

The Role of the Therapeutic Relationship in Psychopharmacological Treatment Outcomes: A Meta-analytic Review

Christine M. Wienke Totura, Ph.D., Sherecce A. Fields, Ph.D., Marc S. Karver, Ph.D.

Objective: Patient nonadherence to psychopharmacological treatment is a significant barrier to effective treatment. The therapeutic relationship is known to be a critical component of effective psychological treatment, but it has received limited study. A meta-analysis was conducted to examine the role of the therapeutic relationship in the delivery of effective psychopharmacological treatment.

Methods: PubMed, PsycINFO, CINAHL, Google Scholar, Ingenta, and the Web of Science–Science Citation Index were searched, including reference lists of found articles. Meta-analytic methods were used to examine the association between the physician-patient therapeutic relationship and outcomes in psychopharmacological treatment.

Results: Eight independent studies of psychopharmacological treatment reported in nine articles met the inclusion criterion

(1,065 participants) of being an empirically based study in which measures of the therapeutic relationship were administered and psychiatric treatment outcomes were assessed. The overall average weighted effect size for the association between the therapeutic relationship and treatment outcomes was $z=.30$ (95% confidence interval=.20–.39), demonstrating a statistically significant, moderate effect.

Conclusions: Findings indicate that a positive therapeutic relationship or alliance between the physician and the psychiatric patient is associated with patient improvement over the course of psychopharmacological treatment. Results suggest that more attention should be paid to psychiatrist communication skills that may enhance the therapeutic alliance in psychopharmacological treatment.

Psychiatric Services 2018; 69:41–47; doi: 10.1176/appi.ps.201700114

Efficacious psychopharmacological treatments for a wide variety of mental disorders have been identified (1). Clinicians are increasingly aware of these treatments to deliver the most effective services to their patients. However, patient participation, engagement, and adherence to treatment regimens are essential components of effective treatment. A number of studies show that medical outcomes are poorer when patients receive an inadequate dose of treatment (2). Patient nonadherence to medication is a significant problem throughout clinical medicine (3,4). Treatment adherence is even more problematic in psychiatric populations because mental health impairments lead to poor insight, reasoning difficulties, and low motivation to comply with treatment regimens (5). Therefore, to improve medication adherence and maximize the likelihood of achieving desirable outcomes, research should focus on identifying factors associated with increasing patient engagement and participation in treatment.

A number of studies examining patient-provider interactions have been conducted in the fields of medical and psychotherapy treatment. For example, in studies of both

general and specialty medical practitioners (including family medicine, internal medicine, and oncology), a positive physician-patient relationship and physician-patient communication have been moderately correlated with a variety of health outcomes, including decreased psychiatric symptoms, resolution of general medical symptoms, improved functional status, decreased blood pressure, improved blood sugar levels, and better pain control (6,7). Similarly, in the psychotherapy treatment literature, the therapeutic relationship or alliance has been found to be one of the most robust predictors of adult and youth mental health treatment outcomes across various psychotherapy approaches (8,9).

Clearly, variables related to the therapeutic relationship are important components in many psychotherapeutic and general medical approaches with diverse patient populations. The therapeutic alliance may also be important for patients who receive psychopharmacological services for a wide variety of mental health issues. In fact, the therapeutic relationship may be more important for psychiatry than for general medicine. The effectiveness of psychopharmacological treatment requires taking medications outside the

treatment session, and the role of the therapeutic relationship may be critical in this regard. Some psychiatric medications take time before a therapeutic effect is evident, and many have side effects (10). Because adult patients are usually responsible for their medication compliance, alliance development seems a particularly relevant factor for managing effectiveness expectations and side effects that could mitigate adherence.

A strong therapeutic relationship may therefore encourage patient willingness to continue medication use despite unpleasant side effects or the lack of immediate therapeutic effect. In this study, we conducted a comprehensive literature review and meta-analysis of the association between the therapeutic relationship and psychopharmacological treatment outcomes among adult psychiatric patients. On the basis of previous studies, we expected to find a significant relationship between the therapeutic relationship and treatment outcome variables.

