Borderpolar: Diagnosis and Treatment of Patients with Bipolar Disorder and Borderline Personality Disorder

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Faculty Disclosure

- **Mark Zimmerman, MD** has no financial relationships to disclose relating to the subject matter of this presentation.

Disclosure

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration).
  - There are no FDA-approved treatments for borderline personality disorder (BPD). All drugs discussed in this presentation for the treatment of BPD is off-label.

- Applicable CME staff have no relationships to disclose relating to the subject matter of this activity.

- This activity has been independently reviewed for balance.

Learning Objectives

- Review the level of comorbidity between bipolar disorder and borderline personality disorder (BPD)
- Identify the differences between patients with borderpolar and BPD, and between patients with borderpolar and bipolar disorder
- Assess the empirical literature on the treatment of patients with both bipolar disorder and BPD

Origin of the Term

A colleague approached me and said that she was referring a patient to the partial hospital program who had borderpolar. Having not previously heard this term, clarification was sought, and it was explained that the patient had both BPD and bipolar disorder. My colleague further explained that this term is frequently used in the psychiatrist chat room she visits as a shorthand for patients with both disorders who are severely ill and have high levels of psychosocial morbidity. A PubMed search on the term borderpolar did not turn up any citations.

BPD = borderline personality disorder.

Prevalence of BPD in Clinical Settings

Prevalence of BPD in Clinical Settings

- Largest clinical epidemiology study—Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project

- Sample: 3674 psychiatric outpatients
  - Gender: 60.2% female, 39.8% male
  - Mean age: 38.8 years

- Method of assessment
  - Semi-structured interview (SIDP-IV)

SIDP-IV = Structured Interview for *DSM-IV* Personality.
Zimmerman M, et al. *Ann Clin Psychiatry*. 2017;29(1):54-60.

Prevalence of BPD in Clinical Settings

- Results
  - Overall prevalence: 10.6% (390/3674)
  - Principal diagnosis: 80/390 (20.5%)
  - Comorbid diagnosis: 310/390 (79.5%)

Zimmerman M, et al. *Ann Clin Psychiatry*. 2017;29(1):54-60.

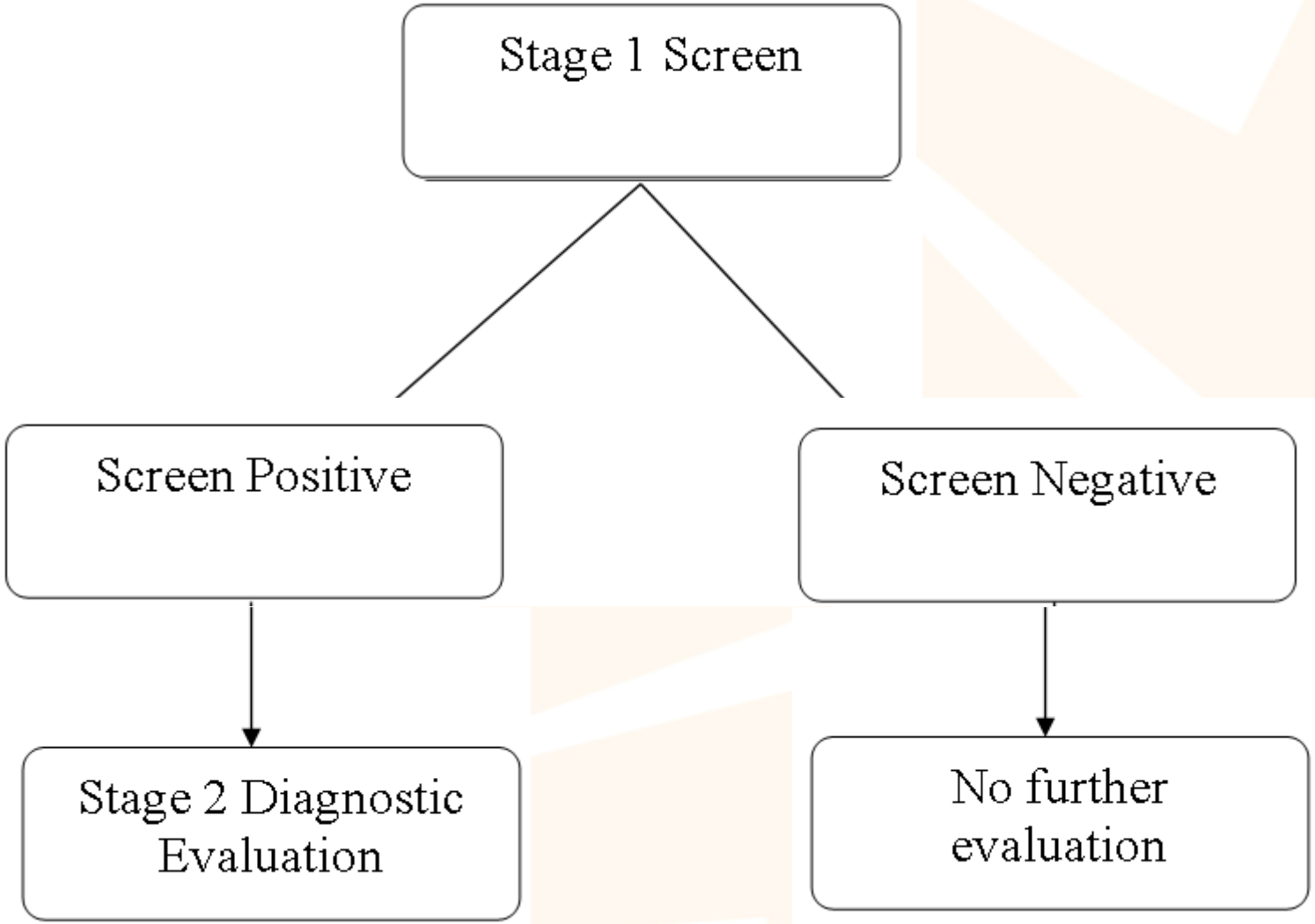
Prevalence of BPD: Association with Diagnosis

DSM-IV disorder	Patients with principal diagnosis, n	Patients with BPD, n (%)	Odds ratio[a]	95% CI
Major depressive disorder	1,222	144 (11.8%)	1.20	0.96 to 1.5
Dysthymic disorder	67	1 (1.5%)	0.13	0.02 to 0.91
Bipolar I disorder	71	24 (33.8%)	4.52	2.7 to 7.5
Bipolar II disorder	96	26 (27.1%)	3.28	2.1 to 5.2
Panic disorder	36	1 (2.8%)	0.24	0.03 to 1.7
Panic disorder with agoraphobia	127	14 (11.0%)	1.05	0.59 to 1.8
Social phobia	52	4 (7.7%)	0.70	0.25 to 1.9
Posttraumatic stress disorder	106	16 (15.1%)	1.52	0.88 to 2.6
Generalized anxiety disorder	171	8 (4.7%)	0.40	0.20 to 0.82
Obsessive-compulsive disorder	47	1 (2.1%)	0.18	0.03 to 1.3
Alcohol abuse/dependence	33	1 (3.0%)	0.26	0.04 to 1.9
Drug abuse/dependence	21	2 (9.5%)	0.89	0.21 to 3.8
Undifferentiated somatoform disorder	26	2 (7.7%)	0.70	0.17 to 3.0
Intermittent explosive disorder	26	0 (0.0%)	—	—
Adjustment disorder	211	2 (0.9%)	0.08	0.02 to 0.31

Zimmerman M, et al. *Ann Clin Psychiatry*. 2017;29(1):54-60.

