Do Comorbid Anxiety Disorders Moderate the Effects of Psychotherapy for Bipolar Disorder? Results From STEP-BD

Thilo Deckersbach, Ph.D.

Amy T. Peters, B.A.

Louisa Sylvia, Ph.D.

Anna Urdahl, B.A.

Pedro V.S. Magalhães, M.D., Ph.D.

Michael W. Otto, Ph.D.

Ellen Frank, Ph.D.

David J. Miklowitz, Ph.D.

Michael Berk, M.D., Ph.D.

Gustavo Kinrys, M.D.

Andrew Nierenberg, M.D.

Objective: At least 50% of individuals with bipolar disorder have a lifetime anxiety disorder. Individuals with both bipolar disorder and a co-occurring anxiety disorder experience longer illness duration, greater illness severity, and poorer treatment response. The study explored whether comorbid lifetime anxiety in bipolar patients moderates psychotherapy treatment outcome.

Method: In the Systematic Treatment Enhancement Program randomized controlled trial of psychotherapy for bipolar depression, participants received up to 30 sessions of intensive psychotherapy (family-focused therapy, interpersonal and social rhythm therapy, or cognitive-behavioral therapy) or collaborative care, a three-session comparison treatment, plus pharmacotherapy. Using the number needed to treat, we computed effect sizes to analyze the relationship between lifetime anxiety disorders and rates of recovery across treatment groups after 1 year.

Results: A total of 269 patients (113 women) with a comorbid lifetime anxiety disorder (N=177) or without a comorbid lifetime anxiety disorder (N=92) were included in the analysis. Participants with a lifetime anxiety disorder were more likely to recover with psychotherapy than with collaborative care (66% compared with 49% recovered over 1 year; number needed to treat=5.88, small to medium effect). For patients without a lifetime anxiety disorder, there was no difference between rates of recovery in psychotherapy compared with collaborative care (64% compared with 62% recovered; number needed to treat=50, small effect). Participants with one lifetime anxiety disorder were likely to benefit from intensive psychotherapy compared with collaborative care (84% compared with 53% recovered; number needed to treat=3.22, medium to large effect), whereas patients with multiple anxiety disorders exhibited no difference in response to the two treatments (54% compared with 46% recovered; number needed to treat=12.5, small effect).

Conclusions: Depressed patients with bipolar disorder and comorbid anxiety may be in particular need of additional psychotherapy for treating acute depression. These results need to be replicated in studies that stratify bipolar patients to treatments based on their anxiety comorbidity status.

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Bipolar disorder, characterized by recurrent episodes of mania and depression, is a chronic and debilitating illness. Pharmacotherapy is the first line of treatment but often fails to bring patients to sustained remission (1, 2). The limited efficacy of pharmacotherapy alone has motivated the study of adjunctive psychosocial interventions. Randomized controlled trials support the efficacy of psychosocial treatment modalities (for a review, see Miklowitz [3]), such as family-focused treatment, family psychoeducation (4–7), cognitive-behavioral therapy (CBT) (8, 9), interpersonal and social rhythm therapy (10, 11), and group psychoeducation (12), in improving medication adherence, preventing mood episode recurrences, reducing residual mood symptoms, and improving psychosocial functioning.

Depression in bipolar disorder constitutes one of the major unresolved problems (13–15). Even with pharmacological treatment, patients experience significantly greater impairment (16) and longer time to recovery from depressive than manic episodes (17, 18), as well as high levels of residual depressive symptoms between episodes (19). Adjunctive psychotherapy has demonstrated important benefits for acute depression (14, 20). The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), a National Institute of Mental Health-sponsored study of the effectiveness of treatments for bipolar disorder, evaluated the efficacy of psychotherapy for depression in bipolar disorder (21). This large, multisite randomized trial of bipolar depressed patients treated with mood stabilizers compared an intensive psychosocial intervention (up to 30 sessions of CBT, family-focused therapy, or interpersonal social rhythm theory in 9 months) with a brief psychosocial treatment, collaborative care (consisting of three sessions in 6 weeks). Results indicated

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that adjunctive intensive psychotherapy was more beneficial in achieving and reducing time to recovery from a depressive episode than brief psychosocial treatment. No differences were found among the three intensive psychosocial treatments in their capacity to aid and sustain recovery (21).