METHODS

Search Strategy

The literature search included PubMed, PsycINFO, CINAHL, publication alerts from Ingenta, and Web of Science–Science Citation Index databases. Combinations of the following search terms were used: therapeutic relationship, therapy relationship, treatment relationship, relationship, patient, physician, psychiatrist, psychiatry, behavior, empathy, interaction, patient perception, communication, and alliance. Authors of relevant articles were searched in the aforementioned databases to determine whether they had published additional research, and the reference lists of found articles were searched for any studies not returned by the literature search. Finally, Google Scholar was used to search for studies that may have been harder to find with the standard databases and for unpublished manuscripts. Published journal articles or dissertations written in or translated into English until February 2014 were included. The search yielded 296 results.

Study Inclusion Criteria

The meta-analysis used the following inclusion criteria: empirically based studies examining the therapeutic relationship (that is, measures were administered explicitly assessing the therapeutic alliance or relationship) and examining the association between the alliance measure and physician-related medication management outcomes for adult patients.

In cases in which abstracts provided insufficient information to adequately assess eligibility, the full article was reviewed to avoid elimination of appropriate articles. Nine articles that met criteria were retained. [A flow diagram of study selection is presented in an online supplement to this article.] Two of these articles used data from the same study, and only one effect size was then computed. Therefore, eight studies were included in the final meta-analysis, with 59 samples of data across multiple alliance and treatment measures.

Data Extraction

Data entry used a standardized form. For each of the eight studies, the following information was coded: author, publication year, relationship variables, outcome variables, number of patients, patient age, type of prescribing health professional, sample size, and relationship to outcome effect size. Two independent raters (CMWT and SAF) coded each study. One of the authors (MK) discussed coding discrepancies with each rater, and all were resolved through repeated review until consensus was reached.

Statistical Analysis

Fisher's z was computed for small sample size by using the statistical software Comprehensive Meta-Analysis, Version 2 (11). Means and standard deviations (SDs) or correlations were preferred to compute effect sizes. When correlations were used, Fisher's z was calculated from r . In the one other case, mean and SD values were used to calculate Fisher's z . Positive z values indicate better outcomes as a function of increased alliance. All eight studies included sufficient information to calculate effect size. If a study employed more than one measure of alliance or outcome, involved different conditions and did not supply an overall effect, or involved distinct groups, then individual effect sizes were calculated and averaged to provide an overall effect size for the study. For studies reporting a nonsignificant relationship between alliance and outcome, the effect size was conservatively imputed to be zero. Inverse relationships were entered as negative values. Fifty-nine individual effect sizes were calculated across measures, samples, and conditions, which were pooled to provide a composite effect size per study, or eight overall effect sizes weighted by sample size. Cochran's Q homogeneity statistic was used to determine whether a random or fixed-effects model would be required. We intended to examine potential moderators of the association between the therapeutic relationship and outcome (9), but we had too few studies to adequately power an analysis.

Meta-analysis typically involves accounting for publication bias (that is, studies with nonsignificant results are less likely to be published) (12). Two approaches examined publication bias: funnel plot (Duval and Tweedie's trim and fill [13]) and fail-safe N (that is, the number of additional "negative" studies [with a zero intervention effect] needed to increase the p value above .05 [14]).

