

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF PSYCHIATRY

TIME TO ANTIPSYCHOTIC DISCONTINUATION AFTER REMISSION AMONG PATIENTS WITH MAJOR DEPRESSIVE DISORDER WITH PSYCHOTIC FEATURES AT TIKUR ANBESSA SPECIALIZED HOSPITAL: A CROSS-SECTIONAL STUDY

BY: ASSAMIN ASSAFAW (MD)

A RESEARCH THESIS TO BE SUBMITTED TO THE DEPARTMENT OF PSYCHIATRY IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE SPECIALITY CERTIFICATE IN PSYCHIATRY

MARCH, 2026

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ADVISORS:

1. Dr. Getahun Belay (MD, Assistant Professor Of Psychiatry)
2. Professor Solomon Teferra (MD, PhD, Consultant Psychiatrist, Specialist in Addiction Psychiatry)

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ADDIS ABABA, ETHIOPIA

ACRONYMS/ ABBREVIATIONS

AP: Antipsychotic

AAU: Addis Ababa University

APA: American Psychiatric Association

CHS: College of Health Sciences

DSM-5: Diagnostic and statistical manual for mental disorder fifth edition

DoP: Department of Psychiatry

ECT: Electroconvulsive Therapy

EPS: Extrapyramidal Side Effects

LMICs: Low- and Middle-Income Countries

MDD: Major Depressive Disorder

MDD-PF: Major Depressive Disorder with Psychotic Features

NICE: National Institute for Health and Care Excellence

OPD: Outpatient Department

PI: Principal Investigator

RCT: Randomized Control Trial

REC: Research and Ethics Committee

SoM: School of Medicine

SPSS: Statistical Package for the Social Sciences

SSRIs: Selective Serotonin Reuptake Inhibitors

STOP-PD II: Study of The Pharmacotherapy of Psychotic Depression II

TASH: Tikur Anbessa Specialized Hospital

WFSBP: World Federation of Societies of Biological Psychiatry

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Abstract

Background: Major depressive disorder with psychotic features is a severe and disabling condition that requires both antidepressant and antipsychotic treatment. Most international guidelines recommend maintaining antipsychotics for 4-6 months after clinical remission, but data on actual duration and discontinuation practices in our setting is limited for major depressive disorder with psychotic feature treatment.

Objective: The objective of this study is to determine the time to antipsychotic discontinuation after remission among patients with major depressive disorder with psychotic features at Tikur Anbessa Specialized Hospital, 2025.

Methods: A retrospective cross-sectional study was conducted among cases with major depressive disorder at TASH who had a follow-up for the past 5 years. Census method was used to select eligible patient records from the psychiatry follow-up EMR registry. Data on demographics, clinical profiles, antipsychotic treatment duration, remission, and discontinuation status was collected. Descriptive statistics was used to summarize the data and chi-square test to measure the association between categorical variables and results were presented using tables, graphs and charts.

Result: A total of 234 MDD patients were included in the study with a mean (±SD) age of 39.6 ± 14.6 years, of whom 60 (25.6%) had MDD with psychotic features, and 62 (60 MDD-PF + 2 MDD as augmentation) patients initiated antipsychotic treatment, with risperidone, 58.3% and olanzapine, 25% being the most commonly prescribed. Clinical remission was achieved in 56.4% patients receiving antipsychotics. Prolonged antipsychotic treatment was found in 65.7% patient, and 48.6% patients still continued antipsychotic treatment following remission for a mean duration of 16.2 months (median: 15.5 months, IQR:9.4 months). Comorbid medical illness was the only factor significantly associated with remission ($p = 0.011$).

Conclusion: The findings provide evidence on rational antipsychotics use and treatment practices for patients with major depressive disorder with psychotic features who start treatment at tertiary care setting. It supports the need to develop an institutionalized or national treatment protocol; help to improve psychiatric care while

reducing the unnecessary prolonged antipsychotics use to ease the burden on both patients and the healthcare system.

Keywords: Major depressive disorder, Psychotic features, Time to antipsychotic discontinuation, clinical remission, Ethiopia.

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Introduction

1.1 Background

Major Depressive Disorder with Psychotic Features (MDD-PF), previously known as psychotic depression, is characterized by the presence of mood-congruent or mood-in congruent psychotic symptoms, such as delusions or hallucinations, during depressive episodes (1). Commonly identified psychotic symptoms are mood congruent, usually manifesting as nihilistic type delusions, with the belief that bad things are about to happen on self or others (2). This is usually associated with greater symptom severity, functional impairment, or risk of suicide than non-psychotic depressive disorders (3).

The current standard treatment approaches for MDD-PF includes a combination of antidepressants and antipsychotic medications (4) or, in some cases, Electroconvulsive therapy (ECT) (5). Although the combination of antidepressants and antipsychotics was widely accepted as the first-line treatment for acute episodes in patients with MDD-PF, there is no strong evidence to say that the combination of an antidepressant with an antipsychotic is more effective or superior than an antidepressant alone according to some studies (6).

In balancing between risks and benefits of different treatment options, most studies suggested that initial monotherapy with an antidepressant should be the preferred option for many patients with MDD-PF. Initial antidepressant monotherapy and adding an antipsychotic if the patient does not respond for the monotherapy (7). Even if combination treatment is necessary the optimal antipsychotic duration as a maintenance treatment is unclear and needs risk benefit analysis (8,9).

An observational study done among patients with major depressive disorder with psychotic features found that about 50% of patients recover within two to three months, and the large majority of patients recover within six to twelve months (10).

However, how long should patients stay on medications after remission remains a point of discussion among patients with MDD-PF (7).

It usually associated with determining the optimal continuation and maintenance period, but in what dose the antipsychotics to be tapered once remission has achieved is not clear.

Multiple international guidelines tried to investigate time to antipsychotic discontinuation and its determinants after remission among patients with psychotic depression, and found minimal evidence to guide clinicians on long-term treatment strategies, regarding the continuation or discontinuation of antipsychotics (7, 8, 10- 11). Most guidelines stressed on the importance of antipsychotics as a maintenance treatment options once remission is achieved (12) and clinicians should be guided by their own individualized and personalized care model weighing patient-specific relapse risk against potential long-term side effects when treating psychotic depression, especially in settings where clinical resources are limited (13).

Most experts discontinue the antipsychotic treatment after four months of sustained recovery, but maintaining the antipsychotic for at least six to 12 months was found to be a reasonable decision once patients who relapsed while discontinuing the antipsychotics during maintenance treatment of prior episode (13,14). One study recommended slow tapering of antipsychotics usually by 25% once remission is achieved on a weekly basis. If any symptoms of relapse recurs during the tapering the study recommended to titrate the dose back up to the full dose used initially to achieve remission (14).

Accordingly, the American Psychiatric Association (APA) and the National Institute for Health and Care Excellence (NICE) clinical guidelines recommend that antipsychotics can be discontinued within 3 to 6 months after remission of psychotic symptoms, while antidepressants may be continued for maintenance therapy (1,12,15).

Despite multiple recommendations, clinical practice in low-resource settings including Ethiopia have not develop its own guideline on the duration of antipsychotic treatment after remission. Patients with MDD-PF often kept on antipsychotic medication for

unspecified prolonged periods, at times lasting years. According to a study done in Ethiopia absence of standardized treatment protocols, limited access to trained mental

health professionals and concerns about relapse as some of the contributing factors identified for longer duration of treatments in a general psychiatric patients (16).

Similarly, most studies found that longer period of antipsychotic use among patients with MDD-PF after remission is strongly associated with adverse outcomes including metabolic syndrome (17), extrapyramidal side effects, poor drug adherence, and decreased quality of life (4). This made it crucial to review the patterns and duration of antipsychotic discontinuation and associated factors for longer period use among patients with MDD-PF once remission is achieved in resource limited settings like ours (9).

1.2. Problem Statement

Despite multiple international guidelines recommend clear evidence favoring combination treatment for patients with MDD-PF in acute phases (13), clinicians often hesitate to discontinue antipsychotic medication treatments beyond remission period resulting adverse side effects including metabolic syndrome and extrapyramidal symptoms. This is mostly resulted from a lack of consensus and still persists on how to balance relapse prevention with minimizing medication burden (18).

Even though, most international guidelines recommend tapering off and discontinuation antipsychotics within a few months of remission in MDD-PF, clinical observations at tertiary level Tikur Anbessa specialized hospital, Ethiopia showed that many patients remain on antipsychotics for months to years once remission has achieved. This practice usually causes unnecessary antipsychotics related adverse effects including EPS and metabolic side effects for patients (17), which is evident in our day to day practices.

This is mostly associated with a combination of patient-related factors like age and adherence, clinician uncertainty and lack of locally agreed guidelines on how long to continue antipsychotics treatment once remission is achieved.

To date, no study in Ethiopia has investigated the actual duration of antipsychotic use in patients with MDD-PF once clinical remission is achieved or identified the determinants contributing to prolonged use. This represents a critical evidence gap, as prolonged exposure to antipsychotics carries significant risks and may not align with best-practice recommendations.

Significance of the Study

At Tikur Anbessa Specialized Hospital (TASH), many patients with MDD-PF remained on antipsychotic treatment for longer months, and at-times for years without clear justification despite symptom remission and usually patients are prone to unnecessary antipsychotics related side effects.

This study aimed to conduct a clinical audit of the patterns of antipsychotics use after clinical remission among patients with MDD-PF who are followed up at TASH for the past five years. This clinical audit will provide valuable knowledge on current practices at TASH psychiatry unit by highlighting the duration and identifying factors associated with prolonged antipsychotics use after remission in comparison with the international guidelines.

The study also aims to raise awareness among psychiatry care providers including resident physicians about the need for regular antipsychotics medication reviews and structured discontinuation plans after remission to decrease adverse side effects. This finding will improve unnecessary side effects, poor medication adherence and increased healthcare.

Findings from this study will also support the development of hospital-level recommendations and training materials for future treating psychiatry teams. By generating local evidence, the study also hopes to contribute toward safer, more

efficient, and standardized care for patients with major depressive disorder with psychotic features.

It a will also serve as a baseline study for future prospective multi-centered studies with a strong study design for future researchers who wants to study on the subject.

In addition, this study generates relevant evidences for MOH health policy makers to guide their policy discussions on rational use of antipsychotics for all patients in general and patients with major depression with psychotic features in particular in Ethiopia context.

Overall, the findings of this study is important in promoting local evidence-based clinical practice with a strong focus on patient safety. The results also support the development of standardized national treatment protocols for major depression with psychotic features patients, helping to improve psychiatric care while reducing the unnecessary use of antipsychotics and easing the burden on both patients and the healthcare system.

Literature Review

3.1. Major Depressive Disorder with Psychotic Features

Major Depressive Disorder with Psychotic Features (MDD-PF), historically referred to as *psychotic depression*, is a severe form of depression characterized by the presence of psychotic symptoms—delusions and/or hallucinations during a major depressive episode (1). Unlike primary psychotic disorders such as schizophrenia and other schizophrenia spectrum disorders, the psychotic symptoms in major depressive disorder with psychotic features are typically mood-congruent and occur exclusively during depressive episodes (19).

These mood-congruent psychotic symptoms usually manifested as nihilistic type of delusions, where patients believe that bad things might and are about to happen with associated feelings of guilt and negative self-concept (20,21). At times it can be manifested with mood-congruent psychotic features like thoughts of persecution, or thought insertion, which often indicates a more complex clinical presentation and poorer prognosis (20,21). It is associated with higher rates of functional impairment, suicide attempts, and hospitalization when compared to those with non-psychotic depression (14, 23, 24).

According to studies, the rates of psychotic depression are considerably higher, and the lifetime prevalence of major depressive disorder with psychotic features was around 0.4–1%, but due to overlapping features with schizophrenia and bipolar disorder; the prevalence tends to *be under-diagnosed* (24).

