

Non-Compliance and Related Factors in Patients With Bipolar I Disorder: A Six Month Follow-Up Study

Sanaz Azadforouz,¹ Amir Shabani,^{2,*} Shabnam Nohesara,² and Masoud Ahmadzad-Asl²

¹Babol University of Medical Sciences, Babol, IR Iran

²Tehran Psychiatric Institute, Mental Health Research Centre, Iran University of Medical Sciences, Teharn, IR Iran

*Corresponding author: Amir Shabani, Bipolar Disorders Research Group, Tehran Psychiatric Institute, Mental Health Research Center, Iran University of Medical Sciences, Tehran, IR Iran. E-mail: am.shabani@gmail.com

Received 2014 October 07; Revised 2015 February 10; Accepted 2015 July 04.

Abstract

Background: Medication treatment compliance among bipolar patients is quite widespread.

Objectives: Treatment compliance depends on multiple factors. The aim of this study was to evaluate the predicting factors of noncompliance in patients with bipolar I disorder admitted to an Iranian hospital during a six-month follow up period.

Materials and Methods: This cross-sectional study included 47 bipolar I disorder subjects who were admitted to the Iran psychiatric hospital and that were chosen using a non-randomized convenient sampling model. The patients were assessed at baseline, and at two and six months after admission. For evaluating the patients, we used the medication possession ratio (MPR), the drug attitude inventory (DIA-10), the young mania rating scale (Y-MRS) and the scale for the assessment of positive symptoms (SAPS). The data were analyzed using a general linear model by SPSS 16 software.

Results: The repeated measures analysis revealed that medication compliance increased successively ($P = 0.045$), and age, gender and symptom severity did not alter the pattern.

Conclusions: There is an increasing pattern in treatment compliance in bipolar I disorder patients, regardless of the known predicting factors for nonadherence.

Keywords: Bipolar Disorder, Non-Compliance, Treatment Compliance

1. Background

Medication treatment compliance among bipolar patients is quite widespread. Montoya et al. reported that 40% of bipolar patients are partially or completely nonadherent (1). Other studies have indicated that 20% - 70% of bipolar patients are poorly adherent (2-7). Guscott and Taylor (8) have noted that poor compliance is the principle reason for the discrepancy between efficacy and effectiveness in bipolar patients (8). Non-compliance is a frequent cause of relapse among patients (9, 10). Gonzalez-Pinto et al. observed rates of suicide that were 5.2 times greater in non-adherent patients than in patients on lithium (11). The effects of noncompliance include worsening symptoms, reduction in the quality of life, more hospital admissions and increased suicide behavior (12-19). Commonly encountered reasons for noncompliance in bipolar patients include negative attitudes toward the illness (3, 7, 20-26), poor insight (3, 20-30) severity of depression (3, 20-25), manic symptoms (3, 11, 20-25, 30, 31), younger age (9, 30, 32-34), male gender (9, 11, 30, 33-35), psychotic symptoms (21, 29, 30), loneliness (32), being unmarried (9, 11, 33, 34, 36, 37) and substance abuse (3, 11, 20-26, 30, 32). Colom et al. as

well as Scott and Godwin, reported the major risk for non-adherence in teenagers and elderly (3) was the duration of treatment (34, 38).

2. Objectives

Although contradictory findings in adherence research have brought increased attention in other countries, researchers in Iran have not yet shown adequate interest. Based on "a scientometric analysis of studies on mood disorders in Iran 1", only 75 articles on bipolar disorder were published up to January 2008 (39).

Therefore, this paper aims to present the pattern of compliance and also evaluate some factors relating to adherence.

3. Materials and Methods

This study was a prospective longitudinal and naturalistic study of patients who were hospitalized in the Iran Psychiatric hospital, Tehran, Iran.

3.1. Sampling and Participants

All patients who were admitted were supervised by the attending psychiatrist and assessed regarding the inclusion and exclusion criteria.

The inclusion criteria were being 18 years or older; being able to speak Persian; living in Tehran, Karaj or the suburbs; being diagnosed as type one bipolar disorder by a board certified psychiatrist based on the diagnostic and statistical manual of mental disorders, 4th edition (DSM-IV-TR) (40) and having the same diagnosis using the structured clinical interview for DSM-IV axis I disorders (SCID-I) performed by a trained resident of psychiatry; having at least one landline and one cell phone to facilitate contact; and providing informed written consent. The exclusion criteria included being mentally retarded or having any other permanent cognitive decline. The sampling was conducted in May 2008 and 50 patients were enrolled in the study. Three patients dropped out, and the assessment was repeated for the remaining 47 patients two and six months later.

3.2. Procedure

This study was conducted by five psychiatric residents who were trained to assess patients. Also, the inter-rater reliability for the rating scales were checked for reliability (39).

All participants had follow-up visits at two and six months after admission. The two follow up visits were free of charge and were held in an outpatient setting, unless the patient required admission due to any indication. The administrative assistant reminded the patients about their appointments (39).

