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A CROSS-SECTIONAL DESCRIPTIVE STUDY OF CLINICAL FEATURES AND COURSE OF ILLNESS IN A SOUTH AFRICAN POPULATION WITH BIPOLAR DISORDER

By

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Declaration

I, the undersigned, hereby declare that the work contained in this thesis is my own original work and that I have not previously in its entirety or in part submitted it at any university for a degree.

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Dr. Christoffel Grobler

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Date

Dedication

For my mother Celine,
who encouraged my passion for reading

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Abstract

There is generally a lack of studies examining prevalence and phenomenology of bipolar disorder in Africa. In literature, a unipolar manic course of illness in particular is reported to be rare.

The purpose of this study was to investigate and describe the course of illness and clinical features in a cross-section of patients diagnosed with bipolar disorder attending public hospitals in Limpopo Province, South Africa and to determine the rate of a unipolar manic course in this sample of patients.

This was a descriptive, cross-sectional study of patients presenting with a history of mania between October 2009 and April 2010, to three hospitals in Limpopo Province. A purposeful sample of 103 patients was recruited and interviewed using the Affective Disorders Evaluation.

This study confirms that a unipolar manic course is indeed much more common than rates suggested in present day literature with 57% of the study sample only ever experiencing manic episodes.

The study also confirms the debilitating nature of bipolar disorder with more than two-thirds being unemployed in spite of a quarter of the study

subjects having a tertiary education. The high rates of attempted suicide, history of violence and history of drug abuse all furthermore points to the devastating effects bipolar disorder has on individuals and their families.

Treatment choice appeared to be a combination of a mood-stabilising agent in combination with an anti-psychotic. It was found that two-thirds of study subjects had consulted with faith- or traditional healers.

Significant gender differences appeared in that females were more likely to suffer from comorbid anxiety disorders, have a history of sexual trauma, and be HIV positive whilst men were more likely to have a forensic- and substance-abuse history, experience hallucinations and receive clozapine.

Patients presenting with a unipolar manic course of illness, as described in this thesis, may contribute to the search for an etiologically homogeneous sub-group which presents unique phenotype for genetic research and the search for genetic markers in mental illness. A unipolar manic course therefore needs to be considered as a specifier in diagnostic systems in order to heighten the awareness of such a course of illness in bipolar disorder, with a view to future research.

Key phrases: “affective disorders”, “bipolar disorder”, “recurrent”, “mania”, “unipolar mania”.

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Abbreviations used

ADE	Affective Disorders Evaluation
AESOP	Aetiology and Ethnicity of Schizophrenia and Other Psychoses
AIDS	Acquired immunodeficiency syndrome
CCMD-3	Chinese Classification of Mental Disorders, 3rd Edition
CGI	Clinical Global Impression of severity
CNV's	Copy-number variants
DAM	Depressive and Manic episodes
DSM	Diagnostic and Statistical Manual of Mental Disorders
EAOO	Early age of onset
EMBLEM	European Mania in Bipolar Longitudinal Evaluation of
GAD	Generalised anxiety disorder
GC	Cuban Glossary Medication
GWAS	Genome-wide association studies
HIV	Human immunodeficiency virus
ICD	International Classification of Diseases
MHCU	Mental Health Care User
MO	Manic Only episodes
NEC	Not elsewhere classified
NIMH	National Institute for Mental Health
OCD	Obsessive-compulsive disorder
PMHC	Polokwane-Mankweng Hospital Complex
PTSD	Posttraumatic stress disorder
SASH	South African Stress and Health
SASOP	South African Society of Psychiatrists
SCID	Structured Clinical Interview for DSM-IV
STEP-BD	Systematic Treatment Enhancement Program for Bipolar Disorder
TB	Tuberculosis
UK	United Kingdom
USA	United States of America
WHO	World Health Organization
ZCC	Zion Christian Church

Chapter 1
Introduction

There is generally a lack of studies examining prevalence and phenomenology of bipolar disorder in Africa. (1) In literature, a unipolar manic course of illness in particular is reported to be rare. (2) The purpose of this study was to investigate and describe the course of illness and clinical features in a cross-section of patients diagnosed with bipolar disorder attending public hospitals in Limpopo Province, South Africa and to determine the rate of a unipolar manic course in this sample of patients.

The distinction between schizophrenia (dementia praecox) and manic depressive insanity as proposed by Kraepelin in 1896 was the subject of vigorous debate in the first decades of the 20th century. (3) This debate on the dichotomous nature of psychotic illness could in one way be seen as the nosological birth of bipolar disorder in the sense that it was the first attempt at drawing a clear line between these two illnesses. However, our modern understanding of bipolar disorders as they are known today is credited to Falret and Ballarger in many circles. (4)

The study could potentially aid in presenting new data for the inclusion of a new diagnostic category within the psychotic spectrum of disorders or

at the very least unipolar mania could come to be used as a specifier in the bipolar spectrum of mental illness.

Considering that finding phenotypes for disorders continues to be a challenge in psychiatric genetic research, a case will be made that the data presented in this study could possibly signify the existence of a homogeneous phenotype on the schizophrenia-bipolar spectrum. This phenotype could possibly lay the foundation for future genetic studies.

The idea for this MD came about in 2006 while I was working at Mokopane Hospital in Limpopo Province where I noticed that the number of patients presenting with manic symptoms, carrying a diagnosis of bipolar disorder, far outnumbered those presenting in the depressive phase of the illness. They seemed to have a recurrent unipolar manic course, the mania accompanied by severe psychotic symptoms of a schizophrenic nature from the onset of the illness, and they seldom presented either to hospital or out-patient clinics with symptoms of depression.

Presenting my literature findings at the South African Society of Psychiatrists (SASOP) Conference of August 2008, a psychiatrist from Cape Town approached the presenter and observed that he was seeing

the same phenomenon in the Xhosa speaking population. In informal discussions with other South African psychiatrists working in rural areas, they concur that bipolar depression is hardly ever seen. And considering that a poster presentation summarising the findings of this study at the 2012 SASOP Conference in September was voted the “Best Poster” by both the Scientific Judging Committee as well as congress delegates gives credence to the fact that a unipolar course in bipolar mood disorder is an area ready to be researched in South Africa.

The subsequent journey that was born out of curiosity inevitably led me to delve ever deeper into the history of bipolar disorder and along the way I could not help but become increasingly aware of the shortcomings of our profession’s diagnostic classification system with regard to the schizophrenia/bipolar dichotomy and the psychotic spectrum illnesses. All the while observing my own clinical approach to our field of practise carefully, I also became acutely aware of our inability to decide which drugs works best for which presentations – and our heavy dependence on a sometimes very undependable pharmacopeia of drugs. In the process we attributed the successes of our drugs to hypothetical drug actions in the brain and rationalised away the numerous treatment failures, hiding behind terms such as “treatment resistance” or “unwanted side effects”.

I do believe that our understanding of the brain and mechanisms of action of psychotropic drugs have increased immensely in the last two decades and that these drugs have undoubtedly made a huge contribution to improved quality of life for many of our patients with severe and enduring mental illness. Still, the arguments put forth in her book " The Myth of the Chemical Cure" (5), by Joanna Moncrieff, have to be considered if we are to be honest with ourselves. In this book Moncrieff makes a compelling argument for a drug-centred- versus a disease-centred model of approach to mental illness. I believe that many psychiatrists start following this approach unintentionally when they are faced with patients that are particularly hard to fit into contemporary diagnostic classification systems.

The current area of research that will in future possibly have the biggest influence on approaches to diagnosis and classification of major psychiatric illness is molecular genetic studies. The researchers in the field of genetic studies have already begun challenging and will possibly in future overturn in particular our dichotomous view of the distinction between schizophrenia and bipolar disorder. (6) The so-called "Kraepelinian Dichotomy" presumes that schizophrenia and bipolar disorder are distinct entities with separate underlying disease processes

and treatments and is based on Emil Kraepelin's view that schizophrenia and manic-depressive illness are two separate illnesses. (7)

The Kraepelinian Dichotomy has probably survived in part because individuals diagnosed with 'typical schizophrenia' are recognised to be different from those having 'typical bipolar disorder' on the basis of clinical features and outcome. The dichotomy is conceptually simple and appeals to clinicians as it allows psychiatrists to demonstrate diagnostic expertise in an often complex patient with a confusing clinical picture. (6)

However, a substantial body of evidence from genetic studies is accumulating, challenging this dichotomous view, and providing convincing evidence that genetic susceptibility is shared between bipolar disorder and schizophrenia. The main findings of these genetic studies consist of family studies; genome-wide association studies (GWAS) and analysis of structural genomic variation or rare copy-number variants (CNV's).

In the largest family study of the two disorders ever conducted, overlap in genetic susceptibility across bipolar and schizophrenia is shown. More than two million families identified from a Swedish population and hospital discharge registers showed that there is an increased risk of

both schizophrenia and bipolar disorder in first-degree relatives of probands with either disorder. Evidence from half-siblings and adopted-away relatives has furthermore revealed this increased risk to be due to genetic factors. (8)

In a genome-wide association study of European individuals, molecular genetic evidence for a substantial polygenic component to the risk of both schizophrenia and bipolar disorder involving thousands of common alleles of very small effect was shown. This study provides compelling evidence that the aggregate polygenic contribution of many alleles of small effect adds to susceptibility for schizophrenia but also influences susceptibility to bipolar disorder. (9)

Recent studies of de novo copy-number variants (CNV's) indicate that they may also have an influence on the risk for developing bipolar disorder albeit slightly less so than for schizophrenia. Malhotra et al estimate the overall frequency of de novo CNV's of more than 10 kb to be approximately 4% in bipolar disorder and 5% to 10% in schizophrenia. These authors' preliminary findings also suggest that individuals with early onset of mania might constitute a subclass of bipolar disorder in which there is a greater contribution of rare alleles of

large effect. They conclude that rare spontaneous mutations are an important contributor to risk for bipolar disorder. (10)

Hamshere maintains that “cases with a rich mixture of clinical features of bipolar mood episodes and the psychotic symptoms typical of schizophrenia (a broadly defined schizoaffective illness) may be particularly useful for genetic studies”. (11) This statement lends credibility to this current study as being possibly very important for doing genetic research on this particular group of patients who seem to present a very specific phenotype on the schizophrenia-bipolar spectrum.

It is envisaged that the present study will help to define a specific phenotype on the schizophrenia-bipolar spectrum. Defining accurate phenotypes in psychiatric genetics is important for future research in disentangling the ethiopathogenesis of these illnesses.

Chapter 2
The History of Bipolar Disorder

2.1 Introduction

The purpose of this chapter is to orientate the reader as to the history of bipolar disorder. Starting from the classical period and the initial use of terms such as mania and melancholia, through the commencement of contemporary concepts of bipolar disorder and ending with the evolution of our current nosology in existing diagnostic manuals.

2.2 The Classical Period

Most present-day authors on the history of bipolar disorder seem to agree that the concept of bipolar disorder was first recognised by Greek and Roman physicians in the classical period between 500 and 400 BC. (12) Hippocrates is credited with the shift of Western medicine away from the religious to the “rational.” He believed doctors should analyse symptoms on a case-by-case basis, instead of having blanket causes for each disease. To accomplish this, he developed the practice of Clinical Observation that had four stages; diagnosis, prognosis, observation and treatment. He also believed that the Four Humours (fluids in the body) were the keys to health and healing. (13)

Blood, the liquor of vitality, made the body hot and wet. *Choler,* bile or gastric juice, made the body hot and dry. *Phlegm* was colourless secretions as in sweat, tears and nasal secretions and also made the body cold and wet. Phlegm was also found in the brain, where one of its roles was to cool the eagerness of the blood. Black bile or *melancholy* was the one hidden humour, seen only insofar as it led to the darkening of other fluids, such as blood and stools; it made the body cold and dry. (14)

Hippocrates was also the first to systematically describe mania and melancholia. He based his work on the views of Pythagoras and Hippocrates's scholars, Alcmaeon and Empedocles of Crotona. Alcmaeon experimented with the brains of animals trying to find the auditory and visual channels of the brain. He believed that the origin of diseases was to be found in the disturbed interaction of body fluids in the brain. (15)

Psychiatry was one of Hippocrates's main interests and he supplemented the abovementioned theories with superb bedside observations as well as longitudinal follow-up. He furthermore formulated the first classification of mental disorders -namely melancholia, mania and paranoia. (16) Hippocrates and his school also

described organic and toxic delirium, post-partum psychosis and coined the term “hysteria”. Hippocrates described personality in terms of humoral theories dividing the different types of personality into choleric, phlegmatic, sanguine and melancholic. Hippocrates thought the brain to be the organ of mental functions and mental disorders. He writes in his famous work ‘On the Sacred Disease’:

> The people ought to know that the brain is the sole origin of pleasure and joy, laughter and jests, sadness and worry, as well as dysphoria and crying. Through the brain we can think, see, hear and differentiate between feeling ashamed, good, bad, happy … Through the brain we can become insane, enraged, we develop anxiety and fear, which can come in the night or during the day, we suffer from sleeplessness, we make mistakes and have unfounded worries, we lose the ability to recognize reality, we become apathetic and we cannot participate in social life. We suffer all these things mentioned above through the brain when it becomes ill.

It would appear to the modern-day psychiatrist reading the above quote that Hippocrates is referring to mental illnesses such as generalised anxiety disorder, major depressive disorder, manic symptoms and psychosis.

Investigating the origins of the word “mania” is challenging as it could suggest a number of different meanings. In the classical period four meanings for “‘mania” were described (4) :

1. A reaction to an event meaning rage, anger or excitement;
2. A biologically defined disease;
3. A divine state; and
4. A kind of temperament, especially in its mild form.

Caelius Aurenianus suggests in his book on chronic diseases:

> In the Phaedrus, Plato declares that there are two kinds of mania, one involving a mental tension that arises from a bodily cause of origin, the other divine or inspired, with Apollo as the source of inspiration. This latter kind, he says, is now called ‘divination’, but in early times was called ‘madness’; that is, the Greeks now call it ‘prophetic inspiration’ (*mantice*), though in remote antiquity it was called ‘mania’. Plato goes on to say that another kind of divine mania is sent by Father Bacchus, that still another, called ‘erotic inspiration’, is sent by the god of love and that a fourth kind comes from the Muses and is called ‘protrepic inspiration’ because it seems to inspire men to song. The Stoics also say that madness is of two kinds, but they hold that one kind consists in lack of wisdom, so that they consider every imprudent person mad; the

> other kind, they say, involves a loss of reason and a concomitant bodily affection. (17)

As with the previous quote from Hippocrates, one gets the distinct impression that again reference is being made to modern biological psychiatric concepts e.g. “tension arising from a bodily cause of origin” and “a loss of reason and a concomitant bodily affection”. Hence it appears the even the philosophers of old seemingly were not at odds with the idea that certain changes in behaviour of individuals may be ascribed to something going awry in their physiology.

It is held that Socrates’s proposition: “The highest of all good things are given to us by mania” referred to “divine mania”, or “creativity”; or, like some authors would suggest today “hypomania”, “hyperthymia” or a “hyperthymic temperament”. (18)

However, the Greeks also associated melancholia or melancholic personality with genius and creativity. In in his book ‘Problemata Physica’, Aristotle asks: “Why are extraordinary men in philosophy, politics or the arts melancholics?” And Hippocrates declared to the citizens of Abdira, after examining the philosopher Democritus that their

fellow citizen suffered not from melancholia- “but is simply a genius”. (16)

Aretaeus of Cappadocia was however, the first of his contemporaries to explicitly link mania and melancholia and may arguably be considered the first to conceptualise the bipolar nature of this disease. Born in Alexandria, he was the most prominent representative of the ‘Eclectics’ who were not bound by any systems of therapy. Aretaeus was very careful in his description of diseases, favoured observation of details and was free of dogma and superstition. The position of Aretaeus, as described in his book ‘On the Aetiology and Symptomatology of Chronic Diseases’ can be summarised as follows (19):

1. Melancholia and mania have the same aetiology, namely disturbance of the function of the brain.
2. Mania is worsening of melancholia.
3. Mania is the phenomenological counterpart of melancholia.

Aretaeus’s concepts of melancholia and mania were broader than modern concepts and probably included depression, psychotic depression, schizoaffective disorders, mixed states, schizophrenia with affective symptomatology and organic psychoses.

He differentiated between melancholia (a biologically caused disease) and reactive depression (a psychologically caused state).

Not all authors however agree that the concept of mania and melancholia as described by Hippocrates, Aretaeus and other ancient Greek and Roman physicians could be considered akin to our modern day understanding of bipolar affective disorder. Healy cogently argues that "whilst terms such as mania, melancholia, insanity, dysphoria, dysthymia, paranoia and lunacy all go back to the Greeks and Romans, manic-depressive disease does not and indeed could not". Healy reasons that visible signs made it reasonable for the Greeks to locate the problem in the body of the sick person and today we depend on what people say to make a diagnosis with the result that mental illness is "negotiated" between doctor and patient.

Healy claims: "to argue that Hippocrates describes manic-depression involves a careful selection of the facts and a gross selection of text". (20) For Hippocrates, the foreheads of maniacs and melancholics would commonly have literally felt hot with fevers that gave rise to delirious or frenzied states. Mania, therefore, was probably what would today be seen as delirium. Before antibiotics, high fevers gave rise to agitated and raving states far more commonly than any 'mental disorder' did and

against a background of terrifying and lethal epidemics, what is now called “manic-depressive illness” was almost an irrelevance, a rare disorder. (20)

2.3 Commencement of the contemporary concept of bipolar disorder

The conclusion that bipolar disease was a distinct entity was drawn for the first time in France in the middle of the 19th century at the *l’Hospice de La Salpêtrière* in Paris by Jean-Pierre Falret. In 1851 Falret issued a statement in the hospital gazette describing a separate entity of mental disorder, which he named *folie circulaire*, characterised by a continuous cycle of depression, mania and free intervals of varying length. Three years later Falret published the ‘*Leçons Cliniques de Médecine Mentale faites à l'Hospice de la Salpêtrière*’ and presented the concept to the *Académie de la Médicine*. (21)

In 1854 Jules Baillarger, arguing forcefully against Falret, presented his concept of *folie à double forme* in a paper as well as a presentation to the *Académie de la Médicine*. (22) Falret and Baillarger could therefore be seen as the fathers of our modern concept of bipolar disorder albeit in this fairly reluctant nuptial as their concepts varied considerably and there seemed to be some animosity between the two colleagues. Baillarger assumed a type of disease in which mania and melancholia

change into one another but the interval is of no importance. Falret in contrast, involved the interval between the manic and melancholic episode in his concept.

Both concepts, however, found widespread distribution in France and soon also in other European nations. In 1863 Karl Kahlbaum, who supported Falret's view and opposed Baillarger, introduced both *"folie circulaire"* and *"folie à double forme"* into German psychiatry in his book 'The Grouping and Classification of Mental Disorders', (23) contributing in this way to the establishment of the two terms in German psychiatry.

Karl Kahlbaum is an intriguing figure in the history of psychiatry and his contribution to the field of psychiatry appears to be undervalued as he rarely presented material and wrote only 16 papers. It fell to Ewald Hecker his colleague, and later brother-in-law, to outline many of his ideas. (20) At the sanatorium in Gorlitz near Dresden where they worked, they introduced innovative reforms such as greater patient freedom and removal of restraints. When discussing patients, they shunned fashion and described their cases in a new way, considering the longitudinal course of a patient's condition -an approach, Kahlbaum argued, that should give rise to clinical entities or syndromes. (23)

In 1882 Kahlbaum outlined two affective disorders – cyclothymia and dysthymia – against a background of circular or cyclic insanity. Circular insanity, he argued, was a severe disorder that led to hospitalisations for both manic and depressive episodes and in which the patient was typically psychotic. Cyclothymia in contrast, was a pure mood disorder, which showed minimal intellectual derangement and typically did not require hospitalisation. Patients cycled from "excess vitality to lack of vitality" which is a state that might today be referred to as "bipolar type II". (24)

2.4 The Kraepelinian Dichotomy – opposition, alternative options and personal misgivings

Debatably referred to as the "father of modern psychiatry", Emil Kraepelin's separation of 'endogenous' psychosis into 'dementia praecox' and 'manic depressive insanity' was extremely important for the development of psychiatry .(25) Contrary to popular belief, Kraepelin himself was not rigid concerning his taxonomies or concepts and was open to persuasion by data-orientated research.

He often revised his concepts, discussing his doubts and questions in publications as illustrated in the following extract:

> Apart from our experience that in a whole series of manic episodes a depressive one can occur unexpectedly, and those cases are immensely rare in which apart from manic irritability not the slightest feature of depression is visible, it is absolutely impossible to distinguish these manic episode fits of circular insanity from periodic mania. But if periodical mania is identical with circular insanity we cannot deny the possibility that also periodic melancholia, or at least some of the cases designated so, must in fact be understood as a kind of circular insanity in which all the episodes take on a depressive hue, just as in periodic mania they all have a manic tinge. (26)

In the quotation above it would appear that Kraepelin was also of the view that periodic or unipolar mania was a rare occurrence. He also comments on a debate still taking place today as to when a patient presenting with a depressive episode might not be in fact suffering from a bipolar type of illness.

Kraepelin stressed the relationship between the syndromes of depression and mania, contributing to the current understanding of manic-depressive illness and also described cases of manic irritability with no features of depression, which he termed “periodic mania”. (27)

Kraepelin did not however use periodicity as a distinguishing feature of the “manic-depressive insanities” because in his view periodicity was also characteristic of “epileptic insanity, histerical insanity and dementia praecox”. (28) Fascinatingly, it was this general tendency to periodicity which gave rise to the mediaeval English word “lunatic”, meaning a person affected with intermittent insanity – the intermittency being attributed to changes in the moon. (29)

Kraepelin’s system, albeit eagerly embraced by many clinicians, also elicited much criticism from the moment it was propagated. Hoche attacked what he considered to be an unwarranted assumption of a linear relationship between localised brain lesions or microchemical alterations and the clinical symptoms of psychotic illness. Attempts to identify mental “diseases” on the basis of relationships between anatomical changes and mental phenomena are bound to be futile he felt. Instead he argued that psychopathology should limit its aim to achieving an exact description of symptom complexes that are aetiologically neutral. (30)

Bonhoeffer, in a similar line of reasoning, used the example of alcoholism to illustrate how the same aetiology can result in widely different clinical diseases and that conversely, diverse aetiological

factors may lead to identical clinical manifestations. (31) Conrad maintained that the sharp distinction between schizophrenia and bipolar illness was “Kraepelin’s most questionable misjudgement”, claiming that both the clinical evidence (cases with early depressive or manic symptoms and a periodic course that later develops delusional features) and genetic evidence (schizophrenia in the pedigrees of pure bipolar cases) suggest that the two clinical forms are different expressions of a single “endogenous psychosis”. (32)

Alternative views in this protracted controversy of the two major psychoses included the so-called Wernicke-Kleist-Leonhard School whose classification of bipolar disorders as we know them today were really very complicated. Wernicke took a fundamentally different approach to the psychoses, proceeding largely from concepts derived from neurology, postulating that disturbances (resulting from different aetiologies) of the three functional brain systems involving the association cortex; psychomotor, psychosensory and intrapsychic – supporting respectively the awareness of one’s body, awareness of the external world and awareness of one’s own personality, lead to psychotic syndromes that can be classified as somatopsychoses, allopsychoses and autopsychoses. (33) These ideas influenced Kleist

and Leonard, who developed a complex classification of psychoses incorporating Wernicke's notion of a functional cerebral system.

Karl Kleist (a colleague of Wernicke at Halle) opposed Kraepelin's concept of manic-depressive insanity, differentiating between unipolar *("einpolig"*) and bipolar *("zweipolig"*) affective disorders and recognising unipolar mania as a separate entity. (34) The concepts of Wernicke and Kleist were completed by Leonard. Karl Leonard (a colleague of Kleist) classified the "phasic psychoses" into "pure phasic psychoses" (such as "pure melancholia" or "pure mania") and "polymorphous phasic disorders".(35) Within the affective disorders, Leonhard was the first to propose the distinction between bipolar and unipolar disorders that has since been adopted by mainstream classifications. Neither Kleist nor Leonard considered unipolar mania to be a component of bipolar disorders in present-day terms.

Another conceptualisation was proposed by Kretschmer who introduced an example of multidimensional classification of the major psychoses, suggesting a typology of character trait clusters underlying the predisposition to for example schizophrenia or affective psychoses. Kretchmer suggested that the psychoses are not circumscribed disease entities but episodes rooted in the biological constitution of the individual

with all the possible transitions between sub-clinical manifestations and florid psychosis. (36)

As suggested earlier however, Kraepelin himself was anything but dogmatic in his views and had the intellectual integrity to accept many of the arguments of his critics. He surmised in 'Patterns of Mental Disorder' that "it is natural to turn away from arranging illnesses in orderly well-defined groups and to set ourselves instead the undoubtedly higher and more satisfying goal of understanding their essential structure". As regards the dichotomy of affective and schizophrenic disorders, Kraepelin conceded that "we cannot distinguish satisfactorily between these two illnesses and this brings home the suspicion that our formulation of the problem may be incorrect". (7)

2.5 Schizoaffective disorder

The first psychiatrist of modern times to describe schizoaffective disorder appears to be Karl Kahlbaum. (23) Kraepelin however, appeared more interested in the conundrum of these "in-between-cases" and more intent on solving this annoying enigma. Critical of his own taxonomy, he speculated that mental disorders can have elements of both dementia praecox and manic-depressive insanity and that they can also have a different course and a different prognosis to that of dementia praecox.

(7) In the wake of an investigation by his pupil and colleague Zendig, Kahlbaum's doubts became stronger.

In a paper, 'Contributions to Differential Diagnosis of Manic-Depressive Insanity and Dementia Praecox' by Zendig, (37) he reported that approximately 30% of Kraepelin's sample diagnosed with dementia praecox had a course and outcome not corresponding to the diagnosis. He attributed the better outcome to incorrect diagnosis in the first place.

The term "schizoaffective disorder" was introduced by Kasanin (38) thereby challenging Kraepelin's dichotomous view that two separate diseases account for severe mental illness. Kasanin recognised the diagnostic significance of mood symptoms in psychotic patients and consequently establishing at last a connection between schizophrenia and bipolar disorder.

