

## **Is Your Depressed Patient Bipolar?**

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## **ABSTRACT**

Accurate diagnosis of mood disorders is critical to their effective treatment. Distinguishing between major depression and bipolar disorders, especially the depressed phase of a bipolar disorder, is essential, since they differ substantially in their genetics, clinical course, outcomes, prognosis, and treatment. In current practice, bipolar disorders, especially bipolar II disorder, are underdiagnosed. Misdiagnosing bipolar disorders deprives patients of timely and potentially lifesaving treatment, particularly considering the development of newer and possibly more effective medications for both depressive features and the maintenance treatment (prevention of recurrence/relapse). This article focuses specifically on how to recognize the identifying features suggestive of a bipolar disorder in patients who present with depressive symptoms or who have previously been diagnosed with major depression or dysthymia. This task is not especially time-consuming, and the interested primary care or family physician can easily perform this assessment. Tools to assist the physician in daily practice with the evaluation and recognition of bipolar disorders and bipolar depression are presented and discussed.

## INTRODUCTION

Studies have demonstrated that a large proportion of patients in primary care settings have both medical and psychiatric diagnoses and require dual treatment.<sup>1</sup> It is thus the responsibility of the primary care physician, in many instances, to correctly diagnose mental illnesses and to treat or make appropriate referrals. Much progress has been made over the past two decades in establishing the importance of depressive disorders in primary care settings and in improving their recognition and correct diagnosis. As bipolar disorders tend to be a less-recognized illness, however, the possibility of bipolar disorder in a patient who presents with depressive features is rarely contemplated. Not a single mention of bipolar depression was made in a recent statement from the International Consensus Group on Depression and Anxiety.<sup>2</sup> This lack of attention has serious consequences, as morbidity and mortality, such as functional impairment and suicide, are substantially greater in bipolar disorders than in major depression, and the psychiatric treatments of the two disorders are distinctly different.<sup>3-5</sup> Whereas antidepressants are the treatment of choice for major depression, current guidelines recommend that antidepressants not be used in the absence of mood stabilizers in patients with a bipolar disorder,<sup>6</sup> although more research is needed to clarify optimal treatment for patients with bipolar disorder who do not have type I disorder.<sup>7</sup>

Distinguishing between major depressive (unipolar) disorder and bipolar disorders, especially the depressive phase of bipolar disorders, is extremely important before instituting treatment for depression. “Unipolar” depression is characterized by a single mood pole, that of major depression, and fulfills specific defined criteria (APA).<sup>8</sup> Table 1 summarizes current *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision* (DSM-IV-TR) criteria for major depressive disorder. Bipolar disorders can be seen as having three distinct

phases: the *depressed phase*, which mimics the clinical picture of major depression (lower pole), the *manic* or *hypomanic phase* (upper pole), and *euthymia*, or the asymptomatic phase. Tables 2 and 3 summarize diagnostic criteria for hypomania and mania. Manic and hypomanic episodes are characterized by grandiosity, inflated self-esteem, diminished need for sleep, increased goal-directed activity and talkativeness. Mania and hypomania are distinguished by the fact that mania is of longer duration, causes more functional impairment, and may be associated with psychotic features. Sometimes patients present with mixed episodes, in which patients experience both manic and depressive symptoms, with associated severe functional impairment. It is important to note that for a diagnosis of bipolar I disorder, only one lifetime manic or mixed episode is required.<sup>9</sup> For a diagnosis of bipolar II disorder, the manual specifies that at least one hypomanic and one depressive episode occur in the absence of manic or mixed episodes.<sup>9</sup>

### **HOW COMMON ARE BIPOLAR DISORDERS?**

In the past, bipolar disorder was believed to have a prevalence approximating 1.5%<sup>10</sup>; however, more recent evidence suggests that actual prevalence rates approach 5.5% when the *spectrum* of bipolar illness is considered.<sup>11-15</sup> This represents a continuum of mood states that includes the traditionally accepted bipolar I and bipolar II disorders, as well as mood swings that do not satisfy the DSM-IV defined criteria for bipolar I and II disorders, but still result in significant functional impairment.<sup>12,15-18</sup> This broader concept of bipolar disorders is currently evolving, and remains an area of some debate among experts. Suffice it to say that bipolar disorders appear to be much more common than previously believed, and are thus likely to be encountered with more frequency in the primary setting than previously thought.

