REVIEW ARTICLE

Unipolar & Bipolar Disorder: A Primary Care Perspective

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Mood disorders are a group of mental health conditions that afflict an estimated 21 million American adults each year. Due to the high incidence of mood disorders, including depression and bipolar disorder, in the general population, a family physician must be prepared to recognize and appropriately evaluate, diagnose and treat, a patient with a persistent alteration in their mood. This article will provide a general overview of two major types of mood disorders: unipolar and bipolar disorders, and will provide primary care physicians with additional tools for approaching such conditions in the adult population.

INTRODUCTION

In a given year, approximately 20.9 million Americans or nearly a tenth of Americans, aged 18 and older, suffer from a mood disorder.[1, 2] The vast majority of all patients suffering from a mood disorder present to the primary care physicians' office first, and sometimes, they never follow up with a psychiatrist. Despite a substantial segment of the American population being impacted, this group of mental disorders remains among the most difficult to diagnose and treat in the primary care setting. One of the most common reasons is thought to include the primary care physician's lack of fluency and/or aid in distinguishing the fine line between normal variation and mental disease. However, an even more significant factor may also be consternation, borne of compassion, about rendering a psychiatric disorder diagnosis, which still carries a significant social stigma and may further complicate daily life for the patient.

In this article, we will attempt to provide guidance to enhance the primary care physician's ability to and confidence in diagnosing, treating, and if necessary, referring a patient to a psychiatrist, with a particular focus on unipolar depression and bipolar disorders. While this article will not eradicate the social stigma associated with these illnesses, we hope that earlier detection may help patients' to better cope with their condition before it may become debilitating and in a subset cause the attempts and completions of life ending measures.

IMPACT

UNIPOLAR DEPRESSION

Unipolar depression is an umbrella term that includes several disorders such as dysthymic disorder and major depressive disorder, the latter being the leading cause of disability among Americans ages 15-44.[3] In a given year, nearly 14.8 million American adults, or about 6.7 percent of the American population age 18 and older suffer from major depressive disorder.[1, 2] Major depressive disorder can arise at any age but the average age of onset is 32.[4] Women are two times more likely to develop major depression disorder and have a lifetime risk of 20% versus 10 % in males.[5, 6] On the other hand, dysthymic disorder has an incidence of 1.5% for the American adults.[1] The most recent census data suggest the current adult population 18yo+ is 239,516,413 and this suggests 3,592,746 adult Americans currently suffer from this condition.[2] The median age of onset for dysthymic disorder is 31.[1]

BIPOLAR DISORDER

Similarly to unipolar depression, bipolar disorder also afflicts a significant number of people both in America and worldwide.

- The World Health Organization ranks bipolar disorder as the sixth leading cause of disability among people ages 15-44.[3]
- In a given year, 8,161,765 American adults, or about 2.6% of the population age 18 and older, are affected by bipolar disorder.[1, 2]
- The median age of onset for bipolar disorders is worryingly young at just 25 years.[4]

ETIOLOGY

Due to the multifactorial etiology of unipolar and bipolar disorders, treatment requires a deep understanding of the mood disorders, along with an intricate balance of skill that providers must possess to successfully treat such ailments.[7] Although there is a particularly strong link that exists between family history and diagnosis of unipolar and bipolar disorders; due to their historical under recognition and under diagnosis, it is not so simple for a physician to collect a history with

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positive family history with a diagnosis of a mood disorder. Therefore, the physician must also look to a family history of an undiagnosed unipolar or bipolar disorders.

- Patients who have first-degree relatives with major depression should be observed more closely for symptoms of unipolar and bipolar disorders.[5]
- Patients with one parent who is bipolar have a risk of 27% to 29% of developing the disorder; while patients with two affected parents have a 50% to 74% chance.[5]
- Studies using monozygotic twins as subjects show that the genetic contribution to developing major depression is 37%, while that of developing bipolar disorder is 80%.[7]

CLINICAL PRESENTATION

As a primary care physician, once you suspect your patient is suffering from a mood disorder, it will become critical to try to eliminate other possible mood disorders as possibilities, and then to distinguish unipolar depression from bipolar disorder. Unlike a variety of physical illnesses that can be observed and diagnosed at an isolated point in time, an accurate diagnosis of mood disorder requires a thorough history of symptoms prior to as well as presenting at the visit. This can be a daunting task for physicians; most notably due to time limitations and heavy patient reliance on historical clues. A sound rapport with the patient is thus an essential component to successful diagnosis and treatment of patients with mood disorders. Refer to Tables 1 and 2 for presenting symptoms of depression and mania.

