Bipolar disorder in rural Ethiopia

Community-based studies in Butajira for screening, epidemiology, follow-up, and the burden of care

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To Emebet Hailu Woldegiorgis, for giving me more than beyond her imagination. She has always been to me an honest, a kind and amazing person who brought me up as a loving elder sister and as a mother, with lots of commitments and dedications to me as she brought me up replacing my mother since my early childhood and even as a father, as I lost my dad while I was a small kid, and finally for being instrumental for the materialization of this thesis, taking all my personal responsibilities together with her own personal life as a married woman, which means to me a lot. Her compassion toward severely mentally ill is amazing.
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Abstract


**Background:** The challenges of research in economically stunted countries’ settings remains a profound concern and is linked to socioeconomic development of these countries. More research is needed regarding psychiatric morbidity in rural areas of the developing and poverty stricken countries. The present studies were undertaken within the framework of a broader ongoing community-based project on the course and outcome of major psychiatric disorders in the rural Butajira district located in Ethiopia. This thesis treats the course and outcome of bipolar I disorder in the district.

**Objectives:** Through appraising mental health and population based research in a rural Ethiopian district, to evaluate the utility of modern research instruments, and to obtain baseline information relating to bipolar I disorder in the poverty stricken rural Butajira district of Ethiopia. The specific objectives were:
1. Evaluating and comparing two different screening methods of case detection and identification for schizophrenia and bipolar I disorder in the adult population of Butajira district.
2. Assessing the prevalence and clinical characteristics of of bipolar I disorder in Butajira at the community level.
4. Determining Neurological Soft Signs in community-identified cases of bipolar I disorder in Butajira district in comparison with healthy controls.
5. Assessing the burden of care among caregivers of those affected by bipolar I disorder identified in the Butajira Study.

**Methods:** The district’s entire adult population aged 15-49 was identified through a double-sampling design. In the first stage of screening, door-to-door interviews were conducted by lay trained high school completed individuals who knew the culture of the people. Females interviewed females whereas males interviewed males. Additionally, the key-informants method was used to identify cases that would be missed by the CIDI or otherwise. The final confirmatory diagnostic interview was conducted by clinicians using the SCAN on door-to-door basis as well. The probable cases that fulfilled the lifetime DSM-IV diagnosis of bipolar I disorder were assigned for assessment by other baseline research instruments such as Neurological Evaluation
Scale (NES), Young Mania Rating Scale, Hamilton Rating Scale for Depression, LCSS, PANS and SANS, BISS, BII, FIS and so on. Cases so identified with bipolar I disorder were subject to a follow-up for up to 2.5 years on the average (range 1 to 4 years). Two of the main clinical outcomes assessed were relapse to a mood episode, and remission from a mood episode. Outcomes were assessed annually by the instruments, and were further assessed monthly by trained psychiatric nurses. We also did a cross-sectional study of caregivers of bipolar I disorder cases, and assessed objective burden on the caregivers as considered from social, family strain, occupational and financial domains.

**Results:** Information provided by the key informants was better at detecting schizophrenia or chronic psychiatric disease, whereas the CIDI was better at detecting affective disorders. Of the around 100,000 adults living in Butajira, 83.3% were found by the project’s census, of which 82% (68,378 subjects) were successfully screened by the CIDI, yielding 2,161 CIDI positive. These, together with 719 cases identified by the key informants, were invited for the SCAN interview, of which 74.7% agreed. This yielded 315 SCAN positive cases for bipolar I disorder, and complete information could be collected on 295 of these. Lifetime prevalence was estimated as 0.6% for males and 0.3% for females. The mean age of onset of the manic phase was 22.0 years and that of the depressive phase was 23.4 years. For 22.7% of the cases the illness started with a depressive episode and for the remaining 77.3% it started with a manic episode. Over half of the cases (55.9%) had never sought help from modern health care sector, and only 13.2% had ever been admitted to psychiatric hospital. At follow-up, 65.9% had experienced a relapse and 31.1% had persistent illness, while only 5% of the patients were in remission for most of the follow-up time. The bipolar I cases, as compared with healthy controls, performed worse on several items of NES, thus having more neurological dysfunction compared to controls. Caregivers were largely (80.3%) first-degree relatives and spouses. Overall, 84% of the caregivers reported difficulties in at least one of the domains of family burden. Of these, 58.7% reported a severe degree of difficulties. Caregivers reported a high level of difficulties in intrafamilial relationships and social restrictions, disruption in earning a livelihood, and financial difficulties.

**Conclusions:** The prevalence of bipolar I disorder is comparable to the prevalences reported from other countries, and our findings support the cross-cultural validity of the concept of bipolar I disorder. Majority of the cases are not treated in contrast to that in the developed countries. The burden of care for the caregivers is substantial in the population studied.

**Key words:** Butajira, bipolar I disorder, screening, epidemiology, neurological soft signs, burden of care.
List of original papers

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


Acronyms

AA: Addis Ababa
APA: American Psychiatric Association
BII: Basic Information on the Informant
BISS: Basic Study on the Study Subject
CIDI: Composite International Diagnostic Interview
DALYs: Disability Adjusted life years
FIS: Family interview Schedule
GBD: Global Burden of Disease
ICD: International Classification of Diseases
LCSS: Life Chart Score Sheet
NES: Neurological Evaluation Scale
NSS: Neurological Soft Signs
SCAN: Schedules for Clinical Assessment in Neuropsychiatry
SPSS: Statistical Package for the Social Sciences
WHO: World Health Organization
YLD: Years Lived with Disability
Background

Mental disorders

Overview

Mental and physical health make up two fundamental ingredients of life that are intimately blended together and mutually interdependent. Since its Alma Ata Declaration in 1978, World Health Organization (WHO) defines good health as a state of complete physical, mental and social well-being and not as merely the absence of disease or infirmity.

Furthermore, various mental health experts have given a variety of definitions to mental health. Concepts of mental health include subjective sense of vivacity, perceived self-efficacy, autonomy, proficiency, intergenerational dependence, and self-actualization of one’s intellectual and emotional potential, among others. It is virtually impossible, however, to define mental health comprehensively because the concepts of mental health are diverse in different cultural contexts worldwide. Despite the differences in definitions as to what constitutes mental health, there seems to be an agreement among mental health experts that mental health is broader than a mere lack of mental disorders.

Progress in neuroscience and behavioral medicine has revealed that similar to many physical illnesses, mental and behavioral disorders are the outcome of complex interplay among biological, psychological and social factors. Scientific evidence from the branch of behavioral medicine has established a vital connection between mental health and physical health.

There are two known key pathways through which mental and physical health reciprocally shape each other. The first functional pathway consists of physiological systems that include the neuro-endocrine and immune systems. Anxious and depressed moods are recognized to initiate a surge of adverse changes in endocrine and immune functioning, and build up increased vulnerability to an array of physical illnesses (Spiegel et al. 1989; Ferketich et al. 2000). The second pathway includes health behavior and is expressed in activities such as nutrition, physical exercise, sexual practices, smoking, consumption of addictive substances, and adherence to prescribed medical treatment modalities. Young people, for instance, with psychiatric disorders like depression and substance dependence are more likely to engage in smoking and
high-risk sexual behavior, which increase the risk of physical illnesses (Spiegel et al. 1989; Kielcot-glaser et al. 1999; Ranrakha et al 2000).

The relationship between children and their parents or significant others during childhood are also important in that irrespective of other known risk factors, children denied of nurture could be more vulnerable to mental and behavioral disorders either in their childhood or later in life. Children need loving, thoughtful, and stable caring so that they are able to develop normally such functions as language, intellect, and emotional regulation. Children and adolescents learn through direct experience, through information, and by observing others which as learning later on could affect health behavior. Failure may be because of mental disorders, illness or death of significant others. Regardless of the specific cause, when children are deprived of nurture from their caregivers they are more likely to develop mental and behavioral disorders, either during their childhood or late in life.

Social factors like chaotic urbanization, poverty and rapid technological development are also important. The nature of modern time urbanization could have detrimental effects for the mental health through the influences of increased stressors and adverse life events like overcrowded and polluted environments, poverty and dependence on a cash economy, high levels violence, and reduced social support (Desjarlais et al., 1995). The association between mental health and poverty is fundamental as well. The relationship between poverty and mental health is multifaceted and multidimensional. The poor and the destitute have a higher prevalence of mental and behavioral disorders including substance use disorders. The higher prevalence may be explainable both by higher causation of disorders among the poor and by the drift of the mentally ill into poverty.

**Magnitude of mental disorders**

Recent analyses done by the WHO showed that neuropsychiatric conditions had an aggregate point prevalence of about 10% for adults worldwide (World Health Organization 2001). About 450 million people were estimated to be suffering from mental and related disorders. These conditions include unipolar depressive disorder, bipolar disorders, schizophrenia, epilepsy, alcohol and selected substance abuse disorders, Alzheimer’s and other dementias, posttraumatic stress disorder, obsessive compulsive disorder, panic disorders and several others (World Health Organization 2000).

Surveys conducted in developed as well as in poverty stricken countries indicate that during the entire lifetime, more than 25% of individuals develop one or more mental
or behavioral disorders (Regier, et al. 1988; Wells et al. 1989; Almeida-Filho, 1997). Most of these studies have found the overall prevalence of mental disorders to be about the same among men and women, although there may be differences in the distribution of the specific disorders within each gender. Notably, depressive disorders are significantly more common among women, whereas substance abuse disorders are more common among men.

Mental disorders in primary health care settings

The cross-cultural study conducted by WHO at 14 sites (Goldberg & Lecrubier 1995; Ustun & Sartorius 1995) showed that 24% of all patients in the studied settings had a mental disorder. The most common diagnoses in primary care settings were depression, anxiety, and substance abuse disorders (Cho, Nam et al. 1998; Kessler, Berglund et al. 2003; Cho et al. 2007; Lee et al. 2007; McCrone et al. 2007). These disorders were found to be present either alone or in combination with one or more physical disorders.

The high prevalence of depression in primary care setting could in part be due to the contribution of bipolar spectrum disorders. Patients with these latter disorders do not complain of the hypomania they have experienced, but complain only about their depressive symptoms. Not uncommonly, their hypomania often is not recognized even by their relatives as illness. Thus, the prevalence of depression in primary care setting could include a contribution from bipolar II disorder, which poses a challenge for diagnosis even among the expert community (Akiskal 1996). By the same token, the relatives of patients with bipolar I disorder having more frequent but less severe or sparsely distributed episodes of mania, might not be seen as abnormally changed mood state related to illness but could mistakenly be attributed to the patient’s misbehaviour. Therefore, these patients are brought to primary care setting only when he or she is depressed. When in the hypomanic or manic state, these patients often experience pleasure and optimism with lots of energy, as a result of which they not considered by themselves or by others as being in a state of illness with potentially serious consequences. Similarly, patients with a state of dysphoric or agitated depression experienced during a mixed bipolar II or bipolar I episode could be mistaken as a unipolar agitated depression (Benazzi 2004; Akiskal et al. 2005; Kiejna et al. 2006; Benazzi, 2007), leading to treatment by antidepressives rather than by mood stabilisers.

Psychiatry is undergoing very rapid development both as a clinical discipline as well as in scientific research. As a result, there has been substantial progress in identifying and delineating suitable criteria for various diagnostic categories based on empirical
evidence, as witnessed in the successive revisions of the DSM and ICD diagnostic systems. However, due to the complexities inherent in the discipline of psychiatry, an increasing awareness regarding the limitations of nosology has also emerged. For instance, the delineation between the disorder of major depression from the multifaceted manifestations of the bipolar spectrum disorders becomes problematic.

This is particularly relevant for countries like Ethiopia where integration of the mental health services has come to the forefront in government agenda, whose ambition is to expedite the integration of mental health services into the existing primary healthcare system. The goal is to offer training to upgrade the proficiency, with respect to mental health care, of the nursing staff and health officers at the primary health care level.

Impact of mental disorders

Mental disorders and related conditions have a huge impact on the affected individuals themselves, on their families, and in their communities. These affected persons have to endure the difficult symptoms manifested by these disorders. They also suffer for not being able to involve themselves in vocational or leisure activities, often owing to stigma and discrimination. They worry about not being able to bear their responsibilities towards their families and friends, and they are afraid of being a burden to the others.

It has been estimated that at least one family in four has a family member suffering from a mental or behavioral disorder at any point in time (World Health Organization 2001). The family members of the affected individuals are required not only to provide physical and emotional support, but also to bear the brunt of stigma and discrimination which is present worldwide. The available evidence regarding the burden of care suggests that it is extensive (Pai & Kapur 1982; Fadden et al., 1987; Winefield & Harvey, 1994; Ogilvie, 2005). Burden includes economic difficulties, emotional reaction to the illness, the stress of coping with disturbed behavior, the disruption of household chores, and restriction of social activities. The expenditure for the treatment of the mental illness is often borne by the family members particularly in the economically disadvantaged part of the world; the treatment costs are incurred to access treatment at the traditional healing centers, or at poorly staffed mental health service provision centers located far away and with poor facilities.

Besides the direct burden discussed above, also indirect forms of the negative consequences of mental disorders are considerable. Families, in which their beloved family member suffers from a mental disorder, make numerous adjustments and
compromises that impede the other family members from attaining their full capacity at work, in social relationships and leisure activities, and their health is affected as well (Gallagher & Mechanic 1996). These are the human components of the burden of mental disorders, which are difficult to appraise and quantify even though they are important aspects of human suffering. Family members often have to spend a major part of their time to look after their beloved mentally ill relatives, and they suffer an economic and social deprivation since they are not fully productive. They also endure fear of anticipated re-emergence of the illness in the patient and expect abrupt and unforeseen disruption of their lives.