Although psychosocial interventions have proved beneficial for the treatment of acute depressive episodes, it is unclear how the efficacy of these interventions is moderated by comorbidity. Bipolar disorder is complicated by high rates of comorbidity with other DSM-IV conditions (22). Anxiety disorders, such as panic disorder, social anxiety disorder, obsessive-compulsive disorder (OCD), posttraumatic stress disorder (PTSD), and generalized anxiety disorder, are especially prevalent in bipolar disorder, with epidemiological and clinical samples suggesting that between 20% and 50% of individuals with bipolar disorder also have a lifetime anxiety disorder (22–31). Relative to bipolar patients without an anxiety disorder, individuals with both bipolar disorder and a comorbid anxiety disorder experience longer illness duration, greater illness severity, higher rates of suicide, and overall poorer treatment response (23, 32–35).

Given that comorbid anxiety is associated with a more severe course of bipolar disorder, we hypothesized that it could be a moderator of treatment response to psychotherapy for depression in bipolar disorder. The purpose of this study was to investigate whether comorbid anxiety moderates the likelihood that patients will recover from depression in response to intensive psychotherapy or collaborative care, using data from the STEP-BD randomized controlled trial of psychotherapy for bipolar depression.

Method

Study Design

STEP-BD was a multisite, nationwide clinical research program designed to study the treatment effectiveness and phenomenology, course, and outcome of individuals with bipolar disorder. The study evaluated best-practice treatment options used for bipolar disorder, including mood stabilizing medications, antidepressants, atypical antipsychotics, and evidence-based psychosocial interventions. It is the largest multisite study of bipolar disorder to date, enrolling 4,361 participants across 21 sites. A detailed description of the nature, scope, and overall design of the research program is provided by Sachs et al. (36).

Embedded within STEP-BD was a randomized controlled trial of psychotherapy for bipolar depression (3). In the study, participants were randomly assigned to receive an intensive psychosocial treatment (up to 30 sessions of CBT, interpersonal social rhythm theory, or family-focused therapy in 9 months) or a minimal psychosocial intervention, collaborative care, consisting of three sessions over 6 weeks. All four psychosocial treatments included psychoeducation, relapse prevention planning, and illness management interventions. Collaborative care was a brief intervention drawing on the most common psychosocial strategies shown to offer benefit for bipolar disorder (37, 38). In contrast, the three intensive treatments were designed as enhanced versions of core psychoeducational interventions with specific treatment targets. CBT focused on restructuring cognitive distortions, problem solving, and activity scheduling (8, 9); family-focused therapy emphasized family psychoeducation, communication enhancement, and problem-solving training (4–7); and interpersonal social rhythm theory concentrated on the stabilization of social rhythms and interpersonal problems, such as grief, role transitions, role disputes, and interpersonal difficulties (10, 11).

Participants

Included in this analysis is a subset of participants (N=269/293) enrolled in the STEP-BD randomized controlled trial of adjunctive psychotherapy, with diagnostic information available regarding the presence or absence of a lifetime comorbid anxiety disorder. Diagnoses were based on the results of the Mini-International Neuropsychiatric Interview (39), administered by a certified clinical interviewer (psychiatrist, psychologist, social worker, or psychiatric nurse), with corroborating information from the Affective Disorders Evaluation (36), administered by a study psychiatrist.

Participants, ages 18 or older, met DSM-IV criteria for current bipolar I or II disorder and a current major depressive episode and were treated or willing to initiate treatment with a mood-stabilizing medication. Participants were also not currently undergoing psychotherapy or, if so, were willing to discontinue nonstudy psychotherapy or taper sessions to one or fewer per month. All eligible patients were English speaking and willing and able to give informed consent. Participants were excluded from the study if they required immediate treatment for current DSM-IV substance or alcohol abuse or dependence disorder (excluding nicotine); met criteria for a DSM-IV current mixed episode or depression not otherwise specified; were pregnant or planning a pregnancy in the next year; had a history of intolerance, nonresponse, or medical contraindication to paroxetine or bupropion; or required initiation of or dosage changes in antipsychotic medications. For further details regarding the participants, study design, assessment, and treatment in the randomized psychosocial pathway of STEP-BD, see the review by Miklowitz (3).