## **MISDIAGNOSING BIPOLAR DEPRESSION AS UNIPOLAR DEPRESSION**

Awareness of a condition is a prerequisite for making the diagnosis. To paraphrase Voltaire, if you don't know about it you can't look for it; if you don't look for it, you can't find it. There is compelling evidence that both psychiatrists and primary care physicians miss the diagnosis of bipolar disorder, especially bipolar II disorder.<sup>19-21</sup> Patients may also fail to mention the presence of manic, and more commonly, hypomanic, symptoms in a past or current episode.<sup>22</sup> This may be in part related to poor insight which is predominant during manic episodes, but may be present in all phases of the illness, and even during remission.<sup>23-25</sup> Despite low patient reporting rates and low physician pick-up rates, screening for bipolar disorders in patients presenting with depressive symptoms is seldom conducted, even in patients with a high risk of bipolar disorders.<sup>26</sup> As many as 40% of both in- and out-patients diagnosed with depression are subsequently found to have bipolar disorders.<sup>27,28</sup> Most striking is that these were patients who had already experienced at least 1 manic or hypomanic episode prior to receiving the diagnosis of major depression. Similar findings have been demonstrated in other studies.<sup>29,30</sup> In addition, an average of 8 years elapses from time of first presentation to correct diagnosis in patients with bipolar disorder.<sup>31</sup>

Therefore the problem of diagnosing bipolar disorders is threefold: current diagnostic classification failings contribute in part (see below), while failure of the physician to recognize previous hypomanic or manic symptoms and failure of patients to report them, also play a role.

## **CONSEQUENCES OF MISDIAGNOSIS**

Missing the diagnosis of a bipolar disorder could have serious and even occasionally fatal consequences for a person with the illness. Lifetime risk of suicide attempts among patients with

bipolar disorders ranges from 25% to 50%,<sup>32</sup> and estimates of completed suicide in persons with a bipolar disorder diagnosis are between 10% and 15%.<sup>7</sup> Epidemiologic data also reveal that suicide attempts occur 30 times more frequently during depressive episodes than during manic or hypomanic states.<sup>4</sup>

Misdiagnosis and inappropriate treatment can also prolong suffering and contribute to worsening occupational, family, and social problems. The situation is particularly concerning because the use of antidepressants in bipolar depression, especially without the concomitant use of a mood stabilizer, may actually worsen the course of the disease. Antidepressants have been shown to contribute to rapid-cycling,<sup>28,33</sup> in which patients experience more mood swings than are normally seen, with at least 4 episodes of mania/hypomania and/or depression over a 1 year period. Rapid-cycling patients experience more episodes of illness, with progressively shorter periods of wellness and a diminished response to medication.<sup>34</sup> At the present time, it is unclear whether the use of mood stabilizers in conjunction with an antidepressant protects against the development of rapid cycling.

## **DISTINGUISHING BETWEEN UNIPOLAR AND BIPOLAR DEPRESSION**

As previously mentioned, a critical distinction between unipolar and bipolar depression is the presence of a history of manic or hypomanic symptoms in patients with bipolar disorders. It is more frequently patients with bipolar II disorder that are misdiagnosed, than those with bipolar I disorder,<sup>20</sup> for the following reasons: (1) Often the patient feels remarkably well when hypomanic and is therefore unlikely to spontaneously report these episodes and may even deny them when directly questioned. (2) Patients with hypomania don't present with psychotic symptoms, nor are they hospitalized, so there may be no indication or records of a previous

hypomanic episode. (3) Several prominent researchers have argued that the usual duration of hypomanic symptoms is actually only 1 to 3 days,<sup>12,15,35-38</sup> and that current DSM-IV-TR diagnostic criteria (requirement for 4 days of hypomania) could incorrectly preclude the appropriate diagnosis in patients with hypomania of shorter duration. (4) Clinically, patients with mild hypomania may present with irritability rather than the euphoria, or an exaggerated sense of well-being that is often associated with an elevated mood state, further challenging the physician.

