Magnitude and factors associated with treatment non-adherence among patients with depressive disorders at St. Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia, 2019: A cross sectional study

Yadeta Alemayehu¹*, Henock Asfaw², Million Girma¹

¹ Department of Psychiatry, College of Health Science, Mettu University, Mettu, Ethiopia, ² Department of Psychiatry, School of Nursing and Midwifery, College of Health and Medical Science, Haramaya University, Harar, Ethiopia

* yadoalex45@gmail.com

Abstract

Background
Inadequate adherence to treatment is among the main underlying causes of depression becoming a chronic problem. In developing countries due to limited access to health care, inaccurate diagnoses, and scarcity of medications, poor adherence may become an even larger obstacle in the treatment of depression. The current study aims to assess the magnitude and factors related to treatment non-adherence among patients with depressive disorders.

Objective
To assess the magnitude and factors associated with treatment non adherence among patients with depressive disorders at St. Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia, 2019.

Methods
A hospital-based cross-sectional study was conducted among 415 respondents using systematic random sampling technique. Medication adherence was assessed by using Medication Adherence Rating Scale. Data was entered to Epi-data version 3.1 and analyzed using SPSS version 20. Binary logistic analysis was done and P-values less than 0.05 were considered statistically significant.

Results
The prevalence of treatment non-adherence among patients with depressive disorders was 26% (95%CI; 21.2, 32.5). Previous suicide attempt (AOR = 3.05, 95%CI; 1.82, 5.12), medication side effects (AOR = 2.46, 95%CI; 1.47, 4.11), moderate to high self-stigma (AOR =
2.60, 95%CI: 1.45, 4.66), and poor quality of life (AOR = 2.47, 95%CI: 1.42, 4.28) were significantly associated with treatment non-adherence among patients with depressive disorders.

Conclusion and recommendation

Treatment non-adherence is a common problem among patients being treated for depressive disorders. Previous suicide attempts, medication side effects, moderate to high self-stigma, and poor quality of life were significantly associated with treatment non-adherence. Appropriate interventions should be developed to promote measures to facilitate adherence in this group of patients, and address the associated factors when applicable.

Introduction

Treatment adherence is the extent to which a person’s behavior such as taking medications, following a diet, and/or executing lifestyle changes correspond with medical or health advice provided by health care providers [1]. Patients may choose not to fill their medications at the pharmacy and to forego starting treatment altogether, they may take more or less medication than advised, or they may take it at the wrong times. This may lead them to stop treatment early before the intended effect of the medication occurs [2, 3].

In low and middle income countries, in addition to poor access to health care, lack of diagnostic certainty, and scarcity of medications, poor adherence is a major challenge in the treatment of the common illnesses such as diabetes, depression, and HIV/AIDS [1].

Depression is a significant mental illness that affects more than 300 million people of all ages across the world. According to a World Health Organization report in 2017, depression was the third leading contributor to the worldwide burden of diseases and is predicted to become the second leading cause of the global burden of disease by the year 2030 [4, 5]. In Ethiopia, depressive disorders contribute to about 6.5% of the total burden of diseases, which is the highest share of burden in comparison to other mental disorders [6].

Patients with depressive disorders are better treated and recover earlier when they follow the provided medications according to the clinicians’ prescription [2]. Despite expectations, patients at times fail to follow prescribers’ instructions, either discontinuing antidepressant medications early, or taking a lower dose of the prescribed medication [7]. Given this reality, patient adherence is a critical aspect of effective clinical management [8].

Inadequate adherence to treatment is among the main underlying causes of depression becoming a chronic problem [9]. An untreated episode of depression lasts 6 to 13 months; most treated episodes of depression last about 3 months. The withdrawal of antidepressant medications before 3 months has elapsed often results in the return of the symptoms of the illness [10].

According to studies done in different parts of the world, the magnitude of treatment non-adherence among patients with depressive disorders ranges from 10% to 67% [11–16]. A systematic review and meta-analysis study showed the magnitude of psychotropic medication non-adherence among patients with a diagnosis of major depressive disorder to be 50% [17].

