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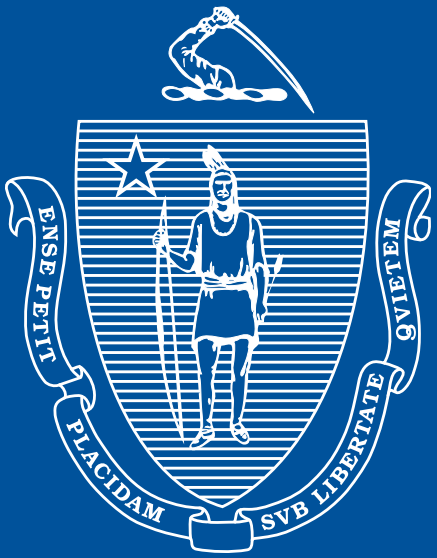
Clinical Practice Guidelines for the Treatment of Bipolar DIsorder in Adults



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CLINICAL PRACTICE GUIDELINES FOR THE TREATMENT OF

BIPOLAR DISORDER IN ADULTS

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Psychosocial Interventions as an Adjunct to Pharmacotherapy in Bipolar Disorder

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OBJECTIVE: TO SUMMARIZE THE EVIDENCE AND MAKE TREATMENT RECOMMENDATIONS REGARDING THE USE OF PSYCHOSOCIAL INTERVENTIONS AS AN ADJUNCT TO PHARMACOTHERAPY FOR BIPOLAR DISORDER.

METHODS: WE REVIEWED PUBLISHED OUTCOME STUDIES SINCE 1975 IDENTIFIED IN MEDLINE AND PSYCHLIT SEARCHES.

RESULTS: AVAILABLE STUDIES ARE INITIAL AND OF HIGHLY VARIABLE METHODOLOGICAL RIGOUR. EVIDENCE IS MOST ROBUST FOR THE EFFICACY OF PSYCHOEDUCATION AND FAMILY THERAPY, AND THESE RECEIVED THE HIGHEST LEVEL OF RECOMMENDATION AS INTERVENTIONS. GROUP THERAPY, COGNITIVE-BEHAVIOURAL THERAPY, AND BEHAVIOURAL FAMILY MANAGEMENT THERAPY ARE SUPPORTED BY WEAKER EVIDENCE AND RECEIVED A LOWER-LEVEL TREATMENT RECOMMENDATION. AVAILABILITY OF ONLY A SINGLE INTERPERSONAL AND SOCIAL RHYTHMS THERAPY TRIAL LIMITED THE CONFIDENCE OF THE RECOMMENDATION FOR THIS INTERVENTION.

CONCLUSIONS: CONTROLLED TRIALS ARE NEEDED TO REPLICATE EARLY OUTCOME STUDIES AND GUIDE TREATMENT RECOMMENDATIONS. ACCUMULATED EVIDENCE OF FAVOURABLE PSYCHOSOCIAL INTERVENTION OUTCOMES SUPPORTS, WITH VARIABLE CONFIDENCE, THEIR USE AS ADJUNCTS TO PHARMACOTHERAPY IN THE TREATMENT OF BIPOLAR DISORDER.

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KEY WORDS: BIPOLAR, PSYCHOSOCIAL, PHARMACO-

Bipolar disorder is often associated with severe social and occupational deficits that persist after the acute phase and during maintenance on pharmacotherapy (1-3). The majority of discharged bipolar patients experience functional impairment after discharge from hospital (4). These issues reflect the impact of a number of problems relating to the disorder: acceptance of the illness by the patient and family, adherence to medication and other management, alcohol and substance abuse, *suicide, possible victimizations*, and social risk factors. Financial and employment difficulties (5), self-esteem injury, divorce (6), and relationship dysfunction (5) are all losses the bipolar patient may have to face. Anticipated lack of fulfilment in future relationships or educational and occupational plans may also contribute to a sense of loss. Because bipolar disorder is a chronic illness with recurrences and relapses, denial, anger, ambivalence, and anxiety may develop as the patient and family adjust to the diagnosis (7). Denying or minimizing the vulnerability of relapse is a coping mechanism often adopted by those with the illness and their caregivers. Prodromal mood instability preceding the development of the disorder frequently predisposes the patient and family to conflict (8).