3.3. Instruments

1) The demographic and clinical variables questionnaire included demographic characteristics and certain clinical features such as history of treatment and previous admissions (39).

2) The structured clinical interview for DSM-IV axis I disorders (SCID-I) is a semi-structured interview used to diagnose the axis I disorders of DSM-IV (41, 42). The Persian clinical version of the SCID-I has been standardized for the Iranian population (43).

3) The Hamilton depressive rating scale-7 (HDRS-7) (44) is widely used in psychiatric research with favorable reliability and validity (45). It has been standardized for the Iranian population (46). McIntyre et al. reported that the 7-item HDRS had as much effectiveness as the 17-item scale and the total score of the HDRS-7 ranges from 0 to 26 (44).

4) The young mania rating scale (YMRS) is an 11-item clinician-administered scale used to measure the severity

of manic symptoms. The total score of the YMRS ranges from 0 to 60, and the Persian version proved to be reliable and valid (47, 48).

5) The scale for the assessment of positive symptoms (SAPS) is a 35-item, five section clinician-administered scale used to measure the severity of psychiatric symptoms. The Persian version proved to be reliable as well (49-51).

6) The drug attitude inventory-10 (DAI-10) (shortened version) is a self-report inventory rating the patient's attitude to the drugs taken. This inventory has previously been used on Iranian bipolar patients (39, 48). Hogan et al. confirms the reliability and discriminative validity of the DAI-10. This instrument includes questions with true or false options. Complete compliance is shown by a score of six or more true answers (15, 52, 53).

7) The medication possession ratio (MPR) is defined as subtraction from the numbers of days' supply the patients should have received to take their medication as prescribed. The MPR was calculated for study patients at the two and six-month follow-up visits after admission: MPR calculations were limited to individuals who were taking at least 75% of the prescribed drug doses. The MPR method has been used to quantify treatment adherence in a number of earlier studies (32, 54-57). Using the MPR scores, the patients were categorized as good adherence (MPR score \geq 80), moderate adherence (MPR score 50 - 80) and poor adherence (MPR score \leq 50) (54, 55, 58).

3.4. Data Analysis

The data were analyzed with SPSS 16 software and the chi-square, one-way ANOVA, Kruskal-Wallis and general linear models were used. A one-sample Kolmogorov-Smirnov test showed the number of previous episodes that led to hospitalization, and the symptom severity at the end of the follow-up did not have a normal distribution. A P value $<$ 0.05 was considered as significant.

4. Results

In this study, 47 patients, with type one bipolar disorder were examined. The average age (mean \pm SE) of the studied patients was 33.7 ± 1.8 . Regarding gender, 32 patients (68.1%) were males and 15 (31.9%) were females. The mean number of previous episodes leading to hospitalization was 3.1 ± 0.5 . The mean age of illness onset was 25.8 ± 10 . The average period of their disorder was 8.1 ± 10 years. Considering the marital status, this study included 24 single patients (51.1%), 7 divorced or widow/widower patients (14.9%) and 16 married patients (34.0%).

In this study, the severity of the symptoms of mania and depression were measured by applying the YMRS

and HDRS questionnaires at the beginning and end of the follow-up course. Based on this, the severity of the symptoms of mania was 20.4 ± 1.7 in the beginning and 4.0 ± 1.0 at the end. The severity indicated a significant statistical decline (Wilcoxon, $P < 0.001$).

Depression severity was 4.3 ± 0.57 in the beginning and 2.9 ± 0.47 at the end, which also shows a significant decline ($P = 0.008$).

Based on the SAPS questionnaire, 31 patients (66%) had psychotic symptoms in the beginning of study.

The level of medical compliance of all patients was calculated by the MPR formula. Accordingly, two people (4.3%) had a low level of drug compliance, 15 people (31.9%) had a medium level, and 30 (63.8%) had a high level.

The average grade of the DAI was 2.1 ± 0.75 in the beginning of the study, and this grade changed to 2.7 ± 0.8 at the end of the six-month period. This indicates that there was no increase in 0.85 ± 1.1 of the DAI in the course in the follow-up period (Wilcoxon, $P = 0.27$).

There was no significant statistical correlation between the MPR at the end of the research and the grade of the primary and final DAIs (coefficient correlation was 0.16 and 0.06 in the two subjects, respectively; $P < 0.05$). MPR was also unrelated to the severity of mania and psychosis.

In the bivariate analysis, there was no significant relationship between primary depression and compliance (Table 1). However, in the multi-variable analysis, there was a small inverse relationship (Table 2). Moreover, there was no significant relationship between the primary or final DAI scores and compliance ($r = 0.12$, $P = 0.46$).

In the binary analysis, it was shown that there was no significant relation between compliance and age of admission, age at disease onset, disease duration, sex, marital status, number of episodes leading to hospitalization, symptom severity and the presence of psychosis at the beginning and the end of study (in all cases $P > 0.1$) (Table 1).