RESULTS

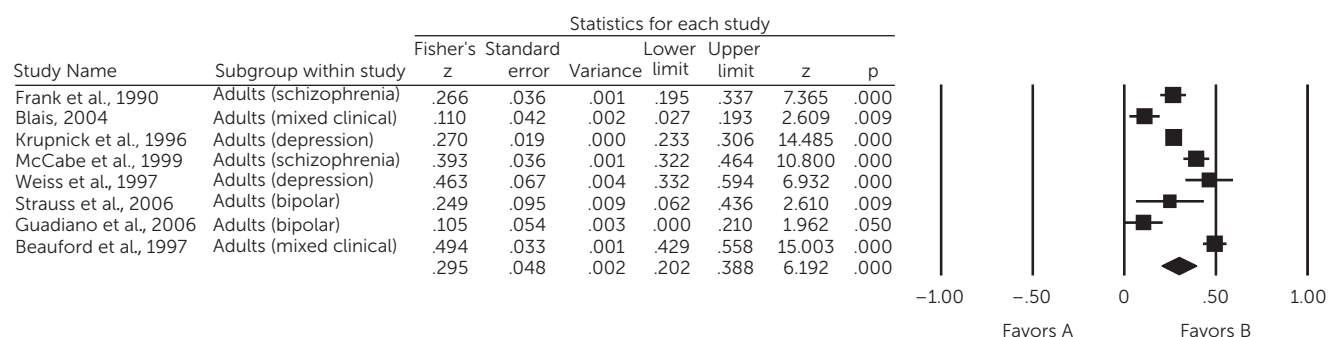
Study Characteristics

Participant demographic characteristics and effect sizes (eight different studies with 59 distinct samples) are reported in Table 1 and Figure 1. Four studies (five reports) involved treatment of affective disorders (depression or bipolar disorder) (15–19), two involved treatment of schizophrenia (20,21), and two involved a mixed clinical population (22,23). Therapeutic alliance measures across studies included domains such as collaboration, shared goals, bonding with the therapist,

TABLE 1. Articles included in a meta-analysis of the association between the therapeutic relationship and psychopharmacological treatment outcomes

Article	Measures				Participants		Overall effect size (z)
	Relationship	Timing of relationship measurement	Outcome	Patients	Health professionals	Study N	
Beauford et al., 1997 (22)	Therapeutic alliance assessed by chart review (6-point scale)	Early treatment	Overt Aggression Scale	Adults; mixed clinical population; mean age=41.9	Inpatient physicians	311	.49
Blais, 2004 (23)	Inpatient Treatment Alliance Scale	Early and middle treatment	10-item Schwartz Outcome Scale, amount of trouble	Adults; mixed clinical population, primarily depression; mean age=47	Psychiatrists	73	.11
Frank and Gunderson, 1990 (20)	Psychotherapy Status Report	Early and middle treatment	Psychiatric Status Scale, Inpatient Multidimensional Psychiatric Scales, Menninger Health-Sickness Rating Scales, Camarillo Dynamic Assessment Scales, Katz Adjustment Scales; Global psychopathology; paranoid hallucinations, delusions and expansiveness; agitation and hostility; anxiety and depression; withdrawal, retardation, and apathy; cognitive disorganization; primary process thinking; verbal-ideational productivity; ego weakness; denial of illness; adaptive regression; interpersonal relations; social dysfunction; behavioral disturbance; occupational functioning; self-sufficiency	Adults; schizophrenia; age range 18–35	Psychotherapists with M.D.s	48	.27
Gaudiano and Miller, 2006 (15)	Working Alliance Inventory	Early and middle treatment	Bech-Rafaelsen Mania Scale, Hamilton Rating Scale for Depression, Global Assessment of Functioning	Adults; bipolar disorder; mean age=42	Psychiatrists	61	.11
Krupnick et al., 1996 (16); Meyer et al., 2002 (17) ^a	Modified Vanderbilt Therapeutic Alliance Scale	Early, middle, and late treatment	Hamilton Rating Scale for Depression, Beck Depression Inventory, composite outcome score	Adults; depression; mean age=37.7	Psychologists and psychiatrists	225	.27
McCabe et al., 1999 (21)	Modified Helping Alliance Scale	Early treatment	Lancashire Quality of Life Profile	Adults; schizophrenia; mean age=48.9	Primary therapists	258	.39
Strauss and Johnson, 2006 (18)	Working Alliance Inventory	Early treatment	Hamilton Rating Scale for Depression, Bech-Rafaelsen Mania Scale	Adults; bipolar disorder; mean age=44.09	Psychiatrists	58	.25
Weiss et al., 1997 (19)	California Pharmacotherapy Alliance Scale	Early treatment	Hamilton Rating Scale for Depression, Beck Depression Inventory	Adults; depression; mean age=41.9	Psychiatrists	31	.46