Kraepelin admitted later "- … it is becoming increasingly clear that we cannot distinguish satisfactorily between the two illnesses …" and:

> The cases which are not classifiable to either manic depressive insanity or dementia praecox are unfortunately very frequent. We have to live with the fact that the criteria applied by us are not

sufficient to reliably differentiate in all cases between the two disorders and that there are many overlaps in this area. (7)

Kraepelin's about-turn was not widely recognised for over 50 years. Instead, the dichotomy became a keystone of psychiatry.

Nearly 100% of functionally psychotic patients were diagnosed with schizophrenia during the 1950s and 1960s (39) and Kraepelin's reversal was only revived in the 1970s when the diagnosis of schizoaffective disorder increased among psychotic patients at the expense of schizophrenia and studies started to question the disease specificity of the diagnostic criteria. Some authors concluded that schizoaffective disorder was either a subtype of schizophrenia (40) or a disease separate from bipolar mood disorder (41). Others implied that schizoaffective disorder and schizophrenia were indistinguishable from psychotic bipolar disorder (42) and some implied schizoaffective disorder and schizophrenia were a single disease (43) (44).

This search for disease specificity of diagnostic criteria is continuing today as can be seen in the preparation of the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM 5), where the DSM Task Force of the American Psychiatric Association has gone to great lengths

to consult with stakeholders in order to produce more disease specific diagnostic criteria.

Considering the historical origins of the concept of schizoaffective psychosis and its pivotal position in nosology, the genetics involved particularly deserves special interest.

Three studies during the 1970s and 1980s investigated the risk of psychosis in first-degree relatives of probands with schizoaffective illness. Angst found the risk of schizophrenia and affective disorder to be approximately equal in first-degree relatives of schizoaffective probands and the risk of schizoaffective illness less than that of either of the prototypical psychotic illnesses. (45) In two other studies, one by Tsuang and the other by Baron, schizoaffective disorder was found to be more closely related to affective illness than schizophrenia, both authors concluding that schizoaffective illness is genetically not separate from the major psychoses. (46) (47)

These findings led to the continuum theory in the 1980s, which was strongly endorsed by several authors who argued that the psychoses are represented on a continuum from pure affective illness to deteriorating schizophrenia. (48) (49) This concept considers psychotic

symptoms as disease non-specific and not diagnostic and is supported by substantial heritability and molecular genetic data since genes linked to psychosis appear to be inherited similarly across diagnoses.

Crow argues that schizoaffective disorder, schizophrenia and bipolar disorder represent a spectrum of variation at a single genetic locus that regulates severity of symptoms irrespective of diagnosis. Crow infers that no unequivocal demarcation of the functional psychoses can be made on the basis of symptoms, outcome or response to treatment and concludes that the affective psychoses and schizophrenia are related to each other on a continuum and that this continuum has a genetic basis. (50)

Lake and Hurwitz take the continuum theory one step further, viewing the concept of a continuum as consistent with a single disease and arguing that this single disease is a mood disorder that can account for the symptoms typically assigned the diagnoses of schizoaffective disorder or schizophrenia. These authors state: “If schizoaffective disorder, schizophrenia and psychotic mood disorders are essentially the same disease, schizoaffective disorder and schizophrenia are redundant diagnoses.” Their argument is substantiated by their review of more than

60 articles published since 2000 on the relationship between schizoaffective disorder, schizophrenia and mood disorders. (39)

The dichotomous view of Kraepelin has however survived and may be explained by the fact that early research focused on schizophrenia and not bipolar disorder. The massive data thus accumulated on schizophrenia are interpreted as supportive of the validity of schizophrenia as a distinct disorder but subsequent focus on bipolar patients has revealed considerable overlap. Eloquently articulated by Kendell and Jablensky:

> Unfortunately, once a diagnostic concept such as schizophrenia … has come into general use, it tends to become reified. That is, people too easily assume that it is an entity of some kind that can be invoked to explain the patient's symptoms and whose validity need not be questioned. (51)

2.6 Bipolar disorder born again

In 1966, the next phase in the understanding of bipolar disorders saw the light in the form of two large studies, one by Angst ('On the Aetiology and Nosology of Endogenous Depressive Psychosis') (52) and the other by Perris ('A Study of Bipolar and Unipolar Recurrent Depressive

Psychoses') (53). These two authors confirmed and further developed the opinions of Falret and the "Wernicke-Kleist-Leonhard School"- namely that unipolar and bipolar disorders are distinct entities. Both the authors showed that unipolar mania was clinically and genetically very strongly related to bipolar disorder and contended that the assumption regarding the separation of the group of unipolar mania was an artefact. Thus, 67 years after Kraepelin's creation of manic-depressive insanity and some 150 years after Falret's and Baillarger's statements, the concept of bipolar disorders experienced a 'rebirth'. (54)

2.7 Nosology in modern times – The history of the Diagnostic and Statistical Manual of Mental Disorders and the International Classification of Diseases

In order to gain an understanding of our modern concept of bipolar disorder and how we arrived at it, it is important to consider the history of the development of the psychiatric classification systems that predominate in the psychiatric literature. To this end there are two diagnostic classification systems that are mainly used in research i.e. the DSM and the International Classification of Diseases and Related Health Problems (ICD).

There are also other national and regional psychiatric associations that have developed substantial adaptations of the ICD to suit their particular circumstances. Notable in this instance are the Chinese Classification of Mental Disorders (CCMD-3) published by the Chinese Society of Psychiatry in 2001 (55), the French Classification of Child and Adolescent Mental Disorders prepared by the French Federation of Psychiatry (56), the Third Cuban Glossary of Psychiatry (GC-3) (57) and the Latin American Guide of Psychiatric Diagnosis produced by the Latin American Psychiatric Association. (58)

The CCMD-3 deserves mention in particular as it appears to be the only classification system that allows for the diagnosis of “unipolar mania”, considering it a valid entity in Chinese patients. (55)

The ICD is a medical classification system that provides codes to classify disease. Under this system, every health condition is assigned a unique category and given a code. It is published by the World Health Organization (WHO) and used worldwide for morbidity and mortality statistics and reimbursement systems. The system is designed to promote international comparability in the collection, processing, classification and presentation of statistics. It is revised periodically and is currently in its tenth edition. (59)

The ICD-6, published in 1949, was the first to contain a section on mental disorders. ICD-6 included ten categories for psychoses, nine for psychoneuroses and seven for disorders of character, behaviour, and intelligence. The American Psychiatric Association Committee on Nomenclature and Statistics developed a variant of the ICD-6 that was published in 1952 as the first edition of the DSM (DSM-I). In part because of the lack of widespread acceptance of the mental disorder taxonomy contained in ICD-6 and ICD-7, the WHO sponsored a comprehensive review of diagnostic issues that was conducted by the British psychiatrist Erwin Stengel. His report can be credited with having inspired many of the recent advances in diagnostic methodology -most especially the need for explicit definitions as a means of promoting reliable clinical diagnoses. (59)

The phenomenon of recurrent mania was interestingly enough given separate diagnostic status in ICD-9, “296.1 (0-6) Manic disorder, recurrent episode. Any condition classifiable to 296.0, stated to be recurrent. Excludes: circular type, if there was a previous attack of depression” (60) but this category disappeared in ICD-10; patients with two or more episodes of mania are now understood to be bipolar and are included under the category of bipolar disorders. (61) DSM-III (62) and DSM-III-R (63) included all manic episodes under bipolar disorders.

The nearest diagnostic category to unipolar mania in DSM-IV-TR (64) is “bipolar disorders not otherwise specified”, which includes recurrent hypomanic episodes with no intercurrent depressive features.

Fascinating, however, as mentioned earlier, is that CCMD-3 gives separate nosological status to recurrent unipolar mania. This separate status is largely based on a prospective ten-year follow-up study by Xu and Chen in 1992 [60] demonstrating that in Chinese patients presenting with recurrent mania, no depressive episodes were observed in a ten-year follow-up period, as well as field trials prior to publication indicating that recurrent mania remains a valid entity in China. Lee states that: “These findings question the obligatory labelling of Chinese patients with recurrent mania as bipolar.” (65)

Similar to DSM and ICD, the CCMD-3 is a medical classification based on both symptoms and etiological as well as pathological factors. In CCMD-3, it appears that Chinese psychiatrists sought consensus with ICD-10 on the one hand but at the same time maintained a nosology that considered Chinese cultural characteristics. Therefore, broad similarities between the ICD-10 and CCMD-3 exist. The CCMD-3 task force, however, is of the opinion that a separate nosological status for unipolar mania will facilitate research into its biologic correlates,

treatment response, and outcome. Unipolar mania therefore remains in the CCMD-3. (65)

2.8 DSM and the evolution of the diagnostic entity of bipolar disorder

The DSM is published by the American Psychiatric Association and provides a common language for the classification of mental disorders. It is used by clinicians, researchers, drug-regulating agencies, health insurance companies, pharmaceutical companies and policy makers around the world in varying degrees. It has attracted controversy and criticism as well as praise and since first being published has gone through several revisions with the fifth edition due for publication in 2013.

2.8.1 DSM I

DSM-I was published in 1952, was 130 pages long and listed 106 mental disorders. (66) The DSM evolved from systems for collecting psychiatric hospital statistics and a manual developed by the United States Armed forces as US psychiatrists were involved in the selection, assessment and treatment of soldiers during World War II. (59)

A fundamental etiological classificatory distinction in DSM-I is a division

between: (1) mental disorders caused by brain impairment, and (2) mental disorders of psychogenic origin suggesting a basic distinction between mental disorders with physical causes (e.g. brain damage) and mental disorders with psychological causes.

> The basic division in this nomenclature is into those mental disorders associated with organic brain disturbance, and those occurring without such primary disturbance of brain function, and not into psychoses, psychoneuroses, and personality disorders. Other categorizations are secondary to the basic division.

The Psychotic Disorders were grouped in DSM-I in the following way: affective disorders (characterised by severe mood disturbance, with associated alterations in thought and behaviour, in consonance with the affect): schizophrenic reactions (characterised by fundamental disturbances in reality relationships and concept formations, with associated affective, behavioural, and intellectual disturbances, marked by a tendency to retreat from reality, by regressive trends, by bizarre behaviour, by disturbances in stream of thought, and by formation of delusions and hallucinations): and paranoid reactions (characterised by persistent delusions and other evidence of the projective mechanism). (66)

Bipolar Mood Disorder in DSM-I was classified under the psychotic disorders as follows: “Psychotic Disorders - Affective Reactions, which could be sub-classified as Manic depressive reaction, manic type, Manic depressive reaction, depressed type, Manic depressive reaction, other and Psychotic depressive reaction”.

Schizoaffective disorder in DSM-I was classified as “schizophrenic reaction, schizo-affective type”. Unipolar Mania in this context would possibly have been diagnosed as “manic depressive reaction, manic type”.

2.8.2 DSM II

DSM-II was published in 1968 and included 182 disorders. (67) Whereas DSM-I featured three major categories of mental disorders, DSM-II organised mental disorders into ten categories. It was quite similar to DSM-I. The term “reaction” was dropped but the term “neurosis” was retained. Still reflecting the predominating psychoanalytic approach of the day, DSM-II also included biological perspectives and concepts of Kraepelin’s system of classification.

In the foreword by Ernest Gruenberg, Chairman of the Committee on Nomenclature and Statistics of DSM-II, it is indicated that the intention of

the DSM to provide a service to the psychiatrists of the United States and to present a nomenclature usable in all mental hospitals, psychiatric clinics and office practice.

Gruenberg goes on to state that it in fact could have a wider usage because of the growth of psychiatric work in general hospitals as well as in community mental health centres. It was also suggested for use in consultations to courts and industrial health services. Gruenberg concedes that it could not incorporate all the accumulated new knowledge of psychiatry at that particular point in time but that the Committee on Nomenclature and Statistics attempted to put down what they judged to be generally agreed upon by well-informed psychiatrists of the day. In the case of diagnostic categories about which there was controversy concerning the disorder's nature or cause, the Committee attempted to select terms which it thought would least bind the judgment of the user.

Gruenberg states:

> Inevitably some users of this Manual will read into it some general view of the nature of mental disorders. The Committee can only aver that such interpretations are, in fact, unjustified. Consider, for example, the mental disorder labelled in this Manual as

> "schizophrenia," which, in the first edition, was labelled "schizophrenic reaction." The change of label has not changed the nature of the disorder, nor will it discourage continuing debate about its nature or causes. *Even if it had tried, the Committee could not establish agreement about what this disorder is; it could only agree on what to call it.* (Italics inserted by author for emphasis.) (67)

Classification of mental illness became more categorised and mood disorders were classified as follows:

- Major affective disorders (affective psychoses)
    - Involutional melancholia
    - Manic-depressive illness, manic type (Manic-depressive psychosis, manic type)
    - Manic-depressive illness, depressed type (manic-depressive psychosis, depressed type)
    - Manic-depressive illness, circular type (manic-depressive psychosis, circular type)
        - Manic-depressive illness, circular type, manic
        - Manic-depressive illness, circular type, depressed
    - Other major affective disorder (affective psychoses, other)

- Unspecified major affective disorder
    - Affective disorder not otherwise specified
    - Manic-depressive illness not otherwise specified

In DSM-II, unipolar mania would possibly have been diagnosed as "manic-depressive psychosis, manic type" or "affective Psychosis, other" or "unspecified major affective disorder".

And under the section 'Psychoses not Attributed to Physical Conditions Listed Previously' which includes schizophrenia, schizoaffective disorder is classified as "schizophrenia, schizoaffective type" with the choice of specifiers being either "excited" or "depressed".

2.8.3 DSM-III

In 1974, Robert Spitzer was appointed as the chairman of the APA Task Force on Nomenclature and Statistics, which was officially formed to coordinate DSM-III with the ninth edition of the WHO's ICD and to update the manual to reflect the current state of knowledge on mental disorders. A key aim was to base categorisation on informal English descriptive language rather than assumptions of etiology, although the DSM's categorical approach assumed each particular pattern of symptoms in a category reflected a particular underlying pathology. (62)

Described as the so-called “neo-Kraepelin” approach (a term originally coined by George Klerman who reported a Kraepelinian revival in psychiatry), (68) the movement supported Kraepelin’s biological approach to psychiatry as opposed to Freudian psychoanalysis. (69)

In contrast to DSM-I and DSM-II, DSM-III provided specific diagnostic criteria as guides for making each diagnosis since “such criteria enhances inter-rater diagnostic reliability”. DSM-III also recommended the use of a multiaxial system for evaluation to ensure that certain information that may be of value in planning treatment and predicting outcome for each individual was recorded on each of five axes.

A controversy emerged regarding the elimination of the concept of neurosis, a mainstream psychoanalytic concept but considered vague and unscientific by the DSM task force. In his introduction in DSM-III, Spitzer goes to some length explaining the task force’s position stating specifically that “the term neurotic disorder is used in DSM-III without any implication of a special etiological process”. (63)

Bipolar mood disorder is classified under the heading “Affective disorders” and it is detailed as follows:

> Major Affective Disorders include Bipolar Disorder and Major Depression, which are distinguished by whether or not there has ever been a manic episode. A category of Manic Disorder is not included in this classification; instead, when there have been one or more manic episodes, with or without a history of a major depressive episode, the category Bipolar Disorder is used. Bipolar Disorder is sub classified at the fourth digit as Mixed, Manic, or Depressed.

Schizophrenia is classified as a “Schizophrenic disorder”, the essential features described thus:

> The presence of certain psychotic features during the active phase of the illness, characteristic symptoms involving multiple psychological processes, deterioration from a previous level of functioning, onset before age 45, and a duration of at least six months.

An explanatory footnote apologetically states:

> Although Schizophrenia is most likely a group of disorders of differing aetiologies, common usage refers to "Schizophrenia" rather than the technically more accurate term, Schizophrenic Disorders.

Schizoaffective disorder is categorised under the section “Psychotic Disorders Not Elsewhere Classified”.

Notably it is acknowledged that the boundaries of the concept of schizophrenia are unclear and that some approaches to defining the concept have emphasised the tendency toward a deteriorating course or an underlying disturbance in certain psychological processes with specific pathognomonic symptoms. In DSM-III the concept was not limited to illnesses with a deteriorating course, although a minimal duration of illness was required since the accumulated evidence at the time suggested that illnesses of briefer duration (called Schizophreniform Disorder in DSM-III) are likely to have different external correlates such as family history or likelihood of recurrence.

DSM-III recommends that individuals who develop a depressive or manic syndrome for an extended period relative to the duration of certain psychotic features or before the psychotic features appear not be classified as having schizophrenia but rather as having either an “Affective Disorder” or Schizoaffective Disorder”. It is specifically suggested that the diagnosis of “Schizoaffective Disorder” be made whenever the clinician is unable to differentiate between a manic episode and schizophrenia. (70)

2.8.4 DSM-III-R

In 1987 the DSM-III-R (63) was published as a revision of DSM-III. It contained 292 diagnoses.

Bipolar disorders are classified under the “Mood Disorders” and three diagnostic groups are recognised namely “Bipolar Disorder”, “Cyclothymia” and “Bipolar Disorder Not Otherwise Specified”.

The diagnostic criteria for a manic episode did not differ greatly from those set out in DSM-III however.

Schizoaffective disorder is classified under the “Psychotic Disorders Not Elsewhere Classified” and it is stated:

> The approach taken in this manual emphasizes the temporal relationship of schizophrenic and mood symptoms. This diagnostic category should be considered for conditions that do not meet the criteria for either Schizophrenia or a Mood Disorder, but that at one time have presented with both a schizophrenic and a mood disturbance and, at another time, with psychotic symptoms but without mood symptoms.

Under the heading “Cautions in the use of DSM-III-R” the following cautionary statement is made:

> The Use of DSM-III-R in Different Cultures; When the DSM-III-R classification and diagnostic criteria are used to evaluate a person from an ethnic or cultural group different from that of the clinician's, and especially when diagnoses are made in a non-Western culture, caution should be exercised in the application of DSM-III-R diagnostic criteria to assure that their use is culturally valid. (63)

2.8.5 DSM-IV

The DSM-IV was published in 1994 and consisted of 297 disorders. (71) A key change from previous versions was the inclusion of a “clinical significance” criterion which required that symptoms cause “clinically significant distress or impairment in social, occupational, or other important areas of functioning”.

In the Introduction the revision process is thus described:

> The third edition of the DSM-III represented a major advance in the diagnosis of mental disorders and greatly facilitated empirical research. The development of DSM-IV has benefited from the substantial increase in the research on diagnosis that was generated in part by DSM-III and DSM-III-R. Most diagnoses now

have an empirical literature or available data sets that are relevant to decisions regarding the revision of the diagnostic manual.

The task force for DSM-IV and its Work Groups conducted a three-stage empirical process that included comprehensive and systematic reviews of the published literature, reanalyses of already-collected data sets, and extensive issue-focused field trials.

Twelve DSM-IV field trials were conducted aimed at comparing alternative options and studying the possible impact of suggested changes. Field trials compared DSM-III, DSM-III-R, ICD-10, and proposed DSM-IV criteria sets in five to ten different sites per field trial. The field trials included more than 70 sites and evaluated more than 6,000 subjects.

Bipolar mood disorder is again assigned to the “Mood Disorders” and the group is somewhat expanded with the inclusion of Bipolar II Disorder. This group consists of: “Bipolar I Disorder”, “Bipolar II Disorder”, “Cyclothymic Disorder” and “Bipolar Disorder Not Otherwise Specified”.

Also now included is “Other Mood Disorders” which included “Mood Disorder Due to a General Medical Condition”, “Substance-induced Mood Disorder” and “Mood Disorder Not Otherwise Specified”.

Specifiers are added to describe the most recent mood episode as “Mild”, “Moderate”, “Severe Without Psychotic Features”, “Severe With Psychotic Features”, “In Partial Remission”, “In Full Remission”, “Chronic”, “With Catatonic Features”, “With Melancholic Features”, “With Atypical Features”, “With Postpartum Onset”.

Specifiers describing course of recurrent episodes were also added and included “Longitudinal Course Specifiers” – “With Full Interepisode Recovery”, “Without Full Interepisode Recovery”, “With Seasonal Pattern” or “With Rapid Cycling”.

Schizoaffective disorder now falls under the heading “Schizophrenia and Other Psychotic Disorders” and described is as “ a disturbance in which a mood episode and the active-phase symptoms of Schizophrenia occur together and were preceded or are followed by at least 2 weeks of delusions or hallucinations without prominent mood symptoms”. (71)

2.8.6 DSM-IV-TR

A text revision of DSM-IV, known as DSM-IV-TR was published in 2000. (64) Diagnostic categories remained the same and for the most part the criteria for diagnoses were unchanged. The text sections contained some extra information on some diagnoses and the diagnostic codes were updated to maintain consistency with the ICD.

In the introduction, the following rationale is given for the revised text:

> One of the most important uses of DSM-lV has been as an educational tool. This is especially true of the descriptive text that accompanies the criteria sets for DSM-IV disorders. Given that the interval between DSM-lV and DSM-V is being extended relative to the intervals between earlier editions (from 7 years between DSM-III and DSM-III-R and between DSM-III-R and DSM-IV, to at least 12 years), the information in the text (which was prepared on the basis of literature dating up to 1992) runs the risk of becoming increasingly out-of-pace with the large volume of research published each year.

It is stated that a revision of DSM-IV text was undertaken in order to bridge the span between DSM-lV and DSM-V. The goals of DSM-IV-TR being to correct any factual errors that were identified in the DSM-lV text;

to review the DSM-IV text to ensure that all of the information was still up-to-date; to make changes to the DSM-IV text to reflect new information available; to make improvements that will enhance the educational value of DSM-IV and to update those ICD-9-CM codes that had been changed since the 1996 coding update. All changes proposed had to be supported by empirical data as with DSM-IV. (64)

There are no significant changes in terms of diagnostic categories and criteria with regard to mood disorders and in particular bipolar mood disorder between DSM-IV and DSM-IV-TR. There appears to be no noteworthy changes in terms of the conceptualisation of schizoaffective disorder either between these last two DSM's.

2.8.7 DSM-5

The fifth edition of DSM, is currently in planning, preparation and consultation and is due for publication in 2013 and there appears to be a move away from roman numerals in the title of the publication. The APA has a website (http://www.dsm5.org) (72) concerning the development of DSM 5, which includes draft versions. Diagnoses are discussed under headings such as "Proposed revised criteria" and "Rationale" in order to orientate the reader to the difference between DSM IV criteria, the proposed changes, and the rationale behind the suggested changes. As

part of the development process, these preliminary draft revisions to the current diagnostic criteria for psychiatric diagnoses are available for public review and the content of the website is updated regularly. (72)

It is proposed that the diagnostic category for bipolar disorder be listed in DSM-5 in the category “Bipolar and Related Disorders” as opposed to “Mood Disorders” which is where it was listed in DSM-IV. It has also been proposed that the “Mixed Episode” diagnosis be eliminated in favour of a “Mixed Features Specifier”, which would apply to manic, hypomanic, and depressive episodes. Criteria for a manic episode will not change significantly except for increased energy/activity that has been added as a core symptom of manic and hypomanic episodes.

The category “Bipolar and Related Disorders” will probably include the following; “Bipolar I Disorder”, “Bipolar II Disorder”, “Cyclothymic Disorder”, “Substance-Induced Bipolar Disorder”, “Bipolar Disorder Associated with a Known General Medical Condition” and “Bipolar Disorder Not Elsewhere Classified”.

The diagnosis of “Bipolar Disorder Not Elsewhere Classified” is reserved for individuals with manic or hypomanic and depressive symptoms that do not meet diagnostic criteria of any other disorder from the “Bipolar

and Related Disorders" chapter and are not attributable to the direct physiological effects of a substance or a general medical condition.

Specifiers will most likely include;

- Current or Most Recent Episode Manic
- Current or Most Recent Episode Hypomanic
- Current or Most Recent Episode Depressed
- With Mixed Features
- With Psychotic Features
- With Catatonic Features
- With Atypical Features (for depression)
- With Melacholic Features (for depression)
- With Rapid Cycling
- With Suicide Risk Severity
- With Anxiety, mild to severe
- With Seasonal Pattern
- With Postpartum Onset

It would appear at this stage that DSM-5 will continue not to consider the clinical course of the disorder with regard to polarity. This is in spite of the fact that, considering experience in everyday practice, there is no

doubt that clinicians deem a clearly determined predominant polarity over the course of the illness important in order to decide the long-term maintenance treatment. Considering this fact, Colom and Vieta proposes the introduction of a specifier for “Predominant Polarity” as a course specifier in DSM-5 in order to help clinicians make therapeutic decisions. (73)

“Unipolar Mania” will therefore continue to find itself relegated to “Not Elsewhere Classified” (NEC) status. On the website it is at present specifically explained that “to aid in the sub-classification of this diverse group of conditions, the recorded name of the condition should not be “Bipolar Disorder NEC”, but, rather, one of the diagnostic terms provided” which in this case shall be “Uncertain Bipolar Conditions”. Since unipolar mania does not fit with any of the “recorded” names and neither is it allowed to be classified as under “NEC”, only “Uncertain Bipolar Conditions” is left, which appears to be an even further downgrading of status for unipolar mania.

Schizoaffective disorder now finds itself in the diagnostic category of “Schizophrenia Spectrum and Other Psychotic Disorders” and the following diagnostic criteria are proposed on the website: (72)

A. An uninterrupted period of illness during which, at some time, Criterion A symptoms of Schizophrenia are present, and there is also either a Major Depressive Episode or a Manic Episode.

B. During the lifetime duration of the illness, delusions and/or hallucinations are present at least for 2 weeks in the absence of a major mood episode (depressive or manic).

C. A major mood episode is present for the majority (≥ 50%) of the total duration of the time after Criterion A has been met. (Note: periods of successfully treated mood symptoms count towards the cumulative duration of the major mood episode).

D. Disturbance is not due to direct physiological effects of a substance (e.g., a drug of abuse, medication) or a general medical condition.