It is worth mentioning that in the analysis model, in order to avoid the multiple collinearity confounding variable effect, the variable named "present age of patient" was not entered due to its high linear correlation with the other variable named "age in the beginning of disorder" ($r = 0.37$, $P < 0.001$) (Table 2). Furthermore, based on the results of the general linear model analysis, it is shown that a significant relation could not be determined between the background elements being studied and drug compliance.

5. Discussion

This study was conducted over a six-month period in order to assess the risk factors that affect treatment compliance in type one bipolar disorder. After analyzing the

data, no significant relation was found between drug compliance (MPR) and age, sex, marital status, psychosis and the severity of mania in bipolar patients. Additionally, the relation between treatment attitude and MPR was not significant.

However, the increase in treatment compliance was significant during the six months. Meanwhile, there was significant relation between drug use during the period one month before admission and the patient's attitude.

The results of our study were consistent with those of Sajatovic et al. (26, 57, 58), Keck et al. (31), and Zeber et al. (59) in terms of an absence of any significant relation between treatment adherence and the patient's age. However, Baldessarini et al. (60), Sajatovic et al. (32, 57), Shabani and Eftekhar (61) and Berk et al. (30) showed a significant relation between noncompliance and younger age. Conversely, some research reports that patients with an older age have better adherence (60). One of the reasons for the relation in the Baldessarini study may be the high number of samples, compared to this study, which had a small sample size.

Considering the absence of a relation between the patient's sex and treatment adherence, our study result is consistent with that of Baldessarini et al. (60), Sharifi et al. (56), Sajatovic et al. (26, 32, 57, 58, 62), and also of other research such as Yen et al. (29), Colom et al. (3) and Scott and Pope (38). In the studies of Berk et al. (30), Lingam and Scott (63) and Gonzalez-Pinto et al. (11) adherence was less in men, while in the study of Ghorayshizadeh et al. (64) it was less in women, however, this could be because the study sample had the same number of men and women. In Sajatovic et al. research (26), 88.7% of research samples were men and this could be the reason for the relation between treatment nonadherence and the male gender. Furthermore, the low number of samples in this study may be a reason for the lack of correlation.

Considering the absence of a relation between marital status and treatment adherence, the results of this study are consistent with that of Yen et al. (29), Sajatovic et al. (32, 57), Colom et al. (3) Scott and Pope (38), Alaghand-Rad et al. (51), Sharifi et al. (56) and Zeber et al. (59), however, Berk et al. (30), Ghorayshizadeh et al. (64), Gonzalez-Pinto et al. (11), Frank et al. (36) and Aagaard et al. (37). One of the reasons for noncompliance is being divorced or widowed. In the current study, 51.1% of the participants were never married and most of them lived within a family and under their control. This can be the reason for the absence of a relation between marital status and adherence, so it is recommended that the participants in future studies be divided based on whether they live alone or with others.

The lack of a significant relationship between the severity of mania and adherence, is consistent with Sajatovic

Table 1. Demographic Factors in Patients With Bipolar Disorder and Their Relationship With Drug Compliance^a

	All Patients (n = 47)	Poor Compliance (n = 2)	Moderate Compliance (n = 15)	High Compliance (n = 30)	P Value
Current age, y	33.7 ± 1.8	27.5 ± 6.5	34.6 ± 2.6	33.7 ± 1.8	0.67 ^b
Onset of disease, y	25.8 ± 1	26.5 ± 6.5	26.9 ± 1.7	25.2 ± 1.3	0.95 ^b
Duration of disease, y	8.1 ± 1	1	7.7 ± 1.5	8.8 ± 1.4	0.29 ^b
Manic symptom severity in beginning, No. ^c	20.4 ± 1.7	18	21.7 ± 2.9	19.8 ± 2.2	0.86 ^b
Manic symptom severity at end, No. ^c	4 ± 1	7.5 ± 1.5	4.7 ± 2	3.4 ± 0.9	0.18 ^d
Depression symptom severity in beginning, No. ^c	4.3 ± 0.57	3 ± 3	5 ± 1.1	4.1 ± 0.7	0.68 ^d
Depression symptom severity at end, No.	2.9 ± 0.47	3 ± 3	2.7 ± 0.9	2.96 ± 0.56	0.87 ^d
Sex					0.13 ^e
Male	32 (68.1)	NA	10 (31.3)	22 (68.7)	
Female	15 (31.9)	2 (13.3)	5 (33.3)	8 (53.3)	
Marital status					0.66 ^e
Single	24 (51.1)	2 (8.3)	6 (25)	25 (66.7)	
Widow	7 (14.9)	NA	2 (28.6)	5 (71.4)	
Married	16 (34)	NA	7 (43.8)	9 (56.2)	
Number of previous episodes, No.	3.1 ± 0.5	0.5 ± 0.5	3.3 ± 0.88	3.2 ± 0.7	0.36 ^d
Psychotic symptom in beginning ^f	31 (66)	2 (6.5)	11 (35.5)	18 (58.1)	0.48 ^e
Psychotic symptom free in beginning ^f	16 (34)	NA	4 (25)	12 (75)	0.48

Abbreviation: NA, not available.