^a Same study, two articles

FIGURE 1. Meta-analytic plot of Fisher's z effect sizes and 95% confidence intervals in eight studies of the association between the therapeutic relationship and psychopharmacological treatment outcomes^a

^a Favors A results suggest a negative effect; favors B results suggest a positive effect. The diamond indicates the overall meta-analytic effect and 95% confidence interval.

active participation, and perceived value of treatment. Psychopharmacology treatment outcomes measured included aggression, anxiety, depression, general well-being, and level of autonomous functioning. Four studies involved outpatient treatment (15–19), three involved inpatient treatment (21–23), and one had a mixed inpatient-outpatient sample (20). In seven studies, the therapeutic relationship was measured either early in treatment or both early and midtreatment, allowing for a prospective relationship to outcome (15,18–23). Some researchers measured the alliance three times: in early, middle, and late treatment (16,17; the data utilized in these articles are from the same study and therefore count in the analyses as only one study). Studies varied by treatment duration; the longest was up to 28 months (15).

Participant Characteristics

The meta-analysis sample consisted of 1,065 participants (mean \pm SD = 122 \pm 101.7 participants per study), with a mean age of 41.2 (range 16–87 years). Only three studies provided information on the gender of patients; these studies were approximately equally divided between males and females (19,22,23). Length of treatment varied across studies (range of inpatient treatment, 16 days to four months; range of outpatient treatment, 11 sessions to 28 months). Only three studies reported the number of treating clinicians (range of four to 81) (16,19,20).

Test of Study Heterogeneity

Cochran's Q suggested heterogeneity ($Q=44.49$, $p<.001$). The error observed between studies was different from that explained by sampling error, suggesting the need for a random-effects model (24,25), which assumes that effects are randomly distributed within studies (26).

Effect of Publication Year on Effect Size

A moderate, nonsignificant correlation occurred for publication year and sample size ($r=.406$, $df=16$, $p=.118$). A small, nonsignificant correlation between publication year and effect size occurred ($r=-.078$, $df=16$, $p=.774$). Sixty-eight percent of studies were published after 2010, and all were published after 2003.

Publication Bias

Studies with nonsignificant results are at risk of being unpublished and thus excluded from meta-analyses (12). Publication bias was examined with the following two approaches.

Funnel plot. As expected, larger studies were clustered around the combined effect size toward the top of the plot, and smaller studies gathered toward the bottom of the plot (11). A plot of observed and inputted studies revealed no bias toward positive effect sizes (Figure 2). Duval and Tweedie's trim-and-fill analysis imputed no additional studies to the left or right of the mean with a random-effects model, leaving the effect size the same ($z=.30$, 95% confidence interval [CI]=.20–.39, $SE=.048$, $z=6.192$, $p<.05$).

Classic fail-safe N. Fail-safe N analysis indicated that 65 nonsignificant studies would be needed to reverse the significant positive effect size found in the eight studies (11). This is above the criterion benchmark of five times the number of studies plus ten (12)—in this case 50 studies—indicating that a file drawer problem is unlikely present.

Therapeutic Alliance and Psychiatric Medication Management

The point estimate (weighted mean) composite effect size was .30 (CI=.20–.39, $SE=.048$, $z=6.192$, $p<.05$). Effect sizes ranged from $-.11$ to $.49$, a medium effect size (27). This indicates a statistically significant association between the therapeutic alliance and outcomes of psychiatric medication management (Table 1).