Assessment of Primary Outcomes

At each outpatient visit (intensive psychotherapy: up to 30 sessions over 9 months; collaborative care: up to three sessions over 6 weeks) clinical status was assessed using the Clinical Monitoring Form (36). Intraclass interrater reliability coefficients (referenced to gold standard ratings for Clinical Monitoring Form depression and mania items) ranged from 0.83 to 0.99 (36). Clinical status designations of "recovered" or "not recovered" were based on the presence or absence of DSM-IV criteria for symptoms of depression and mania/hypomania. Recovered status was defined as two or less moderate mood symptoms for ≥8 consecutive weeks (36).

Statistical Analyses

The hypothesized moderator of recovery associated with psychosocial treatments was the presence at baseline of any lifetime comorbid anxiety disorder. We tested this hypothesis by using the general strategy for exploratory moderator analyses in randomized controlled trials described by Kraemer and Kupfer (40), whose criteria for treatment moderators require that 1) the potential moderator precedes treatment, 2) the potential moderator is uncorrelated with the form of treatment, and 3) the moderator of treatment has an interactive effect with treatment on the outcome. Moreover, Kraemer and Kupfer recommend that p values not be used to define moderators of treatment because of the potential for the moderator status to change with sample size.

TABLE 1. Demographic and Clinical Characteristics of 269 Bipolar Depressed Patients With and Without a Lifetime Anxiety Disorder

Characteristic	Lifetime Anxiety Disorder (N=177)		No Lifetime Anxiety Disorder (N=92)		Overall (N=269)		Lifetime Anxiety Disorder Compared With No Lifetime Anxiety Disorder		
	Mean	SD	Mean	SD	Mean	SD	df	t	p
Age (years)	40.47	9.97	39.73	12.28	40.22	11.64	264	–0.49	0.63
Age at illness onset (years)	21.44	9.97	23.83	10.10	22.24	10.06	264	–0.61	0.54
Depressive severity[a]	7.16	2.28	7.34	2.33	7.22	2.29	267	0.63	0.53
Mania severity[b]	1.18	1.06	1.06	1.12	1.14	1.08	267	–0.85	0.4
Number of sessions	9.75	10.66	8.23	9.71	9.23	10.35	267	–1.13	0.26
Baseline Global Assessment of Functioning scale score	55.61	9.21	57.89	9.46	56.40	9.34	264	1.9	0.06
Comorbid conditions	3.69	2.30	1.20	1.40	2.84	2.39	266	–9.52	<0.01
	N	%	N	%	N	%	N	χ^2	p
Female	114	65	46	50	160	59	267	5.76	0.02
Education (>1 year of college)	135	76	76	83	211	78	262	2.03	0.13
Married	66	37	20	22	86	32	269	6.73	0.01
Diagnosis							269	1.02	0.31
Bipolar I disorder	115	65	54	59	169	63	—	—	—
Bipolar II disorder	62	35	38	41	100	37	—	—	—
>10 Manic episodes	106	60	38	41	144	54	269	8.34	0.01
>10 Depressive episodes	105	60	45	50	150	57	264	2.56	0.11
Baseline medications									
Mood stabilizers	58	33	19	21	77	29	269	4.35	0.04
Antidepressants	93	53	26	28	119	44	269	14.47	<0.01
Atypical antipsychotics	54	31	22	24	76	28	269	1.23	0.25
Anxiolytics	52	29	14	15	66	25	269	6.56	0.01
Anticonvulsants	106	60	40	44	146	54	269	6.57	0.01
Lithium	50	28	39	42	89	53	268	5.33	0.02

[a] Depressive severity refers to the summary score of depression symptoms from the Clinical Monitoring Form recorded within 1 week of the date of randomization to treatment.
[b] Mania severity refers to the summary score of mania symptoms from the Clinical Monitoring Form recorded within 1 week of the date of randomization to treatment.

