

# Studies on psychotic disorders in rural Ethiopia

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*To Teferra Abebe, my beloved father*



## TABLE OF CONTENTS

<b>Table of contents</b>	i
<b>Abstract</b>	iii
<b>List of publications</b>	vi
<b>Tables</b>	vii
<b>Figures</b>	vii
<b>Abbreviations</b>	viii
<b>1 Preface</b>	1
<b>2 General introduction</b>	3
2.1 Ethiopia: brief country profile	5
2.1.1 Historical background	5
2.1.2 Geography and demographics	6
2.1.3 Culture and religion: Christianity, Islam, Animism	7
2.1.4 Politics and economy	8
2.1.5 Health service in Ethiopia with emphasis on mental health	8
2.2 Why does Ethiopia need mental health research?	9
2.3 The need to study psychotic disorders in Ethiopia	10
2.4 Psychosis in traditional societies	11
2.4.1 Problems of measurement of mental disorders in traditional societies	11
2.4.2 The Composite International Diagnostic Interview (CIDI) and psychosis	12
2.5 The epidemiology of schizophrenia in the world: emerging evidence	14
2.6 Khat	15
2.6.1 History of khat	15
2.6.2 Botany of khat	15
2.6.3 Chemistry of khat	16
2.6.4 Varieties of khat	16
2.6.5 Khat chewing: social aspects and effect on individuals	17
2.6.6 Khat and health	18
2.6.7 Legal status of khat	19
<b>3 Aims of the research</b>	20
3.1 General aim	20
3.2 Specific aims of the different papers	20

<b>4</b>	<b>Settings and methods</b>	21
4.1	Butajira	21
4.2	Borana area	22
4.3	Study design	23
4.4	Case identification and establishment of the cohort in Butajira	23
4.5	Statistical methods	25
4.6	The Borana semi-nomadic population study	25
4.7	Qualitative study on khat in Butajira	27
<b>5</b>	<b>Ethical considerations</b>	29
<b>6</b>	<b>Summary of results and discussion</b>	30
<b>7</b>	<b>Strengths and limitations</b>	35
<b>8</b>	<b>Conclusions and recommendations</b>	37
<b>9</b>	<b>Acknowledgements</b>	38
<b>10</b>	<b>References</b>	40

## ABSTRACT

### Background

Studies on course and outcome of schizophrenia coming from low income countries are increasingly becoming important to challenge the existing dogma claiming good outcome in these countries. Besides clinical course and outcome, mortality is considered a very important outcome measure for schizophrenia. Culture and tradition play a significant role in the manifestations of severe mental illnesses (SMI). Khat is a culturally accepted plant endemic to Eastern Africa, which is chewed by people for its stimulating effect. It is believed that Khat influences the course and outcome of schizophrenia although systematic studies are scarce. Patients with SMI continue to chew khat despite advice from their doctors to desist. Reasons for this behavior were not fully investigated before.

### Objectives

- To describe the 5-year clinical course and outcome and mortality of schizophrenia in Butajira.
- To explore traditional views on psychosis in the semi-nomadic Borana population.
- To describe the perceived causes and preferred treatment for SMI in the semi-nomadic Borana population
- To explore reasons for khat chewing behavior in people with SMI in Butajira.

### Methods

The studies were done in two sites: Butajira and Borana. The Butajira study involved screening, using CIDI and Key Informants (KIs), of more than 68,000 adults aged 15-49. Of these, 321 people were diagnosed with schizophrenia and were followed-up for five years to look into their clinical course and outcome, including mortality. A qualitative study involving 37 men with SMI and 30 female caregivers was conducted in Butajira to study reasons why patients continue to chew khat despite their physicians' advice against it. The Borana study of a remote semi-nomadic population in southern Ethiopia, used qualitative methods involving 56 KIs to identify descriptions of psychosis, perceived causes and preferred treatment in the community. Cases identified by the KIs also underwent SCAN interview for confirmatory diagnosis.

## Results

The five year follow-up of schizophrenia patients showed that 45% of participants were continuously symptomatic with 30.3% having had continuous psychotic episode. About 20% had experienced continuous remission. Being single (OR = 3.41, 95% CI = 1.08-10.82, P = 0.037), on antipsychotic treatment for at least 50% of follow up time (OR = 2.28, 95% CI = 1.12-4.62, P = 0.023), and having a diagnosis of paranoid subtype of schizophrenia (OR = 3.68, 95% CI = 1.30-10.44, P = 0.014) were associated with longer period of remission.

A total of 38 (12.4%) patients, thirty four men (11.1%) and four women (1.3%) died during the 5-year follow-up period. The mean age (SD) of the deceased for both sexes was 35 (7.35): 35.3 (7.4) for men and 32.3 (6.8) for women. The most common cause of death was infection, 18/38 (47.4%) followed by severe malnutrition, 5/38 (13.2%) and suicide 4/38 (10.5%). The overall SMR was 5.98 (95% CI = 4.09 to 7.87): 6.27 (95% CI = 4.16 to 8.38) for men and 4.30 (95% CI = 1.02 to 8.52) for women. Patients residing in rural areas had lower mortality with adjusted HR of 0.30 (95% CI = 0.12-0.69) but those with insidious onset had higher mortality with adjusted HR 2.37 (95% CI = 1.04-5.41). Treatment with antipsychotics for less than 50% of the follow-up time was also associated with higher mortality, adjusted HR 2.66 (1.054-6.72).

In the Borana study, the incongruity between local and psychiatric concepts in the CIDI lay mainly in the fact that KIs described characteristics of *marata* (madness) in terms of overt behavioral symptoms instead of thought disturbances. Following the focus group discussions, participants identified 8 individuals with schizophrenia and 13 with a psychotic mood disorder, confirmed by SCAN interview.

Supernatural causes such as possession by evil spirits, curse, bewitchment, 'exposure to wind' and subsequent attack by evil spirits in postnatal women; bio-psycho-social causes such as infections (malaria), loss, 'thinking too much', and alcohol and khat abuse were mentioned as causes of SMI. The preferred treatments for severe mental illness included mainly traditional approaches, such as consulting Borana wise men or traditional healers, prayer, holy water treatment and, finally, seeking modern health care.

Regarding khat and SMI in Butajira, reasons given by patients as well as caregivers were more or less congruent: social pressure, a means for survival by improving function, combating medication side effects, to experience pleasure and curbing appetite.

**Conclusion**

Schizophrenia runs a chronic and non-remitting course and was associated with very high premature mortality in Butajira. Continued treatment with antipsychotics has been a consistent predictor of favorable outcome and reduced mortality.

Case identification in studies of psychotic disorders in traditional communities are likely to benefit from combining structured interviews with the key informant method. Planning mental health care in traditional communities needs to involve influential people and traditional healers to increase acceptability of modern mental health care. Patients with SMI chewed khat for some important reasons that clinicians need to consider in their management.

**Key words**

Attribution, caregivers, course and outcome, key informant method, khat, longitudinal study, mortality, psychotic disorders, qualitative methods, schizophrenia, semi-nomadic, severe mental illness, treatment, Ethiopia, sub-Saharan Africa

## LIST OF PUBLICATIONS

The following original papers form the basis for the thesis. They will be cited in the text with the Roman numerals corresponding to each paper.

- I. Teferra S, Shibre T, Fekadu A, Medihn G, Wakwoya A, Alem A, Jacobsson L. Five-year clinical course and outcome of schizophrenia in rural Ethiopia. (Revised manuscript 'under review' in the journal *Schizophrenia Research*)
- II. Teferra S, Shibre T, Fekadu A, Medihn G, Wakwoya A, Alem A, Kullgren G, Jacobsson L. Five-year mortality in a cohort of people with schizophrenia in rural Ethiopia. (manuscript)
- III. Shibre T, Teferra S, Morgan C, Alem A. Exploring the apparent absence of psychosis amongst the Borana pastoralist community of Southern Ethiopia. A mixed method follow-up study. *World Psychiatry* 2010;9(2):98-102.
- IV. Teferra S, Shibre T, Jacobsson L. Perceived Causes of Severe Mental Illnesses and Preferred Treatment for the Mentally Ill among the Borana Semi-Nomadic Community, Southern Ethiopia. (manuscript)
- V. Teferra S, Hanlon C, Alem A, Jacobsson L, Shibre T. Khat-Chewing in Persons with Severe Mental Illness in Ethiopia: A Qualitative Study Exploring Perspectives of Patients and Caregivers. *Transcultural Psychiatry* 2011. (in press)

## TABLES

Table 1	Religion in Ethiopia.
Table 2	List of topic guides used in the qualitative study in Borana semi-nomadic population.
Table 3	List of topic guides used in the qualitative study of khat in Butajira.
Table 4	Symptoms of severe mental illnesses described by the key informants and psychotic symptoms in CIDI among the Borana semi-nomadic population, Southern Ethiopia.
Table 5	Brief characteristics of SCAN interviewed individuals and DSM-IV diagnosis suggested by key informants in Borana, Southern Ethiopia.

## FIGURES

Figure 1	Map of Africa. Shaded area shows Ethiopia and its neighbours in the horn of Africa.
Figure 2	<i>Coffea arabica</i> and <i>Catha edulis</i> Forsk.
Figure 3	The chemical structures of khat alkaloids in comparison with amphetamine.
Figure 4	Khat is wrapped in false banana leaves to maintain its freshness; the different brands are advertised.
Figure 5	Khat bolus in the mouth of a chewer.
Figure 6	One of the three khat memorial stamps launched by the Ethiopian Postal Service in 2008.
Figure 7	The Butajira study site.
Figure 8	The Borana study site.
Figure 9	The couple seen in this picture lives in Didi Hara, one of the study sites in Borana and cattle is their source of livelihood.
Figure 10	Flow chart summarizing the cohort identification and 5 year follow-up status of patients with schizophrenia in Butajira, Ethiopia.

**ABBREVIATIONS**

AAU	Addis Ababa University
APA	American Psychiatric Association
ART	Antiretroviral Treatment
CIDI	Composite International Diagnostic Interview
CSA	Central Statistics Agency
DIS	Diagnostic Interview Schedule
DOSMeD	Determinants of Outcome in Schizophrenia
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4 <sup>th</sup> Edition
DSS	Demographic and Surveillance System
FDRE	Federal Democratic Republic of Ethiopia
FGD	Focus Group Discussions
HDI	Human Development Index
HIV/AIDS	Human Immuno Deficiency Virus/ Acquired Immuno Deficiency Virus
IPSS	International Pilot Study on Schizophrenia
KI	Key Informants
LAMIC	Low and Middle Income Countries
mhGAP	Mental Health Gap Action Program
RCT	Randomized Controlled Trials
SCAN	Schedule for Clinical Assessment in Neuropsychiatry
SMR:	Standardized Mortality Ratio
SNNPRS:	Southern Nations Nationalities and People's Regional State
SRQ	Self Reporting Questionnaire
WHO	World Health Organization

## 1 PREFACE

### **Choosing Psychiatry as a career: personal reflections**

*"Canst thou not minister to a mind diseased, pluck from the memory a rooted sorrow, raze out the written troubles of the brain, and with some sweet oblivious antidote cleanse the fraught bosom of that perilous stuff which weighs upon the heart?"* Source: 'Macbeth' by William Shakespeare

One of my fascinations in science has been the human brain and how it works. Early in medical school, I remember spending more time studying the embryology, anatomy, and histology of the brain. In human physiology, the CNS was my favorite subject. Concepts such as thinking and memory were very interesting to me. 'Which part of the brain is responsible for thinking?' was my question. I was frustrated to learn that there was no specific answer this question. When I started doing clinical rotation, I found psychiatry of utmost interest to me. It proved to be the subject very close to my heart. It was then that I decided to specialize in psychiatry, though there was no such a program at that time in the country. By chance, I was assigned to work as a General Practitioner (GP) in Butajira where I had met the field researchers in the Butajira study of Course and Outcome of Schizophrenia and Bipolar Disorders Dr. Alemayehu Negash, Dr. Teshome Shibre and Dr. Teferra Beyero. They became my friends and I had a chance to have a closer look at the mental health research process. After four years of work as a GP, I was given the chance to pursue specialty training. Then, I applied to join the postgraduate program at the Department of Psychiatry-a joint program run by the department and University of Toronto known by the name Toronto Addis Ababa Psychiatry Project (TAAPP).

It is no big surprise if I say Psychiatry is not regarded as the most lucrative specialty in medicine. It is a specialty which attracts the least number of applicants even in high income countries such as the UK (Fazel & Ebmeier, 2009). In fact, it is a specialty that is feared and at best avoided by many junior physicians who want to pursue a clinical specialty. Not only patients with severe mental illness and their families but also the field of psychiatry and the mental health professionals are highly stigmatized (Shibre et al., 2003; Schulze, 2007; Sartorius et al., 2010). I learnt this grim reality when I started seriously considering a career in psychiatry. I always remember the reaction people had when I disclosed my intention to join the postgraduate program in psychiatry. 'Why are you interested in Psychiatry?' was the most frequent question that I received both from physicians and lay friends and families. This is also the most important question applicants are asked when they undergo interview for admission into the program. I remember being asked the question 'Why are you interested in psychiatry?' and to the surprise of my interviewers I replied 'Partly it is my fascination with human behavior, and partly I don't know.' That was what I felt when I was asked that question. Later on I learnt that some of them even doubted my sanity because, I suspect, they had never heard such response from their earlier interviewees. I still feel the same. I knew that I

wouldn't be making money or get prestige from joining the field. So, what was my motive? It was a passion. It was like falling in love. One wouldn't answer with certainty if asked why he loved a particular girl. He would simply say I loved her. I suspect a very powerful unconscious process plays a role in most decisions we make! But after I started practicing psychiatry, I started to appreciate the difference I could make in people's lives. Beyond the infatuations I had, I found practice of psychiatry to be both challenging and rewarding. It is emotionally challenging to see a young man's dreams crumble by schizophrenia. And yet it is very rewarding to see the disturbing abnormal experiences a patient has disappear with treatment!

