Original Article

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Adherence to Pharmacological Treatment among Patients with Schizophrenia

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ABSTRACT

Adherence to medication refers to the extent to which an individual corresponds with the prescribed medication dosing regimen. Medication non-adherence among patients with schizophrenia is extremely common, broadly ranging from 4% to 72%. This has serious consequences for individuals as well as the health system, such as relapse of symptoms, re-hospitalization, aggression, suicide, cognitive deterioration, loss of job and arrest, victimization, and overall unfavorable outcome. Factors determining adherence are divided into medication-related such as side effects, patient-related such as lack of insight, illness-related such as persecutory delusions, sociocultural such as stigma, and clinician-related factors such as poor therapeutic alliance. Adherence is best achieved by exploring the reasons for non-adherence with appropriate management plans to deal with them. It can be improved by providing basic strategies that must routinely accompany every prescription and specific interventions, such as psycho-social ones, antipsychotic long-acting injections, reminders, service interventions, and even financial incentives.

Keywords: Adherence, medication, schizophrenia

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INTRODUCTION

Among all mental disorders, schizophrenia is one of the most serious,[1] and it is considered one of the top 10 causes of long-term disability in the entire world, affecting about 1% of people.[2] Typically, schizophrenia is a chronic disease, with significant psycho-social and medical consequences. It is characterized by a constellation of abnormalities in thinking, emotion, and behavior. Patients diagnosed with schizophrenia have a heterogeneous clinical presentation with no single pathognomonic symptom.[3]

The course of the disorder encompasses a prodromal phase, active phase, and residual phase. The active phase includes hallucinations, delusions, and disorganized thinking, whereas the prodromal and residual phases are characterized by attenuated active symptoms, such as odd beliefs, magical thinking, and interpersonal and self-care deficits.[4]

A characteristic feature of schizophrenia is the presence of positive and negative symptoms. Delusions, hallucinations, and disorganized behavior are considered to be positive symptoms that reflect distortion of normal function. The absence of motivation and interest or blunted affect and alogia are stated as negative symptoms that largely account for the long-term morbidity and poor outcome in functioning in these patients.[5]

A literature review suggests that the annual incidence of schizophrenia is about 0.15 per 1,000. The point prevalence is 4.6 per 1,000, whereas the lifetime prevalence is estimated to be 4.0 per 1,000, and lifetime morbid risk is approximately 7.2 per 1,000 persons.[6]

In males, schizophrenia usually develops in the mid-20s with an average onset between 20 and 25 years, while in females, it develops in the late 20s with an average onset between 25 and 30 years.[7]

The genetic influence in the etiology of schizophrenia is the most important, with about 80% of the risk being inherited. Many environmental factors in early life also contribute, which interact with the genetic vulnerability. Together, these risk factors render the individual prone to the emergence of symptoms in later life.[8]

Treatment of schizophrenia initially includes antipsychotic drugs, some of which relieve delusions and hallucinations (positive symptoms) by dopamine receptor blockage, whereas others may also address the negative symptoms.[9] Thus, antipsychotic agents enhance recovery through the control of symptoms, improve quality of life, restore basic life functioning, and prevent relapse.[10]

A significant component in treatment is enhancing the quality of life through successful jobs and relationships and not just reducing the signs and symptoms.[9]

Antipsychotic medication alone is insufficient to address the complex social, financial, and health needs of patients with schizophrenia. Thus, the consensus is the combination of antipsychotic medication and psycho-social interventions that range from psycho-education, assertive community treatment, supported employment, cognitive behavioral therapy, family interventions,

family-based services, token economy, skills training to psycho-social interventions for substance misuse, and weight reduction.[11]

Nearly 40% of schizophrenic patients with treatment continue to experience psychotic symptoms that can impede their functional ability, hindering work, relationships, self-care, and independent living.[12]

Patients with schizophrenia have lower life expectancy and poor physical health secondary to a number of contributing factors, such as lifestyle risks, adverse effects of medication, mental stress, loss of motivation, and healthcare provision. They may also have a significantly higher incidence of chronic obstructive airway disease, diabetes mellitus Type 2, and ischemic heart disease.[13]

Medication adherence is the extent to which an individual's behavior corresponds with the prescribed medication dosing regimen, timing, and dosage and medication intake intervals. Medication non-adherence is a common issue worldwide with significant costs particularly in chronic diseases that need long-term treatment.[14]

