Advances in Bipolar Disorder: a Focus on Bipolar 2 Disorder

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DIAGNOSING BIPOLAR II DISORDER

Are there really different types of bipolar disorder? Why does it matter?

- Bipolar Disorder (BD) II is common
- Not a "less severe" form of BD I
- BD II is often *misdiagnosed*, leading to *inadequte treatment*
- BD II often co-travels with other disorders, making recognition and treatment more *challenging*
- Many are unsure how to treat BD II and its comorbidities

History of Bipolar II Disorder Diagnosis

- Historically, BD II was subsumed under non-specific categories such as manic-depressive illness, unipolar disorder, and bipolar affective disorder
- In the 1960's, David Dunner identified groups of patients who had been hospitalized for depression and had histories of hypomania but not mania
  - Higher rates of suicide
  - Differences in course of illness, response to pharmacotherapy than those with depression alone or those with depression + mania
- I994: Bipolar II disorder was officially recognized in the DSM IV

Diagnosis of Bipolar II Disorder

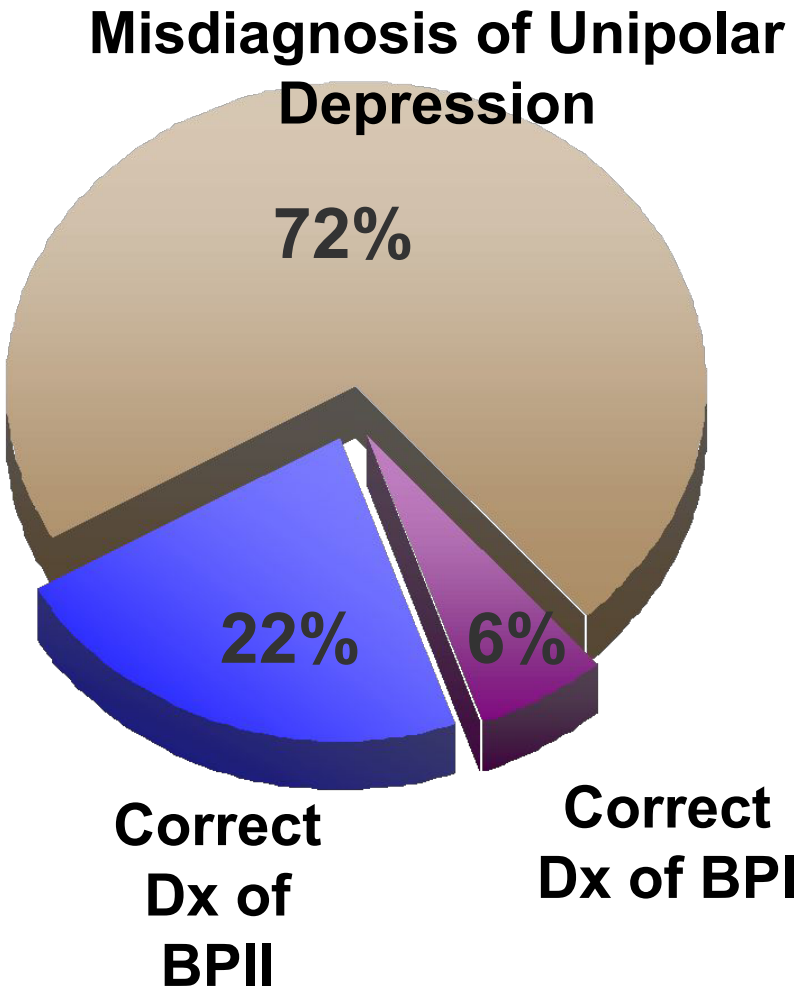
DSM 5-TR Diagnostic Criteria for Bipolar II Disorder

A. Presence of history of at least 1 major depressive episode
B. Presence or history of at least 1 hypomanic episode
C. No presence or history of manic episode
D. A and B not better explained by another disorder

