The Package of Care for Patients With Bipolar Depression

Eduard Vieta, M.D., Ph.D.

Although pharmacotherapy is the mainstay of the comprehensive program of medical care for the management of patients with bipolar disorder, the additional benefits of psychosocial interventions for the patient, family, and caregivers are now being recognized and increasingly adopted. Several facets of bipolar disorder can be addressed more effectively by instituting adjunctive psychosocial interventions. Recent clinical evidence indicates that combining pharmacotherapy with psychosocial interventions, which are tailored to patients' individual needs, may decrease the risk of relapse, improve patient adherence, and decrease the number and length of hospitalizations. A multidisciplinary approach may also enhance long-term patient outcomes such as mood stability, enhanced occupational and/or social functioning, and overall quality of life. Psychoeducation helps individuals become active and informed participants in the management of their illness, promoting a collaborative relationship between patients and their caregivers. However, psychosocial interventions are not useful for all patients with bipolar illness and may be more useful in addressing some problems than others. Evidence would suggest that psychosocial interventions, with continuing pharmacotherapy, are best used as prophylaxis and during periods of remission to prevent further episodes. Further randomized, clinical trials will help to define which components of psychosocial intervention are most effective in patients with bipolar disorder. *(J Clin Psychiatry 2005;66[suppl 5]:34–39)*

Most patients with bipolar disorder require a comprehensive and long-term program of medical care to help them overcome the symptoms and functional impairment associated with this highly recurrent psychiatric illness. Although pharmacotherapy is the mainstay of such a program, the additional benefits of psychosocial interventions for the patient, family, and caregivers are now being recognized and psychotherapy is increasingly being adopted. Numerous studies have examined the effects of adding psychosocial treatment to traditional and emerging pharmacotherapeutic options for bipolar disorder. This article considers aspects of bipolar disorder that may be improved by psychosocial interventions and the recommended goals of a combined package of pharmacotherapy and psychotherapy. In addition, clinical evidence for the effectiveness of a number of psychosocial interventions in the management of bipolar disorder is reviewed.

From the Clinical Institute of Neuroscience, Hospital Clinic, University of Barcelona, IDIBAPS, Barcelona, Spain.

This article is derived from the roundtable "The Burden of Bipolar Illness," which was held April 30, 2004, in New York, N.Y., and supported by AstraZeneca Pharmaceuticals, LP.

The author would like to acknowledge the editorial assistance of Aruna Seth, Ph.D. (PAREXEL Medical Marketing Services [MMS], Hackensack, N.J.). AstraZeneca provided financial support for this assistance.

Dr. Vieta has served as a consultant for AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen-Cilag, Lundbeck, Novartis, and Sanofi; has received research grants from AstraZeneca, Eli Lilly, GlaxoSmithKline, Janssen-Cilag, and Novartis; and has participated in speakers/advisory boards for AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen-Cilag, Organon, Pfizer, and UCB.

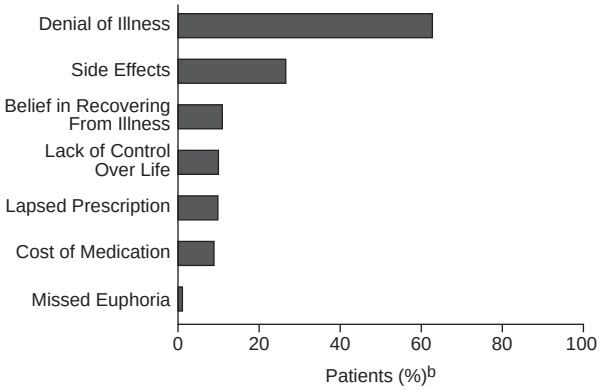
Corresponding author and reprints: Eduard Vieta, M.D., Ph.D., Clinical Institute of Neuroscience, Bipolar Disorders Program, Hospital Clinic, University of Barcelona, IDIBAPS, Villarroel 170/Rossello 140, 08036 Barcelona, Spain (e-mail: evieta@clinic.ub.es).

