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Assessment of Drug Therapy Problems and Associated Factors Among Ambulatory Patients with Schizophrenia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia:

A Cross-Sectional Study

By: Gubae Temtem

A Thesis Submitted to

The Department of Pharmacology and Clinical Pharmacy, School of Pharmacy in Partial Fulfillment of the Requirements for the Degree of Master of Pharmacy in Pharmacy Practice.

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This is to certify that the thesis prepared by Gubae Temtem entitled "Assessment of Drug Therapy Problems and Associated Factors Among Ambulatory Patients with Schizophrenia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia": A Cross-Sectional Study and submitted in partial fulfilment of the requirements for the degree of Master of Pharmacy in Pharmacy Practice complies with respect to originality and quality.

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Abstract

Assessment of Drug Therapy Problems and Associated Factors Among Ambulatory Patients with Schizophrenia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Cross-Sectional Study

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Addis Ababa University, 2018

Among the severe mental disorders schizophrenia is one of the major ones and requires rapid treatment at the early signs of a psychotic incident. In most chronic illness, patients encounter drug therapy problems (DTPs) and if not resolved; the problems may have clinical consequences and causes morbidity, mortality, decreased quality of life, increased health care costs, and can do other harms. Studies regarding DTPs in patients with schizophrenia are insufficient hence; the objective of this study is to assess DTPs and associated factors among ambulatory patients with schizophrenia at Tikur Anbessa Specialized Hospital (TASH). A hospital based cross-sectional study was conducted for a period of 5 months and a total of 118 patients with schizophrenia in psychiatry clinic between July10 and December 8, 2017 were included in the study. The data was then analyzed by using Statistical Package for Social science (SPSS) version 20. The identified DTPs were documented as per the classification of Cipolle. Descriptive statistics, cross-tabulation, binary and multiple logistic regressions were used to analyse the collected patient data and $P < 0.05$ was considered as significance. The findings of this study showed that the prevalence of DTP was 52.50 %. Adverse drug reaction was the most identified DTP followed by dose low and ineffective drug. The most common drug involved in DTP was risperidone. DTP had a significant association with age, source of medication, duration of schizophrenia treatment and number of medications taken by the patient. The prevalence of medication non adherence was 58.5%. Lack of information about drug side effects, drug product unavailability and/or unaffordability, forgetfulness and patient thought being cured or worse were the major reasons for non adherence.

Key words: Schizophrenia**,** Adherence, Drug therapy problems, Antipsychotic medications.

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Abbreviations and acronyms

ADR	Adverse drug reaction
APA	American Psychiatric Association
AOR	Adjusted Odds Ratio
DDI	Drug-drug interaction
DTP	Drug Therapy problem
ECT	Electroconvulsive therapy
EPS	Extrapiramidal symptoms
FDA	US Food and drug administration
FGA	First generation antipsychotics
HAART	Highly Active Antiretroviral Therapy
LAI	Long acting antipsychotic injection
MDD	Major depressive disorder
MMAS	Morisky Medication Adherence Scale
NICE	National Institute for health and clinical Excellence
OAP	Oral antipsychotic
PI	Principal investigators
PRN	When necessary
SD	Standard Deviation
SGA	Second generation antipsychotics
SPSS	Statistical Package for Social Sciences
TASH	Tikur Anbessa Specialized Hospital
TD	Tardive dyskinesias
WHO	World Health Organization

1. Introduction

1.1. Background

Among severe mental disorders schizophrenia is one of the major ones and it is a disabling disorder that requires rapid treatment at the early signs of a psychotic incident (Melle et al., 2006). It is a chronic mental disorder has3 major symptom clusters which are positive, negative and cognitive symptoms (Tandon et al., 2013). Schizophrenia is severe psychiatric disorder hypothesized that an alteration of multiple brain neurotransmitters plays a key role to develop schizophrenia thus number of medications were developed and used targeting these neurotransmitters (Lang et al., 2007).

Previous studies show that occupancy of dopamine 2/3 receptors has been shown to be associated with therapeutic response and neurological adverse effect, adult patients dopamine 2/3 occupancy above 65% with good clinical response and neurological symptoms are more likely to be observed with dopamine 2/3 occupancy above 80%. Hence, dopamine receptor occupancy is therapeutic window that maximizes therapeutic benefits and minimizes adverse effects (Kapur et al., 2000).

In 2017 world health organization (WHO) reported that, schizophrenia affected 21 million people worldwide (WHO, 2017). According to the reports of WHO one in two people living with schizophrenia does not receive treatments. The life-time prevalence of schizophrenia in Ethiopia is estimated to be 0.5%, according to study done at Butajira, Ethiopia (Kebede et al., 2003). In the United States, during 2009-2011, an estimated 382,000 emergency department visits related to schizophrenia occurred among adults aged 18-64, with an overall emergency department visit rate of 20.1 per 10,000 (Albert and McCaig, 2015). In the same country, the annual prevalence of schizophrenia averages 15 per 100,000, the point prevalence averages approximately 4.5 per population of 1000, and the risk of developing the illness over one's lifetime averages 0.7% (Tandon et al., 2008).

Schizophrenia considerably causes higher economic burden hence efforts that focus on measures to reduce the risk of relapse, particularly amongst recently diagnosed patients, such as improved adherence programs, may lead to better clinical and economic outcomes in the management of schizophrenia (Nicholl et al., 2010). Treatment for schizophrenia needs to consider different factors such as, comorbid conditions, past therapeutic response, and

adverse effects, as well as patient choice and expectations from treatment should also be identified and addressed (Kane and Correll, 2010).

There are a number of drugs which are widely used by psychiatrists for treating schizophrenia, and now days the typical antipsychotics are being replaced with atypical antipsychotics more and the atypical antipsychotics are being prescribed more to a much larger and more diverse clinical population (Crystal et al., 2009). Moreover there are individual treatment options and stages of treatment protocols for patients who fail to respond to adequate trials of antipsychotic (Kane et al., 1988). According to the Ethiopian National Drug List Sixth Edition, antipsychotic drugs like Chlorpromazine Hydrochloride, Clozapine, Fluphenazine Decanoate, Fluphenazine Hydrochloride, Haloperidol, Haloperidol Decanoate, Olanzapine, Pimozide, Risperidone, Thioridazine Hydrochloride and Trifluoperazine Hydrochloride are listed medicines to facilitate suitable use and management of the problem (EFMHACA, 2010).

Antipsychotics are associated with therapeutic effect as well as a number of undesired effects like neurological, central nerves system and metabolic or endocrine effects (Ahmad et al., 2016). Patients with schizophrenia are at increased risk of metabolic and other cardiac risk factors, and most antipsychotic drugs also increase the risk of weight gain and metabolic Syndrome (De Hert et al., 2012). For example the well-known atypical anti-psychotic clozapine can cause fatal agranulocytosis that requires immediate medical attention which is age and gender associated (Stahl, 2013). Thus, before treating patients with clozapine, clinicians must consider patients with a clozapine monitoring system and if the patient has a white blood cell count below 2,000 cells per mm^3 or a granulocyte count below 1,000 cells per mm3, clozapine must be switched. So it is important for psychiatrists to be aware of cardio metabolic risks in their patients so that appropriate lifestyle and pharmacologic interventions can be planned(Ayano, 2016).

Drug therapy problem cause significant morbidity and mortality in healthcare as well as increasing cost of care and this also applies to mental health care (Richardson et al., 2014). The pharmaceutical care practitioner is responsible for identifying drug therapy problems which helps the patient to achieve treatment goals and get the best possible out comes from drug therapy (Cipolle et al., 2012). Unfortunately, even in some developed nations, the responsibility of clinical pharmacists in mental health on drug related problems is also under utilized(Richardson et al., 2014).

In 1990 when drug therapy problem investigated, DTP was described and assessed based on indication, effectiveness, safety, and adherence(Strand et al., 1990). The purpose of assessing DTP is to improve an individual patient's quality of life by decreasing medication-related problems and optimizing therapeutic outcome (Cipolle et al., 2012).

1.2. Statement of the problem

Schizophrenia is one of the most severe psychiatric disorders that is associated with a chronic relapsing course and causes human power loss in a significant proportion of patients even if there is treatment advances which significantly change the course and outcome (Kane and Correll, 2010). Patients with schizophrenia have premature mortality outcome which is twice as that of the general population (Fekadu et al., 2015). In rural Ethiopia study by Fekadu *et al* (2015) showed that the commonest cause of premature death associated with schizophrenia were infectious conditions 49.6% because these patients may not complain when they have a problem and these leads to under diagnosed of physical illness and unable to take additional treatments.

In most low and middle income countries mental health services, especially, specialized mental health care are not easily accessible and there are limitation for treatment utilization for people with schizophrenic disorders (Lora et al., 2012). Study done by Lora *et al* (2012) showed that the median value for treatment coverage was 31%, this implies that 69% of the people with schizophrenic disorders were not receiving treatment, about 80% of population were also treated in outpatient facilities even in the most basic mental health care.

Patients with schizophrenia have lack of awareness about their illness due to poor insight, and do not perceive their need for medication and these implies high rates of non-adherence, relapse and worse outcomes of the problem(Aldebot and de Mamani, 2009). There are different factors associated with relapse of schizophrenia where a number of previous hospitalizations and numbers of inappropriate use of different types of antipsychotic drugs were also associated with relapse of schizophrenia (San et al., 2013, Chabungbam et al., 2007). A follow up study in rural Ethiopia on the long-term course and outcome of schizophrenia in Patients with schizophrenia indicated that the outcome result was poor and the percentage of patients experiencing continuous illness was very high where over one third of the patients, 37.8%, had episodic course while 19.0% had continuous psychotic illness and only 11.9% were continuously in full remission following a single episode. Majority of the

patients had at least two relapses during the 10-year follow-up period, 57% of the participants had either episodic course or continuous psychotic symptoms(Shibre et al., 2015).

Study between the periods 1996-1998 and 2010-2012 in the U.S, indicated that there were significant increases in the proportionate use of psychotherapy and psychotropic medications during the study period in which the increments were from 4.2% to 6.0% and from 5.5% to 8.9%, respectively and antipsychotic medications use increased from 0.2% to 1.2% which shows number of medications, complexity of drug regimens and availability of new drug therapies potentially increase the risks of DTP and it indicates that a potential concern about the quality of care (Olfson et al., 2015). The use of second-generation antipsychotics(SGA) nearly tripled from 1995 to 2008 in the United States, more than 16 million prescriptions for drugs such as aripiprazole, clozapine and quetiapine, where more than half of those prescriptions in 2008 were for uses with uncertain scientific evidence, according to a study from Stanford University and the University of Chicago based on more than 1,700 physician surveys(Smith, 2012).

A cross-sectional study conducted in Southwest Ethiopia: showed that Psychotic relapse was high for those patients compliant to medication 69 % lower than that of patients who were not compliant to medications (Fikreyesus et al., 2016). In a person with schizophrenia adherence to medication is the main confront to the effectiveness of antipsychotic medications there are different factors for patients to be non-adherence, a qualitative study in butajira Ethiopia showed that; Economic factors, family support in the care of patients, lack of knowledge about the nature of the illness, substance use, Stigma, lack of insight and medication side effects were the major factors considered to be most important for non adherence. For this reason ensuring treatment adherence is associated with better clinical outcome(Teferra et al., 2013).

In most chronic illness patients encounter DTPs hence if it is not resolved, the problems have clinical consequences and causes morbidity, mortality, decreased quality of life, increased health care costs, and can do other harms (Dalton and Byrne, 2017). Therefore every healthcare practitioner is responsible for helping patients with problems that require a certain level of professional activity to identify, prevent, or resolve such kind of DTP (Cipolle et al., 2012).

Studies regarding DTPs in patients with schizophrenia are limited in Ethiopia hence the principal aim of this study is to identify DTPs and medication adherence, which influence treatment outcome. The thesis may be useful to other researchers as a baseline reference material while conducting further studies on related topics. The findings of this study might also help to influence the development of treatment guidelines and policies for the prevention and management of DTP in patients with schizophrenia. This in turn, may help to facilitate the rational use of the drugs to get the best possible outcomes from drug therapy and improves the management of schizophrenia and help patients to achieve their goals of therapy.

1.3. Literature Review

1.3.1. Schizophrenia

Schizophrenia is the major and the most important form of psychotic illnesses, with a group of heterogeneous conditions that affects a person's thoughts, feelings and behaviour can be occurred by various causes such as environmental and genetic factors (Howes and Kapur, 2009). It is believed to be caused by an imbalance in the brain's natural neurotransmitters or chemicals (Rapoport et al., 2012). According to Rapoport *et al* (2012) described that psychosis is the result of a deviation in neurodevelopmental processes that begins before the onset of symptoms. Persons with schizophrenia may not have the same manifestation that can have different combination of symptoms, different severity, different responses to different treatments and different intervals of symptoms occurrence (Keshavan et al., 2011, Lally and MacCabe, 2015).

1.3.2. Treatment of schizophrenia

Schizophrenia is treatable with both pharmacological and psychotherapy. Antipsychotic drugs are the mainstay of treatment for patients with schizophrenia therefore patients should get timely and standard antipsychotic treatment from the mental health care providers (Anderson and Kurdyak, 2017, Lally and MacCabe, 2015). In Australia a cohort study by McMillan *et al* (2017) showed the most common antipsychotic drug prescribed was risperidone oral and LAI (long acting injection) which were 31% among the total prescription.