DISCUSSION

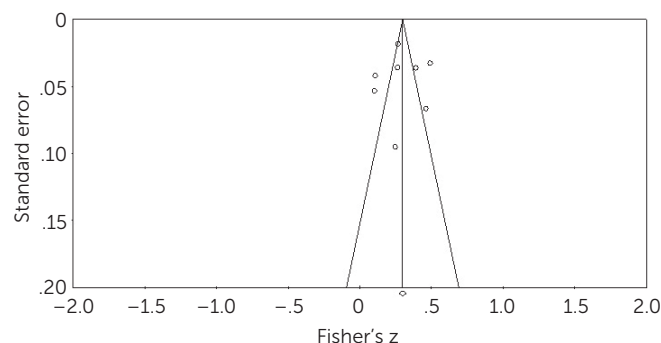
This first meta-analytic review examining the therapeutic relationship in psychiatric medication management indicated that a higher-quality physician-patient relationship was related to better mental health treatment outcomes. Across eight empirical studies, the average effect size was $z=.30$, a medium effect size commensurate with that found in

the literature on the therapeutic alliance or relationship in adult and child psychotherapy (8,28–30). The findings suggest that the therapeutic alliance is just as important in pharmacotherapy adherence as it is in psychotherapy participation. In addition, the effect size suggests that there is considerable variability in the association between the therapeutic relationship and the success of psychiatric medication management. Many physicians form high-quality relationships with their patients, resulting in positive outcomes; however, many relationships need improvement, given the less-than-optimal treatment outcomes in some studies.

Successful psychopharmacological treatment relies on patients' adherence to prescribed medications (31–34). Considering that research has suggested that the therapeutic alliance predicts outcomes across various clinicians and therapies (8), it should not be surprising that it is also important in facilitating positive medication management outcomes, in particular with psychiatric patients (35–37). The results of this meta-analysis suggest a possible mechanism—namely, that a strong physician-patient alliance contributes to improved medication adherence, which may result in positive treatment outcomes. Because the meta-analysis did not assess medication adherence, future research should examine whether medication adherence mediates the relationship between alliance and treatment outcomes or whether the alliance has a more direct curative effect. An alternative possibility is that other unmeasured variables related to the therapeutic alliance may be the actual mechanisms. Specific physician behaviors, such as providing acknowledgment and support (38) or a credible rationale for medication use (39), may be directly related to treatment adherence or outcome, but such behaviors may also result in patients' experiencing positive feelings toward their treating physician. Other understudied variables that may be related to the association between therapeutic alliance and positive treatment outcomes include treatment dose (length of sessions), time between sessions, early symptom change, patient empowerment in managing his or her psychiatric illness, patient motivation to change, or even organizational or agency factors (for example, warmth of the physician's administrative staff). In addition, development of attachments and empathy (40), patient misunderstanding or forgetting prescription instructions, economic barriers or barriers related to the family or the environment, failure to remember to take medications consistently, and regular physician assessment of adherence may also contribute to medication adherence (41).

Given the significant relationship between the therapeutic alliance and outcomes found in a very small sample of studies, each study was carefully examined for limitations in methodological quality. First, the studies used diverse measures to assess alliance, and most did not focus exclusively on the relationship between alliance and outcome in medication management. Several studies included physicians who delivered both psychotherapy and pharmacotherapy (20,22,23), some studies combined data from individuals

FIGURE 2. Funnel plot of standard error by Fisher's z in eight studies of the association between the therapeutic relationship and psychopharmacological treatment outcomes



who were receiving only psychotherapy with data from those also receiving pharmacotherapy (16), others focused on physicians delivering only medication management (15), and others reported alliance ratings for a treatment team, which included a prescribing psychiatrist (16,17,20–23). Thus it was difficult to determine what aspects of the alliance were associated with favorable relationships and whether alliance in the context of psychotherapy or psychopharmacology with the psychiatrist or physician was responsible for treatment effects. However, the effect size found is consistent with that in the psychotherapy literature. If the studies had included only measures of the alliance in pharmacological treatment, the relationship between the alliance and medication management outcomes might have been stronger.

In addition, methodological issues might explain why two of the studies demonstrated weaker associations between alliance and outcomes (15,23). In the study by Blais (23), the aggregation of the alliance construct across the perspectives of multiple informants and helping professionals may have diluted the study's ability to identify a stronger alliance-to-outcome effect size. Moreover, study effect sizes may have been attenuated as a result of the long time lag between assessment of the alliance and of discharge outcomes. In studies with long treatment duration, it might be more effective to assess patterns of alliance over time. This is an area for future research. Furthermore, the effects were stronger for the relationship between the alliance and change in depression symptoms, compared with symptoms of mania, and for the relationship between the alliance and change in overall functioning scores. Additional studies are needed to provide adequate power to assess moderating effects such as these.

