Is it MDD or Bipolar Disorder?

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**Position:** Dr. Tohen is the Professor and Chairman of the Department of Psychiatry and Behavioral Sciences at The University of New Mexico Health Sciences Center in Albuquerque, NM.

**Education:** Dr. Tohen earned his medical degree from the National University of Mexico and his Doctorate in Public Health (Epidemiology) from Harvard University. His postdoctoral training included a residency in Psychiatry at the University of Toronto and a fellowship at McLean Hospital, Harvard Medical School. Dr. Tohen also obtained an MBA degree from the Indiana University Kelly School of Business.

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**Position:** Dr. Trivedi is a psychiatrist and the Julie K. Hersh Chair in Depression Research and Clinical Care at UT Southwestern Medical Center in Dallas, TX.

**Education:** Dr. Trivedi completed his medical studies at Baroda Medical College in Baroda, India, and he completed his residency in Psychiatry at University General Hospital Medical College in Baroda, India, and Henry Ford Hospital in Detroit, Michigan. Dr. Trivedi is board certified by the American Board of Psychiatry and Neurology.
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Objectives

- Review the prevalence and burden of major depressive disorder (MDD) and bipolar disorder (BD)
- Discuss the clinical features of MDD and BD
- Address the difficulties in differential diagnosis between MDD and BD
Polling Question

In your clinical experience, what percentage of patients originally diagnosed with MDD were later found to have BD?

A. < 10%
B. 11% to 25%
C. 26% to 50%
D. > 50%
BASICS OF MAJOR DEPRESSIVE DISORDER (MDD)
Lifetime Prevalence of MDD

- The data below are from a nationally representative United States face-to-face household survey that was conducted using the fully structured World Health Organization World Mental Health Survey version of the Composite International Diagnostic Interview.

MDD, major depressive disorder; SE, standard error.


• Overall lifetime prevalence of MDD across all ages was 16.6%
Burden of MDD

MDD: Burden of Illness

**Total Economic Burden**
$210.5 billion

**Workplace Costs**
$102 billion

**Suicide**
20x the general population

**Suicide-related Costs**
$9.7 billion

**Education**
60% elevated risk of failure to complete secondary school*

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*in high income countries

MDD, major depressive disorder.

BASICS OF BIPOLAR DISORDER (BD)
Lifetime Prevalence of BD

- The data below are from a nationally representative United States face-to-face household survey that was conducted using the fully structured World Health Organization World Mental Health Survey version of the Composite International Diagnostic Interview.

- Overall lifetime prevalence of BD across all ages was 3.9%.

BD, bipolar disorder; SE, standard error.
Burden of BD

*For patients developing BD in their mid-20s.
BD, bipolar disorder.

DISCUSSION
Polling Question

In your experience, which do you consider to be the strongest indicator of BD when a patient presents with depression?

A. Family history of BD
B. History of psychiatric hospitalization
C. History of treatment-resistant depression
D. Antidepressant-related mania/hypomania
Case Presentation*

- Consuelo is a 35-year-old, married, Hispanic woman diagnosed with MDD
  - She is currently employed as a nurse aid and has two children aged 7 and 9 years
  - She previously suffered from anxiety and depression
  - Father has a history of depression; maternal grandmother has a history of BD

- Recent complaints include:
  - Feeling sad and irritable
  - Decreased appetite and loss of 3 lbs in the last month
  - Anhedonia; loss of interest in work and spending time with her family
  - Tiredness fluctuating with feeling of increased energy
  - Insomnia (early and middle)
  - Difficulty at work and taking care of her children
  - Wishes to be dead but no specific suicide plans
  - Feeling of guilt of not being a “good wife”

- She had a partial response to an SSRI, but still reports “being down most days”

- She is referred by her primary care provider who is concerned about Consuelo’s depression continuing to be unresponsive to treatment

*Fictional case presentation.

BD, bipolar disorder; MDD, major depressive disorder; SSRI, selective serotonin reuptake inhibitors.
BD Is Often Underdiagnosed

- Outpatients (n = 649) receiving treatment for depression

BD, bipolar disorder; MDQ, Mood Disorder Questionnaire.

Misdiagnosis of BD: NDMDA Survey (2000)

- Patients were incorrectly diagnosed with:
  - Unipolar depression: 60%
  - Anxiety disorders: 26%
  - Schizophrenia: 18%
  - Borderline or antisocial PD: 17%
  - Alcohol abuse/dependence: 14%
  - Schizoaffective disorder: 11%

35% were symptomatic for more than 10 years before correct diagnosis

BD, bipolar disorder; NDMDA, National Depressive and Manic-Depressive Association; PD, personality disorder.

BD Versus Unipolar Depression

BD is often incorrectly diagnosed as MDD. For every 10 patients eventually diagnosed with BD, ~3 remain misdiagnosed for 10 years or more.