My interest in research is not as difficult to answer as my decision to join psychiatry. It stems from the three vulnerabilities: my inclination to literature which helped me read on diverse issues and write, my inherent quest for information which made acquisition of new knowledge a passion, and my interest in pursuing an academic career. So, it was so natural for me to engage in research activities. I know it is so daring of me to claim the status of a researcher. But, the decision to register for a PhD while I was still a resident tells the story. I am not saying doing research is an easy task. It could be fun but one has to survive to be able to do research. It needs a lot of investment in terms of time and energy which could be considered a luxury for most practitioners in Ethiopia. Numerous challenges ranging from individual to systemic factors exist. These challenges are common to most low income countries. Among the challenges are factors such as environmental, socio-political, economic, and lack of research infrastructure including trained personnel and standardized instruments (Alem & Kebede, 2003). In these countries mental health often gets the least attention because of other competing priorities. Decisions often are not based on evidence. The little research output that exists warms the shelves. Another source of dismay in the research community who live in low income countries is the fact that many reputable journals are reluctant to accept papers that come from these countries (Patel & Sumathipala, 2001). Against all odds, Ethiopian mental health research is a very thriving one and probably an example to other resource limited countries. I feel very privileged to be part of this vibrant research community!

## 2 GENERAL INTRODUCTION

Mental health research has tremendously contributed to the development of mental health service in Ethiopia. When a handful of pioneers started doing research in this country, they had the vision of generating important knowledge that would help improve the lives of many Ethiopians. Among these early studies, the 18% psychiatric morbidity reported in a general medical outpatient setting (Giel & van Luijk, 1968), and a similar proportion (18%) reported from outpatient attendants in Nekemte hospital (Jacobsson, 1985) showed how important psychiatric symptoms are in the general medical setting and the need to integrate mental health care in the general health care system. Subsequent studies mainly focused on describing the epidemiology of severe mental disorders such as the prevalence and course and outcome of severe mental disorders in adults and children, laying the foundation for further studies on a wide range of issues including more sophisticated studies such as RCTs and genetic studies. Though there were several studies of such kind, the 'Butajira study on course and outcome of schizophrenia and bipolar disorders' is probably the most outstanding one. It is actually the largest community based mental health research in Africa. This project was initiated in 1998 as a collaborative undertaking between Departments of Community Health and Psychiatry in Addis Ababa University and Division of Psychiatry in Umeå University Sweden, with a financial support from the Stanley Medical Research Institute to establish a rural community based mental health research focusing on severe mental disorders. After appropriate training and preparation, data collection was embarked. More than 68,000 adults aged 15-49 (82% of the total population) were interviewed in a period of 3 years to identify cases with psychotic and affective disorders using the Composite International Diagnostic Interview (CIDI) version 2.1 (WHO 1997) which identified 2159 suspected cases. Supplementary data was also obtained from Key Informants in the area who identified 719 cases. Suspected cases (2,285) underwent SCAN interview. A total of 860 cases of schizophrenia, bipolar disorder and major depressive disorder were identified.

The cohort of patients with these disorders has been on active follow up for the past decade. Patients get their monthly clinical and treatment status recorded. They also undergo comprehensive evaluation annually. The majority had no access to modern mental health care before the commencement of the project. Now, they all get free psychiatric care, supported by the project, close to their home. Several reports on schizophrenia, bipolar disorder and major depressive disorder have been published in many reputable journals. Earlier reports focused on methodological issues and describing sociodemographic correlates of severe mental disorders and impact of illness on family members (Shibre et al., 2002; Shibre et al., 2003; Kebede et al., 2003; Alem et al., 2004). The findings reported added to the existing knowledge base on these important disorders which affect millions of people across the world. Moreover, it was instrumental in showing to the outside world some of the peculiarities in this low income setting such as schizophrenia having a high male to female ratio (5:1) and an earlier age of onset in females (Kebede et al., 2003). *The*

*emphasis in this thesis is the intermediate (i.e. 5-year follow up) clinical course and outcome of schizophrenia and mortality. Additional issues that have been investigated are khat and severe mental illness and perceived causes of severe mental illness and preferred treatments of the mentally ill.*

Khat is an amphetamine-like mild stimulant which is widely chewed by patients and other people in Ethiopia for its stimulant effect. A large population survey of 10,468 adults from Butajira showed that 55.7% of the sample had used khat at sometime in their lives, 50% were current users and 17.4% reported using on a daily basis. Khat use was associated with being male, being Muslim (80% of current chewers used khat to gain concentration for prayer), higher educational achievement and tobacco-smoking. An interesting finding in this study was the lack of association of khat with mental distress (Alem, Kebede & Kullgren, 1999). It is not surprising, given the high prevalence of khat chewing in the community, to see most of our patients in the cohort chew khat. We did a qualitative study to explore the perspectives of patients and their families on khat. The findings from this study are included in this thesis.

Another project, which makes the basis for some of the papers in this thesis, is the Borana mental health research project. Borana is located in Oromia region, southern Ethiopia, 600 km from the capital, close to the Kenyan border. The study was initiated in 2000, again with the financial support from the Stanly Medical Research Institute, to study the lifetime prevalence and sociodemographic correlates of psychiatric disorders and substance abuse in three districts in this semi-nomadic population. Using the Oromiffa version of CIDI, more than 1,800 adults aged 15 and above were interviewed. The lifetime prevalence of ICD-10 mental disorders was 21.6% out of which 10.1% had substance abuse. No cases of schizophrenia were detected (Beyero et al., 2004). The absence of schizophrenia in this population was a unique finding which led us to question the validity of the methods employed. So, we embarked on doing a mixed method (both qualitative and quantitative) study to explore how psychosis manifests in this traditional community, their perceptions of causes and preferred treatment. The findings will be reported in this thesis. Similar to Butajira, the Borana had no access to mental health care. The commencement of the research project in the area brought free mental health care to the patients living in the area as well.

Besides local benefit of access to mental health care for patients in the study sites, the knowledge generated from these studies has also contributed nationally to raise awareness about mental health problems in the country and influenced policy makers to pay better attention to mental health issues. Positive developments seen in the country in the past few years in the mental health arena include strengthening of the process of integration of mental health care into the general health care system, the development of a 'National Mental Health Strategy', and accelerated training of lower to higher level mental health workers. The research projects have also contributed tremendously in the area of mental health research capacity building which the nation will harness in the years to come.

The thesis is based on three papers from the Butajira schizophrenia cohort and two papers from the Borana mental health research focusing on psychosis. From the Butajira schizophrenia cohort there are two papers on intermediate course and outcome of schizophrenia (one on five-year clinical course and outcome and the other on five-year mortality) and a qualitative study exploring the use of khat. Two papers from the Borana mental health research project (one methodological paper and another paper exploring perception and treatment of severe mental disorders in the traditional Borana community) are presented.

To help the reader understand the context in which the research is done, a brief introduction to the country is presented, followed by some controversial issues regarding the epidemiology of psychosis with emphasis on the prototype psychotic disorder: schizophrenia. The impact of cultural factors on manifestations of schizophrenia is also presented. Methodological problems encountered in studying psychosis in traditional societies are also presented. Details of the settings and the methods of the researches are presented. Results are summarized followed by brief discussions.

## 2.1 Ethiopia: brief country profile<sup>1</sup>

### 2.1.1 Historical background

Ethiopia, or Abyssinia, as it has sometimes been known, is one of the three or four most ancient states of the world. It belongs to ancient civilizations such as China, Greece, Iran and Egypt. The name Ethiopia comes from the Greek word *Aithiops*, meaning a country of people of 'sun-burnt face'. The term Abyssinia, or *Habesh*, means people of 'mixed race' and probably originated in the Middle East. The name Ethiopia refers more to the country where as the people are informally called Habesha. The official contemporary name of the country is Federal Democratic Republic of Ethiopia (FDRE).

Ethiopia is known to the rest of the world by good or bad things. The good things that characterize the country include Lucy, the first *homo erectus*, Coffee (being the origin and home to the best coffee in the world - *Coffea Arabica*), great long distance runners (for instances Abebe Bikila and Haile Gebresilassie) and the history of independence (being the only black country that was never colonized). But the terrible drought and famine, such as the one that happened in 1984 and the bloody protracted civil war gave the country a bad image to the outside world.

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<sup>1</sup> <http://en.wikipedia.org/wiki/Ethiopia>

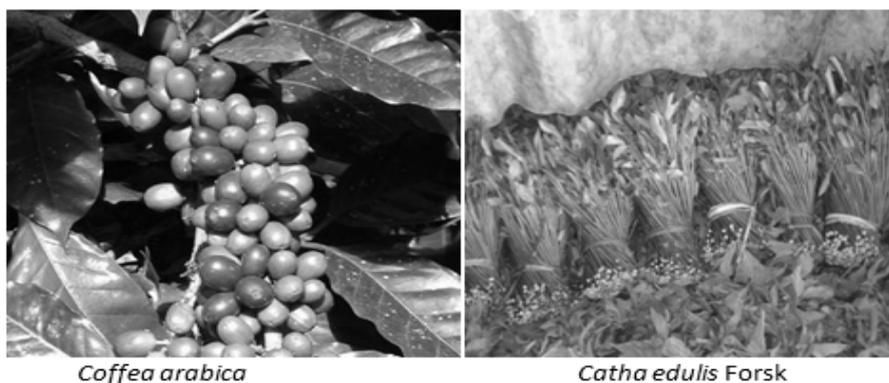
### 2.1.2 Geography and demographics

Ethiopia is a big country with an area of more than 1 million square kilometers located in the horn of Africa. It is located in one of the hot spots in the world surrounded by the stateless Somalia and the war torn Sudan. It shares more than a thousand kilometers of border with these two trouble stricken countries. It also shares borders with two new nations: Eritrea and South Sudan. Another small country, Djibouti in the East and Kenya in the south share borders with Ethiopia. The country is organized in an ethnic based federal system which has 9 regional states and two city administrations which have relative independence in managing their day to day affair.



Figure 1. Map of Africa. Shaded area shows Ethiopia and its neighbours in the horn of Africa<sup>2</sup>.

<sup>2</sup> <http://www.mapsofworld.com/africa-country-groupings/horn-of-africa-political-map.html>



**Figure 2.** Ethiopia is the origin of Coffee and khat: two stimulants!

Despite its proximity to the equator, it has a pleasant weather because of its high altitude. The country has diverse topographical features from the *Dalol* depression found in Eastern part of the country, 120 meters below sea level to the *Ras Dashen* Mountain in the northern part of the country, 4,620 m above sea level.

Most people live in the highlands and the vast lowland is sparsely populated with cattle herding people. There are two seasons: the long dry season and the rainy season. The rainy season has two parts the long one covers mid-June to mid-September where as the small rainy season covers February to March.

Ethiopia has an amazing diversity of cultures, people, language, religious beliefs. The country has more than 80 ethnic groups. Some think that this diversity is vulnerable for the nation while others think it as a source of strength as evidenced by the unified action of every citizen against the European colonizers.

### **2.1.3 Culture and religion: Christianity, Islam, Animism**

Ethiopia is a multicultural and multireligious country. It is one of the first Christian countries in the world. It accepted Christianity as a state religion in the 4<sup>th</sup> AD. But, it is also a country where other religions are widely practiced. Ethiopia is also a country which accepted and gave shelter to the earliest Muslims when they were persecuted in their country. Traditional beliefs, commonly known as Animism is also practiced by a minority of the population. The following table shows the different types of religions practiced in Ethiopia. It compares the two recent censuses done in the country with respect to number and growth of religion.

**Table 1.** Religion in Ethiopia.

Year	Christian	Ethiopian Orthodox	Protestants	Catholics	Muslims	Animists	Other
1994	32,689,482 (61.6%)	26,844,932 (50.6%)	5,366,360 (10.1%)	478,190 (0.9%)	17,427,387 (32.8%)	2,444,085 (4.6%)	531,323 (1.0%)
2007	46,420,822 (62.8%)	32,154,550 (43.5%)	13,748,842 (18.6%)	517,430 (0.7%)	25,058,373 (33.9%)	1,921,881 (2.6%)	517,430 (0.7%)
Growth	13,731,340 (1.2%)	5,309,618 (-7.1%)	8,382,482 (8.5%)	39,240 (-0.2%)	7,630,986 (1.1%)	-522,204 (-1.2%)	-13,893 (-0.3%)

Source: Central Statistics Agency- the 1994 and 2007 censuses conducted in the country.

#### 2.1.4 *Politics and economy*

Throughout most of its three millennia of history, the country has been ruled by kings and emperors who served both as heads of state and Ethiopian Orthodox Church. The last Ethiopian King was Hialesellasié who ruled the country for nearly 50 years. He was removed from power by a popular revolution which was hijacked by the military. The feudal system was abolished and a socialist system was introduced in its place. It was in similar time that a group of students went to the bush to fight the military dictatorship which was eventually defeated after a 17 year bloody civil war which seriously retarded the country's progress. After defeating the Dergue, The Ethiopian People's Revolutionary Front (EPRDF) has been ruling the country since 1991. Another group fighting for Eritrean independence, Eritrean People Liberation Front (EPLF), also claimed victory and the country was officially split into two and lost its long access to the sea and joined the group of landlocked countries.

The country has been relatively free from civil war in the past two decades which resulted in significant improvement in the economy and other related activities. It is one of the largest recipients of aid money in the world. In recent years, it has been praised for improving the lives of its citizens, improving health and sanitation, increasing education and decreasing poverty. Despite these encouraging results, the country still remains one of the poorest countries in the world standing at 157<sup>th</sup> out of 169 countries in the UNDP country report of Human Development Index in 2010<sup>3</sup>.