On the other hand, as many as 35% to 60% of patients with bipolar disorders may experience an episode of major depression before experiencing a manic episode,<sup>27</sup> making the distinction between bipolar disorders and major depression (unipolar depression) substantially more difficult if not impossible. The presence of hypomanic or manic episode(s) is required in order to meet criteria for a diagnosis of bipolar disorders, and until that seminal episode occurs, it would be virtually impossible to diagnose anything other than major depression. However, as soon as the event occurs, the prior “misdiagnosis” needs to be updated to reflect the true bipolar disorder.

## **MAKING THE CORRECT DIAGNOSIS**

In light of these challenges, what strategies can the busy primary care physician use to significantly increase the recognition of bipolar disorders and bipolar depression, and particularly bipolar II depression (where frank mania has not been evidenced) in daily practice? Screening for hypomania and manic symptoms, identifying features that may be indicative of bipolar disorders, and careful patient interviews that include, when possible and appropriate, evidence from at least 1 other informant, are helpful to making the correct diagnosis.

## **Screening for Manic and Hypomanic Symptoms**

Ruling out bipolar disorders should be a routine part of the workup for all patients who present acutely with depressive symptoms or who report a history of depression. As is the case with other medical disorders, the use of a brief, standardized screening instrument can be quite helpful. The Mood Disorder Questionnaire (MDQ) is a good tool for this purpose.<sup>39</sup> The MDQ is a 1-page questionnaire with 13 yes/no items and 2 additional questions regarding function and timing of symptoms (Appendix A). In a validation study of the MDQ, a score of 7 or above yielded a sensitivity of 73% and a specificity of 90%.<sup>39</sup> Any patient can easily complete this survey in less than 5 minutes, enabling its integration into a routine office visit, when the patient can fill it out prior to seeing the physician. It is important to note there is recent evidence to suggest that the MDQ tends to underdiagnose bipolar II disorder due to its requirement for moderate to severe impairment of functioning, when improved functioning is frequently seen in those with hypomania.<sup>40</sup> The author has recommended removing the impairment criterion in order to appropriately diagnose bipolar II disorder.

## **Identifying Features of Bipolar Depression**

A generation ago, it was widely believed that there were no differences between unipolar depression and bipolar depression.<sup>41</sup> Since then, a number of clinical features have been recognized that may be used to distinguish between major depression (unipolar) and the depressed phase of a bipolar disorder (bipolar depression) or at least increase awareness of the possibility of a bipolar disorder diagnosis in a patient presenting with symptoms of depression (Table 4). These include younger age at onset (ie, < 25 years),<sup>28,41-43</sup> the presence of atypical symptoms,<sup>14</sup> such as excessive sleepiness, and weight gain, as well as symptoms of psychomotor

retardation,<sup>30</sup> the presence of psychotic features,<sup>22,44</sup> and the presence of comorbid substance abuse.<sup>10,11</sup> A family history of bipolar disorder can also point to the possibility of a bipolar diagnosis<sup>45-47</sup> (see the Family History Screen by Weissman et al.<sup>48</sup>) Other features that can suggest the presence of bipolar illness in a depressed patient include multiple depressive recurrences (> 3 episodes), brief duration of the depressive illness (< 3 months), and past or current antidepressant-induced mania or hypomania,<sup>49</sup> as well as the presence of mixed depressive episodes, in which hypomanic symptoms are present during a depressive episode.<sup>50</sup> An acute, but not prolonged, response to antidepressants, where response to the antidepressant wears off over time is also suggestive of a bipolar disorder.<sup>49</sup>

Bipolar illness is also characterized by a more pronounced seasonal pattern than is observed in major depression, with winter depressions being the most common.<sup>51</sup> There is a greater likelihood of mood disturbance occurring during the postpartum period; as many as half of all women with bipolar spectrum disorder experiencing an episode of depression, mania, or mixed states after the birth of a child.<sup>51</sup> In fact, for many women, the first presentation of a bipolar disorder is a postpartum episode.<sup>52</sup> Any woman without a prior psychiatric history who develops postpartum depression should be closely followed and monitored, as the risk for developing a bipolar disorder may be especially high.

