PREVALENCE AND PREDICTORS OF NEW EPISODES IN PATIENTS WITH BIPOLAR I DISORDER AT DR. GEORGE MUKHARI HOSPITAL OVER A ONE YEAR PERIOD (JUNE 2007-JUNE 2008)

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DECLARATION

I, **Theona Ballyram**, hereby declare that the work on which this dissertation is based , is original (except where acknowledgements indicate otherwise) and that neither the whole work nor part of it has been, is being, or shall be submitted for another degree at this or any other university, institution for tertiary education or examining body.

T. Ballyram

Name and surname Signature

Date: 12 July 2010

DEDICATION

To my dear husband, Jayendra.

ACKNOWLEDGEMENTS

I hereby wish to express my deep gratitude and appreciation to my supervisor, **Professor S.T. Rataemane** whose guidance, wisdom and inspiration has facilitated the entire process of this dissertation.

I sincerely wish to thank all the staff members at DGMH psychiatry unit for their assistance in the accessing of records in order for me to collect my data.

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And last, but not least I would like to express a special thanks to my husband, whose patience and understanding is deeply appreciated and without whom this endeavour would not have been possible.

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LIST OF ACRONYMS

DSM IV TR:	Diagnostic and Statistical Manual of Mental Disorders 4th edition, text revised
HIV:	Human Immuno-deficiency virus
DGMH:	Dr. George Mukhari Hospital
MEDUNSA:	Medical University of Southern Africa (University of Limpopo)
OPD:	Out-patient department
MREC:	Medunsa Research and Ethics Committee
Pt:	Patient/s
Med condition:	Medical condition

ABSTRACT

Background: Bipolar disorder is a lifelong illness typically presenting with frequent relapses and/or recurrences. Bipolar disorder carries a high morbidity and mortality and can cause significant functional impairment. In understanding the relapsing course of the illness, chronicity may be reduced by preventing or delaying the occurrence of new episodes.

Objectives: The objectives of this study were to establish the prevalence of new episodes in patients with bipolar I disorder and to determine predictors of new episodes.

Methods: This was a retrospective, descriptive study based on the review of medical records of patients with bipolar I disorder seen at Dr. George Mukhari Hospital – psychiatry unit between the period of 1 June 2007 to 1 June 2008. Data concerning socio-demographic parameters of the patients and psychiatric information was collected using a data collection sheet.

Results: Data was extracted and analysed from a total of 143 patient records. Ninety (63%) experienced new episodes and fifty-three patients (37%) did not have any new episodes. Seventy-nine patients (55%) had one or more manic episodes (mean=0.64) and nineteen (13.38 %) had one or more depressive episodes. (Mean=0.14). The maximum number of new episodes was 2 and the mean was 0.78. The most recent episode was manic in seventy-six patients (84%). The mean number of hospital admissions was 0.88. Of the patients that had new episodes, the age ranged from 18 to more than 55 years, the vast majority were black (94%) and of Christian faith (97%). More than half were female (58%) and single (49%), with 1-2 children (48%). The majority achieved high school education (60%), and were unemployed (70%). Only 47% were receiving a disability grant. New episodes were more prevalent in patients who experienced a younger age of onset of illness (41% in the 18-24 year age group) and who were ill for more than ten years (43%). Less than half had a positive family history of mental illness (43%), 39% had a history of substance use, the most common substance being alcohol (54%), and 39% suffered from one or more comorbid medical illnesses. 78% of the patients who had new episodes were on antipsychotics, 93% were on mood stabilisers, and 69% were on a

combination of mood stabilisers and antipsychotics. The only factor that was significantly predictive of new episodes was poor compliance.

Conclusion: There is a high prevalence of relapse in patients with bipolar I disorder, particularly to the manic pole. Compliance with medication remains a serious problem and is associated with the occurrence of new episodes. Improved treatments should include biopsychosocial strategies, identification of risk factors for relapse/recurrence and early and consistent intervention.

CHAPTER 1
INTRODUCTION

1.1 BACKGROUND

Bipolar disorder can be described as a chronic mental illness with marked mood and behavioural dysfunction. The illness is characterised by frequent episodes of relapse and/or recurrence and not much is known about factors that may precipitate new episodes. According to the WHO, bipolar disorder is the sixth leading cause worldwide of disability-adjusted life years in individuals aged 15 to 44 years (Schaffer *et al*, 2006). Bipolar disorder also has a high morbidity and mortality due to suicide, increased incidence of medical illnesses, cognitive deficits with changes in brain morphology and significant impairment of psychosocial functioning. It is therefore no longer sufficient just to focus treatment on the symptoms of acute episodes, but also to understand the course of the illness, reduce chronicity by preventing or delaying episode recurrence and develop timely interventions by optimizing treatment strategies (Judd *et al*, 2006; Yatham *et al*, 2009; Altman *et al*, 2006).

1.2 DEFINITION OF TERMS

An episode can be defined as:

1. Symptoms leading to an inpatient treatment in a mental hospital.
2. The manifestation of symptoms leading to an outpatient treatment with the following additional criteria:

a) Impairment in the usual activities of the patient or a change in the social, occupational or academic functioning of the patient

b) Repeated consultation with primary care, a psychiatrist or a general practitioner because of new onset symptoms or worsening of already existing symptoms (Marneros *et al*, 2008).

Relapse is defined as any new episode within 8 weeks of syndromal recovery in bipolar disorder and recurrence is defined as any new episode after 8 week syndromal recovery/remission (Tohen *et al*, 2003). The words relapse, recurrence, and episode are used interchangeably in literature on bipolar disorders (Altman *et al*, 2006). Relapse and

recurrence will be used synonymously for the purposes of this study and is considered if manic or depressive symptoms fulfilled DSM-IV-TR criteria for a mood episode. Therefore, in this study, reference to a new episode will include the first episode, as well as any subsequent episode, relapse, or recurrence.

1.3 PROBLEM STATEMENT AND SIGNIFICANCE OF THE STUDY

Patients diagnosed with bipolar I disorder present an ongoing challenge in terms of management and rehabilitation at Dr. George Mukhari Hospital. A deeper understanding of the relapsing nature and chronic course of the illness will be beneficial in developing effective guidelines and strategies aimed at reducing the number of relapses/recurrences. This will ultimately improve the prognosis and long term outcome of the disorder, which will subsequently reduce the economic burden on the health system. Assessing epidemiological variables and the effect of co-occurring conditions will prove to be advantageous in terms of improving patient care and providing crucial biopsychosocial management.

1.4 RESEARCH GOAL

This study will determine the profile of patients with bipolar I disorder seen at Dr George Mukhari Hospital - psychiatry department; and will determine the prevalence and possible predictors of new episodes in these patients.

1.5 RESEARCH QUESTION

What is the prevalence of new episodes in patients diagnosed with bipolar I disorder; and which predictors for new episodes can be identified in these patients?

1.6 OBJECTIVES OF THE STUDY

(i) To assess the prevalence of new episodes.
(ii) To evaluate the distribution of bipolar I disorder by socio-demographic factors.
(iii) To determine possibe predictors of new episodes.

1.7 COMPONENTS OF THE DISSERTATION

Chapter 2 contains a review of the literature, followed by a description of the methodology in chapter 3. The results of the study are presented in chapter 4 and discussed in chapter 5. The dissertation ends with recommendations and a conclusion.

CHAPTER 2
LITERATURE REVIEW

2.1 INTRODUCTION

The spectrum of bipolar disorders accounts for up to 5% of the general population and up to 50% of all depressions. The less than optimal outcome of mood disorders cannot be attributed to underdiagnosis and suboptimal treatment alone. According to recent reports, the incidence of mood disorders may be increasing in younger people, particularly associated with the rising rate of substance use disorders. Bipolar disorder is also increasingly being diagnosed in childhood and adolescence. Studies also suggest that there are higher rates of relapse/recurrence, chronicity and treatment resistance than previously thought, however; the proportion of patients with a poor prognosis might be overestimated (Akiskal, 2009). Nonetheless, bipolar disorder remains an intriguing illness that is worthy of ongoing, high quality research.

2.2 PREVALENCE OF BIPOLAR DISORDER

Lifetime (and 12 month) prevalence is 1% (0.6%) for bipolar I, 1.1% (0.8%) for bipolar II and 2.4% (1.4%) for subthreshold bipolar disorder (Merikangas *et al*, 2007). According to data from the National Comorbidity Survey Replication, the lifetime prevalence of bipolar I and II disorders collectively is 3.9% (Kessler *et al*, 2005). Sociodemographic factors like younger age & low income, as well as the presence of psychiatric comorbidity were associated with higher prevalence rates (Schaffer *et al*, 2006). The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) represented a large prospective examination of bipolar disorder and examined the association between clinical features and risk of recurrence. By one year, 22.4% of patients had experienced depressive recurrence and 6.4 % had hypomanic/manic/mixed recurrence. Approximately half the participants experienced at least one recurrence by two years of follow up; and it has been shown that more than 90% of patients with bipolar disorder experience recurrences during their lifetimes (Perlis *et al*, 2006). In the Systematic Treatment Optimization Program for Early Mania Project (STOP-EM); the first mood episode was depressive in 52.9% of the patients, hypomanic in 11.8% and

manic in 35.3%. Depressive recurrences were more common than manic recurrences and more patients achieve remission from a manic episode than from a depressive one (Yatham *et al*, 2009).