UNIPOLAR DEPRESSION

Unipolar depression most often appears in the form of major depressive disorder and/or dysthymic disorder. Common presentations for major depression include depressed mood, lack of interest in things once pleasurable (also termed anhedonia), changes in sleep, decreased concentration and energy, significant changes in weight, feelings of hopelessness and guilt, psychomotor agitation or retardation, and recurrent thoughts of death. According to the Diagnostic and Statistical Manual of Mental Disorders V (DSM-V), the criterion for diagnosis is five or more of the aforementioned symptoms being present for at least two weeks. Patients do not have to admit to a depressed mood to be diagnosed with major depression but if they don't admit to a depressed mood, they must admit to anhedonia.[8]

Note, when screening for unipolar disorder, one must also rule out bipolar disorder.

BIPOLAR DEPRESSION

Bipolar disorder is classified as either Type I or Type II. Bipolar disorder has recurrent episodes of depressed mood with each episode lasting at least 2 weeks. In bipolar Type I disorder the patient has both mania (severely elevated mood causing impairment of judgment such as law disobedience) and depression, while only one manic episode is necessary for this diagnosis. In bipolar Type II disorder patients have episodes of both hypomania (mild elevation in mood without causing impairment of judgment) and depression.[8]

In contrast to bipolar Type II disorder, patients need not have any history of depression in bipolar type I diagnosis.

For the diagnosis of a manic episode, either hospitalization or 3 of the symptoms in Table 2 must be presenting in the patient and can be easily recalled with the acronym DIG FAST.

TABLE 1:

Presenting Symptoms of Depression

Symptoms of Depression "People From SAD CREW"
Psychomotor agitation or retardation
Feelings of hopelessness or guilt
Sleep changes
Anhedonia
Depressed mood
Concentration(decreased)
Recurrent thoughts of death
Energy (decreased)
Weight changes

TABLE 2:

Presenting Symptoms of Mania

Symptoms of Mania "DIG FAST"
Distractibility
Irresponsibility
Grandiosity
Flight of ideas/Increased goal oriented activity
Agitation (Psychomotor)
Sleep (decreased need)
Talkativeness/pressured speech

Carlat, D. The psychiatric review of symptoms: a screening tool for family physicians. American Family Physician 58(7): 1617-1624, 1998.

SCREENING

The U.S. Preventative Services Task Force (USPSTF) recommends screening all adult and pediatric (age 12-18) patients for depression when the physician has services in place to ensure correct diagnosis, favorable treatment, and follow up.[9, 10]

Physicians have several options at their disposal to utilize for screening purposes, from simple self-reported questionnaires to more complex instruments.

We have found self reporting screening tests to be quite convenient and accurate for the proper diagnosis of unipolar disorder. The simplest of these screening tests consists of one question that asks "are you depressed?"

The PHQ-2, a two question screening test, addresses the patients' mood and anhedonia. The questions are:

- During the past month, have you been bothered by feeling down, depressed, or hopeless?
- During the past month, have you been bothered by little interest, or pleasure doing things?

Longer self-reporting screening tools used include:

- Zung Self-Rating Depression scale
- The PHQ-9
- Beck Depression Inventory (BDI-II)
- The Center for Epidemiologic Studies-Depression Scale (CES-D).

With the exception of the PHQ-9, the above tests must be followed up with a full clinical interview focusing on psychiatric history. The PHQ-9 asks each specific symptom of major depression and therefore establishes the diagnosis of major depression without any requirement for further confirmation. This screening test can also be used to track patient symptoms and responsiveness to treatment. The above-mentioned questionnaires are available at www.depression-primarycare.org/clinicians.

The previously mentioned screening tests are all based on patient self-reporting. Another widely used screening test is the Hamilton Depression Scale (HDRS). Unlike the other screening tests, HDRS requires a trained professional to administer it. The results of the HDRS are positively correlated to the BDI-II with a Pearson r of 0.71, meaning there is more than a 70% chance of the same diagnosis using either screening tool.[11]

Currently, there are no fixed screening guidelines for bipolar disorder, except when considering use of Antidepressants or when the patient presents with conclusive symptoms of bipolar or unipolar.

