ADHERENCE TO ANTIDEPRESSANTS IN PSYCHIATRY: A DESCRIPTIVE SURVEY OF OUTPATIENTS IN JOHANNESBURG, GAUTENG

by

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SUPERVISOR: MRS H HENDERSON

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Declaration

I, Lian Taljaard, hereby declare that the study entitled: ***Adherence To Antidepressants In Psychiatry: A Descriptive Survey Of Outpatients In Johannesburg, Gauteng*** is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references.

Lian Taljaard

Student no: 4717-542-7

February, 2016

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Perhaps the somatic insanity

Is but our last

Wake-up call:

To embrace the senses

Of this, our only owned existence.

And to love, to always, always love.

extract from

Meaning in Madness

by

Roger B. Granet, M.D.

Summary

Title: Adherence to Antidepressants in Psychiatry: A Descriptive Survey of Outpatients in Johannesburg, Gauteng.

By: Lian Taljaard

Degree: Master of Arts in Social Science

Subject: Psychology

Supervisor: Mrs. Henderson

Summary: Pharmacological treatment is often required in the management of psychiatric disorders. Non-adherence to medication represents a significant health concern that prevents patients from fully benefitting from their treatment, and can lead to negative consequences for individuals, their families and the healthcare system. The adherence rates to antidepressant medications in a sample of psychiatric outpatients in the Johannesburg Metropolitan district of Gauteng Province were examined. A descriptive survey method was employed to systematically collect data from n=377 patients using a structured, non-clinical questionnaire and the 8-item Morisky Medication Adherence Questionnaire. Variables were analysed using descriptive and correlational statistical methods. Antidepressant adherence rates were reported as 47.7% (low), 31.3% (medium) and 21% (high). These high rates represent a concern in antidepressant treatment, and health care practitioners and health systems must take this into consideration when planning and developing interventions to improve adherence in this area. The current study found significant correlations between antidepressant adherence rates and some medication-, health system- and moderating variables. Based on these findings, interventions that provide appropriate health-related education about treatment and improved social support systems may be effective in addressing antidepressant non-adherence in psychiatric outpatients in this region.

Key terms:

Adherence; Non-adherence; Medication; Antidepressant(s); Psychiatry; Psychiatric outpatient(s); Johannesburg; Survey; Questionnaire; Morisky Medication Adherence Questionnaire.

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CHAPTER 1

STUDY BACKGROUND

1.1. Introduction

Up to one in three South Africans could experience a psychiatric disorder at some point during their lives, and 16.5% have experienced one in the past 12 months (Williams, Herman, Stein, Heeringa, Jackson, Moomal & Kessler, 2008; Khasakhala, Sorsdahl, Harder, Williams, Stein, & Ndetei, 2011). Nearly one in ten (9.8%) could experience Major Depressive Disorder during their lives, and this rate goes up to nearly half (43.7%) for South Africans living with HIV/AIDS (Freeman, Nkomo, Kafaar, & Kelly, 2007; Herman, Stein, Seedat, Heeringa, Moomal & Williams 2009). Due to the chronic nature of many psychiatric disorders, prolonged treatment is often required (Nolen-Hoeksema, 2011), and psychotropic medication such as antidepressants, antipsychotics, anxiolytics, mood stabilisers and sedative hypnotics are commonly prescribed in the treatment of these conditions (Bulloch & Patten, 2010; Panksepp, 2004). Antidepressant medication has become the most common treatment used in Major Depressive Disorder (MDD), but is also prescribed in the treatment of Bipolar I Mood Disorder (BMD-I), as well as Obsessive-Compulsive Disorder (OCD) and Generalised Anxiety Disorder (GAD) (Centers for Medicare and Medicaid Services, 2015; Linde, Kriston & Rücker, 2015). A public hospital-based study (Janse van Rensburg, Taljaard, & Wilson, 2014) from a sample of n=91 psychiatric outpatients in Gauteng Province found that nearly all patients were prescribed more than one psychotropic medication (89%), and of those more than half (57%) were prescribed antidepressants.

To support the successful management of these psychiatric conditions the treatment relies heavily on the patient's continued commitment to the prescribed treatment regimen, and herein lies one of the major contributors to less than desired treatment outcomes - non-adherence to the treatment regimen. There are many reasons why patients who have been prescribed antidepressants may cease taking their medication (Brown & Bussell, 2011; Gumnick & Nemeroff, 2000; Lanouette, Folsom, Sciolla, & Jeste, 2009; Moret, Isaac, & Briley, 2009; Procyshyn, Barr, Brickell, & Honer, 2010; Sajatovic et al., 2011; Venturini, Sung, Nichol, & Sellner, 1999). According to the US Surgeon General Regina Benjamin, "Doctors, nurses, pharmacists and other health care professionals can help prevent many serious health complications by initiating conversations with their patients about the importance of taking medication as directed" (Benjamin, Press statement. November 2, 2011). This is especially important for people with chronic health conditions, who may have a number of medications to take each day. Adherence to antidepressant medications in psychiatric populations therefore becomes a significant public health issue.

The terms *compliance* and *adherence* have been used interchangeably across different settings around the world. It is important to recognise that adherence suggests a patient-centred approach, whereas compliance implies a health care provider-centred approach, and that the different subtext of each concept is also an important aspect (Salvo & Cannon-Breland, 2015). "Compliant patients submit to the prescriptions of doctors and take their medicine, or follow their advice, a phrase that also means accepting punishment", suggesting that *compliance* is considered to have negative associations and suggests yielding or submission (Vermeire, Hearnshaw, Van Royen, & Denekens, 2001, p. 332). In contrast, adherence incorporates the broader notions of concordance (agreement and harmony), cooperation and partnership. The World Health Organization (WHO) has thus defined adherence as "the extent to which a person's behaviour - taking medication, following a diet, and/or executing lifestyle changes - corresponds with agreed recommendations from a health care provider" (World Health Organization, 2003, p. 3). The current study accepts the definition of the term *adherence* provided by the WHO (World Health Organization, 2003), and will be referring to this description throughout the text.

Non-adherence may be deliberate (e.g., due to adverse side effects) or accidental (e.g., due to forgetting), and can manifest in various ways, such as: forgetting to take one's medication; incomplete or incorrect dosage taken; medication taken at the wrong time; stopping medication altogether; non-participation in recommending health programmes; breaking of appointments or not renewing prescriptions (Ho, Bryson, & Rumsfeld, 2009; Jamaluddin Moloo, 2014). Furthermore, non-adherence may refer to several distinct aspects of medication-taking behaviours, i.e., failure to attend an initial appointment, failure to have the prescription filled, having the prescription filled, but failing to take the medication, not following the frequency or dose instructions on the prescription, deliberate errors or use of inadvertent combinations (Hovstadius & Petersson, 2011; Kronish, Rieckmann, Halm, Shimbo, Vorchheimer, Haas & Davidson, 2006).

Non-adherence to medication is a universal issue in medicine that has been extensively researched (Blackwell, 1996; Cramer & Rosenheck, 1998; Cramer, 1995). Due to the difficulties in measuring adherence, care should be taken in generalising estimates, but non-adherence can be expected in approximately 30-50% of all patients, irrespective of disease, prognosis or setting (Hohmann, Neumann-Haefelin, Klotz, Freidank, & Radziwill, 2014; Acosta, Hernández, Pereira, Herrera, & Rodríguez, 2012; Brown & Bussell, 2011; Tacchi, & Scott, 2005;Donovan, 1995; Morris & Schulz, 1992; Sacket & Snow, 1979). Patients with psychiatric diagnosis were also found to have higher rates of non-adherence in comparison to those with organic illness (Kardas, 2011). A profile of psychiatric patients admitted to a general public hospital in Gauteng revealed that nearly half (47%) of patients admitted for

any psychiatric disorder were non-adherent to their respective medications at the time (Janse van Rensburg, 2007). In terms of specific psychiatric disorders, non-adherence rates were estimated to be: 51-69% depression, 57% for Anxiety Disorders, 30-60% in Schizophrenia , 21-50% for Bipolar Mood Disorder; 35% for Alcohol Use Disorder and13% in HIV/AIDS related psychiatric conditions (Buckley, Foster & Patel, 2009). In terms of different medication categories, Bulloch and Patten (2010) analysed data from the Canadian Community Health Survey and found that non-adherence rates of 34.7% of users of antipsychotics, 38.1% in patients taking sedative-hypnotics, 44.9% in mood stabilisers and 45.9% of users of antidepressants.

Adherence is viewed as a primary determinant of treatment effectiveness, and poor adherence attenuates optimum clinical benefit (World Health Organization, 2003). Non-adherence to medication in psychiatry is associated with a worse prognosis, greater probability of relapse, rehospitalisation and increased resource consumption (Erwin & Peters, 1999; Siegel, Karus, & Schrimshaw, 2000). Poor treatment adherence in psychiatry is associated with decreased likelihood of achieving a reduction in symptoms and recovery, as well as increased risk of relapse and hospitalization and suicide attempts. In addition, the World Health Organization reports that the financial costs incurred by non-adherent patients are significantly higher due to increased treatment costs (World Health Organization, 2003). High levels of adherence have been positively correlated with treatment outcomes in depression, independent of the type of antidepressant drugs used (Thompson, Peveler, Stephenson, & McKendrick, 2000). Furthermore, higher rates of medication adherence may translate into economic benefits. This is seen in the form of direct savings by decreased use of expensive health services caused by disease exacerbation, crisis, relapses or rehospitalisation of patients. Indirect savings can be attributed to the improvement of the quality of life and a patient's social and work roles (Agh, 2012; World Health Organization, 2003).

Leo, Jassal and Bakhai (2005) identified: (1) medication factors (complex regimens, adverse effects, costs, availability); (2) illness factors (cognition/memory, reasoning interference); (3) concurrent substance abuse or dependence; (4) patient factors (denial, beliefs and attitudes, stigma); (5) physician factors (inadequate information provided, inadequate follow-up of response to treatment); (6) patient-physician factors (poor alliance/communication); and (7) social and environmental factors (supportive network, financial resources, inaccessibility and unavailability of treatment resources) as reasons for non-adherence to psychiatric treatment. In addition to patient attitudes and beliefs, literature indicates community attitudes and beliefs as being associated with adherence levels (Botha, Koen, & Niehaus, 2006; Fung, Tsang, & Chan, 2010; Hugo, Boshoff, Traut, Zungu-Dirwayi, & Stein, 2003; Weiss, Chang,

Rauch, Smallwood, Schechter, Kosowsky et al., 2012). Although non-adherence to medication in psychiatry has long been identified as problematic in the international community (DiMatteo, 2004; Gillis, Trollip, Jakoet, & Holden, 1987; Leo et al., 2005; Vermeire et al., 2001), there is currently a scarcity of evidence of rates and contributing factors of non-adherence to antidepressant treatment in the local South African psychiatric setting(Mahaye, Mayime, Nkosi, Mahomed, Pramlal, Setlhabana & Oosthuizen, 2012).

The South African Depression and Anxiety Group (SADAG) recognise the important role of adherence to treatment in psychiatry, and seek to address the issue of non-adherence in the mental health context of South Africa. SADAG is a non-profit organisation (NPO), Section 21 company that was established in 1994 to provide mental health care advocacy to users across South Africa (NPO Registration number: 013-085-NPO), (see Appendix VI for Certificate of Registration). SADAG is currently the country's largest and most recognised mental health advocacy initiative. SADAG routinely provides its members with different free telephonic counselling initiatives, such as: Suicide Crisis-; Trauma-; Bipolar-; Sleeping Disorder-; Substance Abuse-; Mental Health- and the Support Group Helplines (SADAG, 2015). SADAG aims to increase public awareness of anxiety and mood disorders, disseminate information and provide continuous support to mental health care users. SADAG works closely with various mental health patients with various psychiatric conditions on an on-going basis by providing a variety of services to support patients on their journey to recovery and, to help patients manage their mental health treatment and care. These services include, but are not limited to, regular follow-up telephone calls and lay counselling, on-site outpatient support, SMS communications, distribution of printed and electronic resources and on-line information. Through their regular and close contact with patients, SADAG has become increasingly aware of non-adherence to taking medication and recognises the importance of investigating this issue.

1.2. Research problem

1.2.1. Statement of the Research Problem

Non-adherence to prescribed antidepressant medications is a remarkably common human experience. This behaviour and its impact on disease management are magnified in chronic illnesses in psychiatric patients. For people with chronic mental illnesses, non-adherence to treatment substantially adds to the burden of disease and leads to poorer long-term outcomes in these conditions. Firstly, it is associated with decreased likelihood of achieving a reduction in symptoms and recovery. Secondly, non-adherence increases the risk of

relapse and hospitalisation and suicide attempts. Finally, the direct or indirect financial costs incurred by non-adherent patients, as well as health care systems, are significantly higher due to increased treatment costs (Leo et al., 2005). Non-adherence to psychiatric medication, therefore, has a profound impact on the psychiatric disease course and recovery. In addition, it can have detrimental effects on the patient's long-term functioning, including social adjustment and academic or vocational productivity and performance (Agh, 2012; Pareek & Kalia, 2013; Robinson, Long, Chang, Able, Baser, Obernchain & Swindle, 2006; Wang, Simon, & Kessler, 2003).

Evidence suggests that non-adherence to treatment can be expected in approximately half of all patients in psychiatric settings (Tacchi, & Scott, 2005; Brown & Bussell, 2011b; Hohmann et al., 2014). These rates increase when specific conditions such as depression (51 % - 69%) or other Anxiety Disorders (57%) are considered (Buckley, Foster & Patel, 2009). In antidepressant medication specifically, Bulloch and Patten (2010) reported non-adherence rates of 45.9%. Adherence to pharmacological treatment in chronic conditions can be influenced by several interacting factors such as age, gender, race, beliefs about illness and treatment, stigma, type of medication, complexity of treatment regiment, medication related adverse effects, costs, availability, type and severity of illness, concurrent substance abuse or dependence, inadequate information and follow-up, poor social support structures, as well as inaccessibility and unavailability of treatment resources (Barbui & Conti, 2014; Hung, 2014; Kane, Kishimoto, & Correll, 2013; Przemyslaw Kardas, Lewek, & Matyjaszczyk, 2013; Leo et al., 2005; Pampallona, Bollini, Tibaldi, Kupelnick, & Munizza, 2002; Procyshyn et al., 2010; World Health Organization, 2003). Considering the multi-faceted problems to which non-adherence to antidepressants may contribute to, it becomes critically important to determine these adherence rates and, with reference to the current research specifically, the contributing factors of these rates in order to address the issue of non-adherence to antidepressant medication in the South African psychiatric population.

1.2.2. Research questions and study hypotheses

Studies measuring non-adherence rates and identifying factors that contribute to non-adherence varies widely in study design, assessment instruments, populations and sampling selection methods (Leo et al., 2005; Procyshyn, et al., 2010; Kardas et al., 2013; Perestelo-perez & Serrano-aguilar, 2013; Brown & Bussell, 2011). It is also apparent there is a great deal of variability across these studies as to which of these factors are statistically significantly correlated with treatment adherence rates. With this in mind, two main research questions have been identified in the current study:

(1) What are the rates of non-adherence to antidepressant medication in a sample of psychiatric outpatients living in Johannesburg, Gauteng? (2) Which variables have a significant correlation with antidepressant treatment adherence in this sample of psychiatric outpatients? The second main research question has been divided into five specific sub-questions; 2a) Which patient-related variables significantly correlate with antidepressant treatment adherence rates in this sample? 2b) Which illness-related variables significantly correlate with antidepressant treatment adherence rates in this sample of psychiatric outpatients? 2c) Which medication-related variables significantly correlate with antidepressant treatment adherence rates in this sample of psychiatric outpatients? 2d) Which health system-related variables significantly correlate with antidepressant treatment adherence rates in this sample of psychiatric outpatients? 2e) Which moderating factor-related variables significantly correlate with antidepressant treatment adherence rates in this sample of psychiatric outpatients?

Informed by the literature cited above and further discussed in Chapter 2, it is clear that adherence rates vary greatly across psychiatric conditions, treatment settings and treatment regiments themselves, and a number of factors that could have a negative impact on treatment adherence that have been identified by the literature (Pampallona et al., 2002; WHO, 2003; Kane et al., 2013; Hung, 2014). The hypotheses of the current study are based on the assumptions that the study design, the adherence-measuring instrument, participant selection methods and adherence rates would not have a significant influence on the adherence rates observed. This is due to the multiple confounding factors in this study, such as the heterogeneity of previous study designs, definitions, settings, samples, conditions, instruments and results. Therefore, it is expected that the antidepressant medication adherence rates observed in the current study would be similar to previous studies using different research methods, instruments and conceptual definitions.In addition, although an indirect measurement (self-report questionnaire) of adherence rates were used, it is assumed that this may not necessarily imply significantly over- or under-reporting of adherence rates observed in the current study sample (Bauer Parker, Schillinger, Katon, Adler, Adams, Karter et al., 2014; Bulloch & Patten, 2010; Leo et al., 2005; Morisky Malotte, Choi, Davidson, Rigler, Sugland, & Langer, 1990; Morisky & Dimatteo, 2011; Perestelo-perez & Serrano-aguilar, 2013). The literature referenced here also informed the formulation of the current study's hypotheses which will discussed in detail in Chapter 3.

1.3. Purpose of the study

Non-adherence to pharmacological treatment in psychiatry poses a serious problem and significant public health issue in mental health care. Adherence in psychiatry is also influenced by a myriad of factors that are still not clearly understood. Relevant, local evidence on the rates of non-adherence and identifying factors that may contribute to these rates is essential in any attempts to address this issue.

Based on the literature cited in the previous section of this chapter, the current study set out to determine the rates of non-adherence and possible contributing factors that influence antidepressant medication adherence rates in a sample of psychiatric outpatients in Johannesburg, Gauteng. To date, there have been no large-scale studies that aim to objectively determine the rate of antidepressant medication adherence in Gauteng, suggesting a shortage of local evidence measuring and describing non-adherent behaviours of psychiatric outpatients. It is important to ascertain the scope of this problem, as well as gain an understanding of the mechanisms and dynamics of its functioning, if health care providers and health systems wish to address the problem more effectively. The purpose of the current investigation was to identify and describe the scope of non-adherence to antidepressant medication in psychiatric outpatient in this particular region, and to provide evidence of contributing factors that influence these rates to gain a better understanding of its underlying causes.

1.3.1. Aim of the study

Overall, the goal of this particular investigation was to contribute to the body of knowledge regarding antidepressant adherence of outpatients, with various psychiatric diagnoses, in the Gauteng Province of South Africa, with a specific focus on antidepressant medications. In this study, the researcher sought to examine the rates of non-adherence to antidepressant medications by psychiatric outpatients in a previously unstudied population and to identify possible factors that may contribute to non-adherence in this sample. To achieve this, data was systematically collected and variables were analysed using descriptive and correlational statistical methods.

1.3.2. Study objectives

The following specific objectives have been identified in the study:

i. Distribute a structured, non-clinical (i.e., non-clinician administered) questionnaire relating to information about mental health care users' socio-demographical- and illness- and treatment profile, supplemented with a self-report adherence measuring questionnaire to a sample of psychiatric outpatients residing in Johannesburg, Gauteng.

ii. Describe the socio-demographic profile (i.e., age, gender, race, home language), clinical profile (i.e., type of DSM-IV-TR diagnosis, comorbid conditions, duration of illness), and medication profile (i.e., type of antidepressant prescribed, the number of antidepressants prescribed, perceived adverse reactions from medication), and medication profile of this sample of psychiatric outpatients from the data collected by the research instrument.

iii. Determine the rates for non-adherence to antidepressant medications in a sample of psychiatric outpatients in Johannesburg, Gauteng.

iv. Identify and discuss the variables that significantly correlate with antidepressant medication adherence rates in this sample of psychiatric outpatients.

1.4. Significance of the study

Non-adherence to medication for psychiatric disorders is a significant public health concern that prevents patients from realising the full benefits of their treatment and negatively impacts on individuals, their families and the health care system (Agh, 2012; Leo et al., 2005; Pareek & Kalia, 2013; R. Robinson et al., 2006; Wang et al., 2003). Understanding non-adherence and determining its rates and influencing factors are therefore a key challenge to address in order to enhance the quality of care for patients with psychiatric disorders. At the very least, health care providers are required to take on the responsibility of gaining a better understanding of non-adherence behaviour in order to provide appropriate care to patients. New evaluation data and information from this specific sample can inform patient care and planning by providing indices of the extent to which patients adhere to their prescribed antidepressant medication regime, as well as identifying factors that may contribute to these adherence levels. The information gathered from this study could be used by patients, health care practitioners and health care systems to identify possible areas for greater understanding, as well as targeted intervention in these patients. The findings reported here may also be used as an information source for those wishing to

inform any interventions that patient-, illness-, medication- as well as structural or health-system factors to increase antidepressant treatment adherence in psychiatric outpatients.

1.5. Definition of concepts

For the purposes of the current study, adherence was determined by the application of the Morisky 8-item Medication Adherence Questionnaire (MMAQ-8), (Morisky, Green, & Levine, 1986), and indicated by a total score that ranges from zero (low adherence) to eight (high adherence). Instead of dichotomously categorising patients as *adherent* or *non-adherent*, three levels of adherence were applied to the current study results (low, medium and high), in accordance with the guidelines of the MMAQ-8 (Morisky, Ang, Krousel-Wood, & Ward, 2008). Low adherence was indicated by a total score ranging between zero and less than six, a total score ranging between six and less than eight indicates medium adherence, and a total score of eight on the MMAQ-8 indicated high adherence. However, adherence has been defined by studies differently across various settings and illnesses. There are also various methods for measuring medication adherence, and currently there is no universally accepted "gold standard" measuring these rates (Lee Ahn, Kim, Hong, Hong, Kim & Morisky, 2013; Vik, Maxwell, & Hogan, 2004). Each adherence measurement approach has strengths and weaknesses and each rests on specific assumptions (O'Brien, Petrie, & Raeburn, 1992). Regardless, at the very least, one can assume that patients who admit to non-adherence to their medication are most likely being honest about it. Therefore, by the mere virtue of asking patients to report about their adherence to their antidepressant treatment can be a relatively accurate, efficient and cost-effective method for determining rates of antidepressant medication adherence.

1.6. Conceptual framework

Like most health-promoting behaviours, having to take medication regularly for a long period of time involves a conscious commitment to a new healthy behaviour and requires a change in daily habits. The World Health Organization identifies several psychological approaches that may be helpful in intervening with non-adherent patients (World Health Organization, 2003). These theories as discussed below can offer an interesting and innovative conceptual framework for investigating antidepressant medication adherence behaviours in psychiatric outpatients in this particular region of South Africa. Despite decades of research undertaken to understand the psychology of non-adherence (DiMatteo, 2004), these rates have not

improved much, and the situation is especially difficult in the case of medications used to control chronic illnesses such as psychiatric diagnoses (Bosworth, Granger, Mendys, Brindis, Burkholder, Czajkowski, Granger et al., 2011).

Leventhal & Cameron (1987) provided a very useful overview of the history of adherence research. They outlined five general theoretical perspectives on adherence: biomedical perspective, behavioural perspective, communication perspective, cognitive perspective, and self-regulatory perspective. These perspectives are discussed in greater detail in the following chapter. Although these theories and models can provide a conceptual framework for organising thoughts about adherence and other health behaviours, each perspective encompasses several theories with its own advantages and disadvantages, and no single approach may be readily translated into a comprehensive understanding of adherence.

Recent approaches that are more specific to health behaviours may provide more helpful frameworks. This includes stage perspectives, such as the transtheoretical model and cognitive perspectives (Brawley & Culos-Reed, 2000; Munro, Lewin, Swart, & Volmink, 2007a; Ozmete & Hira, 2011; Redding, Rossi, & Rossi, 2000; World Health Organization, 2003). These approaches are also included in a broader discussion of the relevant theoretical perspectives in the following chapter. These theories are specifically located within the realm of adherence to long-term medication (defined as medication treatment of three months or more), describing their key characteristics and examining their relevance with regard to adherence to treatment for tuberculosis (TB) and human immune virus/ acquired immunodeficiency syndrome (HIV/AIDS) (Munro et al., 2007). These theoretical models focus on understanding, predicting and improving adherence. Their common components involve health professional–patient communication, patients' cognitive and social processes (e.g., beliefs, norms) and patients' resources (e.g., financial, psychological and social support), (World Health Organization, 2003).

Studies vary widely in methodologies, and operational definitions of adherence are as varied as the diseases, regimens and patients examined (Rahman, Dignan, & Shelton, 2005; Unni, 2008). Informed by these previous theories, the information–motivation–behavioural skills model (IMB), Fisher and Fisher (1992) borrows elements from earlier work to construct a conceptually-based, generalisable and simple model to guide thinking about complex health behaviours. According to this dynamic model, a patient will adhere to his or her treatment if he or she is physically and mentally able to (patient's capability to follow the medication regime), has the information (patient's knowledge and understanding of his or her condition and treatment) and motivation (patient's attitude and beliefs about the condition and treatment) to behave adherently (Fisher, Fisher, Misovich, Kimble, & Malloy, 1996). The IMB

constructs, and how they pertain to patient adherence, are discussed in further detail in Chapter 2.

Interventions based on Fisher and Fisher's (1992) IMB model have been effective in influencing behavioural change across a variety of clinical applications, such as simple drug use, medication switching or duplication (American Pharmacists Association, 2013; Martin Wiley-Exley, Richards, Domino, Carey & Sleath, 2009; Mayberry & Osborn, 2014). In both prospective and correlational studies, the information, motivation and behavioural skills constructs have accounted for between 30% - 40% of the variance in behaviour change (Munro, Lewin, Swart, & Volmink, 2007b).

1.7. Design of the study

1.7.1. Research paradigm

According to Weaver and Olson (2006, p. 460), investigations are guided by a certain paradigm, which they describe as "patterns of beliefs and practices that regulate enquiry within a discipline by providing lenses, frames and processes through which an investigation is accomplished". In the positivist tradition, social scientists support the idea that the social sciences should match the methodology of the natural sciences (Babbie & Mouton, 2011). Therefore, they often use experiments, surveys and statistics in an effort to ensure rigorous measures and allow for the testing of hypotheses (Neuman, 2011). This positivist, quantitative approach is best suited to answer the research questions in this particular study by systematically gathering information from a large number of people and generate quantifiable data to determine the strength of the relationship between variables through statistical tests.

1.7.2. Research design

A research design is usually highly detailed and structured, which allows for easy collation and statistical presentation of results (Shaughnessy, Zechmeister & Jeanne, 2011). Bhattachejee (2012) explains that descriptive research can be used to identify and count the frequency of a particular response among participants. This definition was applied to the current study as a systematic collection of data from a sample population of psychiatric patients using a survey questionnaire. The research design of the current study focused on measuring the rate and frequency of specific variables, and to determine the antidepressant

medication adherence rates and, identify possible reasons for non-adherence among psychiatric outpatients in the Gauteng Province of South Africa. A descriptive, multi-mode survey design was employed by the current study.

1.8. Research method

The current study employed a mixed-mode survey, i.e. collecting data using different ways in which the assessment instruments were presented to the participants. This entailed using the same questionnaire, but allowing the participants to choose the most convenient mode of completion, namely the pen-and-paper questionnaire, a telephonically administered questionnaire or completing the questionnaire online (internet). Mixed-mode surveys provide the benefit of increasing the response rate of respondents, as well as limiting the exclusion of participants (Tobin, Thomson, Radhakrishna, & LaBorde, 2012). The research method utilised by the current study is discussed in Greater detail in Chapter 3.

1.8.1. Research setting and population

Pavlichev (2004) defined the target population for a survey as the entire set of units for which the survey data are to be used and, for which the findings are meant to be generalisable to the entire population. In the current investigation, the target population was defined as all individuals 18 years or older who were prescribed at least one antidepressant medication (as classified by the Monthly Index of Medication Specialities (MIMS, November 2014), at the time of the study, and resided in the Gauteng Province of South Africa.

1.8.2. Sample and sampling procedures

Howitt and Cramer (2011, p. 432) describes purposive sampling as sampling “with a particular purpose in mind, such as when a particular sort of respondent is sought” rather than a representative sample." A non-probabilistic, purposive sampling method is often used because the procedures used to collect data from a sample are more efficient and cost-effective in comparison with probability sampling techniques (Howitt & Cramer, 2011). Given the objectives of the current study, the nature of the research project, availability of financial resources and the population and the sample size, a non-probability sample design, namely purposive sampling, was selected for the current investigation.

1.8.3. Data collection

Data collection commenced in October 2014 after ethical approval was obtained from the Ethics Committee of the Department of Psychology from the University of South Africa (UNISA), refer to Appendix IV, and SADAG, (Appendix V referred). A database containing information on psychiatric outpatients from SADAG was accessed to invite potential participants to the study. As part of routine database updating and follow-up procedures, patients were informed of the study and invited to participate if they expressed an interest in doing so. Once informed consent was received (Appendix II), participants were assigned a coded participant number and was requested to complete a structured, non-clinical questionnaire, accompanied by a well-established medication adherence rating scale (Appendix I). Patients were provided with the option of completing the survey through any one of three formats that were deemed most convenient for them (via telephone interview, self-completed paper-and-pen based or electronic/ on-line). Participants' responses were captured and coded according to the structured datasheet (Appendix III) in a designated database using Statistical Package for the Social Sciences® (SPSS) computer software version 22. Data from a total of n=377 eligible patients were included in the final analysis of the results.

1.8.4. Research instrument

A structured non-clinical questionnaire was developed that comprised four sections to elicit specific information: 1) socio-demographic information, 2) clinical information and 3) medication information. This was supplemented with 4) the well-established self-report 8-item Morisky medication adherence questionnaire (MMAQ-8), (Morisky et al., 1986). Adherence to antidepressant medication (as measured by the MMAQ-8), was determined by the summated score (ranging from 0 to 8) of “positive” or correct responses. A total score ranging between zero and less than six indicated low adherence, medium adherence by a score between six and less than eight, and high adherence indicated by a score of eight (Morisky et al., 2008).

1.8.4.1. Validity and reliability of the MMAQ-8

The MMAQ-8 was found to have a moderate level of reliability (Cronbach's alpha is 0.83) and high levels of concurrent and predictive validity (De Las Cuevas, Peñate, & Sanz, 2014; Oliveira-Filho, Barreto-Filho, Neves, & Lyra Junior, 2012), and, was also validated by a study

in which a chemical marker was used for measuring actual medication-taking behaviour (Morisky et al., 1990).

1.8.5. Data analysis

Responses to the structured questionnaire and MMAQ-8 were coded according to the structured datasheet (Appendix III). Variables were analysed and described using standard descriptive and where indicated, correlational statistical tests. Descriptive results were expressed as frequencies (n=), and percentages (%) of the sample. Between-group tests were conducted using the Chi-square $\chi 2$ test to assess the relationships between categorical variables. Fisher's exact test was used for 2 x 2 tables or where the requirements for the $\chi 2$ test could not be met. The relationship between continuous and categorical variables was assessed by the t-test or analysis of variance (ANOVA) for more than two categories. The relationship between two continuous variables was assessed by Pearson's correlation coefficient. The accepted level of significance (alpha level and p-value) was $< .05$ for the appropriate statistical tests, and 2-tailed level of significance was reported on.

1.9. Ethical considerations

The current study was conducted according to the ethical guidelines and principles of the international Declaration of Helsinki (World Medical Association, 2013). Participants were protected by informing them of the nature and purpose of the research, their rights and that their participation was on a voluntary basis. In the current study, the researcher acknowledged the rights of the respondents to choose to participate in the study by explaining the purpose and informing them of their rights regarding their participation and withdrawal during the process. Potential participants were given the opportunity to decide voluntarily whether to take part in the study or not. Other than the possibility that participants may potentially feel inconvenienced by the survey, no additional expected risks were anticipated by taking part in this research survey. This possible inconvenience was likely to be minimal as the survey was kept brief and took approximately ten to fifteen minutes to complete. Furthermore the questionnaire could be completed at any convenient time, place and in one of three modes that was convenient for potential respondents. Additionally, participants could possibly experience slight psychological discomfort by divulging personal information for research purposes. Emphasis was placed on the anonymous and confidential nature of the information during the introduction of the study and informed consent form. The

SADAG 24-hour emergency helpline number was also provided to all participants if they felt they needed support. Confidentiality of participant information was maintained by using a unique coded identifier for participants during the entire research process. No names were linked to the information at any point, and all results were reported anonymously.

1.10. Study limitations

Self-report measures offer easy-to-use, inexpensive and convenient tools for measuring adherence rates, especially in certain study designs, such as the current descriptive study. However, this kind of measurement is also subject to biases, such as social desirability, recall bias and response bias (Shi, Lui, Koleva, Fonseca, Kalsekar & Pawaskar, 2010). Participants were selected based on their accessibility and by the personal judgement of the researcher, and all potential participants did not have an equal opportunity to take part in the survey. However, Daniels (2012) noted that non-probability sampling techniques, such as purposive sampling used in this particular study, may be more appropriate in study designs that are descriptive in nature, when the target population under investigation is difficult to access, an accurate sampling frame does not exist and, it is not within the scope of the study to generalise its findings to the broader population. The current study meets the above criteria which motivated the researcher's choice of the sampling method used. As outlined in Chapter 3, steps were taken to minimise the potential impact of the study limitations on data quality and were taken into consideration during the discussion of the results. In spite of these limitations discussed, the current study still constitutes novel research in this particular area, thus providing meaningful conclusions and recommendations for health care users, providers and health care systems.

Chapter 2 introduces the reader to the literature review on the research topic, and provides a descriptive overview of previous studies investigating treatment. This is followed by Chapter 3, which describes the approach, methods and instruments used in the current study. Chapter 4 reports on the results of the study after statistical analysis of the data were performed, and briefly discuss these results in the context of the current study. The final chapter (Chapter 5) provides a more detailed discussion of the results relating to research findings in the literature. In addition, Chapter 5 also provides recommendations for patients and health care providers on potential targets for improving antidepressant adherence and, suggests possible directions for improvement in future studies.

1.11. Chapter summary

In this chapter the reader was introduced to the current research study by providing a background to the study and identifying the area of concern. The purpose of the study was subsequently formulated and supplemented by eliciting the significance of this particular investigation. Specific concepts used in the study were also defined, and a background of the theoretical framework that guided the study was provided. In addition to this, an overview of the study design, methods, context, sample, instrument and analysis procedures utilised was provided. Individuals with psychiatric disorders are considered a minority and a vulnerable population, and ethical considerations regarding these aspects were also mentioned. This chapter concluded with a brief overview of the limitations of this investigation.

CHAPTER 2

LITERATURE REVIEW

2.1. Introduction

Non-adherence to medication use is a global challenge in psychiatry that has been extensively researched over the past decades (Vermeire, et al., 2001; Blackwell, 1996, as cited in Bulloch, et al., 2010, p. 47; World Health Organization, 2003). The scope of the problem has reached endemic proportions. Nearly half of all patients given pharmacological treatment for chronic conditions do not take sufficient doses to achieve a positive therapeutic effect (Sacket & Snow 1979; Haynes, McKibbon & Kanani, 1997 as cited in Joyce, 2002; Keller, Hirschfeld, Demyttenaere & Baldwin 2002; Sherbourne, Schoenbaum, Wells & Croghan, 2004; Gopinath, Katon, Russo & Ludman, 2006; Åkerblad, 2007).

In this chapter, the researcher first defines the term *adherence*, followed by a background discussion of adherence in psychiatry, and the pharmacological treatments identified in the study. A subsequent discussion on the measurement of adherence follows. The researcher describes the types of non-adherence based on the existing literature. Factors which influence non-adherence and the consequences of this behaviour are also discussed in greater detail in the subsequent sections. This is followed by a brief overview of the types of psychotropic medication that were identified in the study. In the final section, the researcher discusses the behavioural theories that explain non-adherence. Lastly, the conceptual framework of the study is presented and discussed.

2.2. Definition of adherence

The World Health Organization (WHO) has defined adherence as “the extent to which a person's health behavior - taking medication, following a diet, and/or executing lifestyle changes - corresponds with agreed recommendations from a health care provider” (WHO, 2003, p. 3). Non-adherence may be deliberate or unintentional, and it is accepted that non-adherence refers to various aspects of medication-taking behaviours. The medical domain has traditionally accepted the term *compliance*, which is associated too closely with blame. This perspective would typically prefer objective measurements as biomarkers or its metabolites in serum or urine samples of psychiatric patients.

Although this is a reliable method for assessing adherence, it is also more intrusive, inconvenient and expensive compared to other indirect methods of measurement (Shi et al.,

2010). Strong emphasis must be placed on the need to differentiate adherence from compliance. The key distinction is that *adherence* requires the patient's agreement to the recommendations and is a better way of describing the dynamic and complex interactions required over various domains over extended periods to sustain optimal health in people with mental illnesses.

In the current study, the adherence rates of patients were defined by the application of the 8-item Morisky Medication Adherence Questionnaire (MMAQ-8), a reliable and validated 8-item, self-report measure of medication-taking behaviour (Morisky et al., 1986; Morisky et al., 2008). The MMAQ scores range from zero to eight and have been classified into three adherence levels: high adherence (8 points), medium adherence (6 to < 8 points) and low adherence (< 6 points).

2.3. Background to adherence

Non-adherence is a universal issue in medicine, and has been extensively researched (Blackwell, 1996; Nichol, Venturini & Sung, 1999; Cramer, 2004; Bulloch & Patten, 2010; Chong, Aslani, & Chen, 2011; Kardas, Lewek, & Matyjaszczyk, 2013). These studies attempted to determine rates of adherence using different methods in a variety of diseases and patient samples, and research focused on the extent, determinants and strategies to improve adherence (Vermeire et al., 2001; Julius, Novitsky & Dubin, 2009). The question of how to measure adherence has perplexed researchers, and the difficulty of the problem has hindered the development of a *gold standard* method of measurement (Lee et al., 2013). This is a challenge for medication adherence research and measurement in itself, as it presents a key obstacle to the generalisability of study findings. Despite these challenges, it is estimated that between 25%-50% of all patients, irrespective of disease, prognosis or setting, are non-adherent to their treatment (Morris & Schulz, 1992; Sacket & Snow, 1979; Donovan, 1995, as cited in Vermeire et al., 2001, p. 334; Vergouwen, Bakker, Katon, Verheij & Koerselman, 2003; Bambauer, Adams, Zhang, Minkoff, Grande, Weisblatt et al., 2006; Olfson, Marcus, Tedeschi & Wan 2006). These high rates make it crucial to investigate this phenomenon in order to gain a better understanding of its key elements and processes and would allow for the development of more effective intervention strategies that can be employed. However, it is not within the scope of this study to provide in-depth recommendations for potential intervention methods to address non-adherence in psychiatry, but simply to describe the rates and potential contributing factors of non-adherence to antidepressant medications in this specific sample in sufficient detail.

2.3.1. Adherence in psychiatry

Kardas (2011) conducted a multi-centre study and found that psychiatric patients had significantly higher rates of non-adherence in comparison to those with organic illnesses ($p <$ .05). According to Cramer and Rosenheck (1998), patients with psychiatric disorders also show a greater degree of non-adherence to treatment than those with physical disorders. The observed mean adherence rate for patients with physical disorders was 76%, whereas psychiatric patients on antipsychotics had a mean adherence rate of 58%, and patients on antidepressants had a mean adherence rate of 65%. A profile of psychiatric patients admitted to a general public hospital in Gauteng revealed that nearly half (47%) of patients admitted for any psychiatric disorder were non-adherent to their respective medications at the time (Janse van Rensburg, 2007). However, it is unclear from this paper which definition of non-adherence was used. Venturini, Sung, Nicho and Sellner (1999) also found that roughly 30% of all patients with psychiatric disorders discontinue their medication in the first month and 44% stop taking it within the first 3 months of initiation (Lin, Von Korff, Katon, Bush, Simon, Walker, & Robinson, 1995, as cited in Moosa, 2007). However, the reasons for non-adherence in these patients could not be observed.

In terms of different psychiatric disorders, non-adherence rates were estimated for the following: depression 51-69%, Anxiety Disorders 57%, Schizophrenia 30-60%, Bipolar Mood Disorder 21-50%; Alcohol Use Disorders 35%; and HIV/AIDS-related psychiatric conditions 13% (Buckley *et al*., 2009). A review by Julius et al., (2009) showed that non-adherence ranges between 28% - 52% for Major Depressive Disorder, 20%-50% for Bipolar Bood Disorder, and 20% - 72% in Schizophrenia.

2.3.2. Adherence in depression

Major Depressive Disorder is associated with enormous personal suffering for affected patients, great distress to their family and friends and contributes to major economic and societal costs (Wells, Stewart, & Hays, 1989; Greenberg, Stiglin, Finkelstein, & Berndt, 1993; Wang, Simon, & Kessler, 2003, as cited in Aikens, Nease, Nau, Klinkman, & Schwenk, 2005). The South African Stress and Health Study, the first nationally representative epidemiological study undertaken in the country to determine the prevalence of psychiatric disorders, estimated that 9.8% of South Africans have been diagnosed with a mood disorder (Herman et al., 2009). A South African investigation into the association between mental disorders and lost income through simulations by Lund, Myer, Stein, Williams and Flisher (2013) found that the mean estimated lost income due to severe depression and anxiety

disorders was USD $4,798 per adult per year, after adjusting for age, gender, education, marital status, and household size. To put this into perspective, Lund et al.(2013) further explained that projections of the total annual cost in lost earnings for South Africans with severe depression and anxiety ($4,798 per person), extrapolated from the sample, was USD $3,626,666,995, at the initial observed 12-month prevalence rate of 3.25% (Herman et al., 2009). However, their calculations relied upon outdated statistics of the South African adult population (20-64 years) of 23,257,556 based on the 2001 South African census (Statistics South Africa, 2003). This amount could be significantly higher by current measures.

Myers and Branthwaite (1992) found that the relapse rates in unipolar mood disorders are as high as 80% one year after patients stop taking their prescribed antidepressant medication, and 60% of patients stop their treatment within 3 months of beginning their treatment. However, the reasons for this could not be observed. Nevertheless, in support of the previous finding, it was observed that between 30% and 83% of patients who begin antidepressants discontinue treatment prematurely (Melfi, Chawla & Croghan, 1998; Peveler, Grorge, Kinmonth, Campbell, & Thompson, 1999). A review of quantitative evidence of factors associated with non-adherence reported rates for medication adherence in depression ranging between 30.0% and 97.0% (Pampallona et al., 2002). The wide range in adherence rates reported here may be due to the fact that their review of 32 observational studies conducted between 1973 and 1999 reported on adherence measured by various methods, such as appointments kept, direct pill count of pills actually taken, plasma levels, as well as *ad hoc* composite measures of medication intake.

Although some of these studies did not report on the factors associated with non-adherence in patients with depression, other studies have suggested that improved adherence was associated with the use of Fluoxetine, imipramine rather than any other antidepressant, high education level, married status and good social adjustment, no adverse reactions, female gender, referral or prescription by a psychiatrist, and no personality or Substance Use Disorders (Croghan, Lair, Engelhart, Crown, Copley-Merriman, Melfi, Buesching et al., 1997; Last, Thase, Hersen, Bellack, & Himmelhoch, 1985; Matas, Staley, & Griffin, 1992; Robinson, Gilbertson, & Litwack 1986; Simon, VonKorff, Wagner, & Barlow, 1993).

2.3.3. Adherence to medication

Due to the chronic nature of many psychiatric disorders, prolonged treatment of these conditions is often required (Nolen-Hoeksema, 2011). Psychotropic medication, such as antidepressants, antipsychotics, anxiolytics, mood stabilizers and sedative hypnotics are

used in the treatment of psychiatric conditions (Panksepp, 2004; Bulloch & Patten, 2010). In psychiatry, antidepressants play a pivotal role in the treatment and management of various psychiatric conditions, such as Major Depressive Disorder, Generalised Anxiety Disorder, Social Phobia and Specific), Obsessive-Compulsive Disorder, Eating Disorders, Posttraumatic Stress Disorder and the psychological effects of living with chronic pain (Royal College of Psychiatrists, 2012).