Adherence to treatment involves visiting the physician regularly, complying with requirements of the treatment program, and following the prescription. Partially or completely not adhering to the prescribed drugs, taking non-prescribed medication, discontinuing follow-ups, or missing appointments are all indicators of non-adherence to treatment.[15]

It is estimated that only 50% of patients with chronic diseases (any physical or mental condition that lasts for more than a year and needs continuous care) take their medications as prescribed. Therefore, improving adherence to medication is a major priority of the public health system.[16]

Alipour et al. (2020) found that patients having serious mental disorders, including schizophrenia, may have non-adherence rates that are equal to or worse than that of patients with organic diseases, with rates of non-adherence to antipsychotic drugs reaching up to 89%.[17]

Medication non-adherence among patients with schizophrenia remains a dominant problem, highlighting the need for new approaches to support patients, such as by frequent telephone contact, to improve adherence.[18]

The estimated rate of non-adherence in patients with schizophrenia in one study is 50%, broadly ranging from 4% to 72%,[19] whereas in another study, the range is from 42% to 74%.[20] According to Turkish studies, 69.5% have partial adherence.[15]

A study in Washington showed that 74% of outpatients with schizophrenia stop taking antipsychotics within two years of leaving hospital.[21]

In addition, there are some variations in adherence rates in patients with schizophrenia over time; for example, up to 25% of patients are non-adherent whether partially or completely 10 days after discharge from hospital, and this percentage increases to 50% at one year and to 75% by two years.[22]

Consequences of medication non-adherence

Medication non-adherence among schizophrenic patients has serious consequences for individuals as well as the country, frequently leading to higher rates of relapse and exacerbation of psychotic symptoms, frequent hospital admissions, frequent emergency visits,[23] increased aggressive behaviors, and a worse overall outcome, compared to adherent patients.[24]

Relapse of illness may endanger both the patient and other people. In about two-third of cases, re-admission to hospital is the result of non-adherence or partial adherence. After a year of the first hospital admission, 40% of relapse results from medication non-adherence.[25] Furthermore, it is estimated that the risk of relapse is 3.7 times higher in non-adherent subjects than in patients with good treatment adherence.[26]

Other consequences of non-adherence include increased cognitive deterioration,[26] negative social outcomes such as loss of job and arrest,[27] victimization,[28] poor quality of life, reduction of treatment effectiveness, less response to subsequent treatment, increased co-morbid physical illnesses, wastage of health care resources, and increased risk of suicide.[29] Moreover, the suicide risk in patients with schizophrenia who are non-adherent is 3.75 times higher than in those who are adherent.[30]

In addition, lack of treatment adherence has significant costs and is associated with a marked increase in the health services usage. It is estimated that about 40% of the cost associated with schizophrenia treatment is due to non-adherence, involving an annual expenditure of more than 10 billion dollars and 400 million pounds in the United States and the United Kingdom, respectively. [26]

Table 1: Consequences of medication non-adherence in schizophrenic patients.

Relapse	Arrest
Re-admissions	Victimization
Emergency visits	Poor quality of life
Aggression	Reduction of treatment effectiveness
Suicide	Less response to subsequent treatment
Cognitive deterioration	Increased co-morbid physical illnesses
Loss of job	Wastage of health care resources

Etiology of medication non-adherence

Adherence to medication is not a simple issue, as there are multiple factors that can influence it. These factors can be divided into five major groups: medication-related, patient-related, illness-related, sociocultural, and mental-health service-provider-related,[31] which can also be titled as clinician-related factors.[22]

Medication-related factors involve the drug being perceived to be ineffective, complex medication regime, intolerable side effects, such as weight gain, akathisia,[22] and sexually adverse effects,[32] concerns about drug–drug interaction,[33] or higher frequency of medication.[34] It appears that there is an important positive association between obesity and distress from weight gain and medication non-adherence.[35]

Patient-related factors are lack of insight or denial of illness, co-morbid substance misuse and/or personality disorder, being male and young, personal beliefs about the illness,