ROLE OF PSYCHOSOCIAL INTERVENTIONS IN TREATING BIPOLAR DISORDER

Several facets of bipolar disorder can be addressed more effectively by instituting adjunctive psychosocial interventions than by relying on medications alone. For example, education programs for patients, relatives, and the general public can improve awareness and understanding of bipolar disorder and help patients cope better with their illness. However, results of the GAMIAN-Europe/BEAM survey I, which involved 12 patient advocacy groups in 11 countries, found that this improvement in awareness and understanding of the illness is not sufficiently accomplished and there is an urgent need for patients to receive more information on bipolar disorder.[1] An analysis of completed questionnaires from patients with bipolar disorder (N = 1041) showed that over 70% felt that more information about their illness would be helpful, especially regarding the nature of the disease, how to manage symptoms on a day-to-day basis and in the long term, and availability of medications and their comparative efficacy and safety.[1]

Adherence to medication is a vital factor in the success of the long-term management of any chronic medical or

Figure 1. Reasons for Nonadherence in Patients With Bipolar Disorder[a]



[a]Data from Keck et al.[4]
[b]Patients may have cited more than 1 reason.

psychiatric condition, and improving adherence to medication is particularly important for patients with bipolar disorder, among whom approximately one third are known to take less than 30% of their medication as prescribed.[2] Nonadherence or poor adherence with psychotropic medications is frequently associated with recurrent affective episodes.[3–5] In a study of 140 patients receiving maintenance therapy, of whom 71 were noncompliant, the most common reason for poor compliance was denial of disease, accounting for 63% of the noncompliant patients (Figure 1).[4] Psychosocial intervention, particularly psychoeducation, has the potential to improve medication adherence by improving patients' insight into their condition and helping them to recognize the need for continuing medications.[6]

Nonadherence or poor adherence to medication may not only result in relapse and recurrence of mood episodes, but also in rehospitalization and suicide.[5] In a review of 11 studies that monitored adherence to treatment and patient outcomes, psychotherapeutic interventions (such as cognitive-behavioral therapy [CBT] and interpersonal group therapy, including education to promote illness awareness and the importance of treatment adherence) were most likely to result in positive long-term outcomes.[5] Psychotherapy, when combined with pharmacotherapy in long-term maintenance strategies, may decrease the risk of relapse, improve patient adherence, and decrease the number and length of hospitalizations.[5,7–10] Therefore, a multidisciplinary approach to the management of bipolar disorder integrating pharmacotherapy and psychosocial interventions may enhance long-term patient outcomes, such as mood stability, enhanced occupational and/or social functioning, and overall quality of life.

Cognitive impairment, which is frequently observed in patients with bipolar disorder and is related to poor functional outcome, may also be reduced with psychosocial intervention.[11] In a recent report, patients in all stages of bipolar illness, including those between acute episodes, had lower scores for verbal learning and memory, as well as for selective attention and executive function, than healthy subjects.[12] Patients experiencing depressive episodes were particularly affected by cognitive impairment.[12] The study also showed that patients with a history of psychotic symptoms, bipolar I disorder, longer duration of illness, and a high number of previous manic episodes were more likely to have neuropsychological disturbances. Psychosocial interventions may therefore help patients deal with the cognitive sequelae of bipolar disorder and achieve greater levels of functioning.

Psychoeducation helps individuals become active and informed participants in the management of their illness, promoting a collaborative relationship between patients and their caregivers. Patients' expectations of treatment, for example, should be managed through discussion of the options available, expected therapeutic effects (efficacy-effectiveness gap), possible side effects, and likely need for long-term medication. Limitations of pharmacologic therapy, such as medication refractoriness and treatment-emergent mania or depression, should also be discussed. Well-informed patients are psychologically better equipped to recognize these limitations, have increased confidence to engage in greater dialogue with their physicians, have less anxiety when new treatments are introduced, and are more likely to express treatment preferences and develop appropriate coping mechanisms. Self-monitoring of mood, life-charting, avoidance of high-risk situations and behaviors, identification of triggers, and regular sleep and medication patterns should be encouraged. The adoption of such measures may also help to reduce suicide risk.

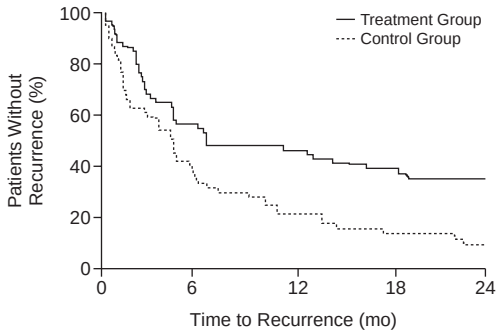
PRINCIPLES AND GOALS OF COMBINING PHARMACOTHERAPY AND PSYCHOSOCIAL INTERVENTIONS