Over the past 50 years, antidepressants have become the main treatment modality for depressive disorders. According to Ban (2014), prior to this, the treatment of depression (formerly known as melancholia) was in line with contemporary beliefs about the condition at that time, and until the 19th century there was little documentation of the results of these treatments. Historically, the treatment approach to depression included the use of warm baths, psychotherapy and bodily exercise treatments, and this approach continued until the 1960's when antidepressants replaced these methods (Ban, 1981; Hunter & Macalpine, 1964). More recently, the British National Clinical Practice Guidelines (NICE) published international guidelines recommending that newer selective serotonin reuptake inhibitors (SSRI's) should be the first-line treatment for depression (NICE, 2004). In general, SSRIs, selective noradrenaline reuptake inhibitors (SNRIs), noradrenaline and dopamine reuptake inhibitors (NDRIs) and mirtazapine, a tetracyclic agent, were encouraged over the use of tricyclic antidepressants and monoamine oxidase inhibitors (MAOI's). Newer melatonergic agents may also be employed. These antidepressant classes were recommended in view of their increased tolerability and safety in patients. This is supported by other international societies, such as the American Psychiatric Association (APA), (Silverman, Galanter, Jackson-Triche, Jacobs, Lomax, Riba, Yager et al., 2015; Gelenberg, Freeman, Markowitz, Rosenbaum, Thase, Trivedi, Silbersweig et al., 2010), the Canadian Network for Mood and Anxiety Treatments (CANMAT) (Kennedy, Lam, Parikh, Patten, & Ravindran, 2009) and the British Association of Pharmacology (BAP) (Cleare, Pariante, & Young, 2015).

These recommendations by the international societies are similar to treatment guidelines adopted in the local South African context. The South African Society of Psychiatrists (SASOP) provided guidelines that apply to the current private health care settings (Emsley, Colin, Flisher, Grobler, Hawkridge, Potocnik, et al., 2013) and the National Department of Health (The South African National Department of Health, 2012) provides treatment guidelines for psychiatric disorders in the published Standard Treatment Guidelines and Essential Medicines List for South Africa, which typically apply to public health care settings in South Africa. These documents recommend the use of an SSRI above older tricyclic or MAOI's as the first-line treatment for moderate to severe depression, while psychotherapy or cognitive-behavioural therapy (CBT) is recommended in patients with mild depression. A

particular reference by SASOP is made to Fluoxetine or switched to an alternative mirtazapine and bupropion, for example, in patients who experience SSRI-induced sexual dysfunction adverse reactions (Emsley et al., 2013). The NDoH Primary Health Care level (PHC) - typically used by outpatients in the public sector - (The South African National Department of Health, 2014), also makes reference to Fluoxetine or amitriptyline (a tricyclic) if a sedating antidepressant is required.

Earlier work by Johnson (1973) in primary care settings in the United Kingdom indicated that up to two-thirds of patients being treated with tricyclic-type antidepressant medication for depression stopped taking them within a month of starting treatment. Katon, von Korff and Lin (1992) assessed the extent to which patients receiving prescriptions for antidepressant drugs actually obtained supplies of medication. It was found that only 20% of patients prescribed antidepressants of the tricyclic type filled four or more prescriptions within 6 months, while 34% of patients who had been prescribed newer antidepressants did so (Katon et al., 1992). This indicated that patients receiving tricyclic antidepressants were adhering less to their treatment regime when compared with patients taking newer antidepressants, but both groups displayed low levels of adherence to medication treatment. Both these studies (Johnson, 1973; Katon et al., 1992) reported on the efficacy of an intervention that was implemented, but did not include the reasons for non-adherence to treatment reported by patients. Reasons for non-adherence by psychiatric patients are discussed in greater details in the following section of this chapter.

Gasquet, Bloch, Cazeneuve, Perrin and Bouhassira (2001) conducted a large national survey of a representative sample of the general French population in order to assess antidepressant non-compliance frequency and the factors that influence it. Data was collected by telephone interview to assess two types of non-adherent behaviours: 1) premature interruption of treatment and 2) omitting doses. Their results reported that 36.9% of people taking antidepressants were non-adherent (15.4% by treatment interruption and 21.5% by dosage modification). They reported that 15% of the subjects admitted to early termination of their treatment, and 22% admitted to reducing their dose without discussing it with their doctor (Gasquet et al., 2001).

In terms of different psychotropic medication classes, a study by Bulloch and Patten (2010), used data from the Canadian Community Health Survey, and reported non-adherence of 34.7% for patients on antipsychotics, 38.1% on sedative-hypnotics, 44.9% on mood-stabilisers and 45.9% for patients on antidepressants, respectively. Although an abstract from the publication by Gasquet et al., (2001) was available in English, the full-text was only

available in French language. This made drawing any comparisons between studies challenging due to the language barriers.

2.3.4. Adherence in the local context

Although there are South African studies that investigated non-adherence to antiretroviral (ARV) treatment (Goudge & Ngoma, 2011; Catz, Kelly, Bogart, Benotsch, McAuliffe, 2000; Kagee, 2008; Kagee, Nothling & Coetzee, 2012), very few recent studies have focused on the adherence rates to antidepressants in the local psychiatric outpatient setting. Local ARV medication adherence rates among n=272 HIV positive men and women with alcohol problems were reported on (Catz et al., 2000). Adherence to ARV therapy was measured using a 14-day timeline interview to recall day by day all medication doses taken and missed during the past two weeks. They (Catz et al., 2000) reported a 43% adherence rate to HIV medication, and noted that depression and anxiety (as measured by the Center for Epidemiologic Studies-Depression Scale (CES-D) and Beck- Symptom Inventory), were not significantly associated with HIV medication adherence ($p = .595$). This figure of 43% non-adherence to ARV therapy falls within the range of non-adherence rates to psychotropic medications and psychiatric conditions previously noted. Kagee, Nothling and Coetzee (2012) specifically reported on the barriers (poverty-related, institution-related and social barriers to clinic attendance and pill-taking) to ARV treatment and noted that food insecurity, stigma and discrimination were the main barriers to treatment adherence experienced by a sample of 10 patients at a public hospital.

One local study by Sharif, Ogunbanjo and Malete (2003), did investigate non-adherence amongst psychiatric patients in the Mpumalanga Province. However, this was a qualitative study, and no objective measurement was used to determine the rate of non-adherence to their medication. Nevertheless, the following themes indicating reasons for non-adherence to treatment by patients with any psychiatric illness were identified: patients' religious and spiritual beliefs; adverse reactions to medication; perceived non-response to treatment; fear and denial; lack of family and health care systems support, as well as social stigma.

Mahaye, et al. (2012) assessed the medication adherence in a sample of 92 psychiatric outpatients in the KwaZulu-Natal Province using the same adherence measuring instrument as the current study (MMAQ-8), but instead focused only on antipsychotic medication in a smaller sample of Schizophrenia patients (n=95). Their (Mahaye, et al., 2012) observational study measured high adherence levels amongst 12.6% of the study sample, moderate adherence levels amongst 50.8%, and low adherence levels amongst 37% of participants.

Mahaye, et al., (2012) noted that significant predictors of adherence to antipsychotic medication were age (p = .045) and race (p = .055). The impact of variables such as the type of condition (Schizophrenia only), employment status, educational level and medication related variables such as the number, formulation, and frequency of intake were however insignificantly associated with adherence levels.

One study (Janse van Rensburg et al., 2014) did, however, investigate medication adherence and clinic attendance in a sample of n=91 psychiatric outpatients with various psychiatric diagnoses at a regional public hospital in Johannesburg, Gauteng. They (Janse van Rensburg et al., 2014) conducted a 3-month pilot-intervention in 2012 to assess its effectiveness in improving adherence. The pilot-intervention programme included: weekly phone calls, free telephonic counselling, reminder SMS-messages, printed and electronic psycho-educational information on conditions and treatment and, access to free support groups (Janse van Rensburg et al., 2014). Although the adherence scale component of this questionnaire was based on the MMAQ-8, this was a pilot study, and therefore the reliability and validity of the tool could not be established.

In their study Janse van Rensburg, Taljaard and Wilson (2014) observed that the majority of patients were female (76%) with White (35%) and Black (34%) ethnicity. The average age of patients was 41.9 years, while nearly two-thirds (58.2%) were older than 40 years. More than two-thirds (64.8%) of patients spoke English, with Afrikaans being the second most common spoken language (19.8%). More than two thirds of patients (61.5%) were not in a relationship with a partner at the time (single, divorced or widowed). The majority of these participants (75%) were unemployed, and from the quarter of those who were employed, 69.6% were working full-time and 30.4% part-time. Participants' most common DSM IV-TR axis I diagnoses were Major Depressive Episode or Disorder (22%); Bipolar Mood Disorder (n = 12; 13.2%); Anxiety Disorders (n = 8; 9%) and Psychosis due to General Medical Conditions (n = 8; 9%). The most common medication categories prescribed to these patients were antidepressants (57%), antipsychotics (56%), mood stabilisers (38.5%), anxiolytics/sedative medication (31.8%) and other general medical treatment (17.6%). For most participants (89%), more than one medication was prescribed. Prior to the pilot-intervention, roughly 80% of the patients reported that they were adherent by taking their medication as suggested by their doctor. However, 60 of the 74 patients who indicated that they were adherent to their medication gave reasons for non-adherence in a subsequent follow-up question. Therefore, a non-adherence rate of 15.4% prior to the pilot-intervention was defined as a more accurate estimate of non-adherence rates (Janse van Rensburg et al., 2014).

After the pilot-intervention (3 months), only 11.4% of participants reported that they skipped doses of their medication during the intervention. The majority (88.6%) indicated that they took their medication as prescribed by their doctor and none of the patients indicated that they stopped taking their medication completely (Janse van Rensburg et al., 2014). The most common reasons for non-adherence to medication prior to the pilot-intervention were forgetfulness, lack of reminder support, perceived adverse reactions, unavailability of medication at pharmacies, beliefs about medication and stigma, as well as lack of knowledge (Janse van Rensburg et al., 2014). Although it is possible that patients who took part in this pilot- intervention to increase medication adherence may have also participated in the current investigation, it is unlikely that the effect of the pilot-intervention had any significant impact on the adherence rates observed in the current study. The pilot-intervention took place over a relatively short period (3 months), and concluded in 2012, two years after the current study took place. To the best of the researcher's knowledge, this local study by Janse van Rensburg, Taljaard and Wilson (2014) provided the only description of medication adherence behaviours in a sample of psychiatric outpatients that took place in the same geographical area as the current study (Johannesburg, Gauteng).

Although it provides valuable socio-demographical-, clinical- and treatment information, as well as adherence behaviours in this sample, there are several limitations to this study. Firstly, it did not measure adherence rates using a validated instrument, and although their instrument was based on the MMAQ-8, the reliability and validity of the tool could not be established as this was a pilot-study. Secondly, adherence rates were dichotomously grouped as *adherent* and *non-adherent* based on patients' self-reported response to a single item on a questionnaire that was being pilot-tested. This leaves the study limited as it does not allow one to create a profile for partial-adherence behaviours. Thirdly, their study sample included a relatively small sample (n=91), and did not perform statistical calculations to determine which variables were significantly correlated with adherence rates. To date, no large-scale studies that aim to objectively determine the rate of adherence to antidepressant medications in Gauteng have been conducted, suggesting a shortage of local evidence measuring and describing non-adherent behaviours of psychiatric outpatients. It is important to ascertain the scope of this problem, as well as gain an understanding of the mechanisms and dynamics of its functioning if health care providers and health systems wish to address the problem more effectively.

2.4. Types of medication

The medications identified in this study were listed according to their pharmacological classification from the Monthly Index of Medical Specialities (MIMS, September, 2014). The following categories have been identified under the Central Nervous System (CSN) class: central nervous system stimulants (CSNS); sedative hypnotics (SH); anxiolytics (ANX); antidepressants (AD); antipsychotics (ANTIP) and; Anti-epileptics (ANEPIL), (MIMS, September, 2014). It is not within the scope of this study to provide a detailed discussion of the mechanisms of action or neurophysiological effects of these medications, but and serves as a general guide instead, and should not be used for clinical reference or to inform pharmacological treatment of patients. Proprietary names of the medications are not provided, but grouped according to their active ingredients only.

Table 1 identifies the antidepressant medications prescribed to psychiatric outpatients who participated in this observational study, and lists the common indications and mechanisms of action of these medications. This information was obtained from the electronic Medicines Compendium (eMC), (Datapharm, 2015). The eMC contains up to date, easily accessible information about medicines licensed for use in the UK, all of which have been checked and approved by either the UK or European government agencies which license medicines such as the UK Medicines and Healthcare Products Regulatory Agency (MHRA) and the European Medicines Agency (EMA), (Datapharm Communications Limited, 2015). The eMC contains: 1) Summaries of Product Characteristics (SPC), which provide health care professionals such as doctors, pharmacists and nurses information on how to prescribe and use the medicine correctly, and is based on clinical trials and gives information about dose, use and possible side effects and; 2) Patient Information Leaflets (PIL), which is written by pharmaceutical companies and is a patient-friendly version of the SPC, and typically contains information on what the medication is used for, what to do before taking the medication, how to take and store the medication, and possible adverse reactions (Datapharm Communications Limited, 2015). It is worth noting that the information reported in Table 1 only serve to provide a general guide.

Table 1: Mechanisms of action, active ingredients and indications of antidepressants recorded in the current study

Antidepressant medication classification	Mechanisms of action	Active ingredient	Indication in adults
Tricyclic	Thought to increase the synaptic concentration of noradrenaline and serotonin in the CNS by inhibiting their re-uptake by the pre-synaptic neuronal membrane.	Amitriptyline	Symptoms of depression (especially where sedation is required). Nocturnal enuresis where organic pathology is excluded.
	Believed to be inhibition of the neuronal re-uptake of noradrenaline and serotonin 5HT to about the same extent	Imipramine	Treatment of symptoms of depressive illness.
	Blocks alpha-adrenergic, histamine H1, and some types of serotonin receptors.	Mianserin	For the treatment of Major Depression.
Mono-Amine Oxidase inhibitors	Non-hydrazine monoamine oxidase inhibitor	Tranylcypromine	Treatment of symptoms of depressive illness especially where phobic symptoms are present or where treatment with other types of antidepressants has failed. It is not recommended for mild depressive states resulting from temporary situational difficulties.
	Involves the selective, reversible inhibition of MAO-A. This inhibition leads to a decrease in the metabolism and destruction of monoamines in the neurotransmitters. This results in an increase in the monoamines, relieving depressive symptoms.	Moclobemide	For the treatment of Major Depression.
Selective serotonin re-uptake inhibitors	(5-HT) re-uptake inhibitor with high affinity for the primary binding site. It also binds to an allosteric site on the serotonin transporter. Has no or low affinity for a number of receptors including 5-HT_{1A}, 5-HT_2, DA D_1 and D_2 receptors, α_1-, α_2-, β-adrenoceptors, histamine H_1, muscarine cholinergic, benzodiazepine, and opioid receptors	Escitalopram	Treatment of Major Depressive Episodes. Treatment of Panic Disorder With or Without Agoraphobia. Treatment of Social Anxiety Disorder (Social Phobia). Treatment of Generalised Anxiety Disorder . Treatment of Obsessive-Compulsive Disorder.
	Selective inhibitor of serotonin reuptake, and this probably accounts for the mechanism of action. Fluoxetine has practically no affinity to other receptors such as α_1-, α_2-, and β-adrenergic; serotonergic; dopaminergic; histaminergic$_1$; muscarinic; and GABA receptors	Fluoxetine	Treatment of the symptoms of major depressive illness, with or without associated anxiety symptoms, especially where sedation is not required. Treatment of Obsessive-Compulsive Disorder. Complement of psychotherapy for the reduction of binge-eating and purging activity.
	Potent inhibitor of the serotonin (5-HT)-uptake. Tolerance to the inhibition of 5-HT-uptake is not induced by long-term treatment with citalopram. With no, or minimal, effect on noradrenaline (NA), dopamine (DA) and gamma aminobutyric acid (GABA) uptake.	Citalopram	Treatment of depressive illness in the initial phase and as maintenance against potential relapse/recurrence. Treatment of Panic Disorder With or Without Agoraphobia
	Inhibitor of neuronal serotonin (5-HT) uptake *in vitro* and *in vivo,* but is without affinity for muscarinic, serotonergic, dopaminergic, adrenergic, histaminergic, GABA or benzodiazepine receptors	Sertraline	Treatment and prevention of symptoms of depressive illness, or reoccurrence of further episodes including accompanying symptoms of anxiety.
	Potent and selective inhibitor of 5-hydroxytryptamine (5-HT, serotonin) uptake	Paroxetine	Treatment of Major Depressive Episode Treatment of Obsessive Compulsive Disorder Treatment of Panic Disorder With and Without Agoraphobia Treatment of Social Anxiety Disorders/Social phobia Treatment of Generalised Anxiety Disorder Treatment of Post-raumatic Stress Disorder
Serotonin & noradrenaline re-uptake inhibitors	Inhibitor of serotonin and noradrenaline reuptake ODV, and reduce β-adrenergic responsiveness after both acute (single dose) and chronic administration	Venlafaxine	Treatment of Major Depressive Episode. For prevention of recurrence of Major Depressive Episodes.

Antidepressant medication classification	Mechanisms of action	Active ingredient	Indication in adults
Serotonin & noradrenaline re-uptake inhibitors	It weakly inhibits dopamine and noradrenaline reuptake, with no significant affinity for histaminergic, dopaminergic, cholinergic, and adrenergic receptors.	Duloxetine	Treatment of Major Depressive Disorder. Treatment of diabetic peripheral neuropathic pain. Treatment of Generalised Anxiety Disorder .
	Non-clinical data suggests a 5-HT_3, 5-HT_7, and 5-HT_{1D} receptor antagonist, 5-HT_{1B} receptor partial agonist, 5-HT_{1A} receptor agonist and inhibitor of the 5-HT transporter, leading to modulation of serotonin , norepinephrine, dopamine, histamine, acetylcholine, GABA and glutamate neurotransmission	Vortioxetine	Treatment of Major Depressive Episodes
Noradrenaline & dopamine re-uptake inhibitors	Selective inhibitor of the neuronal re-uptake of catecholamines (noradrenaline and dopamine) with minimal effect on the re-uptake of indolamines (serotonin) and does not inhibit either monoamine oxidase	Bupropion	An aid to smoking cessation in combination with motivational support in nicotine-dependent patients.
	Potent inhibitor of noradrenaline reuptake. It has only a weak effect on the 5-HT reuptake and does not affect the uptake of dopamine	Reboxetine	Acute treatment of depressive illness/ and for maintaining the clinical improvement in patients initially responding to treatment
Tetracyclic	Use- and voltage-dependent blocker of voltage gated sodium channels. It inhibits sustained repetitive firing of neurones and inhibits release of glutamate	Lamotrigine	Prevention of depressive episodes in patients with bipolar I disorder who experience predominantly depressive episodes
	Centrally active presynaptic α_2-antagonist, which increases central noradrenergic and serotonergic neurotransmission. The enhancement of serotonergic neurotransmission is specifically mediated via 5-HT_1 receptors, because 5-HT_2 and 5-HT_3 receptors are blocked	Mirtazapine	Treatment of episodes of depression
Melatonergic Specific	MT_1 and MT_2 receptors agonist and 5-HT_{2C} antagonist. Has no effect on monoamine uptake and no affinity for α, β adrenergic, histaminergic, cholinergic, dopaminergic and benzodiazepine receptors	Agomelatine	Treatment of Major Depressive Episodes.
Lithium	Related to inhibition of neurotransmitter receptor mediated processes involving beta-adrenoceptors	Lithium Carbonate	Treatment of acute episodes of mania or hypomania and for the prophylaxis of recurrent manic-depressive illness.
Others	Triazolopyridine derivative chemically unrelated to known tricyclic, tetracyclic and other antidepressant agents. It has negligible effect on noradrenaline re-uptake mechanisms. May concern noradrenergic potentiation by mechanisms other than uptake blockade	Trazodone	Anxiety, depression, mixed anxiety and depression.

2.5. Measurement of adherence

Researchers and clinicians have used various methods in an attempt to accurately and reliably assess patient adherence to medication, as well as to identify non-adherent patients (World Health Organization, 2003). Although a number of methods are available for the measurement of adherence to medications, accurate assessment continues to be a challenge, and there remains a debate as to which approach is the most reliable and valid. This is because, currently, there is no universally accepted "gold Standard" for measuring adherence (Vik, Maxwell, & Hogan, 2004). Adherence to pharmacological treatment in psychiatry may be measured using biological measurements, clinician ratings, pill count, health professional reports and patient self-reporting (Moosa, 2007). The majority of medication adherence studies used indirect measures such as pill counts and self-reported questionnaires. This is because direct methods such as biological samples are not always possible, feasible, appropriate or cost effective (Vik Maxwell, & Hogan, 2004).

2.5.1. Biological measurements

This approach implies a direct method of measuring medication adherence through the use of biomarkers or its metabolites in serum or urine samples of psychiatric patients. This is a reliable method for assessing adherence, but it is also more inconvenient and expensive (Evans & Spelman, 1983, as cited in Moosa, 2007). Some patients may object to giving blood specimens, regarding these as unnecessary and intrusive. Additionally, results may be influenced by other drug or food interactions, physiological variability, change in dosing schedules and the half-life of the medication (Smith, Psaty, Heckbert, Tracy & Cornell, 1999).

2.5.2. Clinician ratings

Health care provider ratings and the clinician's subjective rating of the patient's response to treatment are other methods of measuring medication adherence (Moosa, 2007). An alternative, more direct surveillance method by clinicians may be the clinical observation of the medication being taken. Despite being inexpensive and comprehensive, it was noted that clinician ratings may not be the most accurate method for measuring the rates of medication adherence (Gordis, 1979; Stewart, 1987). Limitations of this method include the tendency to overestimate adherence, assessment of global perceptions rather than the frequency of behaviour (e.g., "Did you take all your medications yesterday?" vs. "How many medications

did you take yesterday?"), treatments may be shared by several health providers from whom the data must also be collected (Quittner, Modi, Lemanek, Ievers-Landis, & Rapoff, 2008).

2.5.3. Pill counts

Moosa (2007, p. 42) stated that this method of measuring medication adherence "... involves either a standard pill count or use of drug packs with a built-in counting system." The former requires that patients bring their medication to the appointment with the health care provider. The latter system records when the container is opened. However, this only measures the bottle opening, and not whether the medication was actually ingested by the patient. Additionally, both approaches also require that patients do not give out or share their medication (Moosa, 2007). Multiple variables need to be considered in this deceptively simple approach. If patients are required to bring their medication to the health care provider for counting, missing data will result, particularly from the least adherent patients. Some patients may throw away their medication to appear more adherent (Sajatovic, Velligan, Weiden, Valenstein & Ogedegbe, 2010).

2.5.4. Self-reporting

Self-reporting medication adherence scales or surveys are simple and economical methods to detect non-adherence. According to (Lavsa, Holzworth & Asnani, 2011), the "first published and most commonly used adherence scale is the Morisky Medication Adherence Questionnaire (MMAQ)," (Morisky, et al., 1986). Overall, MMAQ is found to be simple to administer and score, and is validated in many populations, in different languages and different disease conditions, making it a good tool to measure adherence across patient populations (Toll, McKee, Martin, Jatlow & O'Malley, 2007; Tan, Patel & Chang, 2014; Suárez, Pérez, Valentín, Palomo, Cepeda & Aguiar, 2011; Mahaye et al., 2012; Lavsa, Holzworth & Asnani, 2011). Morisky et al., (2008), stated that the advantages of utilising the MMAQ-8 lie in the 8 simple questions that are asked, and the ease of scoring these items (each yes answer = 1 point and; no = 0 points), For these reasons, the MMAQ-8 was used to measure the adherence rates of antidepressant medication in the current study, and will be discussed in greater detail in Chapter 3.

2.6. Types of non-adherence

2.6.1. Primary non-adherence

Primary non-adherence typically involves scenarios where health care practitioners provide prescriptions, but the medication is never filled or collected. This can also include non-participation in health programmes or the breaking of appointments (Morris & Schulz, 1992). There is a direct failure to follow doctors' instructions regarding the prescription. (Gellad, Grenard & McGlynn, 2009, as cited in Jimmy & Jose, 2011). Over the past 20 years studies have shown that this type of non-adherence is motivated by patient's beliefs about their treatment, illness and prognosis, as well as their experiences with medications (Benson, 2002). Patients can exhibit different medication-taking behaviours for different medications because they weigh the perceived risks and benefits for each medication separately. This suggests that adherence interventions should be modifiable to patients' beliefs about different medications (Gadkari & McHorney, 2012). Several studies of various designs, populations and illnesses assessing primary non-adherence found between 1% and 21% of prescriptions unfilled or unclaimed within pharmacies (Jackevicius, Paterson, & Naglie, 2007; Jones & Britten, 1998; Kirking, Zaleon, & Kirking, 1995; Skutnik & Katsanis, 2011). A survey of adults with chronic cardiovascular diseases (asthma, hypertension, diabetes, hyperlipidaemia, osteoporosis) reported that adherent patients were more likely to show higher perceived need, fewer adverse reaction concerns, and better knowledge about their condition and their medication when compared to non-adherent patients (McHorney & Gadkari, 2010).

2.6.2. Secondary non-adherence

Secondary non-adherence relates to patients who stop taking their medication after starting it without the recommendation of their health practitioner, take an incorrect dose or at wrong times, may forget one or more doses of the medication, or by failing to obtain a repeat prescription due to unavailability or inaccessibility to their medication (Morris & Schulz, (1992). Jimmy and Jose (2011) stated that this form of non-adherence is rarely intentional, but arises from patients' ability and resource limitations that inhibit patients to follow their prescribed treatment recommendations. A general secondary non-adherence rate of 50% for various types of drug therapies was observed by Hovstadius and Petersson (2011) using patient registry data in the Swedish general population. They noted that higher rates of secondary non-adherence contribute significantly to unnecessary medical spending, and efforts are needed to improve secondary adherence.

2.7 Factors influencing adherence

Several publications (World Health Organization, 2003; Leo et al., 2005; Kane, Kishimoto & Correll, 2013) have reported on the factors that could have a negative impact on treatment adherence across various settings. The World Health Organization categorised the determinants of non-adherence into five dimensions: (1) social and economic (e.g., unstable living conditions, medication cost, lack of financial resources, burdensome work schedules and low health literacy); (2) health system-related (e.g., provider communication skills, provider-patient relationship and no continuity of care); (3) treatment-related, (e.g., complexity of medication use, medications with social stigma associated, duration of therapy, negative side effects); (4) condition-related (e.g., chronic conditions, psychiatric disorders, lack of symptoms); and (5) patient-related (e.g., negative beliefs about treatment, cognitive impairment, visual impairment), (World Health Organization, 2003). However, Leo, Jassal & Bakhai (2005), described the following six factors why psychiatric patients do not adhere to their medication: (1) medication factors (complex regimen (i.e. polypharmacy, adverse effects, duration and dosage, availability); (2) illness factors (cognition/memory, concentration interference and hopelessness); (3) patient factors (denial, beliefs and attitudes, stigma); (4) physician factors (inadequate information provided, inadequate follow-up of response to treatment); (5) patient-physician factors (poor alliance/communication); and (6) social and environmental factors (supportive network, financial resources, inaccessibility and unavailability of treatment resources). More recently, Kane, Kishimoto and Correll (2013) identified the following five factors associated with non-adherence in patients with psychotic disorders: (1) patient characteristics such as sex, age, race and education; (2) illness characteristics such as duration, phase, severity or comorbidity, substance use cognitive function; (3) provider/ system characteristics include access to treatment, reimbursement or psycho-education; (4) family/ caregiver characteristics, including perceived need for treatment and support, stigma and availability of other support systems. They also noted (5) other characteristics such as financial constraints or transport related problems that may influence adherence to treatment.

It is clear from the literature above that, although there is some overlap, the grouping of these factors is not universally agreed upon. For this reason, an adapted model was developed that could best describe non-adherent behaviours relevant to the current study sample, and was informed by the literature cited here and the data that was collected with the research instrument. The following factors were subsequentlyidentified in the current study: patient factors; treatment factors; illness factors; health system factors and; moderating factors.

2.7.1. Patient factors

According to (Moosa, 2007), these include factors such as age, sex, and social conditions. Non-adherent patients are more likely to be younger, of lower socio-economic status and to have a lower level of education (Davis, 1968; Allan, 1988). Other factors include forgetfulness, inadequate knowledge, lack of insight, fear of being stigmatised, lack of financial resources, and co-morbid conditions, which have been found to negatively affect adherence rates (Owen, Fischer, Booth & Cuffel, 1996; Perkins, 2002; Löffler, Kilian, Toumi & Angermeyer, 2003).

A systematic literature review on the psychosocial and behavioural factors associated with medication non-adherence in both chronic physical and mental disorders noted patient characteristics such as age, gender and race were only significantly associated with adherence in a very small number of the twenty-four studies (published between 1966 and 2011), (12, 5 and 3 respectively), (Zeber, Manias, Williams, Hutchins, Udezi, Roberts & Peterson, 2013). In South Africa, antipsychotic medication adherence was measured in a psychiatric outpatient setting in KwaZulu-Natal Province using the MMAQ-8, and also observed an insignificant association between gender and adherence (Mahaye et al., 2012). However, they (Mahaye et al., 2012) found that only age (p = .045) and race (p = .055) were significantly correlated with medication adherence. However, from the thirty-two studies included in a systematic review of observational studies measuring antidepressant adherence in Depressive Disorders (Perestelo-perez & Serrano-aguilar, 2013), only a very small number of studies indicated that patient factors such as gender and race were predictive of adherence (1 and 1, respectively). In general, the literature seems to indicate that all these factors are not highly correlated with treatment adherence in the majority of the studies.

On the other hand, patient beliefs about medication and treatment efficacy were reported to be highly influential in treatment adherence in a qualitative study investigating reasons for non-adherence to treatment in psychiatry (Sharif, et al., 2003). Furthermore, Janse van Rensburg e. al., (2014) also reported that one of the common reasons psychiatric outpatients gave for not adhering to their medication regime was patient beliefs about medication. However, they did not report whether it had a significant correlation with medication adherence. To minimise the impact of outlying variables on the current study results, those who indicated they spoke languages other than Afrikaans or English comprised only a small percentage of the study sample (11.4%), and were grouped into the “other official SA languages” category (i.e., Northern Sotho: n=6; Sotho: n=10; Swazi: n=3; Tswana: n=8; Venda: n=1; Xhosa: n5; and Zulu: n=10). Similarly, patients who indicated

they were Coloured (n=23), Indian (n=7) or Mixed race (n=2) were also grouped into the "other SA populations"

In the current study, the following five patient-related variables were identified:

- Age: Age was calculated in years from patients' date of birth until December, 2014, upon conclusion of the study. The following age categories were also defined; 18-29, 30-39, 40-49, 50-59 and, 60 and older.
- Gender: Biologicalsex was dichotomously grouped as male or female.
- Race: Racial distribution of patients was grouped into the following categories; Black, White and, any other race
- Language: The main languages spoken by patients were grouped into the following categories; English, Afrikaans and, other official South African languages.
- Treatment beliefs: Perceived need for pharmacological treatment was dichotomously categorised as "yes" or "no".

2.7.2. Illness factors

Potential illness-related factors for non-adherence in psychiatry may also be influenced by issues such as illness severity, unique characteristics and symptoms associated with various psychiatric conditions, comorbid illnesses, previous history of episodes, cognitive impairment or lack of illness insight (Higashi, Medic, Littlewood, Diez, Granström & De Hert, 2013; Perestelo-perez & Serrano-aguilar, 2013).

Findings from a Spanish psychiatric outpatient setting noted that illness related factors such as the type of mood disorder patients were diagnosed with or illness severity were insignificantly correlated with medication adherence (Tamburrino, Nagel, Chahal & Lynch, 2009). However, they used the Medication Adherence Scale (MAS) and the Medical Outcomes Study (MOS) – different from the current study - in measuring adherence. Regardless, De Las Cuevas, Panate and Sans (2014) did use the same instrument as this current study (MMAQ-8), and also noted similar insignificant correlations between medication adherence and diagnosis and illness severity. Contrastingly, earlier onset of diagnosis was significantly associated with non-continuous antidepressant use within 6 months of initiating their treatment ($p = .034$) in a sample of n=189 patients newly dispensed with an antidepressant in a psychiatric outpatient clinic during 2006 and 2007 in Hong Kong

(Yau, Chan, Wing, Lam, Lin, Lam & Lee, 2014). Al-Jumah, Ahmad Hassali, El Tahir, and Al Qhatani (2014), measured antidepressant medication adherence using the MMAQ-8 among n=403 psychiatric outpatients in Saudi Arabia. They noted that a shorter duration of illness in and less depression severity was associated with higher adherence levels.

In the current study, the following five illness-related variables were identified:

- Main diagnosis: This is defined as the primary DSM-IV-TR Axis I and II diagnoses reported, and excludes general medical related conditions.
- Comorbid conditions: This was defined as the type and number of DSM-IV-TR diagnoses reported by patients.
- Age of onset of main diagnosis: This is defined as the age at which patients received their primary DSM-IV-TR diagnosis
- Duration of illness: This is defined as the number of months since patients have received their primary diagnosis until December, 2014, upon conclusion of the study, as extracted from the database.
- Severity of illness: Patients' perceived severity of their condition was defined by the participants' response to the question "Do you think or feel your condition makes it difficult for you to do your daily activities?"

2.7.3. Treatment factors

Treatment related factors such as length of treatment (Moosa, 2007), complex treatment regimens (Blackwell, 1996; Razali & Yahya, 1995) and side-effects (Bostwick, 2010; Taj, Tanwir, Aly, Khowajah, Tariq, Syed, Shahzada et al., 2008; Yau et al., 2014) can all have a detrimental effect on treatment adherence. A meta-analysis found that Escitalopram and sertraline were superior to other antidepressants when considering both effectiveness and safety (Gartlehner, Thieda, Hansen, Gaynes, Deveaugh-Geiss, Krebs & Lohr, 2008). It is worth noting that this meta-analysis had several limitations such as different measuring instruments used, it included studies with low methodological quality, in different settings (inpatient and outpatient) and clinical profiles (single disorder and comorbid diagnoses). However, other analyses (Thaler, Morgan, Van Noord, Gaynes, Hansen, Lux, Gartlehner et al., 2012; Agency for Healthcare Research and Quality, 2014), have found that no SSRI is more superior to the other. Although Zeber and his colleagues (2013) observed that some studies did not report a significant correlation with medication-related factors and lower

adherence levels (Yood, Mazor, Andrade, Emani, Chan & Kahler, 2008; van Geffen, Gardarsdottir, Hulten, Dijk, Egberts & Heerdink, 2009; Wamala, Merlo, Bostrom, Hogstedt & Agren, 2007; Wroth & Patman, 2006), the majority of studies included in their systematic review did observe significant correlations between poor adherence and various antidepressant treatment characteristics such as the use of tricyclic antidepressants (Akincigil, Bowblis, Levin, Walkup, Jan & Crystal, 2007; Cooper, Brown, Vu, Palenchar, Gonzales, Ford & Powe, 2007; Keller, Hirschfeld, Demyttenaere & Baldwin, 2002), complex treatment regimen (Bucci, Possidente &Talbot , 2003), and the presence of unpleasant adverse reactions (Shigemura, Ogawa, Yoshino, Sato, & Nomura, 2010).

In the current study, the following five treatment-related variables were identified:

- Type of antidepressant: The following categories were identified as classified by the MIMS (September, 2014); tricyclic antidepressants, monoamine oxidise inhibitors (MAOI), selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine selective reuptake inhibitors (SNSRIs), norepinephrine and dopamine reuptake inhibitors (NDRIs), melatonergic agents, lithium and, others.

- Duration of treatment: This is defined as the number of months patients have been taking their current antidepressant medication until December, 2014, upon conclusion of the study, extracted from the database.

- Dosage: This is defined as once a day, twice a day, three times daily, or more than four times a day.

- Polypharmacy: This is defined as the number of medications (including all central nervous system medications), patients are currently prescribed.

- Adverse reactions: Patients' experiences with adverse reactions were defined through participants' response to the question, "Are you currently experiencing any adverse reactions from your antidepressant medication?"

- Knowledge of how to cope with adverse reactions: Patients' knowledge of how to cope with any potential medication-related adverse reactions were defined through participants' response to the question, "Do you know how to handle or cope with any potential side-effects from your antidepressant medication?"

2.7.4. Health system factors

Moosa (2007) provided the following health-care related factors that influence non-adherence in psychiatry: poor patient-health care provider relationships may cause poor adherence; failure of psychiatrists to establish good rapport with patients may govern much of the efficacy of care (Pereira & Pinto, 1997). Therefore, a good therapeutic agreement with a doctor who is positive about the treatment outcome may lead to better adherence. Other factors that may have a negative impact on adherence include poor services and medication distribution systems, lack of staff training, overworked health care providers, insufficient ability to provide education and continuity of care to patients, and inability to establish community support systems or groups (Carpenter, Morrow, Del Gaudio & Ritzler, 1981; Craig, Huffine & Brooks, 1974). Furthermore, Price and Kovar (2013) identified barriers to high-quality care, limited support and lacking health insurance as risk factors for non-adherence to antidepressant medications in their literature review.

Lack of social support has also been reported to be a predictor of non-adherence to antidepressant medication (Voils, Steffens, Flint, & Bosworth, 2005). However, this particular international study only included a small sample (n=85) from both in- and outpatients aged 59 years or older. An international systematic review of systematic reviews found that health care system factors such as medication costs and co-payments were found to influence adherence rates negatively in chronic illnesses such as arthritis and cancer (Mathes, Jaschinski, & Pieper, 2014). Additionally, Banerjee and Varma (2013) assessed factors that influenced adherence to depression treatment in an outpatient setting in India observed that the majority of patients were non-adherent due to health facility-related factors (long distance from health care facilities, long waiting hours and unavailability of medication). Although they also measured adherence using the MMAQ-8 (Bengali language), this sample only included patients with unipolar depression, as defined by the ICD-10 (World Health Organization, 1992), and not the DSM-IV-TR classification system used in the current investigation (American Psychiatric Association, 2000), as well as excluding patients with other comorbid conditions.

The current study did not investigate other health system-related issues such as staff training, the frequency of patient-provider communication, distance from health care facilities, waiting hours or medication availability, and this may warrant further study and exploration.

In the current study, the following five health systems-related variables were identified:

- Health care system: The types of health care service patients made use of was categorised as private or public. Furthermore, the distinction was made between patients' prescribing practitioners, i.e., from a psychiatrist or general practitioner

- Health insurance: This was defined as patients' medical aid or social grant status. Patients were asked to indicate if they received any financial aid for their treatment in the form of medical aid or a social grant by responding "yes" or "no" to the corresponding questions.

- Lack of support: Patients' perceived need for support with adhering to their medication was defined by the participants' response to the question "Do you feel you need more support to help you stick to your antidepressant medication?"

2.7.5. Moderating factors

These factors were identified as additional barriers that may restrict or hinder patients from taking their prescribed medication optimally, and include poor socio-economic conditions, lower level of education and literacy, unstable or poor living arrangements, lack of access to clinics (long distance to travel, cost of transport), insufficient support systems, and stigmas and attitudes associated mental disorders (Jin, Sklar, Min Sen Oh, & Chuen Li, 2008; Price & Kovar, 2013; Mathes, Jaschinski, & Pieper, 2014). The availability of support in the form of family, friends, or caregivers to assist or supervise medication is associated with increased outpatient adherence to treatment (Moosa, 2007, as cited in Fenton, McGlashan, Victor & Blyler, 1997). However, these factors are continuously interacting and influencing each other, that ultimately results in non-adherent behaviour. For example, patients report that treatment effectiveness and barriers to access are among the most critical aspects of depression care (Cooper et al., 2000).

Early literature summarised (Pampallona et al., 2002) and concluded that, although patient education was commonly assessed for its impact on treatment adherence, studies did not show consistent findings. Although lower levels are generally associated with poorer treatment adherence, findings have been mixed and suggested that education level and its impact on adherence are still not clearly understood. Additionally, marital status and living arrangements (i.e., alone versus with another person) were not significant predictors of adherence to treatment in a sample of n=134 patients with Major Depressive Disorder (MDD), (Sirey, Bruce, Alexopoulos, Perlick, Raue, Friedman & Meyers, 2001). Similarly, a study investigating reasons for premature discontinuation of treatment with SSRIs in n=406

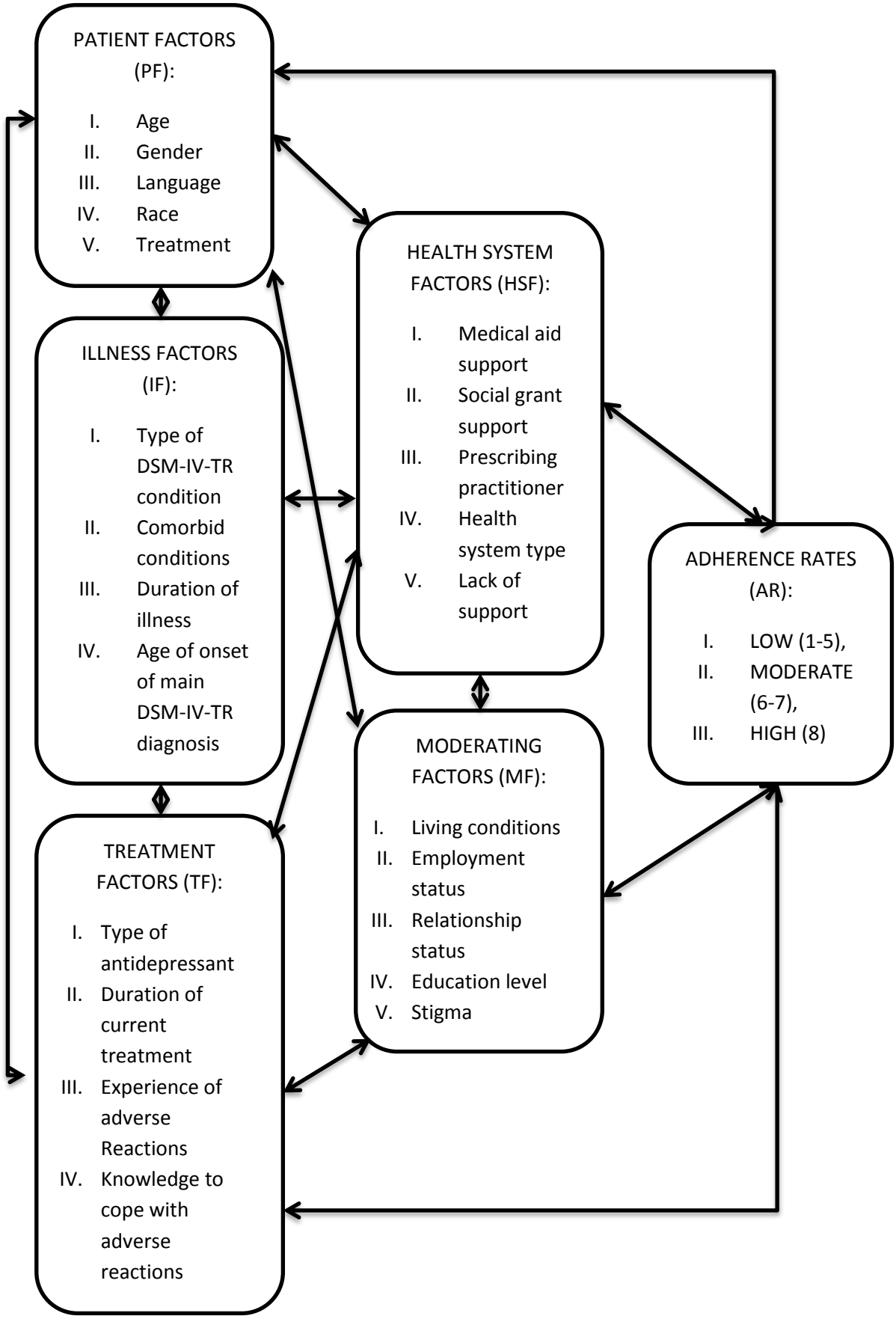
patients with MDD, and reported that treatment non-adherence was not significantly associated with marital status or education (Goethe, Woolley, Cardoni, Woznicki & Pie, 2007). More recently, an analysis of n=228 hypertensive patients with depression found that education level was not significantly correlated with adherence levels, (Bogner & de Vries, 2008).

