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Association Between Therapeutic Alliance, Care Satisfaction, and Pharmacological Adherence in Bipolar Disorder

Louisa G. Sylvia, PhD^{*,†}, Aleena Hay, BA[‡], Michael J. Ostacher, MD, MPH[§], David J. Miklowitz, PhD^{||}, Andrew A. Nierenberg, MD^{*,†}, Michael E. Thase, MD^{||}, Gary S. Sachs, MD^{*,†}, Thilo Deckersbach, PhD^{*,†}, and Roy H. Perlis, MD, MSc^{†,‡}

^{*}Bipolar Clinical and Research Program, Massachusetts General Hospital and Harvard Medical School, Boston, MA

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Reprints: Louisa G. Sylvia, PhD, Bipolar Clinical and Research Program, 50 Staniford St, Suite 580, Boston, MA 02114, (lsylvia2@partners.org).

AUTHOR DISCLOSURE INFORMATION

As of July 1st, 2012, the authors disclose the following: Dr Sylvia is a consultant for Concordant Rater Systems. In the past 2 years, Dr Ostacher has served on advisory/consulting boards of Pfizer and Schering Plough (now Merck); he has received speaking fees from AstraZeneca, Bristol-Myers Squibb, Eli Lilly & Company, and Pfizer. Dr Deckersbach's research has been funded by the National Institute of Mental Health (NIMH), NARSAD, TSA, and OCF. He has received honoraria, consultation fees and/or royalties from Medacorp, Massachusetts General Hospital (MGH) Psychiatry Academy, Brain Cells Inc, Systems Research and Applications Corporation, Boston University, the Catalan Agency for Health Technology Assessment and Research, the National Association of Social Workers Massachusetts, and Oxford University Press. He has also participated in research funded by NIH, NIA, Janssen Pharmaceuticals, The Forest Research Institute, Shire Development Inc, Medtronic, Cyberonics, and Northstar. Dr Miklowitz does not have any support or funding to disclose. Dr Nierenberg is a full time employee of the MGH. In the past 12 months (as of June 21, 2010), he has served as a consultant to the Appliance Computing Inc (Mindsite) and Brandeis University. Through the MGH Clinical Trials Network and Institute (CTNI), he has consulted for Brain Cells, Inc; Dianippon Sumitomo/Sepracor; Labopharm; Merck; Methylation Science; Novartis, PGx Health, Shire; Schering-Plough; Targacept; and Takeda/Lundbeck Pharmaceuticals. He received grant/research support through MGH from NIMH, PamLabs, Pfizer Pharmaceuticals, and Shire. He received honoraria from Belvoir Publishing, Hillside Hospital, American Society for Clinical Psychopharmacology, Columbia University, IMEDEX, MJ Consulting, New York State, MBL Publishing, Physicians Postgraduate Press, SciMed, SUNY Buffalo, University of Wisconsin, and the University of Pisa. Dr Nierenberg is a presenter for the MGH Psychiatry Academy (MGHPA). The education programs conducted by the MGHPA were supported through Independent Medical Education grants from the following pharmaceutical companies: in 2008 AstraZeneca, Eli Lilly, and Janssen Pharmaceuticals; and in 2009 AstraZeneca, Eli Lilly, and Bristol-Myers Squibb. No speaker bureaus or boards since 2003. He is on the advisory boards of Appliance Computing, Inc; Brain Cells, Inc; Eli Lilly and Company; and Takeda/Lundbeck and Targacept. Dr Nierenberg owns stock options in Appliance Computing, Inc, and Brain Cells, Inc. Through MGH, he is named for copyrights to the Clinical Positive Affect Scale and the MGH Structured Clinical Interview for the Montgomery-Åsberg Depression Scale exclusively licensed to the CTNI. Ms Hay is a consultant for GENOMIND. Dr Thase has received federal funding from the NIMH. Dr Thase has received research support from Eli Lilly and Company, GlaxoSmithKline, and Sepracor, Inc. Dr Thase has provided scientific consultation to AstraZeneca; Bristol-Myers Squibb Company; Eli Lilly & Co; Forest Laboratories; GlaxoSmithKline; MedAvante, Inc; Neuronetics, Inc; Novartis; Otsuka; Ortho-McNeil Pharmaceuticals; Pfizer (formerly Wyeth Ayerst Pharmaceuticals); Schering-Plough; Shire US Inc; Supernus Pharmaceuticals; Takeda (Lundbeck); and Transcept Pharmaceuticals. Dr Thase has been a member of the speakers' bureaus for AstraZeneca, Bristol-Myers Squibb Company, Eli Lilly & Co, and Pfizer (formerly Wyeth Ayerst Pharmaceuticals). Dr Thase has equity holdings in MedAvante, Inc, and receives royalty income from American Psychiatric Publishing, Inc; Guilford Publications; Herald House; and W. W. Norton & Company. His wife is employed as the senior medical director for Advogent (Advogent does business with BMS and Pfizer/Wyeth). Over his lifetime, Dr Sachs has served as a member of the speakers' bureaus for Abbott Laboratories, AstraZeneca Pharmaceuticals, Bristol-Myers Squibb, Eli Lilly & Co, GlaxoSmithKline, Janssen Pharmaceuticals, Memory Pharmaceuticals, Novartis Pharmaceuticals, Pfizer, Sanofi-Aventis, and Wyeth. Dr Sachs has received research support from Abbott Laboratories, AstraZeneca Pharmaceuticals, Bristol-Myers Squibb, Eli Lilly & Co, GlaxoSmithKline, Janssen Pharmaceuticals, Memory Pharmaceuticals, the NIMH, Novartis Pharmaceuticals, Pfizer, Repligen, Shire, and Wyeth. In his lifetime, Dr Sachs has served on advisory/consulting boards of Abbott Laboratories, AstraZeneca Pharmaceuticals, Bristol-Myers Squibb, Cephalon, CNS Response, Elan Pharmaceuticals, Memory Pharmaceuticals, Merck, Novartis Pharmaceuticals, Organon, Otsuka, Pfizer, Schering Plough, Sepracor, Repligen, Sanofi-Aventis, Shire, Sigma-Tau, Solvay Pharmaceuticals, and Wyeth. Dr Sachs and his spouse own stock in Concordant Rater Systems. In the past 12 months, Dr Sachs has received research support from GlaxoSmithKline, the NIMH, and Repligen. In the past 12 months, Dr Sachs has served on the advisory/consulting boards of AstraZeneca Pharmaceuticals, Bristol-Myers Squibb, Cephalon, Concordant Rater Systems, Janssen Pharmaceuticals, Merck, Otsuka, Pfizer, Schering Plough, Sepracor, and Repligen. Dr Perlis receives speaker's bureau/consulting fees from AstraZeneca, Eli Lilly & Co, Proteus Biomedical, and Concordant Rater Systems. Dr Perlis receives royalties and has a patent for the Concordant Rater Systems.

