Update on Borderline Personality Disorder: *What Every Clinician Needs to Know*

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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.

Overview

- Epidemiology of BPD
- Prevalence of BPD in clinical settings
- Underrecognition of BPD in clinical settings
- Screening for BPD
- Telling patients they have BPD
- Longitudinal course of BPD
- Empirically supported psychotherapies for BPD
- Pharmacotherapy of BPD

BPD = borderline personality disorder.

Disclosure

COMMENTARY

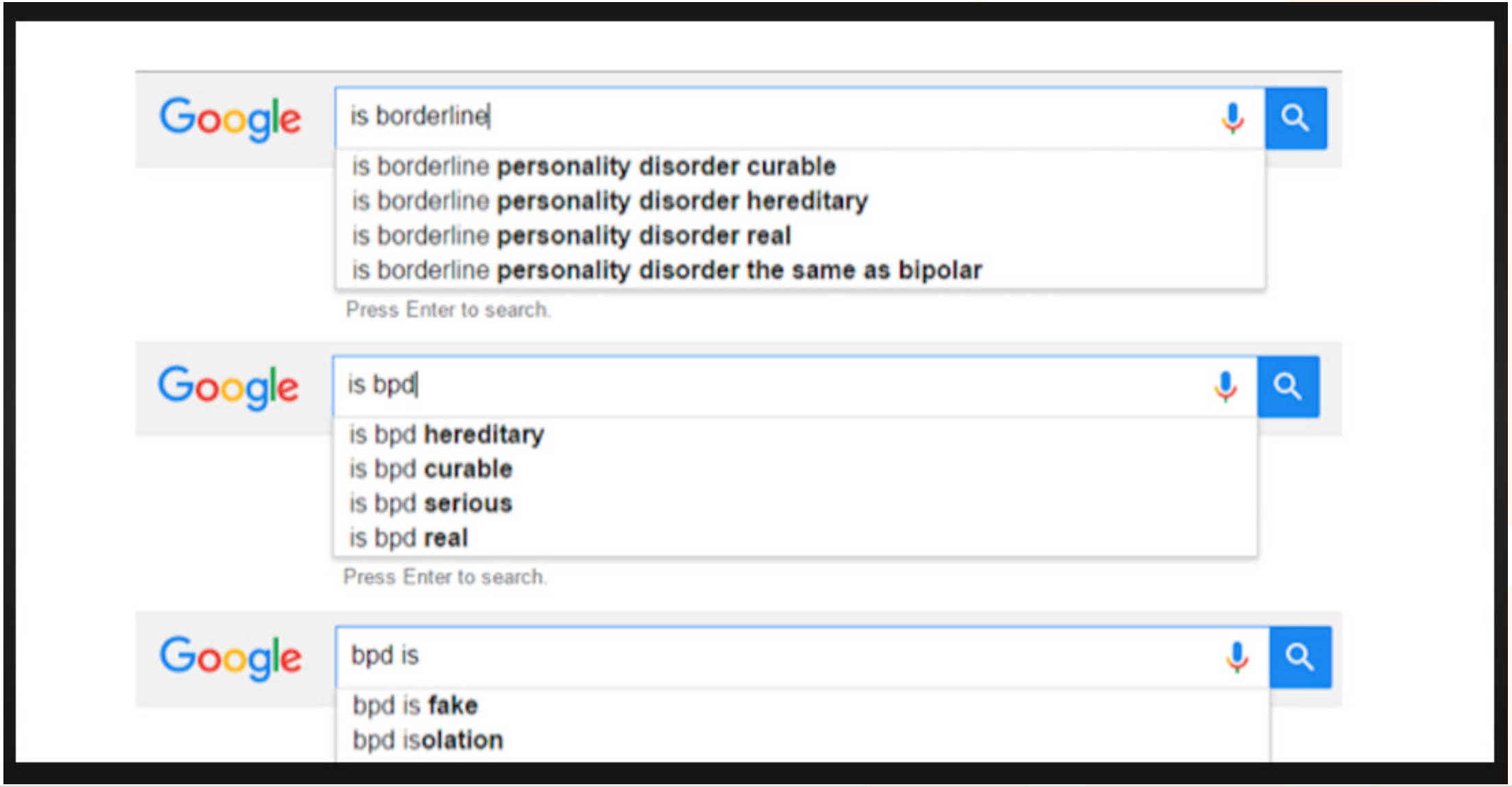
Borderline Personality Disorder

A Disorder in Search of Advocacy

Mark Zimmerman, MD

Zimmerman M. *J Nerv Ment Dis*. 2015;203(1):8-12.