Screening

The 2-Stage Diagnostic Process



Brief Review of the Statistics of Screening

Screening Test	Gold Standard Diagnosis: Present	Gold Standard Diagnosis: Absent	Total
Positive	a	b	a+b
Negative	c	d	c+d
Total	a + c	b + d	

Zimmerman M, et al. *J Clin Psychiatry*. 2004;65(5):605-610.

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		Gold Standard Diagnosis: Present	Gold Standard Diagnosis: Absent	Total
Screening Test	Positive	a	b	a+b
	Negative	c	d	c+d
	Total	a + c	b + d	

Sensitivity = a/(a+c)
Specificity = d/(b+d)
Positive Predictive Value = a/(a+b)
Negative Predictive Value = d/(c+d)

Zimmerman M, et al. *J Clin Psychiatry*. 2004;65(5):605-610.

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Zimmerman M, et al. *J Clin Psychiatry*. 2004;65(5):605-610.

Screening for Bipolar Disorder and BPD

- Why do you screen?
- Who do you screen?
- When do you screen?
- How do you screen?
  - Screening questionnaires
  - Screening questions

Screening for BPD

- Screening for BPD
  - Screening questionnaires are not used
  - Polythetically defined criteria

BPD Criteria: 5 of 9

1. Avoid abandonment
2. Unstable relationships
3. Identity disturbance
4. Impulsivity
5. Suicidality/self-injury
6. Affective instability
7. Emptiness
8. Anger
9. Stress-induced paranoia/dissociation

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.* Arlington, VA: American Psychiatric Association Publishing; 2013.

Screening for BPD

- Screening for borderline personality
  - Screening questionnaires are not used
  - Polythetically defined criteria
  - Psychiatric review of systems
- Can a “gate criterion” be identified to screen for BPD
  - High sensitivity
  - High negative predictive value

BJPsych | The British Journal of Psychiatry (2017)
210, 165–166. doi: 10.1192/bjp.bp.116.182121

Short report

Clinically useful screen for borderline personality disorder in psychiatric out-patients

Mark Zimmerman, Matthew D. Multach, Kristy Dalrymple and Iwona Chelminski

Zimmerman M, et al. *Br J Psychiatry*. 2017;210(2):165-166.

Which Criterion?

1. Avoid abandonment
2. Unstable relationships
3. Identity disturbance
4. Impulsivity
5. Suicidality/self-injury
6. Affective instability
7. Emptiness
8. Anger
9. Stress-induced paranoia/dissociation

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.* Arlington, VA: American Psychiatric Association Publishing; 2013.

Analysis of the MIDAS Project Data

- 3674 psychiatric outpatients
  - 60.2% female
  - 87.1% white
  - 38.8 years
- Semi-structured interview
  - BPD section of the SIDP-IV

Zimmerman M, et al. *Br J Psychiatry*. 2017;210(2):165-166.

Results

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Power
Odd-even split				
Validation sample (n=1,837)	94.3%	81.6%	37.5%	99.2%
Cross-validation sample (n=1,837)	91.4%	82.3%	38.2%	98.8%
Temporal split				
First third (n=1,225)	92.5%	76.9%	32.8%	98.8%
Middle third (n=1,225)	91.5%	83.7%	39.7%	98.8%
Last third (n=1,224)	94.5%	85.1%	42.6%	99.3%
All Patients (n=3,674)	92.8%	81.9%	37.9%	99.0%

Zimmerman M, et al. *Br J Psychiatry*. 2017;210(2):165-166.

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Which Criterion?

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2. Unstable relationships
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4. Impulsivity
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Zimmerman M, et al. *Br J Psychiatry*. 2017;210(2):165-166.

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2. Unstable relationships
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4. Impulsivity
5. Suicidality/self-injury
6. **Affective instability**
7. Emptiness
8. Anger
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Zimmerman M, et al. *Br J Psychiatry*. 2017;210(2):165-166.

Screening in Patients with Bipolar Disorder

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Power
All Patients (n=3,674)	92.8%	81.9%	37.9%	99.0%
Major Depressive Disorder (n=1,222)	91.0%	81.6%	39.8%	98.5%
Bipolar Disorder (n=166)	93.0%	54.3%	46.5%	94.0%
No Major Depressive/Bipolar Disorder (2,287)	92.8%	81.9%	37.9%	99.0%

Zimmerman M, et al. *J Clin Psychiatry*. In press.

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Zimmerman M, et al. *J Clin Psychiatry*. In press.

Assessing Affective Instability

SIDP-IV questions

Has anyone ever told you that your moods seem to change a great deal?

IF YES: What did they say?

Do you often have days when your mood changes a great deal—days when you shift back and forth from feeling like your usual self, to feeling angry or depressed or anxious?

IF YES: How intense are your mood swings?

How often does this happen in a typical week?

How long do the moods last?

Other Studies of the Sensitivity and Negative Predictive Value of the Affective Instability Criterion

Author	Sample	Sensitivity	NPV
Farmer and Chapman (2002)	149 “symptomatic volunteers”	92%	98%
Grilo et al (2004)	130 Hispanic substance abusers	97%	98%
Grilo et al (2001)	668 CLPS study	94%	90%
Korfine and Hooley (2009)	45 hospitalized and community BPD	91%	---
Leppänen et al (2013)	71 BPD patients in psychotherapy trial	89%	---
Nurnberg et al (1991)	100 psychiatric outpatients	100%	100%
Pfohl et al (1986)	131 psychiatric patients	93%	97%
Reich et al (1990)	159 psychiatric outpatients	97%	99%

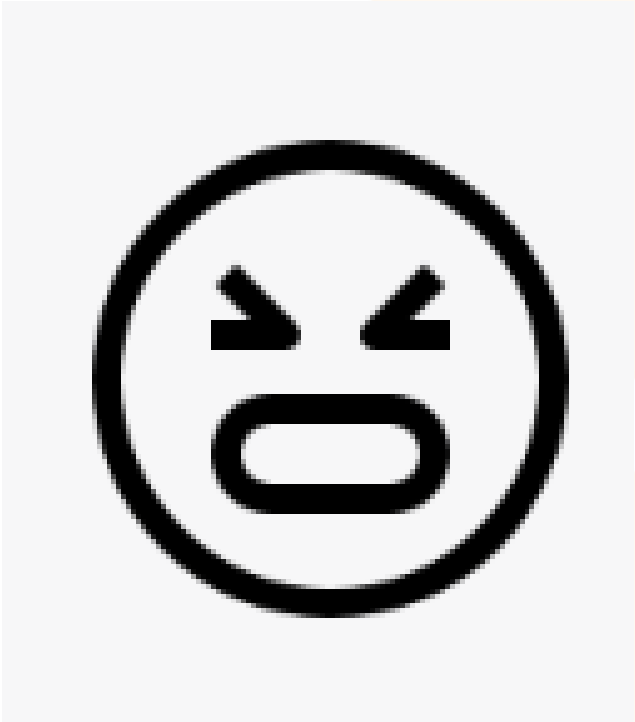
NPV = negative predictive value; CLPS = Collaborative Longitudinal Personality Disorders Study.