Recommendation 4: Therapeutic Alliance and Psychoeducation

Therapeutic Alliance

All psychosocial and medical interventions need to be employed with sensitivity to the importance of the therapeutic relationship between the individual and the provider. A supportive therapeutic relationship should be established in order for the individual to trust the clinician and the team, and thus collaborate with treatment. This relationship will also inform the clinician of early symptom relapse. Part of an essential ingredient of this alliance is an atmosphere in which the individual may feel free to discuss various aspects of his or her illness, including satisfaction or dissatisfaction with medications. The clinician and/or team should create an atmosphere in which the individual can feel free to discuss what he/

she experiences as negative in the treatment process so that continued participation in meaningful and effective treatment is enhanced. Periodic reassessment of the treatment plan, including a psychosocial history, in collaboration with the individual, to make modifications in accord with the individual's preferences and needs should be practiced. The clinician and/or team should work closely with the individual's family when permission is given. Decisions about which treatments are pursued is a shared process between the individual seeking services and the clinician. For the clinician and/or team working with individuals who are culturally diverse, regular consultation with a competent bilingual and bicultural clinician or cultural consultant should be strongly considered when the clinician and/or team are not familiar with the individuals' culture. For individuals who are limited or non-English speakers, the availability of a competent interpreter for the clinician and/or team at all times is critical.

Maladaptive coping frequently involves ignoring recommended pharmacotherapy regimens, which results in illness exacerbation (9). In recent-onset manic patients, partial compliance rates with lithium have been reported to be as high as 70% (3), and noncompliance rates often reach 60% on this medication (10-12). Almost all compliant patients seriously consider discontinuing lithium at some stage, and if they do, they discontinue it abruptly (13). Patients receiving carbamazepine may have higher rates of adherence (14). The prediction of medication noncompliance is complicated by the contribution of numerous factors, including the nature of the patient-physician relationship (15), the patient's understanding of the illness, previous history of poor medication adherence (7), and patient dislike of having "mood controlled" (10). Abrupt discontinuation of medication carries with it a high risk of relapse (17).

The frequency and the timing of illness episodes are probably affected by social environment stressors (18). Prior to illness recurrence, bipolar patients seem to experience more life events than controls without mental illness (19,20), *perhaps including developmental stressors such as early parental loss (Agid, 1999),*and in a prospective study, the relative risk of recurrence was markedly elevated in those with high life stress scores (21, *Hammen & Gitlin, 1997*). Several prospective studies have reported a positive correlation between high expressed emotion as a measure of family affective tone and poor outcome among bipolar patients (3,22).

Various psychotherapeutic approaches have been used with bipolar patients with putative mechanisms of change hypothesized to involve closer monitoring of affective symptomatology, earlier environmental modification following life events, enhanced compliance with pharmacotherapy, enhanced social support, improved

familial adjustment, regulation of daily routines, and enhancement of coping strategies (23). The major psychotherapeutic modalities that may be helpful for some patients are psychoeducation, group therapy, cognitive-behavioural therapy, family therapy, and the 2 newer therapies of interpersonal and social rhythm therapy, and behavioural family management for bipolar disorder. The evidence supporting these interventions suffers from considerable methodological shortcomings. The recommendation to include a psychosocial dimension of care in selected patients is based on a strong clinical consensus that there is at least preliminary support for psychosocial interventions as an adjunct to pharmacotherapy. This situation may soon be improved as several methodologically rigorous trials using manualized psychotherapies as an augmentation to medication maintenance are now in progress (24). Although the recommended psychosocial modalities will be discussed separately, clinical practice often involves a synthesis of approaches adapted to the patient's needs and preferences, as well as the therapist's resources.

Psychoeducation

Psychoeducation has been an important component of many of the group and family interventions reported below, with evidence suggesting that this psychoeducational component was important in facilitating compliance with treatment and favourable clinical outcome. Several controlled studies used the psychoeducational approach exclusively and reported enhanced compliance with lithium. A 6-session psychoeducation intervention, designed from a cognitive therapy perspective, improved lithium compliance and clinical outcome in a randomized controlled trial (25). In that study, patients receiving the intervention had a lithium noncompliance of 21% and significantly fewer hospital admissions than the control group, which received "treatment as usual" and had a lithium noncompliance rate of 57%. In another study, bipolar patients randomized to formal educational lectures on video tape and a written transcript significantly enhanced both their attitude toward and compliance with lithium as compared with the control group (26,27).

