Studies on Affective Disorders in Rural Ethiopia

Abebaw Fekadu
To Tamirat Fekadu, the kindest person I have ever known
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Abstract

Background
Affective disorders are poorly defined and studied in sub-Saharan Africa despite their substantial public health impact.

Objectives
Overall objective
To describe the epidemiology of selected affective disorders in rural Ethiopia.

Specific objectives
1. To describe the validity and utility of the concept of minor depressive disorder (mD).
2. To describe the manifestation, prevalence and the short-term clinical and functional course and outcome of bipolar disorder.

Subjects and methods
Population
Zay community residents (age ≥16), and residents of Butajira (ages 15-49), in Southern Ethiopia.

Study design
Population-based cross-sectional and longitudinal studies

Case identification
For the identification of cases with bipolar disorder, a two stage process was employed. An initial screen used key informants and interview with the Composite International Diagnostic Interview (CIDI) to identify cases with probable bipolar disorder. A second confirmatory diagnostic assessment stage employed the Schedules for Clinical Assessment in Neuropsychiatry (SCAN). For the identification of cases with mD, data from the CIDI was used.

Follow-up
312 cases with bipolar disorder from Butajira were followed up for a mean of 2.5 years (ranging 1-4 years) through monthly clinical assessments and annual symptom and functional ratings.
Results
The CIDI was administered to 1714 adults among the Zay and to 68,378 adults among the Butajira residents. The prevalence of mD among the Zay and Butajira was 20.5% and 2.2% respectively. Up to 80% of cases with mD had used services for their symptoms, while a third to a half of cases had thought about self harm. Up to a sixth of cases had attempted suicide. Age, marital status, education and somatic symptoms were independently associated with mD.

The prevalence of bipolar disorder among the Zay was 1.8%. During a 2.5-year follow-up of 312 cases with bipolar disorder from Butajira, 65.9% relapsed (47.8% manic, 44.3% depressive and 7.7% mixed episodes) while 31.1% experienced persistent illness. Female gender predicted depressive relapse whereas male gender predicted manic relapse. Only being on psychotropic medication predicted remission (OR=3.42; 95% CI=1.82, 6.45). Disability was much worse among bipolar patients than in the general population and was predicted by symptom severity.

Conclusions
This is the largest study on mD and bipolar disorder in Africa. mD appears to have potential clinical utility in this setting given its association with service use and risk. The identified risk factors for mD also suggest potential aetiological continuity with major depression. The relatively high prevalence of bipolar disorder among the Zay may be related to genetic predisposition perhaps mediated through a founder effect, but other factors need exploring. In relation to the outcome of bipolar disorder, this study indicates that, contrary to previous assumptions, the course of bipolar disorder is characterised by both manic and depressive relapses in a relatively proportionate fashion. Bipolar disorder also leads to significant levels of disability. This is the only prospective outcome study of bipolar disorder in Africa where cases were monitored systematically at short assessment intervals. Therefore, findings are likely to be more robust than previous reports.

Key words
bipolar disorder, depressive disorder, affective disorder, mood disorder, prevalence, outcome, cross-sectional study, prospective study, longitudinal study, isolated population, Ethiopia, Africa, developing countries
List of publications

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals.


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<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
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<td>APA</td>
<td>American Psychiatric Association</td>
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<td>BDI</td>
<td>Beck Depressive Inventory</td>
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<td>CEE</td>
<td>Central and Eastern Europe</td>
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<td>CIDI</td>
<td>Composite International Diagnostic Interview</td>
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<tr>
<td>CIS</td>
<td>Commonwealth of Independent States</td>
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<td>DHSCCL</td>
<td>Depression Section of the Hopkins Symptom Checklist</td>
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<td>DIS</td>
<td>Diagnostic Interview Schedule</td>
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<td>DSM</td>
<td>Diagnostic and Statistical Manual of Mental Disorders</td>
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<td>DZ</td>
<td>Dizygotic</td>
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<td>FDRE</td>
<td>Federal Democratic Republic of Ethiopia</td>
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<td>GBD</td>
<td>Global Burden of Disease</td>
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<td>GDI</td>
<td>Gender Development Index</td>
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<td>HDI</td>
<td>Human Development Index</td>
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<td>HEW</td>
<td>Health Extension Worker</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<tr>
<td>HSCL</td>
<td>Hopkins Symptom Checklist</td>
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<td>ICD</td>
<td>International Classification of Diseases</td>
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<td>mD</td>
<td>Minor Depressive Disorder</td>
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<td>MDD</td>
<td>Major Depressive Disorder</td>
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<tr>
<td>mhGAP</td>
<td>Mental Health Gap Action Programme</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>MZ</td>
<td>Monozygotic</td>
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<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
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<td>OR</td>
<td>Odds Ratio</td>
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<td>PET</td>
<td>Positron Emission Tomography</td>
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<td>PHQ</td>
<td>Patient Health Questionnaire</td>
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<td>PPP</td>
<td>Purchasing Power Parity</td>
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<td>PSE</td>
<td>Present State Examination</td>
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<tr>
<td>Acronym</td>
<td>Description</td>
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<td>SCAN</td>
<td>Schedules for Clinical Assessment in Neuropsychiatry</td>
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<td>Health Outcomes Study Short Form</td>
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<td>SNNPR</td>
<td>Southern Nations Nationalities and Peoples Region</td>
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<td>SPI</td>
<td>Standardised Psychiatric Interview</td>
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<td>SRQ</td>
<td>Self Reporting Questionnaire</td>
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<td>UN</td>
<td>United Nations</td>
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<td>UNDF</td>
<td>United Nations Development Fund</td>
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<td>UNDP</td>
<td>United Nations Development Programme</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>WHO AIMS</td>
<td>World Health Organization Assessment Instrument for Mental Health Systems</td>
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Foreword

Like most Ethiopians, I was born in a rural village to a farmer family. Being the youngest of nine, I had many advantages that my oldest siblings did not. I was spared the hard toils of the farm and was mainly expected to tend the cattle. It also meant having the support of my older siblings and a chance to spend periods in the towns and cities. But it did not spare me the long, hard walks to and from school or the general hardships of an Ethiopian rural life and the lack of resources. I had a desire to be a medical doctor before starting regular school, probably because one of my older sisters was a nurse. I am only one of the few lucky individuals to realise their dream. Barriers to fulfilling one’s dreams did not stem from just the lack of resources or opportunities. Growing up in North Ethiopia during the military rule, it was easy to be imprisoned, tortured or even killed. Schools were not just places for learning - they were places for intimidation. For the best part of my high school years, rigorous and daily physical exercises were mandatory. Not attending the weekly political indoctrination or biweekly “development” work, lasting several hours, was enough to get one put into prison. When I completed high school at Theodore II Secondary School, my interest and hope to do Medicine had all but evaporated. Thanks to the kind encouragement of a relative who had known the Gondar College of Medical Sciences, I chose to join medical school. I have not regretted this decision except on a few occasions in the early part of my career as a doctor.

I was assigned to work in Eritrea close to the military front. We (myself and a very good Eritrean doctor) were expected to do everything in the general hospital: from treatment of ascariasis and doing simple circumcisions to treating congestive heart failure in children and doing laparotomies and amputations. We had clinics for the army, and our wards expanded constantly with the increase in military engagements. One of the most gratifying aspects of practicing medicine during that period was to see the dramatic effect of some treatments. One such example was quinine. Seeing a patient comatose from cerebral malaria open their eyes for the first time following treatment with quinine was perhaps the most gratifying experience. But the challenges were equally notable. Travelling to Asmara, a 53 kilometre distance, took over five hours because of the numerous checkpoints. There were many soldiers with psychological difficulties that I was not able to help. With limited training to deal with these problems it was easy to dismiss the needs of
these soldiers and attribute their symptoms to fear and malingering. At 21 years of age, I was too young to rely on my own experience to understand the personal difficulties of these soldiers. Spending a sleepless night in the hospital operation room on the night before the EPLF took over the town, listening to heavy artillery and gun shots with limited support and supply for the wounded soldiers and other patients was the most difficult time in the early days of my career.

But these difficult experiences were not the reason I chose to do psychiatry. I had a transient interest to do psychiatry as a medical student. But my initial work at Amanuel Hospital was opportunistic. On my return from Eritrea, there was a vacancy at Amanuel Hospital, into which I was accepted to work. I had initial doubts whether I should do it. But once I settled into the job my experience of working with severely ill patients with psychosis was as gratifying as treating patients with cerebral malaria. The main problem was that there was no postgraduate training in psychiatry in Ethiopia. There was no opportunity to train in the old scheme through which the senior psychiatrists were trained. I had to wait for 10 years before I got the chance to train in the UK. However, this time of waiting was not wasted. I was introduced to the exciting world of research by Professors Atalay Alem and Derege Kebede. Professor Atalay had just completed his PhD from Umeå University and Professor Derege was head of the then Department of Community Health. They were just planning to carry out a large scale population-based study on the prevalence and course of severe mental disorders. I was invited to join them in this endeavour. As an aside to this, I was asked to lead a similar study among the Rift Valley islanders (residents of the Zeway islands and shores) often known as the Zay. I trained in the use of the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) and related instruments at the Nottingham SCAN Training Centre, one of the WHO designated training centres, with my colleague and dear friend Dr Daniel Fekadu.

My UK training was arranged initially by Professor Sir David Goldberg and Professor Robert Howard from the Institute of Psychiatry with the help of Professor Atalay Alem. I was then accepted to join the Cardiff training scheme. This was a fantastic training scheme with excellent trainers. The Associate Medical Director, Dr Delyth Alldrick was my first supervisor and an outstanding person as well as clinician. My MSc supervisor, Professor Michael O'Donovan, and Dr Alldrick have made a lasting impression on me. After completing my membership (residency training) I moved to London to do specialist registrar training (post-
residency training). I was fortunate in more ways than one. I got different outstanding mentors and colleagues (Professor Martin Prince, Dr Anthony J Cleare, Professor Peter McGuffin) and most importantly met my future wife (Dr Charlotte Hanlon).

While in London, I got the opportunity to do a PhD in Umeå University. The university has a track record of training Ethiopians. Key to the success of the training are Professors Lars Jacobsson and Gunnar Kullgren, who are outstanding supervisors and understand the need of Ethiopian trainees. Professor Atalay Alem, a protégée of these trainers, has been a key catalyst in the expansion of academic and clinical training in Ethiopia. He played an important part in my registration on the PhD programme.

I have been back in Ethiopia working at the Department of Psychiatry, Addis Ababa University, and Amanuel Hospital, for the last one year. As I had waited for 10 years to go abroad to do psychiatry training, I had to wait for 10 years before returning to Ethiopia. I forfeited some modest opportunities from the early stages of my training because of my decision to return. I have no regrets. Things have changed for the better for psychiatry in Ethiopia. The challenges don’t seem so insurmountable. Now we can think of future days when patients can receive treatment nearer their homes. There is commitment for this from different governmental and non-governmental bodies. We can now envisage that most (not just 0.5%) patients with severe mental disorders will have access to effective treatment. There is nothing better than being part of this.
General introduction

This thesis presents results of a research work on affective disorders conducted in Ethiopia between 1998 and 2006. The first impetus for the studies came from a collaborative undertaking between Addis Ababa University and Umea University in the mid-1990s. Initially the level of mental distress was assessed in over 10,000 adult participants in selected communities in Butajira (Alem et al 1999). Shortly after this survey, the two studies that formed the basis for this thesis were conducted. The first, the Butajira study on the course and outcome of schizophrenia, bipolar disorder and major depression was initiated in 1998 following an extensive preparation in the preceding two years. There were three main research questions: What is the prevalence of severe mental disorders in a traditional rural community in Ethiopia? Given some of the uncertainties surrounding the WHO study on the outcome of schizophrenia, what would the course of these disorders be in this rural setting with low exposure to modern treatment? What are the determinants of the prevalence and outcome of these disorders? When the vast data collection effort over the 3 major districts of Butajira ended in 2001, nearly 70,000 adults were assessed using the Composite International Diagnostic Interview, version 2.1 (CIDI) (WHO, 1997). Although the prevalence of both schizophrenia and bipolar disorder in this study turned out to be similar with that of reports elsewhere, the distribution of schizophrenia was highly unusual in that most cases were male (in a 5:1 ratio). The outcome of schizophrenia was also less favourable (Kebede et al 2005; Alem et al 2009) than reported elsewhere in developing countries (Sartorius 1977; Jablensky et al 1992; Leff et al 1992; Hopper et al 2000; Hopper et al 2007; WHO 1979). Although these findings from the Butajira cohort may require further investigation, they were striking.

Almost at the same time as the preparation for the Butajira study was under way, there was observation of some admissions to Amanuel psychiatric hospital in Addis Ababa from the Zeway islands. The residents of these islands (the Zay population or simply called the Zay) are social isolates, who were believed to have migrated from the Northern parts of the country several centuries earlier. This unusual background led to curiosity, and desire to learn about the distribution of mental disorders in this population. In addition to assessing the distribution of mental disorders among the Zay, the interest was also in exploring aetiological clues to mental disorders, for example, by investigating if there was any differential prevalence of illness
between those living on the islands and those living on the shores. The subsequent finding was unexpected and of some interest. All those identified with severe mental disorders almost exclusively had bipolar disorder. As the lead investigator of the study, the candidate developed interest in affective disorders. Thus the focus of this thesis on affective disorders is not entirely coincidental. Part of the thesis comes from the studies on affective disorders among this isolated population.

At the time of the initial survey and for some years after, there were only nine psychiatrists and only one psychiatric hospital in the country. Many had questioned the wisdom of conducting large scale studies in Ethiopia as they saw the research efforts as distraction from what they believed should be the focus of clinicians - treating patients. The first part of the introduction deals with this question. However, there are other important facts not discussed in that section and deserve mention.