Farmer RF, et al. *Compr Psychiatry.* 2002;43(4):285-300. Grilo CM, et al. *J Consult Clin Psychol*. 2004;72(1):126-131. Grilo CM, et al. *Acta Psychiatr Scand.* 2001;104:264-272. Korfine L, et al. *J Pers Disord*. 2009;23(1):62-75. Leppänen V, et al. *Nord J Psychiatry.* 2013;67(5):312-319. Nurnberg HG, et al. *Am J Psychiatry*. 1991;148(10):1371-1377. Pfohl B, et al. *Compr Psychiatry.* 1986;27(1)22-34. Reich J, et al. *Ann Clin Psychiatry* 1990;2:189-197.

Telling Patients They Have BPD

The Issue

Many clinicians state they are hesitant to discuss the diagnosis of BPD with their patients due to concerns about patients' negative reactions to being so diagnosed



Zimmerman M, et al. *Ann Clin Psychiatry*. 2018;30(3):215-219.

The Question

Are patients with BPD less satisfied/more upset with the initial evaluation than patients without BPD?

Zimmerman M, et al. *Ann Clin Psychiatry*. 2018;30(3):215-219.

The Sample

- MIDAS project
- 1093 patients presenting to the Rhode Island Hospital partial hospital program
  - 35.1% men, 62.7% women, 2.2% transgender
  - Mean age = 36.8 years
  - 29.7% graduated college
  - 75.5% white, 6.5% black, 10.1% Hispanic
  - 15.6% BPD, 56.6% MDD, 43.2% GAD, 26.0% PTSD

GAD = generalized anxiety disorder; MDD = major depressive disorder; PTSD = posttraumatic stress disorder.

Zimmerman M, et al. *Ann Clin Psychiatry*. 2018;30(3):215-219.

The Measure:
Clinically Useful Patient Satisfaction Scale (CUPSS)

- Designed to assess satisfaction with the initial encounter
    - Goal: Predict retention in treatment and outcome
- Focus on clinician behavior and interpersonal interaction
- Also evaluate office setting (“control” items)
- Global rating of satisfaction
- Designed for use in various settings

Zimmerman M, et al. *Psychiatry Res*. 2017;252:38-44.

The Results

- Mean scores on the items differed in the BPD and non-BPD patients by two-tenths of a point, or less, on the 5-point scale
- Extremely satisfied with the initial evaluation
  - (74.9% vs 75.1%, χ^2 = .003, ns)
- Diagnosis was explained in a clear way (strongly agree)
  - (76.0% vs 80.6%, χ^2 = 1.87, ns)

ns = not significant.

Zimmerman M, et al. *Ann Clin Psychiatry*. 2018;30(3):215-219.

Conclusions

1. Patients with BPD do not differ from other patients in their satisfaction with the initial evaluation
2. The patients with BPD were as likely to indicate that their diagnosis was explained in a clear way, perceive their doctors as being interested in them, and believe that their doctors understood their problems
3. Clinicians should approach the diagnosis of BPD in the same way that they make other psychiatric diagnoses

Zimmerman M, et al. *Ann Clin Psychiatry*. 2018;30(3):215-219.

Frequency of Co-occurrence

Frequency of Bipolar Disorder in Patients with BPD

- BD-I (9 studies, 634 patients) – 9.3%
- BD-II (8 studies, 949 patients) – 10.9%

BD-I = bipolar I disorder; BD-II = bipolar II disorder.

Zimmerman M, et al. *Dialogues Clin Neurosci.* 2013;15(2):155-169.

Frequency of BPD in Patients with Bipolar Disorder

- Frequency of BPD in patients with BD-I (12 studies, 598 patients) – 10.7%
- Frequency of BPD in patients with BD-II (7 studies, 261 patients) – 22.9%

Zimmerman M, et al. *Dialogues Clin Neurosci.* 2013;15(2):155-169.

Is BPD Part of the Bipolar Spectrum?

Characteristics of Both Bipolar Disorder and BPD

- Impairing
- High rate of substance use disorders
- High frequency of anxiety disorders
- Suicidality
- Most commonly present for depression
- Underdiagnosed

Zimmerman M, et al. *Dialogues Clin Neurosci.* 2013;15(2):155-169.

Is BPD Part of the Bipolar Spectrum?

- More than 2 dozen studies have directly compared individuals with bipolar disorder and BPD
- Multiple reviews of the topic
  - Most reviews conclude they are valid, distinct disorders

Paris J. *Harv Rev Psychiatry*. 2004;12(3):140-145. Magill CA. *Can J Psychiatry*. 2004;49(8):551-556. Smith DJ, et al. *Harv Rev Psychiatry*. 2004;12(3):133-139. Bassett D, et al. *Bipolar Disord*. 2017;19(5):320-323. Bayes A, et al. *Curr Opin Psychiatry*. 2014;27(1):14-20. Ghaemi SN, et al. *Acta Psychiatr Scand*. 2014;130(2):99-108. Parker G. *Br J Psychiatry*. 2014;204:252-253. Paris J, et al. *J Nerv Ment Dis*. 2015;203(1):3-7.

Validity of the Distinction: *Clinical Characteristics*

Characteristic	BPD	Bipolar Disorder
Age of onset	Younger	
Relationship difficulties	More frequent	
Sensitivity to criticism	Greater	
Impulsivity	Greater	
Hostility/anger	Greater	
Suicide attempts	More common	

Bayes A, et al. *Psychiatry Res*. 2018;264:416-420. Bayes AJ, et al. *Acta Psychiatr Scand*. 2016;133(3):187-195. Bøen E, et al. *J Affect Disord*. 2015;170:104-111. Eich D, et al. *J Affect Disord*. 2014;169:101-104. Henry C, et al. *J Psychiatr Res*. 2001;35(6):307-312. Mazer AK, et al. *Behav Brain Res*. 2019;357-358:48-56. Perroud N, et al. *Depress Anxiety*. 2016;33(1):45-55. Reich DB, et al. *Compr Psychiatry*. 2012;53(3):230-237.

Validity of the Distinction: *Neurobiological Substrates*

Characteristic	BPD	Bipolar Disorder
Cortical metabolism	Lower	
Functional network connectivity		Greater
Hippocampal volume	Smaller	

Bayes A, et al. *Psychiatry Res*. 2018;264:416-420. Bayes AJ, et al. *Acta Psychiatr Scand*. 2016;133(3):187-195. Bøen E, et al. *J Affect Disord*. 2015;170:104-111. Eich D, et al. *J Affect Disord*. 2014;169:101-104. Henry C, et al. *J Psychiatr Res*. 2001;35(6):307-312. Mazer AK, et al. *Behav Brain Res*. 2019;357-358:48-56. Perroud N, et al. *Depress Anxiety*. 2016;33(1):45-55. Reich DB, et al. *Compr Psychiatry*. 2012;53(3):230-237.