2.3 EPIDEMIOLOGY OF BIPOLAR DISORDER

Male and female prevalence is 0.8% and 1.1% for bipolar I, 0.9% and 1.3% for bipolar II and 2.6% & 2.1% for subthreshold bipolar. The age of onset ranges between late adolescence and early 40's. The mean age of onset is 18.2 years and the average number of lifetime episodes is 77.6. Patients with this disorder spend an average of a decade of their lives in illness episodes (Merikangas *et al*, 2007). In the STOP-EM project, 54% had comorbid substance abuse, 26% had a comorbid GMC, 30.2% of the patients had a family history of depression and 10% had a family history of bipolar disorder. An anxiety disorder was present in 10% of patients and 9.4% had a previous suicide attempt. There was a significant association between non-compliance with treatment and substance abuse. Noncompliance rates were 37% and substance abuse rates were as high as 54% (Yatham *et al*, 2009).

2.4 PREDICTORS OF NEW EPISODES

2.4.1 The number of previous episodes and the interval between episodes

Kessing, Hansen and Anderson (2004) showed that the risk for relapse increased as the number of previous episodes increased and another study found that patients with a higher number of past episodes relapsed earlier than those with fewer episodes (Altman *et al*, 2006). Hence, the risk of relapse increases with every new episode and a history of four or more episodes is significant (Judd *et al*, 2008). However, there are a few studies e.g. the STEP-BD trial (Perlis *et al*, 2006) and a study by Bromet *et al* (2005) that do not support this observation. Polarity of the index episode serves as a predictor of polarity of subsequent episodes and depressive polarity is more frequent than manic/hypomanic polarity (Colom *et al*, 2006). Patients with a more severe course of bipolar illness and a greater number of episodes, with more hospital admissions also suffer greater neurocognitive decline. The opposite may also be true: patients with neurocognitive

impairments may be more vulnerable to developing a severe and recurrent course of bipolar disorder, and this may represent an endophenotypic marker of genetic vulnerability (Thompson *et al*, 2005).

2.4.2 Substance use

More than 60% of patients with bipolar I disorder and 48% of patients with bipolar II disorder meet criteria for a lifetime diagnosis of substance abuse/dependence. The use of substances can precipitate a new episode, increase its duration, shorten remission, increase the severity of symptoms and complicate management (Altman *et al*, 2006). Substance use is a predictor of noncompliance, which subsequently precipitates relapse/recurrence (Yatham *et al*, 2009). Substance use preceding onset of bipolar illness was associated with manic polarity according to one study and a comorbid substance use disorder was associated with an increased risk of manic recurrence (Colom *et al*, 2006; Perlis *et al*, 2006). Studies by Strakowski *et al* (2005; 2007) showed that alcohol use disorders were common co-occuring conditions that negatively affected outcome in bipolar patients, and that cannabis use was associated with rapid cycling and with more time in affective episodes. Alcohol usage may be associated with depressive onset and cannabis with manic onset in bipolar disorder (Colom et al, 2006).

2.4.3 Stressful life events

There is a significant relationship between stressful life events and an increased risk of relapse or recurrence, as well as a longer time to recovery. The impact of these events is also modified by other factors such as introverted and obsessional personality traits, which increases the risk for relapse. Stress induced sleep deprivation may also be a predictor of relapse, particularly for mania. The “kindling” effect suggests that repeated stress can precipitate an episode and that an increased vulnerability and sensitivity to stress occurs with the progression of the illness resulting in minimal or no stress causing a subsequent episode to occur (Altman et al, 2006). One study by Wals *et al* (2005) concluded that first admissions of adults with mania were often preceded by death in the family or other major stressful event while another study by Colom *et al* (2006) showed

that patients who had a stressful life-event associated with the onset of the condition were more prone to depressive polarity.

2.4.4 Sociodemographic factors

The influence of sociodemographic factors are limited and not convincing, but some studies have shown that female sex predicts depressive relapses, while male gender predicts manic relapses (Fekadu *et al*, 2006). Variables that were not associated with relapse or recurrence were age, age at illness onset and duration of illness, marital and socioeconomic status, level of education, family history of bipolar disorder and number of previous episodes (Perlis *et al*, 2006). Other studies found that an earlier age of onset predicted relapse/recurrence of mood episodes, increased risk of comorbid substance abuse/dependence as well as a longer time to remission (Yatham *et al*, 2009; Ernst and Goldberg, 2004; Kora *et al*, 2008). Only one out of five studies found female sex to be associated with an increased risk of future episodes and in other studies, the male gender predicted a longer time to remission (Altman *et al*, 2006; Kora *et al*, 2008). Poor job functioning and lack of social support has also shown to be predictive of relapse. Studies have shown that a positive family history of substance abuse predicts poorer outcome, and that a family history of mental illness is associated with an increased risk of relapse; however, some other studies did not share these findings (Altman *et al*, 2006).

2.4.5 Treatment compliance

One event of discontinuing medication without medical advice to do so is considered as non-compliance (Yatham *et al*, 2009). Non-compliance with pharmacological treatment in bipolar disorder ranges from 20% to 60% and this is a significant predictor of a new affective episode (Lingam and Scott, 2002). In the McLean- Harvard First Episode Mania Study, the use of psychotropics grew less with time due to problems with compliance and by two year follow up there was a 36% rate of no medication use (Tohen *et al*, 2003). This is in keeping with results from other studies, however, the relapse/recurrence rate seems to be lower in patients receiving combined psychotherapy and pharmacotherapy compared to those receiving pharmacotherapy alone (Mousavi, Moalemi and Sadeghi, 2004). Drug treatment is effective in most patients with bipolar disorder but it does not

adequately prevent relapse especially in patients with severe illness. Non-compliance also perpetuates occupational and social problems that are associated with relapses in bipolar disorder (Lingam and Scott, 2002).

2.4.6 Psychiatric comorbidities

The STEP-BD trial and another study found that a comorbid anxiety disorder or the presence of a lifetime eating disorder was associated with increased risk of depressive recurrence (Perlis *et al*, 2006; Altman *et al*, 2006). A study by Schaffer *et al* (2006) found that almost 52% of patients with bipolar disorder also met the criteria for a comorbid anxiety disorder and that this was associated with increased morbidity and treatment resistance. The presence of comorbid psychiatric conditions or a history of childhood psychopathology were predictors for longer episodes (Kora *et al*, 2008).

2.4.7 Subsyndromal symptoms

Patients with subsyndromal symptoms are about four times more likely to relapse than patients without; and the polarity of the subsyndromal symptoms predicts subsequent relapses of the same polarity (Frye *et al*, 2006). For every residual manic symptom present at the time of recovery, the risk of recurrence increased by 20% and for every residual depressive symptom, the risk of depressive recurrence increased by 14%. Residual manic symptoms increase the risk for both manic and depressive recurrence, therefore aggressively targeting subthreshold symptoms can improve outcome in bipolar disorder (Perlis *et al*, 2006). At least four different studies show that bipolar patients who have residual subsyndromal symptoms after recovery have subsequent affective episodes more than three times earlier than asymptomatic recoverers do. They also have more lifetime episodes, more cycling, more mixed episodes, a higher rate of comorbid cyclothymic disorder as well as a more chronic and disabling course of illness. Hence incomplete recovery is an extremely robust correlate of time to major episode relapse (Judd *et al*, 2008). The presence of residual affective symptoms has also been found to impair cognitive function in mood disorders (Thompson *et al*, 2005).

2.4.8 Family Burden and High Expressed Emotions

In a study that looked at family caregivers of patients with bipolar disorder, 90% of caregivers had experienced significant levels of burden in terms of time, money and energy. Patients living with an overburdened caregiver may have an increased risk of relapse (Zergaw *et al*, 2008). High expressed emotions add to the severity of symptoms and can contribute to recurrence of depressive episodes (Altman *et al*, 2006).

2.4.9 Insight

A patient's illness concept is a powerful predictor of medical adherence, and patients with impaired insight or a negative attitude toward treatment may become non-compliant. A study by Yen et al examined the predictive value of insight on the adverse clinical outcomes of bipolar disorder and found that impaired insight into treatment and a greater number of previous hospitalisations significantly increased the risk of poorer clinical outcome in bipolar disorder in a two-year period (Yen *et al*, 2008).

2.4.10 Other clinical factors

A greater proportion of time spent in an episode in the past year, the presence of rapid cycling, or a history of psychotic symptoms was associated with earlier relapse/recurrence (Perlis *et al*, 2006; Altman *et al*, 2006). According to results from the McLean-Harvard First Episode Mania Study, strong predictors of new manic episodes were initial mood congruent psychotic features, low premorbid occupational status, & initial mania. Predictors of a future depressive episode were initial mixed dysphoric states, presence of other psychiatric or medical comorbidities and higher occupational achievement (Tohen *et al*, 2003).