Mood Disorders: Comparison of Criteria

	Bipolar I Disorder	Bipolar II Disorder	Major Depressive Disorder
Major Depressive Episode	Typical, but not required	Yes	Yes
Manic Episode	Yes	No	No
Hypomanic Episode	Common, but not required	Yes	No

Under-recognition of Bipolar Disorder in Patients with Major Depressive Episodes (N=250)



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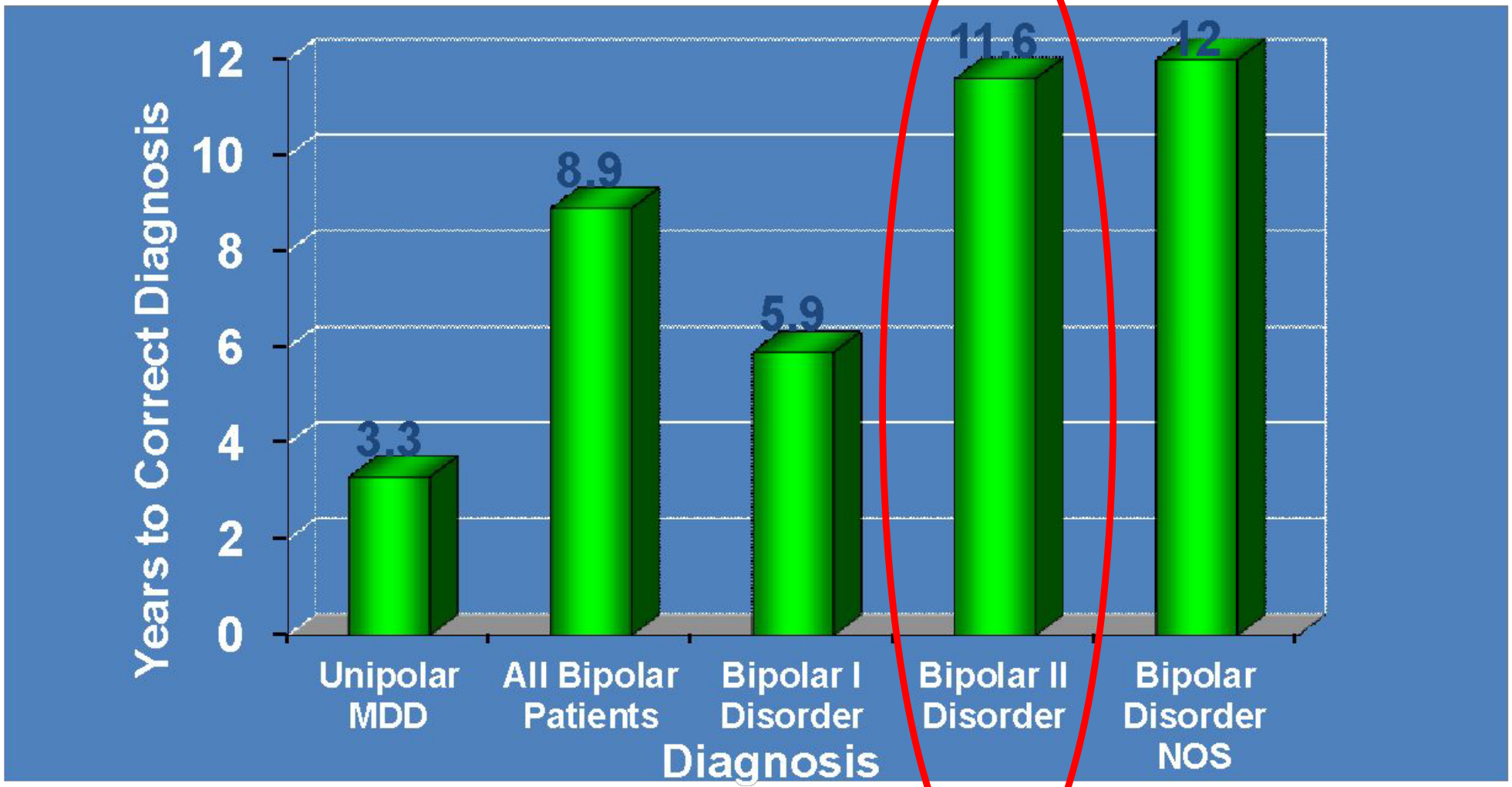
Hantouche EG, et al. *J Affect Disord.* 1998;50:163-173.