According to a WHO report, the determinants of non-adherence are categorized in to different dimensions as: social and economic, health system-related, therapy-related, condition-related, and patient-related [1]. In another study determinants of treatment adherence were
Different studies show factors like duration of illness, severity of illness, previous history of admission, comorbid physical illness, lack of social support, presence of self-stigma, and substance use are correlates of treatment non-adherence among patients with depressive disorders [18–22]. In addition, those patients who have poor quality of life tend to be less adherent to their treatments [23].

There is a paucity of epidemiologically reliable data targeting magnitude and related factors of treatment non-adherence among patients with depressive disorders in Ethiopia, so this study will provide valuable data for clinicians, researchers and governmental bodies to address the problem.

**Method and materials**

**Study design and period**

A hospital based cross-sectional study was conducted from May 6 to June 13, 2019

**Study area**

The study was conducted at St. Amanuel mental specialized hospital (St. AMSH). The hospital is the only specialized mental health hospital in the country and was established in 1930. It is located in the western part of Addis Ababa in Addis Ketema sub city. St. AMSH provides care for patients coming from the entire nation of Ethiopia.

**Source population**

All patients with depressive disorders on follow up at St. Amanuel mental specialized hospital.

**Study population**

Patients with depressive disorders who had a follow up visit at St. Amanuel mental specialized hospital during the study period.

**Sample size and sampling technique**

The sample size was calculated by using single population proportion formula; since there was no published study in Ethiopia, the population proportion (P) was taken to be 50%. The sample size was calculated to be 384 participants. Considering, a 10% (39 participants) rate of non-response resulted in a total sample size of 423.

Systematic random sampling technique was used to select representative samples of patients with depressive disorders who had at least one follow up visit at the outpatient department of St. AMSH. The first participant was selected by lottery method then continued by every 2 intervals (k). The data was collected from every other patient with depressive disorders on follow up.

**Inclusion criteria**

Adult (age ≥ 18) patients with depressive disorders presenting for a follow up visit at St. Amanuel mental specialized hospital during the data collection period.
Study measurements

**Medication adherence:** assessed using the Medication Adherence Rating Scale (MARS). A total score of less than 6 was considered non-adherent [24].

**Self-stigma:** Based on the 24-item Internalized Stigma of Mental Illness scale (ISMI), where a mean score of 1.00–2.00 indicates minimal to no self-stigma, a score of 2.01 to 2.50 indicates mild self-stigma, a score of 2.51 to 3.00 indicates moderate self-stigma, and a score of 3.01 to 4.00 indicates severe self-stigma [25].

**Social support:** Based on the Oslo social support scale. The total score ranges from 3–14 which will be interpreted as: [3–8] poor social support, [9–11] moderate social support, and [12–14] strong social support [26].

**Current substance use:** those who non-medically used at least one substance (alcohol, Khat, cigarette and others) within the last 3 months [27].

**Khat:** is a stimulant drug found in leaves of an East African shrub that contains cathinone and cathine.

**Suicide attempt:** The question on suicide was asked whether the participant had felt so desperate that they had attempted suicide and is recorded as yes or no [28].

**Quality of Life:** using EUROHIS-QOL 8-item index; which has a score ranging from 8 to 40; and the average score level was taken to classify participants into poor or good quality of life groups [29].

**Chronic depression:** if the duration of depressive disorder is greater than or equal to 2 year it’s considered to be chronic [30].

**Comorbid medical illness:** is a diagnosed medical or surgical problem. It was confirmed by reviewing patient’s chart and asking the patient.

**Severity of illness:** was assessed using CGI severity scale; scores 1–3 were considered as mild, 4 as moderate and 5–7 as severe depressive disorder [31].

**Level of Insight:** A total score of zero is regarded as “no insight”, total score of 1–2 is “partial insight”, and a total score of 3 is interpreted as “full insight” based on three adopted questions [32].

**Income:** Using the World Bank poverty line cutoff, those with an average monthly income of less than 1.9$/day were considered as low income [33].

Data collection procedures

Data was collected by face-to-face interview, in addition to chart review. Socio-Demographic variables were collected using a semi-structured questionnaire.

Medication adherence was assessed using Medication Adherence Rating Scale. The total score of 6 or more indicate adherence and less than 6 indicate non adherence [24] The internal consistency (Cronbach’s alpha) of MARS in the current study is 0.86.

Severity of depression was assessed by using the improved Clinical Global Impression scale which has an objective CGI question that was filled by observing clinician and subjective CGI questions that was answered by participants [31].