The research programmes have had significant impact on service development in Ethiopia and had contributed to the development of a successful postgraduate training programme. In all the places where a research programme was implemented, required treatments, including treatments for acute medical conditions, were provided free of charge. The research programme has also lead to the establishment of permanent psychiatric clinics, by providing training and supervision of psychiatry nurses and medications in collaboration with the regional health bureau. The Butajira research programme offers a model outreach service to patients with severe mental disorders that has not been replicated anywhere in the country. Plans for modelling other service programmes are being considered. Many of the researchers who participated in the research programme have eventually become trainers in the university psychiatry residency programme. One of the main attractions of training in mental health is also the Butajira research project, which they visit at the end of their attachment. In addition to these welcome consequences, other practical and theoretical considerations have played a role in the decision to undertake the researches.

1) Understanding the magnitude of mental disorders by running well designed studies is crucial for better service advocacy. This is particularly important to assist in rationally distributing the scarce resources. The research programme has already led to important international links and also had local policy implications.
2) Understanding the risk factors for mental disorders is important in planning curative and preventative interventions. Given that socio-economic challenges and the rapid social changes are important risk factors, it is relevant to assess how these risks change and how they impact on mental health.

3) As was found to be the case, most patients are treatment naïve. This meant that studies were conducted in a more or less naturalistic condition. Although unfortunate, it is important to explore the implications of this as many studies in the Western world are based on patients who have received treatment.

4) It should also not be assumed that aetiological factors for mental disorders are uniform across the world. This is further discussed in the introduction. At this stage, it is sufficient to say that it is crucial to understand these factors to understand the nature of mental disorders as well as provide appropriate care.

5) ‘Translational’ studies are not optional. Ethiopia cannot rely on international research products as the application of these products in the Ethiopian context will be unique.

6) Finally, it is important that Ethiopian scientists take their responsibility seriously and make scientific contributions to the international community. They should not just be users of research.

The rationale for the studies on affective disorders forming the basis of this thesis should be seen in the above context. Having established this, it will now be attempted to present the main contents of the thesis.

The thesis starts by providing brief background to Ethiopia. This part is genuinely brief and is aimed at providing a background as it relates to affective disorders. To help understand findings and implications in context, a more detailed background on the history of affective disorders and researches from Africa are presented. Prevalence and outcome studies are also discussed. As cultural reflection is crucial, particularly in relation to depressive disorders, a cursory discussion to some of the key cultural issues is provided. This will also help readers understand that the issue was not taken lightly and will clarify some of the potential limitations and benefits of the studies.
The five reports that form the main content of the thesis are the following:

1) Two studies on the validation of the concept of minor depression in Ethiopia; one coming from the Zay data; the second coming from the Butajira data. The findings are complementary for the most part.

2) One study on the prevalence of bipolar disorder among the Zay.

3) One study on the short-term clinical outcome of bipolar disorder.

4) One study on the functional outcome of bipolar disorder with additional content on symptomatic outcome. This comes from the Butajira study.

The discourse on methods will focus on detailed description of the Zay setting. As Butajira has been described in various reports, there will only be limited details on Butajira. Details on case identification procedures and statistical procedures will be presented. A brief description of results will lead on to the discussion of the meaning and implication of the findings. All the reports forming the basis of the thesis have been published and are appended at the end.

**Background to Ethiopia**

Ethiopia (Figure 1) is the second largest in geographical terms and the second most populous country in sub-Saharan Africa. The country lies between 3° and 15° north of the equator. With a surface area of about 1.1 million square kilometres, it is the size of France and Spain combined (Pankhurst 2001). Its diverse geography is habitat to numerous bird and animal life that is endemic to Ethiopia. As with many African countries, Ethiopia is culturally diverse and home to a large number of ethnic populations: over 80 linguistic groups live in Ethiopia. Ethiopia is also one of the oldest nation states in the world, and in Africa, with ancient civilisation predating that of many European countries. Ethiopia is also one of the very few countries in Africa that managed to maintain its independence during the colonial period.
Although the recent past of Ethiopia has been promising, the country has experienced, and continues to have, severe challenges over the centuries. A largely agrarian society living in the rural countryside, the reliance on natural resources and reliable seasonal patterns has made Ethiopia victim to natural disasters, mainly successive draughts and famine. Its overstretched governments with mixed intentions have also exposed the nation to numerous wars and man-made disasters. Thus, the country remains one of the least developed countries in the world and in Africa. Low healthy life-expectancy (50 years), high child (109/1000 live births) and maternal mortality (673/100 000 live births) remain major challenges. Health resources are focused on treating infectious diseases, which contribute to the majority of the mortality. Even though mental disorders have been estimated to constitute 12% of the total burden of disease in Ethiopia when disability is taken into account as well as excess mortality (Abdulahi et al 2001), mental health services receives a mere 1.7% of the health budget. Furthermore,

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1 Data available at http://www.who.int/gho/countries/eth.pdf
money for mental health is almost exclusively allocated to the hospital service located in Addis Ababa (WHO and Ministry of Health 2006).²

The main index for measuring the level of a country’s development is the Human Development Index (HDI). The HDI looks beyond Gross Domestic Product (GDP) and defines wellbeing according to three broader dimensions: life expectancy, considered in terms of duration of healthy life lived; being educated, measured in terms of gross enrolment in education and adult literacy; and by having a decent standard of living, measured in terms of purchasing power parity, PPP, income).³ With 54.7 years of life expectancy; 35.9% of adult literacy rate and 779 PPP, Ethiopia has a HDI score of 0.414. This is well below the HDI of developed countries such as Sweden (0.963) and the UK (0.947) as well as the average score for sub-Saharan Africa (Figure 2). According to the Human Development Reports (HDR) of 2009, Ethiopia ranks 171st of 182 countries. The comparison of the development level of Ethiopia with sub-Saharan Africa and other country groups is shown in Figure 2.

![Figure 2. Comparison of the Human Development Index of Ethiopia with different countries and regions.](http://example.com/image.png)

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² Available at: http://www.who.int/mental_health/evidence/ethiopia_who_aims_report.pdf
³ Source: http://hdrstats.undp.org/en/countries/country_fact_sheets/cty_fs_ETH.html
⁴ Source: UNDP Human Development Report 2009
To demonstrate this further, Figure 3 compares the HDI of Ethiopia with its neighbouring East African countries - Eritrea, Kenya and Sudan as well as two high income countries (Sweden and United Kingdom). As can be shown, despite faster growth in the past 10 years (shown in Figure 2), the HDI of Ethiopia is lower than each of these countries. Data uses the 2009 HDR\(^5\).

The figure also shows the Gender-related Development Index (GDI), a summary index representing the gender disadvantage of women. This index is essentially based on the HDI variables and cannot be larger than the HDI. Therefore the figure is somewhat a misrepresentation. A better representation would be comparing the GDI value (0.403) to the HDI value (0.414). Thus the GDI value is 97.3% of its HDI value. With this figure, Ethiopia is only equal with Sudan.

\[\text{Figure 3. Figure comparing the Gender-related Development Index (GDI) and the Human Development Index (HDI) of Ethiopia with its neighbours and two high income countries (Sweden & United Kingdom).}\]

\(^5\) Available at: http://hdr.undp.org/en/countries/
A third index, the Human Poverty Index (HPI) measures the proportion of people living under a certain threshold in the three dimensions assessing HDI. The HPI value for Ethiopia is 50.9% and with this index Ethiopia ranks 130th of 135 countries with this index. All the three indices (HDI, GDI and HPI) represent the low base Ethiopia is starting from and the steep effort that will be required to overcome this disadvantage.

**Implication of the country-context for affective disorders**

The preceding summary clearly shows the enormous challenges that Ethiopia faces. These challenges have not been noticeably mitigated by the efforts of the past few years. In terms of mental health, particularly affective disorders, this has very important implications.

1) Socio-economic problem as a source of mental/emotional distress. There is extensive literature showing the link between deprivation or poverty and mental disorders, particularly depression and other common mental disorders (Examples: Lund et al 2010; Patel et al 1999; Patel and Kleinman 2003; Saraceno et al 1997; Saraceno et al 2005). The interaction between poverty and mental disorders is complex and the precise mechanisms remain undetermined. Figure 4 attempts to model this complex interaction. For Ethiopia, it is not just the multiple deprivation that is a risk factor for mental disorders. Additional factors are highlighted below.

2) The steep effort required to change the current socio-economic difficulties is likely to lead to disruption of the existing social fabric. This could be an important risk factor for affective disorder. Change may be positive but tolerability of change depends on different factors: for example, desire for the change, resources to deal with the change and consequences of the change. Those with limited resource to deal with these changes are likely to be affected the most.

3) Resources to meet the mental health needs: mental health is often not a priority area in most countries. This is particularly the case in restructuring countries like Ethiopia. The total health budget for a population of 77 million people was under half a billion dollars in 2006, of which only 1.7% was allocated to mental health (WHO and Ministry of Health 2006).

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6 Available at: [http://www.who.int/mental_health/evidence/ethiopia_who_aims_report.pdf](http://www.who.int/mental_health/evidence/ethiopia_who_aims_report.pdf)
Figure 4. A model showing a complex interaction of poverty (equated with multiple deprivation) at the individual level. For the most part this is supported by evidence from both low income and high-income settings. Arabic numerals here represent references supporting the link between poverty and depression as an example. References list is given in Appendix A.

These factors are more important for onset and maintenance of affective and anxiety disorders than other psychiatric disorders. Affective and anxiety disorders are generally more prevalent and are more likely to be triggered by social disruptions and economic distress. At the structural level, resources are generally focused on psychotic disorders. This is endorsed in standard recommendations (e.g., Chisholm et al 2007; Giel and Harding 1976; WHO 2008). Again in Ethiopia, 98% of the budget on mental health is spent on the centralised institution, Amanuel Hospital (WHO and Ministry of Health 2006)\(^7\), a centre primarily responsible for the care of psychotic disorders.

\(^7\) Available at: http://www.who.int/mental_health/evidence/ethiopia_who_aims_report.pdf
Additionally the focus on psychotic disorders means patients with bipolar disorder are subsumed under the psychosis. It is established that bipolar disorder has different treatment approach compared with the other psychotic disorders like schizophrenia. Therefore the expertise in the care of patients with bipolar disorder and the general care they receive is inferior. Similarly resources and expertise available for the treatment of non-psychotic depression is very limited. However, we know that the burden of disease from the less severe depressive disorders is much more substantial. In this context, it important to highlight the public health relevance of affective disorders and the potential challenges of addressing the public health need. The thesis highlights some of the treatment gap as well as the burden or disability caused by affective disorders.

**Why study affective disorders in Ethiopia**

Affective disorders are important public health problems worldwide. Among the working adult population, depression and bipolar disorder form two of the top ten causes of disability. For the year 2000, depression was estimated to be the leading cause of life lived with disability and the fourth leading cause of the total global disease burden (Üstün et al 2004). Bipolar disorder is also an important contributor to the disease burden (Murray and Lopez 1997). The burden from affective disorders emanates from the high lifetime prevalence of affective disorders (10%-15%), their tendency for recurrence and chronicity, and their association with high disability and premature mortality. The excess mortality results from both natural and unnatural causes: the risk of suicide in both depression and bipolar disorder ranges between 8% and 15% (Bostwick and Pankratz 2000; Brodersen et al 2000; Guze and Robins 1970; Harris and Barraclough 1997; Sharma and Markar 1994). Excess mortality from natural causes such as cardiovascular, respiratory and infectious diseases is well recognised too (Høyer et al 2000; Ösby et al 2001) There is also evidence that less severe or sub-threshold affective conditions are associated with a high burden within the population due to associated morbidity, disability and cost. Because of this, there is interest to expand the definition of what is considered to be a pathological affective state, with unofficial classification systems extending the group to include sub-threshold states with various names (e.g., Akiskal and Pinto 1999; Angst et al 2003).

The public health importance of affective disorders has also been demonstrated in African countries, including Ethiopia. In Ethiopia,
depression is one of the leading causes of disease burden, ranking above some of the major infectious diseases such as HIV (Abdullahi et al 2001). Both major depression and bipolar disorder have been found to be associated with an approximately three-fold increased risk of premature mortality compared with the general population (Fekadu et al 2009; Mogga et al 2006). It is therefore important to assess the broader public health impact of affective disorders by estimating their prevalence and implications for service use, as well as evaluating their course. As questions remain whether these disorders, particularly depression, are the same disorders in low-income settings as described in current classification systems, a section is also dedicated to discussing this issue.

**Affective disorders - general theoretical background**

Defined by the occurrence of pervasive disturbance of mood, affective disorders encompass a large group of contiguous disorders that range from mild depression to the extremes of manic psychosis. Reference to these disorders can be traced throughout the recorded history of mankind, but the modern understanding of these disorders is just over 100 years old.

Ordinary changes in mood as part of normal day-to-day human existence enhance the experience and enjoyment of life. Such affective changes are commensurate with the triggering circumstances and, to a large extent, are under the control of the individual concerned. In affective disorders, however, the sense of control is lost and the affective changes are disproportionate to the circumstances in terms of quality, quantity and duration. According to current nosology, depression and bipolar disorder are the main diagnostic classes subsumed under the affective disorder category.

The term depression is, to some extent, rather loosely applied in the West so that the serious and disabling nature of the disorder is not always fully appreciated. Mania, the core diagnostic feature of bipolar disorder, has also become part of a growing cultural consciousness, and the association with creativity and success has sometimes meant that the depth of disability due to mania is overlooked. In Africa, although depression is increasingly recognised as an important public health problem, the validity of the concept is often challenged and studies in bipolar disorder are rare. The aim of this section is to provide a theoretical framework for understanding affective disorders in Africa and to summarise the clinical and research findings of affective disorders in Africa within the context of current scientific
knowledge. Studies from Ethiopia are subsumed under this. The discussion here will begin by attempting to place affective disorders within culture.

**Culture and affective disorders**

The importance of culture in relation to mental health and disorder is recognised by most researchers and practitioners. The Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV; APA 1994) includes a section on what are termed “culture bound syndromes” which are defined as “recurrent, locality-specific patterns of aberrant behaviour and troubling experience that may or may not be linked to a particular DSM-IV diagnostic category” (APA 1994). The aim of this DSM-IV section is to supplement the multi-axial diagnostic system of DSM-IV and serve the needs of those working in multicultural communities where persons affected by “culture bound syndromes” are likely to belong to minority groups. The application of the term ‘culture- bound syndrome’ in settings where the majority of the population endorses such culture bound states is unclear. For example, eating disorders such as anorexia nervosa, which are probably quite culture bound, are not considered so because they belong to the dominant Western culture and considered to be part of universal, mainstream mental disorder. Despite this important limitation, the inclusion of culture bound syndromes in DSM-IV highlights the need to consider the influence of culture in making a diagnosis of mental disorder.