Validity of the Distinction

- Neuropsychological profiles
- Maladaptive self-schemas
- Temperament
- History of childhood abuse and neglect
- Family history of bipolar disorder

Atre-Vaidya N, et al. *J Nerv Ment Dis*. 1999;187(5):313-315. Bayes A, et al. *Psychiatry Res*. 2018;264:416-420. Bayes AJ, et al. *Acta Psychiatr Scand*. 2016;133(3):187-195. Eich D, et al. *J Affect Disord*. 2014;169:101-104. Feliu-Soler A, et al. *Psychiatry Res*. 2013;210(3):1307-1309. Gvirts HZ, et al. *Eur Psychiatry*. 2015;30(8):959-964. Mazer AK, et al. *Behav Brain Res*. 2019;357-358:48-56. Perroud N, et al. *Depress Anxiety*. 2016;33(1):45-55.

Why is Differential Diagnosis Important?
Treatment Implications

BPD—psychotherapy primary, medication is adjunctive

Bipolar disorder—medication is primary, psychotherapy is adjunctive

Zimmerman M, et al. *Dialogues Clin Neurosci.* 2013;15(2):155-169.

Problem with Differential Diagnosis

- Either/or
- What about the comorbid group?

Survey of Clinicians' Practice Regarding the Diagnosis of Bipolar Disorder and BPD

- Online survey of members of Royal College of Psychiatrists
- 648 respondents
  - Response rate of 8.1%
- 70% did not consider the 2 disorders as part of the same illness spectrum
- 94% indicated that they rarely diagnosed both disorders

Saunders KE, et al. *Eur Psychiatry*. 2015;30(8):965-974.

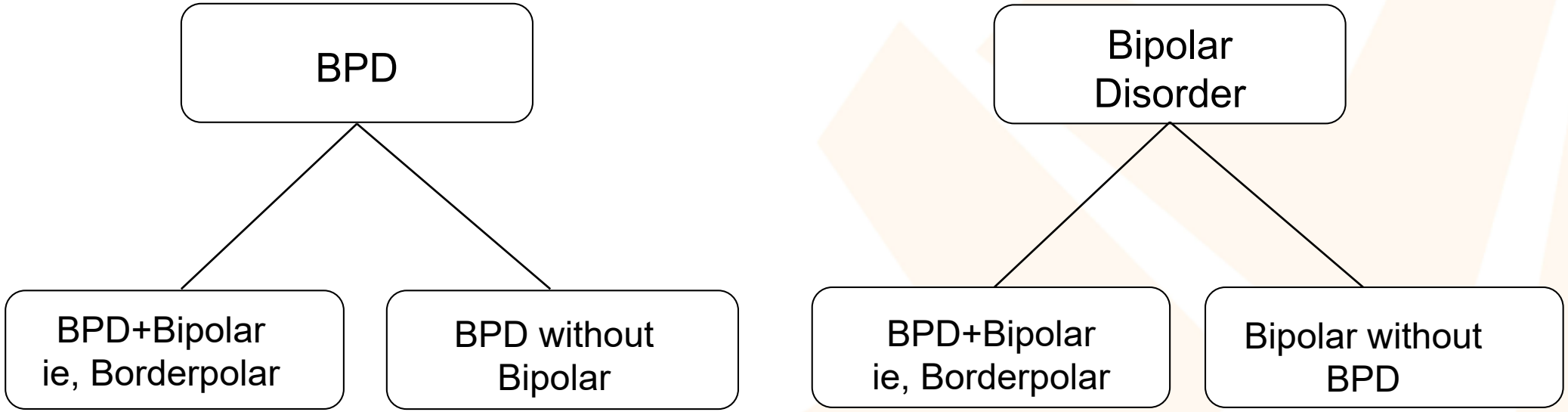
Importance of Recognizing Borderpolar

Comparisons

- Bipolar disorder with vs without BPD
  - ie, Borderpolar vs bipolar disorder
- BPD with vs without bipolar disorder
  - ie, Borderpolar vs BPD

Frías Á, et al. *J Affect Disord*. 2016;202:210-219.

Comparisons



Borderpolar vs Bipolar Disorder

- More mood episodes
- More often hospitalized
- Earlier age of onset of bipolar disorder
- Greater suicidality
- Greater hostility
- Higher prevalence of substance abuse and anxiety disorders
- Greater childhood adversity

Frías Á, et al. *J Affect Disord*. 2016;202:210-219.

Borderpolar vs Bipolar Disorder

- No data on
  - treatment response
  - functioning
  - time unemployed
  - receiving disability payments
  - family history
  - longitudinal course

Frías Á, et al. *J Affect Disord*. 2016;202:210-219.

Journal of Personality Disorders, 28(3), 358-364, 2014

COMORBID BIPOLAR DISORDER AND BORDERLINE PERSONALITY DISORDER AND HISTORY OF SUICIDE ATTEMPTS

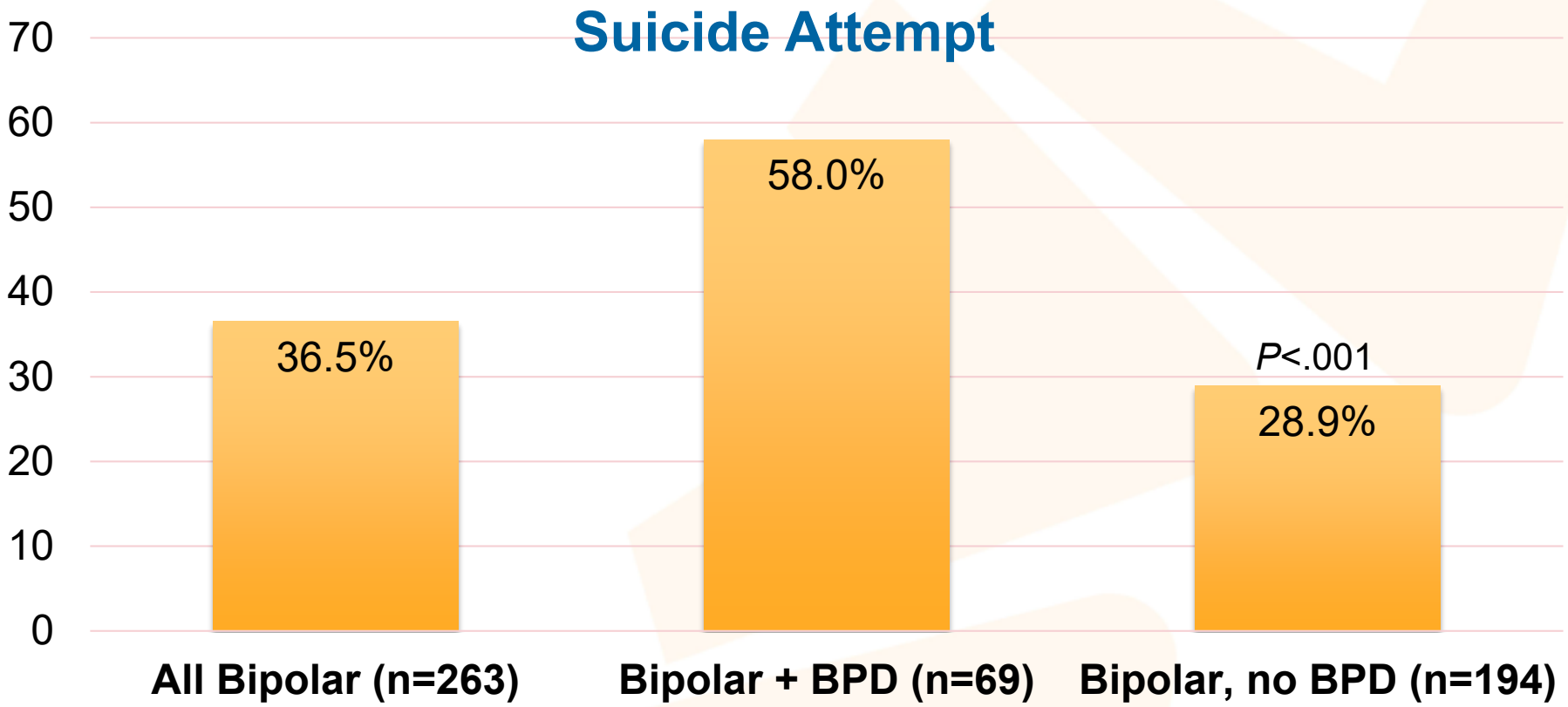
Mark Zimmerman, MD, Jennifer Martinez, BA, Diane Young, PhD, Iwona Chelminski, PhD, Theresa A. Morgan, PhD, and Kristy Dalrymple, PhD