perception of illness severity, concerns about dependency on the prescribed drugs, concerns about long-term side effects, lack of knowledge of medication, misunderstanding the instructions, and simply forgetting medication,[22] which is the most common cause of missing medication dose.[36] Other factors are negative attitudes/beliefs about medication,[37] maladaptive coping skills or personality traits,[38] previous history of non-adherence, and chronic medical diseases.[36] In addition, it is estimated that up to 25% of patients with schizophrenia when effectively treated report missing (i.e., craving for or desire to) their psychotic experiences (missing the voices, missing the feeling of power), which thus acts as a motive for non-adherence to medication.[22,39] According to a Pakistani study, 36% of patients mentioned that "I forgot to take my medication," and 32% of them reported that "I thought that I am better now, and do not need to take my medication."[40] Lack or impaired insight into illness is one of the key reasons that are associated with non-adherence to antipsychotic medication. It is estimated that nearly 60% of patients suffer from moderate-to-severe impairment of insight. Individuals with impaired insight are likely to deny or minimize the need for treatment, have negative attitudes/beliefs toward medication, and have more tendencies to stop taking their drugs. Patients with first-episode psychosis were studied for a year, and it revealed that non-adherent persons had a lower level of insight at baseline at one year compared to the adherent patients. In another study, patients with first-episode schizophrenia treated with antipsychotics and who appeared to have impaired insight at six months were associated with 1.4 increased risk of non-adherence to medication.[41]

Moreover, illness-related factors cover specific symptoms such as loss of interest,[31] persecutory and/or grandiose delusions/thoughts, severe psychotic symptoms,[42] suspiciousness,[35] hostility, cognitive impairment, and depressive symptoms.[41]

Furthermore, sociocultural factors include beliefs of family about the illness and about medication, peer pressure, religious beliefs,[22] low educational level, low socioeconomic status,[35] insufficient income, transportation, homelessness,[43] living alone,[44] lack of family/social support,[45] location of treatment services,[46] racial and ethnic minority,[47] and stigma.[31]

Lastly, clinician-related factors include perceiving the clinician as dismissive or authoritative, not feeling listened to or consulted, poor given explanation of treatment,[22] less emotional support from the physician,[31] and poor therapeutic alliance.[35]

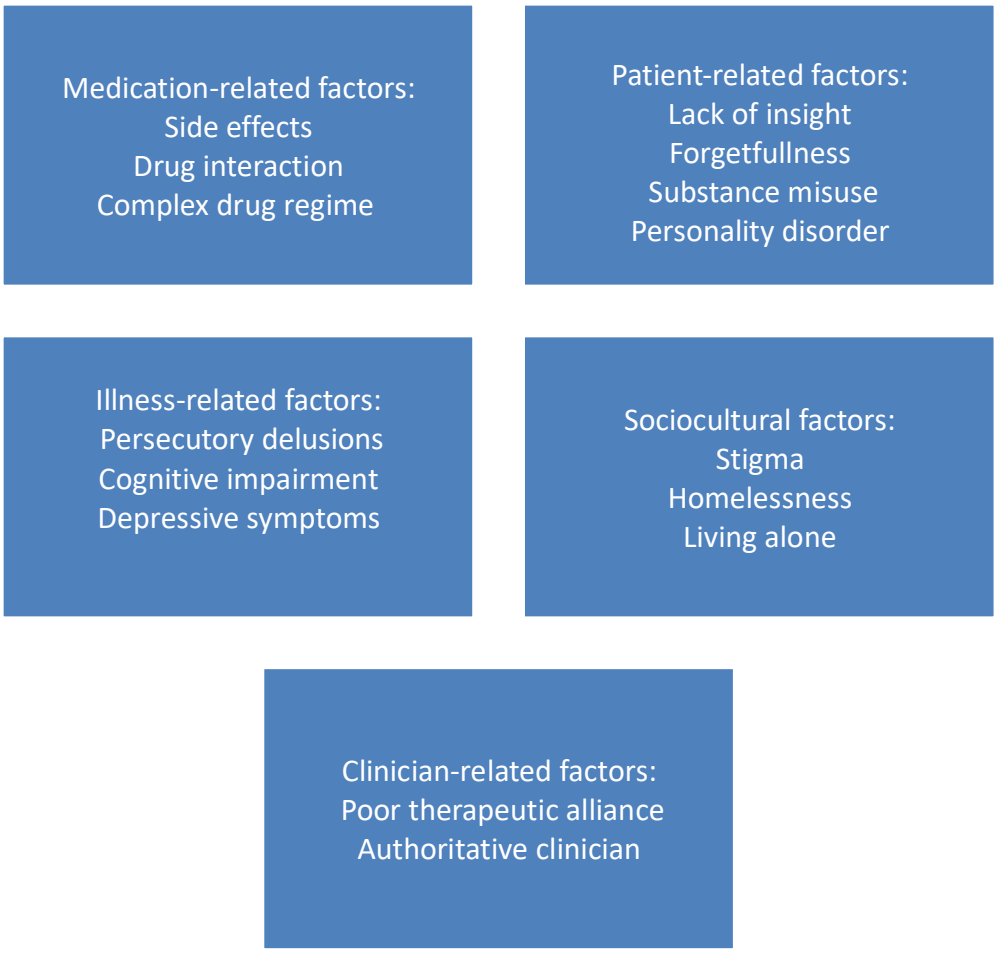

Figure 1: Reasons behind non-adherence to medications among patients with schizophrenia.