Many studies also did not provide information on the physicians or on the number of physicians in the study. The alliance measures used in the studies also varied extensively. The Working Alliance Inventory was the most frequently used, but it was used in only two studies. This raises the question of whether each study measured the same construct. However, the consistently significant findings across studies suggest that each measured the same alliance construct. Furthermore, sample heterogeneity existed in the eight studies.

However, the consistent results suggest the importance of the relationship between alliance and outcome despite the diversity in samples and measures. Unfortunately, the small number of studies did not allow for moderator analyses to examine patterns attributable to theoretical or methodological issues. For example, alliances may have more or less impact depending on the problem or diagnosis treated, the outcome examined (which varied across studies), the alliance measures used, and the treatment settings (inpatient versus outpatient). Although this meta-analysis included a small sample of relevant work, the findings provide justification for more research in this area. Furthermore, some findings may have been inflated because of shared method variance or temporal similarity (in some studies, alliance measures were completed at the same time as outcome measures [15,16,20,23]). Variability in timing of alliance ratings may have had an impact on effect sizes. Alliance assessments in middle to late treatment may have inflated the relationship between alliance and outcomes, especially if the alliance assessments occurred after patients began experiencing potential improvements.

Despite some limitations, three studies were the most methodologically sound of those reviewed, with the clearest evidence of a moderate relation (average $r=.26$) between the therapeutic relationship and psychiatric medication management (15,18,19). Higher-quality studies should be conducted to further elucidate outcomes.

The aforementioned limitations indicate several areas for future research. There is a need for more studies of psychiatrists across levels of experience, of clinicians delivering only pharmacotherapy, and in outpatient settings. The literature would benefit from studies focusing on medication management for a variety of patients (for example, various diagnoses and stages of development) who are typically seen for brief appointments. If the alliance is found to serve a truly important role in pharmacotherapy, then research should examine its mechanisms in medication management and whether they vary depending on the characteristics of the patients being treated or the type of medication prescribed. Moreover, psychotherapy alliance measures have been developed on the basis of certain assumptions, such as one-hour therapy sessions, weekly meetings, and treatment success as assessed by conversations between the therapist and the patient. Given that these assumptions do not typically apply to medication management, treatment process measures are needed that reflect treatment considerations in psychiatric practice (such as brief appointments rather than weekly meetings and not considering physician-patient conversations as the primary treatment ingredient). Finally, we conducted a thorough review of existing research and noted a lack of studies focused exclusively on the alliance-outcomes relationship in pharmacotherapy, which suggests a major gap in the literature on the therapeutic alliance that needs to be addressed.

CONCLUSIONS

More high-quality studies on the role of the therapeutic alliance in psychopharmacological treatment are needed. This

meta-analysis included some studies of lower quality and studies that were highly diverse. Nevertheless, it found evidence of a relationship between alliance and outcomes, suggesting that the therapeutic alliance is important in achieving optimal psychopharmacology outcomes. Thus the training of psychiatrists prescribing psychotropic medications should emphasize communication skills to enhance the therapeutic alliance. Research is clearly needed to effectively develop the skills that will contribute to positive prescriber-patient relationships. This review contributes to the literature by encouraging better research on the therapeutic alliance in psychiatric medication management.

AUTHOR AND ARTICLE INFORMATION

Dr. Totura is with the Department of Psychology, Auburn University, Auburn, Alabama. Dr. Fields is with the Department of Psychology, Texas A&M University, College Station. Dr. Karver is with the Department of Psychology, University of South Florida, Tampa. Send correspondence to Dr. Totura (e-mail: christine.totura@auburn.edu).

The authors thank Sarah Tarquini for assistance with study coding.

The authors report no financial relationships with commercial interests.