†Department of Psychiatry, Harvard Medical School, Boston, MA

‡Yale University, Department of Psychology, New Haven, CT

§Stanford University School of Medicine, Department of Psychiatry & Behavioral Sciences, Stanford, CA

||Department of Psychiatry and Behavioral Sciences, UCLA Semel Institute, Los Angeles, CA

¶University of Pennsylvania School of Medicine, Philadelphia, PA

#Center for Experimental Drugs and Diagnostics, Massachusetts General Hospital and Harvard Medical School, Boston, MA

Abstract

Objectives—We sought to understand the association of specific aspects of care satisfaction, such as patients' perceived relationship with their psychiatrist and access to their psychiatrist and staff, and therapeutic alliance with participants' likelihood to adhere to their medication regimens among patients with bipolar disorder.

Methods—We examined data from the multicenter Systematic Treatment Enhancement Program for Bipolar Disorder, an effectiveness study investigating the course and treatment of bipolar disorder. We expected that participants ($n = 3037$) with positive perceptions of their relationship with their psychiatrist and quality of psychopharmacologic care, as assessed by the Helping Alliance Questionnaire and Care Satisfaction Questionnaire, would be associated with better medication adherence. We utilized logistic regression models controlling for already established factors associated with poor adherence.

Results—Patients' perceptions of collaboration, empathy, and accessibility were significantly associated with adherence to treatment in individuals with bipolar disorder completing at least 1 assessment. Patients' perceptions of their psychiatrists' experience, as well as of their degree of discussing medication risks and benefits, were not associated with medication adherence.

Conclusions—Patients' perceived therapeutic alliance and treatment environment impact their adherence to pharmacotherapy recommendations. This study may enable psychopharmacologists' practices to be structured to maximize features associated with greater medication adherence.

