ECONOMIC BURDEN OF SCHIZOPHRENIA AND BIPOLAR DISORDERS IN ETHIOPIA

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DISSERTATION APPROVAL

This dissertation was submitted by Ababi Zergaw Giref under the direction of the Chairperson of the dissertation committee listed below. It was submitted to the School of Graduate Studies and approved in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Public Health at Addis Ababa University.

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ABSTRACT

In Ethiopia, economic burden of schizophrenia and bipolar disorders was a virgin area of research untapped for the last many decades. On the other hand sporadic epidemiological studies indicate that mental health problems are major public health concern in the country. However, despite high magnitude of the problems, the extent and the longitudinal time change of family and caregiver burden due to schizophrenia and bipolar disorders is unknown. Therefore, this dissertation has tried to give answers to the following research questions: What is the extent of economic burden of schizophrenia and bipolar disorders in Ethiopia? How does burden change overtime in families of patients with schizophrenia and bipolar disorders? Are families with a member with schizophrenia and bipolar disorder face different disease burden compared to families with physical disorders?

To answer these research questions one year longitudinal prospective study with economic and family caregiver burden measurements on families of 249 schizophrenia, 190 bipolar, 55 diabetes, hypertension and asthma patients and 659 families who are with other sickness in the community was carried out. Population average generalized estimating equation and time series generalized least squares analyses were used to estimate the extent and the change over time of burden in the families of patients with schizophrenia and bipolar disorders.

Using the prevalence based and the human capital approach, economic burden estimations at societal level were also made. As a result in the analysis of six waves of data, families of patients with schizophrenia were found to experience persistent burden for about eighty-three percent of the year. The change in family burden due to time was statistically significant with a mean family burden score of 3.10 (z = -20.86, P>|z|= 0.001). In terms of caregiver characteristics, female caregivers, caregivers in farming occupation, whose monthly living expenses were very little, who had paid more out-of-pocket for mental health services, who were angry at the patient, who were worried about the patient, who were over involved in controlling the patient, and who had lost more days of work were found to be more burdened. Overall in 2005, the total burden of schizophrenia to families in Ethiopia ranged approximately between $2.12 million to $9.97 million.

As observed in families of patients with schizophrenia, in a comparative analysis, bipolar patient family caregivers were also found to be more burdened for about 8 to 10 months of the year than family caregivers of patients with diabetes, hypertension and asthma and sick controls in the community. The average difference in family caregiver burden score between bipolar and diabetes, hypertension and asthma patient family caregivers was 4.36 (z = -8.75, P>|z|= 0.001); while the difference due to time between the two groups was 3.42 (z= -4.27, P>|z|= 0.001). Similarly, the average difference in family caregiver burden score between family caregivers of bipolar patient and sick controls in the community was 3.7 (z= -4.88, P>|z| 0.001). In terms of longitudinal caregiver burden difference, bipolar patients family caregivers were found to be more burdened than family caregivers of sick controls in the community with a burden score difference of 2.97 (z= -5.17, P>|z|= 0.001). Over the year, patients with bipolar disorder lost a mean of 93.52 cumulative days of work. Consequently, in the year 2005, bipolar disorder patents living in a community under clinical follow-up lost 112.8 million days of work.

In sum the total economic burden of schizophrenia and bipolar disorders in Ethiopia ranged approximately $378.62 to $469.47 million. Out of this total economic burden the direct cost was found to be 1.25 percent to 3.66 percent of the country's public health expenditure in the year 2005. This amount of burden is very huge for poor countries like Ethiopia. It is a hidden economic loss. Generally the figure shows that the country's health care system should try to reduce the high level of hidden sufferings of families and caregivers so as to keep the level of burden low. Future studies need to focus more on how to devise feasible intervention strategies to lessen economic and family burden due to schizophrenia and bipolar disorders

Key words: schizophrenia; bipolar disorder; caregiver burden; family burden; economic burden; panel data**;** population average generalized estimating equation; time-series generalized least squares, Ethiopia.

To those who have suffered the most

LIST OF ORIGINAL PAPERS

This doctoral dissertation consists of the present summary and the following papers, which are referred to by their Roman numerals.

I. Ababi Zergaw, Damen Hailemariam, Atalay Alem, and Derege Kebede. Longitudinal comparative analysis of economic and family caregiver burden due to bipolar disorder. *African Journal of Psychiatry* 2008; 11(3): 191-198.

II. Ababi Z. Giref, Damen Hailemariam, Atalay A. Ejigu, Derege K.Tesema. Longitudinal analysis of burden due to bipolar disorder patients living in a community under clinical follow-up (Submitted).

III. Ababi Z. Giref., Damen Hailemariam. Panel data analysis of burden in families of patients with schizophrenia (Submitted).

IV. Ababi, Z. Giref., Atalay, A. Ejigu. Time-series generalized least square analysis of caregiver burden in families of patients with schizophrenia (Submitted).

DEFINITIONS

Bipolar disorder	a severe mental illness characterized by recurrent episodes of elated or depressed mood.
Burden causing event	an event that demands care and support from caregiver as a result of a schizophrenic or bipolar patient’s illness
Caregiver burden	the emotional, social, and financial stresses that caring for a relative or friend with schizophrenia and bipolar disorders imposes on the caregiver
Economic burden	the burden experienced by individuals, families and communities with schizophrenia and bipolar disorders as a result of cost of caring and lost opportunity
Family burden	the emotional and economic strain that family members, neighbors and friends of a patient with schizophrenia or bipolar disorders experience
Schizophrenia	severe universally common psychiatric illness characterized by distortions in thinking, perception and inappropriate emotions

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ABBREVIATIONS

AR-1	autoregressive correlation order one
BRHP	Butajira Rural Health Program
CBPQ	Childhood Behavioral and Psychological Questionnaire
CIDI	Composite International Diagnostic Interview
DALY	Disability Adjusted Life Year
DHA	diabetes, hypertension and asthma
DSM-IV	Diagnostic Statistical Manual-IV
FC	friction cost method
GDP	gross domestic product
GEE	generalized estimating equation
GNP	gross national product
HC	human capital approach
ICD-10	International Classification of Diseases-10
ILO	International Labor Organization
PA-GEE	population average generalized estimating equation
RQC	Reporting Questionnaire for Children
SCAN	Schedule for Comprehensive Assessment in Neuropsychiatry
SCC	sick controls in the community
UK	United Kingdom
USA	United States of America
WHO	World Health Organization

STATEMENT OF ORIGINAL AUTHORSHIP

"I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which to a substantial extent has been accepted for the award of any other degree or diploma of the university or other institute of higher learning, except where due acknowledgment has been made in the text."

Signature________________________________

Name ___________________________________

Date____________________________________

“Thanks to the creator God, I have not been left for a hyena”

A50 year old mother of a schizophrenic son in Butajira describing her suffering.

“One of the most elusive diseases known to man and unknown to medicine”

James Joyce, whose daughter was diagnosed with schizophrenia

“We experience this terrible feeling of loss and grieve for the son we knew. There is also that terrible loss of our expectations. We feel cheated out of watching him mature and flower the way adolescents do when they grow into young adults… it is mourning without end … He is very much still with us, seeming eternally twelve years old needing constant care and attention.”

Martin S. Willick, an American psychiatrist whose twenty-eight year old Harvard going son was diagnosed with schizophrenia

1. INTRODUCTION AND BACKGROUND

1.1. Introduction

In Ethiopia, economic burden of schizophrenia and bipolar disorders was a virgin area of research untapped for the last many decades. This may be largely due to disease priority of communicable and nutritional problems and way of thinking in disease burden measurement where morbidity and mortality from communicable and nutritional problems was dominant over morbidity like disability in schizophrenia and bipolar disorders. This dissertation has addressed this untapped area of research for the first time and has revealed the sufferings of families and caregivers. It has estimated the extent of the burden in Ethiopia. The dissertation has not only addressed the issue for the first time, but it has also applied modern methods of longitudinal data analysis.

The first chapter of the dissertation had made background review of international literature available in the field of mental health, schizophrenia and bipolar disorders. It has reviewed global perspectives of economic burden of mental and behavioral disorders with particular emphasis on schizophrenia and bipolar disorder. It has identified types of health care costs, emotional and economic strain, conceptual and estimation issues and limitations of scope in the international literature. It has also included background introduction about psychiatric epidemiology and mental health in Ethiopia. In chapter two and three it has stated the research questions and the rationale for the dissertation. Aims of the dissertation were described in chapter four. In chapter five details of the study methodology was explained along with justification for the paradigm and analytic methodology. Chapter six and seven have presented ethical consideration and results of the study. Chapter eight put the findings in perspective with limitations of methodological assumptions. Conclusive remarks and implications for policy and practice along with future directions were dealt in chapter nine.

1. 2. Background

The World Health Organization (WHO) has recently proposed that mental health is a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community (1). Yet, mental illness and mental health have been neglected by most governments and societies, this was revealed through the use of DALYs (2) - the new global burden of disease measurement.

DALYs has shown us that mental and behavioral disorders have large burden on individuals, families and communities, furthermore, in the future as a result of increasing mental and behavioral problems due to population increase and epidemiological transition, the economic burden on individuals, families and the societies will be on the rise unless some measures are taken to tackle the problems of mental and behavioral disorders. Even if mental and behavioral disorders affect people in all groups of society in all countries, the poor are disproportionately affected by these disorders. 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 (3).

The association between poverty and mental disorders is a vicious cycle (4), this vicious cycle of poverty and mental disorders may be operative at different levels and the cycle at the family level may well be operative at the community and country levels. Poverty causes economic deprivation, low education, and unemployment. These results of poverty may lead to high prevalence of mental and behavioral disorders with lack of care and severe course. Continuing the cycle, mental and behavioral disorders have economic burden with increased health expenditure, loss of job and reduced productivity. This economic burden may lead to poverty, completing the vicious cycle.

1.2.1. Economic burden of mental and behavioral disorders

Mental and behavioral disorders are the results of interaction of biological, psychological and social factors (4), these factors associated with the prevalence, onset and course of mental and behavioral disorders include poverty, sex, age, conflicts and disasters, major physical diseases, and the family and social environment. The development of mental disorders and caring for them may result in economic burden on individuals, families and communities.

Economic burden due to mental and behavioral disorders is the burden experienced by individuals, families and communities with mental health and behavioral problems as a result of cost of caring or lost opportunity (4, 5). The burden could be in the form of loss of income, employment; out of pocket expenses, reduced productivity, days out of role, emotional strain, and disturbed social relations. There is also the constant fear that recurrence of illness may cause sudden and unexpected disruption of the lives of family members.

With respect to the above point, some mental health economic studies (4, 6), mainly from industrialized countries, have estimated the aggregate economic costs of mental disorders. In the United States the aggregate yearly costs of mental disorders accounted for about 2.5 percent of gross national product (GNP). In the Member States of the European Union the cost of mental health problems is estimated to be between 3 percent and 4 percent of GNP, of which health-care costs account for an average of 2 percent of GNP (7). Studies from Europe (7) have estimated expenditure on mental disorders as a proportion of all health service costs: in the Netherlands, this was 23.2 percent and in the United Kingdom inpatient expenditure was 22 percent.

Though scientific estimates are not available for other regions of the world, it is likely that the costs of mental disorders as a proportion of the overall economy are high too. The impact on the quality of life of patients and their families would also be so high. The economic burden of mental illness also includes the cost of organizing and operating mental health services; the expenses related to crimes caused by the mental and behavioral disorders.

The overall economic burden of mental disorders on sufferers, family and friends, employers and society is wide ranging (8). On sufferers it has cost of health care and treatment, reduced productivity as a result of work disability and lost earnings and other costs of anguish and suffering, treatment side-effects and suicide. On family and friends it has costs of informal care giving, less productivity due to time off work, and other costs of anguish, isolation and stigma. On employers it has cost of contributions to treatment and care and low productivity as a result of diminished productivity of a worker with mental disorder. On society, it has cost of provision of mental health and general medical care, reduced productivity, and other costs of loss of lives, untreated illnesses with unmet needs and social exclusion.

1.2.2. Loss of productivity as economic burden

As described earlier most methodologically sound studies have been conducted in the United States and the United Kingdom. In the United States, mental illness is considered responsible for an estimated 59 percent of the economic costs deriving from injury or illness-related loss of productivity, followed by alcohol abuse at 34 percent. A report from Canada revealed that absences for psychological reasons had increased 400 percent from 1993 to 1999, and that the costs of replacement, together with those of salary insurance, amounted to Can $ 3 million for the year 2001 (6, 7, 9, 10).

A survey on psychiatric morbidity in the United Kingdom showed that people with psychosis took an average of 42 days a year off work (1, 10). The same survey reveals that in many developed countries, 35 to 45 percent of absenteeism from work is due to mental health problems. According to a study from Harvard Medical School (10), the average number of work loss days attributable to psychiatric disorders was 6 days per month per 100 workers; and the number of work cutback days (getting less done than usual) was 31 days per month per 100 workers. Even if an employee does not take sick leave, mental health problems can result in a substantial reduction in the usual level of activity and performance.

Therefore, substantial proportion of economic burden of mental health problems stems from difficulties in contributing productively when at work, finding and keeping paid employment and achieving career progression. Such studies are limited in developing countries; however, it has been shown that lost productivity is associated with mental disorders. A mental health service research in India and Pakistan (11) has identified evidence on service use and costs in two districts in the respective countries. Combining patient and family health care costs, the economic burden of depression and anxiety in Bangalore was 700 Indian Rupees per month, and in Rawalpindi it was more than 3000 Pakistani Rupees per month. This was estimated to be equivalent to between 7 and 14 days of an agricultural worker's wages in India, and approximately 20 days work in Pakistan.

In addition to mental health problems, abuse of alcohol and other substances are serious public health tribulations in both developed and developing countries (10). Worldwide, alcohol abuse accounted for 4 percent of the total burden of diseases in the year 2000. In Latin American countries, alcohol was the leading risk factor for the global burden of diseases in the same year. Alcohol abuse is also responsible for neuropsychiatric disorders, domestic violence, child abuse and neglect, and productivity loss. In Asia, substance abuse is considered the main cause in 18 percent of cases presenting problems in the workplace. In Thailand, the percentage of substance abusers aged 12–65 years varies from 8.6 percent to 25 percent in different regions of the country. In New Zealand, with a population of 3.4 million, alcohol-related lost productivity among the working population was estimated to be US$ 57million a year. Diseases related to alcohol and substance abuse are therefore serious public problems. They affect development of the human and social capital, creating not only economic costs to society as a whole, including the health system, but also social costs in terms of injuries, violence and crime. They also affect the well-being of future generations (7).

The health and economic burden of mental and behavioral disorders is wide-ranging, long-lasting and huge. Unfortunately, unlike in developed countries where studies on the economic burden of mental and behavioral disorders exist, there is a dearth of such studies in Africa. Yet, a great need for such information exists for use in sensitizing policy-makers in governments and civil society about the magnitude and complexity of the economic burden of mental and behavioral disorders.

In Kenya, a hospital based study (12) revealed that in the financial year 1998/99, the Kenyan economy lost approximately US$13.4 million due to institutionalized mental and behavioral disorder patients; the total economic cost of mental and behavioral disorder per admission was US$2,351; while the unit cost of operating and organizing psychiatric services per admission was US$1,848. The out-of-pocket expense borne by patients and their families per admission was US$51; and the productivity loss per admission was US$453.

In South Africa**,** 25 to 30 percent of the general hospital admissions are directly or indirectly related to alcohol abuse (4, 7). Almost 80 percent of all assault patients presenting to an urban trauma unit in Cape Town were either under the influence of alcohol, or injured because of alcohol-related violence. The majority of victims of train-related accidents, traffic accidents had blood alcohol levels exceeding the legal limits. Fetal alcohol syndrome is also common cause of mental disability in the country.

With regard to such economic studies, the condition in Ethiopia is much different because there is no economic burden study, but different prevalence studies (13-19) indicate that mental health problems are one of the major public health problems in the country; increasing from about 10 percent to about 30 percent in the period of four decades, that is, from 1960s (8.6 percent) to the late 1990s (31.8 percent). In the year 1998 burden of disease study (20) in Butajira has revealed that neuropsychiatric conditions constitute 11 percent of the disease burden in the rural community.

1.2.3. Economic burden of schizophrenia

Schizophrenia, characterized by distortions in thinking, perception, and by inappropriate emotions, is a severe, universally common psychiatric illness (21-24). The illness begins in late adolescence or early adulthood and follows a variable course, ranging from complete symptomatic and social recovery to chronic or recurrent course, with residual symptoms and incomplete social recovery (23, 25). It causes a high degree of disability in self care, occupational performance, functioning in relation to family and household members, functioning in a broader social context and social stigma (23, 24). Co-morbidity with depression, limited help seeking, rejection of treatment, suicide, cardiovascular diseases, cancer, increased cigarette smoking, recreational use of alcohol and psychoactive drugs are common in patients with schizophrenia (23-27). Often patients with schizophrenia live for many years with the illness and severe disability, remaining dependent on others for basic support (26-28). Patients' dependence on others and the fact that it often leads to mental and social disability, makes it one of the most costly illnesses.

Cost of illness studies found schizophrenia to disproportionately consume health care resources (29-34) and its burden represented 0.3 to 3 percent of annual healthcare budget in developed countries (25, 27, 35-39). Also family burden studies (40-44) had found families with schizophrenia patients to experience high level of burden in various dimensions of life. Studies from the US in 1985 and 1992 estimated the family economic burden associated with schizophrenia to be in the range of \$2.47 to \$8.65 billion (26, 27). The burden of schizophrenia on UK families in 1997 was estimated at £1.9 million (35). Also studies from India and Nigeria found the main brunt of financial burden of caring for schizophrenia patient was borne by families (45, 46). Other existing international literatures on schizophrenia additionally show that its burden has been extensively explored (46-53).

The burden is thought to be multidimensional affecting the life of caregivers, the rest of the family and their social network. Some of the dimensions include paying for medical services, supervising treatment adherence, feelings of loss, worrying about the future, disturbance in family functioning, and social stigma (25, 54). On the other hand high expressed emotion, that is, the attitude and behavior of caregivers towards the patient with schizophrenia, especially critical comments, hostility, lack of warmth or emotional over involvement, predicts course (52, 55) and quality of life in patients (56, 57).

Predictors of burden in schizophrenia were described in cross-sectional studies. A study to assess the relationship between caregiver burden and behavioral disturbances of the affected identified burden in relationship during acute illness as most important predictor (53). Another cross-sectional study on burden of care and general health in families of patients with schizophrenia revealed burden to be high for mothers, carers with less education, carers of younger patients and carers of patients with more hospitalizations (42).

In longitudinal studies people with schizophrenia and concurrent depressive symptoms were found to have poorer long-term functional outcomes compared to the non-depressed (58) and relatives' distress was found related to patient's anxiety-depressive behavior and high expressed emotion (52). In other longitudinal studies patient negative symptoms were found to impact caregivers' burden over time (43).

Schizophrenia burden was also described to be stable over time while reduction was found among relatives who adopt less emotion focused coping strategies and received more practical support from their social network (41). However, in low income countries, there are no longitudinal family and caregiver burden studies in schizophrenia. As a result longitudinal family and caregiver burden is largely unknown and family intervention strategies are rarely integrated to clinical services compounding the effect of poorly organized mental health systems.

1.2.4. Economic burden of bipolar disorder

As schizophrenia, bipolar disorder is a severe mental illness characterized by recurrent episodes of elated or depressed mood. Bipolar disorder is a major global public health issue (59, 60) due to the recurrent and chronic nature of the illness (61-64), and is associated with a large burden for individuals with the disorder, their families and society (65-71). The disorder is associated with elevated mortality, with approximately 18.9 percent of patients dying through suicide (68). In addition, psychosocial impairment is common in bipolar disorder as patients often experience problematic occupational, social and family functioning (61). Functional disability or reduced efficiency at work, loss of productivity because of absence from work, and high level of caregiver distress are some of the factors worsening the burden (65, 72-74). Non-compliance mixed depressive – manic symptoms, co-morbid medical disorders, substance use and alcohol abuse are among the factors that complicate treatment of patients with bipolar disorder (75).

Economic studies have found the burden of bipolar disorder to be extremely high. In 1990 the economic burden of bipolar disorder in the US was estimated to be $15.5 billion due to lost productivity in work performance (72). In the same year, patients in treatment lost an estimated 152 million cumulative days from work and untreated patients lost 137 million days. In 1991, the burden of bipolar disorder among adult Americans based on 1.3 percent lifetime prevalence was estimated at $45 billion (65); of which $8 billion was due to loss of productivity because of suicide and $6 billion was due to lost productivity of caregivers who provide care for family members with the disorder. Another estimate for the 1998 incident cases of bipolar disorder in the US was estimated at 24 billion US dollars (66). In the UK, in 1998, the annual burden of bipolar disorder was estimated at $3 billion (67). In the Netherlands, based on 5.2 percent prevalence of bipolar disorder the total burden of the disorder was estimated at $1.83 billion (71). The burden in Australia in 2004 assuming a 2.5 percent lifetime prevalence and the same pattern of health service, was estimated between AUD$3.97 to AUD$4.95 billion (70). It has also been estimated that bipolar disorder has dramatically increased use of health care resources by patients (76) and their caregivers (74).

In most developing countries, particularly in sub-Saharan Africa, resources for mental health care are very scarce (77) and the delay in seeking treatment for bipolar disorder is long (75). Therefore, it is expected that individual patients and their families would bear the brunt of the burden. Morbidity due to the recurrent nature of the illness, often exacerbated by co-existing medical conditions, has an undoubtedly large economic impact on individuals with the illness, their families, the health system and wider society. For example, it is known that family caregivers of bipolar patients have an increased use of health services themselves (74). Patients with bipolar disorder tend to have high demand for health services and yet the disorder is under-diagnosed and often inappropriately treated (75, 78-81). Manic episodes of the illness are very disruptive of daily life, work and family relationships (82). During the acute phase of the illness family caregivers may be highly demanded to be involved in care giving. Not only during acute period of the illness, even during remission residual symptoms may still be present demanding family care giving (82, 83).

Bipolar disorder has direct and indirect costs resulting in economic and family caregiver burden. Cross sectional studies and data base analyses have shown this burden (65-70, 72). However, little is known about how the economic and family caregiver burden in families with bipolar disorder patients changes over time. Furthermore, almost all studies of the economic and caregiver burden of bipolar disorder have been conducted in high-income countries. In low-income countries, families already living in poverty may be disproportionately affected by having a family member with bipolar disorder, in spite of the strong support networks existing in traditional societies.

1.2.5. Types of health care cost

Costs associated with schizophrenia and bipolar disorders include direct, indirect and intangible costs of the illnesses. Direct costs are actual money expenditures and in-kind contributions incurred by patients, their families, and third parties to purchase medical goods and services. Costs of non-medical goods and services ordinarily incurred to obtain medical services such as transportation to medical facilities are additional direct costs. In-kind contributions are donations of goods or services that would otherwise have to be purchased through actual cash outlays. These include shelter, food, utilities, etc. Indirect costs are losses in productivity associated with symptoms, treatment, disability and premature death. Indirect costs include the value of lost opportunities to work in the general economy because of sick leave, disability leave and unemployment associated with illness or in the household. Relatives who divert time from work to provide care or assistance with household work also incur opportunity costs. Indirect costs associated with schizophrenia include morbidity, mortality, and productivity losses borne by relatives (26, 28, 37, 39, 65).

Intangible costs entail pain and suffering as well as changes in quality of life. Although central to complete understanding of the impact of illness, intangible costs are not ordinarily considered in assessing the economic burden of illness because they have not been successfully quantified in a monetary sense (26, 66). Such costs cannot be expressed in monetary terms, but are nevertheless significant. They include effects on the patient (e.g., despair and the side effects associated with medication) and on the carer (e.g., isolation, uncertainty, stress). Collectively, these may be treated as intangible costs or as important facets of patient or carer quality of life, the effects of which are to cause social withdrawal and to push up the direct costs of treatment (27).

1.2.6. Emotional and economic strain

These costs of managing schizophrenia and bipolar disorders can result in family burden. The term family burden refers to the emotional and economic strain that family members, neighbors, and friends of a mentally ill person experience. This burden can have various effects on families and caregivers. First, it can influence the roles they play in relation to the patient. The patterns and the roles within a family can change because of the patient's problems. Second, it can reduce their leisure activities and social contacts. Finally, it can threaten their own mental and physical health, sometimes forcing them to cut down on their normal daily duties. Clearly this reduction in activity can have financial consequences both for the family and caregivers of schizophrenia and bipolar disorders and for society as a whole (39).

In addition to opportunity costs, in-kind contributions and the value of time spent away from other productive activities, relatives caring for individuals with schizophrenia and bipolar disorders may themselves develop stress-related mental disorders. A study reported that 23 percent of relatives caring for schizophrenic patients in the family home had neurotic disorders, most commonly depression, confirmed by direct clinical interviews. Family interaction studies showed that post-hospital course of illness correlated strongly with family emotional climate. Patients whose relatives displayed high levels of criticalness, hostility and emotional over involvement were at increased risk of relapse and readmission to inpatient care. Similar findings of such studies revealed that relapse rates 9 months after hospital discharge were 92 and 15 percent among patients with high expressed emotion (EE) and low EE families, respectively (26).

Day-to-day care of such patients particularly caring for a person with schizophrenia can be both demanding and exhausting. The uninhibited social behavior of a patient, (stress related) family disputes and a lack of understanding and sympathy from neighbors and friends can leave carers feeling anxious, depressed, physically ill, guilty or bewildered. A study of 408 families in the USA with a mentally ill family member (80 percent with schizophrenia) showed that care giving absorbed most of their spare time (66.5 hours per month) and employment (27). Stress, hostility and emotional over-involvement may produce high levels of EE causing further deterioration as patients living with high-EE families have a worse prognosis than patients in low-EE households.

Increased cost of management of schizophrenia and bipolar disorders and additional family burden could also result from therapy refractory and recurrent cases. Approximately 25 percent of all schizophrenic patients believed to be therapy refractory and do not respond satisfactorily to consistently applied neuroleptic treatment for at least 12 months (84). Review of long term follow up studies in Australia suggests that only 25 percent of patients with schizophrenia can be expected to recover from their psychosis without residual handicap or need for re-hospitalization (85). About 40 percent will suffer recurrent psychotic episodes, social disability, and periods of unemployment, and 35 percent will remain identifiably psychotic, require some level of continual care, and never be employed. Although the prevalence of treatment-resistant patients is not known, studies suggest that between 5 percent and 30 percent of patients fail to respond or be only partially responsive to standard forms of treatment (85).

1.2.7. Conceptual and estimation issues

Analyzing economic impact of schizophrenia and bipolar disorders requires consideration of numerous conceptual and estimation issues. The conceptual issues involve using either prevalence-based or incidence-based cost approach. Prevalence based cost approach estimates the direct and indirect economic burden incurred in a period of time (usually one year) resulting from a disease or illness. This approach is appropriate if the results of the analysis are to be tied to cost control, since it identifies the major components of current expenditures and it identifies possible targets for economy. On the other hand, incidence based cost approach represents the lifetime costs resulting from a disease or illness. These costs refer to the total lifetime costs of all cases with onset of disease in a given base year. This approach is appropriate if the analysis is aimed at making decisions about which treatment or strategy to implement, because it provides the basis for predictions about the likely savings from programs that reduce incidence or improve outcomes (29, 86, 87). However, because of difficulty in estimating long-term prognosis of an illness and its economic consequences, studies using the prevalence-based approach are more common than studies using the incidence-based approach (66).