Mood Disorder Questionnaire (MDQ), a one-page questionnaire that covers symptoms, timing and duration. Some other useful screening tools include the Bipolar Spectrum Diagnostic Scale, the My Mood Monitor Checklist (also called M-3). The above stated screening methods are available at www.dballiance.org/pdfs/MDQ.pdf. It is important to recognize the resources listed above possess a high negative predictive value and thus are good at ruling out mood disorders but by no means do they suffice to confirm a diagnosis.[12] When suspecting bipolar disorder, all other etiologies first must be ruled out before diagnosis of bipolar disorder can be made.

A majority of bipolar patients self-report their self-assessment of depression to their primary care physicians. Rather than reporting the mania present, it is often misdiagnosed as having unipolar depression. Up to 30% of patients exhibiting depressive symptoms actually may have a bipolar disorder.[13] It bears repeating that a patient does not need to have any history of depression to be diagnosed with bipolar Type I disorder and the requirement that the individual simultaneously meet full criteria for both mania and major depressive has been removed from DSM-V.[14] Signs that should alert the primary care provider to bipolar disorder in a patient with depressive symptoms, include a family history of bipolar disorder, precipitation of a hypomanic or manic episode in response to an anti-depressant treatment, symptoms arising before age 25, failure to respond to three or more trials of an antidepressant medication, abrupt onset and offset of episodes, possible seasonal pattern or the presence of atypical depressive symptoms such as hypersomnia.[15]

EXCLUDING OTHER CAUSES

It is important to note, before making a mood disorder diagnosis, one must rule out physical causes such as thyroid disease and anemia. This can be easily performed by ordering a complete blood count and a thyroid stimulating hormone level. In addition to the above labs, in the elderly patient, workup should also include a vitamin B12 level, a serum folate, and a rapid plasma reagin.[16] B12 and folate deficiencies can present with depressive symptoms mimicking a mood disorder. One must look closely at the patient's medication list to rule out medication-induced conditions. Some common medicines that can cause depression-like features are antihypertensives (such as beta-blockers), methyldopa (Aldomet) and clonidine (Catapres).[17] Digitalis may also cause such symptoms. Parkinson's disease drugs

and interferon have also been linked to emerging depressive symptoms.[17] 50% of patients treated with interferon (Pegasys), experience a major depressive episode and it is now recommended prior to starting interferon therapy to prophylactically start the patient on antidepressants, especially if the patient also has a history of depression.[18] Other medications that have been associated with changes in mood are corticosteroids and oral contraceptives.[17] Symptoms of depression often co-exist with other health conditions and comorbidities. 10% to 15% of all depression is attributable to chronic medical illnesses such as renal disease, Parkinson's disease, cancer, diabetes, heart disease and stroke.[18] Thus, with an ever-increasing geriatric population, primary care physicians are destined to see increasing numbers in their future practice.

Refer to Table 3 for other etiologies of mood disorders.

TREATMENT

Treating mood disorders promptly enhances the patient's health prospects through reduction of the risk of relapse and an increased response rate to medications. Therefore, when properly screened and diagnosed early, treatment can help control their serious distress, and/or social/occupational impairments. Please refer to Table 4 (*page 48)* and Table 5 (*page 51*) for a summary of commonly used medications to treat depression and mania, as well as known side effects of these medications.

TABLE 3:

Other etiologies of mood disorders (Mnemonic "Nine Hand")

Categories	Examples
Neurologic	CVA, Parkinson's, Alzheimer's/other dementia, Seizures, Multiple sclerosis, Huntington's
Infectious	HIV, Syphilis
Neoplastic	Pancreas, Brain tumor
Endocrine	Thyroid, Hypothalamic-pituitary-adrenal disorders
Hematologic	Acute intermittent porphyria, Anemia
Autoimmune	Neuropsychiatric systemic lupus erythematosus, Rheumatoid Arthritis
Nutritional	B12, Folate deficiencies
Drugs	Illicit drugs, Prescription medications such as steroids, beta blockers, interferon

UNIPOLAR DEPRESSION

According to the American Psychiatric Association's Practice Guideline for the treatment of patients with depression, three phases exist in the treatment of major depression.[19] The first phase is called the acute phase, during which the goal is to put the patient into remission. This is accomplished by carefully selecting the appropriate treatment: psychopharmacology, psychotherapy, or electro-convulsive treatment (ECT).