Specify Type:

- Bipolar Type: If the disturbance includes a Manic or a Mixed Episode (or a Manic or a Mixed Episode and Major Depressive Episodes)

- Depressive Type: If the disturbance only includes Major Depressive Episodes
- Specify if: With Catatonic Features

Criticism expressed by a number of authors was considered in the revised criteria. Maj reported the inter-rater reliability of the DSM-IV criteria for schizoaffective disorder to be unsatisfactory. (74) Addressing the controversy regarding the diagnostic validity of schizoaffective disorder, Malhi et al (75) indicated that the distinctions between the diagnostic categories of schizophrenia, schizoaffective disorder and bipolar disorder are not clearly established through findings from neuropsychological, neuroimaging, molecular neurobiology, or genetic epidemiology studies.

On the contrary, evidence seems to imply overlap across current diagnostic boundaries in the heritability and pathophysiology of psychotic and affective disorders which suggests that schizoaffective disorder exists as the mid-point on a continuum between schizophrenia and bipolar disorder. It is proposed by the authors that these two disorders be incorporated onto one dimension as a suitable alternative to the current state of affairs. Malhi et al. also recommend that schizoaffective disorder should be omitted in future revisions of the DSM

in order to allow for the development of a meaningful nomenclature that rests upon investigation of differences and similarities between disorders. (75)

In Hecker's review of schizoaffective disorder, he suggests that the fifth edition of the DSM provides the opportunity to improve the reliability and clinical utility of the schizoaffective disorder diagnosis and since the criteria has been unchanged since 1987, a serious need exists to revise current criteria. (76)

Jager et al also found no clear boundaries between schizophrenia, schizoaffective disorder and affective disorders with respect to psychopathological symptoms in their review and also express a need for revision and unification of the current diagnostic concepts of schizoaffective disorder. (77)

Whether the proposed changes for schizoaffective disorder in DSM-5 will change the future directions that classification systems for the psychotic disorders will take remains to be seen. Considering the present system, schizoaffective disorder as a diagnostic entity certainly has value but may become extinct once the psychotic illnesses are to be considered

on a continuum and a dimensional approach to diagnosis find favour amongst members of our profession.

Chapter 3
Unipolar Mania

3.1 Introduction

Considering the reasons for embarking on this study as explained in the first chapter, it would make sense to discuss the literature on “unipolar mania” in some detail.

3.2 Unipolar mania literature review

In 1966, after the two studies by Angst (52) and Perris (78) referred to in the previous chapter, relatively few studies appeared in the literature on the entity of unipolar mania thereafter. The reluctance to study unipolar mania was probably due to the strong opinion Angst and Perris voiced, both claiming that unipolar and bipolar disorders were distinct entities. Angst and Perris also felt that any assumption made regarding the separation of the group of unipolar mania was an artefact, as unipolar mania was so strongly related to bipolar disorder. (27)

In general, the occurrence of a manic only course in bipolar patients is estimated to be in the region of 10% to 20% (2), but rates have been found to vary substantially from a low of 1,1% (79) to a high of 65,3%. (80)

One of the challenges in the research on recurrent bipolar mania is, however lack of consensus on the defining criteria. Different authors have used different criteria for the diagnosis of recurrent mania with respect to the number of manic episodes, diagnosis of manic episode, and inclusion/exclusion of the depressive symptoms in the intercurrent period. (27)

In studies published in the last three decades, there appears to be some consensus on the presence of at least three manic episodes with no depressive episodes, but there is no consensus on the timeframe for the same.

Abrams and Taylor reported on 50 manic probands of whom 14 had never experienced a depressive episode. These authors concluded that unipolar mania was clinically homogeneous with bipolar disorder. (81) Nurnberger et al reported on 241 patients attending a “Lithium Clinic” of whom 38 had never been treated for depression. There was no difference in the age of onset, family history or response to lithium to support unipolar mania as a distinct clinical entity. (82)

In a more sophisticated replication of their earlier study, Abrams et al examined 77 manic patients. Again there was no significant difference

between bipolars and unipolars on a wide range of variables with two exceptions: the first-degree relatives of unipolar manic patients had a morbidity risk for unipolar depression of 10,5% while the risk for relatives of bipolars was only 3,4%. Abrams et al concluded, however, that unipolar mania clinically, historically and demographically was indistinguishable from bipolar illness. (83)

In a study reporting on chart reviews of 247 patients admitted to the University of Iowa Psychiatric Hospital with a history of at least one manic episode, Pfohl et al found that there were few clinically meaningful differences between patients with unipolar mania and bipolar disorder and that unipolar mania was not supported as a separate entity from bipolar disorder. (84) Considering that some of these study subjects might have been seen to have a unipolar manic course after having had only one manic episode, results may be considered doubtful, as the definition of unipolar mania in this study was “≥ 1 manic episode, no depressive episodes”.

Makanjuola’s study of 45 patients presenting with possible diagnosis of mania to two psychiatric units in Nigeria showed that recurrent manic disorder without depressive episodes is the rule rather than the exception among Yoruba Nigerian patients and that mania appears to

occur predominantly as a recurrent unipolar disorder. (85) In a follow-up study, Makanjuola confirmed his previous impression and found recurrent unipolar mania to be four times as common as bipolar disorder. In this study of 104 patients, 55 exhibited a recurrent unipolar manic course. (86)

Khanna et al found in their study of 95 manic patients admitted to a psychiatric hospital in eastern India that the prevalence of recurrent mania in this sample was high. Sixty percent of the sample had two manic episodes without an episode of depression. Among those with three lifetime episodes of illness, 48% had only manic episodes. Even when unipolar mania was defined as four or more lifetime episodes of mania without any episodes of depression, 44% fulfilled the criterion. (87) At a Lithium Clinic in Hong Kong, in a study by Lee, it was found that 36% of patients manifested manic-only episodes during affective relapse. (88)

In a retrospective cohort study of 50 elderly manic in-patients, Shulman and Tohen identified six (12%) who met criteria for a course of unipolar mania, suggesting that the concept of unipolar mania should not be buried yet and that further investigation of neuro-radiological findings and clinical course is merited. (89)

In response to this study, Lee and Yu emphasise in their letter in the British Journal of Psychiatry that more attention to unipolar mania is plainly in order, as the non-Western cultures make up 80% of the world but are poorly prepared to publish in the English literature. Lee and Yu claimed that there was sufficient evidence of a higher prevalence of unipolar mania in non-Western cultures such as Africa, China and India. (90)

In a study aimed at determining the rate of unipolar mania and comparing its characteristics with those of other affective disorders in a psychiatric hospital in the Fiji Islands, Aghanwa found the rate of recurrent unipolar mania to be 47,2%, thereby adding to the evidence in support of the inclusion of recurrent mania as a useful category in the international psychiatric nosology. (91) Yazici et al found the rate for unipolar mania to be 16,3% with unipolar manic patients tending to have more psychotic features and be less responsive to lithium. Yazici et al concluded that unipolar mania may be a nosologically distinct entity. (92)

In a prospective, longitudinal observational study of mood disorders by Solomon et al, endorsed by the National Institute for Mental Health (NIMH), individuals seeking treatment for mood disorder related symptoms at five academic medical centres in the USA were recruited.

Inclusion criteria for this particular study stipulated that participants had to be at least 17 years of age, with an IQ > 70, able to speak English and of white race for testing of genetic hypotheses.

A total of 163 patients with Bipolar I and 66 with schizoaffective disorder with no history of major depression entered the study. After a minimum of 15 years of prospective follow up, 27 subjects had not suffered any subsequent major depressive episodes. Contrary to expectation is the fact that manic recurrences developed in the five subjects who were treated with a mood stabiliser more than 90% of the follow-up time but no manic recurrences developed in the two subjects who were given very little treatment with a mood stabiliser during follow up.

Solomon et al conclude that, although rare, unipolar mania remains a valid diagnostic entity and that any efforts to understand the biological underpinnings of manic-depressive illness need to account for this. (93)

In a community-based study, looking at the prevalence and characteristics of bipolar I disorder in Butajira, Ethiopia through a door-to-door screening of the district's entire population, 315 cases were identified. Negash et al found that, of the 295 for whom complete information could be collected, 59,8% did not report any depressive

episodes and that their illness started with a manic episode in 77,3% of the cases.

In attempting to explain the high rate of cases not reporting depressive episodes, Negash proposes the reasons to be firstly that it was a community-based sample, secondly that recall bias might have led to under reporting milder episodes of depression, and thirdly that depressive symptoms may be seen as part of normal life rather than as a psychiatric disorder. Lifetime prevalence of bipolar I was estimated to be 0,6% for males and 0,3% for females. (94)

Reporting on this same study, Fekadu et al found that nearly two thirds od cases had relapsed over two and a half years and contrary to expectation, bipolar relapses were characterised by both manic and depressive relapses in almost equal proportion. (95)

Perugi et al also studied unipolar mania in order to define clinical and nosographic utility. From a sample of 155 consecutive inpatients with a DSM-III-R diagnosis of mania seen at the Institute of Psychiatry at the University of Pisa, Italy, patients were selected that had a history of at least three major affective episodes and ten years' duration of illness. Of the 87 patients included in this study, 19 (21,8%) presented a course of

illness characterised by recurrent unipolar manic episodes without a history of major or mild depression.

In spite of some similarities in terms of sex distribution, age of onset and polarity of first episode, some characteristics that were deemed of clinical and prognostic importance in the unipolar manic group included absence of suicidal attempts, more chronic course and less severe social and occupational disability. Perugi et al conclude that their data suggest clinical and prognostic validity of keeping unipolar manic patients as a separate subgroup. These authors also recommend that further research is needed to investigate and explore the possible therapeutic and genetic implications. (96)

A retrospective comparative study by Dakhlaoui et al of medical files of patients admitted with bipolar I (using DSM-IV criteria) between 1997 and 2001 to a psychiatric ward in the Razi Hospital, Tunisia, found that 65,3% of the sample of 72 patients had a unipolar manic course of illness (at least two manic episodes without depression).

Comparing two groups (Group 1 comprising those with unipolar mania who presented with at least two manic episodes without depression and Group 2 the rest of the sample) in terms of socio-demographic profile,

family psychiatric history and comorbidity, it was found that there were no significant difference in terms of socio-demographic features and family psychiatric history.

However, it was found that the bipolar group tended to abuse substances significantly more that the unipolar group. A significant difference was also observed regarding the 'first episode season' with the unipolar group presenting with their first episode more in "summer-autumn" and the bipolar group in "winter-spring".

Insisting that unipolar mania was a clinical reality in their daily practice, Dakhlaoui et al also suggested it was the "predominant presentation of bipolar disorder in Tunisia". (80)

3.3 Unipolar mania research – Western- vs. non-Western Countries

It thus becomes clear that there seems to be a considerable difference in findings regarding the entity of unipolar mania when one compares studies from Western vs. non-Western countries as shown in Table 3.1 and Table 3.2.

3.3.1 Table 3.1: Studies from Western countries

Table 3.1				
Author	**Country**	**Year**	**Definition**	**Rate of Unipolar Mania**
Perris (78)	Sweden	1966	≥ 1 manic episode, no depressive episodes	4,5%
Abrams & Taylor (81)	USA	1974	"never had a depressive episode"	28%
Abrams et al. (83)	USA	1979	2 manic episodes with no depressive episodes	18%
Nurnberger et al. (82)	USA	1979	≥ 1 manic episode with no treatment for depression	15,7%
Perris(79)	Sweden	1982	≥ 1 manic episode, no depressive episodes	1,1%
Pfohl et al. (84)	USA	1982	≥ 1 manic episode, no depressive episodes	33,6%
Shulman & Tohen (89)	Canada	1994	3 manic episodes with no depressive episodes and 10 years elapsed since hospitalisation for 1st manic episode	12%
Solomon et al. (97)	USA	2003	No depressive episode in 15-year prospective follow-up study of manic patients	16,5%
Perugi et al. (96)	Italy	2007	≥ 3 manic episode, 10 years of illness with no depressive episodes	21,8%
Average				**16,8%**

3.3.2 Table 3.2: Studies from non-Western countries

Table 3.2				
Author	**Country**	**Year**	**Definition**	**Rate of Unipolar Mania**
Makanjuola (86)	Nigeria	1985	≥ 2 manic episode, no depressive episodes	53%
Khanna et al. (87)	India	1992	≥ 4 manic episode, no depressive episodes	44%
Lee (98)	China	1992	≥ 2 manic episode, no depressive episodes	36%
Aghanwa (91)	Fiji Islands	2001	≥ 3 manic or hypomanic episodes, no depressive episodes and affective illness of at least 4 years	47,2%
Yazici et al. (92)	Turkey	2002	≥ 4 manic episode, no depressive episodes in 4 year follow-up	16,3%
Negash et al. (94)	Ethiopia	2005	Non report of depressive episode in a community-based study	59,8%
Dakhlaoui et al. (80)	Tunisia	2008	≥ 2 manic episodes without depression	65,3%
Average				**45,94%**

The high percentage (28%) found by Abrams and Taylor (81) and Pfohl et al (33,6%) (84), could be attributed to their generous definition of unipolar mania. With regard to the study by Yazici et al (92) in Turkey, the authors failed to describe the selection of his cohort in sufficient detail.

Selection bias could in fact be an important limiting factor in almost all studies mentioned, as the majority of studies, with the exceptions of Makanjuola (85), Solomon et al. (93) and Negash (94), were all retrospective chart reviews of patients admitted for manic episodes.

One should also consider the fact that not all patients with manic episodes would necessarily be admitted to or present in a hospital. Some could be seen by private practitioners or traditional healers and yet others may not present for help at all. The other studies mentioned also appear to have some selection flaws for example, the subjects in the study by Makanjuola were all in-patients (85) and in Solomon's study only white patients were included. (93)

From the abovementioned studies and comments by the various authors, it becomes clear that there is a need to continue to investigate the course of illness of bipolar disorder in South Africa and pay particular attention to a unipolar manic course. It should be interesting to see whether findings will replicate those from other non-Western countries and, in particular those from Africa.

Chapter 4
Purpose and Methodology

4.1 Purpose of the study

The purpose of this study was to investigate and describe the course of illness and clinical features in a cross-section of patients diagnosed with bipolar disorder and attending public hospitals in Limpopo Province, South Africa.

From this information, the author wanted to determine the rate of a unipolar manic course in this specific sample and to ascertain whether it is possibly an entity distinct from bipolar mood disorder as it is generally conceptualised in modern-day psychiatric literature. The issue of unipolar mania as a clinical entity remains unresolved and research in this area from South African may assist in clarifying this conundrum. If unipolar mania is found to be as prevalent in South Africa as compared to the rest of Africa, it will have diagnostic and treatment implications, as well as implications for genetic research.

4.2 Study design

Descriptive, cross-sectional study.

4.3 Methodology

A purposeful sample of 103 patients presenting with a history of mania between October 2009 and April 2010, to three hospitals in the Limpopo Province namely Mankweng-, Mokopane- and George Masebe hospitals, was recruited and interviewed using the Affective Disorders Evaluation (ADE). (99)

4.4 Background to the hospitals

For clarification, it needs to be explained that there are three categories of hospitals in South Africa. The most common names used to refer to these categories are “District”, “Regional” and “Tertiary” although these names are at present being changed to “Level 1”, “Level 2” and “Level 3” hospitals and, as their names imply, they offer different levels of service. Unfortunately the national Department of Health has yet to adopt a firm definition of each category or to define what services should be available at each facility. A district hospital is defined as a facility at which a range of outpatient and inpatient services are offered. This is the first level of referral and generalist staff (ordinary general practitioners) are available and patients have access to basic diagnostic and therapeutic services.

Regional hospitals are Level 2 facilities that provide care requiring the intervention of specialists and general practitioners. Tertiary Hospitals or

Level 3 facilities provide specialist and sub-specialist care. Most of the care here requires the expertise of clinicians working as sub-specialists or in rarer specialties (e.g. sub-specialties such as urology, neurosurgery, plastic surgery and cardiothoracic surgery). (100)

Apart from this, there are also specialised hospitals that cater for high incidence chronic conditions for example psychiatric hospitals and TB hospitals.

All Level 1- or district hospitals should provide psychiatric services but only some of them will be allowed to admit patients in accordance with the Mental Health Care Act (No. 17 of 2002). These facilities are known as “designated facilities” and mental health care users (MHCUs) are admitted for 72 hours before being transferred to a “listed facility”, which will then provide intermediate- to long-term care. The purpose of the 72-hour observation period is to rule out and/or treat any medical conditions that could mimic psychiatric illness. (101)

Limpopo Province has the fourth largest population in South Africa with roughly five million people. It is considered to be a poor province, with approximately 87% of its people living in rural areas and with 23% of households having no access to piped water.

Mankweng Hospital is part of the Polokwane-Mankweng Hospital Complex (PMHC) situated in the Capricorn District of Limpopo Province. The PMHC comprises two hospitals, Pietersburg Campus and Mankweng Campus, 30 kilometres north east of Polokwane, the largest town in the province. The combined bed capacity is 1 016. PMHC provides tertiary services to all district and regional hospitals in Limpopo Province and also serves as a regional hospital to the Capricorn District.

Mankweng Psychiatric Unit is a 40-bed adult unit making provision for 20 males and 20 females. It is known as the ”Mankweng Child and Family Unit” as this is what the original intention for the unit was, but the unit was subsequently never utilised as such since its establishment in 1998. It functions as a “designated” psychiatric facility, admitting patients in accordance with the Mental Health Care Act.

Mokopane Hospital is a Level 2 Hospital in the Mokgalakwena Municipality of the Waterberg area of Limpopo Province. It renders services at Level 2, providing specialist services for psychiatry, obstetrics and gynaecology, internal medicine, surgery and orthopaedics as well as paediatrics. It has a bed capacity of 260 and has made beds available for psychiatric patients in the medical wards. Mokopane

Hospital also functions as a designated facility, also admitting patients under the Mental Health Care Act.

George Masebe Hospital is a district (Level 1) hospital in the Waterberg area and renders a service to the local community, which consists of Bakenberg and Rebone. It is a 143-bed hospital and renders a psychiatric service as a “listed” facility making provision for 72 hours observation. Psychiatric patients are admitted to the medical wards and managed by medical officers. The hospital has a community psychiatric nurse who is very involved in the management of the inpatients as well. Outreach by a specialist psychiatrist to the psychiatric clinic is provided by a visiting psychiatrist from Mokopane Hospital.

For the purpose of orientation Figure 4.1 shows the map of South Africa and neighbouring countries. Figure 4.2 shows the nine provinces and the location of Limpopo Province in particular. Figure 4.3 is a map of Limpopo Province, indicating the location of the three hospitals where the study was conducted.

Figure 4.1 Map of Southern Africa

Figure 4.2 Map of South Africa

Figure 4.3 Map of Limpopo

4.5 Ethical considerations

The research protocol (Protocol no. 136/2009) and informed consent document (Appendix B) were presented to the University of Pretoria, Faculty of Health Sciences Research Ethics Committee and approved on 26/08/2009 (Appendix C).

Letters requesting permission to see patients and access patient records were sent to the Chief Executive Officers of the three hospitals involved and permission was obtained (Appendix D).

Ethical approval to conduct the study was requested and obtained from the Limpopo Department of Health and Social Development Research Ethics Committee on 04/11/2009 (Appendix E).

Patients admitted under the Mental Health Care Act as either assisted or involuntary patients were not requested to participate in the study until such time that they were deemed able to give informed consent and provide an adequate history.

Personal information, names and file numbers of patients were handled with utmost confidentiality but were documented for future reference, follow up and verification of information.

4.6 Informed consent

Subjects agreeing to participate in the study signed informed consent. Those not conversant in English had the informed consent form explained to them in Northern Sotho by an interpreter fluent in the native language. The interpreter was asked to read through the informed consent document first and was given an opportunity to ask questions to clarify content. Hereafter the interpreter then explained the content of the informed consent document to the study subject and the study subject would be given an opportunity to ask questions as well. Study participants were also given the researcher's personal cell phone number so that they could request any additional information at a later stage should they wish to.

Informed consent included: purpose of the study, procedure, potential risks, benefits to the individual and others, consent to family members being interviewed, an invitation to ask questions, name and address of researcher and a statement to the effect that the person was free to choose not to participate without incurring displeasure or disadvantage.

Patients who were incapable of giving either informed consent or providing a good history of their illness were not included in the study.

4.7 Measuring instrument

After signing the informed consent form, a questionnaire, the Affective Disorder Evaluation (ADE) (99), was completed by the researcher for every study subject. See Appendix F for an example of the ADE. The researcher was assisted by registered nurses fluent in Northern Sotho, who translated the questions to non-English-speaking participants.

The ADE is a standardised tool for initial clinical assessment of patients possibly suffering from bipolar disorder. Developed for the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), the main objective of the ADE is to provide an efficient way of making a reliable current and lifetime diagnosis of bipolar disorder. (102) The ADE uses an adaptation of the mood disorder modules from the Structured Clinical Interview for DSM-IV (SCID). (103) These modules assess current mood episode and lifetime mood disorder diagnosis and flow in an orderly sequence designed to reflect the DSM-IV mood disorder classification.

4.8 Sample size

The sample size was calculated with the objective of prevalence of a unipolar manic course determination in mind. Under the assumption that the expected prevalence of a unipolar manic only course in the study

population is 35%, a sample size of 88 patients was considered to be able to estimate the prevalence to an accuracy of 10% with 95% confidence.

4.9 Data analysis

The data summary covered descriptive statistics like mean, standard deviation, median, range and 95% confidence intervals for continuous variables whilst for categorical variables (nominal and ordinal) use was made of proportion, percentages cross-tables and 95% confidence intervals. Survival curves comparing subgroup, e.g. sex, age categories etc., employed hazard ratios. Testing was done at the 0,05 level of significance.

4.10 Methodological limitations

As the researcher is not a speaker of Northern Sotho, interpreters were used for those study subjects not fluent in English. Language and the use of interpreters constitute a challenge in all cross-cultural research situations. In this population specifically there are frequently no specific translations available for a word and the interpreter then had to explain concepts to the study subjects.

Interpreters were mostly registered nurses whose native language was Northern Sotho and who worked in the particular psychiatric unit providing care for psychiatric patients. When possible, use was made of registrars training to become psychiatrists, who were fluent in Northern Sotho.

Selection bias could be a limiting factor as not all patients with manic episodes may necessarily seek help at a hospital but might go to either private practising doctors or traditional healers. Only those presenting to hospital were included in the study.

As with most questionnaires, when history is being taken, patients might not be able to remember everything about their illness in detail and recall bias is therefore a definite limitation of this study. In order to avoid recall bias, information from clinical records in hospital files as well as collateral information from family members was obtained if available.

4.11 Definition of recurrent unipolar mania

One of the challenges in the research of recurrent bipolar mania is a lack of consensus on the defining criteria. Different authors have used different criteria for the diagnosis of recurrent mania with respect to the number of manic episodes, diagnosis of manic episode, and

inclusion/exclusion of the depressive symptoms in the intercurrent period. (27)

In the studies published in the last decade there appears to be some consensus on the presence of at least three manic episodes with no depressive episodes, but there is no consensus on the timeframe for the same.

Aghanwa defined “recurrent mania” as three previous episodes of mania or hypomania (ICD-10) and the presence of affective illness for at least four years. (91)

On the other hand, Yazici et al defined recurrent mania by the occurrence of at least four episodes of mania (DSM-IV) and at least four years of follow up without any depressive episode.(92)

Thus, a critical issue that remains unresolved concerns the maximum number of manic/hypomanic episodes that a person must experience in a particular timeframe without any depressive episodes so as to enable a psychiatrist to make a confident diagnosis of recurrent unipolar mania. One should consider however that this issue is not unique to making a

diagnosis of only recurrent unipolar mania but is equally important when making a diagnosis of recurrent unipolar depression.

For the purposes of this study, a unipolar manic course was considered in all patients who had never experienced a major depressive episode. However, the rate of unipolar mania was also established for those in the sample who were diagnosed with bipolar disorder in particular and had three or more lifetime number of phases without the occurrence of any depressive episodes.

Chapter 5
Results

5.1 Introduction

The results as given here were obtained from the ADE. The order in which the results are presented was however changed in an effort to make the order chronologically more logical and in keeping with the order similar to that used when doing a general psychiatric clinical interview.

In the ADE, under the main heading of 'Medical History', there is a subsection dealing with women's health issues. The results hereof are presented at the end of this chapter so as to not confuse the reader.