For the assessment of insight the following dichotomous questions were asked and a score of 1 is assigned for yes and a score of zero for no for any item answered: Do you accept that you have an illness? Do you think that you require treatment? And, do you think you require your medications to stay well? The total score ranges between 0 and 3. A total score of zero is regarded as “no insight”, total score of 1–2 is “partial insight”, and a total score of 3 is interpreted as “full insight” [32].

Quality of Life was assessed using EUROHIS-QOL 8-item index. It’s prepared by WHO and validated in patients with depressive disorder. It has eight questions that were answered
by participants and it was taken as poor quality of life if average score level was < 24 and good quality of life if average score was ≥ 24 [29].

**Data quality control**

All questionnaires were translated into Amharic and back translated into English to check its consistency. The questionnaires were pretested at St. Paul’s Millennium Medical College Hospital on 5% (n = 22) of sample size that was not included in the main study. Data collectors were trained on the questionnaires and data was collected by psychiatric nurses. Data collectors were supervised daily and the filled questionnaires were checked daily by the supervisor and principal investigator.

**Data processing and analysis**

Coded and checked data were entered into the computer using EPI Data version 3.1 and imported to statistical package for social science (SPSS) window software version 20. Descriptive statistics such as frequency, percentage, mean and median were computed and presented using tables and charts in the current manuscript. Bi-variable binary logistic analysis was performed to determine each of explanatory variables and variables with p-value less than 0.2 during bi-variable analysis were entered to multivariable analysis. Multivariable binary logistic regression analysis was conducted to determine the presence of a statistically significant association between explanatory variables and outcome variables. P values less than 0.05 were considered statistically significant and strength of the association was presented by adjusted odds ratio with 95% C.I.

**Ethical consideration**

Ethical clearance was obtained from ethical review committee of St. Amanuel mental specialized hospital. Formal letter of permission was obtained from St. Amanuel mental specialized hospital. Data collectors clearly explained the aims of the study to study participants. Study participants had the opportunity to refuse or discontinue participation at any time during the course of the study, and they were further given the chance to ask anything about the study. Data was collected after obtaining written consent from participants. Confidentiality was assured throughout the study period.

**Results**

**Socio-economic and demographic characteristics of respondents**

Of the 423 total sample size, responses were received from 415, yielding a response rate of 98.11%. Eight patients failed to complete the expected questionnaires; six of them were due to lack of sufficient time for an interview, and two of them became agitated after initiating the interview. The respondents’ mean age was 36 years (standard deviation (SD): 10.11). Females made up 220 (53%) of the participants. More than half of the participants (227 (54.7%)) were Orthodox, almost half of the respondents (187 (45.1%)) were married, and 123 (29.6%) had completed college. About 250 (60.24%) were employed, and 314 (75.7%) were city dwellers. (Table 1).

**Respondents’ clinical characteristics**

More than half (54.6%) of participants have had multiple episodes of the illness. A slight majority, 292 (70.4%), had chronic depressive disorders, 215 (51.81%) had full insight, and 34.46% of respondents have attempted suicide at some point in their lives. 55.2% of
respondents had moderate severity of depression. Using EUROHIS-QOL 8-item the mean quality of life score in this study was 23.53 (SD 3.12). (Table 2).

**Current substance use history of respondents**

From the total of 415 respondents 91(21.9%) used alcohol, and 59(14.2%) used Khat within three months prior to data collection time (Fig 1).

**Magnitude of treatment non-adherence**

In this study about one fourth of respondents 108(26%) were non adherent to their treatment (Fig 2).

**Factors associated with treatment non adherence**

Being female, single, having low-income, having multiple episodes of depression, experiencing medication side effects, history of suicidal attempt, level of self-stigma, limited social support, and poor quality of life were variables with p-values less than 0.2 in bivariable binary logistic regression.