The impact of mental disorders in the community is substantial and diverse. There is a cost in providing care, the loss of productivity, and some legal problems associated with mental disorders including violence incidents. One specific kind of the burdens is the health burden. This has traditionally been measured only in terms of incidence/prevalence and mortality. While these measures are well-suited for acute manifestations of diseases whose ultimate consequence is either death or full recovery, the utilization of these measures for assessing the burden of chronic and disabling diseases has serious limitations. This is the case for mental and behavioral disorders in particular, which more frequently cause disability rather than immediate death. One way to evaluate the chronicity of disorders and the disability caused by them is the Global Burden of Disability (GBD) methodology (Murray and Lopez 1997a, b, c; Mathers et al., 2000, 2001). In the initial estimates developed for 1990, mental and neurological disorders accounted for 10.5% of the total DALYs lost due to all diseases and injuries (Murray and Lopez, 1997). This rate displayed for the first time the high burden due to these disorders. The corresponding estimate for 2000 was 12.3% of the total DALYs. Three neuropsychiatric conditions rank among the top twenty leading causes of DALYs for all ages. In the age group 15-44 years, six neuropsychiatric conditions rank among the top twenty, namely unipolar depressive disorders, alcohol use disorders, self-inflicted injuries, schizophrenia, bipolar disorders and panic disorder. In the calculations of DALYs, the latest estimate from Australia has placed mental disorders as the leading causes of disability burden (Mathers et al., 2001). From the analysis of trends, it has become evident that this burden will increase to 15% in the year 2020.

Taking the disability part of health alone, GBD 2000 estimates show that mental and neuropsychiatric conditions account for 30.8% of all years lived with disability (YLDs). In actual fact depression causes the largest amount of disability, accounting for 12% of all disability. Six neuropsychiatric conditions listed in the top twenty causes of disability (YLDs) worldwide include unipolar depressive disorders, alcohol use
disorders, schizophrenia, bipolar I disorder, Alzheimer’s disease and other dementias, and migraine.

The disability caused by mental and neurological disorders is high in all regions of the world. However, as compared to the developed countries, this disability constitutes a lesser proportion of the total disability in developing countries, mainly because of the huge burden of communicable, maternal, perinatal and nutritional conditions in those regions. Nonetheless, neuropsychiatric disorders cause 17.6% of all YLDs in Africa (World Health Organization, 2001). The contribution of maternal depression to child mortality rate does not seem to have been given adequate and timely attention.

**Economic costs to the society**

The economic impact of mental disorders is all-embracing, ongoing and huge. These disorders demand a variety of costs on individuals, families and communities. Part of this economic burden is evident and measurable, while a part of it is almost not feasible to measure. Among the measurable components of the economic burden are health and social service needs, lost employment and diminished efficiency, impact on families and caregivers, and the negative impact of premature mortality, levels of crime and public safety.

**Quality of life**

Mental and behavioral disorders cause substantial interference in the lives of those who are affected and in their families. Though the whole range of misery and anguish is not measurable, one of the methods to evaluate its impact is by using quality of life (QOL) instruments (Lehman et al., 1998). A number of studies have reported their findings on the quality of life of individuals with mental disorders, concluding that the negative impact is not only extensive but unrelenting (UK700 Group, 1999). It has been shown that QOL persists to be poor even after improvement from mental disorders because of social factors that include sustained stigma and discrimination.

The Toll of human suffering from mental disorders and the brunt born by the affected individuals, their significant others and the society at large is compounded by the fact that mental disorders are common, have much earlier ages of onset than most chronic physical diseases, have high rates of chronicity victimizing the affected individuals to high risks of impairment and disablement, and by their low rate of treatment. It is believed that all these make them the most burdensome illnesses of mankind (Kessler et al., 1997).
Risk factors for mental disorders

A variety of factors determine the prevalence, onset and outcome of mental and behavioral disorders. These include social and economic factors such as gender and age, serious threats such as conflicts and disasters, the presence of major physical diseases, and the family environment.

Poverty

Poverty and poverty-related conditions such as unemployment, low educational level, deprivation and homelessness are widespread not only in poor countries, but also affect a sizeable minority of the rich countries. Data from cross-national surveys in Brazil, Chile, India, and Zimbabwe show that common mental disorders are about twice as frequent among the poor as among the rich (Patel et al., 1999). In the USA, children from the poorest families were reported to be at increased risk of disorders in the ratio of 2:1 for behavioral disorders and 3:1 for comorbid conditions (Costello et al., 1996). A review of 15 studies found the median ratio for overall prevalence of mental disorders 2.1:1 for one year and 1.4:1 for lifetime prevalence between the lowest and the highest socioeconomic classes (Khon et al., 1998). Similar results have been reported from recent studies carried out in North America, Latin America and Europe (WHO International Consortium of Psychiatric Epidemiology, 2000).

There is also evidence that the course of mental disorders is determined by the socioeconomic status of the affected individuals (Kessler et al., 1994; Saraceno & Barbui, 1997). This could at least partly be an effect of service-related variables, including barriers to accessing health services. Poor countries have few resources for mental health care and these resources are often unavailable to the poorest sections of every society. Even in affluent countries, poverty and associated factors such as lack of insurance coverage, lower levels of education, unemployment, and the racial, ethnic and linguistic minority status create insurmountable barriers to obtaining care. In addition, poor people often have higher mental health concerns when seeking treatment for physical problems.

On the other hand there is also a question of which of several factors that link mental health with poverty. Poverty and mental disorders are twin evils when considering circumstances prevailing in the poverty stricken parts of the world. Although the relationship between mental and behavioral disorders (including those related to alcohol abuse) on the one hand, and the economic development of communities and
countries on the other hand has not been explored in a systematic way, it appears, however, that the vicious cycle of poverty and mental disorders at the family level may well be operative in strongly influencing and reinforcing each other at the community level as well.

In the Butajira setting, for instance, only 2% of the cases perceived their neighbourhood as being above the average of the catchment area in terms of socio-economic level, whereas about 20% perceived their neighbourhood as belonging to the socio-economic level below that of the average of the catchment area. Despite such perceived categorization by the study subjects, these differences could hardly be appreciable to that extent for outsiders coming to Butajira by any means. Therefore, though we didn’t make any objective assessment of the socio-economic status of the cases and their relatives, we could infer from our field studies and from our observations how poverty stricken the district is and how psychiatric disorders in such a setting could further lead to downhill deterioration of the QOL of those affected and their significant others.

**Gender**

There has been an increasing interest to study gender differences regarding the prevalence, risk factors, and the course of mental and behavioral disorders. A community study using sound methodology has revealed some interesting differences (Gold, 1998). The overall prevalence of mental disorders does not seem to be different between men and women. However, by the currently accepted nosological classification, anxiety and depressive disorders are more common among women, while substance use disorders and antisocial personality disorder are more common among men. Many studies revealed a higher prevalence of depressive and anxiety disorders among women, the usual ratio being between 1.5:1 and 2:1. These findings have been reported in both developed and in a number of developing countries (Patel 1999).

Many factors have been incriminated for the higher prevalence of depressive and anxiety disorders among women. Of course, one cannot deny that genetic and biological factors have some role in the contribution in this regard. This is reflected in particular by the close temporal relationship between higher prevalence of these disorders and reproductive age range with related hormonal changes. Dysphoria related to hormonal changes as part of the menstrual cycle and just after childbirth is a well documented phenomenon. Indeed, depression within a few months of delivery of child can be the beginning of a recurrent depressive disorder. Psychological and social factors are also other significant contributors for the gender differences in depressive
and anxiety disorders. Even in bipolar disorders women suffer more from depressive and mixed episodes compared with men whereas men tend to suffer more from manic episodes. On the other hand, there may be more actual and perceived stressors among women. The traditional role of women in societies exposes them to a greater stress as well as makes them have lesser possibilities to change their stressful environment.

An additional factor for the gender differences in the distribution of common mental disorders is likely to be the high rate of domestic and sexual violence to which women are exposed. Domestic violence is found in all regions of the world and women bear the major burden of it as victims (WHO, 2001). A WHO multi-country study on women's health and domestic violence found that lifetime prevalence estimate of domestic violence is 15%-71% (Claudia Garcia-Moreno, 2003; World Health Organization, 2005). Sexual violence is also common In general, the percentage of women who reported sexual abuse by a partner ranged from 6% in Japan and Serbia and Montenegro to 59% in Ethiopia, with the majority of settings falling between 10% and 50% in their life (World Health Organization, 2005). These traumatic events have psychological consequences, depressive and anxiety disorders being the most common. A Nicaraguan study found that women with emotional distress were six times more likely to report spousal abuse compared with women without such distress (Ellsberg et al., 2000), which further underscores the importance of the problem. Moreover, women who had experienced severe abuse during the preceding year were 10 times more likely to experience emotional distress than women who had never experienced abuse. Abuse against women is also a strong stressor that might pave a way for the development or triggering of major psychiatric disorders such as major depressive disorder, bipolar disorder (I or II) and schizophrenia, resulting in subsequent disability, at least in those who are vulnerable to these disorders.

Age

Age is an important correlate of mental disorders. Overall, the prevalence of some disorders tends to rise with age. Predominant among these is the depressive disorder. Depressive disorder is common among elderly people. Studies show that 8-20% of the elderly being cared for in the community and 37% of those being cared for at the primary level are suffering from depressive disorder. A study on a community sample of people over 65 years of age found depression among 11.2% in this population (Newman et al., 1998). Another study, however, found the point prevalence of depressive disorders to be 4.4% for women and 2.7% for men, although the corresponding figures for lifetime prevalence were 20.4% and 9.6%. Depression is more common among older people with physically disabling disorders (Katona & Livinstone, 2000). The presence of depression further increases the already existent
disability among this population group. Typically, depressive disorders among elderly people go undetected more often than among younger adults because their symptoms are often mistakenly attributed as part of the aging process.

Nonetheless, there is also a concern for a significant burden of mental disorders in general among the younger population. In a recent Surgeon General’s report in USA (DHHS 2001), a concern about a public crisis that the USA is facing in mental health of infants, children, and adolescents has been expressed. According to this report, around 10% of the young people suffer from mental illness severe enough to cause some level of impairment, yet fewer than one in five receive treatment. The situation in the so-called developing countries is apparently worse as there is no awareness at large.

The overall prevalence of mental and behavioral disorders among children has been studied in developed as well as in developing countries. It appears that 10-20% of all children have at least one mental or behavioral problem. Severe psychiatric disorders like bipolar I disorder and schizophrenia start at an early age, from early teens to early adulthood, affecting the youngest segments of population who are preparing to enter the labor force or who are planning to attend or attending higher education, or are already employed after higher education. In short, these disorders target the productive section of any society affecting their participation in different social responsibilities. Therefore, these psychiatric disorders could be described as a sword with two sharp edges, one directed toward the affected person and his or her significant others, and the second one directed towards the society at large. Mental and behavioral disorders of childhood and adolescence are very costly to the society in terms of human suffering as well as in financial aspects.

**Conflicts and disasters**

Conflicts, including wars, civil wars and man-made disasters affect a large number of people, and they result in severe trauma, displacement, and subsequently lead to increased mental problems. Globally, over 60 million people are estimated to be refugees and internally displaced and globally their number seems to be growing. Each new natural or man-made disaster forces out more people from their homes. Displaced people, no matter what the cause of their displacement, confront health and social challenges that others never experience. They lose partners, children, parents, and the security that comes with stable community life. Women and girls are exposed to the risk of sexual violence and exploitation, and in the chaos that follows all disasters, lose whatever access to health and social services they may have had.
Furthermore, millions of persons every year are affected by natural disasters including earthquakes, floods, typhoons, hurricanes and large-scale calamities (IFRC, 2000). Such disasters take a heavy toll on the mental health of the people struck by these catastrophes. Most of the affected victims live in economically stunted countries, where capacity to deal with these problems is extremely limited. Thus, between one-third and one-half of all the persons are affected and suffer from mental distress. The most frequent diagnosis they give rise to is post-traumatic stress disorder, frequently together with depressive disorder or anxiety disorders. Conflicts, wars and natural disasters might serve as a fertile ground for the onset of serious psychiatric conditions like bipolar I or II disorders, schizophrenia and major depressive disorder.

**Major physical diseases**

The occurrence of major physical diseases affects the mental health of individuals as well as of entire families. Most of the seriously disabling or life-threatening diseases, including cancers in both men and women, have this impact.

HIV has been spreading at a shocking rate in many parts of the world. At the end of 2000, a total of 36.1 million people had been victims of and living with HIV/AIDS and 21.8 million died of it (UNAIDS, 2000). Of the 5.3 million new victims of this infection in 2001, 10% were children and about half were women. More than 10% percent of the reproductive age population of 16 countries of Sub-Saharan Africa is currently a victim of HIV infection. The HIV/AIDS pandemic has further lowered economic growth and as a result of this grave situation life expectancy has been reduced by upto 50% in the hardest hit countries. In many countries HIV/AIDS is now considered as a danger to national security. With neither cure nor vaccine, prevention remains crucial response, with care and support for those infected with HIV offering a vital entry point.

The mental health outcomes of this epidemic are varied. A proportion of individuals suffer psychological consequences (disorders as well as distress) as a result of being infected. The effects of intense stigma and discrimination against people with HIV/AIDS also play a major role in psychological distress. Disorders range from anxiety or depressive disorders to adjustment disorders (Maj et al., 1994). Cognitive defects are also detected if due attention is given to it (Maj et al., 1994; Starace et al., 1998). In addition family members also suffer the consequences of stigma and of premature death among their infected family members. The psychological effects on members of families thus broken and children thus orphaned are likely to be extensive. Furthermore, the very nature of the psychiatric disorders like bipolar I disorder puts these individuals at high risk to contracting HIV/AIDS (Rahav et al., 1998; Hutton et
al., 2001; Lykins et al., 2006; Klein et al., 2008). The same is true for patients with schizophrenia who, though they are sexually passive most of the time, could contract the illness by being raped or exploited because of their poor judgment or unawareness of the consequences of the act itself. On the other hand, the very fact that one knows he is infected by such serious medical illnesses is a strong stressor leading to the development of serious psychiatric illnesses such as bipolar I, disorder Major Depressive Disorder in predisposed individuals and early onset dementia as a direct effect of the HIV virus in the brain.

These complex interplays whereby a physical illness leads to psychosocial consequences for individuals, families and community levels and, on the other hand, high risk behaviours or mental illnesses have a potential to make people victims of the HIV epidemic requires a holistic approach in assessing this public health problem in order to determine its impact on the society so that to put in place relevant guidelines for intervention.