Keywords

therapeutic alliance; clinical practice; medication adherence; bipolar disorder; treatment

Bipolar Disorder Is A Chronic Mental Illness Frequently Characterized by recurrent episodes of major depression and abnormal mood elevation. Pharmacotherapy is the foundation of treatment for bipolar disorder,^{1–3} but effectiveness of anti-psychotics,⁴ as well as lithium and valproate,⁵ is undermined by poor medication adherence. Adherence rates for bipolar disorder are low, typically ranging from 20% to 60%.^{5–8} Inadequate adherence has been associated with greater risk of hospitalization,^{4,9} worsening course and functional impairment,¹⁰ suicide,¹¹ and higher healthcare costs.¹² Despite the importance of medication adherence in improving outcomes, little is known about the role of the provider and ancillary staff in enhancing patients' perception of adherence in bipolar disorder.¹³ Four important factors have been identified as impacting medication adherence in clinical populations: patient-related (eg, age, gender, ethnicity), psychological (eg, insight, attitudes about medications), medication-related (ie, adverse effects), and social/environmental (eg, quality of therapeutic alliance).¹⁴ Given the low adherence rates found in bipolar disorder and the negative impact of nonadherence on outcomes, a focus on these factors that affect medication adherence is imperative. Of these factors, providers have a direct influence on

the therapeutic alliance and functional aspects of the clinic (eg, waiting times, perceived pleasantness of staff, efficiency in scheduling appointments).^{15–17} This is highlighted by therapeutic alliance accounting for nearly 20% of the variance due to medication adherence in individuals with major depressive disorder.¹⁸

The quality of the patient-provider relationship, or therapeutic alliance, improves treatment retention, adherence, and subsequent outcomes. These data are consistent across psychiatric illnesses, including substance abuse,¹⁹ unipolar depression,²⁰ and schizophrenia,²¹ with recent evidence for bipolar disorder.^{22,23} Aspects associated with improving adherence for individuals with bipolar disorder were providers who “conveyed confidence” in patients’ ability to participate in treatment and who encouraged “keeping in regular contact” with their patients.²³ Similarly, Sajatovic et al²⁴ found that treatment adherence in bipolar disorder is enhanced if the therapeutic alliance is more interactional. For example, providers who acknowledged individual feelings of patients and supported self-management of a chronic illness were associated with higher rates of medication adherence in bipolar disorder.¹⁶ Similarly, individuals with schizophrenia were found to be less adherent to their medication regimens when the strength of the therapeutic alliance was low.²⁵ In major depressive disorder, patients were also more likely to be adherent if their providers collaborated with them on their treatment.¹⁸ In patients with schizophrenia and major depression, understanding and validating patients concerns about medications and educating patients about medications and their adverse effects were identified as key factors associated with higher rates of medication adherence.^{26–28}

A recent meta-analysis of more than 20 bipolar studies on medication adherence concluded that in addition to patient (ie, demographics, severity and phase of illness, past suicide attempts, psychiatric comorbidity, and course of illness) and treatment factors (ie, type and intensity), systems-associated factors (ie, access and costs of care) are important aspects of medication adherence.²⁹ This is important as it suggests that patients’ treatment environment, not just the quality of their relationship with their provider, may impact medication adherence. Increased satisfaction of care provided has also been associated with decreased hopelessness and better life functioning in individuals with bipolar disorder, suggesting that understanding factors of care that may impact adherence could improve treatment outcomes of individuals with bipolar disorder.³⁰

This study examined the association of patients’ perceptions of therapeutic alliance with their psychiatrist, care satisfaction, and medication adherence over one year in a large, representative clinical cohort of individuals with bipolar disorder from the multicenter Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). We hypothesized that positive perceptions of one’s psychiatrist (eg, knowledgeable, friendly, supportive) and treatment setting (eg, good staff, high accessibility) would be positively associated with medication adherence over time.