Borderpolar vs Bipolar Disorder: *History of Suicide Attempts*

- Patients: 3465 psychiatric outpatients
- Methods: Evaluated with semi-structured interviews

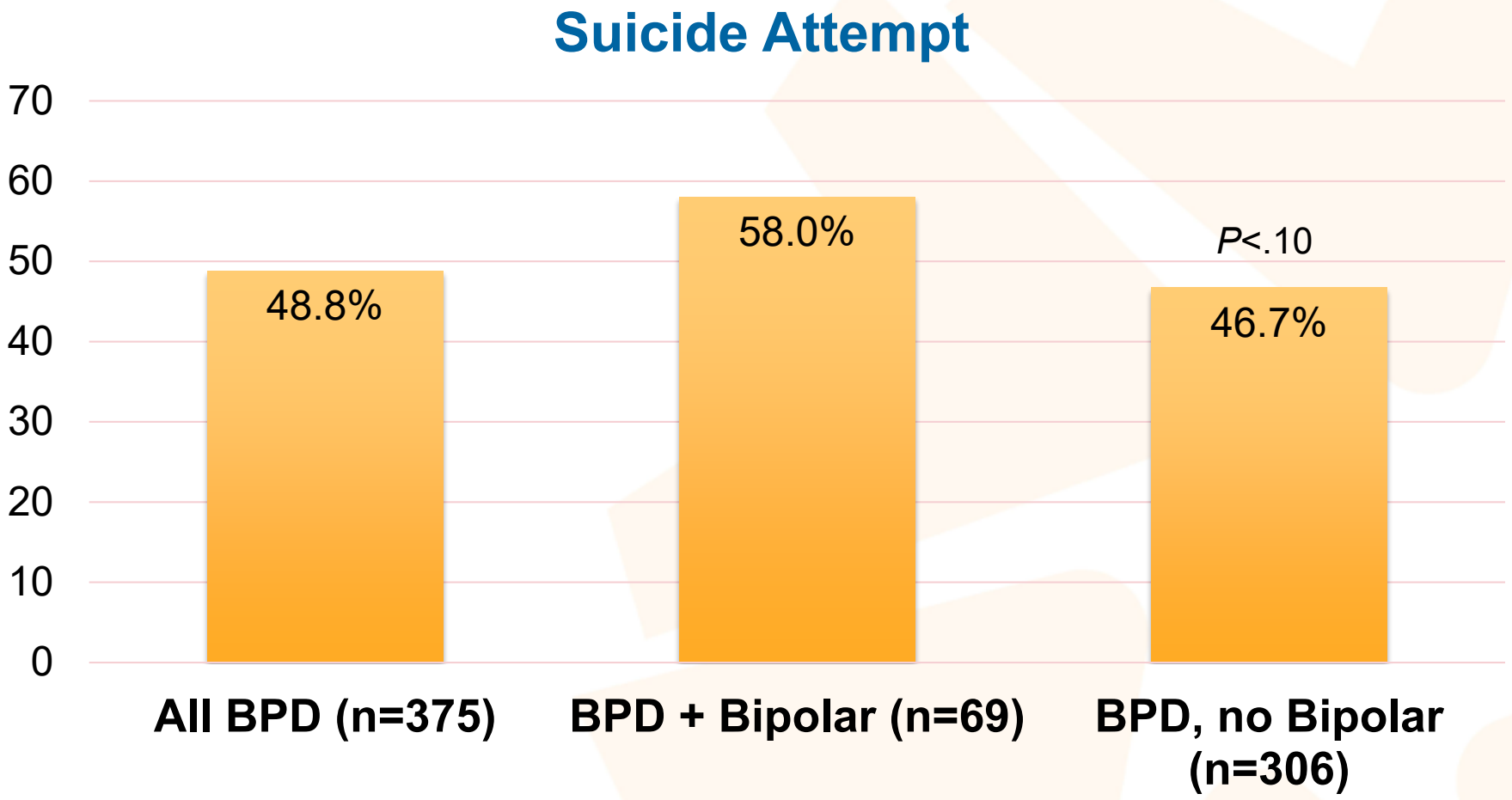
Zimmerman M, et al. *J Pers Disord*. 2014;28(3):358-364.

History of Suicide Attempts in Patients with Bipolar Disorder with and without BPD



Zimmerman M, et al. *J Pers Disord*. 2014;28(3):358-364.

History of Suicide Attempts in Patients with BPD with and without Bipolar Disorder