There are several ways in which a culture may affect affective disorders. Culture can modify the manifestation of affective disorders (*pathoplastic* effect). As will be discussed in subsequent sections, in developing country settings as compared to the West, somatic rather than psychological manifestations are reported to be more common in depression whereas behavioural rather than cognitive manifestations tend to predominate in manic episodes. Culture may also lead to disorders (*pathogenic* effect). For example, khat use is culturally acceptable in some countries, including Ethiopia, and has been associated with mental disorders including affective-like conditions.

In a broader sense, specific cultures have culturally sanctioned states that may relate to, but are not synonymous with, mental disorder. For example, in Ethiopia, people recognise a condition called *woqabi*, which is a possession state that could explain a multitude of somatic and psychological complaints (Hanlon et al 2009). Some people with depression are likely to explain their experience in terms of *woqabi* even though the illness...
General introduction

Attribution woqabi is not specific to depression. A more widely recognised cultural condition, included in the DSM-IV as a culture-bound syndrome, is Zar. Zar is the name of a syndrome as well as its cause. Zar refers to a spirit that possesses someone, usually a woman. The behavioural manifestation of the spirit in the possessed person is also termed Zar. Zar is believed to have originated in Ethiopia and is known to occur in the Sudan, Egypt, Iran, Saudi Arabia and Yemen (Boddy 1988; Torrey 1967). In the study settings in this report, the author’s impression was that Zar was much more common among the Zay than in Butajira.

The possession can occur in episodes, characterised by episodic behavioural manifestations, or as a chronic state with episodic intense influences by the Zar spirit. The impact on the possessed individual can be negative, for example, leading to chronic ill-health. However, for others the effect of Zar possession can be positive, providing the person with power to tell fortunes and perform healing of others, usually persons with ill health or other misfortunes related to malevolent spirits including the Zar spirits. The acute behavioural disturbances usually occur around public holidays such as the Ethiopian New Year or Meskel (the date of the finding of the True Cross according to the Ethiopian Orthodox Church). The person often experiences “dissociative episodes that may include shouting, laughing, hitting the head against a wall, singing, or weeping” (APA 1994). The person often shakes their head violently sideways while making a chanting noise at the same time. The behaviour is fairly stereotypical and preparations are made in advance for the “falling” of the spirit on the person. These episodes are generally brief and are not considered pathological in Ethiopia and the East African countries where Zar is known to occur.

Where effective cultural remedies exist for such culturally accepted conditions, medicalising the experience by mapping onto Western categories of mental disorder may be inappropriate. That said, there is nothing to stop a culture bound syndrome co-occurring with a known psychiatric syndrome in which case biomedical treatments may have a role to play. Finally, culture may also act to protect against onset of mental disorder - in rural Ethiopian women, adherence to traditional perinatal customs was found to protect against onset of postnatal depression (Hanlon et al 2010).

Depression is a prototypical area for consideration of the interaction between culture and mental disorders. Depression is considered a Western cultural concept by some (Jadhav 1996; Summerfield 2008). Leighton and colleagues in their pioneering work among the Yoruba tribes of Nigeria
Abebaw Fekadu (Leighton et al 1963), were struck by the lack of a similar concept to depression among their key informants, although symptoms of anxiety and depression were plentiful. They concluded that in the case of depression they had come across a condition where genuine cultural difference was at play (Leighton et al 1963). In Ethiopia, in a study of 100 key informants, depression was regarded as the least common disorder of seven mental health conditions under consideration (Alem et al 1999). Similarly, in perinatal women from Butajira, although depressive symptoms were recognised and seen as problematic for some women, they were not considered to constitute an illness entity (Hanlon et al 2009).

Some studies have searched systematically for distinguishing features of depression among African patients, with a particular focus on somatic symptoms and their relevance in the diagnosis of depression (Okulate et al 2004; Patel et al 2001a, b). Certain somatic complaints such as tiredness, heartache and sleep problem were also more commonly found among depressed women (Patel et al 2001a, Ebigbo 1986). However, it has not been possible to identify any relevant distinguishing feature for depression in Africa that is of sufficient diagnostic weight. Other studies have also identified locally defined syndromes that may be equivalent to depression in some African cultures (Bolton et al 2001; Patel et al 2001b). Local idioms of distress such as ‘kufungisisa’ (‘thinking too much’) from Zimbabwe (Patel et al 2001a and 2001b) or ‘brain-fag syndrome’ (Prince 1960) were found to have had high concordance with depression (Patel et al 2001a and 2001b).

‘Ode Ori’ is a term for a condition related to a ‘spirit-attack’ and the term literally means “hunter of the head” (Makanjuola 1987). It is a diagnosis given by Yoruban traditional healers for persons predominantly presenting with depression and anxiety symptoms. Individuals with this diagnosis have multiple somatic complaints such as sensation of an organism crawling through the head and other parts of the body, noises in the ears and palpitations (Makanjuola 1987). Although the majority of individuals with Ode Ori had major depression, the range of conditions found was diverse and included schizophrenia, mania, other psychotic disorders and agoraphobia.

A separate question is whether the lack of culturally appropriate terminology for depression as a syndrome, the use of local idioms of distress and the tendency towards somatic rather than emotional presentations might affect the ability of clinicians to detect depression in Africa? This is a possibility. A related barrier to the diagnosis of depression may be the ‘understandability’ of depressed affect in settings where there are seemingly ‘obvious’ reasons
for people to be downcast. It is argued that when such ‘understandable’ reasons exist, the diagnosis of depression only adds to the burden of individuals who already have a lot to deal with (Summerfield 2008). There is some truth in this and clinicians have to be careful not to overdiagnose depression. However, it is equally apparent that not all persons exposed to psychosocial adversity in the African context will develop depressive symptoms, and, where depression is present, the associated disability and suffering may compound a person’s life difficulties. Moreover, some suggest that depression may be more common in Africa precisely because of the ubiquity of these ‘understandable’ reasons (Stein and Gureje 2004). Clearly further studies are required to clarify the interaction between factors such as conflict, poverty, change, migration, loss, physical ill-health and depression in the African setting.

**Cultural validation of depression as an example**

It is to be acknowledged that the level of certainty attached to a diagnosis of depression is not equivalent to certain other medical conditions, for example a diagnosis of malaria. When one makes a diagnosis of malaria, the subjective experiences of the patients are supported by unequivocal external validators or gold standards; for example, a blood film showing a plasmodium parasite or serological assays. The lack of such externally validating criteria makes the diagnosis of depression less secure, even if one is considering severe depression. Diagnostic criteria provided in international classification systems, such as the DSM-IV (APA, 1994) or the Diagnostic Criteria for Research provided in the International Classification of Diseases (WHO 1992) improve diagnostic accuracy and diagnostic agreement (reliability) but do not necessarily improve diagnostic validity. In the absence of firm biological correlates, mental health researchers have relied on alternative methods of validation of their diagnostic concepts.

An important model for the validation of mental disorders was proposed by Guze and Robins taking schizophrenia as a model (Guze and Robins 1970). They described five phases of validation: “clinical description, laboratory study, exclusion of other disorders, follow-up study and family study”. Mental health researchers have employed the last two with some success but laboratory tests are at a preliminary stage. Follow-up studies focus on predictive validity, i.e., prediction of treatment response and illness course (Guze and Robins 1970). Family studies may be considered to provide “convergent validity”, that is, convergence of a known measure tapping into an aspect of depression, such as disability or service use, or, in this case, the
established association of depression with family history (Guze and Robins 1970). Such a broad view of validity has good utility (Kendell and Jablensky 2003) and has been used in some developing countries as part of the measurement of depression (Bolton et al 2002; Fekadu et al 2008; Hanlon et al 2008; Hanlon et al 2008; Mogga et al 2006). Thus, although psychiatric diagnostic entities lack confirmatory biological criteria, most are, “by virtue of information about outcome, treatment response and aetiology that they convey...are...invaluable working concepts for clinicians” (Kendell and Jablensky 2003) and researchers. The lack of biological concomitant for the diagnosis of depression should not therefore invalidate the diagnosis of depression.

The author would like to highlight some further points providing indirect support for the validity of the diagnosis of depression in developing countries.

a) **Historical continuity of disorders:** knowledge regarding the major psychiatric disorders has endured over time and place. What appears to change is not so much the description of the disorder but the attribution and intervention. Syndromes of depression, anxiety, psychotic disorders, “hysteria”, organic brain disorders (for example dementia) were well documented in Africa, Asia and the Middle East even before we find clear documentation from the West (Ndetei and Mburu). This indicates that depressive disorders, although now diagnostically standardised, are conditions that have persisted throughout the documented history of mankind.

b) **Phasic nature of understanding:** Understanding of mental disorders has changed over the years passing through stages. Thus in some developing countries, the current causal attribution is similar to erstwhile attributions in the West (Ndetei and Mburu 2006). Nevertheless, qualitative work from East and Western Africa has identified local terminologies of psychiatric disorders or what one might call “psychiatric diagnostic equivalents”. These cultural equivalents were consistent with what would be considered schizophrenia, mania, depression, anxiety and conversion/dissociative disorders in modern psychiatric nosology (Ndetei and Mburu 2006). Similar concepts are also identified in Latin America (Incayawar 2008). The implication of this is that, although the current understanding of depression in low income countries such as Ethiopia is limited, the level of understanding is likely to change further. The attributions are also likely to change through time.
c) Predictability of human response - The experience of psychiatric disorders are in most instances understandable in the context of response to life events or stress; for example loss events precipitating depression and threatening events precipitating anxiety (Kendler et al 2003; Kendler et al 2006). These are universal experiences with comparable natural paradigms. Some of these responses are mediated by established physiological mechanisms. As accumulating evidence demonstrates, many psychiatric disorders are associated with identifiable neurochemical and anatomical changes (Belmaker and Agam 2008; Freedman 2003; Muller-Oerlinghausen et al 2003; Stein 2002). Thus, despite the possible variations in behavioural expression, underlying changes and mechanisms of mental disorder are likely to be universal. This may indicate the presence of a shared “pathophysiological” or neuroanatomical substrate.

Culture and manifestation of affective disorders

There is general consensus that culture can affect the manifestation of psychiatric disorders. As discussed above, in terms of depression, there is a suggestion that depression in low income countries like Ethiopia manifests with physical symptoms and vague aches and pains. Culture can sanction certain syndromes that are not known in other cultures. For example Zar is a sanctioned cultural syndrome in Ethiopia and East Africa. The degree of influence of culture on the manifestation of different disorders may be tentatively ranked as shown in Figure 5.

![Figure 5](image_url)

**Figure 5.** Impact of culture on the manifestation of some psychiatric disorders - arrow indicating direction of increasing impact.
Culture can affect what causal attributions people form and where they seek treatment. For example, in the United Kingdom, most people would attribute depression to stresses in life and recommend counselling as the treatment of choice (Priest et al 1996). In Ethiopia, depression would not be recognised as a problem. If considered a problem, it is attributed to a loss of equilibrium in the physical, spiritual and social forces (Jacobsson and Merdasa 1991). The preferred form of treatment is spiritual.

However, the influence of culture may become less potent with globalisation, mediated through global media, education, urbanisation and international travel (Bhugra and Mastrogianni 2004). The impact of globalisation and the media may be illustrated from the publications of a local (Ethiopian) newspaper commenting on appetite suppressant drugs. Anorexia nervosa is extremely rare in Ethiopia. It is also uncommon for young women to know about drugs that could be taken to help with weight loss. However, the English edition of The Reporter has this to say for its readers: “Diet pills give you a strong chance of helping you lose weight. That is why they are so easily packagable worldwide because so many people struggle with weight issues and want to change it without doing the work which is normally involved... Before you take diet pills you must acknowledge what the risks are because the false claims companies provide are not enough to fill your mind.”

The potential interaction between depression and globalisation, and related factors that affect the manifestations of depression, is depicted in Figure 6.

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8 Available at: http://en.ethiopianreporter.com/content/view/1466/1/ Accessed on 09/08/2009
Four case examples are provided below to demonstrate some of the subtle influences of culture on the manifestations of both major depressive disorder and bipolar disorder. All of these cases were seen by the author; three among the Zay and one from Addis Ababa.

Case 1: Ms B is a single lady in her mid 30’s living on one of the Zeway shores. She was evaluated by one of the research psychiatrists who believed she had a bipolar disorder but was uncertain whether her presentations related to a manic episode or a Zar possession episode. This lady had a history of recurrent Zar episodes. These episodes usually occurred around the time of the New Year. During these episodes, Ms B becomes flamboyant, dresses colourfully and tells people their fortunes. These episodes tend to last for a day or two. In recent times, the episodes have lasted longer, and her altered behaviour persists even when she was in public places. She has become overtalkative, hyperactive and her fortune telling has also become more pronounced. Her father also had developed episodes of hyperactivity and overtalkativeness. She was treated for a bipolar disorder with a good response.

Case 2: Ms C is a young lady living on one of the Zeway island shores. She was seen for a second opinion. This young lady had a series of domestic stresses. In the three weeks leading to her assessment she had become more restless and difficult to understand when she talked. The research psychiatrist considered that she may have a bipolar disorder but requested a second opinion as he was unsure. She was then assessed in detail over several days without treatment. Her speech was indeed difficult to follow and was interrupted by episodes of brief trance-like states during which her speech was even more difficult to follow. She also appeared unsteady when she walked. She was able to focus and speak coherently when encouraged to do so. She was not hyperactive or elated during the assessment. She admitted to a number of depressive symptoms in addition to irritability. She thought she was possessed by evil spirit. She was successfully treated with imipramine.

