

Medication adherence and associated factors among psychiatric patients in Mozambique:
longitudinal analyses of data from 2022–2024

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Abstract

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Background:

Mental disorders are a major contributor to global disability and mortality, with medication nonadherence presenting a significant barrier to effective treatment. Research on adherence among psychiatric patients is particularly sparse in low- and middle-income countries (LMICs). This study examined the relationship between psychiatric medication adherence and clinical and sociodemographic factors in outpatient psychiatric settings in central Mozambique.

Methods:

We conducted a longitudinal study using data from 803 outpatient psychiatric patients (1,811 total follow-up visits) attending eight healthcare facilities in Mozambique from February 2022 to January 2024. The primary exposure variables in this study include primary diagnoses (epilepsy, schizophrenia-related disorders, other psychotic and delusional disorders, depression-related disorders, mental and behavioral disorders due to substance use, and all other diagnoses). "All other diagnoses" grouped together any ICD-10 code psychiatric diagnoses with fewer than 15 patients each. Primary medications (Carbamazepine, Haloperidol, Amitriptyline, Thioridazine, and all other medications). "All other medications," grouped together those medications with fewer than 15 patients each. Sociodemographic characteristics include age (<18, 18-35, 36-55, and over 56 years), gender (female and male), and marital status (single, married, divorced, separated, widowed, and common-law). Patient adherence was

determined by a combination of pill counts and patients self-declaring they took their medication as prescribed. We analyzed medication adherence and its association with sociodemographic and clinical variables using non-parametric Kaplan-Meier and semi-parametric Cox proportional hazards models. A multivariate linear mixed model was employed to analyze the association between psychiatric medication and clinical/sociodemographic variables and changes in weight, the World Health Organization Disability Assessment Schedule (WHODAS), and blood pressure over time.

Results:

Approximately 93% of patients (N = 729) were non-adherent to their medication at least at one follow-up visits during the study period, with a median time in treatment prior to non-adherence of 60 days (mean: 52 days; 95% CI: 51, 53). In fully-adjusted models, patients aged 56+ had a 31% higher hazard of nonadherence compared to those aged 18-35 (aHR: 1.31; 95% CI: 1.10, 1.57). Patients prescribed amitriptyline had a 54% higher hazard of nonadherence compared to those prescribed carbamazepine (aHR: 1.54; 95% CI: 1.19, 1.99). For each 30 days in treatment, disability scores decreased by an average of 0.13 (95% CI: -0.16 to -0.09) while systolic blood pressure decreased by 0.46 mmHg (95% CI: -0.18 to -0.10) and diastolic blood pressure decreased by 0.15 mmHg (95% CI: -0.23 to -0.06). Patients diagnosed with schizophrenia-related disorders and those in the 'all other diagnoses' group had higher disability scores ($a\beta = 2.0$; 95% CI: 0.88, 3.17, and $a\beta = 1.8$; 95% CI: 0.69, 2.91, respectively), compared to patients with epilepsy. Male patients on treatment had a marginally lower diastolic blood pressure ($a\beta = -4.39$ mmHg; 95% CI: -8.51, -0.27) compared to females. Patients in the 'all other medication' group had a weight 3.21 kg lower (95% CI: -6.41, 0.01) compared to those taking carbamazepine.

Conclusions:

Currently, the typical patient who initiates essential psychiatric treatment in Mozambique is only able to maintain adherence to their medication for 60 days. Patients prescribed amitriptyline and older patients are at a higher risk of non-adherence. Consistent engagement in treatment is linked to lower disability scores and blood pressure. There is an urgent need for research into adherence support strategies, especially for these high-risk groups within Mozambique's mental health patient population.

Background

The World Health Organization (WHO) defines mental, neurological, and substance use disorders (MNS) as an adulteration of thought and emotions produced by inadequacy or deterioration of psychosocial functioning depending on biological, psychological, and social factors (1). MNS are leading causes of disability, premature mortality (2), high economic costs (direct and indirect) due to lost work time (3), and reduced productivity (2). According to the 2020 data, MNS disorders account for 14% of the global burden of disease. This indicates an increase from previous years, highlighting the growing impact of these disorders worldwide (4). This burden is particularly significant in low- and middle-income countries, where 75% of those affected do not receive the treatment they need (5). Across all age groups, schizophrenia, depression, epilepsy, dementia, alcohol dependence, and other mental, neurological, and substance use disorders constitute 13% of the global burden of diseases and account for 10.4% of disability-adjusted life years globally in 2010 (6). In addition, patients with mental disorders in Africa are stigmatized, making it a hidden challenge for help-seeking. Societal issues such as armed conflict, post-conflict situations, and poverty, common in Africa, are also known to be detrimental to mental health (7).

Across Mozambique, a country with a population of 33.8 million as of 2024 (8), over 23.9% of patients attending primary care may have common mental disorders (9). The prevention, care, and treatment of mental disorders have been historically neglected compared with other health conditions (10). Despite efforts by the Ministry of Health to close the treatment gap through a task-shifting approach, systematic barriers such as lack of resources, supervision issues, and medication stock-outs contribute to the poor quality of mental health care. Nonadherence to treatment poses a significant challenge among psychiatric patients, with reported rates ranging from 20% to 60% globally (11). Nonadherence can present itself in several ways, such as not taking medications as prescribed (wrong dosage or frequency), stopping the medication entirely, attending follow-up appointments irregularly, or, in some cases, not attending at all. The rate of nonadherence to typical antipsychotics is notably higher in Africa compared to other continents, with figures ranging from 46.9% to 93.3%, in contrast to 11% in China and 25.6% in Bulgaria (12). Further, the problem of inadequate adherence to medical treatment is expected to grow in developing nations due to limited and uneven access to healthcare services and medications(13) .