^aValues are expressed as mean ± SE or No. (%).

^bOne-way ANOVA test.

^cAccording to YMRS.

^dKruskal-Wallis test.

^eFisher's Exact test.

^fAccording to SAPS.

et al. (32, 57) and Zeber et al. (59) and inconsistent with Gonzalez-Pinto et al. (11) and Keck et al. (31).

Considering the lack of a significant relationship between psychosis and adherence, this study was consistent with Sajatovic et al. (26, 32, 57, 58) and Zeber et al. (59) and inconsistent with Rosa (65) and Berk et al. (30). Berk et al. report a significant relation between the existence of psychosis and the severity of manic symptoms with treatment adherence. The reason for this may be more aggressive treatment and the improvement of symptoms, which leads to a better acceptance of treatment (30).

The significant relationship found between depression and adherence was inconsistent with Sajatovic et al. 2009 (26) and Sajatovic et al. 2008 (58).

In this study, there was no relationship found between drug attitude and treatment adherence, and this result

was inconsistent with Sharifi et al. research (56). In Sharifi et al. study, there was no relation in a two-week period. However, in the 4th, 6th and 8th weeks, they report a positive relationship between a good attitude and treatment adherence. The relation between treatment attitude and drug consumption during the period one month before admission was significant in this study (56).

Considering the increase in adherence during the six-month follow-up, the result was inconsistent with Scott and Pope (38), Goodwin and Jamison (34), Colom et al. (66) and Sharifi et al. (56). In Sharifi et al. study, the follow-up duration was two months and treatment acceptance decreased during the two months, therefore, a longer follow-up period and intermittent visits in the two and six months may be the reasons for the increasing adherence in the current study (56).

Table 2. Linear Relationship Model Independent of the Underlying Factors Associated With Medication Adoption Rate (in Percent) at the end of Follow-Up in Patients With Bipolar I Disorder^a

	Correlation Coefficient	Power ^b	P Value
Duration of disease	0.007	0.093	0.535
Onset of disease	0.002	0.061	0.748
Disease severity (YMRS) at the beginning of follow up	0.005	0.081	0.599
Disease severity (YMRS) at the end of follow up	0.005	0.080	0.603
Severity of depression (HDRS-7) at the beginning of the follow up	-0.018	0.511	0.049
Severity of depression (HDRS-7) at the end of the follow up	0.009	0.187	0.278
Sex	0.001	0.053	0.859
Marital Status	0.003	0.062	0.916
Psychotic symptoms at the beginning of the follow up	0.032	0.240	0.206

^aNote: The current age of the patients had a high linear correlation with the age of onset variable (Pearson $r = 0.73$, $P < 0.001$), therefore, to avoid the confounding effect of multiple collinearity it was not entered into the model analysis.

^bComputed using $\alpha = 0.05$.

In this study, mania severity decreased significantly from the first interview to the six-month follow-up interview. This is inconsistent with Amini et al. (46) study in which a significant decrease in symptoms during a one-year follow-up was not observed. Considering the fact that Amini's follow-up was longer, it was probable that the patients experienced recurrence during the second half of the year.

In this study, the increase in the drug attitude score was not significant during the six months. This might be due to three reasons: 1-the patients entered the study when they were transferred from the emergency room to hospital wards, and their severe symptoms were remitted; 2-since the questionnaires were filled out by residents, they may have presented a high opinion of treatment in order to please them; 3-high rating in the questionnaires.

The level of compliance in our study was less than Sajatovic's study (62) in which he reported 80.7% of samples had good compliance. This could be related to the fact that Sajatovic et al. carried out a one-month follow-up, and also the questionnaires used to evaluate drug attitude used a self-report format (62). In contrast, our study was a six-month study and the questionnaires were filled in by the

residents. Meanwhile, drug acceptance was divided into three groups: good, medium and bad. The rate of good compliance in this study was more than in Baldessarini et al. study. He reports adherence of 28% in a one-year follow-up (60).

Therefore, it is suggested that future studies be conducted with a larger number of participants and for longer periods of time. Since this study was done in a specialized center, most samples were of the severe type of the disease, and for this reason the results cannot be popularized. It is recommended that for future studies outpatients should also be included. Moreover, it is suggested that the patients in primary care settings be taken into future studies.

On the other hand, it seems that the follow-up of the patients may have had a positive effect on the span of the disease. Therefore, it is suggested that future studies be carried out with a control group. Finally, a significant relation was not found with the existence of psychosis, the severity of mania or demographic factors, or the importance of comorbidities, such as substance abuse. It is suggested that further studies should be conducted using other research data that includes psychiatric disorders or substance abuse.