Case 3: Mrs A is a woman in her early 40’s. She was working as a secretary for a large firm. She brings up her 16 year old son and his younger sister on her own following her divorce several years ago. She was a confident woman with a good relationship with the head of the firm. She had managed all her difficulties and hassles successfully until about three months earlier when she had a dream that she was going to die. She understood this dream literally and was extremely concerned that she was going to die. But this was
not the only problem. She had persistent early morning wakening; she had lost her appetite and a significant amount of weight. She had lost her confidence and become too intimidated to approach her manager. She felt worthless and did not see the point of living. She believed that she was going to die and had begun to prepare for this eventuality. To this end she had decided to live in a monastery, abandoning her children, and had started the difficult initiation process. When the author saw her, she fulfilled DSM-IV criteria for depression, with numerous biological symptoms present. She did not know what depression was and did not think her experience was due to depression. Instead she was convinced that it was a spiritual issue and that she had fallen victim of the devil but she agreed to try psychiatric treatment. With medication and physical exercises, she moderated her decision. Although she remained more religious, she abandoned the idea of living in a monastery. Her symptoms improved and she continued in her work.

Case 4: Mr D was a single man in his late 50’s who was living on one of the Zeway islands. He had about four separate periods of brief excitement during which he was hyperactive and overtalkative. These periods were often associated with fever and acute gastrointestinal symptoms such as diarrhoea and vomiting. No physical cause, such as malaria, was identified during any of the acute episodes of behavioural disturbance. Mr D denied experiencing these behavioural disturbances but was able to recall the physical symptoms. He received a SCAN diagnosis of bipolar disorder. Mr D also had a nephew with confirmed and severe bipolar disorder requiring multiple admissions. However, the study design required that all those with a diagnosis of severe mental disorders have an independent assessment by a senior psychiatrist. The psychiatrist made the diagnosis of behavioural disturbance due to unidentified medical causes. Mr D was therefore not included as a case with bipolar disorder. Unfortunately Mr D committed suicide about five years after the study was completed. On further review of the case with people who knew him, he had frequent episodes of hyperactivity when he run around his house naked and climbed trees when he did not have apparent physical symptoms. Neighbours had thought that he was doing this in order to feed his bees as he was a successful beekeeper.

Case 1 (Ms B) demonstrates that culturally sanctioned conditions, in this case Zar, can occur together with a DSM-IV disorder, in this case bipolar disorder. The distinction can be difficult as in this case when the cultural condition predates the DSM-IV disorder. The diagnosis required cultural awareness, detailed assessment and consultation. But the diagnosis of bipolar disorder also showed predictive validity, i.e., response to treatment.
Case 2 (Ms C) again demonstrates the need for careful evaluation when one is unsure about the influence of culture. The decision is not always easy. Again the diagnosis of depression has shown predictive validity.

Case 3 (Mrs A) shows that disorders like depression can have substantial consequences on an individual's life. Mrs A was prepared to change the course of her life drastically despite the potentially serious impact of her decisions. Making the diagnosis of depression was fairly straightforward given the nature of her symptoms. Although she did not believe in the diagnosis of depression she was willing to collaborate with treatment. But it was also important that she managed her fears based on her explanatory model. Although she did not go to live in the monastery in order to prepare for her death, she had changed her lifestyle (she has become much more religious and observant of the required religious rituals). The diagnosis of depression had both convergent and predictive validity. The treatment took into consideration her explanatory model, but in a way that did not affect her life drastically.

The story of Mr D is very unfortunate. Because Mr D was evaluated in the context of a research project, the decision about diagnosis and treatment was cross-sectional. But the case illustrates that the issue of culture does have a biomedical dimension. Explanatory models are not just related to pure socio-cultural issues. The main reason this person was not considered to have bipolar disorder was because of the concurrent physical symptoms. Although the exact diagnosis was undetermined, it was presumed that acute febrile illnesses such as malaria common in the area were considered the causes for the episodic behavioural changes. There was a possibility that this unfortunate outcome could have been prevented with appropriate treatment.

What Aubrey Lewis said in 1961 still holds true: “There is no convincing evidence that the aetiology and pathology (including the psychopathology) of the varieties of mental disorder is different from what it is in Europeans, or that the incidence is grossly different, or that very diverse traditions, religious and social institutions have had more than pathoplastic influence on the manifestations of mental illness” (Lewis 1962). The same may be said of bipolar disorder.
Studies of affective disorders in Africa

**Historical background**

Some have suggested that the syndromes of depression and psychosis (which would include some manic states) were well documented in Africa even before the existence of any clear documentation in the West (Ndetei and Mburu 2006). However, in the past century, the study of affective disorders has been overshadowed by debate over whether depression actually existed in the continent. We can trace the historical understanding of depression in Africa over four overlapping phases and that of bipolar disorder in three phases. As depression is inherently a Western concept, the phases are described in comparison to those in the West.

*Depression*

**Phase 1: Depression viewed as a rare disorder in Africa.** Reports from the end of the 19th century until the mid 1950s originated from “asylum” based clinical observations. Depression was diagnosed in less than 2% of hospital admissions. This observation lead to the view that depression was a rare phenomenon in Africa (Carothers 1953 and 1962; Lambo 1956). Depression, if it occurred was furthermore considered to be mild and of short duration (Carothers 1962; Lambo 1956). The presumed lack of responsibility of the native African and his use of projective defences were hypothesised to account for the absence of depression.

**Phase 2: Depression is not as rare as presumed but that it is not as common as in the West.** After the mid 1950s, almost in conjunction with the beginning of independence (Prince 1967), studies involving populations outside the asylums, including limited ethnographic and measurement-based assessments, were conducted. These studies identified depression as an important problem but conceded that its occurrence is not likely to be as frequent as was found from the West and that it presented with somatic symptoms. Thus, there was more interest in the concept of masked depression although what this constituted was not always clear. Leighton and colleagues (Leighton et al 1963), in their pioneering epidemiological study believed they had come across a genuine cultural difference in depression.

**Phase 3: Depression occurred as commonly but with a marked difference in symptom profile from that found in the West.** Reports from the mid-1970s to the mid 1980s come from clinic-based as well as limited community-based
studies (German 1972; Binitie 1981; Hanck et al 1981; Keegstra 1986; Makanjuola and Olafia 1987). Although depression was considered an important problem, the focus continued to be on the uniqueness of presentations and the prevalence of the disorder in the different subgroups. Thus some symptoms of depression were believed to be more prominent than others. The prevalence and presentation of depression was also believed to be different between the literate and the illiterate, the westernized and the non-westernized, and East and West African (German 1972). The main exception in this regard was the report by Orley and Wing (1979), in which depression was found to be as prevalent in a Ugandan village as in a sample from London. This study also found that guilt, a symptom considered rare amongst depressed patients from Africa, was significantly more common among Ugandan women. This was further confirmed in a study of women in Zimbabwe (Abas and Broadhead 1997).

Phase 4: In recent studies Depression is reported to occur as commonly and to have similar manifestation to that in the West. The availability of structured interview instruments to identify cases facilitated the study of the prevalence, phenomenology and risk factors of mental disorders within the community. Thus several community-based studies describing the epidemiology and phenomenology of depressive disorders were reported from the late 1970s. Despite some variations, which may be partly attributable to methodological differences, these studies reported the prevalence and phenomenology of depressive disorders in Africans as similar to that found in the Westerners. Due to their methodological sophistication and the involvement of native psychiatrists who may be presumed to have more intimate knowledge of the culture, these later studies may be considered the best available evidence on the prevalence and phenomenology of depression in Africa.

Bipolar Disorder

Bipolar disorder is a neglected area of research in Africa and there are only few studies on its epidemiology and phenomenology. The reason for this neglect is partly to be found in the general neglect of mental health and mental health research in the continent. It is also part of the universal phenomenon: there is a relative dearth of research activity in bipolar disorder compared with schizophrenia (Clement et al 2003) and depression. As most studies from Africa are based on clinical samples, it may also be easier to recruit patients with schizophrenia than bipolar disorder. Finally, if there was a tendency to misdiagnose bipolar disorder as schizophrenia as
was found to be the case in the West (Mukherjee et al 1983; Jones and Gray 1986), then bipolar disorder may not register as an important problem to warrant spending limited research fund on. However, this possibility has not been explored.

As has been the case for depression, the primary interest of studies on bipolar disorder was to identify potential differences of presentation and outcome of bipolar disorder in Africa compared with the West. Drawing a historical parallel with depression is difficult, but based on reports that included samples with diagnosis of manic or bipolar disorder, three main stages may be identified.

1) Early studies before the bipolar-unipolar distinction was formulated or employed have claimed mania to be the more common presentation of affective disorders although this was still considered to be a rare phenomenon. These were reports mostly coming from hospital/asylum-based studies.

2) Further clinic-based and retrospective studies in the early 1980s described the tendency of bipolar disorder to present predominantly with manic episodes or relapses rather than with both manic and depressive relapses as reported in the West. In addition to these clinic-based studies, a few community-based studies attempted to describe the cross-sectional prevalence of hypomania/mania (Orley and Wing 1979; Majkanjuola 1982, 1985 and 1989).

3) Population-based cross-sectional studies and studies of course and outcome, at the beginning of this century described the prevalence and the prospective course of bipolar disorder (Fekadu et al 2004; Fekadu et al 2006; Kebede et al 2006; Kebede and Alem 1999; Negash et al 2005).

**Classification and clinical manifestation of affective disorders**

Most of the psychiatric centres in Africa use either the fourth edition of the DSM-IV (APA 1994) or the tenth edition of the International Classification of Diseases (ICD-10) (WHO 1992) classification systems.

Both the ICD-10 and DSM-IV have overlapping profile of classes for affective disorders. The occurrence of mania defines bipolar disorder. The DSM system has two main groups for bipolar disorder: bipolar I disorder in which there is a history of mania, and bipolar II disorder in which there is a history of only hypomania alternating with major depressive disorder. The ICD-10 has a category for single manic episode and bipolar affective disorder is
essentially equivalent to bipolar I disorder in the DSM-IV. Bipolar II in ICD-10 is listed under a residual category of “Other” disorders.

The ICD-10 classifies depression in a dimensional way from the outset based on symptom severity (mild, moderate, and severe) and symptom profile (depression with and without somatic syndromes and with and without psychotic symptoms) (Table 1). The DSM-IV classifies depression in to minor and major depressive disorder and further classifies major depressive disorder according to symptom severity (mild, moderate, and severe). It also uses symptom profiles or descriptors (melancholic, seasonal, catatonic etc) (Table 1). Both systems have a category for chronic mild depression (dysthymia) and a residual category for depressive disorders that cannot be grouped within the main classes.

The use of either diagnostic system is acceptable and is a matter of local practice. But the ICD-10 classes are used for international disease reporting purposes.

Table 1. Diagnostic classes of depression according to the 2 major international classification systems.

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Classification system</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DSM-IV</td>
</tr>
<tr>
<td></td>
<td>ICD-10</td>
</tr>
<tr>
<td>Depressive Disorders</td>
<td>Major depressive disorder, single episode</td>
</tr>
<tr>
<td></td>
<td>Major depressive disorder, recurrent</td>
</tr>
<tr>
<td></td>
<td>Further specification according to:</td>
</tr>
<tr>
<td></td>
<td>- severity (mild, moderate, severe, severe with psychosis)</td>
</tr>
<tr>
<td></td>
<td>- features (melancholic, catatonic, atypical)</td>
</tr>
<tr>
<td></td>
<td>- pattern (postpartum onset, seasonal pattern)</td>
</tr>
<tr>
<td></td>
<td>- course (chronic, with or without full interepisode recovery)</td>
</tr>
<tr>
<td></td>
<td>Depressive episode (mild, moderate, severe, severe with psychotic features)</td>
</tr>
<tr>
<td></td>
<td>Recurrent depressive disorder</td>
</tr>
<tr>
<td></td>
<td>Other depressive episodes (including atypical depression and masked depression)</td>
</tr>
<tr>
<td>Persistent depression</td>
<td>Dysthymic disorder</td>
</tr>
<tr>
<td>Adjustment Disorder</td>
<td>Adjustment disorder with depressed mood</td>
</tr>
<tr>
<td></td>
<td>Adjustment disorder with brief or prolonged depressive reaction</td>
</tr>
<tr>
<td>Depression due to physical factors or use of substances</td>
<td>Affective disorder due to a general medical condition</td>
</tr>
<tr>
<td></td>
<td>Substance-induced affective disorder</td>
</tr>
<tr>
<td>Residual categories</td>
<td>Minor depressive disorder, brief recurrent depressive disorder</td>
</tr>
<tr>
<td></td>
<td>Mixed anxiety depression</td>
</tr>
</tbody>
</table>

Organic depression
Clinical syndromes

Depression

Table 2 details the main features of depression as represented in the main diagnostic systems. The central feature is one of a depressed or low mood, loss of interest and possibly loss of energy for at least two weeks (APA 1994; WHO 1992). These core symptoms are associated with various biological (also called vegetative or somatic or melancholic) symptoms such as change of appetite and weight, sleep disturbance, reduced libido, disturbance of menstruation, constipation, and psychomotor retardation or agitation.

Table 2. Main clinical features of depression included in DSM-IV and ICD-10.

<table>
<thead>
<tr>
<th>Symptom type</th>
<th>Diagnostic criteria</th>
<th>DSM-IV</th>
<th>ICD-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core</td>
<td>Depressed mood</td>
<td>Depressed mood</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Loss of interest</td>
<td>Loss of Interest</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lack of energy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td>Poor concentration</td>
<td>Poor concentration or indecisiveness</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Guilt</td>
<td>Loss of confidence or self esteem</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Worthlessness</td>
<td>Inappropriate guilt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hopelessness</td>
<td>Pessimistic view of future Recurrent thoughts of death or suicide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suicidal thoughts</td>
<td>Any suicidal behaviour</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suicidal plans</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suicide attempt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biological</td>
<td>Weight disturbance (loss or gain)</td>
<td>Weight disturbance (loss or gain)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Appetite disturbance (Decrease or increase)</td>
<td>Appetite disturbance (decrease or increase)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sleep disturbance (decrease or increase)</td>
<td>Sleep disturbance (decrease or increase)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Psychomotor agitation or retardation</td>
<td>Psychomotor agitation or retardation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fatigue or loss of energy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusion</td>
<td>Mixed states</td>
<td>Substance induced</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Substance or General Medical Condition (GMC) induced</td>
<td>GMC induced</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bereavement</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cognitive problems may be reflected in slow thinking, reduced speed and latency of speech, reduced volume of speech, subjective impairment in concentration, registration and recall, associated with objective impairment in psychometric testing. Memory disturbance may be severe and resemble dementia (depressive pseudodementia). So called negative or depressive
cognitions include negative views of self, the world, and the future (pessimism). Vague pessimistic outlook and a tendency to worry unnecessarily in mild depression develop into hopelessness, worthlessness and excessive guilt when the depression becomes moderately severe. Patients may be unable to distract themselves from these repetitive thoughts (depressive ruminations). Suicidal thoughts or behaviour may follow.