Another conceptual issue is how to calculate the value of human life. In this regard there are two prominent approaches: the human capital approach and the willingness to pay approach. The human capital approach views an individual as producing a stream of output that is valued at market earnings, and the value of life is the discounted future earnings. The term human capital (HC) derives from the observation that variation in earning over a person's lifetime is due to investment on human capital through education, on the job training, and work experience. The HC approach is based on the concept of potential productive output that may be lost due to morbidity and mortality. According to this method potentially lost production is estimated until the age of retirement. This approach is more commonly used in cost-benefit and cost-effectiveness analyses (29, 86, 87).

In contrast, the willingness to pay approach values life according to what individuals are willing to pay for a change that reduces the probability of illness or death. This is more difficult to measure since it takes into account perceptions of pain and suffering associated with a disease condition. Also the HC approach has limitations because it implicitly assumes that a worker cannot be replaced. Particularly for most industrialized countries where excess supply of skilled labor exists, the HC approach becomes questionable. Therefore, in an attempt to measure actual rather than potential production loss, another method-the friction cost method (FC) has been developed (86). This method modifies the HC approach by allowing for worker replacement by other workers. The FC method adjusts cost calculations by stating that, when a person is absent from work or terminates employment, the actual productivity loss from the job continues only until the time at which other workers assume that job or fill that vacant position. That means in the FC method the productivity loss from a job will continue only until the time a substitute worker fills that vacant job. This period of time that is required for worker replacement is the friction period. However, this method is not yet widely accepted (29, 86, 87).

With regard to issues mentioned above, many important determinants of cost of illness cannot be measured easily and require estimation. This estimation involves issues of psychosocial costs (pain and suffering), reduced productivity (output losses), non-market activities (value of care giving services provided by families of patients that ordinarily would be purchased in the market place), and non-health related costs (transportation to providers, criminal justice expenditures, incarcerations). Other estimation issues include accounting for consumption, costs versus charges, estimation of lifetime earnings, co-morbidity, and the discount rate. The issue of co-morbidity is of particular interest since co-morbid condition may account for additional days of care. In addition to the conceptual and estimation issues, a comprehensive economic evaluation requires definition of outcomes and their relationship with costs. In other words, indicators of cost-effectiveness need to be built up (29, 86, 87).

1.2.8. Limitations of scope

Studies cited are mainly from Europe and America, particularly from the United Kingdom (UK) and United States of America (USA) and many of them have used secondary data and lack comparability because of methodological differences. Some of the studies fail to indicate alternative methods of mental health service delivery, fall short of showing association of cost of illness to outcome(s) of the diseases and are unable to make full consideration of cost components. In order to make better decision with regard to cost control and resource use the contribution of specific studies undertaken in the context of a specific country is immense. Therefore, it is very necessary to carryout economic burden study on schizophrenia and bipolar disorders in the context of Ethiopia. Economic burden studies which can help in health policy and decision-making are very few, despite the fact that resources are scarce and disproportionately distributed in the country. Economic study is about choice, which is concerned with the best alternative use of limited resources (88); it is a tool to identify the most efficient way of meeting a stated objective. Its main function is to allow policy-makers, managers and clinicians to make choices by assessing the cost and benefits of achieving the stated objectives by different alternative methods.

1.2.9. Psychiatric epidemiology and mental health in Ethiopia

Mental health is vitally important aspect of public health that has long been neglected. As a result, the burden of mental health disorders on social well-being and economic productivity has long been underestimated. These previously underestimated conditions with an immense consequence of disability impose high burden on individuals, communities and health services. In Ethiopia, even though mental health problems are mentioned as one of the priority areas for government action, only very little has actually been done up to now; in addition, despite high burden of disease due to mental health problems, no economic burden studies on mental health in the country. Particularly, the burden of major mental illnesses-schizophrenia and bipolar disorders- is not quantified and translated into economic terms. It is important to translate this burden into economic terms to better understand the magnitude of schizophrenia and bipolar disorders and to bring them to the attention of policy makers in order to facilitate strengthening mental health interventions.

Ethiopia is a low income group country with an approximate area of 1104 sq. km. and population size of 81,021,000. Out of this population number 49.2 percent of males and 33.8 percent of females are literate and life expectancy at birth for males is 55 years while it is 58 years for females. In the country the proportion of health budget to gross domestic product in the year 2005 was 4.9 percent. Ethiopia has no mental health and substance abuse policy and no national mental health program or programs for special population groups. Nonetheless, it has an established mental health financing system, but details about expenditure on mental health are not available. The primary sources of mental health financing are tax based out-of-pocket expenditure by the patient or family and grants. Mental health is part of the country's primary health care system and actual treatment of severe mental disorders is available at the primary care level, however, there are no community care facilities for patients with mental disorders (77, 89).

A village in the highlands of the study area

Government health institutions are the sole source of mental health services. Unlike other health service delivery in the country, non-governmental organizations are not involved in delivering mental health care. The country has data collection system or epidemiological study on mental health. The training and research division of the Amanuel Specialized Mental Hospital has been established recently for this purpose. Also there is a follow-up study project in Butajira, south Ethiopia, on course and outcome of schizophrenia and bipolar disorders which is underway since 1991 by the Department of Psychiatry, Faculty of Medicine-Addis Ababa University. The project is funded by the

Stanley Medical Research Institute. Besides, to the follow-up study on schizophrenia and bipolar disorder, the project sometimes runs a clinical trial studies.

The above general introductory remark can give a clue that mental health problems are rampant in the country and there is a fertile ground for the problem as the country is known for its poverty, poor health status of its populations, war and famine. Nevertheless, in the country still there is no national or comparative study on mental health. Therefore, it can be said that psychiatric epidemiology and the study of mental health in Ethiopia is relatively new field which is at its infancy.

The history of psychiatry in Ethiopia dates back to the late 1930s, however, it is from 1965 onwards that modern psychiatry is gaining ground in the country. Before this period little is known about the prevalence of mental illness in Ethiopia (14). A series of epidemiological surveys in the then Kaffa Governorate by Giel in the late sixties and in Addis Ababa by Kortmann in mid eighties were the first psychiatric morbidity studies whereby prevalence rate of 8.6 and 9.1 percent for rural and urban villages respectively were reported in the Governorate and a prevalence of 12 percent was reported for Addis Ababa (13, 14).

At about the same time (1970) in Nekempte, Western Ethiopia, a Swedish professor had found mental disorders, suicidal and aggressive behaviors due to alcohol intoxication to be common occurrences amongst the general in- and outpatient populations (14). In this study, it was observed that 18 percent of the patients seen at the outpatient clinic of the general hospital had psychiatric illness. Moreover, in the late 1980s, studies on the general population of mothers and children reported prevalence of mental illness ranging from 12 percent to 23 percent (13). Interview instruments used in these studies were Kessel classification, 24-item self Reporting Questionnaire of WHO, 10-item reporting Questionnaire for children of WHO and 64-item tapping externalizing and internalizing behavior problems taken from Achenbach's questionnaire; and most of the studies were based on small sample size. Relatively, large scale psychiatric epidemiological studies using recently developed instruments were conducted in the capital city and in the rural part of the county during the 1990s.

A village in the lowlands of the study area

A study conducted in the capital city Addis Ababa, between January and March 1994 on a study population of 10, 203, which were selected by cluster sampling method proportionate to size from the entire city, reported 11.7 percent prevalence of mental distress (90). In the study, problem drinking and suicidal ideation were explained to be among the mental health problems prevailing in the study community. Another survey conducted in the city between September and December 1994 on 1420 randomly selected individuals aged 15 and above revealed 5 percent weighted lifetime and 3.8 percent one month prevalence for affective disorders (15). This study has also revealed prevalence of severe cognitive disorders, bipolar disorders, depressive episodes, recurrent depressive episodes, persistent mood disorders, neurotic and somatoform disorders. The study found sex (women had increased risk than men), age (increasing risk with increasing age), family history of mental illness, marital status, educational attainment, family size, and employment to be determinants or sociodemographic risk factors of the psychiatric illnesses.

A small town in the highlands

In comparison to the above findings, similar cross-sectional studies conducted in the rural part of the country (Butajira) have reported slightly higher prevalence rates for most of the illnesses (18, 19). In the year 2001 a community based study on schizophrenia in the same locality (91) has screened 68,378 adult population of age above 14 years and according to International Classification of Diseases (ICD-10) and Diagnostic Statistical Manual IV (DSM-IV) criteria the prevalence of schizophrenia was found to be 4.7/1000. Since, persons with schizophrenia lives longer with disability this prevalence rate is high. This study has also shown that relatives of a schizophrenic patient mostly faced financial problems to care for their ill relatives.

It was also found that attitudes of the community add to the seriousness of mental health problems; in an area of central Ethiopia with an epilepsy prevalence of 5.2 per thousand, a door to door survey of 1500 households revealed that 45 percent of those interviewed believed that the disorder could be transmitted by physical contact at the time of an attack; three quarters would not allow a family member to marry a patient with epilepsy and would not employ such a person (92)

There are also reports of mental health studies on children and adolescents. Prevalence of childhood behavioral and mental disorders in Ambo district Western Ethiopia in the age group of 5 to 15 years had reported 17.7 percent of prevalence of mental health problems in the study subjects. This shows high estimate of psychiatric morbidity among the child and adolescent age groups. Previous prevalence estimates of psychiatric disorders among children, using instruments like Reporting Questionnaire for Children (RQC) and Childhood Behavioral and Psychological Questionnaire (CBPQ) range between 5.2 to 25 percent (93, 94). A study done in Butajira, Southern Ethiopia, using the Diagnostic Interview for Children and Adolescents (DICA) showed that 3.5 percent of children had at least one or more diagnoses of childhood behavioral and emotional disorders (95).

Another International Labor Organization (ILO) sponsored pilot study on 1000 children (528 laborers and 472 non-laborers) in Addis Ababa; using DICA gave prevalence of 19 percent and 12 percent for one or more psychiatric disorders among child laborers and non-laborers respectively (96). This study showed that physical, sexual and emotional abuses were more common among child laborers than among non-laborers. Symptoms of separation anxiety and simple phobia were significantly higher among the laborers than the non-laborers.

In the year 2003, prevalence estimate of mental and behavioral problems using psychiatric interview instruments on 2000 child laborers and 400 non-laborers identified 170 children to have mental health problems. The RQC interview screened 8.5 percent of the children as probable cases of mental and behavioral disorders. All of the 170 children were further interviewed for specific psychiatric diagnosis using DICA and it was found that the prevalence of mental or emotional health problems in the child laborers was 4.9 percent with phobia or irrational fear, enuresis or bedwetting and separation anxiety the major mental health disorders identified in the child laborers. Combinations of these disorders were also seen in some of the child laborers (97).

Early starting of a market in one of the study areas

Another descriptive epidemiological survey of mental disorders among an isolated island community on Lake Zeway in Southeastern Ethiopia (98), revealed that out of 1714 individuals involved in the study, 18.3 percent were having ICD-10 diagnoses excluding substance use disorders. Likewise the lifetime prevalence and sociodemographic correlates of psychiatric disorders among the Borana semi-nomadic community (99), in which 1854 people aged 15 years and above were interviewed has shown that the lifetime prevalence of ICD-10 mental disorders, including substance abuse, was 21.6 percent. Affective disorders were found in 1.7 percent of the study population, whereas neurotic and somatoform disorders constituted 14 percent. No cases of schizophrenia were detected. The prevalence of substance use was 10.1 percent.

Another special population group mental health study on 3000 women who were systematically selected from a random start point has shown that depressive episode, somatoform disorder and recurrent depressive episodes were major lifetime mental health problems with prevalence of 6, 3 and 2 percent respectively (100). In the study it was reported that women who suffered from domestic violence also reported more symptoms of mental distress and the low status of women in the society, lack of general awareness about women's rights and weakness in the law enforcement system were some of the reasons for the wide spread violence and problems of mental health.

The subject of mental health should be seen from a wider perspective as their effect on societal functioning is so huge; if things regarding mental health are seen from a wider perspective and quantified in terms of economic burden it would be possible to make proper management of psychiatric problems and have locally appropriate health plan. But, if this is not actually done and appropriate attention is not paid to prevent mental health problems, it would be difficult to understand our society's functional level; furthermore, reduced functionality of our community may result in accumulation of disability days which will further predispose us to abject poverty.


Health post in the highlands of the study area

Poverty creates the conditions for malnutrition, illness, social strife, political instability, and despair; studies indicate that poverty is one of the prime indicators of mental illness (4, 7). With this regard one can envisage the severity of mental health problems for Ethiopia with its large proportion of population living in poverty.

On this subject matter even if literature is inadequate in the country, it can be understood that the problems of mental health in Ethiopia are so high and available epidemiological prevalence figures should be taken as a lower bound, because people are usually reluctant to report such private situations like mental health. In addition, it can be understood that if more representative sample is taken from all over the country, these prevalence findings would have risen high. As a result the economic burden will also be high.

In a traditional society like Ethiopia where most of the population seeks help for mental health problems from traditional and spiritual healers, the burden on caring families would be more than it could be imagined, particularly in the rural areas where the opportunity to seek modern health service help is so limited, the burden in which families are experiencing will be tremendous; on the other hand even if families with a family member of mental health problems are caregivers for the sick at a household level, their involvement in the mental health care system is limited. This makes the system to be ineffective and inefficient. Moreover, many of these issues remain poorly researched in Ethiopia.

2. THE RESEARCH QUESTION

In Ethiopia, mental health problems are not given priority in strategy or action, although mental health was mentioned as a priority in the government's official health policy document. It could be because of lack of data, among many other factors, on the extent of mental disorders in the general population (15, 17, 101). Few studies conducted in the metropolis of Addis Ababa, some urban and rural areas revealed prevalence range of 7 to 31.8 percent among the population groups studied (13-20, 102). In 1998, burden of disease study in Butajira, Southern Ethiopia, has revealed that depression and schizophrenia had contributed for 11 percent of the total DALYs lost (20). In the same area, an ongoing course and outcome study on schizophrenia and bipolar disorders reported prevalence of 4.66 and 3.15 per 1000 cases respectively (103).

However, despite high magnitude of the problem, economic burden of schizophrenia and bipolar disorders is not quantified and translated into economic terms. In addition, the extent and the longitudinal time change of family and caregiver burden is unknown in the country. Therefore, this dissertation had tried to give answer to the following research questions:

1. What is the extent of economic burden of schizophrenia and bipolar disorders in Ethiopia?
2. How does burden change overtime in families of patients with schizophrenia and bipolar disorders?
3. Are schizophrenia and bipolar disorder families and physical disorder families equally burdened?

3. RATIONALE FOR THE DISSERTATION

Most of the studies quantifying economic burden of schizophrenia and bipolar disorders originate from developed countries where the level of health care provision is quite different to that available in developing countries. In addition, most of these studies from the developed world are cross-sectional clinic-based studies, community based studies are rare.

On the other hand, in low income countries, there are very few cross-sectional studies on family and caregiver burden of schizophrenia and bipolar disorders, along side, there are no longitudinal economic burden studies. As a result longitudinal family and caregiver burden is largely unknown and family intervention strategies are rarely integrated to clinical services compounding the effect of poorly organized mental health systems.

In such situations of traditional societies where caring for a family member is a norm like in Ethiopia, it is expected that individual patients and their families would bear the brunt of burden due to schizophrenia and bipolar disorders. This burden needs to be explained in order to unveil the economic burden of schizophrenia and bipolar disorders on families and caregivers. However, caring for schizophrenia and bipolar disorders is poorly researched in Ethiopia and in most low income developing countries. These were the rationales of the dissertation to conduct longitudinal family and caregiver burden study on schizophrenia and bipolar disorders. It was believed that the findings of the study will influence resource allocation starting at policy and managerial level down to the affected.

4. AIMS OF THE DISSERTATION

In low-income countries, families already living in poverty may be disproportionately affected by having a family member with schizophrenia or bipolar disorders. Compounding this effect, the way of thinking in disease prioritization and measurement has made the economic burden of schizophrenia and bipolar disorders to be deeply masked. Therefore, the aims of this dissertation were to estimate the population average economic burden caused by schizophrenia and bipolar disorders in Ethiopia and to bring into light the extent of burden caregivers, families and the society are experiencing. The study had also aimed to describe the change overtime of burden on families and caregivers due to schizophrenia and bipolar disorders.

Specifically the study had aimed to

1. describe the extent of economic burden of schizophrenia and bipolar disorders at family and societal level.
2. make comparative analysis of economic and caregiver burden of families of patients with bipolar disorder to families of patients with other physical disorders.
3. explain the pattern of burden families and caregivers with patients of schizophrenia and bipolar disorders are experiencing over time.
4. describe the burden experienced by patients with bipolar disorder who are living in a community under clinical follow-up.

5. METHODS

5.1. Study setting

The study was done in Meskan and Mareko Wereda, a rural district in Gurage Zone, the Southern Nations, Nationalities and Peoples Regional State in Ethiopia. The estimated size of the District is 797 km^2, of which Butajira town covers approximately 9 km^2. The district is commonly referred to as Butajira. It is located in the south-central part of Ethiopia at an average altitude of 2,100 meters above sea level with a range of 1,750 meters in the low lands to 3,400 meters in the mountainous areas. The district is administratively subdivided into 45 sub-districts and has a population of about 260,000, with over 100, 000 of them between the ages of 15 and 45 years (104). Out of the 45 sub-districts nine rural and one urban sub-district are under continuous demographic surveillance by the Butajira Rural Health Program (BRHP). The BRHP registers events such as birth, death, marriage, new household, out-migration, in-migration, and internal movements. The district community is predominantly Muslim and from the Gurage ethnic group which is further divided into minor ethnic groups. The Meskan, Mareko, Sodo, and Dobi are major tribal groups. The population speaks Guragigna, the national language Amharic, is also widely spoken in the area. The main occupations are farming and small-scale business. Most houses in rural areas are tukuls. In the town, housing is typically dense and crowded, usually with corrugated iron roofs. In the district there are one hospital, 2 health centers, 5 health stations, 12 health posts 5 private clinics and more than 11 drug shops. Health problems have predominantly been associated with infectious and maternal causes. In the year 2000, acute febrile illnesses, liver diseases, diarrheal diseases, tuberculosis and HIV/AIDS were identified as major causes of adult death (105).

One form of patient transportation in front of a health station

However, trends towards higher incidence of non-communicable diseases were also observed (20). In line with this fact, extensive mental health survey in the rural district conducted for about three years was completed in May 2001. This base line survey was done to screen the entire population between 15 to 49 years (estimated to be over 100,000) for psychotic and affective disorders. The survey identified over 800 cases of major mental disorders by interviewing 68,378 adults using the WHO Composite International Diagnostic Interview (CIDI), Version 2.1 (106) and key informants from 44 sub-districts. Identified possible cases for mental disorders were confirmed by Schedule for Comprehensive Assessment in Neuropsychiatry (SCAN) (107). The study was launched to describe the course and outcome of schizophrenia and bipolar disorders in a rural setting. Finally, identified cases of 321 schizophrenia, 217 bipolar disorder, 215 major depression and 93 mania patients were enrolled to the course and outcome study and undergo follow-up assessment every six months. This extensive baseline epidemiological survey has turned out to be one of the best examples of population laboratories on the continent of Africa.

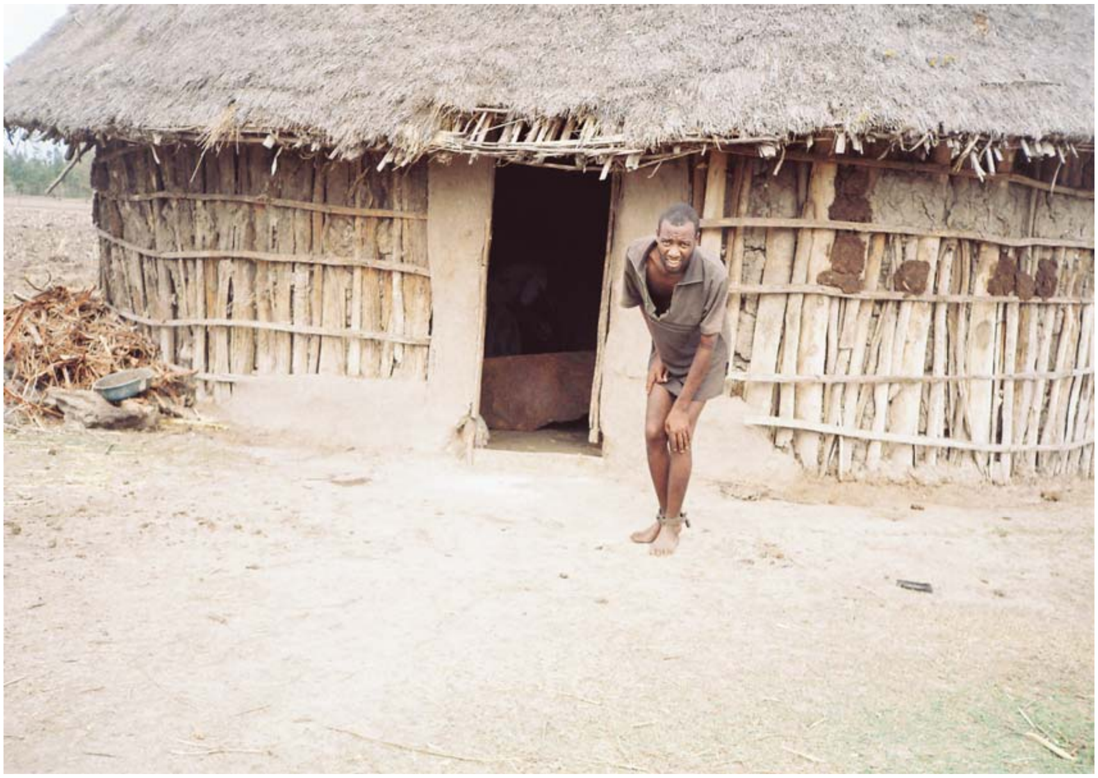
Family members supporting schizophrenic patient transported to a psychiatric clinic

5.2. Study design

The design of the study was a longitudinal prospective cohort involving families with and without schizophrenic and bipolar disorders patients. The follow-up period was one year and follow-up data collection at the community level, was carried out every two months. In establishing a time frame of such studies two recognized approaches are used: prevalence and incidence based. Prevalence based approach examine costs incurred during a given time period, regardless of the time of disease onset. This approach estimates the total costs of treating patients in a given interval independent of when patients were first diagnosed or the stage reached in disease progression. In contrast, the incidence-based approach focuses on all the future costs associated with cases (treating individuals or a cohort of patients) from the time of first diagnosis or treatment (with onset of illness in the base year) until death (29, 86, 87, 108).

When practice patterns and technology do not change overtime, both methods yield the same results. However, if changes in practice patterns and technology are anticipated, incidence-based costs will reflect these changes. The prevalence approach is better suited to answering policy questions about cost control. The incidence approach on the other hand, is better suited to decision making about treatment on research strategies. The incidence approach requires collection of primary data based on knowledge of the likely course of a disease and its duration, i.e., survival rates since onset, type and cost of medical care for the duration of the illness and impact of the illness on employment, income and unpaid work (29, 86, 87, 108).

In this study, the prevalence-based approach was used. Because, all inhabitants of the district were screened for mental health disorders and identified cases are already under treatment and no case finding has been continued.



Schizophrenic patient restrained and standing in front of his hut

5.3. Study subjects

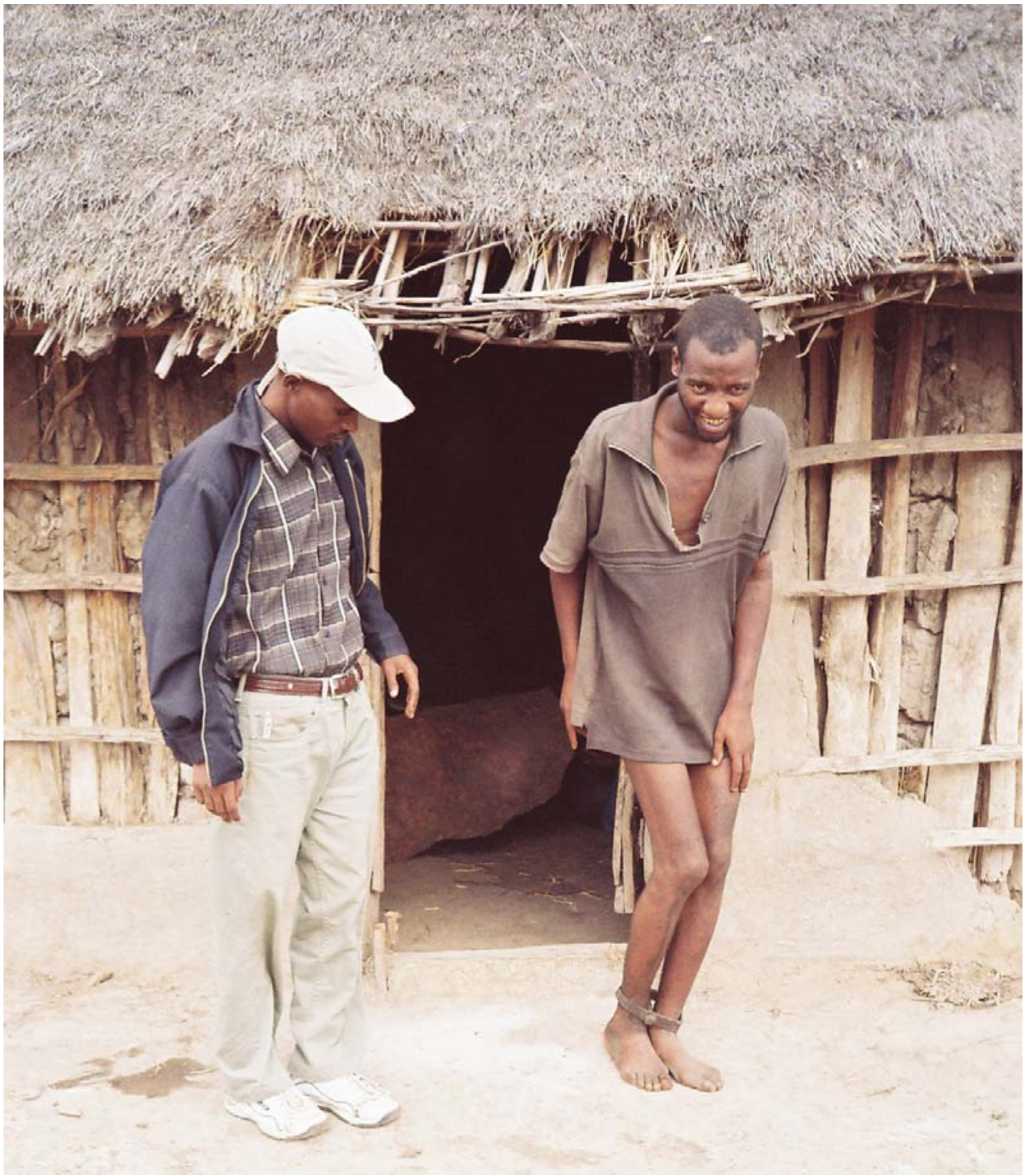
As pointed out in section 5.1 and 5.2, the study was done in Meskan and Mareko Wereda, a rural district in southern Ethiopia. In the district a course and outcome study project on schizophrenia and bipolar disorder is underway since the early 1990s. The project had screened all 83,282 adult population of the district for bipolar disorder by house to house survey using the WHO Composite International Diagnostic Interview (CIDI), Version 2.1 (106). The present study used a prospective longitudinal design involving all identified families with schizophrenia and bipolar disorder patients. Two control groups of families were selected from follow-up clinics and from the community. The first control group included all families of follow-up attendees for diabetes, hypertension and asthma (DHA) in health institutions of the district and the second control group was composed of randomly chosen families from the community. From each group of families, family caregivers were selected using the method followed by Perlick et al. caregiver burden study (109).