Ethiopian standard treatment guidelines for tertiary hospital for the management of schizophrenia could not be found for this study; however different countries suggested standard guidelines/algorithms for the management of schizophrenia like American Psychiatric Association Practice Guideline for the Treatment of Patients with schizophrenia (APA**)**(Lehman et al., 2004), National Institute for Health and Clinical Excellence (NICE) schizophrenia guideline from the United Kingdom, The Maudsley Prescribing Guidelines in Psychiatry (Taylor David, 2015), Texas medical algorithm project procedural manual(Argo et al., 2008),Scottish Intercollegiate Guidelines Network (SIGN).Management of schizophrenia. Edinburgh: SIGN; 2013 and these all protocols have analogous schizophrenia management guidelines scope, focus, goals and medication management protocols. The Texas Medication

Algorithm project has provided a six-stage pharmacotherapeutic algorithm for the treatment of schizophrenia (Argo et al., 2008). (Table 1)

Table 1: Texas Medication Algorithm treatment protocols for patients with schizophrenia

Treatment stage	**Treatment recommendation**	**Treatment response**
Adequate dose titration and treatment duration should be assessed and how well the patient has respond to the chosen treatment should be evaluated		
Stage 1	First episode schizophrenia • Trial of a single (second generation antipsychotic) SGA	• Full response- continue the treatment • No response or partial response go to stage 2
Stage 2	• Monotherapy with one of the second generation antipsychotic not tried during stage one or with a first generation antipsychotic	• Full response- continue the treatment • No response or partial response go to stage 3
Stage 3	• Clozapine trial It is effective in treatment resistance schizophrenia and in patients having a history of comorbid substance abuse, sucidality or violence, persistence positive symptoms greater than two years independent of presiding antipsychotic trials.	• Full response- continue the treatment • No response or partial response reexamine the diagnosis and check for substance abuse, medication adherence and psychosocial stress then go to stage 4
Stage 4	Clozapine Augmentation Clozapine plus one of ➢ FGA(First generation antipsychotic) ➢ SGA ➢ ECT(Electroconvulsive therapy)	• Full response- continue the treatment • No response or partial response go to stage 5
Stage 5	Monotherapy with a FGA or SGA antipsychotic that was not tried at stage one or two	• Full response- continue the treatment • No response or partial response go to stage 5
Stage 6	Combination of therapy with SGA plus FGA plus a combination of ECT or another agent such as a mood stabilizer.	

Different guidelines and literatures recommend that antipsychotics should be used at lower effective doses based on individual responses and tolerability of patient in a different treatment phases(McGorry et al., 2011, Lehman et al., 2004). Different guidelines and studies

revealed that risperidone at dose of (2–4 mg/day) is an effective initial treatment choice, although dosage adjustments may be required for those special populations(McGorry et al., 2011). And some standard textbooks lowered the dose of risperidone to 1mg (Kaplan, 2015).

The recommendation to the patient who does not have a response with antipsychotic treatment at 4–6 weeks is to switch to other antipsychotic medication from different class or the same class (Taylor David, 2015, Lehman et al., 2004). A review on atypical antipsychotics reviewed that one of risk factor for poor efficacy and effectiveness of antipsychotic is early non response to treatment and hence switching or augmenting antipsychotic treatment in patients showing early non response helps to improve the probability of later treatment outcomes (Murray et al., 2017). A retrospective cohort study from 2001 to 2009 was done to examine treatment outcomes in patients with schizophrenia, and it states that if there is a justification of treatment resistance for patients with schizophrenia, initiating clozapine was more effective than initiating a regular antipsychotic medication, since patients put on clozapine had lower rates of hospital admission antipsychotic discontinuation, than patients put on other antipsychotic medications (Stroup et al., 2015).

A number of treatment guidelines for schizophrenia recommend antipsychotic combination is considered only based on clear justifications and circumstances like when the patient fails to respond to sequential monotherapy, if the patient is not responding well with clozapine, and other justifiable circumstance like, during cross-titration or as needed for breakthrough symptoms and in most of the cases, treatment should return to antipsychotic monotherapy as soon as the situation becomes stable (Taylor David, 2015, Lehman et al., 2004).

A retrospective cohort study was done to compare the effects of FGA-LAI and SGA-LAI versus an oral antipsychotic (OAP). The results found that patients on SGA-LAI were more adherent and persistent to their medication and less likely to use another antipsychotic medication than patients on OAP. While there was no clear information if such difference was seen on patients on FGA-LAI, however FGA-LAI patients were more likely to have antipsychotic polypharmacy compared to OAP patients(Pilon et al., 2017).

1.3.3. Prevalence of DTP in patients with schizophrenia

Several drug therapy problem classifications have been proposed and described in the literature. Most of these hold the assessment of indication, effectiveness, safety, and

adherence. According to Cipolle *et al* (2012) drug therapy problem can be categorized as 7 categories (Table2).

Table 2: Drug Therapy Problems According to Cipolle Classification

	Drug therapy Problems	**Categories of drug therapy problems**
1	Indication	Unnecessary drug therapy
2		Needs additional drug therapy
3	Effectiveness	Ineffective drug
4		Dosage too low
5	Safety	Adverse drug reaction
6		Dosage too high
7	Adherence	Non adherence or noncompliance

A complete DTP components data among patients with schizophrenia couldn't be found for this study although; there are studies which were done on some components of the DTPs.

Several studies also revealed that antipsychotic drug prescribing in different settings were constantly differing from recommended guidelines which were stated in different studies (Ramadas et al., 2010, McMillan et al., 2017, Kogut et al., 2005, Choi et al., 2011). A study in the US found out that almost 40% of people with first-episode psychosis in community mental health clinics were receiving medications incompatible with guidelines; thus by correcting their drug treatment modalities patients could be benefited to get in to remission (Robinson et al., 2015).

Study done by Schill and Olsson (2016) on the doses of antipsychotics given by 22 psychiatrists to 20 stable outpatients with schizophrenia, the dose of antipsychotics given to a patient was subjective to the doctor they meet rather than the severity of the disease. The study shows psychiatrists considered 4.45 mg/day of haloperidol to be clinically equivalent to 20 mg/day of olanzapine which is a lower dose than determined by an international consensus study of antipsychotic dosing (Schill and Olsson, 2016).

A national audit in England and Wales in 2014 on six antipsychotic prescribing standards antipsychotic monotherapy, dose, adherence and substance misuse, adequate trials, clozapine and clozapine augmentation revealed that of the total sample, antipsychotic polypharmacy occurred in 15.9% from those clozapine augmentations was 5.3%, high dose was 10.1% where only 25.2% of high dose prescribed had documented justification. Medication

adherence was reported as having been investigated in 85.6% of those and not on clozapine and in 87.8% of those on clozapine, 34(9.4%) cases has appeared to have only received one antipsychotic prior to start clozapine,72.1% of cases had received antipsychotic at optimal dose for at least four weeks. Of these, 84.8% had received a different antipsychotic at optimal dose for at least four weeks a delayed time to initiate clozapine. As a result the audit revealed that there were a significant number of variations with standards of NICE guidance (Patel et al., 2014).

Retrospective cohort study done on clinical audit of antipsychotic in Australia showed 62.5% patients were discharged on a single antipsychotic within the recommended dose range and on the other hand 15.5% patients had antipsychotic combinations and high-dose treatment were not in line with clinical guidelines and recommendations(McMillan et al., 2017). According to Study done in India Antipsychotic Prescription Pattern of Patients with schizophrenia, 4% of patients had received high dose of antipsychotics, 31% of patients were on combination of typical and atypical antipsychotics and 24% of patients were receiving low doses, when compared with Maudsley and national guidelines (Ramadas et al., 2010). Cohort study which was done by McMillan *et al* (2017) in Australia indicates that a considerable amount of, antipsychotic prescribing did not align with clinical guidelines in particular poly pharmacy 32.5%, and antipsychotic high-dose 20.5%,was seen.

A systematic review on longitudinal study antipsychotic prescriptions by Tsutsumi *et al* (2011) in Japan reviewed that physicians switch antipsychotics without adjusting entire dose range and chose to prescribe antipsychotic polypharmacy without trying an adequate number of antipsychotics. There was 27.4% antipsychotic switch the reason provided for 47.4% of the antipsychotic switch was ineffectiveness and this happened despite the fact that the monotherapy dose was below the suggested range; polypharmacy was 17.8% within 2 years period (Tsutsumi et al., 2011).

Amongst the most common challenges with antipsychotic medications use was the side effects of the medications. Antipsychotic medications are associated with neurological, metabolic and other side effects (Lehman et al., 2004, Ahmad et al., 2016). Observational study done in united Arab emirates (UAE) on adverse drug reactions (ADR) in psychiatry outpatient department in 2016, the occurrence rate of ADR was found to be 10.2%, weight gain was 18 (16.07%) followed by somnolence 8 (7.14%) were the most often reported ADR and majority of the cases the drug was withdrawn 46 (41.1%) to manage ADRs (Sridhar et

al., 2016). Observational study in 2017 at tertiary care center psychiatry outpatient department had reported overall incidence rate of ADRs were 6.41%, and central nervous system 46.73% were the most often indicated ADR (Gawali et al., 2017).

In the United States, a cohort study shows the association of age and psychotropic prescription patterns among schizophrenia and schizoaffective patients. Adults ages 35–49 were less likely to fill prescriptions for antidepressants than younger and older age groups whereas use of sedative/hypnotics has increased with age, however the use of mood stabilizers decreased with age (Stroup et al., 2018).

Most antipsychotics use is not recommended during Pregnancy. Study in the United States on pregnant women on antipsychotic medication indicated the frequency of use of second-generation antipsychotics at any time during pregnancy increased threefold, from 0.4% to 1.3%, over the ten-year period, while the use of first-generation antipsychotics remained stable at around 0.1% (Park et al., 2017).

In 2001 WHO reported that adherence to long-term therapy for chronic illnesses in developing countries were lower than 50% (WHO, 2001). A study done in Gondar University Hospital, Northwest Ethiopia on psychiatric patients rate of non-adherence to antipsychotic medications, patients with schizophrenia were found to be the most non adherent 75.7% and different variables such as age, medication regimen, income, educational status, marital status, and occupational status of the respondents($P > 0.05$) were not significantly associated with non-adherence (Endale Gurmu et al., 2014). Antipsychotic ADRs can cause patients not to adhere to the treatment plan, according to a cross-sectional nationwide study done by DiBonaventura *et al* (2012) extra pyramidal symptoms (EPS)/agitation, sedation/cognition, prolactin/endocrine and metabolic side effects were significantly associated with non-adherence.

A systemic review showed that there are different factors which affected medication adherence for chronic illness, such as socio-economic-related factors, health care team and system-related factors, condition-related factors, therapy-related factors, and patient-related factors(Kardas et al., 2013). A study done on factors associated with medication adherence among patients with schizophrenia in Northern Ethiopia, positive attitude to medication and illness insight had positive association with adherence (Eticha et al., 2015). According to the study patients with schizophrenia also showed that fewer side effects had positive association

with adherence and other factors like khat chewers being illiterate and older age group had negatively associated with medication adherence (Eticha et al., 2015).

Pharmacists have a role and responsibility in the management and patient care for patients with schizophrenia. Since pharmacists have the training in the area of drug related problems and drug therapy management, a well-trained and expert pharmacists can take an active role in the mental health care management team (Rubio-Valera et al., 2014). A study in Belgium by Somers *et al* (2013), in a geriatric ward, 304 drug therapy problems were identified by a clinical pharmacist and the most common drug-related problems were, inappropriate dose 31%, drug–drug interaction 20%, and adverse drug reaction 15%.

2. Objective of the study

2.1. General objective

To assess drug therapy problems, medication adherence and associated factors among ambulatory patients with schizophrenia at TASH

2.2. Specific objectives

- To determine the prevalence of DTP among ambulatory patients with schizophrenia at TASH.
- To identify associated factors of DTP for patients with schizophrenia at TASH.
- To determine the most common drugs involved in DTP for patients with schizophrenia at TASH.
- To assess treatment adherence for patients with schizophrenia at TASH.
- To identify associated factors of non adherence for patients with schizophrenia at TASH.

3. Methods

3.1. Study Setting

The study was conducted at TASH, Addis Ababa, Ethiopia. Tikur Anbessa Specialized Hospital is one of the biggest, teaching referral governmental hospital in the country affiliated with Addis Ababa University. The psychiatry unit provides service to the public with senior and resident psychiatry specialists and it is one of the specialty clinics in TASH. Within one year period 230 patients with schizophrenia were treated and the clinic provides service for all mental illness 4 days per week in the morning time. On average 30 patients with different types of mental illness visited per day and a total of 2000 patients expected to visit the clinic within the five month study period.

3.2. Study design and period

This study was institution based cross-sectional study involving chart review and patient interview at psychiatric clinic, ambulatory patients with schizophrenia. Data collection was done for 5 months from July to December 2017. All of the sample populations were screened for DTPs.

3.3. Population

3.3.1. Source population

The source population of the study was all patients with schizophrenia attending the hospital.

3.3.2. Study population

The study population was all patients with schizophrenia that visit the hospital between July10 and December 8, 2017.

3.4. Eligibility criteria

3.4.1. Inclusion criteria

- Patients who were 14 years and above with schizophrenia on treatment follow up at psychiatry clinic.
- Patients who had been on for at least two months on treatment with antipsychotic medication.
- Patients who had complete registration charts
- Patients who consented and who gave assent to participate in the study

3.4.2. Exclusion criteria

- Patients who had emergency condition such as current aggravated and unconscious condition and capable of impairing response.

3.5. Sampling method

All patients with schizophrenia in psychiatry clinic of TASH between July10 and December 8, 2017 and who fulfilled the inclusion criteria were candidates for the study. Since schizophrenia is less frequent case than other cases (within one year period, September 2016-September 2017, 230 patients with schizophrenia were treated in TASH) all available samples based on available patient flow during study period were consecutively taken. Of those 230 patients, 56% (129) that were treated from July 10 – December 8, 2017 were taken as study participants. During the five month data collection period, daily participants were used and similar or repeated visitors were not counted again in the sample. So the total candidates for study after the inclusion criteria were 123 patients. Among the eligible participants 5 were excluded because of incompleteness of their personal data, the data of 118 subjects was finally analyzed.

3.6. Study variables

3.6.1. Dependent variable

- Drug therapy problems
- Adherence

3.6.2. Independent variables

- Socio-demographic information such as (age, sex, marital status, educational background, etc.)
- Clinical characteristics such as **(**Duration of treatment, Number of drugs, Presence of co morbidity, Presence of ADR(in the case of adherence)

3.7. Data collection Instruments and procedure

A well-structured standard checklist and questionnaire was used to collect relevant information from patients and patient charts. The relevant information about each patient (socio demographic and patient's clinical characteristics) was collected from patient interview questionnaire (annex II). The records were retrospectively reviewed for laboratory

results, current medications, comorbidities with their treatment, relevant previous medical and medication histories and ADR were collected using data abstraction format from chart (annex II).

For data collection a psychiatry nurses were recruited for patient interview and the principal investigator (PI) and one clinical pharmacist were involved in chart review. The actual DTPs were identified by the PI.