**Family and environmental factors**

Mental disorders are firmly rooted in the social environment of the individual. Social factors influence the onset, course, and outcome of psychiatric disorders. People go through a series of significant events in life, minor as well as major. These may be wanted or unwanted life events. It has been observed that there is an accumulation of life events immediately before the onset of mental disorders (Brown et al., 1972; Leff et al., 1987), even though unwanted events predominate before the onset or relapse of depressive disorders. A higher occurrence of all events pave the ways also for other mental disorders. Studies suggest that all significant events in life act as stressors and, coming in quick sequence, predispose the individual to mental disorders. This effect is not limited to mental disorders and has also been demonstrated to be associated with a number of physical diseases such as myocardial infarction. Of course, life events are only one of several interacting factors (such as genetic predisposition, personality, and coping style) in the causation of disorders.

The relevance of life events research lies mainly in identifying individuals who are at a higher risk because of experiencing major life events in quicker succession. Initially this effect was observed for depressive disorder and schizophrenia, but subsequently an association has been found between life events and a variety of other conditions including bipolar I disorder as well as suicide.

The social and emotional environments within the family also play a role in mental disorders. Although attempts to link serious mental disorders such as bipolar I and
depressive disorders to the family environment have been made for a long time (Fadden et al., 1987; Kuipers et al., 1990; Perlick et al., 1999), some definitive advances have been made in the recent past. There is a clear correlation between the family social emotional environment and the relapse in schizophrenia or the onset of major depressive disorder (MDD) and bipolar I disorder. Initial observations had suggested that patients with schizophrenia who went back to stay with parents after a period of hospitalization relapsed more frequently. This led to some research on the cause of this phenomenon. Most studies have used the concept of “expressed emotion” of family members toward the individual with schizophrenia. Expressed emotion in these studies has included critical comments, hostility, and emotional over-involvement (Butzlaff et al., 1998).

A large number of studies from all regions of the world have demonstrated that expressed emotionality can predict the course of schizophrenia including relapses. There is also evidence that changing the emotional environment within the families can have an additive effect on prevention of relapses by antipsychotic drugs. These findings are useful for improving the care of selected patients within their family environment and also to recall the importance of social factors in the course and treatment of severe mental disorders.

**Ethiopia: Mental health and psychiatric services**

**General description of Ethiopia**

Ethiopia is one of the largest countries in Africa with an area of more than one million square kilometers. After cessation of its previous province Eritrea, it has become one of the few landlocked African nations. Ethiopia is situated in the horn of Africa bordering Djibouti in the east, Somalia in the south east and south, Kenya in the south, Sudan from Northwest to South West, and Eritrea in the North. Over 85% of its population lives in rural areas. Ethiopia has a federal democratic republic government composed of 9 National Regional States (NRS) and two administrative councils. Regional divisions are mainly ethnic based.

Ethiopia is one of the oldest countries in the world which is an independent state and has never been colonized. Until the 1974 coup by the military junta, Ethiopia was a monarchy. Following the Coup, all the imperial institutions were abolished and a pro-Communist state was established in 1975 by the junta. Subsequently, the Ethiopian People’s Revolutionary Democratic Front’s (EPRDF) long armed struggle overthrew
the 17-year military junta dictatorship in 1991. After the 1991 victory by the EPRDF a transitional government of Ethiopia was established and afterwards in 1995 the EPRDF became the ruling party of the Federal Democratic Republic of Ethiopia.

Topographically, Ethiopia is mainly divided into the highland plateau, the Great Rift Valley, and lowland areas. Altitude ranges from 116 meters below sea level in the Danakil depression to 4,620 meters at the peak of Mount Ras Dashen, Africa’s fourth highest peak. Geographically, Ethiopia is called a roof of Africa as it contains approximately 85% of the highlands and 50% of the mountains. The climate is predominantly that of tropical type, but it is mainly influenced by the altitude. Thus, highlands and mountainous areas have more temperate climate. Most of the towns are established in highland areas and the population density is also the highest in the highlands of the country. The central and larger part of the country, where the majority of the population lives, is an elevated plateau varying in height between 2000 and 3000 meters above the sea level (Kloos 1993). The lowland areas are located mainly in the northeast, southeast, south, and southwest parts of the country. Climatic conditions in Ethiopia are characterized by frequent irregularities leading to drought and famine for the past many years.

According to the 2007 Census the country is inhabited by nearly 80 million people, of whom 45% are below 15 years of age, making it the second most populous nation in Africa following Nigeria. The average population density is 49 per square kilometer. Ethiopia is also among the least urbanized countries of the world with less than 14% of the country urbanized as of 1994. Orthodox Christianity and Islam are the major religions. The official language of the country is Amharic; however, some NSRs have their own local official languages (HSDP 1998, Health Indicators 1999). The life expectancy is 53.5 years for females and 50.9 years for males. The country is a home for about 80 ethnic groups with their respective population varying from 18 million to less than 100 (CSA 1998), and more than 80 different languages are spoken in the country.

Demographic and Health Survey (DHS) began in the country in 2000 with aim of providing the latest and reliable data on fertility and family planning, child mortality, children’s nutritional status, utilization of maternal and child health services and knowledge about HIV/AIDS (Yeman Berhane). According to this survey, 62% of males and 77% of females are illiterate; less than one-fifth of the households have access to piped drinking water; More than three-fourth of the households do not have toilet facilities. Furthermore, the survey revealed that one-fourth of the women of childbearing age died from pregnancy or pregnancy-related conditions. Maternal mortality was 871 deaths per 100,000 live births for the period 1994-2000. Neonatal
mortality rate is 49 per 1000, infant mortality rate is 97 per 1000 and under-five child mortality rate is 166 per 1000 live births (CSA 2000a). At the end of 2000, there were an estimated 2.6 million Ethiopian citizens living with HIV/AIDS, of whom 250,000 were children below the age of 5 years. The cumulative number of deaths from the time of the recognition of the epidemic was estimated at about 1.2 million in 2000, and was predicted to increase to 1.7 million by year 2002 (MOH). However, the effect of parental, particularly maternal mental illness on the children’s physical as well as mental health and its long-term effect in the long-term is a neglected and not researched area.

Agriculture is the backbone of Ethiopian Economy and it accounts for 54% of the Gross Domestic Product (GDP). For about 80% of the country’s population, agriculture is the mainstay of living. The main export farm products are coffee, hide and skin and oil seeds. The prolonged civil war and centrally commanded economic system in the period before 1991 resulted in a catastrophic economic situation with steady annual deterioration in the GDP. With economic re-structuring after 1991 the economy was reported to be stabilizing with a downward trend of inflation, which was hoped to be eliminated after 1998 (HSDP 1998). However, the last conflict with Eritrea could have a backlash on the staggering economy. Though the economy is said to be recovering, the structural adjustment programs, increasing privatization, uncontrolled inflation, global environmental change and rising food prices have awfully been widening the gap between the poor and the rich within the country. A significant proportion of the country’s population has been sinking in poverty and the country is one of the least developed nations of the world with per capita Gross National Product (GNP) of not more than US $100. Because of this, an outmigration to the developed part of world and to Arab countries has become commonplace for survival.
Need for epidemiological field studies

In Economically disadvantaged countries, one of the most important challenges in developing effective public health intervention programs in mental health, is a paucity of information regarding the magnitude of the specific mental disorders and the factors influencing their occurrence, and the potential effectiveness of the various intervention alternatives. In many of these countries, available data are derived from health services that are limited and biased towards non-psychiatric disorders. Moreover, the reporting system in Ethiopia still in operation is the oldest one that categorizes the psychiatric disorders as follows: 1) psychoses; 2) neuroses; 3) other neuropsychiatric disorders; and 4) epilepsy. Such a classification approach does not meet the current nosological advances and hinders studying diagnosis-specific magnitude of psychiatric conditions and its repercussions, thus making difficult informed decision in reorienting public health focus in a dynamic environment.

In order to make significant impacts on the health of a population, decisions should be based on evidence obtained from studies using valid scientific methods. Such information should ideally be obtained from community based studies. Epidemiology, being a discipline devoted to the study of the frequency, distribution and determinants of health related events in human populations that guide appropriate intervention, is the appropriate major public health tool world-wide. As the discipline gains experiences and techniques from the social science arena, it draws and provides a holistic examination of public health problems, adding a socio-cultural dimension in its description and reasoning.

Health problems that are prevalent in economically disadvantaged countries result from many complex and often inter-related adverse conditions. Thus, any intervention that does not take into consideration this complexity is bound to fail. As these countries have very limited resources to expend, good evidence-based decision is more critical here than anywhere else.

The need for evidence-based health planning and policy based on information about the onset, course and outcome of major psychiatric disorders justifies the creation of field laboratories like those in other fields (Tollman, 2000). Field sites are believed to provide a fertile ground for a variety of health, social, behavioral, and intervention studies.

This potential of a field site has been exploited in the Butajira Study on Course and Outcome of Schizophrenia and Bipolar Disorders Project catchment area, on which the present thesis is based. Our research on Bipolar I disorder aims to shed some light into
the very broad public health challenge of this country. It attempts to provide baseline
information that influences mental health in rural Ethiopian context, addresses
methodological issues, and the effect of the illness on healthy household members.

**Epidemiology of mental health in Ethiopia**

Studying community samples is especially important, since the majority of people
with mental disorders do not seek treatment for their psychological distress. Concentrating on clinical populations alone overlooks many who suffer from the most
common psychiatric disorder. Results from a number of large-scale studies support the
notion that psychiatric disorders are common in the general population. The National
Institute of Mental Health, Epidemiological Catchment Area (ECA4) survey, and
National Comorbidity Study (NCS5) are such studies that have shaped mental health
policy and practice to a great extent in the USA. The OPCS National Psychiatric
Morbidity Survey in Great Britain, Taiwan’s Community Survey of minor psychiatric
morbidity, and the Shatin Community Mental Health Survey in Hong Kong, have
similarly provided invaluable mental health related data for their respective countries.

When it comes to Ethiopia, Professor R. Giel, an expatriate psychiatrist from the
Netherlands who worked in the 1960s in Ethiopia, conducted hospital and community-
based studies on the prevalence of mental disorders. He reported the first batch of
information regarding the magnitude of these disorders in the country. In one of these
studies, it was reported that at a general hospital outpatient clinic in Addis Ababa
(AA), psychiatric morbidity was found in 18% of the patients, and it was the second
largest morbidity following gastrointestinal conditions (Giel & van Luijk, 1968). The
majority of his study subjects reported unexplained physical somatic symptoms that
could not be explained by general medical check-up and laboratory investigations.
Another study conducted in a regional hospital outpatient clinic in Jimma town,
western Ethiopia, came up with the result of 6.8% of the morbidity of mental disorders
(Giel & van Luijk, 1968). A similar study was conducted in the Police Force Hospital
in AA and its results showed that of the attendants of the clinic, 16.2% had psychiatric
morbidity.

Another expatriate psychiatrist from Sweden working at Nekemt hospital, also in
western Ethiopia (Jacobsson, 1985a), reported 18% prevalence of psychiatric disorders
among outpatient clinic attendants. A ten-year (1960-1970) retrospective inpatient
analysis from this hospital showed that every year, 0.7-2.3% of the inpatients had
psychiatric diagnosis (Jacobsson, 1985b). There were also rural village studies at
around the same period. The results of the studies were similar to the results reported
worldwide at that time. These surveys were followed by a number of other studies.
Subsequent studies started to use WHO prepared screening and diagnostic instruments. The first of such instruments to be used was the Self Reporting Questionnaire (SRQ). Kortman & Horn (1988) were the first expatriate psychiatrist to use SRQ among literate adult population in AA. A collection of review articles about mental health in Ethiopia was published in a special issue (Acta Psychiatrica Scandinavica, 1999, Vol 100, Supplement No 397).

The mid 1990s and the following years were marked by research endeavours using the latest WHO diagnostic instruments for community-based studies and studies in clinical settings. This was followed by simultaneous use of other relevant diagnoses-based instruments to obtain relevant information on baseline and follow-up data. This was facilitated by the establishment of collaboration among the Departments of Community Health and Psychiatry at Addis Ababa University, the Amanuel Psychiatric Hospital in Addis Ababa, and the Department of Psychiatry at Umeå University in Sweden. The main diagnostic instruments used since then have been the Composite International Diagnostic Interview (CIDI) and the Schedule for Clinical Assessment in Neuropsychiatry (SCAN). These two diagnostic instruments were translated into Amharic language (the national language of the country) and reliability tests were done. CIDI has also been translated into Oromifa, the second mostly spoken language in Ethiopia. Another diagnostic instrument used during this period has been the Diagnostic Interview for children and Adolescents (DICA), which has also been translated into Amharic language.

The first study in Ethiopia using CIDI was conducted in AA on a sample of 512 adults by Rashid et al. (1996). They found a prevalence of 13.6% for mental disorders. In their study 2% of their sample fulfilled DSM-III-R diagnostic criteria for psychotic disorders. In a subsequent study, a sample of 1420 individuals aged 15 and above were assessed for psychiatric disorders employing the CIDI. According to this study, the weighted lifetime and one-month prevalence of schizophrenia and schizoaffective disorders, respectively, were 0.4% and 0.3% for schizophrenia and 0.5% and 0.4% for schizoaffective disorders. The weighted lifetime and one-year prevalence of affective disorders was 5.0% (for women 7.7% and men 3.2%) and 3.8% (for women 5.9% and men 3.8%).

Studies were also conducted in one of the districts lying 132 kilometers south of AA. One of such study assessed 501 subjects using CIDI and reported an aggregate weighted life prevalence of 31.1% for psychiatric morbidity. The most frequent diagnosis found in this study was dissociative disorders and the study did not detect any psychotic disorder. In a survey conducted on a sample of 10468 adults from rural
and semi-urban areas of the same district, lifetime suicide attempt was reported by 3.2% of the studied individuals. The corresponding lifetime prevalence of suicide attempt for the sample of 10,203 individuals from AA was 0.9%.