#### 2.1.5 *Health service in Ethiopia with emphasis on mental health*

Ethiopia has a poor health status even by sub-Saharan African standard. Up to 80 percent of the country's health problems originate from infectious diseases. Health problems related with poverty still predominate. But reports coming in recent years from the health sector in Ethiopia are very encouraging. There has been a huge expansion of health service even in remote parts of the country with deployment of

<sup>3</sup> <http://hdr.undp.org/en/statistics/>

primary health care workers. More than 30 thousand female health extension workers have been deployed so far. Despite these developments, the health indicators published in the year 2006/07, showed that 77/1000 infants and 123/1000 under five children die. More than 600/100,000 mothers die. The life expectancy of the population was shown to be 53.4 years for males and 55.4 years for females.

Historically, modern mental health care in Ethiopia is linked with the Fascist Italian invasion of the country in 1932. Prior to that, traditional and religious treatment modalities were practiced like in any other traditional society. The only specialized mental hospital, known currently by the name Amanuel Specialized Mental Hospital was established in 1948. This hospital soon became a subject of huge stigma because of the abominable conditions patients were kept. The hospital was run by few staff, and there were more patients than the beds. The officials running the Ministry of Health of Ethiopia at that time were reluctant to even mention its existence (Giel, 1999). In the past 30 years the hospital has undergone a transformation from an asylum into an acute care mental hospital where patients are treated for a specified length of time and discharged into the community. With the start of a psychiatric nursing training program in the 80s by the support of the WHO, the concept of primary mental health care was introduced which continued to the present with more than 40 psychiatric units in general health care setting throughout the country, staffed by one or two psychiatric nurses. The latest report by the MOH, Ethiopia, showed that there were 461 psychiatric nurses working in the psychiatric units distributed throughout the country. In the past decade the number of psychiatrists has shown a dramatic increase following the start of a residency program by the department of psychiatry at Addis Ababa University in collaboration with department of psychiatry at University of Toronto, a program known by the acronym TAAPP. Currently, there are more than 40 psychiatrists working in the country, most of them working in public institutions. There are regional psychiatric departments and units staffed by psychiatrists. The country has also embarked on training middle level specialist mental health workers such as the training of mental health officers with a bachelor's degree and master's degree who will work as clinicians in zonal and district hospitals. The integration effort is underway with the implementation of an initiative by the WHO: the mhGAP initiative. The country has been building its research capacity as well. The department of psychiatry at Addis Ababa University has been instrumental in the production of relevant data that would help in policy and planning for the country's mental health development activities. Despite these encouraging developments, there are still millions of Ethiopians suffering from severe mental disorders who have no access to basic mental health care.

## 2.2 Why does Ethiopia need mental health research?

In the presence of many killer diseases in Ethiopia, some people think paying attention to mental health issues is a luxury. When this exists in the policy maker's mind, the possibility for progress will be hampered. Inputs from research could be one way of convincing policy makers to give attention to issues of public health

importance. The global initiative Millennium Development Goals (MDG) which Ethiopia strives to achieve has eight goals. Four out of the eight goals which include 1) eradication of extreme poverty hunger-Goal 1; 2) reduce child mortality-Goal 4; 3) reduce maternal mortality-Goal 5; 4) Combat HIV/AIDS-Goal 6 are linked with mental health. Addressing poverty has been the country's main focus for the past several decades. The rhetoric of poverty being our number one enemy is often heard. But, it has been shown that mental health is intricately related with poverty: poverty causing mental illness and poor mental health leading to poverty (Patel & Kleinman, 2003). So, to come out of the vicious cycle of poverty, the country needs to engage in comprehensive health care that includes mental health as well. Studies done in Ethiopia have clearly shown that maternal depression could lead to a two-fold increase in diarrheal disease in infants (Ross, et al., 2011) and increased mortality (Deyessa, et al., 2010). The presence of antenatal common mental disorder symptoms were found to be also associated with prolonged labor (Hanlon et al., 2009). The country has made significant progress in HIV care, with hundreds of thousands of PLWHA getting access to free treatment. But, one challenge in this area is the high number of non-adherence with as high as 25% of patients discontinuing their medication. In addition to increased morbidity and mortality, there is a risk of development of resistance for the antiretroviral medications. Studies in HIV/AIDS clinics in Ethiopia showed that close to 40% of HIV patients suffered from depression. A depressed person cannot have the motivation and energy to continue taking medication. In fact, it was shown in studies coming from other countries that the presence of depression was associated with poor adherence to ART (Ollisah, et al., 2010). Addressing depression is important in improving adherence. Mental disorders were also shown to account for 11% of the total burden of diseases in Ethiopia (Abdullahi, et al., 2001). The value of mental health research goes beyond convincing policy makers that mental health is an important issue. It also includes adapting evidence based cost effective and relevant mental health interventions for the country and monitoring of the impact of interventions and developing the local resource into a more scientifically sound practice.

### **2.3 The need to study psychotic disorders in Ethiopia**

Though there are many different forms of psychosis, schizophrenia is the prototype and the most important form of psychosis. It is a chronic debilitating mental disorder that affects millions of people across the world. The life-time prevalence of schizophrenia was reported to be 0.5% in Butajira (Kebede, et al., 2003). It was also the number one diagnosis for admission to the only mental hospital in the country accounting for 56.1% of the total cases admitted (Fekadu, et al., 2007). Besides causing immense suffering to patients and their families, the economic cost of the disorder is also huge (Mueser & McGurk, 2004; Shibre, et al., 2003). In the burden of disease study in Butajira, schizophrenia was one of the most important conditions associated with high burden (Abdullahi, et al., 2001). Patients with this disorder also die 10-15 years younger than their non-schizophrenic healthy counterparts (Saha, et al., 2007). Common causes of death in schizophrenia were reported to be related with

cardiovascular diseases, suicide, and smoking related (Osby, et al., 2000; Brown, 2000; Brown, et al; 2010). Despite progress in treatment of schizophrenia, both in pharmacotherapy and psychosocial interventions, there was a worsening of the gap in mortality between the patients and the general population over the past several decades (Saha, et al., 2007). Important causes of premature death in schizophrenia remained undressed while the public health effort to prevent premature death in the general population resulted in improvements. So studying this important disorder will have an impact in reducing overall disease burden, decrease stigma on patients and caregivers, improve quality of life of these patients and, above all, decrease premature mortality.

## **2.4 Psychosis in traditional societies**

Culture has many definitions. The most commonly used definition refers to the shared behavior that is passed from generation to generation that prescribes certain behaviors and actions (Kulhara & Chakrabarti, 2001). It has both internal components such as shared values, beliefs and external components such as artifacts and institutions. Culture influences the manifestations of mental disorders such as schizophrenia (Jablensky & Sartorius, 1975). It plays an important role in conceptualizations of mental illness (Kleinman, 1980). Generally western culture follows a predominantly biomedical model where as the non-western society follows a traditional and religious view as causes of mental illness. This attribution style also influences their choice of treatment. Studies done in Ethiopia showed the importance of cultural and traditional beliefs on people's attribution styles and the modes of treatment when some member of the family developed mental illness. For instance studies done several decades ago showed that people exclusively held traditional and religious views regarding causes of mental illnesses and their preferred treatment was religious and traditional (Kortmann, 1987a; Jacobsson & Merdasa, 1991). Pathways to care study done in Ethiopia also found modern mental health care to be the last resort, the median first contact time being 38 weeks. Most patients were brought to modern mental health care after exhausting other alternative care at traditional and religious places (Bekele et al., 2009). But despite these seemingly dichotomous views people are pragmatic in their approach to treatment (Patel et al., 1995b; Saravanan 2008). Probably there could be other factors contributing to the delay in seeking modern mental health care such as stigma related to mental health institutions, geographical access and cost of care.

### **2.4.1 Problems of measurement of mental disorders in traditional societies**

One challenge in doing epidemiological studies in non-western settings is the measurement of psychiatric disorders. Transcultural application of instruments developed for the western countries proved to be a challenging task. Variations in culture and other sociodemographic factors such as literacy were believed to affect

these instruments. For instance, it was reported from Nigeria that manifestations of schizophrenia symptoms significantly varied between rural illiterate people and urban literate. The latter having a more similar manifestation to western patients (Jablensky & Sartorius, 1975). The validity of using western diagnoses into African settings has been challenged by many authors such as Prince who reported distinctive symptoms which he called 'the hallmark of African psychiatric symptoms'. He wondered whether the predominantly somatic complaints represented depression and why they were so common. He argued that African syndromes were different from the European ones and suggested a different approach to diagnosis (Prince, 1983). For instance, an attempt to use SRQ in Ethiopian patients proved to be a challenging exercise as most of the questions were understood differently from what the questions intended to measure. It was found that 37% of the 'yes' answers to the non-psychotic items and 68% of the 'yes' answers to the psychotic items were not valid responses. It was observed that even the seemingly simple SRQ was found to be too difficult to understand: more than one fourth of the questions were found to be understood differently by Ethiopians (Kortmann, 1987b). The fact that the close to 70 percent of the psychosis section of the SRQ was difficult to understand showed that psychotic symptoms were difficult to understand by Ethiopians. There were so many instances of similar challenges in application of diagnostic instruments in traditional societies. One of the main activities of the Mental Health division of the WHO was to address such challenges and develop instruments that could be used in different cultures to enable cross-cultural comparison by creating uniformity in assessment and reporting (Flaherty, et al., 1988). Several instruments were developed that have been in use for the past several decades. DIS was the first fully structured psychiatric instrument developed to be administered by lay interviewers, followed by the CIDI (Kessler & Üstün, 2004).

#### **2.4.2 The Composite International Diagnostic Interview (CIDI) and psychosis**

The CIDI is a fully standardized structured diagnostic interview for the assessment of mental disorders. It was jointly developed by the WHO and the former US Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) by a project that was initiated in 1979 (Robbins, et al., 1988). Since version 1 came out in 1990, it has undergone several revisions by a team of experts from around the world led by the WHO-CIDI Advisory Board. Version 2.1, modified to meet the DSM-IV criteria, was released in 1997. It was revised to be consistent with diagnostic items both in ICD-10 Diagnostic Criteria for Research (WHO, 1993) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; APA, 1994). The CIDI core Version 2.1 (1998) contains almost all major psychiatric disorders. The CIDI has been translated into many languages and used very widely for clinical and research purposes in addition to epidemiological studies of mental disorders (Wittchen, 1994).

The greatest advantage of CIDI is that it is designed to be administered by lay interviewers with no special clinical training because conducting large scale epidemiological research using clinicians is not feasible because either they are in short supply or are very expensive. This enabled researchers to conduct large scale community based psychiatric research at a very low cost (Robbins et al., 1998). No clinical judgment is required on the part of the interviewer. The training on how to administer the questions can be given over a brief period of time, usually one to two weeks. It is highly structured and therefore there is no room for the common sources of unreliability such as questions asked, the nature of answers given, time criteria, interpretation of information, and interpretation of diagnostic criteria. Interviewers are instructed to strictly follow the directions in the question and are not allowed to give any explanation. Better reliability was considered to be a necessity for a better validity. Several studies have shown that the CIDI had a good to excellent reliability including culture. Validity studies have been minimal compared with reliability, part of the reason being the extensive validity study of its predecessor, DIS, but with the existing evidence it was deemed to be acceptable, but the validity of the psychosis module was not clearly established (Wittchen, 1994, Andrews, 1998). But DIS was shown to have low sensitivity for schizophrenia when compared against standard clinical diagnosis (Burnman, et al., 1983; Wittchen, 1985). After different researchers started using CIDI in different countries, the psychosis section proved to be problematic with many reports indicating low sensitivity to pick psychosis. These reports come not only from non-western countries, but also from developed countries as well (Rosenman, et al., 1997; Cooper, et al., 1998). Reports from different non-western countries showed that the CIDI had a very low sensitivity for picking psychosis in these settings (Helzer et al., 1985; Eaton et al., 1989; Kessler et al., 1994; Youssef et al., 1999; van Os et al., 2001). In a study done in Addis Ababa, Ethiopia, the Amharic version of the CIDI was found to have high reliability. The lifetime prevalence of schizophrenia reported by the CIDI was 0.2% (Rashid et al., 1996). Why CIDI does have low sensitivity for psychosis? One reason could be the way the CIDI is conducted. Diagnosing psychosis probably needs a clinical judgment. In addition to that, psychotic symptoms are probably more influenced by culture so other supplementary methods are needed to fill this gap. In the Butajira study on course and outcome of SMI, key informants were used to supplement the inherent weakness of the CIDI to diagnose psychosis. In fact, it proved to be a useful strategy because more cases of schizophrenia were identified by KIs than the CIDI (Shibre, et al., 2002). The pitfall of using only CIDI was seen in a community based study in the traditional semi-nomadic Borana population involving more than 1800 adults. Not surprisingly, there were no cases of psychosis detected (Beyero, 2004). This was probably the result of low sensitivity of the CIDI to pick psychosis in traditional societies hence the need for a supplementary method.

## 2.5 The epidemiology of schizophrenia in the world: emerging evidence

Schizophrenia is often considered an egalitarian disorder. It is believed to affect men and women equally; doesn't discriminate color, socioeconomic status or educational status. This belief, or 'dogma' as some authors like to call it (McGrath, 2006), stems from the WHO multicenter epidemiological studies that were done around 4 decades ago. The most pervasive of these dogmas is the notion that schizophrenia has a better outcome in developing countries (Sartorius et al., 1977; Jablensky, 1992; Sartorius et al., 1996; Harrison et al., 2001; Hopper et al., 2007). But several reports from different countries started to challenge many of the long held beliefs. For instance, a review of the epidemiological studies in the past 100 years showed that there was at least a 40 percent excess in the incidence of schizophrenia in men giving a male to female ratio of 1.4:1 (Aleman, et al., 2003; McGrath et al., 2004). They also found a wide variation in incidence and prevalence in different countries. They found up to five fold variation in incidence and prevalence of schizophrenia in different countries in the world (McGrath et al., 2004; Saha et al., 2005; McGrath, 2006; Messias et al., 2007). The occurrence of schizophrenia was also shown to be significantly affected by several factors such as migrant status, urban birth or residence, and advanced paternal age (McGrath et al., 2004; Sipos et al., 2004; Malaspina et al., 2001). So, the evidences show that schizophrenia is not an egalitarian disorder. This fact turned out to be merely a myth. This calls for a new direction in the epidemiology of schizophrenia (McGrath & Susser, 2009). The notion of good outcome in developing (LAMIC) countries has also been a subject of fierce debate among epidemiologists. There has been an outpouring of data from LAMIC countries which challenged this dogma. Several studies from these countries showed that patients with schizophrenia had poor clinical course and outcome and high mortality (Patel, et al., 2006; Saha, Chant & McGrath, 2007; Cohen, Patel, Thara, & Gureje, 2008; Alem et al., 2009).