Results will thus be arranged (and discussed in Chapter 6) under the following main headings:

- Socio-demographic variables
- History
- Course and clinical features
- Treatment
- Substances
- Diagnosis
- Women's health issues

5.2 Socio-demographic variables

5.2.1. Table 5.1 Hospitals subjects were recruited from

Table 5.1		
Hospital	**Frequency**	**Percentage**
George Masebe	15	14.56
Mokopane	31	30.10
Mankweng	57	55.34
Total	103	100

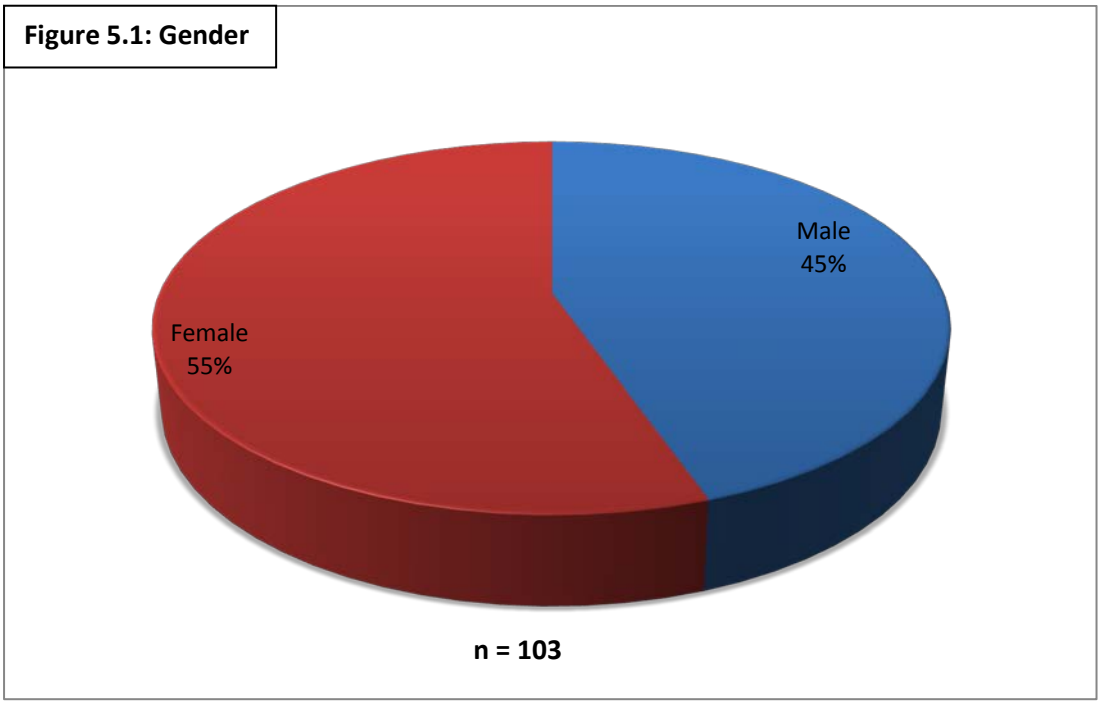
5.2.2 Table 5.2 Inpatient / outpatient status of subjects

Table 5.2		
Current status	**Frequency**	**Percentage**
In-patient	61	59.22
Out-patient	42	40.78
Total	103	100

5.3 Identifying information

5.3.1 Figure 5.1 Gender

Figure 5.1: Gender



5.3.2 Table 5.3 Mean age

Table 5.3				
Variable	**Mean**	**Standard Deviation**	**Min age**	**Max age**
Age	36.6	11.9	12	73

5.3.3 Table 5.4 Marital status

Table 5.4		
Marital status	**Frequency**	**Percentage**
Single	72	69.9
Married	24	23.3
Widowed	5	4.85
Divorced	2	1.94

5.3.4 Table 5.5 Religious affiliation

Table 5.5		
Religious affiliation	**Frequency**	**Percentage**
Zion Christian Church	65	63.11
Christian	26	25.24
None	8	7.77
Other	4	3.88
Total	103	100

5.3.5 Table 5.6 Education

Table 5.6		
Education	**Frequency**	**Percentage**
None	8	7.77
Primary	14	13.59
Secondary	55	53.4
Tertiary	26	25.24
Total	103	100

5.3.6 Table 5.7 Employment

Table 5.7		
Occupation	**Frequency**	**Percentage**
Employed	12	11.65
Unemployed	72	69.9
Retired	5	4.85
Student	7	6.8
Self employed	7	6.8
Total	103	100

5.3.7 Table 5.8 Financial support

Table 5.8		
Monetary support	**Frequency**	**Percentage**
None	1	0.97
Pension	1	0.97
Part time employment	3	2.91
Fulltime employment	13	12.62
Family	31	30.1
Social grant	54	52.43
Total	103	100

5.4 History

5.4.1 Table 5.9 Family history of mental illness

Table 5.9		
Family history	**Frequency**	**Percentage**
Bipolar Mood Disorder	59	57,3
Alcohol abuse	51	52,5
Substance abuse	30	30,9
Suicide	17	16,5
Suicide attempts	12	11,7
Schizophrenia	12	11,7
Other mood disorders	4	3,9

5.4.2 Table 5.10 History of trauma

Table 5.10		
History of trauma	**Frequency**	**Percentage**
Sexual	6	5,8
Physical	25	24,3

5.4.3 Table 5.11 History of suicide attempts

Table 5.11		
Suicide attempts	**Frequency**	**Percentage**
Yes	28	27,2
No	75	72,8
Total	103	100

5.4.4 Table 5.12 Type of suicide attempt

Table 5.12		
Type of suicide attempt	**Frequency n=28**	**Percentage**
Hanging	9	32.14
Overdose	6	21.43
Ingestion of poison	4	14.29
Cutting own throat	3	10.71
Setting self alight	2	7.14
Ate broken glass	1	3.57
Stabbed self in abdomen	1	3.57
Stopped eating	1	3.57
Attempted drowning	1	3.57
Total	28	100

5.4.5 Table 5.13 History of violence/forensic history

Table 5.13		
History	**Yes**	**No**
Violence	51	52
Forensic history	32	71

5.4.6 Table 5.14 Medical history

Table 5.14		
Medical history	**Frequency**	**Percentage**
Head trauma with loss of consciousness	17	16,5
History of seizures	8	7,8
Diabetes	2	1,9
Thyroid disease	1	0,9

5.4.7 Table 5.15 HIV status

Table 5.15		
HIV Status	**Frequency**	**Percentage**
Positive	9	8.74
Negative	39	37.86
Unknown	55	53.4
Total	103	100

5.5 Course and clinical features

5.5.1 Table 5.16 Age of onset

Table 5.16				
Variable	**Mean age of onset**	**Standard deviation**	**Min age**	**Max age**
Mania	25.17	8.49	12	57
Depression	26.16	9.37	12	52

5.5.2 Table 5.17 Age of onset bracket: mania

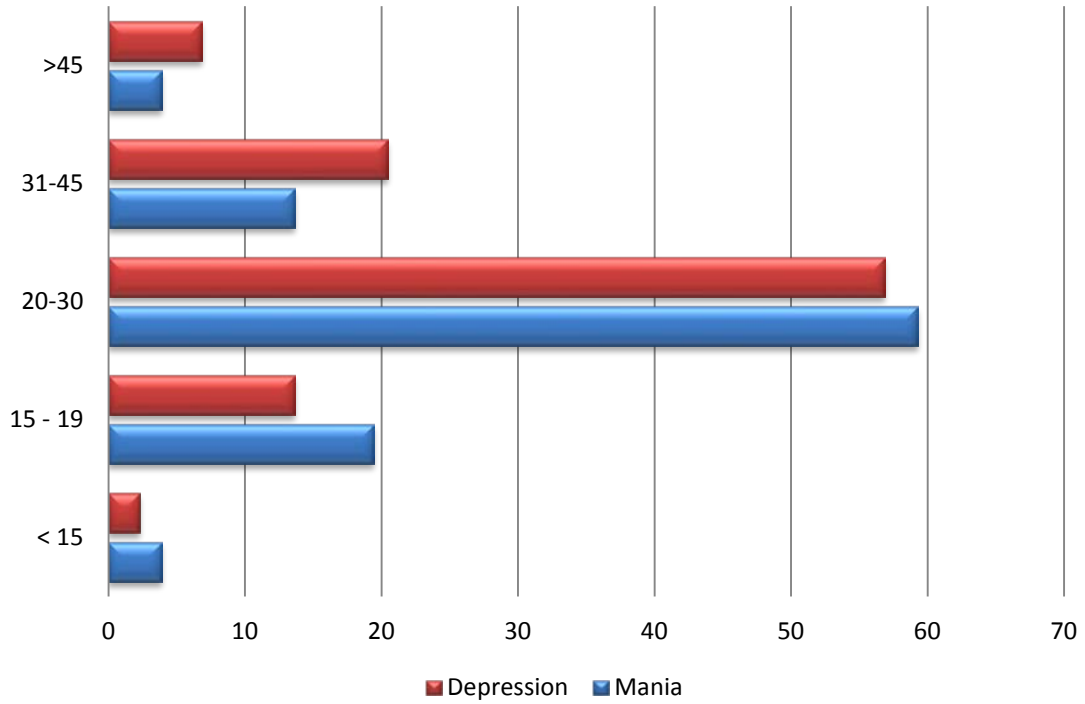
Table 5.17		
Age of onset bracket	**Frequency**	**Percentage**
< 15	4	3.88
15 - 19	20	19.42
20 - 30	61	59.22
31 - 45	14	13.59
> 45	4	3.88
Total	103	100

5.5.3 Table 5.18 Age of onset bracket: depression

Table 5.18		
Age of onset bracket	**Frequency**	**Percentage**
< 15	1	2.27
15 - 19	6	13.64
20 - 30	25	56.82
31 - 45	9	20.45
> 45	3	6.82
Total	44	100

5.5.4 Figure 5.2 Age of onset bracket

Figure 5.2: Age of Onset Bracket



5.6 Episode pattern

5.6.1 Table 5.19 Pattern of mood symptoms – Depressive and manic episodes versus manic only episodes

Table 5.19		
Episode pattern	**Frequency**	**Percentage**
Depressive and manic episodes	44	42.72
Manic only episodes	59	57.28

5.6.2 Table 5.20 Pattern of mood symptoms; manic only episodes – 2 or less phases versus 3 or more phases

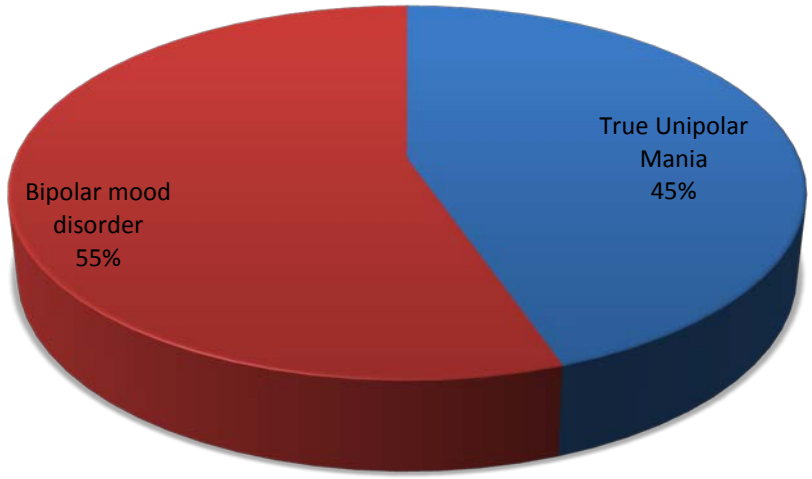
Table 5.20		
Manic only episodes	**Frequency**	**Percentage**
2 or less phases	11	20.75
3 or more phases	42	79.25
Total	53	100

5.6.3 Table 5.21 Pattern of mood symptoms – True unipolar mania versus bipolar mood disorder

Table 5.21		
Pattern of mood symptoms	**Frequency**	**Percentage**
"True unipolar mania" - 3 or more phases	42	44.68
Bipolar Mood Disorder	52	55.32
Total	94	100

5.6.4 Figure 5.3 Pattern of mood symptoms

Figure 5.3: Pattern of Mood Symptoms



n = 94

5.6.5 Table 5.22 Seasonal pattern

Table 5.22		
Seasonal pattern	**Frequency**	**Percentage**
Yes	13	12.62
No	90	87.38

5.6.6 Table 5.23 Lifetime number of phases

Table 5.23		
Lifetime number of phases	**Frequency**	**Percentage**
Zero	1	0,9
1	5	4,8
2	11	10,7
3	7	6,8
4	10	9,8
5 - 12	49	47,6
13 - 52	19	18,5
≥ 53	1	0,9
Total	103	100

5.6.7 Table 5.24 Number of manic episodes

Table 5.24		
Number of manic episodes	**Frequency**	**Percentage**
1	11	7.77
2	13	12.62
3 - 4	20	19.42
5 - 9	42	40.78
10 - 20	13	12.62
20 - 50	4	3.88
Total	103	100

5.6.8 Table 5.25 Number of depressive episodes

Table 5.25		
Number of Depressive Episodes	**Frequency**	**Percentage**
0	63	61.17
1	10	9.71
2	8	7.77
3 - 4	12	11.65
5 - 9	7	6.8
10 - 20	2	1.94
20 - 50	1	0.97
Total	103	100

5.6.9 Table 5.26 Depressive episodes features

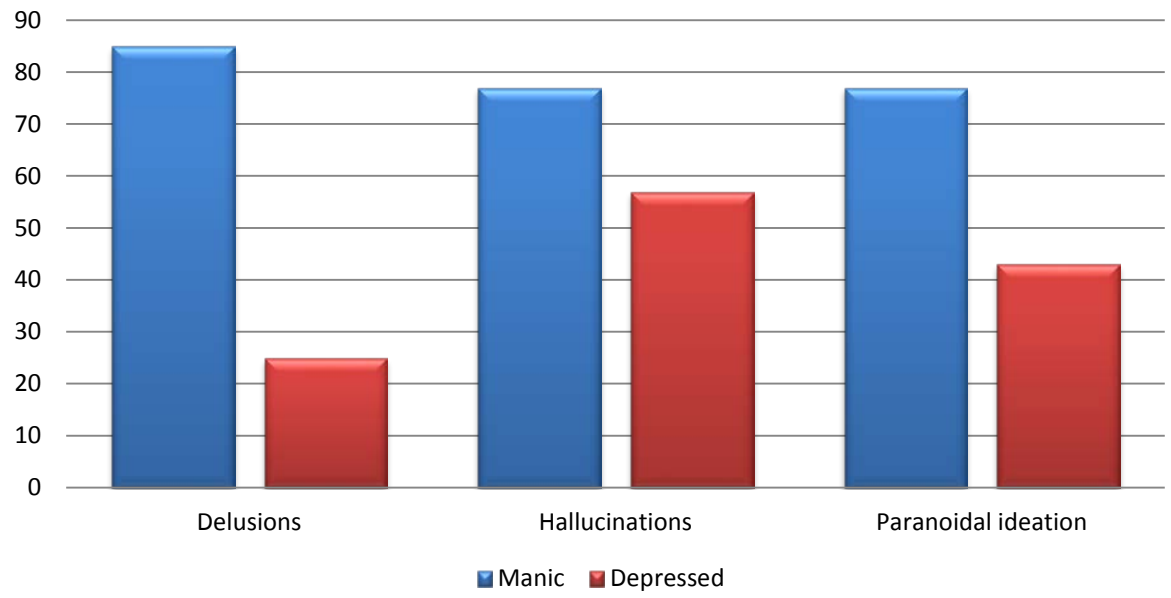
Table 5.26		
Depressive episode features	**Frequency (n = 44)**	**Percentage**
Worthlessness	44	100
Irritability	41	93,2
Sudden onset	39	88,63
Leaden paralysis	31	70,45
Hallucinations	25	56,82
Anger	22	50,0
Paranoid ideation	19	43,18
Delusions	11	25,0

5.6.10 Table 5.27 Mood elevation features

Table 5.27		
Mood elevation features	**Frequency (n=103)**	**Percentage**
Increased energy	101	98,06
Easily annoyed	94	91,26
Delusions	88	85,43
Extraordinary accomplishment	80	77,67
Hallucinations	79	76,7
Paranoid ideation	79	76,7
Decreased appetite	57	55,34
Risky pleasure	47	45,63
Increased libido	35	33,98
Increased spending	23	22,33

5.6.11 Figure 5.4 Psychotic features

Figure 5.4: Psychotic Features – Manic- vs. Depressive Episodes



5.7 Treatment

5.7.1 Table 5.28 Attended traditional healers

Table 5.28		
Attended Traditional Healers	**Frequency**	**Percentage**
Yes	66	64.08
No	37	35.92

5.7.2 Table 5.29 Current medication

Table 5.29 reflects the medication patients were on at the time of the interview.

Table 5.29		
Current Medication	**Frequency**	**Percentage**
Valproate	69	66,90
Haloperidol	51	49,51
Orphenadrine-HCl	43	41,75
Zuclopethixol depot	36	34,95
Risperidone	23	22,33
Lithium	22	21,36
Clozapine	11	10,68
Quethiapine	6	5,82
Clonazepam	5	4,85
Citalopram	4	3,88
Carbamazepine	3	2,91
Olanzepine	3	2,91
Trifluoperazine	1	0,9
Fluoxetine	1	0,9

5.7.3 Table 5.30 Anti-psychotics

Table 5.30 reflects previous medication the patient had ever received.

Table 5.30	
Antipsychotics	**Frequency**
Haloperidol	96
Zuclopethixol depot	59
Risperidone	25
Fluphenazine	15
Clozapine	15
Quethiapine	7
Other First Generation Anti-psychotics (FGA)	9
Olanzepine	4
Trifuoperazine	4

5.7.4 Table 5.31 Mood stabilizers

Table 5.31 reflects previous medication the patient had ever received.

Table 5.31	
Mood stabilisers	**Frequency**
Valproate	81
Lithium	37
Carbamazepine	7

5.7.5 Table 5.32 Anti-depressants

Table 5.32 reflects previous medication the patient had ever received.

Table 5.32	
Anti-depressants	**Frequency**
Citalopram	7
Fluoxetine	3
Amitrityline	2
Clomipramine	1
Ethipramine	1

5.7.6 Table 5.33 Extra-piramidal side-effects and Tardive Dyskinesia

Table 5.33 reflects the presence of either extra-piramidal side-effects or tardive dyskinesia at the time of the interview.

Table 5.33		
Side effects	**Yes**	**No**
Current EPSE	8	95
Tardive dyskinesia	4	99

5.8 Substances

5.8.1 Age of onset

Tables 5.34 to 5.36 reflect the age at which interviewees started to abuse substances. Apart from alcohol, cannabis and nicotine, none reported any other substances of abuse. Considering that the population where this sample came from live in rural areas, what is suggested is a lack of access to other substances available in the area.

5.8.1.1 Table 5.34 Age of onset of alcohol use

Table 5.34		
Alcohol use age of onset	**Frequency**	**Percentage**
Never	57	55.34
< 10	1	0.97
10 - 15	4	3.88
16 - 20	30	29.13
21 - 25	6	5.83
> 25	5	4.85
Total	103	100

5.8.1.2 Table 5.35 Age of onset of cannabis use

Table 5.35		
Cannabis use age of onset	**Frequency**	**Percentage**
Never	83	80.58
10 - 15	4	3.88
16 - 20	10	9.71
20 - 25	5	4.85
> 25	1	0.97
Total	103	100

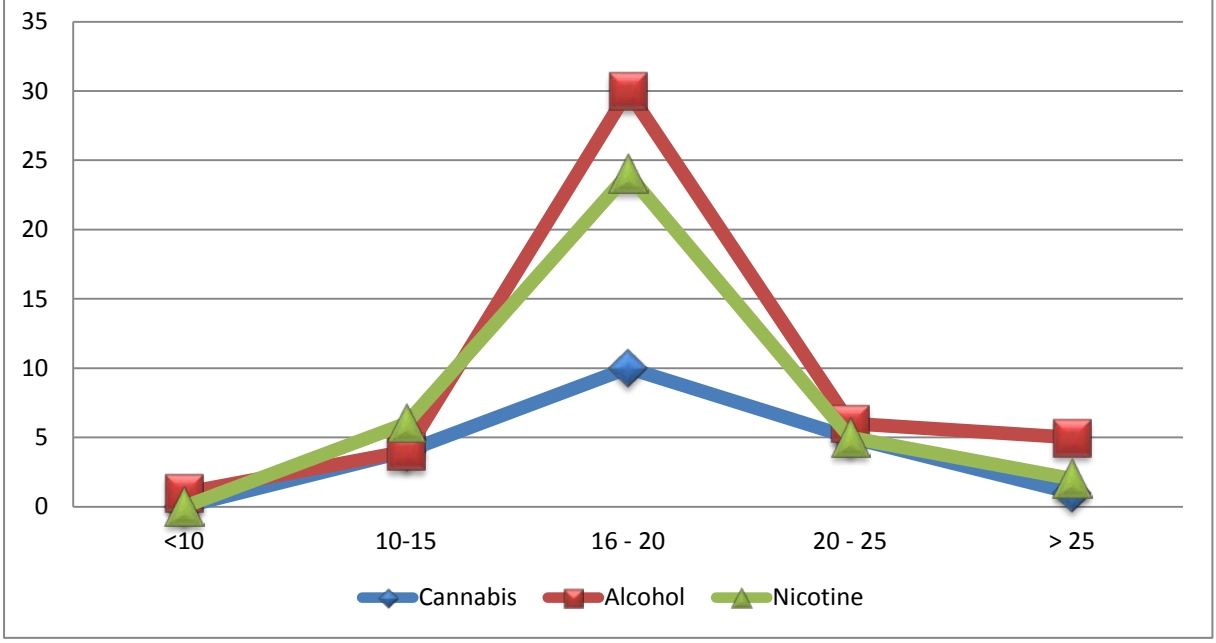
5.8.1.3 Table 5.36 Age of onset of nicotine use

Table 5.36		
Nicotine use age of onset	**Frequency**	**Percentage**
Never	66	64.08
10 - 15	6	5.83
16 - 20	24	23.3
20 - 25	5	4.85
> 25	2	1.94
Total	103	100

5.8.2 Figure 5.5 Substances – Age of onset comparison

Figure 5.5 summarises the age at which subjects started to use substances.

Figure 5.5: Substances Age of Onset Comparison



5.8.3 Summary of current versus past use or abuse

Tables 5.37 to 5.39 reflect a summary of current versus past use or abuse.

5.8.3.1 Table 5.37 Alcohol

Table 5.37	
Alcohol	**Yes**
History of abuse	40%
Current abuse	10%
Current use	18%

5.8.3.2 Table 5.38 Cannabis

Table 5.38	
Cannabis	**Yes**
History of abuse	18%
Current abuse	6%
Current use	9%

5.8.3.3 Table 5.39 Nicotine current use

Table 5.39	
Nicotine	**Yes**
Current use	32%

5.9 Diagnosis

5.9.1 Table 5.40 Axis 1 diagnosis

Table 5.40		
Axis I Diagnosis	**Frequency**	**Percentage**
Bipolar disorder	94	91.26
Schizo-affective disorder	7	6.8
Schizophrenia	1	0.97
Substance induced psychotic disorder	1	0.97
Total	103	100

5.9.2 Table 5.41 Other axis 1 diagnosis

Table 5.41		
Other Axis I Diagnosis	**Frequency**	**Percentage**
Anxiety disorder	51	49.51
Substance abuse/dependence	13	12.63
Other	3	2.91
None	36	34.95

5.9.3 Table 5.42 Comorbid anxiety disorder

Table 5.42		
Comorbid anxiety disorder	**Frequency**	**Percentage**
GAD	21	41.18
PTSD	14	27.45
Panic disorder	8	15.68
Social phobia	7	13.72
OCD	1	0.97
Total	51	100

5.9.4 Table 5.43 Bipolarity Index Score

Table 5.43		
Bipolarity index score	**Frequency**	**Percentage**
81 - 100	52	50.49
71 - 80	29	28.16
61 - 70	17	16.5
51 - 60	4	3.88
41 - 50	1	0.97
Total	103	100

5.9.5 Table 5.44 Clinical Global Impression of severity (CGI)

Table 5.44		
CGI	**Frequency**	**Percentage**
Normal, not ill	4	3.88
Borderline mentally ill	9	8.74
Mildly ill	22	21.36
Moderately ill	41	39.81
Markedly ill	18	17.48
Severely ill	8	7.77
Extremely ill	1	0.97
Total	103	100

5.10 Women's health issues

As alluded to earlier, results of the subsection dealing with women's health issues in the ADE under the main heading of "Medical History", are to be shown here. Menstrual history, parity, contraceptive method and surgery for hysterectomy or oophorectomy are all elicited in the section dealing with women's health issues.

Although not a specific question in the ADE, all women were asked whether they had taken any psychotropic medication while pregnant and whether their offspring had any developmental problems after birth, when enquiring about parity. Results of mood symptoms associated with pregnancy, post-partum onset of symptoms and peri-menstrual exacerbation are presented in this section even though it is enquired about in the section 'Pattern of mood symptoms' in the ADE as it was thought to make more sense presenting it together with women's issues.

5.10.1 Table 5.45 Menarche

Table 5.45		
Menarche Age	**Frequency**	**Percentage**
Never	1	1.75
Twelve	2	3.51
Thirteen	5	8.77
Fourteen	6	10.53
Fifteen	15	26.32
Sixteen	17	29.82
Seventeen	5	8.77
Eighteen	3	5.26
Nineteen	1	1.75
Twenty	2	3.51
Total	57	100

5.10.2 Table 5.46 Cycles

Table 5.46		
Cycles	**Frequency**	**Percentage**
Regular	29	50.87
Irregular	15	26.32
Postmenopausal	11	19.29
Hysterectomy	1	1.76
Never menstruated	1	1.76
Total	57	100

5.10.3 Table 5.47 Contraception

Table 5.47		
Contraception	**Frequency**	**Percentage**
None	31	54.39
Abstinence	8	14.03
IMI	7	12.28
Oral Birth Control	4	7.02
Barrier	4	7.02
Other	3	5.26
Total	57	100

5.10.4 Table 5.48 Took medication while pregnant

Table 5.48		
Took medication while pregnant	**Frequency**	**Percentage**
Yes	26	45.61
No	17	29.82
Unknown	14	24.56
Total	57	100

5.10.5 Live births vs. miscarriages

In Table 5.49 to Table 5.52 an effort was made to ascertain whether there was any reason to believe that taking medication while pregnant was associated with either miscarriages or developmental problems in the offspring. Table 5.49 looks particularly at which drug was taken during pregnancy.

5.10.5.1 Table 5.49 Live births

Table 5.49	
Live Births	**Frequency**
One	13
Two	8
Three	14
Four	3
Five	2
Six	1
Seven	2
Ten	1
Twelve	1
Total	45

5.10.5.2 Table 5.50 Miscarriages

Table 5.50		
Miscarriages	**Frequency**	**Percentage**
Zero	40	70.18
One	10	17.54
Two	5	8.77
Three	1	1.75
Five	1	1.75
Total	57	100

5.10.5.3 Table 5.51 Miscarriages while taking medication

Table 5.51					
Miscarriages while taking medication					
Medication	**Frequency**				
	One	**Two**	**Three**	**Five**	**Total**
Lithium	0	2	0	1	3
Valproate	7	3	1	0	11
Carbamazepine	1	0	0	0	1
Haloperidol	1	0	0	0	1
Clopixol depot	0	0	0	0	0
Quethiapine	1	0	0	0	0
Total	10	5	1	1	17

5.10.6 Developmental problems in offspring

Every woman in the study who had children was specifically asked whether there were any noticeable developmental problems in their children. None answered in the affirmative. This does not necessarily mean that there were no developmental problems but again could just be an indication of the fact that the subjects from this sample lives in

very poor and rural areas with little access to child psychiatric services. Hence developmental problems may go unnoticed or undiagnosed.