---

Table 1. Socio-economic and demographic characteristics of study participants.

| Variables                | Frequency(n = 415) | Percentage (%) |
|--------------------------|--------------------|----------------|
| Sex                      |                    |                |
| Female                   | 220                | 53.02          |
| Male                     | 195                | 46.98          |
| Age                      |                    |                |
| 18–24                    | 56                 | 13.49          |
| 25–34                    | 130                | 31.33          |
| 35–44                    | 121                | 29.16          |
| 45–54                    | 65                 | 15.66          |
| >55                      | 43                 | 10.36          |
| Religion                 |                    |                |
| Christian                | 308                | 74.22          |
| Muslim                   | 107                | 25.78          |
| Marital status           |                    |                |
| Married                  | 187                | 45.06          |
| Single/divorced/widowed  | 228                | 54.94          |
| Occupation               |                    |                |
| Employed                 | 250                | 60.24          |
| Unemployed               | 165                | 39.76          |
| Education status         |                    |                |
| No formal education      | 70                 | 16.86          |
| Primary education        | 111                | 26.75          |
| Secondary education      | 111                | 26.75          |
| Tertiary and above       | 123                | 29.64          |
| Residency                |                    |                |
| Urban                    | 314                | 75.66          |
| Rural                    | 101                | 24.34          |
| Average income           |                    |                |
| <1.9$/day                | 278                | 66.98          |
| ≥1.9$/day                | 137                | 33.02          |

https://doi.org/10.1371/journal.pone.0271713.t001
Medication side effects, history of suicidal attempt, poor social support, poor quality of life, and moderate to high levels of self-stigma were found to have a statistically significant association with medication non-adherence at a p-value less than 0.05 in multivariable binary logistic regression variables.

The odds of being non adherent was 3.05 times greater among respondents with a lifetime history of suicidal attempt than among those without a history of suicidal attempt (AOR = 3.05, 95%CI; 1.82, 5.12).

When compared to those who did not have medication side effects, the odds of being non adherent was 2.46 times higher among those who had medication side effects(AOR = 2.46,95% CI;1.47, 4.11).

The odds of being non adherent was 2.6 times higher among those with moderate to high self-stigma compared to those with minimum to low self-stigma (AOR = 2.60,95%CI;1.45, 4.66).

When comparing respondents with poor quality of life to those with good quality of life, the odds of being non adherent was 2.47 times higher (AOR = 2.47,95%CI; 1.42, 4.28) (Table 3).

Table 2. Clinical characteristics of the study participants.

| Variables                        | Frequency | Percentage (%) |
|----------------------------------|-----------|----------------|
| Episode                          |           |                |
| First Episode                    | 181       | 43.61          |
| Multiple episode(≥2)             | 234       | 56.39          |
| Chronicity of depression         |           |                |
| Chronic                          | 292       | 70.36          |
| Non-chronic(acute)               | 123       | 29.64          |
| Levels of Insight                |           |                |
| No Insight                       | 55        | 13.25          |
| Partial Insight                  | 145       | 34.94          |
| Full Insight                     | 215       | 51.81          |
| Comorbid medical condition       |           |                |
| Yes                              | 105       | 25.30          |
| No                               | 310       | 74.70          |
| Suicidal attempt                 |           |                |
| Yes                              | 143       | 34.46          |
| No                               | 272       | 65.54          |
| Severity of depression           |           |                |
| Mild                             | 146       | 35.18          |
| Moderate                         | 229       | 55.18          |
| Severe                           | 40        | 9.64           |
| Level of stigma                  |           |                |
| No/Minimal                       | 86        | 20.73          |
| Mild                             | 190       | 45.78          |
| Moderate                         | 119       | 28.67          |
| Severe                           | 20        | 4.82           |
| Level of Social support          |           |                |
| Poor                             | 166       | 40.00          |
| Moderate                         | 180       | 43.37          |
| Strong                           | 69        | 16.63          |
| Quality of life                  |           | 23.53 ± 3.12SD |

→SD = standard deviation

https://doi.org/10.1371/journal.pone.0271713.t002
Discussion

In the current study the frequency of treatment non adherence among patients with depressive disorder was 26% (95% CI; 21.9%-30.6%). This finding is consistent with previous studies done in Spain (30.1% [22]), in United Kingdom (30% [16]) and in USA (28% [34]).
However, it was lower than studies done in Nigeria (55.7% [32]), Saudi Arabia (52.9% [14]), India (66.9% [11]), Japan (63.1% [12]), and Thailand (59% [13]). The possible reason for this discrepancy might be the differences in populations and scales. For instance, the Nigerian study used Morisky medication adherence rating scale and was among patients with severe mental illness not specific to depression; similarly the study in Saudi Arabia used Morisky medication adherence rating scale and had a 6 months minimum duration of treatment in the Saudi Arabian study; this longer duration might affect adherence rate as patients might lose confidence in a treatment if their illness has not improved during this time, causing them to quit the treatment. The studies done in India and in Japan used Morisky Medication Adherence Scale and medication possession rate respectively, unlike the one used in the