It is against the backdrop of these diverse views on epidemiology of schizophrenia that we are doing our studies on the epidemiology of schizophrenia. The Butajira project on course and outcome of schizophrenia and bipolar disorders is probably the largest community based study in Sub-Saharan Africa. It was initiated in 1998 with the aim of collecting community based data from a predominantly rural setting. In a span of 3 years more than 68,000 adults aged 15-49 (82% of the total population) were interviewed to identify cases with psychotic and affective disorders using the Composite International Diagnostic Interview (CIDI) version 2.1 (WHO 1997) which identified 2159 suspected cases. Supplementary data was also obtained from Key Informants in the area who identified 719 cases. Suspected cases (2,285) underwent SCAN interview. A total of 321 cases of schizophrenia were identified. The findings from this cohort added further to the heterogeneity of schizophrenia epidemiology. Some of the key findings published before include an estimated prevalence of 4.7/1000, a younger age of onset for females (mean age of 23.8 for males and 21 for females), and a very high male to female ratio (5:1) (Kebede, et al., 2003). Among the sociodemographic correlates, being male, under 35 years of age, unmarried, educated

and living in urban areas were all associated with the risk of schizophrenia (Kebede, et al., 2004). Short-term symptomatic and functional outcome (using SF-36) was also reported. It was found that the patients in this cohort had significantly diminished health related quality of life; moreover, the majority had significant functional impairment (Kebede, et al., 2005). Again short term clinical course and outcome showed that the majority had a non-remitting clinical course (Alem, et al., 2009).

## 2.6 Khat

Khat is an evergreen shrub that is believed to have originated from Ethiopia. It grows in many Eastern and Southern African countries and the Arabian Peninsula. Its fresh leaves are chewed and the juice is swallowed to exert its stimulating effect. It has many names in different countries but in the scientific literature, it is known as khat. Other names include qat, chat, qaadka, miraa, tohai, tschat, Abyssinian tea, African tea, African salad, and so on. In Ethiopia it is widely known by the name *chat* (ጫት) in Amharic and *jima* in Oromo language.

### 2.6.1 History of khat

There is some controversy regarding the origin of khat. Some authors argue that khat originated in Yemen while others say the origin is in Ethiopia. The former say a herder named *Awzulkernayien* discovered the stimulant effect when his goat that ate khat got excited and he was tempted to try it on himself which made him spend a sleepless night. It was later introduced into the Harrar City by the founders of the walled city. Other theories based on Sir Richard Burton's book, 'First Footsteps in East Africa' published in 1856, says it was the other way round i.e. khat being introduced to Yemen from Abyssinia. Among scholars there seems to be a consensus about Ethiopia being the origin of khat. Khat was mentioned in the chronicles of King *Amda Tsion* who reigned from 1314-1344 AD. It was reported that during the war with King Amda Tsion the Muslim Sultan of Ifāt, Sabrad Dīn threatened to plant khat after defeating him because Muslims loved the plant (Getahun & Krikorian, 1973). In the earlier days, the chewing of khat was predominantly confined to the Eastern part of the country and mainly frequented by the Muslim community. But, later on, the habit rapidly spread to the central highlands and to the western parts of the country and crossed over religious and ethnic boundaries. Currently, there is no place in the country where khat is not chewed.

### 2.6.2 Botany of khat

The first Botanical properties were described by the Swedish Botanist Peter Forskal who studied khat while he lived in Arabia (Yemen) in the eighteenth century. His work was published posthumously in 1775 by Niebuhr. He coined the term *catha edulis*, the scientific name for khat. Niebuhr added the name Forsk after *catha edulis* in memory of Peter Forskal (Dhaifalah & Šantavý, 2004). So, it is common to find the

name *catha edulis* Forsk in some literature that deal with khat. It belongs to the family Celastraceae. Khat tree can grow as tall as 15 to 20 meters but usually kept short to facilitate harvesting the fresh leaves. It is drought resistant plant which grows in highlands and can be harvested throughout the year (Getahun & Krikorian, 1973).

### 2.6.3 Chemistry of khat

The interest to identify the active chemicals in khat began in the 19<sup>th</sup> century. Fliückiger and Gerock isolated the first alkaloid in 1887 and called it *katine*. Later on, Mosso isolated another alkaloid in 1891 and named it *celastrine*. Katine and celastrine were shown to have psychoactive properties by Beitter in 1901 and he discovered that these two alkaloids were the same and he coined the name cathine. In 1930, Wolfers observed Cathine to be a norpseudoephedrine, S,S(+) phenylpropanolamine, responsible for the psychoactive properties of khat but von Brücke noted in 1941 that cathine's stimulant property was low. But they used dried leaves of khat in their analysis. Later on, studies using fresh khat leaves showed the presence of a more potent alkaloid than cathine. This more potent alkaloid was the precursor of cathine and found in greater proportion in fresh khat leaves. In 1958 the United Nations Economic and Social Council asked the WHO to investigate khat and the UN Narcotics lab discovered the most potent alkaloid, S(-)-alpha-aminopropiophenone, which was named cathinone, in 1975. The alkaloids found in khat were shown to be structurally similar to amphetamine (Kalix, 1990). One of the pioneers in the study of khat pharmacology, Peter Kalix, called cathinone a 'Natural Amphetamine' in one of his reports (Kalix, 1992).

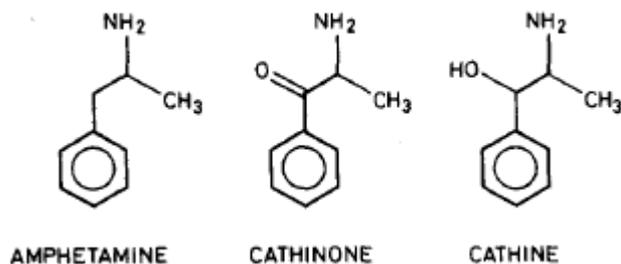


Figure 3. The chemical structures of khat alkaloids in comparison with amphetamine.

### 2.6.4 Varieties of khat

Based on the place it comes from, there are different varieties (brands) of khat in Ethiopia. The price of a bundle varies based on brand. Some of the brands include: *abu mismar*, *asano*, *awoday*, *baherdar*, *beleche*, *gelemso*, *gurage*, *kuto*, *wondo*, *wollene* and so on. Khat shops advertise the brands they have on their shops to attract customers. *Awoday* and *beleche* are the most expensive brands: a bundle

selling 80 and 50 birr respectively; while, *gurage* and *gelemso* are the cheapest and preferred by the low income chewers. Studies done by Geissshüsler and Brenneisen in 1987 on different samples collected from Addis Ababa and Awedai in Harrar (Ethiopia), Anivorano (Madagascar) Nairobi and Mombasa (Kenya), Sanaa (Yemen) on different varieties of khat showed a considerable variability in the content of the psychoactive chemicals. Among the Ethiopian samples, the khat from Wollene had the highest cathinone content of 1.87% followed by Awedai (Harrar) with a cathinone content of 1.73%. Kenyan khat was found to be the most potent with a cathinone content of 3.32%. One hundred gram of fresh khat contains on average 36 mg cathinone, 120 mg cathine and 8mg norephedrine (Geissshüsler & Brenneisen, 1987).



**Figure 4.** Khat is wrapped in false banana leaves to maintain its freshness; the different brands are advertised (Pictures provided by Ephrem Tesema).

### 2.6.5 Khat chewing: social aspects and effect on individuals

People give different reasons for chewing khat. In situations where khat chewing is associated with some traditional practices and events such as weddings and festivities, chewing usually happens as part of the ritual in group settings. Some people chew khat to enhance their performance by feeling more energetic and staying awake such as for farming or studying. But solitary as well as group chewing can take place in urban areas as a form of leisure activity and pastime. The chewing of khat usually takes hours. There has been reports of khat causing decreased productivity, deprivation and disruption in family life by diverting the income to buying khat instead of supporting the family in its basic needs (Elmy et al., 1987; Selassie & Gebre, 1996; Belew et al., 2000). It was also implicated in the spread of HIV in Ethiopia by making people engage in unsafe casual sex which is the most important mode of HIV transmission (Kebede et al., 2005; Dawit et al., 2006). Chewers keep a bolus of fresh leaves in their cheeks and swallow the juice intermittently. This limits the amount of khat they take. They use sugar, coke and tea during chewing to counter the sour taste of the leaves. Many chewers smoke cigarettes and, nowadays, there is increasing use of hookah (water pipe) during chewing in urban areas in Ethiopia. Enzymes in saliva are believed to contribute in the digestion of khat and the psychoactive chemicals can be absorbed through the buccal mucosa (Nencini, 1986;

Toennes, 2003). Nowadays, there are many places in urban areas known by the name *mekamia* bet or khat chewing places which offer their clients fresh khat and other services. A chewer passes through three phases during the day: prechewing known by the name *harara* time which is around lunch time characterized by some form of craving; the chewing phase where the person chews and feels the high which usually lasts for 2 hours followed by the post chewing phase known as *mirkana*. The feeling of high, excessive talking and optimism is usually replaced by quiet withdrawal and pessimism. Chewers often drink alcohol to counteract the feeling of anxiety, dysphoria and sleeplessness, an activity known by the name *chebsi*, meaning breaker of the state of khat intoxication.



Figure 5. Khat bolus in the mouth of a chewer.

### 2.6.6 Khat and health

Several reports exist that address the adverse consequences of khat on physical and mental health. Because khat has amphetamine-like action, the three systems in the body that are most likely to be affected by khat are the cardiovascular, gastrointestinal and nervous system. But other systems such as the respiratory, genitourinary and endocrine systems can be affected as well (Cox, 2003). Myocardial infarction has been reported to be common in khat chewers in the afternoon unlike the typical time where MI occurs i.e. in the morning (Al Motarreb, 2002a, 2005). The tannins in khat are responsible for diseases of the gastrointestinal tract such as periodontitis, esophagitis, and gastritis (Al Motarreb, 2002b). A case series of seven Somali khat chewers with liver cirrhosis has been reported (Peevers, 2010). The effect of khat on the mind has been a subject of interest for many researchers. Khat causes psychological dependence. In chronic khat chewers, withdrawal symptoms that involve frightening dreams which last for one to two nights were reported to occur besides being lethargic, feeling hot in lower extremities and the desire to chew khat (Al Motarreb, 2002b). More severe psychological reactions such as psychoses were

reported as well. In a review published in 2007, Warfa reported more than twenty cases of khat induced psychosis. It was difficult to establish a causal relationship, but the onset of psychotic symptoms was temporally related with khat chewing (Warfa, 2007). There are few community based studies which show the association of khat with the development of severe mental illnesses (Bhui, 2006; Odenwald, 2005). A study done at Amanuel Specialized Mental Hospital in Ethiopia described the role of khat in frequent relapse of cases with psychosis (Bimerew, 2007).

### 2.6.7 Legal status of khat

Controversies abound regarding the legal status of khat. As such there are no internationally agreed strict criteria for labeling drugs as legal or illegal. Criteria used differ from country to country. This holds true especially for drugs which are considered 'soft' such as khat and cannabis. Khat is legal in Australia, Djibouti, Ethiopia, Kenya, Somalia, Uganda, Yemen, UK, and the Netherlands but illegal in Tanzania, almost all the Arab countries, the rest of Europe and North America (Klein & Metaal, 2010). Various sociocultural and economic factors make the banning of khat in Ethiopia difficult. Khat is deeply embedded in some cultures in Ethiopia. It is also the third largest source of foreign currency. For instance, according to official data, the country earned more than 200 million USD in 2010. It continues to be an important source of foreign currency. This calls for a more pragmatic approach of harm reduction strategy to mitigate the problems associated with khat chewing.



**Figure 6.** One of the three khat memorial stamps launched by the Ethiopian Postal Service in 2008.

### 3 AIMS OF THE RESEARCH

#### 3.1 General aim

The general aim of the studies in the two sites was to describe course and outcome of schizophrenia (Butajira study site), describe the influence of tradition on psychosis (Borana study site) and explore perspective of family and patients on khat and severe mental illnesses (Butajira study site).

#### 3.2 Specific aims of the different papers

1. Describe the five-year clinical course and outcome of schizophrenia and its determinants (Paper I).
2. Describe the five-year mortality in schizophrenia using Standardized Mortality Ratio (SMR) and list possible causes of deaths and associated factors and suggest solutions to mitigate the problem (Paper II).
3. Describe the influence of culture on the manifestations of psychosis by exploring how people conceptualize psychosis in the community and comparing it with CIDI (Paper III).
4. Describe the perceived causes and preferred treatment for SMI in a traditional society (Paper IV).
5. Explore reasons from patients and caregivers why patients with SMI continue to chew khat despite advice from their physicians to desist (Paper V).

## 4 SETTINGS AND METHODS

### 4.1 Butajira



**Figure 7.** The Butajira study site (Source: Butajira INDEPTH DSS).

The Butajira district is a predominantly rural locality in central Ethiopia found about 132 km from the capital of Ethiopia, Addis Ababa. It owes its name to a small town that serves as the seat of the administration in the district. In fact, the district was formally known as Meskan and Mareko Woreda at the time the study was started. *Woreda* is the second from the last in the political administrative structure of Ethiopia and translated here as district. The district had 45 kebeles, the smallest political administrative units. Only one of the kebeles was excluded from the study because of geographical inaccessibility. The total population of the district at the time of the study was estimated to be 227,135, about 45% of this belonged to the age group 15-49 (OPHCC, 1996). This age group was the subject of the epidemiological study.