Estimating non-adherence to medication

Many methods of medication adherence monitoring are available. The most commonly used method is self-report, but it is most likely to overestimate adherence. Urine and serum testing provide adherence information only for the days immediately before testing, and it is not available for all drugs. Pharmacy refill rates can be used too to monitor adherence but are problematic if patients change pharmacies or use multiple pharmacies. Furthermore, pharmacy refill rates provide no information about drug ingestion. Similarly, counting pills cannot be considered a measure of actual ingestion of medication.[48]

Management of medication non-adherence

Exploring the attitudes and reasons for poor drug adherence with appropriate management strategies planned is one way to improve adherence to medication.[49] Accumulated research data concluded that

individually tailored multi-component interventions have the best chance to improve adherence.[50]

Improving adherence to antipsychotic medication includes basic strategies that must routinely accompany every prescription and specific interventions. Moreover, these specific interventions can be subdivided into five headings: psychosocial interventions, antipsychotic long-acting injections, reminders including electronic methods, service interventions, and financial incentives.[51]

Basic strategies to accompany prescribing are crucial to improve adherence, such as involving patients in decisions and choice of their drug, listening to them, understanding their beliefs and concerns about the medication and their illness, warning them of potential side effects before starting medication, increasing dosage gradually, or explaining that adverse effects should disappear; these can decrease the risk of side effects impairing adherence. Potential side effects can be managed by dose reduction, starting a specific treatment, changing time of taking the drug, or changing to another antipsychotic. For example, a greater dose can be given at night if the antipsychotic is causing sedation, it can be swallowed with water if the drug is resulting in dry mouth, a weight loss program can be maintained in case of weight gain, anticholinergic agent can be used to deal with antipsychotic-induced Parkinsonism, and another antipsychotic can be switched to in order to deal with side effects of prolactin elevation like galactorrhoea or sexual dysfunction. In addition, adherence can be improved by simplifying the prescription regimen in those with complex ones.[51]

Psychosocial interventions to enhance adherence to antipsychotic drugs are psycho-education, behavioral interventions, motivational interviewing, and cognitive methods.[51]

Psycho-education is defined as a process of teaching patients with mental disorders about the nature of their illness including etiology, progression, consequences, treatment, and prognosis.[52] Behavioral interventions cover skills learning, practice of activities, behavioral modeling, and reinforcement methods.[51] Motivational interviewing is an effective intervention to enhance the patient's motivation for changing behavior and improving adherence to medication.[53] Principles of both motivational interviewing and cognitive behavioral therapy can be combined and called adherence therapy, which is a brief patient-centered approach and aimed at amplifying benefits of treatment, modifying beliefs about illness and treatment, resolving ambivalence toward taking drugs,[54] and discussing stigma.[1] Successful cognitive and behavioral interventions that improve adherence are those that enhance the therapeutic relationship.[51] It is estimated that motivational techniques or concrete problem solving are successful intervention programs that improve medication adherence among schizophrenic patients.[55]

Long-acting injection (LAI) formulations of antipsychotics were developed to enhance treatment adherence and may improve

outcomes in schizophrenia, administration schedules ranging from fortnightly to every three months. LAIs with FDA approval for treatment of schizophrenia are aripiprazole monohydrate, fluphenazine decanoate, haloperidol decanoate, olanzapine pamoate, paliperidone palmitate, and risperidone microspheres. Current schizophrenia treatment guidelines recommend LAI use in patients who are insufficiently adherent to medication and for patients who prefer such treatment.[56] Maintenance therapy with LAI has been shown to reduce risk of relapse and re-hospitalization.[57]

Reminders are helpful in unintentional non-adherence when the patient forgets to take medication. But this method is unlikely to help when non-adherence is intentional. Reminders may involve written notes to take medication that are placed in prominent places, setting alarms for taking drugs, or having medication pre-packed in packets labeled with the day and time to be ingested.[51] Other technologies are being increasingly used to maintain adherence to medication, such as simple reminders to take medication via cell phone or SMS messages.[58]