2.5 COMPLICATIONS OF BIPOLAR DISORDER

2.5.1 Suicide and Accidents

Risk for suicide among patients with bipolar disorder is more than 20 times greater than that for the general population, is amongst the highest for any disorder, and often occurs early in the illness. Risks of accidental and other forms of injury or violent death are also

high among bipolar patients (three times higher than the current US national rate). One study suggested that accidents are associated with manic-hypomanic morbidity especially if psychosis is present, and suicidality is associated with depressive or mixed-dysphoric morbidity and possibly a history of suicide attempt. Accidents, injuries and suicide contribute to excess mortality in patients with bipolar disorder (Khalsa *et al*, 2008).

2.5.2 Neuro-cognitive Impairment

There is a growing body of evidence that people with bipolar disorder who are in remission have persistent cognitive impairment through a variety of cognitive facets, including immediate and visuospatial declarative memory, executive function and attention and concentration. Euthymic patients have also been found to have significant psychomotor retardation. Psychotropic medication may exert a negative effect on neurocognitive functioning, particularly lithium and antidepressants that have anticholinergic effects, however, some studies indicate that the cognitive impairments seen in bipolar disorder are unlikely to be the primary effect of psychotropic drugs (Thompson *et al*, 2005).

2.5.3 Rapid Cycling

Rapid cycling refers to the occurrence of four or more mood episodes during the previous 12 months according to the DSMIV-TR and is a specifier of the longitudinal course of illness presentation and is associated with a greater morbidity (Muzina and Calabrese, 2002). In a French study involving 1090 patients, only 9% were classified as rapid cyclers. Rapid cyclers are more likely to be female, have an earlier age of onset, a longer duration of illness and attempt suicide more often. The study also found that rapid cyclers show more depressive symptoms and less psychotic symptoms. The presence of thyroid disease, cyclothymic temperament, and the use of antidepressants is also associated with rapid cycling in bipolar patients (Azorin *et al*, 2008).

2.6 BIOPSYCHOSOCIAL MANAGEMENT

Bipolar disorder may be the most expensive mental illness in U.S. private health plans as well as to employers (Bauer *et al* 2006a). The cornerstone of management for bipolar

disorder is evidence-based pharmacotherapy with the adjuvant use of structured psychotherapies like cognitive behavioural therapy, group psychoeducation, family therapy as well as interpersonal and social rhythm therapy (Beynon *et al*, 2008; Vieta 2009). The outcome in bipolar disorder is worsened by the problems of suboptimal clinical outcomes, fragmented care, long term functional deficits and incurred expenses, as well as low medication response rates. Studies show that collaborative and ongoing care for bipolar patients improves clinical and functional outcome in the long term, enhances pharmacotherapy, and improves quality of life. Easy access to community clinics and primary health care services could help diagnose and manage patients more effectively, resulting in fewer emergency room and psychiatric triage visits and thus resulting in better cost effectiveness and fewer relapses/recurrences (Bauer *et al*, 2006a; Bauer *et al*, 2006b).

2.7 CONCLUSION

Despite guideline-based treatment, bipolar disorder is a highly recurrent, predominantly depressive illness and an improved understanding of the way in which predictors mediate risk of relapse or recurrence can help create strategies to modify the risk and thus improve outcome (Perlis *et al*, 2006). Current treatments for bipolar disorder do not provide complete long term protection against subthreshold symptoms, relapses/recurrences and switches; and the impact on functional recovery is limited. Improved treatments should include more integration of rehabilitative and psychosocial strategies with better medication, and early and consistent intervention (Tohen *et al*, 2003).

CHAPTER 3
METHODOLOGY

3.1 STUDY DESIGN

This study was a retrospective, descriptive study based on the review of medical records of patients with bipolar I disorder seen between the period of 1 June 2007 to 1 June 2008. This design is appropriate to determine the prevalence of new episodes and to describe the variables surrounding the relapses and recurrences. A data collection chart that depicts patient socio-demographic and psychiatric information was used as the research tool.

3.2 DESCRIPTION OF THE SITE OF THE STUDY

The study was conducted at the psychiatry unit at Dr. George Mukhari Hospital, which is a tertiary healthcare facility that provides specialist psychiatric services.

3.3 STUDY POPULATION

3.3.1 Study sample

The sample included all patients with a diagnosis of bipolar I disorder attending Dr George Mukhari Hospital-psychiatry unit; either as an inpatient or as an outpatient within the period of 1 June 2007 to 1 June 2008.

3.3.2 Selection Criteria

During the selection process, the following criteria were adhered to:

(i) The patient, to whom the file belongs, must have been diagnosed with bipolar I disorder according to DSM IV TR.

(ii) The patient must have received treatment at Dr George Mukhari Hospital-psychiatry unit.

(iii) The patient had to have been seen at the unit between 1 June 2007 and 1 June 2008.

(iv) Participants were men and women aged 18-70 years.

(v) Patients with bipolar II disorder, substance induced mood disorder, mood disorder due to a general medical condition and schizoaffective disorder were excluded from the study.

3.4 DATA COLLECTION

The Dr. George Mukhari Hospital psychiatry unit register for all inpatients and outpatients was used to compile a list of file numbers for all the patients with bipolar I disorder treated at the unit during the study period. The list was then used to locate the patients' files, and once they were retrieved, the above selection criteria were applied. The relevant data was extracted from patient files and recorded on a data collection chart (Appendix A), which comprised the following two sections:

(i) Section 1: Socio-demographic data such as age, gender, marital and occupational status, etc.

(ii) Section 2: Psychiatric data such as number of new episodes, polarity of episodes, family history of mental illness, etc.

The data collection chart was personally completed by the researcher. Each data collection sheet has a specific identification number so that the names and hospital numbers of patients do not appear on the data collection chart in order to ensure patient confidentiality.

3.5 DATA CAPTURING AND ANALYSIS

A quantitative analysis of the data was performed by using the information obtained from the data collection chart. The relevant data was captured electronically and analysed with assistance from a biostatistician. Data was captured in MS-Excel, data capturing was verified, and validation checks were performed. All statistical analyses were performed on SAS, Release 9.1.3, running under Microsoft Windows Vista Business. Categorical data was summarised by frequency counts and percentages. Basic descriptive statistics (mean, standard deviation, minimum and maximum values) were calculated for the number of manic and depressive episodes, for the total number of new episodes as well as for the number of hospital admissions. In addition, 95% confidence intervals were calculated for the mean values. A logistic regression analysis was performed with a new

episode as the dependent variable and the following as predictor variables: comorbid substance use, compliance, family history of mental illness, age, gender and total duration of mental illness. Where applicable, p values $\leq 0,05$ were considered significant.

3.6 ETHICAL CONSIDERATIONS

The following ethical considerations were carried out:

(i) Ethical clearance was requested and obtained from the MEDUNSA Research and Ethics Committee, University of Limpopo, Faculty of Medicine, prior to conducting the study.

(ii) Consent was obtained from the superintendent at Dr George Mukhari Hospital for the use of the facilities as well as to gain access to patients' files.

(iii) The highest level of confidentiality and anonymity was maintained regarding the information obtained from the patients' files. Patients' names and hospital numbers do not appear on the data collection charts and the information is used for the purpose of the study only. All study materials and discussions surrounding the data remained between the study team members only, and confidentiality was honoured.

CHAPTER 4

RESULTS

4.1 THE WHOLE STUDY POPULATION (n=143)

The study was conducted using data from all the patients with a diagnosis of bipolar I disorder at Dr. George Mukhari Hospital-psychiatry unit within the period of 1 June 2007 to 1June 2008. Data was extracted and analysed from a total of 143 patient records, and will be described in detail in this chapter.

4.1.1 Socio-demographic variables

Table I: Socio-demographic variables

Variable	Frequency	Percent
Age		
18 – 24	21	14.69
25 – 34	41	28.67
35 – 44	35	24.48
45 – 54	29	20.28
> 55	17	11.89
Gender		
Female	87	60.84
Male	56	39.16
Ethnicity		
Black	138	96.50
White	2	1.40
Asian	1	0.70
Other	2	1.40
Marital status		
Single	75	52.45
Married	34	23.78
Divorced	20	13.99
Separated	2	1.40
Living in	9	6.29
Widowed	3	2.10
No of children		
none	47	32.87
1 - 2	58	40.56
3 – 4	30	20.98
> 4	8	5.59
Level of education		
No formal	4	2.80
Primary	23	16.08
Secondary	83	58.04
Tertiary	33	23.08
Religion		