Our exploratory analyses of the moderating role of anxiety in psychosocial treatment outcome, therefore, focused on the magnitude of the effect using the binary primary outcome variable of recovery status (recovered, not recovered) and the 95% confidence intervals for sensitivity and specificity according to the Newcombe-Wilson score method without continuity correction (41). The effect size proposed that seems to best reflect clinical significance for binary (success, failure) outcomes is the number needed to treat (42, 43). The number needed to treat is defined as the number of patients one would expect to treat with the investigational treatment (intensive psychotherapy) to have one more responder (or one less nonresponder) than if the same number were treated with the control condition (collaborative care). For a binary outcome, the responder rate difference is defined as the responder rate (r) with the investigational treatment (T) minus the responder rate with the control condition (C) (rT-rC), and number needed to treat=1/(rT-rC). For the investigational treatment better than the control treatment, the number needed to treat ranges from the ideal value of 1 to infinity; for the investigational treatment worse than the control treatment, the number needed to treat ranges from −1 to minus infinity (40). Using the number needed to treat, we compared those with and without lifetime anxiety disorder comorbidity on the magnitude of the between-group (collaborative care compared with psychotherapy) effect size. That is, the number needed to treat for recovered status was estimated separately for those with and without a comorbid lifetime anxiety disorder. An effect size of 2 is considered large; an effect size of 3.5 is considered medium; and effect sizes >9 are considered small (40).

Results

Study Sample

Of the 293 participants enrolled in the psychosocial outcome trial, 269 participants had diagnostic information available on anxiety disorder comorbidity. The 24 participants excluded from this analysis were distributed evenly across treatments (psychotherapy, N=14; collaborative care, N=10). Demographic and clinical characteristics of the included subsample of patients are presented in Table 1. The mean age was 40 years old (SD=11.64). Fifty-nine percent were female (N=160), and 78% (N=211) had greater than 16 years of education. Sixty-three percent (N=169) of these participants met criteria for bipolar I disorder, and 37% (N=100) met criteria for bipolar II disorder.

Consistent with the finding in the full sample (N=293), in this subset of 269 patients, those receiving psychotherapy had significantly higher year-end recovery rates (χ^2=3.83, df=1, p=0.05) than patients in collaborative care.

TABLE 2. Moderator Effects of Comorbid Anxiety Disorders on Collaborative Care and Psychotherapy for Bipolar Depression

Lifetime Anxiety Disorder	N	Number Recovered	Recovered (%)	Number Needed to Treat	SE[a]	95% CI
Yes						
Collaborative care	78	38	49	5.88	7.40	3 to 13
Psychotherapy	99	65	66			
No						
Collaborative Care	42	26	62	50.00	10.10	–6 to 5
Psychotherapy	50	32	64			

[a] Standard error reported is for the responder rate difference.

Anxiety Disorder Pathology

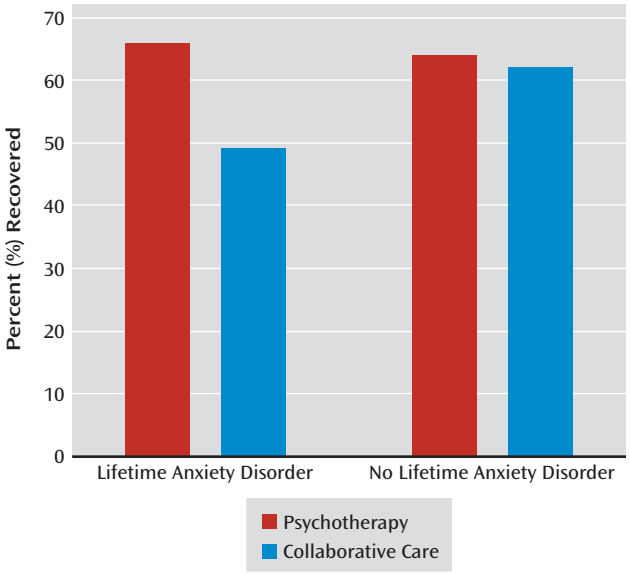
Groups were defined by the presence or absence of any lifetime anxiety disorder. A lifetime anxiety disorder was operationally defined as the presence of any current or past anxiety disorder as assessed by the Mini-International Neuropsychiatric Interview. Sixty-six percent (N=177) of the 269 patients with bipolar disorder met criteria for a comorbid lifetime anxiety disorder, whereas 34% (N=92) did not have a comorbid anxiety disorder (Table 1).