Why BPD Needs Advocates



Epidemiology of BPD

Prevalence of BPD in General Population Studies

- Review of 15 general population studies
- Median prevalence across all studies = 1.1%

Morgan TA, et al. Epidemiology of Personality Disorders. In: Livesley WJ, et al. (Eds). *Handbook of Personality Disorders: Theory, Research, and Treatment*. Second Edition. Guilford Press; 2018.

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

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Prevalence of BPD in Clinical Settings: Implications for Screening

- Screening **recommended** in patients with the following principal diagnoses
  - Bipolar disorder
  - Posttraumatic stress disorder
  - Major depressive disorder
  - Panic disorder
- Screening **not recommended** in patients with the following principal diagnoses
  - Dysthymic disorder
  - Generalized anxiety disorder
  - Adjustment disorder

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Screening for BPD

Screening for BPD

- Screening for borderline personality
  - Screening questionnaires are not used
  - Polythetically defined criteria

BPD Criteria: 5 of 9

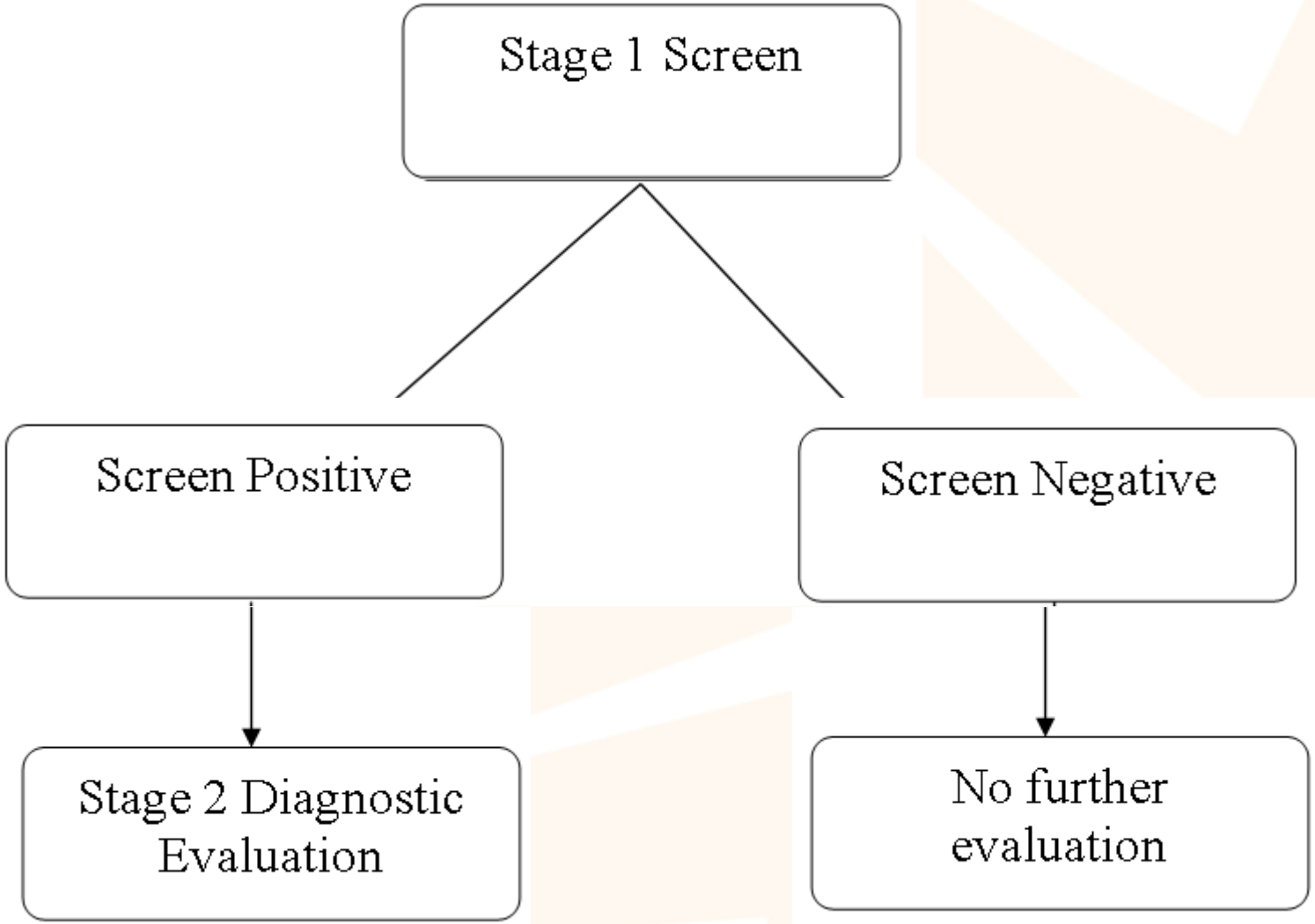
1. Avoid abandonment
2. Unstable relationships
3. Identity disturbance
4. Impulsivity
5. Suicidality/self-injury
6. Affective instability
7. Emptiness
8. Anger
9. Stress-induced paranoia/dissociation