In the current study, the following five moderating variables were identified:

- Relationship status**:** The following relationship categories were identified; married, single, widowed, divorced, relationship and, engaged.
- Education level: The following categories were established to determine the level of education; did not attend school, Primary school - Grade 7 completed, some High (Secondary) school completed - Grade 9, High (Secondary) school completed – Grade 12, Diploma or Degree obtained and, Postgraduate Degree obtained.
- Living conditions: The following categories were identified to describe participants' living arrangements; live on their own, live with a partner, live with family, live with friends or; other.
- Employment status: The following categories were identified to best describe the participants' current employment status; employed working full-time, employed, working part-time, not employed - looking for work, not employed - not looking for work, student, retired and; disabled or not able to work.
- Stigma: Participants' experience with stigma was defined by responding *Yes* or *No* to the question "Are you afraid of what some people may think about you taking antidepressant medication?"

Figure 1 illustrates the conceptual framework utilised by the current study. This framework was informed by the cited literature, the information that was collected in the study as well as consideration for the local context of the setting. Figure 1 represents the various patient-, illness-, treatment-, health system- and, moderating variables identified in the current study, and illustrates how it is possible that each of the individual variables in the five main groups may significantly correlate with variables from any other main variable group or, even with individual variables in the same group (between- and within-groups approach). Ultimately, these variables may (directly or indirectly) have an influence on adherence rates.

Figure 1: Conceptual framework



2.8. Consequences of non-adherence

Although antidepressant medication has been found to reduce depressive symptoms (Regier, Hirschfeld, Goodwin, Burke, Lazar & Judd, 1988; Maixner & Greden, 1998, cited in Aikens et al., 2005), clinical efficacy of the treatment is compromised when patients do not adhere to the prescribed regimen. Adherence is a primary determining factor of pharmacological treatment efficacy in psychiatry, and poor adherence diminishes the clinical and therapeutic benefit of these therapies (World Health Organization, 2003). Non-adherence to medication is associated with a worse prognosis, greater probability of relapse, rehospitalisation and increased resource consumption (Melfi, et al., 1998; Erwin & Peters, 1999; Higashi et al., 2013).

Firstly, it is associated with a decreased reduction in symptoms, as well as increased risk of relapse and hospitalisation and suicide attempts. In addition, financial costs incurred by non-adherent patients are significantly higher due to increased treatment costs (World Health Organization, 2003). According to Thompson, Peveler, Stephenson and McKendrick (2000), levels of adherence have been positively associated with treatment outcomes in depression, independent of the kind of antidepressant medications used. In addition to the clinical impact on the health of patients, higher rates of medication adherence also transforms into financial or economic advantages. This comes in the shape of direct savings through the decreased use of costly health services caused by worsening symptoms, relapses or rehospitalisation of patients. Indirect savings can also be benefited from through the attribution of patients' improved productivity, quality of life, social and work roles (World Health Organization, 2003).

2.9. Psychological theories of adherence

Research that investigated the psychological theories explaining adherence over the past ten years has been limited, but considerable progress has been made since then (World Health Organization, 2003). Although not totally comprehensive and complete, we now have information on the extent of the problem of non-adherence to medication in psychiatry, and there is an increasing awareness of the positive clinical and public impact it can have. Like most health improving behaviours, having to take medication regularly for a long time involves a conscious commitment to a new healthy behaviour and requires a change in daily habits (World Health Organization, 2003). A brief overview of the main theoretical perspectives that describe adherence behaviours is provided in the following section, followed by a detailed discussion of the theoretical approach that guided the current study.

The following psychological approaches outlined by Leventhal & Cameron (1987), provides a helpful overview of the five dominant theoretical perspectives on treatment adherence: Biomedical perspective; Behavioural perspective; Communication perspective; Cognitive perspective; and Self-regulatory perspective. These suggested theories, models and methods provide a conceptual framework to address the challenge of non-adherence. Despite all these efforts after decades of research on adherence to develop a conceptual understanding of this phenomenon, (DiMatteo & DiNicola, 1982; Sherbourne, Hays, Ordway, DiMatteo & Kravitz, 1992; DiMatteo, Giordani, Lepper & Croghan, 2002; DiMatteo, Reiter & Gambone, 2009; Zolnierek & Dimatteo, 2009), adherence rates have not improved much. This can become challenging in the case of chronic illnesses such as psychiatric diagnoses. Although these theories and models offer a conceptual framework for organising the models about adherence, each has its own advantages and disadvantages. No single approach provides a comprehensive understanding of adherence, and more recent approaches that focus on more specific non-adherent behaviours may provide additional information that can inform these existing frameworks (World Health Organization, 2003). Given that the barriers to medication adherence are complex and heterogeneous, psychological theories that aim to understand these health behaviours must be multifaceted and provide the possibility to be modifiable across different settings, illnesses and treatments. Such specialised and comprehensive theories can contribute to a greater understanding of the mechanisms of health behaviours, and lead to successful treatment interventions and adherence-enhancing strategies.

2.9.1. Biomedical perspective

According to Midence and Meyers (1998), the biomedical approach to adherence assumes a paternalistic view, and that patients are passive followers of their doctor's orders regarding their prescribed treatment or therapy. This remains the authoritative perspective in many health care settings. Non-adherence is assumed to be the result of patient characteristics such as demographics. Aspects such as gender and age have been found to be predictors of medication adherence, especially in the case of antiretroviral medications (Langebeek, Gisolf, Reiss, Vervoort, Hafsteinsdóttir, Richter & Nieuwkerk, 2014; De Fatima Bonolo, Ceccato, Rocha, de Assis Acúrcio, Campos & Guimarães, 2013; Blackwell, 1992), and these factors are viewed as the targets that specialised interventions aims to take into consideration. This has helped to clarify the relationships between illness and treatment characteristics on one side, and non-adherence on the other. Keeping in line with this systematic view, solutions and innovations to promote adherence, such as medication

monitoring systems, assessing levels of adherence using biochemical measures, and developing new devices to administer medications, are often grounded in this approach (World Health Organization, 2003).

However, according to Munro, Lewin, Swart & Volmink (2007), a major shortcoming of this approach is that it ignores factors other than patient characteristics that can impact on adherence. Patients' perspectives of their own illness, psycho-social influences and socio-economic environment also play a significant role in medication adherence (World Health Organization, 2003; Blackwell, 1992). The assumption that patients are merely passive compliers makes it unlikely that this theory can contribute significantly to medication adherence (Munro et al., 2007). Instead, patients are active decision makers and more involved in their own treatment, and do not merely receive and follow instructions. They (Munro et al., 2007) suggest that a shift from a paternalistic biomedical model to a model of shared decision-making is necessary.

2.9.2. Behavioural perspective

The Behavioural perspective includes Behavioural Learning Theory (BLT), which concerns itself with the environmental context of patients and the training of skills to manage medication adherence (World Health Organization, 2003). This approach is primarily characterised by the antecedents and consequences of adherence, and their influence on behaviour (Munro et al., 2007). Antecedents are either the internal thoughts of a patient or the external, environmental cues that contributes to non-adherence. Consequences refer to the potential risks or rewards for that particular behaviour. The likelihood of a patient following a specific behaviour will depend on their internal thoughts or the external, environmental setting and what happens before and after the behaviour occurs (World Health Organization, 2003). This perspective emphasises the significance of reinforcement (positive and negative), as a method for influencing adherence behaviour. They (Munro et al., 2007) note that it would be possible to control the adherence behaviour of patients if one could control the events before and after a specific behaviour or act. Practically, these principles can be used to develop interventions that can influence behaviour at each level of influence (i.e., patient, provider and system) to address adherence problems.

Adherence promoting strategies incorporating elements of BLT (Haynes, McDonald, Garg & Montague, 2002), such as using patient reminders (Dunbar, Marshall & Hovell, 1979; Burke, Dunbar-Jacob & Hill, 1997; Atreja, Bellam & Levy, (2005), have been found to improve adherence to chronic medications. However, analysis examining interventions derived from

BLT to improve adherence to ARV therapy concluded that these interventions were as efficacious as those without (Simoni, Pearson, Pantalone, Marks & Crepaz, 2006), or has a negative effect when using electronic reminder systems (Mannheimer, Morse, Matts, Andrews, Child, Schmetter & Friedland, 2006). Therefore, further evidence of the utility of this approach may be needed. BLT has also been critiqued by Blackwell (1992) for lacking an individualised or person-centered approach, and for not considering influences that are not related to risks or rewards. These influences include past behaviour, habits, or lack of acceptance of a diagnosis (Munro et al., 2007). They (Munro et al., 2007) also report that this approach is limited by placing an over-emphasis on external influences on behaviour and, should also consider individuals' perceptions of appropriate risks and rewards.

2.9.3. Communication perspective

According to Ross and Deverell (2004, p. 56), *communication* is "the cornerstone of every patient-practitioner relationship". The Communication approach places an emphasis on the encouragement from health care providers to try to improve their own skills in communicating with patients (Atreja, Bellam, & Levy, 2005). Prior to this, Leventhal, & Cameron (1987) already proposed that improved communication will enhance adherence, and that it can be achieved through good health care provider communication skills and patient psycho-education. This has led to interventions that aim to develop rapport and, educating patients using good communication skills and stressing the benefit of a more equal relationship in the treatment journey (World Health Organization, 2003).

Although adopting a warm and kind interaction style with a patient is a key aspect of this approach, it may be insufficient in itself to change the adherence behaviours of patients. Blackwell (1992) criticises this perspective by arguing that it disregards attitudinal, motivational and interpersonal factors that may interfere with the reception of information and the translation of knowledge into applied knowledge or behaviour change. It is also cautioned (Munro et al., 2007) that communication interventions in isolation may be unlikely to be effective in improving adherence to chronic medications because it ignores the influence of external factors, such as the costs and social barriers related to accessing health care for treatment. Interventions informed by this approach are also restricted to patient-practitioner engagement, and additional social support from family members, friends and support groups may be required to influence the patient’s adherence behaviour. According to Atreja, Bellam, and Levy (2005), the family's role becomes important if a patient is suffering from a chronic or disabling condition that requires continuous care and aid.

2.9.4. Cognitive perspective

Various models have been proposed that emphasise cognitive aspects and processes relating to adherence behaviour. Examples of these include the Health Belief Model (HBM), (Becker, Maiman, Kirscht, Haefner, Drachman & Taylor, 1979), Social–Cognitive Theory (SCT), (Bandura & Simon, 1977), the Theory of Planned Behaviour (TPB), (Ajzen & Fishbein, 1980), and the Protection–Motivation Theory (PMT), (Gochman, 1997). These theories share the assumption that attitudes, beliefs and expectations of future outcomes are major determinants of health related behaviour, and propose that patients will follow behaviour that are most likely to lead to positive health outcomes (Munro et al., 2007). Although these perspectives have focussed their attention on the ways in which patients think about health threats and factors that may hinder or improve positive health outcomes, they have been criticised for not always addressing behavioural coping skills well (World Health Organization, 2003).

It is argued that these Cognitive approaches do not recognise that non-voluntary factors such as power relationships, devoting time and social structures can affect adherence behaviour (Ingham, Woodcock & Stenner, 1991; Gebhardt & Maes, 2001). According to Weinstein, (1988), this perspective also gives little attention to the origin of beliefs and how they can influence other behaviours. This approach only focuses on a single threat to adherence behaviour, and does not consider other potentially competing threats to the patient's mental or physical health (Munro et al., 2007). In addition, two main criticisms of the HMB, for example, where stated. Firstly, the relationships between the relevant variables have not been explicitly formulated (Stroebe, & de Wit, 1996), and no definitions have been constructed for the individual components (Armitage & Conner, 2000). It relies on the underlying assumption that these variables are not moderated by each other and has additive effect affect health behaviour, and that these variables influence adherence directly and remain unmoderated by behavioural intentions (Stroebe, 2000). Secondly, other important aspects of health behaviour, such as the positive effects of negative behaviours and social influence, are not considered (Stroebe, & de Wit, 1996; Stroebe, 2000]. Furthermore, an important limitation of the PMT, for example, is that not all environmental and cognitive variables that could influence health behaviour change, such as social pressures and stigma, are not taken into consideration (Rogers, 2010). In addition, it sub-divides perceived efficacy into categories of response and self-efficacy may be inappropriate – patients may generally not consider themselves capable of performing adherent behaviours without the means to do so (Bandura, 1997).

2.9.5. Self-regulatory perspective

The Self-regulation approach attempts to join environmental aspects and the cognitive responses to health threats (Leventhal, Leventhal & Contrada, 2007). The core of this theory relates to the importance of the patient's own cognitive conceptualisation of their illness and treatment, and emphasises the necessity to examine individuals' subjective experience of health threats to understand the way in which they respond to these threats (Munro et al., 2007). The theory is based on the assumption that people are active, self-regulating problem solvers motivated to avoid and treat health threats (Leventhal, Meyer & Nerenz, 1980; Hale, Treharne & Kitas, 2007). The perceptions and beliefs that patients have about their condition or therapy and their self-efficacy are seen as mediators between the illness and the behavioural response to their health risk (World Health Organization, 2003). Leventhal, Leventhal and Schaefer (1992) explain that patients create personal representations of their illness and its associated treatment, and it is these representations that guide their decision-making and adherence behaviour. Adherence, according to this perspective, requires the belief that patients have the specific coping skills to manage in their own personal, social and cultural environment, the belief that the illness needs to be paid attention to and the adaption of their behaviour to improve their health (Edgar & Skinner, 2003; Benyamini, Gozlan & Kokia, 2004). However, the self-regulation theory offers little guidance related to the development and design of interventions that aim to curb non-adherence in the treatment of chronic conditions of promote positive health behaviours (Munro et al., (2007). While this approach seems innately suitable, there is a lack of specific suggestions as to how these processes would improve adherence (Reynolds, 2003; De Bruin, Sheeran, Kok, Hiemstra, Prins, Hospers & van Breukelen, 2012). Baumeister and Heatherton (1996), also warn against under-regulation, where the patient doesn't exert or manage self-control, as well as misregulation, where self-control is misguided or counterproductive, and therefore fails to lead to improved health outcomes.

These models provide a useful conceptual framework for organising ideas about adherence (World Health Organization, 2003). Each has its advantages and disadvantages, and no single perspective can universally describe and explain adherence behaviours. Regardless, these perspectives have the potential to both improve our understanding of adherence behaviours and inform the design of effective interventions to promote adherence to antidepressant treatment. Despite this, little empirical evidence was located on the effectiveness of these theories in promoting adherence to treatment in chronic conditions (Munro et al., 2007). More recent approaches that are simple, yet transferable and adaptable across heterogeneous chronic conditions and treatments, and consider the demands of following recommended health practices may provide more additional insight.

2.9.6. Information Motivation Behavioural Skills Framework

A more recently developed approach, the information–motivation–behavioural skills model (IMB model), borrowed ideas from previous works to develop a conceptually based, generalisable, and simple model to guide complex adherence behaviours (Fisher & Fisher, 1992), and has been specifically tailored to designing interventions to promote adherence to ART (Fisher et al., 1996). This theory has its roots in the Cognitive perspective, and focuses on three components that result in behaviour change: information, motivation and behaviour skills (World Health Organization, 2003; Munro et al., 2007): a) information, which is the basic knowledge about an illness, and may include how the disease progresses, its expected course and effective treatment options available; b) motivation, which encompasses the personal attitudes towards, perceived social support for, and the patients' subjective perception of how others with the illness may behave and; c) behavioural skills (ability), which includes the specific tools or strategies necessary to perform the adherence behaviour such as social support and other self-regulation strategies. The components also need to be directly relevant to the desired behaviour to be effective (World Health Organization, 2003). Additionally, Fisher, Fisher, Amico & Harman (2006) identified a number of moderating factors such as psychological health (fear of stigma or discrimination), living situations, access to medical care and services, and substance use, which may affect adherence, and were subsequently included in this model.

According to this theory, patients will adhere to their treatment if they are able to (possess the capability to follow instructions), has the information (the knowledge and understanding of their condition and treatment) and motivation (the attitude and beliefs about the condition and treatment), to engage in adherent behaviours (Fisher et al., 1996). The IMB model demonstrates that information is a prerequisite for changing behaviour, but in itself is insufficient to achieve this change (Prochaska, DiClemente & Norcross, 1992). This is because this information is influenced by other treatment, illness or social factors that may affect adherence, and this needs to be taken into consideration. Motivation and behavioural skills are also key determinants and are independent of behaviour change and can also be moderated by a range of contextual factors such as living conditions and access to health services (Fisher & Fisher, 1992; Fisher, et al., 1996). Information and motivation work mainly through behavioural skills which in turn reduce the risk of non-adherent behaviours and, when the behavioural skills are uncomplicated or mastered, information and motivation can have direct effects on behaviour (Munro et al., 2007). The advantage of IMB lies in its simplicity as well as its recent moderately effective application and predictive value in ART adherence, which suggests that it may be a promising model for promoting adherence to other chronic medication therapies as well (World Health Organization, 2003; Amico, Toro-

Alfonso & Fishe, 2005; Amico, Barta, Konkle-Parker, Fisher, Cornman, Shuper, Fisher et al., 2009).

Considering the advantages of the IMB model (simplicity, generalisability, inclusion of moderating factors), this approach was chosen to conceptualise and formulate health behaviours related to antidepressant medication adherence in the current study. The limitations from the Cognitive perspective were also taken into consideration. The current study included non-voluntary factors such as social structures that can affect adherence behaviour, as well as focusing on multiple competing threats to adherence behaviour. Furthermore, the relationships between the identified variables have been explicitly framed and definitions for the individual variables have been clearly formulated. The current study also does not rely on the assumption that these variables are not moderated by each other and are not simply additive in nature, but is cognisant that these variables influences, and are influenced by, several factors that are indirectly related to adherence. In addition, the current study also took into consideration environmental and cognitive variables that could influence health behaviour change, such as social pressures and stigma. However, other limitations of this approach such as patients' origin of beliefs and positive effects of negative behaviours could not be addressed in the current study, and may warrant the need for additional investigation in this sample.

Figure 2 illustrates the conceptualisation of the IMB model (adapted from Fisher et al., 2006) as it applies to antidepressant adherence within the scope of the current study.

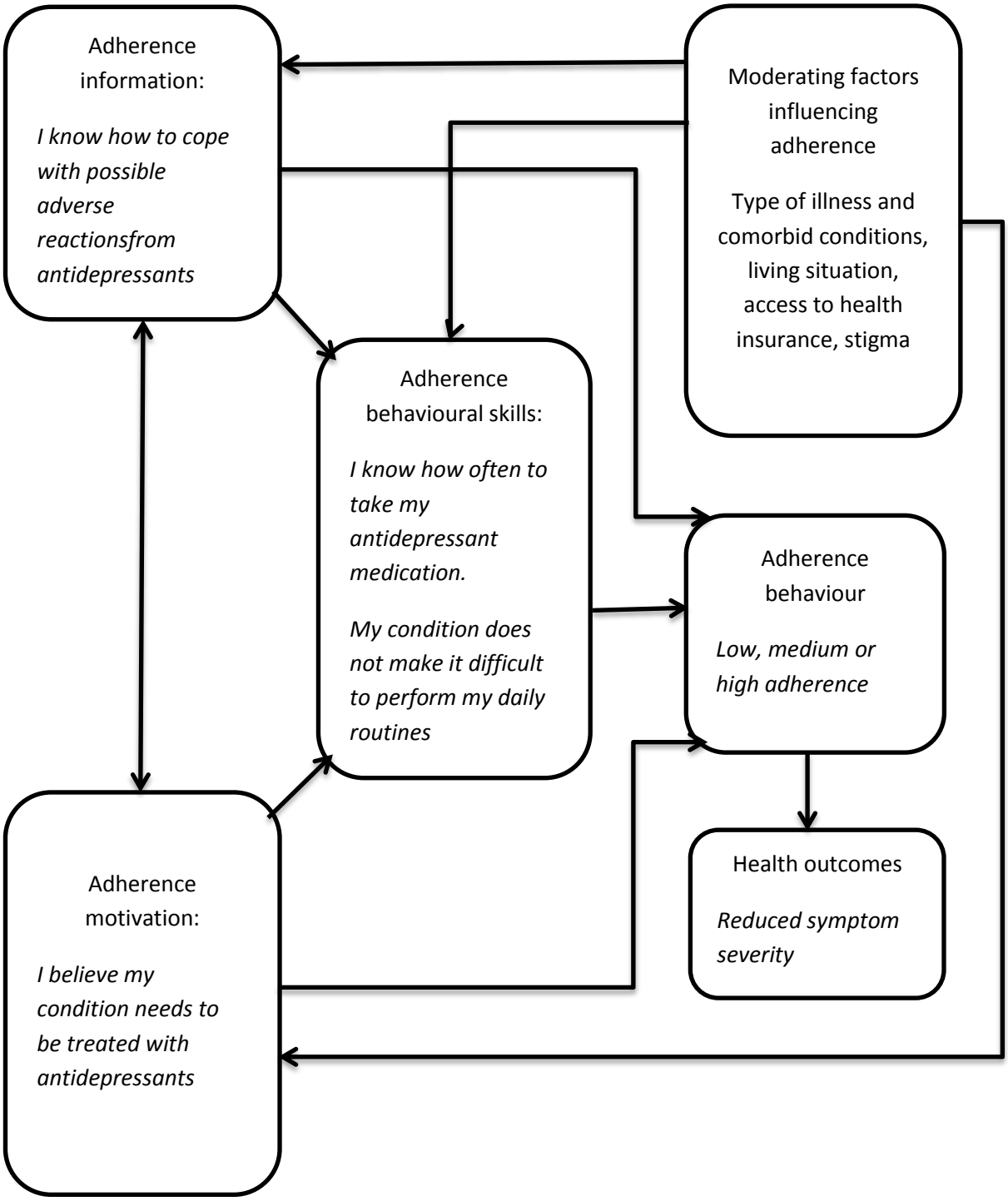


Figure 2: IMB model (adapted from Fisher et al., 2006)

2.10. Chapter summary

The term, *adherence* was defined in the current study by the application of the MMAQ-8, (Morisky, et al., 1986). This was followed by a background discussion of adherence in psychiatry. Evidence suggests that non-adherence to treatment is a tremendous barrier in health care and is estimated that between 25%-50% of all patients, irrespective of disease, prognosis or setting, are non-adherent to their treatment (Morris & Schulz, 1992; Sacket & Snow, 1979; Donovan, 1995; Vermeire et al., 2001; Vergouwen et al., 2003; Bambauer et al., 2006; Olfson et al., 2006). Some local evidence of non-adherence in psychiatry was also provided, however, this was limited. To date, there have been no large-scale studies that aim to objectively determine the rate of adherence to antidepressant medications in Gauteng, suggesting a shortage of local evidence measuring and describing non-adherent behaviours of psychiatric outpatients in this area. A list of the pharmacological treatments identified in the current study was also provided in this chapter. A subsequent discussion on various common methods of adherence measuring instruments was provided (Moosa, 2007). Empirical, descriptive, research that identified various correlates and predictors of adherence and non-adherence were also discussed in this chapter (Blackwell, 1996; Nichol et al., 1999; Vermeire et al., 2001; Cramer, 2004; Bulloch & Patten, 2010; Chong et al., 2011; Kardas et al., 2013), as well as providing an overview of the potential consequences of non-adherence in psychiatry. In the final section, the researcher discussed the behavioural theories that aim to describe, explain and predict non-adherence (World Health Organization, 2003; Munro et al., 2007), and provided the conceptual framework and definitions utilised by the current study.

A tremendous research agenda still remains to understand non-adherent behaviours and to design effective interventions that are generalisable across settings and to address non-adherence to antidepressant medications in psychiatric patients. More accurate, local estimations of the prevalence of non-adherence are also needed to address the different forms that this behaviour can take on. An improved understanding of adherence behaviour could lead to more comprehensive theoretical frameworks and models, and to more effective intervention methods of improving medication adherence in psychiatry. However, it was not within the scope of this study to recommend potential intervention methods to address non-adherence in the current study sample, but to determine the rates and describe factors that contribute to non-adherence in a specific sample and provincial region of South Africa in sufficient detail.

CHAPTER 3

RESEARCH METHODOLOGY

3.1. Introduction

In this chapter, the researcher provides information on the research design and methods of this study. The survey research method has been chosen to determine the rate of non-adherence to antidepressant medication, as well as the factors influencing non-adherence amongst psychiatric outpatients in Gauteng, South Africa. The area of study, population, sample of the population and sampling technique are described. Subsequently, the research instrument used in the study will be elaborated on, which includes a validated, self-reported measure of medication-taking behaviour. This is supplemented with additional items addressing the circumstances surrounding adherence behaviour. Data collection and data analysis procedures are also discussed in this chapter. Lastly, the limitations of the study are described.

3.2. Research questions

The following research questions have been identified based on the aim of the study. In this study, we seek to determine the rates of medication non-adherence, with a specific focus on antidepressant medication, and to identify the variables that significantly influence non-adherence rates in psychiatric outpatients in Johannesburg, Gauteng. With this in mind, two main research questions have been identified in the current study, and the second main research question has been divided into five more specific sub-questions. The current research questions are as follows:

(1) What are the rates of non-adherence to antidepressant medication in a sample of psychiatric outpatients living in Johannesburg, Gauteng?

2a) Which patient-related variables significantly correlate with antidepressant treatment adherence rates in this sample?

2b) Which illness-related variables significantly correlate with antidepressant treatment adherence rates in this sample of psychiatric outpatients?

2c) Which medication-related variables significantly correlate with antidepressant treatment adherence rates in this sample of psychiatric outpatients?

2d) Which health system-related variables significantly correlate with antidepressant treatment adherence rates in this sample of psychiatric outpatients?

2e) Which moderating factor-related variables significantly correlate with antidepressant treatment adherence rates in this sample of psychiatric outpatients?

3.3. Study hypotheses

Studies measuring non-adherence rates and identifying factors that contribute to non-adherence varies widely in study design, assessment instruments, populations, psychiatric conditions, sampling selection methods, treatment settings and treatment regiments themselves (Pampallona et al., 2002; World Health Organization, 2003; Kane et al., 2013; Hung, 2014; Leo et al., 2005; Procyshyn, et al., 2010; Kardas et al., 2013; Perestelo-perez & Serrano-aguilar, 2013; Brown & Bussell, 2011). It is also apparent there is a great deal of variability across these studies as to which of these factors are statistically significantly correlated with treatment adherence rates. For example, literature previously cited suggested that non-adherence to treatment can be expected in approximately 30% – 50% of all patients, irrespective of disease, prognosis or setting (Morris & Schulz, 1992; Sacket & Snow, 1979; Donovan, 1995). Buckley, Foster and Patel (2009) noted that these rates increase further when specific psychiatric conditions such as depression (51 % - 69%), Schizophrenia (30-60%), Bipolar Mood Disorder (21-50%) or other anxiety disorders (57%) are considered. In antidepressant medication specifically, Bulloch and Patten (2010) reported non-adherence rates of 45.9%. Additionally, of the twenty-four articles (published between 1966 and 2011) included in a systematic literature review of psychosocial and behavioural factors associated with medication adherence (Zeber et al., 2013), only five indicated that gender was significantly associated with initial medication non-adherence, four of which in favour of males, and one indicating that females were more adherent than males. A South African study (Mahaye et al., 2012) measured antipsychotic medication adherence in a psychiatric outpatient setting in KwaZulu-Natal Province using the MMAQ-8, and also observed an insignificant association between gender and adherence. A review (Zeber et al., 2013) noted that age, gender and race were only significantly associated with initial medication non-adherence in a very small number of the twenty-four studies included in their review (12, 5 and 3 respectively).

When illness factors are considered, it was found that an earlier onset of diagnosis was significantly associated with antidepressant non-adherence within 6 months of initiating their treatment ($p = .034$), (Yau et al., 2014). Their (Yau et al., 2014) sample included n=189

patients newly dispensed with an antidepressant in a psychiatric outpatient clinic during 2006 and 2007 in Hong Kong. To support their findings, Al-Jumah, Ahmad Hassali, El Tahir, and Al Qhatani (2014), measured antidepressant medication adherence using the MMAQ-8 among n=403 psychiatric outpatients in Saudi Arabia in a similar observational study design. He noted that a shorter duration of illness in and less depression severity (as measured by Montgomery–Åsberg Depression Scale), was associated with higher adherence levels. However, several authors report finding insignificant correlations between these illness factors, as well as other treatment-, health system- and moderating factors and treatment adherence (Pampallona et al., 2002; World Health Organization, 2003; Kane et al., 2013; Hung, 2014; Leo et al., 2005; Procyshyn, et al., 2010; Kardas et al., 2013; Perestelo-perez & Serrano-aguilar, 2013; Buckley et al., 2009; Zeber et al., 2013; Bauer et al., 2014; Zeber, Copeland, Good, Fine, Bauer & Kilbourne, 2008). In an attempt to answer the research questions stated above, research hypotheses need to be generated. The formulation of the current study hypotheses were informed by the literature cited in this study, and is briefly discussed in the following section.

3.3.1. Formulation of study hypotheses

These conflicting findings reported across the studies cited here presented challenges to the formulation of the study hypothesis or predicting the direction of significant correlations that may arise. For this reason, the researcher opted to identify the common factors informed by the literature and formulated individual study hypotheses for each variable related to these factors. However, Rice (1989) cautioned that tests for the statistical significance of individual components such as in the current study are often biased because it increases the probability of finding significant results (i.e., the null hypothesis is rejected when it is actually true, or a Type I error). This provided the motivation for the application of the Bonferroni-Holm correction for multiple comparisons calculator (Holm, 1979). This sequentially rejective correction approach has a large probability of rejecting false hypotheses and strongly controls the family-wise error rate at level alpha (Holm, 1979). A significance value of $p \leq .002$ was therefore used to specify the conditions under which the current study hypotheses would be rejected. The current study therefore called for a total of 25 hypotheses as five overall categories were identified (discussed in chapter 2), and each of these categories included five individual variables. Refer to Table 3 for an overview of the variables and an outline of the various statistical tests performed to test the different hypotheses of the current study. The assumptions of these statistical tests are outlined later in this chapter (see section 3.6.6. Data analysis).

Table 2: Variables and statistical tests performed to test study hypotheses

	Main categories of variables					Statistical test
	Patient-related variables	**Illness-related variables**	**Medication - related variables**	**Health system-related variables**	**Moderating variables**	
Individual variables	a. Age	b. Age of onset of diagnosis c. Illness duration	c. Duration of current treatment			Pearson's correlation coefficient
	b. Gender e. Treatment beliefs	d. Prior hospitalisation (6 months) e. Perceived difficulty of condition	d. Current experience of adverse reactions e. Knowledge to cope with adverse reactions	a. Medical aid b. Social grant c. Prescribing practitioner d. Health care service type e. Require additional support	e. Perceived stigma	Independent sample t-test
	c. Race d. Home Language	a. Main DSM-IV-TR diagnosis	a. Class of antidepressant b. Daily dosage		a. Employment status b. Education level c. Relationship status d. Living arrangements	Analysis of variance (ANOVA)

The null hypotheses for the five main variable categories are the following:

A. Patient-related variables

H_1: Age is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_2: Gender is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_3: Race is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_4: Home language is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_5: Treatment beliefs is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa.

B. Illness-related variables.

H_6: Main DSM-IV-TR diagnosis is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_7: Age of onset of diagnosis is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_8: Illness duration is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_9: Prior hospitalisation (6 months) is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{10}: Perceived difficulty psychiatric condition is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

C. Treatment-related variables

H_{11}: Class of antidepressant is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{12}: Daily dosage is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{13}: Duration of current treatment is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{14}: Current experience of adverse reactions is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{15}: Knowledge to cope with adverse reactions is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

D. Health system-related variables

H_{16}: Medical aid is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{17}: Social grant is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{18}: Prescribing practitioner is not significantly correlated with antidepressant adherence in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{19}: Health care service type is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{20}: Requiring additional support is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

E. Moderating variables.

H_{21}: Employment status is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{22}: Education level is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{23}: Relationship status is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{24}: Living arrangements is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{25}: Perceived stigma is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

3.4. Research paradigm

In order to design a research study, it is important to answer the following questions (Cresswell, 1994; Cresswell, 2003; Groves, Fowler, Couper, Lepkowski, Singer &

Tourangeau, 2009; Goodwin, 2010; Bhattachejee, 2012): a) what epistemology (theory of knowledge embedded in the theoretical perspective) informs the research (e.g., objectivism)? b) what theoretical perspective (ontology) lies behind the methodology in questions (e.g., positivism)? c) what methodology (strategy or plan of action that links methods to outcomes) governs our choice and use of methods (e.g., survey research)? d) what methods(techniques and procedures) do we propose to use (e.g., questionnaire)?

Weaver and Olson (2006, p. 460), define a paradigm as, “patterns of beliefs and practices that regulate enquiry within a discipline by providing lenses, frames and processes through which an investigation is accomplished”. Philosophically, researchers make claims about what is knowledge (ontology), how we know it (epistemology), and the processes for studying it (methodology), (Cresswell, 1994; Bhattachejee, 2012). In the positivist tradition (ontology), social scientists support the idea that the social sciences should match the methodology of the natural sciences. This is based on the analogy that society is not dissimilar from the human body, namely to “heal” the diseases of society (Babbie & Mouton, 2011).

Neuman (2011) describe positivist researchers as scientists who prefer precise quantitative data, often using techniques to collect, analyse and summarise data in numerical value, and focuses on measuring the rate and frequency of variables in a detailed and structured manner in which results can be organised and presented statistically. Positivist social scientists also use experiments, survey and statistics in their search for rigorous measures and testing hypotheses (Neuman, 2011). According to Cresswell (2003), positivism adopts a deterministic philosophy where a) the problems studied reflect a need to examine causes that influence outcomes, b) it reduces phenomena and ideas into a small, discrete set of concepts to test, such as the variables that constitute hypotheses, c) knowledge developed is based on careful observation and measurement of the objective reality that exists "out there" in the world, d) developing numeric measures of observations and studying the behaviour of individuals are paramount, e) there are laws or theories that govern the world, and these need to be tested or verified. For the current research the researcher is concerned with observable and measurable phenomena involving people, events or things, the precise measurement and quantification through rigorous and controlled design and, determining the strength of the relationship between variables through statistical tests (Polit & Beck, 2010). In order to answer the research questions from the current study it is necessary for the researcher to gather information from a large number of people, generate quantifiable data and perform statistical tests on the variables. This positivist, objective, quantitative approach is best suited to answer the research questions of the current study, which is to determine

the rate of non-adherence to antidepressant medication and identify variables that influence these rates through descriptive and correlational statistical methods.

3.5. Research methodology

From this quantitative approach to observing phenomena, descriptive, correlational studies are often utilised (Carson, 2005), when the goal is to provide an account of the characteristics of individuals, groups or behaviours that may inform more complex study designs. The overall aim of descriptive studies is to 'discover new meaning, describe what exists, determine the frequency with which something occurs and categorize information' (Burns and Grove, 1999: p. 24). According to Carson (2005), this kind of study uses descriptive statistics and reported on the frequency and percentage of various characteristics (i.e., medication-taking behaviour). In correlational research, the researcher purposefully sets out to examine relationships between variables and assesses the statistical relationship (i.e., the correlation) between them with little or no effort to control extraneous variables (Stangor, 2010). There are essentially two reasons why researchers are interested in statistical relationships between variables (Stangor, 2010): 1) they do not believe that the statistical relationship is a causal one (i.e., for example the statistical correlation between low adherence rates and prescribing practitioner does not necessarily prove prescribing practitioners cause low adherence rates), and 2) the statistical relationship of interest is thought to be causal, but the researcher cannot manipulate the independent variable because it is either impossible or impractical (i.e., it is likely there are variables that may influence adherence rates beyond the scope of the current study). Additionally, this method is used when researchers set out to generate hypotheses that can be tested in experimental research (Parahoo, 1997; Burns and Grove, 1999). One of the implications arising from correlational research is that it is able to inform the application of experimental study designs that typically set out to test interventions (i.e., to increase treatment adherence), (Carson, 2005).

A descriptive, correlational approach was used to gather information about adherence behaviour of groups of people in the current study, since we are concerned with defining and counting the frequency of variables such as responses among participants, and determine relationships between variables (Shields & Rangarajan, 2013). This approach fits within the aims of the study, which is to determine and describe the rate of non-adherence to antidepressant medication, and to identify variables that may have a significant correlation with non-adherence rates in this sample of psychiatric outpatients.

3.6. Research design

According to Goodwin (2010), cross-sectional study designs take a between-subjects approach, comparing, for example the adherence rates of various groups of people who take a particular treatment. Cross-sectional studies measure variables at one point in time or across groups of individuals, usually of different ages (Howitt & Cramer, 2011). The scope of the current study is to determine the rate of non-adherence to antidepressant medication in psychiatric outpatients in a specific area, and to identify variables that may correlate with non-adherence rates. In the current study this research design has the advantage of enabling the researcher to measure a number of different variables at the same time. Howitt and Cramer (2011) explain that in these study designs any of these variables might explain why something occurs, and it is likely that anything that we are interested in explaining will have a number of different causes rather than a single cause. Therefore, by measuring a number of different variables at the same point in time, it becomes possible to see which of the variables are most strongly related to what it is we are seeking to explain (Howitt & Cramer, 2011).

3.7. Research method

Bhattachejee (2012, p. 73) defines survey research as a "research method involving the use of standardized questionnaires or interviews to collect data about people and their preferences, thoughts, and behaviours in a systematic manner." Social scientists often use survey research to analyse and evaluate behaviour consisting of predetermined questions that are given to a sample of a population (Shaughnessy, Zechmeister & Jeanne, 2011). The questions given to the sample group normally use a written questionnaire as the instrument or tool to collect the data (Bhattachejee, 2012). However, there are a variety of ways to obtain information through surveys. These include telephone surveys, interviews and electronic surveys such as email or internet-based (Goodwin, 2010). Cozby and Bates (2012, p. 73), describes surveys as a way that researchers can obtain a snapshot of how people behave at a given point in time, relying on self-reported information. Bhattachejee (2012), also states that survey designs can be descriptive, exploratory, or explanatory in nature.

The current study had a specific focus on the antidepressant medication adherence behaviours of psychiatric outpatients. It is the purpose of this investigation to describe the rate of non-adherent behaviours to antidepressant medication, as well as determining the factors that influence non-adherence amongst psychiatric out-patients, particularly in the

Gauteng Province of South Africa. Using a survey research design allows the researcher to investigate the medication adherence behaviours of this specific group of people by collecting and analysing the data gathered from only a few people, the research sample, that is thought to be representative of the whole population. The findings of the research survey involving a statistically representative sample can then be considered to be generalisable to the whole population represented by the sample that was investigated. It is for this reason that this design was selected to guide the study rationale. A mixed-mode survey, i.e., collecting data from different forms of media, such as written questionnaires, telephone interviews and internet survey, was employed by the current study. Mixed-mode surveys allow the benefit increasing response rate from respondents, as well as limiting the exclusion of potential participants (Tobin et al., 2012).

An invitation letter was sent via email to all patients on the SADAG registry at the time of the study. The letter provided a brief introduction of the study, explaining the nature, objectives, and the inclusion and exclusion criteria for taking part as well as the rights of participants. The invitation letter also provided patients with options to complete the survey questionnaire. This included an electronic link to the online survey questionnaire which patients could select, a toll-free telephone number and SMS number which patients could contact during office hours and, a fax number was also provided for additional contact methods. Potential participants could then choose which method suited them best.

Bhattachejee (2012) mentions a number of strengths associated with survey research designs. Besides being useful for obtaining a variety of unobservable information, such as individuals' attitudes, perceptions or behaviour, it is also ideally suited when collecting data about a large group. Furthermore, some respondents may prefer the unobtrusive and convenient nature of some of these more remote approaches of data collection. They can respond to the survey questions typically at a time that is suitable for them or in a private setting. Finally, survey research is economical in terms of researchers' time, effort and cost than most other methods. It is for this reason that a questionnaire was selected as the research tool for this study as it: requires less time and is easier to administer compared to many other study designs, and consequently less expensive; can be administered to a large group of people in a short period and, their confidentiality can be emphasised. However, each study method has its own strengths and limitations, and survey research is not excluded from this. Numerous biases such as, sampling bias, social desirability, and recall bias also exist (Bhattachejee, 2012). These will be discussed in more detail, under Section 3.6: Limitations, together with a discussion on how the researcher attempted to minimise the effects of these biases.

3.7.1. Population

Coolican (2009:34) offers a broad definition of a population as “all the existing members of that group”. Pavlichev (2004) defined the target population for a survey as the entire set of units for which the survey data are to be used and which the findings are meant to generalise. For this particular study the target population is defined as all individuals of 18 years and older who were at the time of the study, prescribed at least one antidepressant medication and who resided in Gauteng Province in South Africa. The geographic boundaries of the target population include five (5) districts municipalities, and include the City of Johannesburg, City of Tshwane, Ekurhuleni Metropol, West Rand District and, Sedibeng District Municipalities (Statistics South Africa, 2011), as illustrated in Figure 3.

Figure 3: District Municipalities of Gauteng Province, South Africa.