### Table 3. Bivariable and multivariable binary logistic regression analysis showing association between treatment non-adherence and related factors among study participants.

| Explanatory variables | Treatment non adherence | COR (95%CI) | AOR (95%CI) |
|-----------------------|-------------------------|------------|-------------|
|                       | yes                     | No         |             |
| Sex                   | Female                  | 70         | 150         | 1.93(1.23, 3.04) | 1.70(0.96, 3.01) |
|                       | Male                    | 38         | 157         | 1           | 1           |
| Marital status        | Married                 | 38         | 149         | 1           | 1           |
|                       | Single                  | 50         | 86          | 2.28(1.39, 3.75) | 1.79(0.97, 3.29) |
|                       | Divorced/widowed        | 20         | 72          | 1.09(0.56, 2.01) | 1.57(0.79, 3.10) |
| Income                | < 1.9$/day              | 81         | 197         | 1.67(1.02, 2.33) | 1.26(0.68, 2.36) |
|                       | ≥ 1.9$/day              | 27         | 110         | 1           | 1           |
| Episode               | First                   | 47         | 186         | 1           | 1           |
|                       | Multiple                | 61         | 121         | 1.99(1.28, 3.11) | 1.38(0.79, 2.39) |
| Suicidal attempt      | Yes                     | 62         | 81          | 3.76(2.38, 5.95) | 3.05(1.82, 5.12) |
|                       | No                      | 46         | 226         | 1           | 1           |
| Severity of depression| Yes                     | 30         | 116         | 1.68(0.42,1.12) | 1.14(0.64,2.05) |
|                       | No                      | 15         | 25          | 0.43(0.20,0.92) | 1.15(0.44,2.98) |
| Treatment side effect | Yes                     | 64         | 101         | 2.97(1.89,4.66) | 2.46(1.47,4.11) |
|                       | No                      | 44         | 206         | 1           | 1           |
| Level of stigma       | No/mild                 | 43         | 233         | 1           | 1           |
|                       | Moderate to high        | 65         | 74          | 4.76(2.99,7.58) | 2.60(1.45, 4.66) |
| Social support        | Poor                    | 55         | 111         | 2.13(1.08,4.23) | 0.93(0.49,1.76) |
|                       | Moderate/Strong         | 53         | 196         | 1           | 1           |
| Quality of life       | Poor                    | 75         | 131         | 3.05(1.91,4.87) | 2.47(1.42, 4.28) |
|                       | Good                    | 33         | 176         | 1           | 1           |

→ * indicates statistically significant association, Hosmer and Lemeshow Test = .748

https://doi.org/10.1371/journal.pone.0271713.t003
current study (MARS). The study in Thailand also used medication possession ratio which varies from the current study.

However, the frequency of non-adherence was lower in the study done in United Kingdom 10% [15]. The possible reason might be the difference in age groups as the UK study only included participants above 50 years but the current study included all adults. The other possible reason is the difference in socio-economic status; accessibility and affordability of medication and minimal side effects can explain the improvements in adherence [35].

Those who had attempted suicide in their life were 3.05 times more likely to be non-adherent than those who had not attempted suicide. This is supported by studies done in India [36] and in Czech Republic [21] This association might have occurred because depressive disorders are the main underlying cause of suicidal behavior among mental disorders. If depression is not appropriately treated due to non-adherence, suicidal behavior as a symptom of depression will remain untreated [36, 37].

Patients who had medication side effects were 2.46 times more likely to be non-adherent than those who don’t have medication side effects. This association is supported by a study done in Malaysia [18] and other systematic reviews in Spanish and English languages [22]. The association might be related to intolerance of the medication adverse effects, thinking that the side effects of the medications are harmful; in addition a prescriber’s inadequate knowledge and skill in managing the illness and related adverse effect can have an impact and cause patients to prematurely stop medications [38].