Acknowledgments

We hereby express our gratitude to the authorities of the of mental health research center, the research network of mental health, Aida Taheri, Chejreh Najad Abbasi, Zahra Mousavi, Kambiz Zangeneh and Mojhgah Taban (responsible for the scheme coordination), for their kind cooperation in this study.

Footnotes

Authors' Contribution: Sanaz Azadforouz collected the clinical data and drafted the manuscript. Amir Shabani conceived and designed the evaluation and drafted the manuscript. Shabnam Nohesara re-evaluated the clinical data and revised the manuscript. Masoud Ahmadzad-Asl analyzed the clinical and statistical data and revised the manuscript. All authors read and approved the final manuscript.

Declaration of Interests: None declared.

References

1. Montoya A, Perez Sanchez Toledo J, Gilaberte I, Gonzalez-Pinto A, Haro JM, Vieta E, et al. Patterns of drug treatment for manic episode in the clinical practice. Outcomes of the Spanish sample in the EMBLEM Study. *Actas Esp Psiquiatr.* 2007;35(5):315-22. [PubMed: 17885823].

2. Lingam R, Scott J. Treatment non-adherence in affective disorders. *Acta Psychiatr Scand*. 2002;**105**(3):164–72. [PubMed: [11939969](#)].
3. Colom F, Vieta E, Martinez-Aran A, Reinares M, Benabarre A, Gasto C. Clinical factors associated with treatment noncompliance in euthymic bipolar patients. *J Clin Psychiatry*. 2000;**61**(8):549–55. [PubMed: [10982196](#)].
4. Connelly CE. Compliance with outpatient lithium therapy. *Perspect Psychiatr Care*. 1984;**22**(2):44–50.
5. Keck PJ, McElroy SL, Strakowski SM, Bourne ML, West SA. Compliance with maintenance treatment in bipolar disorder. *Psychopharmacol Bull*. 1997;**33**(1):87–91. [PubMed: [9133756](#)].
6. Licht RW, Vestergaard P, Rasmussen NA, Jepsen K, Brodersen A, Hansen PE. A lithium clinic for bipolar patients: 2-year outcome of the first 148 patients. *Acta Psychiatr Scand*. 2001;**104**(5):387–90. [PubMed: [1172321](#)].
7. Perlick DA, Rosenheck RA, Kaczynski R, Kozma L. Medication non-adherence in bipolar disorder: a patient-centered review of research findings. *Clin Approaches Bipolar Disord*. 2004;**3**(2):56–64.
8. Guscott R, Taylor L. Lithium prophylaxis in recurrent affective illness. Efficacy, effectiveness and efficiency. *Br J Psychiatry*. 1994;**164**(6):741–6. [PubMed: [7952980](#)].
9. Colom F, Vieta E. Treatment adherence in bipolar patients. *Clin Approaches Bipolar Disord*. 2002;**1**:49–56.
10. Suppes T, Baldessarini RJ, Faedda GL, Tohen M. Risk of recurrence following discontinuation of lithium treatment in bipolar disorder. *Arch Gen Psychiatry*. 1991;**48**(12):1082–8. [PubMed: [1845226](#)].
11. Gonzalez-Pinto A, Mosquera F, Alonso M, Lopez P, Ramirez F, Vieta E, et al. Suicidal risk in bipolar I disorder patients and adherence to long-term lithium treatment. *Bipolar Disord*. 2006;**8**(5 Pt 2):618–24. doi: [10.1111/j.1399-5618.2006.00368.x](#). [PubMed: [17042834](#)].
12. Kulhara P, Basu D, Mattoo SK, Sharan P, Chopra R. Lithium prophylaxis of recurrent bipolar affective disorder: long-term outcome and its psychosocial correlates. *J Affect Disord*. 1999;**54**(1-2):87–96. [PubMed: [10403151](#)].
13. Robinson D, Woerner MG, Alvir JM, Bilder R, Goldman R, Geisler S, et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Arch Gen Psychiatry*. 1999;**56**(3):241–7. [PubMed: [10078501](#)].
14. Caton CLM, Koh SP, Fleiss JL, Barrow S, Goldstein JM. Rehospitalization in Chronic Schizophrenia. *J Nervous Ment Dis*. 1985;**173**(3):139–48. doi: [10.1097/00005053-198503000-00002](#).
15. Svarstad BL, Shireman TI, Sweeney JK. Using drug claims data to assess the relationship of medication adherence with hospitalization and costs. *Psychiatr Serv*. 2001;**52**(6):805–11. doi: [10.1176/appi.ps.52.6.805](#). [PubMed: [11376229](#)].
16. Muller-Oerlinghausen B, Wolf T, Ahrens B, Glaenz T, Schou M, Grof E, et al. Mortality of patients who dropped out from regular lithium prophylaxis: a collaborative study by the International Group for the Study of Lithium-treated patients (IGSLI). *Acta Psychiatr Scand*. 1996;**94**(5):344–7. [PubMed: [9124081](#)].
17. Muller-Oerlinghausen B. Arguments for the specificity of the antisuicidal effect of lithium. *Eur Arch Psychiatry Clin Neurosci*. 2001;**251**Suppl 2:1172–5. [PubMed: [11824842](#)].
18. Yerevanian BI, Koek RJ, Mintz J. Bipolar pharmacotherapy and suicidal behavior. Part I: Lithium, divalproex and carbamazepine. *J Affect Disord*. 2007;**103**(1-3):5–11. doi: [10.1016/j.jad.2007.05.019](#). [PubMed: [17628692](#)].