Appropriateness of medical therapy was evaluated using various references and guidelines. Micromedex® drug interaction checker was used to identify drug-drug interactions and absolute contraindications and major drug interaction were selected as a significant drug interaction, whereas moderate and minor interactions were omitted.

The identified DTP was documented as per the classification of Cipolle (modified) (Cipolle et al., 2012). Adherence was measured using validated Morisky Medication Adherence Scale-8(AnnexII, Part-lll). The MMAS-8 is a generic self-reported, medication-taking behavior scale, used for a wide variety of medical conditions. In this study, the questionnaire was prepared in English and translated to Amharic and back-translated to English to check consistency.

The existence of DTP was assessed based on established standard guidelines like American psychiatric association practice guidelines for the treatment of patients with schizophrenia**,** The Maudsley Prescribing Guidelines in Psychiatry, Texas medical algorithm project procedural manual and standard book like Kaplan BJ. Kaplan and Sadocks Synopsis of psychiatry which is intended to serve as guide that can aid in the treatment of mental disorders and also it is a tool for clinicians, an essential educational resource for students and practitioners.

3.8. Data Quality Assurance

Before the actual data collection process, pretest was done to ensure the appropriateness of the data collection instruments. One full day training was given to the data collectors to familiarize them with the data collection instrument as well as how to collect the necessary data from charts and conduct patient interview. The PI closely supervised the data collection process and the collected data was checked on daily basis during data collection.

3.9. Data Analysis

The raw data collected from all the participants was checked for appropriateness and quality before data entry. The data wasthen entered by using Epi Info version 7.2.1 and statistical package for social science (SPSS) version 20 was used to analyze the data obtained.

Descriptive statistics such as frequency, percentage, mean and standard deviation (SD) were used to summarize patients' characteristics. Tables and charts were used to present the results. Univariate binary logistic regression analysis was performed to relate each dependent variable to DTPs and adherence. Among the univariate analysis, those variables with $p< 0.20$ were selected for multi-variable binary logistic regression analysis. Multi-variable binary logistic regression analysis was used to assess predictability of the dependent variables DTPs and medication adherence. P value < 0.05 was considered statistically significant. Drug risk ratio (frequency of involvement in DTP divided by frequency of prescription) was used to identify drugs that were prone to create DTP.

3.10. Ethical considerations

This study was conducted after obtaining letter of ethical clearance from ethical review committee of AAU (002/17/SPharma), CHS and Permission from departmentof Psychiatry. Written and Verbal informed consent and/or assent were obtained from each study participants and their care givers/family to participate for the interview and to extract data from their medical charts. Patients were informed about the objective of the study and they were told that they have full right to refuse their participation at any time, and this by no means affects the service they get from the institution. Information about the study was given to the health facility and assured about the human subjects' protection. Privacy and confidentiality was ensured during patient interview and review of patient medical charts. Thus, name and address of the patient was not recorded in the data abstraction formats.

3.11. Operational Definitions

Additional drug therapy: Additional drug therapy is required to treat or prevent a medical condition in the patient.

Adherent: If the MMAS - 8 score was ≤ 2.

Non-adherent: If the MMAS - 8 score was > 2.

Adverse Drug Reaction: The drug product causes an undesirable reaction; a safer drug product is required due to risk factors, the drug product causes an allergic reaction and the drug product is contraindicated due to risk factors.

Antipsychotic poly pharmacy: Two or more combination of antipsychotic drugs prescribed at the same time.

Dose High: Dosage is high, need additional monitoring to determine if dosage is too high, the dosing frequency is too short, the duration of drug therapy is too long.

Dose low: The dosage is low to produce the desired response in the Patient, the dosing frequency is long and the duration of drug therapy is short.

DTP: is any undesirable event experienced by a patient that involves, or is suspected to involve, drug therapy, and that interferes with achieving the desired goals of therapy and requires professional judgment to resolve.

Duplicate therapy: multiple drug products are being used for a condition that requires only single drug therapy.

Ineffective Drug: The drug product is not being effective or suboptimal efficacy at producing the desired response in the patient, the dosage form of the drug product is inappropriate.

4. Results

4.1. Socio Demographic and Clinical Characteristics of the Study Participants

A total of 123 patients were enrolled during the study period where all available participants were used and 5 were excluded because of incompleteness of their personal data. Finally, the data of 118 subjects was studied.

The mean age of the participants was 34.04 ±11.5 years and more than half of them 53.4% were between the ages of 25-39. Majority of them 70.3% were male and regarding their education status 77% of them had secondary and higher than secondary educational level. Concerning medication cost coverage 80.5% of the study participants got their medication by payment. About 35.6% of them had substance abuse related problems like Alcohol 5.1%, Cigarette 14.4% and Kath 16.1% (Table3).

Table 3: Socio demographic characteristics of patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

Variable	Category	Number (%)	Mean (SD)	Range
Sex	Male	83 (70.3)		
	Female	35 (29.7)		
Age group	14-24	20 (16.9)	34.04 (11.5)	17 – 72
	25-39	63 (53.4)		
	40-64	32 (27.1)		
	≥65	3 (2.5)		
Marital status	Single	76(64.4)		
	Married	34(28.8)		
	Divorced	7(5.9)		
	Widowed	1(0.8)		
Source of medication	Free	23 (19.5)		
	Paid	95 (80.5)		
Substance use	Alcohol use	6 (5.1)		
	Kath use	19 (16.1)		
	Cigarette smoking	17 (14.4)		
Educational status	No formal education	3 (2.5)		
	Primary	24 (20.3)		
	Secondary	42 (35.6)		
	Tertiary	49(41.5)		

In the case of the duration of schizophrenia treatment, about 45.8% of the study participants were on treatment for 1 to 5 years and 37.3% of them had frequent follow up every month. And 67.8% of the study participants were taking one medicine with mean and SD of 1.54 (0.993) medications per day (Table 4).

Table 4: Clinical characteristics of patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

Clinical characteristics	Category	Number (%)	Mean (SD)
Co morbidity	No	87 (73.7)	
	Yes	31 (26.3)	
Number of co morbidity	No	87 (73.7)	0.32 (0.58)
	One	24 (20.3)	
	Two or more than two	7 (5.9)	
Duration of schizophrenia treatment	<1 year	24 (20.3)	
	1-5 years	54 (45.8)	
	>5 years	40 (33.9)	
Frequency of follow up	< 1 month	7 (5.9)	
	Every month	44 (37.3)	
	Every two months	26 (22.0)	
	Other	41 (34.7)	
Number of drug ordered	1 drug	80 (67.8)	1.32(0.47) Range of (1-7) drugs
	>2 drug	38 (32.2)	

Of the total study participants, one fourth (26.3%) of the study participants had comorbid conditions and the common comorbidities identified were MDD 11.9% and neurological problems were 10.2% (figure 1).

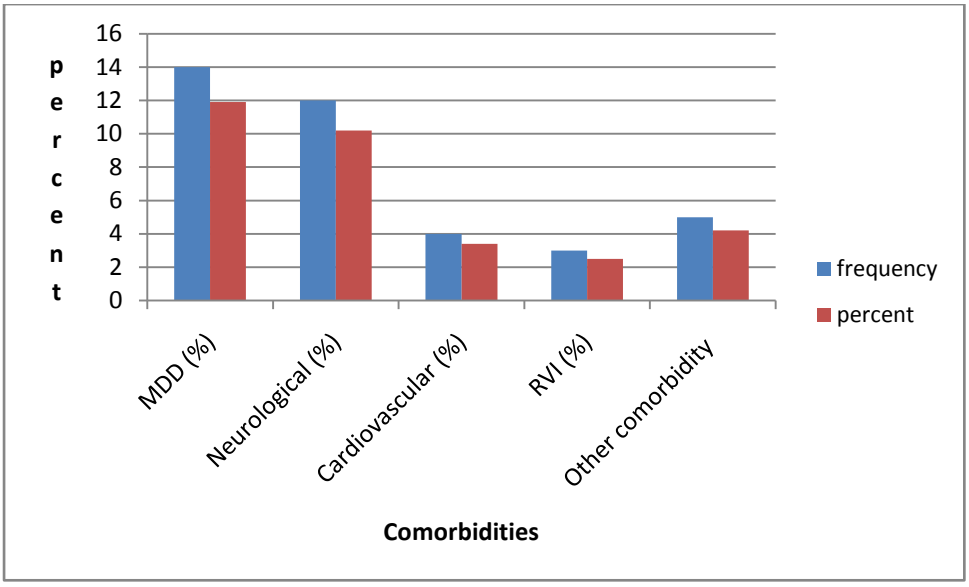


Figure 1: Common comorbidities to schizophrenia patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

Other comorbidity* - metabolic, hepatic problem, renal problem

4.2. Pattern of Antipsychotic Drug Uses among the Study Participants

Risperidone was the primarily preferred antipsychotic drug for prescription and was prescribed for 47% of the patients followed by Fluphenazine depot 7.7%. Most of the study participants 91.5% were prescribed an oral antipsychotic (Table 5).

Table 5: The most common drug prescribed for patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

Most common drug prescribed	Frequencies		
		N	(%)
The most common drug prescribed	Risperidone	79	47.0%
	Fluphenazine depot	13	7.7%
	Chlorpromazine	12	7.1%
	Haloperidol	11	6.5%
	Olanzapine	5	3.0%
	Thioridazine	1	0.6%
	Trifluperazine	1	0.6%
	Trihexyphenidyl	9	5.4%
	Clonazepam	4	2.4%
	Carbamazepine	3	1.8%
	Fluoxetin	9	5.4%
	Other medication*	21	12.5%
Total		168	100.0%

Other medication*– (Cardiovascular drugs, Drugs used for diabetic and metabolic conditions, drugs for neurological problems, HAART)

4.3. Identified Drug Therapy Problems

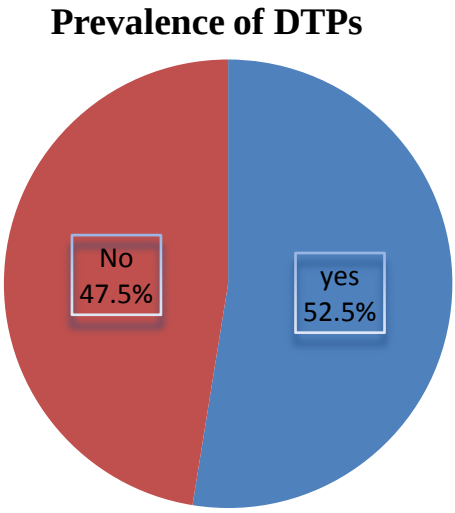


Figure 2: Proportion of DTPs among patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

As indicated in figure 2 DTPs were found in 52.5 % of the study subjects. A total of 88 DTPs were identified from 62 study participants. The most common DTP categories identified in this study were ADRs 26.1%, dose low 20.5%, ineffective drug 20.5% followed by drug interaction18.2% (Table 6). In this study neurological movement disorders mainly tardive dyskinesias (TD) occurred in 5(4.2%) patients. Among these patients one DTP was identified in 42(35.6), two DTPs in 14(11.9%) and three DTPs in 6(5.1%). From the total study participants the average number of DTPs per patient was 0.75.

Table 6: Magnitude of specific DTPs among patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

Type of DTP	Magnitude of specific DTPs	Number of DTP	Total	(%)
Dose low	Dose low	18	18	20.5
Dose high	Dose high	2	2	2.3
Drug Interaction	Drug interactions	16	16	18.2
Unnecessary drug therapy	Duplicate therapy	3	4	4.5
	Non drug therapy indicated	1		
Need additional therapy	Untreated medical condition	7	7	8.0
Ineffective drug	More effective alternative	10	18	20.5
	Dosage form inappropriate	8		
Adverse drug reaction	Undesired effect	14	23	26.1
	Contraindication present	1		
	Unsafe drug for patient	8		
Total			88	100

4.4. Drugs involved in specific type of DTP

In this study from the total DTPs identified dose-low was seen in the drugs prescribed in which risperidone 6.8%, haloperidol 5.7%, fluphenazine depot and chlorpromazine 3.4% (Table 7). The most identified drug interaction occurred between risperidone and fluoxetin 7 drug interaction 44% out of the total drug interaction was between these two drugs.

Haloperidol drug risk ratio is 1.09, chlorpromazine drug risk ratio is 0.75 and fluphenazine depot drug risk ratio is 0.54 were drugs with the highest drug risk ratio. All of these drugs had a risk ratio of above 0.5 which indicates that DTP may occur in half of the times these drugs are used. Haloperidol is one of the drugs with a higher drug risk ratio. In the contrary risperidone drug risk ratio is 0.11 the most commonly used drug with the lowest drug risk ratio.

Table 7: Antipsychotic medications in relation to their specific DTPs among patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

Major Drugs involved in specific type of DTP								
DTP	**Risperidone**		**Fluphenazine depot**		**chlorpromazine**		**Haloperidol**	
	N	%	N	%	N	%	N	%
Dose low	6	10.70	3	37.50	3	30.00	5	38.50
Dose high	2	3.60	1	12.50				
Non drug therapy indicated							1	7.70
Duplicate therapy	1	1.80	2	25.00	2	20.00		
Untreated medical condition	4	7.10	1	12.50	1	10.00	1	7.70
More effective alternative is available	8	14.30	1	12.50			1	7.70
Dosage form inappropriate	6	10.70					1	7.70
Undesired effect	9	16.10			2	20.00	2	15.40
Unsafe drug for patient	7	12.5			1	10.00		
Contraindication present							1	7.70
Drug interactions	13	23.20			1	10.00	1	7.70
Total	56	100	8	100	10	100	13	100

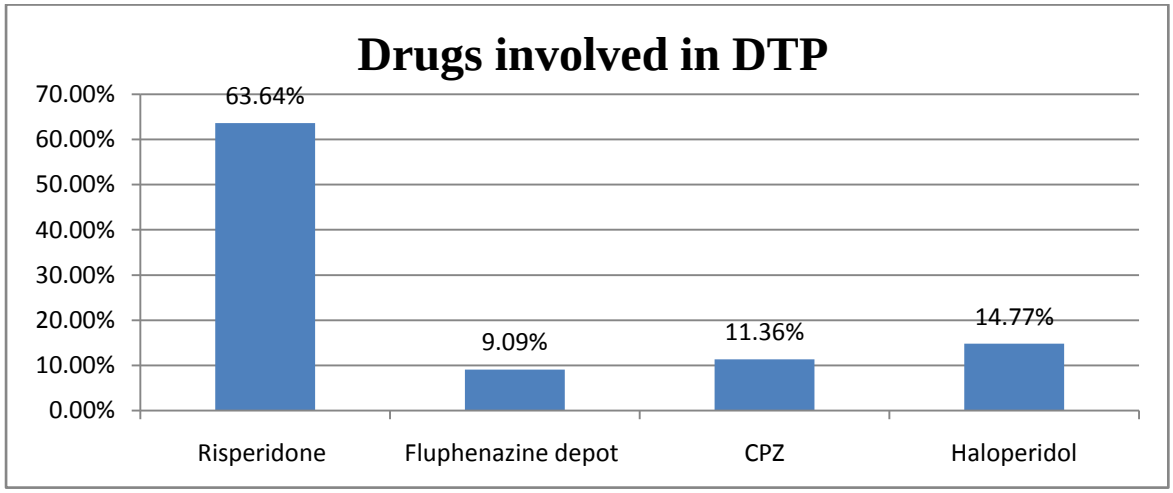


Figure 3: Drugs involved in DTPs among patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

4.5. Predictors of Occurrence of Drug Therapy Problems

Risk factors for DTPs that fulfilled the criteria for multi-variable logistic regression analysis among the univariate analysis, those variables with p<0.2 include age, source of medication, comorbidity, cigarette smoker, khat chewer, total number of medication and duration of schizophrenia treatments. In this study age, source of medication that had got a drug for free or payment, duration of schizophrenia treatment and number of drug prescribed were considered as a risk factor for the occurrence of DTP.