Poor adherence is a multifactorial phenomenon that can result from five major interacting factors: the health team and health system, the patient, therapy, social/economic factors, and clinical factors (14). Medication non-adherence can undermine healthcare effectiveness, resulting in poor health outcomes and increased costs. These consequences include frequent hospital admissions, relapses or recurring symptoms, a heightened risk of suicide or dependency, reduced functionality, increased absenteeism, rebound effects, comorbidities such as weight gain and cardiometabolic disorders, and higher mortality rates (14, 15, 16). A recent study found that patients with schizophrenia or bipolar I disorder who begin treatment with oral second-generation antipsychotics experience weight gain and increased cardiometabolic health issues, even after changing or discontinuing the medication. This weight gain, continuing into the first year of treatment, may worsen health outcomes for these patients, who already have a higher risk of cardiometabolic conditions (16).

A recent pilot study conducted in Mozambique revealed that mental health patients were adherent to medication in only 17% of follow-up visits and showed improvement in daily living activities in 26.6% of these visits (18). However, this study did not investigate the factors influencing medication adherence or the potential effects of mental health treatment on patients' physical health and disability scores over time.

Research on adherence and related factors, as well as adherence support interventions, is limited across sub-Saharan Africa, and no studies have yet been published in Mozambique. This study seeks to bridge that gap by exploring associations of medication non-adherence with primary diagnosis, medication type, and sociodemographic factors among outpatient psychiatric patients in Mozambique. Moreover, it examines how the primary medications prescribed to these patients are linked to changes in the World Health Organization Disability Assessment Schedule (WHODAS) score, weight, and blood pressure. The findings will offer valuable insights into the factors driving medication non-adherence and its biological implications, providing an evidence base to guide and inform strategies for addressing this widespread challenge among psychiatric patients in Mozambique and other low- and middle-income countries (LMICs) more broadly.

Method

Study Design and Study Setting

We conducted a secondary data analysis using cohort data collected as part of the baseline data collection phase of the System Analysis and Improvement Approach for Mental Health (SAIA-MH) cluster randomized controlled trial (19). This trial employed a cluster-randomized design across 16 clinics (eight intervention and eight control) providing primary mental health care in Sofala and Manica provinces of Mozambique. Detailed information on health facility eligibility and selection is available in the published trial protocol (19). The current secondary analysis of trial data uses data from control facilities. The trial protocol was reviewed and approved by the University of Washington IRB and the National Ethics Committee in Mozambique (CNBS).

Study Population and Data Source

The current study utilized data from 803 outpatient psychiatric patients and their 1,811 routine follow up visits with psychiatric technicians between February 2022 and January 2024 at eight primary healthcare facilities in the Sofala and Manica provinces of Mozambique. This study included a census of all patients who were either new to the treatment or who had not been seen at the facilities for psychiatric treatment for at least six months at the initiation of the study baseline period of February 2022 to January 2024. These patients completed WHODAS disability screening at their first visit and received care from psychiatric technicians for mental health conditions that required medication. Patients who were being treated solely for medical conditions unrelated to mental health were not included in the study.

Data Collection

During the provision of routine primary mental healthcare, psychiatric technicians collected clinical data from patients using enhanced paper-based registries and patient charts. These newly introduced registries and charts facilitated the systematic tracking of patient visits, medications dispensed, and the progression of disability over time (using the WHODAS). To ensure this information was efficiently managed and updated, research assistants digitized the patient data monthly using the CommCare application. This process of data collection and digitization allowed for a comprehensive and accurate compilation of clinical data, essential for the detailed analysis and assessment of patient outcomes within the study.

Exposures

The primary exposure variables in this study include primary diagnoses (epilepsy, schizophrenia-related disorders, other psychotic and delusional disorders, depression-related disorders, mental and behavioral disorders due to substance use, and all other diagnoses). "All other diagnoses" grouped together any ICD-10 code psychiatric diagnoses with fewer than 15 patients each, including acute stress reaction, anorexia nervosa, bipolar affective disorder, dementia, dissociative disorders, eating disorders, hyperkinetic disorders, insomnia, mental and behavioral disorders associated with the puerperium, migraine syndromes, mild intellectual disability, mood [affective] disorders, neurasthenia, nonorganic enuresis, nonorganic insomnia, nonorganic sleep disorders, organic amnestic syndrome, other behavioral and emotional disorders, paranoid personality disorder, phobic anxiety disorders, sexual dysfunction not caused by organic disorder, tic disorders, trigeminal neuralgia, and unspecified personality and behavioral disorders in adults. Primary medications (Carbamazepine, Haloperidol, Amitriptyline, Thioridazine, and all other medications). "All other medications," grouped together those medications with fewer than 15 patients each, include: B-complex, biperiden, chlordiazepoxide, chlorpromazine, clonazepam, fluphenazine, imipramine, phenobarbital, phenytoin, sodium valproate, tramadol, and trifluoperazine. Sociodemographic characteristics included age (<18, 18-35, 36-55, and over 56 years), sex (female and male), and marital status (single, married, divorced, separated, widowed, and common-law).

Outcomes

Our primary outcome of interest was adherence to treatment. This metric was determined through a dual-question approach. The first question involved directly asking the patient if they adhered to the prescribed medication (i.e., taking the treatment as prescribed). The second aspect involved cross-referencing the patient record to confirm whether the patient attended the follow-up appointment before exhausting their medication supply. The patient needed to fulfill these two conditions to be considered adherent to the treatment at every visit.

The secondary outcomes of our study included weight (measured in kilograms), systolic and diastolic blood pressures (measured in mmHg), and the WHODAS score. The WHODAS score is a tool used to measure health and disability across six domains of functioning: cognition, mobility, self-care, social interactions, life activities, and societal participation. We used WHODAS 2.0 with a maximum possible score of 48. Higher scores indicate greater levels

of disability. WHODAS is designed to be universally applicable across different cultures and adult populations (20). As part of routine clinical delivery, these variables are measured at each visit per protocol. However, missing data exists in these outcomes over time.