When considering treatment via pharmacology, it is important to keep in mind the cost of drug, severity of symptoms, side effect profile, and prior response to pharmacological treatment. Patient autonomy is an important contributor in guiding the physician to prescribe appropriate treatment, especially for mild to moderate depression where symptoms and side effects must be weighed.

Some patient presentations that may lead the physician to consider starting with psychopharmacology are: "prior response to medication, moderate to severe symptomatology, preference of patient, significant sleep or appetite disturbance, or agitation."[19] Clinical features that should encourage starting with psychotherapy are: "prior positive response to therapy, co-occurring axis II disorders, mild-moderate symptoms, and significant psychosocial stressors" in which the patient would benefit from therapy.[19]

The main classes of antidepressants that are recommended as first line therapy are selective serotonin reuptake inhibitors (SSRIs), atypical antidepressants such as bupropion (Wellbutrin) and mirtazapine (Remeron), selective norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants. Monoamine oxidase inhibitors (MAOIs) have also been used in the past but are no longer first line therapy. With each class of medication, there are side effects that should be carefully explained to the patient. With TCAs, the side effects to consider are cardiac arrhythmias (QTc prolongation), anticholinergic effects, and sedation. With the SSRIs, the main class side effects are sexual dysfunction, weight gain, and nausea/vomiting. With the SNRIs, the most common side effects are hypertension, and diaphoresis. Mirtazapine's side effects include severe weight gain due to appetite stimulation, as well as sedation. Bupropion side effects include insomnia and decreased seizure threshold. For patients that are smokers, consider the use of bupropion since this medication also has proven efficacy for smoking cessation.

Psychotherapy, such as cognitive behavioral therapy, can be used to treat mild or moderate depression in conjunction with medication.[20] Also, psychotherapy should be considered as first line treatment in women who are breastfeeding, pregnant, or wish to become pregnant. However women with severe depression (suicide attempts, functional incapacitation,

TABLE 4:

Major Depression treatment choices and its side effects

Class of Medication	Side Effects
Selective serotonin reuptake inhibitors: Fluoxetine (Prozac) Sertraline (Zoloft) Paroxetine (Paxil) Fluvoxamine (Luvox) Citalopram (Celexa) Escitalopram (Lexapro)	Dizziness, Headaches, Gastrointestinal, Sexual dysfunction
Selective neuroepinepherine reuptake inhibitors: Venlafaxine (Effexor)	Headache, Nausea, Vomiting, Diarrhea, Sweating, Increased blood pressure
Duloxetine (Cymbalta)	Dry mouth, Nausea, Constipation, Decreased appetite, Insomnia, Sweating and Dizziness
Atypical antidepressants:	Headache, Dizziness, Decrease seizure threshold, Weight loss
Bupropion (Wellbutrin) Mirtazipine (Remeron)	Sedation, Weight gain, Increased appetite, Agranulocytosis, Somnolence
Trazodone (Desyrel)	Sedation
Tricyclic antidepressants: Amitriptyline (Elavil) Imipramine (Tofranil) Nortriptyline (Pamelor)	QT prolongation, Sedation, and Anticholinergic effects

or weight loss) may need to be started on antidepressant medication if the benefits outweigh the risks.[21] It is important to recognize that during the acute phase, patients are going to be symptomatic, which in turn would lead them to be poorly motivated and pessimistic during treatment; this could subsequently affect adherence to medication.

Once any modality of treatment has been started, usually 4 to 8 weeks are given to evaluate whether a particular treatment is working. If there is absolutely no change in symptoms after 4 weeks, the treatment must be modified. In patients being treated solely with anti-depressant medication, slowly increasing the dosage of the current medication is the first step, providing the patient can tolerate the side effects, keeping in mind that suicidal/homicidal risk must be assessed at each visit. If the patient cannot tolerate the increase in dosage of medication or prefers not to increase the dosage, the alternative is to switch the patient to another non-MAOI anti-depressant medication in the same class or a different class. For those patients that have more complex disease with symptoms not controlled on one agent, it might take two different medications to treat the patient's symptoms adequately. In this case, one would add a second non-MAOI anti-depressant of a different class then the initial drug. For example, adding bupropion to an SSRI. Other options of medications to add would be lithium or a second-generation anti-psychotic.