As age increases from (14-24) age group to (40-64) and (>65) significantly associated with DTP (p 0.014) and (0.030) respectively. Patients between the ages of (40-64) were 7 (0.144) times less likely to develop DTPs compared to age group (14-24) and patients at the ages of >65, were 22.7 (0.044) times less likely to have DTP it seems that there are negative association between age and DTP which implies the higher the age of the patient less likely for the occurrence of DTP. Source of medication had also associated with DTP (p<0.024), patients who have got medication by payment OR 0.24, 4 times less likely to develop DTPs compared with those who has gotten by free. The other risk factor for the occurrence of DTP was duration of schizophrenia treatment in which as the duration of treatment increases it is positively associated with DTP. When the duration of treatment is >5 years (p<0.013) the patient is 5.8 times more likely to develop DTP compared with those who have been on treatment less than one year. This indicates as the number of physician visit increases incidence of DTP also increases because more documented patient and medication history can be found. On this study the number of drug prescribed at a time was also had statistically significant association with DTP patients who took two and more than two medications were 6 times more likely to develop DTP than those who took one medicine per day (p value 0.007). (Table 8)

Table 8: Predictors for the occurrence of DTPs among patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

Variable	category	Drug-therapy Problem (%)		COR (95%CI)	AOR (95%CI)	p value
		No	Yes			
Age	14-24	9(16.1)	11(17.7)	1	1	
	25-39	29(51.8)	36(58.1)	0.83(0.30-2.32)	0.535(0.152-1.886)	0.33
	40-64	16(28.6)	14(22.6)	0.52(0.17-1.61)	0.144(0.031-0.671)	0.014*
	≥ 65	2(3.6)	1(1.6)	0.33(0.03-4.32)	0.044(0.003-0.741)	0.030*
Cigarette	No	44(78.6)	57(91.9)	1	1	
smoker	Yes	12(21.4)	5(8.1)	0.322(0.105-0.98)	0.499(0.099-2.521)	0.400
Khat chewer	No	43 (76.8)	56 (90.3)	1	1	
	Yes	13 (23.2)	6 (9.7)	0.35(0.125-1.01)	0.774(0.165-3.624)	0.745
Source of	Free	5 (8.9)	18 (29.0)	1	1	
Medication	Paid	51 (91.1)	44 (71.0)	0.24(0.08-0.70)	0.241(0.070-0.826)	0.024*
Duration of	<1 year	16 (28.6)	8 (12.9)	1	1	
schizophrenia	1-5 years	23 (41.1)	31 (50)	2.70(0.99-7.37)	2.303(0.681-7.781)	0.179
Treatment	>5 years	17 (30.4)	23 (37.1)	2.70(0.94-7.77)	5.820(1.451-23.342)	0.013*
Comorbidity	No	47 (83.9)	40 (64.5)	1	1	
	Yes	9 (16.1)	22(35.5)	2.87(1.19-6.94)	1.270(0.319-5.063)	0.734
Number of	1 Drug	47 (83.9)	33 (53.2)	1	1	
Drug	≥ 2 Drugs	9 (16.1)	29 (46.8)	4.59 (1.92-10.96)	5.936(1.623-21.713)	0.007*
prescribed						

4.6. Adherence Status and Identified Reasons for Non Adherence

Adherence status using the Morisky scale revealed that 69(58.5%) of the participants had poor adherence, while 35(29.7%) of them had medium and 14(11.9%) of them had good adherence.

For the purpose of data analysis, the original three categories of adherence were re-categorized in to two. High and medium adherence were re-assigned as adherent with a score of less than or equal to two and low adherence was regarded as non-adherent with a score of greater than two.

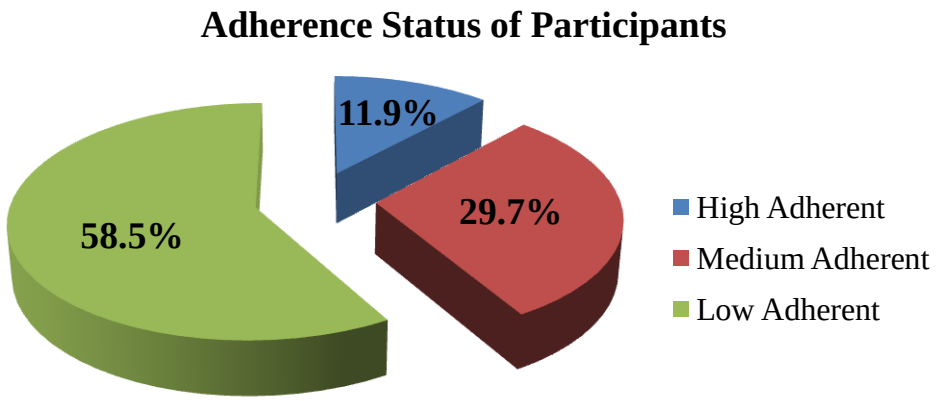


Figure 4: proportion of adherence among patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

The reason for poor adherence were lack of information about drug side effects, drug product not available/not affordable, forgetfulness, patient thought like feeling cured or worse and patients that were not following the appointments properly (Table 9).

Table 9: Reasons for Non-adherence among patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

	Reason for non-adherence	Number	Present (%)	
1	Forgetfulness	56	15	Patient
2	Patients didn't follow the appointments properly (Poor follow-up by Patients)	43	11.5	Related factors.
3	Patient felt better	49	13.2	
4	Patient felt worse	46	12.4	
5	Drug product not available/not affordable	64	17.2	Health
6	Lack of information about the side effects of the drug(healthcare provider-patient relationship)	93	25	Care team And system
7	Unclear information about proper drug usage (Directions not understood)	20	5.4	related factors
	Total	371	100	

4.7. Predictors of Non-adherence

On this study educational status was associated with adherence status and as the education of the patient increases from primary and less than primary level to secondary and higher than secondary level the patient was 4(0.263) times less likely to be non-adherent (p<0.014) (0.090-0.767).

Table 10: Predictors for the occurrence of non-adherence among patients with schizophrenia attending at psychiatry clinic of Tikur Anbessa Specialized Hospital, July10 - December 8, 2017

Variable	category	Adherence status		COR(95%CI)	AOR(95%CI)	p value
		Adherent	Non-adherent			
Khat chewer	Not chewer	45(91.8)	54(78.3)	1	1	
	Current chewer	4(8.2)	15(21.7)	3.13(0.97-10.1)	2.70(0.81-8.97)	0.105
Undesired effect	no	40(81.6)	64(92.8)	1	1	
	yes	9 (18.4)	5 (7.2)	0.35(0.10-0.11)	0.40(0.12-1.38)	0.147
Educational status	Primary and Lower than primary	5(10.2)	22 (31.9)	1	1	
	Secondary and Higher than secondary	44(89.8)	47 (68.1)	0.24(0.09-0.70)	0.26(0.09-0.77)	0.014*

4.8. Examples of Drug Therapy Problems Identified in the Study Subjects

Besides quantitative analysis, document report was made on each study participant in the patient report card. Here is some of the core issues observed in the document analysis.

Case 1: The patient had partial insight and was psychotic before 3 months so 0.5mg of risperidone is not in the range of therapeutic dose of stabilization phase. (Dose is low)

Case 2: This patient is non-adherent and he lives in a street and his condition was fair within a year of antipsychotic treatment but he was not taking his medication properly so depot medication should be considered rather than giving risperidone the whole time. Not the right choice dosage form for the patient (dosage form inappropriate).

Case 3: When switching between first generations, antipsychotics equivalent doses should be given equivalent dose of haloperidol 5mg is 25mg of fluphenazine depot every 4weeks. Testing dose of 12.5mg should have to be given for 2 weeks and the dosage should be adjusted rather than giving (12.5mg every 4 weeks) because patient's condition was still the same and he was non adherent .(dose low).

Case 4: The patient had chronic schizophrenia and developed TD and Trihexyphenidyl was prescribed for him who were C/I but his condition was the same. He had delusion on the day of examination. Switching to another medication is better rather than continuing the same medication (risperidone 2mg).(Undesired effect and inappropriate choice of drug)

Case 5: The patient developed sexual dysfunction and decreased libido. He was on risperidone and different guideline indicates risperidone causes this S/E and recommend to switch to lower propensity of ED or to give medication which can improve his sexual dysfunction because it can make the patient prone to non adherence and treatment discontinuation. ADR (undesired effect).

Case 6: Overweight, the patient gained body weight of 8-9kg after starting risperidone before 7 months and now he is taking Olanzapine 15mg. ADR (undesired effect).

Case 7: This patient is taking Efavirenz based HAART and he develop psychotic problem. Hence, HAART should be evaluated and should be changed to Nevirapine based treatment if the psychotic problem prolongs more than a month. (Unsafe drug)

The details are presented in the Annex part lV

5. Discussion

The present study had aimed to assess drug therapy problems, adherence and associated factors among patient with schizophrenia.

The research found out that from 118 cases of schizophrenia the prevalence of DTP was 88 (52.5%), with the majority of study participants, 70.3%, being male. The result was comparable with the study conducted in northern Ethiopia in which the majority, 72%, of them were male (Eticha et al., 2015). In line with this study, male predominance of schizophrenia was reported in the Indian study (57.9% vs 42.1%) (Patted H Usharani, 2018). It is also related with the study conducted in Asian countries (Banerjee et al., 2013) where 58.76% of males and 41.24% were female.

In the current study the average age was 34.0 in which most of them (more than 50%) were found in 25-39 years. Study in northern Ethiopia where the mean age of patients with schizophrenia was 30.5, with the majority, 48.1% , of them were between 25 to 34 years (Eticha et al., 2015). A study done in India (Patted H Usharani, 2018) also showed average age was 35.6 years 70% of them were <40years (Patted H Usharani, 2018). The results were also similar with the study by Banerjee *et al* (2013) where 78.6% were <40years.

In the current study risperidone was the most common drug prescribed 47.0%, followed by fluphenazine depot 7.7%, which was found to be higher than the finding in cohort study done in Australia which indicated that second generation antipsychotics (SGA) were the most common prescribed antipsychotics, in particular risperidone oral and long-acting injection was the most common prescribed agent which was 31% (McMillan et al., 2017). This might be due to availability of different antipsychotics in Australia. This study was in accordance with study done in India risperidone 44.71% was the most common antipsychotic prescribed followed by olanzapine 34.81% and aripiprazole7.12% (Kumar et al., 2017). Another retrospective study conducted in India shows the commonest antipsychotic drug prescribed was olanzapine 48.6%, followed by risperidone 45.8% (Patted H Usharani, 2018).

In this study the prevalence of DTP was 88 (52.5%); DTP was common among patients with chronic illness even if the complete DTP was not found in schizophrenia and different studies report the prevalence of DTP was high for patients with chronic illness (Hussen and Daba, 2017, Ogbonna et al., 2014).

The current study was relatable with the study done in India on antipsychotic prescription pattern of patients with schizophrenia on 29 patients who had received in patient treatment for schizophrenia. Four patients 13.79% were receiving high doses, 7 patients 24.13% were receiving low doses and 31% of them were on combination of typical and atypical antipsychotics (Ramadas et al., 2010).

In this study it was found out that ineffective drug was given to 18 study participants out of whom 10 of them were needed to be switched to another drug due to suboptimal antipsychotics efficacy for the patient's condition. Hence another drug choice from different class or the same class should be considered based on recommendations of different guidelines, response and tolerability (Taylor David, 2015). In an observational study in India a total of 58 (26%) patients had switched over from one antipsychotic to another in which the study was prospective, observational study at tertiary care hospital in Delhi, and antipsychotic agents were switched to other antipsychotic agent due to various reasons, including lack of efficacy, adverse drug reactions, high cost or non-availability of the drug (Kumar et al., 2017). When compared to the above study, the difference in study design may increase the prevalence in contrast to the current study. In our study the physicians rationalization for the increased prescription of risperidone was cost and non-availability of other antipsychotic drugs which in turn made it difficult for psychiatrists to switch to another antipsychotic and this is also supported by Indian study (Kumar et al., 2017).

According to Cipolle DTP classification, the second most common DTP in our study was dose low, seen in 18 (20.5% of DTP) study participants and dose high was 2 (2.3% of DTP), this finding is relatable with the findings of study done in a tertiary care center in India in which dose low were (24.13%) (Ramadas et al., 2010). Study done by Kogut *et al* (2005) on atypical antipsychotic medications showed about one third of Patients were prescribed at a dosage that was not within the recommended range. The degree of inappropriate dosing was about 27%; where patients received a medication below-range dosage which was below the range recommended in the product labeling. Use of high dose was 6% of patients received medication at dosages that were higher than recommended in the product labeling(Kogut et al., 2005).