### **Interviewing a Family Member or Other Informant**

There are a number of reasons why it is advisable to attempt to interview the patient's spouse, parent, child, "significant other," or close friend. Patients may fail to recall manic or hypomanic symptoms, or have no insight into the impact their symptoms may have had on their functioning. On the other hand, many patients value their heightened activity and energy during hypomanic

states and fail to report them as pathologic. Other patients may fear the stigma associated with bipolar disorders. Interviewing someone close to the patient can often provide historical clues to the correct diagnosis.<sup>22</sup>

## **TREATING THE PATIENT WITH BIPOLAR DEPRESSION**

While correct identification of bipolar depression often lies in the hands of the primary care physician, referral or close consultation with a psychiatrist must be strongly considered in treating these patients. The psychopharmacology of the spectrum of bipolar disorders, and its many incarnations, is much more complicated and entails greater risk than that of major (unipolar) depression.<sup>53</sup> Additionally, in these patients polypharmacy is the rule, with only 20.6% of patients with bipolar disorders being managed with monotherapy.<sup>54</sup>

A comprehensive discussion of pharmacotherapy for bipolar disorders is beyond the scope of this paper, however some key issues will be mentioned. Lithium has been the “gold standard” of treatment of bipolar disorders for many decades. In more recent years, the emergence of several anticonvulsants with mood stabilizing properties, among them divalproex, carbamazepine, and lamotrigine, as well increasing recognition of the utility of atypical antipsychotics such as olanzapine, risperidone, quetiapine, and ziprasidone has bolstered the physician’s armamentarium for treating bipolar disorders.

Numerous agents are approved for treating mania, among them a number atypical antipsychotics such as olanzapine, risperidone, quetiapine, and ziprasidone. Recently, the olanzapine-fluoxetine combination was approved for treatment of depressive episodes in bipolar disorders; this combination was demonstrated to efficacious based on an 8-week randomized controlled double-blind trial in patients with bipolar depression.<sup>55</sup> While there was no evidence

of treatment emergent mania in this study,<sup>55</sup> the risk for developing of mania associated with the use of fluoxetine will need to be adequately evaluated. Lithium, olanzapine, and lamotrigine are FDA-approved for maintenance therapy; lamotrigine's approval specifies use for maintenance therapy of bipolar I disorder.

The emergence of multiple newer agents for treating bipolar disorders has meant that medications can be selected for not only efficacy, but also tolerability. Lithium has numerous side effects, a narrow therapeutic index, and a fatal overdose risk,<sup>56</sup> however it is the only agent demonstrated to data to reduce risk of suicide in patients with bipolar disorders.<sup>57-59</sup> Divalproex, which is used preferentially for manic rather than depressive states, is associated with weight gain, tremor, hepatotoxicity, and many drug-drug interactions.<sup>60</sup> Carbamazepine, while never FDA-approved for the treatment of bipolar disorders, has been studied and shown to be efficacious, but requires serum level monitoring and carries a risk hyponatremia and a low risk of blood dyscrasia.<sup>61</sup> Lamotrigine has demonstrated efficacy in bipolar depression<sup>62</sup> and in prevention of depressive recurrence in subjects with bipolar disorders.<sup>63,64</sup> It must be carefully titrated and monitored to avoid the possibility of serious rash,<sup>65</sup> but does not require blood monitoring and is associated with minimal weight gain, sexual side effects, sedation, or cognitive impairment. Olanzapine, quetiapine, and risperidone, and some of the other atypical antipsychotics have been associated with the dysmetabolic syndrome marked by weight gain,<sup>66</sup> an increased risk of diabetes,<sup>67</sup> and elevated triglycerides occasionally accompanied by pancreatitis. Therefore monitoring of patients is required when these agents are to be used in the longer term, in conjunction with the ADA/APA Consensus Statement on Antipsychotic Medications and Obesity.<sup>68</sup>