One study done in China found the rate of psychotic symptoms among young adult MDD patients was 9.1% (25), and similarly, another study done in a European found 18.5% patients who met the criteria for major depression also fulfilled the criteria for a major depressive episode with psychotic features (24) compared to 14.7% in the United States (26).

in one African study depression was found affecting more than 29 million people and the prevalence was more common among patients with chronic diseases (27). For

example, studies done in Nigeria and South Africa revealed that the prevalence of MDD was around 32.5% (28) and 34.8%(29) respectively among patients with chronic illness. Similarly, in sub- Saharan African countries, there was a decreased of evidence on the pooled prevalence of MDD and single studies done in Uganda and Tanzania revealed the overall prevalence of MDD to be 29.3% (30), and 42.4% (31) among youths, traumatic adults and patients with chronic illness, respectively.

Regarding the prevalence of major depressive disorders with psychotic features, there is little evidences in the general population of most African countries as most studies done focused on general psychotic symptoms or illnesses, without saying whether the psychotic symptoms happen during depressive episodes or not.

This shows that more research is needed in African context on the accurate prevalence of depression with psychotic symptoms, using better study designs and tools that can separate different types of mental illness, which will have prognostic indicators in terms of treatment type and duration.

In Ethiopia too, there is limited evidences regarding the prevalence of Major depressive disorder with psychotic features as few studies have been conducted. In one study done at Hawassa in 2019 among patients diagnosed with cancer, the prevalence of depression was around 21.58% in general populations (32). In this study despite there were no randomization during the study, it concluded around 15% patients diagnosed with MDD has comorbid psychotic features as a severity sign (32).

3.2. Treatment Options and Recommended Duration

A combination of antidepressants and antipsychotics is the recommended first-line pharmacological treatment option for patients with MDD-PF currently. The commonly combinations treatment options include selective serotonin reuptake inhibitors (SSRIs) with second-generation antipsychotics such as risperidone, olanzapine, or quetiapine (7,19,33,34), but first generation antipsychotics can also be used despite common adverse side effects associated with it including severe form of EPS (35). In severe or treatment-resistant MDD-PF, Electroconvulsive therapy (ECT) is considered highly

effective and the treatment of choice according to different studies and in many areas of care (5).

A Swedish registry based study tried to examine the outcomes of combination treatment over a two years period and the study found a lower rate of relapse, measured and defined by defined by hospital readmission, suicide attempt, or suicide (8). The study concluded patients on combination therapy has lower rate of relapse compared to those on antidepressant monotherapy (36.6% vs. 42.3%, $p < 0.01$) (8).

Most International guidelines recommend discontinuing antipsychotics within 3 to 6 months of remission (14), while maintaining antidepressants for longer-duration as a relapse prevention strategy.

For example, the American Psychiatric Association (APA) advises maintaining antipsychotic treatment for at least 4 to 6 months after symptom remission (1,37). It suggests tapering antipsychotics gradually after symptom resolution, and during tapering assessing patient's clinical stability, comorbid illnesses and social support are highly indicated, as these two factors are important good prognostic factors (36,37).

In 2013, a study done in Canada with an aim of examining and addressing the uncertainty about how long to continue antipsychotics treatment for patients with psychotic depression once remission achieved. In the study, researchers tried to highlight a critical clinical dilemma between balancing relapse risks versus long-term side effects of antipsychotics (38). They came up with Study of the Pharmacotherapy Of Psychotic Depression (STOP-PD II) trial aimed to evaluate whether continuing olanzapine after achieving remission with sertraline-olanzapine treatment reduces the risk of relapse compared to early discontinuation (38).

This study was a three-phase multicenter randomized double-blind placebo - controlled trial (RCT) done among patients aged 18-85 years old with non-bipolar major depression with psychotic features and patients underwent up to 12 weeks of open-label treatment with sertraline and olanzapine, followed by an 8-week stabilization phase once remission achieved. Those who maintained remission were randomized to

either continue olanzapine or switch to placebo for 36 weeks, with all participants continuing sertraline.

The study tried to compare the risk of side effects associated with prolonged use of antipsychotics versus early discontinuation by comparing of risk relapse as a primary outcomes whereas with drug side effects including metabolic changes and the influence of age as secondary outcomes (38).

Over a 36-week period, the study found that only 20.3% of participants on continued olanzapine relapsed compared to 54.8% on placebo (hazard ratio = 0.25; $p < 0.001$). The findings recommended a robust support for the continuation of antipsychotic medication during the maintenance phase of psychotic depression for relapse prevention. The study also found a 20% difference in relapse risk among older adults based on prior relapse rates of ~35% upon discontinuation versus ~15% with continuation and recommended an evidence-based guidelines regarding antipsychotic tapering in patients with MDD-PF (38).

Another study done by Rothschild tried to outline the complexities and limitations in the treatment of major depressive disorder with psychotic features and highlighted persistent gaps in clinical management. According to this study combination of antidepressants and antipsychotics was widely accepted as the first-line treatment for acute episodes, but there was minimal evidence for psychiatrists and other mental health clinicians to guide on the continuation or discontinuation of antipsychotics.

The author found clinician's hesitancy to maintain antipsychotic therapy beyond remission due to concerns over adverse effects despite clear evidence favoring combination treatment in acute phases. It also highlighted lack of consensus among clinicians in balancing relapse prevention with minimizing medication burden mainly because of lack of standardized treatment practices and guidelines. Similarly, higher rate of relapse following antipsychotics discontinuation within the first 6 months was found and recommended long-term antipsychotics treatment strategies by analyzing the risks of relapse versus side effects associated prolonged use were recommended (22).

Other studies also highlighted the need for empirical data to guide maintenance antipsychotics treatment decisions by emphasizing on the need for personalized care models focusing on patient-specific risk of relapse against potential long-term side effects (23).

The study further recommended in investigating time to antipsychotic discontinuation and its determinants with good methodology, especially in low resource clinical settings for future researchers (23).

According to the above studies the clinical uncertainty and diversity in treatment approaches for psychotic depression beyond the acute phase is common (22,38). In their findings STOP-PD II offered a rigorous experimental framework to evaluate risk-benefit analysis of continuing versus discontinuing antipsychotics comparing relapse prevention and associated metabolic risks (38), Rothschild provided a real-world challenges and clinician hesitancy regarding the timing of discontinuing antipsychotics after remission (22). Both studies highlighted the need to have further studies with an empirical data to guide maintenance treatment decisions and emphasized the importance of personalized care models (26) that weigh patient-specific relapse risk against potential long-term side effects (22,26).

Similarly, despite several international guidelines recommend continuation of antipsychotic medications for a limited period following remission among patients with psychotic depression. Almost all studies lack specificity regarding tapering strategies or long-term safety in diverse clinical contexts suggested that relapse risks should weighed against the burden of prolonged use of antipsychotics including metabolic syndrome, extrapyramidal symptoms, and poor quality of life (4,39,40)

For instance, the American Psychiatric Association advises maintaining antipsychotic treatment for at least 4 to 6 months after symptom remission (1) while the National Institute for Health and Care Excellence suggests a similar approach, highlighting the risks of premature discontinuation (36). The World Federation of Societies of Biological Psychiatry (WFSBP) also supports individualized continuation based on clinical risk factors and it acknowledges the absence of robust evidence guiding long-term use (41).

In the context of Africa, there is no objective Africa-specific practice guideline used as an exclusive treatment guideline for major depression with psychotic features. However, South African journal of Psychiatry recommended combinations of antidepressant and antipsychotics as first line treatment option, which is consistent with the international evidences drawn from the APA, NICE and CANMAT(42).

Accordingly, the guideline recommended 6-9 months of continued antidepressant use and tapering of antipsychotics within 3-6 months once remission has achieved for major depression with psychotic features. The guideline also recommended longer period of maintenance treatment for recurrent cases (42).

In the context of Ethiopian guidelines recommended combination treatment for the treatment of major depressive disorder with psychotic feature. Despite treating with antipsychotics along with antidepressant is common, antipsychotic discontinuation practices are not standardized. This lack of clear standardized practice is leading to a personal bias for the clinicians, which results in prescribing patterns of antipsychotics largely dependent on clinician experience. Psychiatrist and treating physicians are reluctant and at times due to fear to stop antipsychotics even though remission is achieved for longer period (16).

This practice and lack locally standardized guidelines usually led patients to develop unnecessary antipsychotic related side effects, including metabolic and EPS (35). When prescribed for longer duration even though remission has achieved and at time, premature discontinuations associated with early relapse of the depression.

3.3. Prolonged Antipsychotic Use and Its Consequences

Despite evidence-based recommendations recommended the use of antipsychotics for 4-6 months after remission (1) various international studies report prolonged use of antipsychotics well beyond the advised 6-month period.

For instance, one study done in the United States found that nearly 60% of patients with MDD-PF remained on antipsychotics for over 12 months (43). This extended and prolonged uses of antipsychotics despite remission were associated with serious

adverse effects including decreased adherence due to side effects, extrapyramidal symptoms, cognitive dulling and metabolic syndrome like, weight gain, diabetes, or dyslipidemia (17,44).

In sub-Saharan Africa, studies found prolonged use of antipsychotics were often influenced by clinician uncertainty, fear of relapse, inadequate patient educations and medication monitoring along with poor follow-up systems (45).

3.4. Factors Associated with Prolonged Antipsychotic Use

Varies studies have identified multiple factors associated with the need to have longer duration of antipsychotic use in MDD-PF patients. These includes clinical factors like severe psychotic symptoms, patients resistance to treatment, history of relapse in previous treatment, and the presence of other comorbid psychiatric illness (46). There are also patient related factors identified including patients poor insight about the illness, poor social support, medication non-adherence, older age (47).

Other studies also found that clinician-related factors such as overestimation of relapse risk, limited awareness of guidelines, cautious approach to discontinuation (43), and system related factors; lack of follow-up, non-specialist prescribers, and absence of local guidelines (34) were strongly associated with prolonged antipsychotics use. In general, understanding of determinants of prolonged antipsychotic use among patients with MDD-PF is essential for designing interventions that promote appropriate medication use and improve long-term outcomes for patients.