In this study 2 patients were taking their medications without tapering to minimum effective dose on the maintenance phase of treatment starting from acute phase of treatment. Different guidelines like APA recommendations in stable phase of treatment the dose of medications

should be tapered to minimum effective dose (Lehman et al., 2004). Remington and colleagues also in a randomized control trial showed that patients, who take their dose of antipsychotics every other day instead of daily, still respond well to the treatment which might indicate that patients sometimes instinctively know their minimal effective dose more accurately than their psychiatrists do, and are therefore consciously noncompliant with the doctor's prescription. Gradually reducing the dose to the minimal effective dose: a dose by which the patient does not suffer from side effects, but does not relapse should be considered(Remington et al., 2011).

In the present study antipsychotic combination was 3(3.4%). A study in Nigeria 4.6% of patients with schizophrenia had antipsychotic combination use (Adeponle et al., 2007). However in Korea and Amanuel Mental Specialized Hospital Addis Ababa, antipsychotic combination were 9.0% and 28% respectively (Choi et al., 2011, Tesfaye et al., 2016). Non availability of clozapine may lower the incidence in our hospital since mostly antipsychotic combinations are used when treatment with clozapine failed to manage the condition.

In this study undesired effect occurred in 14 participants 15.9% and this was higher than study done on antipsychotic prescription in India and UAE 6.41% and 10.2% respectively (Gawali et al., 2017, Sridhar et al., 2016). On the other hand it is lower than the study done on adverse drug reactions in psychiatry outpatients of India which undesired effect rate was 20.4% and another observational study in India also showed the overall prevalence of ADRs was found 43.5% which mild and moderate in severity (Jayanthi et al., 2013, Ahmad et al., 2016). The reason for the lower rate of undesired effect in our study might be due to the under documentation of undesired effects in medical record charts and it was only reviewed from medical record charts. And similar scenarios were shown by different researches Cortese *et al* (2004) explain that it might be due to physicians under-detecting and under-recording of EPS. And another study by Butler and Chandrakanth (2016) concerning monitoring of extrapyramidal side effects in patients on antipsychotic treatment stated that documentation regarding EPS was found only in 14% of patient records. A study in India on atypical antipsychotic drugs in psychiatry OPD revealed that healthcare professionals has to follow and assess ADRs of antipsychotics, which in turn has an impact on long-term adherence and successful treatment out comes gives significant input in better patient management(Piparva et al., 2011).

A Cohort study on atypical antipsychotics showed TDs occurred with an incidence rate of 0.74% and EPS with an incidence rate of 3.7%. Even though TD is rare in atypical drugs, if occurs once it may be more persistent compared with typical drugs (Tenback et al., 2010). In our study the most common undesired effect was TD 5(4.2%) patients, however on previous studies central nervous system effect was the most common undesired effect (Gawali et al., 2017, Jayanthi et al., 2013).

The results of our study showed the occurrence of 16 major drug interactions which were identified in 13.6% of study participants. Among them Risperidone and fluoxetin had the highest frequency which is lower than study done in Pakistan indicating that 51.7% patients had drugs-drug interaction(DDI), the reason might be in the current study the sample size is lower than the study in Pakistan and the Pakistan included many psychotic illness other than schizophrenia(Khan et al., 2017). Retrospective cross-sectional study on the prevalence of DDIs in the psychiatric ward of Ayub Teaching Hospital Pakistan, had higher prevalence of DDIs when compared to our study 64.8%, this might be due to the higher sample size they used in which the patients were admitted to the hospital and were using different drugs during the whole hospital stay which also included routine use of medications and PRN(when necessary) medications, however our study was done in outpatient department of psychiatry clinic where majority of patients were using a single 67.8% antipsychotic drug(Ismail et al., 2012).

In this study using bivariate analysis it was observed that as age increases from (14-24) age group to (40-64) and (>65) significantly associated with DTP ($p<0.014$) and (0.030); Patients between the ages of (40-64) were 7(0.144) times less likely to develop DTPs compared to age group (14-24) and patients at the ages of >65, were 22.7(0.044) times less likely to have DTP it seems that age has protective effect to develop DTP which implies the higher the age of the patient less likely for the occurrence of DTP. The reason for this might be the most common age for the peak presentation of the disease is during young age specially people aged 12-24 years (Patel et al., 2007). The other explanation for this might be as age increases patients may become more cooperative to the treatment plan and thus helps to improve therapeutic alliance with the psychiatrist. Supported by study conducted at South Africa the relapses of schizophrenia is more likely to occur in younger patients, age group <50 years were more likely to relapse(Kazadi et al., 2008). Source of medication was also significantly associated with DTP (p0.024), it seems the physician tends and feels free to prescribe different class and

choice of medication for patients who were able to pay; hence the patient can get the medication from any other pharmaceutical sources. The reason for this might be insufficient medication supply in the hospital or most patients who got their medications freely may not be able to pay for their medication. Duration of schizophrenia treatment >5 years as well had an association with DTP (p0.013) AOR 5.8 times more likely to develop DTP compared with the duration of treatment less than one year, cross-sectional study in Amanuel mental hospital in Ethiopia also showed that longer duration of antipsychotic treatment significantly associated with antipsychotic combination because antipsychotic combination is used since a single drug could not managed the problem(Tesfaye et al., 2016). In addition number of medication who took two and more medications had been significantly (p0.007) associated with DTP, as the number of drug increases the probability of drug interaction, increased risk of undesired effects and other drug related factors may also increase(Alomar, 2014).

Prevalence of antipsychotic drug non adherence was found to be 58.5%, in which, 69 of the total study participants were non adherent to their treatments. This finding was in line with the study conducted in Nigeria in which the prevalence of treatment non-adherence was 51.7%(Effiong and Umoh, 2015). The result was higher than a cross sectional study done by Girma *et al* (2017) at Amanuel Mental Specialized Hospital where non adherence rate was 48.4% and lower than the study done in Gondar University Hospital, Northwest Ethiopia, were schizophrenic patients non adherence rate was 75.7% (Endale Gurmu et al., 2014). The reason might be in the current study measure of adherence was measured using MMAS-8 scales but the study at Amanuel Mental Specialized Hospital and Gondar University Hospital used MMAS-4 scales to measure adherence which might under or over report the prevalence. A cross-sectional study in England and Wales on quality of care received by individuals, audit of schizophrenia treatment showes there was high prevalence of non-adherence for those patients who were not in remission or in partial remission, rate of adherence for remission patients were very high 86% (Patel et al., 2014).

In this study using bivariate analysis, educational status was significantly associated with non adherence, where patients with educational level high school and greater than high school were 0.26, 4 times less likely to be non-adherent than patients who only had primary and lower than primary school education. This was similar with the study done in northern Ethiopia where educational status was to some extent associated with adherence and illiterate patients were (AOR = 0.13) 7 times less likely to be adherent (Eticha et al., 2015). And it is

backed with a systemic review that indicated educational status was considered as a factor for non-adherence in chronic illness treatment including psychiatry (Kardas et al., 2013).

6. Limitations of the Study

- The cross-sectional nature of the study didn't allow a follow up, and it was a non-interventional study.
- Self-reported measure of adherence was used to measure adherence, which could have caused overestimation of adherence.
- ADRs were reviewed only from medical record charts.
- The result of the study may not be generalized to all hospitals because the sample size was small

7. Conclusion

In conclusion, the findings of this study showed that the prevalence of DTP was 52.50 %. ADR was the most identified DTP followed by low dose and continued use of ineffective drug for the patient condition respectively. The most common drug classes involved in DTP was risperidone and the prevalence of medication non adherence was 58.5%.

DTP had a significant association with age, source of medication, duration of schizophrenia treatment and number of medications taken by the patients. Educational status of the patient was significantly associated with adherence. Lack of information about drug side effects, drug product unavailability or unaffordability, forgetting, patient belief of being cured or illness worsened were the major reasons for poor adherence.

8. Recommendation

Based on the findings of this study, the following recommendations are suggested

- For optimal management strategies on schizophrenia, national standard treatment guideline must be developed to minimize the incidence of DTP. Psychiatrists who treat the patient as off label dosing or treatment based on diverse patient needs, their best clinical judgment must be clearly documented on patient charts.
- Availability of different antipsychotics helps the psychiatrist to prescribe based on different standard guidelines, individual conditions and patient preference and this helps to minimize DTP and adherence problems.
- Among the risk factors associated with medication non adherence was the level of education hence counseling and education on adherence are the first step to adjust the problem of non-adherence.
- The health sector policy makers should continue to include clinical pharmacists in the hospital. The role of clinical pharmacists should also be geared to identify, solve, and prevent DTPs rather than overlapping on the already existing dispensing pharmacists.
- Continuous monitoring for drugs that have potential drug-drug interactions and psychiatrists should monitor patients for signs of adverse drug effects, including doing laboratory tests as necessary.
- These findings provide a national benchmark for improving drug treatment for patients suffering from schizophrenia.
- Further studies with a follow up of patients are required.

Reference

Adeponle, A., Obembe, A., Adeyemi, S. & Suleiman, G. 2007. Polypharmacy in psychiatric outpatient practice in northern Nigeria. *African journal of psychiatry,* 10**,** 215-218.

Ahmad, A., Hussain, A., Farhat, S., Parveen, S., Sawhney, V. & Ashai, Z. 2016. Prevalence and Severity of Adverse Drug Reactions (ADRs) in patients subjected to different Anti-psychotic drugs in an Out-Patient Department of a Psychiatry Hospital in Kashmir; a prospective observational study. *International Journal of Pharmacology,* 5**,** 12-16.

Albert, M. & Mccaig, L. F. 2015. Emergency Department Visits Related to Schizophrenia Among Adults Aged 18-64: United States, 2009-2011. *NCHS data brief***,** 1-8.

Aldebot, S. & De Mamani, A. G. W. 2009. Denial and acceptance coping styles and medication adherence in schizophrenia. *The Journal of nervous and mental disease,* 197**,** 580.

Alomar, M. J. 2014. Factors affecting the development of adverse drug reactions. *Saudi pharmaceutical journal,* 22**,** 83-94.

Anderson, K. K. & Kurdyak, P. 2017. Factors associated with timely physician follow-up after a first diagnosis of psychotic disorder. *The Canadian Journal of Psychiatry,* 62**,** 268-277.

Argo, T., Crismon, M., Miller, A., Moore, T., Bendele, S. & Suehs, B. 2008. Texas Medication Algorithm Project procedural manual. *Schizophrenia treatment algorithms. Austin, Texas: Texas Department of State Health Services*.

Ayano, G. 2016. Second Generation Antipsychotics: Pharmacodynamics, Therapeutic Effects Indications and Associated Metabolic Side Effects:. *Journal of Schizophrenia Research,* 3.

Banerjee, I., Roy, B., Sathian, B., Banerjee, I., Chakraborty, P. K. & Saha, A. 2013. Socio demographic profile and utilization pattern of antipsychotic drugs among schizophrenic inpatients: a cross sectional study from western region of Nepal. *BMC psychiatry,* 13**,** 96.

Butler, M. & Chandrakanth, J. 2016. Monitoring of extrapyramidal side effects in patients on antipsychotic treatment: a completed audit cycle. *Irish Journal of Psychological Medicine,* 33**,** 165-169.

Chabungbam, G., Avasthi, A. & Sharan, P. 2007. Sociodemographic and clinical factors associated with relapse in schizophrenia. *Psychiatry and clinical neurosciences,* 61**,** 587-593.

Choi, H. J., Jung, S. H., Kang, M. H., Lee, J. S., Bae, J. N. & Kim, C. E. 2011. Antipsychotics prescribing patterns of patients with schizophrenia admitted to Korean general hospital psychiatric unit: 2001 to 2008. *Clinical Psychopharmacology and Neuroscience,* 9**,** 17.

Cipolle, R. J., Strand, L. M. & Morley, P. C. 2012. *Pharmaceutical care practice: the patient-centered approach to medication management,* McGraw Hill Professional.

Cortese, L., Jog, M., Mcauley, T. J., Kotteda, V. & Costa, G. 2004. Assessing and monitoring antipsychotic-induced movement disorders in hospitalized patients: a cautionary study. *The Canadian Journal of Psychiatry,* 49**,** 31-36.

Crystal, S., Olfson, M., Huang, C., Pincus, H. & Gerhard, T. 2009. Broadened use of atypical antipsychotics: safety, effectiveness, and policy challenges. *Health Affairs,* 28**,** w770-w781.

Dalton, K. & Byrne, S. 2017. Role of the pharmacist in reducing healthcare costs: current insights. *Integrated pharmacy research & practice,* 6**,** 37.

De Hert, M., Detraux, J., Van Winkel, R., Yu, W. & Correll, C. U. 2012. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. *Nature Reviews Endocrinology,* 8**,** 114-126.

Dibonaventura, M., Gabriel, S., Dupclay, L., Gupta, S. & Kim, E. 2012. A patient perspective of the impact of medication side effects on adherence: results of a cross-sectional nationwide survey of patients with schizophrenia. *BMC psychiatry,* 12**,** 20.

Effiong, J. H. & Umoh, K. A. 2015. Medication Non Adherence in Schizophrenia: Prevalence and Correlates among Outpatients in a Tertiary Healthcare Facility in Uyo, South-South Nigeria. *Clinical Medicine and Diagnostics,* 5**,** 107-113.

EFMHACA. September 2010. *LIST OF MEDICINES FOR ETHIOPIA* [Online]. Food, Medicine and Healthcare Administration and Control Authority of Ethiopia Available: http://apps.who.int/medicinedocs/documents/s17816en/s17816en.pdf

Endale Gurmu, A., Abdela, E., Allele, B., Cheru, E. & Amogne, B. 2014. Rate of nonadherence to antipsychotic medications and factors leading to nonadherence among psychiatric patients in Gondar University Hospital, Northwest Ethiopia. *Advances in Psychiatry,* 2014.

Eticha, T., Teklu, A., Ali, D., Solomon, G. & Alemayehu, A. 2015. Factors associated with medication adherence among patients with schizophrenia in Mekelle, Northern Ethiopia. *PloS one,* 10**,** e0120560.

Fekadu, A., Medhin, G., Kebede, D., Alem, A., Cleare, A. J., Prince, M., Hanlon, C. & Shibre, T. 2015. Excess mortality in severe mental illness: 10-year population-based cohort study in rural Ethiopia. *The British Journal of Psychiatry,* 206**,** 289-296.