Years to Correct Diagnosis From First Seeking Professional Help



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Ghaemi SN et al. *J Clin Psychiatry* 2000; 61(10):804-808.

Mixed Features are Common in BD II

64% of patients with BD II experienced at least one visit with mixed depression (defined as the presence of subthreshold hypomania concurrent with at least mild depression)

Mixed presentations are associated with worse treatment outcomes, higher suicide rates and higher rates of psychiatric and medical comorbidities

Angst J. et al. *European Archives of Clinical Psychiatry and Neuroscience* 2012; Betzler F et al. *International Journal of Psychiatry in Clinical Practice* 2017; Miller S. et al. *American Journal of Psychiatry* 2016; Suppes T. et al. *Archives of General Psychiatry* 2005

Borderline PD and BD II

About 20% of individuals with BD II also have BPD

BPD is twice as common in BD II as BD I

Transient episodes of affective instability and emotional lability associated with BPD can be confused with hypomanic episodes

BPD is often misdiagnosed as BD II (in one study, 40% of patients with DSM IV defined BPD were given a diagnosis of BPD)

Zimmerman M. et al. *Journal of Clinical Psychiatry* 2010;
Zimmerman M. et al. *Dialogues in Clinical Neuroscience* 2013

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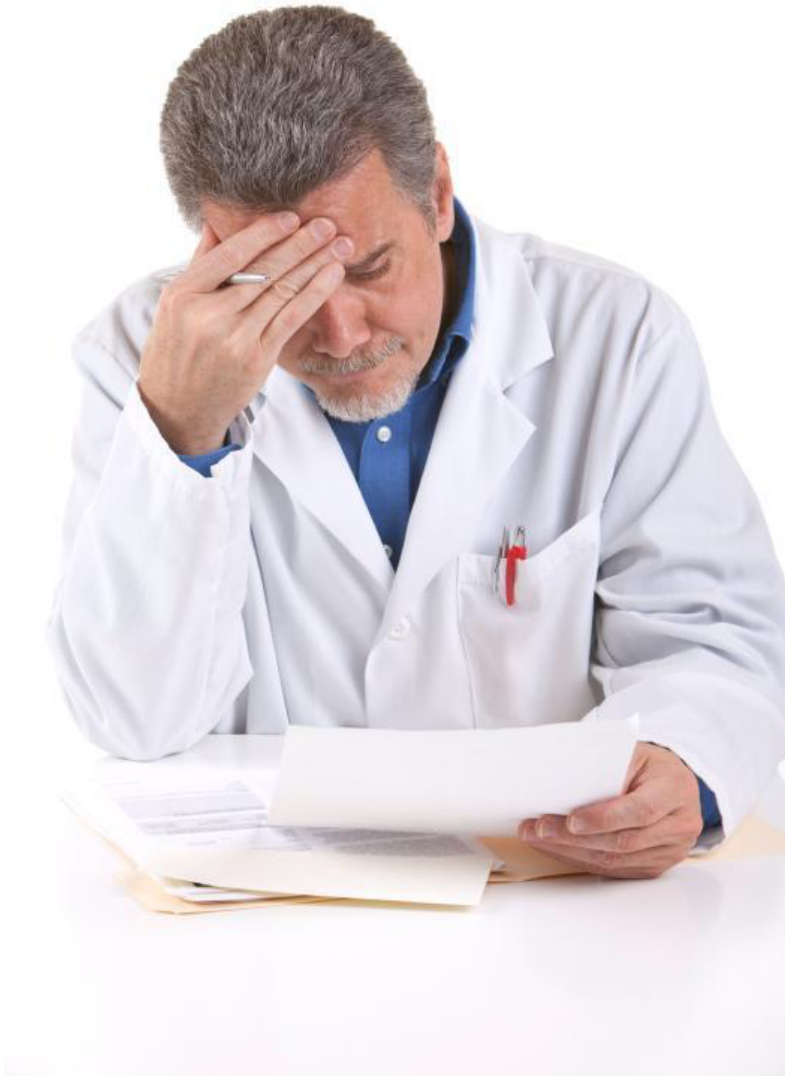
Treatments for BD II