In more severe depression, delusions, normally mood congruent, such as those involving ill health and poverty develop. Hallucinations, usually auditory, may also develop and these are also normally mood congruent. Some patients may develop the so called atypical features in which reversed biological features (increased sleep, appetite and weight), preserved affective reactivity, extreme (leaden) anergia, and interpersonal rejection sensitivity are manifest.

As indicated above, there have been suggestions of a unique symptom profile among patients from Africa. The depression was believed to present with less subjective complaint of depressed mood, increased somatic symptoms and markedly reduced libido. Guilt and worthlessness were reported to be replaced by vague persecutory ideas. The depression was also considered to be of mild severity and shorter duration (Lambo 1956; Collomb and Zwinggelstein 1962; German 1987). Latest studies and clinical observations have not substantiated these claims. Several well designed studies have shown that the symptom profile of depression among clinical (Keegstra 1986; Majodina and Johnson 1983) and community (Orley and Wing 1979; Abas and Broadhead 1997) samples was similar to that found among patients from the West. Contrary to expectations, the acclaimed study by Orley and Wing (1979) and Abas and Broadhead (1997) found that the proportion of women with thoughts of guilt in the two African settings was actually larger than that from London. Similarly, contrary to the claims of a milder illness course, studies from Africa have reported a high burden from depression (Abdullahi et al 2001) and association of depression with significant level of disability and mortality (Mogga et al 2006). These latest findings should at least prove that there are no robust data supporting the existence of unique depressive symptom profile for African patients. Nevertheless, with increasing literacy and globalisation, any presumed unique profile of depressive symptomatology is likely to disappear.

Other depressive disorders include minor depression, brief recurrent depressive disorder, dysthymic disorder and mixed anxiety depressive disorder. Mixed anxiety depressive disorder is said to be most relevant in
general medical settings while some reports indicate that minor depression is associated with help seeking and risk behaviour and may be a useful diagnostic construct in rural African settings (Fekadu et al 2007 and 2008).

**Mania**

The central feature of mania is one of elated or irritable mood lasting for at least a week (APA 1994; WHO 1992). Associated behavioural and cognitive symptoms include increased energy and hyperactivity ranging from semi-purposeful engagements to disruptive restless behaviour. Disinhibition with increased sexual energy, excessive socialising behaviour and overtalkativeness, indiscrete and inappropriate behaviour, overspending and engagement in unproductive business ventures are additional behavioural symptoms. Patients are optimistic and confident, this generally giving way to grandiosity and grandiose delusions. Summary of these is presented in Table 3.

**Table 3.** Main clinical features included for the diagnosis of mania in DSM-IV and ICD-10 classification systems.

<table>
<thead>
<tr>
<th>Symptom type</th>
<th>Diagnostic criteria</th>
<th>DSM-IV</th>
<th>ICD-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core</td>
<td>Elated or irritable mood</td>
<td>Elated or irritable mood</td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td>Flight of ideas</td>
<td>Reduced attention</td>
<td>Distractibility</td>
</tr>
<tr>
<td></td>
<td>Racing thoughts</td>
<td></td>
<td>Inflated self esteem</td>
</tr>
<tr>
<td></td>
<td>Distractibility</td>
<td></td>
<td>Grandiosity</td>
</tr>
<tr>
<td></td>
<td>Inflated self esteem</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grandiosity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behavioural</td>
<td>Overtalkativeness or Pressure of speech</td>
<td>Overtalkativeness</td>
<td>Increased energy</td>
</tr>
<tr>
<td></td>
<td>Increased goal-directed activity</td>
<td></td>
<td>Hyperactivity</td>
</tr>
<tr>
<td></td>
<td>Psychomotor agitation</td>
<td></td>
<td>Overspending</td>
</tr>
<tr>
<td></td>
<td>Increase pleasurable activities</td>
<td></td>
<td>Aggressive behaviour</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Disinhibition</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Poor sleep</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>Poor judgment</td>
<td>Enhanced perception</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overoptimism</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Excessive writing behaviour</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Psychotic symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Functional impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusion</td>
<td>Substance or GMC* induced or antidepressant induced</td>
<td>Substance induced</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Organic mental disorder</td>
<td></td>
</tr>
</tbody>
</table>

*GMC=General Medical Condition*
Mania among African patients is not believed to have unique manifestations (Fekadu et al 2004) although Carothers had suggested that “it is common in Africans to see states of confusion with excitement, which tend to resolve spontaneously within a limited time, but may be masked during this time by any degree of violence, externally directed as a rule”.

There are no reports from Africa on cyclothymic disorder, a disorder in which dysthymic symptoms alternate with hypomania for 2 years or longer with any inter-episode recovery not lasting longer than 2 months (APA 1994; WHO 1992).

**Epidemiology of affective disorders in Africa**

Depression is said to be inherently unreliable of the psychiatric diagnostic categories (Lopez-Ibor 1990). This is partly manifested by the large variation in its prevalence worldwide. But variations in study setting, the diagnostic system, the rating scales used are also important sources of variability. Thus an international report shows a lifetime rates ranging from 1.5% in Taiwan to 19% in Beirut, with annual rates ranging from 0.8% in Taiwan to 5.8% in New Zealand (Weissman et al 1996). This variation is also reflected in studies from Africa.

As shown in Table 4 the prevalence of depression in Africa varies from 0.5% among the Ethiopian nomadic population to 40% among participants exposed to severe armed conflict (Table 5). Excluding studies among special population groups, for example studies among those exposed to violence, the prevalence of depression in most studies is between 5% and 10%. Furthermore, as shown in figure 1, despite the wide variation of prevalence between countries, the rate is more consistent within countries. The review here has excluded all prevalence reports that did not use systematic methods to ascertain cases. Therefore only studies since 1979 are included.
Studies of depression among the elderly are few. What is available suggests that depression may be common in this population. In a representative elderly population (ages 65 and over) from Nigeria, the lifetime prevalence of major depression was 26.2% and the 12 month prevalence was 7.1% (Gureje et al 2007). Diagnosis was predicted by female gender and increasing levels of urbanization. The high prevalence in this study contrasts with the very low prevalence in the general adult population in a similar setting in Nigeria.
employing similar case identification procedures (The WHO Mental Health Survey Consortium 2004). The authors reason that this higher rate among the elderly may be due to the tendency of the elderly to endorse depressive symptoms. They also suggest the dwindling social support, the lack of personal resources to cope with the harsh economic conditions, failing physical care with inadequate medical care may explain the higher rate. However, these findings require replication.

**Figure 7.** Prevalence trend in community studies over time.

Elderly individuals with MDD also had impaired quality of life and impairment in functioning in home, work and social roles. The same group of researchers also found a high rate of comorbidity with medical conditions (Gureje et al 2008). Interestingly, a much higher proportion of individuals with MDD (47.2%) were rated as having severe global impairment compared to those with arthritis (20.6%), chronic spinal pain (24.2%) or those with high blood pressure (25.0%). Again more studies would be required replicating these findings as well looking at presentations of depression in the elderly, and the impact of various social factors, such as displacement or migration, the HIV/AIDS epidemic, loss of social support, the rapid social change, poverty and conflict.

The case is different for bipolar disorder with very few studies providing prevalence figures. The study by Orley and Wing (1979) reported the prevalence for hypomania to be 2.0% among men and 2.2% among women. The overall prevalence can be recalculated at 2.1%. The other two reports
come from Ethiopia. In a large rural community study, the prevalence of bipolar disorder was 0.5% (Negash et al 2005) while among a geographically and possibly genetically isolated population group the prevalence was 1.8% (Fekadu et al 2004). Both studies ascertained cases using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (WHO 1997). A study using the Composite International Diagnostic Interview (CIDI) among an urban setting has reported a prevalence of 0.3% (Kebede and Alem 1999).

The peak age of onset is 30-40 years for unipolar depression and 50-70 years for psychotic depression and mid to late 20’s for bipolar disorder. There is a female predominance of approximately 2:1 in unipolar depression where as this is not the case for bipolar disorder. In Africa, studies have not indicated clear gender preponderance for depression. However, more studies are required before concluding that the most consistent finding in the epidemiology of depression, i.e., a two-fold increased risk of depression among women, is not the case in Africa. If indeed women and men were found to have similar risk of depression, various reasons may be explored as potential explanations. A study that explored possible interaction between culture, gender and depression compared college students from Ghana and the USA (Eshun et al 1998). The study showed that students from the USA were more likely to engage in “dangerous activity” while female Ghanaian students were more likely to engage in ruminative thinking style in response to depressed affective. The study does not answer the question as to why most studies did not find depression to be more prevalent among women. But it points to potential areas for exploration. Social support is one of the key mediators of the onset of depression and is worth exploring if it explains the lack of difference. Other important factors include literacy, which may affect reporting of depressed affective. Low rate of school enrollment is one of the expressions of gender disadvantage in developing countries.

**Aetiology of affective disorders with special reference to the African setting**

Complex hereditary and neurobiological models have been put forward to explain the causes of depression and bipolar disorder. Studies from Africa have focused on measuring potential socio-demographic risk factors for depression but complex biological models are rarely investigated.

In general, as in most psychiatric disorders, family studies have shown the importance of genetic factors in the development of affective disorders. For bipolar disorder, the risk in monozygotic (MZ) twins is 40-70% while in
dizygotic (DZ) twins and all other first degree relatives it is 5-10% (Muller-Oerlinghausen et al 2002). The mode of inheritance is complex with several genes, each making small contributions, likely to be involved. Morphological changes are also reported in neuroimaging studies. These include increase in size and reduction in glucose utilization in the amygdala and basal ganglia. Parts of the prefrontal cortex are found to be smaller in bipolar patients compared to controls (Blackwood and Muir 2004). Reduction in grey matter volume in the subgenual prefrontal cortex are also identified in positron emission tomography (PET) and magnetic resonance imaging (MRI) studies. Neuropsychological tests have shown impairment in memory and concentration during illness episodes that also persist after recovery (Blackwood and Muir 2004).

Twin studies in (unipolar) depression show concordance rates of approximately 40-50% in MZ and 25% in DZ twins (McGuffin et al 1991; Price 1968) although the MZ concordance rates seem to be lower for community sampled depression (McGuffin et al 1996). Importance of genetic factors was further confirmed with adoption studies showing increased rates of illness in biological relatives compared to adopted relatives of probands (Mendlewicz and Rainer 1977). The exact mechanism through which genetic factors confer risk is not established. Useful explorations have employed pharmacogenetic studies focusing on the identification of polymorphic variations. Associations of depression and polymorphisms at the serotonin (5-HT) receptor subtypes (e.g. 5-HT₂C receptor), of tryptophan hydroxylase (the rate limiting enzyme for the synthesis of 5-HT) or the 5-HT transporter have been reported.

Morphological brain changes have also been demonstrated. Computed tomography scans had shown features of cerebral atrophy among the elderly with depression (Jacoby and Levy 1980). Vascular changes are also associated with depression (Alexopoulos et al 1996) and this was demonstrated in MRI studies in which a linear relationship between severity of white matter lesions and measures of depression was shown (de Groot et al 2000). Decreased volume in cortical regions, mainly frontal cortex and subcortical regions (hippocampus, amygdale) has also been reported. These findings are further supported by functional neuroimaging studies.

Although no similar studies exploring the potential biological mechanisms of causation have been reported from Africa, several socio-demographic risk factors were found to be associated with depression. Thus increasing age, lower education level (Bhagwanjee et al 1998; Bolton et al 2004), lack of
regular income (Ndetei and Vadher 1982), somatic illness (Carta et al 2001) and current physical health problem (Rumble et al 1996) were associated with depression. Life events (Gagiano et al 1989; Gureje 1986; Ndetei and Vadher 1984), particularly loss events (Gureje 1986) were associated with increased depression. In a controlled study, Ndetei and Vadher (1984) not only reported higher rate of life events in the depressed group in the 27 weeks preceding the onset of depression but that there was a sharp increase in this in the 6-9 weeks before the onset of depression. Broadhead and colleagues (2001) have shown that support during crisis reduced risk of depression. Beiser and Collomb (1981) looked at the impact of change on those migrating from rural to urban setting. Outcome of change in terms of its causing depression or mental distress was determined not by change per se but by social contingencies which modify the situation as well as by personal assets which individuals bring with them. The role of traditional attitudes measured antenatally in the onset of postnatal depression was explored in a mixed methods study in Ethiopia (Hanlon et al, 2010). This study was conducted in Butajira, a predominantly rural community in Southern Ethiopia. The study prospectively evaluated (during last trimester of pregnancy and shortly after child birth, the impact of holding certain traditional values, for example carrying out certain rituals supposed to be protective of illness or attacks from evil spirits after childbirth among 1065 women. Holding traditional values around child birth was protective of postnatal depression in general, but when postnatal mothers were unable to carry out traditional acts that they ascribed to during pregnancy, they were more likely to be depressed.