Butajira has an interesting landscape and climate which makes it suitable for epidemiological studies. That was the reason for the establishment of the Demographic and Surveillance site (DSS) in the area in 1986 to monitor vital health statistics, a collaborative undertaking between department of public health, AAU and Umea University. It has an altitude ranging from 1500-3,500 mts and a climate ranging from lowland to highland in a relatively small area. The estimated size of the District is 797 km<sup>2</sup>, of which Butajira town covers approximately 9 km<sup>2</sup>. It is also one of the most densely populated areas in the SNNPRS with 325 inhabitants/km<sup>2</sup>. Gurage is the predominant ethnic group, which has subdivisions (tribes) such as Meskan, Mareko, Sodo, Siliti and *Dobi*. Islam is the religion for two-thirds of the population. Coptic Christians (known in Ethiopia as Orthodox Christian) is the second dominant religion. The different tribes have their own version of the Gurage language. The official language in the region is Amharic, the national language, which is widely spoken in the area, and is used for written communication as well. Farming and small scale trades are the two main occupations in the area, farming being the major one. They grow cereals, spice (pepper), false banana and khat (a mild stimulant). The majority of residents in the area are illiterate (Berhane & Byass, 2002).

The presence of the DSS was the reason why mental health research was initiated in the area. The establishment of the DSS and mental health research projects helped improve the health of the community as they brought some health services such as mental health service closer to the community. It also enabled us to have normative data for the community to compare with the findings from our study cohort.

#### 4.2 Borana area

The Borana semi-nomadic study area is a remote, rural region with poor developed infrastructure, and no mental health services at all. The Borana are among the few nomadic groups that still exist in the world today. They reside in all but two districts of the zone extending over a savannah grassland area of more than 400 km diameter in the southern part of Ethiopia, bordering Kenya. They are part of the big Oromo ethnic group in Ethiopia. They also reside in Northern Kenya. It was reported that the Borana in Kenya originally came from Ethiopia during the great Oromo movement in the 10<sup>th</sup> Century. The Borana zone covers a total area of 94,000 km<sup>2</sup> and has a population of 966,467 (CSA, 2007), Religion: 98% Animists, 1% Christian, 1% Muslim. The Borana pastoralists move from place to place in search of grazing land and water for their cattle, especially during severe periodic drought seasons, which occur as frequently as every two to three years. This study was conducted in the villages of Megado, Dida Yabello and Dida Hara and, according to data from the register of local administrations the total population aged over 18 years in the three districts was 10,598. These villages were the site of an earlier epidemiological study (Beyero, et al., 2004).

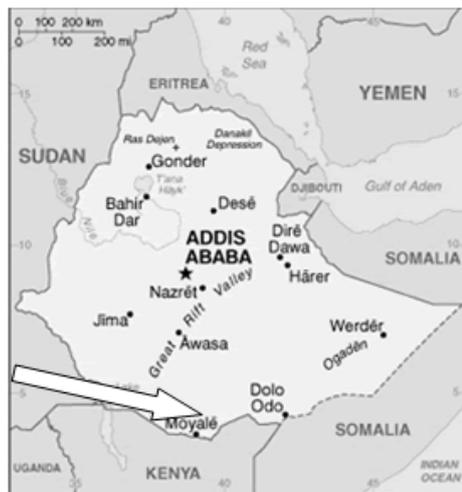
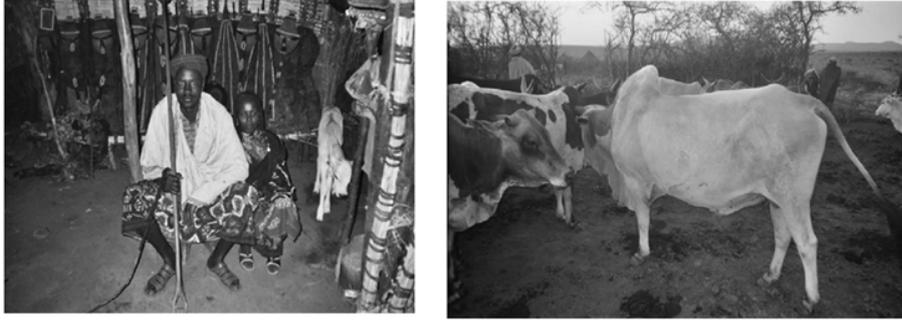


Figure 8. Map of Ethiopia<sup>4</sup>: arrow shows where Borana is located.

<sup>4</sup> <https://www.cia.gov/library/publications/the-world-factbook/geos/et.html>



**Figure 9.** The couple seen in this picture lives in Didi Hara, one of the study sites in Borana, and cattle is their source of livelihood.

### 4.3 Study design

1. The Butajira study on course and outcome of schizophrenia and bipolar disorder: Three study designs were employed in this study.
  - i. Cross-sectional design to identify cases using CIDI (WHO, 1997a) and SCAN (WHO, 1997b) and collect baseline socio-demographic data. Key Informant method was used to identify cases with possible SMI.
  - ii. Qualitative method was also used in the study of khat among patients with SMI.
  - iii. Prospective cohort study design was employed to follow course and outcome of cases with Schizophrenia.
2. The study on psychosis among the Borana semi-nomadic population used two study designs
  - i. Qualitative method was employed in the study using key members of the Borana community to identify cases with possible SMI as well as study attribution and preferred treatment for SMI in the Borana semi-nomadic population
  - ii. Cross-sectional study design was employed to identify cases using key informants, collect baseline socio-demographic data and SCAN interview to confirm the diagnosis of identified cases.

### 4.4 Case identification and establishment of the cohort in Butajira

In 44 of the 45 *kebeles*, a house-to-house survey was conducted to screen 82% of the adult population in the district, aged 15-49 to identify cases with SMI between March 1998 and May 2001. Details of the establishment of the cohort and the follow-up status of the schizophrenia cohort in particular are presented in a flow chart (fig 8).

### **Inclusion criteria into the cohort**

- i. Age between 15 and 49. Individuals older than 49 years of age were not included because the age group 15-49 was believed to give the highest case yield.
- ii. Residence in the area of at least 6 months to ensure stability of the cohort.
- iii. Being diagnosed as a case by the SCAN.

### **Instruments used**

#### **1. Screening**

##### **The Composite International Diagnostic Interview (CIDI): the modules on psychosis and affective disorders.**

The first step was to translate and test the CIDI version 1.0 for reliability and feasibility of use and acceptability by respondents (Rashid et al., 1996).

Fifteen male and 15 female high school graduates were recruited from the area and received a two weeks training by trained professionals on how to administer CIDI. Female interviewers administered the interviews, going door-to-door throughout the district, to females and males to males to make it more acceptable to the population. These lay interviewers interviewed 68,378 adults belonging to the stated age group: 11,562 (16.9%) in urban areas and 56,816 (83.1%) in rural areas. Of these 432 and 1,734 were found to be positive from urban and rural areas respectively.

**Key Informants (KIs):** Case vignettes were used to train KIs selected from the area. These KIs were expected to supplement some of the inherent weaknesses of the instruments that are based on subjective reports of symptoms. They were also able to report vagrant cases that were missed during the house to house survey. They identified a total of 719 cases.

#### **2. Diagnosis**

**Schedule for Clinical Assessment in Neuropsychiatry (SCAN):** It is an instrument developed by the WHO as a diagnostic instrument to be used by psychiatrists and psychiatry residents who received a one week SCAN training either in Nottingham, UK, a WHO designated SCAN training center, or Addis Ababa. They administered the interview to positive cases identified by the CIDI interview and KIs. The SCAN is a semi-structured instrument which allows for clinical judgment.

- 3. Baseline and follow-up assessment:** a monthly case summary and an annual SCAN interview were used during follow-up. Broad rating Schedule and Verbal Autopsy forms were used to investigate the deceased.

## 4.5 Statistical methods

### *Data processing and analysis (Papers I and II)*

For the Butajira course and outcome study, a full time editor scrutinized the interview forms for completeness, accuracy and consistency. Double data entry was used using the Epi-Info (version 6) program. CIDI and SCAN data entry programs were used to enter data obtained by these two instruments. Follow-up data was entered into the Epi-Info program.

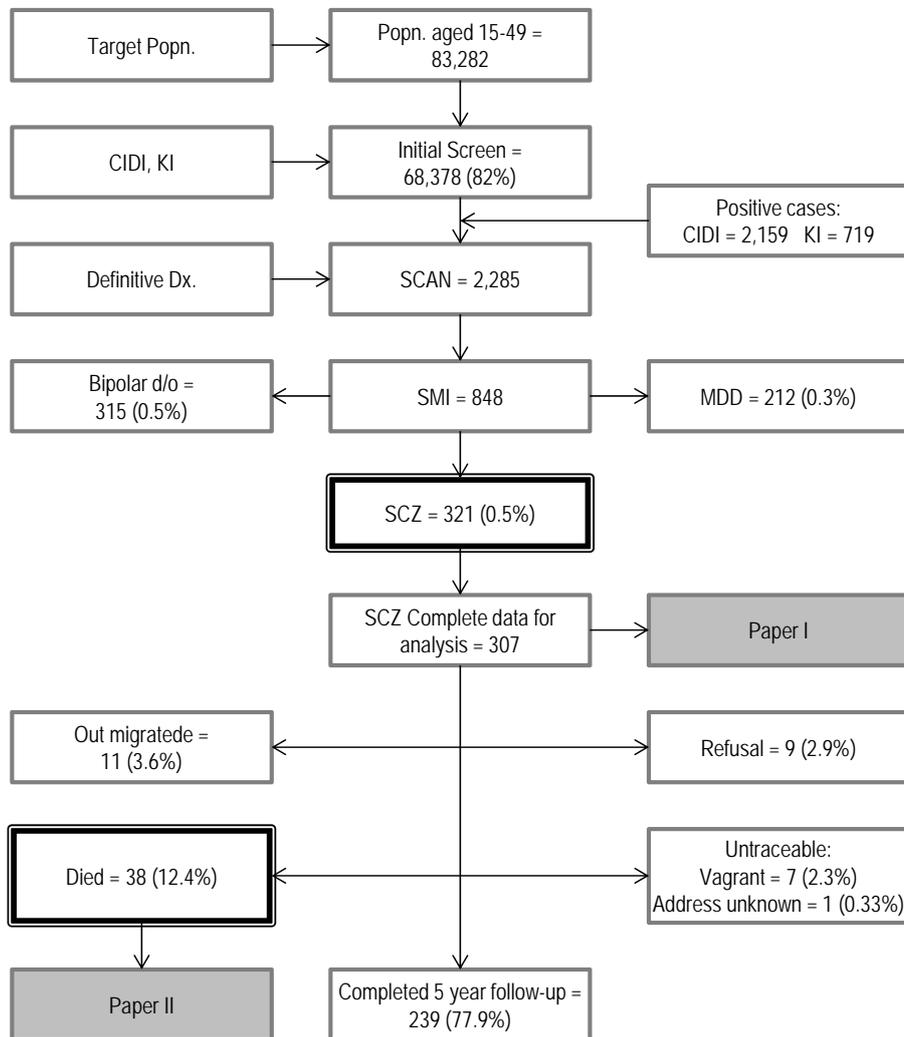
For the quantitative studies, data was analyzed using Statistical Package for Social Sciences (SPSS) version 17 and Stata 11. Frequency and cross-tabs were performed to summarize the results. Regression methods such as logistic regression and Cox regression were used to test associations for binary outcomes such as being in 'remission or not' or 'alive or dead' respectively. Both crude and adjusted odds ratios and hazard ratios were calculated for the clinical course and outcome and mortality respectively. Relevant socio-demographic and clinical factors that were believed to affect course and outcome and mortality were included as explanatory variables. Mortality rate and SMR was calculated using the DSS population as reference.

## 4.6 The Borana semi-nomadic population study

### *Data collection and analysis (Papers III and IV)*

We used Key Informants selected from the three kebeles. Six groups of informants, each consisting of between 8 and 10 participants, were organized in each of the three study sites or villages. We selected one male group and one female group from each kebele to get as diverse opinion as possible. Instead of using case vignettes, we conducted an open discussion asking the participants to tell us how they identify someone who has severe mental illness in their community (see table 2 for topic guides used). We listed the symptoms they gave us and asked each of them to identify someone in their village who had those symptoms. They gave us a list of names. We asked them to bring those people for interview. A SCAN interview was done by a psychiatrist, one of the investigators, who had a good command of both English language and the local Borana Oromo language. Eight cases of schizophrenia and 13 cases of psychotic mood disorder were diagnosed using SCAN after they were identified by the KIs.

**Figure 10.** Flow chart summarizing the cohort identification and 5 year follow-up status of patients with schizophrenia in Butajira, Ethiopia.



CIDI = composite international diagnostic interview; d/o = disorder; Dx = diagnosis; KI = key informants; MDD = major depressive disorder; Popn = population; SCAN = schedule for clinical assessment in neuropsychiatry; SCZ = schizophrenia; SMI = severe mental illnesses.

**Table 2.** Topic guides used in the qualitative study in Borana semi-nomadic population.

- |    |   |
|----|---|
| 1. | Have you ever heard about or seen someone with severe mental illness?                       |
| 2. | How common do you think severe mental illnesses are in Borana?                              |
| 3. | What do you believe are the markers or main symptoms of mental illness?                     |
| 4. | What do you think causes such illness?  |
| 5. | How does the community care for mentally ill people?  |
| 6. | Do you think there are people who have such symptoms in your area?                          |
| 7. | Are you aware of mentally ill people who committed suicide or migrated to the nearby towns? |

For the qualitative studies, interviews were tape recorded along with field notes. Multiple coding, comparison and negotiation took place among researchers. Predominantly thematic (content) analysis was undertaken to summarize the main findings. Descriptive analysis of the subjects who underwent SCAN interview was conducted using SPSS version 17.