Statistical Analysis

We used descriptive statistics to summarize baseline characteristics of the study population, using frequencies and percentages for categorical and dichotomous variables and mean and standard deviation (SD) for continuous variables. We conducted survival analysis—a statistical method designed to model time-to-event (21) data—to examine factors related to medication non-adherence.

We employed a non-parametric Kaplan-Meier model and a semi-parametric Cox proportional hazards model to estimate survival (time to non-adherence) across various exposure variables. These models were adjusted for clustering within each facility to account for variability among facilities. The differences in survival among each category of our exposure variables were compared using the log-rank test. To determine which baseline factors influence the duration until non-adherence to medication, we utilized multivariate Cox proportional hazards regression models. Non-adherence was defined as the event of interest, and 'time' was measured as the number of days for which medications were supplied until the first occurrence of non-adherence. For analysis purposes, patients were categorized into three groups based on their follow-up visits: The first group consisted of 240 patients who attended the clinic only once and did not return. For these individuals, the time to event was assumed to be the duration of their initial medication supply. The second group, comprising 489 patients with more than one visit, was followed until their first non-adherence event. The time to event for this group was calculated as the total duration of medication supplied during the observation period. The third group included 57 patients who remained adherent throughout the study. For these patients, the last adherent visit and the cumulative duration of medication supply until that point were used to determine the time to event. Right censoring was applied to these 57 patients, who were consistently adherent until the end of the study period. There were also 17 patients who were left censored due to a lack of complete data on medication duration. We reported the hazard of failing to adhere to the first medication, the adjusted hazard ratio (aHR), with 95% confidence intervals (CI) and p-values. Adjusted models included variables for primary diagnoses, primary medication, age, sex, and marital status.

A multivariable generalized linear mixed model was employed to examine the associations of primary medications, primary diagnosis, age, sex, marital status, and the duration of 30 days in treatment with changes in the outcome variables: weight, blood pressure, and WHODAS score. These models incorporated a patient-level random intercept to account for individual patient variability. We reported the adjusted estimates ($a\beta$) with their 95% CI. All tests were 2-sided and $p < 0.05$ was used to denote statistical significance. All analyses were conducted using R statistical software, version 4.3.1.

Results

Most study participants were aged 18-35 years (60%), with a mean age of 31 years. The majority were male (53%), single (63%), and had a normal body mass index (BMI, 18.5-24.9 kg/m²) with 62% falling into this category and an average BMI of 19 kg/m². Sixteen percent of participants were HIV positive, 18% were current alcohol users, and 9% were current drug users. A mental health assessment indicated that 3% had thought of suicide at enrollment. At enrollment, the mean WHODAS score was 11; the mean systolic blood pressure was 95 mmHg; the mean diastolic blood pressure was 78 mmHg; and the mean weight was 49 kg. (see **Table 1**).

Approximately 93% (729 out of 786) of patients failed to adhere to their primary medication at least once during the study period. In our non-parametric Kaplan-Meier analysis, after adjusting for facility clustering, the median survival time before non-adherence was 60 days, and the mean survival time was 52 days (95% CI: 51, 53). There was no significant difference in median survival time between male and female patients, both being 60 days (p-value = 0.70 from the log-rank test for sex-specific differences). In age-stratified groups, median survival times ranged from 52.5 days for individuals under 18 years old to 60 days for those aged 56 and older (p-value for age-specific differences = 0.10). The median survival time was similar across marital status groups (60 days), except for individuals who were divorced, with a median survival time of 33.5 days (p-value for differences across marital status groups = 0.20).

For patients with mental and behavioral disorders due to substance use and those in the “all other diagnosis” group, the median survival time was 45 days (see **Figure 1**). In contrast, patients with epilepsy, schizophrenia-related disorders, other psychotic and delusional disorders, and depression-related disorders had a median survival time of 60 days (p-value for differences across diagnoses < 0.001). Patients taking Amitriptyline had a median survival time of 45 days, while those taking carbamazepine, haloperidol, thioridazine, and the “other medication” group had a median survival time of 60 days (p-value for differences across medications < 0.001).

In fully-adjusted semi-parametric Cox regression models, individuals aged 56+ had a 31% higher hazard of non-adherence compared with those aged 18-35 (aHR: 1.31; 95% CI:

1.10, 1.57) (see **Table 2**). Patients prescribed amitriptyline had a 54% higher hazard compared to those prescribed carbamazepine (aHR: 1.54; 95% CI: 1.19, 1.99). Additionally, patients in the 'all other medications' group had a 19% higher hazard compared to those prescribed Carbamazepine (aHR: 1.19; 95% CI: 1.01, 1.41). Patients in the 'all other diagnoses' group had a 20% higher hazard compared to those with epilepsy (aHR: 1.20; 95% CI: 1.02, 1.41). Gender and marital status were not associated with nonadherence in fully-adjusted analyses .

In fully-adjusted generalized linear mixed models, for each 30 days in treatment, WHODAS score, systolic blood pressure, and diastolic blood pressure all showed significant reductions over time, with an average reduction of 0.13 (95% CI: -0.16, -0.09), 0.46 mmHg (95% CI: -0.81, -0.10), and 0.15 mmHg (95% CI: -0.23, -0.06), respectively (see **Table 3**). Across all visits, patients diagnosed with schizophrenia related disorders and patients in the 'all other diagnoses group' had 2.0 (95% CI: 0.88, 3.17) and 1.8 (0.69, 2.91) higher disability scores, respectively, compared with patients diagnosed with epilepsy. During the study period, male patients weighed 3.32 kg more than female patients (95% CI: 0.63 to 6.02). Additionally, males had a marginally lower diastolic blood pressure (DBP) compared to females, with a difference of 4.39 mmHg (95% CI: -8.51 to -0.27). Patients in the 'all other medication' group had a weight that was 3.21 kg lower (95% CI: -6.41, 0.01) compared to those taking carbamazepine.