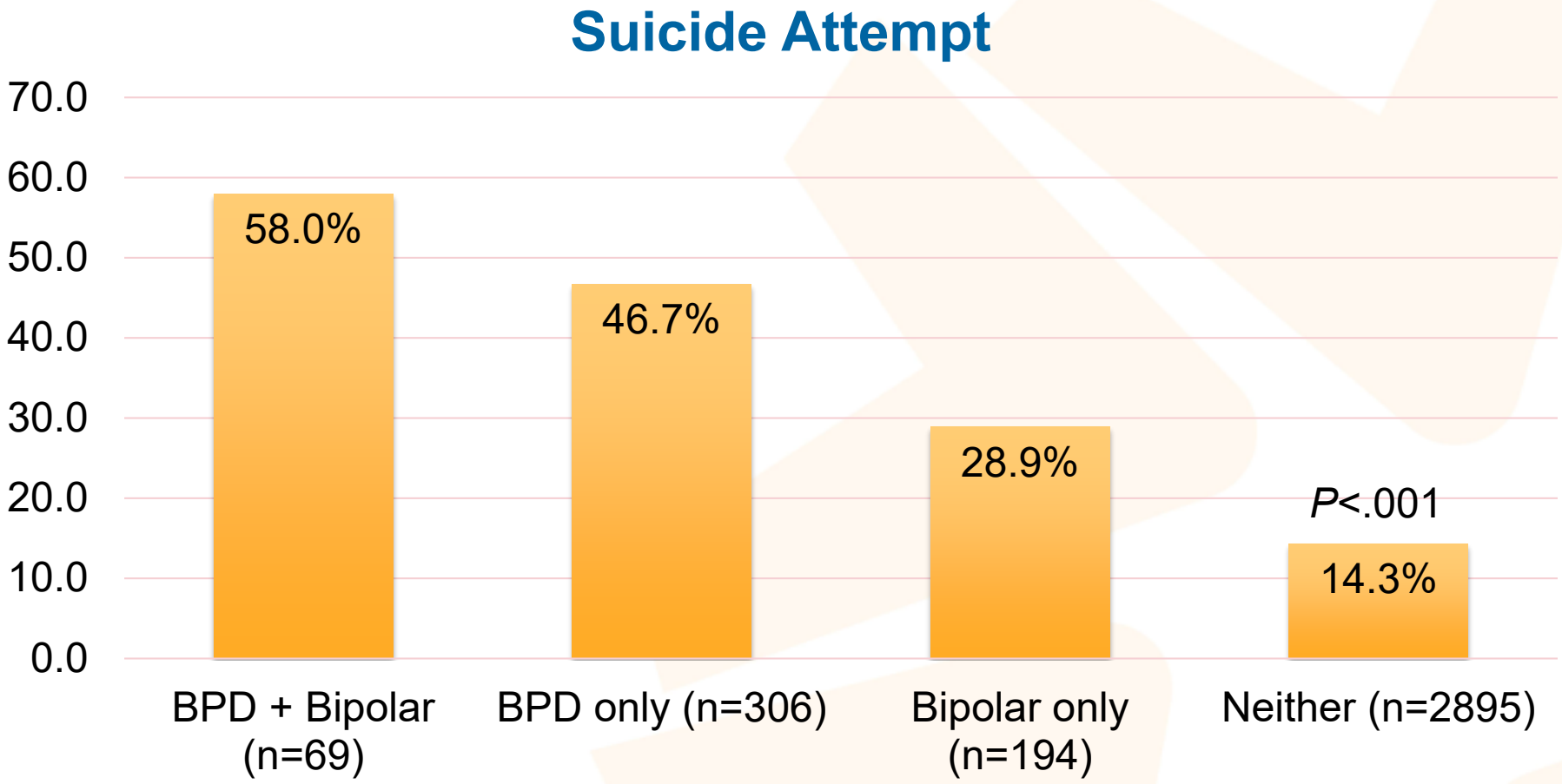
Zimmerman M, et al. *J Pers Disord*. 2014;28(3):358-364.

Borderpolar vs BPD

- Very little research
- No differences in suicide attempts, hospitalizations, childhood adversity, longitudinal course, comorbid disorders

Richard-Lepouriel H, et al. *J Affect Disord*. 2019;244:33-41. Parker G, et al. *Br J Psychiatry*. 2016;209(3):209-215. Bayes A, et al. *J Affect Disord*. 2016;204:103-111. Gunderson JG, et al. *Am J Psychiatry*. 2006;163(7):1173-1178. Goodman G, et al. *J Nerv Ment Dis*. 1998;186(10):616-622.

History of Suicide Attempts in Patients with and without BPD and Bipolar Disorder



Zimmerman M, et al. *J Pers Disord*. 2014;28(3):358-364.

Patients with BPD and Bipolar Disorder (Borderpolar): *A Descriptive and Comparative Study*

Patients: 3465 psychiatric outpatients

Methods: Evaluated with semi-structured interviews

Sample:

Borderpolar	n=59
BD-I/BD-II	n=128
BPD	n=330

Zimmerman M, et al. Submitted for publication.

Borderpolar vs Bipolar Disorder: *Overall Comorbidity*

Disorder	Borderpolar (n=59)	Bipolar (n=128)	*P*-value
≥ 3 Axis I disorders*	71.2%	44.5%	.001
No. current psychiatric disorders	4.3	2.4	.001
Any personality disorder**	59.4%	37.0%	.05

***Not including bipolar disorder; **Not including BPD.**
Zimmerman M, et al. Submitted for publication.

Borderpolar vs Bipolar Disorder: *Anxiety Disorder Comorbidity*

Disorder	Borderpolar (n=59)	Bipolar (n=128)	*P*-value
Panic disorder	32.2%	21.9%	ns
Specific phobia	25.4%	14.1%	ns
Social phobia	49.2%	38.3%	ns
PTSD	**49.2%**	**9.4%**	**.001**
OCD	**28.8%**	**10.2%**	**.001**
GAD	30.5%	33.6%	ns

OCD = obsessive-compulsive disorder.

Zimmerman M, et al. Submitted for publication.

Borderpolar vs Bipolar Disorder: *Substance Use and Other Disorders Comorbidity*

Disorder	Borderpolar (n=59)	Bipolar (n=128)	*P*-value
Alcohol abuse/dependence	8.5%	6.3%	ns
Drug abuse/dependence	**13.6%**	**4.7%**	**.05**
Any substance use disorder	**22.0%**	**10.9%**	**.05**
Any eating disorder	8.5%	7.8%	ns
Any somatoform disorder	**16.9%**	**6.3%**	**.05**
Any impulse control disorder	27.1%	15.6%	ns

Zimmerman M, et al. Submitted for publication.

Borderpolar vs Bipolar Disorder: *Personality Disorder Dimensional Scores*

Disorder	Borderpolar	Bipolar	*P*-value
Paranoid[a]	**2.1**	**0.9**	**.01**
Schizoid[a]	0.7	0.5	ns
Schizotypal[a]	0.9	0.6	ns
Antisocial[b]	**1.7**	**0.5**	**.001**
Histrionic[a]	**1.7**	**1.0**	**.05**
Narcissistic[a]	**1.8**	**1.0**	**.05**
Avoidant[a]	**2.4**	**1.4**	**.05**
Dependent[a]	**1.5**	**0.6**	**.01**
Obsessive-compulsive[a]	2.0	1.6	ns

[a]Borderpolar (n=31–32), Bipolar (n=80–81); [b]Borderpolar (n=44), Bipolar (n=96).
Zimmerman M, et al. Submitted for publication.

Borderpolar vs Bipolar Disorder:

Psychiatric Disorders in First-Degree Relatives (Morbid Risk %)

Disorder	Borderpolar (n=279)	Bipolar (n=128)	*P*-value
GAD	8.2	5.5	ns
MDD	**29.1**	**22.9**	**.05**
Bipolar disorder	**11.3**	**6.5**	**.01**
Panic disorder	5.5	4.5	ns
Social phobia	2.2	1.5	ns
PTSD	**9.0**	**1.4**	**.001**
OCD	2.2	2.2	ns
Specific phobia	**1.9**	**0.6**	**.05**
Alcohol use disorder	**28.3**	**17.0**	**.001**
Drug use disorder	**20.4**	**8.2**	**.001**

Zimmerman M, et al. Submitted for publication.

Borderpolar vs Bipolar Disorder: *Symptom Severity at Evaluation*

	Borderpolar (n=59)	Bipolar (n=128)	*P*-value
CGI of depression severity	3.0	2.7	ns
Subjectively experienced anger	**3.4**	**2.3**	**.001**
Expressed anger	**2.4**	**1.4**	**.001**
Psychic anxiety	2.9	2.5	ns
Somatic anxiety	2.4	2.1	ns
Suicidal ideation	**1.8**	**1.1**	**.01**
Chronic episode (> 2 years)	**32.2%**	**18.3%**	**.05**

CGI = Clinical Global Impression.
Zimmerman M, et al. Submitted for publication.