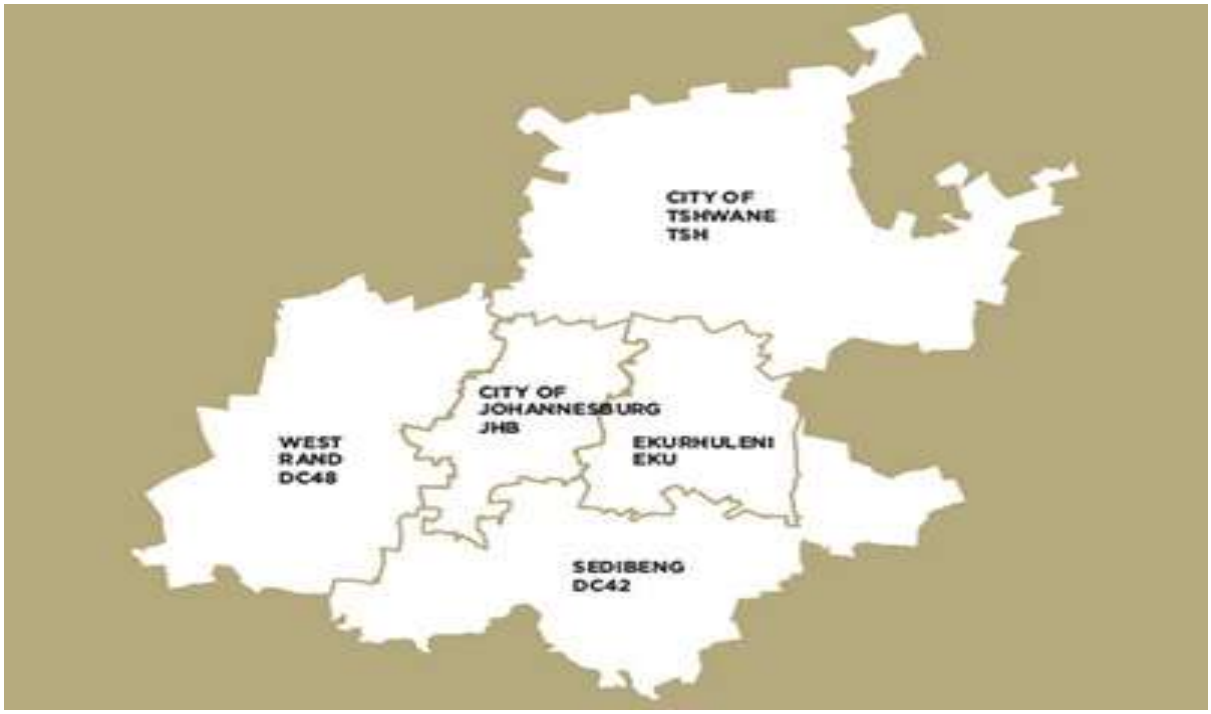


***Image obtained from: http://www.localgovernment.co.za/provinces/view/3/gauteng**

The total size of the population for Gauteng Province was 12, 272, 263 (City of Johannesburg: 4, 434, 827; City of Tshwane: 2, 921, 488; Ekurhuleni Metropol: 3, 178, 470; West Rand District: 820, 995; Sedibeng District: 916, 484), (Statistics South Africa, 2011)**.**

The total size of the target population was determined based on the utilisation or prescription patterns of antidepressant medication in this specific region of the country. The most recent, relevant literature available to the researcher at the time of the study was a drug utilisation review of antidepressant medication by Laher (2013). The review was conducted using information obtained from what was described as, “two (2) datasets from medical

warehousing companies" (Laher, 2013, p. ii). These datasets comprised of 1 year's medical records from health care practitioners on prescriptions and patient information. Dataset A was collected in 2009, and dataset B in 2011. Although from different socio-economic areas (and time), both dataset sources originate from the Johannesburg Metropolitan District (Laher, 2013). Data from this review was collected from a total of 7394 patients who were prescribed antidepressants (Dataset A n=6 555 + Dataset B n=839), which comprises approximately 0.17% of the entire population of the Johannesburg area at that time (Statistics South Africa, 2011).

Le Roux (2014) also described "off-label" prescription patterns of antidepressants among adults in South Africa. Although this study had a much larger sample (consisting of over 1, 220, 289 patients), no provincial demarcation or description could be observed. Burger, Van der Westhuizen, Lubbe, and Serfontein (2009) also conducted an analysis of prescribing patterns of antidepressants in South Africa, but focused on children and adolescents only, which is not within the scope of the study. It is to the best of the researcher's knowledge that the investigation by Laher (2013) provided the most relevant and applicable information to provide a scope of the prescription patterns of antidepressants that is of interest to the current study.

3.7.2. Sample and sampling procedure

With a population size estimated to be n=7394, confidence level specified at 95% and confidence interval (margin of error) of 5%, the sample size was calculated to be 366. This calculation was done using four popular, free on-line sample-size calculators (SurveyMonkey, 2015; Creative Research Systems, 2015; aosoft, 2015; (Maple Tech, 2015). A consensus of 366 was found between three of the four calculators used, which motivated the researcher's decision to estimate the size of the population. The excluded sample size calculator estimated a sample size of 367, and this difference is likely attributable to slight formulation or calculation differences.

A non-probability, purposive sampling method was utilised in this particular investigation based on the time, financial and other resource limitations experienced by a researcher at this level. It allowed the investigator to collect a large amount of information in a relatively short time at a lower cost. Random sampling of population is not possible due to the fact that participants have to self-identify and report taking antidepressant medication. Unlike other types of research in which random samples can be drawn (i.e., from a documented sampling frame), there is no 'master list' of individuals who are prescribed antidepressant

medication for Gauteng Province. Accordingly, the non-random sample in this study may not relate to the experiences of all the individuals who are receiving this particular pharmacological treatment. However, findings can be generalised to psychiatric outpatients who were living in Gauteng Province during this time.

3.7.2.1. Nonprobability sampling technique

Distinctive of non-probability sampling methods is that samples are chosen based on the investigator's judgement, rather than random (Hughes, 2006). Some researchers view non-probability sampling procedures as less "superior" when compared to probability sampling procedures, because they are not "truly" representative. This is because this sampling method does not give all individuals in the population an equal chance to be in the sample (Daniels, 2012). Despite this, there are still strong theoretical and practical reasons that motivate for their use. This sampling method is often used because the procedures used to select data from a sample are easier, quicker and cheaper when compared with probability sampling techniques (Howitt & Cramer, 2011). Researchers following a quantitative research design may feel that they are compelled to use non-probability sampling techniques due to some inability to use probability sampling (e.g., lack of access to a list of the population). However, in instances where it is not possible to use probability sampling techniques, non-probability sampling provides, at least, a feasible alternative. It ensures that the quantitative study design is not simply abandoned because meeting such criteria is time consuming and costly to the researcher. This has the potential to reduce the potential for researchers to study certain types of population, such as those that are vulnerable or difficult to reach (e.g., psychiatric patients), or in cases where a list of the entire population simply does not exist (Goodwin, 2010).

Additionally, a researcher is not always practically able to gain a true random sample, and this technique can also be expensive. It is not within the scope or aim of this study to generalise the findings to the population as a whole. Information obtained from this non-probabilistic study may still be valuable as it can contribute to the body of knowledge on this health issue. The credibility of findings can be improved by approximating random selection methods during sampling procedures, removing as many sources of bias as possible and comparing findings with investigations similar in design, nature and instruments. The researcher attempted to seek, identify and access the target group, inviting all (within the scope of the study) who the researcher had access to, and who were available and willing to participate. More information on how these techniques were employed by the current study can be found under the Limitations section of this chapter (3.6.5. Sampling method). Often,

given the objectives of a study, the nature of the research project, availability of time and financial resources, the population and sample size and characteristics, a non-probability sample design, for example, purposive sampling can be a favourable choice (Daniels, 2012).

3.7.2.2. Purposive sampling

Howitt and Cramer (2011, p. 432) describes purposive sampling as sampling "with a particular purpose in mind, such as when a particular sort of respondent is sought" rather than a representative sample. It is a type of haphazard sample obtained from predetermined types of individuals (Cozby & Bates, 2012). A purposive sample is a non-representative set of a larger population, and is fashioned to serve a very specific theoretical or practical need for a research study. For the current research project the researcher had a specific group in mind, (i.e., psychiatric outpatients currently prescribed at least one antidepressant medication). It was not possible to identify and target this entire study population due to a lack of information. This meant that the study population are not all known and gaining access to patients were therefore difficult as it presented challenges in identifying potential participants. Daniels (2012) described circumstances in which non-probability sampling would be more favourable than probability sampling techniques. Non-probability sampling techniques such as purposive sampling used in this particular study may be more appropriate when the a) objectives of the study are explanatory or descriptive in nature, b) time is a valuable resource, c) there is a need to target specific groups in the population, d) there is no need to make inferences from the sample, e) the purpose of the study is to provide an illustrative example, f) a homogenous population that is difficult to access and, g) an accurate sampling frame is not available.

The current study meets the above criteria as it provided an illustrative example that is descriptive in nature, the target population under investigation is difficult to access, an accurate sampling frame does not exist and, it is not within the scope of the study to generalise its findings to the broader population. These reasons motivated the researcher's choice of sampling method.

3.7.2.3. Inclusion and Exclusion Criteria

The sampling frame included participants who were, at the time of the study:

- living in Gauteng Province,

- 18 years and older,
- diagnosed with a psychiatric condition and,
- prescribed at least one antidepressant medication.

In terms of the Mental Health Care Act (MHCA) (South African Government, 2004), all psychiatric outpatients were considered voluntary health care service users, and therefore considered to have the capacity to make an informed decision about their own mental health care and also to give informed consent to participate in this investigation. However, patients who were admitted to hospital for their psychiatric condition and were being treated on an inpatient basis were not considered voluntary users and/or able to make informed decisions about their health. For this reason, patients who were treated as inpatients were excluded from the current study.

3.7.3. Research Instrument

3.7.3.1 Structured, non-clinical component

A structured non-clinical (i.e. non clinician administered) questionnaire was developed that comprised of four sections to elicit specific information; 1) socio-demographic information, 2) information about diagnosis, and 3) medication. This was supplemented with a scientifically validated self-report 4) medication adherence scale (Morisky, Green, & Levine, 1986).

The development of the questionnaire was informed by the conceptualisation framework of the study, and pilot tested locally at a psychiatric outpatient clinic at a public regional referral hospital in Johannesburg, Gauteng (Janse van Rensburg et al., 2014). Socio-demographical information included the following items: gender, age, race, marital status, living arrangements, employment status, educational level, main language, disability grant status and medical aid status.

The clinical profile included items on type and duration of psychiatric diagnosis (according to DSM-IV-TR Axis I, II & III criteria), recent hospitalisation, prescribing practitioner, and perceived difficulty of their psychiatric condition. Information regarding medication included type, frequency of intake, duration and number of antidepressant medication they are currently taking, perceived adverse reactions, perceptions and beliefs about treatment and stigma associated with antidepressant medication.

3.7.3.2. Adherence rating scale component

Adherence was measured using the eight-item Morisky Medication Adherence Questionnaire (MMAQ-8) in English which is an updated version of the original published version MMAQ-8 (Morisky et al., 1986), and one of the most commonly used self-report adherence scales (Lavsa, Holzworth & Ansani, 2011). Although the validity and reliability of the original scale were established in patients with hypertension, it has since also been validated in patients on tricyclic antidepressants (George, Peveler, Heilinger & Thompson (2000). Similar to the current study, Mahaye and colleagues (2012), investigated adherence to antipsychotic medication at an outpatient setting in KwaZulu-Natal Province, and also used the MMAQ-8. The need for contextual consensus also motivated the choice to use the MMAQ-8 in this particular investigation. The MMAQ-8 is a structured self-report measure of medication-taking behaviour that has been used widely in various countries, such as Germany, Brazil, Ethiopia, Nigeria, Malaysia and Iran, and medical and psychiatric illnesses such as hypertension, diabetes, tuberculosis and mood disorders, in both inpatient and outpatient settings (De La Cuevas & Penate, 2015; Al-Qazaz, Hassali, Shafie, Sulaiman, Sundram & Morisly, 2010; Korb-Savoldelli, Gillaizeau, Pouchot, Lenain, Postel-Vinay, Plouin, Sabatier et al., 2012; Lee et al.,, 2013; Fadare, 2014; Tesfay, Girma, Negash, Tesfaye, & Dehning, 2013; Jamous, 2014; Aikens et al., 2005; Lupattelli, Spigset, Björnsdóttir, Hämeen-Anttila, Mårdby, Panchaud & Nordeng, 2015).

According to Tan, Patel and Chang (2014, p. 1), the Morisky scale has advantages over other patient self-report adherence instruments due to its “widespread use in different diseases, populations and countries, high degree of concordance with pharmacy fill data or electronic monitoring devices, and does not contain many items, resulting in less response burden.” Additionally, the simplicity of questions and ease of scoring of instrument holds additional benefit, as it does not require a skilled professional to administer (Lavsa et al., 2011). Each item on the MMAS measures a specific medication-taking behaviour (Morisky et al., 2008). Each of the first seven (7) items is presented in a dichotomous (“yes or no”) format, and the eighth (8^{th}) question is answered on a five-point Likert-rating scale: (“never/rarely”, “once in a while”, “sometimes”, “usually”, and “all the time”). According to Lavsa, et al,. (2011, p. 4), “patients generally want to answer *yes* when asked questions, and the questions in this scale are worded in such a way that answering *yes* identifies non-adherent behaviours”. By “reversing the wording of the questions about the way patients might experience failure in following their medication regimen, since there is a tendency for patients to give their physicians or other health care providers positive answers.” (Morisky et al., 2008, p. 2).

To reduce response bias, the questions on the MMAQ-8 are phrased in such a way to reduce social desirability bias, where six (6) of the first seven (7) questions that must be answered negatively by responding “no”, and item five (5) answered positively by responding “yes”. Each ‘‘no’’ response in the scale for items 1 through 7 is scored as 1, and each ‘‘yes’’ response is scored as 0 (except for item 5 where each ‘‘yes’’ response is scored as 1 and each ‘‘no’’ response is scored as 0). For Item 8 on the five-point Likert-rating, the scores 0 to 4 was standardised by dividing the result by 4 to calculate a summated score with a maximum of 8 (Morisky et al., 2008).

It is worth noting that some consensus and discrepancies exist with regards to the categorisation or coding of the total scores or into different levels of adherence (i.e., high, medium/moderate and, low). Fadare's (2014) investigation in a Nigerian out-patient setting used the following codes/ categories to classify adherence levels; High: (0), Medium: (1-2), and Low (0>2). In the South African context, (Mahaye et al., 2012), trichotomised categories into: High (8), Moderate (5>7) and Low (0>4) in a psychiatric out-patient setting. However, in a validation study of a French version of the MMAQ-8 in hypertensive adults (Korb-Savoldelli et al., 2012), scores were categorised as Low (0 <6), Moderate/ Medium (6 to <8), and High (8). This categorisation was similar in an investigation by in patients with type-2 diabetes in Korea (Lee et al., 2013), a study in a Palestinian military setting (Jamous, 2014), a multinational, web-based study across 18 countries in Western, Northern, and Eastern Europe; North America; and Australia (Lupattelli et al., 2015), and, in a translation of the Malaysian version of the MMAQ-8 both used the same classification (Al-Qazaz et al., 2010). To support this, a recent validation study of the MMAQ-8 (Morisky et al., 2008) also categorised highly adherent patients with a total score of 8 on the scale, medium adherers had a score of 6 to <8, and low adherers a score of 0 <6. It is in support of the evidence above that the researcher was motivated to categorise adherence levels of the total MMAQ-8 scores of the current study into the following groups - Low (0 <6), Medium (6 to <8), and High (8) - as it is the most commonly utilised, implemented and scientifically supplemented categorisation.

3.7.3.2.1. Validity and reliability of the medication adherence scale

As previously mentioned, the scale was originally developed as a four-item self-report measure of adherence in patients with hypertension, and has been supplemented with additional items addressing the circumstances surrounding adherence behaviour (Morisky et al., 1986). More recently, (Morisky et al., 2008) the 8-item scale was found to be significantly correlated with the previously validated 4-item scale and had improved psychometric

properties, namely a Pearson correlation of 0.64; p <.05 and, Cronbach's alpha value of 0.83, (being above the acceptance threshold). The MMAQ-8 was found to have a moderate level of reliability and high levels of concurrent and predictive validity, particularly in low-income, minority patients, which was validated with a chemical marker for actual medication-taking behaviour (Morisky et al., 1990).

3.7.4. Data collection

A database containing information on psychiatric out-patients from the South African Depression & Anxiety Group (SADAG) was accessed to invite potential participants to the study. The South African Depression and Anxiety Group (SADAG) is a non-profit, Section 21 company established 20 years ago to provide mental health care advocacy to users across South Africa. SADAG is currently South Africa's largest and most recognised advocacy initiative and support network for individuals and families affected by mental illness (See Appendix VI for Certificate of Registration). SADAG, routinely provides its members with, for example, different free telephonic counselling initiatives, such as the: Suicide Crisis Line; Trauma Line; Bipolar Helpline; Sleeping Disorder Helpline; Substance Abuse Helpline; Mental Health Helpline; and the Support Group Helpline. It also boasts with a national mental health referral service, and provides free mental health information. SADAG's work is guided by a Scientific and Advisory Board of registered mental health professionals, including psychiatrists and psychologists, and functions closely with patients and other health care providers on an ongoing basis. Patients are often referred to SADAG after their discharge from hospital for additional information, telephone counselling and other support services such as support groups. These include patients diagnosed with various psychiatric conditions, and come from varying socio-economic backgrounds. Basic information is collected from patients when they contact SADAG for information or support (SADAG, 2014).

This information relates to patients; contact information, basic socio-demographical information such as gender, age, main language and Province of residence. It also includes some clinical information such as their primary DSM-IV-TR diagnosis, and the types of psychotropic medication they are prescribed. Although the DSM-5 (American Psychiatric Association, 2013) was already available a year prior to the current study, these revised diagnostic criteria was not yet widely used in South Africa, and the diagnoses recorded in this sample group was mostly done prior to the publishing of the DSM-5, and still relied upon the DSM-IV-TR (American Psychiatric Association, 2000) criteria. This provided the researcher enough justification to keep the research aligned to the DSM-IV-TR criteria.

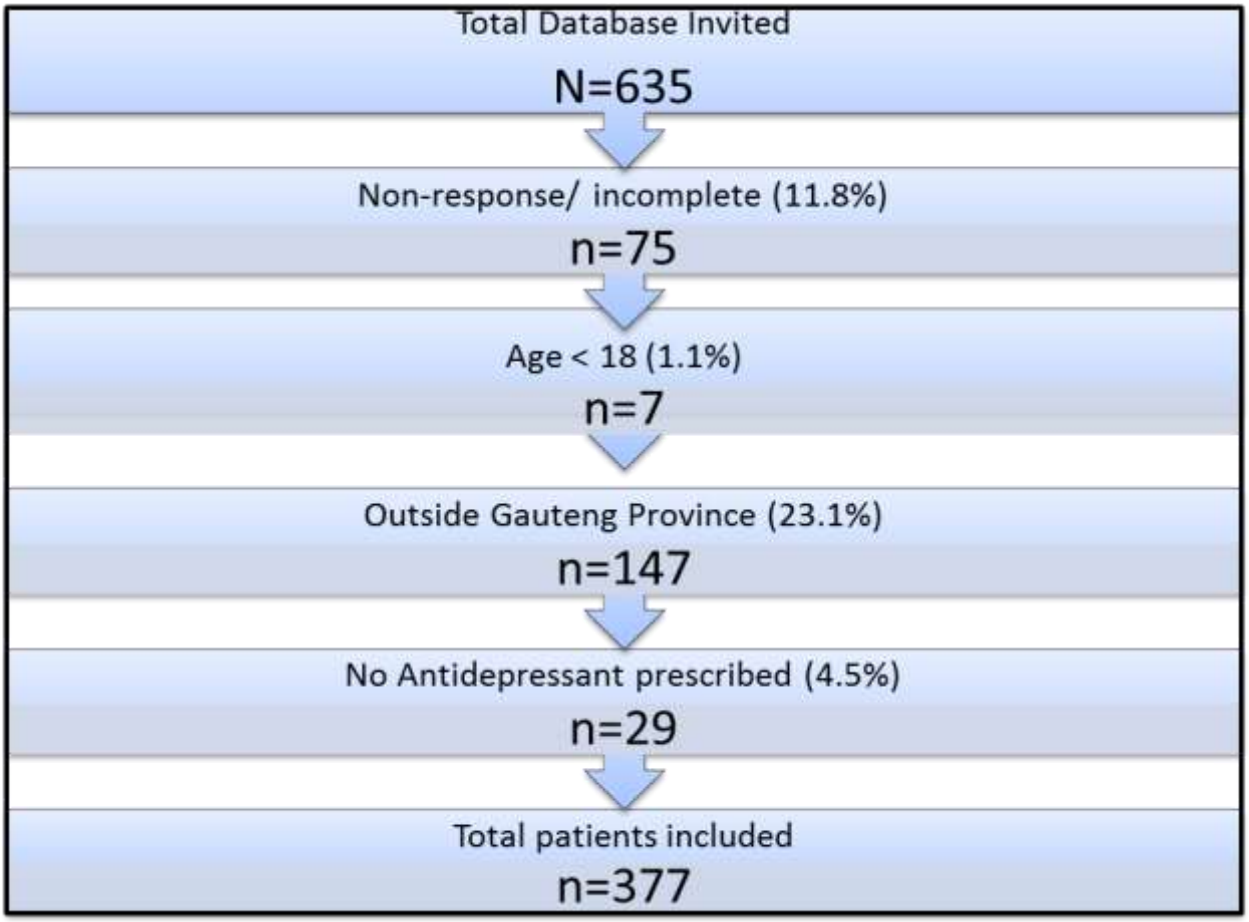
The founder/director of SADAG granted approval for access to the database (Appendix V). After ethical clearance to conduct the study was obtained from the Ethics Committee of the Department of Psychology at UNISA (Appendix IV), potential participants were invited to participate.

It is important that this information is routinely updated, and this occurs on an annual basis. In line with this organisational procedure, patients were contacted, introduced to the study and invited to participate. Signed informed consent was obtained from respondents via fax or email before data collection commenced. Once informed consent had been received (Appendix I), participants were assigned a coded participant number and were requested to complete the structured, non-clinical questionnaire (Appendix II). The survey was completed in one of three formats or modes that were deemed most convenient for the participant, (telephone interview, and self-completed paper-and-pen based or online / web-based).

Participants' responses were captured and coded according to the structured datasheet (Appendix III) in a designated database using the Statistical Package for the Social Sciences (SPSS) ® computer software version 22. Data collection commenced in October, 2014, after ethical approval was obtained, and invitations to participate in the survey were sent to a total of n=635 patients. Reminders were sent during the second, fourth and seventh weeks of data collection, and data collection stopped in December 2014.

During this process, follow-up telephone calls were made to respondents who had incomplete information or missing items, in an attempt to minimise the impact of incomplete survey data as much as possible. Despite the investigators' utmost efforts, not all missing information could be obtained, and such cases were therefore excluded from the analysis. Respondents who did not meet the inclusion criteria were then extracted from the database. The total number of patients that were included in the final analysis of the study was n=377. Figure 4 outlines the framework used to extract the relevant data from the completed database.

Figure 4: Data extraction framework



3.7.5. Data analysis

The data analysis assessed the mode in which participants completed the survey (manually, telephone or on-line), as well as demographic information such as age and age group, sex, main language spoken at home, relationship status, race, living arrangements, medical aid and social grant status, educational level. Clinical information included type of DSM-IV-TR Axis I, II and II diagnosis (grouped into mood-, anxiety-, substance use or abuse-, psychotic-, personality disorders, general medical conditions and conditions normally diagnosed during childhood and adolescence), duration lived with diagnoses (in months), hospitalisation within the six months prior to the data collection and perceived difficulty of their psychiatric condition**.** According to the literature cited in Chapter 2, the above mentioned variables may contribute to non-adherence to treatment in psychiatric conditions. The aim of the analysis was to determine if these variables were not only significantly correlated with adherence to antidepressant medications in this study sample, but also to determine if significant correlations existed between these variables.

Medication information assessed included the type of psychotropic medication currently taken. For analysis purposes, medications were divided into the common groups of psychotropic drugs, according to the Monthly Index of Medicine Specialities (MIMS), September 2014: antidepressants (tricyclic antidepressants, monoamine oxidise inhibitors (MAOI), selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine selective reuptake inhibitors (SNSRIs), norepinephrine and dopamine reuptake inhibitors (NDRIs), melatonergic agents and, lithium. The duration of current pharmacological treatment medication use (in months), was recorded, the prescribing practitioner and whether the patient was receiving private or public health care treatment, and the frequency of medication intake. Whether patients perceived any adverse reaction from their antidepressant treatment was also assessed, along with knowledge of how to cope with any potential adverse reactions. Beliefs about their medication and perceived stigma were also assessed.

The information obtained through the research instrument was collected, coded and stored on the Statistical Package for Social Sciences (SPSS) V20.0 software (IBM® SPSS® Statistics), for analysis. All categorical and numerical variables were analysed and described using standard descriptive and correlational methods. Descriptive results were expressed as frequencies (n=), and percentages (%) of the sample. Between-group tests were conducted using the Chi-square $\chi 2$ test to assess the relationships between categorical variables. Fisher's exact test was used for 2 x 2 tables or where the requirements for the $\chi 2$ test could not be met. The relationship between continuous and categorical variables was assessed by the t-test or ANOVA for more than two categories. The relationship between two continuous variables was assessed by Pearson's correlation coefficient. The accepted level of significance (alpha level and p-value) was $< .05$ for the appropriate statistical tests, and 2-tailed level of significance was reported on.

Normality was assessed to determine sample skewness and kurtosis and testing significance using the Shapiro-Wilk test (Bland, 2000). The total score on the MMAQ-8 scale was treated as the dependant variable across three independent variables (gender, age category and language). For gender (male and female), the results showed a statistically insignificant deviation from the normal distribution ($p = .26$). Similarly, statistical insignificant deviations across the five different age categories (18 – 29 years; 30 – 39 years; 40 – 49 years; 50 – 59 years; 60 years and older), as well as the three main race groups (Black; White and other South Africans) were also found ($p = .48$ and $p = .511$ respectively). Therefore, parametric correlational statistical tests were used where appropriate. To minimise the impact of outlying variables on the study results, those who indicated the spoke languages other than Afrikaans or English comprised only a small percentage of the study

sample (11.4%), and were grouped into the “other official SA languages” category (i.e., Northern Sotho: n=6; Sotho: n=10; Swazi: n=3; Tswana: n=8; Venda: n=1; Xhosa: n5; and Zulu: n=10). Similarly, patients who indicated they were Coloured (n=23), Indian (n=7) or Mixed race (n=2) were also grouped into the “other SA populations”. Data from a total of n=377 participants were included for the final analysis of the data.

3.8. Limitations of the study

Controversy still remains regarding the measurement of adherence in patients, as there is currently no “gold standard” to assess these rates (Vitolins, Rand, Rapp, Ribisl, & Sevick, 2000; Dolder, Lacro, Dunn, & Jeste, 2002; Culig & Leppée, 2014). Therefore, each adherence measurement approach has its own strengths and weaknesses, and each rests on the judgement of the investigator and the nature of the study. Although self-report measures are easy-to-use, inexpensive, useful and convenient tools for measuring adherence, especially in certain study designs such as the current observational study, they are also subject to measurement bias such as social desirability, recall bias and response bias (Shi et al., 2010), which are discussed below.

3.8.1. Self-reporting of adherence

There have been mixed findings about the accuracy of self-reported or subjective measurement of adherence to medication. There is also strong evidence to support its validity (McDonald, Garg & Haynes, 2002; Farmer, 1999). Recent investigations have found that self-reporting questionnaires actually show a moderate-to-high concordance when compared with electronic-based monitoring systems (Garber, Nau, Erickson, Aikens, & Lawrence, 2004; Shi et al., 2010). Self-reporting on medication was also reported to be an acceptably valid measure of adherence in psychiatric patients when compared to their objective measurement (blood serum levels) (Jónsdóttir, Opjordsmoen, Birkenaes, Engh, Ringen, Vaskinn, Andreassen, 2010). Although these particular studies did not look at the MMAQ-8 specifically as self-report instrument, and it is true that the type of self-report used may matter when comparing with non-self-reporting measures (Garber et al., 2004), Krousel-Wood, Islam, Webber, Re, Morisky and Muntner (2009) did find a statistically significant correlation ($r = 0.46$; $p < .001$) between the MMAQ-8 scale and pharmacy script rates. Additionally, Osterberg & Blaschke (2005) concluded that self-reports can easily and effectively measure adherence. Furthermore, it has been reported that self-reporting on

medication is a reasonably valid measure of adherence in psychiatric outpatients when compared with an objective measurement of blood serum levels (Garber et al., 2004; Jónsdóttir et al., 2010), as well as with other objective measures of adherence in several different illness populations (Krousel-Wood et al., 2009; Nguyen, La Caze, & Cottrell, 2014).

3.8.2. Social desirability

Crutzen and Göritz (2010) described social desirability as intentional deception by individuals when there is some perceived negative consequence of admitting to non-adherence. Patients may provide inaccurate or biased (typically in a positive way or upwardly) information regarding their medication-taking behaviour (Morisky & Dimatteo, 2011). Patients may therefore have the tendency to distort their responses according to the perceived expectations of health care providers (Furr, 2010).

If a patient says that he or she is not taking their medication, it would, almost certainly, be safe to believe them. However, patients who claim to be adherent to their treatment may be underreporting their non-adherent behaviours to avoid any potentially negative associations such as health care provider disapproval. However, it was clearly and explicitly stated (during the informed consent procedure, beginning of the survey questionnaire as well as prior to completing the adherence scale component) that patients need not fear any negative outcomes or repercussions based on the information the information they provide. This method was employed in an attempt to reduce the bias of social desirability in the current study.

This tendency of individuals to distort responses (typically in a positive way or upwardly biased) that are, according to them, consistent with what is expected of them is what Crutzen and Göritz (2010) described as social desirability. To minimise the potential impact of potential social desirability bias in the current study, a brief message was presented to patients before completing the adherence scale component of the research instrument. Assurance was provided that their responses would not count against them in any way, that no personal information is linked to their responses, which was protected by assigning a unique identifier to all participants, and that they would continue to receive their treatment regardless of their responses on the survey questionnaire. They were reminded that it was to the benefit of the study that they be honest in their responses. It is worth noting that the research was not able to infer the levels of social desirability of participants in the study due to the largely remote nature of investigation.

3.8.3. Recall bias

Alternatively, patients may also have the tendency to recall/ remember incorrectly when or whether they took their medications (recall bias), therefore making inaccurate attributions about the origins of memories, knowledge and their beliefs about their medication-taking behaviour (Delgado-Rodríguez & Llorca, 2004). Individuals may find it even more difficult to remember or accurately retrieve events that happened in the past if a long period has passed between the time of the event and the time of recall (Lupattelli et al., 2015). Research investigations of past events may therefore be susceptible to the restrictions of a patient's memory, as well as the potential influence of their illness (or treatment) on his or her memory (Hassan, 2005). . This means that the data being collected can be flawed, and thereby unreliable (Hasssan, 2005; Pannucci & Wilkins, 2010). To minimise the potential impact recall bias may have on data from the current study, some methodological approaches were considered such as the use of standardised and pilot-tested questionnaires and reduced length of recall period where possible.

Standardised questionnaires are tested across different setting on different populations, and the development of such tests aim specifically to reduce any bias that may influence the collection of data. The current study utilised a scientifically validated adherence measuring instrument tested across different populations, settings, illnesses and treatments (Toll et al., 2007; Tan, Patel & Chang, 2014; Suárez et al., 2011; Mahaye et al., 2012; Lavsa, et al., 2011). This instrument also does not enquire about very specific information that may have occurred a long time ago. In cases where patients were asked to recall a specific event (such as when they missed a dose of their prescribed antidepressant), they were not expected to recall specific information that occurred more than two weeks prior to the study. Additionally, Coughlin (1990) stated that aspects such as interviewing technique and the motivation of respondents are methods that play a central role in reducing recall bias. These aspects are also under the control of the investigator, and were carefully considered during the data collection phase. The current study attempted to address these issues by also relying upon and adhering to a semi-structured, non-clinician administered questionnaire that was previously pilot-tested in public psychiatric outpatient setting in Johannesburg, Gauteng (Janse van rensburg et al., 2014), which should be similar to the current study target population. As previously mentioned, assurance was provided to participants that their responses would not count against them in any way, that no personal information is linked to their responses, and that they would continue to receive their treatment regardless of their responses on the survey questionnaire. This served as a motivation for patients to provide honest answers as there would be no negative consequences to them.

3.8.4. Interviewer bias

Interviewer bias is described by Privitera (2013), as the tendency for the approach, words, or expressions of a researcher to influence the responses of a participant when they are in contact. These aspects also highlight the importance of investigator skills and characteristics. Recognition and awareness of this bias by the researcher, attention to the characteristics of the respondents and, adequate training will maximize the accuracy of the survey findings. Researcher selection, training, skills and approach to questioning are therefore key determinants of the quality of the data that is being collected and play an important role in reducing this potential bias. The researcher undertook training in administering this specific questionnaire in similar psychiatric outpatient settings. Additionally, the researcher was also involved in the pilot-testing of the questionnaire.

3.8.5. Sampling method

This relates to information gathered in a process that does not give all the individuals in the population equal chances of being selected (non-random sampling method), (Bhattachejee, 2012). The sampling method in this particular study is not random, and the results may not be generalisable to the general public. However, the findings from the current study may be generalisable to the specific sub-population of psychiatric outpatients receiving antidepressants and, who live in the Gauteng Province of South Africa. Participants were selected on the basis of the purposive judgment of the researcher the ability to access a large number of potential participants who are difficult to identify or target. However, Daniel (2012) stated that in certain investigations, not dissimilar from the current study, non-probability sampling may actually be a methodological strength; when the nature of the study has a descriptive or exploratory purpose, when time is a limited resource, when a very specific target population needs to be reached, when the aim is not to make statistical inferences and generalise, when an accurate sampling frame is not available and, when ease of procedural and practical implementation is of importance. The reader can refer back to section 3.5.2.2. as to how these issues relate to the current investigation.

3.9. Ethical considerations

The current study was conducted according to the ethical guidelines and principles of the international Declaration of Helsinki (World Medical Association, 2013).Participants were protected by informing them of the nature and purpose of the research, their rights and that

their participation was on a voluntary basis. In the current study, the researcher acknowledged the rights of the respondents to choose to participate in the study by explaining the purpose and informing them of their rights regarding their participation and withdrawal during the process. Potential participants were given the opportunity to decide voluntarily whether to take part in the study or not. Other than the possibility that participants may potentially feel inconvenienced by the survey, no additional expected risks were anticipated with taking part in this research. This possible inconvenience was likely to be minimal as the survey was kept brief and took approximately ten to fifteen minutes to complete. Furthermore the questionnaire could be completed at any convenient time, place and in one of three modes that was convenient to potential respondents. Additionally, participants could possibly experience slight psychological discomfort by divulging personal information for research purposes. Emphasis was placed on the anonymous and confidential nature of the information during the introduction of the study and informed consent form. The SADAG 24-hour emergency helpline number was also provided to all participants if they felt they needed support. Confidentiality of participant information was maintained by using a unique coded identifier for participants during the entire research process. No names were linked to the information at any point, and all results were reported anonymously.

3.9.1. Confidentiality

Confidentiality was maintained by using a unique coded identifier for participants during the entire research process. No names were linked to the information at any point, and all results were reported anonymously. This confidentiality agreement (Appendix II) was clearly stated in the informed consent form provided to the participants. Only the researcher was able to identify participants and, all files and data were kept in a password-protected computer and locked filing cabinet at SADAG premises to ensure safety of information.

3.9.2. Informed consent

Respondents should never be deceived or lied to when they participate in a study. Before completing the questionnaire, participants were asked to read and sign a patient information and informed consent form. This form included clearly articulated information about the aim of the study and how the results were to be used, the voluntary nature of participation, freedom to withdraw at any time and assurance of confidentiality. It was clearly stated that by completing the form, informed consent was being granted by participants to take part in

the study. The nature and purpose of the study were explained to potential participants in their own language and at their level of understanding, and they were given the opportunity to have any questions they might have had answered satisfactory. However, the research instrument was only made available in the English language.

The following was clearly and explicitly explained verbally so that participants were fully aware of the following key aspects relating to this study:

i. The goal and reason for conducting the research
ii. How long research may take and what is required from them
iii. How it was to be done, e.g. questionnaire/interviews
iv. Any possible risks and/or benefits of taking part
v. The right to withdraw at any time without any negative repercussions
vi. Measures taken to ensure personal information is kept safe

3.9.3. Non-maleficence, beneficence and justice

All participants were treated with respect during the research process. Further consideration by the researcher was kept in mind to limit any potential emotional harm to participants. Careful attention was paid to the emotional state of participants during any contact sessions. If any questions in the interview made participants feel uncomfortable or the topic became too sensitive, they were given the choice to stop, withdraw, continue at another time, or make use of the counselling or support group services. A SADAG toll-free helpline number was also provided in the unlikely event of a participant experiences an emergency situation during the completion of the questionnaire and follow-up and referral services were facilitated. This supported the patients' right to access health care if needed and could assist patients with emergency referral services to their closest, relevant health care provider.

3.9.4. Voluntary participation

The right to self-determination is based on the principle of respect for persons taking part in research studies. It means participants had the right to decide themselves whether to

participate in any study or not, without being penalised in any way (Brink, 1996). As psychiatric outpatients, participants of 18 years and older are (according to the Mental Health Care Act (South African Government, 2004)), considered voluntary users of health care services. In the initial dialogue between the researcher and the prospective participant, the researcher asked the participant if they wanted to take part in the study without forcing or coercing them in any way. In essence, the researcher adhered to the principle of voluntary participation, which states that patients should participate only by free and informed choice. In addition, participants were notified that they were free to leave the study at any time, whether or not the questionnaire was completed.

3.9. Chapter summary

The researcher provided information on the research design and methods of this study. A quantitative, descriptive survey research method was chosen to determine the rate of non-adherence to antidepressant medication, as well as the factors influencing non-adherence amongst psychiatric out-patients in Gauteng, South Africa. The area of study, population, sample of the population and sampling technique were also described. The current study took place in the Gauteng Province of South Africa, and the target population was identified as psychiatric outpatients who were, at the time of the study, prescribed (in part) least one antidepressant medication. Purposive sampling technique was utilised to identify and reach the target sample. Subsequently, the research instrument used in the current study was elaborated on (structured, non-clinical questionnaire), which included a validated, self-reported measure of medication-taking behaviour (MMAQ-8). Data collection and data analysis procedures were also discussed, and concluded with the study limitations and ethical considerations.

CHAPTER 4

RESULTS

4.1. Introduction

This chapter reports and discusses the findings of the investigation phase of this research study. The purpose of this study was to determine levels of antidepressant medication adherence amongst psychiatric outpatients in Gauteng, and identify possible factors that may contribute to this non-adherence. Non-adherence to medication is a significant public health concern that prevents patients from realising the full benefits of their treatment, and negatively impacts on individuals, their families and the health care system (World Health Organization, 2003). The researcher is therefore of the opinion that it is important to determine the rates of non-adherence to antidepressants and identify possible factors that may contribute to this; as a lack of this information presents a key challenge to quality care for patients with psychiatric disorders currently prescribed this medication. In line with the objectives of the study discussed in the previous chapter, the following section will report on the results of the current study by: a) describing the socio-demographical, clinical profile and medication information of psychiatric outpatients who completed the survey; b) reporting on the levels of non-adherence to antidepressant medications of this sample of psychiatric outpatients; and c) identify variables relating to patient characteristics, psychiatric condition, antidepressant treatment, health system and moderating variables that have a significant influence antidepressant adherence rates.

4.2. Data analysis

The data were analysed using the SPSS® version 22. Data was coded from the structured, non-clinical questionnaire completed by psychiatric outpatients who were prescribed at least one antidepressant medication. Patient demographics, clinical and medication information and possible contributors to non-adherence rates of patients for all categorical and numerical variables were analysed and described using descriptive and, where indicated, correlational statistical methods. Between-group tests were conducted using the Chi-square $\chi 2$ test to assess the relationships between categorical variables. Fisher's exact test was used for 2 x 2 tables or where the requirements for the $\chi 2$ test could not be met. The relationship between continuous and categorical variables was assessed by the t-test or ANOVA for more than two categories. The relationship between two continuous variables was assessed by Pearson's correlation coefficient. Due to the many study hypotheses, the Bonferroni-Holm

correction for multiple comparisons calculator was applied, which has a large probability of rejecting false hypotheses and strongly controls the family-wise error rate at level alpha (Holm, 1979). A significance value of $p \leq .002$ was therefore used to specify the conditions under which the current study hypotheses would be rejected.

4.3. Results

4.3.1. Sample

The majority of the patients were female (79.58%; n=300), between 18 and 39 years of age (57.3%; n=116), English speaking (57.56%; n=217), married (n=143; 37.93%) and living with their family (n=165; 43.77%), completed a diploma or degree (40.85%; n=154) and were employed full-time (56.5%; n=213), as well as having access to medical aid support (67.37%; n=254). The majority of patients completed the survey questionnaire through the online method (81.43%; n= 307).

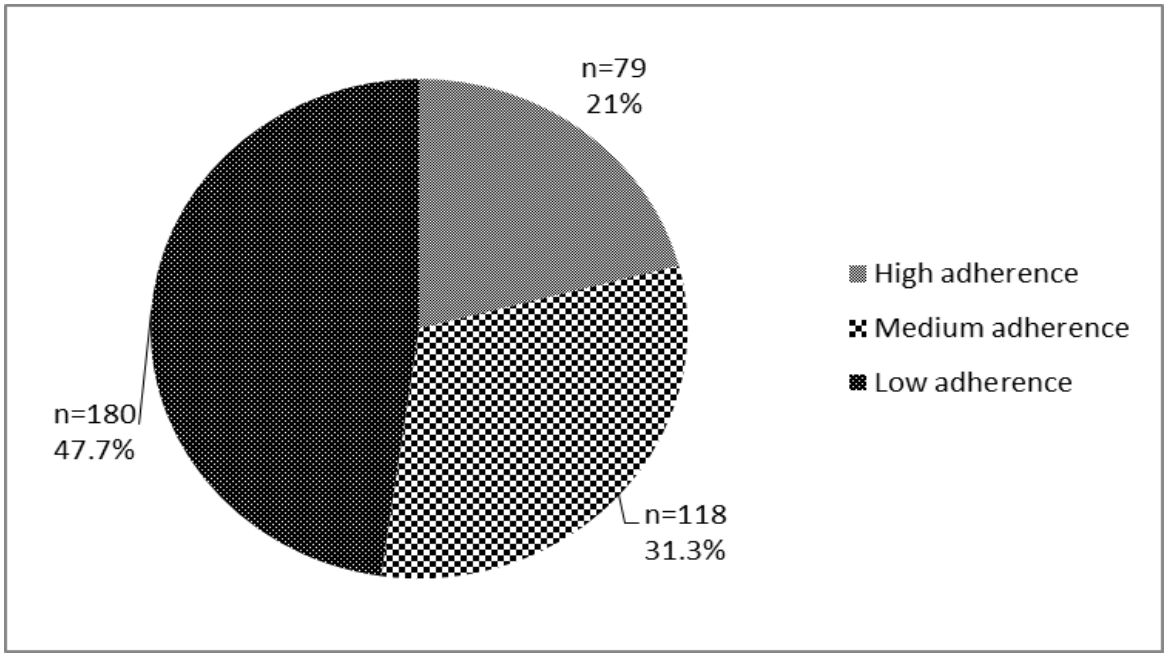
Table 3: Summary of socio-demographical information of the total sample of psychiatric outpatients in Gauteng (n=377).

		Frequency (n)	Percent (%)	Cumulative Percent
Method Completed	Manual	19	5	5
	On-line	307	81.4	86.5
	Telephone	51	13.5	100
Sex	Male	77	20.4	20.4
	Female	300	79.6	100
Age Group	18-29	102	27.1	27.1
	30-39	114	30.2	57.3
	40-49	81	21.5	78.8
	50-59	52	13.8	92.6
	60+	28	7.4	100
Main language	English	217	57.6	57.6
	Afrikaans	117	31	88.6
	Other official SA languages	43	11.4	100
Population	Black South Africans	45	11.9	11.9
	Other South Africans	32	8.5	20.4
	White South Africans	300	79.6	100
Relatioship status	Married	143	37.9	37.9
	Single	111	29.4	67.4
	Widowed	8	2.1	69.5
	Divorced	49	13	82.5
	Relationship	54	14.3	96.8
	Engaged	12	3.2	100
Living arrangements	On my own	81	21.5	21.5
	Partner	113	30	51.5
	Family	165	43.8	95.2
	Other	18	4.8	100
Employment status	Employed, working full-time	213	56.5	56.5
	Employed, working part-time	36	9.5	66
	Unemployed, looking for work	47	12.5	78.5
	Unemployed, not looking for work	21	5.6	84.1
	Student	37	9.8	93.9
	Unable to work	23	6.1	100
Education level	Did not complete high school	26	6.9	6.9
	High school (Gr. 12)	130	34.5	41.4
	Diploma / Degree	154	40.8	82.2
	Post-graduate degree	67	17.8	100
Medical aid support	Yes	254	67.4	67.4
	No	123	32.6	100
Social grant support	Yes	23	6.1	6.1
	No	354	93.9	100

4.3.2. Medication adherence questionnaire

The total scores on the MMAQ-8 ranged between a minimum of 0.25 and 8. The average score for the total sample of n=377 psychiatric outpatients in the current study was 5.59 (*SD* =2.08), suggesting low levels of antidepressant adherence rates in general across the entire sample. More specifically, nearly half of all patients (n=180; 47.7%) reported with low antidepressant medication adherence rates, while a third of psychiatric outpatients reported with medium levels of adherence, and only a fifth of all patients reported with high rates of antidepressant medication adherence. This is illustrated in Figure 5.