Antidepressant therapy in patients with bipolar disorders presents unique difficulties. While treatment with antidepressant monotherapy is discouraged in current guidelines for bipolar disorder treatment,<sup>6,7</sup> use of antidepressants may be necessary in some patients. The current APA guideline<sup>7</sup> recommends use of bupropion and paroxetine as first-line antidepressant therapy, however, these are the only antidepressants that have been evaluated for use in bipolar disorders in randomized controlled trials to date that have demonstrated a relatively low risk of manic switch, therefore conclusions cannot be drawn regarding their supremacy over other antidepressants in treatment of bipolar disorders. Clinicians generally agree that other SSRIs, such as sertraline, are just as effective and safe, and that MAOIs are also relatively unlikely to promote switching into mania.

Another reason to consider a psychiatric referral is that patients with bipolar disorders have a highly variable course of illness with evolving, difficult-to-predict, clinical features. Careful charting of mood symptoms (Appendix B) and ongoing psychiatric assessment are often required to clarify each patient's particular pattern of disease and provide optimal treatment. The extremely high incidence of comorbid substance abuse also complicates disease management and increases treatment noncompliance and negative outcomes.

Finally, the degree of psychosocial morbidity for people with bipolar disorders can be substantial.<sup>7</sup> The divorce rate is 2 to 3 times higher than that of the general population,<sup>45</sup> and a majority of people so diagnosed experience some form of chronic occupational, social, or family difficulties,<sup>7</sup> which may be alleviated to some extent by adjuvant psychosocial interventions.<sup>7</sup> All of these problems are more appropriately dealt with in a mental health setting.

## **CONCLUSION**

Bipolar disorders are a very serious group of illness that are undoubtedly more commonly seen in primary care settings than was previously appreciated. They are associated with greater morbidity and mortality than major (unipolar) depression, and treatments for unipolar depression and bipolar depression differ significantly. However, according to Bowden, “[e]very systematic study ... finds ... a large proportion of patients with bipolar disorders receive a diagnosis of major depression.”<sup>22</sup> This problem will persist until primary care physicians and even general psychiatrists develop a keen awareness of the possibility of the diagnosis of a bipolar disorder in patients presenting with symptoms of depression. This is particularly true for patients with bipolar II disorder, as their history does not include the more easily identifiable mania seen in bipolar I disorder. It is therefore imperative that physicians consider the differential diagnosis of bipolar disorders to be a routine component of the workup of any patient presenting with depressive symptoms or a history of depression. In addition, there is a need to address and revise existing diagnostic criteria for bipolar disorders in order to facilitate increased and appropriate recognition of the illness.

Although the diagnosis of bipolar disorder is frequently missed, there are several very useful strategies that can help physicians improve diagnostic accuracy: screening for manic symptoms, identifying features of the depression that are more typical of bipolar disorders, and interviewing a family member/significant other. Once the diagnosis is made, referral to a psychiatrist or working in close collaboration with a psychiatrist should result in the safest and most comprehensive treatment.

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**Table 1:** Diagnostic Criteria for Major Depressive Disorder

**Major Depressive Episode**

- Five or more of the following symptoms (present for at least 2 weeks):
  1. Depressed mood most of the day, nearly every day
  2. Markedly diminished interest or pleasure in all, or almost all activities most of the day, nearly every day
  3. Significant weight loss or weight gain
  4. Insomnia or hypersomnia nearly every day
  5. Psychomotor retardation or agitation nearly every day
  6. Fatigue or loss of energy nearly every day
  7. Feelings of worthlessness or excessive or inappropriate guilt nearly every day
  8. Diminished ability to think or concentrate or indecisiveness nearly every day
  9. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt, or specific plan for committing suicide
- Includes a change from previous functioning.
- At least one symptom is either depressed mood or loss of interest or pleasure.
- Note: Do not include symptoms due to a medical condition/mood incongruent delusions or hallucinations
- Symptoms do not meet criteria for a Mixed Depressive Episode
- The symptoms cause clinically significant distress/Impairment in social occupational, or other important areas of functioning
- The symptoms are not due to a substance (drug abuse/medication) or general medical condition (eg, hypothyroidism)

- The symptoms are not better accounted for by bereavement

### **Single Episode**

- Presence of a single Major Depressive Episode.
- The Major Depressive Episode is not better accounted for by Schizoaffective Disorder and is not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

- There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode.