Discussion

In the current study of outpatient psychiatric patients in Mozambique, we found major gaps in adherence to essential psychiatric medication. Only 7% of patients maintained adherence throughout the study follow-up period, with the median duration of adherence being just 60 days following the initiation of psychiatric medication. This rate of adherence is lower compared to a 2020 meta-analysis, which reviewed forty-six studies published in English before December 2017 globally. The meta-analysis found that, on average, 49% of patients with major psychiatric disorders did not adhere to their psychotropic medication regimen (22). Importantly, 40% of these studies were conducted in Low- and Middle-Income Countries (LMICs), and 25% were conducted in Sub-Saharan Africa. The elevated non-adherence rate observed in our study could be attributed to the method used to measure adherence time, which relied on the duration of medication supply. This approach may be particularly unreliable in our context, as the reasons for the prescribed duration of medication were not always clear. While many studies have used medication duration as a proxy for adherence time (23), numerous factors affect medication supply in developing countries, including limited supplies, restricted access to pharmacies for prescription pickups, and the necessity for patients to return to clinics for refills. In Mozambique, the requirement for patients to return to the clinic every 30-60 days for medication is likely a significant reason for non-adherence.

Despite the overall high rates of nonadherence, our study identified specific sub-groups at an even higher hazard of medication noncompliance. Particularly, patients over 56 years of age exhibited a 30% higher hazard of medication non-adherence compared to those aged 18-35. This finding is consistent with findings from the study by Abdulbari et al., who reported that patients aged 21-30 years were significantly more compliant with drug treatment than those over 30 years old (24). In contrast, a study in Qatar examining medication compliance among patients with psychiatric disorders suggested that younger age might be a risk factor for medication non-adherence. This indicates that older individuals could adhere better to medication regimens due to a better understanding of their illness, its progression, and their prior treatment experiences. (25). In the Mozambican and LMIC contexts, further research is necessary to examine potential differential barriers to medication adherence by age. For instance, older individuals might face more challenges traveling long distances to clinics for regular medication, may struggle with physical limitations or comorbidities that hinder their ability to access care, may have less access to transportation, and might benefit from additional

medication adherence support, such as community health worker visits or mobile health interventions.

In our study, primary diagnosis and prescribed medication were significant predictors of medication adherence. Patients in the 'all other diagnoses' group had a 20% higher hazard of non-adherence compared to those with epilepsy ($p = 0.01$). Other studies in Sub-Saharan Africa have shown that epilepsy has higher medication adherence compared to other mental, neurological, and substance use conditions (26). These studies also indicated that patients with epilepsy exhibited higher medication adherence scores. These findings contrast with those reported by other studies on epilepsy, potentially due to differences in socio-cultural factors and variations in other population characteristics (26, 27). In addition, patients prescribed Amitriptyline had a 50% higher hazard of non-adherence compared to those prescribed Carbamazepine. In our study, 116 patients (15% of the sample) were prescribed Amitriptyline as their primary medication. Among these, 29 were diagnosed with nonorganic sleep disorders, 26 with depressive episodes, 19 with bipolar affective disorder, and seven with epilepsy, among other conditions (see **Table 4**). Previous research has shown that patients taking older generation tricyclic antidepressants, including Amitriptyline, often experience significant side effects such as insomnia, anxiety, dry mouth, and weight gain (28, 29, 30). Potential causes of non-adherence may include the prevalence of negative side effects associated with tricyclic antidepressants, a general shortage of psychotropic medications, and possibly disproportionate stockouts of amitriptyline (32). There is an increased need for a variety of medications to treat sleep disorders, depressive episodes, and bipolar disorder in Mozambique and other similar LMICs. Relying solely on older generation tricyclics, which may have more side effects and lower efficacy, is insufficient

In our examination of the impact of treatment duration, primary medications, primary diagnoses, and sociodemographic factors on disability scores, we found that even with challenges related to non-adherence to medication, each 30 days in mental health treatment resulted in a meaningful and statistically significant lower disability scores over time. We also found that schizophrenia patients had higher disability scores than patients diagnosed with epilepsy. This difference might be attributed to the more chronic and debilitating nature of schizophrenia, which often requires more complex and sustained interventions. No association was found between disability scores and gender, age, marital status, or primary medication. Future research should explore the mechanisms behind the reduction in disability scores and

test strategies to promote adherence and maximize gains in activities of daily living. Additionally, research should investigate how to sustain these improvements over time. It may also be necessary to provide differentiated care for patients with schizophrenia, who tend to have higher disability scores at baseline, rather than applying the same overall treatment structure to all patients. This tailored approach could better address the specific needs of different diagnoses.

Patients in the 'all other medication' group had a weight that was 3.21 ($p = 0.04$) kg lower compared to those taking carbamazepine. This finding aligns with a clinical trial that compared carbamazepine and haloperidol in treating mania, revealing that haloperidol resulted in higher dropout rates due to side effects, whereas carbamazepine was deemed potentially effective despite causing some drowsiness and gastrointestinal issues (33). We also found that males experienced lower diastolic blood pressure (4.39 mmHg; $p = 0.04$) compared to females of similar age, medication, and diagnosis. These results underscore the importance of personalized treatment plans that account for specific diagnoses and individual patient characteristics. The observed weight differences suggest that medication choice can have significant effects on physical health, which should be considered when prescribing treatments. The finding of lower diastolic blood pressure in males highlights potential gender differences in response to treatment, indicating the need for further research to optimize treatment strategies for different patient groups. Healthcare workers should focus on enhancing medication adherence through tailored interventions, especially for those on medications with significant side effects or in populations with higher risks of non-adherence like Mozambique.