#### 4.7 Qualitative study on khat in Butajira

##### *Data collection and analysis (Paper V)*

Using purposive sampling, a total of 37 men with SMI (19 with bipolar disorder, 13 with schizophrenia, five with major Depressive disorder) who engaged in regular khat chewing behavior, identified by the field workers, were selected from the Butajira cohort. Selection criteria were mainly: being well enough to communicate, the ability to speak in Amharic and regular khat chewing habit. They were assigned into either focus group discussion or in-depth interviews. A total of fourteen in-depth interviews were conducted. The other 23 men participated in three focus group discussions, two composed of eight men, the third of seven men. The mean age of the participants was 38 years. The majority (81%) was married; farmers (84%) from the Gurage ethnic group and all except one were Muslim by faith.

There was also a separate focus group discussion held involving 30 female caregivers. Most of them (70%) were spouses of the patients who participated in the study. The remaining were close family members (such as mothers) who were involved in the care of the patients.

Topic guides were prepared to facilitate the discussions, but participants were encouraged to speak freely and initiate discussion about those issues most pertinent to them. The topic guided used are given in a table 3.

**Table 3.** Topic guides used in the qualitative study of khat.

<p><b>I. Clarifying how much and how often the person chews khat</b></p> <ul style="list-style-type: none"> <li>• I understand that you chew khat. How often do you chew? How much do you chew at a time?</li> </ul> <p><b>II. Understanding why people chew khat</b></p> <ul style="list-style-type: none"> <li>• Could you tell me why you chew khat? Anything else?</li> <li>• [Probes: do you chew because your friends do, for prayer, because you are bored, because it makes you feel better...]</li> </ul> <p><b>III Finding out the effect that khat has on them</b></p> <ul style="list-style-type: none"> <li>• What happens to you when you chew khat?</li> <li>• How does khat affect your body?</li> <li>• Does chewing khat affect your mind in any way? How?</li> <li>• Does chewing khat affect you mentally (emotionally, psychologically)? In what way?</li> <li>• Probes: Does khat make your symptoms better or worse? If so, how does it do that?</li> </ul> <p><b>IV. Relationship to medication</b></p> <ul style="list-style-type: none"> <li>• Do you think khat affects your medication in any way?</li> <li>• What do you think would be the opinion of the doctors on your khat chewing?</li> </ul> <p><b>V. Bad effects of khat</b></p> <ul style="list-style-type: none"> <li>• Have you ever had a problem when you used khat?</li> <li>• Did you ever hear of anybody having a problem because they used khat?</li> <li>• Do you think khat could be harmful?</li> <li>• Do you want to keep chewing khat?</li> <li>• Could you stop chewing if you wanted to?</li> <li>• How much money do you spend on khat?</li> </ul>
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NB. A slightly modified version was used to facilitate the discussion with caregivers of people who chew khat.

Interviews were tape recorded along with field notes. Independent coding was done by two researchers. Then comparison of the codes and negotiation on differences took place between the researchers. Predominantly thematic analysis was undertaken to summarize the main findings. Simple descriptive analysis of the participants was conducted.

## 5 ETHICAL CONSIDERATIONS

For both the Butajira and Borana studies, ethical approval was obtained from the Faculty of Medicine, Addis Ababa University. All participants provided consent to be interviewed. CIDI interviews were conducted by female interviewers for female participants and male interviewers for male participants. For the cases identified by the research, a psychiatric clinic was established which provided free medication as well. Patients who also had medical illness identified during the initial evaluation were given free treatment. Funding for the service was provided by the research project.

## 6 SUMMARY OF RESULTS AND DISCUSSION

### Part-I

#### ***Five-year clinical course and outcome and mortality in schizophrenia in Butajira (Papers I and II)***

Consistent with our hypothesis of an unfavorable outcome for schizophrenia in this setting, the 5-year follow-up result of course and outcome of schizophrenia was found to be poor. More than 30% of patients lived in psychotic episode for greater than 75% of the follow-up time; which was higher than the five-year outcome reported for developed centers from high income countries in the WHO IPSS report except one center, Aarhus in Denmark (Leff et al., 1992) whereas, 20% were in remission for a similar period; 45% had not experienced any remission in the 5-year follow-up period. The presence of such a high level of cases with chronic non-remitting course challenges the prevailing opinion of a good course and outcome for schizophrenia in low and middle income countries (LAMICs) (Sartorius et al., 1977; Jablensky et al., 1992; Leff et al., 1992). Despite availability of free medication and close follow-up, 32% of the patients were not on antipsychotic medication for more than 75% of the follow-up time. It was shown that those who took their medication had better outcome than those who were not on treatment, adjusted OR 2.276 (95% CI = 1.121-4.621; P-value = .023).

One of the pioneers of research in course and outcome of psychosis, Emil Kraepelin, described the case of Dementia Praecox, a condition believed to be similar to schizophrenia, a century ago, on patients who were living in asylum in Germany. These cases had generally severe and deteriorating illness course with only permanent cure rate of 2.6-16% (Kraepelin, 1971). The cases in asylum were generally severely ill patients who had lived prior to the era of pharmacotherapy. The introduction of psychopharmacology in the 1950s resulted in improvement in symptoms and prevented relapses in schizophrenia which forced most asylums to be closed and patients were discharged into the community (Hogarty et al., 1974; Schooler et al., 1997). In our study we found that adherence to antipsychotic medication significantly improved the course and outcome but as in most reports, compliance was a very important problem. Studies involving patients with schizophrenia reported a non-compliance rate of as high as 80% (Corrigan et al., 1990). So, improving compliance could be an important step in improving course and outcome. Another factor that was believed to be responsible for the poor course and outcome in our cohort is the delay in initiation of treatment. Our cohort involved a predominantly treatment naïve group with long duration of illness. Several studies show that early intervention can significantly improve outcome in schizophrenia (Loebel et al., 1992; McGlashan, 1996; Wyatt et al., 1997; Haas et al., 1998; Larsen et al., 1998).

Interestingly, single patients had good outcome compared with patients who were married. This finding is most likely related with the culture of the area in which

marriage is arranged and may not reflect the clinical status of patients unlike the situation in western countries where the man has to court his spouse. Some families think if their sick son gets a wife he will be free from the symptoms. For this reason, they arrange marriage even for severely ill patients with schizophrenia. Another interesting finding in our cohort was the absence of a difference in outcome between men and women. It was shown in several studies that women run a more benign course in schizophrenia or other psychotic disorders (Grossman et al., 2006; Goldstein, 1988). So, these peculiar epidemiological findings add to the contemporary view of heterogeneity of schizophrenia instead of being an egalitarian disorder (van Os and Kapur, 2009).

With regards to mortality, which is also an important measure of outcome, a high level of mortality was observed in this cohort. Thirty eight patients died (12.4%) in the 5-year follow-up period. It was disproportionately high for men compared with women. The mean age of death for both sexes was 35 years. The age and sex standardized mortality ratio was (SMR) was 5.98 (95% CI = 4.09 to 7.87). The total SMR was 6.27 (95% CI = 4.16 to 8.38) which suggests a six fold increase in mortality for patients with schizophrenia compared with their age and sex matched healthy counterparts. Men had the highest rate of mortality compared with women. Failure to take medication for at least half of the follow-up period was associated with a two-fold increase in rate of mortality. The most common cause of death was infection which is a potentially treatable condition followed by possible malnutrition, unlike other reports from high income countries which report non-communicable diseases such as neoplasms and circulatory diseases and smoking related deaths as common causes of death in schizophrenia (Brown, 2000). This clearly shows the high degree of poverty in the area. When there is shortage of food in the household, patients are often the last to be fed. This could be the reason for the high rate of malnutrition observed in the deceased cases. The four suicide cases that were observed exclusively occurred in men. Studies show that suicide is more common in men than women even in the general population (Goldstein et al., 1993). But the interesting finding is the absence of suicide in the female patients with schizophrenia. For instance a study done in Butajira adult population reported a life time suicide attempt rate of 3.2%, a significant proportion of women attempted suicide, but men used more lethal methods than women (Alem et al., 1999). Since we recorded successful cases of suicides, there could be women patients with schizophrenia who attempted suicide but not successful.

## **Part-II**

### ***Psychosis in the semi-nomadic Borana population: manifestation, attribution and preferred treatment. (Papers III and IV)***

The lack of cases of psychosis in a previous epidemiological survey was the reason for conducting a qualitative study to find out the possible reasons for this phenomenon. The use of CIDI was not supplemented with Key Informant method unlike the studies

in Butajira. Influential and well informed members of the Borana community that lived in the three kebeles were selected and focus group discussions were held.

**Table 4.** Symptoms of severe mental illnesses described by the key informants and psychotic symptoms in CIDI among the Borana semi-nomadic population, southern Ethiopia.

Symptoms described by Key Informants (KI)	Symptoms in the CIDI 2.1 section G & P
<p><b>Non social Behavior</b> Eats non edible things Hates family members Social withdrawal Inappropriate dressing Going naked Setting fire to houses Self care neglect Neglect family responsibilities Collects garbage Sleeps everywhere (in the jungle) Verbal/physical abuse</p> <p><b>Motor Behavior</b> Aggression/violence Danger to self/others/animals Restless/roaming Disorderly</p> <p><b>Cognitive</b> Inattentive Poorly recognize things unaware of being ill Unwilling to accept help</p> <p><b>Speech</b> Talks too much Talks alone Laughs alone Talks nonsense Talks in obscene language Talks in new languages Shout Quite</p> <p><b>Thought*</b> Suspicious Unrealistic Being followed/insulted/ridiculed</p> <p><b>Emotion</b> Fearful Irritable Noise intolerant</p> <p><b>Perception</b> Sees what others do not see</p> <p><b>Supernatural</b> Guided by spirit (God/evil)</p>	<p><b>Dysfunction</b> Difficulty to initiate goal directed activities Dysfunction in important social &amp; occupational spheres</p> <p><b>Motor behavior</b> Slow to move Difficulty to move at all Moving constantly</p> <p><b>Speech</b> Carry on conversations with hallucinatory voices Neologism Brief, empty, not fluent</p> <p><b>Thought</b> Spied upon/followed Secretly tested/experimented Plot to hurt/poison Someone in love with... Partner unfaithful Thoughts read Hearing others thought Controlled Others hear his/her thoughts Thoughts inserted/withdrawn Sent special message in TV/radio Experiences strange forces</p> <p>Disordered thought &amp; communication</p> <p><b>Perception</b> Hallucinatory experiences</p>

\* This was described only by one participant.

The most important finding from these focus group discussions was the disparity between what the community describes as psychotic symptoms and the items in the CIDI. The finding is summarized in Table 4. Those participants served as key informants to identify patients who they thought had severe mental illnesses. They identified 8 cases with schizophrenia and 13 cases with mood disorders with psychotic features that were confirmed by SCAN interview. The characteristics of the cases identified by the key informants are described in Table 5. As it is often said, culture has an important influence in the manifestations of psychiatric symptoms. As it was stated before, CIDI has been found to be less sensitive in picking cases with psychosis. So, the use of supplementary methods such as key informants proved to be a useful strategy to address the inherent weakness of the CIDI.

**Table 5.** Brief characteristics of SCAN interviewed individuals and DSM-IV diagnosis suggested by key informants in Borana, southern Ethiopia.

Participants characteristics	N=48	
Age range	18-80 (mean 37 SD17.7)	
Sex	Male	26 (54.2%)
	Female	22 (45.8%)
Marital Status	Married	24 (50)
	Never married	19 (39.5%)
	Separated	2 (4.2%)
	Widowed	3 (6.3%)
Number of years at school	0	45 (93.8%)
	1-5	3 (6.3%)
SCAN generated diagnosis	Brief psychotic disorder	2 (4.2%)
	Schizophrenia	8 (16.8%)
	Bipolar I disorder	11 (22.9%)
	Major Depression	6 (12.6%)
	Anxiety Disorder	5 (10.4%)
	Substance related disorder	2 (4.2%)
	Dementia	2 (4.2%)
	No SCAN diagnosis given *	12 (25.2%)

\*(Seizure disorder 4 of the 12 in this group)

**Part-III*****Khat and severe mental illness (Paper V)***

Patients with SMI and their caregivers were able to freely discuss reasons for chewing khat. As reported by the patients and their caregivers, the perceived positive and negative aspects of khat chewing are presented below.

***Positive aspects of khat chewing***

The main reason for chewing khat as described by patients was to resist social exclusion which they could face if they don't chew while participating in social situations and traditional rituals. Interestingly, this was de emphasized by their caregivers who were rather more concerned with the patients' functionality and symptoms. This difference could partly be because of the gender segregation that happens in social situations. It is quite customary for men to gather together and chew while the women tend to other duties. Some patients said khat made them more active and alleviated the side effects of the psychotropic medication they were taking. This report was strongly emphasized by their caregivers who wanted their spouses to be more active and functional. Some even reported encouraging the patient to chew khat in order for him to be functional and look after the family. Other positive aspect of khat was the experience of pleasure reported by the patients. They reported that khat gave them a temporary exit from the difficulties they were having. Yet another positive aspect of khat chewing was the anorectic effect of khat. Because of shortage of food and the medication they take, patients repeatedly reported feeling hungry which they suppressed by chewing khat. Caregivers also reported this same effect of khat.

***Negative aspects of khat chewing***

Patients as well as their caregivers reported several negative experiences that came with khat. The patients reported that khat made them sleepless and rendered the medication they were taking ineffective. Some of them reported exacerbation of their illness. They expressed their concern over the possible adverse effect on their health when combining khat with psychotropic medication which has important implication for compliance. Their caregivers also noted that patients who chewed khat had poor sleep at night and experiences positive symptoms such as hearing voices or being suspicious. Both the patients and their caregivers were ambivalent about the role of khat in causing the mental illness though they were fairly consistent in their belief about its role in exacerbating an existing illness. The other negative aspect of khat chewing was the adverse effect it had on sexuality. Both the patients and their spouses reported that khat weakened the sexual function of men which was a source of distress for some of the spouses. In this study we observed patients with severe mental illness and their caregivers struggle to balance the beneficial effects with the unwanted effects of khat.