Although not common, many infectious diseases may present with affective symptoms (please see Table 5 for details). Presentations that should increase the index of suspicion for an organic basis of a affective disorder include abrupt onset, excessive fatigue, cognitive changes such as disorientation or inattention, physical symptoms including fever, headache, and nausea or vomiting. Due to the neurophilic nature of the Human Immunodeficiency Virus (HIV), there are perhaps more studies on its neuropsychiatric consequences than any other infectious condition. A meta-analytic study has reported a nearly two-fold increase in the risk of depression among those who were HIV-positive study participants compared with those who were HIV-negative (Ciesla and Roberts 2001). A study among homosexual individuals did not find significant elevation in those who were HIV positive (Perkins et al 1994) although the risk increased more substantially 12-18 months before the diagnosis of AIDS (Lyketsos et al 1996). Few studies have
looked at the interaction of HIV infection and depression from Africa. In a large multicentre study by the WHO that involved two countries from Africa (Kenya and Zaire), the rate of depression was elevated only among those with symptomatic infection (Maj et al 1994). This was also reflected in the severity of depression measured with symptom rating scale.

Table 5. Infectious and other relevant causes of affective disorders.

<table>
<thead>
<tr>
<th>Cause Category</th>
<th>Cause details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious</td>
<td>• Acute</td>
</tr>
<tr>
<td></td>
<td>- Malaria</td>
</tr>
<tr>
<td></td>
<td>- Typhoid fever</td>
</tr>
<tr>
<td></td>
<td>• Sub acute</td>
</tr>
<tr>
<td></td>
<td>- Brucellosis</td>
</tr>
<tr>
<td></td>
<td>- Leptospirosis</td>
</tr>
<tr>
<td></td>
<td>- Tuberculosis</td>
</tr>
<tr>
<td></td>
<td>- Lyme disease</td>
</tr>
<tr>
<td></td>
<td>- HIV/AIDS</td>
</tr>
<tr>
<td></td>
<td>- Cysticercosis</td>
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<tr>
<td></td>
<td>• Fungal infections</td>
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<tr>
<td></td>
<td>- Cocciomycosis</td>
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<tr>
<td></td>
<td>- Cryptococosis</td>
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<tr>
<td></td>
<td>- Histoplasmosis</td>
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<tr>
<td></td>
<td>- Candidiasis</td>
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<tr>
<td></td>
<td>• Neurosyphilis</td>
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<tr>
<td>Nutritional deficiencies</td>
<td>• Folate</td>
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<tr>
<td></td>
<td>• Nicotinamide (Pellagra)</td>
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<tr>
<td></td>
<td>• Vitamin B12</td>
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<tr>
<td></td>
<td>• Vitamin B1 (Thiamine)</td>
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<tr>
<td></td>
<td>• Vitamin B6</td>
</tr>
<tr>
<td></td>
<td>• Anaemia</td>
</tr>
<tr>
<td>Endocrinopathies</td>
<td>• Hypothyroidism</td>
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<tr>
<td></td>
<td>• Disorders causing cortisol abnormality</td>
</tr>
<tr>
<td></td>
<td>• Hypopitutarism</td>
</tr>
<tr>
<td></td>
<td>• Diabetes mellitus and hypoglycaemia</td>
</tr>
<tr>
<td>Drugs</td>
<td>• Cardiovascular: methyl-dopa, reserpine, beta-blockers, diuretics, digoxin</td>
</tr>
<tr>
<td></td>
<td>• Endocrine: steroids, oral contraceptives</td>
</tr>
<tr>
<td></td>
<td>• Others: pentazocine, indomethacin, chloroquine, mefloquine</td>
</tr>
<tr>
<td></td>
<td>• Antibacterial: ampicillin, sulfamethoxazole, tetracycline, ethionamide, metronidazole, streptomycine</td>
</tr>
<tr>
<td></td>
<td>• Anticholinesterses: cimetidine</td>
</tr>
<tr>
<td></td>
<td>• Butyrophenones</td>
</tr>
<tr>
<td></td>
<td>• Psychostimulants, including khat</td>
</tr>
<tr>
<td></td>
<td>• Alcohol abuse</td>
</tr>
<tr>
<td></td>
<td>• Traditional herbal medicine</td>
</tr>
</tbody>
</table>
The findings from this WHO study and the preceding study (Leyketsos et al 1996) suggest that the occurrence of depression may be an indication of a symptomatic HIV or may be used as an indicator of illness progression. Equally relevant is that depression has been associated with poorer treatment adherence, treatment failure and risk of mortality (Hartzell et al 2008). There is no evidence suggesting unique symptomatology or presentation of HIV-related depression among Africans (Tom 2009).

Treatment with some antiretroviral drugs, such as AZT can sometimes be associated with affective symptoms, particularly mania. On the other hand, some studies indicate that zidovudine therapy may be protective of HIV-related mania (Mijch et al 1999). If the latter report is proven true, wider availability of antiretroviral therapies may have considerable impact on affective disorder comorbidity in HIV.

One of the main challenge in diagnosing comorbid or secondary depression in chronic infectious conditions like HIV is that many of the symptoms that help diagnose depression may also be part of the manifestation of the infectious condition. It is often necessary to rely on cognitive and emotional symptoms of depression and risk behavior for the diagnosis of depression. If medication is considered necessary in such states, it is important to try and avoid psychotropics with anticholinergic properties. Extensive lists of medical and iatrogenic conditions are described as potential causes of affective disorder. Table 5 focuses on conditions that are considered particularly relevant for Africa.

It is important to note here that depression is often under-recognised among the medically ill (Rodin and Voshart 1986). Two recent studies looked at the occurrence of depression (Ndeitei et al 2009) and suicidality (Ndeitei 2010) among the medically ill in Kenya. Of 2770 inpatients assessed in the former report (Ndeitei et al 2009), 42% were found to have mild to severe depression. Only 4.2% of these had received some sort of psychiatric diagnosis. In the latter study, 10.5% of a similar number of inpatients were found to have some form of suicidal ideation or behavior. The rate of depression may have been a little high in this study because of the use of a rating scale rather than a diagnostic instrument. However, the study confirms the common occurrence of co-morbid depression in the medically ill African patients. It further confirms the high rate of under-recognition as well as the need for innovative intervention to improve the level of detection.
General introduction

Course and outcome of affective disorders with special reference to the African setting

Affective disorders in most cases are lifelong conditions with multiple relapses and switches. Among clinical samples, about 90% of cases with a single manic episode and 75% with single depressive episode will have recurrence. Whereas studies on the course of depression in the African setting are almost non-existent, few studies have looked at the course of bipolar disorder.

One of the outcome studies on depression comes from Benin (Benitie 1981). In this study, compared to anxiety disorders where 61.8% had recovered by the time of follow up 8-9 years later, only 15.8% of those with depression had recovered. Most had residual symptoms (73.7%) and 5.9% had died (2.9% by suicide). Another study from Ethiopia has associated the course of depression with high rate of mortality and disability (Mogga et al 2006).

The outcome of bipolar disorder is better investigated. Most of the work was pioneered by Makanjuola. Based on both cross-sectional and prospective studies he has reported on the clinical outcome of the disorder. Consistent with what was reported previously, he found that bipolar relapses were predominantly of manic nature rather than depressive (Makanjuola 1982; 1985; 1986; 1989). These reports were based on a clinical cohort with infrequent follow-ups that were conducted at clinical settings or centres of traditional healers. Another retrospective study of hospital admissions in Tunisia has also reported the predominance of manic relapse (Dakhlaou et al 2008). Recently, based on a systematic ascertainment of community cases, the clinical and functional outcome of bipolar disorder was reported (Kebede et al 2006; Fekadu et al 2006). Nearly two thirds of the cases had relapsed over two and half years. Contrary to expectation, bipolar relapses were characterised by both manic and depressive relapses in almost equal proportion. Just under a third of cases also had continuous illness. While male gender was associated with manic relapse, female gender was associated with depressive relapse (Fekadu et al 2006). Although the annual scores of the mania rating scale progressively declined, the depression scores remained stable over the follow up years (Kebede et al 2006). Bipolar disorder was also associated with significant level of disability (Kebede et al 2006). Medication with antipsychotic drugs was the only factor associated with remission. Both depressive and bipolar disorders were associated with significantly increased mortality compared to the general population (Fekadu et al 2009). The apparent difference between the study from Nigeria
and Ethiopia may be primarily due to the study designs. In the former study, cases were recruited from clinical settings where manic episodes are likely to predominate and may also be predisposed towards manic relapses where as the community is likely to draw a mixed sample with propensity for manic and depressive relapses. Additionally the follow-up interval in the Nigerian studies was much longer and depressive relapses are more likely to be missed in longer follow up intervals. However, the monthly follow-up intervals in the Ethiopian study are likely to capture the spectrum of relapses. This requires further exploration as it would have therapeutic and aetiological implications.

In summary, the course of bipolar disorder appears to be similar to what has been reported from the West and there is no consistent evidence to suggest the predominance of manic relapses. It is also clear that both bipolar and depressive disorders are severe, causing significant level of disability with a tendency towards chronicity.

**Subthreshold affective states**

The term subthreshold refers to the occurrence of affective symptoms without reaching the level required for making a diagnosis of a specific disorder defined in the international classification systems. The DSM-IV includes a list of conditions for consideration for further research. These include recurrent brief depressive disorder and minor depressive disorder. There is a more extensive list of subthreshold bipolar and depressive states. Epidemiological evidence points to the public health and clinical importance of these subthreshold states. Research findings also suggest continuity and shared aetiology with DSM-IV or ICD-10 defined or categorical disorders. These subthreshold states are three to four times more common than categorical disorders (E.g., Judd et al 1994; Jones et al 2004). Clinically they can represent a prodrome (Howarth et al 1992) or residue of a more severe illness and also tend to be associated with relapse (Judd et al 2000). They are also associated with significant psychosocial disability and high health care need (Judd et al 2002).

The evidence for a shared aetiology for subthreshold states with categorical DSM-IV or ICD-10 disorders comes from family studies, neurophysiological considerations, and evidence of shared socio-demographic risk factors. In a study of twin sibling, the risk of depressive episode in the unaffected sibling was increased in a similar fashion in both those with a depressive disorder diagnosed according to the DSM-IV (APA 1994) or depressive symptoms below the DSM-IV threshold level (Kendler and Gardno 1998). Family
studies also indicate a shared genetic predisposition for both threshold and subthreshold depression (Sherbourne et al. 1994). The evidence from family studies further suggests that the heritability of depressive disorders is more “robust” if less severe presentations of the illness are included (Judd et al. 2002). Neurophysiologic factors are deemed similar in the depressive disorders, particularly between dysthymic disorder and major depressive disorder (Judd et al. 2002). Similarity of correlates between subthreshold psychotic symptoms and categorical disorders (Sherbourne et al. 1994; Jones et al. 2004) also reinforces the view that shared aetiological mechanisms between categorical disorders and subthreshold symptoms might exist.

Minor depressive disorder is a subthreshold condition operationalised in the DSM-IV over 12 years ago. The work by Angst and colleagues describing its symptoms and course gave impetus for its inclusion in DSM-IV (Merikangas et al., 1996). The construct was considered to be particularly useful in primary care settings, among the physically ill, the elderly, and those seeking treatment (Merikangas et al., 1996). For a definitive diagnosis of minor depressive disorder, DSM-IV requires the concurrent occurrence, for at least 2 weeks, of 2 to 4 prespecified depressive symptoms, of which one should be low mood or loss of interest (Criterion A1). These symptoms should cause clinically significant distress or impairment (Criterion A2) and should not be due to the direct physiological effect of a substance, physical illness or injury (Criterion A3) or should not be better accounted for by bereavement (Criterion A4). Lifetime history of major depressive disorder (Criterion B), or manic episodes (Criterion C) should be excluded. The symptoms also should not occur only during major psychotic episodes (Criterion D). Lifetime mood disorders (major depressive, dysthymic, brief recurrent, manic, mixed, and cyclothymic disorders) have to be excluded because symptoms considered to be due to minor depressive disorder could be residual symptoms of an underlying mood disorder, which has not resolved completely, or prodromes of a relapse. Adjustment disorder with depressed mood can also mimic minor depressive disorder. The main distinguishing feature is the onset of the depressive symptoms in response to an identifiable stressor in adjustment disorder (APA, 1994).

Even though the operational criteria for minor depressive disorder were published in the DSM-IV 12 years ago, varied definitions have continued to be employed in descriptive (Pincus et al., 1999; Rapoport et al., 2002), intervention (Judd et al., 2004; Williams et al., 2000), and outcome studies (Cuijpers et al., 2005; Pincus et al., 1999). Consequently, there remains a need to assess the validity and usefulness of this diagnostic construct. The
impact and relevance of this group of disorders in resource-poor settings is also not evaluated.

**Concluding remarks and recommendation for future research**

Current evidence suggests that both depressive and bipolar disorders are important public health problems in Africa. Contrary to what has been taken as a dogma, depression is frequent in Africa and has similar manifestations to what is described in the West. Identified risk factors are also similar to what is expected and found in studies from the West further suggesting potential aetiological similarities of the disorder. However, important questions remain. Despite a degree of within country consistency of prevalence reports, there is a wide variation across countries. This is not unique to studies from Africa and geographic and cultural differences are not likely to fully account for this. Some of the difficulty may be to do with measuring instruments, but marked differences are reported even when studies were conducted by the same group of researchers using the same instruments. Identifying the reason behind such differences is important to understanding the nature of the disorder and methods of intervention as well as to increase the credibility of scientific studies of depression. The family unit remains the crucial element in the effective treatment of the African patient. Studies to understand the role of the family and effective ways of supporting them is important. The impact of the ongoing use of first generation antipsychotics for the prophylaxis of bipolar disorder should be evaluated and studies on the outcome of both bipolar disorder and depression are also required. A pan-African study of affective disorders with shared methodology and looking at cross-country differences in prevalence and the impact of socio-cultural factors as well as globalization on the presentation of affective disorders may be necessary. However, the enormity and challenge of such a task should not be underestimated. Studies on the different models of care for affective disorders, on the role of primary care in detection and management of affective disorders, and on the role of traditional healers are required. Given the huge mental health gap in Africa, traditional healers may be seen as potential resources, but requires a careful evaluation of their potential role. The role of traditional remedies in the treatment of affective disorders and their potential adverse impact also needs evaluation. Although the adverse interaction between HIV infection and affective disorders is to some extent known, how the care of affective disorders may be integrated into HIV programmes is not clear. Study in this area is also warranted.
Aims of the study

General Aims
The overall aim of the study was to describe the prevalence and determinants of affective disorders in rural Ethiopia

Specific Aims
The specific aims of the study were to determine:
1) The prevalence of minor depressive disorder (Paper I and Paper II)
2) Potential aetiological continuity of minor depressive disorder with major depressive disorder by assessing predictive factors (Paper I and Paper II)
3) The clinical utility and validity of the diagnosis of minor depressive disorder (Paper I and Paper II)
4) The prevalence of bipolar disorder (Paper III)
5) The clinical manifestations of mania (Paper III)
6) The clinical outcome of bipolar disorder (Paper IV)
7) The functional and symptomatic outcome of bipolar disorder (Paper V)
Participants and methods

Settings
The study was conducted in two sites: Butajira district and the Zeway islands. The Butajira setting has been well described in previous reports and will be discussed here only briefly. The Zeway islands and population will be described in more detail.