Service interventions ensuring that services are readily accessible to patients are likely to improve adherence. These include ensuring ready access to emergency departments, setting appointments with minimal delay, and using prepayment cards to reduce total prescription costs.[51]

Furthermore, financial reinforcement is emerging as a potential plan to enhance adherence to medication in severe mental illness.[59] Financial incentives provision to improve adherence in patients taking antipsychotic drugs is a promising intervention[60] but raises ethical issues.[51]

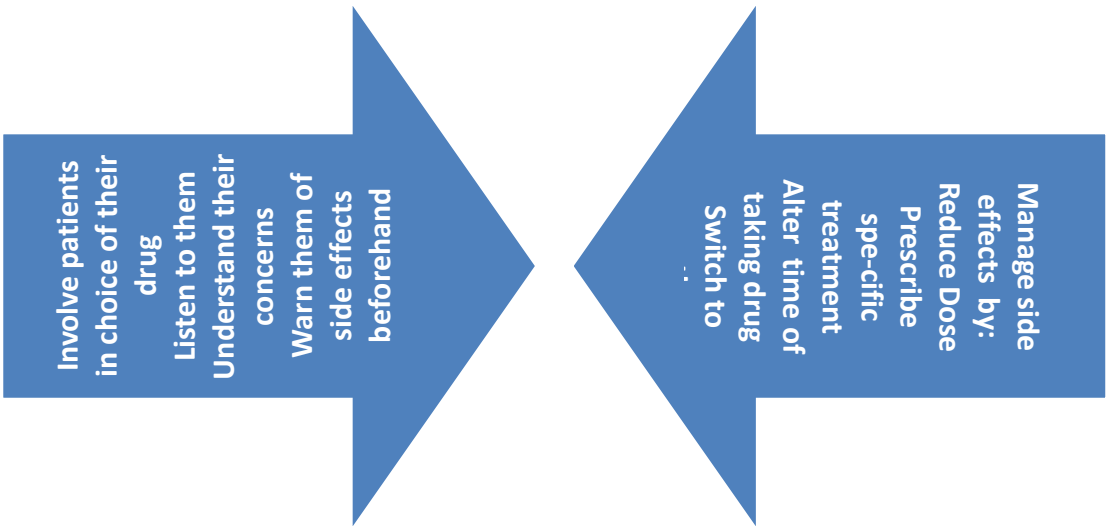

Figure 2: Basic strategies to enhance adherence to medication among patients with schizophrenia.