Figure 5: Distribution of antidepressant adherence rates of the total sample of psychiatric outpatients in Gauteng (n=377)



The literature previously cited suggested that non-adherence to treatment can be expected in approximately 30% – 50% of all patients, irrespective of disease, prognosis or setting (Morris & Schulz, 1992; Sacket & Snow, 1979; Donovan, 1995; Buckley, Foster and Patel (2009) noted that these rates increase further when specific psychiatric conditions such as depression (51 % - 69%), Schizophrenia (30-60%), Bipolar Mood Disorder (21-50%) or other anxiety disorders (57%) are considered. In antidepressant medication specifically, Bulloch and Patten (2010) reported non-adherence rates of 45.9%. Locally, Mahaye, et al. (2012) reported low adherence in 37% in a sample of psychiatric outpatients in the KwaZulu-Natal Province using the same adherence measuring instrument as the current study (MMAQ-8). However, they (Mahaye et al., 2012) focused on antipsychotic medication in a smaller sample (n=92) of schizophrenic patients specifically. Furthermore, Janse van

Rensburg (2007) noted that nearly half (47%) of patients admitted to a general public hospital in Gauteng for any psychiatric disorder were non-adherent to their respective medications at that time (Janse van Rensburg, 2007). The results from the current study suggests that non-adherence to antidepressant medication in this sample of psychiatric outpatients reflect that of findings reported in both international and local contexts. This lends strength to the current study argument that non-adherence to antidepressant medication presents a significant concern in local psychiatric outpatient settings.

In response to Question 8, patients were asked to rate on a five-point Likert scale how often they have difficulty remembering to take their antidepressant medication. Although nearly half of patients indicated that they never or rarely forget to take their antidepressant medication (n=187; 49.6%), the other half of the sample did however report increased difficulty in remembering to take their medication at the prescribed treatment regime. This is still a significant proportion of patients that could benefit from targeted adherence interventions. Question 1 and 8 in this scale support each other in the measurement of medication taking behaviour by firstly determining the scope of antidepressant non-adherence, and secondly determining the degree to which these behaviours occur among psychiatric outpatients. In addition, more than one in ten patients reported that they did not take their antidepressant medication the day prior to completing the survey questionnaire (n=52; 13.8%). Furthermore, more than a third of psychiatric outpatients (n=140; 37.13%) indicated that they missed a daily dose of their medication in the two weeks preceding the study.

The current study did not dichotomously group patients into *adherent* and *non-adherent* categories, but instead complied with the MMAQ-8 scoring guidelines that grouped patients into three adherence categories namely, low-, medium- and high adherence. However, responses from specific questions on the MMAQ-8 may be used to categorise patients as non-adherent. For example, it may be stated that 13.8% of psychiatric outpatients were non-adherent to their antidepressant medication the day prior to completing the survey questionnaire. Additionally, it can be stated that more than a third of psychiatric outpatients (n=140; 37.13%) were non-adherent two weeks preceding the study. Finally, nearly half of the patients indicated that they are sometimes non-adherent to their antidepressant medication (n=183; 48.54%). Table 4 provides the distribution of the total sample of psychiatric outpatients' responses to the 8-item self-report medication adherence questionnaire (MMAQ-8) in frequencies and percentages of the total study sample. During data collection, specific reference to antidepressant medication was made.

Table 4: Distribution of responses to the MMAQ-8* by psychiatric outpatients in Gauteng (n=377)

Self-report Medication Adherence Questionnaire Questions	Response	Frequency (n=)	Percentage (%)
1. Do you sometimes forget to take your medication?	Yes	183	48.5
	No	194	51.5
2. Were there any days during the past 2 weeks when you did not take your medication? (ed.)	Yes	140	37.1
	No	237	62.9
3. Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	Yes	123	32.6
	No	254	67.4
4. When you travel or leave home, do you sometimes forget to bring along your medication	Yes	87	23.1
	No	290	76.9
5. Did you take your medication(s) yesterday?	Yes	52	13.8
	No	325	86.2
6. When you feel like your symptoms are under control, do you sometimes stop taking your medication?	Yes	114	30.2
	No	263	69.8
7. Taking medication every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	Yes	138	36.6
	No	239	63.4
8. How often do you have difficulty remembering to take all your medicine?	Never/ rarely	187	49.6
	Once in a while	112	29.7
	Sometimes	55	14.6
	Usually	21	5.6
	All the time	2	.5

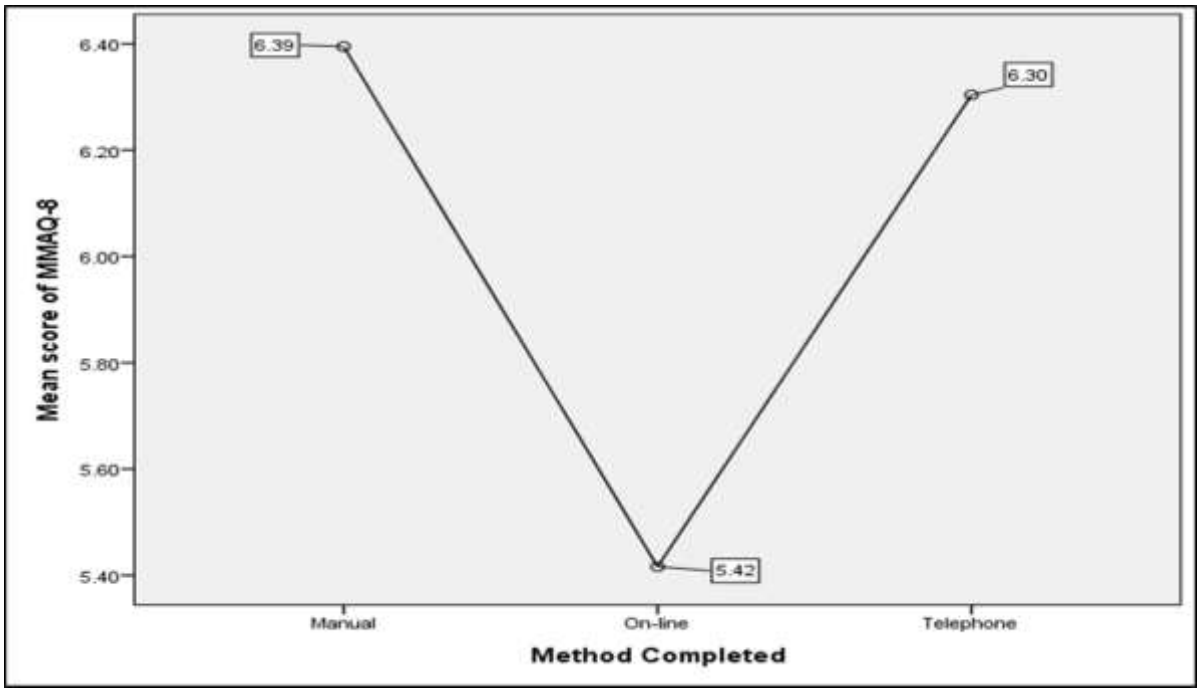
* Morisky, Green & Levine, 1986.

In response to Question 1 patients were asked if they “sometimes forget to take” their antidepressant medication. Nearly half of the patients indicated that they do sometimes forget to take their medication (n=183; 48.54%). This is the most frequently reported reason for non-adherent behaviour in this particular sample of psychiatric outpatients. Other frequently reported reasons for non-adherence to antidepressant medication as measured by the MMAQ-8 includes: “feel(ing) hassled about sticking to their antidepressant treatment plan”, (n=138; 36.6%), “cut(ting) back or stopped taking antidepressant medication without telling their doctor because they felt worse when they took it”, (n=123; 32.62%), or “stop(ped) taking antidepressant medication when feeling like symptoms were under control” (n=114; 30.2%).

Based on the high rates of poor adherence behaviours observed in the current study, it appears that non-adherence to antidepressant medication in psychiatric outpatients represents a significant health concern. The following chapter discusses these findings and provides recommendations that may be relevant to the target population.

The majority of the participants preferred to complete the survey questionnaire on-line (81.43%; n= 307), while 13.53% (n=51) completed the questionnaire telephonically, and 5.04% (n=19) completed it manually (pen-and-paper). The large proportion of on-line responses could be attributed to several factors; Firstly, the primary recruitment method was through online advertising on a website, which provided an electronic link to the survey questionnaire and may have facilitated convenience; secondly, compared to other modes of completion, the online mode provided more anonymity to participants, which may have been more suitable to them; thirdly, the majority of the sample (57.3%) were in the younger age categories (19 – 39 years), and may feel less intimidated and more accustomed to technology; and fourthly, the majority of participants indicated that they are employed and working full-time, and therefore may have less time available to use other methods. The benefits of using online questionnaires to conduct surveys may have had a strong influence on the large proportion of completed responses in the total sample. Results from the one-way ANOVA indicated mean MMAQ-8 scores of 6.39, 5.42 and 6.3 for manual, online and telephone completion groups respectively, and resulted in a statistically significant effect (F (2, 374) = 5.64, p = .004). A Tukey post-hoc test revealed that the mean MMAQ-8 score was statistically significantly lower among those who completed the survey on-line compared to those who completed the questionnaire telephonically (M = 5.1, SD = 2.1, p = .012). However, there were no statistically significant differences between on-line and manual groups (p = .11) or between manual and telephone groups (p = .985).

Figure 6: Mean MMAQ-8 scores of sample of psychiatric outpatients in Gauteng by mode of completion (n=377)



The results shown in Figure 1 above clearly indicate that the on-line method of completing the survey had a significant effect on total MMAQ-8 scores, with a much lower mean score for this group. This does not necessarily mean that individuals who preferred the online mode of administration are less adherent to their antidepressant medication, but the assumption can be made that poor or low adherence in this sample is more likely to be reported through more indirect methods. Patients may be more likely to report on non-adherence when they are not directly faced with their health care provider for fear of possible repercussions. It is also worth noting that the reason for the insignificant correlation found between the differences in mean MMAQ-8 scores of patients who completed the survey manually (6.39) and online (5.42), which is greater by 0.6 than the difference in mean MMAQ-8 scores of patients who completed the survey telephonically (6.3), may be due to the small number of patients who completed the survey telephonically (n=51). These findings are discussed in greater detail in the following chapter.

4.3.3. Patient-related variables

4.3.3.1. Gender

The gender distribution of participants in this study was 79.58% (n=300) female and 20.42% (n=77) male, with a ratio 3.9 females to 1 male. Seedat, Williams, Herman, Moomal, Williams and Jackson (2009) investigated the mental health service use by South Africans based on the first nationally representative epidemiological survey that assessed the prevalence of common mental health disorders in the country (Herman et al., 2009). Although the study did not find significant gender differences for accessing mental health services in the 12 months preceding the study, women did have higher rates of treatment seeking for any psychiatric condition, and especially for mood disorders. Additionally, stratification by gender provided the following predictors of service use (Seedat et al., 2009) study: (i) women with any psychiatric condition were more likely to receive any kind of treatment compared to men and; (ii) men diagnosed with a mood disorder specifically were less likely be receiving treatment. The reasons for these findings could not be inferred from the study. Furthermore, a review on antidepressant use in South African by privately insured mental health care users (Roux, 2014) found that 14.8% of all patients (n = 1 220 289) and 9.3% of men compared to 19.4% of women were prescribed at least one antidepressant. Findings by Laher (2013) also concluded that females formed the majority of users (66%) of antidepressants in a drug utilisation review from the Gauteng Province.

These gender differences in mental health service use between men and women may influence the skewed representation of women in this current survey. If more females access mental health services in South Africa and fewer males receive this specific treatment under investigation, then it is unsurprising to see a biased representation of females in the current study.

Results from the Pearson's chi-square test did reveal that the proportion of males (6.5%; n=5) in this study diagnosed with Schizophrenia or any other psychotic disorder was statistically significantly more when compared to the proportion of females (1%; n=3) with the same diagnosis ($\chi 2$ (1) = 8.903, p = .003). Additionally, compared to females (45.1%; n=170), males (12.5%; n=47) were significantly less likely to present with only one DSM-IV-TR diagnosis ($\chi 2$ = 11.055, p = .05). Male patients in this study sample (88.3%; n=68) were also found to be significantly less likely to indicate that their condition required treatment with medication ($\chi 2$ = 5.274, p = .022) when compared to females (95.3%; n=286). With regards to the antidepressant medication category specifically, females (8.3%; n=25) were found to be significantly more likely to be prescribed a tricyclic type ($\chi 2$ = 6.872, p = .009) when compared to males (0%; n=0). These results will be discussed in greater detail in the following chapter.

However, results from the Pearson's chi-square test found no significant correlations between males and females and any other socio-demographical variables such as age group (p = .323), main language spoken (p = .536), relationship status (p = .212), race (p = .266), living arrangements (p = .063), employment status (p = .966), level of education (p= .621), or if they were the beneficiaries of medical aid or social grant support (p = .433 and p = .872, respectively). Additionally, gender was not correlated with any clinical-related variables such as DSM-IV-TR main diagnosis (p = .347), any mood disorder (p = .338), any anxiety disorder (p = .487), any substance use or abuse disorder (p = .446), or ADHD (p = .344). Additionally, hospitalisation within 6 months prior to this study (p = .268), perceived difficulty of condition (p = 0.628), patients' prescribing practitioner (p = .44), and type of health care service (p = 0.138), were also not significantly correlated with gender. In terms of medication-related variables, males and females did not differ significantly by type of sedative/hypnotic (p = .331), anxiolytic (p = .891), anti-psychotic medication (p = .308), or antidepressant type medication prescribed.

Additionally, knowledge of how to cope with possible medication-related adverse reactions (p = .169), current experience of adverse reactions (p = .321), the need for additional adherence support (p = .311), medication perceived as necessary (p = .231), and perceived social stigma, did not reveal any significant gender differences. Results from the

independent sample t-test also revealed that there was no statistically significant difference between the mean MMAQ-8 scores of males (*M* = 5.34, *SD* = 2.07) and females (*M* = 5.64, *SD* = 2.07, *t* (375), = -1.12, *p* = .841).

4.3.3.2. Age

The age of participants ranged from 18 to 77 years, with the mean age 39.07 years, range of 59, and standard deviation of 12.66. The median age was 37 years, with a mode of 29. The confidence level (95%) was 1.28, suggesting a high level of representativeness. Nearly two thirds of patients (57.3%; n=216) were younger than 40 years. One in five patients (21.49%; n=81) were in the 40-49 age group, and one in five (21.22%; n=80) were fifty years or older. Results from the one-way ANOVA revealed a statistically significant difference in the mean age of patients who completed the survey through the three different modes (*F* (2, 374) = 14.07, *p* = .001). A Tukey post-hoc test revealed that the mean age was statistically significantly lower among those who completed the survey on-line (*M* = 37.5, *SD* = 11.59 years) compared to those who completed the questionnaire telephonically (*M* = 45.16, *SD* = 3.43, *p* = .001), or manually (*M* = 48.16, *SD* = 18.01 years, *p* = .001). However, there were no statistically significant differences in the mean age of patients who completed the survey manually and telephonically (*p* = .633). Specifically, patients who were between 18 - 39 years were significantly more likely to complete the survey on-line compared to patients who were older than 40 years (*p* = .05). These results will be discussed in greater detail in the following chapter.

However, in the current study, age was not correlated with any clinical variables such as DSM-IV-TR main diagnosis (*p* = .095), any mood disorder (*p* = .377), any anxiety disorder (*p* = .275), any substance use or abuse disorder (*p* = .055), Schizophrenia or any other psychotic disorder (*p* = .664), ADHD (*p* = .402), personality disorder (*p* = .267) or any general medical condition (*p* = .912). Furthermore, hospitalisation within 6 month prior to this study (*p* = .867), perceived difficulty of condition (*p* = .218), patients' prescribing practitioner (*p* = .518), and type of health care service (*p* = .692), were also not significantly correlated with age.

In terms of medication-related variables, age did not correlate significantly between patients who were prescribed respiratory stimulants, (*p* = .596), any sedative/ hypnotic (*p* = .536), any anxiolytic (*p* = .994), or any anti-psychotic medication (*p* = .522), and patients who did not receive the same medication. With regards to the antidepressant medication category specifically, age was found to have an insignificant correlation between patients who were

prescribed any tricyclic (p = .853), any MAOI (p = .164), any SSRI (p = .620), any SNRI (p = .886), any NDRI (p = .279), any tetracyclic agent (p = .385), any melatonergic agent (p = .164), lithium (p = .726), or any other type (p = .618), and patients who were not prescribed the same medication. Finally, the Pearson's product moment correlation found a statistically insignificant correlation between age and total MMAQ-8 score at 2-tailed analysis (r (377) = 1, p = .224).

4.3.3.3. Population

Nearly four out of every five patients (79.58%; n=300) indicated their race as being White. Slightly more than one in ten patients (11.94%; n=45) were Black. A study that investigated the mental health service use of South Africans with mood, anxiety and substance abuse disorders (Seedat et al., 2009) found a significant difference between racial groups with respect to the type of services accessed. They (Seedat et al., 2009) classified service providers as general medical providers (medical doctor, nurses or other health professionals not in a mental health setting), mental health specialists (psychiatrist, psychologist, other mental health professionals), human services (religious or spiritual advisor, social worker), and complementary and alternative medicine (CAM) (traditional healer, chiropractor or other healer not in a health setting). The mental health and general medical sectors together were also defined as `any health care'. Their study found that Black South Africans were most likely to have accessed the CAM sector, while White South Africans were more likely than Black South Africans to have seen a psychiatrist, as well as having used other mental health services. They (Seedat et al., 2009) further considered the effect of race in patients with a 12-month disorder and stratified by gender. It was also reported that White females and males and Coloured females had the highest odds of seeking mental health services, which could explain the large variation between race categories, particularly between White and Black South Africans.

In South Africa, in order to receive a diagnosis of a mental health condition, one has to be evaluated by a psychiatrist or psychologist, and can only be prescribed an antidepressant medication by a psychiatrist or medical doctor. The low rates of Black South Africans that access these services, and higher access rates by Whites South Africans, may explain the large discrepancy between these two groups in the current study sample. The current survey questionnaire specifically enquired who participants' prescribing practitioners are, with medical doctor or psychiatrist as the only choices provided. Therefore, data on alternative referring/ prescribing practitioners where not collected in the current study.

Results from the one-way ANOVA revealed a statistically significant differences in the mean age of patients and population (race) (F (2, 374) = 21.84, p = .001). A Tukey post-hoc test revealed that the mean age was statistically significantly lower among Black South Africans (M = 30.71, SD = 9.79 years, p = .028), when compared to White South Africans (M = 40.77, SD = 12.49 years) or South Africans from any other population (Indian, Coloured and Mixed race) (M = 34.94, SD = 12.43 years). There were no statistically significant differences in the mean age of White South Africans or South Africans from any other population (p =.293). Additionally, there was no significant difference between population and total MMAQ-8 scores (p = .5).

4.4.3.4. Home language

More than half of patients in this study (57.56; n=217) reported English as their home language. One in three (31.03%; n=117) patients were Afrikaans speaking. One in ten patients (11.41%; n=43) indicated that their home language was one of the remaining 9 official South African languages (i.e., Northern Sotho, Sotho, Swazi, Tswana, Venda, Xhosa and Zulu). The survey questionnaire was distributed in English language only. This is likely the cause for the large number of patients who indicated that this is the main language spoken by them. It is also the second most spoken language in Gauteng Province (13.3%), where the survey was conducted (Statistics South Africa, 2011). Results from the one-way ANOVA also revealed a statistically significant differences in the mean age of patients and main language spoken (F (2, 374) = 9.16, p = .001). A Tukey post-hoc test revealed that the mean age was statistically significantly lower among those who spoke any South African language (M = 31.49, SD = 10.51 years) other than English (M = 40.24, SD = 13.29 years, p = .001) or Afrikaans (M = 39.71, SD = 11.21 years, p = .001). However, there were no statistically significant differences in the mean age of patients who spoke English and Afrikaans as a main language (p = .927). Additionally, there was no significant difference between main language and total MMAQ-8 scores (p = .672).

This suggests that the main language spoken by patients did not have a significant influence on the reported levels of adherence on the MMAQ-8. Due to the limited time and financial resources available, the researcher chose to make the survey available in English only, and not to translate the survey questionnaire into other languages. This is a possible avenue for further investigation.

4.3.3.5. Perceived need for pharmacological treatment of condition

Nearly all patients (88.3%; n=333) indicated that they felt their psychiatric condition required the treatment of antidepressant medication. Results from the Pearson's chi-square test found no significant correlations between patients who indicated the need for pharmacological treatment of their condition and those patients who did not (6.1%; n=23), and any socio-demographical variables such as mode of completion (p = .377), age group (p = .994), main language spoken (p = .59), relationship status (p = .753), racial group (p = .266), living arrangements (p = .167), employment status (p = .723), level of education (p = .137), or if they were the beneficiaries of medical aid or social grant support (p = .574 and p = .259, respectively). However, gender was found to be significantly correlated with this variable. Results from the Chi-square test revealed that males were significantly more likely to indicate that their condition does not require pharmacological treatment ($\chi 2$ (1) = 5.27, p = .022).

Furthermore, no clinical information such as diagnostic-related variables was significantly correlated with patients' perceived need for antidepressant treatment of their psychiatric condition. This included the type and number of DSM-IV-TR diagnoses patients had received (p = .706), prior hospitalisation within six months preceding the study (p = .091), condition perceived as difficult or interfering with daily routines (p = .797), their prescribing practitioner (p = .522), or type of health care service provider (p = .403) were also not significantly correlated with patients' perceived need for pharmacological treatment of their condition. In addition, medication related information such as type of treatment prescribed, did not have a significant correlation with patients' perceived need for pharmacological treatment of their psychiatric condition. The number of antidepressants patients were taking (p = .229), their daily dosage (p = .514), current experience of medication-related adverse reactions (p = .827), knowledge of how to cope with these possible adverse reactions (p = .614), or perceived social stigma (p = .438), were also not significantly correlated with patients' perceived need for pharmacological treatment of their condition.

Finally results from the independent t-test indicated that there was no significant correlation between patients who believe their psychiatric condition requires the treatment of antidepressants (M = 5.71, SD = 2) compared to those who did not feel their condition required antidepressant medication, and their total MMAQ-8 scores (M = 4.6, SD = 2.42, t(375), = 3.364, p < .006).

In summary, although the majority of patient-related variables such has age (p = .224), gender (p = .841), race (p = .5) or home language (p = .672) did not significantly correlate with low adherence rates in psychiatric outpatients in the current study sample, patients'

beliefs about their treatment did have a significant correlation with low adherence rates ($p <$ .006). Specifically, psychiatric patients who indicated they did not believe that their psychiatric condition requires the treatment of antidepressant medication (M = 4.6, SD = 2.42), reported with lower adherence rates when compared to patients who indicated they believe that their psychiatric condition requires the treatment of antidepressant medication (M = 5.71, SD = 2). However, when the Bonferroni-Holm correction for multiple comparisons (Holm, 1979) calculation was considered, this resulted in a statistically insignificant correlation, as it is greater that p = .002. Therefore, under the Bonferroni-Holm correction conditions the results indicate that we fail to reject the following study null hypotheses concerning patient-related variables:

H_1: Age is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_2: Gender is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_3: Race is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_4: Home language is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_5 Treatment beliefs is not significantly correlated with antidepressant adherence rates this sample of psychiatric outpatients in Gauteng Province of South Africa

This means that in the current study sample none of the patient-related variables correlate significantly with antidepressant adherence rates.

4.3.4. Illness-related variables

4.3.4.1 Diagnostic profile

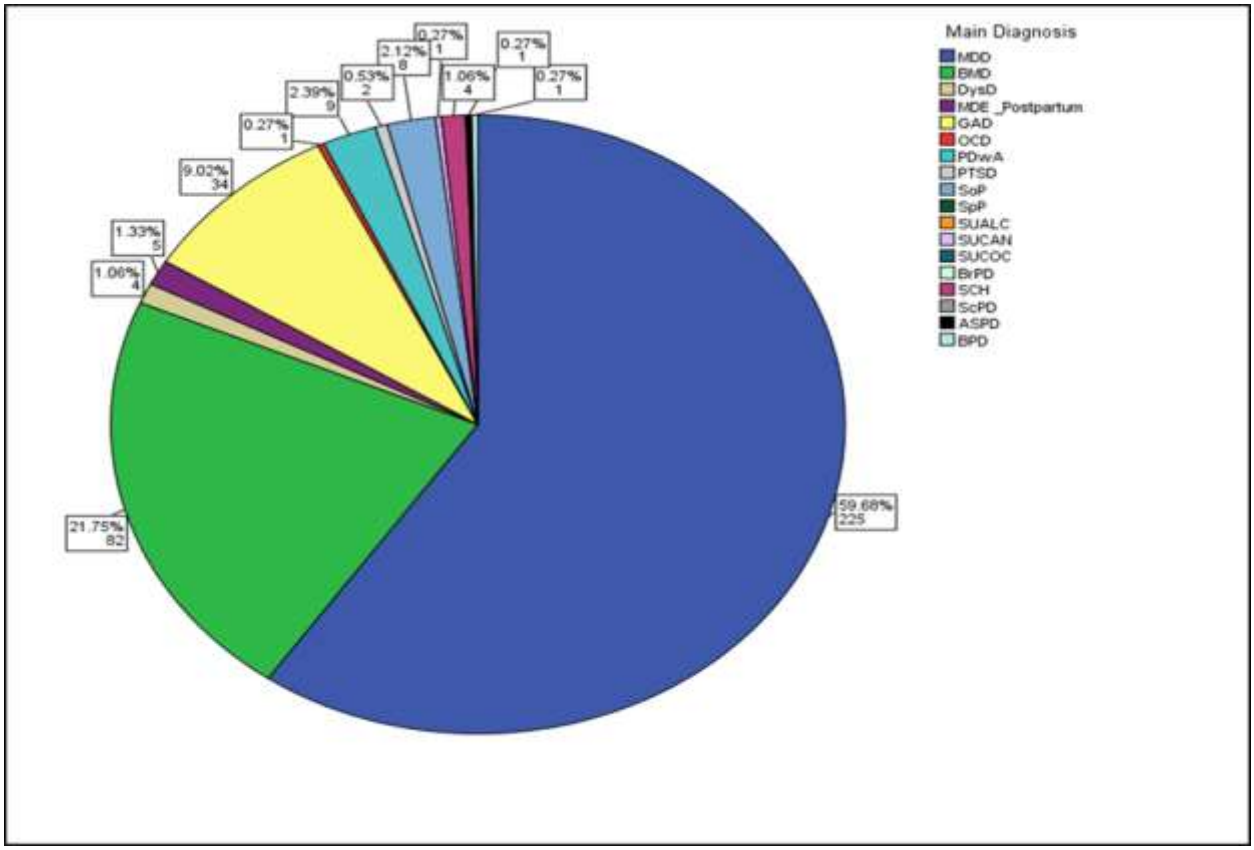
A description of the clinical profile of the 377 participants, including Axis I DSM-IV-TR diagnoses, Personality Disorders (Axis II), and Mental Disorders Due to a General Medical Condition (Axis III), is provided. Participants could select more than one diagnosis if it was applicable. Five broad categories for Axis I were considered when participants' diagnoses were reviewed. These were: Mood Disorders (n=317; 84.1%); Anxiety Disorders (n=165; 43.8%); Schizophrenia and Other Psychotic Disorders (n=8; 2.1%); Substance-Related

Disorders, (n=10; 2.7%); and Disorders Usually First Diagnosed in Infancy, Childhood, or Ado lescence (n=11; 2.9%). In the current study, this refers specifically to Attention-Deficit/Hyperactivity Disorder (ADHD). Additionally n=23 (6.1%) of patients were diagnosed with an Axis II Personality Disorder and 5.3% (n=20) had other general medical conditions (Axis III) that may relevant to their psychiatric diagnosis.

DSM-IV-TR Axis II diagnoses that were documented for participants included: Borderline Personality dDsorder (BPD), (5.04%; n=4 males and n=15 females); Anti-social Personality Disorder, (ASPS), (n=4 females; 1.06%); and Schizoid Personality Disorder (ScPD), (n=3 females; 0.8%). Only two (n=2) patients were diagnosed with only an Axis II condition, without any Axis I comorbid diagnosis. General medical diagnoses were documented for (n=23) participants and included: epilepsy (n=7); diabetes (n=4), metabolic syndrome (n=2); and other conditions (n=9), (i.e., breast cancer (n=1), Parkinson's disease (n=1), Prader Willi Syndrome (n=1), traumatic head injury (n=1), and stroke (n=1).

Of the total sample, only n=18 (1.8%) had any type of Mood Disorder identified in the study and a comorbid DSM-IV-TR Axis III diagnosis (general medical condition). In terms of main Axis I and II DSM-IV-TR diagnoses, Figure 8 below shows that Major Depressive Disorder was the most common diagnosis (59.7%; n=39 males and n=187 females) indicated by participants, followed by Bipolar Mood Disorder (n=82; 21.8%; n=12 males and n=70 females), and Generalised Anxiety Disorder s (23.1%; n=18 males and n=69 females). N=9 (2.4%) patients indicated a main diagnosis of Panic Disorder With or Without Agoraphobia. Although Social Anxiety dDsorder was reported in nearly one in ten patients (10.13%; n=38), data revealed that this diagnosis did not present in patients in isolation from other mood or anxiety disorders.

Figure 7: Distribution of individual Axis I & II DSM-IV-TR diagnoses of sample of psychiatric outpatients in Gauteng (n=377)



Key: *Major Depressive Disorder* ***(MDD)****; Bipolar Mood Disorder* ***(BMD)****; Dysthymic Disorder* ***(DysD)****; Major Depressive Episode-Postpartum Onset* ***(MDE_Postpartum)****; Generalised Anxiety Disorder* ***(GAD)****; Obsessive-Compulsive Disorder* ***(OCD)****; Panic Disorder With or Without Agoraphobia* ***(PDwA);*** *Posttraumatic Stress Disorder* ***(PTSD)****; Social Phobia* ***(SoP)****; Specific Phobia* ***(SpP)****; Substance Abuse or Dependence - Alcohol* ***(SU_ALC)****; Substance Abuse or Dependence - Cannabis* ***(SU_CAN);*** *Substance Abuse or Dependence - Cocaine* ***(SU_COC)****; Brief Psychotic Disorder* ***(BrPD);*** *Schizophrenia* ***(SCH)****; Schizoid Personality Disorder* ***(ScPD)****; Antisocial Personality Disorder*

The mean number of disorders for each patient was 1.67, with the median and mode observed as 1, and standard deviation was found to be 0.960. More than half (n=217; 57.6%) of patients had a single diagnosis, while one in four (n=98; 26%) had received two diagnoses. One in ten patients (n=39; 10.34%) indicated they were diagnosed with three comorbid disorders. The minimum diagnosis per patient is one, and the maximum is seven, with a sum of 630 DSM-IV-TR diagnoses recorded across n=377 patients. This is illustrated in Table 4 below. Finally, the number of diagnoses did not have a significant correlation with patients' total MMAQ-8 scores (p = .84). In the current study, n=226 patients reported with a diagnosis of MDD, and a significant portion of these (n=19 males and n=58 females) reported with a comorbid Anxiety Disorder of any type (34.1%).

Table 5: Distribution of number of DSM-IV-TR diagnoses of sample of psychiatric outpatients in Gauteng (n=377)

Number of DSM-IV-TR diagnoses	**Frequency** ***(n=)***	**Percentage** ***(%)***	**Cumulative Percentage** ***(%)***
1	*217*	*57.6*	*57.6*
2	*98*	*26.0*	*83.6*
3	*39*	*10.3*	*93.9*
4	*17*	*4.5*	*98.4*
5	*5*	*1.3*	*99.7*
7	*1*	*.3*	*100.0*

Patients' main diagnosis did not correlate significantly with any demographic variables such as age groups (p = .334), relationship status (p = .775), employment status (p = .815), living arrangements (p = .224), education level (p = .367), race (p = .747), or medical aid or social grant support (p = .957 and p = .309 respectively). Furthermore, patients' total MMAQ-8 scores was not significantly correlated with any specific DSM-IV-TR main diagnosis (p = .095), any Mood Disorder (p = .962), any Anxiety Disorder (p = .67), any Substance-Related Disorder (p = .993), Schizophrenia and Other Psychotic Disorders (p = .782), ADHD (p = .576), any personality disorder (p = .914) or any general medical condition (p = .947).

Additionally, the presence of any comorbid anxiety disorder (p = .663), comorbid substance use or abuse disorder (p = .623), comorbid Schizophrenia or Other Psychotic Disorder (p = .719) or comorbid Axis II Personality Disorder (p = .791), showed no significant correlation with MMAQ-8 scores between patients who reported with these diagnoses and that did not .Hospitalisation within 6 months prior to this study (p = .867), perceived difficulty of condition (p = .218), patients' prescribing practitioner (p = .518), and type of health care service (p = .692) were also not significantly correlated with patients' total MMAQ-8 scores.

4.3.4.2. Age at which initial diagnosis was received

The mean age at which patients received their initial diagnosis is 30.97 years old (std. deviation 12.85), and ranges between 9 to 70 years old. The median and mode was 30 years and 25 years respectively. The number of months patients have lived with their diagnoses ranges from 1 to 491 (years?), with a mean of 94.62 (7.88 years). The median

number of months is 59, and the mode is 11 months. The standard deviation is 98.66. The confidence level (95%) was found to be 9.99. One in ten patients received their first psychiatric diagnosis between the ages of nine and fifteen years (10.34%), while nearly a quarter of the study sample received their initial diagnosis before the age of twenty (24.93%). More than half of patients in the current study were diagnosed between 20 and 40 years of age (n=201; 53.32%).

A Tukey post-hoc test revealed that the mean average age at which patients received their main diagnosis was statistically significantly lower (therefore at a younger age) among those who spoke other official South African languages (*M* = 25.74, *DS* = 10.23 years) when compared to patients who spoke English (*M* = 31.03, *SD* = 13.43 years, *p* = .035) or Afrikaans (*M* = 32.77, *SD* = 12.2 years, *p* = .006). There were no statistically significant differences between the English and Afrikaans language groups (*p* = .458).

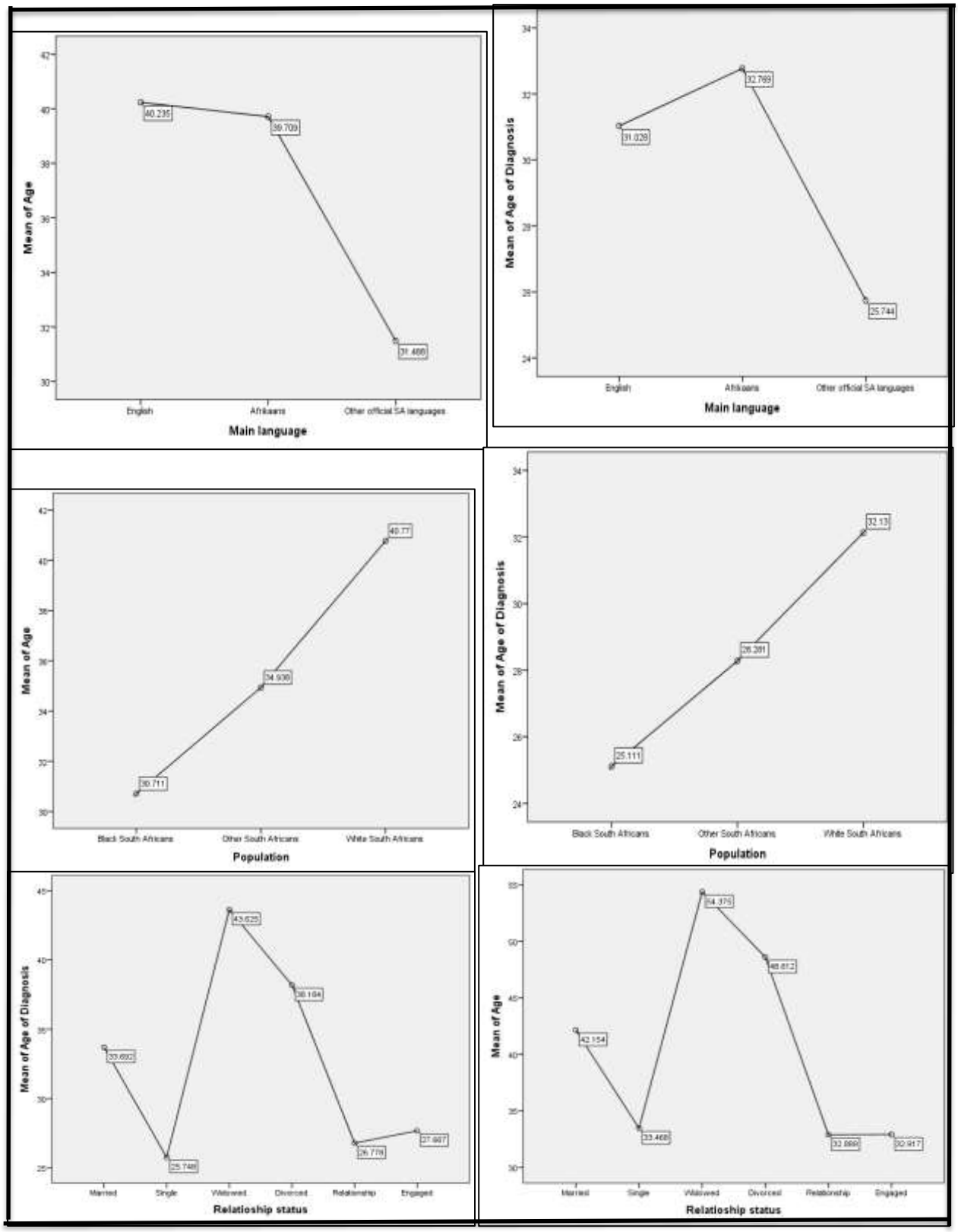
Table 6: Frequency distribution of age at which the sample of psychiatric outpatients received their initial diagnosis (n=377).

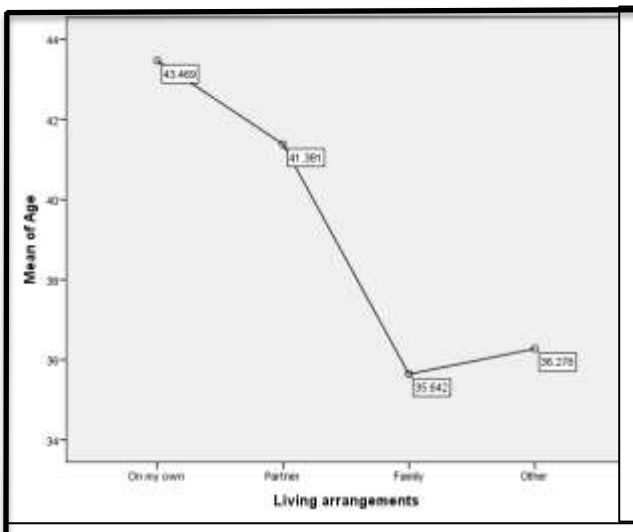
Age (years) at which main diagnosis was received	Frequency (n)	Percentage (%)	Cumulative Percentage
9 - 15	39	10.34	10.34
16 - 20	55	14.59	24.93
21 - 25	50	13.26	38.20
26 - 30	47	12.47	50.66
30 - 35	63	16.71	67.37
36 - 40	41	10.88	78.25
41 - 45	24	6.37	84.62
46 - 50	26	6.90	91.51
51 - 55	15	3.98	95.49
56 - 60	10	2.65	98.14
60 +	7	1.86	100.00

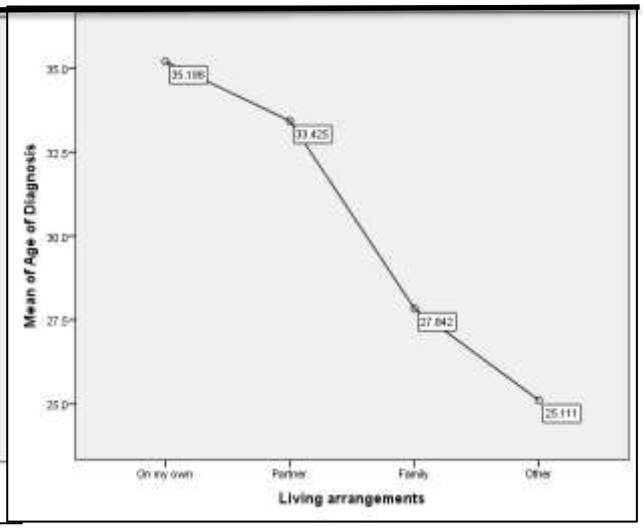
It is worth noting that the average age of patients and the average age at which patients received their diagnosis follow similar trends across the study sample. This may reflect the similar findings observed under heading 4.4.3.4. Home language', namely that the mean age was statistically significantly lower among those who spoke other South African languages (*M* = 31.49, *SD* = 10.51 years) when compared to English (*M* = 40.24, *SD* = 13.29 years, *p* = .001) or Afrikaans (*M* = 39.71, *SD* = 11.21 years, *p* = .001). Figure 8 provides an illustration of the similarity in trends between the mean age of the study sample at time of data collection and mean age at receiving initial psychiatric diagnosis across the different language groups. These findings will be discussed in greater detail in the following chapter.

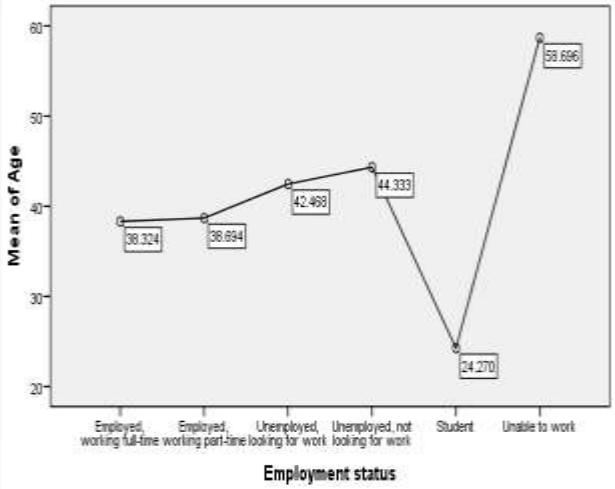
Figure 8 on the following two pages clearly illustrate the similar trends between the mean age of patients at time of data collection and the mean age at which they received their initial psychiatric diagnosis across the various socio-demographical variables identified in the current study. These trends may indicate that socio-demographical factors do not have a significant influence on the age at which patients receive their initial diagnosis. This may suggest that patients in the current study sample access mental health care service similarly across age. Alternatively, it seems that patients' socio-demographical profile does not have an influence on the age at which they receive their first psychiatric diagnosis. These findings may be useful for those who wish to target age-specific interventions aimed at improving adherence rates in this sample.

