• Maintain a high level of suspicion for bipolar depression in anyone presenting with an MDE; 1 in 5 patients being treated for depression in primary care actually has bipolar I or II disorder.

• Be vigilant for clusters of symptoms and features that may suggest bipolar depression:
  - Strong indicators are:
    • Family history of bipolar disorder in a first-degree relative
    • History of antidepressant-induced mania or hypomania
    • Early age of onset
    • Recurrent pattern of illness
    • Atypical symptoms of depression (e.g., hypersomnia, hyperphagia, fatigue)
  - Suggestive features include:
    • Psychotic features
    • Lack of response to antidepressant therapy
    • Abrupt onset of and end to MDE

Among patients diagnosed with bipolar disorder, 50% experience a major depressive episode (MDE) first, before a manic episode.

Depression predominates symptomatic time.

The diagnostic criteria for an MDE are the same regardless of whether the MDE occurs in the context of major depressive disorder (MDD) or bipolar disorder.

One of the greatest diagnostic challenges is that early in bipolar disorder, an individual may not have had enough episodes to have had a history of mania, which is necessary for diagnosing the illness. Further, people often do not recognize manic or hypomanic symptoms as part of the illness; rather, they are typically motivated by depressed states to seek help.

An MDE is like a fever in that a number of things could be causing it. The patient has the symptom of depression, but underneath it, what is the driving condition?
• Patients with bipolar disorder typically are complex: Comorbid psychiatric illnesses are commonly seen in these patients and can confound diagnosis.

• In the landmark STEP-BD trial, the most frequent lifetime comorbidities in patients with bipolar disorder were:
  - Anxiety disorder
  - Substance use disorder
  - ADHD
  - Eating disorder

When I take a history, I explore the past with my patient to look for a pattern that has been building over time, such as a childhood diagnosis of ADHD that was difficult to manage followed by high levels of anxiety and irritability in adulthood. This longitudinal perspective is important. Look beyond the comorbidities, which might be marked and predominate the clinical picture, and dig under the surface to determine whether bipolar disorder lies underneath.

• For a patient who presents with an MDE, investigate whether mania has occurred in the past, because the diagnosis of bipolar I disorder requires a lifetime history of at least 1 manic episode.

• Utilize a mnemonic such as DIGFAST to guide questions that can help uncover past manic or hypomanic episodes:
  - D = Distractibility
  - I = Indiscretion or disinhibition
  - G = Grandiosity
  - F = Flight of ideas
  - A = Activity increase
  - S = Sleep deficit or decreased need for sleep
  - T = Talkativeness

In my practice, when I ask a patient about history, I start with strengths. I ask, “What were you good at?” Then, “What were your challenges?” Quite often with bipolar disorder, you will see that there were roots of it earlier in a patient’s life. So, I ask the same questions about each life stage—childhood, adolescence, and adulthood—to establish a developmental history, all the while looking for episodes of mania or hypomania. Then, I obtain the patient’s family and medical histories. Gathering collateral information from a patient’s partner, family members, or caregivers—with the patient’s consent—is also an important aspect of history-taking. I can obtain additional perspectives on the patient’s past mood episodes and be alerted to current issues. I always let the patient know when I’ve spoken to someone they trust. In my experience, this candor helps strengthen the therapeutic alliance.
Up to 69% of patients with bipolar disorder are initially misdiagnosed.10

Patients with bipolar disorder go through a mean of 3.5 other diagnoses and 4 HCPs before receiving an accurate diagnosis.10

The most common misdiagnoses in patients with bipolar disorder are:
- MDD
- Anxiety disorder
- Schizophrenia
- Personality disorder
- Substance use disorder

Per current guidelines, use a screening tool or other structured instrument for documenting mania to decrease the potential for bipolar disorder to be missed or confused with another diagnosis.11

One such tool is the MDQ, a 13-item patient questionnaire that assesses past symptoms, as well as their concurrence and the degree to which they have caused problems for the patient.12

Additionally, to further aid the diagnostic process, screeners may help quantify a patient’s current depression. The PHQ-9 is a 9-item questionnaire via which the patient indicates the frequency of depressive symptoms experienced over the past 2 weeks and specifies the extent of functional difficulty associated with them.13

In my practice, we administer the PHQ-9 and MDQ to all patients who present with an MDE. I believe these 2 screeners are commonly used tools because they can provide systematic data that anyone on the multidisciplinary care team can collect; they can also be downloaded for free.

Several other instruments are also widely accessible. Regardless of your choice, I believe the most important point is that screeners play a key role in the diagnostic process. I think of it like an internist’s knowledge that a patient’s blood pressure is elevated before a detailed clinical interview: It informs the conversation and next steps.

Further, some screeners, like the PHQ-9, can be administered throughout the management process to assess the patient’s progress and response to treatment.
Screeners are not validated diagnostic instruments. Using the internist metaphor again, the clinician knows that a patient's blood pressure is elevated but must figure out why. Similarly, a clinician whose patient screens positive on the PHQ-9 or the MDQ must now investigate further with a detailed clinical interview—the last step in the process before a formal diagnosis can be made.

For a patient who screens positive for an MDE or a lifetime history of mania, conduct a detailed clinical interview to confirm the diagnosis of bipolar disorder and exclude other diagnoses. The interview comprehensively evaluates the patient's history, including duration and severity of episodes, impact of the episodes on psychosocial functioning, and previous treatments and response. A detailed clinical interview may also include a complete medical history, physical examination, and laboratory tests, in part to thoroughly assess the patient for comorbid medical conditions. As many as 55% of patients with bipolar disorder have at least 1 medical condition, and metabolic comorbidities are the most prevalent. The etiology of these abnormalities is complex; factors such as lifestyle choices, genetic vulnerability, and the use of certain medications may play a role.

There are many details about a patient's illness, such as sleep and sleep cycles, impulsivity, school- or work-related issues, and relationship difficulties, that can offer important insights to the clinician but that a simple history or screener may not fully elucidate. The patient interview can help us dig deeper. Thoroughly exploring a patient's medical history and assessing metabolic risk factors are important for 2 reasons: They can rule out other causes of depressive symptoms, such as fatigue associated with hypothyroidism, and they can inform treatment decisions with respect to the risk-benefit ratios of various medications. Therefore, in my practice, in addition to weighing patients, I usually order lab tests for thyroid function, vitamin D, and testosterone (in men), as well as a complete blood count and a metabolic panel. Over time, metabolic parameters should be routinely monitored in patients with severe mental illness, including bipolar disorder, due to their increased risk for CVD compared with the general population.
References:

ADHD, attention-deficit/hyperactivity disorder; CVD, cardiovascular disease; HCPs, health care professionals; MDQ, Mood Disorder Questionnaire; PHQ-9, Patient Health Questionnaire–9 Item; STEP-BD, Systematic Treatment Enhancement Program for Bipolar Disorder.