Psychoeducation may also be effective in improving patients' partners' knowledge about the illness, medication, and social support strategies for at least 6 to 18 months (28,29), but the effect of these interventions on major mood disorder relapse and retention of educational benefit is not known.

Psychoeducation should include but not be limited to the following topics as appropriate:

1. *Recognition and acceptance of illness*
2. *Identifying triggers to relapse and early signs of trouble*
3. *Standardizing daily routines*
4. *Dealing with friends and family and minimizing stressors*
5. *Learning how to cope with mood changes*
6. *Medication education*
7. *Potential risks of substance use*
8. *Information about self-help groups*
9. *Family Planning*
10. *Risk of sexually transmitted diseases*
11. *Information regarding resources and referrals to support services such as, Day Treatment, Social Day Programs, Supported Education and Employment (SEE), the American Psychiatric Association (www.psych.org), the American Psychological Association (www.APA.org), Career Centers (www.looksmart.com), the Knowledge Exchange Network (www.mentalhealth.org), the Manic Depressive Association (www.namda.org), Mass Rehabilitation Commission (MRC)(www.state.ma.us/mrc.htm), the National Alliance for the Mentally Ill (www.nami.org), and the National Institute for Mental Health (www.mentalhealth.org), [These references should not be considered an endorsement of the sources cited. The Committee has not reviewed the content of the information distributed by these organizations or that which is posted on their websites. There are many other sources of information and referrals which are available to individuals, their caregivers, and clinicians.]*
12. *Efforts should be made to make psychoeducation understandable, given the individual's language, culture, and reading level.* Overall, the quality of evidence for psychoeducation is "1," that is, there is at least one randomized controlled trial, and the working group classification of recommendation was "A," that is, good support for the intervention to be considered in clinical practice.

Recommendation 5: Family Therapy

Family Therapy

Early reports of eclectic-based family therapy in bipolar patients without systematic follow-up concluded that this intervention could enhance lithium compliance, reduce relapse, and improve family communication (30). Subsequently, several other more systematic family therapy studies have reported improvement in global outcome. A randomized controlled trial of 6 inpatient family intervention sessions in 169 inpatients assessed global function outcome 18

months after discharge. Of the 21 bipolar patients (14 female) in the treatment group, the female patients demonstrated immediate and long-term improvement in social, family, leisure, and occupational performance, as well as family attitude toward treatment, compared with the female controls and male bipolar patients, who demonstrated either no benefit or negative effect (31,32). Interpretation of this study is limited by unreported rates of illness relapse or rehospitalization and uncertainty about control of the medication regimen.

Overall, the quality of evidence for family therapy is "1," that is, at least one randomized control trial, and the working group classification of recommendation was "B," that is, fair support for the intervention to be considered in clinical practice.

Due to scheduling and other constraints, family therapy may be difficult to fully utilize. However, family members can and should be integral partners in the rehabilitation process through regular involvement and contact, as confidentiality allows. There is a wide spectrum and level of involvement that the family may have in the treatment plan so that treatment plans can reflect the uniqueness of each family system. The family often has more contact and a longer history with the individual, which can often have a positive effect on treatment outcomes.

Recommendation 6: Group Therapy

Group Therapy

Several open, uncontrolled trials provide the most robust assessment of group therapy (plus lithium) in the treatment of bipolar patients. The overall frequency and length of hospitalization per year diminished (16.8 to 3.6 weeks of hospitalization per year), while rates of regular employment and lithium compliance significantly improved over 2 years among 13 lithium-responsive bipolar patients involved in interpersonal group therapy (33). A follow-up report on this trial noted a generally higher rate of lithium compliance in the group therapy patients. Delineating the psychotherapy-specific effects from the nonspecific effects of close follow-up, however, is not possible (34). Outpatient group therapy in bipolar patients (12 women, 10 men) focusing on interpersonal relationships has been reported to reduce hospital admissions over a 4-year period (35). The significance of these results is uncertain given a dropout rate of greater than 50%. The persistence of reduced hospitalization rates and improved psychosocial and economic functioning was perceived to have been a benefit of group therapy and has extended beyond a decade of the intervention (36). Group psychotherapy in

combination with psychoeducation and case management may also be an effective approach in the male geriatric outpatient population (37).