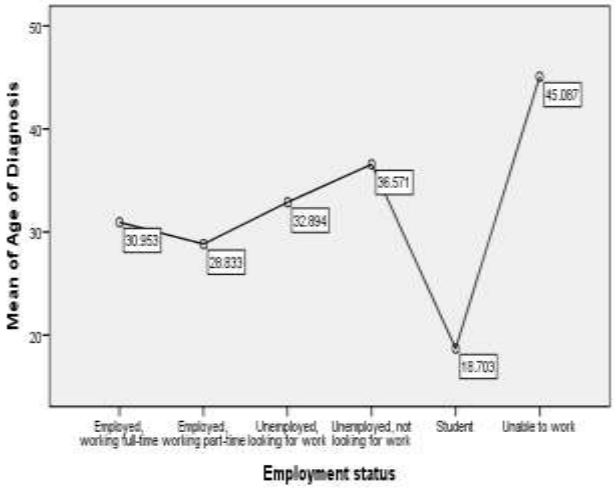
Figure 8: Mean age of sample at time of data collection compared to mean age at receiving initial diagnosis of sample of psychiatric outpatients in Gauteng across socio-demographical variables (n=377)

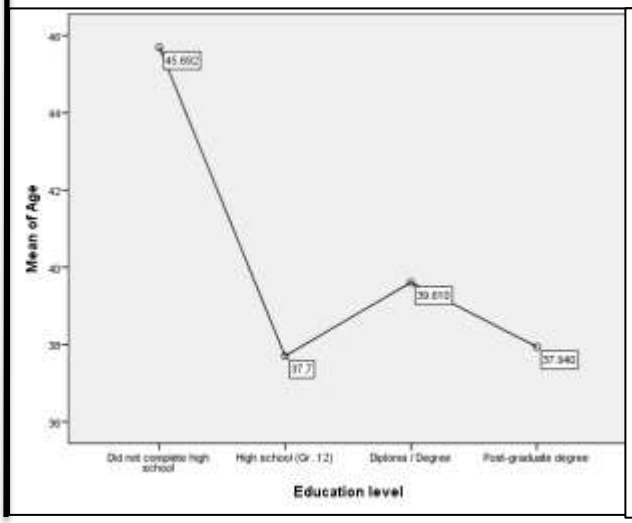


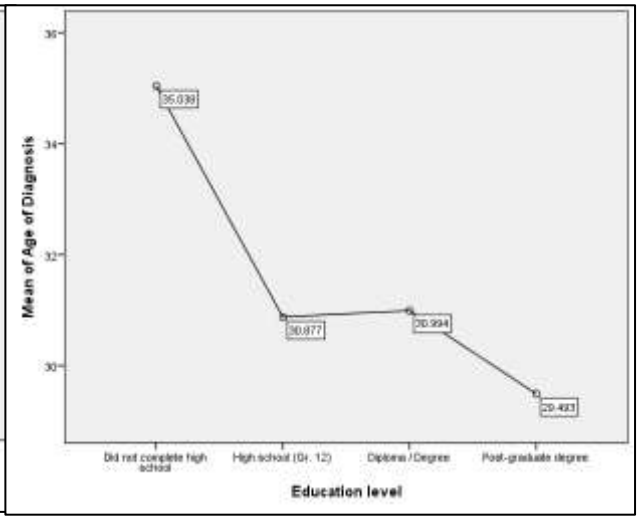

Mean of Age
43.469
41.361
35.642
36.278
On my own
Partner
Family
Other
Living arrangements


Mean of Age of Diagnosis
35.198
33.425
27.842
25.111
On my own
Partner
Family
Other
Living arrangements


Mean of Age
38.324
38.694
42.498
44.333
24.270
58.696
Employed, working full-time
Employed, working part-time
Unemployed, looking for work
Unemployed, not looking for work
Student
Unable to work
Employment status


Mean of Age of Diagnosis
30.953
28.833
32.894
36.571
18.703
45.067
Employed, working full-time
Employed, working part-time
Unemployed, looking for work
Unemployed, not looking for work
Student
Unable to work
Employment status


Mean of Age
45.692
37.7
39.610
37.940
Did not complete high school
High school (Gr. 12)
Diploma / Degree
Post-graduate degree
Education level


Mean of Age of Diagnosis
36.039
30.877
30.994
29.493
Did not complete high school
High school (Gr. 12)
Diploma / Degree
Post-graduate degree
Education level

4. 3.4.3. Previous hospitalisation

Participants were asked if they had been hospitalised for their psychiatric condition in the six months prior to the study. The majority of patients (82.76%; n=312) responded that they had not been hospitalised, while one in six patients (17.24%; n=65) indicated that they had been hospitalised in the past six months (n=10 males; n=55 females). As noted previously, gender (p = .268) and age (p = .867) were not significantly correlated with hospitalisation 6 months prior to the study. Other socio-demographical variables such as mode of questionnaire completion (p = .753), main language (p = .726), population grouping (p = .856), relationship status (p = .296), living arrangements (p = .75), employment status (p = .305), and education level (p = .654) were not significantly correlated with hospitalisation 6-months prior to participation in this study. More specifically, main DSM-IV-TR diagnosis (p = .616), any Mood Disorder (p = .213), Substance-Related Disorders (p = .815), Schizophrenia or Other Psychotic Disorders (p = .192), any Personality Disorder (p=0.556) or general medical condition (p = .136) were also not significantly correlated with hospitalisation 6-months prior to participation in this study

Additionally, the presence of a comorbid Anxiety Disorder (p = .124), comorbid Substance-Related Disorder (p = .622), comorbid Schizophrenia and Other Psychotic Disorders (p = .427), or comorbid Personality Disorder (p = .566) was also not significant correlated with hospitalisation 6 months prior to the study. However, when compared to patients who did not have the same comorbid DSM-IV-TR diagnoses, patients diagnosed with Generalised Anxiety Disorder ($\chi 2$ = 6.702, p = .01), any Specific Phobia ($\chi 2$ = .494, p = .023) or Bipolar Mood Disorder ($\chi 2$ = 3.926, p = .048), were significantly more likely to have been hospitalised for their psychiatric condition in the 6 months preceding the study. Patients who indicated that they were hospitalised for their psychiatric condition 6 months prior to the study were significantly less likely to have received their prescriptions from a general practitioner ($\chi 2$ = 14.803, p = .04). These findings will be discussed in greater detail in the following chapter.

Patients who reported hospitalisation 6 months prior to the study was not significantly correlated with perceived difficulty of their psychiatric condition (p = .421), perceived the need for pharmacological treatment (p = .091), type of health care system accessed (p = .337), current experience of medication-related adverse reactions (p = .317) or perceived social stigma (p = .221), Finally, patients' MMAQ-8 scores were also not significantly correlated with hospitalisation in the six months prior to the study (p = .867). These findings may indicate that recent hospitalisation (6 months prior to study) by patients in the current

study sample is not significantly influenced by their demographical or treatment profile, but instead by their clinical profile.

4.3.4.4. Perceived difficulty of condition

Participants were asked if their psychiatric condition makes it difficult for them to take care of their daily tasks by responding “Yes” or “No”. Three quarters of patients (76.13%; n=287) indicated that their condition make it difficult for them to perform their daily activities, whereas nearly a quarter of (23.87%; n=90) patients did not experience the same challenges to performing daily activities as a result of their psychiatric condition. The perceived difficulty of patients’ psychiatric condition was also not significantly correlated with demographical variables such as age group (p = .532), main language (p = .561), population (p = .23), relationship status (p = .873), living arrangements (p = .487), employment status (p = .791), or education level (p = .255).

However, a significant correlation was shown between the participants’ perceived difficulty of (psychiatric) condition and clinical-related variables, namely main diagnosis (p = .001). Specifically, patients who had been diagnosed with any DSM-IV-TR Mood Disorder (p = .004) were significantly more likely to indicate that their condition makes it difficult for them to perform their daily activities. However, when analysed individually, none of the specific mood disorders identified in this study (Major Depressive Disorder, Bipolar Mood Disorder, Dysthymic Disorder and Major Depressive Episode – Postpartum Onset) was significantly correlated with perceived difficulty of condition.

Additionally, the presence of any DSM-IV-TR Axis II or III disorder was also not significantly correlated with perceived difficulty of condition. Furthermore, the presence of any DSM-IV-TR Anxiety Disorder or any Substance-Related Disorder was also not significantly correlated with perceived difficulty of condition. Patients in the current study who were diagnosed with a Mood Disorder and any comorbid Anxiety Disorder ($\chi 2$ = 5.075, p = .024), or comorbid Schizophrenia ($\chi 2$ = 16.159, p = .01) were significantly more likely to indicate that their condition makes it difficult for them to perform their daily activities. These results will be discussed in greater detail in the following chapter.

In summary, none of the illness-related variables such has main DSM-IV-TR diagnosis (p = .095), age of onset of psychiatric illness (p = .52), illness duration (p = . 548), perceived difficulty of psychiatric condition (p = . 218) or recent (6 months prior to the study) hospitalisation (p = . 274) were significantly correlated with antidepressant adherence rates in this study sample. Therefore, the results indicate we fail to reject following study hypotheses concerning illness-related variables:

H_6: Main DSM-IV-TR diagnosis is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_7: Age of onset of diagnosis is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_8: Illness duration is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_9: Prior hospitalisation (6 months) is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{10}: Perceived difficulty psychiatric condition is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

This means that in the current study sample, none of the illness-related variables correlate significantly with antidepressant adherence rates.

4.3.5. Medication-related variables

4.3.5.1. Number of medications

A total of 762 central nervous system (CNS) medications were recorded across the entire study sample of 377 patients. The total number of psychotropic medications for patients ranged between one and seven, (M = 2.1, SD = 1.22). Half of all patients (50.13%; n=189) were prescribed between one and three medications. The number of antidepressants patients were prescribed did not have a significant correlation with any socio-demographical variables such as age group (p = .935), gender (p = .173), main language spoken (p = .238), relationship status (p = .886), population (p = .525), living arrangements (p = .312), employment status (p = .853), level of education (p = .497), or if they were the beneficiaries of medical aid or social grant support (p = .054 and p = .39, respectively).

However, patients in this sample who were prescribed a total of three antidepressants (n=18; 4.8%) were significantly more likely to have received a diagnosis of a comorbid Substance-Related Disorders ($\chi 2$ (2) = 6.489, p = .039), and specifically Cocaine Abuse or Dependence ($\chi 2$ (2) = 10.696, p = .005). No other significant correlations were observed when any other DSM-IV-TR diagnoses were considered in the analysis. Additionally, the

number of antidepressants prescribed did not have any significant correlations with other clinical-related variables such as the type (p = .077) or number (p = .708) of DSM-IV-TR diagnoses, hospitalisation within six months prior to the study (p = .075), perceived difficulty of psychiatric condition (p = .163), duration of treatment (p = .94), prescribing practitioner (p = .372) or type of health care system (p = .523). No significant correlations were observed between the number of psychotropic medications (p = .52) or number of antidepressants (p = .81) patients were prescribed and their total MMAQ-8 scores. The findings reported in this paragraph will be elaborated on in the following chapter.

4.3.5.2. Medication category

Table 7 illustrates the distribution (in frequencies and percentages) of all 762 psychotropic medications recorded for the entire study sample of 377 psychiatric outpatients as classified according to the Monthly Index of Medical Specialities (MIMS) September, 2014. The most frequent medication category prescribed to patients were antidepressants, comprising of nearly two thirds (64.44%; n=491) of all the CNS medications recorded in this study. The most common class of all antidepressants prescribed (n=491) was selective serotonin re-uptake inhibitors, which comprised of nearly half (n=236; 48.07%) of all the antidepressants prescribed. The most commonly prescribed SSRI was Escitalopram, comprising of a third (n=74; 31.36%) of all SSRI's prescribed. The number of antidepressant medications that participants reported being prescribed ranged between one (1) and three (3) antidepressants prescribed to each patient (M = 1.32).

As seen in table 5, of all antidepressants from any category, Escitalopram was also the most commonly prescribed antidepressant of all comprising of (n=74; 15.07%) all antidepressants prescribed to participants in this sample. This was followed by venlafaxine, which was the most commonly prescribed SNRI (n=57; 67.86%), and then Fluoxetine (n=60; 25.42%), also an SSRI. The fourth most commonly prescribed CNS medication was quetiapine, an anti-psychotic of the atypical class (n=55), and it was also the most common atypical anti-psychotic prescribed (63.22%). The second most common atypical anti-psychotic prescribed was risperidone (n=12; 13.79%). Other common CNS medications include citalopram (n=64), comprising of 19.49% of all SSRI prescribed to patients in this study; bupropion, (n=45), the most commonly prescribed NDRI (95.74%), and sertraline (n=45), comprising of 18.64% of all SSRI's prescribed. Table 7 presents the distribution of all the psychotropic medications that the sample of psychiatric outpatients in Gauteng (n=377) were prescribed at the time of the current study.

Table 7: Distribution of psychotropic medications of psychiatric outpatients in Gauteng (n=377)

Medication Category	Frequency in total prescriptions (n)	Percentage of total prescriptions (%)	Medication classification	Frequency in drug category (n)	Percentage in drug category (%)	Active ingredient	Frequency in drug classification (n)	Percentage in drug classification (%)
Central Nervous System Stimulants	11	1.44	Respiratory Stimulants	11	100.00	Methylphenidate	11	100.00
Sedative Hypnotics	32	4.20	Benzodiazepines	7	21.88	Loprazolam	3	42.86
						Temazepam	2	28.57
						Epilizine	1	14.29
						Flurazepam	1	14.29
			Others	25	78.13	Zolpidem	21	84.00
						Zopiclone	4	16.00
Anxiolytics	72	9.45	Benzodiazepines	68	94.44	Alprazolam	23	26.74
						Clobazam	20	23.26
						Lorazepam	16	18.60
						Diazepam	5	5.81
						Oxazepam	3	3.49
						Etifoxine	1	1.16
			Others	4	5.56	Buspirone	4	100.00
Antidepressants	491	64.44	Tricydic	25	5.09	Amitriptyline	22	88.00
						Imipramine	2	8.00
						Mianserin	1	4.00
			Mono-Amine Oxidase inhibitors	2	0.41	Tranylcypromine	1	50.00
						Moclobemide	1	50.00
			Selective serotonin re-uptake inhibitors	236	48.07	Escitalopram	74	31.36
						Fluoxetine	60	25.42
						Citalopram	46	19.49
						Sertraline	44	18.64
						Paroxetine	12	5.08
			Serotonin & noradrenaline re-uptake inhibitors	84	17.11	Venlafaxine	57	67.86
						Duloxetine	26	30.95
						Vortioxetine	1	1.19
			Noradrenaline & dopamine re-uptake	47	9.57	Bupropion	45	95.74
						Reboxetine	2	4.26
			Tetracyclic	58	11.81	Lamotrigine	45	77.59
						Mirtazapine	13	22.41
			Melatonergic Specific	2	0.41	Agomelatine	2	100.00
			Lithium	15	3.05	Lithium Carbonate	15	100.00
			Others	22	4.48	Trazodone	22	100.00
Anti-psychotics	97	12.73	Butyrophenones	3	3.09	Haloperidol	3	100.00
			Atypical anti-psychotpics	87	89.69	Quetiapine	55	63.22
						Risperidone	12	13.79
						Olanzapine	8	9.20
						Aripiprazole	5	5.75
						Clonazepam	4	4.60
						Ziprasidone	2	2.30
						Flupenthixol	1	1.15
			Others	7	7.22	Sulpiride	7	100.00
Anticholinergics	2	0.26	Anticholinergics	2	100.00	Orphenadrine	2	100.00
Anti-epileptics	57	7.48	Anti-epileptics	57	100.00	Lamotrigine	19	33.33
						Sodium Valproate	15	26.32
						Clonazepam	12	21.05
						Carbamazepine	5	8.77
						Pregabalin	3	5.26
						Topiramate	3	5.26

Patients who were prescribed a tricyclic antidepressant (such as amitriptyline, comprising of 88% of all tricyclics prescribed), were significantly more likely to have a diagnosis of Bipolar Mood Disorder (BMD) ($\chi 2$ (1) = 7.348, p = .007), or Borderline Personality Disorder (BPD), ($\chi 2$ (1) = 9.106, p = .003). 16% of patients on tricyclic antidepressants also had a diagnosis of BPD, compared to only 3.41% of patients with the same diagnosis who were not prescribed this type of antidepressant. Furthermore, patients with a diagnosis of BMD were also significantly more likely to receive a prescription for lithium ($\chi 2$ (1) = 7.638, p = .006). In addition to BMD, lithium was also significantly correlated with the diagnosis of brief psychotic disorder ($\chi 2$ (1) = 6.821, p = .001) as well as cocaine use or abuse disorder ($\chi 2$ (1) = 11.147, p = .001). Although the local SASOP treatment guidelines does not make reference to amitriptyline in the treatment if BMD, particular reference is made to lithium as an effective treatment in the acute manic and depressive phase of this condition (Emsley et al., 2013). This may be due to the mood-stabilising effect this treatment has earned its reputation for. Selective serotonin re-uptake inhibitors (SSRI's) were not significantly correlated with any DSM-IV-TR Axis I or II diagnosis in this study sample. Antidepressants in the "Other" class (in this study only trazodone was recorded) was found to be significantly correlated with the diagnosis of Alcohol Abuse or Dependence ($\chi 2$ (1) = 6.71, p = .01) and Cocaine Abuse or Dependence ($\chi 2$ (1) = 7.137, p = .008). Trazodone was also found to be significantly correlated with a diagnosis of Schizoid Personality Disorder, ($\chi 2$ (1) = 4.161, p = .041). Reference to Trazodone is made (Emsley et al., 2013) for the treatment of dementia, particularly Substance-Induced Dementia, which supports the significant correlations observed between this medication and Substance-related Disorders observed in the current study sample. These significant correlations will be discussed in greater detail within the context of the study in the following chapter.

The prescription of any noradrenaline and dopamine re-uptake inhibitor (NDRI) was not significantly correlated with any DSM-IV-TR Axis I or II diagnosis. Although MDD was significantly correlated with the prescription of an NDRI medication in the current study sample ($\chi 2$ (1) = 4.563, p = .033), closer inspection into the specific NDRI's identified in the study (Buproprion and Reboxetine), no statistically significant correlations were observed between these two medications (p =.057 and p =.221 respectively). These results will be elaborated on in the following chapter.

Table 8 summarises the correlations between DSM-IV-TR Axis I and II diagnoses identified in the current study sample and the class of antidepressants psychiatric outpatients were prescribed. Pearson Chi-Square, Fishers Exact test and p -values are presented. Significant correlations in the table are highlighted in bold and grey-scale shaded background.

Table 8: Correlations between DSM-IV-TR Axis I & II diagnosis and prescribed antidepressant medication classes for psychiatric outpatients in Gauteng (n=377)

Main DSM IV-TR diagnosis	Tricyclic			MOAI			SSRI			SNRI			NDRI			Tetracyclic			Melatonergic			Lithium			Other		
	Pearson Chi-Square value	*p* value	Fishers Exact test value	Pearson Chi-Square value	*p* value	Fishers Exact test value	Pearson Chi-Square value	*p* value	Fishers Exact test value	Pearson Chi-Square value	*p* value	Fishers Exact test value	Pearson Chi-Square value	*p* value	Fishers Exact test value	Pearson Chi-Square value	*p* value	Fishers Exact test value	Pearson Chi-Square value	*p* value	Fishers Exact test value	Pearson Chi-Square value	*p* value	Fishers Exact test value	Pearson Chi-Square value	*p* value	Fishers Exact test value
Major Depressive Disorder	.174 (a)	.677	.414	1.343 (b)	.246	.519	.139 (a)	.709	.746	.008 (a)	.928	1	4.563 (a)	**.033**	.04	.05 (a)	.823	.884	.083 (b)	.773	1	2.589 (a)	.108	.116	.132 (a)	.716	.824
Bipolar Mood Disorder	7.348 (a)	**.007**	.011	.797 (a)	.372	1	1.625 (a)	.202	.239	.608 (a)	.435	.494	.017 (a)	.897	.866	1.255 (a)	.263	.271	.797 (b)	.372	1	7.683 (c)	**.006**	.015	1.804 (a)	.179	.222
Dysthymic Disorder	.287 (b)	.592	1	.022 (d)	.883	1	.287 (b)	.592	1	1.159 (b)	.282	.597	.59 (b)	.442	1	.287 (b)	.592	.489	.022 (d)	.883	1	.168 (b)	.682	1	.251 (b)	.617	1
Major Depressive Disorder - Post-partum Onset	.581 (c)	.446	1	.044 (b)	.835	1	2.096 (b)	.148	.162	3.627 (c)	.057	.077	.000 (c)	.984	1	1.486 (c)	.223	.615	.044 (b)	.835	1	.339 (c)	.561	1	.507 (c)	.477	1
Generalised Anxiety Disorder	.755 (a)	.385	.47	.821 (b)	.365	.409	1.587 (a)	.208	.257	.013 (a)	.91	1	1.149 (a)	.284	.277	.017 (a)	.896	1	.603 (b)	.437	1	.083 (c)	.773	1	.002 (a)	.968	1
Obsessive-compulsive Disorder	.206 (c)	.65	1	.131 (b)	.718	1	.32 (a)	.572	.659	2.211 (a)	.137	.192	1.55 (c)	.213	.335	.842 (c)	.359	.552	.131 (b)	.718	1	.009 (c)	.926	1	1.518 (c)	.218	.383
Panic Disorder w. & w/o Agoraphobia	1.837 (c)	.175	.227	2.513 (b)	.113	.239	.004 (a)	.947	1	.732 (a)	.392	.457	.003 (a)	.959	1	2.397 (a)	.122	.134	.293 (b)	.588	1	.743 (c)	.389	.42	.017 (c)	.896	.751
Post-traumatic Stress Disorder	.597 (c)	.44	.436	.174 (b)	.667	1	.293 (a)	.589	.696	.098 (a)	.754	1	1.079 (c)	.299	.401	1.903 (c)	.168	.287	.174 (b)	.677	1	.036 (c)	.85	1	.041 (c)	.84	.691
Social Phobia	1.092 (c)	.296	.493	.225 (b)	.635	1	.248 (a)	.618	.725	3.473 (a)	.062	.067	.185 (c)	.667	.802	.161 (a)	.688	.816	3.535 (b)	.06	.192	1.751 (c)	.186	.381	1.692 (c)	.193	.26
Specific Phobia (any)	.215 (b)	.643	1	.016 (d)	.899	1	1.061 (b)	.303	.56	3.44 (b)	.064	.126	1.155 (b)	.282	.336	.55 (b)	.458	1	.016 (d)	.899	1	.125 (b)	.723	1	.187 (b)	.655	1
Alcohol Use or Abuse Disorder	.507 (c)	.447	1	.038 (b)	.845	1	1.118 (b)	.29	.434	9.949 (c)	**.002**	.007	1.041 (c)	.308	.602	1.297 (c)	.255	.601	.038 (b)	.845	1	.296 (c)	.587	1	6.71 (c)	**.01**	.057
Cannabis Use or Abuse Disorder	.36 (b)	.549	1	.027 (d)	.869	1	3.809 (b)	.051	.071	4.163 (b)	**.041**	.076	.241 (b)	.642	.496	.921 (b)	.337	1	.027 (d)	.869	1	.21 (b)	.647	1	1.85 (b)	.174	.261
Cocaine Use or Abuse Disorder	.143 (b)	.706	1	.011 (d)	.918	1	3.29 (b)	.07	.143	7.013 (b)	**.008**	.049	.293 (b)	.588	1	1.851 (a)	.174	.284	.011 (d)	.918	1	11.147 (b)	**.001**	.078	7.137 (b)	**.008**	.113
Brief Psychotic Disorder	3.482 (b)	.062	.187	.016 (d)	.899	1	1.061 (b)	.303	.56	.867 (b)	.352	1	.441 (b)	.507	1	.748 (b)	.387	.395	.016 (d)	0899	1	6.821 (b)	**.009**	.115	.187 (b)	.665	1
Schizophrenia	.36 (b)	.549	1	.027 (d)	.869	1	.009 (b)	.924	1	.015 (b)	.902	1	.739 (b)	.39	1	.083 (b)	.773	.568	.027 (d)	.869	1	.21 (b)	.647	1	.314 (b)	.575	1
Attention Deficit/ Hyperactivity Disorder	.111 (c)	.739	.535	.06 (b)	.806	1	.012 (c)	.913	1	.11 (c)	.740	1	.303 (c)	.582	.638	1.23 (c)	.267	.386	.06 (b)	.806	1	.775 (c)	.379	.346	.702 (c)	.402	1
Schizoid Personality Disorder	.215 (b)	.643	1	.016 (d)	.899	1	.027 (b)	0869	1	.213 (b)	.644	.532	.441 (b)	.507	1	.748 (b)	.387	.395	.016 (d)	.899	1	.125 (b)	.723	1	4.161 (b)	**.041**	.165
Anti-social Personality Disorder	.287 (b)	.592	1	.022 (d)	.883	1	.287 (b)	.592	1	.017 (b)	.895	1	.548 (b)	.459	.421	.287 (b)	.592	.489	.022 (d)	.833	1	.168 (b)	.682	1	.251 (b)	.617	1
Borderline Personality Disorder	9.106 (c)	**.003**	.016	.089 (b)	.765	1	.001 (a)	.971	1	.12 (c)	.729	1	2.263 (c)	.132	.133	.107 (c)	.744	1	.089 (b)	.765	1	.226 (c)	.635	.485	.005 (c)	.942	1

a) 0 cells (0%) have an expected count of less than 5
b) 2 cells (50%) have an expected count of less than 5
c) 1 cells (25%) have an expected count of less than 5
d) 3 cells (75%) have an expected count of less than 5

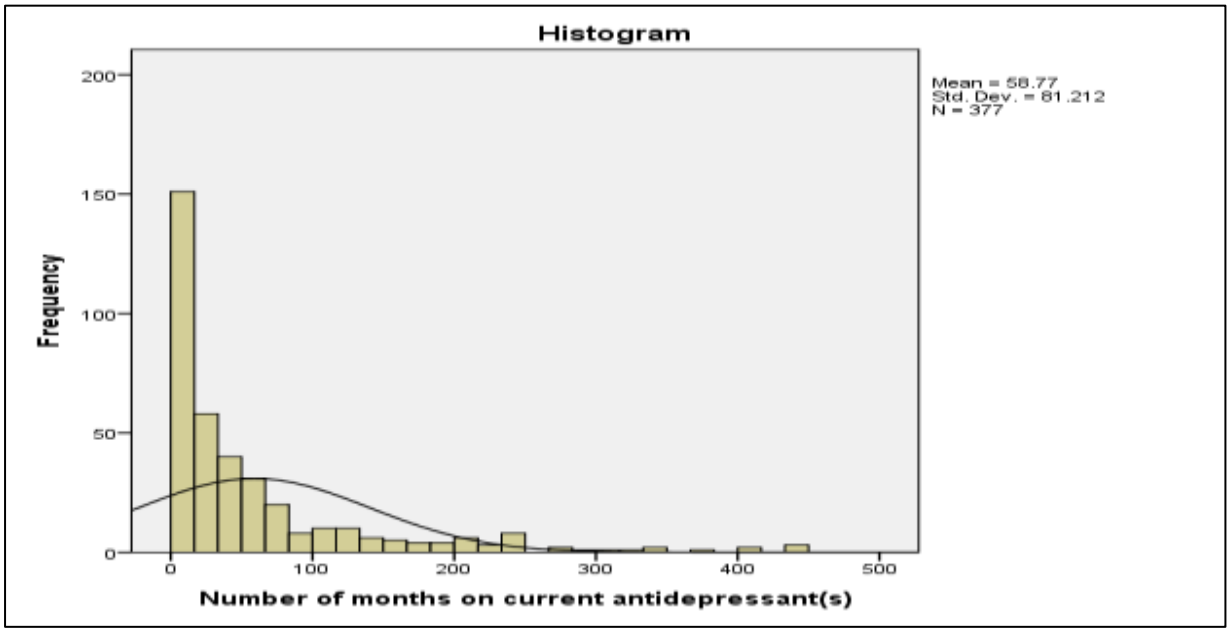
There were no significant correlations observed between specific antidepressant medication such as tricyclics (*p* = .672), MOAI's (*p* = .331), SSRI's (*p* = .735), SNRI's (*p* = .666), NDRI's (*p* =.694), tetracyclic antidepressants (*p* =.948), melatonergic agents (*p* =.569), lithium (*p* = .361) or antidepressants in the "Other" category (*p* = .742) and patients' total MMQ-8 scores.

4.3.5.3. Duration on current antidepressant medication

The number of months patients have been taking their current antidepressant medication ranged from 1 to 447 (37.25 years) (*M* = 58.77 months/ 4.9 years; *SD* = 81.21 months/ 6.7 years). The median number of months was 25, and the mode was 4 months.

Many of these patients may have volunteered to participate in the study soon after having received a psychiatric diagnosis or having been discharged from hospital. These patients may have contacted or have been referred to SADAG for additional outpatient support services by their respective health care providers. The standard treatment phase for antidepressants (The South African National Department of Health, 2012; Emsley et al., 2013) namely acute, continuation, and maintenance, ranges between 1 and 12 months. However, only a third of patients (33.2%; n=125) in this study were on their current antidepressant(s) for twelve months or less, suggesting the majority of patients required chronic pharmacological treatment for their conditions.

Figure 9: Distribution of the number of months psychiatric outpatients have been on their current antidepressant(s)



Half of all patients (n=191; 50.7%) were on their current antidepressant(s) for up to two years (24 months), while 5% of patients (n=19) have been on their current antidepressant for more than two decades (240 months). The disproportionate distribution of the number of months patients have been on their current antidepressant(s) may be a reflection of the chronic nature of psychiatric conditions discussed in Chapter 2. It is also worth noting that these findings only relate to patients' current antidepressant prescription, and no information of previous pharmacological treatments was recorded. Therefore, patients may have been treated with antidepressants for a longer duration than what has been identified in this current study. Finally, the number of months patients have been on their current antidepressant treatment was not significantly correlated with any socio-demographical variables, clinical variables or medication-related variables. Similarly, insignificant correlations were observed when patients' total MMAQ-8 scores were considered for analysis.

4.3.5.4. Daily dosage

The majority of participants (65.25%; n=246) only needed to take a single dose of antidepressant medication per day. A third (30.5%; n=115) needed to take their dose twice daily. No significant correlations were observed between any socio-demographic variables and the number of times patients had to take their medication. When clinical variables were considered for analysis, patients diagnosed with MDD (n=226) were significantly more likely to be required to take their medication four times daily $\chi 2(3) = 9.303$, $p = .026$ when compared to patients without this diagnosis. However, only two (n=2; 0.53%) of the study sample reported a daily antidepressant dosage of four times daily. The significant correlation reported here may be as a result of the low number of patients in the current study sample who needed to take their antidepressant medication four or more times a day. A significant correlation was also found for patients who had been diagnosed with ADHD $\chi 2(3) = 18.813$, $p < .001$, and the number of daily medication dosages. Patients who had received a diagnosis of ADHD were more likely to report a daily antidepressant dosage of four times or more. No significant correlations were observed when other clinical-related variables were considered for analysis. Patients' daily dosage also did not show a significant correlation with patients' total MMAQ-8 scores ($p = .406$).

4.3.5.5. Current experience of adverse reactions

Participants were asked if they were currently experiencing any adverse reactions from their antidepressant medication. A slight majority of patients in the study (54.38%; n=205) reported no adverse reactions to the antidepressant medications, whereas n=172 patients (45.62%) indicated that they were experiencing adverse reactions to the antidepressant medications). The current study did not include descriptions of the type of adverse reactions to antidepressant medication that were experienced. Therefore due to this particular limitation in this study the results are only indicative of whether a patient is attributing the presence of any adverse reaction to their antidepressant medication. It is suggested that this area should be explored further in subsequent studies. These findings can only comment on patients' subjectively perceived medication-related adverse reactions, and is not able to distinguish this from any other symptoms that may be related to the patient's condition. This limitation should be taken into account when results are interpreted.

The reported presence of medication-related adverse reactions did not have a significant correlation with any socio-demographic or clinical-related variables identified in the study. However, when specific medication categories were considered in the analysis, patients who were prescribed sedative-hypnotics from the "Other" class (Zolpidem and Zopiclone was identified in this study) were significantly more likely to report that they perceived medication-related adverse reactions ($\chi 2$ (1) = 5.404, p = .02) when compare to patients who were not prescribed these medications. Furthermore, patients who reported that they perceived medication-related adverse reactions showed some degree of correlation with medication adherence rates. Specifically, psychiatric outpatients from the current study who indicated they perceived antidepressant-related adverse reactions scored lower on the MMAQ-8 (M = 5.35, SD = 2.16) when compared to patients who did not report perceived antidepressant - related adverse reactions (M = 5.78, SD = 2), but only approached statistical significance (t(375) = 2.536, p = 0.51).

4.3.5.6. Knowledge to cope with adverse reactions

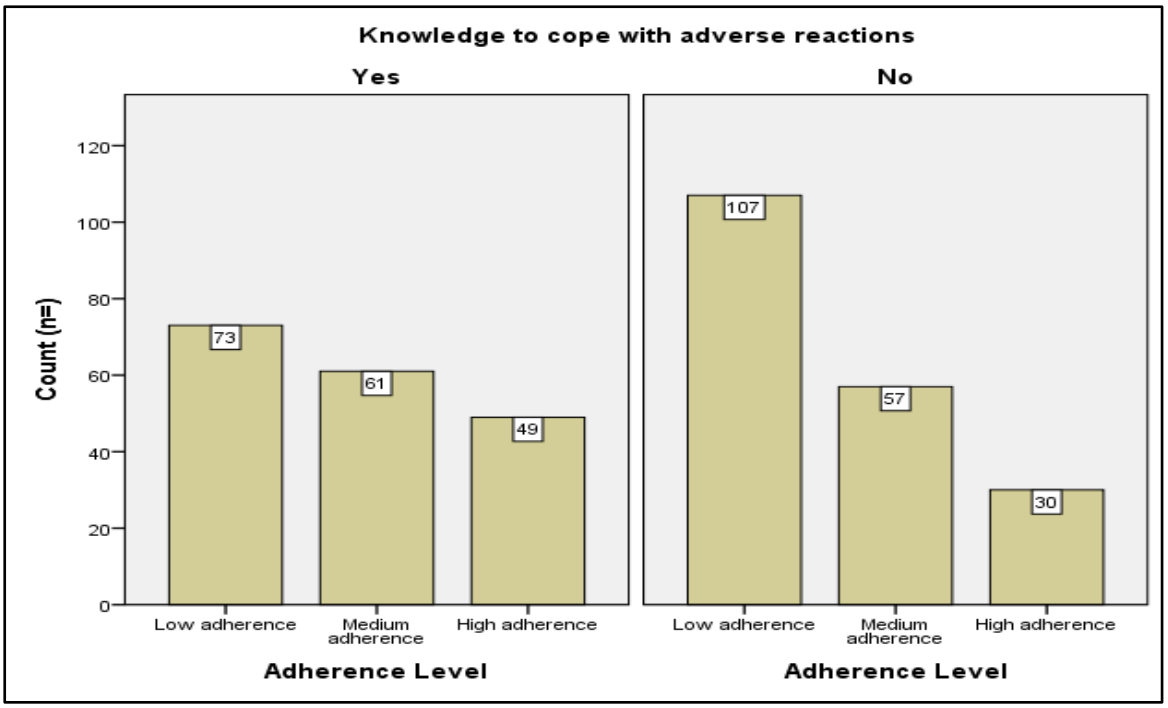
Participants were asked if they were able to cope with the adverse reactions from the medication. Of all the patients (n=377), less than half (48.5%; n=183) indicated that they know how to deal with possible adverse reactions from their antidepressant medication, while the majority (51.5%; n=194), did not. Of the 172 patients that indicated they were experiencing adverse reactions, only 70 (40.7%) stated that they knew how to deal with possible antidepressant medication-related adverse reactions. The majority of patients

(n=102; 59.3%) stated that they do not know how to cope with the potential adverse reactions of their antidepressant medication.

Patients' knowledge of how to cope with possible adverse reactions from medications did not have any significant correlation with any socio-demographical variables. No significant correlations were observed for clinical-related variables either. However, knowledge of how to cope with possible adverse reactions had a significant negative correlation with the number of months patients have lived with their main diagnosis, and number of months patients have been on their current antidepressants. The smaller the number of months since receiving their diagnosis, the more likely the patients were to indicate that they did not know how to deal with possible medication-related adverse reactions (r = -.225, p < .001). Similarly, as the number of months the patients have been taking their current antidepressant decreased (r = -.133, p < .001) the more likely patients were to indicate that they do not know how to deal with possible medication-related adverse reactions. Therefore, psychiatric outpatients in the current study who received their initial diagnosis more recently and consequently have been prescribed their current antidepressant medication more recently. These individuals were more likely to indicate that they did not know how to deal with possible antidepressant medication-related adverse reactions. These trends may reflect that time is sometimes needed for the patients to adjust to taking antidepressant medication or to learn coping strategies to manage the potential medication-related adverse reactions. Alternatively, patients who have received their initial diagnosis a longer time ago and have been taking their current antidepressant treatment for a longer duration may have gained knowledge and experience in in how to cope with the related adverse reactions.

Finally, patients' knowledge of how to cope with possible adverse reactions from medications had a significant correlation to their total MMAQ-8 scores (t(375) = 20.135, p < 0.001). Psychiatric outpatients who reported that they did not know how to cope with the possible antidepressant medication-related adverse reactions had a significantly lower mean score on the MMAQ-8 (M = 5.14, SD = 2.25) compared to patients who reported that they knew how to deal with potential antidepressant medication-related adverse reactions (M = 6.05, SD = 1.76). This may be an area of opportunity for adherence interventions to target, and medication-related psycho-education and support may prove beneficial in increasing adherence in this population.

Figure 10: Knowledge to cope with adverse reactions and adherence levels of psychiatric outpatients in Gauteng (n=377)



In summary, although the majority of medication-related variables such as class of antidepressant (p = .289), daily dosage (p = .406), duration of current antidepressant treatment (p = .052) or the experience of medication-related adverse reactions (p = .51) were not significantly correlated with low adherence in the current study, a statistically significant correlation was observed in patients who reported that they do not know how to deal with potential antidepressant medication-related adverse reactions ($p < 0.001$). Specifically, psychiatric patients who indicated they did not know how to cope with the possible antidepressant medication-related adverse reactions had a significantly lower mean score on the MMAQ-8 (M = 5.14, SD = 2.25), compared to patients who reported they know how to cope with the possible antidepressant medication-related adverse reactions (M = 6.05, SD = 1.76). Additionally, when the Bonferroni-Holm correction for multiple comparisons (Holm, 1979) calculation was considered, this still resulted in a statistically significant correlation, as it is smaller than p = .002.

The results therefore indicate that we fail to reject the following study null hypotheses concerning medication-related variables:

H_{11}: Class of antidepressant is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{12}: Daily dosage is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{13}: Duration of current treatment is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

H_{14}: Current experience of adverse reactions is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

Alternatively, the researcher rejects the study null hypothesis namely, H_{15} that states knowledge to cope with adverse reactions is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

This means that we can accept that class of antidepressant, daily dosage, duration of current treatment and current experience of adverse reactions is not significantly correlated with antidepressant adherence rates in the current study sample. However those who reported they do not know how to cope with potential antidepressant medication adverse reactions, scored significantly lower on the MMAQ-8 compared to patients who reported they know how to cope with potential antidepressant medication adverse reactions and therefore knowledge to cope with adverse reactions significantly correlates with antidepressant adherence rates.

4.3.6. Health system-related variables

4.3.6.1. Medical aid and social grant status

The majority of patients indicated that they did have medical aid (67.37%; n=254), and a third of patients do not have medical aid (32.63%; n=123). Additionally, the majority of patients indicated that they do not receive any form of a social grant (93.9%; n=354). Only a very small number of patients (n=23; 6.1%) were recipients of some form of social grant. From the total sample, (n=100; 26.53%), one in four patients indicated that they do not have access to either form of financial support (medical aid or social grant) for mental health care treatment.

Results from the independent sample t-test also revealed that patients who had medical aid support were significantly younger (*M* = 37.83, *SD* = 11.96 years), when compared to those

who did not (*M* = 41.65, *SD* = 13.66 years), *t*(375) = -2.77, *p* = .009. Additionally, those who had social grant support were significantly older (*M* = 47.22, *SD* = 16.62 years) when compared to those who did not (*M* = 38.55, *SD* = 12.19 years), *t*(375) = 3.22, *p* = .001. Finally, there was no statistically significant correlation between patients who had medical aid (*p* = .648), or social grant support (*p* = .782) and total MMAQ-8 scores when compared to patients who did not receive the same kind of financial benefits.

4.3.6.2. Prescribing practitioner

The majority of patients received their prescription for their medication from a psychiatrist (males = 67.53%, n=52; females = 72%, n=216; total = 71.09%; n=268), while nearly a third (28.91%; n=109) indicated that they receive their prescription from a general practitioner. No socio-demographical variables such as mode of completion (*p* = .22), gender (*p* = .44). age group (*p* = .705), main language spoken (*p* = .577), relationship status (*p* = .536), population (*p* = .767), living arrangements (*p* = .562), employment status (*p* = .482), level of education (*p* = .825), or if they were the beneficiaries of medical aid or social grant support (*p* = .916 and *p* = .208, respectively) were significantly correlated with patients' prescribing practitioners.

Patients' prescribing practitioner did not have a significant correlation with the majority of DSM-IV-TR Axis I and II diagnoses, except for Bipolar Mood Disorder (BMD), and Borderline Personality Disorder (BPD). Patients diagnosed with BMD were significantly more likely to receive their prescribed treatment from a psychiatrist (24.4%) than form a general practitioner (3.96%), $\chi 2$ (1) = 16.125, $p < .001$. Similarly, patients who were diagnosed with BPD were also significantly more likely to receive their prescribed treatment from a psychiatrist (4.24%) than form a general practitioner (0%), $\chi 2$ (1) = 16.125, $p < .001$). In addition, patients who reported that they were hospitalised for their psychiatric condition within six months prior to the study were significantly more likely to receive their medication from a psychiatrist $\chi 2$ (1) = 14.803, $p < .001$, as well as patients who made use of private health care services $\chi 2$ (1) = 6.719, *p* = .009.

In addition, there were no significant correlations observed between patients' prescribing practitioners and any drug category, specific pharmacologic treatment class or other medication-related information such as number of medications prescribed or current experience of adverse reactions. Finally results from the independent t-test indicated that there was no significant correlation between patients who receive their prescribed medication from a psychiatrist (*M* = 5.6, *SD* = 2.09) compared to those who receive their

treatment from a general practitioner, and their total MMAQ-8 scores (*M* = 5.4, *SD* = 2.05, *t*(375), = 1.221, *p* = .502). These findings will also be discussed in greater detail in the following chapter.

4.3.6.3. Health care system type

Participants were asked if they make use of a public or a private funded health care service. Three quarters of patients indicated that they receive their prescription of antidepressant medication from a private health care provider (75.33%; n=284), while one in four (24.67%; n=93) indicated they receive their antidepressant medication from a public/ government health care provider. No socio-demographical variables such as mode of completion (*p* = .332), gender (*p* = .138), main language spoken (*p* = .072), relationship status (*p* = .079), race grouping (*p* = .09), or living arrangements (*p* = .341), were significantly correlated with health care system type used by patients. However, patients older than 60 years of age were significantly more likely to make use of public health care services (16.1%) compared to private health care users (3.9%) of the same age ($\chi 2$ (4) = 19.555, *p* = .022. Additionally, patients who were unable to work were significantly more likely to make use of public health care services compared to patients who were employed ($\chi 2$ (5) = 16.164, *p* = .006. Patients who indicated that they did not have medical aid support were significantly more likely to make use of public health care services (49.5%) compared to patients who reported that they made use of private health care services ($\chi 2$ (1) = 15.92, *p* = .001. Finally, patients who indicated that they received social grant support were also significantly more likely to make use of public health care services (19.4%) compared to patients who reported that that they made use of private health care services s ($\chi 2$ (1) = 37.858, *p* = .001. These results will be discussed in greater detail in the following chapter.