Thus, caregivers were selected based on the following criteria:

a) is a spouse, parent or spouse equivalent to the patient;
b) has most frequent contact with the patient;
c) helps to support the patient financially;
d) has most frequently been a collateral in the patient's treatment; and
e) is contacted by treatment staff in case of emergency. To be included in the sample as a caregiver, the chosen caregiver had to satisfy at least three of the criteria.

Consequently, this study sampled all 249 schizophrenia and 190 families of bipolar patients who were under follow-up during the survey, the first control group of 55 families with DHA patients (35 diabetes mellitus, 12 hypertension and 8 asthma), and the second control group of 659 randomly selected families in the community. The total sample size of the study comprised of 1153 families of patients and caregivers.

During data collection from families of controls from the community, a family member was considered as a caregiver if any other illness had affected a family member and care had been given to the ill person by other family member(s). Therefore, in each of the groups, illness was defined as having an individual family member whose normal functioning was interrupted due to a health problem.



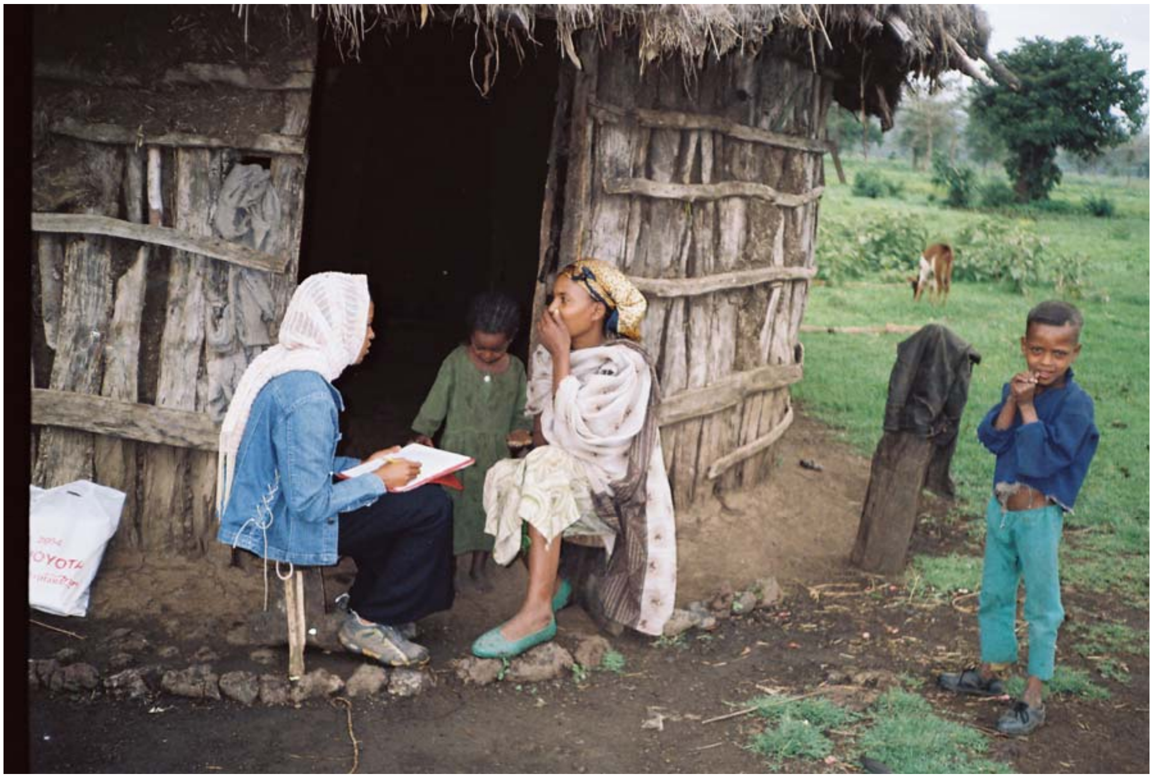
Data collector visiting a schizophrenic patient

5.4. Sampling

The second control group for the purpose of comparison was selected using registration list during the baseline survey of adult population of the district as a sampling frame. Thus, from the 68,378 individuals screened for mental health disorders, 659 subjects were randomly selected based on computer generated random numbers. And their families were involved in the study as control. The size of this control group was determined based on the size of 439 cases of the study. As a result, controlling for each case and 50 percent allowance for non-response were selected.

5.6. Data collection

The data collection was carried out every two months for one year; starting in July 2004 and ending in June 2005. Data collection instruments were developed and pre-tested three times in a nearby community. The purpose of these repeated pre-tests was to increase the reliability and validity of interview instruments. Accordingly, interview instruments with reliability test coefficient less than 0.40 were dropped; and reliable burden measurement scales was obtained with improvement of Cronbach's alpha from 0.535 during the second pretest to 0.839 during the third. It was also tried to improve the validity of interview instruments by constructing as many questionnaire items as possible. In each of the pre-testing sessions, one week extensive training was provided for data collectors and supervisors. Using the refined final interview instruments, data were collected on family economic and caregiver burden. Data quality and consistency cross-checks were made by another group of trained supervisors recruited for the purpose. The data quality and consistency cross-checking was implemented by randomly selecting 5 percent of total interviews done and re-interviewing study subjects. For data entry EpiInfo 6 version 6.04d statistical software was used while SPSS 11.0 and Stata/SE 8.2 for Windows were used for data analysis.



Data collector interviewing a caregiver

5.6.1. Burden measurement

Longitudinal burden measurements (six in total within a year) were made on out-of-pocket medical expenses for health services, time lost due to care giving and the extent of family caregiver burden. Out-of-pocket medical expenses included cost of: travel, medical examination, drugs and injections, laboratory service, food and accommodation; and the time lost due to care giving included time lost in accompanying patient to and from health institute and lost days of work due to care giving at home. There were 15 questionnaire items constituting family caregiver burden. Also there were 14 questionnaire items constituting family burden, with response categories on a five-point scale (see tables 1 and 2).

Table 1. Questionnaire items constituting family caregiver burden in schizophrenia, Butajira-Ethiopia, 2005

To what extent the:

a) patient’s illness causes sleep disturbance?

b) patient’s illness creates burden on job?

c) patient’s illness limits social relation movement?

d) patient’s illness creates burden as to ignore other family members?

e) patient’s illness creates feeling of unhappiness?

f) patient’s illness creates worry about the future?

g) to what extent were you ashamed due to the patient’s illness?

h) when you think about the patient, to what extent do you feel guilty?

i) how much do you worry by saying that I am unable to cope-up more than this?

j) to what extent patient’s illness create health problem?

k) to what extent your relationship with the patient was in crisis due to the patient’s illness?

l) to what extent the patient causes physical injury on you?

m) to what extent life was problematic and challenging for you due to the patient’s illness?

n) to what extent the patient’s illness creates burden on you as to think of suicide? and

0) to what extent were you happy about patient’s social relationships?

During each interview, family caregivers were asked about the extent of burden they and their family had experienced in the month prior to interview using the 15 questionnaire items of family caregiver burden and the 14 questionnaire items of family burden. Thus, family and caregiver burden score of 1 to 5 was given based on the frequency of occurrence of a ‘burden-causing event’: 1 = did not happen at all in the month; 2 = happened at least once per week in the month; 3 = happened at least twice per week in the month; 4 = happened at least 3 to 6 times per week in the month; and 5 = happened almost every day per week in the month.

Table 2. Questionnaire items constituting family burden, Butajira-Ethiopia, 2005

To what extent:

a) patient’s illness creates financial problem on the family?

b) the patient’s illness affected possibility of getting family income?

c) the patient’s illness creates problem in celebrating holidays?

d) the family feels no financial alternative source for the patient’s illness?

e) the patient’s illness causes financial strain on family need to go somewhere?

f) the patient’s illness creates burden on the family’s children?

g) family relationship was disturbed due to the patient’s illness?

h) the family feels lonely and isolated due to the patient’s illness?

i) the family feels that nothing can be done for the patient’s illness?

j) the patient was isolated by family members and others you consider family?

k) the family was worried thinking about relapse of patient’s illness?

l) patient’s health condition was felt as a burden to the family?

m) patient’s condition has affected family’s quality of life? and

n) to what extent patient’s health behavior was challenging and difficult?

5.6.2. Burden estimation

In the estimation of burden direct and indirect cost estimations were involved. In estimating the indirect cost, two methods of estimation were used. The first one was estimating lost days of work using a day’s wage and the other method was estimating lost days of work using average estimated value of lost time (as the value of lost time estimation was made by the study subjects). Direct cost extrapolation at societal level was made by taking into consideration the out-of-pocket medical expense made by families, one percent life time prevalence as a lower margin and average life time prevalence of different studies done at different times in urban and rural Ethiopia (15, 16, 19, 91, 98, 99, 110) as a higher margin; and assuming that each case of schizophrenia and bipolar disorders cared by all respective families. Likewise, the indirect cost of loss of annual cumulative working days due to care giving was estimated by assuming $0.92 as a wage for a day's work. In general financial costs, time lost and lost days of work were considered as a burden and estimates were extrapolated to societal level by multiplying added costs of mean out-of-pocket medical expense, lost time, lost days of work by the estimated lifetime prevalence of schizophrenia and bipolar disorders in the adult population of age 15 years and above in Ethiopia. These assumptions were made in the dissertation that use the prevalence based and the human capital approach of economic burden estimation.

5.6.3. Data collection procedures

Interview date forms were prepared to be filled by each data collector during each interview period. The purpose of using the interview dates forms was to make durations of each interview to be equally spaced. Making interviews equally spaced will lay the ground to meet the assumption of repeated measure data analysis, besides other assumptions discussed in the data analysis section. However, due to work nature and unavailability of study subjects in their residential area, interviews were not equally spaced. This had a significant implication on the choice of data analysis approach (see section 5.7).

5.7. Data analysis

There were six waves of data used in the analysis. Descriptive analyses were made in terms of mean out-of–pocket medical expenses for health services; cost of travel, time lost traveling to-and-from health institutions, time lost at health institutions; lost days of work in the month prior to the interview; patients' ability to work and compliance to treatment and frequency of substance use. Longitudinal economic and family caregiver burden comparisons of caring for bipolar patients were made using two arms of control. The first arm was family caregivers of DHA patients and the second arm was family caregivers of sick controls in the community (SCC). Chi-square and t-test were used to compare socio-demographic characteristics.

From time one (baseline) through six (end of the study); family and caregiver burden were computed as the respondent's average responses across the 14 items constituting family burden and the 15 items constituting caregiver burden. Finally, a population average generalized estimating equation was used to explain the change over time in family and caregiver burden. To account for unmeasured effects in longitudinal caregiver burden, time series analyses were made using feasible generalized least square regression with panel-specific autocorrelation. Burden estimates were extrapolated to societal level. For the purpose of comparison all costs were converted to US$ by using the mean exchange rate for 2005 of Ethiopian currency Birr 8.6810 = 1US$ (111).

5.7.1. Justification for the paradigm and analytic methodology

In the present study burden measurements were done repeatedly. Methods used to analyze repeated measures data range from the simple to the complex. One of the simple approaches for the analysis of repeated measures is to compare groups at each time point, by using either t-tests or some nonparametric equivalent (112-115). However, such testing assumes that each time point is of separate interest and is independent. This is unlikely; the tests are not independent. Therefore, their interpretation is difficult. The separate tests do not give an overall answer to whether or not there is difference and provide no single estimate. The application of methods for the analysis of repeated measures data are discussed further in the next sections in relation to justification of choice in the analytic methodology of the economic burden of schizophrenia and bipolar disorders.

5.7.2. Applying repeated measures analysis

My plan of analysis was to make comparisons using the repeated measures analysis of variance (RM- ANOVA). To make this analytic approach applicable in my study, the following assumptions should be met (116, 117): i.e., the populations are normally distributed; samples are independent, the population variances are all equal and, assumption of sphericity. In line with these statistical facts, problems encountered when applying the repeated measure ANOVA in my study were:

1. There were unequal population sample size in each group of my study subjects; as a result there is unequal variance and covariance in my sample which on the other hand might violate analytical assumption.
2. The other problem was that in each of the six repeated measures, study subjects were different in numbers and characteristics. This has arisen from loss or participation of different number of study participants at different times of measurement. Such a problem may hinder making comparisons between groups and evaluate changes across time.

3. The dissertation planned to make interview durations to be equally spaced. But due to work nature and unavailability of study subjects in their residential areas, interviews were not equally spaced. Each study subject has an unequally spaced interview dates between consecutive measurements. So, the data are unbalanced requiring other alternative methods.

At this time one may turn to other alternative(s) for repeated measures data analysis. One of the other alternative approaches to repeated measure analysis is to employ multiple regression analysis (118). The multiple regression approach generates results identical to the repeated measures ANOVA, by utilizing a series of orthogonal contrast variables. Another option when sphericity is violated is to use the multivariate tests. However, multivariate tests can be less powerful. The multivariate approach, Multivariate Analysis of Variance (MANOVA), invokes a different sort of logic, that is, rather than treating several measurements over time as a single dependent variable repeatedly measured, the multivariate approach treats the repeated measurements as separate dependent variables generated by one individual (117, 118).

Recent development in analyzing repeated measures data is the use of mixed models. To understand the use of mixed model in analyzing repeated measure data, let me re-examine some points and assumptions about repeated measures analysis. The standard repeated-measures analysis assumes equal correlation between individuals. This method of analysis has strong assumptions about the data (119). The first assumption is equal variance across groups. The second assumption is there should be balanced data; that is, after repeated observations, all individuals should have the same number of measurements. (Unfortunately, subjects in the study do have missing values due to missed visits, dropouts, or subjects not completing all questionnaires… etc). The third assumption is equal time intervals between repeated observations on the same unit. For example, suppose that measurements for two subjects are taken on the same day. If the second measurement of the first subject is taken thirty days after initial measurement, and the second measurement of the second subject is taken thirty-two days after the initial measurement, one cannot assume that these two measurements were taken at the same level of time. One last assumption is equal correlation between repeated observations on a subject, meaning that correlation between measurements at time 1 and 2 are the same as correlation between measurements at time 1 and 3, etc., However, consecutive observations on the same subject tend to be more highly correlated than observations on the same subject taken further apart in time (119).

In comparison, the mixed model analysis has fewer assumptions and restrictions than the repeated measures ANOVA model. It does not have the assumption of equal correlation between observations. Alternatively, the covariance structure of the data can adequately model data in which the observations are not independent. The mixed model also uses all available data on subjects and is unaffected by missing data. Mixed model has fewer limitations and assumptions and models the data more accurately because it accommodates the missing data and takes into account the correlations between repeated observations (119).

However, when the focus of interest is on marginal distribution of the outcome, then the population average generalized estimating equation (PA-GEE) is the method of choice. GEEs are termed marginal models or population average models. Marginal models can be considered as extensions of general linear models for the situation of correlated data. The basic premise of marginal models is to make inferences about the population averages. Marginal models or the GEE approach have become popular method for analyzing longitudinal data. It provides a flexible approach to modeling the mean and the pair wise within-subject association structure. It is flexible enough for use in analyzing response variables that are not normally distributed. It can handle inherently unbalanced designs and missing data with ease. These are the reasons why I have used the PA-GEE analytic approach for the data analysis (120-124). I also believe that in such situations one has also to look for unmeasured effects. To look for unmeasured effects random effects-modeling or generalized least square analysis can be used as in paper IV of this dissertation.

6. ETHICAL CONSIDERATIONS

Before launching the study, ethical approval was obtained from the Faculty of Medicine, Addis Ababa University. Subjects' agreement to participate in the study was requested and the interview process was carried out after an informed consent was obtained from each participant. The right of selected study participant was fully respected as to refuse in taking part in the study and/or discontinue the interview. The confidentiality nature of any information in the study was assured by data collectors and supervisors. The identified cases of mental illness were under clinical follow-up and some were taking medications, however, counseling, psychological support and other similar help were rendered to those who were in need.

7. RESULTS

7.1. Burden in families of patients with schizophrenia (Paper III).

In traditional societies like Ethiopia, where caring for a family member is a norm, the longitudinal time change of burden in families with schizophrenia patients is unknown. Therefore, this study had aimed to fill this research gap in burden studies of families with schizophrenia patients in a rural developing country setup by involving 210 families of patients with schizophrenia for one year. During the year, families had spent $16.52 out-of-pocket due to schizophrenia and on average they had lost 3.12 (sd = 4.54) days of work due to care giving in one month. In the families the mean family burden score over the year was 2.42 (sd= 0.87) and the median family burden score was 2.29. Both the mean and the median family burden scores showed that family burden causing events were happening at least one to two times per week in all the months of the year.

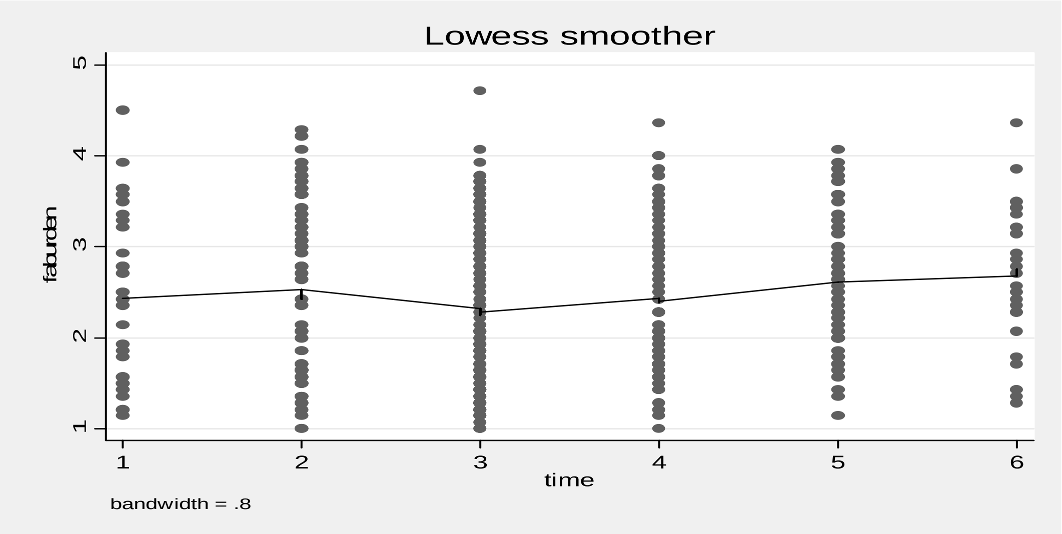


Figure 1 Time series response profile plots with LOWESS mean smoother of burden scores in families with schizophrenia, Butajira-Ethiopia, 2005

Longitudinally families were constantly experiencing burden between the score of 2 and 3 throughout the study year (see fig. 1). Similar results were observed during family burden analysis using family burden median scores (see fig. 2). The median scores were at the higher side of the scale for about 8 months (from time one to two and from time five to six). After 6 to 8 months of the study (i.e., at time three and four) families were experiencing relatively low level of burden. But, then after, they were experiencing relatively higher levels of burden than the other times. Furthermore, throughout the year more than 25 percent of the families were found to experience burden causing events 3 to 6 times per week with burden scores of 3.21 to 4.29.

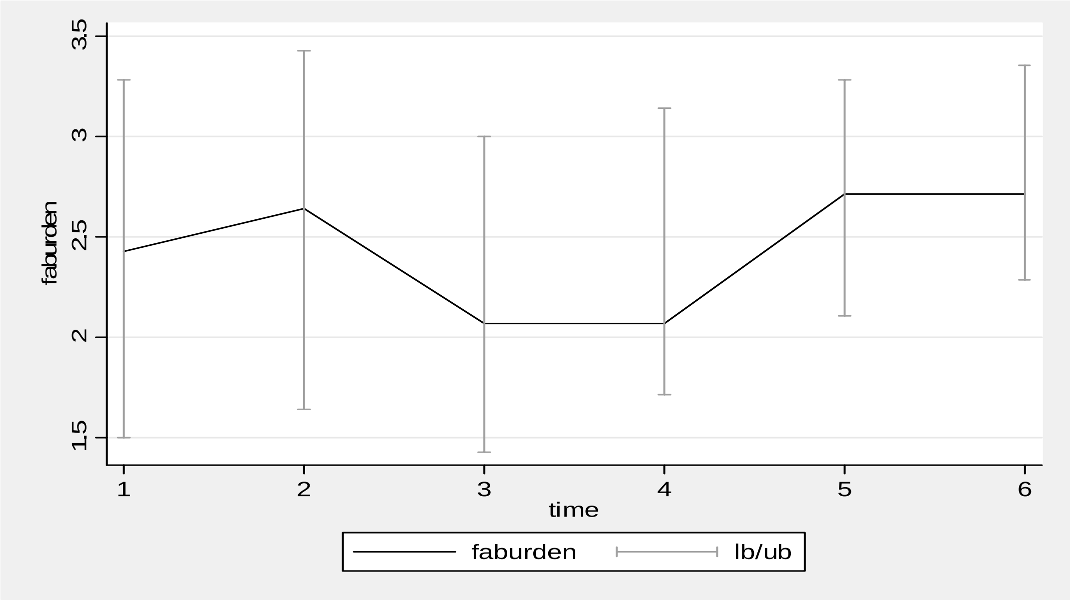


Figure 2 Time series median burden scores with inter quartile range in families with schizophrenia, Butajira-Ethiopia, 2005

The mean and standard error plots of family burden of schizophrenia patient families also showed that mean family burden scores were on the higher side of the scale for most periods of the study except at time 3. For the other periods the mean family burden score were greater than 2.4. It was only at time 3 that the mean family burden score was between 2.2 and 2.4. That means for about 10 months, burden causing events were happening on schizophrenia patient families at least twice per week (see figure 3).

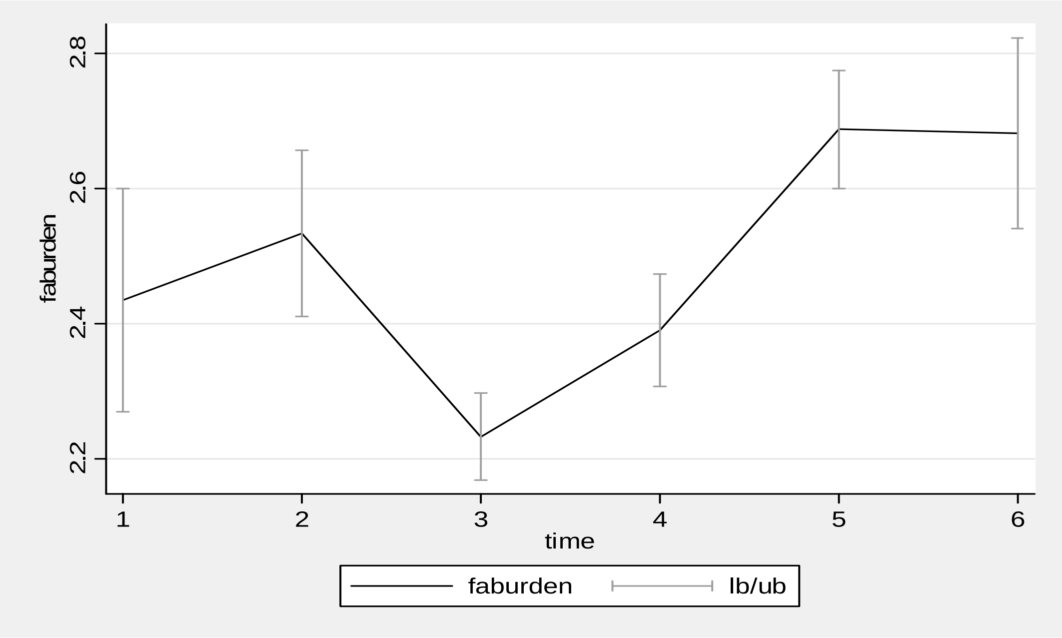


Figure 3 Time series mean and standard error plot of burden scores in families with schizophrenia, Butajira-Ethiopia, 2005

Further analysis of family burden using a population average generalized estimating equation with autoregressive working correlation (see table 3) demonstrated that over the year change in family burden due to time was statistically significant with a mean family burden score of 3.10 (z = -20.86, P>|z|= 0.001). In addition, it was also found that the interaction among the variables of being a family of schizophrenia patient, family burden and time was statistically significant with family burden score of 2.46 (z= 55.95, P>|z|= 0.001).

In summary, this study found that the economic and family burden due to schizophrenia was high for families with schizophrenia patients. Throughput the study period, schizophrenia patient families were constantly experiencing burden due to their schizophrenic relatives.

Table 3. Population average generalized estimating equation analysis of burden in families with schizophrenia patients, Butajira-Ethiopia, 2005.

```
_____________________________________________________________________________________
GEE population-averaged model                              Number of obs       = 262
Group and time vars:   idnumber ndate                      Number of groups   = 76
Link:                   identity                           Obs per group: min = 2
Family:                 Gaussian                                          avg = 3.4
Correlation:                 AR(1)                                        max = 6
                                                           Wald chi2(6)     =   3884.20
Scale parameter:             0.0824217                     Prob > chi2       =    0.0000

                                          (standard errors adjusted for clustering on subjects)
_____________________________________________________________________________________
                     |             Semi-robust
Family burden        |  Coef.    Std. Err.       z            P>|z|      [95% Conf. Interval]
_____________________________________________________________________________________
Time                 | -.66          .03       -20.86    0.000       -.72      -.60
Family size          |  .03          .01         1.79    0.074       -.00       .04
Children under 15 | -.00          .01        -0.35    0.727       -.03       .02
Type of residence  | -.02          .03        -0.72    0.475       -.09       .04
Annual income       | -.00          .00        -1.07    0.283       -.00       .00
Interaction          |  .02          .00        55.95    0.000        .02       .02
Constant             | 2.44          .13        18.17    0.000       2.18      2.71
_____________________________________________________________________________________

Estimated within subject correlation matrix R:
         c1        c2       c3       c4       c5        c6
r1  1.0000
r2  0.0440  1.0000
r3  0.0019  0.0440  1.0000
r4  0.0001  0.0019  0.0440  1.0000
r5  0.0000  0.0001  0.0019  0.0440  1.0000
r6  0.0000  0.0000  0.0001  0.0019  0.0440  1.0000
```

7.2. Caregiver burden in families of patients with schizophrenia (Paper IV)

In low income countries, there are no time series caregiver burden studies in schizophrenia. As a result longitudinal caregiver burden is largely unknown and family intervention strategies are rarely integrated to clinical services compounding the effect of poorly organized mental health systems. Therefore, to fill this research gap the study had aimed to make time-series analysis of caregiver burden in families of patients with schizophrenia. Also in this study 210 families of patients with schizophrenia had participated. In the families the overall mean caregiver burden score over the year was 2.14 (sd= 0.81). In table 4 the participation pattern of caregivers is shown. As shown in the table, caregiver burden standard deviation between subjects was 0.63 (minimum 1.07, maximum 4.2) and the within subject standard deviation was 0.62 (minimum 0.46, maximum 4.01).