3.5 Conceptual Framework

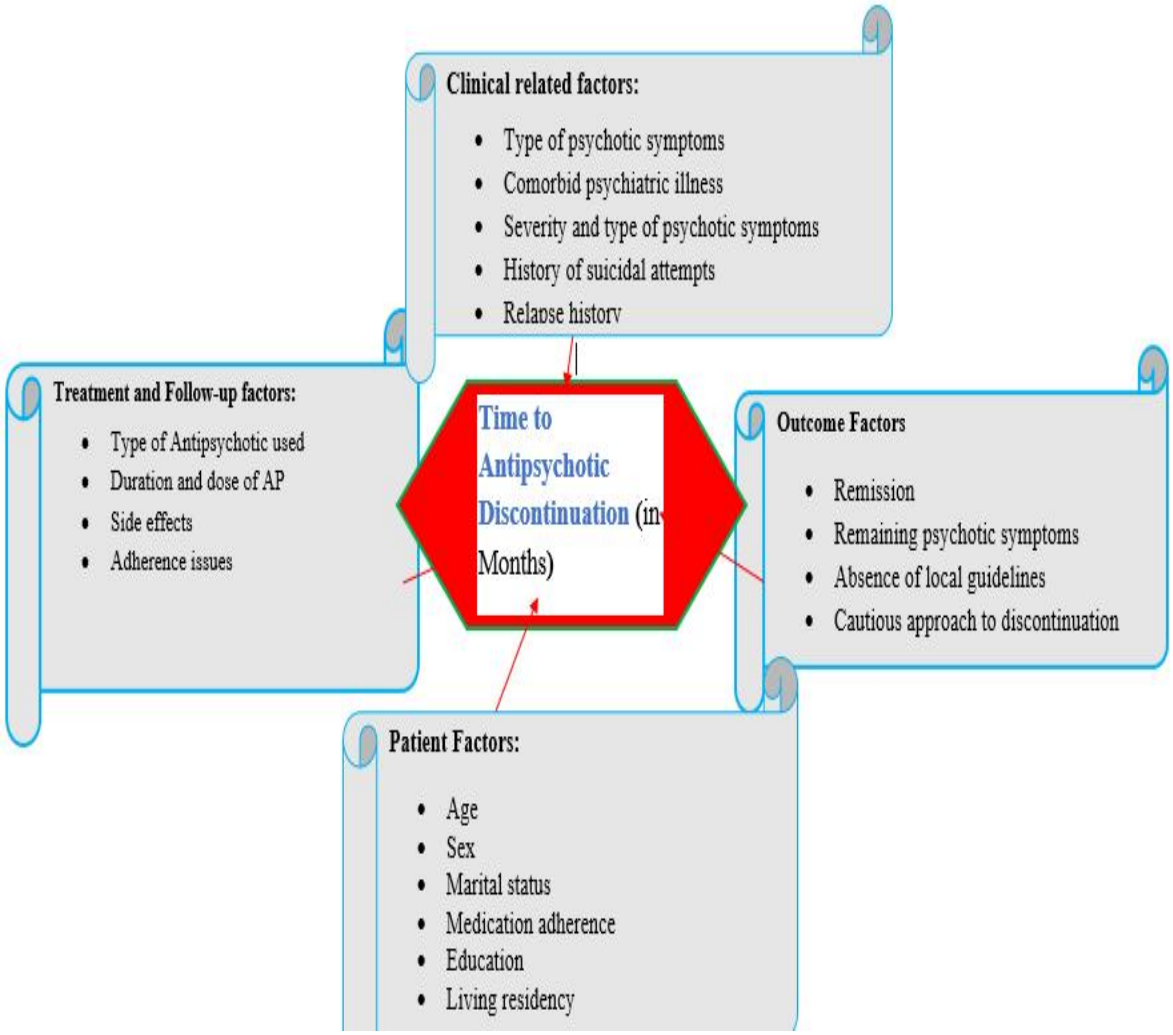


Figure 1 : Conceptual framework of variables associated with Time to antipsychotic discontinuation after remission among MDD-PF patients [adapted and modified from different literature reviews] (9, 43, 47)

Research Question

The research questions guiding this study were:

1. What is the average duration of antipsychotic use after remission among patients diagnosed with MDD-PF at Tikur Anbessa Specialized Hospital?
2. What is the proportion of prolonged antipsychotic treatment after remission of psychotic symptoms and what are the possible factors are associated with prolonged treatment?
3. To what extent do antipsychotic discontinuation practices following clinical remission for patients diagnosed with MDD-PF at TASH align with regional and international guidelines?

Objectives

5.1 General Objective

- To assess the time to antipsychotic discontinuation after clinical remission among patients with major depressive disorder with psychotic features at Tikur Anbessa Specialized Hospital (TASH).

5.2 Specific Objectives

1. To estimate the proportion of patients with major depressive disorder with psychotic features at TASH who remain on antipsychotic treatment beyond six months after treatment remission.
2. To determine the median time to antipsychotic discontinuation after clinical remission in patients with major depressive disorder with psychotic feature at TASH.
3. To identify socio-demographic, clinical, and treatment-related factors associated with prolonged antipsychotic use in patients with MDD-PF.
4. To assess adherence in comparison to international recommendations for antipsychotic use among MDD-PF patients.

Methods and Materials

6.1. Study Setting and period

6.1.1. Study setting

The study was conducted at Tikur Anbessa Specialized Hospital (TASH)**,** one of the largest teaching and tertiary specialized hospitals in the country, operating under the Addis Ababa University in Arada, Sub city, Addis Ababa Ethiopia. It is the largest and the oldest hospital in the country, which is giving high quality service. As a major healthcare institution, it serves as both a clinical and center of excellence in academia, providing specialized care while training future medical professionals including specialization and subs-specialization programs in psychiatry. The hospital started a 3-year post-graduate training program since 2003 G.C under Addis Ababa University. As national referral center, TASH has psychiatry outpatient clinics that provide ongoing care for patients with different psychiatric illness including major depressive disorder with psychotic features.

6.1.2. Study period

- Data was collected from 22 October 2025 – 12 December 2025**.**

6.2. Study Design

A an institution based retrospective cross-sectional study design using a chart review was conducted to assess the duration of antipsychotics use before discontinuation after achieving remission and identify its factors for prolonged use. This clinical audit was done by reviewing electronic medical records of already diagnosed cases with Major depressive disorder who had been on follow up at TASH psychiatry OPD.

6.3. Study Population and Eligibility Criteria

6.3.1. Source Population

- All patients diagnosed with MDD and had follow up at TASH psychiatry OPD for the past 5 years.

6.3.2. Study Population

- Patients diagnosed with MDD who had a follow-up for the past 5 years (January 1, 2020, and October 20, 2025) were included in the study

6.3.3. Inclusion Criteria

1. Patients documented in the electronic medical record as having a diagnosis of major depressive disorder, based on ICD-10 or DSM-5 diagnostic criteria.
2. At least 6 months of documented follow-up
3. Complete records on medication use and follow-up.

6.3.4. Exclusion Criteria

1. Patients with comorbid schizophrenia, bipolar disorder, or schizoaffective disorder, or diagnosis changed from major depression to other diagnosis (e.g. bipolar disorder, primary psychosis, OCD…) through time.
2. Patients transferred to another facility before completing follow-up.
3. Records with major missing or illegible key data (e.g. Antipsychotics start/discontinuation dates).

6.4. Sample Size Determination and Sampling Technique

6.4.1. Sample Size determination

- The required sample size for this study was determined based on the availability of complete medical record during the study period.
- Given the limited cases with MDD at TASH Psychiatry OPD, a Census or complete enumeration technique was employed.
- All eligible charts for the past five years, which fulfill the inclusion criteria were included.

6.4.2. Sampling Technique

- Census or complete enumeration method was used to select eligible patient records from the psychiatry follow-up EMR registry. Census technique is chosen for this particular study because of the small number of cases with a diagnosis of major depressive disorder has been observed in our psychiatric clinical setting for the past few years, and this method is ideal in reviewing all eligible patient without sampling error. It is ideal in terms of avoiding selection bias with maximum data accuracy which supports robust conclusion (48).
- Hence, all recorded EMR cases with a diagnosis of MDD according to ICD-10, or DSM-5 criteria who received treatment at Tikur Anbessa in the past five years and who fulfill eligibility criteria were included in this study.

6.4.3. Data collection Procedure

Initially, a total of 300 patients with a diagnosis of major depressive disorder were identified from the EMR registry. During their follow up overtime, some patients' diagnosis were changed to other psychiatric disorder, including bipolar disorder, schizoaffective disorder, schizophrenia and OCD, and these cases were excluded from the study.

After exclusion, 234 charts with a consistent diagnosis of MDD were included in the final analysis. Among them, 60 cases were identified as having MDD with psychotic features.

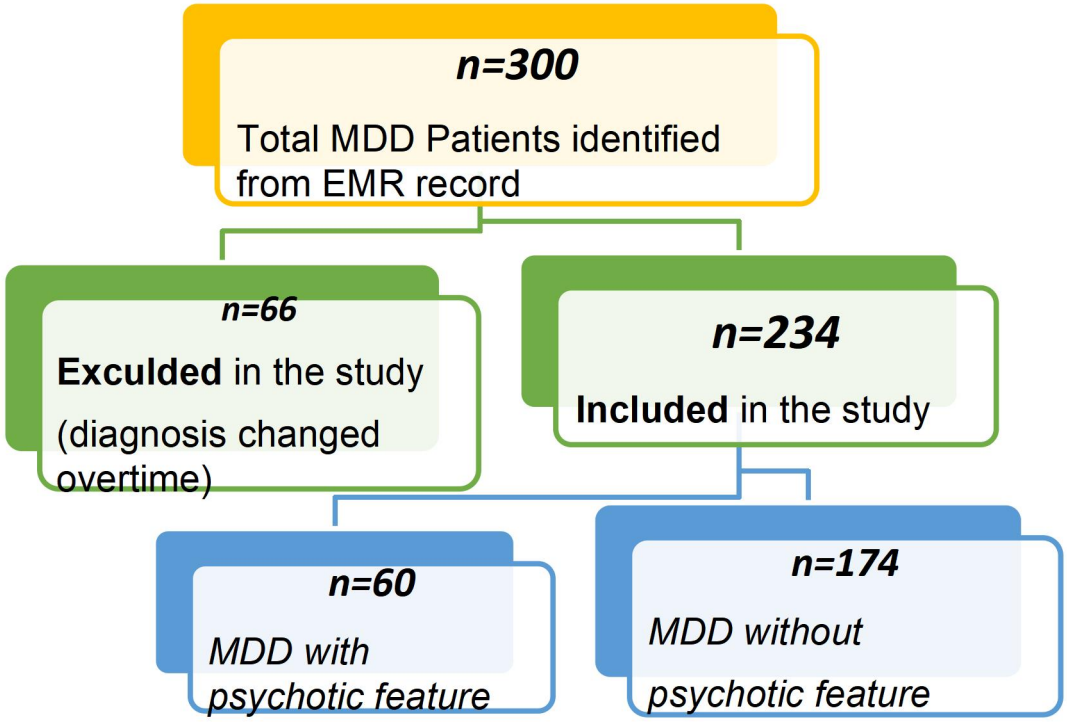


Figure 2: *Data collection Procedure*

6.5. Variables

6.5.1. Dependent Variable

- Time to antipsychotics discontinuation after remission (in months).

6.5.2. Independent Variables

- Socio-demographic factors: age, sex, marital status, educational status, residence, occupation.
- Clinical factors: severity of depression, type of psychotic features, medical and psychiatric comorbidities, suicidal attempt
- Treatment-related factors: type and dose of antipsychotics, treatment side effects, clinical remission, treatment discontinuation, adherence.

6.6. Operational definition of terms

- **Antipsychotic Treatment:** The prescription of any antipsychotic medications to manage psychotic symptoms in depressive disorders.
- **Duration of Antipsychotic Use:** The period, measured in months, from the start of antipsychotic treatment to its documented discontinuation or last follow-up entry.
- **Discontinuation:** Stopping of antipsychotic medication, confirmed by clinician notes or absence of prescriptions for at least three months (9).
- **Prolonged Use:** Continued antipsychotic treatment beyond six months after clinical remission of psychotic symptoms (33).
- **Clinical Remission:** The absence or significant reduction of psychotic features, noted in follow-up assessments by the treating clinician (33).
- **Relapse:** Reappearance of depressive or psychotic symptoms requiring intervention after remission (47).
- **Guideline Adherence:** Consistency of treatment practices with recognized international standards such as APA, NICE, or WFSBP recommendations (36,37,41).
- **Incomplete Chart:** Patient records missing critical data such as diagnosis, medication dates, or follow-up information necessary for analysis (48).

6.7. Data Collection Tools and Procedures

Data Collection Process: Data was collected using the Google form. The questionnaire was pre-loaded into the application. Two registered trained psychiatry clinical staff were recruited as data collectors supervised by the principal investigator (PI). A structured data extraction checklist using Google form was used to collect information from EMR patient records after getting ethical clearance from hospital's HMIS team.

In order to keep uniformity of the data collection process; data collectors were trained and adequately oriented day on the objective of the study, method of data collection, about how to use Google form with day-to-day supervision by the PI. Data collectors (trained psychiatry clinical staff) extracted clinical and demographic variables such as

diagnosis date, medications initiated, dose changes, starting and discontinuation dates from electronic medical records.

6.8. Data Analysis and Statistical Plan

Data from Google form was coded and exported to the Statistical Package for the Social Sciences (SPSS) version 25 for statistical analysis. The study employed statistical analysis to evaluate the duration of antipsychotics use since initiations (in months) and Time to discontinuation after clinical remission. Descriptive statistics (frequencies, percentages, mean, median and standard deviations) were calculated for demographic and other related factors and results were reported as percentages (frequency) for categorical variables or means with standard deviations for continuous variables. Chi-square test was used to measure the association between categorical variables. P-value $\leq$ 0.05 was used to cut significant association between categorical variables in the chi-square test.