19. Clatworthy J, Bowskill R, Rank T, Parham R, Horne R. Adherence to medication in bipolar disorder: a qualitative study exploring the role of patients' beliefs about the condition and its treatment. *Bipolar Disord*. 2007;**9**(6):656–64. doi: [10.1111/j.1399-5618.2007.00434.x](#). [PubMed: [17845282](#)].
20. Jamison KR, Gerner RH, Goodwin FK. Patient and physician attitudes toward lithium: relationship to compliance. *Arch Gen Psychiatry*. 1979;**36**(8 Spec No):866–9. [PubMed: [454105](#)].
21. Miklowitz DJ. Longitudinal outcome and medication noncompliance among manic patients with and without mood-incongruent psychotic features. *J Nerv Ment Dis*. 1992;**180**(11):703–11. [PubMed: [1359003](#)].
22. Maarbjerg K, Aagaard J, Vestergaard P. Adherence to lithium prophylaxis: I. Clinical predictors and patient's reasons for nonadherence. *Pharmacopsychiatry*. 1988;**21**(3):121–5. doi: [10.1055/s-2007-1014662](#). [PubMed: [3406049](#)].
23. Comtois KA, Ries R, Armstrong HE. Case manager ratings of the clinical status of dually diagnosed outpatients. *Hosp Community Psychiatry*. 1994;**45**(6):568–73. [PubMed: [8088736](#)].
24. Weiss RD, Greenfield SF, Najavits LM, Soto JA, Wyner D, Tohen M, et al. Medication compliance among patients with bipolar disorder and substance use disorder. *J Clin Psychiatry*. 1998;**59**(4):172–4. [PubMed: [9590667](#)].
25. Salloum IM, Thase ME. Impact of substance abuse on the course and treatment of bipolar disorder. *Bipolar Disord*. 2000;**2**(3 Pt 2):269–80. [PubMed: [11249805](#)].
26. Sajatovic M, Ignacio RV, West JA, Cassidy KA, Safavi R, Kilbourne AM, et al. Predictors of nonadherence among individuals with bipolar disorder receiving treatment in a community mental health clinic. *Compr Psychiatry*. 2009;**50**(2):100–7. doi: [10.1016/j.comppsy.2008.06.008](#). [PubMed: [19216885](#)].
27. Ghaemi SN, Rosenquist KJ, Ko JY, Baldassano CF, Kontos NJ, Baldessarini RJ. Antidepressant treatment in bipolar versus unipolar depression. *Am J Psychiatry*. 2004;**161**(1):163–5. doi: [10.1176/appi.ajp.161.1.163](#). [PubMed: [14702267](#)].
28. Peralta V, Cuesta MJ. Lack of insight in mood disorders. *J Affect Disord*. 1998;**49**(1):55–8. doi: [10.1016/s0165-0327\(97\)00198-5](#).
29. Yen CF, Chen CS, Ko CH, Yeh ML, Yang SJ, Yen JY, et al. Relationships between insight and medication adherence in outpatients with schizophrenia and bipolar disorder: prospective study. *Psychiatry Clin Neurosci*. 2005;**59**(4):403–9. doi: [10.1111/j.1440-1819.2005.01392.x](#). [PubMed: [16048445](#)].
30. Berk M, Berk L, Castle D. A collaborative approach to the treatment alliance in bipolar disorder. *Bipolar Disord*. 2004;**6**(6):504–18. doi: [10.1111/j.1399-5618.2004.00154.x](#). [PubMed: [15541066](#)].
31. Keck PJ, McElroy SL, Strakowski SM, West SA, Sax KW, Hawkins JM, et al. 12-month outcome of patients with bipolar disorder following hospitalization for a manic or mixed episode. *Am J Psychiatry*. 1998;**155**(5):646–52. doi: [10.1176/ajp.155.5.646](#). [PubMed: [9585716](#)].
32. Sajatovic M, Valenstein M, Blow FC, Ganoczy D, Ignacio RV. Treatment adherence with antipsychotic medications in bipolar disorder. *Bipolar Disord*. 2006;**8**(3):232–41. doi: [10.1111/j.1399-5618.2006.00314.x](#). [PubMed: [16696824](#)].
33. Frank E, Prien RF, Kupfer DJ, Alberts L. Implications of noncompliance on research in affective disorders. *Psychopharm Bull*. 1985;**21**(1):37.
34. Goodwin FK, Jamison KR. Manic-depressive illness: bipolar disorders and recurrent depression. Oxford University Press; 2007.
35. Danion JM, Neunreuther C, Krieger-Finance F, Imbs JL, Singer L. Compliance with long-term lithium treatment in major affective disorders. *Pharmacopsychiatry*. 1987;**20**(5):230–1. doi: [10.1055/s-2007-1017111](#). [PubMed: [3671494](#)].
36. Frank E, Prien RF, Kupfer DJ, Alberts L. Implications of noncompliance on research in affective disorders. *Psychopharmacol Bull*. 1985;**21**(1):37–42. [PubMed: [3983336](#)].
37. Aagaard J, Vestergaard P, Maarbjerg K. Adherence to lithium prophylaxis: II. Multivariate analysis of clinical, social, and psychosocial predictors of nonadherence. *Pharmacopsychiatry*. 1988;**21**(4):166–70. doi: [10.1055/s-2007-1014670](#). [PubMed: [3205885](#)].
38. Scott J, Pope M. Nonadherence with mood stabilizers: prevalence and predictors. *J Clin Psychiatry*. 2002;**63**(5):384–90. [PubMed: [12019661](#)].
39. Shabani A, Taheri A, Azadforouz S, Abbasi CN, Mousavi Z, Zangeneh K, et al. Bipolar Disorder Patients Follow-up (BDPF): methods and materials. *J Res Med Sci*. 2010;**15**(4):229–34. [PubMed: [21526087](#)].
40. American Psychiatric Association. Diagnostic and statistical manual of mental disorder. Washington: American Psychiatric association;