If the patient is still not responding to treatment, they most likely have treatment-resistant depression in which case, ECT is the most effective form of treatment. If a patient's symptoms are partially improving, it is reasonable to wait another 4 to 8 weeks before making any adjustments to the medication. In patients being treated solely with psychotherapy that are having no change in symptoms, the next step is to increase the frequency of the therapy session. ECT is performed two to three times per week. Usually, an acute course of ECT lasts from two to four weeks. ECT has the highest rate of response and remission out of all the other treatment modalities with 70% to 90% of patients getting better.[19]

TABLE 4.1:

Treatment of Unipolar depression - 3 Phases

	Goal	Options	Considerations	Time
Phase 1: Acute	**Remission**	**Pharmacology** **Psychotherapy** **Electro-convulsive treatment**	Cost Severity of symptoms (i.e. sleep or appetite disturbance) Side effects Prior response to treatment type Patient autonomy	4 - 8 weeks modify treatment if no change in 4 weeks
Phase 2: Continuation of Treatment			Monitor for signs of relapse	4 - 9 months
Phase 3: Maintenance			Determine if treatment can be discontinued Factors: • Risk of reoccurrence • Co-existing conditions • Persistence of symptoms	Patient specific

The second phase of treatment is the continuation phase. This phase lasts for 4 to 9 months and the patient is kept at the same dosage of medication used to achieve remission during the acute phase. It is important during this phase to monitor for signs of relapse.

The third and last phase of treatment is the maintenance phase. It is important to make a determination of whether following the continuation phase the patient will likely need to continue the medication. Patients that are euthymic generally focus on the burden and side effects of treatment, while not noticing the benefits. Recurrence is common and occurs in approximately 20% of patients within the first six months following remission. Over a patient's lifetime, they have a 50% to 85% chance of having at least one recurrence.[19] Risk factors to recurrence include earlier age of onset of symptoms, prior history of major depressive disorder, and ongoing sleep disturbances. Patients who have had three or more major depressive episodes should receive maintenance treatment.

There have been no studies on exactly how and when to discontinue treatment in patients that no longer want treatment. Factors that need to be considered are risk of recurrence, other co-existing conditions, persistence of symptoms after remission has been reached. Patients need to be advised not to abruptly discontinue anti-depressants and that the medication needs to be tapered over several weeks. Symptoms that the patient could experience if they suddenly discontinue medication are flu-like symptoms and headache. It is also important to educate the patient that recurrence of symptoms is highest within the first two months of discontinuing treatment. Please refer to Table 4.1 for a summarized view of how to treat unipolar depression.

BIPOLAR DISORDER

The standard of care treatment for patients with bipolar disorder is a mood stabilizer.[22] It is contraindicated to have a patient with bipolar disorder on monotherapy with an antidepressant. Current guidelines recommend that a patient should be on a mood stabilizer regardless of which phase the patient is presenting in.[23] Treatment for bipolar disorder consists of two stages: acute and maintenance. In the acute phase, it is important to choose an appropriate medication for the medication naïve patient. First line medications that are being used to treat mania are lithium (Lithobid), valproate (Depakote), and second-generation anti-psychotics. For a patient that is presenting with acute severe mania or a mixed episode (patients that present with both elevated and depressed mood symptoms at the same time), it is recommended to start lithium or valproate in combination with a second-generation antipsychotic.[22] For patients with less severe symptoms, monotherapy would be adequate with lithium,

valproate, or a second-generation antipsychotic. Valproate is the drug of choice in patients presenting with mixed episodes. If the patient is currently on an antidepressant medication, that medication should be tapered and discontinued. Patient symptoms must be monitored closely within the first 10 to 14 days of treatment to assess for suicidal/homicidal tendencies since the risk may be increased in some patients (see section 9: suicide risk). If symptoms are inadequately controlled with optimized dosages of medication, then addition of another first line agent is necessary.[22]

For a patient that is bipolar and presenting in acute depression that has not been on any treatment modality before, first line treatment is lithium or lamotrigine (Lamictal). When using lamotrigine, the expected response time is approximately 3 weeks.[24] It is not recommended to have the patient on monotherapy with an antidepressant. If a patient fails to respond to optimized treatment, the addition of bupropion, lamotrigine, or paroxetine should be considered. Studies have shown that the use of antidepressants in patients that have a diagnosis of bipolar Type II is higher than in bipolar Type I due to "lower rates of antidepressant-induced switching into hypomania or mania."[22] For a patient that is rapid cycling (4 or more cycles/year of either manic, hypomanic, major depression, or mixed depression) it is important to identify and treat any medical condition that could contribute to the rapid cycling. Also, it is important to taper patient off antidepressants that possibly could be contributing to the rapid cycling. Initial treatment consists of either starting lithium or valproate. Lamotrigine could also be used as an alternative. In most cases of rapid cycling, multiple medications are required to control the symptoms. Either a combination of two mood stabilizers (lamotrigine, valproate, or lithium) or one mood stabilizer plus a second generation antipsychotic are used.[22]