6.9. Data Quality Control and Management

To maintain the quality of the data, data collectors were trained on standard procedures with a regular supervision on a daily basis to review the accuracy of collected data. On the Google form each question was encoded with a mandatory to answer before moving to the next parts. In addition, double data entry and consistency checks were performed. Electronic medical records were excluded from the study if there are incomplete or inconsistent data on the important variables of the study.

6.10. Ethical Considerations

Ethical clearance was obtained from the Research and Ethics Committee of Department of Psychiatry. Hospital administrations and HMIS team was communicated to have permission to access patient's medical records. Patient identifiers were anonymized including their name, and EMR identification. Data was stored in password protected computer. Confidentiality and data security was ensured throughout the process.

6.11. Utilization and Dissemination of Results

The study findings will be disseminated through:

- Thesis submission and defense at the Department of Psychiatry, School of Medicine, College of Health Sciences, Addis Ababa University
- Presentations at academic and professional conferences and submission to peer-reviewed journals
- Sharing with hospital administrators and the Ethiopian Ministry of Health to support guideline development

Result

7.1. Socio-demographic characteristics of patients

A total of 234 participants were included in the study. More than half 128 (54.7%) were aged <40 years, with a mean age of 39.6 ± 14.6 years, the majority 164 (70.1%) were females. Most 215 (91.9%) of participants resided in urban areas. Regarding religion, the majority 154 (65.8%) were Orthodox Christians, and 41 (17.5%) Protestant Christian religion followers. About 96 (41.0%) of patients were single, while 88 (37.6%) were married. Regarding educational status, the majority 55 (23.5%) had primary education (grades 1–8), while about 23 (9.8%) had no formal education. With respect to occupational status, 38.9% of the patients were employed while 28.6% were unemployed. (See Table 1 for details).

Table 1*:* Socio-demographic characteristics of patients diagnosed with major depressive disorder with psychotic features at Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia, 2025 (n=234).

Characteristics	Category	Frequency	Percent
Age group	<40 years	128	54.7
	≥ 40 years	106	45.3
	Mean ±SD	39.6±14.6 years	
	Median	38 years	
Sex	Female	164	70.1
	Male	70	29.9
Residence	Rural	19	8.1
	Urban	215	91.9
Religion	Orthodox	154	65.8
	Muslim	30	12.8
	Protestant	41	17.5

	Others	3	1.3
	Not documented	6	2.6
Marital status	Single	96	41.0
	Married	88	37.6
	Divorced	32	13.7
	Widowed	18	7.7
Educational status	Primary (1-8)	55	23.5
	Secondary (9-12)	53	22.6
	Diploma	37	15.8
	Degree	53	22.6
	Master and above	9	3.8
	No formal education	23	9.8
	Not documented	4	1.7
Occupational status	house-wife	30	12.8
	Employed	91	38.9
	Unemployed	67	28.6
	Farmer	4	1.7
	Student	36	15.4
	Others*	6	2.56

Key; Others*(occupation): broker, Congolese migrant, daily laborer, prisoner, merchant, retire

7.2. Clinical characteristics of patients

Among 234 patients included in this study, the proportion of Major Depressive Disorder with Psychotic Features was found to be 25.6% (60) and the remaining 74.4% (174) had no psychotic features.

In addition, documented history of suicide attempt was found in 9.8% (23), and 38.5% (90) had history of comorbid psychiatric illness: generalized anxiety disorder (GAD) was the most common with 16.8%, followed by PTSD (4.3%), somatic symptom disorder (3.0%), panic disorder (2.1%) and sleep disorders (1.7%) and OCD (1.3%). Other conditions less frequently present (proportions each ≤0.9%) included social anxiety disorder, substance use disorders, and borderline personality disorder, were found in the study.

About 95 (40.6%) of patients had history of comorbid medical illness; among those with comorbidities, the most frequently reported medical conditions were epilepsy 14(6.0%), HIV 9(3.8%), diabetes 7 (3.0%) and hypertension 7 (3.0%) either alone or in combination with other conditions. Other less commonly reported conditions (each ≤1.7%) included cardiac illnesses, hypothyroidism, stroke, Parkinson's disease, systemic lupus erythematous (SLE), and various thyroid disorders.

Antipsychotic was initiated for 62 (2 additional MDD cases as augmentation strategy) patients, and clinical remission was achieved in 56.45% (35) of the patients among those who initiated antipsychotics. Twenty-four (38.7%) patients discontinued antipsychotic medication during their last follow-up, and the main reason was clinical remission with no psychotic symptoms in 18 (75%) and four (16.67%) patients lost follow-up with unknown antipsychotics use status.

Regarding documented side effects, extrapyramidal symptoms (EPS) and metabolic side effects were reported in 5 (8.06%) and 4 (6.45%) respectively. In this study poor medication adherence was reported in 14 (23.33%) patients. (See Table 2 for details).

Table 2: Clinical characteristics and diagnostic pathways of patients diagnosed with major depressive disorder at Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia, 2025.

Characteristics	Category	Frequency	Percentage
Primary label diagnostic (n=234)	MDD	174	74.4
	MDD-PF	60	25.6
History of suicide attempt documented(n=234)	Yes	23	9.8
	No	211	90.2
Comorbid psychiatric illness (n=234)	Yes	90	38.5
	No	144	61.5
Comorbid medical illness (n=234)	Yes	95	40.6
	No	139	59.4
Did antipsychotic initiate? (n=234)	Yes	62	26.5
	No	172	73.5
Any Side effects documented? (n=62)	EPS	5	8.06
	Metabolic	4	6.45
	None	53	85.48
Adherence concerns noted (n=60)	Yes	14	23.33
	No	46	76.67
What was the patient's recent status? (n=60)	Has psychotic symptoms	23	38.3
	No psychotic symptoms	36	60.0
	NA	1	1.7
If the patient still has psychotic symptoms, what symptoms remained? (n=23)	Aggression	4	17.39
	Delusion	6	26.08
	Delusion + Aggression	5	21.73

	Delusion + Hallucination	3	13.04
	Hallucination	4	17.39
	Hallucination+ Aggression	1	4.34
Did the patient achieve clinical remission? (n=62)	Yes	35	**56.45**
	No	27	43.5
Was the antipsychotic medication discontinued after clinical remission at the last follow-up? (n=35)	Yes	18	51.43
	No	17	48.57
What was the reason for antipsychotics medication discontinuation, among patients discontinued treatment? (n=24)	antipsychotic related side effects	2	8.33
	Clinically remission / no psychotic symptoms	18	75.00
	Status unknown (lost to follow up)	4	16.67

7.3. Type of psychotic features present at first presentation

Hallucination, routinely defined as hearing voices or seeing objects which others can not hear or see, and delusion, defined by false and fixed belief which can not be shared by others, were the most common psychotic symptoms reported during first presentation In 27 (45%), and 16 (26.67%) patients, respectively. (See Figure **3** for details).

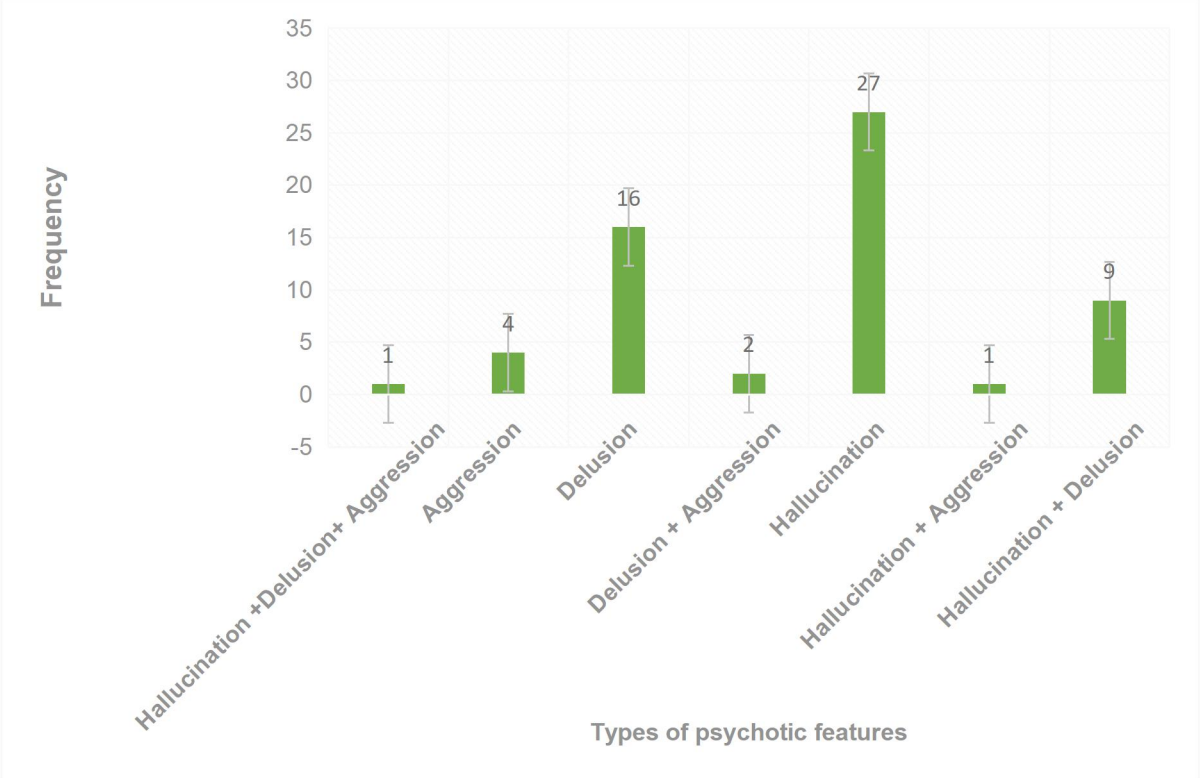


Figure 3: Type of psychotic features present at first presentation among patients diagnosed with major depressive disorder with psychotic features at TASH, 2025.

7.4. Prolonged antipsychotic use after clinical remission

In our study, prolonged antipsychotic treatment after clinical remission was found in 23 (**65.7%)** patients, among patients who achieved clinical remission (n =35), which is defined as continued antipsychotic treatment beyond six months post clinical remission, 12 (34.3%) patients discontinued treatment within 6 months of clinical remission as per recommendation from APA guideline. **(**See Figure 4 for details).

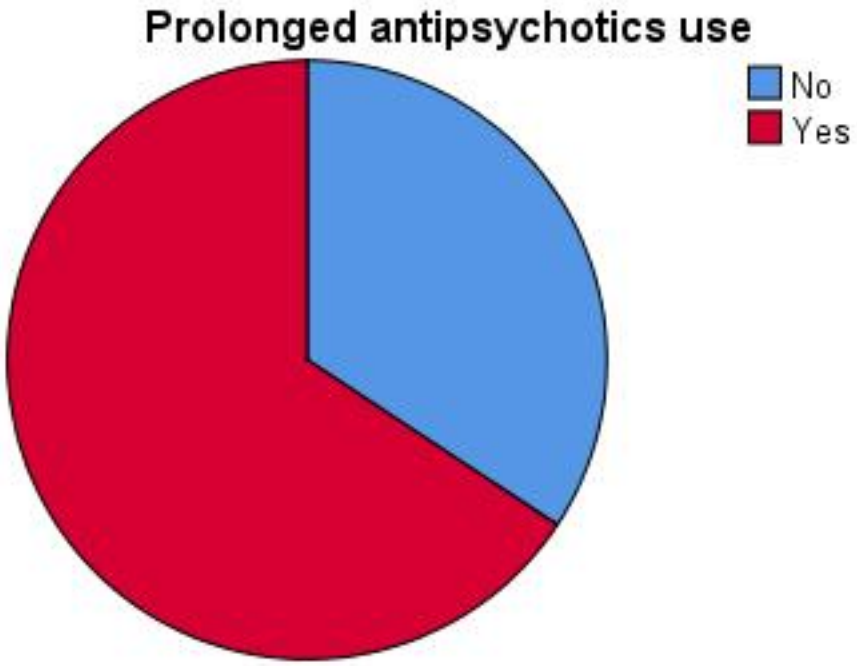


Figure 4: Prolonged antipsychotic treatment among MDD-PF patients who achieved clinical remission at TASH, 2025.