- Understudied relative to BD I
- Fewer studies
- Many are underpowered
- Lower quality evidence
- Often combined populations of BD I and BD II
  - do not report results separately, making it difficult to draw definitive conclusions
- Many of us resort to using treatment for BD I or MDD, despite absence of evidence

Recommendations (CANMAT) for Acute Management of Bipolar II Depression

	Agent		Level of Evidence
First Line	• **Quetiapine**		
Second Line	• **Lithium** • **Lamotrigine** • *Bupropion* (adj)*	• *Sertraline** • *Venlafaxine**	
Third Line	• *Fluoxetine** • *Tranylcypromine* • Ziprasidone#	• Ketamine (IV or sublingual) (adj)^ • Pramiprexole (adj)	
	• Divalproex • Agomelatine (adj) • ECT^ (adj)	• EPA (adj) • N-acetyl cysteine (adj) • T3/T4 thyroid hormones (adj)	

*: for patients with pure depression (non-mixed); # for patients with depression and mixed hypomania: ^: for severely ill/ treatment refractory patients;
adj: adjunctive ECT: electroconvulsive therapy; EPA: eicosapentaenoic acid

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Yatham et al. *Bipolar Disord* 2018:15:1-44.

Recommendations: Maintenance Treatment of BD II

	Agent	Evidence Level
First Line	• Quetiapine	
	• Lithium	
	• Lamotrigine	
Second Line	• Venlafaxine	
	• Fluoxetine	
Third Line	• Carbamazepine • Escitalopram • Other antidepressants	
	• Risperidone* • Divalproex	
No Specific Recommendation	• Olanzapine	Insufficient data

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* Primarily for prevention of hypomania

Adjunctive Psychological Treatments for Bipolar Disorder

Treatment	Maintenance: Recommendation (Level of Evidence)	Acute Depression: Recommendation (Level of Evidence)
Psychoeducation (PE)	**First Line (Level 2)**	Insufficient evidence
Cognitive behavioral therapy (CBT)	**Second Line (Level 2)**	**Second Line (Level 2)**
Family-focused therapy (FFT)	**Second Line (Level 2)**	**Second Line (Level 2)**
Interpersonal and social rhythm therapy (IPSRT)	**Third Line (Level 2)**	**Third Line (Level 2)**
Peer Support	**Third Line (Level 2)**	Insufficient evidence
Cognitive and Functional Remediation	Insufficient evidence	Insufficient evidence
Dialectical behavioural therapy (DBT)	Insufficient evidence	Insufficient evidence
Family/ caregiver interventions	Insufficient evidence	Insufficient evidence
Mindfulness based cognitive therapy (MBCT)	Insufficient evidence	Insufficient evidence
Online interventions	Insufficient evidence	Insufficient evidence

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Yatham et al. *Bipolar Disord* 20[illegible]8;15[illegible]-44.

Psychosocial Interventions

- Pharmacotherapy is the foundation of successful treatment of BD[1,2]
  - The evidence for maintenance medications in BP2 disorder is too small!
- Adjunctive psychosocial interventions may be useful for:[1,2]
  - Acute depressive episodes
  - Prevention of relapse
  - May be particularly effective early in the illness course[3]
- Although less is known about psychotherapy in BD II, available data are promising[4]

1. Reinares et al. *J Affect Disord* 2014;156:46-55; 2. Murray et al. *Clin Psychol Rev* 2017;52:148-63; 3. Yatham et al. *Bipolar Disord* 2018;15:1-44.4. Swartz et al. FOCUS 2014; 12: 251-266

Conclusions

- Bipolar 2 is a common, often misdiagnosed disorder
  - approximately 10 years for correct diagnosis
- First and second line treatments include quetiapine, lithium, lamotrigine, sertraline, venlafaxine, and now ***lumateperone***
  - whether antidepressants alone work is not well known
- Psychotherapy is an important part of care