Alem et al (1999a) also assessed the prevalence of alcohol and khat use in Butajira district. The CAGE questionnaire was used for screening consumption of both substances. In this study, alcohol drinking was reported by 36% of the men and 15% of the women. They found that the overall prevalence of problem drinking was 3.7%. The lifetime prevalence of khat consumption was found to be 55.0% whereas the prevalence of current khat consumption was 50.0% in the same study. In a study using CAGE in AA, it was found that 2.7% of the studied subjects met the criteria for problem drinking.

Epidemiological studies in Ethiopia have not restricted themselves to studying only adult psychiatric morbidity. Studies on mental and behavioral disorders in children have been also carried out for the last more than 10 years. The studies were made possible by translating DICA into Amharic language with the collaboration of Department of Community health and Amanuel Psychiatric Hospital. A first study was conducted in Butajira on a sample of 1447 children to estimate the prevalence of childhood disorders in the community (Ashenafi et al. unpublished). The prevalence of mental disorder among this group was 3.5%. A second study was carried out in one of the districts in AA to see the impact of child labor on children’s mental health (Fekadu, Alem & Hägglöf, 2006). The sample size of this study was 528 child laborers compared with 472 in the control school children, all within the age range 5-15 years. This study showed an aggregate prevalence of any DSM-III-R childhood emotional and behavioral disorders to be 20.1% in the child labor group and 12.5% in the control group.

**Psychiatric services in Ethiopia**

Psychiatric services in Ethiopia started in the only psychiatric hospital in the country located in AA, today known as Amanuel Hospital. This hospital was constructed by Fascist Italy for general purposes during its five-year occupation of the country from 1936-1941. Since the defeat of the Italians, the hospital has been functioning as a mental hospital. The hospital was under the Ministry of Interior Affairs and the Red Cross society until 1948. Under the Ministry of Health (established in 1948) it was first incorporated with Menelik II Hospital, but sometimes thereafter, it started to function as an independent mental hospital given the name from the adjacent Orthodox Christian Church, namely Amanuel Church. For many years it served as an asylum for confining the severely mentally ill. From the late 1960s psychiatric services were
given only by foreign professionals working at Amanuel Hospital and at the University Department clinic in St. Paul’s hospital.

Until 1987, there were only two Ethiopian psychiatrists in the country. Since 1987, psychiatric nursing training was started that marked a breakthrough in mental health service in the country. At present, services are provided by more than 70 centers throughout the country by trained psychiatric nurses. In the 1990s the number of psychiatrists increased to six. At present there are 30 psychiatrists in the country, making a psychiatrist population ratio of one psychiatrist serving about three million people. The number of psychiatrists started to increase since postgraduate training in psychiatry was commenced some years back. However, the insufficiency in mental health service provision in terms of quantity and quality will continue for years to come despite the modest and encouraging changes taking place currently in the country in this respect.

Although there are more than one hundred psychiatric nurses working in different parts of the country, their attrition rate has been increasing as they look for better career opportunities since there has been no established opportunities for career development in the field. Also, they are poorly supported by the Ministry of Health and regional health bureaus, and they are ineffectively supervised, and they work alone for years perhaps with frustration. This trend seems to have started to change lately as the government has become more interested in developing mental health services in the country and in training middle level health professionals at the Bachelor’s and Master’s levels. This ambitious plan is likely to change the face of psychiatric services in the country in the near future.

The main psychiatric service is outpatient service, which is provided at all psychiatric centers. Inpatient service is provided mainly by Amanuel Hospital for civilians and at Armed Forces Hospital for the army. Amanuel Hospital has 350 psychiatric beds for the whole country, whereas the Army Hospital has 30 psychiatric beds. The specialty clinics in psychiatry are also emerging at Amanuel and St. Paul’s Hospitals, though they are still in their early stages of development. The Department of Psychiatry at St. Paul’s Hospital has units for substance use disorders and for child psychiatry. Their emergence was fostered by the starting of the postgraduate training program in psychiatry 7-8 years ago.

In Amanuel Hospital substance use disorder related treatment unit and a unit for forensic psychiatry are fully functional. Other specialty clinic like mood disorders clinic or lithium clinic are planned to start in the near future.
Bipolar spectrum disorders

Overview

Bipolar disorders (BPD) (alternatively known as bipolar affective disorders or manic-depressive illness) are one of the most severe forms of mental illnesses and are characterized by swinging moods. They are devastating diseases with a lifetime prevalence of about at least 5% (Akiskal et al., 2000) in the general population (some estimate it to be around 5 - 8%). They have a chronic, intermittent course and high morbidity, mortality, and are causes of disability.

From the historical perspective, the history of knowledge of these disorders appears to go back as far as the first century BC (Jackson SW, 1986) though it was Arteus of Cappadocia who described the condition almost exactly as it is understood currently in the second Century A. D. (Sydenham Society, 1856).

After nearly two millennia, French alienists revived the interest in studying the disorder. The French psychiatrist Esquirol and his followers did superb work in their clinical description of the various mental illnesses and their courses in their clinical observation. They were also known for their interest in documenting factors that contributed to new episodes, led to their evolution into more malignant forms, or produced recovery. In 1854 the French psychiatrist Baillarger gave one of the first clinical descriptions of a bipolar disorder, which he called folie à double forme (dual-form insanity). Roughly at the same time another French psychiatrist, Jean-Pierre Falret described the same symptoms, which he referred to as folie circulaire (circular madness).

These developments in turn evolved into the German psychiatrist Kraepelin’s description of different affective states under the rubric of Manic-Depressive Insanity (Marneros & Angst, 2000). This delineation represented the concept of the disease as a continuum in that recurrent melancholia, mania, as well as subsyndromal fluctuations of activity, mood, and cognition between affective episodes (which he called temperaments) were postulated by him as part of the same disease process. Episodes of bipolarity periodically erupted from these temperamental substrates, giving rise to the cyclic course of the illness. Similarly as the French authors, Kraepelin revealed diversity of course patterns, including continuous and rapid-cycling forms. Additionally, he illustrated six types of mixed states and made a differentiation
between various admixtures of depression and mania that occur concurrently, thus providing a critical argument in support of the concept of a unitary affective disorder.

Kraepelinian thoughts prevailed until 1960s at which time delineation between unipolar and bipolar mood disorders started to emerge. This demarcation later on was supported by the two diagnostic tools (ICD-10 1992; DSM-IV 1994). As a result of this, much of the thrust on mood disorders and their treatment, have been aimed at major depressive disorder (MDD) and bipolar disorder moving away from Kraepelinian approach (Akiskal, 1996). This in part has been attributable to epidemiologic studies that estimate the lifetime likelihood of occurrence of MDD to be 10 to 17%, whereas the corresponding risk of bipolar I disorder is 0.4 to 1.7%. Even in psychiatric populations, the ratio of unipolar (MDD) to bipolar illness is biased in favor of the former, ranging from 10:1 to 4:1. It is well documented that before the publication of the DSM-III, patients with severe psychotic mania were often diagnosed as “schizophrenic.” A related and more important reason for the relative bias of paying no attention to bipolarity is that non-responders to lithium treatment have been considered as schizoaffective, characterologically unstable, or odd (Grof et al., 1993) so creating a doubt in the relation of their condition to bipolar disorders.

This narrow representation of bipolarity is shifting, based on the evidence of mounting research findings that support viewing mood disorders in a spectrum. Studies have been reporting several overlapping subtypes of bipolar disorders since 1970s (Dunner et al., 1977). Research findings have repeatedly illustrated hypomanic rather than manic features (Dunner et al., 1976; Akiskal et al., 1977; Depue et al., 1981). Furthermore, severe, or more complex evolutive forms of the illness with extreme psychotic (Akiskal et al., 1979), mixed (McElroy et al., 1992), and rapid-cycling (Bauer et al. 1994) forms have greatly been clinically known. Finally, a number of anticonvulsant agents have been shown to be effective in the treatment of all forms of bipolar disorders (Bowden et al., 1994; Post et al., 1995) which is persuasive evidence in support of reconsideration of the current classification of mood disorders. These developments have considerably expanded the boundaries of bipolar illness in line with Kraepelinian conceptualization. This expansion of bipolar boundaries is in line with classical French psychiatrists as well. In this wider bipolar spectrum perspective, both bipolar and cyclic “unipolar” disorders are considered to belong to the same morbid process. As discussed above, currently there are convincing data arguing against the dichotomized approach to mood disorders and supporting a belief of continuum between unipolar and bipolar disorders calling for revision (Akiskal, 1996) of the current nosology related to mood disorders. The mounting clinical observations show greater complexity than imagined, in contrast to the theory of the two fundamental affective forms (Akiskal et al., 1994; 1995). Hence, there are patients
with dysthymic disorder who are observed shifting into hypomanic or manic state; patients with cyclothymia who progress into severe depressive episodes; and patients with unipolar depressive disorder, who develop hypomania and even mania (Akiskal et al., 1983; Akiskal et al., 1995). Hypomanic symptomatology have been also observed intruding into patients experiencing MDD as a result giving rise to agitated depressive and/or anxious dysphoric, restless depressions with flight of ideas (Akiskal et al., 1996).

Temperamental cyclothymia and hyperthymia are also observed as fertile grounds leading to a switch from depression to bipolar I disorder and, in prone individuals, to primarily depressive cycling. In general, rapid-cycling and mixed states are pervasive. However, there are reports on the existence of ultrarapid-cycling forms where depressed, labile moods with mixed features make up patients’ habitual self and are usually mistaken for borderline personality disorder as a result (Akiskal et al., 1996). In current clinical practice these transformations occur so often that the territory of mood disorders cannot be so sharply demarcated between unipolar and bipolar, as noted by Akiskal. Full-blown disorder with mania and strictly unipolar depressive disorder stand for the extremes of a spectrum (Akiskal et al., 1983); recurrent depressive disorder with hypomania occupies the middle territory. However, the difficulty lies in diagnosing the bipolar II disorder as the hypomanic phase of the disorder which is not so disruptive and is short-lived compared to bipolar I disorder, leading to a possible bias towards unipolar recurrent major depressive disorder. Evidence indicative of a shrinking border of unipolar major depressive disorder seems still accumulating given the recent research findings supporting bipolar spectrum disorders (Benazzi et al., 2004; 2006; 2007; Akiskal et al., 2005).

These bipolar spectrum disorders (or bipolar disorder subtypes) include (1): Bipolar I disorder, which is defined by the presence of at least single manic episode; (2): Bipolar II disorder, which is characterized by recurrent MDD with hypomania (which is a challenge to diagnosis) and/or (3): Cyclothymic disorder characterized by mini depressive episodes and hypomanias that could not fullfil the criteria for bipolar I disorder; (4): Bipolar III (Pseudo-unipolar) disorder, denoted by recurrent MDD without spontaneous hypomania but often with hyperthymic and/or bipolar family history; (5): Unipolar depression, with no evidence for hypomania, cyclothymic, hyperthymic disorders or bipolar family history; and (6): Agitated or excited major depressive disorder consisting of few hypomanic admixtures (racing thoughts, sexual arousal, increased energy) (Akiskal et al., 1983).

Another complication of bipolar disorders is increased mortality from suicide, mortality from other causes, and substance abuse. The recent WHO World Mental
Heath Consortium’s report, based on the results of its study in fourteen countries, demonstrated that 76.3% to 85.4% of the serious cases of mental illnesses received no treatment in developing countries whereas this was true for 35-50% for serious cases in the developed countries for the past 12 months. Likewise, a recently conducted community based survey in rural Ethiopia showed that 92.9% of cases with bipolar I disorder did not receive treatment for their illness in the past 12 months (A. Negash et. al in the present thesis). Hence, the burden of psychiatric morbidity in Sub-Saharan countries appears to be even much higher compared with that in developed part of the world.

The bipolar spectrum disorders are fascinating though complex and need some effort to understand them. Their origin and interdependence in terms of switching from one subtype to another, and treatment response are also amazingly interesting.

However, the focus of this thesis is not on bipolar spectrum disorders. The focus of the thesis is on bipolar I disorder which is one of the extremes of the bipolar spectrum disorders. According to the currently accepted nosology, bipolar I disorder is known as the classic manic-depressive illness. Certainly, focusing on this disorder may be conceived as paying attention to the tip of an iceberg neglecting the large group of remaining bipolar spectrum disorders whose prevalence is thought to be no less than 5% among mental disorders.

**Bipolar I disorder**

Bipolar I (or classic manic-depressive) disorder is a frequent, severe, mostly recurrent mood disorder associated with great morbidity and mortality. It is characterized by periods of abnormally elevated mood (mania) that cycle with abnormally lowered mood (depression), or both existing together. The lifetime prevalence of bipolar I disorder is estimated to be 1% to 2.6%. The mortality rate of the disease is two to three times higher than that of the general population. Suicide is the cause of death in 15-20% of these patients and is the third leading cause of death among people aged 15-24 years, and nearly one third of the patients admit at least one suicide attempt. The clinical manifestations of the disease are exceptionally diverse. They range from mild hypomania or mild depression to severe forms of mania or depression accompanied by profound psychosis. It is equally prevalent across sexes with the exception of rapid cycling, a severe and difficult to treat variant of the disorder, and its mixed subtype, which are mostly observed in women. Patients with bipolar I disorder have a high probability of relapse and are symptomatically ill nearly half of the time after onset.
Multiple structural, metabolic, and biochemical defects are apparent in the brain's cortex, subcortex, and deeper regions of the affected individuals. This disorder is highly genetically conditioned but also highly susceptible to environmental stressors: prenatal or perinatal injuries, childhood sexual or physical abuse, difficult life events, substance abuse, and other toxic chemical exposures. Its high morbidity, lost productivity, and suicide risk place a great toll on the society. Since World War II, bipolar I disorder has been steadily worsening with earlier age of onset, greater intensity of symptoms, and development of drug resistance. Incidence in children is rising and misdiagnosis is common. Disciplined management of the many risk factors is essential, including cognitive psychotherapy and support from the family and the community. Lithium has been the foundational treatment, followed by valproate and other mood stabilizers, antidepressants, and anticonvulsants. Several single-nutrient and multinutrient supplements have been proposed to be beneficial.