7.5. Duration and time to antipsychotic discontinuation after clinical remission

Among 35 patients who achieved clinical remission, only 18 patients discontinued antipsychotic treatment, indicating that nearly half of the remitted patients remained on antipsychotics beyond remission. The mean time to discontinuation from achieving clinical remission was approximately ≈12.4 months (range 0.7- 69.4 months). The median difference between clinical remission and treatment discontinuation was 5.54 months (IQR 1.97–14.6), which showed discrepancy between the mean and median indicating positively skewed distribution. **(**See Figure **5** for details**).**

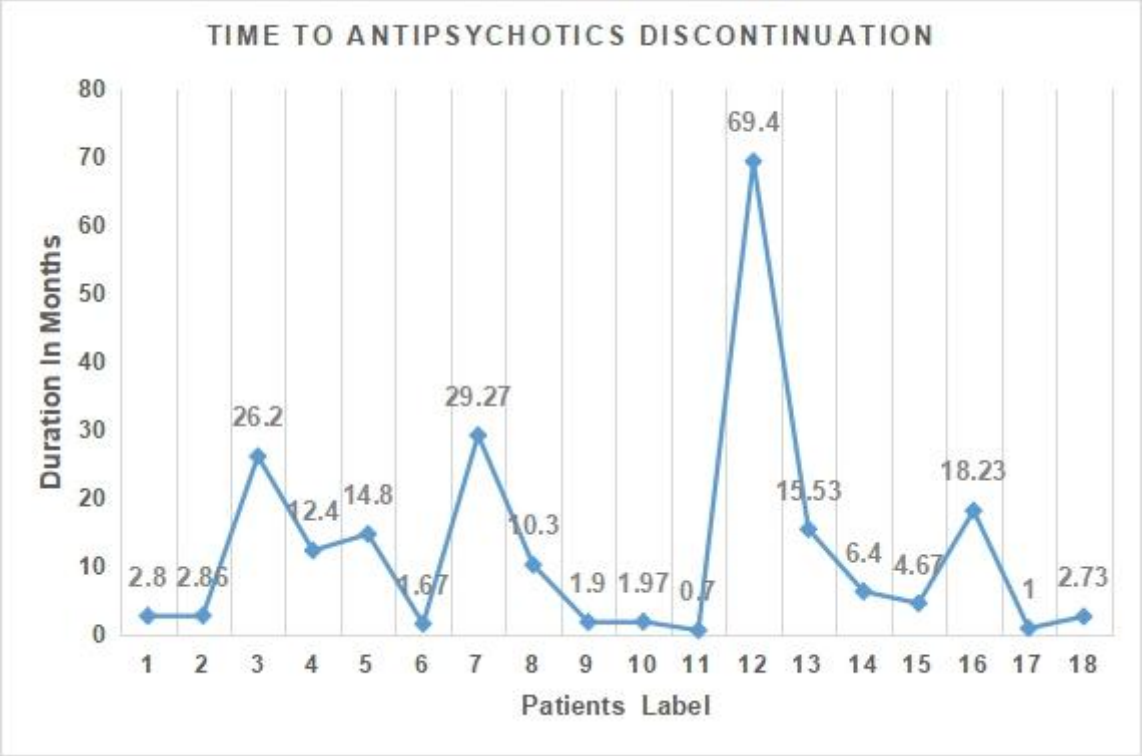


Figure 5: Duration of antipsychotic use before discontinuation (in months) among MDD-PF patients (labeled 1–18) achieved remission at Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia, 2025.

In addition, the mean time taken from initiation of antipsychotic treatment to discontinuation was approximately ≈18.5 months; (median=9.8 months, range≈ 1- 81.9 months).

In contrast, among patients who achieved clinical remission but did not discontinue antipsychotic treatment (n=17) by the end of the data collection period, the mean duration of continued treatment from the time of clinical remission until the end of the study was approximately 16.27 months; (range:0.8-76.73 months), and the wide range suggested data was skewed. The median difference between the two events was 15.5 months (IQR 7.69–18.92). This group of patients continued receiving antipsychotic treatment for an extended period beyond the recommended duration following remission. **(**See figure 6 for details**).**

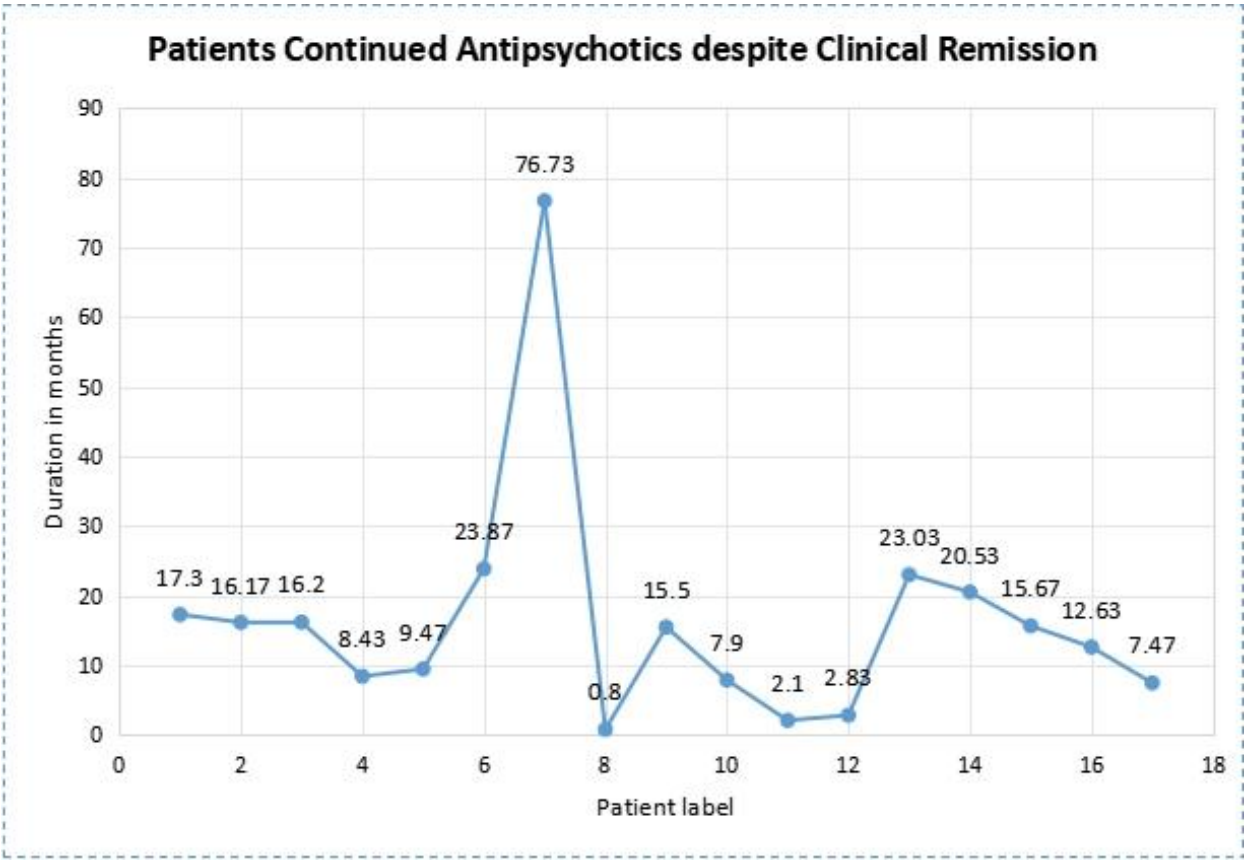


Figure 6: Duration of continued antipsychotic use (in months) from clinical remission to the time of data collection among MDD-PF patients (leveled 1–17) who achieved remission at TASH, 2025.

In addition, those patients still continuing antipsychotic treatment by the end of the data collection period, have been taking *antipsychotic* treatment for an extended period despite remission, and 14 of them have been taking *antipsychotic* treatment for more than 6 months after remission unlike APA guideline.

7.6. Type of Antipsychotic lastly being used

Among those on treatment, the most commonly used antipsychotic was risperidone 35 (58.33%) followed by olanzapine 15 (25%). (See Figure 7 for details)

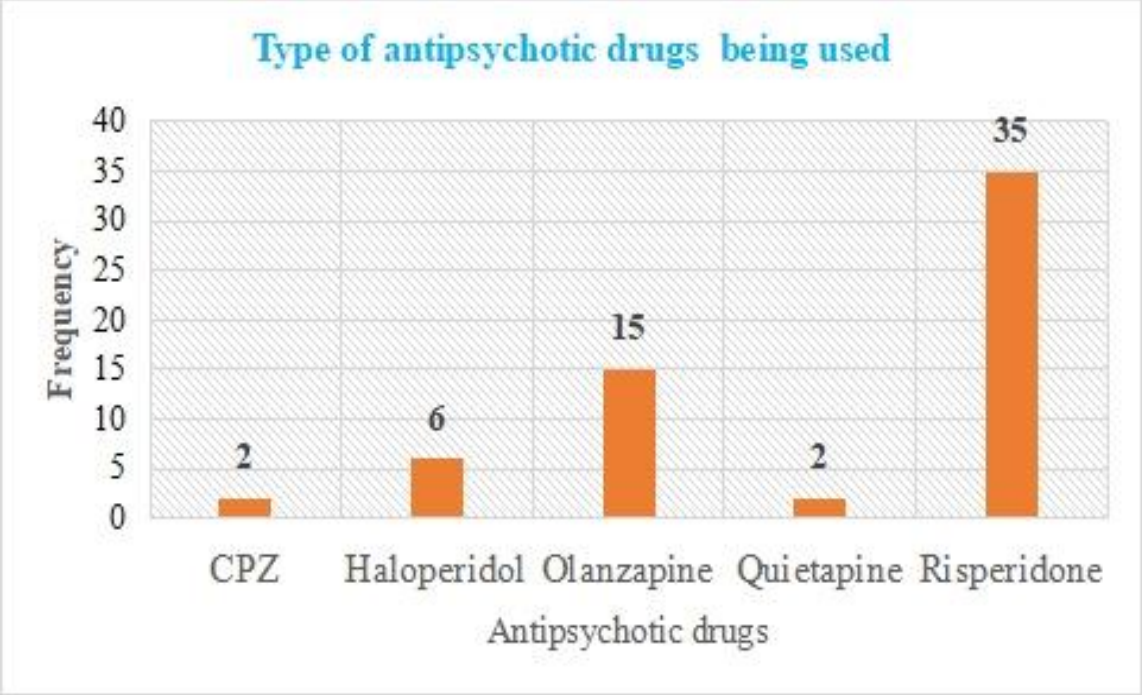


Figure 7: *Type of antipsychotics being used among patients diagnosed with MDD-PF at Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia, 2025.*

7.7. Reason for antipsychotics medication discontinuation

The result of our study found that antipsychotics medication was discontinued for 24 (38.7%) patients from those started antipsychotics treatment. The common reasons for antipsychotics discontinuation was clinical remission (75%), and antipsychotics related side effects (8.3%). Lost follow up was found in 16.7% of patients with unknown antipsychotic use status. (See Figure 8 for details).