5.10.6.1 Table 5.52 Developmental problems in offspring

Table 5.52		
Developmental problems in offspring	**Frequency**	**Percentage**
No	40	70.18
Unknown	17	29.82
Total	57	100

5.10.7 Table 5.53 Peri-menstrual exacerbation

Table 5.53		
Peri-menstrual exacerbation	**Frequency**	**Percentage**
Yes	7	12,82
No	44	77,19
Unknown	6	9,99
Total	57	100

5.10.8 Table 5.54 Mood symptoms associated with pregnancy

Table 5.54		
Mood symptoms with pregnancy	**Frequency**	**Percentage**
Yes	18	31,58
No	31	54,39
Unknown	8	14,03
Total	57	100

5.10.9 Table 5.55 Post-partum onset of symptoms

Table 5.55		
Post-partum onset of symptoms	**Frequency**	**Percentage**
Yes	28	49,13
No	21	36,84
Unknown	8	14,03
Total	57	100

Chapter 6
Discussion

6.1 Introduction

Results will be discussed in the chronological order of the previous chapter. At the end of the chapter special attention will be given to the areas of gender, age of onset of mania and substances. The findings in this study will be compared to the current literature on the subject. In the last part of the discussion, the group of study subjects with Depressive and Manic episodes (DAM) will be compared with the group that had Manic only episodes (MO).

6.2 Recruitment

The majority of patients were recruited from Mankweng Hospital (see Table 5.1). Numbers recruited from each hospital reflect the different size and levels of hospitals. Sixty-one patients were recruited as in-patients while 42 were recruited from out-patients (see Table 5.2).

Hospitals were visited on the days when psychiatric patients were to attend follow up at psychiatric out-patient clinics. The doctors working at out-patients clinics that day were alerted to my presence and were requested to send all patients attending clinic with a diagnosis of bipolar mood disorder to me that day for interview. Hereafter, the wards were

visited and all patients with a diagnosis of bipolar disorder were seen and assessed for their ability to give informed consent. Those that could give informed consent were asked to participate in the study.

6.3 Identifying information

6.3.1 Gender and age

Of the one-hundred-and-three patients interviewed, 46 (44,66%) were male and 57 (55,34%) female (see Figure 5.1). The mean age was 36,6 years with a standard deviation of 11,9. The youngest patient interviewed was 12 and the oldest 73 years of age (see Table 5.3).

6.3.2 Marital status

The majority of participants were not married with 69,9% reporting being single and 1,94% divorced (see Table 5.4). In comparison, the study by Negash et al in Ethiopia found that 63,4% of the patients in their study were married. (94)

6.3.3 Religious affiliation

Most of the patients interviewed (63,11%) were members of the Zion Christian Church (ZCC), (see Table 5.5). The ZCC is a religious denomination with an extremely large following in Limpopo Province, their headquarters, Zion City Moria, situated a mere 5 kilometres from

Mankweng Hospital. It is one of the largest African-initiated churches in southern Africa with congregations throughout South Africa as well as in neighbouring countries.

The ZCC comprises two main congregations which are led by Barnabas Lekganyane (identified by wearing a green badge with a silver star) and Saint Engenas Lekganyane (identified by wearing a green badge with a silver dove), the grandsons of the founder of the church. (104)

In a scientific letter to the African Journal of Psychiatry; Culture, religion and psychosis – a case study from Limpopo province, South Africa, Grobler (2011) describes a family affiliated to the ZCC church that became psychotic and were treated at the Mankweng Hospital Psychiatric Unit. (105) They became psychotic after one of the family members received a prophecy from an elder of the church suggesting that something bad was going to happen to her and her family.

The role of traditional- and faith healers will be discussed in more detail under the section ‘Treatment’, as a large number of patients in this study (64%) also sought help from traditional healers, most of whom would be within the context of the ZCC church, considering that 63% were members of this church.

6.3.4 Education

In spite of the fact that 25,24% had a tertiary education, 69,9% of the sample were unemployed (see Table 5.6). This finding would be similar to that from a study by Kupfer et al. who found that, despite the fact that 60% of patients in their study had completed some college education and 30 % had completed college education, only 64% were currently unemployed and almost 40% were receiving disability support. (106)

6.3.5 Employment

More than two thirds of subjects in the study were not employed with only 11,6% being in gainful employment (see Table 5.7). This is again in sharp contrast to the study by Negash et al who found only 7,6% of subjects in their study to be unemployed. (94)

A possible explanation could be that employment in rural communities is very scarce in this part of South Africa considering that the average unemployment rate for South Africa is 25,53% and 32,46% for Limpopo in particular. (107) Unemployment is most probably related however to the fact that individuals with severe and enduring mental illness are less able to compete in the open labour market because of the nature of their illness as well as stigmatisation. (108)

6.3.6 Financial support

Slightly more than half the sample (52,43%) were receiving a social grant (Disability Grant) and 30,1% of the sample was dependant on their families for financial support (see Table 5.8).

The large number of patients receiving a Disability Grant in this study reflects the severity of the illness. For the majority of these patients, considering the scarcity of work as mentioned above, it is virtually impossible to compete in the open-labour market.

Employment is an often neglected topic of conversation with patients suffering from bipolar disorder as the perception of doctors in rural areas in my experience are that they view bipolar disorder as an illness with a good prognosis.

For this reason they tend not to consider patients with bipolar disorder candidates for a social grant and it is seldom suggested that they may consider applying for a social grant.

6.4 History

6.4.1 Family history of mental illness

Approximately two thirds of patients (57,3%) reported a family history of bipolar disorder (see Table 5.9). Heritability for bipolar disorder was reported to be 59% by Lichtenstein et al in 2009. (8) Barnett described a ten-fold increased risk for bipolar disorder among first degree relatives compared to the general population. (109) This finding supports the impression that the patients in this sample do in fact suffer from a bipolar type illness rather than a schizophrenic type of illness.

A family history of substance abuse was also common, with 52,5% reportedly having had a family member with a history of alcohol abuse in particular (see Table 5.9).

6.4.2 History of trauma

A third of patients interviewed (30,1%) reported some sort of traumatic experience (see Table 5.10) which is in keeping with a study by Neria et al reporting a history of assaultive trauma in bipolar patients with psychosis in 40% of their sample. (110) All subjects reporting sexual trauma were female with 5,8% reporting a history of a sexually traumatic event.

6.4.3 History of suicide attempts

Twenty-seven percent of patients in this study reported having made a suicide attempt (see Table 5.11) which is much higher than the 6,9% in the study by Negash et al in Ethiopia. History of suicide attempts in this study is however similar to estimated rates of suicide reported by Jamison et al in 2000 in patients suffering from bipolar disorder of between 25% and 50%. (111) The life-time suicide risk was found to be 25.6% by Dalton et al in a sample of 336 subjects with a diagnosis of bipolar I, bipolar II, or schizoaffective disorder (bipolar type). (112)

The results in this study is also in keeping with results from the EMBLEM study, which reported a history of suicidal behaviour in 29,9% of study subjects. The EMBLEM study is a two-year prospective, pan-European, observational study on treatment outcomes in patients with bipolar disorder. A history of suicide was associated with female gender, past alcohol or cannabis problems and poor treatment compliance. (113)

The EMBLEM study also revealed, apart from the above, the other main characteristics that differed between those with versus those without a lifetime history of suicidal behaviour were higher level of depressive (but not manic) symptoms at baseline, longer untreated period of bipolar disorder, earlier age at onset of bipolar disorder, recent treatment with

anti-depressants or benzodiazepines, work impairment and less satisfaction with life. (113)

Suicide is known to be the leading cause of mortality in patients with bipolar disorder. (114) Several studies have suggested an association between suicidal behaviour and comorbid alcohol or substance abuse (115), female gender (116), and being unmarried. (117)

Of those attempting suicide, hanging was the method most commonly reported, followed by overdose of medication and ingestion of poison. Attempting to cut one's own throat was a startling choice of method in 10% of those attempting suicide (see Table 5.12), considering that the most frequently employed methods for suicide in South Africa is hanging, followed by shooting, poisoning, overdosing, gassing and burning. (118)

6.4.4 History of violence and forensic history

Half the patients interviewed had a history of violence (Table 5.13) which would be in keeping with 94 subjects reported being "easily annoyed" whilst manic (see table 5.72) and 41 reporting being "irritable" while depressed (Table 5.71). A third of patients reported a forensic history. The high number of patients reporting a forensic history reflects findings

of other studies in which bipolar disorder has been associated with increased rates of violent behaviour. (119) A history of violence in this study is substantially higher than rates reported in the Epidemiologic Catchment Area Surveys which reported a rate of 11% of respondents reporting violent acts in the past year. (120)

6.4.5 Medical history

Seventeen patients (16,5%) had a history of head injury with loss of consciousness and eight (7,8%) had a history of seizures (see table 5.14). This appears to be quite high considering the findings of the New Haven NIMH Epidemiologic Catchment Area Study which specifically looks at the association between head injuries and psychiatric disorders.

The researchers in this study found that all psychiatric diagnoses, except bipolar disorder and schizophrenia, were more prevalent in the group with head injury compared to those with no history of a head injury. (121)

6.4.6 HIV status

Whilst their HIV status was unknown to the majority of patients, nine (8,74%) of the patients in the sample were HIV positive (Table 5.15). There appears to be heightened rates of bipolar affective disorder and secondary mania among individuals with HIV/AIDS. (122) (123) The

present study did, however, not investigate the relation between HIV status and manic symptoms. Discussing risks related to sexually promiscuous behaviour when manic should be part of the psychoeduation of all bipolar patients.

6.5 Course and clinical features

6.5.1 Age of onset

The mean age of onset of first manic episode was 25 years and the mean age of onset of depression was 26 years (Table 5.16). The majority of patients experienced their first manic- as well as depressive episode between 20 and 30 years of age (Table 5.17 and Table 5.18). A comparable study would be that of Negash et al in 2005 in Ethiopia who found the mean age of onset of mania to be 22 years of age and that of depression 23,4 years of age. (94)

In a cross-national epidemiological study of major depression and bipolar disorder, Weismann et al (1994) found noteworthy differences in terms of age of onset of mania between participating countries. These differences ranged from 17,1 in Canada to 29 in West Germany. (124) Leboyer et al (125) provide a comprehensive review of existing data, showing that age of onset can identify homogenous sub-groups of patients with bipolar disorder.

There appears to be a trend towards mania developing earlier, before age 20 (23,3%) and depression developing later in life, after 30 (27,3% of the 44 subjects who had depressive episodes in this sample), (see tables 5.17, 5.18 and figure 5.2). Only 34% of the subjects in this study were younger than 30.

Age of onset findings will be discussed in more detail at the end of this chapter when those subjects with earlier onset of mania are compared with those with later onset of mania.

6.5.2 Episode pattern

6.5.2.1 Pattern of mood symptoms

A significant finding was that, of the 103 patients interviewed with a history of mania, 57,28% had only ever experienced manic symptoms (Table 5.19) As mentioned in Chapter 3, a unipolar manic course in this study was considered in all patients who had never experienced a major depressive episode. An issue that needs clarification however, is what “true” unipolar mania constitutes in terms of amount of manic episodes without any depressive episodes.

If one excludes all the patients who turned out not to suffer from bipolar disorder (Table 5.40), it leaves 94 patients who had a diagnosis of

bipolar mood disorder specifically. Of these 94 patients, 53 reported never having had depressive episodes (Table 5.20) and of this 53 patients, 42 (44,68%), (Figure 5.3) reported "three or more" lifetime number of phases (see table 5.21). This figure of 44,68% reflects those study subjects with a true unipolar manic course if one accepts the criteria of three or more lifetime number of episodes as indicative of a unipolar manic course. This figure is significantly higher than the reported 10% to 20% rate of unipolar mania in the literature in general. (2)

6.5.2.2 Seasonal pattern

Not many patients admitted to seasonal variation or exacerbation of mood symptoms with only 12,62% reporting a seasonal pattern (Table 5.22). This is lower than the figure reported by Kim et al of 20% to 25% (126) but in keeping with the conclusion of Murray et al who found no evidence of seasonal variation in bipolar disorder. (127)

6.5.2.3 Lifetime number of phases

Most patients had “5 to 12” mood episodes in a lifetime (see table 5.23). Lifetime number of manic or depressive episodes were assessed according to the following breakdown; “zero”, “one”, “two”, “3 to 4”, “5 to 9”, “10 to 20” and “20 to 50”. Most patients experienced “5 to 9” episodes

of mania in a lifetime (Table 5.24). Depression was a much rarer expression of the illness and the majority of patients had fewer than five episodes of depression in a lifetime (Table 5.25).

6.5.2.4 Episode features

Crucial to the present study is the ability to elicit the symptoms of depression and to diagnose the presence of a depressive episode, either currently or in the past. This has been reported to be notoriously difficult in cross-cultural settings.

The prevailing language in Limpopo is Sepedi. When enquiring about depressed mood, it's more of describing the emotion, but the phrase "kgatello ya monagano" is used to describe the emotion which means literally “suppressed mind”. In spite of the lack of a word for depression or depressed mood, the follow on questions in the ADE goes to great lengths to elicit other symptoms of a depressive episode.

Bodemer (1984) engaged this challenge in his MD dissertation “The concept of depression – an evaluation of symptoms and signs in a group of black South Africans” reporting that the cultural background of the patient played an integral part in the mode of clinical presentation of depression. Bodemer emphasised specifically the challenge that most

black languages in South Africa do not have an accepted word for depression and although the minority in his study complained of a feeling of depression, all the patients diagnosed with depression complained of a loss of interest or pleasure in all or practically all normal pastimes.

In the group with major depression Bodemer found 89,5% presented with agitation or retardation, 78,9% with somatic complaints, 73,7% with loss of appetite and 73,7% with sleep problems, referring to these symptoms as culture free. (128)

Ellis, in a very eloquently article, highlights the challenges of diagnosing depression in general practice in rural Kwazulu-Natal. Ellis suggests that the traditional African presentation of depression may be divided into four domains; somatic complaints, fatigue variants, message of distress and problematic relationships. This author concedes that this is his “artificial” perspective as an English immigrant doctor working with Zulus and that all cultures can present with depression in a variety of said categories but that in more traditional societies the symptoms of depression are more likely to be delivered metaphorically or symbolically as idioms of distress, linguistic images, metaphors and associative phrases. (129)

In the present study, each subject had to answer specific questions related to past depressive episodes (page 3 of the ADE). The first two questions were; 1) Has there ever been a period when you were feeling down or depressed most of the day, nearly every day, for as long as two weeks? and 2) What about being a lot less interested in things or unable to enjoy things you usually would enjoy nearly every day for as long as two weeks?, reflecting DSM diagnostic criteria for a depressive episode. The interviewer could rate these two questions as “No”, “Probable” or “Definite”.

If either question was rated “Definite”, the interviewer then proceeded to ask the following questions: During that time…

1. …did you have a change in sleep pattern?
2. ….were you down on yourself? Did you feel as if you were a bad person or that you deserved to suffer?
3. ….how was your energy level? Were there things that you should have done and didn’t because you didn’t have enough energy or were simply too tired?
4. ….how was your concentration? Were you able to read the newspaper or watch TV? Did you find that you were easily distracted?
5. ….how was your appetite? Did your weight change?

6. ….were there times when you were so fidgety or agitated it was hard for you to stay still? What about the opposite - thinking or moving more slowly than usual? If I had been there, would I have noticed that something was wrong
7. ….were there times when you were feeling so bad that you felt life was not worth living? What about actually thinking about suicide or harming yourself?

Hereafter the following parameters were enquired about: “Sudden onset”, “Irritability”, “Anger attacks”, “Leaden paralysis”, “Worthlessness”, “Paranoid ideation”, “Delusions” and “Hallucinations”.

Using the above approach, the diagnosis of depression was made with a reasonable amount of confidence. It was found that, while subjects were depressed, the most common accompanying feature was “Worthlessness” (100%) followed by “Irritability” (93,2%) and “Sudden onset” (88,63%). “Leaden paralysis” (70,45%) was also a common finding (see table 5.26).

Manic episodes (or lifetime abnormal mood elevation) were elicited in the following fashion (page 2 of the ADE).

Have you ever had a time…

1. …when you were feeling so good or so hyper that other people thought you were not your normal self?
2. …or you were so hyper you got into trouble?
3. …did anyone say you were “manic”?
4. …when you felt like you could do much more than you are ordinarily capable of?
5. …when you were so irritable that you shouted at people or started fights or arguments? Did you find yourself yelling at people you didn’t really know?

It was then ascertained whether, for the most severe episode identified above, any of the following sounded familiar;

a) During that time, were there any times when your mood was euphoric or expansive or irritable or dysphoric?
b) Were you admitted to the hospital during this time?
c) Altogether, how long did this period last?

Symptoms present to a significant degree during most severe episode identified through the questions set out above were then elicited:

During that time…

1. …were you feeling more self-confident than usual or like you were special, more talented, more attractive, or smarter than usual?
2. …were there nights you got less sleep than usual and found you didn't really miss it?
3. …were there any times you were more talkative than usual, or you found you said much more than you intended? Were there any times you spoke faster than usual?
4. …did you find that you had more ideas than usual? Were there times when your thoughts seemed to be racing through your head?
5. …did you find you were easily distracted?
6. …did you experience difficulties due to making new plans or getting new projects started? Were there times when you were so energised or agitated you couldn't sit still?
7. …did you do anything that was unusual for you or that other people might think was excessive, foolish or risky? Did you do anything that would have caused a problem if you were caught?

The following parameters were then asked about with regard to other features of past episodes of mood elevation: "Increase in risky pleasure",

"Extraordinary accomplishment", "Sudden onset", "Easily annoyed", "Decreased appetite", "Increased energy", "Increased Spending", "Increased libido", "Paranoid ideation", "Delusions" and "Hallucinations".

The most common accompanying features of mood elevation (see table 5.27) appeared to be "Increased energy" (98,06%), followed by "Easily annoyed" (91,26%) and "Delusions" (85,43%). The low number of patients reporting "Increased spending" (22,33%) is perhaps a reflection of the poor socio-economic status of the interviewed population.

It appears that, whilst manic, a significant number of patients experienced psychotic symptoms (see table 5.27 and figure 5.3) with 85,43% reporting delusions, 76,7% hallucinations and 76,7% paranoid ideation. However, while subjects were depressed, hallucinations appeared to be more common as a psychotic feature than delusions and paranoid ideation. These findings described here support the argument that this sample of patients presents with significant psychotic symptoms when manic.

6.5.3 Treatment

6.5.3.1 Attended traditional healers

Two thirds (64%) of those interviewed stated that they had consulted with faith or traditional healers with regard to their mental illness (see table 5.28). This is in keeping with the local culture and the fact that the majority of study subjects belonged to the ZCC faith.

Seeking help from a faith healer is not only culturally acceptable but in fact encouraged by the ZCC church where it is believed that that senior officials in the ZCC (known as *"baruti"*) can use the power of the Holy Spirit to perform healing. This could include the laying-on of hands, the use of holy water, drinking of blessed tea and coffee, and the wearing of blessed cords or cloth. (130)

Robertson explored the issue of collaboration between psychiatry and traditional healers in South Africa. In this article Robertson maintains that there are approximately 250,000 traditional healers in South Africa and that it is estimated that 70% of South Africans consult traditional healers. This means that there are more traditional healers than medical practitioners in South Africa and many people consider traditional healers to be more accessible and provide more holistic care.

Reporting on the findings of three studies by their research group at the Department of psychiatry of the University of Cape Town, Faculty of Health Sciences, Robertson's research group found that the overwhelming majority of the sampled population expressed satisfaction with treatment received from traditional healers.

The first study was conducted amongst traditional healers, the second in hospital on in-patients admitted for serious mental illness and the third in the community. In their second study Robertson's group found that 61% of patients admitted for serious mental illness consulted with African indigenous healers during the previous 12 months.

Robertson goes on to write that traditional healers clearly provide a valuable mental health service but draws a distinction between their usefulness for problems related to daily living and lifestyle problems versus serious mental illness. Robertson states:

> As the treatment measures employed by the traditional healer appear to be limited to relatively non-specific, low potency homeopathic medications combined with suggestion, we should not be surprised that they are effective with the former, but not the latter mental health problems. (131)

6.5.3.2 Medication

The drugs study subjects were taking mostly at the time of interview were valproate, haloperidol and zuclopenthixol depot. A significant amount of patients were also receiving orphenadrine (Table 5.29).

Haloperidol was the most commonly ever prescribed anti-psychotic followed by zuclopenthixol depot (see table 5.30). Valproate was the most popular choice with regards to mood stabilizers ever prescribed (Table 5.31). Of those ever receiving antidepressants, most were prescribed citalopram (Table 5.32).

The choice of medication and prescription habits probably reflects availability of certain drugs in the public service. Most of the study subjects in this study would primarily be initially diagnosed, treated and followed-up by primary health care practitioners. This would be especially true for George Masebe- and Mokopane hospitals. Having said that, at the time of the study there was a fulltime consultant psychiatrist working at Mokopane Hospital who also did an outreach-clinic at George Masebe Hospital. At Mankweng Hospital the out-patient service was rendered by medical officers and registrars working fulltime in the department of psychiatry.

Comparing the above findings with those from the study by Kupfer et al where more than a third of the patients in their study were taking lithium (compared to 21% in the current study) and 40% were taking an anticonvulsant as a mood stabiliser (compared to 85% in the current study), it would appear that prescription habits differ from continent to continent. In the current study a patient would more likely receive an anticonvulsant as a mood stabilising agent than lithium. (106)

Valproate in particular was used much more compared to the study by Kupfer et al. A possible explanation for this could the fact that the subjects in this study comes from a rural and sometimes isolated population where monitoring for lithium levels would be challenging and therefore an anticonvulsant would be chosen rather than lithium as lithium is perceived to carry more risk in terms of toxicity.

More than half the patients in Kupfer et al's study were taking antidepressants compared to only 13,6% in this current study. Twenty-five percent of the patients in Kupfer et al's study were taking benzodiazepines compared to 4,8% in this study.

Considering the small amount of patients receiving anti-depressants, one has to wonder whether this because this population tends to present

with a manic only course of their bipolar illness. The fact that so few patients were receiving antidepressants indicates a different expression of bipolar disorder in this particular population and would support the argument that bipolar disorder presents differently in Africa.

Not many patients exhibited any extra-piramidal symptoms and very few had tardive dyskinesia (see table 5.33), in spite of the fact that the majority of patients received first-generation anti-psychotic drugs. Forty-two percent were taking an anti-cholinergic at the time of interview (Table 5.29).

6.5.4 Substances

The age of onset of substance use appeared to be mostly in the age group “16 to 20” for nicotine, alcohol and cannabis (see tables 5.34, 5.35, 5.36 and figure 5.4). The majority started smoking cigarettes between the ages of 16 to 20 and 32% were still smoking cigarettes at the time of interview (Table 5.36 and Table 5.39).

Whilst 40% gave a history of alcohol abuse, only 18% admitted to current use (Table 5.37). Just 5,8% of participants were still using cannabis at the time of interview but 18,4% had a history of cannabis abuse (Table 5.38).

Substance use and history of abuse will be discussed in detail at the end of this chapter.

6.5.5 Diagnosis

All the subjects assessed by the researcher were referred as having had a history of mania and after assessment with the ADE, a definitive diagnosis was made. Not all patients presenting with mania were diagnosed as having bipolar mood disorder by the researcher after completion of the assessment using the ADE. The patients that received a different diagnosis from bipolar disorder after being interviewed were excluded in the final calculations as to a “true” unipolar manic course as mentioned earlier under the heading “Pattern of mood symptoms”.

Of the 103 subjects interviewed, nine turned out not to have bipolar mood disorder after completion of the ADE (99) which uses DSM-IV-TR criteria (64), with 6,8% (n = 7) diagnosed with schizoaffective disorder, one with schizophrenia and one with substance induced psychotic disorder (Table 5.40).

Anxiety disorders were the most common comorbid condition (49,51%) followed by substance abuse/dependence (12,63%) (Table 5.41).

Generalised anxiety disorder (GAD) was the anxiety disorder mostly encountered (41,18%), followed by posttraumatic stress disorder (PTSD) (27,45%), panic disorder (15,68%), social anxiety disorder (13,72%) and obsessive-compulsive disorder (OCD) (0,79%) (Table 5.42).

At first glance the number of patients presenting with comorbid anxiety disorders seems disproportionately high but the recent literature suggests that comorbid anxiety disorders have been reported at rates of 7% to 32% for GAD, 7% to 38,8% for PTSD, 3,2% to 35% for OCD, 7,8% to 47,2% for social anxiety disorder and 10,6% to 62,5% for panic disorder. (132) (133) (134) (135) (136)

In a study of psychiatric comorbidity in patients with bipolar disorder who entered into the Stanley Foundation Bipolar Treatment Outcome Network, McElroy et al found the lifetime comorbidity for anxiety disorders to be 42% and current comorbidity of anxiety disorders 30%. Findings for GAD and PTSD in particular were however lower compared to the current study with 3% having comorbid GAD (41% in the current study) and 4% comorbid PTSD (27% in the current study). (137)

Similarly, Simon et al, examining anxiety and its correlates in a cross-sectional sample from the first 500 patients with bipolar disorder enrolled

in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), found the prevalence of any lifetime anxiety disorder for the entire sample to be 51,2% and 30,5% for any current anxiety disorder.

Data on prevalence of psychiatric disorders in South Africa are, however scarce and one of the first studies investigating lifetime prevalence of psychiatric disorders in South Africa was the South African Stress and Health (SASH) Study. (138) Stein et al reported the lifetime prevalence of any anxiety disorder in the general population to be 15,8%, GAD 2,7% and PTSD 2,3%. (139)

Examining trauma and posttraumatic stress disorder in an urban Xhosa primary care population, Carey et al interviewed 201 subjects at a South African township primary healthcare clinic. Ninety-four percent of the sample reported exposure to traumatic events and PTSD was found to be present in 19,9% of patients. (140)

Considering the high rates of comorbidity of bipolar- and anxiety disorders as reported on above, the lifetime prevalence of anxiety disorders in the general population in South Africa and the prevalence of PTSD in in an urban primary care population, the rate of comorbid

anxiety disorders including GAD (41%) and PTSD (27%) in this present study suddenly seems less disproportionate.