Patients with moderate to high self-stigma were 2.6 times more likely than those with minimal to mild self-stigma to be non-adherent to the treatment. This association is consistent with studies done in Malaysia [18], Czech Republic [21] and USA [19] The possible reason for the association might be those who were non adherent to the treatment have poor ability to control or recover from the illness, worsening their level of self-stigma [39].

Respondents who reported a poor quality of life were 2.47 times more likely than those who reported a good quality of life to be non-adherent to the treatment. This finding is consistent with the survey done by EU National Health and Wellness Survey (NHWS) [23]. The other possible reason for the association might be that treatment non-adherence can cause a worsening of the illness; and can increase social isolation which is major reflection of poor quality of life. The other reason for the association might be that if a patient with chronic medical disorders including depression fails to adhere to treatment due to their physical, social and psychological health issues, which are indicators of poor quality of life [40, 41].

Although factors like chronicity of depression, severity of depression, number of episodes, comorbid medical illness, lack of social support, level of insight, educational status and current substance use were associated with treatment non adherence in different studies, but they failed to have statistically significant association in the current study. The reason for this variation might be the difference in socio-cultural variations and tools which were employed in the current study.

The limitation of this study is the use of cross-sectional study design, so the current study is unable to show a temporal causal relationship between treatment non-adherence and major associated factors.

**Conclusion and recommendation**

Treatment adherence is a common problem among patients on treatment for depression. Having a history of suicidal attempt, medication side effect, moderate to high self-stigma and poor quality of life were significantly associated with treatment non adherence. Suitable
interventions should be developed to address these factors, and promote measures to facilitate adherence in this group of patients.

Acknowledgments
We would like to give our deepest thankfulness to participants, and staffs of St. Amanuel Mental Specialized Hospital for their cooperation and support throughout data collection process.

Author Contributions
Conceptualization: Yadeta Alemayehu, Henock Asfaw, Million Girma.
Data curation: Yadeta Alemayehu, Million Girma.
Formal analysis: Yadeta Alemayehu, Henock Asfaw.
Investigation: Million Girma.
Methodology: Yadeta Alemayehu, Henock Asfaw, Million Girma.
Software: Yadeta Alemayehu.
Supervision: Yadeta Alemayehu, Henock Asfaw, Million Girma.
Validation: Yadeta Alemayehu.
Visualization: Million Girma.
Writing – original draft: Yadeta Alemayehu, Henock Asfaw, Million Girma.
Writing – review & editing: Yadeta Alemayehu.

References
1. Sabaté E SE, editors. Adherence to long-term therapies: evidence for action: World Health Organization; 2003.
2. Martin LR FC, Maksoudian CR, Wysong K, Faasse K. A perspective on nonadherence to drug therapy: psychological barriers and strategies to overcome nonadherence. Patient preference and adherence. 2018; 72(1527). https://doi.org/10.2147/PPA.S155971 PMID: 30197504
3. Lowry KP DT, Oddone EZ, Bosworth HB. Intentional and unintentional nonadherence to antihypertensive medication. Annals of Pharmacotherapy 2005 Jul; 39(7–8):1198–203. https://doi.org/10.1345/aph.1E594 PMID: 15956238
4. Organization WH. Depression and other common mental disorders: global health estimates. World Health Organization, 2017.
5. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS medicine. 2006; 3(11):e442. https://doi.org/10.1371/journal.pmed.0030442 PMID: 17132052
6. Abdulahi H, Mariam DH, Kebede D. Burden of disease analysis in rural Ethiopia. Ethiopian medical journal. 2001; 39(4):271–81. PMID: 12380227
7. Breggin PR. Psychiatric drug withdrawal: A guide for prescribers, therapists, patients and their families: Springer Publishing Company; 2012.
8. D S. Importance of patient adherence and compliance in the present day. J Bacteriol Mycol Open Access. 2017; 4(5):150–2.
9. Pompoli M, Serafini G, Innamorati M, Venturini P, Fusar-Poli P, Sher L, et al. Agomelatine, a novel intriguing antidepressant option enhancing neuroplasticity: a critical review. The World Journal of Biological Psychiatry. 2013; 14(6):412–31. https://doi.org/10.3109/15622975.2013.765593 PMID: 23590731
10. Sadock BJ, Sadock VA. Kaplan and Sadock’s synopsis of psychiatry: Behavioral sciences/clinical psychiatry: Lippincott Williams & Wilkins; 2011.
11. Banerjee S, Varma RP. Factors affecting non-adherence among patients diagnosed with unipolar depression in a psychiatric department of a tertiary hospital in Kolkata, India. Depression research and treatment. 2013; 2013.
12. Sawada N, Uchida H, Suzuki T, Watanabe K, Kikuchi T, Handa T, et al. Persistence and compliance to antidepressant treatment in patients with depression: a chart review. BMC psychiatry. 2009; 9(1):38. https://doi.org/10.1186/1471-244X-9-38 PMID: 19531229