- 2000.
41. First MD, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM-IV axis I disorders (SCID-I), clinical version (Administration booklet). Washington: American psychiatric Association; 1997.
 42. Gibbon M, Spitzer RL, Williams JBW, Benjamin LS, First MB. User's guide for the structured clinical interview for DSM-IV Axis II personality disorders (SCID-II). Washington: American psychiatric Association; 1997.
 43. Sharifi V, Assadi SM, Mohammadi MR, Amini H, Kaviani H, Semnani Y, et al. A Persian translation of the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: psychometric properties. *Compr Psychiatry*. 2009;**50**(1):86-91. doi: [10.1016/j.comppsy.2008.04.004](https://doi.org/10.1016/j.comppsy.2008.04.004). [PubMed: [19059520](https://pubmed.ncbi.nlm.nih.gov/19059520/)].
 44. McIntyre R, Kennedy S, Bagby RM, Bakish D. Assessing full remission. *J Psychiatry Neurosci*. 2002;**27**(4):235-9. [PubMed: [12174732](https://pubmed.ncbi.nlm.nih.gov/12174732/)].
 45. Kobak KA, Greist JH, Jefferson JW, Katzelnick DJ. Computer-administered clinical rating scales. A review. *Psychopharmacology (Berl)*. 1996;**127**(4):291-301. [PubMed: [8923563](https://pubmed.ncbi.nlm.nih.gov/8923563/)].
 46. Amini H, Sharifi V, Nejatiasafa A, Arbabi M, Tabatabaie M, Alimadadi Z, et al. One year follow-up of patients with bipolar disorder admitted to Roozbeh Hospital. *Iran J Psychiatr Clin Psychol*. 2009;**15**(2):168-74.
 47. Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. *Br J Psychiatr*. 1978;**133**(5):429-35. doi: [10.1192/bjp.133.5.429](https://doi.org/10.1192/bjp.133.5.429).
 48. Berekatain M, Tavakoli M, Molavi H, Maroufi M, Salehi M. Standardization, reliability and validity of the Young Mania Rating Scale. *Psychology*. 2007;**11**(2):150-66.
 49. Andreasen NC. The scale for the assessment of positive symptoms (SAPS). University of Iowa; 1984.
 50. Bell V, Halligan PW, Ellis HD. Diagnosing delusions: a review of inter-rater reliability. *Schizophr Res*. 2006;**86**(1-3):76-9. doi: [10.1016/j.schres.2006.06.025](https://doi.org/10.1016/j.schres.2006.06.025). [PubMed: [16857345](https://pubmed.ncbi.nlm.nih.gov/16857345/)].
 51. Alaghband-Rad J, Boroumand M, Amini H, Sharifi V, Omid A, Davari-Ashtiani R, et al. Non-affective Acute Remitting Psychosis: a preliminary report from Iran. *Acta Psychiatr Scand*. 2006;**113**(2):96-101. doi: [10.1111/j.1600-0447.2005.00658.x](https://doi.org/10.1111/j.1600-0447.2005.00658.x). [PubMed: [16423160](https://pubmed.ncbi.nlm.nih.gov/16423160/)].
 52. Hogan TP, Awad AG, Eastwood R. A self-report scale predictive of drug compliance in schizophrenics: reliability and discriminative validity. *Psychol Med*. 1983;**13**(1):177-83. [PubMed: [6133297](https://pubmed.ncbi.nlm.nih.gov/6133297/)].
 53. Gilmer TP, Dolder CR, Lacro JP, Folsom DP, Lindamer L, Garcia P, et al. Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. *Am J Psychiatry*. 2004;**161**(4):692-9. doi: [10.1176/appi.ajp.161.4.692](https://doi.org/10.1176/appi.ajp.161.4.692). [PubMed: [15056516](https://pubmed.ncbi.nlm.nih.gov/15056516/)].
 54. Valenstein M, Blow FC, Copeland LA, McCarthy JF, Zeber JE, Gillon L, et al. Poor antipsychotic adherence among patients with schizophrenia: medication and patient factors. *Schizophr Bull*. 2004;**30**(2):255-64. [PubMed: [15279044](https://pubmed.ncbi.nlm.nih.gov/15279044/)].