The type of health care service patients made use of (private or public), did not have any significant correlations with any diagnostic information or clinical-related variables such as type and number of DSM-IV-TR diagnoses, hospitalisation within six months prior to the study, or perceived difficulty of condition. In addition, there were no significant correlations observed between the two types of health care systems and the majority of drug categories or specific medication classes.

However, the prescription of specific sedative hypnotic-, anxiolytic-, antidepressant-, and anti-epileptic medications did show significant correlations with the type of health care services patients reported making use of. More specifically, patients who made use of private health care services (7%) were significantly more likely to receive a prescription for

Zolpidem (a sedative hypnotic) when compared to public health care users (1.1%), ($\chi 2$ (3) = 10.348, p = .016). Additionally, although the proportion of patients who received a prescription for Sertraline, an SSRI type antidepressant, who made use of private health care services (13.7%) was much larger than public health care users receiving the same treatment (5.4%), this difference only approached statistical significance ($\chi 2$ (6) = 10.702, p = .052). In addition, public health care patients were significantly more likely to receive a prescription for Buspirone (3.2%), an anxiolytic medication, ($\chi 2$ (1) = 5.511, p = .019, Amytripteline (11.8%), a tricyclic antidepressant medication, ($\chi 2$ (3) = 11.826, p = .008, Lithium (9.7%), an antidepressant, ($\chi 2$ (1) = 10.494, p = .003. and Clonazepam (8.6%), an anti-epileptic medication, ($\chi 2$ (7) = 19.665, p = .006, when compared to private health care users receiving the same treatment (0.4%, 3.9%, 2.1% and 2.1% respectively). These findings may be the result of the difference in access and availability of specific psychotropic medications found across the public and private health care settings. Typically, the options to prescribe a greater variety of psychotropic medication are limited in the local public setting. No other medication related variables significantly correlated with patients' type of health care system. Finally results from the independent t-test indicated that there was no significant correlation between private (M = 5.68, SD = 2.05) compared to public health care system users, and their total MMAQ-8 scores (M = 5.3, SD = 2.1, t(375), = .1.95, p = .163).

4.3.6.4. Perceived need for support

Participants were asked if they needed additional support to help them stay adherent to their medication regime. More than one in four patients (27.85%; n=105) indicated that they felt they did need additional support. There were no significant correlations observed between patients who indicated that they required additional support to adhere to their medication regime and any of the socio-demographical variables such as age, gender, race or home language. There were also no significant correlations observed between patients who indicated that they required additional support to adhere to their medication regime and any individual DSM-IV-TR diagnosis or the majority of other clinical variables.

However, the number of months since patients have received their main diagnosis (t(375) = 6.606, p = .011), as well as the number of months they have been on their current antidepressant medication (t375) = 4.345, p = .038), were significantly correlated with patients' reported need for additional adherence support. Specifically, patients who reported that they need additional support to help them stay adherent to their antidepressant medication had received their diagnosis significantly more recently (M = 70.91, SD = 87.95 months) compared to patients who reported that they did not need additional support to help

them stay adherent to their treatment regimen (*M* = 103.78, *SD* = 101.17). Furthermore, patients who reported that they need additional support to help them stay adherent to their medication had been on their current antidepressant medication for a significantly shorter time period (*M* = 45.75, *SD* = 71.41 months) compared to patients who reported that they did not need additional support to help them stay adherent to their antidepressant treatment (*M* = 63.41, *SD* = 84.35).

Finally, patients who reported that they need additional support to help them stay adherent to their medication (*M* = 4.24, *SD* = 2.21) had a significantly lower MMAQ-8 score $t(375) = 13.001$, $p < 0.001$) compared to patients who reported that they do not need additional support (*M* = 6.1, *SD* = 1.78) to help them stay adherent to their medication had been on their current antidepressant medication (*M* = 6.1, *SD* = 1.78). This may be an area of opportunity for adherence interventions to target, and psycho-social support may prove beneficial in increasing adherence in this population, and is discussed in the following chapter.

In summary, although the majority of health system-related variables such as medical aid benefit ($p = .648$) or social grant status ($p = .782$), prescribing practitioner ($p = .502$), or type of health care service use ($p = .163$) were not significantly correlated with low adherence in the current study, a statistically significant correlation was observed in patients who reported that they need additional support to stay adherent to their antidepressant medication regime ($p < 0.001$). Specifically, psychiatric patients who reported they did need additional support to help them stay adherent to their medication had a significantly lower MMAQ-8 score (*M* = 4.24, *SD* = 2.21) compared to patients who reported that they did not need additional support to help them stay adherent to their medication (*M* = 6.1, *SD* = 1.78).

Additionally, when the Bonferroni-Holm correction for multiple comparisons (Holm, 1979) calculation was considered, this still resulted in a statistically significant correlation, as it is smaller than $p = .002$. Therefore, the results indicate we fail to reject the following study null hypotheses concerning health system-related variables:

H_{16}: Medical aid is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa

H_{17}: Social grant is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa in this sample of psychiatric outpatients in Gauteng Province of South Africa

H_{18}: Prescribing practitioner is not significantly correlated with antidepressant adherence in this sample of psychiatric outpatients in Gauteng Province of South Africa

H_{19}: Health care service type is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa

However, the researcher rejects the study null hypothesis H_{20} that states requiring additional support is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa.

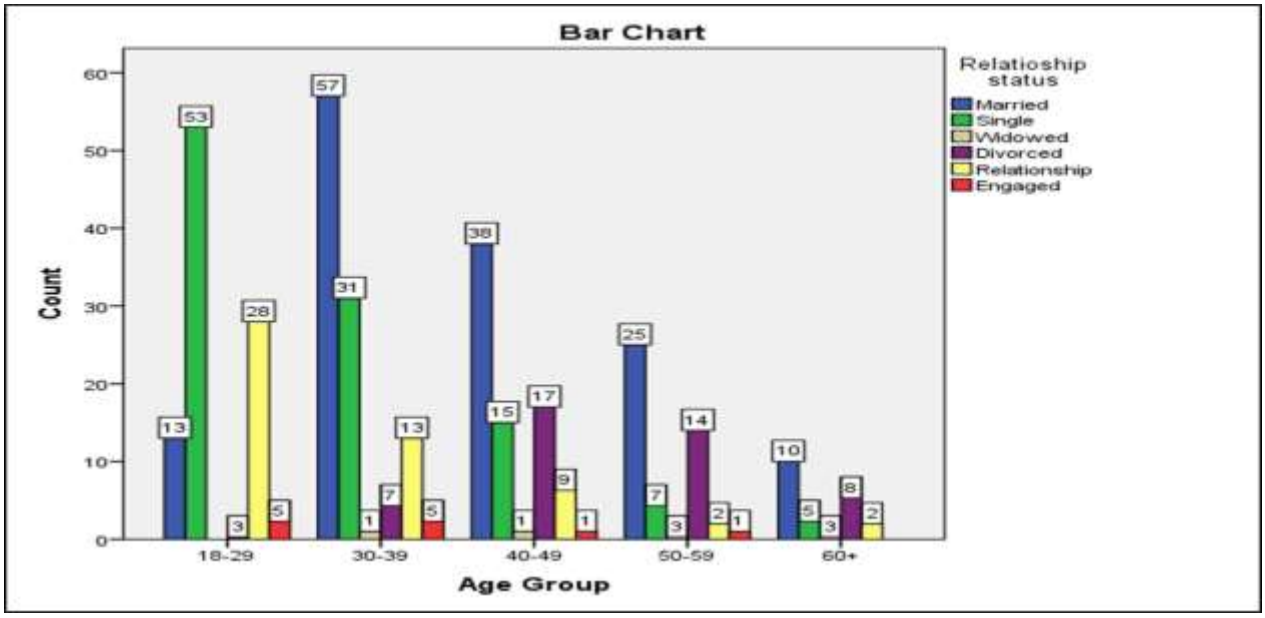
This means that medical aid, social grant, prescribing practitioner and health care service type, do not correlate significantly with adherence rates to antidepressant medication in the current study sample. However, those who reported they required additional support to help them stay adherence to their antidepressant medication scored significantly lower on the MMAQ-8 compared to patients who reported they do not need additional support to help them stay adherence to their antidepressant medication. Therefore the need for additional support correlates significantly with low antidepressant adherence rates in the current study sample.

4.3.7. Moderating variables

4.3.7.1. Relationship Status

Figure 11 illustrates the number of patients in different relationship statuses by age groups.

Figure 11: Distribution of sample of psychiatric outpatients in Gauteng by relationship status and age group (n=377)



The majority of patients (37.93%; n=143) were married. Nearly a third of patients (29.44%; n=111) were single. Results from the one-way ANOVA revealed a statistically significant differences in the mean age of patients and relationship status (F (5, 371) = 21.84, p = 0.001). A Tukey post-hoc test revealed that the mean age was statistically significantly lower among those who were married (M = 42.15, SD = 10.77 years, p = .007), single (M = 33.47, SD = 11.57 years, p = .003), in a relationship (M = 32.89, SD = 11.28 years, p = .001), or engaged (M = 32.92, SD = 9.37 years, p = .001), when compared to widowed (M = 54.38, SD = 10.09 years) or divorced (M = 48.61, SD = 11.96 years). There were no statistically significant differences in the mean age of divorced or widowed patients (p = .757). Additionally, there was no significant difference between relationship status and total MMAQ-8 scores (p = .278).

4.3.7.2. Living arrangements

The majority of patients indicated they live with a family member (43.77%; n=165). Nearly a third of patients (29.71%; n=112) live with a partner, and one in five patients indicated that they live on their own (21.49%; n=81). Results from the one-way ANOVA revealed a statistically significant difference in the mean age of patients and living arrangements (F (3, 373) = 9.44, p = .001). A Tukey post-hoc test revealed that the mean age was statistically significantly lower among patients who were living with family (M = 35.64, SD =11.8 years, p = .001), when compared to patients who were on their own (M = 43.47, SD = 13.84 years), or had other living arrangements (M = 34.94, SD = 12.43 years). Additionally, there was no significant difference between the different living arrangement categories and total MMAQ-8 scores (p = .482).

4.3.7.3. Employment status

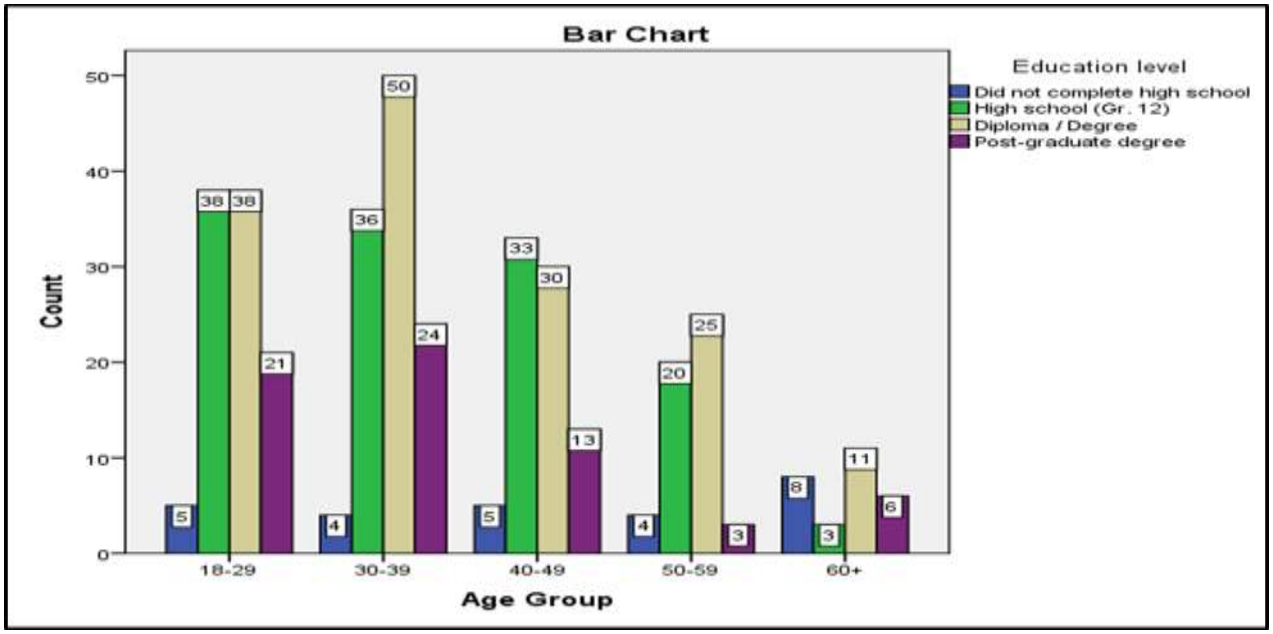
More than half of patients (56.5%; n=213) were working full-time, and more than one in ten patients were unemployed and looking for work (12.47%; n=47). Results from the one-way ANOVA revealed a statistically significant difference in the mean age of patients and employment status ($F($ 5, 371) =32.16, p = .001). A Tukey post-hoc test revealed that the mean age was statistically significantly lower among students (M = 24.27, SD = 7.42 years, p = .001), when compared to all other employment levels. Additionally, patients who were disabled or unable to work were significantly older (M = 58.7, SD = 11.37 years, p = .001) when compared to all other employment levels. However, there were no statistically

significant differences in the mean age of patients who were employed full-time and half-time (p = .1), unemployed and looking for work (p = .153), and those who were unemployed and not looking for work (p = .136). Additionally, there was no significant difference between employment status and total MMAQ-8 scores (p = .294).

4.3.7.4. Education level

The majority (40.85%; n=154) of patients had obtained a diploma or degree, while a third of patients (34.48%; n=130) completed high school, and one in six patients (17.77%; n=67) completed a post-graduate qualification. Results from the one-way ANOVA revealed a statistically significant difference in the mean age of patients and level of education (F (3, 373) = 3.2, p = .023). A Tukey post-hoc test revealed that the mean age was statistically significantly higher among those who had not completed high school (M = 45.69, SD = 17.37 years), when compared to patients who had completed high school (Gr. 12), (M = 37.7, SD = 12 years, p = .017), who had a diploma or degree (M = 39.61, SD = 11.86, p = .013) or a post-graduate degree (M = 37.94, SD = 12.94 years, p = .039). These results will be discussed in greater detail in the following chapter. Additionally, there was no significant difference between education level and total MMAQ-8 scores (p = .838). Finally, patients who completed high school or any higher education level were also significantly less likely to be the recipients of social grant support, when compared to patients who completed some high school or less (p = .23).

Figure 12: Distribution of sample of psychiatric outpatients in Gauteng by education level and age group (n=377)



4.3.7.5. Perceived stigma

Participants were asked if they were afraid of what some people may think about them taking antidepressant medication. More than half of the patients (n=200; 53.05%) indicated that they had fears of stigma relating to the pharmacological treatment of their psychiatric condition. There were no significant associations observed among patients who reported that they had fears of stigma relating to the pharmacological treatment of their psychiatric condition and the majority of socio-demographical variables. However, patients who indicated that they are recipients of a social grant (9%) were significantly less likely to indicate that they were afraid of what some people may think about them taking antidepressant medication compared to patients who indicated that they do have a fear of what others may think of them taking antidepressant medication for their psychiatric condition ($\chi 2$ (2) = 5.03, p = .025). Patients who receive social grant benefits may be more exposed to other patients in similar circumstances, compared to other (privately insured) patients who may be more isolated during their treatment process. Social grant recipients typically congregate to receive their benefits at a particular location on a specific day. This opportunity to meet others in similar circumstances may be missed by patients who do not receive social grant benefits, and may reflect the findings above. However, further investigation is required to determine the causal relationship between these variables.

Finally, patients who reported that they fear social stigma had a significantly lower MMAQ-8 score (M = 5.11, SD = 2.21) compared to patients who did not (M = 6.1, SD = 1.78), t(375) = 14.911, p < 0.001. This may be an area of opportunity for adherence interventions to target, and community engagement and advocacy, psycho-social support and education may prove beneficial in increasing adherence in this population, and will be discussed in greater detail in the following chapter.

In summary, although the majority of moderating variables such as employment status (p = .294), level of education (p = .838), relationship status (p = .278) or living arrangements (p = .482) were not significantly correlated with antidepressant adherence rates in the current study, a statistically significant correlation was observed in patients who reported that they had fears of stigma relating to the pharmacological treatment of their psychiatric condition (p < 0.001). Specifically, psychiatric patients who indicated they did have fears of stigma relating to the pharmacological treatment of their psychiatric condition had a significantly lower MMAQ-8 score (M = 5.11, SD = 2.21) compared to patients who reported that they did not have fears of stigma relating to the pharmacological treatment of their psychiatric condition (M = 6.1, SD = 1.78). Additionally, when the Bonferroni-Holm correction for multiple

comparisons (Holm, 1979) calculation was considered, this still resulted in a statistically significant correlation, as it is smaller than $p = .002$.

Therefore, the results indicate we fail to reject the following study hypotheses concerning moderating variables:

H_{21}: Employment status is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa

H_{22}: Education level is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa

H_{23}: Relationship status is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa

H_{24}: Living arrangements is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa

However, the researcher rejects the study null hypothesis H_{25} that states that perceived stigma is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa. Specifically, those who reported they fear social stigma scored significantly lower on the MMAQ-8 compared to patients who reported they do not fear social stigma related to their antidepressant treatment. This means that employment status, education level, relationship status, and living arrangements do not significantly correlate with antidepressant adherence levels in the current study sample. However, perceived stigma correlated significantly with adherence rates to antidepressant medication in the current study sample.

4.4. Chapter summary

In this chapter the reader was first introduced to the study results with a description of the socio-demographic profile of psychiatric outpatients who took part in the current study. The majority of patients were White (79.36%), female (79.58%), married (37.93%) and living with family (43.77%), were younger than 40 years of age (57.3%), English speaking (57.56%), obtained a diploma or degree (40.85%), working full-time (56.5%) and had medical aid (67.37%). Slightly less than half of the total sample (47.7%) reported with low antidepressant medication adherence rates. The results from the current study suggests that non-adherence to antidepressant medication in this sample of psychiatric outpatients reflect that of findings reported in both international and local contexts. This lends strength to the current

study argument that non-adherence to antidepressant medication presents a significant concern in the local psychiatric outpatient setting. Table 9 presents the study hypotheses could be accepted and rejected based on the analysis of the results. These results are discussed in greater detail in the following chapter.

Table 9: Summary of study hypotheses accepted and rejected

Variable groups	Individual variables	Significance level (*p* value)
Patient-related variables		
	$H_{1:}$ Age	.224
	$H_{2:}$ Gender	.841
	$H_{3:}$ Race	.5
	$H_{4:}$ Home Language	.672
	$H_{5:}$ Treatment beliefs	.006
Illness-related variables		
	$H_{6:}$ Main DSM-IV-TR diagnosis	.095
	$H_{7:}$ Age of onset of diagnosis	.52
	$H_{8:}$ Illness duration	.548
	$H_{9:}$ Prior hospitalisation (6 months)	.274
	$H_{10:}$ Perceived difficulty of condition	.218
Treatment-related variables		
	$H_{11:}$ Class of antidepressant	.289
	$H_{12:}$ Daily dosage	.406
	$H_{13:}$ Duration of current treatment	.052
	$H_{14:}$ Current experience of adverse reactions	.51
	$H_{15:}$ Knowledge to cope with adverse reactions	.001*
Health system-related variables		
	$H_{16:}$ Medical aid	.648
	$H_{17:}$ Social grant	.782
	$H_{18:}$ Prescribing practitioner	.502
	$H_{19:}$ Health care service type	.163
	$H_{20:}$ Require additional support	.001*
Moderating variables		
	$H_{21:}$ Employment status	.294
	$H_{22:}$ Education level	.838
	$H_{23:}$ Relationship status	.278
	$H_{24:}$ Living arrangements	.482
	$H_{25:}$ Perceived stigma	.001*

*Significant at Bonferoni-Holm correction

Table 9 reports on the results of the statistical tests used to determine if there were any significant correlations between adherence rates and the individual variables used to test the study hypotheses. Although treatment beliefs (H_5) resulted in a significant correlation ($p <$ .006), the Bonferroni-Holm correction for multiple comparisons (Holm, 1979) calculation was considered and resulted in a statistically insignificant correlation, as it is greater that $p =$

.002. Therefore, we also fail to reject H_5. There was a strong positive correlation between adherence rates and duration of current treatment (i.e., younger patients were more likely to report with lower levels of adherence), (p = .052), this was statistically insignificant.

There was a statistically significant correlation between adherence rates and knowledge to cope with adverse reactions (H_{12}), (p < 0.001). Specifically, psychiatric patients who indicated they did not know how to cope with the possible antidepressant medication-related adverse reactions had a significantly lower mean score on the MMAQ-8 (M = 5.14, SD = 2.25), compared to patients who reported they know how to cope with the possible antidepressant medication-related adverse reactions (M = 6.05, SD = 1.76). Additionally, when the Bonferroni-Holm correction for multiple comparisons (Holm, 1979) calculation was considered, this still resulted in a statistically significant correlation, as it is smaller than p = .002. For this reason we reject H_{12} that states knowledge to cope with adverse reactions is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa. There was a statistically significant correlation between adherence rates and require additional support (H_{12}), (p < 0.001). Specifically, psychiatric patients who reported they did need additional support to help them stay adherent to their medication had a significantly lower MMAQ-8 score (M = 4.24, SD = 2.21) compared to patients who reported that they did not need additional support to help them stay adherent to their medication (M = 6.1, SD = 1.78). Additionally, when the Bonferroni-Holm correction for multiple comparisons (Holm, 1979) calculation was considered, this still resulted in a statistically significant correlation, as it is smaller than p = .002. For this reason we reject H_{20} that states requiring additional support is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa. There was a statistically significant between adherence rates and perceived stigma (H_{25}) ((p < 0.001). Specifically, psychiatric patients who indicated they did have fears of stigma relating to the pharmacological treatment of their psychiatric condition had a significantly lower MMAQ-8 score (M = 5.11, SD = 2.21) compared to patients who reported that they did not have fears of stigma relating to the pharmacological treatment of their psychiatric condition (M = 6.1, SD = 1.78). Additionally, when the Bonferroni-Holm correction for multiple comparisons (Holm, 1979) calculation was considered, this still resulted in a statistically significant correlation, as it is smaller than p = .002. For this reason we reject H_{25} that states perceived stigma is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa. There was no statistical significant correlations observed between adherence rates and any other variables identified, and therefore fail to reject the remaining study hypotheses. These findings are discussed in the following chapter.

CHAPTER 5

DISCUSSION AND RECOMMENDATIONS

5.1. Introduction

In the previous chapter the researcher discussed the results after statistical analysis of the data collected from a sample of psychiatric outpatients living in the Gauteng Province of South Africa. In this final chapter, the rates of non-adherence to antidepressant medications in this sample, as well as the variables that were found to be significantly associated with these rates are discussed. This chapter initially provides a brief description of the current study sample, following a discussion of the results relating to research findings in the literature. Recommendations based on the findings and suggestions regarding possible directions for future studies are also provided. An overview of the limitations identified in the study is provided and a brief summary concludes the chapter.

5.2. Summary of research design

An observational, descriptive multi-mode survey research approach was carried out to systematically collect data through three methods from a sample of psychiatric outpatients using a structured non-clinical questionnaire. Participants were eligible if they were a) 18 years or older, b) prescribed at least one antidepressant medication, c) not currently hospitalised i.e. treated as an out-patient, and d) living in Gauteng Province, South Africa at the time of the study. The survey questionnaire included socio-demographical information, a clinical- and medication profile as well as the 8-item Morisky Medication Adherence Questionnaire (Morisky et al., 1986). A convenience sampling method was used to select patients through an invitation sent via personal email or telephone call. This sampling method was selected as it allowed the researcher to obtain basic data and trends regarding non-adherence to antidepressant medication without the complications of using a randomised sample, as well as reduce relative costs and time. It also offers a fair degree of external validity with regards to the context (local), and time (current), and sample (patients).

Data collection commenced in October 2014, after ethical approval was obtained from the Department of Psychology Ethics Committee of UNISA and the South African Depression and Anxiety Group. Data collection was completed in December 2014, and was cleaned and coded according to a structured coding sheet (Appendix III).

Data from a total of n=377 patients were included in the final analysis and was reported on anonymously and in a manner that didn't allow for individual participants to be identified. All categorical and numerical variables were analysed and described using standard descriptive and correlational methods using SPSS® (22) software.

5.3. Discussion and conclusions

5.3.1. Discussion of findings

The majority of the patients were female (79.58%; n=300), between 18 and 39 years of age (57.3%; n=116), English speaking (57.56%; n=217), married (n=143; 37.93%) and living with their family (n=165; 43.77%), completed a diploma or degree (40.85%; n=154) and were employed full-time (56.5%; n=213), as well as having access to medical aid support (67.37%; n=254). The majority of patients completed the survey questionnaire online (81.43%; n= 307). The large proportion of online responses in this study could be attributable to several factors: firstly, the primary recruitment method was through online advertising on the SADAG website and electronic newsletter providing a link to the survey questionnaire, and may have facilitated convenience; secondly, compared to other modes of completion, the online provided more anonymity to participants, which may have been more preferable to the targeted population; thirdly, the majority of participants indicated that they are employed and working full-time and therefore, may have less time available to participate in other methods of data collection and; fourthly, the majority of the sample (57.3%) were in the younger age categories (19 – 39 years), and may feel less intimidated and more accustomed to the use of electronic devices. Results from the current study revealed that the mean age was statistically significantly lower among those who completed the survey online (M = 37.5, SD = 11.59 years) compared to those who completed the questionnaire telephonically (M = 45.16, SD = 3.43, p = .001), or manually (M = 48.16, SD = 18.01 years, p = .001), supporting the current study findings above.

Results indicated that those who completed the survey online scored a significantly lower (p = .006) score on the MMAQ-8 compared to those who completed it manually or telephonically. This does not necessarily indicate that individuals who preferred the online mode of administration are less adherent to antidepressant medication when compared to other modes of administration, but likely reflect that low adherence in this study is more likely to be reported through the online mode of survey administration which may offer patients a greater degree of anonymity compared to manual or telephonic modes. However, there was

no statistically significant correlation observed between age and antidepressant adherence in the current study (p = .224).

The gender distribution of patients in this study was 79.58% (n=300) female, and 20.42% (n=77) male, with a 3.9:1 ratio. In South Africa, women have higher rates of mental health treatment seeking overall, and especially for mood disorders (Seedat et al., 2009). Furthermore, the prevalence of major depression in South Africa is significantly higher among females (95% Confidence Interval (CI)), for both lifetime prevalence (1.75 times more likely, (CI) 1.3 – 2.4), and 12-month prevalence (2.17 times more likely, (CI) 1.5 – 3.2) when compared to males (Tomlinson et al., 2009). These authors provide evidence that women are more likely to be diagnosed with major depression, therefore requiring mental health treatment, as well as being more likely to seek out mental health services for this condition to receive treatment. Since antidepressants are used as first-line pharmacological treatment in conditions such as major depression (The South African National Department of Health, 2012; Emsley et al., 2013), but also several anxiety disorders (Royal College of Psychiatrists, 2012), an indication of the gender-based use of mental health services could also be inferred from information on medication prescription data. A drug utilisation review that focussed specifically on antidepressant use in South African by privately insured mental health care users (Roux, 2014) found that only half of the men in the data set were receiving antidepressants when compared to women. Findings by Laher (2013) also concluded that females formed the majority of receivers (66%) of antidepressants in a drug utilisation review. These gender differences in mental health service use and treatment between men and women may influence the skewed representation of women in this current survey. If more women than men access mental health services in South Africa, it is not surprising to find that more females would represent the large majority in a study investigating the adherence rate of antidepressant medications. These findings may account for the disproportionately large number of females found in the current study.

The racial distribution of patients in the current study was also disproportionately in favour of White South Africans. Nearly four out of every 5 patients (79.58%; n=300) were White. Slightly more than one in ten patients (11.94%; n=45) identified as Black South Africans. A study that investigated the mental health service use of South Africans with mood, anxiety and substance abuse disorders (Seedat et al., 2009) found a significant difference between racial groups with respect to the type of mental health services accessed. The study found that Black patients were more likely to have accessed the complementary and alternative medicine (CAM) sector, while White patients were more likely than Black patients to have seen a psychiatrist or other mental health professionals such as psychologists. In South Africa, psychotropic medication such as antidepressants must be prescribed by a

psychiatrist or medical doctor. The low rates of Black South Africans that access these services, and higher rates of White South Africans that do, may explain the large discrepancy between these two groups in the current study sample. This survey questionnaire makes specific reference to medical doctors or psychiatrists only when asking about their prescribing practitioner, and no alternative options were recorded. Previous findings from the local context also observed that White females and males and Coloured females had the highest likelihood of seeking mental health services (Seedat et al., 2009), which may explain the unrepresentative racial distribution in this study. It is therefore likely that younger White females in the current study who are working and have had an influence on their access to medical aid study may have been more likely to access professional care. Access to these services was observed to decrease with age, and is reflected in employment status.

5.3.1.1. Discussion of medication adherence

Nearly half of the patients indicated that they do sometimes forget to take their medication (n=183; 48.54%). Other common reasons for non-adherence to antidepressant medication measured by the MMAQ-8 includes: “feel(ing) hassled about sticking to their antidepressant treatment plan”, (n=138; 36.6%), “cut(ting) back or stopped taking antidepressant medication without telling their doctor because they felt worse when they took it”, (n=123; 32.62%), or “stop(ped) taking antidepressant medication when feeling like symptoms were under control” (n=114; 30.2%). The average score for the total sample of n=377 psychiatric outpatients in the current study was 5.59 (*SD* =2.08), suggesting low levels of antidepressant adherence rates in general. More concerningly, when considering the distribution of the adherence rates in the sample, nearly half of the total sample (n=180; 47.7%) reported with low antidepressant medication adherence rates. In addition, more than one in ten patients reported non-adherence to their antidepressant medication the day prior to completing the survey questionnaire (n=52; 13.8%), while more than a third of psychiatric outpatients (n=140; 37.13%) reported non-adherence in the two weeks preceding data collection.

The results from the current study suggests that non-adherence to antidepressant medication in this sample of psychiatric outpatients reflect that of findings reported in both international and local contexts (Morris & Schulz, 1992; Sacket & Snow, 1979; Donovan, 1995; Buckley, Janse van Rensburg, 2007; Foster & Patel, 2009; Bulloch & Patten, 2010; Mahaye, et al., 2012). This lends strength to the current study argument that non-adherence to antidepressant medication presents a significant concern in local psychiatric outpatient

settings. Non-adherence to antidepressant medication is an important predictor of relapse and recurrence with significant implication for long-term prognosis (Yau et al., 2014), and is associated with decreased reduction in symptoms, as well as increased risk of suicide (Weiss & Gorman, 2005).

Adherence is a key determining factor of pharmacological treatment efficacy in psychiatry, and poor adherence diminishes the clinical and therapeutic benefit of these therapies (WHO, 2003). The results found in this sample in Gauteng highlighted the high rates of non-adherence by determining the scope of the problem, as well as identifying factors that influence these rates. Collaboration and supporting patients' adherence to antidepressant medications throughout their treatment process should be a primary focus area for any who are concerned with providing care to psychiatric patients.

5.3.1.2. Discussion of patient-related variables

Statistical analysis of the data revealed that patients' age in years (p = .15), gender (p = .841), home language (p = .511), and race (p = .5), was not significantly associated with adherence levels in this particular study. The results of these analyses indicate that these specific patient-related variables as measured in this study did not have a significant correlation with antidepressant medication adherence in this sample. A systematic literature review by Zeber and colleagues (2013) on the psychosocial and behavioural factors associated with initial medication non-adherence in both chronic physical and mental disorders observed that gender was not associated with treatment adherence in a majority of the studies. From the twenty-four articles included in the review (published between 1966 and 2011), only five indicated that gender was significantly associated with initial medication non-adherence, four of which in favour of males, and one indicating that females were more adherent than males. Similarly, a local study by Mahaye and colleagues (2012) measured antipsychotic medication adherence in a psychiatric outpatient setting in KwaZulu-Natal Province using the MMAQ-8, and also observed an insignificant association between gender and adherence. However, in contrast with the current study, they found that age (p = .045) and race (p = .055) were significantly correlated with medication adherence rates. However, differences in clinical and treatment characteristics such as diagnosis and prescribed medication may not be comparable to the current study sample characteristics (mostly young and White and female), which is not demographically heterogeneous enough. This may account for the discrepancies between the above observations and findings from the current study.

A systematic review (Zeber et al., 2013) noted that age, gender and race were only significantly associated with initial medication non-adherence in a very small number of the twenty-four studies included in their review (12, 5 and 3 respectively). Observations regarding patient factors such as age, gender and race from the current study seem to be in line with the majority of previous observations made by other investigators (Fischer et al., 2010; Shrank et al., 2006, 2010; Wroth & Pathman, 2006; Fischer, Stedman & Lii J, et al., 2010; Shrank, Hoang, Ettner, et al., 2006; Shrank, Choudhry, Fischer, et al., 2010; Ekedahl & Månsson, 2004), suggesting that these factors may not have a significant correlation with antidepressant non-adherence in this sample. This provides support to the findings from the current investigation. Although findings between various studies have not been consistent, a reasonable explanation for these findings may be that patients included in these studies vary widely across settings and illnesses.

Patients in the current study who indicated they do not believe their psychiatric condition requires the treatment of antidepressants (M = 4.6, SD = 2.42) had a statistically significant lower score on the MMAQ-8 when compared to patients who indicated they do believe their psychiatric condition requires the treatment of antidepressants (M = 5.71, SD = 2), (t(375), = 3.364, p < .006). A qualitative study by Sharif, et al. (2003) investigating reasons for non-adherence to treatment in psychiatry in the South African context, reported that patients' beliefs about treatment and its efficacy were commonly given as reasons for non-adherence. Furthermore, Janse van Rensburg and colleagues (2014) also reported that one of the common reasons psychiatric outpatients from a public, regional referral hospital in Gauteng gave for not adhering to their medication regime, was patient beliefs about medication. However, they did not report whether it had a significant correlation with medication adherence. Males from the current study (88.3%; n=68) were also found to be significantly less likely to indicate that their condition requires treatment with medication ($\chi 2$ = 5.274, p = .022) when compared to females (95.3%; n=286).

Although the majority of patient-related variables such has age (p = .224), gender (p = .841), race (p = .5) or home language (p = .672) were not significantly correlated with adherence rates in psychiatric outpatients in the current study sample, patients' beliefs about their treatment did have a significant correlation with low adherence rates (p = .006). Specifically, psychiatric patients who indicated they did not believe that their psychiatric condition requires the treatment of antidepressant medication (M = 4.6, SD = 2.42), reported with lower adherence rates when compared to patients who indicated they believe that their psychiatric condition requires the treatment of antidepressant medication (M = 5.71, SD = 2). However, when the Bonferroni-Holm correction for multiple comparisons (Holm, 1979)

calculation was considered, this resulted in a statistically insignificant correlation, as $p = .006$ is greater than $p = .002$.

In the current study, none of the patient variables, namely age ($p = .224$), gender ($p = .841$), race ($p = .5$), home language ($p = .672$) or treatment beliefs ($p = .006$) were statistically significantly correlated with adherence rates in the study sample. We can therefore conclude that we fail to reject the following study hypotheses: H_1, H_2, H_3, H_4, and H_5.

It can be challenging for psychiatric patients who need to navigate the uneven terrain of accessing mental health treatment for a condition that has been highly stigmatised (Sirey et al., 2001). Interventions targeting false illness and medication beliefs may be effective in increasing antidepressant adherence in this sample. Additional focus and study may be required to address gender-specific issues regarding treatment beliefs. This may further increase antidepressant adherence rates among males specifically.

5.3.1.3. Discussion of illness-related variables

Since antidepressants have become the primary treatment modality for depression (Emsley et al., 2013), it was not surprising to see that the majority of patients in this study was diagnosed with MDD (n=225; 59.7%). The average age at which patients received their diagnosis is 30.97 (SD = 12.85 years) and have lived with their diagnosis for an average of 7.88 years.

Patients' adherence levels was not significantly correlated with any illness-related variables such as specific DSM-IV-TR main diagnoses ($p = .095$), any Mood Disorder ($p = .962$), any Anxiety Disorder ($p = .67$), Substance-Related Disorder ($p = .993$), Schizophrenia or Other Psychotic Disorder ($p = .782$), ADHD ($p = .576$) or any Personality Disorder ($p = .914$). Similar insignificant observations regarding other illness-related variables such as the number of diagnosed conditions ($p = .708$), age at which diagnosis was received ($p = .52$), and duration of illness ($p = .548$) were observed when considered in the analysis of the data. Finally, patients' perceived difficulty of their condition was also not significantly correlated with antidepressant adherence ($p = .218$). Similar findings have been made in a psychiatric outpatient setting in the United States and Spain (Tamburrino, Nagel, Chahal, & Lynch, 2009; De Las Cuevas, Peñate and Sanz (2014), noting insignificant associations between the type of mood disorder patients were diagnosed with, or illness severity and medication adherence. Although the two studies (Tamburrino et al., 2009; De Las Cuevas et al., 2014) used different measurements in measuring adherence rates (Medication Adherence Scale

(MAS) and MMAQ-8, respectively). These results suggest that illness-related variables do not have a significant correlation with adherence to antidepressant medication in this sample.

In contrast to the current study, Yau and associates (2014) found that an earlier onset of diagnosis was significantly associated with non-continuous antidepressant use within 6 months of initiating their treatment (p = .034). Additionally, antidepressant medication adherence using the MMAQ-8 among n=403 psychiatric outpatients in Saudi Arabia noted that a shorter duration of illness in and less depression severity was associated with higher adherence levels (Al-Jumah et al., 2014).

The different findings between the studies discussed above and this current investigation could be explained by the differences in health care settings across countries or the prioritisation, level of training or support relating to psychiatric services in general of antidepressant medication adherence. In addition to this, in an outpatient setting, access to services or treatment can become a barrier to utilising services, and mental health literacy and stigma may play a significant role in the presentation of patients' clinical features and profile. Finally, differences between study outcome measurements (clinical rating and adherence scales) and study design, clinical profile and sample sizes may also explain the variation between observations made involving illness-related variables and antidepressant medication adherence.

Patients in the current study who were diagnosed with any DSM-IV-TR Mood Disorder (p = .004) and Schizophrenia (p = .01), as well as the presence of a comorbid Anxiety Disorder (p = .024) were, however, significantly more likely to indicate that their condition makes it difficult for them to perform their daily activities. However, these conditions did not have significant correlations with adherence rates in patients from the current study. Furthermore, the proportion of males in the current study (6.5%; n=5) diagnosed with Schizophrenia or Other Psychotic Disorder was statistically significantly more when compared to the proportion of females (1%; n=3) with the same diagnosis ($\chi 2$ (1) = 8.903, p = .003).

Overall, none of the illness-related variables such has main DSM-IV-TR diagnosis (p = .095), age of onset of psychiatric illness (p = .52), illness duration (p = . 548), perceived difficulty of psychiatric condition (p = . 218) or recent (6 months prior to the study) hospitalisation (p = . 274) were significantly correlated with antidepressant adherence rates in this study sample. We can therefore conclude that we fail to reject the following study hypotheses: H_6, H_7, H_8, H_9, and H_{10}.

5.3.1.4. Discussion of medication-related variables

The most common class of all antidepressants prescribed (n=491) to patients in the current study was SSRI's, specifically Escitalopram, comprising of a third (n=74; 31.36%) of all SSRI's prescribed. Recommendations from the South African Society of Psychiatrists (SASOP) that apply to the current private health care setting in South Africa (Emsley et al., 2013) make reference to Fluoxetine as an initial pharmacological treatment modality for the treatment of Major Depressive Disorder. The National Department of Health (South African Department of Health, 2012) provides treatment guidelines for psychiatric disorders in the published Standard Treatment Guidelines and Essential Medicines List for South Africa, which typically apply to public health care outpatient settings in South Africa (South African Department of Health, 2014), and similarly makes reference to Fluoxetine as first-line treatment for moderate to severe depression. Results from the current study suggest that Escitalopram is the most commonly prescribed antidepressant as well the most commonly prescribed SSRI in this particular sample of psychiatric outpatients. This is somewhat incongruent with these treatment guidelines. However, Fluoxetine was observed to be the second most common antidepressant (and SSRI specifically) prescribed to patients in the current study (n=60; 25.42%). Therefore, there does not seem to be a significant deviation from the recommended treatment guidelines in public and private health care services and antidepressant prescribing practices.

A meta-analysis found that Escitalopram and Sertraline were superior to other antidepressants when considering both effectiveness and safety (Gartlehner, Thieda, Hansen, 2008), which may account for the popular use of this medication observed in the current study. It is worth noting that this meta-analysis had several limitations such as different measuring instruments used, included studies with low methodological quality, different settings (inpatient and outpatient) and clinical profiles (single disorder and comorbid diagnoses). However, other analyses (Thaler et al., 2012; AHRQ, 2014), have found that no SSRI is more superior to the other. Additionally, an international consumer report noted that Escitalopram is more expensive than many other antidepressant drugs, but is now available as less-costly generic formulations in some dosage forms (BestBuyDrugs, 2013). Since the majority of patients in this sample had financial support to access private medical insurance (67.37%; n=254), it would be reasonable to assume that cost may not be a significant problem when prescribing antidepressants in this sample. Additionally, the availability of the medication in a cheaper generic formulation can only serve to increase the amount of patients that can access this particular treatment. This may explain the prevalent use of Escitalopram over Fluoxetine in the current study.

There were no statistically significant correlations observed between adherence levels and the different antidepressant categories. When specific SSRI antidepressants were considered for analysis, patients who were prescribed Venlafaxine had on average the highest mean MMAQ-8 score (8), and patients who were prescribed Paroxetine had on average the lowest mean MMAQ-8 score (5.07). However, there was no statistically significant correlation between specific SSRI antidepressant medications and adherence scores $F(7, 374 = .594, p = .735)$, or any other antidepressant category in this study. The insignificance of this large difference in mean MMAQ-8 scores can be attributed to the low number of patients in this study who were prescribed Venlafaxine (n=1; 0.3%), and may be considered a statistical outlier. Additionally, the duration (in months) which patients have been taking their currently prescribed antidepressant medication was also not significantly correlated with adherence levels (r (377) = 1, p = .052). However, the wide range in duration (1 - 446 months) which patients were taking their antidepressant medication observed in this study may reflect the various phases of treatment (acute, continuation, and maintenance, ranging between 1 and 12 months) at which patients are. A third of patients in the current study (33.2%; n=125) were on their current antidepressants for less than a year. Many of these patients may have volunteered to participate in the study soon after having received a psychiatric diagnosis or referred after being discharged from the hospital. However, more than half of the study sample (52.2%) was on their current medication between one and ten years. This may reflect the chronic nature with which psychiatric conditions present and prolonged treatment is often required (Nolen-Hoeksema, 2011). This means that many patients may suffer a lifetime of depression with episodes of longer duration and increasing severity as time progresses (Keller, Hirschfeld, Demyttenaere, & Baldwin, 2002).

Additionally, there was no significant correlations observed between other medication-related variables such as the number of psychotropic medications (p = .52), number of antidepressants (p = .81) current experience of medication-related adverse reactions (p = .051) or daily dosage (p = .406), and adherence scores.