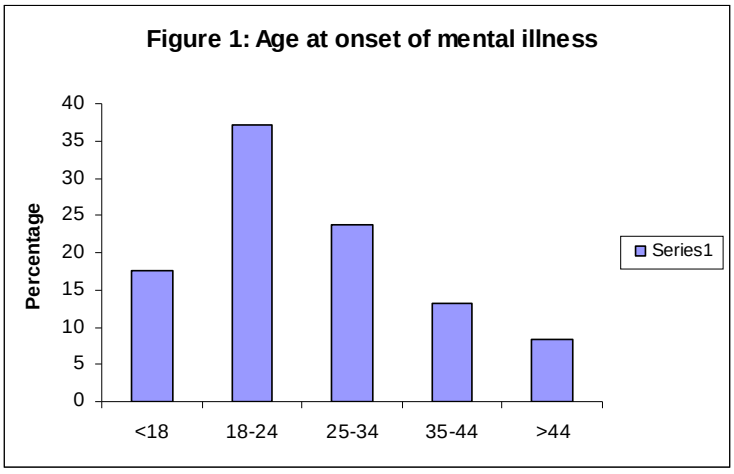
Christian	136	95.10
Traditional	2	1.40
Other	5	3.50
Employment		
Employed	30	20.98
Unemployed	108	75.52
Self employed	3	2.10
Retired	2	1.40
***Receiving disability grant**		
Yes	78	54.93
No	64	45.07

*data regarding the disability grant was missing from one data collection sheet

The age of the patients in the sample ranged from 18 years to older than 55 years. Most of the patients were between 25 and 34 years of age. Table I demonstrates that the vast majority of the patients were black (97%), and that 61% of the sample was female. About half of the patients were single, 24% were married, 14% divorced and the remainder were either living in, separated or widowed. Most of the patients had 1-2 children; and more than half had achieved high school education, while 23% went up to tertiary level and only 3% had had no formal education at all. In terms of religion, 95% were Christian, 2% were from traditional religious groups and 5% belonged to other religions or followed no religion at all. The majority of the patients were unemployed (76%) and about half of the study population was receiving a disability grant.

4.1.2 Age at onset of mental illness

Figure 1: Age at onset of mental illness



37% of the patients first became ill between 18 to 24 years of age and 24% became ill in the range of 25 to 34 years of age. Of note is that 17% had an onset of illness before 18 years of age.

4.1.3 Total duration of mental illness

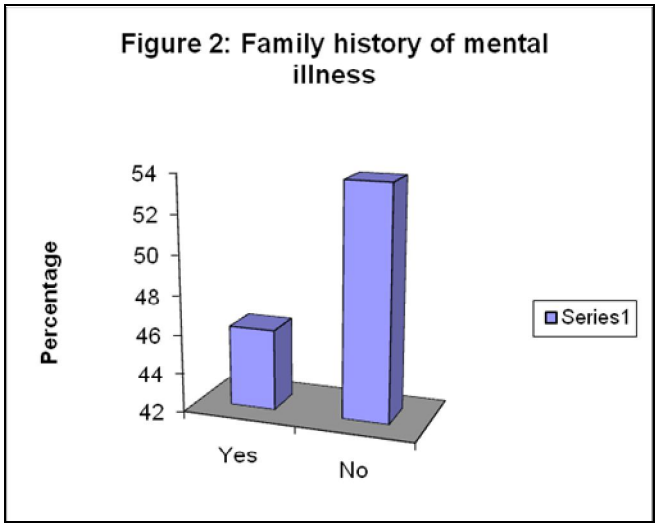
Table II: Total duration of mental illness

Total duration of mental illness	Frequency	Percent
< 1 yr	9	6.29
1 - 5 yrs	32	22.38
5 - 10 yrs	35	24.48
>10 yrs	67	46.85

Table II demonstrates that almost half of the sample had been ill for more than 10 years.

4.1.4 Family history of mental illness

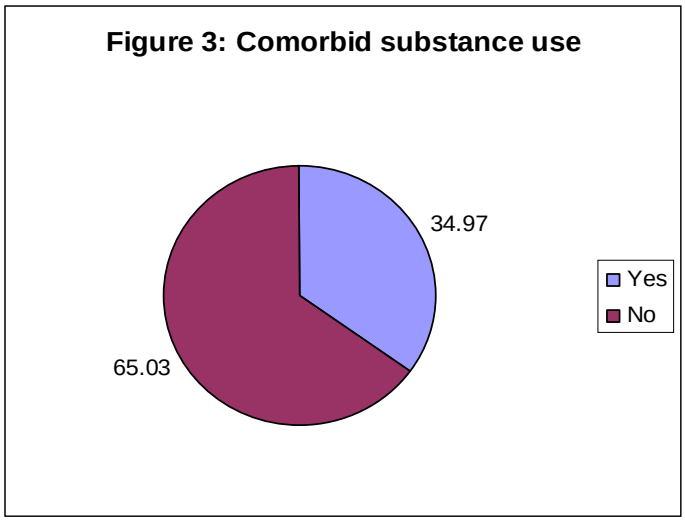
Figure 2: Family history of mental illness



Almost half (46%) of the study population had a family history of one or another mental illness.

4.1.5 Comorbid substance use

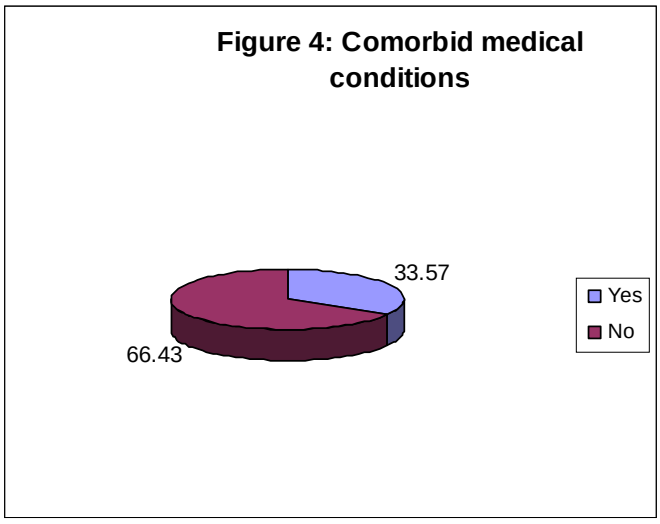
Figure 3: Comorbid substance use



The majority of this study population did not use any substances of abuse (65%). Of the 50 patients that did have a history of substance use, 52% used alcohol only, 12% used cannabis only, 34% used cannabis and alcohol and 2% used cannabis and inhalants.

4.1.6 Comorbid medical conditions

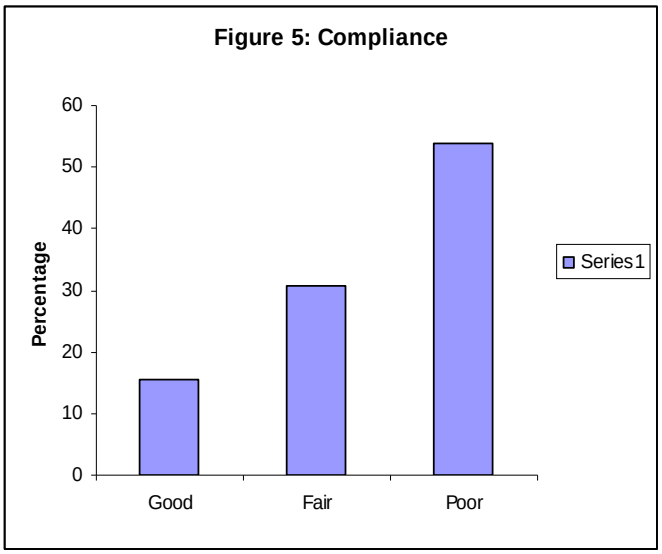
Figure 4: Comorbid medical conditions



34% of the sample had one or more comorbid medical conditions. The most common medical conditions were HIV, diabetes mellitus type II and hypertension.

4.1.7 Compliance

Figure 5: Compliance



Around half the study population (54%) demonstrated poor compliance.

4.2 PATIENTS WHO EXPERIENCED NEW EPISODES (n=90)

During the one year period that was studied, of the 143 patients, 90 (63%) had experienced new episodes and 53 patients (37%) had not experienced any new episodes.

4.2.1 Socio-demographic variables in patients who experienced new episodes

Table III: Socio-demographic variables in patients who experienced new episodes

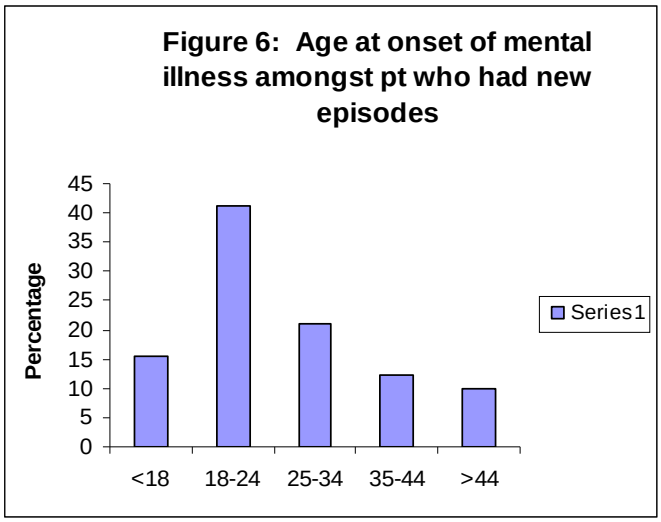
Variable	Frequency	Percent
Age		
18 – 24	12	13.33
25 – 34	26	28.89
35 – 44	22	24.44
45 – 54	21	23.33
> 55	9	10.00
Gender		
Female	52	57.78
Male	38	42.22
Ethnicity		
Black	85	94.44
White	2	2.22
Asian	1	1.11
Other	2	2.22
Marital status		
Single	44	48.89

Married	20	22.22
Divorced	18	20.00
Separated	2	2.22
Living in	6	6.67
Widowed	-	-
No of children		
None	27	30.00
1 – 2	43	47.78
3 – 4	16	17.78
> 4	4	4.44
Level of education		
No formal	2	2.22
Primary	12	13.33
Secondary	54	60.00
Tertiary	22	24.44
Religion		
Christian	87	96.67
Traditional	1	1.11
Other	2	2.22
Employment		
Employed	22	24.44
Unemployed	63	70.00
Self employed	3	3.33
Retired	2	2.22
Receiving disability grant		
Yes	42	47.19
No	47	52.81

Of the patients that had new episodes, 29% were in the age group of 25-34 years and only 10% of those aged 55 years or older had new episodes. More than half were female, 94% were black and 97% were Christian. More than half of the patients that relapsed were also never married and the majority had either 1 or 2 children. Table III demonstrates that 60% of those who experienced new episodes during the 1 year study period achieved secondary level education. Only 27% (employed & self employed) of those who experienced relapses were employed and only around half were receiving a disability grant despite having new episodes.