## 7 STRENGTHS AND LIMITATIONS

The main strength of the Butajira Study on Course and Outcome of Schizophrenia and Bipolar Disorders is the fact that it is a large community based study involving a predominantly treatment naïve patient population in a low income rural African setting where there is generally a dearth of evidence. Another notable strength of this cohort is the low level of attrition (<10%) during the five year follow-up. This five year report on clinical course and outcome is expected to add knowledge regarding the status of schizophrenia in LAMIC countries. The study in the Borana semi-nomadic population is also one of the rare studies involving nomadic populations in the world who. The belief system of these people will shed some light on some transcultural issues regarding manifestations of psychotic disorders as well as how best to measure psychosis. The studies also serve as a major input for service development in the area. The study involving khat has both a clinical as well as public health importance: there is diversity of opinion regarding the impact of khat on mental illness and the first hand information gathered from the patients themselves as well as their close caregivers is important. The findings will shed some new light on the issue and will generate several research questions for further investigations into the beneficial as well as the adverse consequences of khat not only on patients but also on healthy segments of the population who engage in this behavior.

Limitations of the studies in Butajira include the fact that only 15-49 year olds were involved. This has the potential failure to pick patients who were older or younger than the stated age limit. It is known that schizophrenia occurs in people younger than 15 or older than 49 years of age. For instance the peak age of onset for schizophrenia was reported to be between 10 and 25 and women tend to have a bimodal age of onset with the possibility of first onset older than 49 years of age. The mixed nature of the cases with more chronic cases in the cohort could also affect the course and outcome. Our unusual male to female ratio of 5:1 also favors a poor prognosis as it is well known that males with schizophrenia have unfavorable prognosis compared with females (Sadock & Sadock, 2007). Again, the high number of chronic cases in our cohort may partly explain the high mortality observed together with the high number of male patients in the cohort, who generally tend to have higher mortality than women, could raise the mortality rate (Harris & Barraclough, 1998). The other limitation was that information regarding causes of death, especially medical causes, was based on family or caregiver reports which could only give us a gross estimation. So, it was not possible to be sure what the actual cause of death was for the patients. For instance, patients who we claim to have died from malnutrition because of a report of generalized body swelling could be caused by other medical conditions such as nephritic syndrome.

The limitation in the khat study includes the fact that only male khat chewing patients were included in the study. Knowing the perspectives of female khat chewing patients could have made the report more complete. The general limitation of the qualitative studies is the issue of generalizability, because samples are selected based

on purposive sampling method instead of the probability sampling method which usually represents the study population. So, the views expressed by the participants may not necessarily reflect the others who did not participate in the studies.

## 8 CONCLUSIONS AND RECOMMENDATIONS

This research addresses fairly diverse topics from course and outcome of schizophrenia to the role of tradition in the perception of psychosis to the use of khat. The findings in this research provide new insights about the course and outcome of schizophrenia in this low income setting. The dogma that schizophrenia runs a benign course in LAMIC countries is increasingly being challenged by many authors, and this report adds to the existing knowledge base that argues against this pervasive dogma. The very high rate of mortality, especially from potentially preventable and treatable conditions, observed in the cases with schizophrenia also calls for action to address the needs of this vulnerable group of society. Another issue which was addressed was the effect of tradition in the manifestation of psychosis. The challenge of applying western instruments in a traditional non-western setting has been demonstrated. Transcultural adaptation of instruments plus use of innovative methods such as key informants is emphasized. Since psychiatry is an imported science in Africa and mostly confined to big cities, traditional belief systems and treatments play a significant role in most parts of Africa. Expansion of modern mental health care needs to consider existing belief systems and treatment approaches and work in collaboration with the influential leaders and healers in the community to make it more acceptable. Clinicians who treat patients with severe mental illnesses and concurrent khat chewing behavior need to explore the reasons why patients engage in the behavior and address the patients' problems such as side effects which interfere with their mood and functionality instead of giving blanket advice of 'Do not chew!' which is rarely heeded.

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## 10 REFERENCES

- Abdullahi H, Hailemariam D, Kebede D. Burden of disease analysis in rural Ethiopia. *Ethiopian Medical Journal* 2001;39(4):271-81.
- Aleman A, Kahn RS, Selten JP. Sex differences in the risk of schizophrenia: evidence from meta-analysis. *Archives of General Psychiatry* 2003;60(6):565-571.
- Alem A, Kebede D, Kullgren G. The prevalence and socio-demographic correlates of khat chewing in Butajira, Ethiopia. *Acta Psychiatrica Scandinavica (Supplement)* 1999;397:84-91.
- Alem A, Kebede D, Jacobsson L, Kullgren G. Suicide attempts among adults in Butajira, Ethiopia. *Acta Psychiatrica Scandinavica (Supplement)* 1999;397:70-76.
- Alem A, Kebede D. The challenges of doing psychiatric research in developing countries. *British Journal of Psychiatry* 2003;182:185-187.
- Alem A, Kebede D, Shibire T, Negash A, Deyessa N. Comparison of computer assisted SCAN diagnosis and clinical diagnosis of major mental disorders in Butajira, rural Ethiopia. *Ethiopian Medical Journal* 2004;42:137-143.
- Alem A, Kebede D, Fekadu A, Shibire T, Fekadu D, Beyero T, Medhin G, Negash A, Kullgren G. Clinical course and outcome of schizophrenia in a predominantly treatment-naive cohort in rural Ethiopia. *Schizophrenia Bulletin* 2009;35:646-654.
- Al Motarreb A, Al Kebsi M, Al Adhi B, Broadley KJ. Khat chewing and acute myocardial infarction. *Heart* 2002a;87:279-280.
- Al-Motarreb A, Baker K, Broadley KJ. Khat: Pharmacological and Medical Aspects and its Social Use in Yemen. *Phytotherapy Research*. 2002b;16:403-413.
- Al Motarreb A, Briancon S, Al Jaber N, Al Adhi B, Al Jailani F, Salek MS, Broadley KJ. Khat chewing is a risk factor for acute myocardial infarction: a case-control study. *British Journal of Clinical Pharmacology* 2005;59:574-581.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4<sup>th</sup> Edition. 1994.
- Andrews G, Peters L. The psychometric properties of the Composite International Diagnostic Interview. *Social Psychiatry Psychiatric Epidemiology* 1998;33:80-88.
- Bekele YY, Flisher AJ, Alem A, Baheretebew Y. Pathways to psychiatric care in Ethiopia. *Psychological Medicine* 2009;39:475-483.
- Belew M, Kebede D, Kassaye M, Enquoselassie F. The Magnitude of Khat Use and Its Association with Health, Nutrition and Socio-economic status. *Ethiopian Medical Journal* 2000;38(1):11-26.
- Berhane Y, Byass P. Site description: physical geography of the Butajira DSA. Butajira DSS; Ethiopia: 2004. [http://www.idrc.ca/lacro/ev-43008-201-1-DO\\_TOPIC.html](http://www.idrc.ca/lacro/ev-43008-201-1-DO_TOPIC.html).
- Beyero T, Alem A, Kebede D, Shibire T, Desta M, Deyessa N. Mental disorders among the Borana semi-nomadic community in Southern Ethiopia. *World Psychiatry* 2004;3:2.

- Bhui K, Craig T, Mohamud S, Warfa N, Stansfeld SA, Thornicroft G, Curtis S, McCrone P. Mental disorders among Somali refugees developing culturally appropriate measures and assessing socio-cultural risk factors. *Social Psychiatry and Psychiatric Epidemiology* 2006;41:400–408.
- Bimerew MS, Sonn FCT, Korlenbout WP. Substance abuse and the risk of readmission of people with schizophrenia at Amanual Psychiatric Hospital, Ethiopia. *Curationis* 2007;30:74–81.
- Brown S, Barraclough B, Inskip H. Causes of the excess mortality of schizophrenia. *British Journal of Psychiatry* 2000;177:212–7.
- Brown S, Kim M, Mitchell C, Inskip H. Twenty-five year mortality of a community cohort with schizophrenia. *British Journal of Psychiatry* 2010;196:116–121.
- Burnam MA, Karno M, Hough RL, Escobar JI, Forsyth AB. The Spanish Diagnostic Interview Schedule. Reliability and comparison with clinical diagnoses. *Archives of General Psychiatry* 1983;40:1189–96.
- Cohen A, Patel V, Thara R, Gureje O. Questioning an axiom: better prognosis for schizophrenia in the developing world? *Schizophrenia Bulletin* 2008;34:229–244.
- Cooper L, Peters L, Andrews G. Validity of the Composite International Diagnostic Interview (CIDI) psychosis module in a psychiatric setting. *Journal of Psychiatric Research* 1998;32:361–368.
- Corrigan PW, Liberman RP, Engel JD. From noncompliance to collaboration in the treatment of schizophrenia. *Hospital and Community Psychiatry* 1990;41: 1203–11.
- Cox G, Rampes H. Adverse effects of Khat: A review. *Advances in Psychiatric Treatment*, 2003;9:456–463.
- Dawit A, Debella A, Dejene A, Abebe A, Mekonnen Y, Degefa A, Ketema L. Is khat-chewing associated with HIV risk behaviour? A community-based study from Ethiopia. *African Journal of AIDS Research* 2006;5(1):61–69 .
- Deyessa N, Berhane Y, Emmelin M, Ellsberg MC, Kullgren G, Högborg U. Joint effect of maternal depression and intimate partner violence on increased risk of child death in rural Ethiopia. *Archives of Diseases of Childhood* 2010;doi:10.1136.
- Dhaifalah I, Šantavý J. Khat Habit and Its Health Effect. A Natural Amphetamine. *Biomedical Papers* 2004;148:11–15.
- Eaton WW, Kramer M, Anthony JC, Dryman A, Shapiro S, Locke BZ. The incidence of specific DSM-III mental disorders: data from the NIMH Epidemiologic Catchment Area Program. *Acta Psychiatrica Scandinavica* 1989;79:163–78.
- Elmi AS, Ahmed YH, Samatar MS. Experience in the Control of Khatchewing in Somalia. *Bulletin on Narcotics* 1987;39(2),51–7.
- Fekadu A, Desta M, Alem A, Prince M. A descriptive analysis of admissions to Amanuel Psychiatric Hospital in Ethiopia. *Ethiopian Journal of Health Development* 2007;21(2):173–178.
- Fazel S, Ebmeier CP. Specialty choice in UK junior doctors: Is psychiatry the least popular specialty for UK and international medical graduates? *BMC Medical Education* 2009, 9:77.

- Flaherty JA, Gaviria FM, Pathak D, Mitchell T, Wintrob R, Richman JA, Birz S. Developing instruments for cross-cultural psychiatric research. *Journal of Nervous and Mental Disease* 1988;176:257–263.
- Geissshüsler S, Brenneisen R. The content of psychoactive phenylpropyl- and phenylpentenylkhatamines in *Catha edulis* Forsk of different origin. *Journal of Ethnopharmacology* 1987;19:269-277.
- Getahun A, Krikohian A. Chat: coffee's rival from Harar, Ethiopia, I. Botany, cultivation and use. *Economic Botany* 1973;27:353-377.
- Giel R, Van Luijk JN. Psychiatric morbidity in a small Ethiopian town. *British Journal of Psychiatry* 1969;115:149-162.
- Giel R. The Prehistory of psychiatry in Ethiopia. *Acta Psychiatrica Scandinavica* (supplement) 1999;100:2-4.
- Goldstein, JM. Gender Differences in the Course of Schizophrenia. *American Journal of Psychiatry* 1988;145:684-689.
- Goldstein JM, Santangelo SL, Simpson JG, Tsuang MT. Gender and mortality in schizophrenia: do women act like men? *Psychological Medicine* 1993;23:941-948.
- Grossman L, Harrow M, Rosen C, Faull R. Sex Differences in Outcome and Recovery for Schizophrenia and Other Psychotic and Nonpsychotic Disorders. *Psychiatric Services* 2006;57:844-850.
- Haas GL, Garratt LS, Sweeney JA. Delay to first antipsychotic medication in schizophrenia: impact on symptomatology and clinical course of illness. *Journal of Psychiatric Research* 1998;32:151–159.
- Hanlon C, Medhin G, Alem A, Tesfaye F, Lakew F, Worku B, Dewey M, Araya M, Abdullreshid A, Hughes M, Tomlinson M, Patel V, Prince M. Impact of antenatal common mental disorders upon perinatal outcomes in Ethiopia: the P-MaMiE population-based cohort study. *Tropical Medicine and International Health* 2009;14 (2):156–166.
- Harris E, Barraclough B. Excess mortality of mental disorder. *British Journal of Psychiatry* 1998;173:11–53.
- Harrison G, Hopper K, Craig T, Laska E, Siegel C, Wanderling M, Dube KC, Ganey K, Giel R, An Der Heiden, W, Holmberg SK, Janca A, Lee Pwh León CA, Malhotra S, Marsella AJ, Nakane Y, Sartorius N, Shen Y, Skoda C, Thara R, Tsirkin SJ, Varma VK, Walsh D, Wiersma D. Recovery from psychotic illness: a 15- and 25-year international follow-up study. *British Journal of Psychiatry* 2001;178:506–517.
- Helzer EJ, Robins NL, McEvoy TL, Spitznagel EL, Stoltzman RK, Farmer A, Brockington IF. A comparison of clinical and Diagnostic Interview Schedule diagnosis: physician reexamination of lay-interviewed cases in the general population. *Archives of General Psychiatry* 1985;42:657-66.
- Hopper K, Harrison G, Janca A, Sartorius N. Recovery from Schizophrenia: An International Perspective—Results from the WHO-Coordinated International Study of Schizophrenia. Oxford: Oxford University Press, New York 2007.