Poor outcome, or at least moderate impairment in psychosocial adjustment, is common in patients with bipolar I disorder. Residual symptoms, which are common for many bipolar I patients between their episodes (Keller et al 1992, Goldberg et al, 1999), and a lengthy duration of illness prior to beginning an optimal treatment regimen, are often significant determinants of good versus poor outcome (Goldberg et al, 1999). Many patients with bipolar I disorder become relatively functional as the time from their index episode increases, perhaps reflecting an improved adaptation to the stress of having a chronic, recurrent illness. However, more than one half of the patients with bipolar I disorder manifest some degree of functional disability after the onset of their illness, and a core subgroup of 10-15% of patients show profound impairment in multiple areas, with little improvement (Goldberg et al., 1995). Evidence suggests that affective relapse is more damaging to functional outcome in bipolar I patients than in unipolar-depressed patients.

Prominent and common risk factors for poor outcome in mania include rapid-cycling and mixed-affective states, concurrent substance abuse including alcohol, poor or erratic treatment compliance, inadequate medication dosing or follow-up, poor psychosocial support, and late initiation of treatment.

According to the Global Burden of Disease Study, bipolar I disorder is amongst the leading causes of chronic disability worldwide and it has been ranked seventh among the worldwide causes of non-fatal disease burden. Moreover, bipolar I disorder is one of the top ten causes of YLDs causing profound emotional, psychosocial, occupational, interpersonal and medical burden striking the most youngest and productive section of society. From the perspective of illness-related costs, the total USA economic impact of bipolar disorders was estimated at 45.2 billion in 1991, with
much of the indirect expenses (37,630 million) attributable to lost worker productivity and suicide. In 1979, U.S., Department of Health, Education and Welfare estimated that an average woman with onset of bipolar illness at 25 years of age would experience a 9-year reduction of life expectancy and a loss of work-related productivity of 14 years (Bipolar Disorder: course and outcome, 1999).

Thus, the aggregate data from several research findings suggest that the negative effects of bipolar I disorder for the individual, close family members and for the society as a whole are substantial. The mental health initiatives in developing countries require extensive community-based evidence to determine needs and strengthen promotional as well as intervention activities. Such efforts will facilitate developing effective and proper interventions that address the broad bipolar I illness-related needs of the rural affected population and this is what the current thesis attempts to highlight.
Background to the present research project

Prior to launching “The Butajira Study on Onset, Course and Outcome of Schizophrenia and Bipolar disorders”, the Butajira “field laboratory,” the Butajira Rural Health Program (BRHP), has been functioning since mid 1986. BRHP started the demographic surveillance system in January 1987 with continuous registration of vital events. The major aims of the project were to develop and evaluate a system for continuous registration of births and deaths to generate valid data on fertility and mortality, and to provide a study base for essential health research and intervention in the area. Currently, BRHP is a member of the International Network for continuous Demographic Evaluation of Populations and their Health in developing countries (INDEPTH). The project selected one subdistrict (kebele) from Butajira town, and 8 others from the rural areas based on the grounds of proportional probability, to represent the district which consisted of 44 kebeles. The population of the District was 257, 000 in 1999 (CSA 1994).

The Butajira Study on Onset, Course and Outcome of Schizophrenia and Bipolar disorders project has been launched initially with the aim of using the infrastructure of BRHP and relevant data. However, as the former included the whole adult population aged 15-49 years living in the district, its independence and establishing necessary facilities of its own, became inevitable issue that has to be addressed promptly. Because of this, The Butajira Study on Onset, Course and Outcome of Schizophrenia and Bipolar disorders project moved to the Butajira Health Center and subsequently to the newly built Hospital.

The aims of onset, course and outcome project was to screen adult population aged 15-49 years to obtain a cohort with the lifetime diagnoses of schizophrenia, bipolar disorders and major depressive disorder in order to estimate their incidence and prevalence. The project sought to determine mode of onset, course and outcome of these disorders using a prospective design. Ten years have passed since the project was launched.

Within these ten years, a number of baseline, course, and outcome studies have been completed and are ongoing. Various diagnoses-specific effects of these disorders (e.g., neurological soft signs) have been studied. Many of the project’s achievements have generated scientific doctoral theses for Ethiopian candidates.

The onset, course, and outcome project has contributed to human resource development, and building of research capacity at the Faculty of medicine, Addis
Ababa University and Amanuel Psychiatric Hospital, and Department of Community Health at Addis Ababa University. The training has been in a sandwich model that allows doctoral researchers to stay close to their mother institutions and carry on with their routine duties and other responsibilities, in parallel to doing research. The project has also offered a three-year sponsorship for 2 research assistants to attend postgraduate studies in psychiatry. It has also sponsored Masters Level training in health systems management for one additional doctor. The project has also started to provide a continuous platform for research training for those attending postgraduate training in psychiatry at the Department of psychiatry in Addis Ababa.

Besides the above accomplishments, this project has committed itself to provide the community with relevant and available drugs free of charge for psychiatric disorders and for seizure disorders, and it is still doing so. In addition to this, the project has established a psychiatric clinic and trained two psychiatric nurses for local service.

The Onset, Course and Outcome project is a collaborative research undertaking among Departments of psychiatry and Community Health at Addis Ababa University, Amanuel Psychiatric Hospital in Addis Ababa, and the Department of Psychiatry at Umeå University in Sweden. It is also funded by Stanley Medical Research Institute (SMRI) in the USA.

Currently, there is a need to maintain and subsequently to expand the vision and scope of the project in order to widely address diverse mental health problems other than the currently addressed ones, and to expand training opportunities in various subspecialty areas, and to continue research training for those undergoing postgraduate psychiatric training. Study of first episode psychiatric conditions is also a top priority in such a setting. Refining the study instruments developed elsewhere and bearing in mind the cultural context is also an area of focus (see figure 1).
Butajira study project on course and outcome of schizophrenia and bipolar disorders

**Ground for research**
- Cross-sectional baseline studies
- Follow-up outcome studies
- First onset psychoses studies
- Domestic violence and mental illness study
- Intervention drug-trial studies
- Genetic studies
- Maternal mental health studies with focus on the outcome on their offspring
- Economic burden of schizophrenia and bipolar disorder

**Major outputs**
- Research results on course & outcome
- Research results on first onset psychosis
- Trends on mortality

**Ground for training**
- Doctoral training
  - 1 completed
  - Four ongoing
  - Two in process
- Masters
  - 2 completed
- Research training
  - for postgraduate students

**Benefits**
- Planning of better psychiatric care and treatment
- Future interventions for prevention

Figure 1: The activities and outcome of the Onset Course and Outcome Project of Butajira.
Aims of the thesis

The overall aim of this thesis is to assess the magnitude of, and the clinical characteristics of, bipolar I disorder in a predominantly rural socio-cultural context in Butajira district in Ethiopia, its ultimate aim being to indicate the public health interventions that are needed to improve the mental health conditions to policy makers by studying Bipolar I disorder.

The specific aims were:

- Evaluating two screening methods (key informant and CIDI) in detecting major psychiatric disorders in Butajira setting.

- Assessing the prevalence and clinical characteristics of bipolar I disorder in Butajira at Community level.

- Clinical outcome of bipolar I disorder in Butajira district at follow-up during 2.5 years on the average.

- Determining neurological soft signs in community identified cases of bipolar I disorder in Butajira.

- Assessing burden of care among caregivers of cases of Bipolar I disorder identified in Butajira study of onset, course and outcome.
Material and methods

Subjects

Description of the study area

The study was conducted in Meskan and Mareko District whose capital town is Butajira. The name Butajira is used interchangeably for the district usually by researchers. The district is located 135 kilometers south of AA in the south central part of Ethiopia. The district is administratively a part of Gurage zone in Southern Nations, Nationalities and Peoples Regional Government (SNNPRG). The estimated size of the district is 797 km² that lies on average 2100 meters above sea level (ranging 1500-3400 meters). The Butajira town is 9000 hectares in size and is located at 2100 meters above sea level. The climate is cool-to-cold in the mountainous parts and dry-hot in rest of its parts. Therefore, the district has only highland and mountainous topography though the effects of Great Rift Valley that bounds it in the East can be appreciated in terms of climate and vegetation at the periphery. Annual rainfall ranges between 900 and 1,400 mm though it has become more erratic and drought affected. The consequent famine has become frequent for about more than past 10 years. Normally, the main rainy season ranges from June to September, with relatively small rains around the period February to April.

Ethiopia in the Horn of Africa  Butajira study area in southern-central Ethiopia  The Meskan and Mareko District in Butajira study area

Figures 2 (a-c)
The area has rich soil and farming is the mainstay of livelihood. Maize, legumes, and millet are the main crops. Additionally, Enset (a false banana tree), another endemic to Ethiopia plant whose parts are source of staple diet for large section of the country’s population, is grown in areas extending from Butajira town towards north and north-western areas including in parts of the chain of Gurage mountains stretching through the district. Wheat, teff (endemic to Ethiopia cereal staple), red pepper and khat are also grown as cash crops. Extensive crop cultivation and high population density make difficult animal husbandry to a larger extent. In the town, most people are engaged in commercial activities. In the town’s commercial activities, shops, food and drink establishment, workshops, flour mills and transport sector (though inadequate) predominate.

Butajira district is among Ethiopia’s most densely populated parts, about 34 people per 1 km$^2$. The population of the district was estimated at 257,000 in 1999 based on 1994 national census. The proportion of children 14 and less years of age constitutes 46% and that of 65 or more years of age 1.3% which is characteristic of low income countries. The majority of the district population follows Islam.

Figure 3: Farming is the mainstay of livelihood
The health needs of the district’s population is accommodated by 2 health centers and 2 hospitals (one nongovernmental), one specialized center for ophthalmology and epilepsy, as well prosthesis of long bones of the lower limbs and physiotherapy services, 19 functional health posts, and five private drug vendors. There had never been any psychiatric service in the district until the Butajira Study on Course and Outcome of Schizophrenia and Bipolar disorder’s Project was launched. Under the project’s auspices, two psychiatric nurses have been trained for the local service, psychotropic and antiepileptic drugs are dispensed through the hospital’s pharmacy free of charge, primarily for the district’s people with psychiatric and seizure disorders. The project has also one permanent and another optional outreach centers. The permanent center is functional on once weekly basis and the optional one is used to trace the lost to follow-up cases and is located about 25 kms away to the East from Butajira town. This enables the project’s service as much near to the served population as possible. This is dictated by inefficient transport system and low socioeconomic status of cases and their families that the project serves.
The district has one technical school, 14 junior secondary schools, one high school, and 14 elementary schools. There are also three private colleges that have been opened in Butajira town recently. The male to female enrolment ratio is 3.5:1. The literacy rate of the district is about 23% and only less than 2% of its population has education beyond junior secondary school.

The Butajira town is connected to the capital city (AA) currently by asphalted road. The villages in the district are connected to the town by virtually dry-weather roads. There is also another asphalted road connecting Butajira town to Zeway; a town located 50 kms away built near one of the Great Rift Valley’s lakes (Lake Zeway). In the district, only Butajira town gets a 24-hr hydroelectric power and has a digital telecommunication service (both National and International).

Study setting and design

This thesis is a product of the collaboration on mental health research in Butajira, Ethiopia, among the Departments of Psychiatry and Community Health at Addis Ababa University, Amanuel Psychiatric Hospital of the Ministry of Health of Ethiopia, and the Division of Psychiatry at Umeå University in Sweden. The result of this collaboration has been the establishment of the Butajira Study on the Course and Outcome of Schizophrenia and Bipolar Disorders Project that was established from June to September 1997 and funded by Stanley Medical Research Institute (SMRI) and the Swedish Agency for research and Cooperation with Developing countries (SIDA/SAREC). The participating researchers have backgrounds of psychiatry, public health and neurology.

The foundation underlying all the studies was the Butajira Course and outcome Study on Schizophrenia and Bipolar Disorders Project, that has been functional since 1997 in Meskan and Mareko district in Ethiopia. The database created since 1998-2001 was used for analysis. Most of the studies used the cross-sectional data collection method, but in the present thesis we present also the results of clinical short-term outcome at follow-up on the average after 2.5 years, on bipolar I disorder.

Data collection was carried out in entire district excluding only one kebele (a subdistrict consisting of 7500 population) which was inaccessible to any type of transport for data collection and supervision of data collection process and data quality control. The estimated target adult population that aged 15-49 was 100,000 and data collection was conducted by door-to-door search for all eligible individuals. Cases were also screened for substance or alcohol dependence using the relevant SCAN sections. They also underwent general medical examination using an
acceptable general medical examination format to exclude gross chronic or acute medical illnesses, mental retardation, epilepsy, and other gross neurological disorders.

**Subjects of the study**

This thesis is prepared under the framework of and is a cross-sectional study based on baseline data of the study project. The Butajira Study on Course and Outcome of schizophrenia and Bipolar Disorders project conducted a door-to-door survey to screen the entire adult population of Butajira district aged 15-19 years to obtain a cohort for an ongoing epidemiological study on the course and outcome of schizophrenia and bipolar disorders. Lay interviewers and key informants were used at the first stage of screening. Trained high school graduate lay interviewers applied the CIDI (World Health Organization 1997; Andrews and Peters 1998). Key informants were additionally used to identify potential cases that could be missed during CIDI interview (Shibre et al., this thesis). Key informants were selected from each kebele in the district and were given intense orientation on the type of cases the study Project was interested in.