4.2.2 Age at onset of mental illness amongst patients who had new episodes

Figure 6: Age at onset of mental illness amongst patients who had new episodes



New episodes were more common in patients who experienced a younger age of onset of illness (41% in the 18-24 year age group), whereas only 10% of those who had a late age of onset (>44 years) had new episodes.

4.2.3 Total duration of mental illness in patients with new episodes

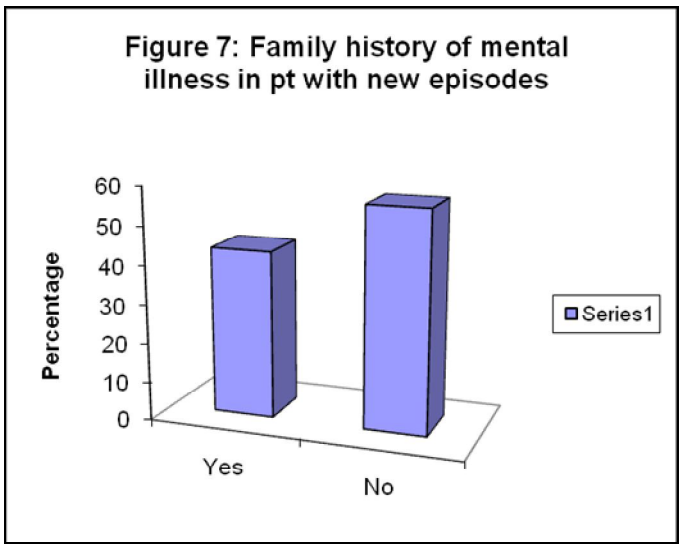
Table IV: Total duration of mental illness in patients with new episodes

Total duration of mental illness	Frequency	Percent
< 1 yr	9	10.00
1 - 5 yrs	20	22.22
5 - 10 yrs	22	24.44
>10 yrs	39	43.33

Almost half of those who were ill for more than 10 years had new episodes, while only 10% of those who had been ill for less than 1 year experienced relapses.

4.2.4 Family history of mental illness in patients with new episodes

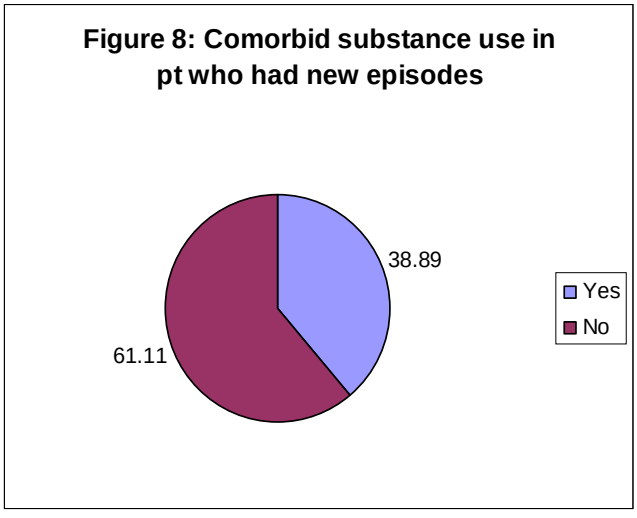
Figure 7: Family history of mental illness in patients with new episodes



Less than half (43%) of those who experienced relapses had a positive family history of mental illness.

4.2.5 a) Comorbid substance use in patients who had new episodes

Figure 8: Comorbid substance use in patients who had new episodes



Substance use was reported in 35 (39%) patients who experienced new episodes.

b) Distribution of the different substances in patients who had new episodes

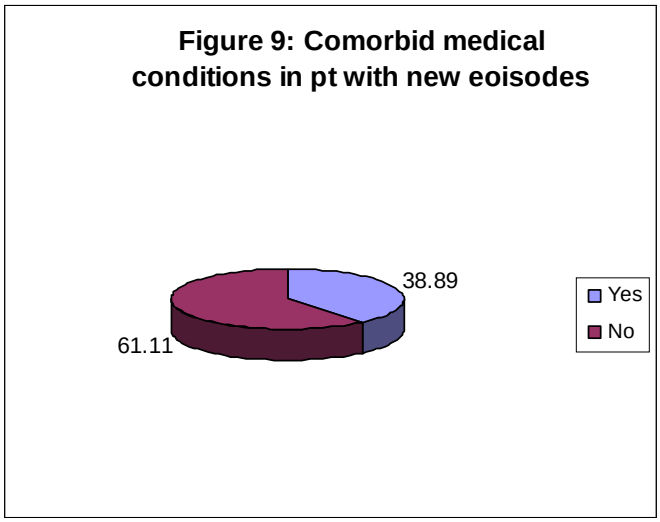
Table V: Distribution of the different substances in patients who had new episodes

Specific substance / s	Frequency	Percent
Alcohol	19	54.00
Cannabis	4	12.00
Alcohol + Cannabis	12	34.00

Amongst the 35 patients who had a history of substance use, 19 (54%) used alcohol only, 4 (12%) used cannabis only and 12 (34%) used a combination of both alcohol and cannabis.

4.2.6 a) Comorbid medical conditions in patients with new episodes

Figure 9: Comorbid medical conditions in patients with new episodes



35 (39%) patients who had experienced relapses suffered from one or more comorbid medical illness.

b) Distribution of the comorbid medical conditions amongst patients who experienced new episodes

Table VI: Distribution of co-morbid medical conditions amongst patients who experienced new episodes

Med condition 1	Med condition 2	Med condition 3	Frequency
Diabetes mellitus			2
HIV			8
Asthma			2
Epilepsy			3

Head injury			2
Hypertension			3
Osteoarthritis			1
Partial blindness			1
Tuberculosis			1
Epilepsy	Migraine		1
Hypertension	HIV		1
Hypertension	Diabetes mellitus		3
Hypertension	Hypothyroidism		1
Hypertension	Osteoarthritis		1
Hypertension	HIV	Head injury	1
Hypertension	Diabetes mellitus	Congestive cardiac failure	2
Hypertension	Diabetes mellitus	Neurocysticercosis	1
Hypertension	Diabetes mellitus	Stroke	1

The nature and distribution of the medical illnesses is represented in Table VI. As was seen in the whole study population, HIV, diabetes mellitus type II and hypertension remained the most common conditions also in the group that experienced relapses.

4.2.7 Medication profiles of patients who had new episodes

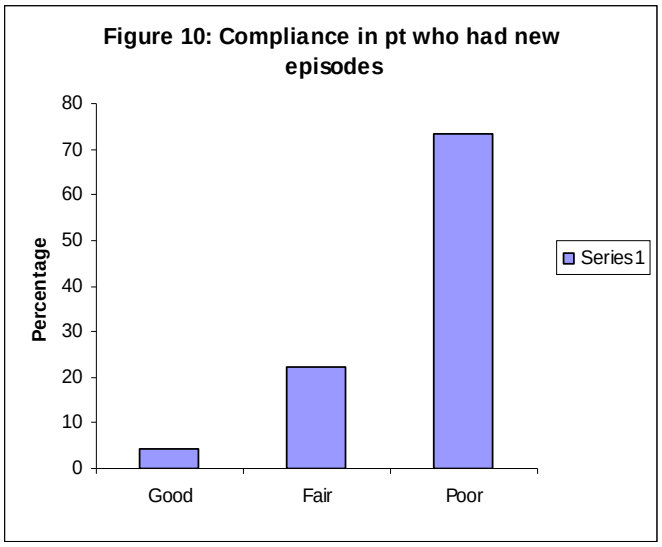
Table VII: Medication profiles of patients who had new episodes