Psychosocial interventions are not useful for all patients with bipolar disorder and may be more useful in addressing some of the problems of the illness than others. For example, patients who are in acute phases of bipolar disorder, especially those who exhibit psychotic features, are unlikely to gain additional benefit from adding psychosocial interventions to their pharmacotherapy.[13,14] Psychosocial interventions, with continuing pharmacotherapy, are best used prophylactically and during periods of remission to prevent further episodes. In this setting, psychosocial interventions should focus on the long-term consequences of bipolar disorder and on ways to lessen these consequences. Because of the chronic and recurring nature of bipolar disorder, there are many different domains to target in the course of the disease. As previously mentioned, effective treatment of acute symptoms is best accom-

Table 1. Goals of Pharmacotherapy and Psychotherapy for Bipolar Disorder

Goals of pharmacotherapy
Treatment of acute episodes
Treatment of psychotic symptoms
Goals of combined pharmacotherapy and psychotherapy
Prophylaxis of recurrences
Treatment of anxiety and insomnia
Prevention of suicide
Avoiding drug abuse
Treatment adherence
Improving impairment
Goals of psychotherapy
Information about and adjustment to chronic illness
Improve interepisodic functioning
Emotional support
Family support
Early identification of prodromal symptoms
Coping with psychosocial consequences of past and future episodes

Figure 2. Delay of Recurrences of Bipolar Disorder Observed When Group Psychoeducation Was Combined With Medication[a,b]



[a]Reprinted with permission from Colom et al.[8]
[b]Total N = 120. Between-group comparison: p < .003.

plished with pharmacotherapy. Some domains are responsive to psychotherapy in combination with pharmacotherapy, such as prophylaxis of recurrence, prevention of suicide and drug abuse, and overcoming functional impairment. Many areas can be addressed by psychotherapy alone, including the need for information about the illness, identification of prodromal symptoms, increasing emotional and family support, and coping with psychosocial consequences of acute episodes (Table 1). It should also be noted that adverse events may occasionally be associated with psychotherapy.[15]

Psychosocial interventions that have been used or are under investigation for maintenance treatment of patients with bipolar disorder include psychoeducation (individual and group sessions), CBT, family-focused therapy, and interpersonal and social rhythm therapy (IPSRT).[16]

EVIDENCE FROM CLINICAL STUDIES

Psychoeducation

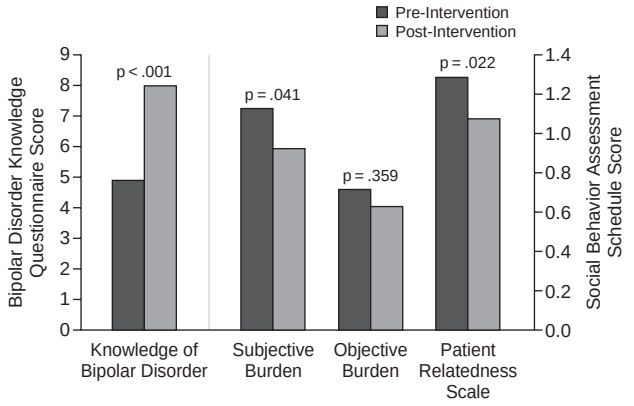
Psychoeducation approaches bipolar disorder as a biological disturbance that can be managed by pharmacologic as well as nonsomatic coping strategies. The primary goals of psychoeducation include reducing rates of relapse and hospitalization and improving functional outcomes by enhancing illness awareness, promoting early detection of prodromal symptoms, increasing medication adherence, and preventing suicidal behavior.[7,13] Because sleep deprivation has been associated with switching to mania, the promotion of healthy sleeping habits is an additional tool to prevent relapse.[13] Further, improvements in patients' quality of life can be expected by reducing stigma and guilt, increasing self-esteem and well-being, reducing comorbidities, and avoiding a stress-inducing lifestyle.[7]

Various psychoeducational approaches have proved effective in clinical studies. In a single-blind, randomized, controlled study, 69 patients who had had a relapse in the previous 12 months received routine care, either alone or combined with 7 to 12 (median = 9) individual treatment sessions with a psychologist.[17] Patients were educated to recognize their own (idiosyncratic) prodromal symptoms of relapse and to seek prompt medical attention when they occurred. Compared with patients who received routine care alone, patients receiving psychoeducation had significantly longer time to manic episodes (p = .008) and fewer manic episodes (p = .013) during the 18-month study. Sessions with the psychologist had no effect on time to depressive episodes or number of depressive episodes. However, overall social functioning measurements and employment rates were significantly improved with psychoeducation.[17]