Received March 8, 2017; revision received May 24, 2017; accepted June 22, 2017; published online September 15, 2017.

REFERENCES

1. Clinical Practice Guidelines. Arlington, Va, American Psychiatric Association. <https://www.psychiatry.org/psychiatrists/practice/clinical-practice-guidelines>
2. DiMatteo MR: Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Medical Care* 42:200–209, 2004
3. Bulloch AGM, Patten SB: Non-adherence with psychotropic medications in the general population. *Social Psychiatry and Psychiatric Epidemiology* 45:47–56, 2010
4. Chappuy H, Tréluyer JM, Faesch S, et al: Length of the treatment and number of doses per day as major determinants of child adherence to acute treatment. *Acta Paediatrica* 99:433–437, 2010
5. Julius RJ, Novitsky MA Jr, Dubin WR: Medication adherence: a review of the literature and implications for clinical practice. *Journal of Psychiatric Practice* 15:34–44, 2009
6. Gabbay M, Shiels C, Bower P, et al: Patient-practitioner agreement: does it matter? *Psychological Medicine* 33:241–251, 2003
7. Street RL Jr, Makoul G, Arora NK, et al: How does communication heal? Pathways linking clinician-patient communication to health outcomes. *Patient Education and Counseling* 74:295–301, 2009
8. Martin DJ, Garske JP, Davis MK: Relation of the therapeutic alliance with outcome and other variables: a meta-analytic review. *Journal of Consulting and Clinical Psychology* 68:438–450, 2000
9. Shirk SR, Karver M: Prediction of treatment outcome from relationship variables in child and adolescent therapy: a meta-analytic review. *Journal of Consulting and Clinical Psychology* 71: 452–464, 2003
10. Chew RH, Hales RE, Yudofsky SC: *What Your Patients Need to Know About Psychiatric Medications*, 2nd ed. Arlington, Va, American Psychiatric Publishing, 2009
11. Borenstein M, Hedges L, Higgins J, et al: *Comprehensive Meta-analysis*, Version 2. Englewood, NJ, Biostat, 2005
12. Sharpe D, Rossiter L: Siblings of children with a chronic illness: a meta-analysis. *Journal of Pediatric Psychology* 27:699–710, 2002
13. Duval S, Tweedie R: A nonparametric “trim and fill” method of accounting for publication bias in meta-analysis. *Journal of the American Statistical Association* 95:89–98, 2000