13. Pruukkanone B, Vos T, Burgess P, Chaiyakunapruk N, Bertram M. Adherence to antidepressant therapy for major depressive patients in a psychiatric hospital in Thailand. BMC psychiatry. 2010; 10(1):64.

14. Al Jumah K, Hassali MA, Al Qhatani D, El Tahir K. Factors associated with adherence to medication among depressed patients from Saudi Arabia: a cross-sectional study. Neuropsychiatric disease and treatment. 2014; 10:2031. https://doi.org/10.2147/NDT.S71697 PMID: 25378929

15. Lingam R, Scott J. Treatment non-adherence in affective disorders. Acta Psychiatrica Scandinavica. 2002; 105(3):164–72. https://doi.org/10.1034/j.1600-0447.2002.1r084.x PMID: 11939969

16. Demyttenaere K, Haddad P. Compliance with antidepressant therapy and antidepressant discontinuation symptoms. Acta Psychiatrica Scandinavica. 2000; 101:50–6. https://doi.org/10.1111/j.1600-0447.2000.tb10948.x PMID: 11019935

17. Semahegn A TK, Manu A, Assefa N, Tesfaye G, Ankomah A. Psychotropic medication non-adherence and its associated factors among patients with major psychiatric disorders: a systematic review and meta-analysis. Systematic reviews. 2020 Dec; ; 9(1):1–8.

18. Ho SC, Jacob SA, Tangisuran B. Barriers and facilitators of adherence to antidepressants among outpatients with major depressive disorder: A qualitative study. PloS one. 2017; 12(6). https://doi.org/10.1371/journal.pone.0179290 PMID: 28614368

19. Sirey JA, Bruce ML, Alexopoulos GS, Perlick DA, Friedman SJ, Meyers BS. Stigma as a barrier to recovery: Perceived stigma and patient-rated severity of illness as predictors of antidepressant drug adherence. Psychiatric services. 2001; 52(12):1615–20. https://doi.org/10.1176/appi.ps.52.12.1615 PMID: 11726752

20. van Servised G, Heise BA, Ellis R. Factors associated with antidepressant medication adherence and adherence-enhancement programmes: a systematic literature review. Mental Health in Family Medicine. 2011; 8(4):255. PMID: 23205067

21. Sedlackova Z, Kamaradova D, Prasko J, Latolavok C, Ociskovh M, Ociskov M, et al. Treatment adherence and self-stigma in patients with depressive disorder in remission: A cross-sectional study. Neuroendocrinology Letters. 2015; 36(2):171–7. PMID: 26071588

22. Martin-Vazquez M-J, Garcia-Toro M, Campaomor F, Pareja A, Aguire I, Salva J, et al. Use and Results of Antidepressant Treatment: Patients’ Perception. Current Drug Therapy. 2011; 6(4):271–7.

23. Pedersini R, Kuehl M. The Burden Associated with Non-Adherence in European Patients with Depression. Value in Health. 2014; 17(7):A329. https://doi.org/10.1016/j.jval.2014.08.606 PMID: 27200562

24. Thompson K, Kularni J, Sergejew A. Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. Schizophrenia research. 2000; 42(3):241–7. https://doi.org/10.1016/s0920-9964(99)00130-9 PMID: 10785582

25. Lysaker PH RD, Yanos PT. Toward understanding the insight paradox: internalized stigma moderates the association between insight and social functioning, hope, and self-esteem among people with schizophrenia spectrum disorders. Schizophr Bull. 2007 Jan; 33(1):192–9. https://doi.org/10.1093/schbul/sbl016 PMID: 16894025

26. Abiola T, Udofia O, Zakari M. Psychometric properties of the 3-item oslo social support scale among clinical students of Bayero University Kano, Nigeria. Malaysian Journal of Psychiatry. 2013; 22(2):32–41.