In the second phase, probable cases thus identified underwent diagnostic assessment by clinicians using SCAN. SCAN interviews were conducted on full-time basis throughout the working hours in Butajira Health Center and in the villages where the probable cases were identified. All patients that met ICD-10/DSM-IV (World Health Organization, 1990; American Psychiatric Association, 1994) diagnostic criteria for bipolar I disorder, schizophrenia and major depressive disorder were included in the third phase of the study, the course and outcome study. All SCAN interviewed cases of Bipolar I disorder, schizophrenia and major depressive disorder also underwent further assessment using other relevant instruments to obtain baseline information. The subjects screened and the procedure followed is displayed in figure 6 below. In this way, 864 cases were identified and later on six patients were excluded because some of them were found to have incomplete data or some neurological conditions. The basis for this thesis is 315 cases of bipolar I disorder which were identified at the end of the data collection period from March 1998 – May 2001.
Tracking down the subjects literally through field studies

Door-to-door survey by trained interviewers

Figures 5 (a-c)
Total eligible population (N = 83,277)

- CIDI non-interviewed (n = 14,899)
  - CIDI Negative (n = 66,217)
    - CIDI interviewed n = 68,378 (82.1%)
      - CIDI positive n = 2,161 (3.2%)
        - Scan invited
      - Identified by Key Informants (n = 719)
        - Scan invited
  - SCAN Non-Interviewed n = 423
    - SCAN Interviewed n = 1738 (80.4%)
      - SCAN Positives (n = 864)
        - Schizophrenia (n = 321)
        - Depression (n = 219)
        - Bipolar I disorder (n = 315)

SCAN Non-Interviewed n = 172

Figure 6. Case identification process at the community in Butajira district
A patient just brought in with the help of a chariot …

… and the same patient, recovered, at follow-up

Figures 7 (a, b)
Instruments

Despite the fact that psychiatric disorders are diseases of the brain, neuroscience measures of brain structure and function in general are still too expensive and impractical and are steadily undergoing refinements, limiting their use for research purposes. Moreover, there are few definitive brain measures for diagnosis, and only a few mental disorders conform to traditional models of disease in medicine. Because of this, psychiatry unlike other areas of medicine, has few diagnostic laboratory tests for underlying brain diseases. Hence, mental disorders are generally defined by a constellation of symptoms and other clinical descriptors.

In the last several decades there has been an appreciable advance in defining suitable criteria for the diagnosis and classification of mental disorders, and this has given rise to systematic and empirical testing. Progress in developing instruments for structured evaluation has been the center of a large amount of endeavor, along with standardization of phenomenologic and diagnostic concepts (Sartorius et al., 1993). The achievement of the DSM and ICD systems indicates the importance of this work. This scientific approach has brought to maturity phenomenologic approaches to psychiatric measurement which are currently vital in epidemiologic, clinical, and services research.

Beginning in the 1970s, specific operational criteria have been developed to standardize the diagnostic process for psychiatric disorders. These are clinically meaningful, practical, with reasonable reliability and logically consistent. While diagnostic criteria were standardized by these operational developments, instruments that translate criteria into questions in an interview also started to develop as a natural companion to the diagnostic systems that were developed in 1990s. These interviews have the advantages of consistent coverage of items, standardized probing, and application. Their precision, ease of use, and reliability have made these instruments popular in research and clinical work.

For large-scale surveys like that of this thesis, fully structured interviews conducted by lay interviewers are necessary to maintain standardization. For this purpose, diagnostic interviews were developed that translate the criteria of diagnostic classifications, namely the International classification of Diseases (ICD) which is in its 10th version nowadays, and Diagnostic and Statistical Manual of Mental Disorders (DSM) in its 4th revised version.
Within the program of the WHO on diagnosis and Classification of mental disorder, the Composite International diagnostic Interview (CIDI) has been developed to cover ICD-10 mental disorder diagnoses. CIDI was developed utilizing cross-national expert consensus. It is a highly structured and standardized instrument with high specificity. Before the establishment of Butajira Study on Course and Outcome Project, CIDI has been translated into Amharic (the official language in Ethiopia) and revisions have been made subsequently. It has also a computer algorithm to be used for analysis.

Another instrument used by Butajira Study on Course and Outcome of Schizophrenia and Bipolar Disorders Project is the Schedule for Clinical Assessment in Neuropsychiatry (SCAN). The SCAN is a set of instruments aimed at assessing and classifying psychopathology and psychiatric disorders in adults. Although structured, the interview is flexible and resembles clinical examination. The assessment approach is a clinical cross-examination of the subject to discover whether a symptom or sign is present during designated period of time, and if so, with what severity. The SCAN has a glossary in which individual items of psychopathology and other information are differentially defined with operationalized rating scales. The glossary is the phenomenologic core of the SCAN, providing a highly refined set of psychopathology, the rating of which is the goal of the clinical cross-examination. It also has the diagnostic algorithm for diagnostic analysis. The SCAN is clinician administered and is based on clinical judgment based on the Glossary. The CIDI, to the contrary, is inflexible and highly standardized so that Clinical Judgment is not required.

A number of other relevant interview instruments were used to obtain baseline information which also served as data collection questionnaires for the prospective follow-up study. These instruments were employed by psychiatric residents, general practitioners and psychiatric nurses and their specifics are described in the respective papers (see figure 8).
Butajira study on the course and outcome of Schizophrenia and Bipolar Disorders

Baseline Questionnaires & Study Forms

To be completed by a psychiatrist
- Diagnostic Schedule
- Hamilton Scale
- Mania Scale
- Negative Symptoms Scale
- Positive Symptoms Scale
- Life Chart Schedule

To be completed by a psychiatric nurse
- Basic Information on Study Subject
- Basic Information on Informant(s)
- Family Interview Schedule
- SF-36 Health Survey
- Major Life Events Inventory

To be completed by a physician
- General Medical Examination
- Neurological Evaluation Scale

Department of Community Health
Addis Ababa University
and
Amanuel Psychiatric Hospital
Ministry of Health
Addis Ababa
February 1998

Figure 8.
Data management and statistical methods

A full-time data editor first ascertained all the completed interview forms for completeness, accuracy and consistency in the field. Data were then entered into computers using the Epi-Info-6 program. The CIDI and SCAN data entry programs were used to enter the data obtained from these respective interviews. A double data entry procedure was employed to ascertain accuracy and consistency of the entered data with subsequent cleaning to maximize its quality.

All the statistical analyses were performed using the SPSS software version 14.0 (SPSS, 2005). All statistical tests were two-sided. Chi-square tests were used when comparing two proportions or when testing independence between two categorical variables. Differences between two groups for quantitative scores were evaluated by the t test. Logistic regression was employed to control for possible confounding effects, and to calculate the odds ratios.

Ethical considerations

The study was reviewed and approved by committees of Departments of Community Health and Faculty of Medicine Addis Ababa University. At the district level, the district’s administrative council agreed that the study could be conducted. Approval letters were sent to respective kebele administrative units in rural as well as in the town. Furthermore, verbal consent was obtained from local leaders and from subjects eligible for the study. When the study subjects were not in a condition to give consent due to their mental state verbal consent was obtained from their immediate family members. Participants’ confidentiality was observed and anonymous release of information was agreed as well. All individuals who were enrolled for the follow-up study who were in episode as well as those previously on medications were prescribed medications free of charge. Those subjects who didn’t have psychiatric conditions but were found to have acute medical conditions were also managed free of charge accordingly. Those cases diagnosed with psychiatric illnesses other than the interest of the project and those with epilepsy were referred to psychiatric clinic within the existing health delivery system and appropriate medications were provided free of charge by the project.
Results with comments

Table 1: The Papers I-V on which this thesis is based (All samples were from the same study population).

<table>
<thead>
<tr>
<th>No</th>
<th>Problem addressed</th>
<th>Study design</th>
<th>Study population</th>
<th>Study period</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>Prevalence and clinical characteristics of bipolar I patients in a community-based study</td>
<td>Cross-sectional</td>
<td>284 cases</td>
<td>1998-2001</td>
</tr>
<tr>
<td>III</td>
<td>Short-Term Outcome of Bipolar I Disorder – community-based study at Butajira</td>
<td>Prospective</td>
<td>312 cases</td>
<td>1998-2003</td>
</tr>
<tr>
<td>IV</td>
<td>Neurological soft signs in bipolar I patients</td>
<td>Case-control</td>
<td>224 cases, 78 controls</td>
<td>1998-2001</td>
</tr>
</tbody>
</table>

We recall (see figure 6) that a total of 83,277 eligible subjects in the district were approached but 68,378 subjects were interviewed by lay interviewers using CIDI which makes the CIDI response rate of 82.1%. A total of 2161 (3.2%) probable cases identified by CIDI interview were found to be eligible for SCAN interview. Key informants simultaneously identified 719 probable cases. Overall 2880 individuals were invited for interview by clinicians employing SCAN. SCAN interview non-response rate was 19.5% (n=423) for CIDI identified cases and 23.9% (n=172) for key informants identified subjects. This makes SCAN response rate of 79.3% (n=2152). Of these cases 864 were found to be positive for one of the diagnostic categories of major psychiatric conditions the project was interested in. Later on, 9 cases having strongly suggestible medical conditions were excluded and 855 cases became the baseline cohort out of which 315 were bipolar I cases on which this thesis is based.
Table 2: A summary of the major findings

<table>
<thead>
<tr>
<th>Paper №</th>
<th>Problem addressed</th>
<th>Major Findings</th>
</tr>
</thead>
</table>
| I       | Evaluation of two screening methods | • Comparison of identifying both schizophrenia and bipolar I disorder was not different between CIDI and key informants.  
• CIDI was superior to Key informant in detecting Affective disorder (45% Vs 30%)  
• However, key informant method was better in detecting Schizophrenia than CIDI (59% Vs 29%) |
| II      | Prevalence and clinical characteristics of bipolar I disorder-a community-based study in Butajira | • The prevalence of Bipolar I disorder in the community is conservatively 5 per1000, but considering the inherent nature of CIDI around 1%.  
• For more than half of the study subjects, age of onset was less than 23 years.  
• The prevalence among males is twice more as among women.  
• The mean age of manic phase was 22 years (22.0 for men, 21 year for women).  
• The mean age at for depressive phase was 23.4 years (24.1 for men, 22.5 for women).  
  o 64.1% of cases reported two or more episodes.  
  o 55.9% of the cases never sought any form of modern health care.  
  o Of the one-third who were ill, 78% were not on any treatment  
  o Only 13.6% had had admission to psychiatric hospital.  
  o Only 7.1% of all the cases were taking medication at the time of survey  
  o 8.6% of the men and 4.7% of the women reported suicide attempt. |
| III     | Clinical outcome in bipolar I disorder at follow-up | • Relapse and remission assessed at follow-up average 2.5 yrs (range 1 - 4 yrs)  
• 65.9% relapsed at least once (47.8% manic, 44.3% depressive)  
• Of those relapsed, 28.5% had psychotic features  
• 31% were continuously ill & 5% were mostly in remission during the follow-up time  
• Use of medication predicted greater remission |
| IV      | Neurological soft signs in bipolar I patients | • Cases performed worse on two sensory integration items and one item from motor coordination subscale compared to controls  
• Cases performed worse in all the items under sequencing of complex motor acts compared to controls |
| V       | Burden of bipolar I patients on their caregivers: community-based study | • 84% reported moderate and 58.7% reported severe burden  
• Burdens were experienced in social, finance, occupational, & strain domains  
• Characteristics & clinical status of the affected bipolar I cases influenced the degree and type of burden  
• The most affected caregivers were siblings and spouses |
An evaluation of two screening methods (Paper I)

Rating instruments are the most common measuring instruments in clinical psychiatric research. They have been used for decades. They have many different applications, but screening, diagnosis, and the measurement of severity, and change are among the most important. Following their use detecting psychiatric morbidity in community samples has been interest over many years. To fulfill this goal a number of epidemiological screening instruments have been devised and among them the most recent ones, the CIDI and SCAN, are mentioned above.

It is beyond doubt that carefully employed clinical research diagnostic interviews conducted by well-trained clinical interviewers produce diagnostic data that are superior to the data obtained in the CIDI. However, the financial and logistic issues limit the use of well-trained and experienced clinical interviewers in large-scale community surveys. Another limitation related to CIDI use is that it is extremely difficult to assess some critical symptoms of certain disorders (Kessler et. al 1994, Kessler 1998) without using clinical interview-based interviewing strategies that use clinical judgment to rate symptoms. Furthermore, there exist methodological challenges expressed in terms of conceptual difficulties such as those associated with culture-bound syndromes (Guarnaccia PJ). There are also difficulties inherent in attempting to find suitable words needed to describe certain critical symptoms that do not exist in some languages (Shweder RA), which might be the case in countries like Ethiopia where more than eighty languages are spoken. Despite these limitations, the reliability of CIDI is said to be within the bounds of acceptability for most of the disorders assessed in CIDI (Wittchen HU).

Keeping these CIDI limitations in mind we also used “Key informants” to include those cases which could have been missed by the CIDI interview. By August 1999, lay interviewers administered the CIDI to 22,324 out of 25,632 expected adult population aged 15-49 years, and identified 524 CIDI positive cases. Also, the key informants alone identified 192 probable cases independently. These resulted in totally 716 probable cases identified by both the screening methods, who were all invited for the diagnostic SCAN interview. Of the 524 CIDI positive subjects, 183 (35%) subjects refused to participate, and of the 192 subjects identified by the key informants, 52 (37%) subjects refused to participate.
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Diagnosed by SCAN</th>
<th>Identified as a case by CIDI alone</th>
<th>Identified as a case by Key informants alone</th>
<th>Identified as a case by both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>132 (100%)</td>
<td>29 (22%)</td>
<td>59 (45%)</td>
<td>44 (33%)</td>
</tr>
<tr>
<td>Affective disorder</td>
<td>87 (100%)</td>
<td>45 (52%)</td>
<td>30 (34%)</td>
<td>12 (14%)</td>
</tr>
<tr>
<td>Either diagnosis</td>
<td>219 (100%)</td>
<td>74 (34%)</td>
<td>89 (41%)</td>
<td>56 (25%)</td>
</tr>
<tr>
<td>Non-cases</td>
<td>262 (100%)</td>
<td>195 (74%)</td>
<td>51 (20%)</td>
<td>16 (6%)</td>
</tr>
<tr>
<td>Total SCAN</td>
<td>481</td>
<td>269</td>
<td>140</td>
<td>72</td>
</tr>
<tr>
<td>SCAN-Refusers (n = 235)</td>
<td>183</td>
<td>52</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Number (percentage) of the subjects identified (classified) as a case by CIDI and Key informants, respectively.

So altogether, 481 probable cases agreed and were interviewed by clinicians using the SCAN (Paper I). Table 3 shows that of the 219 cases diagnosed by SCAN, 130 (59%) were identified as cases by CIDI, and 145 (66%) were identified as cases by the Key informants. So in this respect, these two screening methods are comparable.