This study has several limitations that need to be considered. First, the assessment of treatment adherence was based on the duration of medication supply, which does not necessarily equate to actual patient adherence. Medication supply might be limited due to decisions by physicians to discontinue the treatment or prescribe medications for short durations because of supply shortages or clinical discretion, rather than due to patient non-compliance. Furthermore, logistical challenges in LMICs exacerbate this issue, as patients often need to return to clinics for medication refills within 30 to 60 days, which can be time-consuming and costly compared to simply picking up prescriptions at local pharmacies, as is common in high income countries. Additionally, the use of the ICD-10 classification system for primary diagnosis data may not be entirely accurate or appropriate for the setting (21). Another significant limitation is the reliance on self-reported data to determine if patients took their

medication as prescribed, which cannot be independently verified and may introduce bias. Lastly, since the data were collected from a limited number of hospitals in Mozambique, caution is advised when interpreting the results and making broader inferences about diagnostic and treatment patterns across the country.

This study is the first to utilize a comprehensive dataset from eight clinics in Mozambique, employing a longitudinal approach over a two-year period to investigate medication non-adherence among outpatient psychiatric patients. It examined the relationships between non-adherence and clinical variables such as primary diagnosis, medication type, and sociodemographic factors. Importantly, it also explored how the primary medications prescribed impact changes in WHODAS scores, weight, and blood pressure over time. Our research found a very low adherence rate, with over 90% of patients failing to consistently follow their prescribed regimen. The median survival time among our study population was 60 days, after adjusting for facility-based variability. The study also highlights significant associations between psychiatric diagnoses and a difference in WHODAS scores, underscoring how medication adherence and specific psychiatric disorders, as well as other factors (e.g., gender), significantly affect disability or biological measures. For instance, patients with schizophrenia-related disorders had a higher WHODAS score compared with those with epilepsy. A gender-related pattern was also evident in the clinical measurements, with males displaying lower diastolic blood pressure than females, even after adjusting for various factors. These findings underscore the urgent need for targeted research into adherence support strategies to address the widespread challenge of medication non-adherence in Mozambique and potentially extend these strategies across sub-Saharan Africa.

Reference:

1. Mental health [Internet]. [cited 2024 May 10]. Available from: <https://www.who.int/news-room/fact-sheets/detail/mental-health-strengthening-our-response>
2. WEF_Harvard_HE_GlobalEconomicBurdenNonCommunicableDiseases_2011.pdf [Internet]. [cited 2023 Nov 23]. Available from: https://www3.weforum.org/docs/WEF_Harvard_HE_GlobalEconomicBurdenNonCommunicableDiseases_2011.pdf
3. Canavan ME, Sipsma HL, Adhvaryu A, Ofori-Atta A, Jack H, Udry C, et al. Psychological distress in Ghana: associations with employment and lost productivity. *Int J Ment Health Syst* [Internet]. 2013 Dec [cited 2023 Nov 23];7(1):1–9. Available from: <https://ijmhs.biomedcentral.com/articles/10.1186/1752-4458-7-9>
4. Prevention [Internet]. [cited 2024 Jun 1]. Available from: <https://www.who.int/teams/mental-health-and-substance-use/treatment-care/mental-health-gap-action-programme>
5. Prevention [Internet]. [cited 2024 May 31]. Available from: <https://www.who.int/teams/mental-health-and-substance-use/treatment-care/mental-health-gap-action-programme>
6. Whiteford HA, Ferrari AJ, Degenhardt L, Feigin V, Vos T. The Global Burden of Mental, Neurological and Substance Use Disorders: An Analysis from the Global Burden of Disease Study 2010. *PLoS ONE* [Internet]. 2015 Feb 6 [cited 2024 May 31];10(2):e0116820. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4320057/>
7. Mental Health — SAIA [Internet]. [cited 2024 Apr 18]. Available from: <https://www.saia-strategy.com/saia-mental-health>
8. World Population Clock: 8.1 Billion People (LIVE, 2024) - Worldometer [Internet]. [cited 2024 May 31]. Available from: <https://www.worldometers.info/world-population/>
9. Prevalence and associated factors of common mental disorders in primary care settings in Sofala Province, Mozambique - PubMed [Internet]. [cited 2023 Nov 24]. Available from: <https://pubmed.ncbi.nlm.nih.gov/36632814/>
10. Bh W, V C, M RB, D R, Ba K, A S, et al. Outpatient Mental Health Services in Mozambique: Use and Treatments. *Psychiatr Serv Wash DC* [Internet]. 2016 Jun 1 [cited 2023 Nov 23];67(6). Available from: <https://pubmed.ncbi.nlm.nih.gov/26828400/>
11. Mert DG, Turgut NH, Kelleci M, Semiz M. Perspectives on reasons of medication nonadherence in psychiatric patients. *Patient Prefer Adherence* [Internet]. 2015 [cited 2023 Dec 13];9:87. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4298301/>
12. Adherence to Typical Antipsychotics among Patients with Schizophrenia in Uganda: A Cross-Sectional Study [Internet]. [cited 2023 Nov 24]. Available from: <https://www.hindawi.com/journals/schizort/2023/7035893/>
13. Factors associated with poor adherence to medication among hypertensive patients in twelve low and middle income Sub-Saharan countries - PMC [Internet]. [cited 2024 Mar 1]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6619761/>
14. Medication nonadherence and psychiatry - PMC [Internet]. [cited 2023 Dec 13]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4222796/>
15. Sc C, R H. Medication nonadherence and psychiatry. *Curr Opin Psychiatry* [Internet]. 2013 Sep [cited 2023 Nov 23];26(5). Available from: <https://pubmed.ncbi.nlm.nih.gov/23880592/>
16. Weight gain and comorbidities associated with oral second-generation antipsychotics: analysis of real-world data for patients with schizophrenia or bipolar I disorder - PMC [Internet]. [cited 2024 Apr 18]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8842889/>
17. Medication adherence and subjective weight perception in patients with first-episode psychotic disorder - PubMed [Internet]. [cited 2024 Apr 18]. Available from:

- <https://pubmed.ncbi.nlm.nih.gov/21983497/>
18. Mental Health — SAIA [Internet]. [cited 2024 Apr 18]. Available from: <https://www.saia-strategy.com/saia-mental-health>
 19. Systems analysis and improvement approach to optimize outpatient mental health treatment cascades in Mozambique (SAIA-MH): study protocol for a cluster randomized trial | Implementation Science | Full Text [Internet]. [cited 2024 Jan 2]. Available from: <https://implementationscience.biomedcentral.com/articles/10.1186/s13012-022-01213-8>
 20. WHO Disability Assessment Schedule (WHODAS 2.0) [Internet]. [cited 2024 Apr 18]. Available from: <https://www.who.int/standards/classifications/international-classification-of-functioning-disability-and-health/who-disability-assessment-schedule>
 21. Accuracy of Diagnosis Coding Based On ICD-10 | Asian Pacific Journal of Health Sciences [Internet]. [cited 2024 Jan 17]. Available from: <https://www.apjhs.com/index.php/apjhs/article/view/699>
 22. Psychotropic medication non-adherence and its associated factors among patients with major psychiatric disorders: a systematic review and meta-analysis - PMC [Internet]. [cited 2024 Apr 20]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6966860/#CR6>
 23. Treatment adherence and persistence with long-acting somatostatin analog therapy for the treatment of acromegaly: a retrospective analysis - PMC [Internet]. [cited 2023 Nov 28]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5379584/>
 24. A study of reasons of non-compliance of psychiatric treatment and patients' attitudes towards illness and treatment in Qatar - PubMed [Internet]. [cited 2024 Apr 20]. Available from: <https://pubmed.ncbi.nlm.nih.gov/23566190/>
 25. Psycho-demographic and clinical predictors of medication adherence in patients with bipolar I disorder in a university hospital in Egypt - PMC [Internet]. [cited 2024 Apr 20]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7059429/>
 26. Antiepileptic Drug Adherence and Its Associated Factors among Epilepsy Patients on Follow-ups at Amanuel Mental Specialized Hospital, Ethiopia - PMC [Internet]. [cited 2024 May 10]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9554767/>
 27. Sajatovic M, Mbwambo J, Lema I, Blixen C, Aebi ME, Wilson B, et al. Correlates of poor medication adherence in chronic psychotic disorders. *BJPsych Open* [Internet]. 2021 Jan [cited 2023 Nov 23];7(1). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7791569/>
 28. Health-related quality of life and medication adherence in elderly patients with epilepsy - PubMed [Internet]. [cited 2024 May 10]. Available from: <https://pubmed.ncbi.nlm.nih.gov/30807640/>
 29. Self-Reported Antidepressant Drug Side Effects, Medication Adherence, and Its Associated Factors among Patients Diagnosed with Depression at the Psychiatric Hospital of Nepal [Internet]. [cited 2024 Apr 20]. Available from: <https://www.hindawi.com/journals/drt/2020/7024275/>
 30. JCDR - Depression, Antidepressants, WHO-UMC [Internet]. [cited 2024 Apr 20]. Available from: https://www.jcdr.net/article_fulltext.asp?issn=0973-709x&year=2013&month=June&volume=7&issue=6&page=1131-1134&id=3041
 31. Self-Reported Adverse Drug Reactions, Medication Adherence, and Clinical Outcomes among Major Depressive Disorder Patients in Ethiopia: A Prospective Hospital Based Study [Internet]. [cited 2024 Apr 20]. Available from: <https://www.hindawi.com/journals/psychiatry/2017/5812817/>
 32. The availability of essential medicines for mental healthcare in Sofala, Mozambique - PMC [Internet]. [cited 2024 May 23]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4469619/>

33. Medication Non-Adherence and Disability among Outpatients with Schizophrenia in North-Central Nigeria [Internet]. [cited 2024 Apr 20]. Available from: <https://www.scirp.org/journal/paperinformation?paperid=119773#ref7>

Tables

Table1: Selected socio-demographic characteristics of outpatient psychiatric patients in Mozambique from February 2022 to January 2024.

Patient Characteristics	N=803
Age (Mean/SD) in years	31(14)
<18	77 (9.8%)
18-35	479 (59.8%)
36-55	174 (21.2%)
56+	73 (9.2%)
Sex	
Female	378 (47.1%)
Male	425 (52.9%)
Marital status	
Married	61(7.6%)
Divorced	6 (0.8%)
Separated	26 (3.2%)
Single	507 (63.1%)
Widowed	45(5.6)
Common-law	155(19.3)
WHODAS Score (Mean/SD)	11(7)
0-9	348(43.3%)
9-20	389(48.4%)
20-30	59 (7.4%)
30+	7 (0.9%)
Weight (Mean/SD) Kg	49(23)

Systolic blood pressure(Mean/SD) mmHg	95(49)
<120	269(33.5%)
120-129	276(34.4%)
130-139	79 (9.9%)
140+	53(6.6%)
Missing	126 (15.6%)
Diastolic blood pressure(Mean/SD) mmHg	78(11)
<80	317(39.5%)
80-89	271 (33.6%)
90+	90 (11.2%)
Missing	125(15.7%)
BMI (Mean/SD) kg/m2	19(10)
<18.5	103 (12.8%)
18.5-24.9	501 (62.4%)
25-29.9	77 (9.6%)
30+	25 (3.1%)
Missing	97 (12.1%)
HIV status	
Yes	127(15.8%)
No	462(57.5%)
Unknown	208(25.9)
Missing	6 (0.8%)
TB status	
Yes	32 (4.0%)
No	361 (45.0%)