Table 4. Participation pattern of caregivers in schizophrenia burden study, Butajira-Ethiopia, 2005.

```
Distribution of T_i:   min    5%    25%     50%     75%    95%    max
                         1     1      1       2       4      5      6
 Frequency     Percent     Cumulative                Pattern
-------------------------------------------------------------------------
     67         33.67        33.67         .    .    1    .    .    .
     25         12.56        46.23         .    .    1    1    .    .
     24         12.06        58.29         .    1    1    1    1    .
     13          6.53        64.82         1    1    1    1    1    .
     13          6.53        71.36         1    .    1    .    .    .
     10          5.03        76.38         1    .    1    1    .    .
     47         23.62       100.00         (other patterns)
-------------------------------------------------------------------------
    199        100.00                      X    X    X    X    X    X
-------------------------------------------------------------------------
Summary mean and standard deviations of caregiver burden

Variable                   Mean     Std. Dev.    Min     Max  |   Observations
Caregiver burden   overall  2.14      0.81         1      4.2  |   N =    477
                   between            0.63         1.07   4.2  |   n =    199
                   within             0.62       0.46     4.01 |  T-bar = 2.40
-------------------------------------------------------------------------------
```

In generalized least square regression analysis time was found statistically significant (z= -13.23, P>|z|= 0.001) determinant factor of schizophrenia caregiver burden (see table 5). Time had increased caregiver burden by a unit of 0.47. However, the p-value of its quadratic term Time^2 suggests that its relationship with schizophrenia caregiver burden is not linear, which may mean after some time burden may rest at a certain constant level. In the same analysis it was found that care giving was more burdensome to female caregivers than males (z= -2.43, P>|z| 0.015). In addition, caregivers in farming occupation were more burdened than caregivers in other occupations (z= -2.49, P>|z|= 0.03) and caregivers whose average family living expense per month was less than or equal to $23.04 were more burdened (z= -3.26, P>|z| 0.001) than caregivers with living expense of greater than $23.04.

Table 5. Time series generalized least square analysis of caregiver sociodemographic characteristics vs. burden in schizophrenia, Butajira-Ethiopia, 2005.

Cross-sectional time-series FGLS regression
Coefficients: generalized least squares
Panels: homoskedastic
Correlation: panel-specific AR(1)

Estimated covariances	= 1	Number of obs	= 397
Estimated autocorrelations	= 122	Number of groups	= 122
Estimated coefficients	= 13	Obs per group: min	= 2
		avg	= 3.25
		max	= 6
		Wald chi2(12)	= 9506.41
Log likelihood	= -21.20594	Prob > chi2	= 0.0000

Caregiver burden	Coef.	Std. Err.	z	P>|z|	[95% Conf. Interval]	
Time	-.473	.035	-13.23	0.000	-.543	-.403
Time2	-.012	.005	-2.37	0.018	-.022	-.002
Interaction	.249	.003	67.40	0.000	.242	.257
Sex (female= 1, male= 0)	-.054	.022	-2.43	0.015	-.096	-.010
Age (15-44= 1, 45+= 0)	-.000	.000	-0.14	0.887	-.001	.001
Marital status (married= 1, other= 0)	-.006	.009	-0.66	0.511	-.024	.012
Education (iliterate= 1, other= 0)	-.002	.007	-0.26	0.791	-.017	.013
Occupation (farmer= 1, other= 0)	-.026	.010	-2.49	0.013	-.046	-.005
Family size (n≥ 5= 1, n ≤5= 0)	-.000	.006	-0.07	0.942	-.012	.011
Family relation (mother = 1, other = 0)	-.010	.012	-0.83	0.406	-.034	.013
Living expense (≤$23.04= 1, >$23.04= 0)	-.001	.000	-3.26	0.001	-.001	-.000
Annual income (≤$345.58=1, >$345.58= 0)	.000	.000	1.47	0.141	-.000	.000
Constant	2.337	.092	25.23	0.000	2.155	2.518

The time series analysis of burden with respect to caregiver characteristics and patient behavior (see table 6), revealed angry caregivers at the patient (because of inability of the patient to carryout activity that was thought to be good for the patient) were more burdened than those caregivers who were not angry at the patient (z= -3.73, P>|z|= 0.001). Similarly caregivers who were worried about the patient and over involved in controlling the patient were more burdened than those caregivers who were not worried (z= -3.6, P>|z|= 0.001) or over-involved (z= -2.12, P>|z|= 0.034). At this point, time was again found important determinant of burden, however, unlike the previous result, the p value of its quadratic term Time^2 suggests that its relationship with schizophrenia caregiver burden was linear, which may suggest linear relationship of burden with patients' behavior. On the other hand, caregivers who were caring for unable patients to carry out self care without being told what to do and who were also caring for non-treatment compliant patients were more burdened than caregivers who were not caring for such patients.

Table 6. Time series generalized least square analysis of caregiver characteristics, patient behavior and burden in schizophrenia, Butajira-Ethiopia, 2005.

Cross-sectional time-series FGLS regression
Coefficients: generalized least squares
Panels: homoskedastic
Correlation: panel-specific AR(1)
Estimated covariances = 1 | Number of obs = 401
Estimated autocorrelations = 123 | Number of groups = 123
Estimated coefficients = 10 | Obs per group: min = 2
Avg = 3.26
max = 6
Wald chi2(9) = 6998.49
Log likelihood = 1.294663 | Prob > chi2 = 0.0000

Caregiver burden	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Time	-.455	.039	-11.39	0.000	-.533	-.376
Time2	-.009	.005	-1.68	0.093	-.019	.001
Interaction	.229	.004	51.24	0.000	.220	.237
Was angry at the patient (Ref: No)	-.099	.026	-3.73	0.000	-.151	-.046
Worried about patient (Ref: No)	-.113	.030	-3.67	0.000	-.174	-.052
Patient was self caring (Ref: Yes)	.114	.023	4.89	0.000	.068	.160
Over-control the patient (Ref: No)	-.060	.028	-2.12	0.034	-.116	-.004
Was aggressive toward patient (Ref: No)	.008	.025	0.33	0.742	-.042	.059
Patient was compliant of treatment (Ref: Yes)	.076	.019	3.89	0.000	.038	.115
Constant	2.271	.090	25.01	0.000	2.093	2.449

Further analysis of caregiver burden in relation to average lost days of work due to care giving and out-of-pocket medical expense made for the patients' mental health services have found caregivers who had lost more than 10 days of work over the year to be more burdened than those who had lost less than 10 days of work. This result was statistically significant (z= 7.14, P>|z|= 0.001). Additionally, there was statistically significant difference (z= -2.07, P>|z|= 0.038) between caregivers who had on average paid more than $5.76 out-of-pocket than caregivers who had paid less. In all the analyses the interaction between time and caregiver burden was statistically significant. This emphasizes that caregivers were constantly burdened over the year.

In general, over the year female caregivers, caregivers in farming occupation, caregivers whose monthly living expenses were very little (which implies impoverishment), who had paid more out-of-pocket for mental health services, who were angry at the patient, who were worried about the patient, who were over involved in controlling the patient, and who had lost more days of work were found to be burdened.

7.3. Economic and family caregiver burden due to bipolar disorder (Paper I)

This paper presents the results of one year follow-up study from rural Ethiopia comparing the economic and caregiver burden for families of patients with bipolar disorder to families of patients with other physical disorders. In addition, this paper had reported on the pattern of burden over time. In the study, family caregivers of 139 bipolar patients, 36 DHA (diabetes, hypertension, and asthma) patients and 401 SCC (sick controls in the community) were involved. During the year, bipolar patient family caregivers had the highest mean out-of-pocket medical expenses ($93.93) compared to DHA patient ($64.80) and SCC family caregivers ($56.18).

Longitudinal comparative analysis of family caregiver burden between bipolar and DHA patient family caregivers, using the respondent’s average responses across the

15 items constituting caregiver burden, found that overall, bipolar patient family caregivers were on the higher side of the scores signifying that bipolar patient family caregivers were more burdened than DHA patient and SCC family caregivers (see Fig 4).

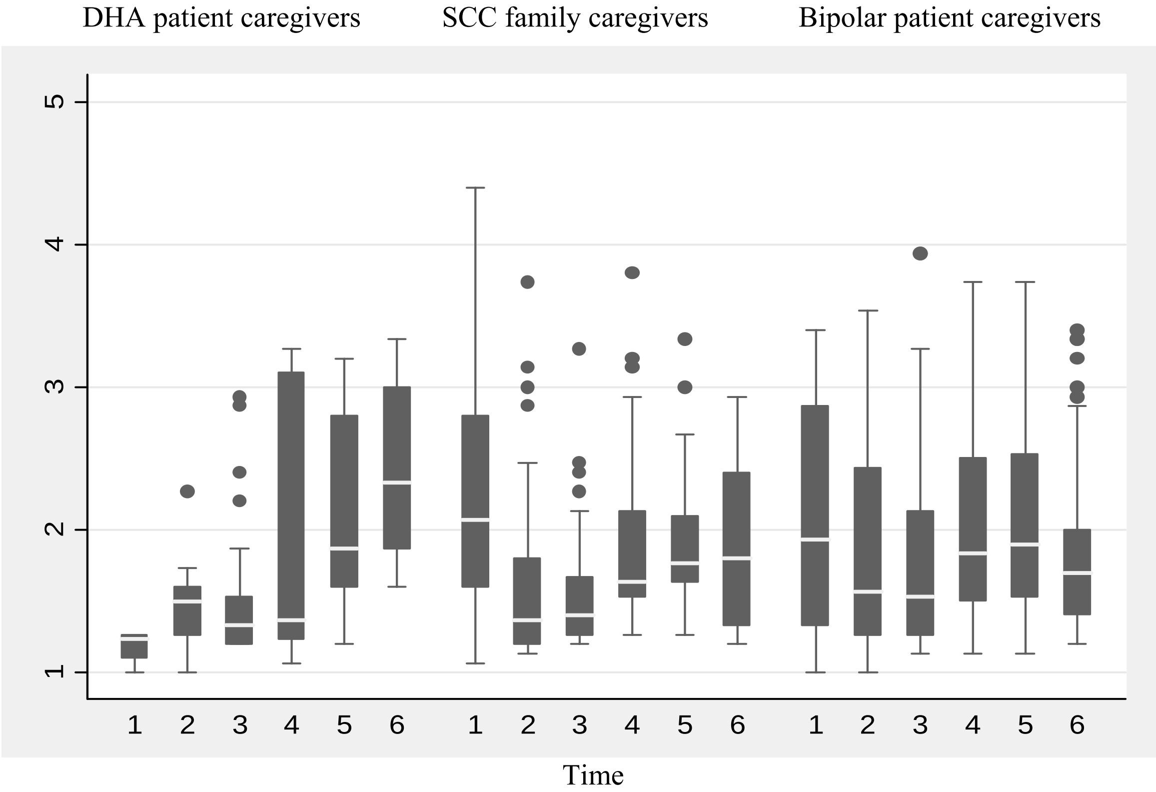


Fig 4. Box plots of family caregiver burden for six follow-up periods, Butajira-Ethiopia, 2005.

Mean and standard error plot comparisons of family caregiver burden between bipolar and DHA patient family caregivers showed that mean family caregiver burden scores of bipolar patient family caregivers were on the higher side of the scale from time 1 through 4, that is, for about 8 months, than mean family caregiver burden scores of DHA patient family caregivers (see figure 5). The mean difference in family caregiver burden between bipolar and DHA patient family caregivers was statistically significant (t = -2.23, P > |t| = 0.03, 95%CI= 0.70, 0.84). However, more variability was observed in DHA patient family caregivers particularly from time three to six.

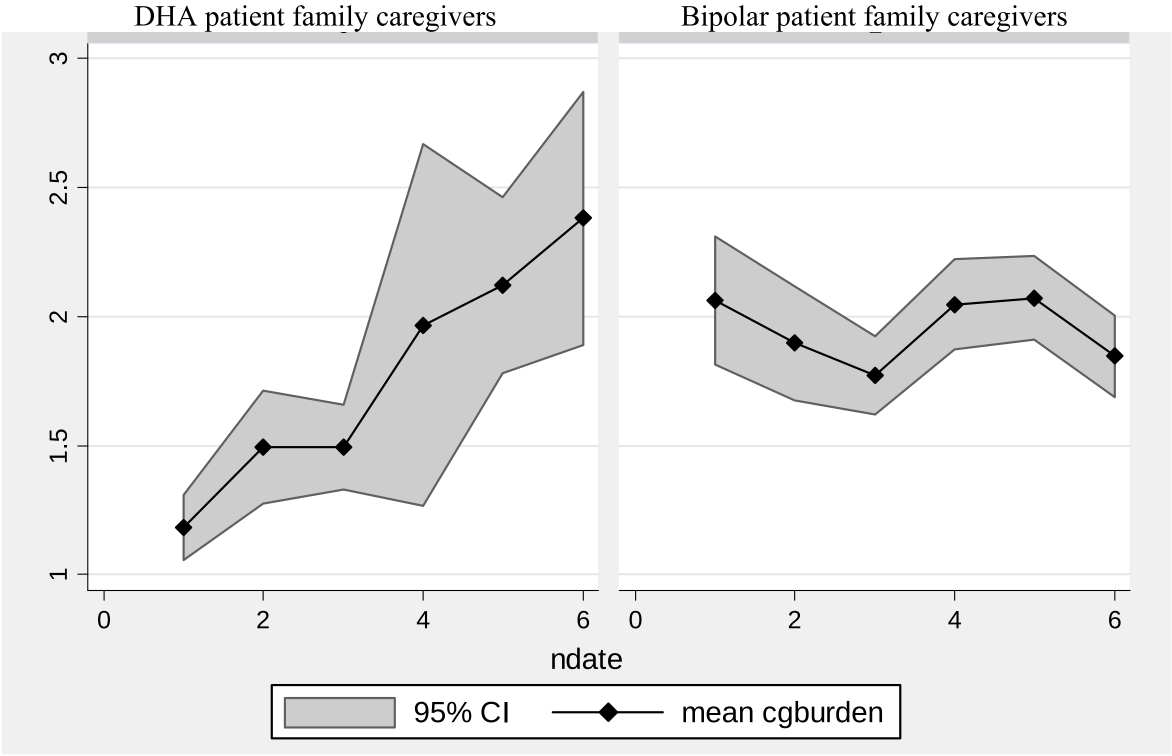


Fig 5. Family caregiver burden mean and standard error plots for bipolar and DHA patient family caregivers, Butajira-Ethiopia, 2005.

A similar result was obtained from mean and standard error plot comparisons of family caregiver burden between bipolar and SCC family caregivers. Bipolar patient family caregivers had higher mean burden scores from time two to five, that is again for about 8 months, than SCC family caregivers (see figure 6). Also this mean difference in family caregiver burden between bipolar patient family caregivers and SCC family caregivers was statistically significant (t = -13.39, P > |t| = 0.0001, 95%CI= 0.34, 0.41). Again in these mean and standard error plot comparisons it was demonstrated that bipolar patient family caregivers had been more burdened than DHA patients and SCC family caregivers. In general, the median burden score analyses and the mean and standard error plot comparisons showed that, across the total 12 month period of the study, bipolar patient family caregivers were more burdened for about 8 to 10 months when compared to DHA patient and SCC family caregivers.

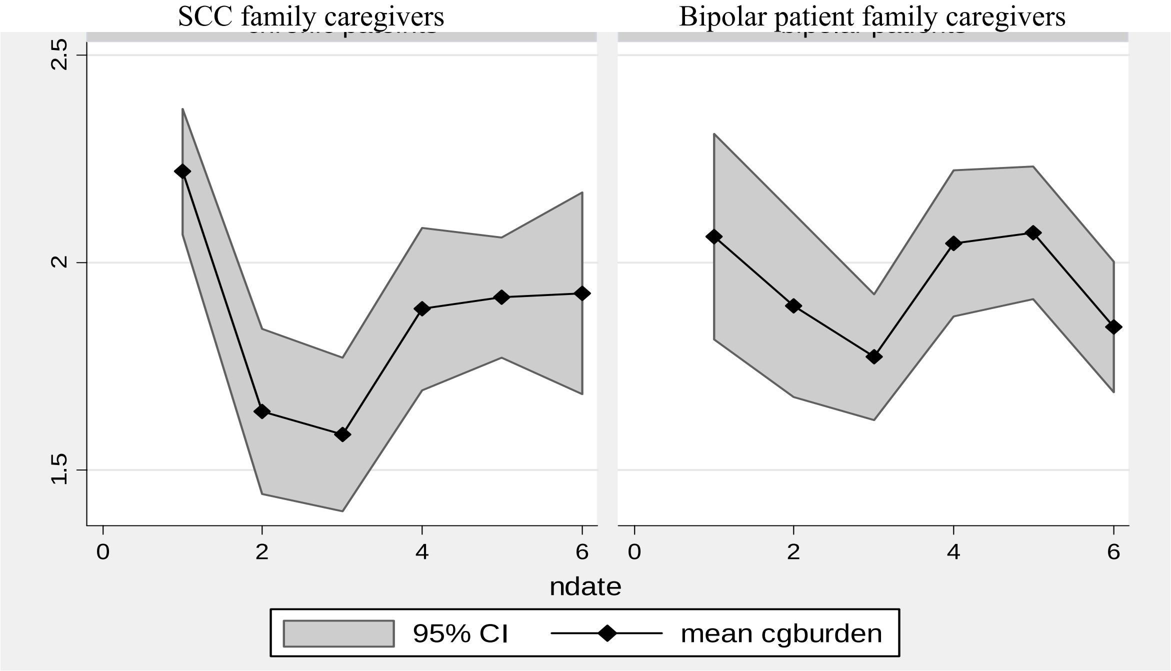


Fig 6. Family caregiver burden mean and standard error plots for bipolar patient and SCC family caregivers, Butajira-Ethiopia, 2005.

Further analysis of family caregiver burden using a population average generalized estimating equation with autoregressive working correlation (see table 7) demonstrated that the average difference in family caregiver burden score between bipolar and DHA patient family caregivers was 4.36 (z = -8.75, P>|z|= 0.001). It was also shown that the difference due to time between the two group of family caregivers was 3.42 (z= -4.27, P>|z|= 0.001). In addition, it was also found that the interaction among the variables of being a family caregiver of bipolar patients, caregiver burden and time was statistically significant with caregiver burden score difference of 3.32 (z= 13.46, P>|z|= 0.001).

Table 7. Population average generalized estimating equation analysis of family caregiver burden between bipolar and DHA patient family caregivers, Butajira-Ethiopia, 2005.

```
GEE population-averaged model                         Number of obs      = 144
Group and time vars:    subject time                  Number of groups   = 44
Link:                    identity                     Obs per group: min = 2
Family:                  Gaussian                                    avg = 3.3
Correlation:                 AR(1)                                   max = 6
                                                      Wald chi2(9)       = 810.55
Scale parameter:             0.2043554                Prob > chi2        = 0.0000

                              (standard errors adjusted for clustering on subject)

                   |              Semi-robust
Caregiver burden | Coef.          Std. Err.        z       P>|z|    [95% Conf. Interval]

Caregiver          | -1.25          0.14          -8.75    0.000     -1.54   -0.97
Time               | -0.29          0.07          -4.27    0.000     -0.43   -0.16
Sex                | -0.01          0.06          -0.24    0.809     -0.12    0.09
Age                | -0.01          0.00          -2.33    0.020     -0.01   -0.00
Marital status     | -0.05          0.06          -0.73    0.464     -0.18    0.08
Educational level  | -0.01          0.06          -0.12    0.903     -0.13    0.11
Occupation         |  0.01          0.06           0.27    0.789     -0.09    0.12
Family size        | -0.00          0.03          -0.25    0.803     -0.04    0.03
Interaction        |  0.21          0.02          13.46    0.000      0.18    0.24
Constant           |  3.11          0.24          13.17    0.000      2.65    3.58

Estimated within-subject correlation matrix R:
         c1        c2        c3        c4        c5        c6
r1   1.0000
r2   0.1914    1.0000
r3   0.0366    0.1914    1.0000
r4   0.0070    0.0366    0.1914    1.0000
r5   0.0013    0.0070    0.0366    0.1914    1.0000
r6   0.0003    0.0013    0.0070    0.0366    0.1914    1.0000
```

Similarly when comparing bipolar patient family caregivers with SCC family caregivers (shown in table 8), the average family caregiver burden score difference was 3.7 (z= -4.88, P>|z| 0.001). In terms of longitudinal caregiver burden difference, bipolar patients family caregivers were found to be more burdened than SCC family caregivers with a burden score difference of 2.97 (z= -5.17, P>|z|= 0.001). Besides, the interaction among the variables of being a family caregiver of bipolar patient, caregiver burden and time was statistically significant with caregiver burden score difference of 2.88 (z= 16.14, P>|z|= 0.001), signifying that when considered longitudinally, care-giving for bipolar patients was more burdensome than care-giving for sick controls in the community (SCC).

Table 8. Population average generalized estimating equation analysis of family caregiver burden between bipolar patient family caregivers and SCC family caregivers, Butajira-Ethiopia, 2005.

```
GEE population-averaged model                    Number of obs       = 141
Group and time vars:      subject time           Number of groups   = 47
Link:                    identity                Obs per group: min = 2
Family:                   Gaussian                                avg = 3.0
Correlation:                 AR(1)                                max = 6
                                                 Wald chi2(9)       = 835.77
Scale parameter:            .1760814             Prob > chi2         = 0.0000
                                       (standard errors adjusted for clustering on subject)

                  |              Semi-robust
Caregiver burden  |  Coef.        Std. Err.          z              P>|z|    [95% Conf. Interval]

Caregiver         | -1.03          0.21          -4.88            0.000    -1.44    -0.61
Time              | -0.30          0.06          -5.17            0.000     -0.41    -0.19
Sex               |  0.05          0.09           0.55            0.581    -0.13     0.23
Age               | -0.00          0.00          -1.12            0.262    -0.01     0.00
Marital status    |  0.00          0.09           0.03            0.972    -0.18     0.18
Educational level | -0.06          0.10          -0.59            0.553    -0.26     0.14
Occupation        |  0.04          0.07           0.60            0.549    -0.09     0.17
Family size       | -0.01          0.02          -0.52            0.604    -0.04     0.02
Interaction       |  0.21          0.01          16.14            0.000     0.19     0.24
Constant          |  2.67          0.33           7.99            0.000     2.01     3.32

Estimated within-subject correlation matrix R:
         c1         c2           c3          c4         c5         c6
r1  1.0000
r2  0.2866    1.0000
r3  0.0821    0.2866    1.0000
r4  0.0235    0.0821    0.2866    1.0000
r5  0.0067    0.0235    0.0821    0.2866    1.0000
r6  0.0019    0.0067    0.0235    0.0821    0.2866    1.0000
```

In summary, the study found that the economic and family caregiver burden due to bipolar disorder was greater for families with bipolar disorder patients than the economic and family caregiver burden of families with diabetes, hypertension and asthma patients or families with sick controls in the community.

7.4. Burden due to bipolar disorder patients living in a community (Paper II)

This paper described the burden experienced by patients with bipolar disorder; and it was found that over the follow-up period, the mean out-of-pocket medical expenditure made by bipolar patients was $10.44 while the cost for round trip travels was $2.74. Thus, the total direct cost per year was $13.18. Furthermore, one month prior to the interviews, each patient lost an average of 12 to 19 days of work. Across the whole study year, patients lost an average of 93.52 cumulative days of work. The mean value of time lost in traveling to visit a health institution and to complete medical examination was estimated at $2.76 with standard deviation of $3.50. This value was also used to estimate burden due to lost days of work. Therefore, the overall annual cost of bipolar disorder to the individual patient was $274.06. This burden was extrapolated and estimated to societal level by multiplying added costs of mean out-of-pocket medical expense ($13.18), value of lost time ($2.76), value of lost days of work (93.52 x $2.76) by an average estimated prevalence of bipolar disorder in Ethiopia (2.9%) among the population of age 15 years old and above (41,609,606) (125). The average estimated 2.9 percent prevalence rate was derived from different studies conducted at different times in Addis Ababa- the capital city; Butajira- south central part of the country which is rural; Borana semi-nomadic and Zeway- isolated island communities (16, 19, 98, 99, 110). Therefore, annual burden of bipolar disorder to Ethiopian society was estimated to be

$331 million. Similarly, in the year 2005 the projected lost days of work to the Ethiopian society was estimated to be 112.8 million, assuming a 2.9 percent life time prevalence rate of bipolar disorder in the general population and 93.52 cumulative lost days of work from each patient annually.

8. DISCUSSION

The economic burden of schizophrenia and bipolar disorders has long been ignored and underestimated mainly due to way of thinking in disease prioritization and burden measurement. Now the time has come to make schizophrenia and bipolar disorders part of disease priorities. Evidences found in this study tell us that the toll of economic burden and suffering of families is undoubtedly huge and unbearable. Because at societal level, the burden imposed by these disorders is very high. The study has clearly shown what our society would have gained if these illnesses were not there. On the other hand productivity loss by family caregivers is a fuel added to the pains of poverty prevailing in most parts of our country. The high extent of burden experienced by caregivers is also the other side of the suffering due to schizophrenia and bipolar disorders. The change overtime is significantly important factor that had been described in the study. Families and caregivers were constantly burdened. In addition, this constant high level of caregiver burden clearly would influence the outcome of service delivery. These and other findings of the study are further discussed below.

8.1. Findings in perspective

Based on estimation of the out-of-pocket medical expense made by families at societal level, by taking into consideration one per thousand life time prevalence as a lower margin and the average 4.7 per thousands life time prevalence of different studies done at different times in urban and rural Ethiopia (15, 19, 126) as a higher margin; and assuming that each case of schizophrenia cared by all respective families, then the total direct cost to the Ethiopian society was approximately between $687,390.69 to $3.23 million. Likewise, the indirect cost of loss of annual cumulative working days due to care giving (by assuming $0.92 as wage for a day's work) was approximately $1.43 to $6.74 million. Therefore in 2005, the total burden of schizophrenia to families in Ethiopia ranged approximately between $2.12 million to $9.97 million.

Compared to other studies in the Western world, the total burden of schizophrenia to families of low income developing country like Ethiopia is very huge. Studies from the US in 1985 and 1992 estimated the family economic burden associated with schizophrenia to be in the range of $2.47 to $8.65 billion (26, 27). According to an international review in 1998 the U.S. incurred a total cost of $32,500 million and in Hungary in 1990 the burden of schizophrenia was $41.1 million (127). The burden of schizophrenia on UK families in 1997 was estimated at ₤1.9 million (35). In Canada this burden was estimated to be $2.35 billion in 1996 (36).

This huge burden was because of families experiencing persistent burden for about eighty-three percent of the year. In addition 75 percent of the families were experiencing high level of burden. Such high level of burden could possibly explained by the fact that about 93 percent of the patients in the families were in their most productive years of life, 85 percent were not able to work on their regular job and about 73 percent were not compliant with treatment regimen. Therapeutic noncompliance may lead to increased burden and decreased cost-effectiveness of interventions compounding the effect of inability of patients to work on their regular job. In some studies more than 60 percent of individuals with schizophrenia fail to take medication as directed (26). Noncompliance and rejection of treatment could increase the burden on families and the health systems. The high level of burden on the families may further be explained by the fact that about 47 percent of the patients were children (daughter/son) and 40 percent were household heads of the family.

When this burden was described in terms of carers' characteristics and patient conditions; over the year female caregivers, caregivers in the farming occupation, whose monthly family living expenses were very little (poor families), who had paid more out-of-pocket for mental health services, and who had lost more days of work were found to be more burdened. In addition, caregivers who were angry at the patient, worried about the patient, over involved in controlling the patient, caring for unable patient to carry out self care and who were caring for non-treatment compliant patients were found to experience more burden.

Overall schizophrenia family and caregiver burden in this rural community was severe. Furthermore, the present findings of caregivers who were angry at the patient, worried about the patient, over involved in controlling the patient, caring for unable patients to carry out self care and who were caring for non-treatment compliant patients to experience more burden signifies the importance of improving coping strategies of caregivers and patients' level of functioning and treatment compliance, because, caregivers who can cope better with the patient's behavior have fewer burdens (43, 48, 128). Improving treatment noncompliance will have important positive consequences for clinical outcome as well as for health care costs. But, some patients were reported fail to take medication as directed, increasing the chance of relapse of the patient's illness. Noncompliant patients had been found to be burdensome for the caregivers. Such patient behavior on the other hand leads to relapse. Relapse is known to be closely linked to noncompliance (33, 129). In such situations family interventions and compliance therapy may help (27, 130, 131). Therefore, the finding of burden in this study due to noncompliance needs to be well addressed and tackled in order to reduce the burden of caregivers and improve course and outcome.