Patients with a lifetime anxiety disorder did not differ significantly from those without a lifetime anxiety disorder in age, bipolar type, education, the number of previous depressive episodes, age at illness onset, depressive severity, mania severity, or the number of therapy sessions completed or with regard to the proportion taking an atypical antipsychotic at study entry (Table 1). However, the lifetime anxiety disorders group consisted of a greater proportion of participants who were women, were married, and had greater than 10 lifetime episodes of mania/hypomania compared with the group with no lifetime anxiety disorders. Participants in the lifetime anxiety disorders group also had more comorbidities, were more likely to be taking a mood stabilizer other than lithium or an antidepressant, anxiolytic, or anticonvulsant, and were less likely to be taking lithium at study entry compared with those without a lifetime anxiety disorder. Participants without a lifetime anxiety disorder had higher levels of global psychosocial functioning, but the relationship fell short of significance. In demographic and clinical variables, these differences between patients with and without lifetime anxiety were not significantly associated with response to intensive psychotherapy or collaborative care, for those with lifetime anxiety, nor for those without lifetime anxiety.

Do Lifetime Anxiety Disorders Moderate Responses to Psychotherapy Compared With Collaborative Care?

We evaluated differential treatment effects of psychotherapy and collaborative care for patients with and without a lifetime anxiety disorder (Table 2, Figure 1). For patients with comorbid lifetime anxiety, 66% (N=65) recovered with psychotherapy, whereas only 49% (N=38) recovered with collaborative care. This corresponded to a small to medium effect size (number needed to treat=5.88). That is, among patients with comorbid anxiety disorders, one would need to treat approximately six patients with intensive psychotherapy compared with collaborative care to see one additional patient recover with psychotherapy. For patients without lifetime anxiety disorders, there was no difference between rates of recovery for those randomly assigned to psychotherapy compared with collaborative care: 64% (N=32) of patients without an anxiety disorder recovered with psychotherapy, and 62% (N=26) of patients without lifetime anxiety disorders recovered with collaborative care. This corresponded to a very small effect size (number needed to treat=50). That is, one would need to treat approximately 50 patients without a lifetime anxiety disorder with intensive psychotherapy compared with collaborative care to see one additional patient recover with psychotherapy.

FIGURE 1. Differential Treatment Effects of Psychotherapy and Collaborative Care for Bipolar Patients With and Without a Lifetime Anxiety Disorder



Effects of Specific Anxiety Disorders

We also investigated the effect of specific lifetime anxiety disorder diagnoses on treatment outcome. Of patients with a lifetime comorbid anxiety disorder, 55% (N=97) met criteria for panic disorder, 42% (N=74) for social phobia, 22% (N=39) for OCD, 36% (N=63) for PTSD, and 38% (N=68) for generalized anxiety disorder. Sixty percent

TABLE 3. Moderator Effects of Specific Anxiety Disorders on Collaborative Care and Psychotherapy for Bipolar Depression

	Psychotherapy			Collaborative Care					
Anxiety Disorder	N	Number Recovered	Recovered (%)	N	Number Recovered	Recovered (%)	Number Needed to Treat	SE[a]	95% CI
Panic Disorder									
Lifetime	59	34	57	38	17	44	7.69	10.30	–14 to 3
Current	32	20	63	19	10	53	10.00	14.29	–6 to 3
Social Phobia									
Lifetime	41	29	71	33	19	58	7.69	11.20	–12 to 3
Current	31	21	68	25	14	56	8.33	13.00	–8 to 3
Obsessive-compulsive disorder									
Lifetime	21	15	71	18	11	61	10.00	15.10	–6 to 3
Current	10	7	70	13	7	54	6.25	20.00	–5 to 2
Posttraumatic stress disorder									
Lifetime	45	28	63	18	8	44	5.56	13.80	–12 to 2
Current	14	9	64	10	4	40	4.17	20.10	–7 to 2
Generalized anxiety disorder									
Lifetime	42	25	60	26	7	27	3.03	11.50	2 to 12
Current	30	18	60	21	4	19	2.44	12.40	2 to 7

[a] Standard error reported is for the responder rate difference.