6.5.6 Bipolarity Index Score

The “Bipolarity Index” is part of the ADE and is a tool for both assessment as well as creating rapport with patients. According to Sachs the index approaches the diagnosis of bipolar disorder not as a categorical question but more on a continuum. Therefore an impression is created of how much and in what ways a patient is ‘bipolar’. (141)

Sachs contends that, at the end of an evaluation, the goal of producing a DSM diagnosis pushes the interviewer toward considering bipolarity as a categorical entity. The “Bipolarity Index” was developed as a useful alternative to categorising bipolarity as present or absent. Most bipolar I patients will score above “60”. (102)

In this current study sample, close to 95% of the subjects scored higher than “60” on the Bipolarity Index (Table 5.43).

Most of the subjects in the study were rated as “Mildly ill” to “Moderately ill” on the CGI at the time of interview (Table 5.44).

6.6 Women's health issues

As explained earlier in this chapter, there is a subsection dealing with women's health issues in the ADE, under the main heading of "Medical History". For this reason women's issues are discussed here in accordance with the order in which results were presented in the "Results" chapter.

Research with regard to the management of bipolar disorder in women during pregnancy and the postpartum period remains scarce. The impact of the illness in women is poorly understood and many questions remain to be answered that could have major treatment implications for women suffering from bipolar disorder during their reproductive years.

The majority of women in the study had their menarche at ages 15 to 16 which is slightly older than the expected 14 to 15 years (see table 5.45). The worldwide average age of menarche is difficult to estimate accurately and varies by geographical region, race, ethnicity and other characteristics. Some estimates suggest that the median age of menarche worldwide is 14. (142)

Age of menarche was found to be 13 to 14 years in a study from Cameroon (143) as well as one from Mozambique. (144) However, in a

study conducted in two small towns in northwest Ethiopia in 2007, the average age at menarche by recall method was 15.8 +/- 1 years, which is more in keeping with the results from the present study. (145) The average age of menarche is about 12.5 years in the United States. (142)

Twenty-six percent of the women in this sample reported irregular menses (see table 5.46) and more than half of them used no contraception at all (Table 5.47). Another neglected topic with regard to psychoeducation of our female patients of childbearing age is the matter of menstrual abnormalities associated with taking psychotropic mediation as well as the importance of using contraception if of childbearing age. Not only should women be informed about the effects of psychotropic medication in their menstrual patterns but they should also be educated about the possible teratogenetic effects of psychotropic drugs on their offspring.

Only 29% (n = 26) stopped taking their medication while pregnant with another 24% (n = 14) were “not sure” or “could not remember” whether they took medication while pregnant (Table 5.48).

In order to come to conclusions with regard to miscarriages suffered by females in this sample, the author also looked at “Live births” and the

medication the patients were taking. Considering that this is the medication they were currently on and not necessarily that which they were taking at the time of falling pregnant, findings need to be interpreted carefully and no clear conclusions can be inferred from this data. It can serve as a guide for future research however.

Table 5.49 reflects the number of “live births” per subject, in other words the females who had children in the study had 45 children all together. Approximately 30% (n=17) of the sample had suffered miscarriages (see table 5.50). The majority of those who had miscarriages were on Valproate (see table 5.51). None of the females who had children were on a depot medication. The rate of miscarriages appears to be higher than expected and significantly higher than the findings of a study on pregnancy outcomes in South Africa by Bello et al who reported that 9.5% of 2467 pregnancies ended in spontaneous abortion and only 2.2% in still births. (146)

A specific question was asked with regard to any noticeable developmental problems in their offspring. Again, the findings should be carefully interpreted considering that this is a very rural and poor population and that developmental problems may not be picked up by either parents or the school system. None however reported any

problems that could be interpreted as being the result of a teratogenetic effect of a particular drug (see table 5.52).

Research on the effects of prenatal exposure to anti-psychotic medication remains scarce but a recent study examining the effects by Johnson et al showed that prenatal anti-psychotic exposure may affect neuromotor performance during infancy. This prospective study conducted at an Infant Development Laboratory in Atlanta, Georgia examined 309 infants who had prenatally been exposed to either anti-psychotics, antidepressants or no psychotropic medication. Johnson et al found that, among six month-old infants, a history of intrauterine antipsychotic exposure, compared to antidepressant or no exposure was associated with significantly lower scores on a standard test of neuromotor performance. (147)

Only 12% (n = 7) of women in the sample reported peri-menstrual exacerbation of mood symptoms (Table 5.53). This appears to be lower than the approximately 60% in other studies. (148) (149)

A third of patients reported mood symptoms associated with pregnancy while 49,13% (n = 28) reported postpartum onset of symptoms (see tables 5.54 and 5.55). Some studies report rates of post-partum mood

episodes of up to 40% after delivery (150) (151), while Freeman et al (152) found that 67% of their group of 50 women with bipolar disorder with children experienced a post-partum mood episode within one month of delivery. Nearly half (49,13%) of the women who had children in this study reported post-partum onset of symptoms.

6.7 Gender comparison

In the present study the following trends with regard to gender appeared:

- Marital status
    - Males were less likely to be married (17% vs. 28%) [p=0.245]
- Education
    - Males were more likely to have secondary education (58% vs. 49%) but less likely to have a tertiary education (21% vs. 28%) [p=0.502].
- Employment
    - Men were more likely to be unemployed (76% vs. 64%) [p=0.281].
- Disability
    - Men were slightly more likely to receive a Social Grant (54% vs. 50%) [p=0.843].

- History of trauma
    - No men reported being the victim of sexual trauma whereas 10% of females reported a history of sexual trauma which is a statistically significant difference [p=0.032].
- History of suicide attempts
    - There did not appear to be a significant difference in reporting of a history of suicidal attempts (26% vs. 28%) [p=1.000] but methods differed significantly.
    - Men were more likely to attempt suicide by hanging (13% vs. 5%) [p=0.293] while women were more like to ingest poison (0% vs. 7%) [p=0.126] or take an overdose (2% vs. 8%) [p=0.221].
- Forensic history
    - Men were significantly more likely to have a forensic history (52% vs. 14%) [p=0.001].
- Medical history
    - Men tended to more often report a history of head trauma with loss of consciousness (21% vs. 12%) [p=0.286] whilst more women reported being HIV positive (14% vs. 2%) which was statistically significant [p=0.040].

- Affective episode features
    - Interesting gender differences emerged with regard to ways in which both depressive episodes as well as manic episodes presented:
        - While depressed, females were more likely to report delusions, anger, irritability, sudden onset, worthlessness and leaden paralysis.
        - Whilst manic, men were more likely to report delusions, hallucinations, paranoid ideation, increased libido and partaking in risky pleasurable activities.
        - The only statistical difference was for hallucinations while manic with 78,26% of men reporting hallucinations compared to 49,12% of women [p=0.004]
- Treatment
    - Slightly more females tended to visit a traditional healer (60% vs. 66%) [p=0.680].
    - With regard to current medication, again some very interesting gender differences emerged:

    - Males were more likely to receive lithium (26% vs. 17%) [p=0.339] and clozapine (19% vs. 3%) [p=0.011] and females more likely to receive valproate (58% vs. 73%) [p=0.141].
    - No males were on anti-depressants whereas 8% of the females were on an anti-depressant [p=0.063].

- Substances
    - Fifty-six per cent of males were currently smoking compared to 12% of females, a statistically significant difference [p=0.001].
    - Males were also statistically significant more likely to have a history of alcohol abuse (60% vs. 22%) [p=0.001] and cannabis abuse (39% vs. 1,75%) [p=0.001].
- Comorbid anxiety disorder
    - Females had virtually double the rate of comorbid anxiety disorders (32% vs. 63%) [p=0.003].
- CGI
    - Males were more likely to be rated “Markedly ill” (19% vs. 10%) to “Severely ill” (15% vs. 1%) [p=0.103].

The literature on the matter of gender differences in bipolar disorder suggests that the clinical features and evolution of illness differ between

men and women. (114) Roy-Byrne et al held that women are more likely to have depressive episodes. (153) Hendrick et al found no gender difference in the total number of depressive or manic episodes. (154)

Kupfer et al found that more men (39,4%) than women (29,29%) had never been married. Men had higher mean educational achievement (in keeping with current study findings), were more likely to be employed (different from current study) but were also more likely to be receiving disability grants (same as current study). (106)

Arnold claims the onset of bipolar disorder to often be later in women than in men and, similarly to the current study found that women tended to have more anxiety disorders. (17) In keeping with the current study, men with bipolar disorder more often had comorbid substance abuse according to Kessing (155) as well as Kawa et al. (156)

Baldessano et al found women had higher rates of PTSD (10,6% M vs. 20,9% F), men were more likely to have a history of legal problems (36% M vs. 17,5% F), and women had more lifetime suicide attempts. In the current study men were also more likely to have a forensic history. (157)

The findings of Nivoli et al are also similar to those of the present study with Nivoli finding that men are more likely to suffer from comorbid substance abuse, women are more likely to have a lifetime history of a suicide attempts, and suicides are often more violent in men with bipolar disorder. (158) Lastly Miquel et al found that manic episodes are more common in men and depressive episodes occur more frequently in women.(159)

Statistically significant differences in the present study in summary are:

- Females were more likely to:
    - Have a history of sexual trauma.
    - Be HIV positive
    - Suffer from a comorbid anxiety disorder
- Males were more likely to:
    - Have a forensic history
    - Experience hallucinations
    - Receive clozapine
    - Smoke cigarettes currently
    - Have a history of alcohol or cannabis abuse

6.8 Age of onset of mania

For the purposes of this particular study and considering the assessment instrument used, the author defined early age of onset (EAOO) as ≤ 19 years of age. In the present study the following trends appeared with regard to age of onset:

- Marital status
    - Considerably less of the EAOO group appeared to get married (12,5% vs. 27,85%) [p=0.175].
- Education
    - Less of the EAOO group obtained secondary education (67% vs. 49%) [p=0.066] or went on to obtain tertiary education (12,5% vs. 29,11%) [p=0.116].
- Employment and financial support
    - The rate of unemployment was virtually equal with more subjects receiving a Social Grant in the later onset group (42% vs. 56%) [p=0.252].
- Family history of mental illness
    - The EAOO group had a slightly increased rate of a family history of bipolar disorder (62,5% vs. 55,7%) [p=0.641].
- History of suicide attempts
    - The EAOO group had a lower rate of suicide attempts (20,83% vs. 29,11%) in this study [p=0.601].

- Treatment
    - A number of differences came to light with the EAOO group receiving more lithium (29,17% vs. 18,99%) [p=0.393], less oral haloperidol (37,5% vs. 53,16%) [p=0.244] but more depot Zuclopenthixol (54,17% vs. 30,88%) [p=0.051] and much more Clozapine (25% vs. 6,33%) [p=0.018]. This was the only statistically significant difference with regard to difference in age of onset and could signify a more severe and disabling course of illness.
    - Another interesting finding was that the EAOO group were more likely to receive Citalopram (12,5% vs. 1,27%) [p=0.081].
- Substance abuse
    - The EAOO group appeared to be slightly less prone to have a history of substance abuse with regard to both alcohol (37,5% vs. 40,5%) [p=0.645] and cannabis (16,7% vs. 18,99%) [p=1.000], which is not in keeping with research findings from other countries.
- Comorbid anxiety disorder
    - The EAOO group had a slightly higher rate of comorbid anxiety disorders (54,17% vs. 48,1%) [p=0.647]

- Bipolarity Index
    - In terms of the Bipolarity Index, the EAOO group had a higher likelihood of scoring “81-100” (58,33% vs. 48,1%) [p=0.166] which again could indicate that this group is the ‘true’ bipolar group.
- CGI
    - The EAOO group was more likely to be rated ‘Markedly ill’ (20,83% vs. 16,46%) to ‘Severely ill’ (12,5% vs. 6,33%) on the CGI, which again could point toward a more severe and disabling course of illness. [p=0.700].

As noted above, the only statistically significant difference that emerged from the above comparison was that the EAOO group was more likely to be prescribed clozapine [p=0.018].

The diagnosis of mania in childhood has been a source of much debate but nowadays it seems clear that early-onset bipolar disorders are not necessarily rare but simply very difficult to diagnose. There appears from the literature to be three sub-groups based on age of onset – early, intermediate and late onset. Bellivier et al. demonstrated by admixture analysis (a method that identifies the theoretical model that best fits with the observed distribution of age at onset in an epidemiological sample of

bipolar patients) three distinct age of onset sub-groups to exist namely early, intermediate and late onset, peaking at 17, 27 and 46 years respectively. (160)

Lin et al examined the clinical and familial characteristics of age at onset in bipolar disorder subjects from families with multiple affected members and defined early onset as ≤ 21 years. (161)

Early onset bipolar disorder is associated with:

- Lifetime panic disorder - Chen and Dilsaver (136)
- Higher rates of psychotic symptoms during affective episodes, particularly in women - Yildiz and Sachs (162)
- Alcohol- and substance abuse - Lin (161)
- More suicidal behaviour - Lin (161)

Kennedy et al, however, maintains that studies investigating age at onset of bipolar disorder have yielded inconsistent results. (163)

6.9 Substance Abuse

In the present study the following trends emerged when the matter of substance abuse was reviewed:

- Employment
    - Although the rate of unemployment was high in both cannabis users and alcohol abusers, those that abused cannabis were even more likely to be unemployed. (78% vs. 68%) [p=0.541].
- Financial support
    - Cannabis abusers were less likely to receive a Social Grant compared to those that abused alcohol. (36% vs. 53%) [p=0.274].
- History of suicide attempt
    - Subjects with a history of cannabis abuse were less likely to have a history of suicide attempts compared to those with a history of alcohol abuse (15% vs. 39%) [p=0.083].
- Comorbid anxiety disorder
    - Subjects with a history of cannabis abuse were less likely than those with a history of alcohol abuse to have a comorbid anxiety disorder (26% vs. 56%) [p=0.051]. This could suggest that alcohol abuse may indicate self-medicating for anxiety.

- CGI
    - Those with a history of cannabis abuse were more likely to be rated as “Severely ill” on the CGI. (21% vs. 14%) [p=0.711].

None of the above findings were found to be statistically significant.

One of the most comprehensive papers with regard to bipolar disorder and substance abuse is a paper by Regier et al (164). The Epidemiological Catchment Area Study, a large epidemiological study of the prevalence of psychiatric disorders in five communities in the United States during the 1980s, found that, compared with individuals with other Axis I disorders, individuals with bipolar I disorder, had the highest lifetime rates of alcohol-use disorders (46%) and drug-use disorders (41%).

Kessler et al confirmed this in their study and found that individuals with mania were 8,2 times more likely to have been drug dependent in the previous 12 months and 8,4 times more likely to have lifetime drug dependence compared to the general population. (165) Brown et al reported that the lifetime rate of drug abuse or dependence for patients

with bipolar disorder ranged from 14% to 65% compared with rates of 6% to 12% in the general population. (166)

6.10 Manic Episodes Only vs. Depressive- and Manic Episodes

In Chapter 3, “unipolar mania” was extensively discussed. The literature suggests there is ample evidence that a huge number of patients in Africa diagnosed with bipolar disorder have a ‘manic only’ or ‘unipolar manic’ course of illness. The present study supports the presence of a high rate of a unipolar manic course of illness.

The question that still needs answering, though, is whether this a different course of bipolar (affective) illness we are seeing in Africa or could this be a different illness altogether? With this in mind the researcher decided to compare the two groups in order to ascertain whether any differences appear which could assist in answering the above questions.

In the present study the following differences appeared when comparing the Depressive and manic (DAM) group with the Manic only (MO) group:

- Mean age
    - The mean age of the MO group was 38,18 years vs. the DAM group at 34,66 years.

- Gender
    - There were more males in the MO group (54% vs. 31%), which was statistically significant [p=0.028].
- Marital Status
    - No obvious difference appeared with regard to marital status (22% vs. 25%) [p=0.815].
- Employment
    - The rate of unemployment was slightly less in the MO group (67% vs. 72%) [p=0.667].
- Financial support
    - More patients received a disability grant in the MO group (57% vs. 45%) [p=0.238].
- Family history of mental illness
    - The MO group reported a family history of bipolar mood disorder (54% vs. 61%) [p=0.548], alcohol abuse (47% vs. 52%) [p=0.692] and suicide (15% vs. 18%) [p=0.790] less frequently.
- History of suicide
    - The MO group reported having attempted suicide significantly less than the DAM group (16% vs. 40%, a statistically significant difference [p=0.013].

- History of violence/forensic history
    - The MO group reported a history of violence more often (50% vs. 47%) [p=0.843] but had a lesser chance at having a forensic history (28% vs. 34%) [p=0.668].
- Medical history
    - Only 3% in the MO compared to 15% in the DAM group reported being HIV positive which was statistically significant [p=0.036].
- Age of onset
    - Age of onset did not appear to differ dramatically between the two groups.
- Mood elevation features
    - Some interesting differences with regard to 'mood elevation features' appeared in the sense that the MO group tended to report more psychotic symptoms (delusions: 89% vs. 79%) [p=0.166], (paranoid ideation: 88% vs. 61%) [p=0.002], (hallucinations: 77% vs. 63%) [p=0.126] but less 'increased energy' (16% vs. 31%) [p=0.100].
    - The difference in paranoid ideation was statistically significant [p=0.002].

- Treatment
    - In keeping with the above, it would appear that the MO group tended to be prescribed more anti-psychotics (haloperidol: 54% vs. 43%) [p=0.321], (zuclopenthixol depot: 49% vs. 38%) [p=0.321], (risperidone: 23%vs. 20%) [p=0.812], (clozapine: 10% vs. 11%) [p=1.000] and fewer mood stabilisers (lithium – 18% vs. 25%) [p=0.473], (valproate: 57% vs. 59%) [p=1.000].
    - None of the patients in the MO group were on anti-depressants (0% vs. 11%), a statistically significant difference [p=0.012].
- Substance abuse
    - The MO group tended to abuse substance more than the DAM group both with regard to a history of abuse and current abuse.
    - History of alcohol abuse (42% vs. 36%) [p=0.550], current alcohol abuse (13% vs. 4%) [p=0.183].
    - History of cannabis abuse (25% vs. 9%) was statistically significant [p=0.042],
    - Current cannabis abuse (8% vs. 2%) [p=0.235].

- Comorbidity
    - The appeared to be a significant difference between the two groups in terms of comorbidity with the DAM group twice as likely to have a comorbid anxiety disorder (20% vs. 43%), a statistically significant finding [p=0.017].
- Bipolarity index
    - There appeared to be a trend towards the MO group scoring lower on the Bipolarity Index (“81-100”: 45% vs. 56%) [p=0.321] and (“71-80”: 33% vs. 20%) [p=0.184].
- CGI
    - There was a slight tendency for the MO group to be scored ‘Markedly ill’ (20% vs. 13%) to ‘Severely ill’ (10% vs. 6%), compared with the DAM group [p=0.058].

Statistically significant differences in the present study in summary are:

- The Depressive and Manic (DAM) group were more likely to:
    - Have a history of attempted suicide
    - Be HIV positive
    - Be prescribed antidepressants
    - Have a comorbid anxiety disorder

- The Manic Only (MO) group were more likely to:
    - Be males
    - Have more psychotic features; in particular paranoid ideation
    - Have a history of cannabis abuse

Research from the non-Western world and in particular Africa seems to indicate that a manic only course in bipolar mood disorder is more prevalent than previously believed. (80) (85) (94) Bipolar disorder also possibly expresses itself differently in different ethnic races. It would appear from studies of bipolar disorder in African, African-Caribbean and African-American patients in both the UK and the USA that they are less likely than white patients to experience depressive episodes before the onset of first mania, experience more severe psychotic symptoms at first mania (167), and are more likely to be misdiagnosed as having schizophrenia. (168)

A number of studies have found that there seems to be an increased rate of psychosis among African-Caribbean people living in the UK (169) (170) as well as an increased rate of mania. Leff et al reported that the African-Caribbean population more often displayed mixed manic and schizophrenic symptoms. (171) In fact, Van Os et al calculated that the rate for mania among African-Caribbean people in Camberwell, south

London, was approximately three times that of the white group in their study. (172)

Kirov and Murray found that, among patients diagnosed as Bipolar I attending a Lithium Clinic in South London, African patients were significantly more likely than whites to show exclusively or mainly manic presentations (64,3% as compared to 28,3% in the white British group in their study). They conclude that “there may be genuine differences between ethnic groups in the form of presentation of bipolar disorder”. (173)

Kennedy et al, in their study of first episode psychosis and mania in Camberwell, London, found that the African-Caribbean and African groups were significantly less likely to have had a previous depressive episode before the onset of mania, were more likely to present with psychotic symptomatology and had a more severe clinical presentation at first mania. (167)

In contrast, Caucasian subjects in studies conducted in Europe and the USA seemed to spend far more time with depressive symptoms than with mania over the course of their illness as shown by Angst (174) and Judd et al. (175) Kennedy et al rightfully insist therefore that ethnic

differences in clinical presentation of affective disorders are clinically important as such differences may lead to misdiagnosis that could have obvious treatment implications. (167)

Lloyd et al found in the AESOP (Aetiology and Ethnicity of Schizophrenia and Other Psychoses) study in the UK, a multi-centre population-based incidence and case-control study of first-episode psychosis, that the incidence of bipolar disorder was higher among black and minority ethnic groups than in the white population. (176) Dean et al in the same study concluded that African-Caribbean ethnicity was independently associated with aggression and that aggression was associated with a diagnosis of mania. (177)

Bearing in mind the findings of this current study and considering the evidence from the literature as referred to in this chapter, there appears to be no doubt that bipolar disorder presents differently in patients of African descent.

Chapter 7
Conclusion

The limitations of this study need to be recognised before the implications of the findings are discussed. Language was probably the biggest obstacle in conducting this study and the fact that interpreters had to be used. The difficulties associated with explaining some concepts - particularly eliciting a history of depressive episodes - were also certainly a limitation. As alluded to elsewhere, eliciting depression may be particularly challenging in South Africa. (128) (129)

However, the way the ADE (99) is designed and the type of questions asked makes it improbable that depressive episodes were missed. The ADE appears to be a dependable instrument for eliciting a history of bipolar disorder including eliciting a history of depressive episodes.

A much more important limitation would be recall bias. The reasons Negash et al (2005) (94) considered explaining the high rate of non-reporting of depressive episodes deserves consideration in the present study as well, in that recall bias might lead to under reporting milder episodes of depression. Depressive symptoms may also be seen as part of normal life rather than as a psychiatric disorder.

Another limitation may be the fact that the methodology could be criticised as this was a purposeful sample with the majority of patients being recruited while hospitalised and all patients being interviewed only once. This precludes generalisation of the findings. In future a prospective study with a control group may be considered as the cross-sectional nature of the study, without a prospective component, makes it impossible to accurately evaluate and predict the course and outcome of the illness.

In consideration of the findings of the present study, one cannot help but being struck again by the debilitating nature of bipolar disorder. And in spite of a quarter of the study subjects having a tertiary education, more than two-thirds were unemployed. Yet only half of them were receiving a disability grant. The majority of the study subjects were not married (70%).

Twenty-seven per cent of subjects had attempted suicide at some point, half the patients interviewed had a history of violent behaviour, and a third had a forensic history. Forty per cent had a history of alcohol abuse and 18% of cannabis abuse. All these factors point to the serious risks associated with this illness, not to mention the challenges faced by the carers of these patients. Primary health care doctors need to be

educated with regard to the debilitating nature of this illness and the perception that bipolar disorder patients do not qualify for disability grants should be changed.

The role of traditional healers is another area that needs to be considered and we need to ask ourselves the question whether we should not attempt to collaborate more with them, considering that two-thirds of this study sample had consulted with faith- or traditional healers. As they clearly provide a service to our mental health care users, we should seriously consider collaborating with traditional healers on certain issues and this is an area ripe for exploring through research.

Most of the subjects in this study appeared to receive a combination of a mood-stabilising agent (70% being on valproate) and an anti-psychotic (50% receiving haloperidol and 35% depot zuclopenthixol). Forty-two percent were receiving orphenadrine. Further research exploring different treatment approaches in bipolar patients in South Africa certainly merits future research to answer the question as to what the appropriate approach would be and whether there is a place for monotherapy using second-generation anti-psychotics.

Significant gender differences also appeared from this study in that females were more likely to suffer from comorbid anxiety disorders, to have a history of sexual trauma, and be HIV positive whilst men were more likely to have a forensic- and substance-abuse history, experience hallucinations and receive clozapine. It would appear, therefore, that the expression of bipolar disorder is certainly different in the two sexes and this may have treatment implications.

Women's health issues in bipolar disorder needs specific attention, considering the possible effects psychotropic drug use can have on women's menstrual pattern and the dangers related to falling pregnant while taking these drugs. Twenty-six per cent of females in this sample reported irregular menses and only 29% stopped taking their psychotropic medication when they fell pregnant.

Although findings with regard to miscarriages need to be carefully interpreted as the drugs the females in this sample were taking are not necessarily the same they were taking whilst being pregnant, one cannot help but be concerned about the fact that 30% had miscarriages. More troubling is the fact that the majority of them were taking valproate. However, as mentioned, one cannot infer that they were taking valproate at the time of being pregnant but it has been shown that valproate

increases the risk of miscarriage and can also cause developmental delay and cognitive defects in the children of mothers taking valproate whilst pregnant. (178)

The fact that a third of females reported mood symptoms associated with pregnancy and nearly half reported postpartum onset of symptoms indicate the need for careful monitoring of our patients both intra- and postpartum.

Twenty-three percent of this study population had an early age of onset of mania – before the age of 20. Although comparison of the two groups, in terms of onset of illness before age 20 versus after, yielded only one statistically significant difference between the early onset- and late onset groups, a number of differences came to light which might indicate a more severe course of illness.

Fewer members of the EAOO group got married, fewer obtained secondary and tertiary education, this group was more likely to receive lithium and depot zuclopenthixol and significantly more were likely to receive clozapine. The EAOO group had a higher rate of comorbid anxiety disorders and were more likely to be rated “Markedly ill” to “Severely ill” on the CGI.