MATERIALS AND METHODS

Procedure

The STEP-BD was a multicenter project funded by the National Institute of Mental Health designed to evaluate the longitudinal outcome of patients with bipolar disorder conducted between 1999 and 2005. This study evaluated naturalistic prospective outcomes among individuals with bipolar disorder, while using the best practice procedures, or empirically based, guideline-informed treatment of bipolar disorder.³¹ Thus, visits with participants’ treating physicians were not standardized across sites, but instead determined by the individual’s treatment goals and plan. Standard assessment visits were scheduled every 3 months during the first year of the study (and then every 6 months thereafter). The aim of

the STEP-BD project was to further these practice procedures for bipolar disorder by developing standard monitoring procedures and assessment techniques.³² To ensure individualized and optimized treatment, psychiatrists were trained on these expert consensus guidelines.³¹ This study design allowed for naturalistic patient-provider interaction. Methods for the STEP-BD study are detailed elsewhere.^{32,33}

Participants

Individuals with bipolar disorder seeking outpatient treatment at a STEP-BD site were invited to join the study (further details on the sites and study design are reported elsewhere).³² The sites selected for this study were bipolar specialty clinics with geographically and demographically diverse patient populations. The primary inclusion criteria were (1) *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* diagnosis for bipolar disorder I, II, or not otherwise specified, cyclothymia, or schizoaffective disorder bipolar type; and (2) the ability to provide informed consent. Written assent was required from a parent or guardian for individuals aged 15 to 17 years. Exclusion criteria were limited to unwillingness or inability to comply with study assessments or to give informed consent to maximize generalizability of the STEP-BD study. Participants who completed the baseline visit were included in these analyses. The final sample consisted of 3337 participants (n = 2371 [65.1%] with bipolar I disorder, n = 966 [26.5%] with bipolar II disorder).

Assessments

The following assessments were utilized to screen participants and to conduct the study-specific analyses. Thus, not all assessments utilized in the STEP-BD project are described here. Of note, the Affective Disorders Evaluation (ADE) and the Clinical Monitoring Form (CMF) (described further below) were developed specifically for this study by the STEP-BD investigators. The ADE and Mini International Neuropsychiatric Interview (MINI) were conducted by 2 separate STEP-BD clinicians (typically by a psychiatrist and a psychologist, respectively) to determine a consensus bipolar diagnosis, and the CMF was completed at each follow-up visit by the participants' psychiatrist to monitor medications, symptoms, and adherence. The predictors of medication nonadherence were the Helping Alliance Questionnaire (HAQ) and Care Satisfaction Questionnaire (CSQ), which were controlled with participants' current mood state (ie, CMF) and other predictors of adherence in this population³⁵ (as measured by the ADE) (assessments described further below).

Affective Disorders Evaluation

The ADE³² is a composite form designed by the STEP-BD investigators as the intake assessment for the treating psychiatrist and utilized to determine the diagnosis of participants at study entry. The ADE includes the mood and psychosis modules from the Structured Clinical Interview for DSM-IV Axis I Disorder.³⁴ Additional details of patient retrospective course that have been found to be associated with medication adherence in this sample³⁵ were also collected by the psychiatrist on the ADE (ie, rapid cycling, suicide attempts, earlier onset of illness), which were included in this analysis as variables to be controlled for in the final analysis (see Statistical Analysis).

Mini International Neuropsychiatric Interview

The MINI³⁶ was administered by a second STEP-BD clinician (typically a psychologist) to confirm the psychiatrist's diagnosis from the administering the ADE. Comorbid Axis I diagnoses were also determined using the MINI, such as current anxiety or alcohol use disorder. These 2 variables were included in this analysis as variables to be controlled for in

the final analysis as they have been found to be associated with medication adherence in this sample³⁵ (see Statistical Analysis).

Clinical Monitoring Form

The CMF³² was designed for this study as a psychiatrist-rated assessment of bipolar mood symptoms and severity. The CMF also tracked medication recommendations and adverse effects. Pharmacological adherence was obtained by asking patients to report the total number of missed doses of each medication that they were prescribed in the preceding week. These data were recorded by the patient's psychiatrist as mg/wk missed. Adherence was calculated for each medication based on number of milligrams missed and summarized as the maximum nonadherence at any given visit. Nonadherence of at least 25% was defined a priori in the STEP-BD protocol as poor adherence at that visit. The CMF was completed at every STEP-BD visit.