Fikreyesus, M., Soboka, M. & Feyissa, G. T. 2016. Psychotic relapse and associated factors among patients attending health services in Southwest Ethiopia: a cross-sectional study. *BMC psychiatry,* 16**,** 354.

Gawali, U. P., Kesari, H. V. & Gawand, K. S. 2017. Adverse drug reaction profile at psychiatry outpatient department of a tertiary care centre. *International Journal of Basic & Clinical Pharmacology,* 6**,** 2428-2433.

Girma, S., Abdisa, E. & Fikadu, T. 2017. Prevalence of Antipsychotic Drug Non Adherence and Associated Factors among Patients with Schizophrenia Attending at Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia: Institutional Based Cross Sectional Study. *Health Science Journal,* 11.

Howes, O. D. & Kapur, S. 2009. The dopamine hypothesis of schizophrenia: version III—the final common pathway. *Schizophrenia bulletin,* 35**,** 549-562.

Hussen, A. & Daba, F. B. 2017. Drug therapy problems and their predictors among hypertensive patients on follow up in dil-chora referral hospital, dire-dawa, ethiopia. *Stroke,* 9**,** 3.3.

Ismail, M., Iqbal, Z., Khattak, M. B., Javaid, A., Khan, M. I., Khan, T. M. & Asim, S. M. 2012. Potential drug-drug interactions in psychiatric ward of a tertiary care hospital: prevalence, levels and association with risk factors. *Tropical Journal of Pharmaceutical Research,* 11**,** 289-296.

Jayanthi, C., Divyashree, M. & Sushma, M. 2013. Adverse drug reactions in psychiatry outpatients: Clinical spectrum, causality and avoidability. *J Chem Pharm Res,* 5**,** 128-35.

Kane, J., Singer, M. & Meltzer, M. 1988. Clozapine for the treatment-resistant. *Arch. Gen. Psychiatry,* 45**,** 789-796.

Kane, J. M. & Correll, C. U. 2010. Past and present progress in the pharmacologic treatment of schizophrenia. *The Journal of clinical psychiatry,* 71**,** 1115-1124.

Kaplan, B. J. 2015. *Kaplan and Sadock's Synopsis of Psychiatry. Behavioral Sciences/Clinical Psychiatry*.

Kapur, S., Zipursky, R., Jones, C., Remington, G. & Houle, S. 2000. Relationship between dopamine D2 occupancy, clinical response, and side effects: a double-blind PET study of first-episode schizophrenia. *American Journal of Psychiatry,* 157**,** 514-520.

Kardas, P., Lewek, P. & Matyjaszczyk, M. 2013. Determinants of patient adherence: a review of systematic reviews. *Frontiers in pharmacology,* 4**,** 91.

Kazadi, N., Moosa, M. & Jeenah, F. 2008. Factors associated with relapse in schizophrenia. *South African Journal of Psychiatry,* 14**,** 52-62.

Kebede, D., Alem, A., Shibre, T., Negash, A., Fekadu, A., Fekadu, D., Deyassa, N., Jacobsson, L. & Kullgren, G. 2003. Onset and clinical course of schizophrenia in Butajira-Ethiopia. *Social psychiatry and psychiatric epidemiology,* 38**,** 625-631.

Keshavan, M. S., Nasrallah, H. A. & Tandon, R. 2011. Schizophrenia,"Just the Facts" 6. Moving ahead with the schizophrenia concept: from the elephant to the mouse. *Schizophrenia research,* 127**,** 3-13.

Khan, Q., Ismail, M., Haider, I. & Khan, F. 2017. Prevalence of QT interval prolonging drug–drug interactions (QT-DDIs) in psychiatry wards of tertiary care hospitals in Pakistan: a multicenter cross-sectional study. *International journal of clinical pharmacy,* 39**,** 1256-1264.

Kogut, S. J., Yam, F. & Dufresne, R. 2005. Prescribing of antipsychotic medication in a medicaid population: use of polytherapy and off-label dosages. *Journal of Managed Care Pharmacy,* 11**,** 17-24.

Kumar, S., Chawla, S., Bimba, H., Rana, P., Dutta, S. & Kumar, S. 2017. Analysis of Prescribing Pattern and Techniques of Switching Over of Antipsychotics in Outpatients of a Tertiary Care Hospital in Delhi: A Prospective, Observational Study. *Journal of Basic and Clinical Pharmacy,* 8.

Lally, J. & Maccabe, J. H. 2015. Antipsychotic medication in schizophrenia: a review. *British medical bulletin,* 114**,** 169-179.

Lang, U. E., Puls, I., Müller, D. J., Strutz-Seebohm, N. & Gallinat, J. 2007. Molecular mechanisms of schizophrenia. *Cellular Physiology and Biochemistry,* 20**,** 687-702.

Lehman, A. F., Lieberman, J. A., Dixon, L. B., Mcglashan, T. H., Miller, A. L., Perkins, D. O., Kreyenbuhl, J., Mcintyre, J. S., Charles, S. C. & Altshuler, K. 2004. Practice guideline for the treatment of partients with schizophrenia. *American Journal of psychiatry,* 161.

Lora, A., Kohn, R., Levav, I., Mcbain, R., Morris, J. & Saxena, S. 2012. Service availability and utilization and treatment gap for schizophrenic disorders: a survey in 50 low-and middle-income countries. *Bulletin of the World Health Organization,* 90**,** 47-54B.

Mcgorry, P. D., Cocks, J., Power, P., Burnett, P., Harrigan, S. & Lambert, T. 2011. Very low-dose risperidone in first-episode psychosis: a safe and effective way to initiate treatment. *Schizophrenia research and treatment,* 2011.

Mcmillan, S. S., Jacobs, S., Wilson, L., Theodoros, T., Robinson, G., Anderson, C., Mihala, G. & Wheeler, A. J. 2017. Antipsychotic prescribing for vulnerable populations: a clinical audit at an acute Australian mental health unit at two-time points. *BMC psychiatry,* 17**,** 139.

Melle, I., Johannesen, J. O., Friis, S., Haahr, U., Joa, I., Larsen, T. K., Opjordsmoen, S., Rund, B. R., Simonsen, E. & Vaglum, P. 2006. Early detection of the first episode of schizophrenia and suicidal behavior. *American Journal of Psychiatry,* 163**,** 800-804.

Murray, R., Correll, C. U., Reynolds, G. P. & Taylor, D. 2017. Atypical antipsychotics: recent research findings and applications to clinical practice: proceedings of a symposium presented at the 29th Annual European College of Neuropsychopharmacology Congress, 19 September 2016, Vienna, Austria. *Therapeutic advances in psychopharmacology,* 7**,** 1-14.

Nicholl, D., Akhras, K. S., Diels, J. & Schadrack, J. 2010. Burden of schizophrenia in recently diagnosed patients: healthcare utilisation and cost perspective. *Current medical research and opinion,* 26**,** 943-955.

Ogbonna, B., Ezenduka, C., Opara, C. & Ahara, L. 2014. Drug Therapy Problems in Patients with Type-2 Diabetes in a Tertiary Hospital in Nigeria. *International Journal of Innovative Research and Development|| ISSN 2278–0211,* 3.

Olfson, M., Druss, B. G. & Marcus, S. C. 2015. Trends in mental health care among children and adolescents. *New England Journal of Medicine,* 372**,** 2029-2038.

Park, Y., Huybrechts, K. F., Cohen, J. M., Bateman, B. T., Desai, R. J., Patorno, E., Mogun, H., Cohen, L. S. & Hernandez-Diaz, S. 2017. Antipsychotic Medication Use Among Publicly Insured Pregnant Women in the United States. *Psychiatric Services,* 68**,** 1112-1119.

Patel, M. X., Bishara, D., Jayakumar, S., Zalewska, K., Shiers, D., Crawford, M. J. & Cooper, S. J. 2014. Quality of prescribing for schizophrenia: evidence from a national audit in England and Wales. *European Neuropsychopharmacology,* 24**,** 499-509.

Patel, V., Flisher, A. J., Hetrick, S. & Mcgorry, P. 2007. Mental health of young people: a global public-health challenge. *The Lancet,* 369**,** 1302-1313.

Patted H Usharani, N. G. H., Nagaraj Mysore Anil Kumar 2018. Antipsychotics in schizophrenia: a retrospective study of drug utilization pattern in outpatient

department of psychiatry at a tertiary care hospital. *IJBCP International Journal of Basic & Clinical Pharmacology,* 7**,** 5.

Pilon, D., Joshi, K., Tandon, N., Lafeuille, M.-H., Kamstra, R. L., Emond, B. & Lefebvre, P. 2017. Treatment patterns in Medicaid patients with schizophrenia initiated on a first- or second-generation long-acting injectable versus oral antipsychotic. *Patient preference and adherence,* 11**,** 619.

Piparva, K. G., Buch, J. & Chandrani, K. V. 2011. Analysis of adverse drug reactions of atypical antipsychotic drugs in psychiatry OPD. *Indian journal of psychological medicine,* 33**,** 153.

Ramadas, S., Kuttichira, P., Sumesh, T. & Ummer, S. A. 2010. A study of an antipsychotic prescription pattern of patients with schizophrenia in a developing country. *Indian journal of psychological medicine,* 32**,** 13.

Rapoport, J., Giedd, J. & Gogtay, N. 2012. Neurodevelopmental model of schizophrenia: update 2012. *Molecular psychiatry,* 17**,** 1228.

Remington, G., Seeman, P., Feingold, A., Mann, S., Shammi, C. & Kapur, S. 2011. " Extended" antipsychotic dosing in the maintenance treatment of schizophrenia: a double-blind, placebo-controlled trial. *The Journal of clinical psychiatry,* 72**,** 1042-1048.

Richardson, T. E., O'reilly, C. L. & Chen, T. F. 2014. Drug-related problems and the clinical role of pharmacists in inpatient mental health: an insight into practice in Australia. *International journal of clinical pharmacy,* 36**,** 1077-1086.

Robinson, D. G., Schooler, N. R., John, M., Correll, C. U., Marcy, P., Addington, J., Brunette, M. F., Estroff, S. E., Mueser, K. T. & Penn, D. 2015. Prescription practices in the treatment of first-episode schizophrenia spectrum disorders: data from the national RAISE-ETP study. *American Journal of Psychiatry,* 172**,** 237-248.

Rubio-Valera, M., Chen, T. F. & O'reilly, C. L. 2014. New roles for pharmacists in community mental health care: a narrative review. *International journal of environmental research and public health,* 11**,** 10967-10990.

San, L., Bernardo, M., Gómez, A. & Peña, M. 2013. Factors associated with relapse in patients with schizophrenia. *International journal of psychiatry in clinical practice,* 17**,** 2-9.

Schill, J. & Olsson, H. 2016. Do doctors agree on doses of antipsychotic medications? *Therapeutic advances in psychopharmacology,* 6**,** 349-354.

Shibre, T., Medhin, G., Alem, A., Kebede, D., Teferra, S., Jacobsson, L., Kullgren, G., Hanlon, C. & Fekadu, A. 2015. Long-term clinical course and outcome of schizophrenia in rural Ethiopia: 10-year follow-up of a population-based cohort. *Schizophrenia research,* 161**,** 414-420.

Smith, B. L. 2012. Inappropriate prescribing. *Monitor on Psychology,* 43**,** 36.

Somers, A., Robays, H., De Paepe, P., Van Maele, G., Perehudoff, K. & Petrovic, M. 2013. Evaluation of clinical pharmacist recommendations in the geriatric ward of a Belgian university hospital. *Clinical interventions in aging,* 8**,** 703.

Sridhar, S. B., Al-Thamer, S. S. F. & Jabbar, R. 2016. Monitoring of adverse drug reactions in psychiatry outpatient department of a Secondary Care Hospital of Ras Al Khaimah, UAE. *Journal of basic and clinical pharmacy,* 7**,** 80.

Stahl, S. M. 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications*, Cambridge university press.

Strand, L. M., Morley, P. C., Cipolle, R. J., Ramsey, R. & Lamsam, G. D. 1990. Drug-related problems: their structure and function. *DICP: the annals of pharmacotherapy,* 24**,** 1093-1097.

Stroup, T. S., Gerhard, T., Crystal, S., Huang, C. & Olfson, M. 2015. Comparative effectiveness of clozapine and standard antipsychotic treatment in adults with schizophrenia. *American Journal of Psychiatry,* 173**,** 166-173.

Stroup, T. S., Gerhard, T., Crystal, S., Huang, C., Tan, Z., Wall, M. M., Mathai, C. M. & Olfson, M. 2018. Psychotropic Medication Use Among Adults With Schizophrenia and Schizoaffective Disorder in the United States. *Psychiatric Services***,** appi. ps. 201700356.

Tandon, R., Gaebel, W., Barch, D. M., Bustillo, J., Gur, R. E., Heckers, S., Malaspina, D., Owen, M. J., Schultz, S. & Tsuang, M. 2013. Definition and description of schizophrenia in the DSM-5. *Schizophrenia research,* 150**,** 3-10.

Tandon, R., Keshavan, M. S. & Nasrallah, H. A. 2008. Schizophrenia,"just the facts" what we know in 2008. 2. Epidemiology and etiology. *Schizophrenia research,* 102**,** 1-18.

Taylor David, P. C. A. K. S. 2015. *The Maudsley Prescribing Guidelines in Psychiatry*, John Wiley & Sons, Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK.

Teferra, S., Hanlon, C., Beyero, T., Jacobsson, L. & Shibre, T. 2013. Perspectives on reasons for non-adherence to medication in persons with schizophrenia in Ethiopia: a qualitative study of patients, caregivers and health workers. *BMC psychiatry,* 13**,** 168.

Tenback, D. E., Van Harten, P., Slooff, C. J. & Van Os, J. 2010. Incidence and persistence of tardive dyskinesia and extrapyramidal symptoms in schizophrenia. *Journal of Psychopharmacology,* 24**,** 1031-1035.

Tesfaye, S., Debencho, N., Kisi, T. & Tareke, M. 2016. Prevalence of antipsychotic polypharmacy and associated factors among outpatients with schizophrenia attending amanuel mental specialized hospital, Addis Ababa, Ethiopia. *Psychiatry journal,* 2016.