However, not all the findings were consistent with the literature on the subject, as the EAOO group in this study had lower rates of suicide attempts and were less likely to have a history of substance abuse.

Arguably the most important finding of this current study is the fact that 57% of study subjects had only ever experienced manic episodes. And even after exclusion of those who were not diagnosed with bipolar disorder, the rate only came down to 56%. If one defines a true unipolar manic course in terms of three or more phases without the occurrence of a depressive episode the rate was still 45%, in stark contrast to the rate of 10% to 20% as reported in the literature (2), but in keeping with findings from Africa (85) (94) and other non-Western countries. (27) (88)

Identifying etiologically homogenous subgroups in psychiatry can aid the profession in developing a reliable and valid nosology for psychiatric disorders. The earlier view that bipolar disorder is a chronic illness with alternating phases of depression and mania together with euthymic intervals, has gradually been replaced by an understanding of the heterogeneity of this disease and the need to identify phenotypic markers associated with sub-forms. The “manic only” group as described in this thesis may contribute to the search for an etiologically homogeneous sub-group. As a unique phenotype, a manic only course

of illness in bipolar disorder present an opportunity for genetic research and the search for genetic markers in mental illness.

It would make sense therefore that we need to consider a unipolar manic course as at least a specifier in the DSM as well as ICD, in order to heighten the awareness of such a course of illness in bipolar disorder, with a view to research and in particular genetic research.

If the Kreapelinian dichotomy continues to survive for the time being and we continue to consider the psychotic disorders categorically, one could also postulate that a certain sub-group of patients currently being diagnosed as bipolar disorder in Africa may in fact have a completely different illness. They may in fact suffer from a psychotic-type illness that lies somewhere on the spectrum between what are currently described as bipolar mood disorder and schizoaffective disorder. An appropriate descriptive name for this illness that could be considered would be “Recurrent Manic Psychotic Illness”.

Chapter 8
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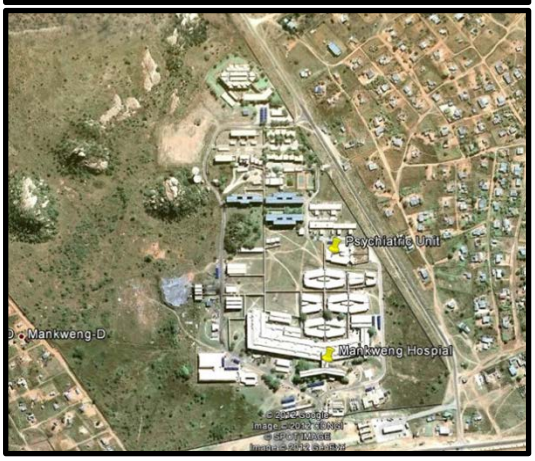
Appendix A

Thesis Photographs

MD Thesis photographs

Mankweng Hospital

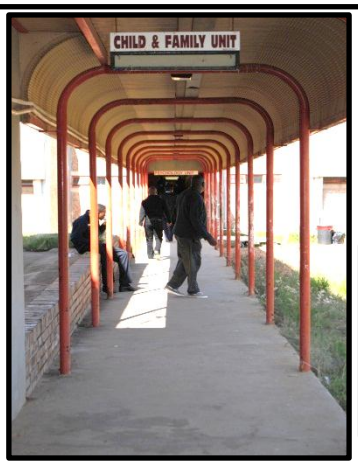


Aerial view of Mankweng Hospital using Google Earth

Mankweng Hospital

Front view of the Administrative Block

Mankweng Psychiatric Unit



The Mankweng Psychiatric Unit, aka "The Child and Family Unit"

Mankweng Hospital

The view from the entrance to the unit

Mankweng Hospital

The MDT at the Unit preparing for a wardround

Mankweng Hospital

More members of the MDT

Mankweng Hospital

The Interview Room

Mankweng Hospital

View from the back of the unit

Mankweng Hospital

The OT and Clinical Psychologist discussing a patient

Mankweng Hospital

The Nurses' Station

Mankweng Hospital

Confusing signage

Mankweng Hospital

The hospital is situated across the road from the University of the Limpopo

Mokopane Hospital

Aerial view using Google Earth

Mokopane Hospital

Entrance to Mokopane hospital

Mokopane Hospital

Some businesses at the entrance

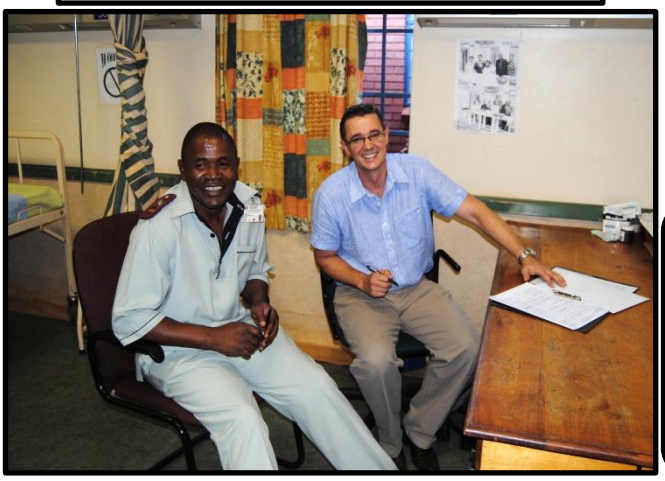
Mokopane Hospital

A Coffee-shop near the entrance to the hospital

Mokopane Hospital

Inside the premises - the gardens are always impeccably kept

Mokopane Hospital



The Interview Room

Mokopane Hospital

A Marula tree outside the Female Medical Ward

Mokopane Hospital

Some marulas in season

Mokopane Hospital

Doing Outreach from Mokopane Hospital ...

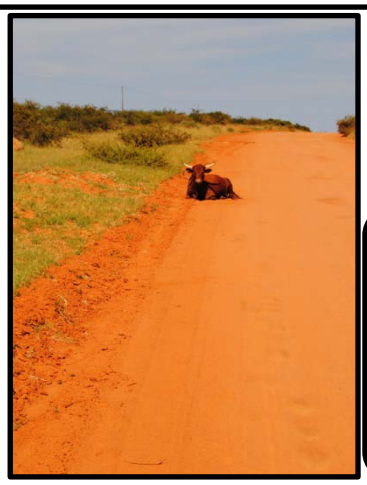
George Masebe Hospital

The road to George Masebe Hospital

George Masebe Hospital

Lovely scenery along the road

George Masebe Hospital



Some obstacles that is sometimes encountered along the way

George Masebe Hospital

And more obstacles to avoid

George Masebe Hospital

A Maize-meal Depot along the way

George Masebe Hospital

A Petrol Filling Station

George Masebe Hospital

Another business selling fuel

George Masebe Hospital

A local shopping centre

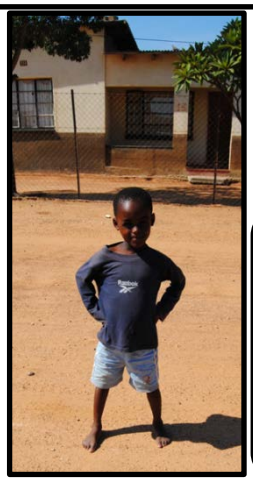
George Masebe Hospital

For low self esteem, may I recommend ...

George Masebe Hospital

Locals have to carry water to their houses

George Masebe Hospital



This dapper young man just begged to have his photograph taken

George Masebe Hospital

An example of an outside toilet

George Masebe Hospital

A rural household, growing their own mielies and sun flower

George Masebe Hospital

My son and I. My wife took the photographs

George Masebe Hospital

Another 27 kilometers to go

George Masebe Hospital

Aerial view using Google Earth

George Masebe hospital

Welcome to George Masebe Hospital

George Masebe Hospital

Entrance to the hospital

George Masebe Hospital

The outside of the ward

George Masebe Hospital

Dual function office

George Masebe Hospital

The Interview Room

George Masebe Hospital

The bravest and most dedicated CPN ever!

George Masebe Hospital

The Nurses' Station in Male Medical Ward

George Masebe Hospital

Mentally ill patients are admitted in the Medical wards

Appendix B

Affective Disorder Evaluation

AFFECT … N (ADE)

Name _____ Date ___ / ___ / _____

D.O.B. ___ / ___ / _____ Age ___ Marital status / domestic partner _____ Referred by: _____

History of present illness:

Current Medications

Indicate medications, daily doses (in mg), and how long patient has been taking each medication (in months).

(01) Lithium _____ mg ____ mo	(05) _____ _____ mg ____ mo	(09) _____ _____ mg ____ mo
(02) Valproate _____ mg ____ mo	(06) _____ _____ mg ____ mo	(10) _____ _____ mg ____ mo
(03) _____ _____ mg ____ mo	(07) _____ _____ mg ____ mo	(11) _____ _____ mg ____ mo
(04) _____ _____ mg ____ mo	(08) _____ _____ mg ____ mo	(12) _____ _____ mg ____ mo

Over the past two (2) weeks, how many days have you been/had…

	Last 2 weeks # of days	Severity (Rate 0-4)	~ % days past year…
… depressed **most of the day**	(13) _____	(14) ___	(15) ~ _____ %
… less interest in **most** activities or found **couldn't enjoy even pleasurable activities most of the day**	(16) _____	(17) ___	(18) ~ _____ %
… **any** abnormal mood elevation	(19) _____	(20) ___	(21) ~ _____ %
… **any** abnormal irritability	(22) _____	(23) ___	(24) ~ _____ %
… **any** abnormal anxiety	(25) _____	(26) ___	(27) ~ _____ %

Other *Current* (past week) Symptoms (0-4)

(28) _____ PI
(29) _____ IOR
(30) _____ LOA
(31) _____ Hallucinations
(32) _____ Delusions
(33) _____ Binge/Purge
(34) _____ Panic Attacks
(35) _____ OCD
(36) _____ Social Phobia
(37) _____ Gen Anx

Rate Associated Symptoms for the PAST WEEK

MORE +2 ----- 0 ----- -2 LESS
0 = usual/none

MDE: Requires at least 5 moderate symptoms (including depressed mood and/or interest).

Depressed mood	Sleep	Interest	Guilt / SE	Energy	Conc / Distr	Appetite	PMR / PMA	SI
(38) ____	(39) ____	(41) ____	(42) ___ or ___ (43)	(44) ____	(45) ___ or ___ (46)	(47) ____	(48) ___ or ___ (49)	(50) ____

(40) Sleeps ___ - ___ hours ❑ EBT ❑ DFA ❑ MCA ❑ EMA ❑ DGOOB ❑ Naps ❑ Anhedonia (51) ❑ LNWL ❑ Passive ❑ Active

Elevation: Mania/hypomania requires at least 3 moderate symptoms, unless only irritable, then at least 4 moderate symptoms are required. (Do not count elevation or irritability in symptom count.)

Self Esteem	Need for sleep	Talking	FOI / Racing thoughts	Distractible	Goal directed activity / PMA	High Risk Behavior
(52) ____	(53) ____	(54) ____	(55) ____	(56) ____	(57) ____ or ____ (58)	(59) ____

(60) Symptoms of **current episode began:** ___ / ___ / _____ ❑ N/A if Current Status = *Recovered*

(61) Immediately **prior to current mood state, mood was:**
❑ euthymic ❑ depressed ❑ elevated ❑ mixed ❑ _____

Prior to onset of current episode…
(62) Well for _____ Months **OR** (63) Time since last episode: _____ Months

(64) In past 2 years, what is the longest period your mood has been consistently normal?
_____ days _____ weeks _____ months

(65) **Dysthymia: Depressed more days than not for > 2 years** (circle one) **Y N**

(66) **Cyclothymia: Many ups and downs for > 2 years** (circle one) **Y N**

(67) Current Clinical Status

(check one)

DSM (+)	DSM (-)
❑ Depression	❑ Continued Sxs
❑ Hypomania	❑ Recovering
❑ Mania	❑ Recovered
❑ Mixed	❑ Roughening

If new episode, estimate onset date:
___ / ___ / _____

ABNOR…IME)

Have you ever had a time…

	No	Probable	Yes		
…when you were feeling so good or so hyper that other people thought you were not your normal self?	❑	❑	❑	If yes, when was that? __ / __ / ____	Age: ___
…or you were so hyper you got into trouble?	❑	❑	❑	If yes, when was that? __ / __ / ____	Age: ___
…did anyone say you were manic?	❑	❑	❑	If yes, when was that? __ / __ / ____	Age: ___
…when you felt like you could do much more than ordinarily capable of?	❑	❑	❑	If yes, when was that? __ / __ / ____	Age: ___
…when you were so irritable that you shouted at people or started fights or arguments? Did you find yourself yelling at people you didn't really know?	❑	❑	❑	If yes, when was that? __ / __ / ____	Age: ___

For the most severe episode identified above, determine:

During that time, were there ***any times*** when your mood was: ❑ euphoric ❑ expansive ❑ irritable ❑ dysphoric

(Was it really too _____, or just better than the times you felt down?)

Were you admitted to the hospital during this time? ❑ hospitalized ❑ not hospitalized

Altogether, how long did this period last? ____ hours ____ days ____ weeks ____ months

Symptoms present to a significant degree during <u>most severe episode</u> identified above

During that time… (Much less) -2—0—+2 (Much more)		
…were you feeling more self-confident than usual or like you were special, more talented, more attractive, or smarter than usual? Were there any times when your thoughts were grandiose?	_____	Self-esteem
…were there nights you got less sleep than usual and found you didn't really miss it?	_____	Need for sleep
…were there any times you were more talkative than usual, or you found you said much more than you intended? Were there any times you spoke faster than usual?	_____	Talking
…did you find that you had more ideas than usual? Were there times when your thoughts seemed to be racing through your head?	_____	FOI/Racing
…did you find you were easily distracted?	_____	Distractible
…did you experience difficulties due to making new plans or getting new projects started? Were you so active that people worried about you taking on so much? Were there times when you were so energized or agitated you couldn't sit still?	____/____	Goal-directed activity/PMA
…did you do **anything** that was unusual for you or that other people might think was excessive, foolish or risky? Did you do anything that would have caused a problem if you were caught?	_____	High-risk behavior

Other features of past episodes of mood elevation ("+" indicates symptom present to a significant degree in any week, "-" indicates absent.)

___ ⇑ Risky pleasure: _____ ___ Extraordinary accomplishment

___ Sudden onset ___ Easily annoyed ___ ⇓ Appetite ___ ⇑ Energy ___ ⇑ Spending

___ ⇑ Libido ___ PI ___ Delusions ___ Hallucinations: _____

Associated stressor: _____

Organic factors:

___ Alcohol abuse ___ Substance abuse

___ Onset <12 wks after ⇑ antidepressant

___ Other: _____

During worst week of episode: Rate: 0 = none, 1 = mild, 2 = moderate, 3 = severe

___ Marital discord ___ Occupational dysfunction ___ Social dysfunction ___ Violence ___ Legal problems

(68) **Mania? Y N** (69) If no, **Hypomania? Y N** If neither, is mood elevation sufficient for BP NOS? **Y N**

Determine number of (hypo)manic episodes

The time we've been talking about is what we would call (hypo)mania.

Using that time as a guide, how many times have you been like that for as long as 1 wk?

(70) Number of phases (circle one): 0 1 2 3-4 5-9 10-20 20-50 Too many to count Indeterminate

(71) When was the last episode of (hypo)mania?

(Do not consider current episode.) Estimated onset: ___ / ___ / _____ Estimated offset: ___ / ___ / _____

How many times have you felt like that in the past year? Mania: ____ Hypomania: ____ Mixed: ____ (72) **Total:** ____

(If the total is >1): How were you feeling between those times? _____

Earliest episode: When was the first time your mood was like that for a week or more? (73) Age: ____ Date onset: ___ / ___ / _____

	No	Probable	Definite
Has there ever been a period when you were feeling down or depressed most of the day, nearly every day, for as long as two weeks?	❑	❑	❑
What about being a lot less interested in things or unable to enjoy things you usually would enjoy nearly every day for as long as two weeks?	❑	❑	❑

If either is "Definite":

Symptoms present to a significant degree during most severe episode

During that time… (Much less) -2—0—+2 (Much more)		
…did you have a change in sleep pattern?	_____	Sleep (___ - ___ hours)
…were you down on yourself? Did you feel as if you were a bad person or that you deserved to suffer?	____/____	Guilt / Self-esteem
…how was your energy level? Were there things that you should have done and didn't because you didn't have enough energy or were simply too tired?	_____	Energy
…how was your concentration? Were you able to read the newspaper or watch TV? Did you find that you were easily distracted?	____/____	Concentration / Distractibility
…how was your appetite? Did your weight change?	_____	Appetite
…were there times when you were so fidgety or agitated it was hard for you to stay still? What about the opposite, thinking or moving more slowly than usual (or feeling like molasses in January)? If I had been there, would I have noticed that something was wrong?	____/____	PMR / PMA
…were there times when you were feeling so bad that you felt life was not worth living? What about actually thinking about suicide or harming yourself?	_____	SI ❑ LNWL ❑ Passive ❑ Active

Other features of past episodes of depression ("+" indicates symptom present to a significant degree in any week, "-" indicates absent.)

(74) ___ Sudden onset (75) ___ Irritability (76) ___ Anger attacks (77) ___ Leaden paralysis
(78) ___ Worthlessness (79) ___ PI (80) ___ Delusions (81) ___ Hallucinations
Associated stressor: _____

Organic factors:
___ Alcohol abuse
___ Substance abuse
___ Other: _____

Determine number of depressive episodes

The time we've been talking about is what we'd call an episode of depression. Using that time as a guide, how many times have you been like that for as long as 2 weeks?

(82) Number of phases (circle one): 0 1 2 3-4 5-9 10-20 20-50 Too many to count Indeterminate

(83) When was last episode of depression? (Do not consider current episode.) Estimated onset: ___ / ___ / _____ Estimated offset: ___ / ___ / _____

(84) How many times have you felt like that in the past year? ____
(If the total is >1): How were you feeling between those times? _____

Earliest episode: When was the first time your mood was like that for a week or more? (85) Age: ____ Date onset: ___ / ___ / _____

PATTERN OF MOOD SYMPTOMS: ❑ NONE APPARENT USUAL ONSET: _____-_____ USUAL OFFSET _____ -_____

(86) Hx Antidepressant induced (hypo)mania ❑ Yes ❑ No ❑ Unknown/not done
↘ If yes, drug: _____, date: ___ / ___ / _____

(87) Perimenstrual Exacerbation: ❑ Yes ❑ No ❑ Unknown/not done ❑ N/A

Mood Sxs associated with Pregnancy: ❑ Yes ❑ No ❑ N/A

(88) Postpartum ❑ Yes ❑ No ❑ N/A

NUMBER OF PHASES: (SEPARATED BY 4 WEEKS OF EUTHYMIA OR AN EPISODE OF OPPOSITE POLARITY)	NO RELIABLE INFO	0	1	2	3	4	5-12	13-52	≥53
(89) LIFETIME									
(90) PAST 12 MONTHS									
(91) MOST EVER IN 12 MONTHS									

(92) Episode pattern: ❑ DEM ❑ DME ❑ MED ❑ MDE ❑ MDMDMD ❑ Inconsistent ❑ Unclear

IS SEASONAL PATTERN SUSPECTED? ❑ YES ❑ NO ❑ UNKNOWN/NOT DONE
↘ If yes, comment: _____

CYCLOTHYMIA (Optional, determine whether patient has/had current or past cyclothymia)		
Other than the times we talked about when you met criteria for depression…		
…have you ever had a period when you had lots of ups and downs, that is, some days you felt too good or even a little high, and other days you felt down and depressed?	Y	N
(If yes)Were the good days really too good, or just better than the bad days?	Y	N
Did the ups and downs follow any pattern?	Y	N
Was there a period of time like that for as long as two years during which you were never without those ups and downs for as long as two months?	Y	N
During that time, what's the longest period that you felt normal?	____ weeks	
Well interval ___/___ - ___/____		
Note: DSM-IV does not specify the number of symptoms of mood elevation required for cyclothymia. Use script to screen for occult periods of mood elevation.		
During those period when you were high, did you find that you…		
…needed less sleep than usual?	Y	N
…felt particularly full of energy?	Y	N
…felt especially self confident?	Y	N
…get a lot more done than usual?	Y	N
…felt physically restless?	Y	N
…talked more than usual?	Y	N
…had unusually good ideas or think especially clearly?	Y	N
…did things that could have caused trouble for you or your family (e.g., lavish spending sprees, reckless driving)?	Y	N
…laugh or joke about things that other people don't find funny (or think are in poor taste)?	Y	N
Cyclothymia	Y	N

DYSTHYMIA (Optional, or if unclear whether patient has mood disorder)		
Have you ever felt down/depressed more often than not for 1-2 years and were never without those feelings for as long as 2 months?	Y	N
During that time, what was the longest period of time that you felt normal? _____ weeks		
During this period of feeling depressed most of the time…		
…did your appetite change significantly?	Y	N
…did you have trouble sleeping or sleep excessively?	Y	N
…did you feel tired or without energy?	Y	N
…did you lose your self-confidence?	Y	N
…did you have trouble concentrating or making decisions?	Y	N
…did you feel hopeless?	Y	N
Are two or more answers coded yes?	Y	N
Did these symptoms cause significant distress or impair your ability to function at work, socially, or in some other way?	Y	N
Dysthymia	Y	N

SUBSYNDROMAL MOOD ELEVATION (Optional, or if unclear whether patient has bipolar disorder)		
Have you ever had even brief periods when your mood was abnormally high or when you were very easily annoyed?	Y	N
In the past 2 months how many weeks have you had without even one day like that? _____ weeks		

PAST PS[illegible] t packet)

Other Psychiatric History (Use DSM criteria. If [illegible]e "No." If patient clearly meets DSM criteria, indicate "Definite." If patient may meet criteria or meets subthreshold criteria, indicate "Probable.")

	No	Probable	Definite	Comment	Age/ Onset
(93) **Panic**					(94)
(95) **Social Phobia**					(96)
(97) **GAD**					(98)
(99) **OCD**					(100)
(101) **Hypochondriasis**					(102)
(103) **Bulimia**					(104)
(105) **Anorexia Nervosa**					(106)
(107) **Personality disorder**					(108)
(109) **PTSD**					(110)
Abuse/Trauma	**Yes**		**No**		
Sexual					
Physical					
Emotional					
Other extreme trauma					

	Yes	No	???	(Type/Date):	Age/Onset
(111) Suicide attempt					(112)
(113) Violence					(114)
(115) Arrests					(116)
(117) Other Legal Problems					(118)

Psychotic Disorders (review patient packet and mental status exam)	No	Probable	Yes	Age/ Onset
Current or historical delusions				
Current or historical hallucinations				
Current or historical formal thought disorder (disorganized speech, tangentiality, loose associations)				
Current or historical negative sxs (flat affect, amotivation, avolition) in absence of depressed mood				
Current or historical bizarre behavior, catatonia, gross disorganization				
Level of occupational or social functioning significantly below expected or achieved prior to sxs onset				

If one or more psychotic symptom above coded "Definite":	Yes	No
Have any of the above symptoms occurred in the **absence** of severe mood symptoms?		
Have any of the above symptoms occurred in the **absence** of intoxication, medication such as steroids, or neurologic or metabolic illness?		
If mood symptoms have been present, have their total duration been brief relative to the total duration of active and residual symptoms?		
Have any of the above positive symptoms persisted for a significant amount of time during any one month period (less if successfully treated)?		
Has there been continuous signs of disturbance for at least 6 months (less if successfully treated)?		

Select the best DSM-IV diagnosis

Determine Psychotic Disorder Diagnosis		
(119) **Any Psychotic Disorder?** Y N	(120) **If so, earliest age of onset:** _____	
(121) **Check appropriate diagnosis below.**		
❑	**Affective Psychosis**	Psychosis only in association with depressive or manic episodes
❑	**Schizoaffective Disorder**	Psychosis persists significantly beyond (>2 wks) resolution of affective episode
❑	**Schizophrenia**	Duration of Affective illness is much less than duration of psychosis
❑	**Secondary Psychosis**	All psychotic sxs attributable to only secondary substance use or a gen'l medical etiology
❑	**Other** _____	

Use DSM criteria and code: "No," "Probable," or "Definite." If uncertain of criteria, indicate "Probable" and check DSM. If patient is short of criteria, indicate "No."