14. Rosenthal R: The "file drawer problem" and tolerance for null results. *Psychological Bulletin* 86:638–641, 1979
15. Gaudiano BA, Miller IW: Patients' expectancies, the alliance in pharmacotherapy, and treatment outcomes in bipolar disorder. *Journal of Consulting and Clinical Psychology* 74:671–676, 2006
16. Krupnick JL, Sotsky SM, Simmens S, et al: The role of the therapeutic alliance in psychotherapy and pharmacotherapy outcome: findings in the National Institute of Mental Health Treatment of Depression Collaborative Research Program. *Journal of Consulting and Clinical Psychology* 64:532–539, 1996
17. Meyer B, Pilkonis PA, Krupnick JL, et al: Treatment expectancies, patient alliance, and outcome: further analyses from the National Institute of Mental Health Treatment of Depression Collaborative Research Program. *Journal of Consulting and Clinical Psychology* 70:1051–1055, 2002
18. Strauss JL, Johnson SL: Role of treatment alliance in the clinical management of bipolar disorder: stronger alliances prospectively predict fewer manic symptoms. *Psychiatry Research* 145:215–223, 2006
19. Weiss M, Gaston L, Propst A, et al: The role of the alliance in the pharmacologic treatment of depression. *Journal of Clinical Psychiatry* 58:196–204, 1997
20. Frank AF, Gunderson JG: The role of the therapeutic alliance in the treatment of schizophrenia: relationship to course and outcome. *Archives of General Psychiatry* 47:228–236, 1990
21. McCabe R, Röder-Wanner UU, Hoffmann K, et al: Therapeutic relationships and quality of life: association of two subjective constructs in schizophrenia patients. *International Journal of Social Psychiatry* 45:276–283, 1999
22. Beauford JE, McNeil DE, Binder RL: Utility of the initial therapeutic alliance in evaluating psychiatric patients' risk of violence. *American Journal of Psychiatry* 154:1272–1276, 1997
23. Blais MA: Development of an inpatient treatment alliance scale. *Journal of Nervous and Mental Disease* 192:487–493, 2004
24. Hunter JE, Schmidt FL: Fixed effects vs random effects meta-analysis models: implications for cumulative research knowledge. *International Journal of Selection and Assessment* 8:275–292, 2000
25. Petitti DB: Approaches to heterogeneity in meta-analysis. *Statistics in Medicine* 20:3625–3633, 2001
26. Higgins JPT, Thompson SG, Spiegelhalter DJ: A re-evaluation of random-effects meta-analysis. *Statistics in Society* 172:137–159, 2009
27. Cohen J: *Statistical Power Analysis for the Behavioral Sciences*, 2nd ed. Hillsdale, NJ, Erlbaum, 1988
28. Cummings CM, Caporino NE, Settipani CA, et al: The therapeutic relationship in cognitive-behavioral therapy and pharmacotherapy for anxious youth. *Journal of Consulting and Clinical Psychology* 81:859–864, 2013
29. Horvath AO, Del Re AC, Flückiger C, et al: Alliance in individual psychotherapy. *Psychotherapy* 48:9–16, 2011
30. Shirk SR, Karver MS, Brown R: The alliance in child and adolescent psychotherapy. *Psychotherapy* 48:17–24, 2011
31. Post RM, Denicoff KD, Leverich GS, et al: Morbidity in 258 bipolar outpatients followed for 1 year with daily prospective ratings on the NIMH life chart method. *Journal of Clinical Psychiatry* 64:680–690, 2003
32. De Nadai AS, Karver MS, Murphy TK, et al: Common factors in pediatric psychiatry: a review of essential and adjunctive mechanisms of treatment outcome. *Journal of Child and Adolescent Psychopharmacology* 27:10–18, 2017
33. Salloum IM, Cornelius JR, Daley DC, et al: Efficacy of valproate maintenance in patients with bipolar disorder and alcoholism: a double-blind placebo-controlled study. *Archives of General Psychiatry* 62:37–45, 2005
34. Scott J, Pope M: Self-reported adherence to treatment with mood stabilizers, plasma levels, and psychiatric hospitalization. *American Journal of Psychiatry* 159:1927–1929, 2002
35. Klein DN, Schwartz JE, Santiago NJ, et al: Therapeutic alliance in depression treatment: controlling for prior change and patient characteristics. *Journal of Consulting and Clinical Psychology* 71:997–1006, 2003
36. Meier PS, Barrowclough C, Donmall MC: The role of the therapeutic alliance in the treatment of substance misuse: a critical review of the literature. *Addiction* 100:304–316, 2005
37. Zeber JE, Copeland LA, Good CB, et al: Therapeutic alliance perceptions and medication adherence in patients with bipolar disorder. *Journal of Affective Disorders* 107:53–62, 2008
38. Perron BE, Zeber JE, Kilbourne AM, et al: A brief measure of perceived clinician support by patients with bipolar spectrum disorders. *Journal of Nervous and Mental Disease* 197:574–579, 2009
39. Gatchel RJ, Oordt MS: Hypertension; in *Clinical Health Psychology and Primary Care: Practical Advice and Clinical Guidance for Successful Collaboration*. Edited by Gatchel RJ, Oordt MS. Washington, DC, American Psychological Association, 2003
40. Cameron KA, de Haes H, Visser A: Theories in health communication research. *Patient Education and Counseling* 74:279–281, 2009
41. Velligan DI, Weiden PJ, Sajatovic M, et al: Assessment of adherence problems in patients with serious and persistent mental illness: recommendations from the Expert Consensus Guidelines. *Journal of Psychiatric Practice* 16:34–45, 2010