Helping Alliance Questionnaire

The HAQ³⁷ Patient Version for Treatment With Psychiatrists (HAQ-PC) is a self-report 19-item questionnaire created to capture key aspects of the therapeutic alliance. These aspects include the collaborative nature of the patient-psychiatrist relationship, patients' perception of psychiatrist, and patients' motivation for treatment (eg, "I want very much to work out my problems"). The HAQ-PC has good internal consistency ($\alpha = 0.93$), test-retest reliability ($r = 0.78$), and convergent validity (ie, with California Psychotherapy Alliance Scale) as well as discriminate validity.³⁷ Of note, the California Psychotherapy Alliance Scale assesses the patient-psychotherapist relationships, not the patient-psychiatrist relationship (which the HAQ measures in this study). The HAQ uses a 6-point Likert scale, and thus, a cutoff score of 5 was selected a priori to determine whether someone "agreed" (5) or "strongly agreed" (6) with each statement to yield clinically interpretable data. It was administered once at the baseline visit.

Care Satisfaction Questionnaire

The CSQ^{38,39} is a 44-item self-rated scale to the 56-item Consumer Assessment of Behavioral Health Services measure. The CSQ assesses patients' perceptions of their behavioral health services, such as their quality of care, the accessibility of psychiatrists, and degree to which they felt treated with "respect" and "courtesy," among other items. The CSQ was administered every 3 months for the first year and then every 6 months for subsequent years; in regression models, we utilized the nearest CSQ to a given visit, including only those visits within 90 days of a CSQ assessment. The CSQ includes dichotomous items (eg, item 17: "In the last 3 months, did your clinician tell you about the risks and benefits of the medications you have taken?"), 4-point ordinal measures (eg, item 13: "In the last 3 months, how often did clinicians explain things in a way you could understand?"), and Likert scales scored 0 to 10 (eg, item 23: rating of all clinicians). For the 4-point ordinal scales, we dichotomized never/sometimes versus usually/always.

Statistical Analysis

Primary analyses used logistic regression with items from the HAQ-PC and CSQ as independent variables, and poor adherence at a given visit as the repeated dependent variable. Thus, nonadherence was the dependent variable and was defined as a dichotomous variable (adherent to medications $\geq 25\%$ vs nonadherent to medications $<25\%$). Thus, missing at least 25% of total doses of any 1 medication was defined as poor adherence. To allow all visits to be incorporated in the analysis, observations were treated as being nested by subject using generalized estimating equations in Stata. Generalized estimating equation is a robust statistical method when using correlated categorical data as response variables.

Visits that did not occur within 90 days of the CSQ (which refers to a 3-month window of time) were treated as missing data. First, crude odds ratios (ORs) were calculated to estimate the association of HAQ-PC and CSQ with medication adherence. These ORs were then adjusted for current symptom severity (as measured by the CMF as it was administered at every visit), as well as for factors that we have previously found associated with poor adherence in this sample to remove the variance accounted for by these variables in the regression equation.³⁵ These factors are rapid cycling, suicide attempts, earlier onset of illness, and current anxiety or alcohol use disorder. All analyses utilized Stata 10.0 (College Station, Tex). Given the exploratory nature of these analyses, we did not use a Bonferroni correction for these analyses.

RESULTS

Demographics for the sample are reported in Table 1. We also present a comparison of patients in this STEP subsample compared with those who were excluded because of missing data.³⁵ Tables 2 and 3 include the distributions or means of the outcome variables for the HAQ-PC and CSQ, respectively. Of note, the average assessment time between visits for the first year of the study was 42.5 (SD = 31.3) days (interquartile range, 24.5–51.0 days).

Several aspects of the therapeutic alliance, or items from the HAQ-PC, were associated with medication adherence (Table 2). When controlling for variables that were associated with poor adherence (ie, rapid cycling, suicide attempts, earlier onset of illness, current anxiety, or alcohol use disorder) and current mood, participants' perceptions of the strength of the therapeutic relationship with their psychiatrist (ie, degree of dependence, having a good relationship, feeling understood, having meaningful exchanges) and the degree of collaboration (ie, having similar ideas about the problem) were positively associated with medication adherence (as evidenced by a significant OR <1.0; Table 2). "Treatment procedures not suiting participants' perceived needs" was the only factor associated with medication nonadherence (as evidenced by a significant OR >1.0; Table 2), but this was not significant after adjusting for factors associated with poor adherence and current mood. Other perceived negative aspects of the relationship, such as distrusting psychiatrists' judgment, perceived distance from the psychiatrist, and having unprofitable exchanges, were not associated with medication adherence (Table 2).