Overall, the quality of evidence for group therapy was "2.3," that is, very significant results from uncontrolled trials from more than one centre comparing results with and without interventions, and the working group classification of recommendation was "C," that is, poor support for the intervention to be considered in clinical practice.

Recommendation 7: Cognitive Therapy

Cognitive Therapy

The cognitive-behavioural literature in the treatment of bipolar disorder is sparse. Cognitive therapy principles were employed in the psychoeducation intervention described earlier. Open reports have suggested a role for cognitive therapy in bipolar depression (23; Zaretsky 1997, unpublished observations). A cognitive-behavioural therapy and psychoeducation-oriented treatment manual was recently designed for the purpose of improving medication compliance and promoting patient awareness of maladaptive information processing in an attempt to prevent illness relapse (38).

Overall, the quality of evidence for cognitive therapy rated a "3," that is, opinions of respected clinical authorities based on clinical experience, descriptive studies, or reports of expert committees, and the working group classification of recommendation was "B," that is, fair support for the intervention to be considered in clinical practice. This recommendation was made despite the limited amount of evidence in view of the strong evidence for its efficacy in unipolar depression and the likelihood that cognitive therapy does not pose significant risks of side effects or a switch into mania.

Recommendation 8: Behavioural Family Management Therapy

Behavioural Family Management Therapy

Adapted from a therapeutic approach used in schizophrenia treatment, this social skill- and education-based family therapy consists of a functional assessment of the family unit, psychoeducation, and training in communication and problem-solving skills (39,40). Twenty-one sessions over 9 months, with additional crisis intervention as required, comprises the treatment. A small (N = 9) uncontrolled trial of this therapy conducted in the

setting of close medication monitoring revealed an 11% rate of mood disorder recurrence during a 9-month posthospital follow-up (39). Randomized controlled behavioural family management clinical trials are currently in progress (40).

Overall, the quality of evidence for behavioural family management therapy merits a "3," that is, opinions of respected clinical authorities based on clinical experience, descriptive studies, or reports of expert committees, and the working group classification of recommendation was "C," that is, poor support for the intervention to be considered in clinical practice.

Recommendation 9: Rehabilitation Services and Interpersonal and Social Rhythm Therapy

Rehabilitation Services

Persons with bipolar disorder who have any of the following characteristics should be offered Rehabilitation Services which may include but are not limited to Occupational Therapy and Vocational Rehabilitation. Rehabilitation Services are indicated if the person demonstrated functional deficits that significantly interfere with participation in daily life responsibilities, roles, and interests. Such areas include: 1) Activities Of Daily Living: grooming, dressing, feeding, medication routine, health maintenance, socialization, functional communication, functional mobility, emergency response, 2) Work and Productive Activities: home management, care of others, educational opportunities, vocational activities, and 3) Leisure Exploration And Leisure Performance: which include the ability to experience and identify new and personally fulfilling leisure interests and the ability to engage and increase skill levels in activities of past leisure pursuits.

Occupational Therapy Serivces provide functional capacity evaluations, treatment, and environmental adaptations to maximize an individual's physical and cognitive abilities. Such services can be useful when determining an individual's readiness to resume life roles and responsibilities (school, work, parenting, driving, etc.) after manic or depressive episodes. Occupational Therapy assists individuals in establishing healthy daily routines and balancing individuals' roles and responsibilities (American Occupational Therapy Association, 2000).

Vocational Rehabilitation Services provides work skill evaluations and training in work skill development. These interventions enhance the individual opportunity to increase functional vocational skills and improve the work behaviours needed to find, obtain, and maintain gainful employment.

Interpersonal and Social Rhythm Therapy

This therapeutic model attempts to unify the social and interpersonal models of affective disorder and the social rhythm stability hypothesis (24,41-43). This hypothesis proposes that mood regulation is in part a function of the regularity of daily activity and social stimulation patterns insofar as these patterns affect biologically based circadian rhythms. According to this model, derived primarily from observations in unipolar depressed patients, mood-disordered patients are particularly susceptible to social and circadian rhythm change (18,42). The goal of interpersonal and social rhythm therapy is to standardize a patient's daily rhythms and resolve key interpersonal problems that destabilize the mood state and/or daily rhythm (24,43). Preliminary evidence from a randomized clinical trial suggests that this therapy with medication is associated with improved regularity of daily rhythms over 52 weeks as compared with control group patients from the same outpatient medication clinic (44). The effect of this intervention on medication compliance, global functioning, and illness course, however, is uncertain at this stage.