Unknown	399(49.7%)
Missing	11(1.3%)
Alcohol use status	
Current user	144 (17.9%)
Never user	494 (61.5%)
Past user	134 (16.7%)
Missing	31(3.9%)
Drug use status	
Current user	69(8.6%)
Never user	454 (81.4%)
Past user	65(8.1%)
Missing	15(1.9)
Thoughts of suicide	
No	775 (96.5%)
Yes	24 (3.0%)
Missing	4 (0.5%)
Patient pregnancy status	
No	794(98.8%)
Yes	6 (0.8%)
Missing	3 (0.4%)
Patient engaged in family planning	
No	768 (95.6%)
Yes	32(4.0%)
Missing	3 (0.4%)

Table 2: Factors related to medication non-adherence among outpatient psychiatric patients in Mozambique from February 2022 to January 2024.

Variables	Nonadherence N(%)	Crude model		Adjusted model	
		HR	95% CI	aHR*	95% CI
Sex: Male	383(93%)	0.96	[0.83, 1.13]	0.97	[0.80, 1.19]
Age(Years)					
18-35(ref)	434(92%)				
<18	74(96%)	1.20	[0.83, 1.73]	1.26	[0.83, 1.92]
36-55	153(92%)	1.18	[1.04, 1.34]*	1.13	[0.92, 1.40]
56+	68(94%)	1.20	[0.84, 1.70]	1.31	[1.10, 1.57]**
Marital Status					
Single(ref)	461(93%)				
Married	55(92%)	1.05	[0.77, 1.45]	1.03	[0.68, 1.58]
Separated	26(100%)	1.00	[0.52, 1.91]	0.94	[0.52, 1.70]
Divorced	5(83%)	1.17	[0.34, 3.95]	0.72	[0.19, 2.77]
Widowed	40(91%)	0.94	[0.70, 1.25]	0.73	[0.51, 1.04]
Common Law	139(935)	1.01	[0.87, 1.17]	0.92	[0.77, 1.12]
Primary med					
Carbamazepine(ref)	366(92%)				
Haloperidol	83(97%)	1.37	[0.85 2.20]	1.38	[0.92, 2.07]
Amitriptyline	108(93%)	1.70	[1.28, 2.26]***	1.54	[1.19, 1.99]**
Thioridazine	61(95%)	1.01	[0.73, 1.41]	0.95	[0.59, 1.55]

All other medications [‡]	109(91%)	1.21	[1.10, 1.33]***	1.19	[1.01, 1.41]*
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Primary Diagnosis

Epilepsy(ref)	372(92%)				
Schizophrenia related disorders	206(96%)	1.07	[0.94, 1.22]	0.98	[0.76, 1.25]
Other psychotic and delusional disorders	43(91%)	1.23	[0.90, 1.69]	1.17	[0.74, 1.83]
Depression related disorders	30(97%)	1.54	[1.28, 1.85]***	1.09	[0.84, 1.41]
Mental and Behavioral disorders due to substance use	48(94%)	1.33	[0.77, 2.30]	1.11	[0.58, 2.14]
All other “rare” diagnoses [∂]	130(92%)	1.51	[1.22, 1.87]***	1.20	[1.02, 1.41]*

Significant codes: 0 ‘****’ 0.001 ‘***’ 0.01 ‘**’ 0.05 ‘*’

* aHR - adjusted hazard ratio

[‡] All other medications with <15 patients grouped together(B complex, Biperiden, Chlordiazepoxide, Chlorpromazine, Clonazepam, Fluphenazine, Imipramine, Phenobarbital, Phenytoin , Sodium Valproate, Tramadol, and Trifluoperazine)

[∂] All diagnoses with < 15 patients grouped together (Acute stress reaction, Anorexia nervosa, Bipolar affective disorder, Dementia, Dissociative disorders, Eating disorders, Hyperkinetic disorders, Insomnia, Mental and behavioral disorders associated with the puerperium, Migraine syndromes, Mild intellectual disability, Mood [affective] disorders, Neurasthenia, Nonorganic enuresis, Nonorganic insomnia, Nonorganic sleep disorders, Organic amnesic syndrome, Other behavioral and emotional disorders, Paranoid personality disorder, Phobic anxiety disorders, Sexual dysfunction not caused by organic disorder, Tic disorders, Trigeminal neuralgia, and unspecified personality and behavioral disorders in adults)

Table 3: Associations of biological variables (WHODAS score, SBP, DBP, and weight) with primary medication and diagnosis among outpatient psychiatric patients in Mozambique from February 2022 to January 2024.