The associations of the CSQ items with medication adherence are reported in Table 3. If patients felt helped and respected by their psychiatrists, they were more likely to be adherent, regardless of factors associated with poor adherence and current mood. The efficiency with which patients were seen (ie, <15 minutes) was also significantly associated with medication adherence. The degree with which patients felt that their psychiatrist discussed medication risks/benefits was not significantly associated with medication adherence.

In Tables 2 and 3, we also report the results' crude OR, or the results without controlling for variables that were associated with poor adherence and current mood. In these analyses, "psychiatrist and I work on our problems together" and "my psychiatrist likes me as a person" were associated with good medication adherence, and "procedures not suited to my needs" was associated with poor medication adherence (Table 2). The results did not differ in regard to participants' perception of their treatment setting (Table 3).

DISCUSSION

This article examined whether positive perceptions of one's care provider (ie, psychiatrist) and treatment setting were associated with better adherence to their pharmacotherapy. We found that patients' perceived collaboration, empathy, compassion, and access to their psychiatrist were positively associated with medication adherence. In contrast, discussion of medication risks/benefits, experience of the psychiatrist in helping others, and the degree to which the patient was motivated to solve his/her problems were not associated with adherence. This study underscores the importance of the patient's perceived relationship with his/her provider, and with the provider's office staff, in influencing his/her adherence. Most of these associations were statistically significant regardless of patient's current mood state and factors associated with poor medication adherence (ie, rapid cycling, suicide attempts, earlier onset of illness, current anxiety, or alcohol use disorder).

This study also offers insight into possible mediators of treatment outcome in bipolar disorder for pharmacotherapy and psychotherapy studies.⁴⁰ The importance of timely appointments is emphasized by the finding that wait times are associated with medication nonadherence. A recent meta-analysis of more than 20 bipolar studies found that "systems-level factors," such as reduced access to care, negatively impacted medication adherence.²⁹ Velligan et al¹⁷ summarized strategies to address medication adherence problems in serious mental illness based on the Expert Consensus Guideline Series in 2009. In this summary, they highlighted the importance of addressing systems-level issues, such as ensuring that phone calls are answered and that appointments are scheduled in a "timely manner." Reilly-Harrington and Sachs⁴¹ also recommend that treatment contracts for individuals with bipolar disorder may help to enhance their treatment adherence. Such treatment contracts are developed by the provider in collaboration with the patient and clearly describe the expectations of treatment, such as patient adherence, provider availability, and accessibility.

The results of this study also highlight the importance of collaborating with patients.^{13,42} Collaboration involves selecting treatment goals and interventions with the patient, such that his/her feedback and input is incorporated in the treatment process. Importantly, the patient is perceived as a comanager of his/her illness with their provider.⁴³ Educating and training psychiatrists on how to develop and maintain collaboration with patients may play an important role in improving medication adherence.^{13,24,44} Further investigation into the association of patient-psychiatrist collaboration and adherence is needed to understand factors that may mediate this relationship. For example, it is possible that psychiatrists may be more motivated to treat adherent patients. It is also likely that individual, patient factors, such as impulsivity, poor insight, denial of illness, and negative attitude toward medication, explain part of (ie, moderate) this relationship.^{14,45,46}

Notably, the patients' perceived strength of the relationship and degree of collaboration with their psychiatrists were associated with adherence, but patients' perceptions of the psychiatrist's knowledge were not. For example, the scale items "the therapist appears experienced in helping people" and "clinicians discussing risks/benefits of medications" were among the few items that were not associated with adherence. This finding contradicts other studies that have found that medication adherence in individuals with bipolar disorder is enhanced by psychoeducation, or knowledge about medication risks and benefits.^{24,44} Thus, given that provider knowledge is often targeted in enhancing adherence,⁴² future research should investigate whether providers who assert their educational background and clinical experience are more effective at increasing medication adherence.

Surprisingly, the patient's motivation to solve his/her problems was not a factor associated with adherence. This finding is in contrast to other literature that has cited the importance of

patients' motivation to get better as a predictor of their improvement and outcome.^{14,47} This may be due to this finding relying on only 1 item of the HAQ-PC. Future research is also warranted to better understand why the patients' degree of respect for providers' point of view, working with their provider, and believing that they are liked by their provider were no longer associated with medication adherence after controlling for mood state and factors associated with poor adherence. Investigating the impact of these factors on adherence would likely improve our ability to personalize medication adherence interventions.