Butajira
Butajira is a predominantly rural district located approximately 130 km south of the Ethiopian capital, Addis Ababa. It is found in the Gurage zone of the Southern Nations Nationalities and Peoples region. When the study was conducted, the district had 45 sub-districts. All except one sub-district were included in the study. This sub-district was excluded because it was difficult to access. Recent administrative restructuring has split the district into two separate districts (Meskan and Mareko). Four of the sub-districts that were included in the study have become part of another district, the Sodo district. Furthermore, some of the sub-districts are now included within the newly defined Silti zone. However, the name “Butajira” will be used throughout this thesis for the sake of simplicity. The study sites are depicted in Figure 8.

The population is predominantly of the Gurage ethnic group and Moslem (65%). About 90% of the population live rurally (FDRE Population Census Commission 2008). Although the proportion of the Butajira population living rurally (90%) seems to be larger than the national average (85%), the national figure for the urban population is inflated because of the large number of people living in the capital city.

During the study period, the population of the Butajira district was estimated to be 227,135 persons. The actual study targeted those aged 15 to 49 years, constituting about 45% of the total population (OPHCC 1996). With an altitude ranging from 1750 to 3400 metres, the climate of the area is almost representative of the climate of the nation: tropical lowlands, cooler highlands and temperate intermediate areas. Malaria is endemic in the lowland areas.
The people live on small-scale subsistence farming, cattle breeding and trading. They grow maize, barley, wheat, sorghum, legumes and Enset (false banana). Enset is a drought-resistant plant. Although growing Enset is relatively easy, the process of converting it to edible food is labour intensive. Khat (Catha edulis) and chilli pepper are the main cash crops. Khat is a mild psychostimulant, about one quarter to one seventh the strength of amphetamine. It is widely grown and consumed in the area. Khat is used in religious rituals, particularly by Moslims. The impact of khat on mental health has not been satisfactorily clarified and well conducted studies in this area are limited.

Butajira is one of the beneficiaries of Ethiopia’s radical health service reform programme. Most of the services described here were not available when the study began. At the community level there are now two female health extension workers (HEW) for a population of about 5000 persons (1000 houses). The primary responsibility of these HEWs is health promotion and prevention of illness through health education, house to house visits, facilitating immunisations and providing simple diagnostic and curative measures (for example for malaria). Now there are five to seven health centres (staffed by nurses and health officers) in each district. There are two hospitals: a public hospital in Butajira town and a second hospital owned by a charitable organisation (Project Mercy) located about five kilometres south
west of Butajira town. There is one psychiatric clinic, established by the research project and staffed by two psychiatric nurses. The nurses receive regular supervision by research psychiatrists working in the project. The clinic provides service for patients coming from a vast area, from within and outside the Gurage and Silti Zones. The health service structure is depicted in Figure 9.

Figure 9. Health service structure and where mental health service fits.

Butajira district hosts a demographic surveillance site (DSS) that monitors vital health statistics. The DSS offers a unique opportunity to standardise relevant events against the routinely gathered data of the DSS.

Zeway islands

The Zeway population lives on the islands and shores of Lake Zeway. The people living on the Zeway islands and the shores of Lake Zeway are commonly called Zay. The lake is the largest and the northern-most lake of the rift valley lakes in Ethiopia. Lake Zeway lies almost in the centre of where the Rift valley crosses Ethiopia (Figure 10). The lake is located 160 kilometres south of the capital city, Addis Ababa. It is 1 636 metres above sea

9 Available at: http://www.idrc.ca/en/ev-43008-201-1-DO_TOPIC.html
level with a surface area of 434 km² and a mean depth of 2.5 metres (Zinabu et al. 2003). Historically, the Zay population mostly lived on the islands. Migration to the shores is only a recent phenomenon, taking place in the last 50 years or so. It is suggested that the term Zay originated from the Tigrigna language, the language spoken by the Tigray ethnic group who live in the north of Ethiopia. The word is said to mean either "hot" or is used as an expression of surprise. The former meaning is derived from the expression 'Z-waai'i', meaning how hot! Weiy in Tigrigna is translated as hot or warm and the word Zay in this case refers to a population living in this hot Rift Valley area. The second meaning expresses the beauty of the area: Z-wai. Wai in Tigrigna is an expression of surprise.

Figure 10. Location map of Lake Zeway, the Zeway islands and the shores where the Zay population lives.

This geographically contained, and culturally and probably genetically homogenous ethnic minority, is one of the most unique ethnic groups in the country. The Zay population resides on three of the five islands and the shores of Lake Zeway (Figure 10); the inhabited islands, Tulugudo, Fundro and Tedecha, are in the Eastern part of the lake. The uninhabited islands, namely Debresina and Gelila, are located near the Western coast and Zeway town (Edetto, 1988). The residents of Debresina and Gelila migrated across
to the nearby shores of Bochesa and Herera over the last 50 years (Edetto 1988). Around the same time some of the residents from Tulugudo migrated out to the shores of Mekdela. Some also live in the nearby Mek and Zeway towns, and Korkiadi village. The shores regularly flood during the rainy seasons and the residents have to move out from some parts (Figure 11). This also means that malaria is endemic to the area.

![Figure 11. Houses flooded during the rainy season, located in the outskirts of Mekdela village, on the Northern borders of Lake Zeway. (Photograph by author)](image)

Those who migrated out have maintained their distinct identity, culture and traditions. The Zay are strongly religious and this is reflected in their culture and lifestyle (Henze 1973). There are also indications of the influence of the 14th Century Orthodox Christian Church movement (Tamrat 1972), suggesting the Zay people have probably been living on the islands since the 14th Century. Endogamy is the rule, but consanguineous marriage is prohibited.

There are three main theories about the origin of the Zay. Two of these consider them to be migrants while the third considers them to have been endogenous to the area. Tamrat (1972) forwarded this last theory. He claimed that before the Zay were evangelised in the 14th Century by monks from the North, the Zay were native to the area. This will date their origin well before the 14th Century. However, if they were part of a larger native population group, it may be difficult to explain the high level of isolation and
distinctiveness of the community. In the second theory, Wolf Leslau (1994) quotes several similarities between the language of the Zay Society and the dialect spoken by the Eastern Gurage, located in a region about 50 kilometres from Lake Zeway. In contrast to the Cushitic language of the surrounding communities, the language spoken by the islanders, Zayigna, is a Semitic language similar to that of the Gurage language and the languages spoken by the Amhara and the Tigray ethnic groups from the north. Based on these observations, Leslau infers that the Zay originated from the Eastern Gurage region. Further evidence that the Zay migrated from outside is forwarded by Edetto (1988). He quotes an early 17th century record that suggests that their origins were the Silti people (Eastern Gurage area) who originally lived on the shores of Lake Zeway enduring intense pressure from the neighbourhood. If this is true then they may have been later pushed onto the islands.

The Zay’s own traditional understanding of their origin is that they are descended from a few ancestors from the North and Central parts of the country. Between the 9th and 11th century (Wondafrash 1993) it is claimed that these ancestors fled intense religious persecution and settled on the islands with valuable religious artefacts. Interestingly, one of the traditions of the Zay is to trace their paternal origin to 25 generations. Based on this they class themselves into three major sub-groups (Wondafrash 1993): Woyzero, Amarayge and Gumarge. The Woyzero claim to have come from Tigray, the northern most part of Ethiopia. This may have some support from the theory proposed by Tamrat (1972) if the monks managed to form or attract families from the North. The Amarayge is said to come from North Shoa, a central part of the country which is predominantly inhabited by the Amhara ethnic group. The Gumarge trace their origin from the nearby regions of the Gurage area. This tradition is in some ways consistent with the theories of origin suggested by Leslau and Edetto. If this is the case, their current lifestyle, language and culture suggests they have completely assimilated into each other through years of isolation, possible endogamy and inbreeding. Despite the absence of firm historical and scientific grounds to trace the origin of the Zay society, it is clear that they are geographical and cultural isolates and have been living in isolation for several hundred years.

The Zay primarily live on fishing and small-scale subsistence farming. They use the water from the lake for drinking. Transportation from the islands is by canoe and privately run motorboats (Figure 12). No health facility exists on the islands, but a periodic antimalarial spray and occasional vaccination campaign are provided. A primary school was built on the largest island by the government in 1974 and subsequently another one was built on Tedecha.
Figure 12. Photographs depicting the main subsistence activities of the islanders. At the top, young men are shown drying their nets and then displaying their morning catch; at the bottom women are shown fetching water. In the centre a young man is leaving Fundro island (one of the five islands) on his boat made from Abatcha tree. (Photographs by author)

Study design

Two study designs were employed.

Cross sectional design: used for the study among the Zay, which included determination of the prevalence of bipolar disorder and the study of minor depressive disorder. The study on minor depressive disorder in Butajira also employed a cross-sectional design.

Prospective design: used for the determination of clinical and functional outcomes of bipolar disorder in the Butajira sample.

Case identification

For the identification of cases with minor depressive disorder as well as bipolar disorder, complete case ascertainment of the target population was attempted. Among the Zay, an initial census was conducted to identify all
Participants and methods

In both study sites individuals were eligible for participation in the study if they had lived in the study areas for at least six months and if they provided informed consent. For the Butajira study, only individuals aged 15-49 years were eligible. This was because the study was focused on severe mental disorders, which are more common in this age group. Therefore, it was assumed that most individuals with severe mental disorders would be included within this relatively restricted age range. Furthermore, around the time of the study, the average life expectancy in the study area was captured within the included age interval. For the Zeway study, all individuals aged 16 and above were invited to participate.

For the identification of cases with bipolar disorder we used a double sampling design in which an initial screening procedure was followed by a confirmatory diagnostic process. The initial screen consisted of key informants and lay interview using the Composite International Diagnostic Interview (CIDI) (WHO 1997). The Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (WHO 1997) were administered by trained psychiatrists for confirmatory diagnosis. For the identification of cases with minor depressive disorder, we used data from the initial screen using CIDI.

Figure 13 and 14 present the case identification procedures in the two study sites.

**Figure 13.** Identification of cohort with bipolar disorder, Zay Study.
Identification of cases with minor depressive disorder (Paper I and II)

The Amharic (the Ethiopian official language) translation of the CIDI, version 2.1 (CIDI 2.1; WHO, 1997) was used for diagnostic assessment.

The initial Amharic translation of the CIDI version 1.0 (Rashid et al., 1996) was updated according to versions 2.0 and 2.1. Fifteen male and fifteen female high school graduates administered the CIDI through a door-to-door interview. Interviewers were trained for two weeks by trainers previously trained by experts from a WHO Collaborative Centre in the Netherlands.
Satisfactory inter-rater agreement was achieved and pilot studies were conducted in urban and rural settings before administration of the CIDI to the study sample. All interviews were conducted by interviewers who were the same sex as the study participant (Figure 15).

For the diagnosis of minor depressive disorder, depressive symptoms from the depression section (section E) of the CIDI 2.1 were used. Diagnostic categories based on section F (Mania section) were excluded. Most of the items in the CIDI are rated using a five-point scoring system with a score of five indicating the presence of a depressive symptom. Therefore only a score of five counted towards the diagnosis of minor depressive disorder. For a definitive diagnosis of minor depressive disorder, we required all the criteria in the DSM-IV (APA 1994) to be fulfilled. Current and lifetime history of major depression, dysthymic disorder, hypomania, mania or cyclothymic disorder were excluded. In settings like rural Ethiopia where untreated physical conditions are common, it is of particular importance to exclude cases where the occurrence of psychiatric symptoms may be explained by physical causes. Interviewers were trained to exclude symptoms caused by physical illness, use of medication or drugs and alcohol. When in doubt, the interviewers recorded the illness which was thought to have caused the symptoms and marked that particular item for the editor's decision. The editor reviewed the completed score sheets (usually on a daily basis) and made the decision as to whether those particular symptoms marked by the interviewers were caused by physical illness or another pathophysiological process. The editor who made these decisions was a trained physician with an additional four years of psychiatry experience. Trained key informants were also used in this study, along with the CIDI, as a first stage screening to identify possible cases with severe mental disorders; schizophrenia, bipolar disorder and major depression. Cases identified through key informants who were not CIDI interviewed were excluded.
Minor depressive disorder was evaluated in terms of two interrelated issues: utility and validity. The utility of the diagnosis primarily refers to the ability of the diagnosis to identify a treatment-seeking population. Validity was explored in relation to the construct of minor depressive disorder as well as its ability to tap into known adverse outcomes such as self-harm and disability (predictive validity). Risk factors for minor depressive disorder were also assessed to determine the potential aetiological continuity of the diagnosis with major depressive disorder.

**Determination of prevalence of bipolar disorder (Paper III)**

Identification of cases involved initial screen with CIDI and key informants. Those selected as key informants were residents of the sub-districts and community leaders with intimate knowledge of their communities. For each sub-district, four to six key informants were selected and were trained before starting the survey. Key informants were also trained prior to undertaking screening of potential cases for further assessment. The performance of rating instruments and key informants was assessed and has been reported separately (Shibre et al 2003).