The efficacy of group psychoeducation in preventing recurrences in remitted patients with bipolar I or II disorder receiving standard pharmacologic treatment was evaluated in a single-blind, randomized, controlled trial undertaken by the Barcelona Bipolar Disorders Program.[8] Patients (N = 120) received 21 weekly sessions of group psychoeducation or 20 sessions of nonstructured group meetings (control group). Experienced psychologists carried out both structured and nonstructured sessions, with 8 to 12 patients in each group. Psychoeducation included lectures and discussion about bipolar disorders, its causes and triggers, medications, and coping strategies.[8]

During treatment and the subsequent 2-year follow-up period, time to recurrence of both manic and depressive episodes and the number of overall recurrences per patient were significantly reduced in the psychoeducation group compared with the control group. Figure 2 shows survival analyses of patients in remission over the 2-year period. The reduction in number of all types of episodes, except manic episodes, was significantly greater in the psychoeducation group than in the control group during the 2-year follow-up period. Some of these improvements can be accounted for by increased adherence to pharmacotherapy. Although the mechanism of action of psychoeducation is unknown, prevention of depressive episodes may have

Figure 3. Benefits of Psychoeducation (family intervention) on Caregivers of Stabilized Bipolar Patients[a]



[a]Data from Reinares et al.[22]

been related to education about the importance of lifestyle regularity, whereas recognition of prodromal symptoms may have played a part in reduced numbers of manic episodes.[8]

Bipolar disorder in patients with comorbid personality disorders has been identified as particularly difficult to treat effectively.[18] In a subgroup of patients included in the above study who had comorbid personality disorders (N = 37), those randomized to the psychoeducation group had significant increases in time to recurrence and reductions in number of total, manic, and depressive episodes over the 2-year follow-up period.[19] The rate of hospitalizations was the same between the 2 groups, but patients in the psychoeducation group had significantly shorter durations of hospitalization than patients in the control group.[19]

Interpersonal and Social Rhythm Therapy (IPSRT)

Interpersonal and social rhythm therapy is individualized psychotherapy that focuses on improving the patient's psychosocial and interpersonal relationships as well as stabilizing social and biological rhythms. Because recurring episodes of bipolar disorder may be triggered by stressful life events and by psychological or physiologic disruptions, psychoeducation is used to help the patient recognize and regulate the foundations of these events as far as possible. In combination with pharmacotherapy, IPSRT may help patients achieve more stable social rhythms and interpersonal relationships, thereby reducing the risk of an affective episode.[20] A randomized, clinical trial is underway to evaluate IPSRT compared with intensive clinical management for patients with bipolar disorder receiving stable medication regimens.

Family-Focused Therapy

The support and cooperation of family and caregivers are very important components of successful management of patients with bipolar disorder. A randomized, controlled, open trial evaluated the effect on patient outcomes of integrating family-focused treatment with individual IPSRT sessions.[9] Thirty patients with bipolar disorder who had just experienced an acute episode were assigned to open treatment (up to 50 weekly sessions of family and individual therapy combined with mood-stabilizing medications), and outcomes over 1 year were assessed. Compared with patients who received standard community care (2 family educational sessions, mood-stabilizing medications, and follow-up crisis management) in a previous study (N = 70),[21] patients in the integrated family/individual therapy group had longer periods without relapsing and greater improvement in depressive symptoms. These preliminary findings have been confirmed recently in a randomized, controlled trial.[9]

In another study, psychoeducation for patients' relatives in group sessions was instrumental in increasing knowledge about bipolar disorder and significantly improving subjective burden among caregivers (Figure 3). During the course of the sessions, blame on the patient was increased in the control family group, but decreased in the psychoeducation group.[22]

Cognitive-Behavioral Therapy (CBT)

Cognitive-behavioral therapy focuses on the interactions between disordered thinking, mood, and behavior. Patients are taught to monitor and change automatic, dysfunctional thinking and behaviors that arise from their mood states, thus improving coping mechanisms and social functioning. The effects of CBT were assessed in a randomized, controlled, pilot study by Scott and colleagues.[23] Forty-two patients received immediate CBT for 6 months or were assigned to a 6-month waiting list with subsequent CBT (control group). After 6 months, those who received immediate CBT had more improvement in depressive symptoms and functioning than those in the control group. A total of 29 patients ultimately received CBT. In these patients, a 60% reduction in relapse rates in the 18 months after beginning CBT, compared with the 18 months before CBT, was observed. This study shows that CBT is beneficial in patients with bipolar disorder and suggests that it may be especially useful in the treatment of bipolar depression.[23]