Overall, the quality of evidence is "1," that is, there is at least one randomized controlled trial of this intervention, but the working group classification of recommendation was only "C," in other words, there was poor support for the intervention to be considered in clinical practice in view of the reliance on a single study without sufficient replication and without extensive published data on the clinical outcomes. The working group recognized, however, that like cognitive therapy, interpersonal and social rhythm therapy presents low risks to patients who are also on other adequate treatment and that the normalizing of social and biological rhythms can be beneficial.

Quality of Psychosocial Evidence

Few studies employed outcome measures that had been demonstrated to be both valid and sufficiently reproducible. Only psychoeducation, cognitive therapy, and brief inpatient family therapy interventions with follow-up during the continuation phase of the illness are supported by some trials, one of which was a single published trial in which bipolar patients were randomized to either the intervention of interest or control treatment (25,27,32). Small sample sizes often increase the risk of a type II error. To date there are no published randomized controlled trials examining the efficacy of interpersonal, behavioural, cognitive, marital and family, group, or social rhythm therapies in bipolar disorder maintenance treatment.

Although research on psychosocial interventions in bipolar disorder is limited and subject to methodological flaws, a recent review article of 32 peer-reviewed studies (Huxley, Parikh, & Baldessarini, 2000) reported on 14 groups, 13 couples or family, and 5 individual therapy interventions in conjunction with standard pharmacotherapy. The sample included a total of 1052 patients. These studies utilized psychoeducational, interpersonal or cognitive-behavioural approaches and reported consistent beneficial effects, which included reduced morbidity, reduced hospitalizations, improved social functioning, and/or improved vocational functioning. While additional research is needed, the results to date strongly support the use of psychosocial approaches with standard psychopharmacology in treating bipolar patients.

Clinical Recommendations

Available research and clinical experience provide strong evidence to support the use of psychoeducation, regardless of the phase of the disorder, but particularly in the first few episodes. The best format for psychoeducation—individual, group, or family-based intervention—remains unclear; each type has some demonstrated efficacy. Maintaining a treatment alliance must remain as a principal objective throughout all phases, relying on supportive therapy principles when the patient is more acutely ill. During the manic phase, no formal psychotherapies have been demonstrated to be useful; instead, psychotherapeutic techniques such as alliance building, limit setting, supportive measures, reduction of stimuli, and behavioural techniques may be needed. During the depressed phase, cognitive-behavioural therapy should be considered for selected patients, particularly those with mild bipolar depression. Some evidence exists to support the use of interpersonal and social rhythm therapy interventions during the continuation and maintenance phases of bipolar treatment. Substantial evidence suggests a role for family therapy intervention in selected cases to reduce stigmatization and negative expressed emotion, which may provoke relapse *and to provide education to improve an individual's ability to recognize the signs and symptoms of relapse*. Patient utilization of support and advocacy groups, for example, the Canadian Mental Health Association and the National Depression and Manic Depression Association, may also be beneficial.

Clinical Implications

- Maintaining a treatment alliance must remain a principal objective throughout all phases, relying on supportive therapy principles when the patient is more acutely ill.
- During the manic phase, no formal psychotherapies have been demonstrated to be useful; instead, psychotherapeutic techniques such as alliance building, limit setting, supportive measures, reduction of stimuli, and behavioural techniques are potential strategies.
- During the depressed phase, cognitive-behavioural therapy or interpersonal and social rhythms therapy should be considered for selected patients.
- Substantial evidence suggests a role for family therapy intervention in selected cases to reduce stigmatization and negative expressed emotion, which may provoke relapse.
- Psychoeducation can be a valuable tool in promoting therapeutic alliance and a collaborative approach to effective treatment.

Limitations

- Review of literature is narrative and data are not quantitatively analyzed.
- Evidence available is initial, is of variable methodological quality.

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