However, when these two screening methods were compared in relation to diagnoses, key informants had identified 103 (78%) out of 132 identified cases with schizophrenia compared to 73 (55%) cases detected by CIDI. On the other hand, CIDI identified 57 (66%) out of the 87 cases with the diagnosis of affective disorders, compared to 42 (48%) cases by the key informants. The differences in effective detection in both instances is significant, the key informants being better in identifying cases with schizophrenia ($\chi^2=15.34$ df 1 < 0.05) and CIDI identifying more cases with major affective disorders ($\chi^2=5.27$ df 1 < 0.05).
We compared performances of the two screening methods to see whether they have differences in identifying acute versus chronic major psychiatric disorders (duration of illness $< \text{or} \geq 2$ years). Key informants identified 69.2% of cases with chronic psychiatric illnesses compared to 57% of cases identified by CIDI and the difference is statistically significant ($\chi^2=4.23$ df 1 $< 0.05$).
Prevalence and clinical characteristics of bipolar I disorder (Paper II)

Studying prevalence and clinical characteristics of any disorder is crucial since priority setting and timely intervention is important in terms of treatment and prevention of undue disability and premature mortality. From the perspective of public health, studying a disorder in such a way helps in health policy matters and priority setting in addressing health problems of major public health concern.

Having in mind this, we found 315 cases at the end of the survey out of CIDI interviewed cases as confirmed by SCAN interviews. Complete information relevant to this paper was obtained for 295 individuals, which comprised the final sample for analyses.

As already mentioned above, the CIDI uses a narrow definition for bipolar disorders. Therefore, our conservative estimate of bipolar I disorder was 0.5%, making the true estimate of prevalence around 1% when adjusting for the CIDI limitation for the disorder. The prevalence estimate for males is 0.6% and it is 0.3% for females (still using narrow CIDI definition).

The female proportion comprised 45%, and the mean age at enrollment to the study was 29.5 years with no gender difference. The majority of them were from the rural setting (83.1%), and illiterate (70.2%). Nearly two-thirds of the subjects were married and nearly one-fifth reported a family history of mental illness.

The mean age at clear recognition of the bipolar I illness was 22.0 years (22.3 yrs for men, 21.2 yrs for women, not statistically different). Based on lifetime recall, the illness started with a depressive episode in 22.7% of the cases, and the mean age at onset of the depressive phase was 23.4 years. The mean age at onset of the manic phase of the illness was 22.0 years.

Of all the cases that were ill at the time of enrollment, more than three-fourths had had at least one previous episode. Overall, 64.1% of the cases had experienced two or more episodes regardless of their clinical status at the time of recruitment.

More than half of the cohort reported that they had never sought help from modern health sector. Only 13.2% had ever been admitted to a psychiatric hospital for their lifetime illness. Although about one third of the patients were still not in remission, only 7.1% had been on treatment for bipolar I illness which started during the year...
preceding the survey, and they had received classical neuroleptics rather than mood-stabilizers. The reported rate of suicide was 8.6% among men and 4.7% among women. The overall suicide attempt was found to be 6.9%. 
Clinical outcome in bipolar I disorder at follow-up (Paper III)

The 315 cases identified in Paper I as having bipolar I disorder were subject to a follow-up for up to 2.5 years on the average (range 1 to 4 years). Two of the main clinical outcomes assessed were relapse to a mood episode, and remission from a mood episode. Relapse was defined as the occurrence of a depressive, manic, or mixed state that fulfills episode criteria according to DSM-IV. Remission was specified either as full remission (lacking affective symptoms), or partial remission (had symptoms but did not fulfill the episode criteria).

Outcomes were assessed annually using the SCAN, the Young Mania Rating Scale, and Hamilton Rating Scale for Depression, administered by trained psychiatrists. Further assessments were done by monthly clinical interviews by experienced psychiatric nurse practitioners and residents.

Medications were available to the patients through the study project and were provided routinely depending on the clinical indication. But only the old-generation psychotropic medications were available (chlorpromazine, haloperidol, fluphenazine decanoate depot, and amitryptyline).

During follow-up, 65.9% had relapsed at least once, of which 47.8% had manic, 44.3% had depressive, and 7.7% had mixed episodes. About three-fourths had only had a single relapse, but the number of episodes in the sample ranged from one to five. Of those who had relapsed, 28.5% had psychotic features (about 17.4% associated with mania, and about 11.1% associated with depression). About 31% of the patients were continuously ill during the follow-up time (with clinical or sub-clinical symptoms), whereas only 5% of the patients were in remission for most of the follow-up time, including 14% of the patients being in remission at least half of the follow-up time.

A predictive factor associated with remission was the female gender when only the sociodemographic variables were considered. However, this association was insignificant when also the use of medication was considered. Being on psychotropic medication for at least half of the time was independently associated with remission.
Neurological soft signs in bipolar I disorder (Paper IV)

Although the biological basis of bipolar I disorder is indisputable, the underlying putative pathogenetic and pathophysiological mechanisms underlying it are poorly understood so far. One of the areas of research interest in the search of such mechanisms has been studying the presence, magnitude, localization, pattern and distribution of neurological soft signs (NSS). The subject has been extensively studied in schizophrenia but not adequately in mood disorders.

The 224 bipolar I disorder patients were compared with 78 healthy control subjects to investigate whether they differed in their performance, using Neurological Evaluation Scale (NES). The proportion of individuals who scored the lower values 0-5 on the NES scales was greater among the controls compared to among the cases in our study. However, the proportion of those who scored more than 5 on NES was greater among the cases compared to the controls. Compared to controls, the cases performed more than twice more poorly in audiovisual integration and graphesthesia, under sensory integration subscale. They also performed more than three and half times worse in one item from motor coordination subscale. They performed poorly in four of the ‘others’ subscales as well. The most significant difference in performance between cases and controls, however, was observed in all of the items under the sequencing of complex motor acts subscale. No difference in performance was found between cases and controls in relation to clinical dimensions (single current episode manic, single manic episode in remission, two or more episodes of bipolar I disorder in one of the phases current relapse or in remission), and sociodemographic characteristics.
Burden of care in bipolar I disorder (Paper V)

Mental disorders have a large impact on the affected individuals, their families and on communities where they reside. The affected individuals suffer not only from distressing symptoms of the disorder, but also suffer because they are incapable of enjoying work and leisure activities, worry about not being able to bear their social responsibilities and are fearful of being a burden for others.

The burden on families ranges from economic difficulties, to emotional reactions to the illness, stress of coping with the disturbed behavior, the disruption of household routine and the restriction of social activities. One of the major psychiatric disorders causing such a formidable burden on families is bipolar I disorder.

We did cross-sectional assessment of 284 caregivers of cases with bipolar I disorder from this largely rural community. We assessed objective burden as considered from social, family strain, occupational and financial domains. Among the assessed caregivers, 84% reported to have experienced at least a moderate degree of burden while 58.7% of them reported a severe degree of burden. Severe degree of burden was reported by 52.1% of caregivers for the social burden domain, 50.0% for finance, and 32.7% for occupational, followed by 24.6% for the family strain objective burden domains. Non-housewife status (P < 0.05), first-degree relationship (P < 0.01), being a spouse (P < 0.001), and self-employment (P < 0.05) increased the likelihood of experiencing the burden of care in financial aspects. Spouses (P < 0.01), parents (P < 0.05), siblings (P < 0.05) and self-employed (P < 0.01) or partially employed (P < 0.01) caregivers experienced greater level of social activities restriction. Spouses (P < 0.01), siblings (P < .05), self-employed (P < 0.01) and partially employed (P < 0.05) caregivers experienced a greater level of family disruption. Non-housewife status (P < 0.01) and age range 35-44 years (P < 0.05) of caregivers predicted difficulties in work-related routines.

Characteristics and the clinical status of the bipolar I affected cases at the time of recruitment were also found to have a relationship with the caregivers’ burden of care. Better economic position (P < 0.05), singlehood (P < 0.05) and marital bond (P < .01) of the cases were inversely related to the social activity restrictions on caregivers. The likelihood of disruption of work-related activities of the caregivers was inversely related to the cases being single (P < 0.01), being married (P < 0.01, and being employed (P < 0.01). Most recent manic (P < 0.05) and depressive (P < 0.05) episodes were found to cause greater interference in occupational activities of the caregivers.
Male gender of cases was associated with a lower burden of care on caregivers. The age range 16-44 years (P < 0.05) of the cases increased the likelihood of burden of care on caregivers in the financial burden domain. However, better economic position of the cases and the cases being married were inversely related to financial constraints on caregivers.
Discussion and conclusions

Major findings

Evaluation of Two Screening Methods

Reliability is a measure of reproducibility and it refers to how frequently interviewers examining the same subject will provide the same diagnosis. In current measures, mainly test-retest and interviewer-observer reliability at the diagnostic level is emphasized. Validity denotes how well the diagnostic tool measures the true disorder status. Thus, reliability and validity are twin concepts. A major challenge in psychiatric diagnosis is ascertaining what the true disorder status really is. Without any objective measure of pathologic processes and states of brain and mind structure and function, the true disorder can only be approximated.

This drawback in psychiatric diagnoses is also reflected in the screening and diagnostic instruments currently used. Although WHO field trials of the CIDI have acknowledged good inter-rater reliability and test-retest reliability, it has a number of limitations (WHO International Consortium in Psychiatric Epidemiology, 2000). Firstly, validity tests appear to be slim and controversial, especially in a trans-cultural context. Secondly, CIDI does not use clinical judgment; hence it involves risks of false positives and false negatives at the level of symptom identification, so its use produces a trade-off between sensitivity and specificity depending on the objectives of the study. Thirdly, acute psychotic disorders appear to be diagnosed with a relatively low reliability and validity. Fourthly, it is extremely difficult to assess some critical symptoms of certain disorders without using clinical interviewing strategies that use clinical judgments. The CIDI includes a number of such symptoms, most notably those involving psychotic delusions and hallucinations needing clinical judgment.

Because of this we decided to involve key informants alongside the CIDI. Our result indicates that key informant method is an important and complementary screening method to CIDI in large-scale epidemiological surveys at least in our setting. This method did better in detecting patients with psychotic disorders (both acute and chronic) compared to CIDI.

Prevalence and Clinical Characteristics of Bipolar I Disorder

Bipolar I disorder patients in Butajira were predominantly from rural area and illiterate. Virtually all of them have average or lower perceived socioeconomic position compared to their catchment area, and nearly half of them were farmers
whereas almost one-third were engaged in domestic work. Furthermore, the vast majority of the cases (88.4%) were ≤ 30 years of age at the time of the illness and more than half the cohort was ≤ 30 years of age at the time of recruitment.

Nearly the entire cohort had never been treated or had been treated inadequately. A large number of the currently ill (at the time of survey) had two or more previous episodes. Of the entire cohort, almost two-thirds had one or more previous episodes at the time of recruitment. Hence, the likelihood of developing chronic recurrent illness with subsequent disability is very high.

Although the married persons predominated in the cohort, marriage is family-arranged in Butajira. Furthermore, marriage in Butajira district is at an earlier age for both women and men. Most women get married before age 20 whereas men get married mostly in their early 20s. As the mean age of onset for both genders is in the early 20s and most of the women get married earlier, probably stigma plays little role in this regard although it surfaces as time goes on. Moreover, women are not in a position to divorce unless their husbands consent. However, when the unmarried group is explored separately, the likelihood of males to get married appeared about two times less compared to their female counterparts. This is suggestive of disorder-related disability that makes males unable to fulfill social sanctions to get married or/and stigma against mental illness. This is in line with a number of other studies reporting that bipolar I patients are either single or divorced. Moreover, according to the Chicago multiple follow-up assessment results, for patients on lithium therapy, approximately 10 – 15% of them were found to have consistently poor outcome. Approximately 50-60% of the assessed patients had a variable degree of outcome, about 15-20% of them having moderately impaired functioning over serial follow-up assessments. Only about 15-20% of the patients appeared to have good overall functioning or remission within their follow-up period. What this pattern of outcome of bipolar I disorder on standard treatment implies to community identified and largely untreated patients in Butajira awaits further answers from the Butajira prospective course and outcome study.

**Neurological Soft Signs in Bipolar I disorder patients**

Neurological soft signs (NSS) are minor neurological abnormalities in sensory and motor performance identified by clinical examination. The term ‘soft’ has been used to indicate signs that do not reflect primary tract or nuclear pathology, whereas the term ‘hard’ is used to indicate any obvious localizable pathological lesion underlying these signs. NSS are categorized into three main neurological domains. These domains are integrative sensory function, motor coordination, and sequencing of complex motor
acts. Additionally, fourth domain ‘others’ is included as a subscale in the NES. Deficits in integrative sensory function are thought to result from parietal lobe dysfunction. Poor performances in complex motor tasks are believed to arise from malfunctioning of the frontal basal ganglia circuitry.

Although these abnormalities are well studied and reported more in schizophrenia, they are found to be non-specific for the disorder. These abnormalities are believed to occur in other psychiatric conditions as well. Studying neurological impairment in patients with bipolar I disorder is of clinical relevance, regardless of the mechanisms by which it occurs. Frontal lobe damage is known to cause severe difficulties in coping with day to day activities of life, in particular in terms of goal-setting, self-regulation and decision-making. It is likely that even minor cognitive deficits may result in considerable social and occupational difficulties. A failure to cope with the demands of work activities or family life could cause stress and hence put the affected individual at greater risk of relapse. Cognitive problems, attributed rightly or wrongly to side-effects from medication, might lead to non-adherence. The recognition of these difficulties and the timely institution of an appropriate psychotherapeutic intervention for coping with these, might be of considerable benefit to patients in preventing or delaying relapse.

We studied 224 cases of bipolar I disorder and 76 controls. Cases were found to perform poorly on items from sensory integration and motor coordination NES subscales. They also displayed abnormality in 50% of the ‘others’ subscale’s items. However, their performance was found impaired in all of the sequencing of complex motor acts subscale items of the NES compared to controls. This appears to be in line with a recent review article that in its summary stated the possibility of neuropsychological deficit at the level of frontal-temporal and subcortical systems. There is also a research report on euthymic bipolar patients and controls that found poor performance of patients in executive function compared to controls.