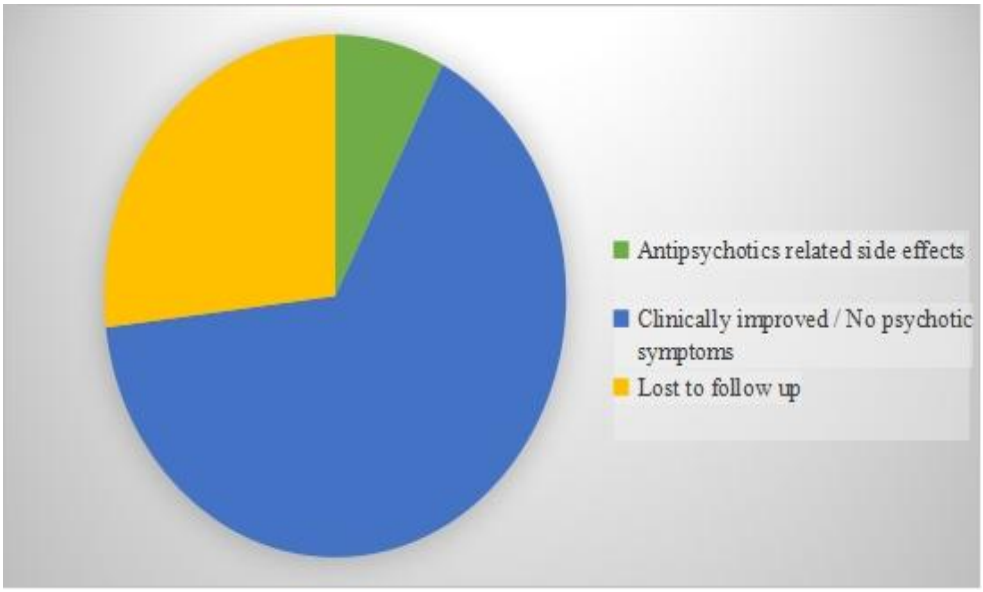


Figure 8: *Reason for antipsychotics medication discontinuation among patients diagnosed with MDD-PF at Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia, 2025.*

7.8. Comparative descriptive analysis; comparison of clinical remission with demographic and clinical factors

The proportion of patients achieving clinical remission varied across different socio-demographic and clinical characteristics. In our study, we found younger patients (aged <40 years) having a higher remission rate (61.3%) compared with those aged ≥40 years (51.6%), suggesting a better treatment response in younger age.

With respect to marital status, clinical remission was most common among single patients (72.0%), followed by married patients (50.0%). The majority of urban residents had achieved clinical remission (57.1%) compared with rural residents (50.0%), which might be due to poor mental health services availability and adherence to follow up in rural settings.

The study also found (60.9%) patients with comorbid psychiatric illness achieved remission compared to (53.8%) without comorbid psychiatric illness. Similarly, absence of comorbid medical illness has better remission rate (71.9%) compared with patients with comorbid medical illness (40.0%).

Chi-square analysis showed that comorbid medical illness was significantly associated with clinical remission ($\chi^2 = 6.41$, $p = 0.011$), whereas age group, marital status, residence, and psychiatric comorbidity were not significantly associated with remission ($p > 0.05$). (See Table 3 for details).

Table 3: Comparison of clinical remission with demographic and clinical factors among patients diagnosed with major depressive disorder with psychotic features at Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia, 2025.

Factors	Category	Clinical remission		X^2_ test	P value
		Yes	**No**		
Age group (n=62)	<40 years	19 (61.3%)	12 (38.7%)	0.59	0.44
	≥40 years	16 (51.6%)	15 (48.4%)		
Marital status	Single	18 (72.0%)	7 (28.0%)	4.72	0.19
	Married	13 (50.0%)	13 (50.0%)		
	Divorced	3 (37.5%)	5 (62.5%)		
	Widowed	1 (33.3%)	2 (66.7%)		
Residence	Urban	32 (57.1%)	24 (42.9%)	0.11	0.74
	Rural	3 (50.0%)	3 (50.0%)		
Comorbid psychiatric illness	Yes	14 (60.9%)	9 (39.1%)	0.29	0.59
	No	21 (53.8%)	18 (46.2%)		
Comorbid medical illness	Yes	12 (40.0%)	18 (60.0%)	6.41	**0.011**
	No	23 (71.9%)	9 (28.1%)		

7.9. Comparison of antipsychotics medication discontinuation after clinical remission

About twenty-two (68.75%) of urban residents discontinued antipsychotic medications, compared with 2 (66.67%) of rural residents. 16 (69.57%) patients without comorbid psychiatric illness discontinued antipsychotic medications, compared with 8 (57.14%) patients with comorbid psychiatric illness. 14 (56.0%) patients without medical illness discontinued antipsychotic medications, compared with 10 (41.7%) among those with comorbid medical illness. Chi-square analysis showed age group, marital status, residence, and psychiatric and medical comorbidities were not significantly associated with *antipsychotic discontinuation following clinical remission.* (See Table 4 for details).

Table 4: Comparison of after antipsychotics medication discontinuation after clinical remission with demographic and clinical factors among patients diagnosed with major depressive disorder with psychotic features at TASH, 2025.

Factors (n=35)	Category	Antipsychotic medications discontinued		X^2_ test	P value
		Yes	**No**		
Age group	<40 years	12 (63.16%)	7(36.84)	0.565	0.452
	≥40 years	12 (75.0%)	4 (25.0%)		
Residence	Rural	2 (66.67%)	1(33.33)	0.006	0.941
	Urban	22 (68.75%)	10 (31.25)		
Comorbid psychiatric illness	Yes	8 (57.14%)	6 (42.86%)	0.589	0.443
	No	16 (69.57%)	7(30.43%)		
Comorbid medical illness	Yes	10 (71.43%)	2(28.57%)	1.846	0.174
	No	14 (60.87%)	9(39.13%)		

Discussion

This study assessed the time to antipsychotic discontinuation after clinical remission among patients with major depressive disorder with psychotic features (MDD-PF) at Tikur Anbessa Specialized Hospital. This study provides comprehensive evidence on socio-demographic, clinical characteristics, comorbidities, and treatment patterns patients and identified a substantial discrepancy of antipsychotics discontinuation between international recommendations and real-world clinical practice, with many patients continuing antipsychotic for prolonged periods following remission.

In this study, comorbid psychiatric disorders were found among 38.5% of patients with a diagnosis of major depressive disorder as a comorbid diagnosis; generalized anxiety disorder, post-traumatic stress disorder and somatic symptom disorder being the most common prevalent comorbidities (6.8%, 4.3%, and 3.0%) respectively. In addition, 40.6% of patients had at least one comorbid medical condition including epilepsy (6.0%), HIV (3.8%), and diabetes (3.0%). The findings suggest the complex nature of depressive disorders, comorbidities, the link between chronic medical illnesses and depression which highlights the need for comprehensive psychiatric assessment during clinical practice.

Similarly, the proportion of depressive disorder with psychotic features was 25.6%**,** among major depressive disorder patients on follow up at TASH for the past 5 years. Our study found higher proportion of major depressive disorder with psychotic features, compared with studies done in Western countries, 18.5% in a five European countries on study done by Ohayon, 2002 (24) and 14.7% in the United States (26). Similarly, our study found higher proportion of MDD-PF compared with other studies, 9.1% in China, 2024 (25) and 15% Hawassa, Ethiopia, 2019 (32).

Our study also found that risperidone (58.3%) and olanzapine (25%) were the most frequently prescribed antipsychotic treatment, similar with standard clinical guidelines, as both drugs are commonly used for psychotic depression due to their efficacy in controlling psychotic and depressive symptoms along with antidepressants (35).

In our study, thirty-five (56.4%) patients achieved clinical remission among patients diagnosed with major depressive disorder with psychotic features, among them 65.7% patients continued antipsychotic treatment beyond six months, which is defined as prolonged antipsychotic treatment (33), despite evidence-based guidelines recommended discontinuation of antipsychotics within 4-6 months clinical remission (12,15,37).

Similarly, 43.6% of patients receiving antipsychotic treatment did not achieve clinical remission despite longer period antipsychotic treatment. This suggested achieving clinical remission remains challenging among substantial number of patients. The severity of illness, delayed help-seeking and prolonged untreated illness, sub-optimal antipsychotic doses, adherence issues (side effects or irregular follow-up), patients attitude towards treatment, comorbid psychiatric and medical illness, and limited access to psychiatric care could be the possible hypothetical explanation for not achieving remission in our study.

Clinical remission was the commonest reason mentioned for antipsychotic discontinuation in 75% who started antipsychotic treatment. Four patients had lost to follow-up with unknown status of antipsychotic use, which is an important concern in psychiatric care because this may lead to relapse, untreated symptoms, and poorer outcomes.

Similarly, among thirty-five patients who achieved remission, 18 (51.4%) of them discontinued antipsychotic treatment, and the mean time to discontinuation is 12.6 months and a median of 5.5 months (IQR 1.97–14.6). Here the mean is misleading as few patients who took for a long time dragged the mean up while 50% of patients took antipsychotics for less than 6 months after achieving clinical remission which is consistent with APA guideline.

We found 65.7% prolonged antipsychotic use among thirty-five patients who achieved clinical remission, which showed higher prevalence compared to 60%, in a study done in the United States, 2017 (43).

There were no other similar study done in the topic up-to my knowledge in African context, but although the exact prevalence were not reported, one study done in South Africa, 2013, found prolonged use among MDD-PF patients was a common problem, and the reasons mentioned were absence of structured discontinuation strategies and risk of relapse (42)

In this study, seventeen (48.6%) of patients still continued antipsychotic treatment after remission for a prolonged period (mean duration: 16.2 months, and median of 15.5 months), and fourteen of them took the antipsychotic medication for more than 6 months despite clinical remission, which showed prolonged antipsychotic use is a common problem. Compared with available international evidences; 9 months in STOP-PD II randomized clinical trial (38), 4 to 6 months in the American Psychiatric Association (APA) guideline (1,37) and 3 to 6 months in the National Institute for Health and Care Excellence (NICE) guideline (38) for discontinuation after remission (12,15), which suggests duration is longer, and needs a practical solution in our setting.

Similarly, compared with available South Africa's recommendation of antipsychotics discontinuation within 3 to 6 months (42), 65.7% of patients continued more than 6 month after clinical remission is significant. The overall cumulative effects resulting unnecessary antipsychotics related adverse effects or poor drug adherence issues.

Although prolonged antipsychotics treatment was significant in our finding, similar study done by Rothschild and colleagues in 2024 suggested maintaining the antipsychotic for at least six to 12 months was found to be a reasonable decision for patients who had a relapse history (13).

Surprisingly, our finding also showed while few patients discontinued treatment relatively early after remission (within few months) and others continued for extended periods (2-5years) highlights a significant gap between evidence-based recommendations and actual prescribing practices in our tertiary care setting.

From our findings, we hypothesize that longer duration of antipsychotic treatment could be reflected from a multi-factorial reasons: clinicians reluctant to discontinue

antipsychotic, frequent rotation of treating resident physicians resulting limited in counter in their subsequent patient visit, limited supervision from the most senior clinicians regarding treatment options and duration, lack of clear documentation of remission status of patients as most documentation identified refilling without symptom remission status or due to fear about future relapse due to absence of guideline supported from similar STOP-PD II RCT study (38). Other important factors could be patient's poor adherence for treatment and follow up resulting with frequent relapses or residual symptoms resulting for prolonged use.

In our categorical factors comparison using chi-square test, we found that comorbid medical illness was the only factor significantly associated with clinical remission ($p = 0.011$) with patients without medical comorbidity more likely to achieve remission. This finding is in line with other studies in which chronic medical conditions can complicate the treatment process and reduce the likelihood of full symptomatic recovery.

To our knowledge, this is the first study in Ethiopia, which tried to investigate time to antipsychotic discontinuation after achieved clinical remission among patients with a diagnosis of MDD-PF, and our study identified prolonged use of antipsychotics despite achieved remission as major and critical gap in our day-to-day clinical practice.

Overall, our findings highlight the gap between guideline recommendations and real time day-to-day clinical practice in our setups despite international evidences support to discontinue antipsychotic treatment with in 4 to 6 months after remission. The variability observed in this study underlines the need for local guideline and structured follow-up strategies regarding antipsychotic treatment in patients with psychotic depression.