Medication 1	**Medication 2**	**Medication 3**	**Frequency**
Risperidone			1
Carbamazepine			1
Haloperidol			3
Lithium			6
Sodium valproate			10
Other			2
Carbamazepine	Antidepressant		2
Carbamazepine	Haloperidol		6
Carbamazepine	Other		2
Carbamazepine	Risperidone		1
Lithium	Haloperidol		7
Lithium	Other		5
Sodium valproate	Antidepressant		1
Sodium valproate	Haloperidol		15
Sodium valproate	Other		5
Sodium valproate	Risperidone		4
Carbamazepine	Haloperidol	Other	5
Carbamazepine	Other	Antidepressant	1
Lithium	Haloperidol	Other	2
Sodium valproate	Haloperidol	Antidepressant	1
Sodium valproate	Haloperidol	Other	8
Sodium valproate	Lithium	Haloperidol	1
Sodium valproate	Risperidone	Other	1

All the patients in the sample (n=143) had been on medication. The following drugs were prescribed either alone or in various combinations: lithium carbonate, sodium valproate, carbamazepine, haloperidol, risperidone, antidepressants or other (which included depot antipsychotics or other first generation oral antipsychotics like chlorpromazine). Table VII represents the treatment profiles of those who had experienced new episodes (n=90). 6 patients (7%) were on an antipsychotic alone, 17 (19%) were on a mood stabiliser only, 62 (69%) were on a combination of mood stabilisers and antipsychotics, 3 patients (3%) were on a combination of mood stabilisers and antidepressants and 2 (2%) were on a combination of mood stabilisers, antipsychotics and antidepressants. No one was on antidepressants only.

4.2.8 Medication compliance in patients who had new episodes

Figure 10: Medication compliance in patients who had new episodes



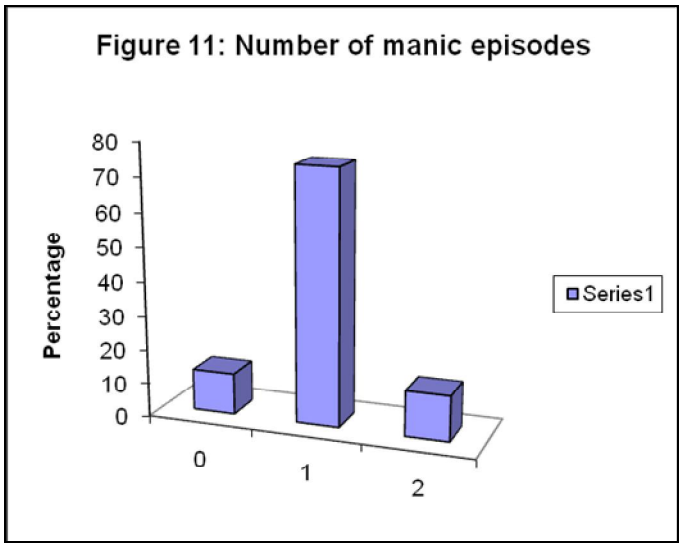
73% of patients who had experienced relapses demonstrated poor compliance.

4.3 DESCRIPTION OF NEW EPISODES

The new episodes that occurred in the 90 patients will be described in this section.

4.3.1 Number of manic episodes

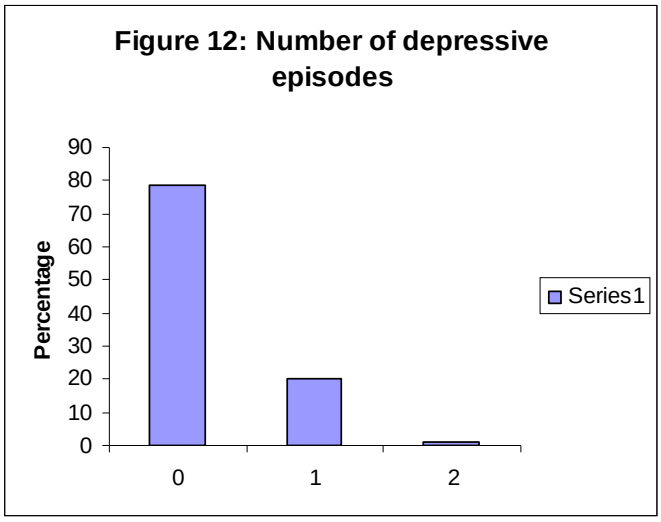
Figure 11: Number of manic episodes



Of the patients that had new episodes during the one year period under study, 12% had no manic episodes at all, 74% had 1 manic episode and 13% had 2 manic episodes (figure 11). Looking at the whole study population, 45% did not have any manic episodes, 47% (67) experienced 1 manic episode and 8% (12) had 2 manic episodes. This means that 55% (79) of the study population had one or more manic episodes during the one year period under study. (Mean=0.64)

4.3.2 Number of depressive episodes

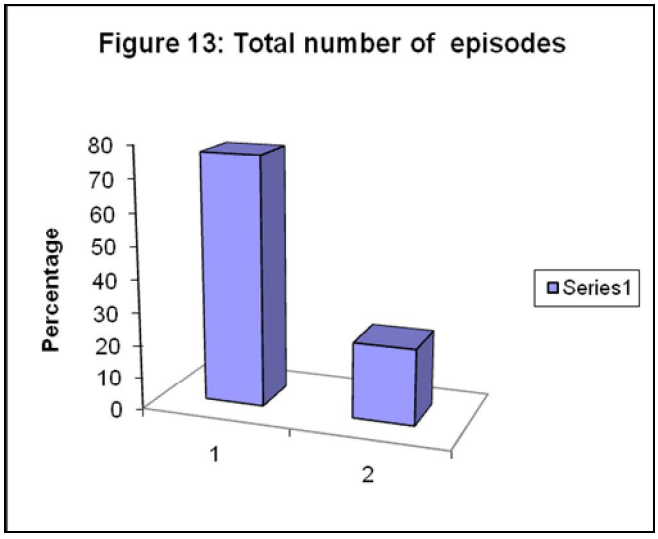
Figure 12: Number of depressive episodes



The majority of the patients who had new episodes did not experience any episodes to the depressive pole (79%); however, 20% did have 1 depressive episode and 1% had 2 depressive episodes (figure 12). Hence, most of the patients in the sample (87%) did not have any depressive episodes in that given year, however, 12.68% (18) had 1 depressive episode and 0.7% (1) had 2 episodes. This implies that 13.38 % (19) of the study population had one or more depressive episodes. (Mean=0.14)

4.3.3 Total number of episodes

Figure 13: Total number of episodes



Amongst the patients who did experience new episodes, 77% had 1 new episode only and 23% had 2 new episodes (figure 13). This means that out of all 143 patients, 37% (53) had no new episodes and 63% (90) did experience new episodes. 48% (69) had 1 new episode and 15% (21) had 2 new episodes. As shown in Table VIII, the maximum number of new episodes during the one year period was 2 and the mean was 0.78. Of note is that no one experienced rapid cycling during the one year period under study.

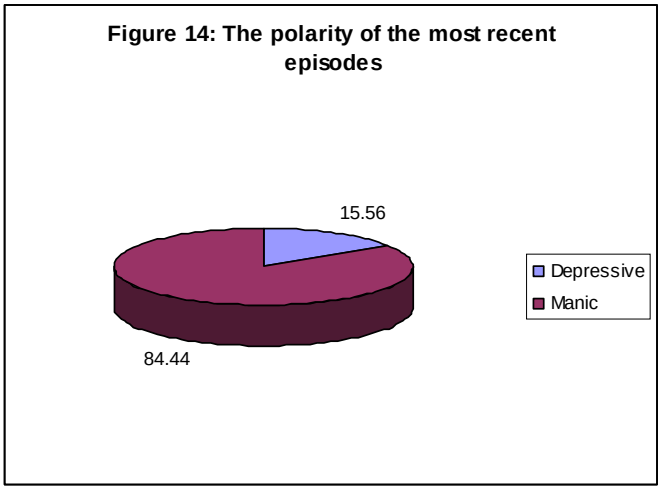
Table VIII: The means procedure for the new episodes

	Number of manic episodes	Number of depressive episodes	Total number of episodes
N	143	142*	143
Mean	0.64	0.14	0.78
Std dev	0.63	0.37	0.69
Min	0.00	0.00	1.00
Max	2.00	2.00	2.00

*data regarding episodes of depression was missing from one data collection sheet

4.3.4 Polarity of the most recent episode

Figure 14: The polarity of the most recent episode



Of the 90 patients that had new episodes, the most recent episode was manic in 76 patients (84%), and depressive in 14 patients (16%).

4.3.5 Total Number of hospital admissions

Table IX: Total number of hospital admissions

No of hospital admissions	Frequency	Percentage
0	23	25.56
1	55	61.11
2	12	13.33

During the one year period that was studied, 61% of those that had relapsed were hospitalised once only and 13% had two hospital admissions. 26% of those who experienced new episodes were managed on an outpatient basis with no admission to

hospital. The mean number of hospital admissions was 0.88 (minimum=0, maximum=2, standard deviation=0.61).