**Note:** This exclusion does not apply if all of the manic-like, mixed-like, or hypomanic-like episodes are substance or treatment induced or are due to the direct physiological effects of a general medical condition.

### ***Recurrent***

- Presence of two or more Major Depressive Episodes.
- **Note:** To be considered separate episodes, there must be an interval of at least 2 consecutive months in which criteria are not met for a Major Depressive Episode.
- The Major Depressive Episodes are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
- There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode.

**Note:** This exclusion does not apply if all of the manic-like, mixed-like, or hypomanic-like episodes are substance or treatment induced or are due to the direct physiological effects of a general medical condition.

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Publishing, Inc, 2000: 375–376

**Table 2:** Diagnostic Criteria for Manic Episode

- A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary)
- During the period of mood disturbance, 3 or more of the following symptoms have persisted (4 if the mood is only irritable) and have been present to a significant degree:
  - (1) inflated self-esteem or grandiosity
  - (2) decreased need for sleep (eg, feels rested after only 3 hours of sleep)
  - (3) more talkative than usual or pressure to keep talking
  - (4) flight of ideas or subjective experience that thoughts are racing
  - (5) distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli)
  - (6) increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
  - (7) excessive involvement in pleasurable activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)
- The symptoms do not meet criteria for a Mixed Episode
- The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features
- The symptoms are not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication, or other treatment) or a general medical condition (eg, hyperthyroidism)

Note: Manic-like episodes that are clearly caused by somatic antidepressant treatment (eg, medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of Bipolar I Disorder

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**Table 3:** Diagnostic Criteria for Hypomanic Episode

- A distinct period of persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual nondepressed mood
- During the period of mood disturbance, 3 or more of the following symptoms have persisted (4 if the mood is only irritable) and have been present to a significant degree:
  - (1) inflated self-esteem or grandiosity
  - (2) decreased need for sleep (eg, feels rested after only 3 hours of sleep)
  - (3) more talkative than usual or pressure to keep talking
  - (4) flight of ideas or subjective experience that thoughts are racing
  - (5) distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli)
  - (6) increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
  - (7) excessive involvement in pleasurable activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)
- The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic
- The disturbance in mood and the change in functioning are observable by others
- The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features
- The symptoms are not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication, or other treatment) or a general medical condition (eg, hyperthyroidism)

**Note:** Hypomanic-like episodes that are clearly caused by somatic antidepressant treatment (eg, medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of bipolar II disorder.

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**Table 4: Features Indicative of Bipolar Disorders**

	<b>Bipolar</b>	<b>Unipolar</b>
Substance abuse	Very high	Moderate
Family history	Almost uniform	Sometimes
Seasonality	Common	Occasional
First episode < 25 years	Very common	Sometimes
Postpartum illness	Very common	Sometimes
Psychotic features < 35 years	Highly predictive	Uncommon
Atypical features	Common	Occasional
Rapid on/off pattern	Typical	Unusual
Recurrent major depressive episodes (>3)	Common	Unusual
Antidepressant-induced mania or hypomania	Predictive	Uncommon
Brief major depressive episodes (avg. <3 months)	Suggestive	Unusual (episode duration usually > 3 months)
Wearing off of antidepressant efficacy	Suggestive	Uncommon
Mixed depression (presence of hypomanic features within the depressive episode)	Predictive	Rare

Data from Calabrese JR, Bowden CL, Sachs G, Yatham LN, Behnke K, Mehtonen OP, et al. A placebo-controlled 18-month trial of lamotrigine and lithium maintenance treatment in recently depressed patients with bipolar I disorder. *J Clin Psychiatry* 2003;64:1013-24; Hirschfeld RMA, Bowden CL, Perlis RH, Gitlin MJ, Suppes T, Keck PE, et al. Practice guideline for the treatment of patients with bipolar disorder (revision). *Am J Psychiatry* 2002;159:1-50; Whybrow PC: A

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## Appendix A

### Mood Disorder Questionnaire

Instructions: This questionnaire is an important part of providing you with the best health care possible. Your answers will help in understanding problems that you may have. Please answer each question as best you can.