The advantages of NES in indicating soft neurological signs are suggested by Arango et al. (1999). They reported that this advantage of NES lies in discriminating something that occurs with low frequency among control subjects, but that is present with high frequency in ill patients including patients who demonstrate generally good intellectual functioning. Based on their study on prediction of neuropsychological performance by NES, they thought of the possibility of neurological soft signs as markers of global cognitive impairment. Based on this assumption, they suggested the possibility of using NES or similar instruments instead of comprehensive neuropsychological test batteries, as their discriminant role is similar (Arango et al., 1999). This may have a potential benefit for low income countries, where
neuropsychological test batteries and the available products of modern technological advancement in the medical field are far beyond a reach.

**Caregiver burden from Bipolar I disorder**

Burden of care from bipolar I disorder on caregivers ranges from economic constraints, to emotional reactions to the illness, the stress of coping with disturbed behavior, disruption of household routine, and the restriction of social activities, in particular at the time of onset or relapse. In addition to providing physical and emotional support, families bear discrimination and stigma as well. Expenses for the treatment at traditional healing centres or at modern health services (if any) are shouldered mainly by the relatives. Caregivers make a number of adjustments and compromises that hamper them and other members of the family from attaining their full potential in work, social relationships, and leisure. Caregivers are often compelled to leave behind a major part of their time to look after their family members with bipolar I disorder, and endure financial and social denial as they are not fully productive. They also seem to be in a continuous fear that recurrence of the illness may cause abrupt and unpredicted disruption of the lives of the family members.

**The burden of bipolar disorders in a sociodemographic context**

Health status of individuals is partly a reflection of their social status in the society they live. Butajira district shares the most typical features found in the rural community in Ethiopia: The vast majority of the districts’ people live in poverty. This is compounded by shortages of rain and crop failure, and further being aggravated by massive population density with shortage of land, 40 persons living per 1km$^2$ in the district, poor housing status, the average household size being 4.7 m$^2$ (PHCC, 1996), which is complicated by high population growth rate, with resultant overcrowding of the households.

Anticipating that a dimensional approach to the bipolar disorder spectrum will become more accepted and included in further revisions of the DSM system, and consequently its prevalence estimated in the order of 5-8%, then the toll that the district’s population is paying in this respect will become more apparent and understandable. The detrimental effect of the illness in the absence of mood stabilizing drugs is unacceptable and unethical from a professional perspective.

When other major mental disorders are added to the magnitude of the burden of bipolar spectrum disorders, combating the detrimental effects of mental illhealth will require reconsiderations in the health policies where mental health is given a greater
priority, and will entail collaborative interventions by the government and the psychiatrists. This collaborative work should also focus on working out guidelines about adequate and functional mental health services, and their integration into the general health service delivery systems, starting from the primary health care level. Persons affected by mental disorders, as compared to by physical disorders, have a much greater burden on the families, neighbours and on the society at large. The government and nongovernment organizations should put maximum effort on making available the essential drugs whose effectiveness is approved by the committee of psychiatric experts in the country. Unless this is done we will find ourselves remain in a vicious cycle.

Validity and generalizability of the current findings

The research site, the Butajira Study on Course and Outcome project’s catchment area (the whole Butajira district), is characterized by the typical features of an Ethiopian rural setting. Its limited access to health services, high population density, high mortality rates, poor sanitation and water supply conditions, poor housing facilities, high illiteracy rate, poverty complicated by repeated droughts, and its reliance of most parts of the country on subsistence agricultural economy, these are the main features shared by many rural areas in the country. Although Ethiopia is known for its ethnic and cultural diversity, the issues that are largely influenced by socio-demographic and environmental factors have a reasonable level of similarity within this diversity.

Conducting a large-scale epidemiological survey in order to obtain reliable data on which much of the analysis is based, it is a big challenge and requires commitment from the stakeholders, logistics, adequately trained reasonable number of manpower, and relevantly organized supportive staff, at the least. However, only two clinicians for the whole district were posted at the field office at the outset of the data collection. The clinicians were intended to conduct clinician-based interviews at the only health center at Butajira town, at the outset by inviting for SCAN interviews the subjects identified by the key informants as well as those who positive by CIDI, as probable cases. However, after having stayed there for about half a year, the number of invited individuals was unexpectedly and exceedingly low. This happened despite the fact that contacts were made and orientations about the aims of the project along with the nature and consequences of the illnesses of study interest, were provided on several occasions to the administrative officials at different levels and by visiting the relatives of the patients who are either in episode or those who are in remission, hoping that they would understand and come. Additionally, the project compensated for the time lost during interviews, by giving per diem to the relatives or to the study subjects in terms of money, and they were also paid if there was a need to spend the night in the
town, and if the study subjects and their relatives came for interview travelling long distances.

In order to understand why patients and their significant others were not coming despite the modest advantages they were obtaining and also free of charge treatments for those who are in episodes, five kebeles (sub-districts) were randomly selected and the author of this thesis with one young man who has been working as CIDI interviewer and who was from the same district, were assigned to assess the situation.

The result of this assessment indicated that mostly patients with schizophrenia (paranoid and chronic patients), acutely ill bipolar I patients, and with those severe depressive disorder were the ones not coming. Furthermore, the attribution by the local people that the psychiatric disorders are caused by evil spirits or curses by ancestors and the elderly, coupled with lack of awareness of the possibilities that these patients could be helped by modern health care systems, were the main factors. This appears reasonable to the author of this thesis, because those who did not come or bring their ill relatives to the project’s office for interview, had never seen the modern health care systems working in the district helping people with mental health problems. So it is very logical if they were reluctant to bring their loved ones with mental disorders to the health centre. They should not be blamed for that. As patients mostly had been ill for many years, with no one helping from the existent health care system in the district, the relatives seemed to have lost confidence in the modern health care providing institutions. The same seems to be true for local kebele and district level officials, who preferred to be passive than actively involving themselves in initiating patients and their families to go to the interview center, and at times actively refusing to send patients to the survey and treatment center.

Based on the results of this assessment, decision was made to transform the passive data collection procedure into an active one. As a result, clinicians started to interview cases identified by both the CIDI interviews, and the key informant identified cases in their respective kebeles. This time the number of clinicians who should do this interview was three and they have to travel throughout the whole district for accomplishing the mission, for a door-to-door clinician administered SCAN and assisted clinical diagnostic interviews. Additionally, the clinicians had to train key informants of the respective kebele so that they could identify cases of interest. Interview of a single eligible potential case by CIDI interviewers was done in three visits if he/she is not at home during previous visits. If he/she was not available during the third visit, looking for that particular person was terminated, assuming a refusal to participate or a change of address or had travelled outside the district. The same procedure was followed for the SCAN interviews as well.
Supervision of CIDI interviewers was also conducted by field supervisors who in their turn were supervised by designated clinicians. Supervision was also carried out in ascertaining whether forms were appropriately filled or whether there were any missing data at the field level. Supervision mechanism for clinicians was also in place by a designated person from the department of community health at Addis Ababa University. Supervision was made in an indirect way by using a neutral person who knew how to apply it, or by other means by estimating the number of households in the respective kebeles that has been covered by the clinicians and data collectors. Overall, the effects of the above mentioned weaknesses were appropriately addressed to the extent which was possible.

This bold and overambitious undertaking of the project would not have been successful had it not been due to the devoted, unyielding and honest clinicians and data collectors, with maximum commitment and neglecting their personal life for the project’s cause. They worked conscientiously day and night for more than three years. Furthermore, the final year was marked by working also during the weekends to finish the survey. The task was accomplished even though all this mentally as well as physically energy draining field work was not supported adequately enough by the project in terms of payment or moral compensation.

Moreover, these three clinicians were expected to conduct interviews throughout the district despite the geographic variation often without lunch walking from door-to-door and coming home late in the evening and not uncommonly exhausted. Evenings were also used to edit what they had done during the day time to avoid mistakes as much as possible and to remember things that were not filled during the day but should be remembered in the evenings. It was expected that the clinicians, in addition to conducting interviews, had had to carry out administrative activities at field level as well as supervisory activities in relation to the CIDI interviewers. Thirdly, the survey was so protracted that some of the cases died, others out-migrated whereas others refused, somehow increasing the SCAN non-response rate (25.3%), even though it is fairly within acceptable range. After the CIDI interviewers and clinicians moved away from one part of the district, there appeared new cases (incident cases) with psychiatric disorders of interest who were not interviewed, although some were interviewed by psychiatric nurses and later by physicians.

Research activities are dynamic and they are performed not only because they are fascinating, but because they are roads to the betterment of the society in several directions.
Conducting a large-scale mental health survey in a rural setting like that in Butajira district or elsewhere, is a complex task not only because it has administrative and logistic repercussions. It is also surrounded by various cultural and traditional beliefs making the task even more complex. Many local concepts, beliefs and behaviors were identified during the interviews. As there is no simple method for approaching the mental health issue in such a context, well designed procedures tailored to local situations are imperative. In the current thesis, a two-stage screening design was used together with the key informant method to be able to obtain data on bipolar I disorder with acceptable level of accuracy. Qualitative method approaches could have assisted in understanding the issues that arose during interviews, enriching the results. In this respect, further studies are required in Butajira district to generate ample and relevant information in this regard.

One important lesson that can be drawn from the survey is that in order to start such a big undertaking, careful planning beforehand is crucial. Planning should consider every aspects of the survey process even though it will not be an easy task, but it would help flexibly adjust field level staff as unpredicted problems arise, set the time limit or completion time and that every resource be tailored to this end with appropriate and adequate monitoring of the field work.

Overlapping projects that share the same manpower and logistics should be avoided as this entails unnecessary delays in the main work and exhausts manpower physically and mentally, compromising the main focus under consideration. Also, it may sometimes become a source of conflict of interest for the data collectors. Such overlapping undertakings had been observed in the field under the frame work of Butajira Study on Course and Outcome of Schizophrenia and Bipolar Disorders Project. The study of mental distress using SF-36, and genetic studies are examples of this situation. Despite these limitations, we believe the results of the study are reasonably reliable and could be generalizable to similar settings.
POTENTIALS OF THE BUTAJIRA PROJECT ON SCHIZOPHRENIA AND BIPOLAR DISORDERS

This thesis is wholly dependent on the database and infrastructure established by the Butajira Study on Schizophrenia and Bipolar Disorders Project. The project was initiated by the collaboration of Amanuel Psychiatric Hospital, Friends of the hospital abroad, Department of Public Health and Epidemiology at Addis Ababa University, Department of Clinical Sciences Division of Psychiatry, Umeå University Sweden, and later on it included the Department of Psychiatry, Addis Ababa University. The Project has been largely funded by the then Stanley Research Foundation (the current Stanley Medical Research Institute, SMRI) in 1997-1998 and until now at the stage of course and outcome phase.

At the outset, the aim of the project was to study the incidence, prevalence, course and outcome of schizophrenia and bipolar disorders. However, under framework of the project were also studied nutritional status of the collected cohort; the projected genetic studies of bipolar I and schizophrenia patients and their first-degree relatives, collecting their DNA (the results have not been known due to different reasons until now). It also carried out drug trials to investigate the effect of trimetoprim as an adjuvant treatment for the presumed infectious origin of the mental disorders (Toxoplasma Gondi). By undertaking these rather ambitious activities, the Project in due course transformed itself into a field laboratory, a rare phenomenon in Sub-Saharan Africa. However, it maintained its focus on major mental disorders. A number of baseline original research reports have been produced and published in international scientific journals. Short-term and intermediate-term outcome papers have also been started appearing in such journals of them is being the one included in this thesis.

As a result of this project’s establishment, two PhDs have already been completed and the current one is the third one. There is also another sisterly project in the area. That study has been based on postnatal maternal depression and its effects on outcome of children born to those mothers who had experienced depression pre- or postnatal. This Project has been a collaborative undertaking with two PhD programs which have been funded by the Well Come Trust based in UK. Additionally, a number of Masters Programs have been accommodated by the Project from Masters students from Addis University Medical Faculty Department of Community Health and Epidemiology scheme. Thus, it became also the first general population-based research site for providing advanced research training for Ethiopian mental health researchers. From its very beginning, the Butajira Study on Schizophrenia and Bipolar Disorders which generated data for baseline studies, recruited a cohort of cases with psychiatric
disorders of interest for prospective research. It has also provided a framework for specialized mental health-related research such as the field randomized drug trials and genetic aspects. In general, the project is a source of good quality data that can improve decision-making in policy formulation and planning health care services and producing high quality human resources needed at the higher level training institutions.

Based on the results and past experience, a number of activities are envisaged in Butajira. The priority in the forthcoming years will be to focus on drug trial studies to find out the possible putative etiological causes of mental disorders, as well as intervention studies, which is a top national priority issue. The project has been getting funding for its activities from SMRI for the past more than 10 years. For how long this will continue, it is not certain. Looking for other additional financial sources may ensure the sustainability of the project’s activities. Since the WHO’s 2001 ground breaking and subsequent reports on the mental health situation, there is an increasing appreciation and a growing concern about the world’s mental health conditions.

**Directions for further research**

It is very apparent that addressing the whole mental health issue is beyond the scope of this thesis. Nevertheless, attempts have been made to identify some crucial problems that are especially relevant to bipolar I disorder in a rural setting. As the thesis work has been carried out in an organized research environment, some of the findings warrant further research that are beyond the scope of this thesis. This future research will of course take into consideration the lessons learnt from the difficulties encountered, and how many of them were solved.

One has to address the impact of extremely low literacy rate on the perception of mental health, and the meaning of living with untreated relatives with bipolar I disorder in the long-term, in relation to aspects like occupational, social, role functioning as a mother, father, husband or wife, etc. For this to happen, stronger culture-sensitive designs and diagnostic instruments need to be adopted. This should be done within the framework of international experts in psychiatry, so that the instrument adoption should be done at least in consensus reaching objective not compromising the standards.
Summary in Amharic

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