Tsutsumi, C., Uchida, H., Suzuki, T., Watanabe, K., Takeuchi, H., Nakajima, S., Kimura, Y., Tsutsumi, Y., Ishii, K. & Imasaka, Y. 2011. The evolution of antipsychotic switch and polypharmacy in natural practice—a longitudinal perspective. *Schizophrenia research,* 130**,** 40-46.

WHO. 2001. *Adherence to long-term therapies a policy for action* [Online]. WHO. Available: http://www.who.int/chp/knowledge/publications/adherencerep

WHO. 2017. *schizophrenia* [Online]. WHO. Available: http://www.who.int/mental_health/management/schizophrenia/en/ 2018].

Annexes

Annex I: English version of informed consent form

Consent Form

Addis Ababa University

School of Pharmacy

Department of pharmacology and clinical pharmacy

Cross-sectional study on assessment of drug Therapy problems in psychiatry unit of TikurAnbessa Specialized Hospital

Greeting:

Hello, my name isGubaeTemtem I am here today to collect data to asses' drug therapy problems in **psychiatry unit** of TikurAnbessa Specialized Hospital, Addis Ababa, Ethiopia. The study is being conducted by GubaeTemtem from Addis Ababa University, school of Pharmacy, department of clinical pharmacy and pharmacology, post graduate program.

The objective of this study is

- To identify the prevalence of DTP in schizophrenic adult patients at outpatient service
- To identify predictors of occurrence of drug therapy problems.
- To assess treatment adherence

This is cross-sectional study so I request you to take part in this study. Your cooperation and willingness is greatly helpful in assessing drug therapy problems in TikurAnbessa Specialized Hospital. The study will be conducted through recording medical findings from your medical chart and interviewing.

Your name will not be written in this form and will never be used in connection with any information we take from the chart and you tell us. The risk will be the lowest, the only risk for the interviewee the time spent to deliver information for us. All information taken from your medical chart or given by you will be kept strictly confidential. Your participation is voluntary and you are not obligated to participate in the study. If you feel discomfort with the study, it is your right to withdraw at any point. If you have questions regarding this study or would like to be informed of the results after its completion, please feel free to contact the principal investigator.

Address of the principal investigator:

GubaeTemtem

Cell phone: +251- 912202973

E-mail: Gubaetemtem@gmail.com

Are you willing to participate in this study?

1. Yes - …….. Continue
2. No - …… Skip to the next participant

Annex II: Data abstraction format from patient interview(English version)

I. Socio-Demographic Characteristics:			
Card No----------	1.Age (in years)---------- Weight in Kg---------- Height in cm----------		
2.Sex	Male ☐	Female ☐	Pregnant: Yes ☐ No ☐
3.Marital status	Single ☐	Married ☐	Divorced ☐ Widowed ☐
4.Educational status	Illiterate ☐ Grade 1-8 ☐	Grade 9-10 ☐ Grade 10-12 ☐	College diploma ☐ University degree and above ☐
5.Source of Medication	payment ☐	free ☐	
6. Residence (current)			
7. Monthly income, ETB	<1500 ☐ 1500-3000 ☐ 3001-5000 ☐ >5000 ☐		

8.Social habits:	Cigarette Smoker	Yes ☐ No ☐	Ex-smoker/ former smoke ☐
	Alcohol Drinker	Yes ☐ No ☐	Ex-drinker/former drinker ☐
	Kchat chewing	Yes ☐ No ☐	Ex-chewer/former chewer

<u>Part II:</u> Clinical characteristics (Obtained from non-medical record chart):

Duration of Schizophrenia treatment (years)	□< 1	□1-5	□6-10	□10+
Frequency of attending follow-up appointments	□ twice a month □ once a month □ every 2 month □ If other, please specify _____			
Current use of if any prescribed Drugs other than in medical record chart and OTC or herbals	□ No □ Yes Ifyes list them_____			

Part-lll: 8-Items Morisky Medication Adherence Scale- (MMAS-8)

No	Items	Yes	No
1	Do you sometimes forget to take your pills?	□1	□0
2	People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?	□1	□0
3	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?	□1	□0
4	When you travel or leave home, do you sometimes forget to bring along your medicine?	□1	□0
5	Did you take all your medicine yesterday?	□0	□1
6	When you feel like your symptoms are under control, do you sometimes stop taking your medicine?	□1	□0
7	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	□1	□0
8	How often do you have difficulty remembering to take all your medicine? **0.** Never **1**. Rarely **2.** Once in a while **3.** Sometimes **4.** Usually **5**. All the time		
	Total score		

Part VI. Data abstraction format

Patients' Medical and Medication Record Chart Review (past and current)

Card Number_____ Unique (ID/Code)_____Age (in year) _____Weight (kg) _____ Height (cm) _____ Body mass index (BMI) [kg/m^2] _____

1. Past medical conditions and medications

Medical condition/ Indication	Drug product (Generic Name)	Dosage regimen (dose, route, frequency, duration)	Date (dd/mm/yy)		Response Effectiveness/ safety profile
			Started	Stopped	

2. Past relevant medical history (hospitalizations, surgical procedures, injuries, pregnancies).

_____

_____

_____

_____

Base line Weight (kg) _____ Height (cm) _____ Body mass index (BMI) [kg/m^2]

3. Schizophrenia Related Medication History
Medical history:
Medication history:
ADR:

4. Recent Relevant Vital Signs (at least for three consecutive results)							
Date	RR	PR	BP	Tem	Spiro		

5. Relevant laboratory series results (Findings, at least for three consecutive results).

Investigations		Measurement Unit	Dates					Normal range
S.No.	Type							
1	Serum K							
2	Serum Na							
3	BUN							
4	Serum Cr							
5	Serum iCa							
6	Serum Cl							
7	Albumin							
8	FBG							
Lipid profile								
1	TG							
2	Total chol.							
3	LDL							
4	HDL							
Liver function tests								
1	AST							
2	ALT							
3	ALP							
4	PT							
5	INR							
7	aPTT							
8	Total Bili.							
9	Indirect Bili.							
Renal function tests								
1	Ketone							
2	Protein							
3	Glucose							
4	WBC							

5	RBC							
6	Nitrites							
7	Cr Cl							
CBC								
1	WBC							
2	RBC							
3	PLT							
4	Hgb							
5	Hct							
6	Neu.							
7	Lymph.							
12	ESR							
Blood glucose								
1	FBS							
2	RBS							
3	HbA1C							

6. Any other investigations/Diagnostic imaging results

_____

_____

_____

_____

7. **Current Medications and DTP**

Date (dd/mm/yy) ----------

Indication	Name of drug(Generic name)	Strength	Dosageform	Route	Frequency	Duration	Date started	Date to be stopped	Response	Comment DTP
Total number of medications										

8. **Adverse Drug Events**

Drug Regimen	**1. Adverse drug reaction**	**Event date**
	2. Drug allergies (drug, timing, reaction-rash, shock, asthma, nausea, anemia and others)	
	3. Other alerts/health aids/special needs (sight, hearing, mobility, literacy, disabilities)	

9. Drug interaction

Is there any drug interaction? ☐Yes | ☐ No

If drug interaction is there, specify it

10. Reason for non-adherence

- Patient forgets to take
- Poor follow up by patients.
- Directions not understood
- Patient felt better or worse
- Drug product not available or affordable
- Fear of adverse events

የአማርኛቋንቋቃለመጠይቅ (Amharic Version Questionnaire)

በአዲስአበባዩኒቨርሲቲፋርማሲት/ቤት

ጥናቱንበተመለከተለታካሚየሚሰጥመረጃ

የፈቃድመጠየቂያናመቀበያፎርም፡፡

አዲስአበባዩኒቨርሲቲ

የፋርማሲ ት/ቤት

የፋርማኮሎጂ እና ክሊኒካል ፋርማሲ ት/ት ክፍል

በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል የአእምሮ ህክምና ክፍል ከመድሀኒትጋርየተያያዙችግሮችበተመለከተግምገማማድረግ።

ጤና ይስጥልኝ:

ስሜ ጉባኤ ተምትም ይባላል። ዛሬ እዚህ የተገኘሁት በዚህ በአእምሮ ህክምና ክፍል ውስጥ ክፍል በሚሰጠው ህክምና ዙርያከመድሀኒትጋርየተያያዙችግሮችላይበተመለከተ ለሚደረግ ጥናት መረጃ ለመሰብሰብ ነው። ይህ ጥናት የሚደረገው በአዲስ አበባ ዩኒቨርሲት ድህረ ምረቃ ፕሮግራም በኩል ለሚሰጠው የየፋርማኮሎጂ እና ክሊኒካል ፋርማሲ ድህረ ምረቃ ት/ት ማሟያነት ነው።

የዚህ ጥናት አላማውም፣

- በተመላላሽ የአእምሮ ህክምና ክፍል ውስጥ በሚሰጠው ህክምና ላይ ከመድሀኒትጋርየተያያዙችግሮችን መጠን ለማወቅ
- የችግሮቹን መነሻ ለማወቅ
- የህክምና ክትትሎን አለመቋረጥ ለመገምገም ሲሆን፤

እርሶም በጥናቱ እንዲሳተፉ በትህትና እጠይቆታለሁ።የእርሶ ተሳትፎ በህክምና አሰጣጡ ላይ የሚታዩ ችግሮችን ለመለየት ከፍተኛ ጠቀሜታ ይኖረዋል። ጥናቱ የሚካሄደው የህክምና ውጤቶን ከካርድዎ በመመልከት እና ቃለመጠይቅ በማድረግ ይሆናል።.

ስሞት በዚህ ጥናት ውስጥ አይገለጽም።እንዲሁም ከካርዶት ከምንወስደው መረጃ ጋርም ሆነ ከቃለመጠይቁ ጋር አይያያዝም።ለጥናቱ የሚሆን መረጃ ለመስጠትከሚሰዉት ጊዜዎትበስተቀርጥናቱምንምየሚሰከትለዉጉዳትየለም። **የ**ሚሰጡትማንኛውምመረጃሁሉሚስጥራዊነቱየተጠበቀነው፡፡በጥናቱየሚሳተፉትፈቃደኛከሆኑብቻስለሆነ

አለመሳተፍወይምበጥናቱ መሳተፍከጀመሩምበኋላማቋረጥሙሉመብትዎነው፡፡ይህን ጥናት አስመልክቶ የሚኖሮትን ጥያቄም ሆነ የጥናቱን ውጤት ማወቅ ከፈለጉ ጥናቱን የሚያካሂደውን ሰው በስተመጨረሻ በተገለጸው አድራሻ ማግኘት ይችላሉ ።

ማንኛውምጥያቄካለዎት

ጉባኤተምትም

የፋርማኮሎጂ እና ክሊኒካል ፋርማሲ ት/ት ክፍል፤ አዲስ አበባ ዩኒቨርሲቲ

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ፈቃደኝነት መገለጫ

በጥናቱ ለመሳተፍ ፈቃደኛ ነዎት

አዎን ፈቃደኛ ነኝ፥ ----------

ፈቃደኛ አይደለሁም፥ ----------

ሀ.<u>የታካሚዉማህበራዊሁኔታዎች</u>(*መመርያ፡ለመረጡትምላሽበየ‘X” ምልክትንያድርጉ*)

ኮድቁጥር_____ ቀን_____

I. ማህበራዊሁኔታዎች				
የካርድ ቁጥር_____		እድሜ፤ (በአመት) ---------- ክብደት(በኪሎግራም):_____ቁመት (በሴንትሜትር):_____		
ፆታ፤	ወንድ ☐	ሴት ☐	ሴትከሆኑ ነፍሰጡር ነዎት?	አዎ☐አይለሁም ☐
የጋብቻሁኔታ፤	ያላገባ/ች☐	ያገባ/ች ☐	አግብቶ/ታየፈታ/ች☐	ሚስቱ/ ባሏየሞተችበት/ባት ☐
የትምህርትደረጃ	ያልተማረ/ች☐ ከ1ኛ-8ኛክፍል☐	ከ9ኛ-10ኛክፍል☐ 11ኛ-12ኛክፍል ☐	ኮሌጅዲፕሎማ ☐ ዩኒቨርስቲዲግሪእናከዛበላይ ☐	
አሁንየሚኖሩበትወረዳእናቀበሌ ----------				
የመድሃኒትዎምንጭ	በግዢ ☐	በነጻ☐	በዱቤ ☐	
በወርየሚያገኙትየገቢመጠን	<1500 ☐ 1500-3000 ☐ 3001-5000 ☐ >5000 ☐ አይታወቅም/የላቸውም ☐			
ማህበራዊየሱስልማድ	ሲጋራያጨሳሉአዎአላጨስምአ☐አልፎአልፎአጨሳለሁ ☐ ድሮአጭስነበርአሁንግንአቁሚያለሁ ☐			
	መጠጥ(አልኮል) ይጠጣሉአዎአልጠጣም ☐ አልፎአልፎእጠጣለሁድ☐ጠጣነበርአሁንግንአቁሚያለሁ ☐			
	ጫትይቅማሉአዎአልቅምምአ☐አልፎእቅማለሁ ☐ ድሮእቅምነበርአሁንግንአቁሚያለሁ ☐			

ለ.ታካሚውንህመምበተመለከተተጨማሪመረጃዎች

የአእምሮ ህመሙን ህክምና ከጀመሩ ምን ያህል ጊዜ ሆኖት? (በአመት)	< 1☐	1-5☐	6-10☐	ከ 10አመትበላይ ☐
ወደጤና ማእከል በምን ያህል ጊዜ ይመጣሉ?	በወርሁለትጊዜበ☐ንድጊዜበየሁለትወሩሌ☐ይጥቀሱ_____☐___ _____ ☐			
በህክምና ካርዶት ላይ ካለው ውጪ ታዞሎት እየወሰዱት ያለ መድሃኒት፣ያለህኪምትእዛዝየሚወስዱት ወይም የባህል መድሃኒት አለ?	አለየለ☐ ☐ ካለ እባኮት የመድሃኒቱን አይነትእና ለምን ህመም እንደሚወስዱት ይጥቀሱ። _____			

መድሐኒቶችንበታዘዘዉመሰረትበአግባቡስለመዉሰድመመዘኛ(ሞሪስኪስምንት)