- Hogarty GE, Goldberg SC, Schooler NR, Ulrich RF. Drug and sociotherapy in the aftercare of schizophrenic patients. II. Two-year relapse rates. *Archives of General Psychiatry* 1974;31:603–8.
- Jablensky A, Sartorius N. Culture and Schizophrenia (Editorial). *Psychological Medicine* 1975;5:113–124.
- Jablensky A, Sartorius N, Ernberg G, Anker M, Korten A, Cooper JE, Day R, Bertelsen A. Schizophrenia: manifestations, incidence and course in different cultures: a World Health Organization ten-country study. *Psychological Medicine Monograph Supplement* 1992;20:1–97.
- Jacobsson L. Psychiatric morbidity and psychosocial background in outpatient population of a general hospital in western Ethiopia. *Acta Psychiatrica Scandinavica* 1985;71:417–426.
- Jacobsson L, Merdasa F. Traditional perception and treatment of mental disorders in western Ethiopia before the 1974 revolution. *Acta Psychiatrica Scandinavica* 1991;84:475–481.
- Kalix P. Cathinone, a natural amphetamine. *Pharmacologic Toxicology* 1992;70:77–86.
- Kalix P. Pharmacological properties of the stimulant khat. *Pharmacology and Therapeutics* 1990;48:397–416.
- Kebede D, Alem A, Deyessa N, Shibre T, Negash A, Beyero T. Sociodemographic correlates of depressive disorder in Butajira, rural Ethiopia. *Central African Journal of Medicine* 2003;49 (7/8):78–83.
- Kebede D, Alem A, Shibre T, Negash A, Fekadu A, Fekadu D, Deyessa N, Jacobsson L, Kullgren G. Onset and clinical course of schizophrenia in Butajira- Ethiopia: a community-based study. *Social Psychiatry Psychiatric Epidemiology* 2003;38:625–631.
- Kebede D, Alem A, Shibre T, Negash A, Deyessa N, Beyero T. The Sociodemographic correlate of schizophrenia in Butajira, rural Ethiopia. *Schizophrenia Research* 2004;69:133–141.
- Kebede D, Alem A, Shibre T, Negash A, Deyessa N, Beyero T, Medhin G. Short term symptomatic and functional outcome of schizophrenia in Butajira, Ethiopia. *Schizophrenia Research* 2005;78:171–185.
- Kebede D, Alem A, Mitike G, Enquselassie F, Berhane F, Abebe Y, Ayele R, Lemma W, Assefa T, Gebremichael T. Khat and alcohol use and risky sex behaviour among in-school and out-of-school youth in Ethiopia. *BMC Public Health* 2005;5:109.
- Kessler R, McGonagle K, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen HU, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. *Archives of General Psychiatry* 1994;51:8–19.
- Kessler R, Ütsun B. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *International Journal of Methods in Psychiatric Research* 2004;13(2):93–121.
- Kleinman A. Depression, somatisation and the new 'crosscultural psychiatry'. *Social Science and Medicine* 1980;11:269–276.
- Klein A, Metaal P. A good chew or good riddance—How to move forward in the regulation of khat consumption. *Journal of Ethnopharmacology* 2010;132:584–589.

- Kulhara P, Chakrabarti S. Culture and schizophrenia and other psychotic disorders. *Psychiatric Clinics of North America* 2001;24(3):449-64.
- Kortmann F. Popular, traditional, and professional mental health care in Ethiopia. *Transcultural Psychiatric Research Reviews* 1987a;24:255-274.
- Kortmann F. Problems in communication in transcultural psychiatry The self reporting questionnaire in Ethiopia. *Acta psychiatrica scandinavica* 1987b;75:563-570.
- Kraepelin E. *Dementia Praecox and Paraphrenia, 1919* (translated by Barkley RM). New York: Robert E. Kreiger;1971.
- Larsen TK, Johannessen JO, Opjordsmoen S. First-episode schizophrenia with long duration of untreated psychosis. *British Journal of Psychiatry (Supplement)* 1998;172:45-52.
- Leff J, Sartorius N, Jablensky A, Korten A, Ernberg G. The International Pilot Study of Schizophrenia: five-year follow-up findings. *Psychological Medicine*. 1992;22,131-145.
- Loebel AD, Lieberman JA, Alvir JMJ, Mayerhoff DI, Geisler SH, Szymanski DO. Duration of psychosis and outcome in first-episode schizophrenia. *American Journal of Psychiatry* 1992;149:1183-1188.
- Malaspina D, Harlap S, Fennig S, Heiman D, Nahon D, Feldman D, Susser ES. Advancing paternal age and the risk of schizophrenia. *Archives of General Psychiatry* 2001;58:361-367.
- McGlashan TH. Early detection and intervention in schizophrenia: research. *Schizophrenia Bulletin* 1996;22:327-345. McGrath J, Saha S, Welham J, El Saadi O, MacCauley C, Chant D. A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. *BMC Medicine* 2004;2(1):13.
- McGrath JJ. Variations in the Incidence of Schizophrenia: Data Versus Dogma. *Schizophrenia Bulletin* 2006;32 (1):195-197.
- McGrath JJ, Susser, ES. Pathways to schizophrenia: New directions in the epidemiology of schizophrenia. *Medical Journal of Australia* 2009;190:S7-S9.
- Messias E, Chen C, Eaton WW. Epidemiology of Schizophrenia: Review of Findings and Myths. *Psychiatric Clinics of North America* 2007;30(3):323-338.
- Mueser KT, McGurk SR. Schizophrenia. *Lancet* 2004;363:2063-72.
- Nencini P, Ahmed AM, Aminconi G, Elmi AS. Tolerance develops to sympathetic effects of khat in humans. *Pharmacology* 1984;28:150-154.
- Odenwald M, Neuner F, Schauer M, Elbert T, Catani C, Lingenfelder B, Hinkel H, Hafner H, Rockstroh B. Khat use as risk factor for psychotic disorders: a cross-sectional and case-control study in Somalia. *BMC Medicine* 2005;3:5.
- Olisah VO, Baiyewu O, Sheikh TL. Adherence to highly active antiretroviral therapy in depressed patients with HIV/AIDS attending a Nigerian university teaching hospital clinic. *African Journal of Psychiatry* 2010;13:275-279.
- OPHCC, Office of Population and Housing Census Commission. The 1994 population and housing census of Ethiopia. Results for southern nations, nationalities and people's region. Vol. 1: Part V. Abridged Statistical Report, Addis Ababa. 1994.

- Osby U, Correia N, Brandt L, Ekblom A, Sparén P. Mortality and causes of death in schizophrenia in Stockholm county, Sweden. *Schizophrenia Research* 2000;45:21-28.
- Patel V, Musara T, Butau T, Maramba P, Fuyane S. Concepts of mental illness and medical pluralism in Harare. *Psychological Medicine* 1995a;25:485-493.
- Patel V. Explanatory Models of Mental Illness in Sub-Saharan Africa. *Social Science and Medicine* 1995b;40(9):1291-1298.
- Patel V, Sumathipala A. International representation in psychiatric literature. Survey of six leading journals. *British Journal of Psychiatry* 2001;178:406-409.
- Patel V, Kleinman A. Poverty and common mental disorders in developing countries. *Bulletin of the WHO* 2003;81:609-615.
- Patel V, Cohen A, Thara R, Gureje O. Is the outcome of schizophrenia really better in developing countries? *Revista Brasileira de Psiquiatria* 2006;28:149-152.
- Peevers CG, Moorghen M, Collins PL, Gordon FH, McCune A. Liver disease and cirrhosis because of Khat chewing in UK Somali men: a case series. *Liver International* 2010;30:1242-1243.
- Prince R. Article review: Africa. *Transcultural Psychiatric Research Reviews* 1983;90:134-139.
- Rashid E, Kebede D, Alem A. Evaluation of an Amharic version of the CIDI and prevalence estimation of DSM-III-R disorders in Addis Ababa. *Ethiopian Journal of Health Development* 1996;10:69-77.
- Robins LN, Wing J, Wittchen H-U, Helzer JE, Babor TF, Burke J, Farmer A, Jablensky A, Pickens R, Regier DA, Sartorius N, Towle LH. The composite international diagnostic interview: An epidemiological instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Archives of General Psychiatry* 1988;45:1069-1077.
- Rosenman SJ, Korten AE, Levings CT. Computerised diagnosis in acute psychiatry validity of CIDI Auto against routine clinical diagnoses. *Journal of Psychiatry Research* 1997;31:581-92.
- Ross J, Hanlon C, Girmay M, Alem A, Tesfaye F, Worku B, Dewey M, Patel V, Prince M. Perinatal mental distress and infant morbidity in Ethiopia: a cohort study. *Fetal & Neonatal an edition of Archives of Disease in Childhood* 2011;96:F59-F64.
- Sadock BJ, Sadock VA (Eds.). Schizophrenia. In Kaplan & Sadock's *Synopsis of Psychiatry: Behavioral Sciences/Clinical Psychiatry* (10th ed.), (p. 468). Philadelphia: Lippincott Williams & Wilkins, 2007.
- Saha S, Chant D, Welham J, McGrath J. A systematic review of the prevalence of schizophrenia. *PLoS Medicine* 2005;2(5):e141.
- Saha S, Chant D, McGrath J. A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time? *Archives of General Psychiatry* 2007;64:1123-1131.

- Saravanan B, Jacob KS, Deepak MG, Prince M, David AS, Bhugra D. Perceptions about psychosis and psychiatric services: a qualitative study from Vellore, India. *Social Psychiatry Psychiatric Epidemiology* 2008;43:231–238.
- Sartorius N, Jablensky A, Shapiro L. Two-year follow-up of the patients included in the WHO International Pilot Study of Schizophrenia. *Psychological Medicine* 1977;7:529–541.
- Sartorius N, Gulbinat W, Harrison G, Laska E, Siegel C. Long-term follow-up of schizophrenia in 16 countries. A description of the International Study of Schizophrenia conducted by the World Health Organization. *Social Psychiatry and Psychiatric Epidemiology* 1996;31:249–258.
- Sartorius N, Gaebel W, Cleveland HR, Stuart H, Akiyama T, Arboleda-Flórez J, Baumann AE, Gureje O, Jorge MR, Kastrup M, Suzuki Y, Tasman A. WPA guidance on how to combat stigmatization of psychiatry and psychiatrists. *World Psychiatry* 2010;9:131–144.
- Schooler NR, Keith SJ, Severe JB, Matthews SM, Bellack AS, Glick ID, Hargreaves WA, Kane JM, Ninan PT, Frances A, Jacobs M, Lieberman JA, Mance R, Simpson GM, Woerner MG. Relapse and rehospitalization during maintenance treatment of schizophrenia. The effects of dose reduction and family treatment. *Archives of General Psychiatry* 1997;54:453–63.
- Schulze B. Stigma and mental health professionals: A review of the evidence on an intricate relationship. *International Review of Psychiatry* 2007;19(2):137–155.
- Shibre T, Kebede D, Alem A, Negash A, Kibreab S, Fekadu A, Fekadu D, Jacobsson L, Kullgren G. An evaluation of two screening methods to identify cases with schizophrenia and affective disorders in a community survey in Ethiopia, *International Journal of Social Psychiatry* 2002;48(3):200–2008.
- Shibre T, Kebede D, Alem A, Negash A, Deyessa N, Fekadu A, Fekadu D, Jacobsson L, Kullgren G. Schizophrenia: illness impact on family members in a traditional society- in rural Ethiopia, *Social Psychiatry Psychiatric Epidemiology* 2003;38:27–34.
- Sipos A, Rasmussen F, Harrison G, Tynelius P, Lewis G, Leon DA, Gunnell D. Paternal age and schizophrenia: a population based cohort study. *British Medical Journal* 2004;329:1070.
- Selassie S, Gebre A. Rapid assessment of drug abuse in Ethiopia. *Bulletin on Narcotics* 1996;48,53 63.
- Toennes SW, Harder S, Schramm M, Niess C, Kauert GF. Pharmacokinetics of cathinone, cathine and norephedrine after the chewing of khat leaves. *British Journal of Clinical Pharmacology* 2003;56:125–130.
- Tsuang MT, Lyons MJ, Faraone SV. Heterogeneity of schizophrenia. Conceptual models and analytic strategies. *British Journal of Psychiatry* 1990;156:17–26.
- van Os J, Hanssen M, Bijl VR, Vollebergh W. Prevalence of psychotic disorder and community level of psychotic symptoms. *Archives of General Psychiatry* 2001;58:663–8.
- van Os J, Kapur S. Schizophrenia. *Lancet*. 2009;374:635–45.
- Warfa N, Kleinb A, Bhuia K, Leaveyc G, Craig T, Stansfelda SA. Khat use and mental illness: A critical review. *Social Science & Medicine* 2007;65:309–318.

- Wittchen HU, Semler G, von Zerssen D. A comparison of two diagnostic methods. Clinical ICD diagnosis vs DSM-III and RDC using the DIS (version II), *Archives of General Psychiatry* 1985;42:677-84.
- Wittchen HU, Robins LN, Cottler LB, Sartorius N, Burke JD, Regier D, participants in the WHO/ADMHA field trials. Cross-cultural feasibility, reliability, and sources of variance of the composite international diagnostic interview (CIDI). *British Journal of Psychiatry* 1991;159:645-653.
- Wittchen HU. Reliability and validity studies in the WHO-composite international diagnostic interview (CIDI): A critical review. *Journal of Psychiatric Research* 1994;28:57-84.
- World Health Organization. The ICD-10 Classification of Mental and Behavioral Disorders: Clinical Descriptions and Diagnostic Guidelines. WHO, Geneva 1992.
- World Health Organization. Composite international diagnostic interview (core version 2.1). WHO, Geneva 1997a.
- World Health Organization. Schedules for Clinical Assessment in Neuropsychiatry, Version 2.1 (SCAN2.1). WHO, Geneva 1997b.
- Wyatt RJ, Green MF, Tuma AH. Long-term morbidity associated with delayed treatment of first admission schizophrenic patients: a re-analysis of the Camarillo State Hospital data. *Psychological Medicine* 1997;27:261-268.
- Youssef AH, Scully JP, Kinsella A, Waddington JL. Geographical variation in rate of schizophrenia in rural Ireland by place at birth vs place at onset. *Schizophrenia Research* 1999;37:233-43.