(N=25) of individuals with lifetime generalized anxiety disorder recovered with psychotherapy, whereas 27% (N=7) recovered in collaborative care. This corresponded to a medium to large effect size (number needed to treat=3.03) favoring response to psychotherapy (Table 3). A similar, although smaller, effect was observed for PTSD. Sixty-three percent (N=28) of individuals with lifetime PTSD responded to psychotherapy, whereas 44% (N=8) recovered in collaborative care. This corresponded to a small to medium effect size (number needed to treat=5.56) favoring response to psychotherapy. There were only small differences in recovery rates for psychotherapy compared with collaborative care for participants meeting lifetime criteria for panic disorder (number needed to treat=7.69, small to medium effect), social phobia (number needed to treat=7.69, small to medium effect), or OCD (number needed to treat=10, small effect).

Current Specific Anxiety Disorders

To determine the role of current anxiety, we also computed the effect size for the relative difference in response rates for intensive psychotherapy compared with collaborative care for patients with current anxiety disorders. The treatment effects for current generalized anxiety disorder and current PTSD resembled the effects for lifetime diagnoses (Table 3). Sixty percent (N=18) of participants with current generalized anxiety disorder recovered with psychotherapy, whereas 19% (N=4) recovered in collaborative care (number needed to treat=2.44). Sixty-four percent (N=9) of participants with current PTSD recovered with psychotherapy, whereas 40% (N=4) recovered in collaborative care (number needed to treat=4.17). There were only small differences in recovery rates for psychotherapy compared with collaborative care for participants meeting criteria for a current diagnosis of panic disorder (number needed to treat=10.00, small effect), social phobia (number needed to treat=8.33, small to medium effect), or OCD (number needed to treat=6.25, small to medium effect). When specific current anxiety disorders were collapsed, the effect for any current anxiety disorder was small (number needed to treat=9.09).

Number of Anxiety Disorders

We also conducted an additional analysis to examine whether recovery rates for psychotherapy and collaborative care differed according to the number of anxiety disorder diagnoses patients exhibited (Table 4). Eighty-four percent of participants with one lifetime anxiety disorder recovered from treatment with psychotherapy, whereas 53% recovered with collaborative care (number needed to treat=3.22, medium to large effect). In contrast, participants with two or more lifetime anxiety disorders did not differ in recovery rates for psychotherapy compared with collaborative care (number needed to treat=12.5, small effect). Fifty-four percent of individuals with two or more anxiety disorders responded to psychotherapy, and 46% responded to collaborative care. A similar pattern of treatment effects was observed for current anxiety disorders. Small to medium treatment effects favoring response to psychotherapy were observed for patients with only one current anxiety disorder (number needed to treat=4.76), whereas there was less of a difference in recovery rates for psychotherapy compared with collaborative care for individuals with two or more current anxiety disorders (number needed to treat=7.69, small to medium effect).

Discussion

To our knowledge, this is the first study investigating the effect of comorbid anxiety as a moderator of response to intensive psychotherapy compared with collaborative care

TABLE 4. Moderator Effects of the Number of Anxiety Disorders on Collaborative Care and Psychotherapy for Bipolar Depression

	Psychotherapy			Collaborative Care					
Anxiety Disorder	N	Number Recovered	Recovered (%)	N	Number Recovered	Recovered (%)	Number Needed to Treat	SE[a]	95% CI
Lifetime									
One anxiety disorder	38	32	84	40	21	53	3.22	9.90	2 to 9
Two or more anxiety disorders	61	33	54	37	17	46	12.5	10.40	–8 to 4
Current									
One anxiety disorder	11	9	71	23	14	58	4.76	15.50	–8 to 2
Two or more anxiety disorders	53	30	68	32	14	56	7.69	11.10	–12 to 3

[a] Standard error reported is for the responder rate difference.

in patients with bipolar depression. Our results suggest that depressed patients with bipolar disorder who have a lifetime anxiety disorder are more likely than patients without anxiety to respond to intensive psychotherapy compared with collaborative care. The between-treatment group effect size for those with lifetime anxiety disorder comorbidity was notably larger than the effect size for those without anxiety disorder pathology. When broken down into individual anxiety disorders, it appears that this moderating effect of lifetime anxiety is particularly pronounced in individuals who suffer from generalized anxiety disorder and PTSD.