4.3.6 Description of variables associated with new episodes

Table X: Variables associated with manic episodes

Variable	Frequency	Percent
Age		
18 – 24	11	13.92
25 – 34	24	30.38
35 – 44	19	24.05
45 – 54	17	21.52
> 55	8	10.13
Gender		
Female	42	53.16
Male	37	46.84
Ethnicity		
Black	74	93.67
White	2	2.53
Asian	1	1.27
Other	2	2.53
Marital status		
Single	41	51.90
Married	15	18.99
Divorced	15	18.99
Separated	2	2.53
Living in	6	7.59
Widowed	-	-
Level of education		
No formal	1	1.27
Primary	9	11.39
Secondary	48	60.76
Tertiary	21	26.58
Employment		
Employed	19	24.05
Unemployed	56	70.89
Self employed	2	2.53
Retired	2	2.53
Family history		
Yes	36	45.57
No	43	54.43
Comorbid substance		
Yes	32	40.51
No	47	59.49

Table XI: Variables associated with depressive episodes

Variable	Frequency	Percent
Age		
18 – 24	2	10.53
25 – 34	6	31.58
35 – 44	4	21.05
45 – 54	6	31.58
> 55	1	5.26
Gender		
Female	17	89.47
Male	2	10.53
Ethnicity		
Black	18	94.74
White	1	5.26
Asian	-	-
Other	-	-
Marital status		
Single	7	36.84
Married	8	42.11
Divorced	4	21.05
Separated	-	-
Living in	-	-
Widowed	-	-
Level of education		
No formal	1	5.26
Primary	3	15.79
Secondary	9	47.37
Tertiary	6	31.58
Employment		
Employed	7	36.84
Unemployed	11	57.89
Self employed	1	5.26
Retired	-	-
Family history		
Yes	7	36.84
No	12	63.16
Comorbid substance		
Yes	6	31.58
No	13	68.42

Of the 79 patients who had manic episodes, the majority (68%) were younger than 45 years of age, while 32% were 45 years and older. Comparatively, 37% of the 19 patients that also had depressive episodes were 45 years of age and older. Slightly more than half of the patients who had manic episodes were female, whereas 89% of depressive relapses occurred in women. About half the patients with manic episodes were single, while the majority (42%) of patients who experienced depressive episodes were married. 32% of

patients with depressive relapses had achieved tertiary education, compared to 27% of patients with manic episodes. 71% of those with manic relapses were unemployed compared to only 58% of those with depressive episodes as well. The prevalence of a positive family history of mental illness was 46% in patients with manic relapses and 37% in those with depressive relapses. Comorbid substance use was reported in 41% of patients who had manic episodes, and in 32% of those who experienced depressive episodes.

4.4 FINDINGS FROM LOGISTIC REGRESSION

Table XII: Findings from Logistic regression

Variable	Wald Chi-Square	p-value
Age	7.6227	0.1064
Gender	0.1120	0.7379
Total duration Of mental illness	7.6958	0.0527
Family history of mental illness	3.3495	0.0672
Comorbid substance use	0.4802	0.4883
Compliance	31.8284	<0,0001

Six variables were assessed as possible predictors of new episodes. These were: age, gender, total duration of mental illness, family history of mental illness, comorbid substance use and compliance. Compliance, assessed as poor, fair or good, was found to be the only statistically significant predictor variable for new episodes ($p < 0,0001$). The odds ratio (OR) estimates, with 95% confidence intervals, were:

(i) Fair vs. poor OR = 0,046 (0,013 ; 0,157)

(ii) Good vs. poor OR = 0,012 (0,002 ; 0,064)

The interpretation is as follows:

(i) The odds for a new episode when compliance is fair, is 0,046 times the odds when compliance is poor

(ii) The odds for a new episode when compliance is good, is 0,012 times the odds when compliance is poor

This indicates that the chance of a new episode occurring is 83 times higher with poor compliance than with good compliance.

CHAPTER 5
DISCUSSION

5.1 SOCIODEMOGRAPHIC DATA

Results from this study show that most of the patients with a diagnosis of bipolar I disorder were between 25 and 34 years of age. The majority were black (97%), and this distribution of ethnicity represents the general distribution in South Africa. Another explanation for the marked racial distribution is that the setting of the study (Dr. George Mukhari Hospital) is the catchment area for mostly outer-lying and rural areas containing socio-economically disadvantaged people. Most of the patients were female (61%) with 1-2 children. Merikangas *et al* (2007) also reported that the illness occurs more frequently in females with a male and female prevalence of 0.8% and 1.1% respectively. Approximately half of this study population was single and more than half had achieved high school education. The unemployment rate was 76% and about half of the study sample was receiving a disability grant for mental illness. Sociodemographic correlates from other studies show that bipolar disorder is inversely related to educational level and occurs more frequently in unemployed or divorced people but is unrelated to race and socioeconomic status (Merikangas *et al*, 2007). The illness had its onset between 18 to 24 years of age in 37% of the patients and onset in the range of 25 to 34 years of age in 24% of the study sample. This is consistent with other studies that describe the age of onset as ranging between late adolescence and early 40's (Merikangas *et al*, 2007). In this study, 17% had an onset of illness before 18 years of age, however some studies report that the age of onset is commonly in childhood or adolescence. Yatham *et al* (2009) for instance found that 50 - 66% of patients with bipolar disorder had the first episode before the age of 19 years; and another study found the mean age of onset to be 18.2 years (Merikangas *et al*, 2007).

Approximately half the patients had been ill for more than 10 years and this is consistent with other studies, demonstrating the chronicity of bipolar disorder. 46% of this study population had a family history of mental illness. The Systematic Treatment Optimization Program for Early Mania (STOP-EM) project had similar findings viz. 40% of the

patients had a family history of mental illness, specifically affective disorders (Yatham *et al*, 2009). Only 35% of the patients in this study used substances of abuse. This finding is less than that observed in other studies. The STOP-EM study found the prevalence of substance use to be 54% and another study found it to be more than 60% (Yatham *et al*, 2009; Altman *et al*, 2006). Co-existing medical illness/s occurred in 34% of this study population compared to a finding of 26% in a Canadian study (Yatham *et al*, 2009). The most common medical conditions were HIV, diabetes mellitus type II and hypertension. The higher prevalence of HIV infection in Africa compared to first world countries may account for the difference in the findings between the two studies. A very important finding was that half the patients demonstrated poor compliance in this study. This factor varies between studies but the overall range for non-compliance with long term treatment is generally between 20-60% (Lingam and Scott, 2002).

5.2 PREVALENCE OF NEW EPISODES AND ASSOCIATED FACTORS

During the one year period and 143 patients who were studied; 90 patients (63%) experienced relapse/recurrence. This result is significantly higher than the findings in many studies. For example, in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) trial, 29% of patients had experienced recurrence by one year and 49% by two years (Perlis *et al*, 2006) and in the McLean-Harvard First Episode Mania Study; new episodes occurred in 40% of 154 patients with bipolar disorder within two years (Tohen *et al*, 2003), while the Health Outcomes of Manic Episodes (HOME) Study observed a 36% prevalence of new episodes by one year (Kora *et al*, 2008). However, some other studies reveal that more than half of the patients have a new episode within 12 months, e.g., in the STOP-EM study; 53.3% of patients experienced a relapse/recurrence during a one year follow up period after the index episode and the mean time to event was 7.9 months (Yatham *et al*, 2009). Studies on bipolar disorder come mostly from developed countries but it has been suggested that bipolar disorder may run a more severe course in developing countries compared with developed countries. An example is the largest community based cohort study on bipolar disorder in Sub-Saharan Africa, which was carried out in Butajira, Ethiopia. The researchers monitored 315 patients prospectively over 2.5 years and found that 66% had relapsed at

least once (Fekadu *et al*, 2006). Contrary to the aforementioned, in the International Pilot Study of Schizophrenia, Leff *et al* found that patients from developing countries who were diagnosed with affective disorders had a better clinical and social outcome compared with patients from developed countries over a five-year period (Fekadu *et al*, 2006).

Of the patients that had new episodes, 28% were in the age group of 25-34 years and only 10% were 55 years and older. More than half of the patients who relapsed were female and more than half were also never married. Only 27% of those who experienced relapses were employed and only half received a disability grant despite having new episodes. Relapses/recurrences were more prevalent in patients who experienced a younger age of illness onset, i.e., 41% in the 18-24 year age group compared to only 10% in those older than 44 years. Other studies found that a younger age of onset predicted a longer duration of that episode (Kora *et al*, 2008). In this study, almost half of patients who were ill for longer than 10 years had new episodes, compared to only 10% of those who had been ill for less than one year. The distribution of a family history of mental illness in patients with new episodes was similar to that of the whole study population (less than 50%). Substance use was reported in 35 patients who experienced new episodes, of which 19 (54%) used alcohol only, 4 (12%) used cannabis only and 12 (34%) used a combination of both alcohol and cannabis. In this study, an overall 78% of the patients who had new episodes were on antipsychotics, 93% were on mood stabilisers, and 69% were on a combination of mood stabilisers and antipsychotics. Of note is that no single patient was on antidepressants alone. These findings are very similar to results from other studies, e.g., in the STOP-EM study, 77% of patients were on an antipsychotic, 87% on a mood stabiliser, and 72% on a combination of a mood stabiliser and an antipsychotic (Yatham *et al*, 2009); and in a study by Tohen et al (2010) 79% were on antipsychotics and 70% on mood stabilizers. In this study, 73% of patients who had new episodes demonstrated poor compliance.