On the other hand in this study, when comparing caregivers of bipolar patients with caregivers of patients with physical disorders, bipolar patient family caregivers were found to be burdened above the median caregiver burden score for about two thirds of the year. Caregiver burden score differences between family caregivers of bipolar patients and the two comparison groups- family caregivers of DHA patients and SCC, revealed that a burden causing event happened at least three to six times per week in the months of the year on family caregivers of bipolar patients, whereas on family caregivers of DHA patients and SCC, burden causing events had not happened in most of the months of the year. In addition, compared to DHA patients and SCC family caregivers, the burden experienced by family caregivers of bipolar disorder patients was for longer period of time. The longitudinal time change of burden experienced by family caregivers of bipolar disorder patients was significantly different from longitudinal time change of burden experienced by family caregivers of DHA patients and SCC. In this longitudinal time change of burden, family caregivers of bipolar patients were found to be more burdened than DHA patients and SCC family caregivers. Moreover, money and time of family caregivers of bipolar disorder patients had been directly and indirectly taxed. They had spent their money for their bipolar relatives seeking medical help and had also lost days of work due to care giving, of course that was not significantly more than the comparison groups.

The study found care giving to be more burdensome for bipolar patient family caregivers. Through time, these caregivers may become overburdened as the longitudinal change in family burden score was persistent for most months of the year. With this regard a previous study has reported that patients living with an overburdened caregiver may have increased risk of relapse, therefore, attention should be paid to those bipolar patient family caregivers (109). In addition, the annual cost of out-of-pocket medical expense ($93.93) made by family caregivers of bipolar patients was substantially higher than the out-of-pocket medical expense made by DHA patient and SCC family caregivers. If we consider this out-of-pocket medical expense at societal level, by taking into consideration one percent life time prevalence as a lower margin and the average 2.9 percent life time prevalence of different studies done at different times in urban and rural Ethiopia as a higher margin; and assuming that each case of bipolar disorder had at least one family caregiver, then the total direct cost to the Ethiopian society was approximately between $39.1 to $113 million (16, 19, 98, 99, 110, 132). Likewise, the indirect cost of loss of working days due to care giving (by assuming $0.92 as a wage for a day’s work) was approximately $5.4 to $15.5 million. Therefore in 2005, the total economic burden of family care giving for patients with bipolar disorder in Ethiopia ranged approximately between $45.5 million to $128.5 million.

Compared to other studies, the total economic burden of care giving for bipolar disorder patients seems minimal (65-67, 70). But, for a low income developing country like Ethiopia, this is another huge sum. In 1990 the economic burden of bipolar disorder in the U.S. was estimated to be $15.5 billion due to lost productivity in work performance (72). In the same year, patients in treatment lost an estimated 152 million cumulative days from work and untreated patients lost 137 million days. In 1991, the burden of bipolar disorder among adult Americans based on 1.3 percent lifetime prevalence was estimated at $45 billion (65); of which $8 billion was due to loss of productivity because of suicide and $6 billion was due to lost productivity of caregivers who provide care for family members with the disorder. Another estimate for the 1998 incident cases of bipolar disorder in the US was estimated at 24 billion US dollars (66). In the UK, in 1998, the annual burden of bipolar disorder was estimated at $3 billion (67). In the Netherlands, based on 5.2 percent prevalence of bipolar disorder the total burden of the disorder was estimated at $1.83 billion (71). The burden in Australia in 2004 assuming a 2.5 percent lifetime prevalence and the same pattern of health service, was estimated between AUD$3.97 to AUD$4.95 billion (70). It has also been estimated that bipolar disorder has dramatically increases use of health care resources by patients (76) and their caregivers (74).

It should not be forgotten that these cost estimates involve a lot of approximation because of uncertainty involved in the calculation. However, it is undeniable that the figures give an insight of how burdensome was family care giving for bipolar disorder patients in a low income developing country. The burden was due to care giving for bipolar patients whose mean age was in the early thirties; more importantly most of the study subjects were in the age group of 30 to 44 years, followed by the age group of 15 to 29 years. Therefore, this population-based sample of patients with bipolar disorder were in the most economically productive years of their life resulting in high productivity loss to society as a result of their illness. The burden upon the affected individual and their family is considerable. This is particularly likely to be the case as 40 percent of study subjects were household heads and 31 to 37 percent were homemakers with an average family size of six, of which three of the members were children under 15 years of age. Ethiopia is one of the one-third of countries worldwide which has no specific budget for mental health care and it would be expected that the majority of people with bipolar disorder do not receive optimal treatment for their condition, thus increasing the burden of the disorder (77). Furthermore, one month prior to the interviews, each patient lost an average of 12 to 19 days of work which is an additional burden. The burden of illness may have been associated with treatment non-adherence and/or co-morbid substance use: out of bipolar patients under treatment, 21 to 36 percent were chewing Khat for most days of the year while they were under treatment. Frequent use of psychoactive stimulants may adversely affect the adherence to treatment. In this regard an outcome study in the area revealed a 66 percent relapse rate among bipolar patients having chronic symptoms during an average follow-up period of 2.5 years (64).

During the year the total annual cost of bipolar disorder to individual patients was $274.06. When compared to study findings of annual individual costs in the Netherlands ($848), UK ($1444), Australia ($8553), and the US ($9619) (67, 70, 71, 73) this cost to individual patients was also low. However, the scope of burden studies, epidemiological patterns, patterns of health service utilizations, cost of medical services, and methodologies of estimating cost in these countries necessarily differ from a study conducted in a rural area of a developing country. A wider view of types of medical services was used in bipolar burden studies from these countries, but in our case a narrower definition of burden was required due to the fact that patients were living in the community where health sector costs were excluded. Nevertheless, the total annual cost of $274.06 to each individual patient was surprisingly high in a country, like Ethiopia, where bipolar disorder had never appeared in the list of leading causes of morbidity and mortality.

Likewise, when compared to the annual lost days of work in studies from the Netherlands and the USA (71, 73), the number of lost days of work (93.52) by each patient and number of projected annual lost days of work (112.8 million) were high in the present study. In the Netherlands study the mean annual days of absence from work was 55.5 per each respondent with a paying job, and the mean annual productivity loss associated with reduced efficiency at work was 7.7 days. In the US study bipolar disorder was associated with 65.5 annual lost days of work per ill worker and 96.2 million lost days of work. The use of different methodologies may contribute to this difference in number of lost days of work. In the present study, the patient's self-report of lost days of work was used while in the Netherlands study, Health and Labor Questionnaire; and in the US study, the WHO Health and Work Performance Questionnaire were used respectively. In addition, most of our study subjects were self employed, while in the Netherlands study 30 percent of the subjects were in a paying job and in the US study the subjects were a representative sample of US workers. On the other hand, the present finding of 112.8 million annual lost days of work was close to the estimate by a US study conducted in 1990 (72), where patients in treatment lost an estimated 152 million cumulative days from work and untreated patients had lost 137 million days.

Generally, using average prevalence rate of schizophrenia and bipolar disorders derived from different studies conducted at different times in Addis Ababa- the capital city; Butajira- south central part of the country which is rural; Borana semi-nomadic and Zeway- isolated island communities, the annual total economic burden of schizophrenia and bipolar disorders to Ethiopian society was estimated to be \$378.62 to \$469.47 million. Out of this total economic burden the direct cost was found to be 1.25 percent to

3.66 percent of the country’s public health expenditure in the year 2005. The burden was immensely high for a poor country where one finds woefully inadequate mental health service in most urban and especially in the rural areas. In such a setting as Ethiopia, individual schizophrenia and bipolar patients and their families need to be supported by a devised scheme of mental health care financing, perhaps making use of existing local associations (e.g. social insurance for burial service assistance) in the community.

8.2. Limitations of methodological assumptions

In this dissertation there are some limitations and methodological assumptions that need to be reiterated. In the issue of comparability of groups, there was relatively low recruitment rate for DHA patients and their caregivers; this was mainly due to availability of very few study subjects diagnosed as DHA patients in the district. Low number of DHA families may affect results of comparisons between bipolar disorder and DHA patient families. Moreover it is likely that DHA patients tend to access services even when services are scarce as these kinds of illnesses are found in higher socioeconomic class of populations, and this may also affect comparability. The other possible methodological shortcoming could be making comparison of community-ascertained cases of bipolar disorders with clinic-ascertained cases of DHA patients.

On the other hand the dissertation does not have data on the missed families so that it was not possible to explore whether or not bias was likely. As in most studies of economic burden of schizophrenia and bipolar disorders the estimate of burden in this study may vary mainly due to cost estimation methodology and data sources on prevalence rate, services utilization, and unit cost of services. Therefore, this would limit the comparability of this study with other international studies. On the other hand there might be uncertainties in the calculation of indirect costs. In addition using the human capital approach in calculating indirect costs might inflate estimates. Another limitation is that costs to the health sector were not included and this might affect the generalizability of the study results to a certain degree.

9. CONCLUSION AND IMPLICATIONS

9.1. Conclusion

Generally more should be done in the direction of lessening the economic and family caregiver burden due to schizophrenia and bipolar disorders. Health policy and priority setting needs to be tuned in accordance with the available evidence of burden from schizophrenia and bipolar disorders and other mental health problems. Family caregivers should be supported through family and follow-up clinic based educational programs. Because, caregivers who can cope better with patients' behavior or who can improve their coping abilities over time has less burden. Families should be supported through a carefully designed intervention strategy to improve level of functioning and treatment adherence of patients. Thus, future studies need to focus more on how to devise feasible intervention strategies to lessen economic and family burden due to schizophrenia and bipolar disorder and also need to define cultural norm of care giving in the study community.

Caregivers are immediate managers of the course and outcome environment where the illness is lived, therefore the existing high level of caregiver burden in context of poverty and scarcity of mental health services in this rural community calls for the support needs of carers through holistic schizophrenia and bipolar disorder clinical management approach.

9.2. Implication for policy

The country's health care system should try to reduce the high level of hidden sufferings of families and caregivers so as to keep the level of burden low. The economic gain from alleviation of this suffering is high, therefore, the results of the study have implications for policy to reduce the level of burden due to schizophrenia and bipolar disorders, increase the type and intake of training on mental health care, allocate resources judiciously and increase input for mental healthcare, improve the quality of mental health service at the community level, emphasize on early identification and assessment of level of family and caregiver burden, give free service or partially covered delivery of health care for families of patients with schizophrenia and bipolar disorders at all levels of the health care system, engage patients in rehabilitation and social activities, establish system of giving psycho-educational support to families and caregivers of schizophrenia and bipolar disorder patients.

9.3. Implication for practice

The level of family and caregiver burden due to schizophrenia and bipolar disorders in the community calls for immediate support of families and caregivers. Therefore, the results of the study have implication for practice to make patients engage in supportive rehabilitation activities such as giving them simple appropriate jobs in their community and improve their treatment compliance. The other implication for practice is to involve caregivers as a partner for the management of patients' illness through regular consultative meetings and establish family support groups; given psycho-educational support to reduce level of caregiver burden not only during the appearance of the patient at the clinic but also by designing feasible family intervention strategies with continuity.

9.4. Future directions

Future studies need to focus more on how to devise feasible intervention strategies to lessen economic and family burden due to schizophrenia and bipolar disorder and also need to define cultural norm of care giving in the study community. Additionally, future studies need to explore ways of improving adherence to treatment of schizophrenia and bipolar patients living in the community, assess availability of health care resources for schizophrenia and bipolar disorder and possible insurance mechanisms for covering the burden to schizophrenia and bipolar patients. In addition, it would be better to conduct nationwide more representative economic burden study of schizophrenia and bipolar disorders along with epidemiological surveys.

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12. APPENDICES (PAPER I-IV)

Paper I

Longitudinal comparative analysis of economic and family caregiver burden due to bipolar disorder

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Declaration of relative contribution:

Ababi Zergaw, the first author of this article is a doctoral candidate who was responsible for the conception, design, analysis and interpretation of the study data. He was the principal investigator who had run the overall research process. He drafted and revised the article producing the final form for publication. He had collected original data, thus, he had full access to all the data in the study, and was responsible for the integrity of the data and the accuracy of the data analysis.

Damen Hailemariam, MD, MPH, Ph.D. was the first advisor of the candidate. He had contributed in the designing stage of the study and critical review of the manuscript. He approved the final version of the article for publication.

Atalay Alem, MD, Ph.D. was the second advisor of the candidate. He had contributed in the designing stage of the study and critical review of the manuscript.

Derege Kebede, MD, MSc. Sc.D. was the third advisor of the candidate. He had contributed in the designing stage of the study and critical review of the manuscript.

Longitudinal comparative analysis of economic and family caregiver burden due to bipolar disorder

Abstract

Objective: to explain comparatively how economic and family caregiver burden in families with bipolar disorder patients change overtime.

Methods: one year follow-up of economic and family caregiver burden was carried out on family caregivers of 190 bipolar, 55 diabetes, hypertension and asthma patients and 659 sick controls in the community. Population average generalized estimating equation was used to make longitudinal comparative analysis.

Results: bipolar patient family caregivers were found to be more burdened for about 8 to 10 months than family caregivers of diabetes, hypertension and asthma and sick controls in the community. The average difference in family caregiver burden score between bipolar and diabetes, hypertension and asthma patient family caregivers was 4.36 (z = -8.75, P>|z|= 0.001); while the difference due to time between the two groups was 3.42 (z= -4.27, P>|z|= 0.001). Similarly, the average difference in family caregiver burden score between family caregivers of bipolar patient and sick controls in the community was 3.7 (z= -4.88, P>|z| 0.001). In terms of longitudinal caregiver burden difference, bipolar patients family caregivers were found to be more burdened than family caregivers of sick controls in the community with a burden score difference of 2.97 (z= -5.17, P>|z|= 0.001).

Conclusion: more should be done to lessen the economic and family caregiver burden due to bipolar disorder.

Key words: Bipolar disorder, burden, caregiver, family.

Introduction:

Bipolar disorder, characterized by recurrent manic and depressive or mixed episodes, is one of the most burdensome illnesses occurring in the early productive years of life. [1-7] Studies from Europe, America and Australia have found the economic burden of bipolar disorder to be substantially high.[2-5, 8, 9] Bipolar disorder follows a chronic course and is associated with significant distress, disability, marital problems and premature mortality.[10,11] Abuse of alcohol, drug and other substances is common, as well as an increased risk of co-morbid medical conditions. Patients with bipolar disorder tend to have high demand for health services and yet the disorder is under-diagnosed and often inappropriately treated.[12-16]

Morbidity due to the recurrent nature of the illness, often exacerbated by co-existing medical conditions, has an undoubtedly large economic impact on individuals with the illness, their families, the health system and wider society. For example, it is known that family caregivers of bipolar patients have an increased use of health services themselves.[17] Manic episodes of the illness are very disruptive of daily life, work and family relationships.[18] During the acute phase of the illness family caregivers may be highly demanded to be involved in care giving. Not only during acute period of the illness, even during remission residual symptoms may still be present demanding family care giving.[18, 19]

Bipolar disorder has direct and indirect costs resulting in economic and family caregiver burden. Cross sectional studies and data base analyses have shown this burden. [2-6, 8, 9] However, little is known about how the economic and family caregiver burden in families with bipolar disorder patients changes over time. Furthermore, almost all studies of the economic and caregiver burden of bipolar disorder have been conducted in high-income countries. In low-income countries, families already living in poverty may be disproportionately affected by having a family member with bipolar disorder, in spite of the strong support networks existing in traditional societies. This paper presents the results of one year follow-up study from rural Ethiopia comparing the economic and caregiver burden for families of patients with bipolar disorder to families of patients with other physical disorders. In addition, this paper reports on the pattern of burden over time.

Methods:

Study subjects

The study was done in Meskan and Mareko Wereda, a rural district in southern Ethiopia. In the district a course and outcome study project on bipolar disorder is underway since the early 1990s. The project had screened all 83,282 adult population of the district for bipolar disorder by house to house survey using the WHO Composite International Diagnostic Interview (CIDI), Version 2.1.[20] The present study used a prospective longitudinal design involving all identified families with bipolar disorder patients. Two control groups of families were selected from follow-up clinics and from the community. The first control group included all families of follow-up attendees for diabetes, hypertension and asthma (DHA) in health institutions of the district and the second control group was composed of randomly chosen families from the community. From each group of families, family caregivers were selected using the method followed by Perlick et al. caregiver burden study. [21]

Thus, caregivers were selected based on the following criteria:

a). is a spouse, parent or spouse equivalent to the patient;

b). has most frequent contact with the patient;

c). helps to support the patient financially;

d). has most frequently been a collateral in the patient's treatment; and

e). is contacted by treatment staff in case of emergency. To be included in the sample as a caregiver, the chosen caregiver had to satisfy at least three of the criteria.

Consequently, this study sampled all 190 families of bipolar patients who were under follow-up during the survey, the first control group of 55 families with DHA patients (35 diabetes mellitus, 12 hypertension and 8 asthmatics), and the second control group of 659 randomly selected families in the community. The total sample size of the study comprised of 904 families of caregivers.

During data collection from families of controls from the community, a family member was considered as a caregiver if any other illness had affected a family member and care had been given to the ill person by other family member(s). Therefore, in each of the groups, illness was defined as having an individual family member whose normal functioning was interrupted due to a health problem.

Data collection

The data collection was carried out every two months for one year; started in July 2004 and ended in June 2005. Data collection instruments were developed and pre-tested three times in a nearby community. The purpose of these repeated pre-tests was to increase the reliability and validity of interview instruments. Accordingly, interview instruments with reliability test coefficient less than 0.40 were dropped. In each of the pre-testing sessions, one week of extensive training was provided for data collectors and supervisors. Using the refined final interview instruments, data were collected on economic and family caregiver burden. Data quality and consistency cross-checks were made by another group of trained supervisors recruited for the purpose. For data entry EpiInfo 6 version 6.04d statistical software was used while SPSS 11.0 and Stata/SE 8.2 for Windows were used for data analysis.

Burden measurement

Longitudinal burden measurements were made using out-of-pocket medical expenses for health services, time lost due to care giving and the extent of family caregiver burden. Out-of-pocket medical expenses included cost of: travel, medical examination, drugs and injections, laboratory service, food and accommodation; and the time lost due to care giving included time lost in accompanying patient to and from health institute and lost days of work due to care giving at home. There were 15 questionnaire items constituting family caregiver burden, with response categories on a five-point scale (see table I).

During each interview, family caregivers were asked about the extent of burden they had experienced in the month prior to interview using the 15 questionnaire items. Thus, family burden score of 1 to 5 was given based on the frequency of occurrence of a 'burden-causing event': 1 = did not happen at all in the month; 2 = happened at least once per week in the month; 3 = happened at least twice per week in the month; 4 = happened at least 3 to 6 times per week in the month; and 5 = happened almost every day per week in the month.

Table I. Questionnaire items constituting family caregiver burden, Butajira-Ethiopia, 2005

To what extent the:

- a) patients illness causes sleep disturbance,
- b) patient's illness creates burden on job,
- c) patient's illness limits social relation movement,
- d) patient's illness creates burden as to ignore other family members,
- e) patient's illness creates feeling of unhappiness,
- f) patient's illness creates worry about the future,

g) to what extent were you ashamed due to the patient's illness,

h) when you think about the patient, to what extent you feel guilty,

i) how much do you worry by saying that I am unable to cope-up more than this,

j) to what extent patient's illness create health problem,

k) to what extent your relationship with the patient was in crisis due to the patient's illness,

l) to what extent the patient causes physical injury on you,

m) to what extent life was problematic and challenging for you due to the patient's illness,

n) to what extent the patient's illness creates burden on you as to think of suicide, and

0) to what extent were you happy about patient's social relationships?

Analysis

Longitudinal economic and family caregiver burden comparisons of caring for bipolar patients were made using two arms of control. The first arm was family caregivers of DHA patients and the second arm was family caregivers of sick controls in the community (SCC). Chi-square and t-test were used to compare socio-demographic characteristics. Descriptive mean comparisons were made in terms of out-of–pocket medical expenses for health services, time lost due to care giving and the extent of family caregiver burden. From time one (baseline) through six (end of the study); family caregiver burden was computed as the respondent’s average responses across the 15 items constituting family caregiver burden. Finally, a population average generalized estimating equation was used to explain the change over time in family caregiver burden. For the purpose of comparison all costs were converted to US$ by using the mean exchange rate for 2005 of Ethiopian currency Birr 8.6810 = 1US$.[22] The study was ethically approved by the Faculty of Medicine Addis Ababa University and oral informed consent to participate in the study was obtained from the study subjects.

Results

Out of the 190 eligible families with a member suffering from bipolar disorder, 26 were inaccessible, six shad changed address, six were unavailable, four refused, two died and seven did not have caregivers, leaving 139 participating family caregivers. From the first control group of 55 families with DHA patients; 12 had changed address, two were unavailable, one refused and four did not have family caregivers, leaving 36 participating families. From the second control group of 659 randomly selected families with sick controls in the community, 472 families participated but only 402 had family caregivers (one also refused). From this group, 146 had changed address and the status of 18 subjects was unknown. Therefore, family caregivers of 139 bipolar patients, 36 DHA (diabetes, hypertension, and asthma) patients and 401 SCC (sick controls in the community) were involved in the final study. The majority of participants were female, married and non-literate (see table II). The mean monthly living expenses of bipolar patient family caregivers was $9.28 (SD = $8.44) while that of DHA and SCC family caregivers was $19.70 (SD= $12.16) and $3.41 (SD= $5.64) respectively. Likewise, mean annual family income of bipolar patient family caregivers was $154.72 (sd= $178.77) while the mean annual family income of DHA patent and SCC family caregivers was $417.64 (sd= $330.22) and $57.01 (sd= $107.73) respectively. Caregivers were found comparable in their socio-demographic characteristics, however, some difference were observed between bipolar and DHA patient in terms of other educational level and occupations. These differences were accounted in further analyses.

Table II. Sociodemographic characteristics of family caregivers, Butajira-Ethiopia, 2005.

Variable	**Bipolar patient family caregivers N=139, (%)**	**DHA patient family caregivers N=36, (%)**	**SCC family caregivers N=401, (%)**
Sex			
Male	56 (40.29)	12(33.33)	163(40.65)
Female	83 (59.71)	24(66.67)	238(59.35)
Age mean(sd)	37.58 (13.87)	37.47(14.76)	34.06(11.96)
Family size mean(sd)	6.23 (2.54)	7.08(3.05)	5.64(2.08)
Marital status			
Married	112 (80.58)	27(75.00)	328(81.80)
Others	27 (19.42)	9(25.00)	73(18.20)
Educational level			
Illiterate	90(64.75)	12(33.33)	256(63.84)
Literate	41(29.50)	12(33.33)	122(30.42)
Others	8(5.75)	12(33.33)	23(5.74)
Occupation			
Farmer	49(35.25)	8(22.22)	136(33.92)
Housewife	65(46.76)	11(30.56)	199(49.63)
Merchant	11(7.91)	6(16.66)	17(4.24)
Other	14(5.76)	11(30.56)	49(12.21)
Relation with the family			
Household head/Father	48(34.53)	8(22.22)	139(34.66)
Mother	70(50.36)	20(55.56)	199(49.62)
Child	12(8.63)	7(19.44)	52(12.96)
Brother/Sister	8(5.76)	-	8(1.99)
Other	1(0.72)	1(2.78)	4(0.99)
Religion			
Orthodox	37(26.62)	18(50.00)	104(25.94)
Islam	90(64.75)	13(36.11)	266(66.99)
Protestant	12(8.63)	5(13.89)	31(7.73)

During the year, bipolar patient family caregivers had the highest mean out-of-pocket medical expenses ($93.93) compared to DHA patient ($64.80) and SCC family caregivers ($56.18). The expense borne by bipolar patient family caregivers ranged from $6.62 (median= $4.38) to $30.55 (median= $2.88) per month. Family caregiver comparisons in terms of lost days of work due to care giving in one month revealed that, on average, bipolar patient family caregivers lost 1.78 days (sd = 4.54) while DHA patient and SCC family caregivers lost 2.66 (sd = 5.78) and 2.32 days (sd = 5.02) respectively. However, these differences in mean out-of-pocket medical expense and lost days of work among caregivers were not statistically significant.

Longitudinal comparative analysis of family caregiver burden between bipolar and DHA patient family caregivers, using the respondent's average responses across the 15 items, found that the median scores of bipolar patient family caregiver burden were at the higher side of the scale for about 10 months (from time one to five), compared to the median family caregiver burden scores of DHA patient family caregivers (see figure 1). It was only at time six that median family caregiver burden scores of DHA patient family caregivers exceeded the median scores of bipolar patient family caregivers. Similar comparison of bipolar and SCC family caregivers also revealed that the median family caregiver burden scores of bipolar patient family caregivers were higher for about 8 months (from time two through five). However, at times one and six the median family caregiver burden scores of SCC family caregivers were on the higher side. But overall, bipolar patient family caregivers were on the higher side of the scores signifying that bipolar patient family caregivers were more burdened than DHA patient and SCC family caregivers.

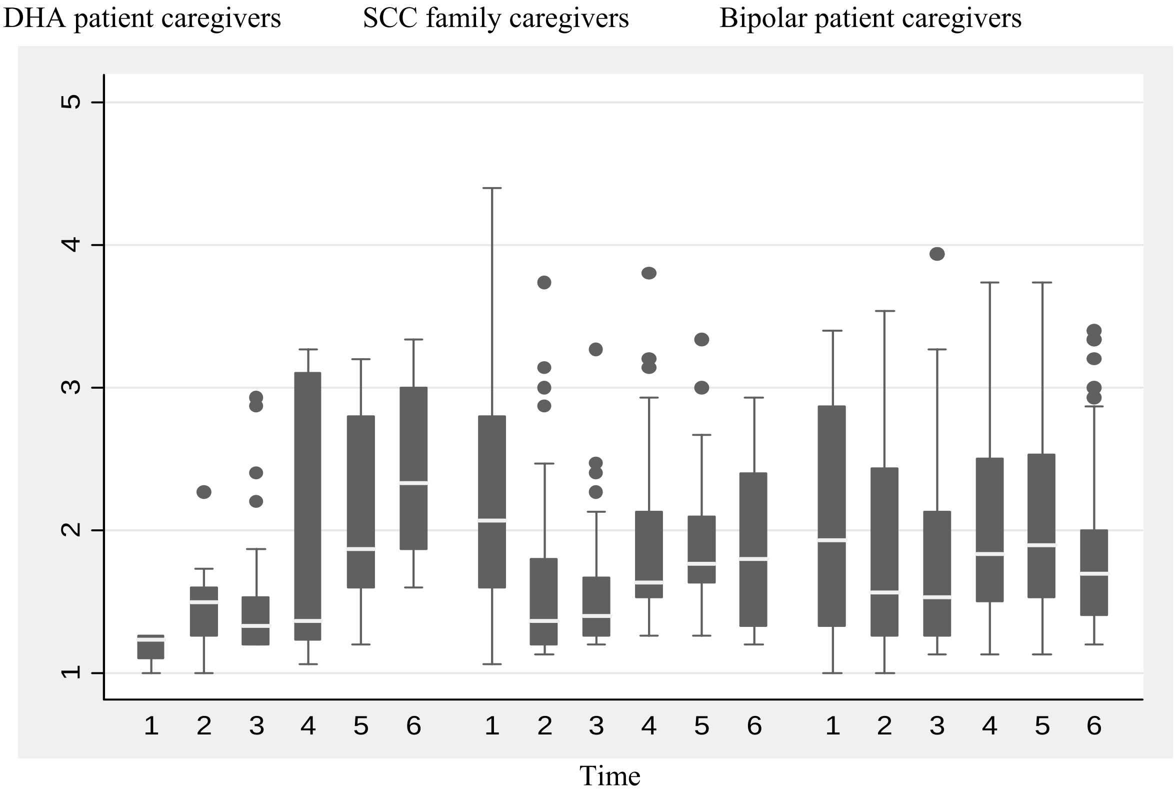

Fig1. Box plots of family caregiver burden for six follow-up periods, Butajira-Ethiopia, 2005.