ተ.ቁ	ጥያቄዎች	አይደለም	አዎ
፩	አንዳንድጊዜመድሐኒትመውሰድረስተውያውቃሉ?	□1	□0
፪	አንዳንድሰዎችከመርሳትውጪመድሐኒቶችንያለመውሰድችግርይታየባቸዋል። ባለፉትሁለትሳምንታትውስጥመድሐኒትያልወሰዱበትቀንአለ?	□1	□0
፫	ሐኪምዎንሳያማክሩበበሽታዎብሶቦትምክንያትመድሐኒትዎንመዉሰድአቋርጠውያዉቃሉ?	□1	□0
፬	ወደሌላቦታሲጓዙወይንምከቤትወጥተውሲሄዱመድሐኒትዎንይዘውከመሄድረስተውያውቃሉ	□1	□0
፭	በትላንትናውዕለትሁሉንምመድሐኒትበትክክልወስደዋል?	□0	□1
፮	የህመሙምልክቶችቀንሰዋልወይምተሸሎኛልብለውአንዳንዴመድሐኒትመውሰድአቋርጠውያውቃሉ?	□1	□0
፯	መድኃኒቶችንበየቀኑመውሰድለአንዳንድሰዎችምቾትይነሳቸዋል። እርስዎበህክምናክትትልዎወቅትበየቀኑወይምአንድምጊዜሳያዛንፉመድሐኒትበትክክልለመዉሰድተሰላችተዉ ያዉቃሉ?	□1	□0
፰	ሁሉንምመድሐኒቶችመውሰድአለመዉሰድዎንማስታወስየከበድዎትጊዜአለ? በፍፁም□አልፎአልፎ□አንዳንድጊዜ□አብዛኛውጊዜ□ሁልጊዜ□		
	ጠቅላላድምር		

መድሀኒትንበአገባቡላለመጠቀምምክንያቶች

NO		አዎ	አይደለም
ነ	ከጤናባልሙያስለበሽታዎበቂማብራሪያያገኛሉ		
2	መድሀኒቴንወስጇስለተሻለኝ		
3	የታዘዘልዎትንመድሃኒት በ ተመጣጣኝዎጋያገኛሉ		
4	ስለመድሃኒትዎየጎንዮሽጉዳትበቂመረጃያገኛሉ		
5	የሚወስዱትንመድሃኒትመውሰድይረሳሉ		
6	የህክምናቀጠሮዎንሳያዛንፉይከታትላሉ		
7	መድሀኒቱያድነኛልብዬስለማላስብ		
8	መድሀኒትስወስድህመሜስለሚባባስብኝ		

Annex lll: DTPs Registration Format (Modified)

DTPs Categories	Common Cause(s) of Drug therapy problem
1. Unnecessary drug therapy	☐ There is no valid medical indication for the drug therapy at this time Duplicate therapy ☐ Multiple drug products are being used for a condition that requires single drug therapy ☐ The medical condition is more appropriately treated with nondrug therapy ☐ Drug therapy is being taken to treat an avoidable adverse reaction associated with another medication ☐ Drug abuse, alcohol use, or smoking is causing the problem
2. Needs additional drug therapy	☐ Untreated medical condition (a medical condition requires the initiation of drug therapy) ☐ Preventive/ prophylactic(preventive drug therapy is required to reduce the risk of new condition) ☐ Synergistic/ potentiating (a medical condition requires additional pharmcotherapy to attain synergistic or additive effect) _____
3. Ineffective drug product	☐ The drug product is not the most effective for the indication being treated (In appropriate drug selection) ☐ Condition refractory to drug ☐ Dosage form inappropriate
4. Adverse drug reaction	☐ The drug product causes undesired effect ☐ The drug product is unsafe drug for patient ☐ The drug product causes allergic reactions ☐ The drug product is ccontraindications'due to safety issues ☐ Others, specify_____
5. In appropriate dose	☐ Dose high ☐ Dose low
6. Drug interaction	☐ Presence of major drug interaction among the medications

Annex lV: Drug Therapy Problems Identified in the Study Subjects

1. The patient had partial insight and was psychotic before 3 months so 0.5mg of Risperidone is not in the range of therapeutic dose of stabilization phase. (dose is low)
2. This patient is non-adherent and he lives in a street and his condition was fair within a year of antipsychotic treatment but he was not taking his medication properly so depot medication should be considered rather than giving Risperidone the whole time. Not the right choice dosage form for the patient (dosage form inappropriate).
3. Multiple drug discontinuations: The patient was taking oral haloperidol 1.5mg even if he was not taking at the time of arrival so he is a candidate for depot medication. Not the right choice for the patient (dosage form inappropriate).and even in the oral form the dosage of haloperidol should be greater than 2mg because he was not in full remission (dose low)
4. This patient was not in full remission fair judgment and insight but his medication was reduced to 2mg of Risperidone the dosage should be increased.(dosage low)
5. When switching between first generations, antipsychotics equivalent doses should be given equivalent dose of haloperidol 5mg is 25mg of fluphenazine depot every 4weeks. Testing dose of 12.5mg should have to be given for 2 weeks and the dosage should be adjusted rather than giving (12.5mg every 4 weeks) because patient's condition was still the same and he was non adherent .(dose low)
6. This patient is still symptomatic and she was taking haloperidol 10mg for more than 7months so another option from the second generation antipsychotic should be considered and switch.(Not the right choice drug for the patient delayed switch)
7. This patient was non adherent and he was taking 6.5mg of haloperidol so rather than giving 12.5mg of fluphenazine depot every 4 weeks, equivalent dose of haloperidol 6.5mg after test dose, 25mg of fluphenazine every 4 weeks should be given. (dose low)
8. The patient had fair insight and inappropriate speech starting from he was on Risperidone (had fair response on Risperidone 5/1/07 on chart written). Other options should be assessed including olanzapin. (Not the right choice drug for the patient, Delayed switch)

9. The patient condition was poor, he was non adherent to his medication and he started fluphenazine so the dose of fluphenazine 25mg should be evaluated and adjusted every 2 weeks. (dose adjustment, frequency inappropriate)
10. The patient had chronic schizophrenia and developed TD and Trihexyphenidyl was prescribed for him which were C/I but his condition was the same. He had delusion on the day of examination. Switching to another medication is better rather than continuing the same medication (Risperidone 2mg).(undesired effect and not the right choice of drug for the patient)
11. This patient only had slight improvement with more than one month of starting treatment so the dosage should be adjusted. (dose low)
12. The patient developed sexual dysfunction and decreased libido. He was on Risperidone and different guideline indicates Risperidone causes this S/E and recommend to switch to lower propensity of ED or to give medication which can improve his sexual dysfunction because it can make the patient prone to non-adherence and treatment discontinuation. ADR (undesired effect).
13. This patient had chronic schizophrenia. If a decision was made to reduce the dose and discontinue medication he should stay at least 1-2 years on full remission early dose reduction (8 months after remission) to discontinue CPZ which was 25mg ,is out of therapeutic effect. The patient should stay on therapeutic maintenance dose for a minimum of 1-2 years. (dose low)
14. The patient had Alzheimer disease which is not treated and he developed drug induced Parkinsonism. He was taking Haloperidol 5mg which was reduced to 2mg and Trihexyphenidyl and clonazepam was added. (ADR and untreated medical condition).
15. Overweight, the patient gained body weight of 8-9kg after starting Risperidone before 7 months and now he is taking Olanzapine 15mg, written on chart (22/2/09, 16/6/09, and 4/12/09). ADR
16. This patient should be on minimum effective dose she was on 4mg of Risperidone starting from acute phase after drug discontinuation, for more than one year on stable phase she is taking the same dosage; dosage should be adjusted on stable phase to minimum effective dose. (dose high)
21. This patient was on the same dosage before discontinuation of treatment and had got improvement. He should be on 15mg of olanzapine rather than 5mg because his

condition was the same as acute phase and consider resuming the same dose and adherence problem should be addressed by educating and counseling the patient. (Dose low).

22. Dosage low; the patient was partial remission on 1.5 mg of haloperidol since 6/10 2008. And should be on minimum therapeutic range.
23. Dosage low: this patient has poor insight and she was taking Fluphenazine Deaconate depot 25mg Im monthly and should be on equivalent dose of haloperidol (Haloperidol 2.5mg/day not 1.5mg)
24. ADR: she had weight gain of more than 15kg after starting treatment and now weighs 75 kilograms within 5 years of treatment. Needs advice on nutrition and close follow up of weight or metabolic work up (undesired effect).
25. He is taking Efavirenz based HAART and he develop psychotic problem initially. Hence, HAART should be evaluated and should be changed to Nevirapine based treatment if the psychotic problem prolongs more than a month.(unsafe drug)
26. She has a difficulty of initiating sleep (Insomnia) so she needs short term benzodiazepine (needs additional treatment).
27. The patient was taking Risperidone 4mg more than two months and he is poorly responding to treatment. (Not the right for patient condition) should switch to other AP drug.
28. This patient had a problem of sexual dysfunction when he was taking thirodazine and Risperidone should not be the option to switch. ADR unsafe drug for the patient.
29. Routine combination of anti-psychotic is not recommended it should be based recommendation of different guidelines because it might causes combination of S/Es CPZ should not be continued for more than 2 years. Unnecessary drug therapy (Duplicate therapy)
30. Akathisia is better treated by benzodiazepine or propranalol. Trihexyphenidyl is considered after other trials including switching to other drug like olanzapine.
31. The patient developed TD. And he was taking 1mg of Risperidone for more than two years and His condition is the same. (Undesired effect)
32. In this patient's case, switching to other anti-psychotic drug should be considered, because he was on Risperidone 4mg and 6mg for more than two years and he is still in partial remission and non-adherent. And also his symptoms have relapsed and he

developed Dystonic reaction switching to olanzapine or other long acting antipsychotic. (Undesired effect and Not the right choice for patients condition)

33. The patient is poorly responding to the treatment and his medication was not in the lowest effective dose range. Haloperidol should be 2mg or more. But maintenance dose can be as low as 1mg/day dose low
34. This patient had fair insight and the dose of CPZ was 50mg starting from 2007.she had one time of drug discontinuation 11/9/08. So the dose of the medication should be increased. (not in full remission)
35. ----------
36. This patient was on haloperidol 0.75mg for more than 2 years and she fulfils the criteria to stop the medication if a decision is made to stop the medication. Gradual tapering and DC treatment (non drug therapy)
37. The patient develops TD (on 2mg of Risperidone) and Trihexyphenidyl was prescribed which should not be given for TD. (Undesired effect and unsafe drug).
38. Risperidone 1 mg is not a therapeutic range and response to treatment was poor (not in full remission). Even if the patient was non adherent to medication, when resuming medication it should be within the therapeutic range.
39. The patient condition hasn't improved and it is difficult to manage. Olanzapine was tried and it was combined with Risperidone but combination in not advised before clozapine trial. Not the right choice for the patient condition.
40. This patient condition hasn't improved and the dosage should be changed or another antipsychotic should be considered. She also developed TD and hyperglycemia so Trihexyphenidyl was prescribed which should not be prescribed for TD. (undesired effect, unsafe drug for condition)
41. The patient discontinued his treatment several times. So depot medication is preferable.(dosage form inappropriate)
42. The patient had multiple drug discontinuations and should be on depot medication; (dosage form unsuitable)
43. Combination of antipsychotics is not advisable unless for a short period or after clozapine trial. In this case, Combination of fluphenazine and thirodazine for more than 6 months is seen. And his blood sugar has increased to 262.8 and is not being treated or monitored.

44. Combination of anti-psychotics should not be given unless with some circumstances and if there is sleep problem short term benzodiazepine should be given.
45. Early dose reduction dosage low at least 1-2 years in full remission to stop anti-psychotic. (She is in full remission since 3/1/09) two months.
46. This patient condition has got only slight improvement. Dosage adjustment for CLD patients Risperidone can increase to 0.5mg every 12 hours (dosage low).
47. This patient's lipid profile is high (TG-330 and Total cholesterol was 256) and also his BMI was 36.49 which is class ll obesity, so he needs additional drug treatment. His weight is 103 kg so he needs medication which has weight neutral on proper dosage form because he is non-adherent to his medication. He is on Risperidone 2mg and his condition was fair. (Needs additional drug therapy for Obesity and Hyperlipidaemia)
48. This patient had chronic schizophrenia and she was taking low dose 100mg CPZ and she is not entering in to remission. Dosage of CPZ should be adjusted.
49. The patient's lipid profile is high (TG-244, total cholesterol 274) and had class l obesity BMI 32.71. He discontinued follow up from Amanuel Hospital and was non adherent. Risperidone is unsafe drug for the patient and depot medication from first generation should be considered.
50. Chronic schizophrenia and has partial insight for more than 4 months. Dosage should be increased to 5mg of Risperidone.
51. Multiple drug discontinuation LA depot medication should be considered.
52. This patient has increased prolactin level and hypogonadism, she also developed TD and she is type l Diabetic patient. Risperidone is unsafe for the patient and contraindicated; her condition is also the same and has poor insight.
53. This patient has treatment resistant schizophrenia and she took different antipsychotics but her condition is the same for more than 5 years. She has hyperlipidimiya and obesity. She is a candidate for clozapine by controlling her weight and lipid profile. She also has developed Absence seizure on 30/8/09 and she didn't get treatment.
54. This patient is not taking her medications properly (multiple drug discontinuation) and her conditions haven't improved. So she is non-adherent and a candidate for long acting depot medication.

55. This patient has been taking Risperidone 8mg for more than 2months but her condition is the same switching to another antipsychotic should be considered.
56. When switching to LA fluphenazine depot gradual tapering and discontinuation of Risperidone should be done and not increasing the dose of Risperidone at the same time of adding depot medication. (Dosage of Risperidone is high).
57. The patient is non-adherent to his medication and his condition has relapsed. Hence depot medication should be considered (dosage form inappropriate)
58. The patient developed dystonia of rolling eyes and face and he needs anticholnergic medication. He also needs additional drug therapy because he developed undesired effect.
59. The patient developed erectile dysfunction and impotence and divorced his wife because of this and Risperidone is highly associated with high risk of prolactin elevation and sexual side effects. Different guidelines recommend that if sexual dysfunction occurred by Risperidone first step is to decrease the dose or discontinue the offending drug. The next step is to switch to a different drug that is less likely to cause the specific sexual problem experienced.
60. The patient had multiple relapses and repeated suicidal ideation and also he was non adherentto his medicationmultiple times. So depot formulations should be considered.