Strength and limitation of the study

Our study has certain strengths and limitations: This study provides valuable early data on the time to antipsychotic discontinuation after remission with baseline demographic, and clinical profiles of patients with major depressive disorder with psychotic features which will be crucial for clinical and public health interventions. It also provides important local evidence on antipsychotic treatment and discontinuation practices in MDD-PF patients, and highlights a critical gap between guideline recommendations and real-world practice. The findings underscore the need for the development of institutionalized or national guidelines for antipsychotic discontinuation period, clinical monitoring and follow-up strategies in MDD-PF.

This study also has some limitations. First, due to the retrospective nature of data, it is difficult to establish causal relationships which is not originally collected for research purposes, some important variables were incomplete or missed which may have affected our results.

Second, the relatively small sample size, single setting study, the statistical power to detect significant association and generalizability to other settings might be difficult. Finally, the clinical remission assessment was based on clinician documentation which may introduce measurement bias unlike standardized rating scales.

Conclusion

In general, our study revealed 25.6% proportion major depressive disorder with psychotic features presentation among major depressive disorder patents on follow up at TASH for the past 5 years. The findings reveal that more over than half of them (56.5%) had achieved clinical remission.

Prolonged antipsychotic treatment was found among 65.7% patients after achieving clinical remission, identified was a major gap in our study. Among 35 patients who achieved remission, 48.6% patients still continuing antipsychotic treatment for approximately 16.2 months (median:15.5 months), despite international evidences recommended to discontinue within 4 to 6 months following remission. Extra-pyramidal symptoms (8.1%) and metabolic side effects (6.5%) were the most common documented antipsychotic related side effects identified in this study.

Overall, our findings highlighted 65.7% prolonged antipsychotic use following clinical remission, which showed gaps between our day-to-day clinical practice and international guidelines supporting to discontinue antipsychotic treatment with in 4 to 6 months after remission (APA). The variability observed in our study, conducted in a tertiary care setting highlighted the need for developing standardized institutionalized or national treatment protocol and structured follow-up strategies. This will promote evidence-based antipsychotics prescription practices and reduces medication related side effects by decreasing unnecessary prolonged antipsychotics use following remission. The overall effects is vital in improving psychiatric care by reduces burden for both patients and the healthcare system.

Recommendations

Based on the findings of this study, we recommend the following recommendations for TASH psychiatry department, ministry of health, health facility leaders, policy makers and other relevant stakeholders.

❖ For Tikur Anbessa Specialized Hospital Department of Psychiatry

There is a need to develop a hospital level protocol at the psychiatry department, with periodic clinical discussions in the morning presentations, grand rounds or individual case reviews. This is important that every resident physicians will have a consensus regarding antipsychotic discontinuation timing following clinical remission to reduce unnecessary prolonged antipsychotic use (>6 months) among major depressive disorder with psychotic feature patients evidenced by prolonged antipsychotic use in 65.7% patients following remission in our setting.

❖ For Clinicians (Resident Physicians and Psychiatrists)

Once sustained clinical remission is achieved, treating clinicians should have a gradual tapering strategy regarding the duration of antipsychotic treatment to guide appropriate discontinuation decisions, with careful monitoring of relapse in every patient with major depressive disorder with psychotic features. In addition, treatment providers should adhere to international guidelines for the use and discontinuation of antipsychotic with accurate and complete documentation of patient information to support effective patient management and continuity of care.

❖ For Researchers:

Future researchers should focus on prospective multicenter longitudinal studies to better understand the ideal duration of antipsychotic treatment, the time to discontinuation after clinical remission, and to explore the factors associated with treatment outcomes including remission and reasons for prolonged treatment, and risk of relapse.

❖ Policy Makers / Ministry of Health

We highlighted the need for developing standardized national treatment protocol and structured follow-up strategies once strong evidences are generated in the area. We also recommended Ministry of Health (MOH) policy makers to use the findings of this study as bench mark data in their discussion along with involving psychiatrists while developing national antipsychotic treatment protocols.

References

1. Publication manual of the American Psychological Association, 6th ed. Washington, DC, US: American Psychological Association; 2010. xviii, 272 p. (Publication manual of the American Psychological Association, 6th ed.).

2. Rothschild AJ. Challenges in the Treatment of Major Depressive Disorder With Psychotic Features. Schizophr Bull [Internet]. 2013 Jul [cited 2025 Jun 28];39(4):787–96. Available from: https://academic.oup.com/schizophreniabulletin/article-lookup/doi/10.1093/schbul/sbt046

3. Parker G, Roy K, Wilhelm K, Mitchell P, Hadzi-Pavlovic D. The nature of bipolar depression: implications for the definition of melancholia. J Affect Disord [Internet]. 2000 Sep [cited 2025 Jul 13];59(3):217–24. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0165032799001445

4. Farahani A, Correll CU. Are Antipsychotics or Antidepressants Needed for Psychotic Depression?: A Systematic Review and Meta-Analysis of Trials Comparing Antidepressant or Antipsychotic Monotherapy With Combination Treatment. J Clin Psychiatry [Internet]. 2012 Apr 15 [cited 2025 Jun 28];73(04):486–96. Available from: https://www.psychiatrist.com/jcp/are-antipsychotics-antidepressants-needed-psychotic

5. Pagnin D, De Queiroz V, Pini S, Cassano GB. Efficacy of ECT in Depression: A Meta-Analytic Review. Focus [Internet]. 2008 Jan [cited 2025 Jun 28];6(1):155–62. Available from: https://psychiatryonline.org/doi/10.1176/foc.6.1.foc155

6. Kruizinga J, Liemburg E, Burger H, Cipriani A, Geddes J, Robertson L, et al. Pharmacological treatment for psychotic depression. Cochrane Database Syst Rev. 2021 Dec 7;12(12):CD004044.

7. Wijkstra J, Lijmer J, Balk FJ, Geddes JR, Nolen WA. Pharmacological treatment for unipolar psychotic depression: Systematic review and meta-analysis. Br J

Psychiatry [Internet]. 2006 May [cited 2025 Jun 28];188(5):410–5. Available from: https://www.cambridge.org/core/product/identifier/S0007125000231504/type/journal_article

8. Al‐Wandi A, Landén M, Nordenskjöld A. Antipsychotics in the maintenance phase for psychotic depression. Acta Psychiatr Scand [Internet]. 2024 Jan [cited 2025 Jun 29];149(1):6–17. Available from: https://onlinelibrary.wiley.com/doi/10.1111/acps.13628

9. Rothschild AJ, Duval SE. How Long Should Patients With Psychotic Depression Stay on the Antipsychotic Medication? J Clin Psychiatry [Internet]. 2003 Apr 15 [cited 2025 Jun 28];64(4):390–6. Available from: https://www.psychiatrist.com/jcp/long-should-patients-psychotic-depression-stay-antipsychotic

10. Coryell W. Affective Syndromes, Psychotic Features, and Prognosis: I. Depression. Arch Gen Psychiatry [Internet]. 1990 Jul 1 [cited 2025 Jun 28];47(7):651. Available from: http://archpsyc.jamanetwork.com/article.aspx?doi=10.1001/archpsyc.1990.01810190051007

11. Al-Wandi A, Holmberg C, Landén M, Nordenskjöld A. A systematic review and meta‐analysis of maintenance treatment for psychotic depression. Nord J Psychiatry [Internet]. 2022 Aug 1 [cited 2025 Jul 6];76(6):442–50. Available from: https://www.tandfonline.com/doi/full/10.1080/08039488.2021.1990997

12. Rothschild AJ. Maintenance treatment of psychotic depression: Is antipsychotic medication needed? Acta Psychiatr Scand [Internet]. 2024 Jan [cited 2025 Jun 28];149(1):3–5. Available from: https://onlinelibrary.wiley.com/doi/10.1111/acps.13639

13. Leadholm AKK, Rothschild AJ, Nolen WA, Bech P, Munk-Jørgensen P, Østergaard SD. The treatment of psychotic depression: Is there consensus among guidelines

and psychiatrists? J Affect Disord [Internet]. 2013 Feb [cited 2025 Jun 29];145(2):214–20. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0165032712005678

14. Rothschild AJ. Treatment for Major Depression With Psychotic Features (Psychotic Depression). Focus Am Psychiatr Publ. 2016 Apr;14(2):207–9.

15. Kendrick T, Pilling S, Mavranezouli I, Megnin-Viggars O, Ruane C, Eadon H, et al. Management of depression in adults: summary of updated NICE guidance. BMJ [Internet]. 2022 Jul 20 [cited 2025 Jun 28];o1557. Available from: https://www.bmj.com/lookup/doi/10.1136/bmj.o1557

16. Siraj J. Assessment of psychotropic medications prescribing pattern in Gebretsadik Shawo General Hospital, South West Ethiopia. Pan Afr Med J. 2023;45:165.

17. De Hert M, Detraux J, Van Winkel R, Yu W, Correll CU. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. Nat Rev Endocrinol [Internet]. 2012 Feb [cited 2025 Jun 28];8(2):114–26. Available from: https://www.nature.com/articles/nrendo.2011.156

18. Gerhard T, Stroup TS, Correll CU, Setoguchi S, Strom BL, Huang C, et al. Mortality risk of antipsychotic augmentation for adult depression. Wright JM, editor. PLOS ONE [Internet]. 2020 Sep 30 [cited 2025 Jun 28];15(9):e0239206. Available from: https://dx.plos.org/10.1371/journal.pone.0239206

19. Tyrka AR, Price LH, Mello MF, Mello AF, Carpenter LL. Psychotic Major Depression: A Benefit-Risk Assessment of Treatment Options. Drug Saf [Internet]. 2006 [cited 2025 Jun 29];29(6):491–508. Available from: http://link.springer.com/10.2165/00002018-200629060-00003

20. Maj M, Pirozzi R, Magliano L, Fiorillo A, Bartoli L. Phenomenology and Prognostic Significance of Delusions in Major Depressive Disorder: A 10-Year Prospective Follow-Up Study. J Clin Psychiatry [Internet]. 2007 Sep 15 [cited 2025 Jun 29];68(09):1411–7. Available from:

https://www.psychiatrist.com/jcp/phenomenology-prognostic-significance-delusions-major

21. Gournellis R, Tournikioti K, Touloumi G, Thomadakis C, Michalopoulou PG, Michopoulos I, et al. Psychotic (delusional) depression and completed suicide: a systematic review and meta-analysis. Ann Gen Psychiatry [Internet]. 2018 Dec [cited 2025 Jun 28];17(1):39. Available from: https://annals-general-psychiatry.biomedcentral.com/articles/10.1186/s12991-018-0207-1

22. Rothschild AJ. Challenges in the Treatment of Major Depressive Disorder With Psychotic Features. Schizophr Bull [Internet]. 2013 Jul [cited 2025 Jun 28];39(4):787–96. Available from: https://academic.oup.com/schizophreniabulletin/article-lookup/doi/10.1093/schbul/sbt046

23. Rothschild AJ, Williamson DJ, Tohen MF, Schatzberg A, Andersen SW, Van Campen LE, et al. A double-blind, randomized study of olanzapine and olanzapine/fluoxetine combination for major depression with psychotic features. J Clin Psychopharmacol. 2004 Aug;24(4):365–73.