Mean and standard error plot comparisons of family caregiver burden between bipolar and DHA patient family caregivers showed that mean family caregiver burden scores of bipolar patient family caregivers were on the higher side of the scale from time 1 through 4, that is, for about 8 months, than mean family caregiver burden scores of DHA patient family caregivers (see figure 2). The mean difference in family caregiver burden between bipolar and DHA patient family caregivers was statistically significant ($t = -2.23$, $P > |t| = 0.03$, 95%CI= 0.70, 0.84). However, more variability was observed in DHA patient family caregivers particularly from time three to six

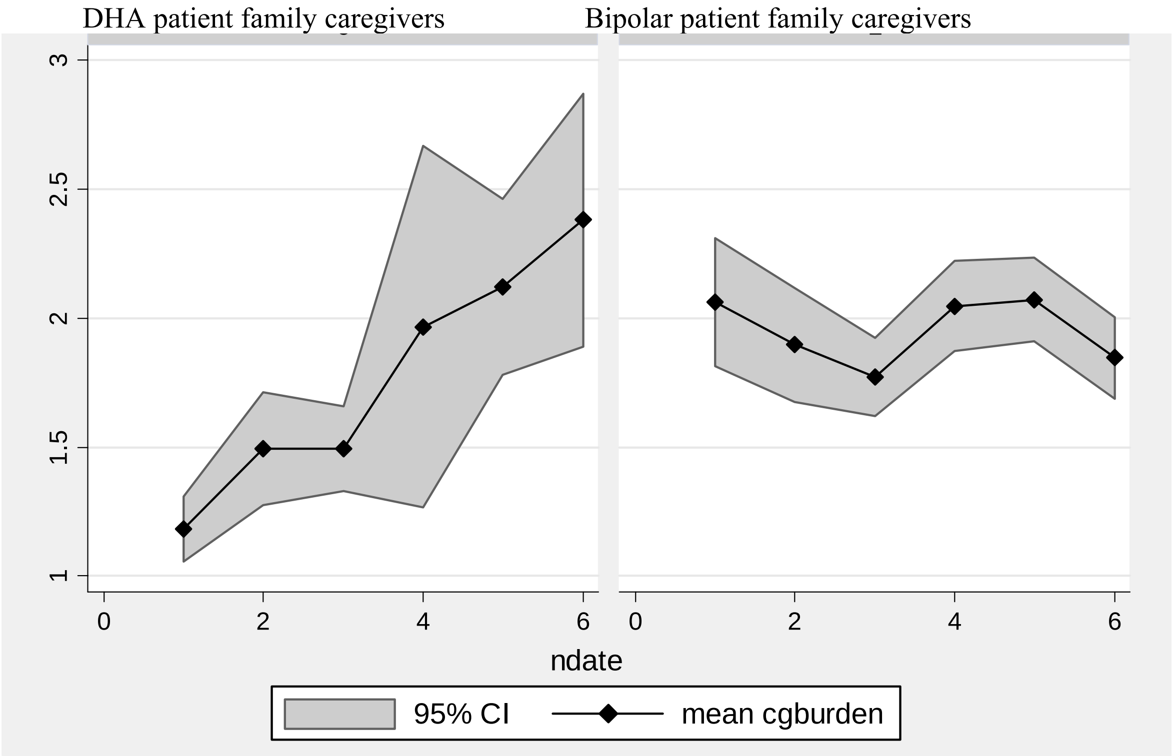

Fig 2. Family caregiver burden mean and standard error plots for bipolar and DHA patient family caregivers, Butajira-Ethiopia, 2005.

A similar result was obtained from mean and standard error plot comparisons of family caregiver burden between bipolar and SCC family caregivers. Bipolar patient family caregivers had higher mean burden scores from time two to five, that is again for about 8 months, than SCC family caregivers (see figure 3). Also this mean difference in family caregiver burden between bipolar patient family caregivers and SCC family caregivers was statistically significant (t = -13.39, P > |t| = 0.0001, 95%CI= 0.34, 0.41). Again in these mean and standard error plot comparisons it was demonstrated that bipolar patient family caregivers had been more burdened than DHA patients and SCC family caregivers. In general, the median burden score analyses and the mean and standard error plot comparisons showed that, across the total 12 month period of the study, bipolar patient family caregivers were more burdened for about 8 to 10 months when compared to DHA patient and SCC family caregivers.

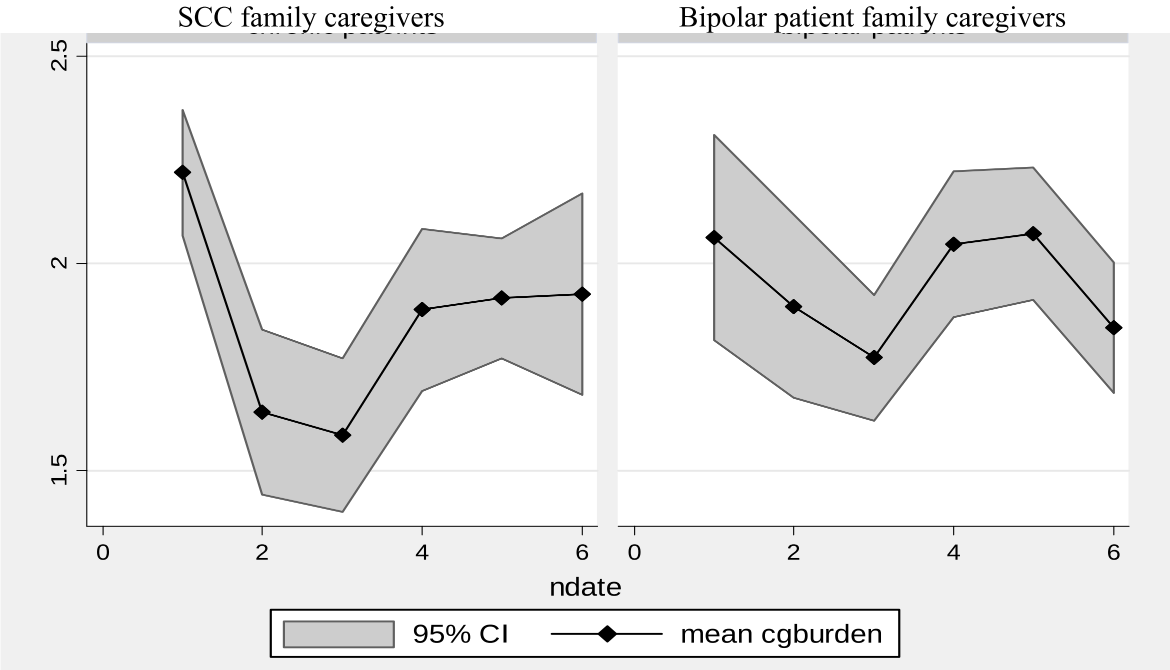

Fig 3. Family caregiver burden mean and standard error plots for bipolar patient and SCC family caregivers, Butajira-Ethiopia, 2005.

Further analysis of family caregiver burden using a population average generalized estimating equation with autoregressive working correlation (see table III) demonstrated that the average difference in family caregiver burden score between bipolar and DHA patient family caregivers was 4.36 (z = -8.75, P>|z|= 0.001). It was also shown that the difference due to time between the two group of family caregivers was 3.42 (z= -4.27, P>|z|= 0.001). In addition, it was also found that the interaction among the variables of being a family caregiver of bipolar patients, caregiver burden and time was statistically significant with caregiver burden score difference of 3.32 (z= 13.46, P>|z|= 0.001).

Table III. Population average generalized estimating equation analysis of family caregiver burden between bipolar and DHA patient family caregivers, Butajira-Ethiopia, 2005.

```
GEE population-averaged model                          Number of obs      =     144
Group and time vars:     subject time                  Number of groups   =      44
Link:                    identity                      Obs per group: min =       2
Family:                  Gaussian                                     avg =     3.3
Correlation:                 AR(1)                                    max =       6
                                                       Wald chi2(9)       =  810.55
Scale parameter:             0.2043554                 Prob > chi2        =  0.0000

                              (standard errors adjusted for clustering on subject)

                 |             Semi-robust
Caregiver burden |  Coef.       Std. Err.        z       P>|z|    [95% Conf. Interval]

Caregiver        | -1.25         0.14          -8.75    0.000     -1.54   -0.97
Time             | -0.29         0.07          -4.27    0.000     -0.43   -0.16
Sex              | -0.01         0.06          -0.24    0.809     -0.12    0.09
Age              | -0.01         0.00          -2.33    0.020     -0.01   -0.00
Marital status   | -0.05         0.06          -0.73    0.464     -0.18    0.08
Educational level  | -0.01       0.06          -0.12    0.903     -0.13    0.11
Occupation       |  0.01         0.06           0.27    0.789     -0.09    0.12
Family size      | -0.00         0.03          -0.25    0.803     -0.04    0.03
Interaction      |  0.21         0.02          13.46    0.000      0.18    0.24
Constant         |  3.11         0.24          13.17    0.000      2.65    3.58

Estimated within-subject correlation matrix R:
         c1        c2        c3        c4        c5        c6
r1   1.0000
r2   0.1914    1.0000
r3   0.0366    0.1914    1.0000
r4   0.0070    0.0366    0.1914    1.0000
r5   0.0013    0.0070    0.0366    0.1914    1.0000
r6   0.0003    0.0013    0.0070    0.0366    0.1914    1.0000
```

Similarly when comparing bipolar patient family caregivers with SCC family caregivers (see table IV), the average family caregiver burden score difference was 3.7 (z= -4.88, P>|z| 0.001). In terms of longitudinal caregiver burden difference, bipolar patients family caregivers were found to be more burdened than SCC family caregivers with a burden score difference of 2.97 (z= -5.17, P>|z|= 0.001). Besides, the interaction among the variables of being a family caregiver of bipolar patient, caregiver burden and time was statistically significant with caregiver burden score difference of 2.88 (z= 16.14, P>|z|= 0.001), signifying that when considered longitudinally, care-giving for bipolar patients was more burdensome than care-giving for sick controls in the community (SCC).

In summary, this study found that the economic and family caregiver burden due to bipolar disorder was greater for families with bipolar disorder patients than the economic and family caregiver burden of families with diabetes, hypertension and asthma patients or families with sick controls at the community.

Table IV. Population average generalized estimating equation analysis of family caregiver burden between bipolar patient family caregivers and SCC family caregivers, Butajira-Ethiopia, 2005.

```
GEE population-averaged model                  Number of obs      =     141
Group and time vars:     subject time          Number of groups   =      47
Link:                   identity               Obs per group: min =       2
Family:                  Gaussian                             avg =     3.0
Correlation:               AR(1)                              max =       6
                                               Wald chi2(9)       =  835.77
Scale parameter:          .1760814             Prob > chi2        =  0.0000
                         (standard errors adjusted for clustering on subject)

                 |          Semi-robust
Caregiver burden | Coef.      Std. Err.    z      P>|z|    [95% Conf. Interval]

Caregiver        | -1.03       0.21     -4.88    0.000    -1.44   -0.61
Time             | -0.30       0.06     -5.17    0.000    -0.41   -0.19
Sex              |  0.05       0.09      0.55    0.581    -0.13    0.23
Age              | -0.00       0.00     -1.12    0.262    -0.01    0.00
Marital status   |  0.00       0.09      0.03    0.972    -0.18    0.18
Educational level| -0.06       0.10     -0.59    0.553    -0.26    0.14
Occupation       |  0.04       0.07      0.60    0.549    -0.09    0.17
Family size      | -0.01       0.02     -0.52    0.604    -0.04    0.02
Interaction      |  0.21       0.01     16.14    0.000     0.19    0.24
Constant         |  2.67       0.33      7.99    0.000     2.01    3.32

Estimated within-subject correlation matrix R:
        c1       c2       c3       c4       c5       c6
r1  1.0000
r2  0.2866   1.0000
r3  0.0821   0.2866   1.0000
r4  0.0235   0.0821   0.2866   1.0000
r5  0.0067   0.0235   0.0821   0.2866   1.0000
r6  0.0019   0.0067   0.0235   0.0821   0.2866   1.0000
```

Discussion

To the best of our knowledge, this is the first study which has comparatively explored how family caregiver burden due to bipolar disorder changes over time. In this study, bipolar patient family caregivers were found to be burdened above the median score for about two thirds of the year. Caregiver burden score differences between family caregivers of bipolar patients and the two comparison groups revealed that a burden causing event happened at least three to six times per week in the months of the year on family caregivers of bipolar patients, whereas on family caregivers of DHA patients and SCC, burden causing events had not happened in most of the months of the year. In addition, compared to DHA patients and SCC family caregivers, the burden experienced by family caregivers of bipolar disorder patients was for longer period of time. The longitudinal time change of burden experienced by family caregivers of bipolar disorder patients was significantly different from longitudinal time change of burden experienced by family caregivers of DHA patients and SCC. In this longitudinal time change of burden, family caregivers of bipolar patients were found to be more burdened than DHA patients and SCC family caregivers. Moreover, money and time of family caregivers of bipolar disorder patients had been directly and indirectly taxed. They had spent their money for their bipolar relatives seeking medical help and had also lost days of work due to care giving, of course that was not significantly more than the comparison groups.

With regard to the extent of burden, our findings were consistent with findings of other studies.[23-27] A longitudinal hospital based study in the US, involving caregivers of bipolar disorder patients, reported that over 90 percent of family caregivers had experienced at least moderate levels of burden whereas over 50 percent of the caregivers had experienced severe levels.[23] Another South American cross-sectional study reported high levels of burden in relatives of people with schizophrenia.[24] In another study from Nigeria, rural families of schizophrenics were reported to shoulder a heavy burden of treatment and transportation for follow-up.[25] The five European centers study on relatives of patients with schizophrenia had also reported that relatives experience high level of burden spending 7 to 9 hours daily with the patient.[26]

As in the South American study our findings also uncovered that there was no difference in family care giving burden due to age and being married. Also, like the European centers study the majority of the caregivers in our study were females. However, in our study there was no family caregiver burden difference between male and female family caregivers. Furthermore, our findings showed that there was no difference in family caregiver burden due to differences in occupation, marital status and educational level among the study subjects. This might be due to similarities among study subjects which might indicate inadequate representativeness of the sample. Moreover, unavailability of difference in terms of educational level, as usually expected, may also mean that caregivers understanding of patients' condition were also similar or this may further need to discover the cultural norm of defining caregiver burden in the study community. Even though, our findings were consistent (in some respect) with these studies, there were methodological differences. In some of the studies family caregivers were assessed clinically so as to know the influence of patients' clinical status on caregivers' burden. They also used different interview instruments and analytic methods.

In our study, care giving was more burdensome for bipolar patient family caregivers. Through time, these caregivers may become overburdened as the longitudinal change in family burden score was persistent for most months of the year. With this regard a previous study has reported that patients living with an overburdened caregiver may have increased risk of relapse, therefore, attention should be paid to those bipolar patient family caregivers.[21] In addition, the annual cost of out-of-pocket medical expense ($93.93) made by family caregivers of bipolar patients was substantially higher than the out-of-pocket medical expense made by DHA patient and SCC family caregivers. If we consider this out-of-pocket medical expense at societal level, by taking into consideration one percent life time prevalence as a lower margin and the average 2.9 percent life time prevalence of different studies done at different times in urban and rural Ethiopia as a higher margin; and assuming that each case of bipolar disorder had at least one family caregiver, then the total direct cost to the Ethiopian society was approximately between $39.1 to $113 million.[28-33] Likewise, the indirect cost of loss of working days due to care giving (by assuming $0.92 as a wage for a day's work) was approximately between $5.4 to $15.5 million. Therefore in 2005, the total economic burden of family care giving for patients with bipolar disorder in Ethiopia ranged approximately between $45.5 million to $128.5 million. Compared to other studies in the western world, the total economic burden of care giving for bipolar disorder patients seems minimal,[2-4, 8] But, for a low income developing country like Ethiopia, this is huge. Of course these cost estimates involve a lot of approximation because of uncertainty involved in the calculation. However, it is undeniable that the figures give an insight of how burdensome was family care giving for bipolar disorder patients in a low income developing country.

Generally more should be done in the direction of lessening the economic and family caregiver burden due to bipolar disorders. Health policy and priority setting need to be tuned in accordance with the available evidence of burden from bipolar disorder and other mental health problems. Family caregivers should be supported through family and follow-up clinic based educational programs. Caregivers who can cope better with patients' behavior or who can improve their coping abilities over time has less burden.[34] Future studies need to focus more on how to devise feasible intervention strategies to lessen economic and family caregiver burden due to bipolar disorder and also need to define cultural norm of care giving in the study community. Finally, the study has been undertaken longitudinally; and it is among the first that described the economic and family caregiver burden of caring for bipolar disorder patients at the community level. However, direct comparison of the results of the study with other studies conducted elsewhere was limited. Also, the sample may not be adequately representative, so the results of the study should be cautiously interpreted.

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Paper II

Longitudinal analysis of burden due to bipolar disorder patients living in a community under clinical follow-up

Short running head: burden due to bipolar disorder patients living in a community

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Abstract

Introduction: there is little existing data on the burden of bipolar disorder experienced by patients living in developing countries. Therefore, it was aimed to describe the burden associated with bipolar disorder in a community sample of patients under clinical follow-up in Ethiopia.

Methods: A sample of 190 patients with bipolar disorder was recruited from a large community survey (n = 68000) and followed up every two months for one year. Data were collected on patients’ sociodemographic characteristics, health service visits, lost days of work and substance use. Annual and projected population levels of burden were calculated.

Results: out of the sampled 190 bipolar patients, 21 to 45 percent had visited health services in the last year, and 21 to 34 percent were unable to perform their regular job. Over the year, patients with bipolar disorder lost a mean of 93.52 cumulative days of work. Consequently, in the year 2005, bipolar disorder patents living in a community under clinical follow-up lost 112.8 million days of work. The annual burden of bipolar disorder to individual patients was a mean of $274.06 per patient. The annual burden of bipolar disorder to society at large was estimated to be $331 million.

Conclusions: the burden of bipolar patients who were living in the community under clinical follow-up was immensely high to poor countries where one hardly finds adequate mental health service in most rural as well as urban areas. Therefore, individual bipolar patients and their families need to be supported by a devised scheme of financing. Future studies need to assess availability of resources to address the burden of bipolar disorder.

Key words: bipolar disorder, burden, community, longitudinal

Significant outcomes:

- The burden of bipolar patients who were living in the community under clinical follow-up was immensely high for a poor country.
- Individual bipolar patients and their families need to be supported by a devised scheme of mental health care financing.

Limitations:

- Costs of bipolar disorder to the health sector were not included.

Introduction

Bipolar disorder is a severe mental illness characterized by recurrent episodes of elated or depressed mood. Bipolar disorder is a major global public health issue (1, 2) due to the recurrent and chronic nature of the illness (3-6), and is associated with a large burden for individuals with the disorder, their families and society (7-13). The disorder is associated with elevated mortality, with approximately 18.9 percent of patients dying through suicide (10). In addition, psychosocial impairment is common in bipolar disorder as patients often experience problematic occupational, social and family functioning (3). Functional disability or reduced efficiency at work, loss of productivity because of absence from work, and high level of caregiver distress are some of the factors worsening the burden (7, 14-16). Non-compliance, mixed depressive – manic symptoms, co-morbid medical disorders, substance use and alcohol abuse are among the factors that complicate treatment of patients with bipolar disorder (17).

Economic studies have found the burden of bipolar disorder to extremely high. In 1990 the economic burden of bipolar disorder in the U.S. was estimated to be $15.5 billion due to lost productivity in work performance (14). In the same year, patients in treatment lost an estimated 152 million cumulative days from work and untreated patients lost 137 million days. In 1991, the burden of bipolar disorder among adult Americans based on 1.3 percent lifetime prevalence was estimated at $45 billion (7); of which $8 billion was due to loss of productivity because of suicide and $6 billion was due to lost productivity of caregivers who provide care for family members with the disorder. Another estimate for the 1998 incident cases of bipolar disorder in the US was estimated at 24 billion US dollars (8). In the UK, in 1998, the annual burden of bipolar disorder was estimated at $3 billion (9). In the Netherlands, based on 5.2 percent prevalence of bipolar disorder the total burden of the disorder was estimated at $1.83 billion (13). The burden in Australia in 2004 assuming a 2.5 percent lifetime prevalence and the same pattern of health service, was estimated between AUD$3.97 to AUD$4.95 billion (12). It has also been estimated that bipolar disorder has dramatically increases use of health care resources by patients (18) and their caregivers (16).

In most developing countries, particularly in sub-Saharan Africa, resources for mental health care are very scarce (19) and the delay in seeking treatment for bipolar disorder is long (17). Therefore, it is expected that individual patients and their families would bear the brunt of the burden. Most of the studies quantifying economic burden of bipolar disorder originate from developed countries where the level of health care provision is quite different to that available in developing countries. In addition, most studies have used clinic-based samples of patients with bipolar disorder. In this paper we describe the burden experienced by patients with bipolar disorder who are living in a community under clinical follow-up in rural Ethiopia.

Methods:

Study design and subjects

The study was conducted in Meskan and Mareko Wereda, rural district in southern Ethiopia. In the district a course and outcome study project on bipolar disorder has been underway since the early 1990s. The project conducted a house-to-house survey and screened all 83,282 of the adult population of the district for bipolar disorder using the WHO Composite International Diagnostic Interview (CIDI), Version 2.1(20). The present study used a prospective longitudinal design involving identified bipolar disorder patients who were being clinically monitored (on a monthly basis) with symptom rating scales. The total sample size was 190 cases.

Data collection

Data collection instruments were developed and pre-tested three times in a nearby community. The purpose of these repeated pre-tests was to increase the reliability and validity of interview instruments. Accordingly, interview instruments with reliability test coefficient less than 0.40 were dropped. In each of the pre-testing sessions one week extensive training was provided for data collectors and supervisors. Using the refined final interview instruments, data were collected on sociodemographic characteristics, health service visits, out-of–pocket medical expenses for health services, time lost travelling to and from health institutions, time lost at the health institutions, lost days of work due to illness and substance use. The latter included asking about frequency of chewing Khat (Catha edulis); a psychoactive stimulant indigenous to most east African countries.

Participants were interviewed every 2 months. Data quality and consistency cross-checks were made by another group of trained supervisors recruited for the purpose. The data quality and consistency cross-checking was implemented by randomly selecting 5 percent of total interviews done and re-interviewing study subjects. The data collection was carried out every two months for one year. (July 2004 to June 2005). EpiInfo 6 version 6.04d statistical software was used for data entry and Stata/SE 8.2 for Windows was used for data analysis.

Analysis

In the analysis mean out-of-pocket medical expense, cost of travel, time lost traveling to-and-from health institutions, time lost at health institutions; lost days of work in the month prior to the interview and frequency of substance use were calculated. Financial costs, time lost and lost days of work were considered as a burden and estimates were extrapolated to societal level by multiplying added costs of mean out-of-pocket medical expense, lost time, lost days of work by the estimated prevalence of bipolar disorder in the adult population (age 15 years and above) in Ethiopia. For reasons of comparability, all costs were converted to US$ using the mean exchange rate for 2005 of Ethiopian currency Birr 8.6810 = 1US$ (21). The study was ethically approved and informed consent to participate in the study was obtained from the study subjects.

Results:

Out of the 190 patients with bipolar disorders eligible for inclusion in the studies, the number participating at each time-point was as follows: 137 at T_1; 150 at T_2, 149 at T_3, 148 at T_4, 141 at T_5 and 131 at T_6. The reasons for missing data included participant change of address, death, refusal, imprisonment, unavailability, and wandering (vagrant i.e. no fixed abode). At each interview time-point, male participation ranged from 51 to 53 percent, whereas female participation was in the range of 47 to 49 percent (see table 1). The mean age of the study subjects was 33.08 years, with standard deviation of 8.88. The minimum age was 15 years and maximum was 61 years. Married participants constituted between 68 to 72 percent of the sample at the different time-points. Most of the study subjects (53 to 65 percent) were non-literate but more than 90 percent were employed. About 40 percent were household heads, and 31 to 37 percent were homemakers. For each interview time-point, the average family size per household was six, with an average of three children under 15 years of age. Over the study period the mean monthly family expense of patients ranged from \$11.63 to \$18.32.

Table 1. Sociodemographic characteristics of bipolar patients living in a community under clinical follow-up, Butajira-Ethiopia 2005.

Variable	**At time 1**	**At time 2**	**At time 3**	**At time 4**	**At time 5**	**At time 6**
	2 months	**4 months**	**6 months**	**8 months**	**10 months**	**12 months**
	(n = 137)	(n = 150)	(n = 149)	(n = 148)	(n= 141)	(n= 131)
Sex						
Male	73 (53.28)	77 (51.33)	76 (51.01)	75 (50.68)	74 (52.48)	67 (51.15)
Female	64 (46.72)	73 (48.67)	73 (48.99)	73 (49.32)	67 (47.52)	64 (48.85)
Age						
Mean	33.11(8.72)	32.81(8.97)	32.65(8.94)	33.18(9.51)	33.16(8.33)	33.58(8.79)
Range	15 - 50	15 - 60	15 - 55	15 - 61	15 - 51	18 - 55
Marital status						
Married, n (%)	93 (67.88)	102 (68.00)	104 (70.27)	106 (71.62)	102 (72.34)	93 (71.54)*
Others, n (%)	44 (32.12)	48 (32.00)	44 (29.73)	42 (28.38)	39 (27.66)	37 (28.46)
Educational level						
Illiterate, n (%)	72 (52.55)	86 (57.72)	90 (60.40)	96 (64.86)	82 (58.16)	76 (58.46)*
Literate, n (%)	65 (47.45)	63 (42.28)*	59 (39.60)	52 (35.14)	59 (41.84)	54 (41.54)
Occupation						
Employed, n (%)	122 (89.05)	133 (88.67)	140 (94.63)	141 (95.27)	132 (93.62)	127 (97.69)*
Unemployed, n (%)	15 (10.95)	17 (11.33)	8 (5.37)	7 (4.73)	9 (6.38)	3 (2.31)
Relationship with the family						
Household head, n (%)	55 (40.15)	63 (42.00)	59 (39.60)	61 (41.22)	59 (41.84)	54 (41.54)*
Housewife, n (%)	43 (31.39)	50 (33.33)	55 (36.91)	52 (35.14)	47 (33.33)	44 (33.85)
Child/daughter/son, n (%)	34 (24.82)	35 (23.33)	32 (21.48)	32 (21.62)	31(21.99)	29 (22.31)
Others, n (%)	5 (3.64)	2 (1.34)	3 (2.01)	3 (2.02)	4 (2.84)	3 (2.30)
Average family size (sd)	5.78 (2.28)	5.97(2.33)	5.97(2.42)	6.31(3.03)	6.13(2.55)	6.05(2.34)
Average No. of children (sd)	2.86 (1.61)	2.97 (1.34)	3.12 (1.43)	3.17(1.44)	3.13(1.44)	3.04(1.46)
Average monthly family expense (sd)	13.75 (14.10)	18.32 (28.59)	14.07 (15.65)	11.63 (11.43)	12.66 (14.76)	11.64 (11.47)

* 1 case was missing

Self-reported health status was ‘not good’ in 18 to 32 percent of study participants over the follow-up period (see table 2); and between 18.5 and 45 percent of bipolar patients visited health services. Over the follow-up period, 21 to 34 percent of patients were unable to work on their regular job. Around half (42 to 64 percent) of patients remained under active clinical follow-up, visiting clinics every month or two months to be assessed clinically; Those who felt well were expected to visit follow-up clinics once a year for a check-up. Out of patients who remained under active clinical follow-up, 48 to 71 percent were taking medication in the month preceding interview. Out of the group of bipolar patients under treatment, 21 to 36 percent were chewing Khat for most days of the year.