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

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

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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

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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%

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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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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 predicitive 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.

Who Should You Screen?

ANNALS OF CLINICAL PSYCHIATRY 2017;29(1):54-60

RESEARCH ARTICLE

Principal diagnoses in psychiatric outpatients with borderline personality disorder: Implications for screening recommendations

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

Prevalence of BPD in Clinical Settings: Implications for Screening

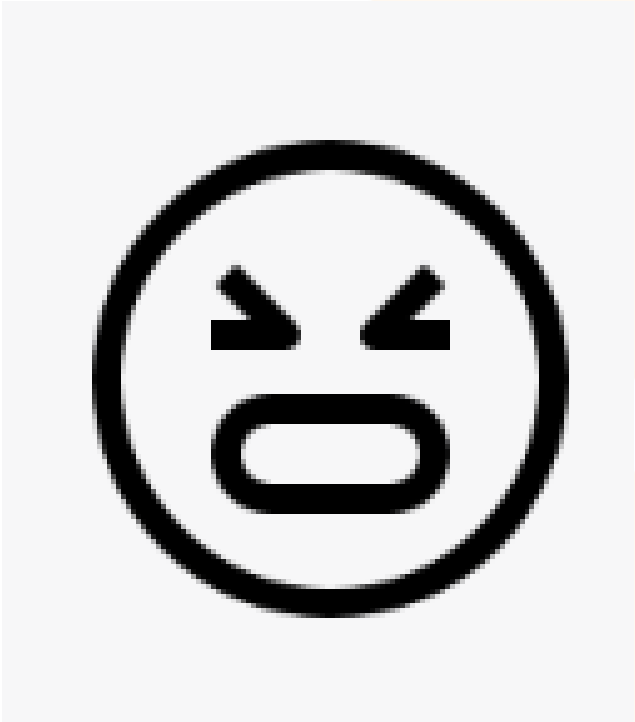
- Screening recommended in patients with the following principal diagnoses
  - Bipolar disorder
  - Posttraumatic stress disorder
  - Major depressive disorder
  - Panic disorder
- Screening not recommended in patients with the following principal diagnoses
  - Dysthymic disorder
  - Generalized anxiety disorder
  - Adjustment disorder

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

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

MDD = major depressive disorder; GAD = generalized anxiety 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.

CUPPS: Sample Items

- Scale length – 16 items (or 18 items for outpatient version)
  - Clinician attitude and behavior (12 items)
    - "The evaluation was thorough and complete."
    - "I was asked for my opinion about treatment."
    - "My doctor seemed genuinely interested in me."
  - Office Environment and Staff (2 items)
  - Overall Satisfaction (2 items)

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.