The difference in response rates between intensive psychotherapy and collaborative care was driven by the apparent cost of anxiety disorder pathology to the collaborative care intervention; patients in intensive psychotherapy responded at similar rates regardless of the historical or current presence of an anxiety disorder (e.g., a 66% and 64% response rate for intensive psychotherapy compared with a 49% and 62% response rate for collaborative care for those with and without a lifetime anxiety disorder, respectively). Hence, those with past or present anxiety disorders appeared to need the more intensive intervention to recover. This effect was strongest when only one anxiety disorder was present (e.g., an 84% response rate compared with a 53% response rate for intensive psychotherapy versus collaborative care); with two or more anxiety disorders, the advantage of intensive psychotherapy was attenuated to a very small effect size (i.e., number needed to treat=12.5).

This apparent cost of anxiety disorder pathology to response rates in collaborative care was not observed for all anxiety disorders. When anxiety disorders were examined separately, patients with generalized anxiety disorder and PTSD had the most differential response to treatment relative to patients with panic disorder, social phobia, or OCD (although evaluation of effect for OCD was limited by sample size). Lower response rates for collaborative care compared with psychotherapy were observed for both current and lifetime generalized anxiety disorder and PTSD.

Our findings also suggest that response to intensive psychotherapy is robust for bipolar patients with one anxiety disorder, whereas efficacy is lost in the brief collaborative care intervention. This apparent effect of intensive psychotherapy stands in contrast to findings on pharmacologic management for bipolar disorder, in which any comorbid anxiety serves as a predictor of poorer response (35, 44). It is possible that individuals with one anxiety disorder need the more intensive intervention to achieve recovery, whereas individuals with multiple anxiety disorders have more treatment-resistant symptoms and are unlikely to achieve recovery even with intensive psychosocial approaches. As such, anxiety comorbidity may emerge as an important variable for the allocation of clinical resources, identifying individuals for whom intensive psychotherapy for bipolar disorder may be particularly important for treatment response. This observation awaits confirmation in a prospective study.

Some additional limitations of the study deserve comment. First, this study did not evaluate the potential role of psychotherapy targeting anxiety pathology directly. That is, we do not know whether the treatment benefits achieved were a result of the degree to which interventions could be applied to current or residual anxiety patterns or a result of the interpersonal and role challenges that accompany anxiety disorders (45–48). It is possible that the components of intensive psychotherapy (e.g., cognitive restructuring for CBT, problem solving for family-focused therapy and CBT, and solving role disputes for interpersonal social rhythm theory) targeted some of these difficulties more substantially than the collaborative care intervention, leading to the differential efficacy observed between the two treatments. Moreover, our analyses were limited by a sample size that was too low to examine individual therapy comparisons (e.g., CBT, family-focused therapy, and interpersonal social rhythm theory). It is also a possibility that the ingredients of certain interventions targeted anxiety pathology more or less than others. Second, there was little consideration of medication strategies, particularly medication changes throughout

treatment that may have contributed to the observed treatment effects. Although our analyses did indicate that baseline differences between those with and without a lifetime anxiety disorder in the proportion of patients taking certain classes of medication were not related to differential treatment response, an assessment of medication use and changes throughout treatment would be needed to help disentangle the relative effects of anxiety pathology and medication strategies on recovery outcome. Finally, randomization to treatments was not stratified based on anxiety status, and thus the results presented in this study should be considered exploratory. Replication in studies that allocate bipolar patients to treatments based on their anxiety comorbidity status is warranted.

Overall, our findings suggest that identifying anxiety in the context of bipolar disorder and understanding its relationship with psychosocial treatment efficacy is of value in terms of allocating clinical resources and improving patient care. Anxiety pathology may serve as an indicator for whom intensive psychotherapy for bipolar disorder may be particularly important with regard to treatment response. Specific aspects of anxiety disorder pathology, such as the anxiety disorder diagnosis and the number of anxiety disorders, deserve consideration in the assessment of the relative advantages of intensive psychotherapy compared with collaborative care. These preliminary results suggest that different psychosocial approaches may be needed for those with and without anxiety.

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Clinical Guidance: Psychotherapy Helpful for Bipolar Depression With Anxiety

Adding intensive psychotherapy to medication for depressed patients with bipolar I or II disorder increases the likelihood of recovery in those who also have a lifetime diagnosis of an anxiety disorder. The analysis by Deckersbach et al. did not show an advantage for depressed bipolar patients without a comorbid anxiety disorder or those with multiple anxiety disorders. Adjunctive intensive psychotherapy is especially effective for generalized anxiety disorder and posttraumatic stress disorder.