Table 2. Bipolar patient characteristics during the survey. Butajira, Ethiopia, 2005.

Variable	**At time1** **2 months** (n = 137)	**At time 2** **4 months** (n = 150)	**At time 3** **6 months** (n = 149)	**At time 4** **8 months** (n = 148)	**At time 5** **10 months** (n = 141)	**At time 6** **12 months** (n = 131)*****
During last 2 months:						
Health status						
Not good, n (%)	44 (32.12)	44 (29.33)	39 (26.17) 83	39 (26.35)	25 (17.73)	29 (22.31)
Good, n (%)	77 (56.20)	80 (53.33)	(55.70)	86 (58.11)	93 (65.96)	81 (62.31)
Very good, n (%)	16 (11.68)	26 (17.33)	27 (18.12)	23 (15.54)	23 (16.31)	20 (15.38)
Visited health services						
Yes, n (%)	62 (45.26)	44 (29.33)	43 (28.86)	36 (24.32)	29 (20.57)	24 (18.46)
No, n (%)	75 (54.74)	106 (70.67)	106 (71.14)	112 (75.68)	112 (79.43)	106 (81.54)
Was unable to work						
Yes, n (%)	46 (33.58)	34 (22.67)	38 (25.50)	31 (20.95)	32 (22.70)	27 (20.77)
No, n (%)	91 (66.42)	116 (77.33)	111 (74.50)	117 (79.05)	109 (77.30)	103 (79.23)
Was under active follow-up						
Yes, n (%)	87 (63.50)	63 (42.00)	75 (50.34)	76 (51.35)	70 (49.65)	66 (50.77)
No, n (%)	50 (36.50)	87 (58.00)	74 (49.66)	72 (48.65)	71 (50.35)	64 (49.23)
Last month:						
Was taking medication						
Yes, n (%)	59 (67.82)	43 (68.25)	49 (65.33)	54 (71.05)	44 (62.86)	32 (48.48)
No, n (%)	28 (32.18)	20 (31.75)	26 (34.67)	22 (28.95)	26 (37.14)	34 (51.52)
Chew khat						
Yes, most days of the week, n (%)	30 (34.48)	21 (33.33)	16 (21.33)	25 (32.89)	23 (32.86)	24 (36.36)
No, not at all, n (%)	57 (65.52)	42 (66.67)	59 (78.67)	51 (67.11)	47 (67.14)	42 (63.64)

* 1 case was missing

In the final estimation of burden, the mean out-of-pocket expense was considered as a direct cost and lost time and days of work were considered as indirect costs. As shown in table 3, the mean out-of-pocket medical expenditure made by bipolar patients was $10.44 while the cost for round trip travels was $2.74. Thus, the total direct cost per year was $13.18. In traveling to visit a health institution, patients lost a minimum of 1.24 hours and a maximum of 1.81 hours, and they had also lost a minimum of 1.83 hours and a maximum of 4.11 hours to complete medical examination and treatment at the institutions. Furthermore, one month prior to the interviews, each patient lost an average of 12 to 19 days of work. Across the whole study year, patients lost an average of 93.52 cumulative days of work. During each interview patients were asked to estimate the value of the time which they lost traveling to-and-from the health institute and at the health institute in relation to their current job. As a result the mean value of time lost was estimated at $2.76 with standard deviation of $3.50. This value was also used to estimate burden due to lost days of work. Therefore, the overall annual cost of bipolar disorder to the individual patient was $274.06. The sum of the direct and indirect costs was considered as burden. This burden was extrapolated and estimated to societal level by multiplying added costs of mean out-of-pocket medical expense ($13.18), value of lost time ($2.76), value of lost days of work (93.52 x $2.76) by an average estimated prevalence of bipolar disorder in Ethiopia (2.9%) (22-27) among the population of age 15 years old and above (41,609,606) (28). Therefore, annual burden of bipolar disorder to Ethiopian society was estimated to be $331 million. Similarly, in the year 2005 the projected lost days of work to the Ethiopian society was estimated to be 112.8 million, assuming a 2.9 percent life time prevalence rate of bipolar disorder in the general population and 93.52 cumulative lost days of work from each patient annually.

Table 3. Bipolar patients' mean annual out-of-pocket medical expense, lost time and days of work, Butajira, Ethiopia, 2005.

Variable	**At time 1** **2 months** (n = 137)	**At time 2** **4 months** (n = 150)	**At time 3** **6 months** (n = 149)	**At time 4** **8 months** (n = 148)	**At time 5** **10 months** (n= 141)	**At time 6** **12 months** (n= 131)*
During last 2 months:						
Mean out-of-pocket medical expense (sd)	0.50 (19.52)	1.42 (5.05)	0.87 (3.20)	1.98 (9.61)	0.45 (1.33)	0.38 (1.47)
Mean cost of travel (sd)	0.79 (1.87)	0.50 (0.91)	0.41 (0.56)	0.48 (1.14)	0.29 (0.42)	0.27 (0.45)
Mean time lost traveling, hours (sd)	1.81 (1.92)	1.65 (1.93)	1.39 (0.82)	1.34 (0.81)	1.24 (0.84)	1.40 (0.92)
Mean time lost at HI, hours (sd)	4.11(11.94)	2.30 (1.74)	1.83 (1.75)	2.42 (2.24)	2.57 (2.21)	3.35 (2.09)
Mean lost days of work last months (sd)	19.39 (9.67)	19.32 (11.10)	14.77 (11.30)	15.23 (11.79)	12.85 (11.24)	11.96 (9.77)

Discussion:

This study attempted to prospectively estimate the economic burden of bipolar disorder in a rural community in a developing country. An average of 75 percent response rate was observed in the study. The mean age of study subjects was in the early thirties; more importantly most of the study subjects were in the age group of 30 to 44 years, followed by the age group of 15 to 29 years. Therefore, this population-based sample of patients with bipolar disorder were in the most economically productive years of their life resulting in high productivity loss to society as a result of their illness. The burden upon the affected individual and their family might be expected to be considerable. This is particularly likely to be the case as 40 percent of study subjects were household heads and 31 to 37 percent were homemakers with an average family size of six, of which three of the members were children under 15 years of age. The mean monthly family living expense of patients ranged from $11.63 to $18.32 which averages to less than a dollar a day. In such a setting, the burden of bipolar disorder would be expected to be high as a result of the compounding effect of poverty.

In the present study 18 to 32 percent of patients reported poor health during the study year and this was reflected in the high number of health service visits; 21 to 45 percent of the patients had one to four visits in the year. These findings are consistent with findings of a multinational Delphi consensus study (18) which found that 23 to 41 percent of bipolar patients visited a primary health care service while in the depressive phase of their illness. Such a high number of health service visits may represents a burden to the health care delivery system. For instance in our study, out of patients who were under active clinical follow-up, 48 to 71 percent were taking medication in the month prior to the interviews. Ethiopia is one of the one-third of countries worldwide which has no specific budget for mental health care and it would be expected that the majority of people with bipolar disorder do not receive optimal treatment for their condition, thus increasing the burden of the disorder (19). Furthermore, one month prior to the interviews, each patient lost an average of 12 to 19 days of work which is an additional burden. These findings are also consistent with the findings of a study on major depression in the area, in which patients lost 15 days of work per month (29). The inability of 21 to 34 percent of the patients to work on their regular job demonstrates the loss of productivity associated with bipolar disorder in Ethiopia. This was despite the presence of a clinical service offering assertive outreach and subsidized medication for these study participants. The burden of illness may have been associated with treatment non-adherence and / or co-morbid substance use: out of bipolar patients under treatment, 21 to 36 percent were chewing Khat for most days of the year while they were under treatment. Frequent use of psychoactive stimulants may adversely affect the adherence to treatment. In this regard an outcome study in the area revealed a 66 percent relapse rate among bipolar patients having chronic symptoms during an average follow-up period of 2.5 years (6).

The annual mean out-of-pocket medical expense of $13.18 by patients was an underestimate since most of the drug cost for bipolar patients was subsidized by the ongoing research project. Depending on the clinical status of patients, amytriptline, chlorpromazine or both drugs may be prescribed. Those patients who felt well on clinical assessment may only receive psychological therapeutic support. Therefore, this could be one of the reasons for the low estimate of annual mean out-of-pocket medical expense. The other reason could be the fact that patients were living in the community and were under clinical follow-up and some of the cases were under medication, thus, the severe form of the illness may have been avoided. The other big factor for the low estimate of annual mean out-of-pocket medical expense could be the level of poverty prevailing in the community as most of the study subjects were living on less than a dollar a day (mean annual family income of $169.39). Moreover, the scarce availability of health care resources for the illness likely resulted in the observed minimal level of expenditure.

Similarly the finding of the total annual cost of $274.06 to individual patients was also low when compared to study findings of annual individual costs in the Netherlands ($848), UK ($1444), Australia ($8553), and the US ($9619) (9, 12, 13, 15). However, the scope of burden studies, epidemiological patterns, patterns of health service utilizations, cost of medical services, and methodologies of estimating cost in these countries necessarily differ from a study conducted in a rural area of a developing country. A wider view of types of medical services was used in bipolar burden studies from these countries, but in our case a narrower definition of burden was required due to the fact that patients were living in the community where health sector costs were excluded. Nevertheless, the total annual cost of $274.06 to each individual patient was surprisingly high in a country, like Ethiopia, where bipolar disorder had never appeared in the list of leading causes of morbidity and mortality and where number of outpatient visits per annum and public health expenditure per capita were 0.33 and $1.54 respectively (30).

Likewise, when compared to the annual lost days of work in studies from the Netherlands and the USA (13, 15), the number of lost days of work (93.52) by each patient and number of projected annual lost days of work (112.8 million) were high in the present study. In the Netherlands study the mean annual days of absence from work was 55.5 per each respondent with a paying job, and the mean annual productivity loss associated with reduced efficiency at work was 7.7 days. In the US study bipolar disorder was associated with 65.5 annual lost days of work per ill worker and 96.2 million lost days of work. The use of different methodologies may contribute to this difference in number of lost days of work. In the present study, the patient's self-report of lost days of work was used while in the Netherlands study, Health and Labor questionnaire; and in the US study, the WHO Health and Work Performance Questionnaire were used respectively. In addition, most of our study subjects were self employed, while in the Netherlands study 30 percent of the subjects were in a paying job and in the US study the subjects were a representative sample of US workers. On the other, hand, the present finding of 112.8 million annual lost days of work was close to the estimate by a US study conducted in 1990 (14), where patients in treatment lost an estimated 152 million cumulative days from work and untreated patients had lost 137 million days.

Generally, the burden of $331 million due to bipolar patients who were living in the community under clinical follow-up was immensely high for a poor country where one finds woefully inadequate mental health service in most urban and especially in the rural areas. In such a setting as Ethiopia, individual bipolar patients and their families need to be supported by a devised scheme of mental health care financing, perhaps making use of existing local associations (e.g. social insurance for burial service assistance) in the community.

The strength of this study is that it was undertaken longitudinally in a developing country and addressed a disease entity to which very little attention has been given in such a setting. A limitation is that costs of bipolar disorder to the health sector were not included. In addition use of non-standardized interview instruments may have limited further comparability of the study results with findings of other studies. Future studies need to explore the role of adherence to treatment of bipolar patients living in the community, availability of health care resources for bipolar disorder and possible insurance mechanisms for covering the burden to bipolar patients.

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Paper III

Panel data analysis of burden in families of patients with schizophrenia

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Panel data analysis of burden in families of patients with schizophrenia

Abstract

Background: in traditional societies the longitudinal time change of burden in families of patients with schizophrenia is unknown.

Aim: to describe how burden in families of patients with schizophrenia changes over time

Method: families (n= 249) with schizophrenia patients were followed prospectively for one year and the change over time in family burden was explained using a population average generalized estimating equation.

Results: families were found to experience persistent burden for about eighty-three percent of the year. The change in family burden due to time was statistically significant with a mean family burden score of 3.10 (z = -20.86, P>|z|= 0.001). As time goes on, family burden due to schizophrenia increases by a unit of 0.66 (z= -20.86, P>|z|= 0.001).

Conclusions: families should be supported through a carefully designed intervention strategy to improve level of functioning and treatment adherence of patients.

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Key words: General, panel data; burden; schizophrenia; family

Panel data analysis of burden in families of patients with schizophrenia

Introduction

Schizophrenia, characterized by distortions in thinking, perception, and by inappropriate emotions, is a severe, universally common psychiatric illness (Jablensky, 2000; WHO, 1973; 2001; Barbato 1998). The illness begins in late adolescence or early adulthood and follows a variable course, ranging from complete symptomatic and social recovery to chronic or recurrent course, with residual symptoms and incomplete social recovery (WHO, 2001; Rössller et al., 2005). It causes a high degree of disability in self care, occupational performance, functioning in relation to family and household members, functioning in a broader social context and social stigma (WHO, 2001; Barbato 1998). Co-morbidity with depression, limited help seeking, rejection of treatment, suicide, cardiovascular diseases, cancer, increased cigarette smoking, recreational use of alcohol and psychoactive drugs are common in patients with schizophrenia (WHO, 2001; Barbato, 1998; Rössller et al., 2005; Terkelsen and Menikoff, 1995; Knapp 1997). Often patients with schizophrenia live for many years with the illness and severe disability remaining dependent on others for basic support (Terkelsen and Menikoff, 1995; Knapp 1997, Frankenburg et al., 1996). Patients' dependence on others and the fact that it often leads to mental and social disability, makes it one of the most burdensome costly illnesses.

Cost of illness studies found schizophrenia to disproportionately consume health care resources (Rice, 1999; Andrews et al., 1985; Salize and Rössller, 1996; Jonsson and Wålinder, 1994; Weiden and Olfson, 1995; Seva, 2002) and its burden represented

0.3 to 3 percent of annual healthcare budget in developed countries (Rössller et al., 2005; Knapp, 1997; 2004; Goeree et al., 1999; Davies and Drummond, 1994; Fisher et al., 2006; Evers and Ament, 1995). Also family burden studies (Magliano et al., 1998; 2002; 2005; Maldonado et al., 2005; Roick et al., 2006) had found families with schizophrenia patients to experience high level of burden in various dimensions of life. Studies from the US in 1985 and 1992 estimated the family economic burden associated with schizophrenia to be in the range of $2.47 to $8.65 billion (Terkelsen and Menikoff, 1995; Knapp 1997). The burden of schizophrenia on UK families in 1997 was estimated at £1.9 million (Knapp, 2004). Studies from India and Nigeria have also found that the main brunt of financial burden of caring for schizophrenia patients to be borne by families (Grover et al., 2005; Yellowe, 1992). Existing international literature on schizophrenia additionally shows that its burden has been extensively explored (Yellowe, 1992; Magliano et al., 2000; 2006; Berglund et al., 2003; Perlick et al., 2006; Dyck et al., 1999; Boye et al., 2001; Lauber et al., 2003). However, in traditional societies where caring for a family member is a norm, the longitudinal time change of burden in families with schizophrenia patients is unknown. Therefore, this study was aimed at filling this research gap in burden studies of families with schizophrenia patients in the setup of a rural developing country.

Methods:

Study subjects

The study was done in Meskan and Mareko Wereda, a rural district in southern Ethiopia. In the district a course and outcome study project on schizophrenia is underway since the early 1990s. The project had screened all 83,282 adult population of the district for schizophrenia by house to house survey using the WHO Composite International Diagnostic Interview (CIDI), Version 2.1 (WHO, 1997). Identified possible cases were confirmed by Schedule for Comprehensive Assessment in Neuropsychiatry (SCAN) (Sartorius and Janka, 1996). The present study used a prospective longitudinal design involving all identified families with schizophrenia patients. From each family, family caregivers as informants of family burden were selected using the method followed by Perlick et al. caregiver burden study (Perlick et al., 1999). Thus, caregivers were selected based on the following criteria:

a) is a spouse, parent or spouse equivalent to the patient;
b) has most frequent contact with the patient;
c) helps to support the patient financially;
d) has most frequently been a collateral in the patient's treatment; and
e) is contacted by treatment staff in case of emergency. To be included in the sample as a caregiver, the chosen caregiver had to satisfy at least three of the criteria.

Consequently, this study sampled all 249 families of schizophrenia patients who were under follow-up during the survey.

Data collection

The data collection was carried out every two months for one year; started in July 2004 and ended in June 2005. Data collection instruments were developed and pre-tested three times in a nearby community. The purpose of these repeated pre-tests was to increase the reliability and validity of interview instruments. Accordingly, interview instruments with reliability test coefficient less than 0.40 were dropped. In each of the pre-testing sessions, one week of extensive training was provided for data collectors and supervisors. Using the refined final interview instruments, data were collected on economic and family burden. Data quality and consistency cross-checks were made by another group of trained supervisors recruited for the purpose. For data analysis Stata/SE 8.2 for Windows was used.

Burden measurement

Longitudinal burden measurements were made on out-of-pocket medical expenses for health services, time lost due to care giving, patients' ability to work and compliance to treatment and the extent of family burden. Out-of-pocket medical expenses included cost of: travel, medical examination, drugs and injections, laboratory service, food and accommodation; and the time lost due to care giving included time lost in accompanying patient to and from health institute and lost days of work due to care giving at home. There were 14 questionnaire items constituting family burden, with response categories on a five-point scale (see table 1).

Table 1. Questionnaire items constituting family burden, Butajira-Ethiopia, 2005

to what extent:

a) patient’s illness creates financial problem on the family,

b) the patient’s illness affected possibility of getting family income,

c) the patient’s illness creates problem in celebrating holidays,

d) the family feels no financial alternative source for the patient’s illness,

e) the patient’s illness causes financial strain on family need to go anywhere,

f) the patient’s illness creates burden on the family’s children,

g) family relationship was disturbed due to the patient’s illness,

h) the family feels lonely and isolated due to the patient’s illness,

i) the family feels that nothing can be done for the patient’s illness,

j) the patient was isolated by family members and others you consider family,

k) the family was worried thinking about relapse of patient’s illness,

l) patient’s health condition was felt as a burden to the family

m) patient’s condition has affected family’s quality of life and

n) to what extent patient’s health behavior was challenging and difficult.

During each interview, family caregivers were asked about the extent of burden that their families had experienced in the month prior to interview using the 14 questionnaire items. Thus, family burden score of 1 to 5 was given based on the frequency of occurrence of a ‘burden-causing event’: 1 = did not happen at all in the month; 2 = happened at least once per week in the month; 3 = happened at least twice per week in the month; 4 = happened at least 3 to 6 times per week in the month; and 5 = happened almost every day per week in the month.

Analysis

There were six waves of data used in the analysis. Descriptive analyses were made in terms of out-of–pocket medical expenses for health services, time lost due to care giving, patients' ability to work and compliance to treatment and the extent of family burden. From time one (baseline) through six (end of the study); family burden was computed as the respondent's average responses across the 14 items constituting family burden. Finally, a population average generalized estimating equation was used to explain the change over time in family burden. For the purpose of comparison all costs were converted to US$ by using the mean exchange rate for 2005 of Ethiopian currency Birr 8.6810 = 1US$ (National Bank of Ethiopia Annual Report 2005/06). The study was ethically approved by the Faculty of Medicine Addis Ababa University and oral informed consent to participate in the study was obtained from the study subjects.

Results

Out of the 249 eligible families with a member suffering from schizophrenia, 21 were of unknown status, nine were unavailable, five refused; four were inaccessible, leaving 210 participating families. In average there were 5.89 (sd= 2.24) household members per family. In each family there was at least one child (sd= 0.42) less than 15 years of age. The majority of families (n=147, 70%) were living in thatch house, while 30 percent (n=63) were living in houses with corrugated iron roofs. The average monthly expense of the families was $6.84 ($5.55), and the average yearly income was $99.90 ($116.22). As family caregivers had assessed their family health status, 34.21 percent (n= 72) had said that their family health status was not good during the year. More than 50 percent (n= 115) had described their family health as being good. The remaining 11 percent (n=23) described their family health status as very good.

Mean age of schizophrenia patients living in the families was 33.13 years (sd= 8.48) with 93 percent of the patients between age 15 to 45 years old. Nearly 50 percent (n= 95) of the patients were single, 36.22 percent (n=71) were married, and 15 percent (n= 30) were widowed or separated. On average 32.65 (n= 64) percent of the patients had visited health service prior two months during each interview, 84.92 percent (n= 166) were not able to work on their regular job, 72.45 percent (n= 142) were not taking medication as prescribed and one month prior to each interview on average each patient had lost 22.94 (sd= 10.97) days of work. With regard to relationship with respective families: 47.18 percent (n= 92) were children (daughter/son); 40 percent (n=78) were household heads, 6.6 percent (n=13) were housewives, 5.65 percent (n=11) were brothers/sisters and 0.51 (n=1) was a cohabite.

During the year, families had spent \$16.52 out-of-pocket due to schizophrenia and on average they had lost 3.12 (sd = 4.54) days of work per month due to care giving. Additionally, during a health service visit family caregivers on average had lost 1.05 (sd= 0.87) hours traveling to a health institute, 2.04 (sd= 3.80) hours to finish treatment and 4.76 percent (n=10) of the caregivers were accompanied by another family member during the health service visit. In the families the mean family burden score over the year was 2.42 (sd= 0.87) and the median family burden score was 2.29. Both the mean and the median family burden scores showed that family burden causing events were happening at least one to two times per week in all the months of the year.

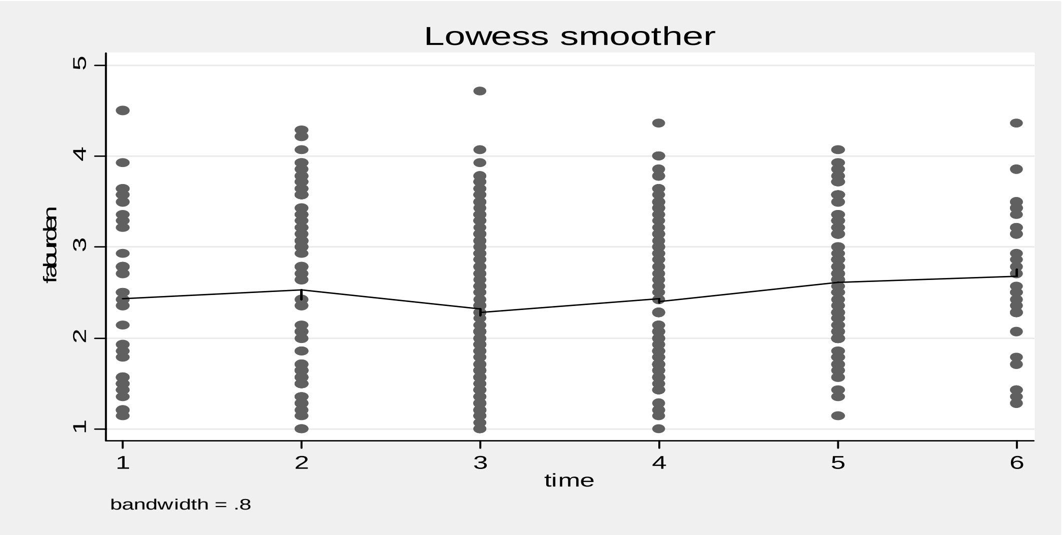

Figure 1 Time series response profile plots with LOWESS mean smother of burden scores in families with schizophrenia, Butajira-Ethiopia, 2005

Descriptive longitudinal analysis of family burden using response profile plot and lowess mean smooth curve had revealed families' constant experience of burden between the scale of 2 and 3 throughout the study year (see fig. 1). This again had shown that families were experiencing at least one to two burden causing events per week in all the months of the study year. Similar results were observed during family burden analysis using family burden median scores (see fig. 2). The median scores were at the higher side of the scale for about 8 months (from time one to two and from time five to six). After 6 to 8 months of the study (i.e., at time three and four) families were experiencing relatively low level of burden. But, then after, they were experiencing relatively higher levels of burden than the other times. Furthermore, throughout the year more than 75 percent of the families were found to experience burden causing events 3 to 6 times per week with median burden scores of 3 to 3.5.

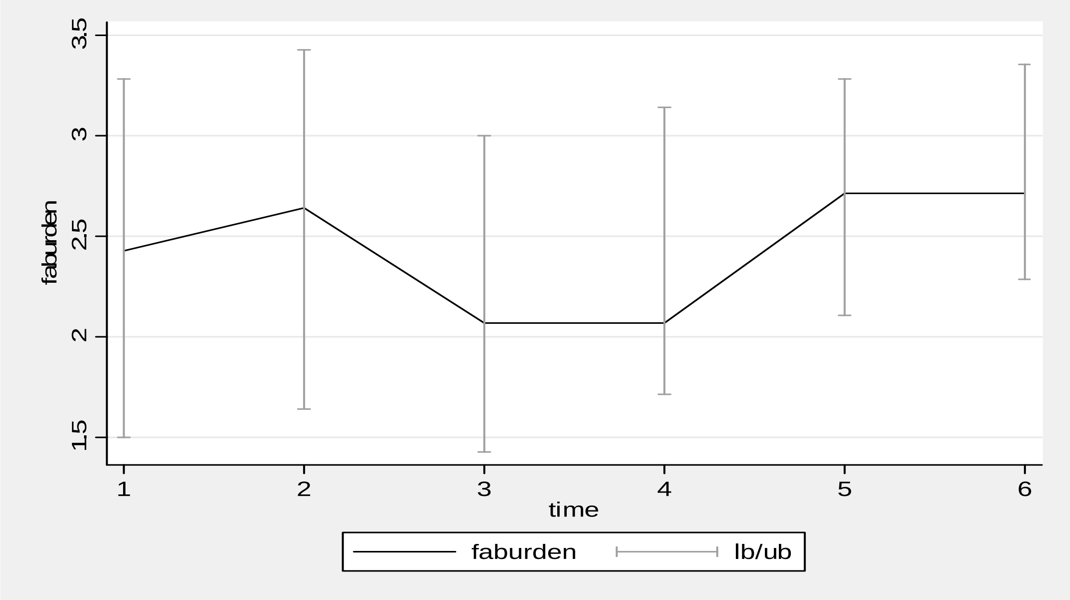

Figure 2 Time series median burden scores with inter quartile range in families with schizophrenia, Butajira-Ethiopia, 2005

The mean and standard error plots of family burden of schizophrenia patient families also showed that mean family burden scores were on the higher side of the scale for most periods of the study except at time 3. For the other periods the mean family burden scores were greater than 2.4. It was only at time 3 that the mean family burden score was between 2.2 and 2.4. That means for about 10 months, burden causing events were happening on schizophrenia patient families at least twice per week (see figure 3).