- |  | YES                      | NO                       |
|--|--------------------------|--------------------------|
| 1 Has there ever been a period of time when you were not your usual self and...  |                          |                          |
| you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble? | <input type="checkbox"/> | <input type="checkbox"/> |
| you were so irritable that you shouted at people or started fights or arguments?   | <input type="checkbox"/> | <input type="checkbox"/> |
| you felt much more self-confident than usual?  | <input type="checkbox"/> | <input type="checkbox"/> |
| you got much less sleep than usual and found you didn't really miss it?  | <input type="checkbox"/> | <input type="checkbox"/> |
| you were much more talkative or spoke much faster than usual?  | <input type="checkbox"/> | <input type="checkbox"/> |
| thoughts raced through your head or you couldn't slow your mind down?  | <input type="checkbox"/> | <input type="checkbox"/> |
| you were so easily distracted by things around you that you had trouble concentrating or staying on track?                           | <input type="checkbox"/> | <input type="checkbox"/> |
| you had much more energy than usual?   | <input type="checkbox"/> | <input type="checkbox"/> |
| you were much more active or did many more things than usual?  | <input type="checkbox"/> | <input type="checkbox"/> |
| you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?                    | <input type="checkbox"/> | <input type="checkbox"/> |

- you were much more interested in sex than usual?
- you did things that were unusual for you or that other people might have thought were excessive, foolish or risky?
- spending money got you or your family into trouble?
- 2 If you checked YES to more than one of the above, have several of these ever happened during the same period of time?
- 3 How much of a problem did any of these cause you – like being unable to work; having family, money or legal troubles; getting into arguments or fights? *Please circle one response only.*
- No problem      Minor problem      Moderate problem      Serious problem
- 4 Have any of your blood relatives (i.e., children, siblings, parents, grandparents, aunts, uncles) had manic depressive illness or bipolar disorder?
- 5 Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?

Courtesy of The University of Texas Medical Branch. This instrument is designed for screening purposes only and is not to be used as a diagnostic tool.

## Appendix B

Mood Chart. *Instructions:* Patient should rate themselves each morning and evening (thus 2 columns for each date of the month). There is a normal range of mood and patient should use all three levels of “normal.” The 3 levels of elevated and depressed mood should be viewed as mild, moderate, severe as defined by the patient.

Name/ Month/Year																																																														
Date: AM/PM	1	1	2	2	3	3	4	4	5	5	6	6	7	7	8	8	9	9	10	10	11	11	12	12	13	13	14	14	15	15	16	16	17	17	18	18	19	19	20	20	21	21	22	22	23	23	24	24	25	25	26	26	27	27	28	28	29	29	30	30	31	31
<b>Mood:</b>																																																														
Severe elev.																																																														
Moderate elev.																																																														
Mild Elevation																																																														
Normal High																																																														
Normal																																																														
Normal Low																																																														
Mild dep.																																																														
Moderate dep.																																																														
Severe dep.																																																														
<b>Circumstances:</b>																																																														
Menses																																																														
Thyroid Function																																																														
Alcohol																																																														
Caffeine																																																														
Hours Slept																																																														
<b>Medication:</b>																																																														
Lithium Dose																																																														
Lithium Level																																																														
Depakote Dose																																																														
Depakote Level																																																														
Lamictal Dose																																																														
Lamictal Level																																																														
Tegretol Dose																																																														
Tegretol level																																																														
<b>Other Meds:</b>																																																														
Antidepressant																																																														
Anxiolytic																																																														
Sedative																																																														
Antipsychotic																																																														
<b>Special Events</b>																																																														