CBT has also been evaluated specifically in another trial with bipolar depressed patients. In a pilot study, responses to CBT in patients with bipolar depression (N = 11) were compared with those in patients with unipolar depression (N = 11).[24] Patients with bipolar depression received mood-stabilizing medications, but no antidepressant therapy was allowed in either group. After 20 weeks of weekly therapy sessions, depression scores were significantly reduced from baseline in both groups. Although negative automatic thinking was significantly reduced in patients with bipolar disorder, measurements of underlying dysfunctional attitude did not change, suggest-

ing that longer courses of treatment, possibly between episodes, may be needed for these patients.[24]

Subsequently, a randomized, controlled trial of CBT designed to assess relapse prevention showed that patients (N = 103) who received 12 months of CBT in conjunction with their regular medications had significantly fewer mood episodes, days in an episode, and number of hospital admissions compared with patients in a medication-only control group.[25] Rates of depressive and manic episodes were significantly improved. In addition, medication adherence was increased (p = .06) and social functioning scores were significantly improved (p = .03) in the patients who received CBT compared with the control group.[25]

A recent trial,[14] however, suggested that patients with bipolar disorder who are acutely ill at the time of treatment may not actually benefit from CBT. No efficacy for preventing relapse was observed in a cohort of patients who had acute depressive symptoms, high numbers of episodes, and comorbid mental disorders.[14] These observations support the view that psychosocial interventions for patients with bipolar disorder are likely to yield the greatest benefit during periods of remission.

In the Barcelona Bipolar Disorders Program, the package of care comprises 2 important elements. First, pharmacotherapy is employed during the acute phases of illness to stabilize mood. In the nomenclature of Ketter and Calabrese,[26] this is treatment that stabilizes mood from above baseline (euthymia) in the case of hypomanic, manic, and mixed states and subsyndromal mood elevation (i.e., drugs that have antimanic properties) and from below baseline in the case of depressive symptomatology (i.e., drugs that have antidepressive properties). Second, treatments that stabilize mood from the center are used prophylactically during periods of remission. These include maintenance doses of pharmacotherapy as well as psychosocial interventions.

An important outcome of psychoeducation in this program has been the empowerment of some patients to have more control over their illness and treatment. Patients who have gained good awareness of their illness and are capable of understanding the properties of their treatments may be able to make minor adjustments to their own medication regimen. In addition, support from family or caregivers is an important component of this program.

CONCLUSIONS

Bipolar disorder is a complex illness that is difficult to treat effectively. Careful observations of patients in the community have revealed that, even with intensive pharmacotherapy, many are at least mildly symptomatic for long periods of time.[27,28] In this situation, every opportunity to improve patients' quality of life and social functioning must be explored and evaluated. Recent clinical evidence indicates that combining pharmacotherapy with psychosocial interventions, which must be tailored to patients' individual needs, has the potential to increase the chances of symptom resolution, long-term remission, and unimpaired social functioning.

Choice of medication is an important consideration for patients who are allowed to self-adjust their dose. The medication should work rapidly for breakthrough depressive symptoms and manic/mixed symptoms without inducing a switch in either direction. Also, the therapy should require only minor dose adjustments to be effective for changes in daily mood. In addition, a treatment that helps patients sleep may address the problem of sleep deprivation, which can induce mania. Allowing psychoeducated patients to make some medication decisions with a rapidly acting, effective agent enables patients to take more control over their illness.

To summarize the data presented here, psychosocial treatment is a critical component of care for patients with bipolar disorder. Empirical evidence demonstrates the complementary benefits associated with combining psychosocial interventions with standard pharmacotherapy. Further randomized, clinical trials will assist in defining which components of psychosocial intervention are most effective in patients with bipolar disorder.