	No	Probable	Definite	Comment	Age / Onset
(122) ADD/ADHD					(123)
(124) Oppositional/Defiant					(125)
(126) Conduct Disorder					(127)
(128) Learning Disorders					(129)
(130) Overanxious/GAD					(131)
(132) Separation					(133)
(134) Avoidant					(135)
(136) Sleep Walking					(137)
(138) Sleep Talking					(139)
(140) Night Terrors					(141)
(142) Enuresis					(143)
(144) Migraine Headaches					(145)
(146) Other:					(147)

Compared to average classmate/peer: Much worse = **-2 — 0 — +2** = Much better (0 = average)	Best term	Worst term
Academic function:		
	Best year	Worst year
Social function:		

PSYCHOACTIVE SUBSTANCE USE HISTORY

	Current use	Age last use	Age peak use	Hx Abuse?	Age onset	Abuse Treatment
EtOH	(148) ____ dr/d	_____	_____	Y N	(149) __ __	(150) Y N if yes, age: __ __
Caffeine	(151) ____ c/d	_____	_____	Y N	(152) __ __	(153) Y N if yes, age: __ __
Nicotine	(154) ____ p/d	_____	_____	Y N	(155) __ __	(156) Y N if yes, age: __ __
MJ	(157) Y N	_____	_____	Y N	(158) __ __	(159) Y N if yes, age: __ __
Amphtetamine	(160) Y N	_____	_____	Y N	(161) __ __	(162) Y N if yes, age: __ __
Cocaine	(163) Y N	_____	_____	Y N	(164) __ __	(165) Y N if yes, age: __ __
PCP	(166) Y N	_____	_____	Y N	(167) __ __	(168) Y N if yes, age: __ __
LSD	(169) Y N	_____	_____	Y N	(170) __ __	(171) Y N if yes, age: __ __
Opiates	(172) Y N	_____	_____	Y N	(173) __ __	(174) Y N if yes, age: __ __
	Y N	_____	_____	Y N	__ __	Y N if yes, age: __ __
	Y N	_____	_____	Y N	__ __	Y N if yes, age: __ __

How old were you when you were first treated for…	**Age**	**Treatment**
…any psychiatric (emotional, psychological, behavioral) problem? (**Dx**: _____)		
…depression?		
…depression with medication or ECT? (if first tx did not include antidepressant meds or ECT)		
…mood elevation (irritability)?		
…mood elevation (irritability) with medication or ECT? (if first tx did not include antimanic meds or ECT)		

Dates/Age	Diagnosis	Place/Clinician	Treatment/Response

Notes:

Treatment	Date	Wks of tx	Max dose (mg/d)	Response	Affective switch* in 1st 12 weeks (circle one)	Comments / adverse effects
Mood stabilizing agents						
❑ (175) Lithium					Y N ?	
❑ (176) Valproate					Y N ?	
❑ (177) Carbamazepine					Y N ?	
❑ (178) Lamotrigine					Y N ?	
❑ (179) Gabapentin					Y N ?	
❑ (180) Clonazepam					Y N ?	
❑ (181) Omega-3					Y N ?	
❑ (182) Ca blocker					Y N ?	
Antidepressants						
❑ (183) Buproprion					(184) Y N ?	
❑ (185) Mirtazapine					(186) Y N ?	
❑ (187) MAOI					(188) Y N ?	
❑ (189) Citalopram					(190) Y N ?	
❑ (191) Fluoxetine					(192) Y N ?	
❑ (193) Sertraline					(194) Y N ?	
❑ (195) Paroxetine					(196) Y N ?	
❑ (197) Fluvoxamine					(198) Y N ?	
❑ (199) Venlafaxine					(200) Y N ?	
❑ (201) Nefazodone					(202) Y N ?	
❑ (203) Heterocyclic					(204) Y N ?	
❑ (205) ECT Uni Bi					(206) Y N ?	
Stimulants						
					Y N ?	
					Y N ?	
Anxiolytics						
❑ (207) Benzodiazepine					Y N ?	
❑ (208) Buspirone					Y N ?	
❑ (209) Beta blocker					Y N ?	
Antipsychotic						
❑ (210) Risperidone					(211) Y N ?	
❑ (212) Clozapine					(213) Y N ?	
❑ (214) Olanzapine					(215) Y N ?	
❑ (216) Quetiapine					(217) Y N ?	
❑ (218) Ziprasidone					(219) Y N ?	
❑ (220) Haloperidol					(221) Y N ?	
❑ (222) Other					(223) Y N ?	
❑ (224) Other					(225) Y N ?	
Other						
❑ (226) Thyroid					(227) Y N ?	
❑ (228) Light					(229) Y N ?	
❑ (230) Verbal tx					(231) Y N ?	

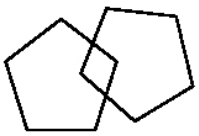
* *Affective switch* is defined as a switch to a new episode of opposite polarity.

Cognitive Screen	Spell	Repeat Items (4)	Subtraction (5)	Date of birth	Oriented (x4)	Memory
	"WORLD" backwards.	Repeat the following: "Detroit, 16, Streetcar, Rainbow"	100-7-7-7-7-7	__ / __ / ____	Person, Place, Day, Date	Recall the last 4 presidents
Errors:	0 1 ≥2	0 1 2 ≥3	0 1 2 ≥3	0 1 2 ≥3	0 1 2 ≥3	0 1 2 ≥3

(232) **Total number of errors:** _____

(233) **MMSE Done?** Y N **(If >1 error, complete MMSE below. If 0 or 1 error, MMSE is optional.)**

The Mini-Mental State Examination[1] (MMSE)

Maximum Score	Score	
		ORIENTATION
5	( )	**What is the (year) (season) (date) (day) (month)?** *One point for each correct response.*
5	( )	**Where are we: (state) (county) (town or city) (hospital) (floor)?** *One point for each correct response.*
		REGISTRATION
3	( )	**Name 3 common objects (e.g., "apple, table, penny").** *One point for each correct reponse.* **Count trials and record. Trials:** _____
		ATTENTION AND CALCULATION
5	( )	**Serial 7's backwards.** *One point for each correct response.* **Stop after 5 answers. Alternatively, spell "WORLD" backwards.**
		RECALL
3	( )	**Ask for the 3 objects repeated above.** *One point for each response.*
		LANGUAGE
2	( )	**Name a pencil and a watch.**
1	( )	**Repeat the following: "No ifs, ands, or buts."**
3	( )	**Follow a 3-stage command: "Take a paper in your right hand, fold it in half, and put it on the floor."** *One point for each part correctly executed.*
1	( )	**Read and obey the following: CLOSE YOUR EYES.**
1	( )	**Write a sentence.**
1	( )	**Copy the following design.** 
Maximum Total 30	**Total Score** _____ (234)	

[1] Folstein et al., *J Psychiatr Res.*, 1975

General	Cooperativeness:			Reliability:		
	Dress:			Grooming:		
Speech ❑ Normal	Rate	Latency	Volume	Detail	Goal directed	Over inclusive
	Major Themes:					
Content ❑ No SI,HI, PI	**Paranoid ideation:**					
	SI: ❑ None evident					
	HI: ❑ None evident					
Psychoses ❑ None	**Hallucinations:** ❑ None evident ❑ Present. If so, describe:					
	Delusions: ❑ None evident ❑ Present. If so, describe:					
Affect ❑ Full and appropriate	Range	Appropriateness	Laughs	Cries	Lability	Irritability

Major Illnesses/Surgeries/Admissions
Childhood: _____
Adulthood: _____
Date of Last Physical Exam: __ / __ / ____ PCP: _____ Phone: _____

Birth History	No	Yes
(235) Full-term uncomplicated vaginal delivery		
Neonatal Jaundice		
Febrile Seizure		
Other Neonatal Insult		

Menstrual History ❑ N/A (Check if male)
(236) Menarche, age: ____
Cycles: ____ days Currently: ❑ Regular ❑ Irregular
Became irregular: __ / __ / ____ Range: ____ - ____ days
Last menstrual period: __ / __ / ____
(237) **Parity**: ___ Conception ___ Miscarriages ___ Abortions ___ Live Births
(238) **Current contraceptive method**: ❑ None ❑ OBC ❑ Barrier ❑ Abstinence ❑ Other ____
❑ Hysterectomy Age ____
❑ Oopharectomy Age ____

Review of Systems

	No	Yes
(239) Allergies		
(240) HT with LOC		
(241) Other LOC		
(242) Seizure		
(243) Migraine		
(244) Multiple Sclerosis		
CVA (Stroke)		
Head		
Neck		
Lymph nodes		
Mouth		
Tongue		
Uvula		

Physical Examination

Vital signs	
(253) Blood pressure: _____ / _____	(254) Pulse: _____
(255) Height: _____ in	(256) Weight: _____ lb.
(257) Handedness: ❑ Left ❑ Right ❑ Ambidextrous	

(258) **Clinically Significant Abnormalities?**
❑ No ❑ Yes ❑ Unclear
If yes, specify clinically significant findings:

		Normal		Comment
		No	Yes	
(245) Peptic Ulcer Disease	**Abdomen**			
(246) Hepatitis	Bowel Sounds			
Irritable Bowel Syndrome				
(247) Asthma	**Thorax**			
Respiratory	Heart			
Cardiac	Breasts			
(248) Eczema	Lungs			
(249) Raynauds	**Skin**			
(250) Stevens Johnson	Frequent Rashes			
Psoriasis				
(251) Diabetes	**Neuro-Endocrine**			
(252) Thyroid	Cranial Nerves			
Lupus				
Traumatic injury	**Extremities/ Joints**			
Rheumatoid Arthritis	Gait			
Osteoarthritis				
Frequent UTI	**Genital/ Urinary**			
STD				
Renal				

If values not known, code: nl = normal Unk = unknown X= never done

Serum Drug Levels:

Date of Last		Results	Dose:	Steady state
__ / __ / ____	Lithium	(259) _____ mMol/L	(260) _____ mg/d	Yes No Unknown
__ / __ / ____	Valproate	(261) _____ µg/ml	(262) _____ mg/d	Yes No Unknown
__ / __ / ____	Carbamazepine	(263) _____ µg/ml	(264) _____ mg/d	Yes No Unknown
__ / __ / ____	(265) Other_____	(266) _____ µg/ml	(267) _____ mg/d	Yes No Unknown
__ / __ / ____	Other_____	_____ µg/ml	_____ mg/d	Yes No Unknown

Chemistry __ / __ / ____	Electrolytes: Na	K	Cl	CO_2	Ca	Creatinine	BUN	Glucose	Albumin	LFT
Hematology __ / __ / ____	WBC		HCT		Plt		MCV		ESR	
Endocrine __ / __ / ____	TSH	T4		FT4		T3		Prolactin		Cortisol
Immunology __ / __ / ____	ANA			HIV				RF		
EKG __ / __ / ____	---									
EEG __ / __ / ____	---									
Imaging __ / __ / ____	CT --- MRI									
Neuropsych __ / __ / ____	---									
Other __ / __ / ____	---									

Notes/comments:

Siblings: ___ F (ages: ___ ___ ___ ___ ___) ___ M (ages: ___ ___ ___ ___ ___)
Children: ___ F (ages: ___ ___ ___ ___ ___) ___ M (ages: ___ ___ ___ ___ ___)

Code: 3= Professionally dx or treated 2= Likely by description 1= Negative ?= No info available	Any Blood relative	Mother	Father	Sister	Brother	Daughter	Son	Maternal GM	Maternal GF	Maternal Aunt	Maternal Uncle	Maternal Cousin	Paternal GM	Paternal GF	Paternal Aunt	Paternal Uncle	Paternal Cousin
Psychiatric hospitalization																	
Bipolar disorder																	
Other Mood Disorder																	
ADD/ADHD																	
Alcohol abuse																	
Substance abuse																	
Schizophrenia																	
Schizoaffective																	
Panic																	
Suicide																	
Suicide Attempt																	
Bulimia																	
Anorexia																	

Social History

Lives is _____ with _____

Occupation _____

Education _____ Military Service _____

Monetary support _____

Involvement in role Rate -2—0—+2
__ Gainful employment __ Student __ Parenting __ Home chores __ Recreation __ Unemployed Impairment ___ % of normal

Notes/comments:

For each of the items below, circle the score next to the c
Characteristics' scores range from 0 (no evidence of bipolar disorder) to 20 (most convincing characteristic of bipolar disorder).

I. Episode Characteristics (268)	
20	▪ Documented acute mania or mixed episode with prominent euphoria, grandiosity, or expansiveness and no significant general medical or known secondary etiology.
15	▪ Clear-cut acute mixed episode or dysphoric or irritable mania with no significant general medical or known secondary etiology.
10	▪ Clear-cut hypomania with no significant general medical or known secondary etiology. ▪ Clear-cut cyclothymia with no significant general medical or known secondary etiology. ▪ Clear-cut mania secondary to antidepressant use.
5	▪ Clear-cut hypomania secondary to antidepressant use. ▪ Episodes with characteristic sxs of hypomania, but sxs, duration, or intensity are subthreshold for hypomania or cyclothymia. ▪ A single MDE with psychotic or atypical features (Atypical is 2 of the following sxs: hypersomnia, hyperphagia, leaden paralysis of limbs) ▪ Any postpartum depression.
2	▪ Any recurrent typical unipolar major depressive disorder. ▪ History of any kind of psychotic disorder (i.e., presence of delusions, hallucinations, ideas of reference, magical thinking).
0	▪ No history of significant mood elevation, recurrent depression, or psychosis.
II. Age of Onset (1st affective episode/syndrome) (269)	
20	▪ 15 to 19 years
15	▪ before age 15 or between 20 and 30
10	▪ 30 to 45 years
5	▪ after age 45
0	▪ No history of affective illness (no episodes, cyclothymia, dysthymia, or BP NOS).
III. Course of Illness / Associated Features (270)	
20	▪ Recurrent, distinct manic episodes separated by periods of full recovery.
15	▪ Recurrent, distinct manic episodes with incomplete inter-episode recovery. ▪ Recurrent, distinct hypomanic episodes with full inter-episode recovery.
10	▪ Comorbid substance abuse. ▪ Psychotic features only during acute mood episodes. ▪ Incarceration or repeated legal offenses related to manic behavior (e.g., shoplifting, reckless driving, bankruptcy).
5	▪ Recurrent unipolar MDD with 3 or more major depressive episodes. ▪ Recurrent, distinct hypomanic episodes without full inter-episode recovery. ▪ Recurrent medication non-compliance. ▪ Comorbid borderline personality disorder, anxiety disorders, or eating disorders, or history of ADHD. ▪ Engagement in risky behaviors that pose a problem for patient, family, or friends. ▪ Behavioral evidence of perimenstrual exacerbation of mood symptoms.
2	▪ Baseline hyperthymic personality (when not manic or depressed. ▪ Marriage 3 or more times (including remarriage to the same individual. ▪ In two or more years,, has started a new job and changed jobs after less than a year. ▪ Has more than two advanced degrees.
0	▪ None of the above.
IV. Response to Treatment (271)	
20	▪ Full recovery within 4 weeks of therapeutic treatment with mood stabilizing medication.
15	▪ Full recovery within 12 weeks of therapeutic treatment with mood stabilizing medication or relapse within 12 weeks of discontinuing tx. ▪ Affective switch to mania (pure or mixed) within 12 weeks of starting a new antidepressant or increasing dose.
10	▪ Worsening dysphoria or mixed symptoms during antidepressant treatment subthreshold for mania. ▪ Partial response to one or two mood stabilizers within 12 weeks of therapeutic treatment. ▪ Antidepressant-induced new or worsening rapid-cycling course.
5	▪ Treatment resistance: lack of response to complete trials of 3 or more antidepressants. ▪ Affective switch to mania or hypomania with antidepressant withdrawal.
2	▪ Immediate near complete response to antidepressant withdrawal.
0	▪ None of the above, or no treatment.
V. Family History (272)	
20	▪ At least one first degree relative with documented bipolar illness.
15	▪ At least one second degree relative with documented bipolar illness. ▪ At least one first degree relative with documented, recurrent unipolar MDD and behavioral evidence suggesting bipolar illness.
10	▪ First degree relative with documented, recurrent unipolar MDD or schizoaffective disorder. ▪ Any relative with documented bipolar illness or recurrent unipolar MDD and behavioral evidence suggesting bipolar illness.
5	▪ First degree relative with documented substance abuse. ▪ And relative with possible bipolar illness.
2	▪ First degree relative with possible recurrent unipolar MDD. ▪ First degree relative with diagnosed related illness: anxiety disorders, eating disorders, ADD/ADHD.
0	▪ None of the above, or no family psychiatric illness.
_____	← **Total score (0 – 100)** (273)

Axis I Mood Disorder Dx: *(Use DSM-IV Codes)*

(274) Current (or most recent) episode: ❑ 296.4_ ❑ 296.5_ ❑ 296.6_ ❑ 296.7 ❑ 296.8_ ❑ 296.2_ ❑ 296.3_ ❑ 295.7_ ❑ Other _____

(275) Lifetime: ❑ BP I ❑ BP II ❑ BP NOS ❑ Unipolar MDD ❑ Schizoaffective BP ❑ Schizoaffective UP ❑ Other _____

(276) Lifetime: ❑ Cyclothymia ❑ Dysthymia ❑ Neither

(277) Other Axis I: _____ _____ _____ _____

(278) Axis II: _____ _____ _____ _____

(279) Axis III: _____ _____ _____ _____

(280) Axis IV (stressors): _____ _____ _____

(281) Axis V (GAF): Current Month = _____ Past Year: Best = _____ Worst = _____

CGI (current month): (282) CGI-BP-Depression = _____ (283) CGI-BP-Elevation = _____ (284) CGI-BP-Overall = _____

GAF Scale (frequently used definitions)

71-80: • No more than slight impairment in functioning, varying degree of every day worry and problems that sometimes get out of hand. Minimal symptoms may or may not be present.

61-70: • Some mild symptoms (e.g., depressed mood and mild insomnia) OR some difficulty in several areas of functioning, but generally functioning pretty well, has some meaningful interpersonal relationships, and most untrained people would not consider him "sick."

51-60: • Moderate symptoms OR generally functioning with some difficulty (e.g., few friends and flat affect, depressed mood and pathological self-doubt, euphoric mood and pressured speech, moderately severe antisocial behavior).

41-50: • Any serious symptomatology or impairment in functioning that most clinicians would think obviously requires treatment or attention (e.g., suicidal preoccupation or gesture, severe OC rituals, frequent anxiety attacks, serious antisocial behavior, compulsive drinking, mild but definite manic syndrome).

31-40: • Major impairment in several areas, such as work, family relationships, judgement, thinking or mood (e.g., depressed woman avoids friend, neglects family, unable to do housework), OR some impairment in reality testing or communication (e.g., speech is sometimes obscure, irrelevant), OR single suicide attempt.

21-30: • Unable to function in almost all areas (e.g., stays in bed all day) OR behavior is considerably influenced by either delusion or hallucinations OR serious impairment in communication (e.g., sometimes incoherent or unresponsive) or judgement (e.g., acts grossly inappropriately)

Recommendations / Plan:

_____

_____

_____

_____

_____

_____

_____

_____

Other Interventions	Offered	Accepted	Comment
Review practical tables for _____			
Baseline laboratory assessment			
Teach Daily Mood Charting			
Collaborative Care video			
Collaborative Care workbook			
Treatment Contract			
Referral to:			
Randomized study entry:			

Follow-up with: _____

Physician's signature: _____ Date: __/__/____

Appendix C

Informed Consent Documents

Sepedi

English

FOROMO YA TUMELO

Nna …… ke dumela go tšea karolo mo go dinyakišišo tša bolwetši bja Bipolar.

Ke kwišiša gore bohlokwa bja dinyakišišo tše ke go hlahloba tshepedišô ya bolwetši le dika tše dingwe go batho ba amilweng ke bolwetši bja Bipolar.

Ke dumela gore letlakala-potšišo le tlatšwe go dipotšišo tše dibotšišwago mabapi le bolwetši bjaka bja Bipolar Mood Disorder.

Ke dumela go fana ka tsedimošo yohle ya go nyakega go kgoniša Dr. Grobler go šala morago tshepedišô ya bolwetši bjaka.

Ke dumelela ba lapa laka go tšea karolo go fana ka lesedi ka bolwetši le go thuša ka maele a leloko lešo.

Ke a kwešiša gore batho ba bang ba tshwenywago ke boletši bjo ba tla kgona go hwetša tsedimošo go maele a tlišwago ke dinyakišišo tše. Le dingaka di tla kgona go phekola seemo sa bolwetši le go booka ka tshwanelo.

Ke kwišiša gore ke tla swanela go bolela ditaba le diphiri tšaka ka botlalo ka kamogelo ya gore ba tla dira tsohle ka maatla go re di se phatlalatšwe.

Ke a kwišiša gore leina laka, botšo bjaka le tše dingwe tše ka lemošang batho gore ke tšere karolo go dinyakišišo di ka se tsebagatšwe dipukung le diphatlalatšwa tsa nyakisiso ye.

Le kwišiša gore kena le kgetho ya gore ke se tsenele dinyakišišo tše ebile nka se bonwe molato goba go hloka hlokomelo go tša maphelo

Ke dumeletswe go botšiša dipotšišo le go hlaloša maikutlo a ka mabapi le dinyakišišo tše.

……	……..
Tshaeno ya Motšeakarolo	Tšatšikwedi
……	……..
Tshaeno ya Monyakišiši	Tšatšikgwedi
……	……..
Hlatse	Tšatšikgwedi

Informed consent form

I …….. hereby agree to participate in this study of bipolar illness.

I understand that the purpose of the study is to examine the course of illness and other clinical characteristics of people suffering from bipolar mood disorder.

I agree that a questionnaire be filled out in which I will be asked a variety of questions related to my illness namely bipolar mood disorder.

I agree to give all information necessary to enable Dr Grobler to effectively plot the course of my illness.

I agree to involve my family members with a view to gaining more information about my illness and also to draw up a family tree.

I understand that other people suffering from bipolar mood disorder might benefit from the information from this study in that it will help doctors to better diagnose the condition and prescribe appropriate treatment.

I understand that I will be expected to share personal information and accept that everything possible will be done to keep my information confidential.

I understand that my name or otherwise identifying information will not be divulged in any dissertations or publications that might arise from this research.

I understand that I am free to choose not to participate in the study without it incurring me any displeasure or disadvantage in any way.

I have been invited and given opportunity to ask any questions and raise any concerns that I might have related to participating in this study.

Signed: …….. **Date: …….**

Dr C Grobler: …… **Date: …….**

Witness: …….. **Date: …….**

Appendix D

Letter from Faculty of Health Sciences Research Ethics Committee, University of Pretoria

100 1908 - 2008

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Health Sciences Research Ethics Committee
Fakulteit Gesondheidswetenskappe Navorsingsetiekkomitee

DATE: 01 / 09 /2009

PROTOCOL NO.	**136/2009**
PROTOCOL TITLE	A cross-sectional descriptive study of clinical features and course of illness in a South African population with bipolar disorder.
INVESTIGATOR	**Principal Investigator:** Dr Christoffel Grobler
SUPERVISOR	Prof. JL Roos
DEPARTMENT	**Dept:** Department of Psychiatry **Phone:** 015 287 5186 **Fax:** 015 296 3836
	E-Mail: dr.stof@mweb.co.za **Cell:** 083 713 5693
STUDY DEGREE	PhD
MEETING DATE	26 August 2009

This **Protocol** and **Informed Consent** Document were considered by the Faculty of Health Sciences Research Ethics Committee, University of Pretoria and approved by a quorum of committee members on 26/08/2009

Members of the Research Ethics Committee:

Prof VOL Karusseit	MBChB; MFGP(SA); MMed(Chir); FCS(SA) - Surgeon
Prof JA Ker	MBChB; MMed(Int); MD – Vice-Dean (ex officio)
Dr NK Likibi	MBBCh – Representing Gauteng Department of Health)
Prof TS Marcus	(female) BSc(LSE), PhD (University of Lodz, Poland) – Social scientist
Dr MP Mathebula	(Female)Deputy CEO: Steve Biko Academic Hospital
Prof A Nienaber	(female) BA(Hons)(Wits); LLB; LLM(UP); PhD; Dipl.Datametrics(UNISA) – Legal advisor
Mrs MC Nzeku	(female) BSc(NUL); MSc(Biochem)(UCL, UK) – Community representative
Snr Sr J Phatoli	(female) BCur(Eet.A); BTec(Oncology Nursing Science) – Nursing representative
Dr L Schoeman	(female) B.Pharm, BA(Hons)(Psych), PhD – Chairperson: Subcommittee for students' research
Y Sikweyiya	MPH; SARETI Fellowship in Research Ethics; SARETI ERCTP; BSc(Health Promotion) Postgraduate Dip (Health Promotion) – Community representative
Dr R Sommers	(female) MBChB; MMed(Int); MPharmMed – **Deputy Chairperson**
Prof TJP Swart	BChD, MSc (Odont), MChD (Oral Path), PGCHE – School of Dentistry representative
Prof C W van Staden	MBChB; MMed (Psych); MD; FCPsych; FTCL; UPLM - **Chairperson**

DR R SOMMERS; MBChB; MMed(Int); MPharmMed.
Deputy Chairperson of the Faculty of Health Sciences Research Ethics Committee, University of Pretoria

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♦ Fax: (012)3541367 / 0866515924 ♦ E-Mail: manda@med.up.ac.za ♦ Web: //www.healthethics-up.co.za ♦

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Appendix E

Letters of Approval from Chief Executive Officers at the Mankweng-, Mokopane- and George Masebe Hospitals

Permission to do the research study at this hospital / clinic and to access the information as requested, is hereby approved.

Title and name of Chief Executive Officer: Dr Khoabane RS

Name of hospital / clinic: Pokwane/Mankweng Hospital Complex

Signature: [signature]

Date: 25/11/09

Permission to do the research study at this hospital / clinic and to access the information as requested, is hereby approved.

Title and name of Chief Executive Officer: DR S.F. NDHAMBI.

Name of hospital / ~~clinic~~: MOKOPANE REGIONAL HOSP.

Signature: .....

Date: 03.12.2009.

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

GEORGE MASEBE HOSPITAL

Ref no: 2/8/4
Enq: Mautjana N.M.
Date: 02/12/2009

Dr. Grobler
Polokwane/Mankweng Complex

REQUEST TO DO RESEARCH AT GEORGE MASEBE HOSPITAL

1. *Receipt of your email with attachments dated 15/11/2009 is acknowledged.*
2. *Permission to do your research study at this hospital and to access information as requested is approved.*
3. *Please rest assured that we will assist in any way possible.*

N.M. MAUTJANA
CHIEF EXECUTIVE OFFICER

Appendix F

Letter from Limpopo Department of Health and Social Development

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH AND SOCIAL DEVELOPMENT

Enquiries: Ramalivhana NJ/Malomane EL

Ref: 4/2/2

4 November, 2009
Dr Christoffel Grobler
Department of Psychiatry
POLOKWANE
0700
South Africa

Dear Dr Christoffel Grobler

"A cross-sectional descriptive study of clinical features and course of illness in a south African population with bipolar disorder"

Permission is hereby granted to Dr Christoffel Grobler to conduct a study as mentioned above in Limpopo Province, South Africa

- The Department of Health and Social Development will expect a copy of the completed research for its own resource centre after completion of the study.
- The researcher is expected to avoid disrupting services in the course of his study
- The research results must be used only for the purpose of the study
- The Researcher/s should be prepared to assist in interpretation and implementation of the recommendations where possible
- The Institution management where the study is being conducted should be made aware of this,
- A copy of the permission letter can be forwarded to Management of the Institutions concerned

HEAD OF DEPARTMENT
HEALTH AND SOCIAL DEVELOPMENT
LIMPOPO PROVINCE

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18 College Str., Polokwane 0700 • Tel: 015 293 6000 • Fax: 015 293 6211 • Website: http/www.limpopo.gov.za

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