The goal of the maintenance phase of treatment is to reduce suicide risk and prevent relapse of symptoms. Maintenance medication is recommended after a depressive episode or a manic episode in a patient that has a diagnosis of bipolar disorder. The best evidence supports use of lithium or valproate for maintenance treatment, but lamotrigine, or carbamazepine can be used. The medication that was used during the most recent depressed or manic episode that led to remission should be continued. Antipsychotic medication can be discontinued during this phase unless needed for continued psychosis management. Maintenance therapy has been done with antipsychotics, but less evidence exists for the efficacy as does for the mood stabilizers. If during the maintenance phase, the patient continues to experience sub-threshold symptoms, another maintenance medication, second generation antipsychotic, or antidepressant should be added.[22]

In prescribing medications to treat bipolar disorder, it is important to know how to monitor the medication and the side effects of each one. The most recognized mood stabilizer used is lithium. Lithium is approved for use in both the acute phase and the maintenance phase of the disease.[14] Lithium's side effects include polyuria, polydipsia, weight gain, tremor, sedation, and gastrointestinal distress. Lithium can also cause diabetes insipidus, thyroid abnormalities and birth defects. A majority of patients will experience some side effects from lithium but most are minor and can be eliminated by changing the dose schedule or lowering the dose. It is important to monitor renal and thyroid functions, as well as lithium and sodium levels, while the patient is on lithium. Certain labs should be checked when there is a change in the patient's presentation. For a stable patient, lithium levels should be checked every six months. The therapeutic serum level is between 0.8 to 1.2 meq/L and it is suggested that serum levels be assessed five to seven days after each increase in dosage.[25] Renal function should be checked every 8 to 12 weeks for the first six months when the patient is first placed on the medication. After that time period, renal function can be checked every 6 to 12 months if the patient is stable. Thyroid function should be checked at least twice within a six-month period upon initiation of treatment with lithium. After that time period, the thyroid can be checked every 6 to 12 months if the patient is stable.[22] It is also important to note that Lithium has an extremely narrow therapeutic index, so patients on Lithium must closely be observed.

Valproic acid is another mood stabilizer used to treat bipolar disorder. It has shown a greater efficacy in treating mania in the acute phase, in contrast to maintenance therapy. Valproate's side effects include gastrointestinal distress, weight gain, elevated liver enzymes, and sedation. Mild leukopenia and thrombocytopenia can also occur but are reversed with discontinuation of the medication. It is important to monitor blood count and liver function tests in these patients. Liver function tests and complete blood count should be performed every six months at a minimum for stable patient. Valproate levels should be checked when suspicions of non-compliance are present or when a patient is placed on any other medication that could change the metabolism of valproate (carbamazepine, carbapenem antibiotics and lamotrigine can decrees valproic acid levels while amitriptyline, diazepam, ethosuximide, phenytoin, and phenobarbital may increase levels). It is also important to keep in mind that if one is considering having the patient on both lamotrigine and valproate, the dose of lamotrigine must be started at half of the normal starting dose because valproate inhibits metabolism of lamotrigine.[22]

TABLE 5:

Biopolar Disorder treatment choices and side effects

Class of Medication	Side Effects
Mood Stabilizers: Lithium (Lithobid)	Polyuria, Polydipsia, Weight gain, Tremor, Sedation, Gastrointestinal distress, Diabetes Insipidus, Thyroid abnormalities, Congenital anomalies (Ebstein's anomaly)
Valproic Acid (Depakote)	Gastrointestinal distress, Weight gain, Elevated liver enzymes, Sedation, Mild leukopenia and Thrombocytopenia
Carbamazepine (Tegretol)	Gastrointestinal distress, Dizziness, Drowsiness, Elevated liver enzymes, Fatigue
Lamotrigine (Lamictal)	Headache, Nausea, Infection, Xerostomia, and Rash
2nd Generation Antipsychotics: Aripiprazole (Abilify), Ziprasidone (Geodon), Risperidone (Risperdal), Quetiapine (Seroquel), Olanzapine (Zyprexa)	Weight gain, Hyperlipidemia, Hyperglycemia, Cardiac arrhythmia (QTc prolongation), Sedation, and Hypotension