REFERENCES

1. Morselli PL, Elgie R, GAMIAN-Europe. GAMIAN-Europe/BEAM survey 1: global analysis of a patient questionnaire circulated to 3450 members of 12 European advocacy groups operating in the field of mood disorders. Bipolar Disord 2003;5:265–278
2. Scott J, Pope M. Self-reported adherence to treatment with mood stabilizers, plasma levels, and psychiatric hospitalization. Am J Psychiatry 2002; 159:1927–1929
3. Colom F, Vieta E, Martinez-Arán A, et al. Clinical factors associated with treatment noncompliance in euthymic bipolar patients. J Clin Psychiatry 2000;61:549–555
4. Keck PE Jr, McElroy SL, Strakowski SM, et al. Compliance with maintenance treatment in bipolar disorder. Psychopharmacol Bull 1997;33: 87–91
5. Sajatovic M, Davies M, Hrouda DR. Enhancement of treatment adherence among patients with bipolar disorder. Psychiatr Serv 2004;55: 264–269
6. Vieta E, Colom F. Psychological interventions in bipolar disorder: from wishful thinking to an evidence-based approach. Acta Psychiatr Scand Suppl 2004;422:34–38
7. Colom F, Vieta E, Reinares M, et al. Psychoeducation efficacy in bipolar disorders: beyond compliance enhancement. J Clin Psychiatry 2003;64: 1101–1105
8. Colom F, Vieta E, Martinez-Aran A, et al. A randomized trial on the efficacy of group psychoeducation in the prophylaxis of recurrences in bipolar patients whose disease is in remission. Arch Gen Psychiatry 2003;60:402–407
9. Miklowitz DJ, Richards JA, George EL, et al. Integrated family and individual therapy for bipolar disorder: results of a treatment development study. J Clin Psychiatry 2003;64:182–191
10. Gonzalez-Pinto A, Gonzalez C, Enjuto S, et al. Psychoeducation and cognitive-behavioral therapy in bipolar disorder: an update. Acta Psychiatr Scand 2004;109:83–90
11. Martinez-Aran A, Vieta E, Colom F, et al. Cognitive dysfunctions in bipolar disorder: evidence of neuropsychological disturbances. Psychother Psychosom 2000;69:2–18
12. Martinez-Aran A, Vieta E, Reinares M, et al. Cognitive function across

manic or hypomanic, depressed, and euthymic states in bipolar disorder. Am J Psychiatry 2004;161:262–270
13. Colom F, Vieta E, Martinez A, et al. What is the role of psychotherapy in the treatment of bipolar disorders? Psychother Psychosom 1998;67:3–9
14. Scott J. What is the role of psychological therapies in the treatment of bipolar disorders? Eur Neuropsychopharmacol 2004;14(suppl 3):111–112
15. Vieta E. Improving treatment adherence in bipolar disorder through psychoeducation. J Clin Psychiatry 2005;66(suppl 1):24–29
16. Colom F, Vieta E. A perspective on the use of psychoeducation, cognitive-behavioral and interpersonal therapy for bipolar patients. Bipolar Disord 2004;6:480–486
17. Perry A, Tarrier N, Morriss R, et al. Randomized controlled trials of efficacy of teaching patients with bipolar disorder to identify early symptoms of relapse and obtain treatment. BMJ 1999;318:149–153
18. Black DW, Winokur G, Hulbert J, et al. Predictors of immediate response in the treatment of mania: the importance of comorbidity. Biol Psychiatry 1988;24:191–198
19. Colom F, Vieta E, Sanchez-Moreno J, et al. Psychoeducation in bipolar patients with comorbid personality disorders. Bipolar Disord 2004;6: 294–298
20. Frank E, Swartz HA, Kupfer DJ. Interpersonal and social rhythm therapy: managing the chaos of bipolar disorder. Biol Psychiatry 2000;48:593–604
21. Miklowitz DJ, Simoneau TL, George EL, et al. Family-focused treatment of bipolar disorder: 1-year effects of a psychoeducational program in conjunction with pharmacotherapy. Biol Psychiatry 2000;48:582–592
22. Reinares M, Vieta E, Colom F, et al. Impact of a psychoeducational family intervention on caregivers of stabilized bipolar patients. Psychother Psychosom 2004;73:312–319
23. Scott J, Garland A, Moorhead S. A pilot study of cognitive therapy in bipolar disorders. Psychol Med 2001;31:459–467
24. Zaretsky AE, Segal ZV, Gemar M. Cognitive therapy for bipolar depression: a pilot study. Can J Psychiatry 1999;44:491–494
25. Lam DH, Watkins ER, Hayward P, et al. A randomized controlled study of cognitive therapy for relapse prevention for bipolar affective disorder: outcome of the first year. Arch Gen Psychiatry 2003;60:145–152
26. Ketter TA, Calabrese JR. Stabilization of mood from below versus above baseline in bipolar disorder: a new nomenclature. J Clin Psychiatry 2002; 63:146–151
27. 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 Methods. J Clin Psychiatry 2003;64:680–690
28. Judd LL, Akiskal HS, Schettler PJ, et al. The long-term natural history of the weekly symptomatic status of bipolar I disorder. Arch Gen Psychiatry 2002;59:530–537

© COPYRIGHT 2005 PHYSICIANS POSTGRADUATE PRESS, INC.