Borderpolar vs Bipolar Disorder: *Childhood Trauma Questionnaire*

	Borderpolar (n=30)	Bipolar (n=80)	*P*-value
Childhood Trauma Questionnaire Total Score[a]	60.6	43.6	.001
Physical abuse	11.7	8.0	.001
Physical neglect	8.4	7.4	.01
Emotional abuse	17.3	12.2	.001
Emotional neglect	12.2	8.9	.01
Sexual abuse	11.0	7.7	.01

Zimmerman M, et al. Submitted for publication.

Borderpolar vs Bipolar Disorder: *Functioning*

	Borderpolar (n=59)	Bipolar (n=128)	*P*-value
Global Assessment of Functioning (GAF) < 50	72.9%	44.5%	.001
Current social functioning[a]	4.2	3.6	.05
Adolescent social functioning[a]	3.4	2.8	.01
Chronic unemployment (> 4 years)	28.8%	10.7%	.01
Persistent unemployment (> 2 years)	51.9%	22.3%	.001
Temporary disability	46.4%	21.4%	.05
History of psychiatric hospitalization	64.4%	46.1%	.05

Zimmerman M, et al. Submitted for publication.

Borderpolar vs BPD: *Overall Comorbidity*

Disorder	Borderpolar (n=59)	BPD (n=330)	*P*-value
≥ 3 Axis I disorders*	71.2%	79.1%	ns
No. current psychiatric disorders	**4.3**	**5.0**	**.05**
Any personality disorder**	59.4%	52.0%	ns

***Not including bipolar disorder; **Not including BPD.**
Zimmerman M, et al. Submitted for publication.

Borderpolar vs BPD:
Anxiety Disorder Comorbidity

Disorder	Borderpolar (n=59)	BPD (n=330)	*P*-value
Panic disorder	32.2%	27.3%	ns
Specific phobia	25.4%	24.2%	ns
Social phobia	49.2%	48.2%	ns
PTSD	**49.2%**	**26.1%**	**.001**
OCD	**28.8%**	**12.1%**	**.001**
GAD	30.5%	32.4%	ns

Zimmerman M, et al. Submitted for publication.

Borderpolar vs BPD: *Substance Use and Other Disorders Comorbidity*

Disorder	Borderpolar (n=59)	BPD (n=330)	*P*-value
Alcohol abuse/dependence	**8.5%**	**18.8%**	**.05**
Drug abuse/dependence	13.6%	13.0%	ns
Any substance use disorder	22.0%	25.5%	ns
Any eating disorder	8.5%	8.5%	ns
Any somatoform disorder	16.9%	15.5%	ns
Any impulse control disorder	27.1%	22.1%	ns

Zimmerman M, et al. Submitted for publication.

Borderpolar vs BPD: *Personality Disorder Dimensional Scores*

Disorder	Borderpolar	BPD	*P*-value
Paranoid[a]	2.1	1.8	ns
Schizoid[a]	0.7	0.6	ns
Schizotypal[a]	0.9	0.9	ns
Antisocial[b]	1.7	1.2	ns
Histrionic[a]	1.7	1.4	ns
Narcissistic[a]	1.8	1.7	ns
Avoidant[a]	2.4	2.1	ns
Dependent[a]	1.5	1.7	ns
Obsessive-compulsive[a]	2.0	1.8	ns

[a]Borderpolar (n=31–32), BPD (n=173–175); [b]Borderpolar (n=44), BPD (n=231).
Zimmerman M, et al. Submitted for publication.

Borderpolar vs BPD:

Psychiatric Disorders in First-Degree Relatives (Morbid Risk %)

Disorder	Borderpolar (n=279)	BPD (n=330)	*P*-value
GAD	8.2	7.2	ns
MDD	29.1	27.3	ns
Bipolar disorder	**11.3**	**3.4**	**.001**
Panic disorder	5.5	5.3	ns
Social phobia	2.2	1.1	ns
PTSD	**9.0**	**2.9**	**.001**
OCD	2.2	1.9	ns
Specific phobia	1.9	0.9	ns
Alcohol use disorder	**28.3**	**20.5**	**.01**
Drug use disorder	**20.4**	**10.6**	**.001**

Zimmerman M, et al. Submitted for publication.

Borderpolar vs BPD: *Symptom Severity at Evaluation*

	Borderpolar (n=59)	BPD (n=330)	*P*-value
CGI of depression severity	3.0	2.8	ns
Subjectively experienced anger	3.4	3.2	ns
Expressed anger	2.4	2.3	ns
Psychic anxiety	2.9	2.8	ns
Somatic anxiety	2.4	2.4	ns
Suicidal ideation	1.8	1.6	ns
Chronic episode (> 2 years)	32.2%	35.5%	ns

Zimmerman M, et al. Submitted for publication.

Borderpolar vs BPD: *Childhood Trauma Questionnaire*

	Borderpolar (n=30)	BPD (n=330)	*P*-value
Childhood Trauma Questionnaire Total Score[a]	**60.6**	**50.1**	**.01**
Physical abuse	**11.7**	**9.3**	**.05**
Physical neglect	8.4	8.1	ns
Emotional abuse	**17.3**	**13.7**	**.005**
Emotional neglect	**12.2**	**10.2**	**.05**
Sexual abuse	11.0	9.1	ns

Zimmerman M, et al. Submitted for publication.

Borderpolar vs BPD: *Functioning*

	Borderpolar (n=59)	BPD (n=330)	*P*-value
Global Assessment of Functioning (GAF) < 50	**43.3**	**46.7**	**.01**
Current social functioning[a]	4.2	3.9	ns
Adolescent social functioning[a]	3.4	3.2	ns
Chronic unemployment (> 4 years)	**28.8%**	**9.6%**	**.001**
Persistent unemployment (> 2 years)	**51.9%**	**24.4%**	**.001**
Temporary disability	**46.4%**	**11.2%**	**.001**
History of psychiatric hospitalization	**64.4%**	**42.4%**	**.01**

Zimmerman M, et al. Submitted for publication.

Treatment

Placebo-Controlled Studies of BPD and Bipolar Disorder

- Patients: 30 with BPD and history of BD-II
- Exclusion: Current MDD, hypomania, BD-I
- Medication: Divalproex sodium (mean dose 850 mg)
- Duration: 24 weeks
- Measures: SCL-90, modified Overt Aggression Scale
- Results: Divalproex sodium significantly more effective on
  - SCL-90 interpersonal sensitivity
  - SCL-90 anger/hostility
  - Modified Overt Aggression Scale

SCL = Symptom Checklist.

Frankenburg FR, et al. *J Clin Psychiatry*. 2002;63(5):442-446.

Open-Label Studies of BPD and Bipolar Disorder

- Aguglia et al
  - 50 patients with euthymic BD-I
  - Focus on impulsivity and aggressiveness
- Martinez and Caballero
  - Case report
- Preston et al
  - Assessed BPD 15 months after entry into a study

Aguglia A, et al. *Int Clin Psychopharmacol*. 2018;33(3):121-130. Martínez JS, et al. *J Clin Psychopharmacol*. 2017;37(2):266-267. Preston GA, et al. *J Affect Disord*. 2004;79(1-3):297-303.