Predictor variables	WHODAS score			SBP (mmHg)			DBP(mmHg)			Weight(kg)		
	$a\beta^*$	SE(β)	95% CI	$a\beta$	SE(β)	95% CI	$a\beta$	SE(β)	95% CI	$a\beta$	SE(β)	95% CI
Intercept	9.68	1.69	[6.35, 13.02]***	98.22	4.54	[89.32, 117.12]***	81.63	2.3	[77.51, 85.75]***	48.9	1.68	[45.59, 52.21]***
Days (30 day)	-0.13	0.02	[-0.16, -0.09]***	-0.46	0.18	[-0.81, -0.10]*	-0.15	0.04	[-0.23, -0.06]***	-0.05	0.08	[-0.20, 0.12]
Sex: Male	-0.34	0.39	[-1.11, 0.42]	2.22	2.61	[-2.90, 7.34]	-4.39	2.10	[-8.51, -0.27]~	3.32	1.37	[0.63, 6.02] *
Age(Years)												
18-35(ref)												
36-55	-0.3	0.47	[-1.22, 0.63]	0.01	3.15	[-6.19, 6.21]	2.48	2.54	[-2.50, 7.47]	0.88	1.66	[-2.38, 4.14]
56+	0.65	0.67	[-0.67, 1.97]	2.33	4.47	[-6.44, 11.10]	3.43	3.60	[-3.63, 10.50]	-2.88	2.35	[-7.49, 1.74]
Marital Status												
Single(ref)												
Married	0.08	0.74	[-1.37, 1.54]	-3.8	4.98	[-13.72, 6.12]	-3.21	3.96	[-11.07, 4.63]	-0.88	2.58	[-6.02, 4.26]
Separated	0.92	1.03	[-1.11, 2.94]	6.17	6.71	[-7.05, 19.39]	-3.00	5.26	[-13.33, 7.33]	4.98	3.53	[-1.98, 11.94]
Divorced	-1.46	2.1	[-5.59, 2.67]	17.09	14.86	[-12.21, 46.38]	-10.46	10.73	[-31.52, 10.61]	0.24	7.65	[-14.84, 15.32]
Widowed	-0.06	0.49	[-1.02, 0.90]	2.56	3.24	[-3.80, 8.92]	-1.41	2.52	[-6.36, 3.55]	3.33	1.61	[-0.90, 6.02]
Primary med												
Carbamazepine(ref)												
Haloperidol	0.62	0.57	[-0.50, 1.75]	-3.97	5.08	[-13.94, 5.99]	-0.93	1.63	[-4.13, 2.27]	-3.57	2.45	[-8.38, 1.22]
Amitriptyline	-0.65	0.61	[-1.86, 0.53]	8.49	5.16	[-1.64, 18.61]	-0.76	1.9	[-4.49, 2.96]	2.14	2.52	[-2.79, 7.09]

Thioridazine	-0.57	0.49	[-1.55, 0.40]	1.18	4.76	[-8.15, 10.51]	-0.5	1.35	[-3.15, 2.15]	-1.71	2.26	[-6.15, 2.72]
All others γ	0.48	0.36	[-0.22, 1.18]	-3.34	3.46	[-10.12, 3.44]	0.97	0.99	[-0.97, 2.90]	-3.21	1.63	[-6.41, 0.01]~
Primary Diagnosis												
Epilepsy(ref)												
Schizophrenia related disorders												
	2.02	0.58	[0.88, 3.17]***	3.39	4.75	[-5.93, 12.72]	-2.74	1.99	[-6.63, 1.17]	0.36	2.36	[-4.28, 5.00]
Other psychotic and delusional disorders												
	-0.51	0.69	[-1.86, 0.86]	8.07	5.62	[-2.96, 19.10]	-0.61	2.36	[-5.24, 4.02]	5.04	2.81	[-0.47, 10.57]
Depression related disorders												
	0.73	0.92	[-1.07, 2.53]	9.37	7.52	[-5.37, 24.12]	3.31	2.95	[-2.47, 9.09]	2.43	3.75	[-4.92, 9.78]
Mental and Behavioral disorders due to substance use												
	1.42	0.8	[-0.16, 2.99]	2.1	6.23	[-10.11, 14.31]	3.48	3.38	[-3.14, 10.11]	2.12	3.12	[-4.00, 8.24]
All other δ	1.8	0.57	[0.69, 2.91]**	1.72	4.54	[-7.19, 10.64]	2.54	2.05	[-1.48, 6.55]	2.28	2.27	[-2.17, 6.73]

Significant codes: 0 '****' 0.001 '***' 0.01 '**' 0.05 '*' ~'

* $\alpha\beta$ - adjusted estimates

Se (β)- standard error of the estimates

DBP- diastolic blood pressure

SBP: systolic blood pressure

γ All other medications with <15 patients grouped together(B complex, Biperiden, Chlordiazepoxide, Chlorpromazine, Clonazepam, Fluphenazine, Imipramine, Phenobarbital, Phenytoin , Sodium Valproate, Tramadol, and Trifluoperazine)

δ All diagnoses with < 15 patients grouped together (Acute stress reaction, Anorexia nervosa, Bipolar affective disorder, Dementia, Dissociative disorders, Eating disorders, Hyperkinetic disorders, Insomnia, Mental and behavioral disorders associated with the puerperium, Migraine syndromes, Mild intellectual disability, Mood [affective] disorders, Neurasthenia, Nonorganic enuresis, Nonorganic insomnia, Nonorganic sleep disorders, Organic amnestic syndrome, Other behavioral and emotional disorders, Paranoid personality disorder, Phobic anxiety disorders, Sexual dysfunction not caused by organic disorder, Tic disorders, Trigeminal neuralgia, Unspecified personality and behavioral disorders in adults)

Table 4: Distribution of Primary Medications Across Different Primary Diagnoses Among Outpatient Psychiatric Patients in Mozambique (February 2022 - January 2024)

Primary medication	Primary diagnosis						Grand Total
	Epilepsy	Schizophrenia related disorders	Depression related disorders	Other psychotic and delusional disorders	Mental and behavioral disorder due to substance use	All others	
Carbamazepine	358(90%)	7(2%)	1(0%)	6(2%)	2(1%)	24(6%)	398
Amitriptyline	7(6%)	1(1%)	26(22%)	2(2%)	6(5%)	74(64%)	116
Haloperidol	1(1%)	53(49%)	1(1%)	12(11%)	25(23%)	17(16%)	109
Thioridazine		34(53%)		11(17%)	10(16%)	9(14%)	64
All other medications	39(40%)	15(15%)	3(3%)	16(16%)	9(9%)	15(15%)	97
Grand Total	405(52%)	110(14%)	31(4%)	47(6%)	52(7%)	139(18%)	784

Figures

Figure 1: Kaplan Meier survival curves (overall and stratified by sociodemographic characteristics) of non-adherence to the primary medication among outpatient psychiatric patients in Mozambique from February 2022 to January 2024.