5.3 DESCRIPTION OF NEW EPISODES

A total of 63% of patients experienced new episodes during the one year period under study with the maximum number of episodes being two. Of the patients who relapsed, the majority (88%) had one or more manic episodes and 21% had one or more depressive episodes. The most recent episode was manic in 84% and depressive in 16%. The ratio of depressive recurrence to manic recurrence is 1:4. These results differ from other studies. In the STEP-BD trial, up to 70% of recurrences were that of depression with a ratio of 2.5:1 for depressive recurrence vs. (hypo) manic/mixed episodes and in the Ethiopian study the ratio of depressive to manic relapse was 1:1.07 (Perlis *et al*, 2006; Fekadu *et al*, 2006). However, studies from some developing countries like India and Nigeria show that the course of bipolar disorder in these countries is characterised by manic rather than depressive episodes. Studies in India have demonstrated an almost seven-fold rate of manic compared with depressive relapses and in Nigeria a three-fold rate of manic compared with depressive relapses has been shown. It has also been suggested that mania is more common than depressive episodes in regions closer to the equator (Fekadu *et al*, 2006). Although depression exists across all cultures, different cultures may vary in their clinical manifestation of depressive symptoms. For example, in a South African study by Mosotho *et al* (2008), Sesotho speaking people suffering from depression displayed somatic complaints (headaches, chest pain and dizziness), perceptual disturbances and disturbances in thinking (suicidal or homicidal thoughts, paranoid delusions). Another study by Ngcobo and Pillay (2008) found that pain and other psychosomatic complaints in African women symbolically represented their emotional status, but that this unfortunately lead to late or no detection of depression in these patients. This may be one of the reasons for depressive episodes being commonly missed in an African context. In addition, people of various South African cultural groups often consult traditional or spiritual healers for mental illness and are more likely to present to a hospital setting for a manic rather than a depressive episode. This could be another reason why manic episodes seem to be more prevalent in a South African context.

Of the patients who had experienced relapse in this study, 61% were hospitalised once, 13% twice, and the remainder were not treated on an inpatient basis at all. Of note is that

no one experienced rapid cycling during the one year period under study. About half of the patients who had manic episodes were female and single, whereas 89% of depressive relapses occurred in women and these women were mostly married. This finding concurs with other studies that report that men may be more prone to mania and women more prone to depressive episodes and that men take longer to reach remission of an episode (Colom *et al*, 2006; Fekadu *et al*, 2006; Kora *et al*, 2008). Only 24% of patients who relapsed had achieved tertiary education and 71% of those with manic relapses were unemployed compared to 58% of those with depressive episodes. Some studies found poor job functioning to be associated with risk for relapse and in the HOME study lower premorbid occupational status was associated with a shorter time to relapse/recurrence (Altman *et al*, 2006; Kora *et al*, 2008). The prevalence of a positive family history of mental illness was 46% in patients with manic relapses and 37% in those with depressive relapses. Comorbid substance use was reported in 41% of patients who had manic episodes, and in 32% of those who experienced depressive episodes. The most common substance reported was alcohol followed by a combination of both alcohol and cannabis. Other studies found that a comorbid substance use disorder particularly cannabis was associated with an increased risk of manic recurrence while alcohol usage may be associated with depressive episodes (Perlis *et al*, 2006; Colom *et al*, 2006).

5.4 PREDICTORS OF NEW EPISODES

In this study, age and gender were not associated with the occurrence of new episodes. This is consistent with other studies and the general understanding is that sociodemographic factors are not strong predictors of outcome. For instance, in the STEP-BD trial, age, marital and socioeconomic status, as well as level of education were not associated with relapse or recurrence (Perlis *et al*, 2006). In another 5 studies, only 1 found that female gender resulted in an increased risk of new episodes; however, several studies did indicate that female gender was associated with depressive episodes and male gender with manic episodes (Altman *et al*, 2006; Fekadu *et al*, 2006). Results from this study indicate that a positive family history of mental illness was not associated with new episodes. This finding varies in different studies. Some studies have shown that a positive family history of mental illness is associated with an increased risk of relapse in patients

with bipolar disorder (Altman *et al*, 2006), but a study by Staner et al, as well as the STEP-BD trial found no significant association between family history and risk of new episodes (Staner *et al*, 1997; Perlis *et al*, 2006). Total duration of mental illness and comorbid substance use were not found to be predictors of relapse/recurrence in this study. One review study, however, mentions that the use of substances can precipitate a new episode and increase the duration and severity of the episode (Altman *et al*, 2006), and another study observed that substance use can indirectly precipitate relapse/recurrence because it predicts noncompliance (Yatham *et al*, 2009), but in the STEP-BD trial, Perlis *et al* (2006) found that the duration of illness did not predict future episodes. Compliance was the only factor in this study found to be statistically significant in serving as a predictor of new episodes, meaning that the chance of a new episode occurring is 83 times higher when compliance is poor. This is in keeping with results from other studies, e.g., a direct correlation was found between the rate of relapse/recurrence and noncompliance with follow up visits and medication in a study by Mousavi, Moalemi and Sadeghi (2004). Poor compliance also indirectly precipitates new episodes in bipolar disorder by perpetuating social and occupational problems (Lingam and Scott, 2002).

CHAPTER 6
CONCLUSION

6.1 LIMITATIONS OF THE STUDY

This study suffers the following limitations. First, there was a possibility of sampling bias because approximately 30-40 patient files either could not be obtained or were not useful. Secondly, the findings in this study might have been influenced by the short duration of the study, i.e., some patients may not have had adequate time to experience a relapse. Thirdly, given that this is a retrospective study, the clinical information drawn from patients' files cannot be guaranteed to be correct and consistent. In addition, different clinicians were involved in patient assessment and management at different points in time; hence, there may not be uniformity in the information recorded in patients' files. Lastly, some patients may have been incorrectly diagnosed or incorrectly listed on the patient register. It is for these reasons that findings cannot be generalised to other settings.

6.2 RECOMMENDATIONS

In the light of these findings, the following recommendations have been made bearing in mind that the goals involve preventative, supportive and dispositional approaches:

(i) Patients with bipolar I disorder be followed up regularly in order to identify those at high risk for new episodes.

(ii) Rating scales be used to monitor symptoms and medication response in order to identify prodromes of relapse.

(iii) Families and patients receive structured and consistent psycho education in order for them to be actively involved in the patient's illness so as to identify signs of relapse as early as possible as a preventative measure.

(iii) Strategies should be implemented to facilitate better compliance with medication e.g. addressing patient concerns and side effects.

(iv) Evaluate for and manage medical and psychiatric comorbidities as well as substance use in order to control factors that may contribute to relapse.

(v) Make mental health services more accessible by mobilizing community health care in order for high-risk patients to be identified early and managed adequately and efficiently.

6.3 CONCLUSION

Bipolar I disorder proves to be a chronic illness with a recurring nature. There is a high rate of relapse and recurrence in the setting of Dr. George Mukhari Hospital, and the majority of the new episodes are to the manic pole. Poor compliance is the greatest contributor to relapse/recurrence and strategies to address problems with compliance should be implemented in order to improve the prognosis of patients.

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APPENDIX A: DATA COLLECTION SHEET (1 JUNE 2007-1 JUNE 2008)

Number: …….

1. SOCIO-DEMOGRAPHIC DATA

Age group: 18-24 ☐ 25-34 ☐ 35-44 ☐ 45-54 ☐ > 55 ☐

Gender: male ☐ female ☐

Ethnic group: black ☐ white ☐ asian ☐ other ☐

Marital status: single ☐ married ☐ divorced ☐ widowed ☐

living in ☐ separated ☐

No. of children: none ☐ 1-2 ☐ 3-4 ☐ >4 ☐

Level of education: no formal ☐ primary ☐ secondary ☐ tertiary ☐

Religion: christian ☐ traditional ☐ other ☐

Employment: unemployed ☐ employed ☐ self-employed ☐ retired ☐

Receiving disability grant: yes ☐ no ☐

2. PSYCHIATRIC DATA

Age at onset of mental illness: <18 ☐ 18-24 ☐ 25-34 ☐ 35-44 ☐ >40 ☐

Total duration of mental illness: <1yr ☐ 1-5yrs ☐ 5-10yrs ☐ >10yrs ☐

Number of manic episodes: ……

Number of depressive episodes: ……..

Specify polarity of most recent episode: ……

Total number of previous episodes: ……

Total number of hospital admissions: ……..

Family history of mental illness: yes ☐ no ☐

Comorbid substance use: yes ☐ no ☐

Specify substance/s: 1……..... 2…… 3……

Comorbid medical condition: yes ☐ no ☐

Specify condition/s: 1……..…….. 2…….. 3…….....

Medication: lithium ☐ sodium valproate ☐ carbamazepine ☐

haloperidol ☐ risperidone ☐ antidepressant ☐

other ☐

Compliance: poor ☐ fair ☐ good ☐