Finally, although patients who reported current experience of adverse reactions from medications had a lower mean score on the MMAQ-8 (M = 5.35, SD = 2.16) compared to patients who did not report current experience of adverse reactions from medications (M = 5.78, SD = 2), this strong correlation is not considered statistically significant t(375) = 2.536, p = 0.51. However, patients who reported that they do not know how to cope with the possible medication-related adverse reactions had a significantly lower mean score on the MMAQ-8 (M = 5.14, SD = 2.25) compared to patients who reported they did know how to cope with the possible medication-related adverse reactions (M = 6.05, SD = 1.76). This may

be an area of opportunity for adherence interventions to target, and medication-related psycho-education and support may prove beneficial in increasing adherence in this sample.

Although Zeber and his colleagues (2013) observed that some studies did not report a significant correlation with medication-related items and lower adherence levels (Yood, Mazor, Andrade SE, et al., 2008; van Geffen, Gardarsdottir, van Hulten, et al., 2009; Wamala, Merlo, Bostrom, et al., 2007; Wroth et al., 2006), the majority of studies included in their review did observe relationships between poor adherence and various antidepressant treatment characteristics such as the use of tricyclic antidepressants (Akincigil, Bowblis, Levin, Walkup, Jan & Crystal, 2007; Cooper, Bebbington, King et al, 2007; Keller, Hirschfeld, Demyttenaere & Baldwin, 2002), complex treatment regimen (Bucci, Possidente &Talbot , 2003), and the presence of unpleasant adverse reactions (Nemerhof, 2003; Shigemura, Ogawa, Yoshino, Sato, & Nomura, 2010; Zeber et al., 2013).

In general, the review (Zeber et al., 2013) suggests there is a strong correlation between adherence and various aspects of pharmacological treatment. In the current study, only the current experience of adverse reactions (showing a strong but statistically insignificant correlation) and knowledge of how to cope with adverse reactions were highly correlated with adherence levels in this sample of patients. The different findings between the studies discussed above and this current investigation, could be explained by the differences in health care settings across countries or the prioritisation and availability of medication, health literacy and stigma in general of antidepressant medication adherence. In addition to this access to services or treatment, in an outpatient setting, can become a barrier to utilising services, and mental health literacy and stigma may play a significant role in the presentation of patients' clinical features and profile.

Finally, differences between study outcome measurements (clinical rating and adherence scales) and study design, clinical profile, and sample sizes may also explain the variation between observations made involving medication-related variables and antidepressant medication adherence.

Although the majority of medication-related variables such as class of antidepressant (p = .289), daily dosage (p = .406), duration of current antidepressant treatment (p = .052) or the experience of medication-related adverse reactions (p = .51) were not significantly correlated with low adherence in the current study, a statistically significant correlation was observed in patients who reported that they do not know how to deal with potential antidepressant medication-related adverse reactions ($p < 0.001$). We can therefore conclude that we fail to reject the following study hypotheses: H_{11}, $H_{12,}$ $H_{13,}$ and $H_{14.}$

However, the researcher rejects H_{15} that states knowledge to cope with adverse reactions is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa. Specifically, those who reported they do not know how to cope with potential antidepressant medication adverse reactions scored significantly lower on the MMAQ-8 compared to patients who reported they know how to cope with potential antidepressant medication adverse reactions. This may highlight an area of opportunity for adherence interventions to target, and providing appropriate and relevant medication-related psycho-education and support may prove beneficial in increasing adherence in this population. A brief discussion of recommendations that may be of relevance are discussed later in this chapter.

5.3.1.5. Discussion of health system-related variables

There were no significant correlations observed between adherence levels and various health system-related variables such as medical aid or social grant status (p = .648 and p = .782 respectively), prescribing practitioner (p = .502), or type of health care system (p = .163). However, patients who reported needing additional support from their health care system to help them stay adherent to their medication had a significantly lower MMAQ-8 score (M = 4.24, SD = 2.21) compared to patients who did not need the support (M = 6.1, SD = 1.78), $t(375) = 13.001$, $p < 0.001$. Lack of social support has also been reported in literature to be a predictor of non-adherence to antidepressant medication (Voils et al., 2005). However, this particular international study only included a small sample (n=85) from both in- and outpatients aged 59 years or older. This may indicate a need for interventions to increase medication adherence in this sample of psychiatric outpatients, and may be an area of opportunity for adherence interventions to target. Psycho-social and educational support and treatment-specific information may prove beneficial in increasing adherence to antidepressant medication in this sample.

An international review found that health care system factors such as medication costs and co-payments were found to influence adherence rates negatively in chronic illnesses such as arthritis and cancer (Mathes, Jaschinski, & Pieper, 2014). Moosa (2007) also cited the following health system factors that might impact negatively on psychiatric treatment adherence in the local South African context: scarce or poorly developed services; poor staff training and lack of capacity to educate patients and to provide continuity of care; inability to establish community support, and poor liaison between the hospital setting and the outpatient setting. Additionally, Banerjee and Varma (2013) assessed factors that influenced adherence to depression treatment in an outpatient setting in India observed that the

majority of patients were non-adherent due to health facility-related factors (long distance from health care facilities, long waiting hours and unavailability of medication). Although they also measured adherence using the MMAQ-8 (Bengali language), this sample only included patients with unipolar depression, as defined by the ICD-10, and not the DSM-IV-TR classification system used in the current investigation (WHO, 1992; APA, 2000), as well as excluding patients with other comorbid conditions.

The current study did not investigate other health system-related issues such as staff training, the frequency of patient-provider communication, distance from health care facilities, waiting hours or medication availability, and this may warrant further study and exploration. However, since the majority of this sample is, married (n=143; 37.93%), living with their family (n=165; 43.77%), working on a full-time basis (56.5%; n=213), as well as having access to medical aid support (67.37%; n=254) through the private health care system (75.3%; n=284), it suggests that they may not be so susceptible to these health system-related issues. Typically, these patients would have easier access to good quality services and treatment, and avoid long waiting queues characteristic of current public health services. This may lead to a general greater satisfaction with the health system for these patients, and may explain why these variables were not significantly correlated with adherence rates in the current study.

It is not possible to say for certain if the finding of other studies can explain the findings of non-adherence in the current study. These reasons include different and additional measurements and scales, as well as different operational and conceptual definitions. It is not clear whether this is due to differences between populations and health care systems or due to differences in the prescribing practitioners; additional studies is needed to verify these results. From the observations above it appears that health system related variables such as perceived lack of support were significantly associated with adherence levels in patients in this particular study, and may warrant further exploration as well as being a possible target for intervention.

Although the majority of health system-related variables such as medical aid benefit (p = .648) or social grant status (p = .782), prescribing practitioner (p = .502), or type of health care service use (p = .163) were not significantly correlated with low adherence in the current study, a statistically significant correlation was observed in patients who reported that they do not know how to deal with potential antidepressant medication-related adverse reactions ($p < 0.001$). We can therefore conclude that we fail to reject the following study hypotheses: H_{16}, $H_{17,}$ $H_{18,}$ and $H_{19.}$

The researcher however rejects the study null hypothesis H_{20} that states requiring additional support is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa. This finding therefore indicates that those patients who reported that they needed additional support to help them stay adherence to their antidepressant medication scored significantly lower on the MMAQ-8 compared to patients who reported they do not need additional support to help them stay adherence to their antidepressant medication. This may highlight an area of opportunity for adherence interventions to target, and improving access to appropriate psycho-social support services to patients and families, may prove beneficial in increasing adherence in this population. A brief discussion of recommendations that may be of relevance are discussed later in this chapter.

5.3.1.6. Discussion of moderating variables

Moderating factors that may influence adherence rates refer to socio-economic circumstances or settings that affect patients in their particular context. The current investigation observed moderating variables such as relationship status (p = .278), living arrangements (p = .482), employment status (p = .294) and education level (p = .838). The availability of social support in the form of family, friends, or caregivers to assist or supervise treatment and recovery, and higher levels of health literacy and stable living conditions are likely to contribute to adherence to treatment in outpatient settings (Moosa, 2007).

Pampallona and colleagues (2002) summarised literature from 1990 – 1999, and concluded that although patient education was commonly assessed for its impact on treatment adherence, studies did not show consistent findings. Although lower levels are generally associated with poorer treatment adherence, findings have been mixed and suggested that education level and its impact on adherence are still not clearly understood (Pampallona et al., 2002). More recently, a latent analysis of n=228 participants with depression and hypertension found that education level was not significantly correlated with adherence levels, whereas relationship status indeed was significantly correlated with adherence levels (Bogner & de Vries, 2008).

Overall, socio-demographic and cultural characteristics do not seem to substantially influence patient adherence to antidepressants in the current study. In a study conducted by Sirey and associates (2001), they noted that race, marital status, and living arrangements (i.e., alone versus with another person) were not significant predictors of adherence to treatment in a sample of n=134 patients with MDD. Similarly, a separate study investigated

reasons for premature discontinuation of treatment with SSRIs in n=406 patients with MDD, and reported that treatment non-adherence was not significantly associated with race, marital status, or education (Goethe, Woolley, Cardoni, Woznicki & Pie, 2007). However, in the current study, patients who reported that they fear social stigma had a significantly lower MMAQ-8 score (M = 5.11, SD = 2.21) compared to patients who did not (M = 6.1, SD = 1.78), $t(375) = 14.911$, $p < 0.001$. Lower perceived stigma was previously found to be significantly related (p = .05) to better treatment adherence in patients with MDD (Sirey et al., 2001). Stigma related to mental health and its associated treatment was also found to be a major barrier to medication adherence for psychiatric patients in later studies (Angermeyer & Matschinger, 2003; Gaebel, Zaske & Bauman, 2006; Mitchell, 2006; Adewuya et al., 2009). The studies cited in this paragraph took place across different social settings, used different measurements and study designs and, therefore, make it difficult to draw meaningful comparisons between the different investigations. From the observations above it appears that perceived stigma specifically, was significantly associated with adherence levels in patients in the current study, and may warrant further exploration as well as being a possible target for intervention. This may be an area of opportunity for adherence interventions to target, and community engagement and advocacy, psycho-social support and education may prove beneficial in increasing adherence in this sample.

In summary, although the majority of moderating variables such as employment status (p = .294), level of education (p = .838), relationship status (p = .278) or living arrangements (p = .482) were not significantly correlated with antidepressant adherence rates in the current study, a statistically significant correlation was observed in patients who reported that they had fears of stigma relating to the pharmacological treatment of their psychiatric condition (p < 0.001). We can therefore conclude that we fail to reject the following study hypotheses: H_{21}, $H_{22,}$ $H_{23,}$ and $H_{24.}$.

However, the researcher rejects the study null hypothesis, $H_{25,}$ that states perceived stigma is not significantly correlated with antidepressant adherence rates in this sample of psychiatric outpatients in Gauteng Province of South Africa. Specifically, those who reported they fear social stigma scored significantly lower on the MMAQ-8 compared to patients who reported they do not fear social stigma related to their antidepressant treatment. This may highlight an area of opportunity for adherence interventions to target, and improving access to appropriate psycho-social and education services to patients and families and may prove beneficial in increasing adherence in this population. A brief discussion of recommendations that may be of relevance are discussed later in this chapter.

5.3.2. Conclusions

As a result of the chronic and often incapacitating nature of psychiatric conditions, adherence to medication is essential to positive treatment response and prevents relapse and recurrence of symptoms (Keller et al., 2002). No prior work has been conducted to determine antidepressant adherence rates or identified factors that contribute to non-adherence in psychiatric patients in this region of South Africa. The current study observed moderate to high levels of non-adherence to antidepressant medication treatment amongst outpatients with various psychiatric disorders in the Gauteng Province of South Africa. This suggests that there is substantial opportunity to address a key challenge in antidepressant treatment, and the findings of the current study highlights this issue and informs the recommendations made here for patients, clinicians, health systems and researchers regarding interventions that may promote psychiatric patients' adherence to antidepressant treatment in this population.

5.4. Limitations of the study

Findings from the current study may be limited because this study collected data through a non-random sampling method, and may, therefore represent a biased study sample. Although resembling findings from many other international studies, several contradictions have also been noted. Due to the heterogeneous methodologies utilised between these investigations, the current study cannot draw meaningful comparisons on many variables. Although the current study included a relatively small sample of patients in comparison to some other international studies, to the best of our knowledge, this is the largest study undertaken in South Africa to measure antidepressant medication adherence rates and identify factors that may contribute to non-adherence behaviours.

The aforementioned methodological and conceptual issues between different medication adherence measuring instruments signify not only a potential problem for the results of this study, it also makes summarising and translating our findings within a consistent and universally accepted framework challenging. This means that results are not easily comparable to other international or local studies, due to the different conceptual definitions and measuring instruments. Varying treatment stages, longitudinal patient medication adherence and associated factors following initial prescriptions, as well as accessibility issues influencing mental health care use as well as the role of the complementary and alternative medicine (CAM) sector were not examined in the current study. Ongoing work can refine, combine and evaluate different study design approaches that measure

adherence and its predictors over time for chronic psychiatric conditions. Finally, this study was conducted in the English language, and making it available in other South African languages may lead to improved response rates among non-English South Africans and a more socio-demographically representative sample.

A key obstacle in measuring adherence stems from the challenge to link the agreement that took place in the prescribing practitioner's office with the patient's medication-taking behaviours outside when they leave. Although, in the near future, this may be overcome with the rise of new technologies such as electronic systems that monitor and promote medication-taking more efficiently and effectively. Nevertheless, this study demonstrated that adherence to antidepressant medication is a complex phenomenon involving various mechanisms of behaviours and factors that affect its occurrence. By being cognisant of the conceptual, operational and methodological heterogeneity surrounding adherence measurements in psychiatry, health care providers, health care systems, researchers and policymakers should take note of the potential inconsistencies when evaluating and drawing comparisons between studies.

Despite these limitations, this study has provided valuable insights into adherence behaviours in this previously unstudied population of psychiatric outpatients. In addition, the current study demonstrated the feasibility of using these methods to assess antidepressant medication adherence rates. There is a need for strategies to be developed and implemented to address significant variables in order to improve medication adherence in psychiatric patients, thereby leading to a better therapeutic outcome. The development and implementation of interventions to improve antidepressant treatment adherence, and consequently patient health outcomes, may need to be more intensive or tailored for certain subgroups of patients with known non-adherence. Patients and prescribing practitioners discussing all the information and misconceptions about antidepressant treatment can address stigma-related barriers to adherence. Providing continuing education and encouragement may strengthen their commitment to taking their antidepressant medication. The increased availability of support in the form of family, friends, or caregivers to assist or supervise medication may also be an effective strategy to improve adherence rates in this sample. Targeted interventions may benefit from focusing on a brief but regular remote follow-up through telephone calls or online platforms, as well as family-focused interventions, may be a convenient way for patients to obtain additional support within their busy schedules. Specialised medication management training for mental health service providers may also effective in improving clinical outcomes in people with psychiatric conditions, as well as improvement in their own clinical skills and knowledge. These could be explored as potential strategies in improving antidepressant adherence rates in psychiatric outpatients in

this area. Further research is also needed to assess additional treatment barriers as well as the efficacy of current efforts to promote antidepressant adherence.

5.5 Recommendations

5.5.1. Recommendations for patients

For patients starting antidepressant treatment for the first time, provision of key psycho-educational material and messages may be beneficial in improving medication adherence, specifically providing information about the possible medication-related adverse reactions, how to deal with these reactions and expected benefits from antidepressants. It is important for patients to be informed about both the potential risks and therapeutic benefits of antidepressant medications in order to make informed decisions about treatment, and not become discouraged by unmet expectations. By discussing all the information and misconceptions about antidepressant treatment with their prescribing practitioner can address stigma-related barriers to adherence. Providing continuing education and encouragement may strengthen their commitment to taking their antidepressant medication.

The increased availability of support in the form of family, friends, or caregivers to assist or supervise medication may also be an effective strategy to improve adherence rates in this sample. This requires a co-ordinated effort by carers involved with the patient, and recovery must be a responsibility shared by clinicians, families and patients.

It is important that patients understand what is expected of them, and written information alone may be insufficient in long-term treatment. Reminder schedules and special medication containers may assist in preventing skipped or missed doses of their treatment. It's important to keep in mind that antidepressants can help recovery. The American Psychiatric Association (American Psychiatric Association, 2000b) recommends that people keep taking their medicine at least for four to five months after they recover from a first depressive episode in order to reduce the risk of relapse. And for people who have had multiple previous episodes, the duration of treatment can be lengthier.

5.5.2. Recommendations for health care providers

Adhering to a prescribed antidepressant medication regimen may be a complex series of behaviours that can have a long-term effect on a patient’s health and well-being. Therefore, understanding issues that influence non-adherence behaviour can enable the health care

providers to identify targeted interventions during the treatment process, and improve the patient's adherence behaviours and long-term health outcomes. It is thus fundamental that relevant health care providers are aware of the magnitude in which patients are non-adherent to antidepressant medication.

The level of involvement by health care practitioners in providing educational strategies to improve patients' perceptions of antidepressants, as well as ongoing follow-up may assist patients to achieve greater long-term adherence to antidepressants. Thus, to benefit patients, providers should attempt to improve patient adherence by facilitating an environment in which patients can feel free to discuss their expectations and concerns about antidepressants. The possibility of increasing frequency of the contact session with a focus on managing expectations of illness and treatment side effects, as well as de-stigmatisation should be explored as a way to improve non-adherence.

By providing training for health care providers on communication skills and facilitating remote contact sessions (such as telephone or other online platforms) may increase patient satisfaction and provide continuous support for patients with busy schedules. Patients should also be orientated on the use of their medication(s), and empowered to not only manage illness symptoms, but also potential medication-related adverse reactions, and should be provided with tools and trained in monitoring adherence.

Targeted interventions may focus on a brief but regular remote follow-up through telephone calls or online platforms, as well as family-focused interventions, may be a convenient way for patients to obtain additional support within their busy schedules. Various ways to increase the convenience of care, such as simplified dosing, self- monitoring of medication regimen, reminders tailoring treatment to daily habits or routines as well as positive reinforcement or rewards for improved adherence may also benefit this type of study sample. Early identification of signs of medication or illness related issues that affect adherence is also essential, and methods to detect these are of paramount importance in addressing non-adherence behaviours.

5.5.3. Recommendations for health care systems

Poor adherence is a multi-level problem, affected by patient's knowledge, attitudes, skills and the environment of the patient; providers' practices; and the health care system (Moosa, 2007). Disclosing one's mental illness can raise a serious dilemma for many patients. On the one hand, they could be subjected to social exclusion and discrimination, but on the other

hand, it may lead to a greater sense of personal empowerment, acceptance and higher self-esteem, as well as enhanced social support. These conflicting issues can provoke uncertainty concerning the nature and suitability of disclosure. Addressing the stigma of mental illness can be achieved through efforts that target multiple levels of society. Several small and large-scale methods of stigma change can be effective (such as patient-specific or general public campaigns) and should be informed by the vast research literature on this issue.

The misconceptions associated with taking antidepressant medication can be contested with messages that these are no different from taking medications for any other condition such as hypertension or diabetes. Prejudice and discrimination toward individuals with any mental illness should be opposed with positive messages that people with mental illnesses are able to live meaningful lives and make independent life choices like many others who are suffering from chronic illnesses. Interventions that include aspects aimed at motivating males specifically to access psychiatric health services could also prove beneficial. This may be facilitated through the incorporation of gender-appropriate messages or encouragement. Finally, addressing medication unavailability, unclear information about drug administration, and poor follow-up may improve the extent to which patients take their antidepressants.

Improvements in adherence can also be achieved by including theoretically informed evidence on interventions that promote psychiatric patients' adherence in psychiatric training modules. This can inform, educate and equip health care providers with skills to safely and effectively deliver services in outpatient settings. Additionally, by providing training to community mental health workers (such as psychiatrists, psychologists, nurses and pharmacists) that place an emphasis on adherence to all facets of treatment may also prove to be beneficial. Specialised medication management training for mental health service providers can be effective in improving clinical outcomes in people with psychiatric conditions, as well as improvement in their own clinical skills and knowledge.

5.5.4. Recommendations for future research

The current study could be extended and improved upon in several areas. Future research in the local context could utilise more scientifically rigorous methodological approaches (random sampling) and more objective measures of adherence could facilitate the comparison of findings across different studies. Further investigations using clinically validated scales measuring various clinical features, medication information, health system and socio-economic motivations why patients are non-adherent may also strengthen,

support and improve on the current study findings. Finally, strategies to address issues such as specific at-risk groups, targeted psycho-education, self-management strategies and ongoing lay support could increase adherence to antidepressant medication in the current study sample. Adherence benefits can be framed in terms of improved capacity for individual and work/family functioning, reduced hospital visits, reduced financial costs, reduced chance of relapse and improved chance of recovery.

Future research could also explore additional treatment barriers as well as the efficacy of current efforts to promote antidepressant adherence. Further research is needed on non-adherence to antidepressant as well as interventions to promote patients' adherence to treatment, as most of the research identified was only recommended for specific settings, illnesses, pharmacological treatments and included small study samples. Results from the current study contributed to the existing body of psychological knowledge to stimulate and structure further research efforts in the local context. Adherence is a complex phenomenon regarding conceptual aspects, accurate assessment and factors affecting its rate. In addition to clinical challenges surrounding treatment decisions, researchers and policymakers must be aware of the potential inconsistencies in terminology and methodological approaches when evaluating non-adherence.

5.6. Summary

This chapter initially presented the reader with a background of the research. This was followed by stating the research objectives, as well as providing a brief overview of the research design and methods used in this study. Consequently, a descriptive overview of the database was included. The conclusions drawn from the study results were provided by discussing the various patient-, illness-, treatment-, health care system- and moderating variables that influenced antidepressant medication adherence in this specific sample, as well as a discussion relating these findings to the referenced scientific literature. The limitations of the research were discussed subsequently. This was supplemented by including recommendations for patients, health care providers, health care systems and future research that could build upon this study.

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Dear potential participant,

Before we begin, please take a moment to consider the following information about the study. My name is **Lian Taljaard**. I am currently doing this study to complete my Master's degree in Research Psychology at the **University of South Africa (UNISA).** I have been collaborating with the South African **Depression & Anxiety Group (SADAG),** and we have become aware that many patients experience difficulty in sticking to their antidepressant medication.

We are doing a survey and need your help to see how often people take their antidepressant medication, and what some of the reasons may be why they do not. We would appreciate your time to answer some questions about you, your diagnosis, and medication.

Ethical clearance to conduct this study was obtained from the UNISA Department of Psychology Human Research Ethics Committee (HREC), and SADAG. Any problems, concerns or complaints about this study can be directed to this Committee through its secretary Cassey Chambers: Tel 011-234 4837; Fax 011-234 4839; email operations@anxiety.org.za OR to my supervisor, Louise Henderson: email: hendeh@unisa.ac.za

To take part, you must be **18 years or older**, AND, currently **prescribed at least 1 antidepressant** medication AND **live in Gauteng** Province, South Africa. You participation would require approximately 10 minutes time to answer some questions about you, your diagnosis, and medication.

If you have questions about the study, you can email or call Lian Taljaard at research@anxiety.org.za; Tel: 011 234 4837; 079 491 4433

If you have an **emergency**, you can **call** 0800 33 33 77, or **SMS** 31393.

1. Who is SADAG?

The SADAG is a non-profit, non- governmental organization established 20 years ago to provide mental health care advocacy to users across South Africa. SADAG is currently the country's largest and most recognised mental health advocacy initiative. SADAG, for example, routinely provides its members with different free telephonic counselling initiatives, such as the: Suicide Crisis Line; Trauma Line; Bipolar Helpline; Sleeping Disorder Helpline; Substance Abuse Helpline; Mental Health Helpline; and the Support Group Helpline. SADAG aims to: increase public awareness of anxiety and mood disorders; disseminate information; and provide support to consumers.

2. What is the study all about?

People sometimes forget to take their medication for many reasons, and non-adherence to antidepressant medications is a remarkably common human experience. This experience and its impact on the treatment are enlarged in chronic illnesses such as mental health conditions. For these people, non-adherence to treatment substantially adds to the burden of the illness and leads to poorer long-term outcomes in these conditions. Non-adherence to antidepressant medication therefore has a profound impact on psychiatric disease course and recovery. In addition, there can be significant detriments to the patient's long-term functioning, including social adjustment and academic or vocational performance. The purpose of this investigation is to determine levels of adherence to antidepressant medication(s) amongst psychiatric outpatients in the Gauteng Province of South Africa, and to identify possible factors that may be contribute to the observed medication adherence levels in this specific sample. This information could help health care providers better understand the reasons why patients sometimes don't take their antidepressant medication(s), and inform the development of interventions that could assist patients.

3. What will happen during the study?

When you have considered the information about this investigation and after you have given your written consent to participate in the study, you will be asked to complete a questionnaire about yourself, what you know and understand about your condition and the antidepressant treatment that you are prescribed. We would also like to ask you some questions about sticking to your anti-depressant medication. This will not count against you in any way whatsoever and no personal information is linked to your answers. You will still be able to see your doctor and

receive your medication as always, regardless of your response. For the purpose of this study, it is important to answer as honestly as you can.

4. Are there any risks involved?

There are no risks involved in taking part in this program. The questions that we ask may be personal to you, and you may feel uncomfortable answering them. However, we can assure you that no personal information is linked to your responses, and any results published would be done anonymously.

5. Are there any benefits involved?

There are no direct benefits involved in taking part in this study (financial or otherwise), and can in no way guarantee to improve your condition. This programme does not take responsibility for the medications you are/ were prescribed. Any adverse effects must be discussed with your doctor. However, the programme does offer assistance/ facilitation to this regard. Being informed about your condition and treatment reduces stigma and can help you on your road to recovery. Additional support structures are also essential in recovery for all those with a mental health condition who find it difficult to adjust to their illness.

6. Will any personal information be made available in the study?

The data from the study will be analysed and reported on anonymously and in a manner that will make it impossible for individual participants to be identified or recognised. The information from this study may be used for publication in professional journals or presented at conferences. Confidentiality will be maintained by using a participant code to disguise the identity of participants during the entire study process. No names will be linked to the information at any point. All data and information will be kept in a protected and locked file in the offices and password-protected computer of SADAG to ensure safety.

7. What happens if there is an emergency?

If at any time during the study, for example when you are answering the questions in the questionnaires or during a personal or telephone discussion, and it becomes clear that you may have to consult a doctor about your condition or treatment, you will be referred for the next available appointment at your closest clinic (See contact number for appointments below). If it turns out that the problem is more urgent and you may need emergency treatment, you will be

directed by the investigator who assists you to answer the questionnaire, and standard referral processes will be employed. Emergency counselling can be made during 8h00 to 20h00 by contacting toll-free 0800 21 22 23, or after hours toll-free 0800 12 13 14.

8. Who can I talk to about the study?

You can contact any of the investigators involved in this study with any question that you may have about the investigation or the Reminder and Support Adherence Program. The investigators on the research team are:

Mr. Lian Taljaard (UNISA/ SADAG): 011- 262 6396; 0800 17 18 19; 0800 21 22 23
Ms Louise Henderson (UNISA) 012-
Ms. Zane Wilson (SADAG): 011- 262 6396; 080017 18 19; 0800 21 22 23

9. What if I do not want to do this?

Participation in this study is totally voluntary. If you decide not to participate, it will not affect your current treatment in any way. Even if after you initially decided to participate and later decide that you would rather not continue, you can stop being in the study at any time and your doctor will continue to treat you as always. If you don't want to be in the study please tell the study team at any time, and you need to answer only those questions that you understand and are comfortable with. The information that is shared will be held in strict confidence and discussed only amongst the research team members.

By signing this form below, you are indicating that:

- this study and the form has been explained to you
- you understand the study, the form and what is expected from you as participant; and
- any questions that you may have had about it, were sufficiently answered

You are indicating that you understand how the information may be used and how your privacy will be protected. By signing this form, you are agreeing to participate in the study. Signing this form, however, does not mean that you have waived any of your legal rights.

- I have read and understood the information above on the study and what will happen during the study. I understand that:

(1) participation in this study is voluntary

(2) I can decline to participate in this study on invitation or at any other time during the study without prejudice and that it can or will in no way be used to my disadvantage

(3) I may refuse to answer any questions I would prefer not to

(4) no information that could identify me will be included in the research report and all responses and assessment scores will remain confidential

(5) in the event of the study results are being published, that my identity and responses to questions will remain confidential

(6) there are no direct risks or benefits involved in participation in this study

(7) there is no remuneration or reimbursement for participating and there are no direct costs to me

- All questions about the purpose and process of and reporting on the study were answered by the investigator to my satisfaction.
- I hereby consent to take part in the Research Study by Mr Lian Taljaard

NAME (PRINT) _____

SIGNATURE _____

DATE _____

1. Information about you

1.1. In what year were you born? (enter 4-digit birth year; for example, 1976) :_____

1.2. Are you: ❑ Male OR ❑Female

1.3. What language do you mainly speak at home?

❑English ❑Afrikaans ❑Ndebele ❑Northern Sotho ❑Sotho
❑Swazi ❑Tswana ❑Tsonga ❑Venda ❑Xhosa ❑Zulu

1.4. What is your relationship status?

❑Married ❑Single ❑Engaged ❑Relationship
❑Widowed ❑Divorced

1.5. Please specify your race

❑Asian ❑Black ❑Coloured ❑Indian ❑White
❑Mixed race

1.6. In which province do you currently live in?

❑Eastern Cape ❑Free-State ❑Gauteng ❑Kwazulu Natal
❑Limpopo ❑Mpumalanga ❑Northern Cape ❑North West
❑Western Cape

1.7. Who do you live with at the moment?

❑On my own ❑A Partner ❑Family (Parents/ siblings)
❑Friends

Other (please specify)_____

1.8. Which of the following categories best describes your employment status?

❑Employed, working Full-time ❑Employed, working Part-time

❑Not employed, looking for work ❑Not employed, NOT looking for work

❑Student ❑Retired ❑Disabled, not able to work

1.9. Do you have Medical Aid Support? ❑Yes ❑No

1.10. Do you receive a Government/ Social Grant? ❑Yes ❑No

1.11. What is the highest level of education you have completed?

❑Did not attend school ❑Primary School (7th grade)
❑Some High School (9th Grade) ❑High School (12th Grade)
❑Diploma / Degree ❑Post-Graduate Degree

2. Information about your ilness

2.1. What is your diagnosis?

❑Major Depression (MD) ❑Bipolar Mood Disorder (BMD)

❑Post-Natal Depression (PND) ❑Generalised Anxiety Disorder (GAD)

❑Obsessive-Compulsive Disorder (OCD) ❑Panic Disorder (PD)

❑Post-Traumatic Stress Disorder (PTSD) ❑Social Anxiety Disorder (SAD)

❑Specific Phobia (SP) ❑Substance Use - Alcohol (Alc)

❑Substance Use -Cannabis (Can) ❑Substance Use -Cocaine (Coc)

❑Brief Psychotic Disorder (BPD) ❑Schizophrenia (Sch)

❑Schizoaffective Disorder (ScD) ❑Anti-Social Personality Disorder (ASPD)

❑Borderline Personality Disorder (BPD)

If your diagnosis is not on the list, please specify which here:_____

2.2. Approximately when did you receive your diagnosis? (month & year, e.g. June 2010)

I_____

2.3. Have you been hospitalised in the past 6 months? ❑Yes ❑No

2.4. Do you think or feel your condition makes it difficult for you to do your daily activities? ❑Yes ❑No

2.5. Do you think your condition needs to be treated with medication? ❑Yes ❑No

3. Information about your medication

3.1. Do you get your anti-depressant(s) prescription from a Psychiatrist OR General Practitioner (GP)?

❑Psychiatrist ❑General Practitioner (GP) ❑Other_____

3.2. Approximately when did you start taking the anti-depressant(s) you are currently prescribed? (month & year, e.g. June 2010)

I_____

3.3. What medication(s) are you currently prescribed?

(1):_____ (2):_____

(3):_____ (4):_____

(5):_____ (6):_____

(7):_____ (8):_____

3.4. How often do you have to take your medication(s)?

❑Once a day ❑Twice a day ❑Three times daily
❑More than four times a day

❑Other (please specify)_____

3.5. Do you know how to deal with potential side-effects of anti-depressants? ❑Yes ❑No

3.6. Are you currently experiencing any side-effects? ❑Yes ❑No

3.7. Do you feel you need more support to help you stick to your medication? ❑Yes ❑No

3.8. Do you think it's necessary for you to take your anti-depressant medication? ❑Yes ❑No

3.9. Are you afraid of what some people may think about you taking anti-depressant medication? ❑Yes ❑No

******We would like to ask you some questions about sticking to your anti-depressant medication. This will not count against you in any way whatsoever and no personal information is linked to your answers. You will still be able to see your doctor and receive your medication as always, regardless of your response. For the purpose of this study, it is important to answer as honestly as you can.******

4. Information about Adherence

1. Do you sometimes forget to take your antidepressant medication? ❑Yes ❑No

2. People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your antidepressant medication? ❑Yes ❑No

3. Have you ever cut back or stopped taking your antidepressant medication without telling your doctor because you felt worse when you took it? ❑Yes ❑No

4. When you travel or leave home, do you sometimes forget to bring along your antidepressant medication? ❑Yes ❑No

5. Did you take your antidepressant(s) yesterday? ❑Yes ❑No

6. When you feel like your symptoms are under control, do you sometimes stop taking your antidepressant medication? ❑Yes ❑No

7. Taking antidepressant medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?
   ❑Yes ❑No

8. How often do you have difficulty remembering to take all your antidepressant medicine?

❑Never/ Rarely ❑Once in a while ❑Sometimes ❑Usually ❑All the time

Thank you for taking the time to complete this survey!

APPENDIX III: Coding Sheet

Record date	dd-mm-yyy
Coded identification	XXX
Mode	Manual (M); Telephone (T); Online/ electronic (O)
Date of Birth	dd-mm-yyyy
Age (years)	DoB subtracted from current date (i.e., 31-12-2014)
Age group	18-29 (1); 30-39 (2); 40-49 (3); 50-59 (4); 60+(5)
Gender	Male (M), Female (F)
Ethnicity	Asian (A); Black (B); Colored (C); Indian (I), Mixed race (M); White (W)
Language	English (E); Afrikaans (A); Ndebele (ND); Northern Sotho (NS); Sotho (S); Swazi (SW); Tswana (TSA); Tsonga (TSO); Venda (VE); Xhosa (XHO); Zulu (ZUL)
Relationship status	Married (M); Single (S); Widowed (W); Divorced (D); Relationship (R); Engaged (E);
Residence	On my own (OWN); Partner (P); Family (FA); Friends (FR); Other (O)
Employment status	Employed, working Full-time (EF); Employed, working Part-time (EP); Not employed, looking for work (UL); Not employed, NOT looking for work (UN); Student (S); Retired (R); Disabled, not able to work (DU)
Education level	Did not attend school (NS); Primary School (7th grade) (SSS); Some High School (SHS); High School (12th Grade) (HS); Diploma / Degree (D); Post-Graduate Degree (PGD); Other (O);
Province	Gauteng Province (G)
Prescribing practitioner	Psychiatrist (PSY); General Practitioner (GP)
Medical aid status	Yes (Y); No (N)
Social grant status	Yes (Y); No (N)
Health care system	Private (PVT); Public (PUB);
Date of main diagnosis	mm-yyy
Diagnosis AXIS I	**Mood Disorders (MD);** Major Depressive Disorder (MDD); Bipolar Mood Disorder I & II (BMD); Dysthemic Disorder (DysD);Post-partum onset MDEpisode (PND); **Anxiety Disorders (ANX);** Generalised Anxiety Disorder (GAD); Obsessive-Compulsive Disorder (OCD); Panic Disorder w/wo agoraphobia (PD); Post-Traumatic Stess Disorder (PTSD); Social Anxiety Disorder (SAD); Specific Phobia (SP); **Substance use or abuse disorders (SUBS);** Alcohol (SUBS_Alc); Cannabis (SUBS_Can); Cocaine (SUBS_Coc); **Schizophrenia & other Psychotic Disorders (PSYCH);** Brief Psychotic Disorder (BrPD); Schizophrenia (Sch); **Disorders diagnosed in childhood (ADHD);**

APPENDIX III: Coding Sheet

Diagnosis AXIS Id (Differential)	As above
Diagnosis AXIS II	**Personality disorders (PD);** Schizoid Prsonality Disorder (ScPD); Anti-Social Personality Disorder (ASPD); Borderline Personality Disorder (BPD);
Diagnosis AXIS III	**General medical conditions (GMC);** Traumatic brain injury (TBI); Epilepsy (EPIL); Diabetes mellitus (DIAB); Hypothyroidism (HYPOTH); Other (O)
Previous 6-month hospitalisation	Yes (Y); No (N); (from current date e.g., 31-12-2014)
Illness severity requires pharmacological treatment	Yes (Y); No (N);
Illness perceived as difficult/ intrusive by patient	Yes (Y); No (N);
Start date of current pharmacotherapy	mm-yyyy
	Central Nervous System Stimulants (CNSS); **Respiratory Stimulants (RS);** Methylphenidate (METHYL); ***Sedative Hypnotics (SH);*** **Benzodiazepines (BENZO);** Temazepam (TAMAZ); Epilizine (EPILI); Loprazolam (LOPRAZ); Flurazepam (FLURAZ); **Others (O);** Zolpidem (ZOLPI); Zopiclone (ZOPIC); ***Anxiolytics (ANXIO);*** **Benzodiazepines (BENZO);** Alprazolam (ALPRAZ); Diazepam (DIAZ); Clobazam (CLOBA); Lorazepam (LORAZ); Oxazepam (OXAZE); Etifoxine (ETIFO); **Others (O);** Buspirone (BUSPI); ***Antidepressants (AD);*** **Tricyclic (TRIC);** Amitriptyline (AMYTR); Mianserin (MIANS); Imipramine (IMIPR); **Mono-Amine Oxidase inhibitors (MOAi)** [INCL.SELECTIVE & NON_SELECTIVE]; **Tranylcypromine (TRANY);** Moclobemide (MOCLO); **Selective serotonin re-uptake inhibitors (SSRI);** Fluoxetine (FLUOX); Citalopram (CITAL); Escitalopram (ESCIT); Sertraline (SERTR); Paroxetine (PAROX); **Serotonin & noradrenaline re-uptake inhibitors (SNRI);** Venlafaxine (VENLA); Duloxetine (DULOX); Vortioxetine (VORTI); **Noradrenaline & dopamine re-uptake inhibitors (NDRI);** Bupropion (BUPRO); Reboxetine (REBOX); **Tetracyclic (TETRA);** Mirtazapine (MIRTA); **Melatonergic Specific (MELOT);**Agomelatine (AGOME); **Lithium (LITHI);** Lithium Carbonate (LITH); **Others (O);** Trazodone (TRAZO); ***Anti-psychotics (ANTIP);*** **Butyrophenones (BUTYR);** Olanzapine (OLANZ); Haloperidol (HALOP); **Atypical anti-psychotics (AT_ANTIP);** Olanzapine; (OLANZ); Quetiapine (QUETI); Risperidone (RISPE); Clonazepam (CLONA); Ziprasidone (ZIPRA); Aripiprazole (ARIPI); Flupenthixol (FLUPE); **Others (O);** Sulpiride (SULPI); ***Anticholinergics (ANCHOL);*** Orphenadrine (ORPHE); ***Anti-epileptics (ANEPIL);*** **Others (O);** Lamotrigine (LAMOT); Clonazepam (CLONA); Sodium Valproate (SODIV); Carbamazepine (CARBA); Pregabalin (PREGA); Topiramate (TOPIR);
DailyDosage	1nce a day (1); 2ce a day (2); 3ce a day (3); 4 Or More (4)
Cope with Side Effects	Yes (Y); No (N);
Currently Experiencing Side Effects	Yes (Y); No (N);
Requires Adherence Support	Yes (Y); No (N);
Medication Perceived As Necessary	Yes (Y); No (N);
Currently experiencing stigma	Yes (Y); No (N);

UNISA university of south africa
Department of Psychology

Ethical Clearance for M/D students: Research on human participants

The Ethics Committee of the Department of Psychology at Unisa has evaluated this research proposal for a Higher Degree in Psychology in light of appropriate ethical requirements, with special reference to the requirements of the Code of Conduct for Psychologists of the HPCSA and the Unisa Policy on Research Ethics.

Student Name: Lian Taljaard **Student no.** 47175427

Supervisor: Ms L Henderson **Affiliation:** Dept. of Psychology, Unisa

Title of project:

Adherence to Anti-Depressant Medications among Psychiatric Out-Patients in Gauteng: A Descriptive Multi-Mode Survey

The proposal was evaluated for adherence to appropriate ethical standards as required by the Psychology Department of Unisa.

Because of the sensitivity of the information being sought and the fact that the participants come from a vulnerable group, the application was approved by the Ethics Committee of the Department of Psychology on the understanding that –

- All ethical requirements regarding informed consent, the right to withdraw from the study, the protection of participants' privacy and confidentiality of the information should be made clear to the participants and adhered to, to the satisfaction of the supervisor;
- If access to participants or data relating to them is gained through institutions acting as intermediaries, all conditions and procedures regarding access to patient data for research purposes that may be required by these institutions are to be met;
- If further counseling is required in some cases, the participants will be referred to appropriate counseling services.

Signed:

Prof. M Papaikonomou

Date: 2014-09-11

[For the Ethics Committee]
[Department of Psychology, Unisa]

The proposed research may now commence with the proviso that:

1) *The researcher/s will ensure that the research project adheres to the values and principles expressed in the UNISA Policy on Research Ethics.*
2) *Any adverse circumstance arising in the undertaking of the research project that is relevant to the ethicality of the study, as well as changes in the methodology, should be communicated in writing to the Psychology Department Ethics Review Committee. An amended application could be requested if there are substantial changes from the existing proposal, especially if those changes affect any of the study-related risks for the research participants.*
3) *The researcher will ensure that the research project adheres to any applicable national legislation, professional codes of conduct, institutional guidelines and scientific standards relevant to the specific field of study.*

26 April 2014

The Registrar

Professional Board of Psychology

HPCSA

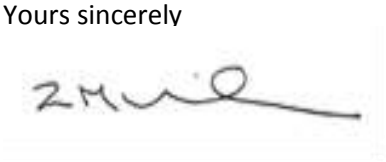
PO Box 205

Pretoria 0001

Dear Sir/ Madam

We hereby declare that we are willing to provide supervision for **Mr. Lian Taljaard**, and look forward to accommodate him for his study entitled **ADHERENCE TO ANTIDEPRESSANTS IN PSYCHIATRY: A DESCRIPTIVE SURVEY OF OUTPATIENTS IN JOHANNESBURG, GAUTENG** from January, 2014 to December, 2014 Mr. Taljaard will be working under close supervision with myself and executive staff to assist with the implementation of the project. We will ensure that the necessary support services are available to complete the study successfully and according to the ethical guidelines prescribed by the relevant health research ethics committee.

Yours sincerely



_____

Ms ZaneWilson

Founder/ Director

The south African Depression & Anxiety Group

SADAG

Email: zane1@medport.zo.za

G.P.-S. 012-0123

CERTIFICATE OF REGISTRATION OF NONPROFIT ORGANIZATION

In terms of the Nonprofit Organisation Act, 1997, I am satisfied that .....

The South African Depression and Anxiety Group

(*name of the nonprofit organization*)

meets the requirements for registration.

The organisation's name was entered into the register on **25 October 2001**

(*date*)

Registration number

013-085-NPO

Director's signature

Date **09 October 2009**

Department of Social Development

IT IS HEREBY CERTIFIED THAT THIS IS A TRUE COPY OF THE ORIGINAL DOCUMENT AND THAT THERE IS NO ERASURE OR ALTERATION THEREON OR THERETO BY AN UNAUTHORISED PERSON.
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2009 -10- 30