**Determination of outcome of bipolar disorder (Paper IV and Paper V)**

The average duration of follow-up was 2.5 years, ranging from one to four years. Determination of clinical outcome (Paper IV) was primarily based on monthly clinical assessments. Annual symptom ratings were also used. Functional outcome was assessed annually using the 36-item Medical Outcomes Short Form (SF-36) (Ware 1992). The SF-36 scores were compared at baseline with available local general population norms (Kebede et al 2004).

**Data management**

The CIDI data were entered into a compatible CIDI data entry program (CIDI Auto), which also allows diagnoses to be made according to ICD-10 and DSM-IV criteria. The data were exported into the Statistical Package for Social Sciences (SPSS) and subsequent analyses was made using SPSS version 11.5. A similar data entry programme was used for the SCAN data. The programme also makes diagnosis according to the ICD-10 and DSM-IV diagnostic algorithms.
**Statistical analysis**

The analytic method included simple frequency distributions and determination of associations. Two-tailed significance was set at $p = 0.05$. All analyses were conducted using SPSS and Amos programmes. Bivariate and multivariate models were fitted to determine associations. For example, the ANOVA model was used to compare mean differences in scores of rating scales. Logistic regression modelling was used for binary outcomes such as the occurrence of a disorder or remission from a disorder. Linear random coefficient models were also fitted to assess factors associated with symptomatic outcomes. Factors included in multivariate analyses were socio-demographic factors and factors considered to be relevant determinants of the specified outcomes in the literature.
Ethical considerations

For the Zay study, ethical approval was granted from the ethics board of Amanuel Psychiatric Hospital, the national ethics board of the Ethiopian Science and Technology Commission, and from Region 4 Health Bureau. The respective Zonal (provincial) and Woreda (district) health bureaus also supported the study. The Butajira study was approved by the Ethics Committees of the Department of Community Health and the Faculty of Medicine, Addis Ababa University. CIDI interviews were conducted by interviewers of the same sex as the participants in order to respect local customs. Only consenting participants were interviewed. Treatment was provided and maintained for patients with established diagnosis of severe mental disorders. Additionally, participants with acute febrile illnesses (e.g. malaria), eye infections, and skin infections were treated free of charge. The study also led to the establishment of psychiatric clinics in both Zeway and Butajira. The Butajira study provides a model mental healthcare service for the region, including the only outreach service in the country.
Results

The study results are presented in three parts. The first part discusses the results related to minor depression. The second part focuses on the prevalence of bipolar disorder, which stands alone as it deals with a different study design and comes from the Zeway study whereas the other two reports on bipolar disorder come from the Butajira study. The third part outlines the outcome of bipolar disorder. Table 6 summarises the results to be presented further.

Table 6. Summary results of the component studies forming the thesis.

<table>
<thead>
<tr>
<th>Source</th>
<th>Problem addressed</th>
<th>Study site</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paper I</td>
<td>Validity of minor depressive disorder diagnosis assessed in terms of symptom construct and impact.</td>
<td>Zeway</td>
<td>Symptom construct: Unitary construct and distinct from bereavement. Impact: Prevalence (lifetime): 20.5% Self-harm: Thoughts of suicide: 33.5%; suicide attempt: 5% Service use: 35.3%</td>
</tr>
<tr>
<td>Paper IV</td>
<td>Clinical outcome of bipolar disorder (mean follow-up duration 2.5 years).</td>
<td>Butajira</td>
<td>High rate of chronicity (31.1%) Relapse: 65.9% (47.8% manic, 44.3% depressive, 7.7% mixed).</td>
</tr>
<tr>
<td>Paper V</td>
<td>Symptomatic and functional outcome of bipolar disorder (mean follow-up duration 2.5 years).</td>
<td>Butajira</td>
<td>Annually measured symptoms of mania reduced over the years; the reduction in depressive symptom scores was less marked. Functioning was significantly impaired compared to the local general population. This was in all domains, including physical functioning.</td>
</tr>
</tbody>
</table>
Minor depressive disorder (Paper I and Paper II)

Symptom construct (validity)

Validity of the construct of minor depressive disorder was evaluated through describing the symptom profile of minor depressive disorder as well as using confirmatory factor analysis. The symptom profile of the diagnosis tapped into the broader symptoms of depression; i.e., core symptoms of depression as well as other vegetative and cognitive symptoms of depression were endorsed. The symptoms of minor depressive disorder best fitted a unitary model. However, minor depressive disorder had symptoms overlapping with both depressive symptoms related to bereavement and major depressive disorder (described in Paper I).

Utility of concept

Minor depressive disorder was found to capture a prevalent and distressing condition. Many of those with the condition used health services (Figure 16).

Figure 16. Utility of minor depressive disorder assessed in terms of prevalence, ability to capture adverse outcomes and service use.
**Continuity with major depressive disorder**

Age, specifically belonging to the 35-54 year age group, being divorced or widowed (OR=2.54; 95% CI 1.23, 5.24), experiencing somatic symptoms such as headache and abdominal pain and lack of employment were significantly associated with receiving a diagnosis of minor depressive disorder. The association of education with minor depression was a little peculiar. Having primary education was protective among the Zay while higher education was associated with the diagnosis of minor depressive disorder among men. In the Butajira participants, both primary and secondary educations were associated with the diagnosis of minor depressive disorder.

**Bipolar disorder among the Zay (Paper III)**

The prevalence of bipolar disorder was 1.8% (n=31). Schizophrenia was almost absent, with only one person receiving the diagnosis. Although more males had bipolar disorder (61.3%; n=19), the difference was not statistically significant. Most persons with bipolar disorder came from one of the islands, the Tullu Gudo island. Over a third of cases (38.7%; n=12) had experienced a single manic episode. Most of the ICD-10 symptoms of mania were manifest, although behavioural symptoms were much more prominent. This is shown in Figure 17.

![Figure 17. Percentage of patients manifesting specific symptoms of mania.](image)
**Clinical and functional outcome of bipolar disorder (Paper IV and Paper V)**

Most people with Bipolar Disorder had a relapsing illness (65.9%) (Figure 18). Both manic and depressive relapses occurred in almost equal proportions (47.8% versus 44.3%) (Figure 19).

![Figure 18. Clinical course of bipolar disorder.](image1)

![Figure 19. Pattern of relapse.](image2)

Most patients also received either antipsychotic medications alone or in combination with antidepressant medications (Figure 19). Experiencing remission for at least the median duration of remission was predicted by taking psychotropic medications. Male gender predicted manic relapse while female gender predicted depressive relapse.

![Figure 20. Pattern of use of psychotropic medications.](image3)

The severity of manic and depressive symptoms showed a significant reduction over the follow-up years. However, the reduction for depressive symptoms was not that marked. A higher proportion of cases with long-standing illness, defined as illness lasting for two years or longer, had functional impairment (42%-57%) compared with those with recent onset illness, i.e., disorder duration shorter than two years, (35%-47%), during the follow-up years. Similarly impairments were also found in social and physical functioning. The severity of depressive and manic symptoms was
associated with functional impairment, while male sex, rural residence and being married were associated with better functional outcome.

Figure 21. Changes in the percentage of persons with functional impairment during follow-up years compared with baseline functioning.
Discussion

Minor depressive disorder (Paper I and Paper II)

This is the first large scale study of minor depressive disorder in a rural setting in sub-Saharan Africa. Minor depressive disorder appears to be an important diagnostic entity with construct validity and the expected symptom profile. Owing to its higher prevalence, minor depressive disorder affects a much larger number of people than major depressive disorder. It also captures the help-seeking population. This is particularly demonstrated among cases from Butajira. The condition also appears to cause a high level of distress as evidenced by the high proportion of cases with suicidal ideation and a history of self-harm. Therefore intervening to reduce minor depressive disorder may be important for the prevention of suicide. However, given the high prevalence, the condition would have major service implications, especially in countries like Ethiopia. Therefore further validation of the diagnosis of minor depressive disorder is important. The lack of clear demarcation in symptom profile from low mood related to bereavement and major depressive disorder also invites further careful evaluation of the disorder. Nevertheless, the limited evidence from this report indicates that the concept of minor depressive disorder is likely to be useful in the rural Ethiopian setting. Doing a further follow-up study of those identified with this disorder may prove useful in validating the validity of the disorder. This is practically possible as the population is accessible and there is also ongoing engagement with the population through the ongoing research projects and data collectors.

One of the striking findings in this report was the marked difference in the prevalence of minor depressive disorder between the Zay and the Butajira population. Several potential explanations may be forwarded.

Measurement error: Measurement error may arise either because of the poor applicability of the instruments in some settings, poor training of interviewers or the inherent nature of some instruments. The CIDI has been used in other studies and its feasibility and applicability in the Ethiopian context has been established (Rashid et al 1996). For the administration of the CIDI in the studies included for this thesis, rigorous training and ongoing supervision was provided throughout the data collection period. Interviewers for both sites were trained by the same group of researchers and some of the interviewers were working in both the Butajira and the Zeway sites. Although
measurement error cannot be completely excluded, it is unlikely to be the main reason for the difference in prevalence in these two settings. Although it is known that for the predecessor of the CIDI, the Diagnostic Interview Schedule (DIS; Robins 1982), lay interviewers underdiagnosed major depression (Helzer et al 1985), this is unlikely to explain the difference in prevalence between the two sites; instead lower prevalence would be reported in both sites.

**Difference in included age groups:** The Butajira participants were aged 15-49 years whereas all age groups were included for the Zay participants. Nearly half of the cases with minor depressive disorder among the Zay were above 35 years of age and about 15% of the cases were above 55 years of age. This would have increased the prevalence of minor depressive disorder among the Zay slightly but doesn’t explain the magnitude of the observed difference.

**Difference in population level risk factors:** There is some indication that some isolated population groups may have higher levels of stress and raised rates of substance abuse and violent deaths (Kraus and Buffler 1979). The level of stress was not systematically assessed among the Zay population, but there was no obvious reason to suspect the occurrence of a higher level of stress among the Zay.

**Threshold effect:** This may arise if the Zay population endorsed depressive symptoms at lower level of depression severity whereas the Butajira participants endorsed symptoms at a higher level of severity. There may be truth in this because minor depression was associated with a much higher level of service use and self-harm in Butajira compared with the Zay. But no other objective measures of disability were administered to know if this was truly the case. Related to this may be the difference in community attitude towards mental disorders leading to differences in reporting. One of the striking things about the Zay was their openness about mental disorder in their community. This may have lead to reporting of symptoms of depression even at a lower level of severity.

**Difference in ethnic vulnerability of depression:** A higher rate of minor depressive disorder among the Zay might have been expected because of the finding of a higher rate of bipolar disorder and the potential for genetic predisposition.

**Category fallacy:** This could arise if the nature of depression was different in the two population groups. However, this is unlikely given that the nature of the symptom profile of minor depressive disorder, associated distress and predictor factors were shared between the two populations.
In conclusion, it is suggested that the difference in prevalence of minor depressive disorder between the two sites is likely to be a true difference but a combination of factors indicated above, rather than a single factor is likely to explain the magnitude of the difference.

Prevalence of bipolar disorder among the Zay (Paper III)

The prevalence of bipolar disorder among the Zay is relatively high. Most prevalence reports on narrowly defined bipolar disorder provide a figure of 1.6% or less (Boyd and Weissmann 1981; Robins et al 1984; Weissman et al 1996; Kessler et al 1997). The prevalence is also higher than that found in Butajira (Negash et al 2005). The prevalence is all the more striking when considered against the much lower prevalence of schizophrenia. This higher prevalence could be due to genetic vulnerability mediated through a founder effect. Other relevant environmental factors that need to be considered include dietary habits, exposure to unique stressors, exposure to perinatal famine and toxic materials.

Diet is perhaps the most distinguishing environmental factor. The regular diet of the Zay is dominated by fish. However, sea food is thought to be protective against mood disorders rather than increasing the risk (Puri 1998; Stoll et al 1999; Peet & Horrobin 2002). Classificatory error is an important consideration. But this seems unlikely given the care taken to ascertain the cases. First cases were identified through a clinical interview using the SCAN. Second, interviewers had access to second opinion when they were in doubt of the diagnosis of a disorder. Third, an additional diagnostic step was required when it was found that most of the identified cases had bipolar disorder. This third step involved clinical diagnosis by senior psychiatrists trained in the UK. In fact, this third step excluded cases who were categorised as having bipolar disorder and may have lead to underestimation in the actual prevalence of bipolar disorder. Given the nature of the population, genetic factors are likely to be operational and may explain the relatively higher rate of bipolar disorder compared with schizophrenia too.

Outcome of bipolar disorder (Paper IV and Paper V)

The observed relapse pattern of bipolar disorder was consistent with that established in the literature. However, it differed from previous reports from Africa (Example, Makanjuola 1982, 1985, 1987 and 1989) or Asia (Khanna et
These studies were based on clinical samples and retrospective assessments. Where prospective assessments were employed, the assessments were carried out at long intervals. Such assessments are likely to be biased towards identifying manic relapse. Given the systematic nature of the assessments and the shorter assessment intervals, findings from the Butajira study are likely to be more robust. The clinical implication of the finding is that depression is an important problem in the course of bipolar disorder in Ethiopia and has to be considered in the management of bipolar disorder. This calls for the need to make mood stabiliser medications, particularly lithium, widely available.

Bipolar disorder is also associated with a high level of functional impairment in several domains of functioning, including physical functioning. The magnitude of the impairment was predicted by the severity of manic and depressive symptoms. This again emphasises the need for providing adequate treatment.

**Gender and affective disorders**

Gender has been consistently found to be a key determinant of affective disorders although this is not the case for bipolar disorder. However, no clear or consistent pattern was identified for the role of gender in the prevalence or manifestation of minor depressive disorder and bipolar disorder in this study. The lack of gender influence on bipolar disorder is to be expected. The lack of gender difference in minor depressive disorder is consistent with studies from Africa on major depressive disorder (Kebede et al 2003; Bolton et al 2004; Gureje et al 2006).

Child bearing was a stressor relevant in the onset of bipolar disorder or for its relapse. This was found to be the case in four of the 12 cases from Zeway.

The association of manic relapse with the male gender and that of depressive relapse with the female gender was to be expected. Overall, the impact of gender on the manifestation or outcome of bipolar disorder was not striking.
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Appendix A

References for model in Figure 4