BD, bipolar disorder; MDD, major depressive disorder.
People With BD Were Depressed for Almost 30% to 50% of the Evaluation Period*

*bEvaluation period for bipolar I and II studies are 12.8 years (n=146) and 13.4 years (n=86), respectively. BD, bipolar disorder.
Journal of Affective Disorders

Two-year outcomes in first-episode psychotic depression: The McLean–Harvard first-episode project

Mauricio Tohen, Hari-Mandir K. Khalsa, Paola Salvatore, Eduard Vieta, Caitlin Ravichandran, Ross J. Baldessarini

Change in Diagnosis in the McLean-Harvard First-episode Psychotic Depression Project: Two-Year Outcomes

Change in Diagnosis of Patients With Psychotic Depression at Baseline

- Retained Diagnosis: 59%
- Diagnosis Changed: 41%

56 patients with a diagnosis of MDD with psychotic features per the *DSM-IV* were prospectively followed.

Change in Diagnosis

- Bipolar: 70%
- Schizo-affective: 30%

*DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; MDD, major depressive disorder.*

Switch to Manic Episode

• Presence of mixed features in a first episode of psychotic depression predicted switch to BD
  – 2.4-fold higher baseline YMRS manic-symptoms (2.12 vs 5.05)
  – OR: 1.18 (1.01-1.38); $P = 0.036$

BD, bipolar disorder; OR, odds ratio with 95% confidence interval; YMRS, young mania rating scale.
Predictors of Diagnostic Switch in First-episode Psychotic Depression

• Validity of *DSM-5* mixed features specifier
  – Presence of mixed features had implications for diagnostic outcomes

• Switch to schizoaffective disorder
  – Presence of mood incongruent features
  – Prodromal thought disorder

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*DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.*

DIFFERENTIATING BIPOLAR DEPRESSION FROM UNIPOLAR DEPRESSION
Clinical Features of MDD and Bipolar Depression

<table>
<thead>
<tr>
<th>Unipolar Depression</th>
<th>Bipolar Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typically occurs after 25 years of age(^1)</td>
<td>Typically occurs before 25 years of age(^1)</td>
</tr>
<tr>
<td>May be preceded by period of gradually worsening symptoms(^1)</td>
<td>Episodes may abrupt; often period or seasonal(^1)</td>
</tr>
<tr>
<td>No history of mania or hypomania(^1)</td>
<td>Treatment-emergent mania / hypomania(^1)</td>
</tr>
<tr>
<td></td>
<td>Heritable; family history is vital(^1)</td>
</tr>
<tr>
<td></td>
<td>History of mania/hypomania, or increased energy and decreased need for sleep(^1)</td>
</tr>
</tbody>
</table>

**Symptoms More Common in Unipolar Depression**

- Anxiety\(^2\)
- Appetite disturbances\(^2\)
- Physical complaints\(^2\)
- Initial insomnia\(^2\)
- Weight loss\(^2\)

**Symptoms More Common in Bipolar Depression**

- Hypersomnia\(^2\)
- Psychomotor retardation\(^2\)
- Fewer physical complaints\(^2\)
- Hyperphagia\(^2\)
- Leaden paralysis\(^2\)

MDD, major depressive disorder.

Indicators of BD Among Patients Presenting With Depression

- Family history of BD\textsuperscript{1}
- Earlier onset of illness\textsuperscript{2}
- Seasonality\textsuperscript{1}
- Number of past episodes\textsuperscript{1}
- History of psychiatric hospitalization\textsuperscript{1}
- Mixed states\textsuperscript{1}
- Mood reactivity\textsuperscript{1}
- History of treatment-resistant depression\textsuperscript{2}
- Antidepressant-related mania / hypomania\textsuperscript{1}

\textsuperscript{1} BD, bipolar disorder.
Factors to Consider When Selecting a Therapy for Patients With Bipolar Depression


Depressive symptom severity\(^1,^2\)

Presence of mixed features, rapid cycling\(^2\)

Comorbid psychiatric and medical illness\(^2\)

Therapy risk-benefit\(^2\)
ISBD Recommendations for Antidepressant Use in BD

- International collaboration of 70 experts in bipolar; 173 studies reviewed
- Antidepressants have a questionable risk-benefit ratio
- Only use in bipolar I or II depressive patients with a past history of good response to antidepressants
- Do not use as monotherapy in bipolar I disorder
- Do not use in presence of mixed features, rapid cycling

BD, bipolar disorder; ISBD, International Society for Bipolar Disorders.
Conclusions

• Depression is often the presenting mood state in BD\textsuperscript{1}
• Screening for a history of mania / hypomania is essential in patients with depression\textsuperscript{1,2}
• Treatment-resistant depression is associated with BD\textsuperscript{1,3}
• Additional information may point to BD, such as family history, early onset, number of past episodes, etc\textsuperscript{2,3}

BD, bipolar disorder.