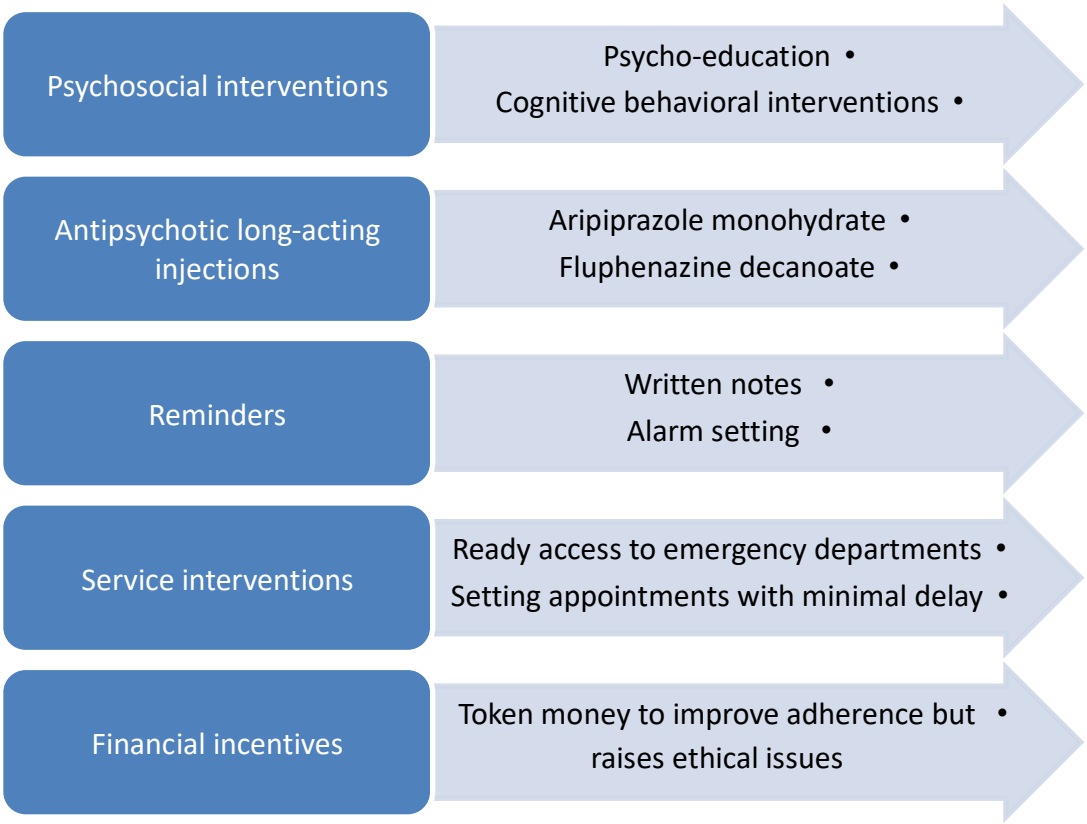

Figure 3: Specific interventions to enhance medication adherence among patients with schizophrenia.

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REFERENCES

1. Saber EH, Abdel- Kader NM, Sayied NE, et al. Effect of psycho educational program on improving of medication adherence among schizophrenic patients. IOSR-JNHS. 2018; 7(6):69–79.
2. Tareke M, Tesfaye S, Amare D, et al. Antipsychotic medication non-adherence among schizophrenia patients in Central Ethiopia. S Afr J Psych. 2018; 24(0):a1124.
3. Ganti L, Kaufman MS, Blitzstein SM. First aid for the psychiatry clerkship. 5th ed. New York: McGraw-Hill Education; 2019.
4. Sadock BJ, Ahmad S, Sadock VA. Kaplan & Sadock's pocket handbook of clinical psychiatry. 6th ed. Philadelphia: Wolters Kluwer; 2019.
5. Correll CU, Schooler NR. Negative symptoms in schizophrenia: a review and clinical guide for recognition, assessment, and treatment. NDT. 2020; 16:519–34.
6. Epping EA, Black DW. Epidemiology and risk factors influencing schizophrenia. In: Schulz SC, Green MF, Nelson KJ (Eds). Schizophrenia and psychotic spectrum disorders. New York: Oxford University Press; 2016. p41–54.
7. Brar JS. Epidemiology of schizophrenia. In: Marcsisin MJ, Gannon JM, Rosenstock JB (Eds). Schizophrenia and related disorders. New York: Oxford University Press; 2017. p89–110.
8. Harrison P, Cowen P, Burns T, et al. Shorter Oxford textbook of psychiatry. 7th ed. Oxford: Oxford University Press; 2018.
9. Ganguly P, Soliman A, Moustafa AA. Holistic management of schizophrenia symptoms using pharmacological and non-pharmacological treatment. Front Public Health. 2018; 6:166.
10. Kassew T, Demilew D, Birhanu A, et al. Attitude towards antipsychotic medications in patients diagnosed with schizophrenia: a cross-sectional study at Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia. Schizophr Res Treat. 2019; 2019:1–9.
11. Asher L, Patel V, De Silva MJ. Community-based psychosocial interventions for people with schizophrenia in low and middle-income countries: systematic review and meta-analysis. BMC Psychiatry. 2017; 17(1):355.
12. Radhakrishnan R, Ganesh S, Meltzer HY, et al. Schizophrenia. In: Ebert MH, Leckman JF, Petrakis IL (Eds). Current diagnosis & treatment. 3rd ed. New York: McGraw-Hill Education; 2019. p207–35.
13. Harrison C, Charles J, Britt H. Comorbidities and risk factors among patients with schizophrenia. FOCUS. 2015; 44(11):781–3.
14. Gast A, Mathes T. Medication adherence influencing factors: an (updated) overview of systematic reviews. Syst Rev. 2019; 8(1):112.
15. Ata EE, Bahadir-Yilmaz E, Bayrak NG. The impact of side effects on schizophrenia and bipolar disorder patients' adherence to prescribed medical therapy. Perspect Psychiatr Care. 2020; 1–6.
16. Fernandez-Lazaro CI, García-González JM, Adams DP, et al. Adherence to treatment and related factors among patients with chronic conditions in primary care: a cross-sectional study. BMC Fam Pract. 2019; 20(1):132.
17. Alipour A, Gabrielson S, Patel PB. Ingestible sensors and medication adherence: focus on use in serious mental illness. Pharmacy. 2020; 8(2):103.
18. Tessier A, Dupuy M, Baylé FJ, et al. Brief interventions for improving adherence in schizophrenia: a pilot study using electronic medication event monitoring. Psychiatry Res. 2020; 285:112780.
19. Singh PM, Karmacharya S, Khadka S. Severity of relapse and medication adherence in patient of schizophrenia: a study from Nepal. J Psychiatr Assoc Nepal. 2019; 8(2):54–8.
20. Dobber J, Latour C, Van Meijel B, et al. Active ingredients and mechanisms of change in motivational interviewing for medication adherence: a mixed methods study of patient-therapist interaction in patients with schizophrenia. Front Psychiatry. 2020; 11:78.
21. Endale Gurmu A, Abdela E, Allele B, et al. Rate of nonadherence to antipsychotic medications and factors leading to nonadherence among psychiatric patients in Gondar University Hospital, Northwest Ethiopia. Advances in Psychiatry. 2014; 2014:1–5.
22. Taylor D, Barnes TRE, Young AH. The Maudsley prescribing guidelines in psychiatry. 13th ed. Hoboken: Wiley; 2018.
23. Grover S, Mehra A, Chakrabarti S, et al. Attitude toward psychotropic medications: a comparison of the elderly and adult patients with affective and psychotic disorders. J Geriatr Ment Health. 2020; 6(2):38–45.
24. Gebeyehu DA, Mulat H, Bekana L, et al. Psychotropic medication non-adherence among patients with severe mental disorder attending at