An important limitation of this study is its reliance on self-reported adherence. Objective assessments (ie, pill counts, electronic monitoring) could have decreased any variance due to error. Another limitation is this study's reliance on self-reported measures of therapeutic alliance. However, it should be noted that self-report measures of assessing therapeutic alliance have been utilized in similar studies.^{16,23,48–50} The generalizability of our data may also be limited as adherence may be overrepresented in a sample that agrees to participate in a research study. For example, medication adherence was assessed only if participants were adherent to the study procedures or attended their medication sessions, which may have biased this sample.⁵¹ We believe that this bias was minimized given that we used a large patient population, or patients receiving medication treatment for a specific condition, regardless of current adherence.⁵² Although the STEP-BD was designed as an effectiveness study, with very few exclusion criteria, these associations should be replicated in community clinics and general health settings. It should also be noted that we pooled subtypes of bipolar disorder, or subtype I, II, not otherwise specified, as well as cyclothymia or schizoaffective disorder bipolar type, given that some data suggest that medication adherence may differ by subtype.⁵³ However, this STEP-BD design feature was based on evidence that these subtypes share many overlapping features and are thus conceptualized as being on the same continuum.^{54,55} In addition, high conversion rates of bipolar II and bipolar not otherwise specified to bipolar I disorder suggest overlapping etiology.⁵⁶ We also note our a priori decision to analyze the CSQ data for association with adherence data in the prior 3 months. This is consistent with the wording of the CSQ, which refers to the past 3 months, but introduces some risk that CSQ scores may have been influenced by medication adherence or response to nonadherence. We also elected not to use Bonferroni corrected *P* values, as these analyses are exploratory and hypothesis generating (and thus we were more concerned about type II than type I error).

In summary, patients' perception of a collaborative therapeutic alliance and an efficient treatment environment positively influence medication adherence. Providers may elect to prioritize these aspects of the therapeutic alliance and clinical practice when treating individuals with bipolar disorder.

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TABLE 1

Demographics

	STEP-BD Patients Included in Analyses		STEP-BD Patients Not Included in Analyses		Group Difference
	n*	%	n*	%	χ^2
Sex (male)	1398	41.6	366	48.9	13.08 [†]
Race (white)	3031	90.3	655	87.4	5.26 [†]
Ethnicity (Hispanic)	187	5.6	43	5.8	0.04
Age [‡]	3358	40.1 (SD, 1.28)	749	37.3 (SD, 1.30)	$t = -5.39$ [†]
Age at onset [‡]	3274	17.2 (SD, 8.83)	713	16.6 (SD, 8.23)	$t = -1.55$
Married	1197	37.2	170	28.5	16.45 [†]
Employed	773	24.0	154	25.8	0.90
Completed some college	2649	82.3	470	78.9	4.03 [†]
History of suicide attempt	1225	37.6	249	35.8	0.80
History of psychosis	1260	38.8	239	34.8	3.90 [†]
History of anxiety disorder	1207	35.9	227	30.3	8.56 [†]
Rapid cycling (ever)	2274	67.7	508	67.8	0.00
Rapid cycling (past year)	1541	45.9	382	51.0	6.43 [†]

* Total sample is not the same for each variable because of missing data.

[†] $P < 0.05$.

[‡] These are continuous variable, so the mean age (and standard deviation) is reported opposed to a percentage, and a t test was used to determine group differences.