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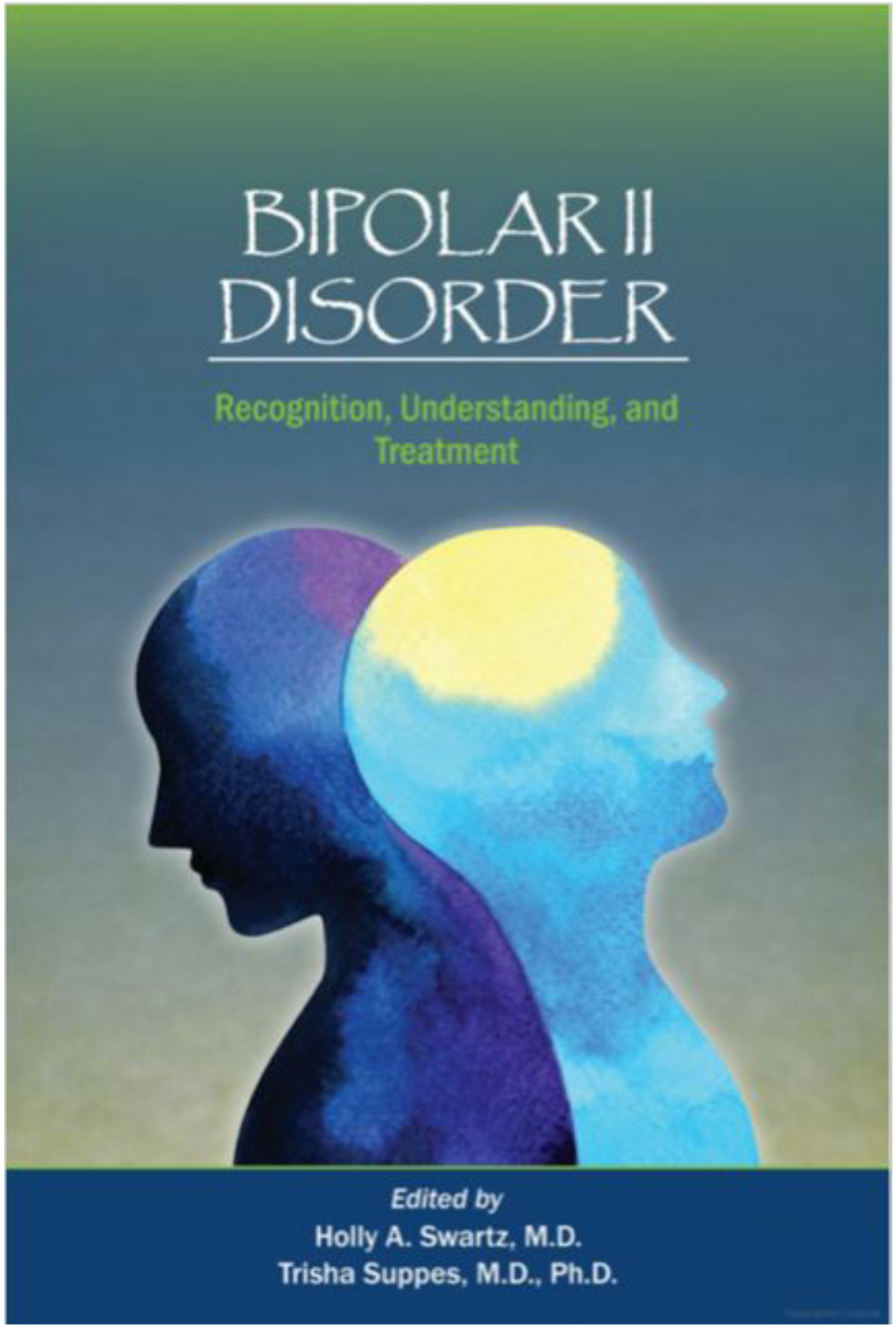

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