Bahir Dar Felege Hiwote Referral Hospital, North West Ethiopia, 2017. BMC Res Notes. 2019; 12(1):102.
25. Lama A, Baruah A. Medication adherence and its association with subjective well-being among persons with schizophrenia. Indian J Psy Nsg. 2019; 16(2):61–6.
26. Torras MG, Tomas EP. Interventions to improve therapeutic adherence in subjects with schizophrenia. Pap Psicol. 2018; 39(1):31–9.
27. Forma F, Green T, Kim S, et al. Antipsychotic medication adherence and healthcare services utilization in two cohorts of patients with serious mental illness. CEOR. 2020; 12:123–32.
28. Czobor P, Van Dorn RA, Citrome L, et al. Treatment adherence in schizophrenia: a patient-level meta-analysis of combined CATIE and EUFEST studies. European Neuropsychopharmacology. 2015; 25(8):1158–66.
29. Semahegn A, Torpey K, Manu A, et al. Psychotropic medication non-adherence and its associated factors among patients with major psychiatric disorders: a systematic review and meta-analysis. Syst Rev. 2020; 9(1):17.
30. Ahmed N, Gandhi S, Baruah A. Effectiveness of specific intervention on treatment adherence of persons with mental illness: a pilot study. Indian J Psychiatry. 2015; 57(4):403–6.
31. Okasha TA, Radwan DN, Elkholy H, et al. Psycho-demographic and clinical predictors of medication adherence in patients with bipolar I disorder in a university hospital in Egypt. S Afr J Psych. 2020; 26(0):a1437.
32. Fatma F, Baati I, Omri S, et al. Medication adherence in schizophrenia. Eur Psychiatr. 2016; 33(S1):S586.
33. Ibrahim AW, Pindar SK, Yerima MM, et al. Medication-related factors of non adherence among patients with schizophrenia and bipolar disorder: outcome of a cross-sectional survey in Maiduguri, North Eastern Nigeria. J Neurosci Behav Health. 2015; 7(5):31–9.
34. Odo HO, Olotu SO, Soni JS, et al. Assessment of adherence to psychotropic medications among out-patients at the pharmacy department of a psychiatric hospital, in Benin City, Nigeria. Asian J Pharm. 2014; 8(4):211–5.
35. Lee Y, Lee M-S, Jeong H-G, et al. Medication adherence using electronic monitoring in severe psychiatric illness: 4 and 24 weeks after discharge. Clin Psychopharmacol Neurosci. 2019; 17(2):288–96.
36. Mamo ES , Gelaw BK, Tegegne GT. Medication adherence among patients with schizophrenia treated with antipsychotics at Adama Hospital, East Shoa Zone, Oromia Regional State. Adv Pharmacoepidemiol Drug Saf . 2016; 5(2):1000200.
37. Descalço NFF, Afonso PMM. Can empathy improve therapeutic adherence in schizophrenia? J Clin Psychopharmacol. 2020; 40(1):89–90.
38. Atram U, Karia S, Shah N, et al. A retrospective study of treatment compliance in psychiatric patients and factors affecting the same. IJMH. 2016; 3(2):178–84.
39. Moritz S, Favrod J, Andreou C, et al. Beyond the usual suspects: positive attitudes towards positive symptoms is associated with medication noncompliance in psychosis. Schizophr Bull. 2013; 39(4):917–22.
40. Girma S, Abdisa E, Fikadu T. Prevalence of antipsychotic drug non adherence and associated factors among patients with schizophrenia attending at Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia: institutional based cross sectional study. Health Sci J. 2017; 11(4):520
41. Kim J, Ozzoude M, Nakajima S, et al. Insight and medication adherence in schizophrenia: an analysis of the CATIE trial. Neuropharmacology. 2020; 168:1–8.
42. Chang JG, Roh D, Kim C-H. Association between therapeutic alliance and adherence in outpatient schizophrenia patients. Clin Psychopharmacol Neurosci. 2019; 17(2):273–8.
43. Ebrahem SM. Alam FH. Effectiveness of psychiatric nursing intervention on adherence to medications and quality of life of schizophrenic patients. AJNS. 2016; 5(6):232–9.
44. Phan SV. Medication adherence in patients with schizophrenia. Int J Psychiatry Med. 2016; 51(2):211–9.
45. Eticha T, Teklu A, Ali D, et al. Factors associated with medication adherence among patients with schizophrenia in Mekelle, Northern Ethiopia. PLoS ONE. 2015; 10(3):e0120560.
46. Ghimire SR. Poor medication compliance in schizophrenia from an illness and treatment perspective. ECPP. 2017; 3(4):131–41.
47. Hernandez M, Barrio C. Families and medication use and adherence among Latinos with schizophrenia. J Ment Health. 2017; 26(1):14–20.
48. Beebe LH. Effect of a telephone intervention upon medication adherence and related outcomes