Psychotherapy Studies of BPD and Bipolar Disorder

Official Treatment Guidelines for BPD

APA

1. Psychotherapy is first-line treatment
2. Recommend symptom-specific medication treatment
   - SSRIs for affective dysregulation or impulsivity
   - Mood stabilizers for impulsivity
   - Antipsychotics for cognitive-perceptual symptoms

NICE (National Institute of Clinical Excellence)

1. Psychotherapy is first-line treatment
2. Do not recommend medication for BPD symptoms
3. Recommend medication for comorbid conditions

SSRI = selective serotonin reuptake inhibitor.

American Psychiatric Association Work Group on Borderline Personality Disorder. Practice Guideline for The Treatment of Patients With Borderline Personality Disorder. October 2001. https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/bpd.pdf. Accessed June 7, 2019.

NICE. Borderline personality disorder: recognition and management. January 2009. www.nice.org.uk/guidance/cg78/resources/borderline-personality-disorder-recognition-and-management-975635141317. Accessed June 7, 2019.

4 Facts about the Pharmacotherapy of BPD

1. No medication has been approved for BPD anywhere in the world
2. Almost all patients with BPD are treated with psychotropic medication
3. Polypharmacy is the rule, rather than the exception
4. A variety of medications are prescribed

Starcevic V, et al. *Curr Opin Psychiatry*. 2018;31(1):69-73.

Real World Pharmacologic Treatment of BPD: European Drug Safety Project

Patients

- 2195 inpatients
- 58 hospitals in Germany, Switzerland, Austria
- Principal diagnosis of BPD (2.5%) of all patients in the study
- Comorbid diagnoses not recorded
- Cross-sectional analysis

Bridler R, et al. *Eur Neuropsychopharmacol*. 2015;25(6):763-772.

European Drug Safety Project Results

Rates of Polypharmacy

- Mean number of medications = 2.8
- 54% on 3+ psychoactive medications

Medications used

- Antidepressants 70.0%
- Antipsychotics 69.1%
- Anticonvulsants 32.5%
- Benzodiazepines 29.6%

Bridler R, et al. *Eur Neuropsychopharmacol*. 2015;25(6):763-772.

Cochrane Review of Pharmacotherapy of BPD: Conclusions

- No evidence of efficacy for symptoms of: Abandonment, emptiness, identity disturbance, dissociation
- Robustness of findings is low
  - Few studies; small sample sizes for most studies
  - Varied measures
  - Exclusion criteria reduce generalizability
- No evidence of efficacy of polypharmacy, and therefore this should be avoided when possible
- Mood stabilizers first-line treatment for affective dysregulation. Second-generation antipsychotics also effective
- Mood stabilizers preferred for impulsivity
- Little evidence for efficacy of SSRIs
  - No studies of SSRIs in patients with MDD and BPD

Lieb K, et al. *Br J Psychiatry*. 2010;196(1):4-12.

Psychotherapy for BPD: More Than DBT

- **DBT**: Dialectical Behavior Therapy
- **MBT**: Mentalization-Based Therapy
- **TFP**: Transference-Focused Psychotherapy
- **SFT**: Schema-Focused Therapy
- **GPM**: Good Psychiatric Management
- **STEPPS**: Systems Training for Emotional Predictability and Problem Solving

Links PS, et al. *Curr Psychiatry Rep*. 2017;19(3):16.

Meta-Analysis of Efficacy of Psychotherapy for BPD

Variable	Stand-alone Design				Add-on Design				*P* Value[b]
	No. of Trials	Hedges *g* (95% CI)[a]	NNT	I^2 (95% CI), %	No. of Trials	Hedges *g* (95% CI)[a]	NNT	I^2 (95% CI), %	
Posttest									
Borderline-relevant outcomes[c]	17	0.32 (0.14 to 0.51)	5.56	49 (0 to 69)	10	0.40 (0.15 to 0.65)	4.50	50 (0 to 74)	.63
Borderline symptoms	10	0.31 (0.04 to 0.57)	5.75	62 (3 to 79)	8	0.56 (0.15 to 0.97)	3.25	76 (43 to 87)	.30
Self-harm and parasuicidal behavior	13	0.32 (0.09 to 0.54)	5.56	55 (0 to 75)	6	0.24 (−0.07 to 0.55)	7.46	41 (0 to 75)	.68
Suicide	10	0.44 (0.15 to 0.74)	4.10	60 (0 to 78)	3	0.35 (0.02 to 0.68)	5.10	10 (0 to 75)	.67
Health service use	13	0.40 (0.22 to 0.58)	4.50	22 (0 to 59)	3	0.16 (−0.13 to 0.46)	11.11	5 (0 to 74)	.17
General psychopathology, anxiety, and depression	13	0.32 (0.09 to 0.55)	5.56	62 (18 to 78)	10	0.53 (0.24 to 0.82)	3.42	62 (4 to 79)	.25

Cristea IA, et al. *JAMA Psychiatry*. 2017;74(4):319-328.

Meta-Analysis of Efficacy of Psychotherapy for BPD: Conclusions

- Various therapies for BPD are effective
- Effects are small
- Effects are not found in trials with low risk of bias
- Control groups using a manual were as effective as BPD specific therapies

Cristea IA, et al. *JAMA Psychiatry*. 2017;74(4):319-328.

Recent Progress in Psychotherapy for BPD: Emergence of Generalist Therapies

- Good psychiatric management
  - Theory-based therapies requiring extensive training not necessary

Links PS, et al. *Curr Psychiatry Rep*. 2017;19(3):16.

So, In the Absence of Data, What Should I Do?

Practical Approach to Diagnosing and Treating Patients with Comorbid Bipolar Disorder and BPD

1. Screen for the diagnoses
2. Tell patients if you make the diagnoses
3. Educate patients about the diagnoses (and prognosis)
4. Don’t let patients define themselves by their disorders
5. Be collaborative
6. Set limits
7. Don’t be rigid
8. Help patients distinguish between the features of the 2 disorders

Practical Approach to Diagnosing and Treating Patients with Comorbid Bipolar Disorder and BPD

9. Be willing to be wrong, and admit it
10. Think long-term
11. Refer for therapy
    Possibly require it
12. Be an island of stability and predictability
13. Set expectations regarding medication
14. Understand the downside of prescribing medication
15. Try to avoid medicating crises
16. See patients regularly

Practical Approach to Diagnosing and Treating Patients with Comorbid Bipolar Disorder and BPD

17. Try to avoid polypharmacy (or poly, polypharmacy)
18. Switching is preferred to augmenting
19. Adequate duration and dosage
20. Involve the family
21. Attend to functioning as well as symptom management
22. Acceptance and self-compassion
23. Promote healthy lifestyle
24. Talk to colleagues about your frustrations and concerns

Conclusions

Practical Take-Aways

- BPD and bipolar disorder are valid, distinct disorders
- 20% of patients with bipolar disorder or BPD also have the other disorder
- Assessment of the affective instability criterion of BPD can be used to screen for the disorder in patients with bipolar disorder
- Patients are accepting of the diagnosis of BPD
- Patients with both disorders (ie, borderpolar) have more severe psychosocial morbidity than patients with only 1 of these disorders
- The treatment literature is very sparse. There are no placebo-controlled studies of patients with BPD and bipolar depression