TABLE 2

Association of Adherence and HAQ-PC

HAQ-PC Item	Endorsed Item % (n = 2091)	Crude OR	95% CI	Adj OR	95% CI
1. Dependence on PSY	85.9	0.79*	0.67–0.94	0.81*	0.69–0.96
2. PSY understands me	66.7	0.80*	0.68–0.94	0.83*	0.71–0.97
3. PSY wants me to achieve goals	84.6	0.88	0.72–1.08	0.90	0.74–1.09
4. I distrust PSY judgment	14.7	0.98	0.78–1.22	0.95	0.77–1.18
5. I'm working with PSY	77.0	0.82	0.69–0.97	0.84	0.71–1.00
6. PSY has similar ideas about problem	70.0	0.78*	0.66–0.91	0.80*	0.68–0.94
7. I respect PSY's views	78.8	0.82*	0.69–0.97	0.84*	0.71–1.00
8. Procedures not suited to my needs	10.1	1.29*	1.03–1.62	1.22	0.97–1.52
9. I like my PSY as a person	82.9	0.93	0.77–1.13	0.94	0.78–1.13
10. PSY and I work on problems together	70.5	0.78*	0.67–0.91	0.80	0.68–0.93
11. PSY slows up progress	9.8	1.25	0.98–1.59	1.22	0.96–1.55
12. Have good relationship with PSY	63.3	0.81*	0.69–0.94	0.82*	0.71–0.96
13. PSY experienced in helping people	83.5	0.91	0.76–1.10	0.93	0.77–1.12
14. I want to work on my problems	96.0	0.95	0.64–1.41	0.92	0.63–1.36
15. PSY and I have meaningful exchanges	68.0	0.79*	0.68–0.92	0.81*	0.70–0.95
16. PSY and I have unprofitable exchanges	13.2	1.17	0.95–1.45	1.12	0.91–1.38
17. We talk about same past events	43.8	0.96	0.82–1.12	0.95	0.82–1.11
18. PSY likes me as a person	62.5	0.85*	0.73–0.99	0.88	0.75–1.02
19. PSY seems distant	15.3	1.16	0.96–1.41	1.12	0.92–1.35

* $P < .05$.Adj indicates adjusted OR to control for mood and factors associated with poor adherence (ie, rapid cycling, suicide attempts, earlier onset of illness, current anxiety, or alcohol use disorder)³⁵; CI, confidence interval; PSY, psychiatrist.

TABLE 3

Association of Adherence and CSQ

CSQ Item (in the Past 3 Months...)	Endorsed Item, [*] n (%)	Crude OR	95% CI	Adj OR	95% CI
How much were you helped by your treatment/counseling?	1549 (61.4)	0.82 [†]	0.73–0.92	0.89 [†]	0.79–1.00
Did your clinician tell you the risks/benefits of your medications?	1920 (79.6)	1.02	0.88–1.18	1.02	0.88–1.17
Did your clinician tell you about different kinds of treatment for your problem?	1691 (67.1)	1.01	0.90–1.13	0.99	0.89–1.11
Did your clinician tell you your right to refuse treatment?	1526 (60.5)	1.07	0.96–1.19	1.05	0.94–1.17
Overall rating of treatment/counseling	Mean, 7.81 (2.08) [‡]	0.97	0.94–1.00	0.99	0.96–1.02
Rating of “main clinician”	Mean, 8.49 (1.88) [‡]	1.00	0.96–1.04	1.01	0.97–1.05
Rating of health plan	Mean, 6.71 (2.44) [‡]	0.99	0.97–1.01	1.00	0.97–1.02
How often did you get treatment as soon as you wanted?	733 (70.0)	0.88	0.71–1.08	0.92	0.74–1.13
How often did you get an appointment as soon as you wanted?	1446 (70.1)	0.96	0.83–1.12	1.01	0.87–1.18
How often did you get help needed by phone?	689 (62.9)	1.01	0.86–1.18	1.03	0.88–1.21
How often did office staff treat you with courtesy and respect?	2351 (93.5)	1.50 [†]	1.12–2.00	1.57 [†]	1.17–2.10
How often did you wait more than 15 min past your appointment?	351 (13.9)	1.22 [†]	1.02–1.45	1.16 [†]	0.97–1.37
How often did clinicians listen to you?	2294 (90.7)	1.06	0.85–1.34	1.15	0.92–1.44
How often did clinicians explain things in way that you could understand?	2322 (91.9)	0.88	0.70–1.10	0.94	0.76–1.17
How often did clinicians show you respect?	2304 (91.1)	0.88	0.71–1.10	0.96	0.77–1.19
How often did clinicians spend enough time with you?	2113 (83.7)	0.89	0.76–1.05	0.95	0.81–1.13
How often did clinicians give you reassurance and support?	2034 (80.6)	0.91	0.77–1.06	0.94	0.80–1.10
How often were you involved in decisions about your treatment/counseling?	2033 (83.5)	0.92	0.79–1.09	0.98	0.84–1.16

^{*} The number of individuals endorsing each item varies, given that the CSQ was administered at multiple time points.

[†] $P < 0.05$.

[‡] These items are continuous variables, and thus the mean and SDs are reported.

Adj indicates adjusted OR to control for mood and factors associated with poor adherence (ie, rapid cycling, suicide attempts, earlier onset of illness, current anxiety, or alcohol use disorder)³⁵; CI, confidence interval.