in outpatients with schizophrenia spectrum disorders (SSDs). Med Clin Rev. 2017; 3(2):1–6.
49. Chandra IS, Kumar KL, Reddy MP, et al. Attitudes toward medication and reasons for non-compliance in patients with schizophrenia. Indian J Psychol Med. 2014; 36(3):294–8.
50. Dahan S, Behrbalk P, Greenberger C. Improving adherence in hospitalized patients diagnosed with schizophrenia: an integrative one-on-one intervention. Arch Psychiatr Nurs. 2016; 30(6):660–5.
51. Haddad PM, Brain C, Scott J. Nonadherence with antipsychotic medication in schizophrenia: challenges and management strategies. PROM. 2014; 5:43–62.
52. Sarkhel S, Singh OP, Arora M. Clinical practice guidelines for psychoeducation in psychiatric disorders general principles of psychoeducation. Indian J Psychiatry. 2020; 62(8):S319–23.
53. Dobber J, Latour C, de Haan L, et al. Medication adherence in patients with schizophrenia: a qualitative study of the patient process in motivational interviewing. BMC Psychiatry. 2018; 18(1):135.
54. Gray R, Bressington D, Ivanecka A, et al. Is adherence therapy an effective adjunct treatment for patients with schizophrenia spectrum disorders? A systematic review and meta-analysis. BMC Psychiatry. 2016; 16(1):90.
55. Salzmann-Erikson M, Sjödin M. A narrative meta-synthesis of how people with schizophrenia experience facilitators and barriers in using antipsychotic medication: Implications for healthcare professionals. Int J Nurs Stud. 2018; 85:7–18.
56. Greene M, Yan T, Chang E, et al. Medication adherence and discontinuation of long-acting injectable versus oral antipsychotics in patients with schizophrenia or bipolar disorder. J Med Econ. 2018; 21(2):127–34.
57. Ljungdalh PM. Non-adherence to pharmacological treatment in schizophrenia and schizophrenia spectrum disorders: an updated systematic literature review. Eur J Psychiatry. 2017; 31(4):172–86.
58. Velligan DI, Kamil SH. Enhancing patient adherence: introducing smart pill devices. Therapeutic Delivery. 2014; 5(6):611–3.
59. Guinart D, Kane JM. Use of behavioral economics to improve medication adherence in severe mental illness. PS. 2019; 70(10):955–7.
60. Noordraven EL, Wierdsma AI, Blanken P, et al. Financial incentives for improving adherence to maintenance treatment in patients with psychotic disorders (money for medication): a multicentre, open-label, randomised controlled trial. The Lancet Psychiatry. 2017; 4(3):199–207.