Another mood stabilizer found to be efficacious in treating bipolar depression in the acute phase is lamotrigine. It has also been found to be effective in the long-term management of bipolar disorder especially in managing recurrent depression.[26] Most common side effects of lamotrigine are headache, nausea, infection, and xerostomia. Patients need to also be educated about the possibility of developing a rash. Although a rash could occur at any time once starting treatment, usually it occurs within the first few months. Rashes that should be considered extremely alarming are those accompanied by fever, sore throat, those involving the face or mucosa, and those that are wide spread over the body. In this case, lamotrigine needs to be discontinued. To minimize the risk of a rash, lamotrigine is started at a low dose and titrated up very slowly. Lamotrigine can also lead to Steven-Johnson syndrome, which is a life threatening condition.[22]

Some atypical antipsychotics have also been shown to be efficacious for the treatment of bipolar disorder. These include quetiapine (Seroquel), risperidone (Risperdal), and olanzapine (Zyprexa). Common class side effects to the second-generation antipsychotics include weight gain, hyperlipidemia, hyperglycemia, cardiac arrhythmia (such as QTc prolongation), sedation, and hypotension. It is important to monitor blood glucose and lipids in these patients, as the use of atypical antipsychotics can lead to an increased risk of diabetes and hypertriglyceredemia.[22] In the case of acute bipolar depression, studies have shown it to be safe to use olanzapine with fluoxetine (Prozac).[27] Please refer to Table 5.1 (*page 52)* for a summarized view of how to treat bipolar disorder.

REFERRING TO A SPECIALIST

The primary care physician must be knowledgeable in making a diagnosis of unipolar and bipolar disorders, and must be familiar with the mainstay initial treatment options, but must also recognize when to refer the patient to a psychiatrist for further evaluation and treatment. Some situations in which a primary care provider should consider referring the patient to a specialist include:

- Severe depression accompanied by life threatening situations involving the patients' lives or the lives of their dependents
- Symptoms not alleviated by initial trials of antidepressants
- The presence of psychotic symptoms
- Depression that is "part of the course" of another major psychiatric illness such as bipolar disorder or schizoaffective disorder.[16]

TABLE 5.1:

Treatment of Bipolar depression - 2 Phases

	Goal	Options	Considerations	Time
Phase 1: Acute	**Remission**	**Pharmacology - mood stabilizer**	Cost Severity of symptoms Side effects Prior response to treatment type Patient autonomy Co-morbidities (i.e. diabetes)	Monitor closely first 10 - 14 days Response within 3 weeks
Phase 2: Maintenance	**Reduce suicide risk; Prevent relapse**	**Pharmacology**	Side effects	Lifetime Check renal and liver functions regularly

SUICIDE RISK

At the time of evaluation of a mood disorder, one must also always assess for the risk of suicide including ideation, plan and intent. It is estimated that as many as 25% to 50% of patients with bipolar disorder attempt to commit suicide.[28] Many patients suffering from unipolar depression actually succeed in committing suicide. According to a study by Angst et al., the incidence of suicide is 27 times greater in patients with unipolar depression, as compared to the general population.[29] Evaluating your patient for suicidality is crucial and, in certain cases, it may become necessary to involuntarily commit a patient that is in your office for psychiatric treatment. It is also important to remember that antidepressants have been shown to increase the risk of suicidal thinking and behavior in some children, adolescents, and young adults in short-term studies of major depressive disorder.[30] This has generally occurred during initial treatment usually within the first one to two months.

CONCLUSION

Mood disorders, such as depression and bipolar disorder, are under diagnosed and undertreated; therefore, screening, in a primary care setting is critical and should be routine. We suggest that practitioners screen patients for depression periodically, particularly when anxiety, chronic conditions, and somatic complaints are present. As a primary care physician, it is important to become familiar with and be able to distinguish unipolar from bipolar disorder, as patients experiencing symptoms of depression, mania and hypomania will primarily present to their primary care's office first and it will be the duty of that physician to properly diagnose, treat and refer the patient.

Although the new standard of diagnosis mental disorders is made by the DSM V, no significant changes have been made from the DSM IV in terms of symptoms or duration of symptoms.[31]

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