 55. Valenstein M, Copeland LA, Blow FC, McCarthy JF, Zeber JE, Gillon L, et al. Pharmacy data identify poorly adherent patients with schizophrenia at increased risk for admission. *Med Care*. 2002;**40**(8):630-9. doi: [10.1097/01.MLR.0000021003.43524.64](https://doi.org/10.1097/01.MLR.0000021003.43524.64). [PubMed: [12187177](https://pubmed.ncbi.nlm.nih.gov/12187177/)].
 56. Sharifi A, Shabani A, Ahmadzad-Asl M. The pattern of adherence in patients with bipolar I disorder; an eight weeks study. *Iran J Psychiatr Behav Sci*. 2009;**3**(2):39-43.
 57. Sajatovic M, Bauer MS, Kilbourne AM, Vertrees JE, Williford W. Self-reported medication treatment adherence among veterans with bipolar disorder. *Psychiatr Serv*. 2014.
 58. Sajatovic M, Biswas K, Kilbourne AK, Fenn H, Williford W, Bauer MS. Factors associated with prospective long-term treatment adherence among individuals with bipolar disorder. *Psychiatr Serv*. 2008;**59**(7):753-9. doi: [10.1176/appi.ps.59.7.753](https://doi.org/10.1176/appi.ps.59.7.753). [PubMed: [18586992](https://pubmed.ncbi.nlm.nih.gov/18586992/)].
 59. Zeber JE, Copeland LA, Good CB, Fine MJ, Bauer MS, Kilbourne AM. Therapeutic alliance perceptions and medication adherence in patients with bipolar disorder. *J Affect Disord*. 2008;**107**(1-3):53-62. doi: [10.1016/j.jad.2007.07.026](https://doi.org/10.1016/j.jad.2007.07.026). [PubMed: [17822779](https://pubmed.ncbi.nlm.nih.gov/17822779/)].
 60. Baldessarini R, Henk H, Sklar A, Chang J, Leahy L. Psychotropic medications for patients with bipolar disorder in the United States: polytherapy and adherence. *Psychiatr Serv*. 2008;**59**(10):1175-83. doi: [10.1176/appi.ps.59.10.1175](https://doi.org/10.1176/appi.ps.59.10.1175). [PubMed: [18832504](https://pubmed.ncbi.nlm.nih.gov/18832504/)].
 61. Shabani A, Eftekhari M. Non Complication after first episode of mania or mix mod stabilizer : A 17 month follow up. *Iranian J Psychiatr Behav Sci*. 2007;**1**(2).
 62. Sajatovic M. predictors of non adherence among individual with BP receiving treatment in common mental health clinic. *Psychiatry*. 2009;**5**:100-7.
 63. Lingam R, Scott J. Treatment non-adherence in affective disorders. *Acta Psychiatrica Scandinavica*. 2002;**105**(3):164-72.
 64. Ghorayshizadeh MA, Kouchaksaraei F, Pezeshki M. Evaluation of Risk Factors of Relapse in Bipolar I Disorders and Its Relation to Demographic Feature. *Med J Tabriz unit Med Sci*. 2009;**31**(2):77-81.
 65. Rosa AR, Marco M, Fachel JM, Kapczynski F, Stein AT, Barros HM. Correlation between drug treatment adherence and lithium treatment attitudes and knowledge by bipolar patients. *Prog Neuropsychopharmacol Biol Psychiatry*. 2007;**31**(1):217-24. doi: [10.1016/j.pnpbp.2006.08.007](https://doi.org/10.1016/j.pnpbp.2006.08.007). [PubMed: [16982121](https://pubmed.ncbi.nlm.nih.gov/16982121/)].
 66. Colom F, Vieta E, Tacchi M, Sanchez-Moreno J, Scott J. Identifying and improving non-adherence in bipolar disorders. *Bipolar Disord*. 2005;**7** Suppl 5:24-31. doi: [10.1111/j.1399-5618.2005.00248.x](https://doi.org/10.1111/j.1399-5618.2005.00248.x). [PubMed: [16225557](https://pubmed.ncbi.nlm.nih.gov/16225557/)].