27. Saiz R, Palfai TP, Cheng DM, Alford DP, Bernstein JA, Lloyd-Travaglina CA, et al. Screening and brief intervention for drug use in primary care: the ASPIRE randomized clinical trial. Jama. 2014; 312(5):502–13. https://doi.org/10.1001/jama.2014.7862 PMID: 25096690

28. Organization WH. Composite International Diagnostic Interview-version 2.1. 1997. Geneva: WHO.

29. da Rocha NS, Power MJ, Bushnell DM, Fleck MP. The EUROHIS-QOL 8-item index: comparative psychometric properties to its parent WHOQOL-BREF. Value in Health. 2012; 15(3):449–57. https://doi.org/10.1016/j.jval.2011.11.035 PMID: 22583455

30. Klein DN. Classification of depressive disorders in the DSM-V: Proposal for a two-dimension system. Journal of abnormal psychology. 2008; 117(3):552. https://doi.org/10.1037/0021-843X.117.3.552 PMID: 18729608

31. Kadouri A, Corruble E, Falissard B. The improved Clinical Global Impression Scale (iCGI): development and validation in depression. BMC psychiatry. 2007; 7(1):7. https://doi.org/10.1186/1471-244X-7-7 PMID: 17284321

32. Ibrahim AW, Yahya S, Pindar SK, Wakil MA, Garkuwa A, Sale S. Prevalence and predictors of sub-optimal medication adherence among patients with severe mental illnesses in a tertiary psychiatric facility in Maiduguri, North-eastern Nigeria. Pan African Medical Journal. 2015; 21(1).
33. Decline of Global Extreme Poverty continues but has slowed [press release]. Washington, USA, September 19 2018.

34. Bosworth HB VC, Potter GG, Steffens DC. The effects of antidepressant medication adherence as well as psychosocial and clinical factors on depression outcome among older adults. Int J Geriatr Psychiatry. 2008 Feb; 23(2):129–34. https://doi.org/10.1002/gps.1852 PMID: 17563920

35. Solmi M MA, Croatto G, Pigato G, Favaro A, Fornaro M, et al. How can we improve antidepressant adherence in the management of depression? A targeted review and 10 clinical recommendations. Braz J Psychiatry. 2020.

36. Alekhya P SM, Priya Darsini T, Reddy SK, Venkata Ramudu R. Treatment and diseases related factors affecting non adherence among patients on long term therapy of antidepressants. J Depress Anxiety. 2015 4(1000175).

37. Rihmer Z GX. Suicide behaviour of patients treated with antidepressants. Neuropsychopharmacol Hung 2006 Mar, 8(1):13–6. PMID: 16841560.

38. Wu CH, Farley JF, Gaynes BN. The association between antidepressant dosage titration and medication adherence among patients with depression. Depression and anxiety. 2012; 29(6):506–14. https://doi.org/10.1002/da.21952 PMID: 22553149

39. Abdisa E, Fekadu G, Girma S, Shibiru T, Tilahun T, Mohamed H, et al. Self-stigma and medication adherence among patients with mental illness treated at Jimma University Medical Center, Southwest Ethiopia. International Journal of Mental Health Systems. 2020; 14(1):1–13. https://doi.org/10.1186/s13033-020-00391-6 PMID: 32760443

40. Voros V FS, Tenyi T, Rihmer Z, Szili I, Osvath P. Untreated depressive symptoms significantly worsen quality of life in old age and may lead to the misdiagnosis of dementia: a cross-sectional study. Ann Gen Psychiatry 2020 Sep 15; 19:52. https://doi.org/10.1186/s12991-020-00302-6 PMID: 32944058; PMCID: PMC7493324.

41. Hayhurst K DR, Massie J, Dunn G, Barnes T, Jones P, et al. Improved quality of life over one year is associated with improved adherence in patients with schizophrenia. European Psychiatry. 2014; 29 (3):191–6. https://doi.org/10.1016/j.eurpsy.2013.03.002 PMID: 23769325