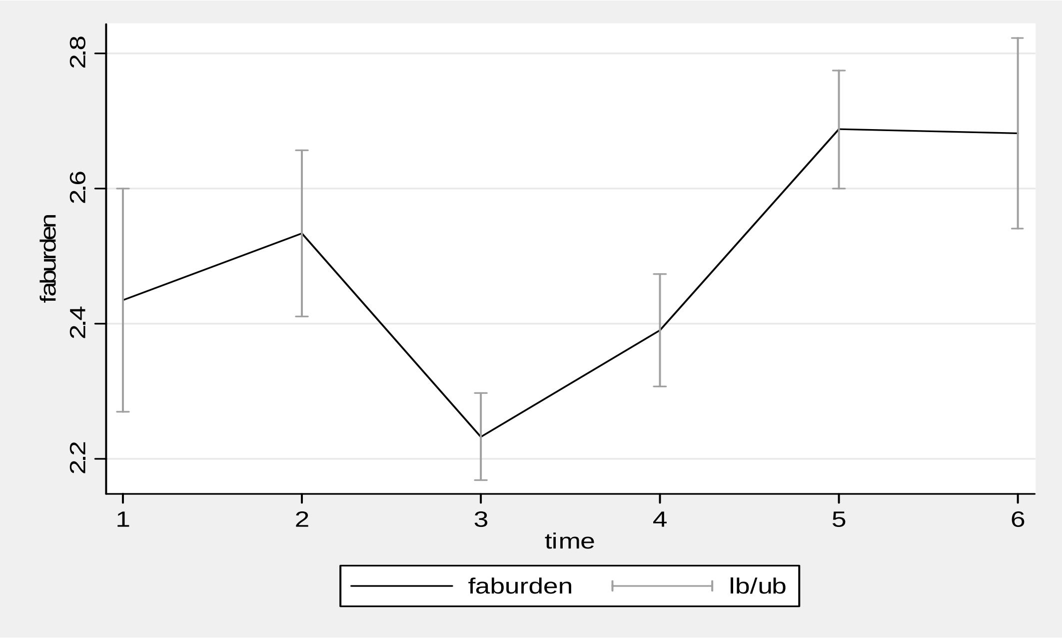

Figure 3 Time series mean and standard error plot of burden scores in families with schizophrenia, Butajira-Ethiopia, 2005

Further analysis of family burden using a population average generalized estimating equation with autoregressive working correlation (see table 2) demonstrated that over the year change in family burden due to time was statistically significant with a mean family burden score of 3.10 (z = -20.86, P>|z|= 0.001). It was also shown that as time goes on, family burden due to schizophrenia increases by a unit of 0.66 (z= -20.86, P>|z|= 0.001). In addition, it was also found that the interaction among the variables of being a family of schizophrenia patient, family burden and time was statistically significant with family burden score of 2.46 (z= 55.95, P>|z|= 0.001).

In summary, this study found that the economic and family burden due to schizophrenia was high for families with schizophrenia patients. Throughout the study period, schizophrenia patient families were constantly experiencing burden due to their schizophrenic relatives.

Table 2. Population average generalized estimating equation analysis of burden in families with schizophrenia patients, Butajira-Ethiopia, 2005.

```
________________________________________________________________________
GEE population-averaged model                      Number of obs      = 262
Group and time vars:  idnumber ndate               Number of groups   = 76
Link:                 identity                     Obs per group: min = 2
Family:               Gaussian                                    avg = 3.4
Correlation:            AR(1)                                     max = 6
                                                   Wald chi2(6)    =  3884.20
Scale parameter:        0.0824217                  Prob > chi2     =    0.0000

                                   (standard errors adjusted for clustering on subjects)
___________________________________________________________________________
                   |           Semi-robust
Family burden      |  Coef.   Std. Err.      z        P>|z|     [95% Conf. Interval]
___________________________________________________________________________
Time               | -.66        .03      -20.86    0.000      -.72     -.60
Family size        |  .03        .01        1.79    0.074      -.00      .04
Children under 15  | -.00        .01       -0.35    0.727      -.03      .02
Type of residence  | -.02        .03       -0.72    0.475      -.09      .04
Annual income      | -.00        .00       -1.07    0.283      -.00      .00
Interaction        |  .02        .00       55.95    0.000       .02      .02
Constant           | 2.44        .13       18.17    0.000      2.18     2.71
___________________________________________________________________________
```

```
xtcorr
Estimated within subject correlation matrix R:
        c1      c2      c3      c4      c5      c6
r1  1.0000
r2  0.0440  1.0000
r3  0.0019  0.0440  1.0000
r4  0.0001  0.0019  0.0440  1.0000
r5  0.0000  0.0001  0.0019  0.0440  1.0000
r6  0.0000  0.0000  0.0001  0.0019  0.0440  1.0000
```

Discussion

This study has explored how family burden due to schizophrenia changes over time in a developing country setup. In the study families were found to experience persistent burden for about eighty-three percent of the year. In addition 75 percent of the families were experiencing high level of burden. Such high level of burden could possibly be explained by the fact that about 93 percent of the patients in the families were in their most productive years of life, 85 percent were not able to work on their regular job and about 73 percent were not compliant with treatment regimen.

The inability of patients to work on their regular job may increase the level of family burden as work responsibilities were reported not to be carried out by the patients. An earlier study has reported decreased level of family burden over time when the level of patient social functioning also gets improved (Magliano et al., 2000). Another longitudinal study has also shown that less severe symptoms of the patient predict lower family burden (Roick et al., 2006). A cross sectional study in the same study area had also reported over 80 percent of schizophrenia patients to have negative symptoms, 67 percent to have continuous course of illness (Kebede et al., 2003) and disorganized symptoms of the patient as important factors affecting families in financial, social and family life domains (Shibre et al., 2003). Therefore, the inability of patients to carry out their job could be one of the explanations for the continuous high level of burden on the families.

The other explanation could be that treatment noncompliance of patients may have increased the level of family burden as families will be required to monitor prescribed drug treatment regimen. Therapeutic noncompliance may lead to increased burden and decreased cost-effectiveness of interventions compounding the effect of inability of patients to work on their regular job. In some studies more than 60 percent of individuals with schizophrenia fail to take medication as directed (Terkelsen and Menikoff, 1995). Noncompliance and rejection of treatment could increase the burden on families and the health systems.

The high level of burden on the families may further be explained by the fact that about 47 percent of the patients were child (daughter/son) and 40 percent were household heads for the family. As to the level of burden, the findings of the study were consistent with some studies who had reported high levels of family burden in families with schizophrenia patients (Maldonado, 2005; Grover, et al., 2005; Yellowe, 1992; Shibre, et al., 2003). Financial burden was the main problem reported by the studies. In the present study the financial burden as an out-of-pocket payment for medical services was found to be 17 percent of families' annual income. This seems much lower when compared to a study finding from India (Grover, et al., 2005) which had reported financial burden to constitute 48 percent of the family income per month. Besides to methodological differences between the studies, in the present study the reason for low reporting could be the provision of drug treatment free of charge.

On the other hand, with regard to how family burden changes over time, the findings of the study were also consistent with that of an international study which had reported family burden in schizophrenia was stable over a year period (Magliano et al., 2000). Through time, these families may become overburdened as the longitudinal change in family burden score was persistent for most months of the year. With this regard a previous study has reported that patients living with an overburdened caregiver may have increased risk of relapse, therefore, attention should be paid to those schizophrenia patient families (Perlick et al., 1999).

Finally, if we consider the out-of-pocket medical expense made by families at societal level, by taking into consideration one per thousands life time prevalence as a lower margin and the average 4.7 per thousands life time prevalence of different studies done at different times in urban and rural Ethiopia (Kebede et al., 2003; Kebede and Alem, 1999; Awas et al., 1999) as a higher margin; and assuming that each case of schizophrenia cared by all respective families, then the total direct cost to the Ethiopian society was approximately between $687390.69 to $3.23 million. Likewise, the indirect cost of loss of annual cumulative working days due to care giving (by assuming $0.92 as a wage for a day's work) was approximately $1.43 to $6.74 million. Therefore in 2005, the total burden of schizophrenia to families in Ethiopia ranged approximately between $2.12 million to $9.97 million. Compared to other studies in the western world, the total burden of schizophrenia to families of low income developing country like Ethiopia is very huge.

Generally more should be done in the direction of lessening family burden due to schizophrenia. Health policy and priority setting need to be tuned in accordance with the available evidence of burden from schizophrenia and other mental health problems. Families should be supported through a carefully designed intervention strategy to improve level of functioning and treatment adherence of patients. Thus, future studies need to focus more on how to devise feasible intervention strategies to lessen economic and family burden due to schizophrenia. Finally, the study has been undertaken longitudinally; and it is among the first that described family burden of schizophrenia patients in a developing country setup. However, direct comparison of the results of the study with other studies conducted elsewhere was limited due to scarcity of other similar longitudinal studies. Also, the sample may not be adequately representative, so the results of the study should be cautiously interpreted.

Acknowledgements

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Paper IV

Time-series generalized least square analysis of caregiver burden in families of patients with schizophrenia

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Time-series generalized least square analysis of caregiver burden in families of patients with schizophrenia

Ababi, Z. Giref., Atalay, A. Ejigu

Abstract

Background: in low income countries, there are no time series caregiver burden studies in schizophrenia. As a result longitudinal caregiver burden is largely unknown. Therefore, to fill this research gap the study had aimed to make time-series analysis of caregiver burden in schizophrenia.

Methods: using a prospective longitudinal design, burden measurements were made on caregiver characteristics, patient behavior, out-of-pocket medical expenses for health services, time lost due to care giving, and the extent of caregiver burden. There were six waves of data used in the analysis. To explain longitudinal caregiver burden, time series analyses were made using feasible generalized least square regression with panel-specific autocorrelation.

Results: over the year female caregivers, caregivers in farming occupation, whose monthly living expenses were very little, who had paid more out-of-pocket for mental health services, who were angry at the patient, who were worried about the patient, who were over involved in controlling the patient, and who had lost more days of work were found to be more burdened.

Conclusions: existing high level of caregiver burden in context of poverty and scarcity of mental health services in the community calls for the support needs of carers.

Key words: time series, schizophrenia, caregiver burden, generalized least squares

Time-series generalized least square analysis of caregiver burden in families of patients with schizophrenia

Introduction

Schizophrenia is common psychiatric illness characterized by alteration in thinking, judgment, and sensory perception (APA, 1994). It causes high degree of disability on individuals with the illness and long lasting burden (WHO, 2001) which primarily falls on families (WHO, 2003; Brand, 2003; Shibre et al., 2003; Yellowe, 1992; Magliano et al., 2002; Maldonado et al., 2005). The burden is thought to be multidimensional affecting the life of caregivers, the rest of the family and their social network. Some of the dimensions include paying for medical services, supervising treatment adherence, feelings of loss, worrying about the future, disturbance in family functioning, and social stigma (Rössller et al., 2005; Foldemo et al., 2005). On the other hand high expressed emotion, that is, the attitude and behavior of caregivers towards the patient with schizophrenia, especially critical comments, hostility, lack of warmth or emotional over involvement, predicts course (Barbato et al., 2000; Boye et al., 1999) and quality of life in patients (Mubarak and Barber, 2003; Hao et al., 2004).

Cross-sectional studies had revealed different caregiver characteristics and patient conditions as predictors of burden in schizophrenia. A study to assess the relationship between caregiver burden and behavioral disturbances of the affected identified burden in relationship during acute illness as most important predictor (Lauber et al., 2003). Another cross-sectional study on burden of care and general health in families of patients with schizophrenia revealed burden to be high for mothers, carers with less education, carers of younger patients and carers of patients with more hospitalizations (Maldonado et al., 2005). In addition cross sectional studies from Ethiopia (Shibre et al., 2003), Nigeria (Yellowe, 1992) and India (Grover et al., 2005) had reported financial burden in families of patients with schizophrenia.

In longitudinal studies people with schizophrenia and concurrent depressive symptoms were found to have poorer long-term functional outcomes compared to the non-depressed (Robert et al., 2007) and relatives' distress was found related to patient's anxiety-depressive behavior and high expressed emotion (Boye et al., 1999). In other longitudinal studies patient negative symptoms were found to impact caregivers' burden over time (Roick et al., 2006) and burden was described to be stable over time while reduction was found among relatives who adopt less emotion focused coping strategies and received more practical support from their social network (Magliano et al., 2002). However, in low income countries, there are no time series caregiver burden studies in schizophrenia. As a result longitudinal caregiver burden is largely unknown and family intervention strategies are rarely integrated to clinical services compounding the effect of poorly organized mental health systems. Therefore, to fill this research gap the study had aimed to make time-series analysis of caregiver burden in families of patients with schizophrenia.

Methods

Study subjects

The study was done in Meskan and Mareko Wereda, a rural district in southern Ethiopia. In the district a course and outcome study project on schizophrenia is underway since the early 1990s. The project had screened all 83,282 adult population of the district for schizophrenia by house to house survey using the WHO Composite International Diagnostic Interview (CIDI), Version 2.1 (WHO, 1997). Identified possible cases were confirmed by Schedule for Comprehensive Assessment in Neuropsychiatry (SCAN) (Sartorius and Janka, 1996). The present study used a prospective longitudinal design involving all identified families with schizophrenia patients. From each family, family caregivers were selected using the method followed by Perlick et al. caregiver burden study (Perlick et al., 1999). Thus, caregivers were selected based on the following criteria:

a) is a spouse, parent or spouse equivalent to the patient;
b) has most frequent contact with the patient;
c) helps to support the patient financially;
d) has most frequently been a collateral in the patient's treatment; and
e) is contacted by treatment staff in case of emergency. To be included in the sample as a caregiver, the chosen caregiver had to satisfy at least three of the criteria.

Consequently, this study sampled all 249 families of schizophrenia patients who were under follow-up during the survey.

Data collection

The data collection was carried out every two months for one year; started in July 2004 and ended in June 2005. Data collection instruments were developed and pre-tested three times in a nearby community. The purpose of these repeated pre-tests was to increase the reliability and validity of interview instruments. Accordingly, interview instruments with reliability test coefficient less than 0.40 were dropped. In each of the pre-testing sessions, one week of extensive training was provided for data collectors and supervisors. Using the refined final interview instruments, data were collected on caregiver burden. Data quality and consistency cross-checks were made by another group of trained supervisors recruited for the purpose. For data analysis Stata/SE 8.2 for Windows was used.

Burden measurement

Longitudinal burden measurements were made on caregiver characteristics, patient behavior, out-of-pocket medical expenses for health services, time lost due to care giving, and the extent of caregiver burden. Out-of-pocket medical expenses included cost of: travel, medical examination, drugs and injections, laboratory service, food and accommodation; and the time lost due to care giving included time lost in accompanying patient to and from health institute and lost days of work due to care giving at home. There were 15 questionnaire items constituting caregiver burden, with response categories on a five-point scale (see table 1).

Table 1. Questionnaire items constituting family caregiver burden in schizophrenia, Butajira-Ethiopia, 2005

To what extent the:

- a) patients illness causes sleep disturbance,
- b) patient’s illness creates burden on job,
- c) patient’s illness limits social relation movement,
- d) patient’s illness creates burden as to ignore other family members,
- e) patient’s illness creates feeling of unhappiness,
- f) patient’s illness creates worry about the future,

g) to what extent were you ashamed due to the patient’s illness,

h) when you think about the patient, to what extent you feel guilty,

i) how much do you worry by saying that I am unable to cope-up more than this,

j) to what extent patient’s illness create health problem,

k) to what extent your relationship with the patient was in crisis due to the patient’s illness,

l) to what extent the patient causes physical injury on you,

m) to what extent life was problematic and challenging for you due to the patient’s illness,

n) to what extent the patient’s illness creates burden on you as to think of suicide, and

0) to what extent were you happy about patient’s social relationships?

During each interview, family caregivers were asked about the extent of burden that they had experienced in the month prior to interview using the 15 questionnaire items. Thus, caregiver burden score of 1 to 5 was given based on the frequency of occurrence of a ‘burden-causing event’: 1 = did not happen at all in the month; 2 = happened at least once per week in the month; 3 = happened at least twice per week in the month; 4 = happened at least 3 to 6 times per week in the month; and 5 = happened almost every day per week in the month.

Analysis

There were six waves of data used in the analysis. Descriptive analyses were made in terms of out-of–pocket medical expenses for health services, time lost due to care giving, patients' ability to work and compliance to treatment and the extent of caregiver burden. From time one (baseline) through six (end of the study); caregiver burden was computed as the respondent's average responses across the 15 items constituting caregiver burden. To explain longitudinal caregiver burden, time series analyses were made using feasible generalized least square regression with panel-specific autocorrelation. For the purpose of comparison all costs were converted to US$ by using the mean exchange rate for 2005 of Ethiopian currency Birr 8.6810 = 1US$ (National Bank of Ethiopia Annual Report 2005/06). The study was ethically approved by the Faculty of Medicine Addis Ababa University and oral informed consent to participate in the study was obtained from the study subjects.

Results

Out of the 249 eligible families with a member suffering from schizophrenia, 21were unknown of status, nine were unavailable, five refused, four were inaccessible, leaving 210 participating family caregivers. In average there were 5.89 (sd= 2.24) household member per family. In each family there was at least one child (sd= 0.42) less than 15 years of age. The majority of families (n=147, 70%) were living in thatch house, while 30 percent (n=63) were living in a corrugated iron house. The average monthly expense of the families was $6.84 (sd= $5.55), and the average yearly income was $99.90 (sd= $116.22). As family caregivers had assessed their family health status, 34.21 percent (n= 72) had said that their family health status was not good during the year. More than 50 percent (n= 115) had described their family health status was good. The remaining 11 percent (n=23) described their family health status as very good.

Mean age of schizophrenia patients living in the families was 33.13 (sd= 8.48) with 93 percent of the patients between age 15 to 45 years old. Nearly 50 percent (n= 95) of the patients were single, 36.22 percent (n=71) were married, and 15 percent (n= 30) were widowed and separated. On average 32.65 (n= 64) percent of the patients had visited health service prior two months during each interviews, 84.92 percent (n= 166) were not able to work on their regular job, 72.45 percent (n= 142) were not taking medication as prescribed and one month prior to each interview on average each patient had lost 22.94 (sd= 10.97) days of work. With regard to relationship with respective families: 47.18 percent (n= 92) were child (daughter/son); 40 percent (n=78) were household heads, 6.6 percent (n=13) were housewives, 5.65 percent (n=11) were brother/sister and 0.51 (n=1) was a cohabite.

During the year, families had spent $16.52 out-of-pocket due to schizophrenia and on average they had lost 3.12 (sd = 4.54) days of work due to care giving in one month. Additionally, during a health service visit family caregivers on average had lost 1.05 (sd= 0.87) hours traveling to a health institute, 2.04 (sd= 3.80) hours to finish treatment and 4.76 percent (n=10) were accompanied by another family member during the health service visit. In the families the overall mean caregiver burden score over the year was 2.14 (sd= 0.81). In table 2 the participation pattern of caregivers is shown. As shown in the table, caregiver burden standard deviation between subjects was 0.63 (minimum 1.07, maximum 4.2) and the within subject standard deviation was 0.62 (minimum 0.46, maximum 4.01).

Table 2. Participation pattern of caregivers in schizophrenia burden study, Butajira-Ethiopia, 2005.

```
Distribution of T_i:   min      5%     25%      50%      75%     95%     max
                         1       1       1        2        4       5       6
 Frequency         Percent     Cumulative                   Pattern
     67             33.67           33.67          .      .      1      .      .      .
     25             12.56           46.23          .      .      1      1      .      .
     24             12.06           58.29          .      1      1      1      1      .
     13              6.53           64.82          1      1      1      1      1      .
     13              6.53           71.36          1      .      1      .      .      .
     10              5.03           76.38          1      .      1      1      .      .
     47             23.62          100.00          (other patterns)
    199            100.00                       X      X      X      X      X      X
```

Summary mean and standard deviations of caregiver burden

```
Variable                    Mean      Std. Dev.     Min     Max  |   Observations
Caregiver burden   overall   2.14          0.81         1      4.2  |    N =     477
                   between                 0.63      1.07      4.2  |    n =     199
                   within                  0.62      0.46     4.01  |  T-bar = 2.40
```

In generalized least square regression analysis time was found statistically significant (z= -13.23, P>|z|= 0.001) determinant factor of schizophrenia caregiver burden (see table 3). Time had increased caregiver burden by a unit of 0.47. However, the p value of its quadratic term Time2 suggests that its relationship with schizophrenia caregiver burden is not linear, which may mean after some time burden may rest at a certain constant level. In the same analysis it was found that care giving was more burdensome to female caregivers than males (z= -2.43, P>|z| 0.015). In addition, caregivers in farming occupation were more burdened than caregivers in other occupations (z= -2.49, P>|z|= 0.03) and caregivers whose average family living expense per month was less than or equal to $23.04 were more burdened (z= -3.26, P>|z| 0.001) than caregivers with living expense of greater than $23.04.

Table 3. Time series generalized least square analysis of caregiver sociodemographic characteristics vs. burden in schizophrenia, Butajira-Ethiopia, 2005

Cross-sectional time-series FGLS regression
Coefficients: generalized least squares
Panels: homoskedastic
Correlation: panel-specific AR(1)

Estimated covariances	= 1	Number of obs	= 397
Estimated autocorrelations	= 122	Number of groups	= 122
Estimated coefficients	= 13	Obs per group: min	= 2
		avg	= 3.25
		max	= 6
		Wald chi2(12)	= 9506.41
Log likelihood	= -21.20594	Prob > chi2	= 0.0000

Caregiver burden	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Time	-.473	.035	-13.23	0.000	-.543	-.403
Time2	-.012	.005	-2.37	0.018	-.022	-.002
Interaction	.249	.003	67.40	0.000	.242	.257
Sex (female= 1, male= 0)	-.054	.022	-2.43	0.015	-.096	-.010
Age (15-44= 1, 45+= 0)	-.000	.000	-0.14	0.887	-.001	.001
Marital status (married= 1, other= 0)	-.006	.009	-0.66	0.511	-.024	.012
Education (iliterate= 1, other= 0)	-.002	.007	-0.26	0.791	-.017	.013
Occupation (farmer= 1, other= 0)	-.026	.010	-2.49	0.013	-.046	-.005
Family size (n≥ 5= 1, n ≤5= 0)	-.000	.006	-0.07	0.942	-.012	.011
Family relation (mother = 1, other = 0)	-.010	.012	-0.83	0.406	-.034	.013
Living expense (≤$23.04= 1, >$23.04= 0)	-.001	.000	-3.26	0.001	-.001	-.000
Annual income (≤$345.58=1, >$345.58= 0)	.000	.000	1.47	0.141	-.000	.000
Constant	2.337	.092	25.23	0.000	2.155	2.518

The time series analysis of burden with respect to caregiver characteristics and patient behavior, revealed angry caregivers at the patient (because of inability of the patient to carryout activity that was thought to be good for the patient) were more burdened than those caregivers who were not angry at the patient (z= -3.73, P>|z|= 0.001) (see table 4). Similarly caregivers who were worried about the patient and over involved in controlling the patient were more burdened than those caregivers who were not worried (z= -3.6, P>|z|= 0.001) or over-involved (z= -2.12, P>|z|= 0.034). At this point, time was again found important determinant of burden, however, unlike the previous result, the p value of its quadratic term Time2 suggests that its relationship with schizophrenia caregiver burden was linear, which may suggest linear relationship of burden with patients' behavior.

Table 4. Time series generalized least square analysis of caregiver characteristics, patient behavior and burden in schizophrenia, Butajira-Ethiopia, 2005.

Cross-sectional time-series FGLS regression
Coefficients: generalized least squares
Panels: homoskedastic
Correlation: panel-specific AR(1)
Estimated covariances = 1
Estimated autocorrelations = 123
Estimated coefficients = 10
Log likelihood = 1.294663

Number of obs = 401
Number of groups = 123
Obs per group: min = 2
Avg = 3.26
max = 6
Wald chi2(9) = 6998.49
Prob > chi2 = 0.0000

Caregiver burden	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Time	-.455	.039	-11.39	0.000	-.533	-.376
Time2	-.009	.005	-1.68	0.093	-.019	.001
Interaction	.229	.004	51.24	0.000	.220	.237
Was angry at the patient (Ref: No)	-.099	.026	-3.73	0.000	-.151	-.046
Worried about patient (Ref: No)	-.113	.030	-3.67	0.000	-.174	-.052
Patient was self caring (Ref: Yes)	.114	.023	4.89	0.000	.068	.160
Over-control the patient (Ref: No)	-.060	.028	-2.12	0.034	-.116	-.004
Was aggressive toward patient (Ref: No)	.008	.025	0.33	0.742	-.042	.059
Patient was compliant of treatment (Ref: Yes)	.076	.019	3.89	0.000	.038	.115
Constant	2.271	.090	25.01	0.000	2.093	2.449

On the other hand, caregivers who were caring for unable patients to carry out self care without being told what to do and who were also caring for non-treatment compliant patients were more burdened than caregivers who were not caring for such patients. Further analysis of caregiver burden in relation to average lost days of work due to care giving and out-of-pocket medical expense made for the patients' mental health services have found caregivers who had lost more than 10 days of work over the year to be more burdened than those who had lost less than 10 days of work. This result was statistically significant (z= 7.14, P>|z|= 0.001). Additionally, there was statistically significant difference (z= -2.07, P>|z|= 0.038) between caregivers who had on average paid more than $5.76 out-of-pocket than caregivers who had paid less. In all the analyses the interaction between time and caregiver burden was statistically significant. This emphasizes that caregivers were constantly burdened over the year. In general, over the year female caregivers, caregivers in farming occupation, caregivers whose monthly living expenses were very little (which implies impoverishment), who had paid more out-of-pocket for mental health services, who were angry at the patient, who were worried about the patient, who were over involved in controlling the patient, and who had lost more days of work were found to be burdened.

Discussion

This cross-sectional time series study is the first of its kind to describe caregiver burden of schizophrenia in rural setup where delivery of mental health services are poorly organized, inadequate and short of resources. In the study caregiver burden was described in terms of carers' characteristics and patient conditions; and over the year female caregivers, caregivers in the farming occupation, whose monthly family living expenses were very little (poor families), who had paid more out-of-pocket for mental health services, and who had lost more days of work were found to be more burdened. In addition, caregivers who were angry at the patient, worried about the patient, over involved in controlling the patient, caring for unable patient to carry out self care and who were caring for non-treatment compliant patients were found to experience more burden. However, burden was not explained in terms of caregiver's age, marital status, educational level, family size, family relationship and annual family income.

The present finding of female caregivers to be more burdened than males, which is consistent with a cross-sectional study in the same area (Shibre et al., 2003) may show the burdensome effect of schizophrenia care giving on females. In traditional societies like Ethiopia, females have many household responsibilities. Thus, in the study area, it can be imagined how females were burdened due to their schizophrenia relatives. Overall caregiver burden in this rural community was severe. Furthermore, the present findings of caregivers who were angry at the patient, worried about the patient, over involved in controlling the patient, caring for unable patients to carry out self care and who were caring for non-treatment compliant patients to experience more burden signifies the importance of improving coping strategies of caregivers and patients' level of functioning and treatment compliance, because, caregivers who can cope better with the patient's behavior have fewer burdens (Roick et al., 2006; Magliano et al., 2000).

Improving treatment noncompliance will have important positive consequences for clinical outcome as well as for health care costs. But, some patients were reported fail to take medication as directed increasing the chance of relapse of the patient's illness. Noncompliant patients had been found to be burdensome for the caregivers. Such patient behavior on the other hand leads to relapse. Relapse is known to be closely linked to noncompliance (Weiden and Olfson, 1995). In such situations family interventions and compliance therapy may help (Knapp, 1997; 2000; Healey et al., 1998). Therefore, the finding of burden in this study due to noncompliance needs to be well addressed and tackled in order to reduce the burden of caregivers and improve course and outcome.

In conclusion, caregivers are immediate managers of the course and outcome environment where the illness is lived, therefore the existing high level of caregiver burden in context of poverty and scarcity of mental health services in this rural community calls for the support needs of carers through holistic schizophrenia clinical management approach. Finally, the study has strong side by addressing schizophrenia caregiver burden longitudinally. However, due to methodological differences it has limitations of comparability with other studies. Future studies may address caregiver burden in schizophrenia using standardized psychiatric assessment tools.

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