24. Ohayon MM, Schatzberg AF. Prevalence of Depressive Episodes With Psychotic Features in the General Population. Am J Psychiatry [Internet]. 2002 Nov 1 [cited 2025 Jun 28];159(11):1855–61. Available from: https://psychiatryonline.org/doi/10.1176/appi.ajp.159.11.1855

25. Wu Y, Zhao X, Li Z, Yang R, Peng R, Zhou Y, et al. Prevalence and risk factors for psychotic symptoms in young, first-episode and drug-naïve patients with major depressive disorder. BMC Psychiatry [Internet]. 2024 Jan 23 [cited 2025 Jun 28];24(1):66. Available from: https://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-024-05517-5

26. Johnson J. The Validity of Major Depression With Psychotic Features Based on a Community Study. Arch Gen Psychiatry [Internet]. 1991 Dec 1 [cited 2025 Jun 29];48(12):1075. Available from:

http://archpsyc.jamanetwork.com/article.aspx?doi=10.1001/archpsyc.1991.01810360039006

27. Esan O, Esan A. Epidemiology and burden of bipolar disorder in Africa: a systematic review of data from Africa. Soc Psychiatry Psychiatr Epidemiol [Internet]. 2016 Jan [cited 2025 Aug 2];51(1):93–100. Available from: http://link.springer.com/10.1007/s00127-015-1091-5

28. Agbir T, Audu M, Adebowale T, Goar S. Depression among medical outpatients with diabetes: A cross-sectional study at Jos University Teaching Hospital, Jos, Nigeria. Ann Afr Med [Internet]. 2010 [cited 2025 Aug 2];9(1):5. Available from: https://journals.lww.com/10.4103/1596-3519.62617

29. Bean J, Möller AT. Posttraumatic Stress and Depressive Symptomatology in a Sample of Battered Women from South Africa. Psychol Rep [Internet]. 2002 Jun [cited 2025 Aug 2];90(3):750–2. Available from: https://journals.sagepub.com/doi/10.2466/pr0.2002.90.3.750

30. Kinyanda E, Woodburn P, Tugumisirize J, Kagugube J, Ndyanabangi S, Patel V. Poverty, life events and the risk for depression in Uganda. Soc Psychiatry Psychiatr Epidemiol [Internet]. 2011 Jan [cited 2025 Aug 2];46(1):35–44. Available from: http://link.springer.com/10.1007/s00127-009-0164-8

31. Smith Fawzi M, Kaaya S, Mbwambo J, Msamanga G, Antelman G, Wei R, et al. Multivitamin supplementation in HIV‐positive pregnant women: impact on depression and quality of life in a resource‐poor setting. HIV Med [Internet]. 2007 May [cited 2025 Aug 2];8(4):203–12. Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1468-1293.2007.00454.x

32. Ayalew M, Deribe B, Duko B, Geleta D, Bogale N, Gemechu L, et al. Prevalence of depression and anxiety symptoms and their determinant factors among patients with cancer in southern Ethiopia: a cross-sectional study. BMJ Open [Internet]. 2022 Jan

[cited 2025 Jul 17];12(1):e051317. Available from: https://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-2021-051317

33. Flint AJ, Meyers BS, Rothschild AJ, Whyte EM, Alexopoulos GS, Rudorfer MV, et al. Effect of Continuing Olanzapine vs Placebo on Relapse Among Patients With Psychotic Depression in Remission: The STOP-PD II Randomized Clinical Trial. JAMA [Internet]. 2019 Aug 20 [cited 2025 Jun 28];322(7):622. Available from: https://jamanetwork.com/journals/jama/fullarticle/2748508

34. Cleare A, Pariante C, Young A, Anderson I, Christmas D, Cowen P, et al. Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British Association for Psychopharmacology guidelines. J Psychopharmacol (Oxf) [Internet]. 2015 May [cited 2025 Jun 28];29(5):459–525. Available from: https://journals.sagepub.com/doi/10.1177/0269881115581093

35. Correll CU, Detraux J, De Lepeleire J, De Hert M. Effects of antipsychotics, antidepressants and mood stabilizers on risk for physical diseases in people with schizophrenia, depression and bipolar disorder. World Psychiatry Off J World Psychiatr Assoc WPA. 2015 Jun;14(2):119–36.

36. Wise J. NICE guidance on depression: 35 health organisations demand “full and proper” revision. BMJ [Internet]. 2019 May 28 [cited 2025 Jun 28];l2356. Available from: https://www.bmj.com/lookup/doi/10.1136/bmj.l2356

37. Publication manual of the American Psychological Association, 6th ed.

38. Flint AJ, Meyers BS, Rothschild AJ, Whyte EM, Mulsant BH, Rudorfer MV, et al. Sustaining remission of psychotic depression: rationale, design and methodology of STOP-PD II. BMC Psychiatry [Internet]. 2013 Dec [cited 2025 Jun 28];13(1):38. Available from: http://bmcpsychiatry.biomedcentral.com/articles/10.1186/1471-244X-13-38

39. Nelson JC, Papakostas GI. Atypical Antipsychotic Augmentation in Major Depressive Disorder: A Meta-Analysis of Placebo-Controlled Randomized Trials.

Am J Psychiatry [Internet]. 2009 Sep [cited 2025 Jun 28];166(9):980–91. Available from: https://psychiatryonline.org/doi/10.1176/appi.ajp.2009.09030312

40. Al-Wandi A, Holmberg C, Landén M, Nordenskjöld A. A systematic review and meta-analysis of maintenance treatment for psychotic depression. Nord J Psychiatry. 2022 Aug;76(6):442–50.

41. Bauer M, Pfennig A, Severus E, Whybrow PC, Angst J, Möller HJ, et al. World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Unipolar Depressive Disorders, Part 1: Update 2013 on the acute and continuation treatment of unipolar depressive disorders. World J Biol Psychiatry [Internet]. 2013 Jul [cited 2025 Jun 29];14(5):334–85. Available from: http://www.tandfonline.com/doi/full/10.3109/15622975.2013.804195

42. Grobler G. Major Depressive Disorder. South Afr J Psychiatry [Internet]. 2013 Aug 30 [cited 2025 Aug 2];19(3):7. Available from: http://www.sajp.org.za/index.php/sajp/article/view/946

43. Simons P, Cosgrove L, Shaughnessy AF, Bursztajn H. Antipsychotic augmentation for major depressive disorder: A review of clinical practice guidelines. Int J Law Psychiatry [Internet]. 2017 Nov [cited 2025 Jun 28];55:64–71. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0160252717300614

44. Correll CU, Detraux J, De Lepeleire J, De Hert M. Effects of antipsychotics, antidepressants and mood stabilizers on risk for physical diseases in people with schizophrenia, depression and bipolar disorder. World Psychiatry [Internet]. 2015 Jun [cited 2025 Jun 28];14(2):119–36. Available from: https://onlinelibrary.wiley.com/doi/10.1002/wps.20204

45. Alem A, Kebede D, Fekadu A, Shibre T, Fekadu D, Beyero T, et al. Clinical Course and Outcome of Schizophrenia in a Predominantly Treatment-Naive Cohort in Rural Ethiopia. Schizophr Bull [Internet]. 2009 Mar 30 [cited 2025 Jun 29];35(3):646–54. Available from: https://academic.oup.com/schizophreniabulletin/article-lookup/doi/10.1093/schbul/sbn029

46. McGrath J, Saha S, Chant D, Welham J. Schizophrenia: A Concise Overview of Incidence, Prevalence, and Mortality. Epidemiol Rev [Internet]. 2008 May 14 [cited 2025 Jun 29];30(1):67–76. Available from: https://academic.oup.com/epirev/article-lookup/doi/10.1093/epirev/mxn001

47. Naz B, Craig TJ, Bromet EJ, Finch SJ, Fochtmann LJ, Carlson GA. Remission and relapse after the first hospital admission in psychotic depression: a 4-year naturalistic follow-up. Psychol Med [Internet]. 2007 Aug [cited 2025 Jul 6];37(8):1173–81. Available from: https://www.cambridge.org/core/product/identifier/S0033291707000141/type/journal_article

48. Vassar M, Holzmann M. The retrospective chart review: important methodological considerations. J Educ Eval Health Prof. 2013;10:12.

49. Valliant R, Dever JA, Kreuter F. Nonprobability Sampling. In: Practical Tools for Designing and Weighting Survey Samples [Internet]. Cham: Springer International Publishing; 2018 [cited 2025 Aug 7]. p. 565–603. (Statistics for Social and Behavioral Sciences). Available from: http://link.springer.com/10.1007/978-3-319-93632-1_18

APPENDIX

Data Collecting Questionnaire

Section A: Socio-demographic Characteristics

Variable	Code
Record ID- Code	_____
1. Sex	1. Male 2. Female
2. Age	_____ (years)
3. Marital status	1. Single 2. Married 3. Divorced 4. Widowed
4. Religion	1. Orthodox 3. Protestant 2. Muslim 4. Catholic 5. Other (specify) ----------
5. Educational status	
6. Occupational status	☐ Employed ☐ Student ☐ Unemployed ☐ Other
7. Residence	☐ Urban ☐ Rural

Section B: Clinical Characteristics

Variable	Code/Response Options
1. What is the primary label Diagnostic?	☐ MDD ☐ MDD-PF
2. History of suicide attempt	☐ Yes ☐ No
3. Comorbid psychiatric illness	☐ No

	☐ Yes
4. If Yes for the above question, specify: _____	specify: _____
5. Comorbid medical illness	☐ No ☐ Yes
6. If Yes for the above question, specify: _____	specify: _____
7. What type of psychotic features were present at first presentation?	☐ Delusion ☐ Hallucination ☐ Aggression
8. Did antipsychotic initiated?	☐ Yes ☐ No

Section C: Treatment and Follow-up Characteristics

Variable	**Code**
1) Date of antipsychotic initiation	____ / ____ / _____ (DD/MM/YYYY)
2) Type of Antipsychotic first used?	☐ Haloperidol ☐ Risperidone ☐ Olanzapine ☐ Quietapine ☐ Other→ If specify_____
3) Type of Antipsychotic Lastly being used?	☐ Haloperidol ☐ Risperidone ☐ Olanzapine ☐ Quietapine ☐ Other→ If specify_____
4) What was the antipsychotic dose (mg) lastly being use?	_____mg

5) Any Side effects documented?	☐ EPS ☐ Metabolic ☐ Combined ☐ None
6) Adherence concerns noted	☐ Yes ☐ No
7) What was the patient's recent status?	☐ No psychotic symptoms ☐ Has psychotic symptoms
8) If the patient still has psychotic symptoms, what symptoms remained?	☐ Delusion ☐ Hallucination ☐ Aggression ☐ Other…

Section D: Outcome Measures

Variable	**Code**
1. Did the patient achieved clinical remission?	☐ Yes ☐ No
2. If yes, when did remission achieved (Date documented on the EMR)?	____ / ____ / _____ **(DD/MM/YYYY)**
3. Did antipsychotics medications discontinued on the last follow-up?	☐ Yes ☐ No
4. What was the reason for antipsychotics medication discontinuation?	☐ Clinically Improved / No psychotic symptoms ☐ Antipsychotics related side effects ☐ Lost to follow-up ☐Not documented
5. Date of antipsychotic discontinuation?	____ / ____ / _____ **(DD/MM/YYYY)**

DECLARATION FORM

This is to certify that the thesis proposal is prepared by Dr**. Assamin Assafaw** entitled: ‘’ TIME TO ANTIPSYCHOTIC DISCONTINUATION AFTER REMISSION AMONG PATIENTS WITH MAJOR DEPRESSIVE DISORDER WITH PSYCHOTIC FEATURES AT TIKUR ANBESSA SPECIALIZED HOSPITAL: A CROSS-SECTIONAL STUDY**’’** to be submitted in partial fulfillment of the requirements of specialty complies with the regulations of the university and meets the accepted standards with respect to originality and quality. This thesis proposal has not been presented for a degree in any other university, and all sources of materials used for the thesis have been duly acknowledged.

ASSURANCE OF PRINCIPAL INVESTIGATORS

I, the undersigned, declare that this postgraduate degree thesis is my original work, has not been presented for a degree in this or any other university and that all sources of materials used for the thesis have been fully acknowledged.

Name of Investigator: Dr. Assamin Assafaw Demelash

Signature: _____

Date of submission: _____

APPROVAL OF THE ADVISORS

This thesis has been submitted to department of psychiatry with my approval as a supervisor.

APPROVAL OF ADVISOR

Name of the first advisor: _____

Signature _____ Date. _____

Name of the second advisor: _____

Signature _____ Date. _____