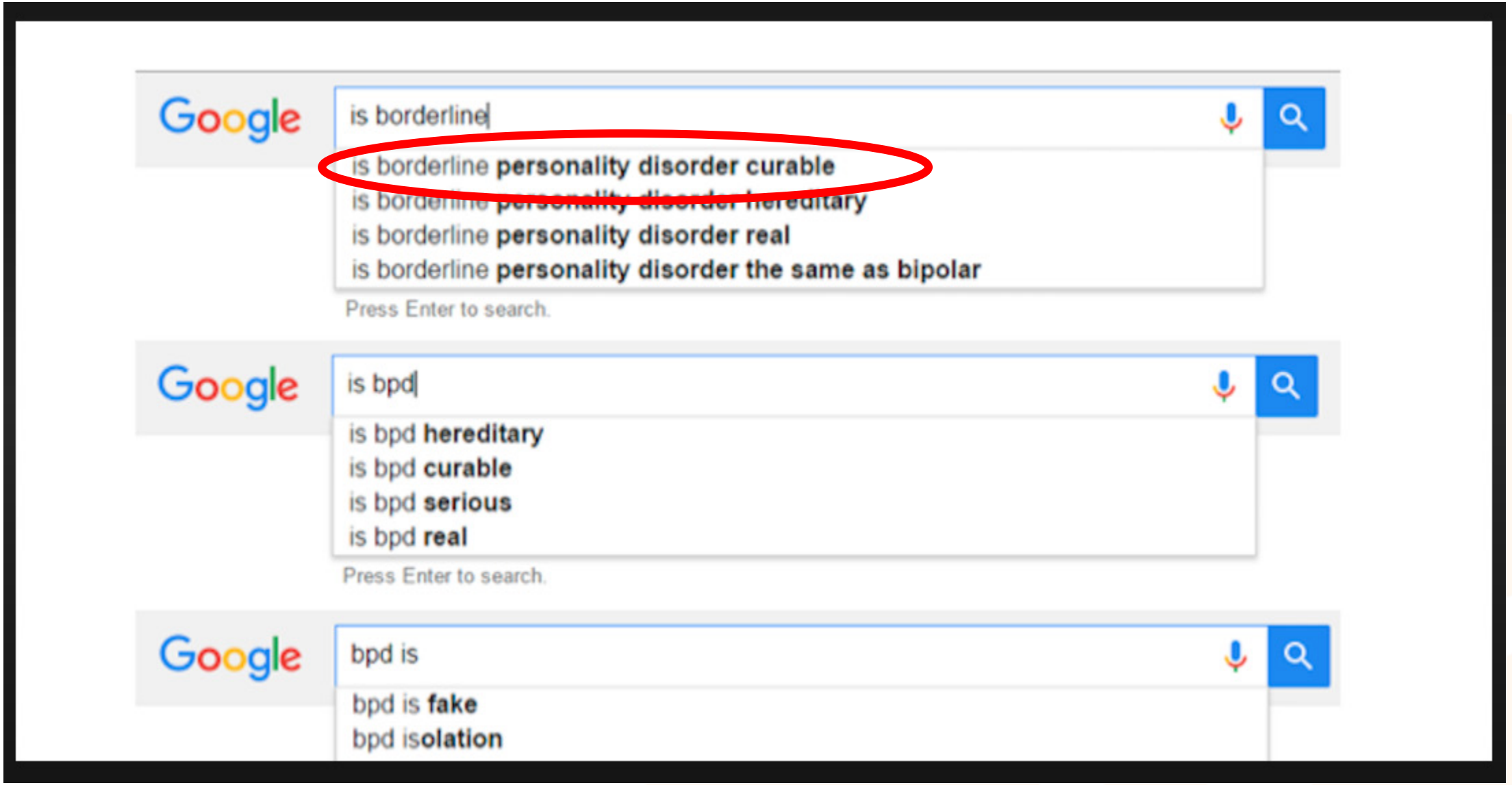
Conclusions

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.

Longitudinal Course of BPD


BORDERLINE PERSONALITY DISORDER
IS THERE HOPE?
HEALINGFROMBPD.COM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Clinician Beliefs

- “When borderline personality disorder (BPD) was first defined, it was considered a severe, chronic, untreatable disorder with poor prognosis.” **Alvarez-Tomás I, et al. *J Pers Disord*. 2017;31(5):590-605.**
- “Many clinicians still believe that borderline personality disorder is a chronic disorder.” **Zanarini MC, et al. *Am J Psychiatry*. 2012;169(5):476-483.**
- “…seminal long-term retrospective studies…largely completed…from 1985 to 1995, indicated that…many patients get better, thereby challenging the widely held view of BPD as an unremittingly chronic condition. Still, the methodological and design limitations that characterized this prior literature diminished its impact, and a firmly entrenched pessimism about the prognosis of patients with BPD has persisted.” **Gunderson JG, et al. *Arch Gen Psychiatry*. 2011;68(8):827-837.**

Prospective Longitudinal Studies

- McLean Study of Adult Development (MSAD)
- Collaborative Longitudinal Personality Disorders Study (CLPS)

Zanarini MC, et al. *Am J Psychiatry*. 2010;167(6):663-667. Gunderson JG, et al. *Arch Gen Psychiatry*. 2011;68(8):827-837.

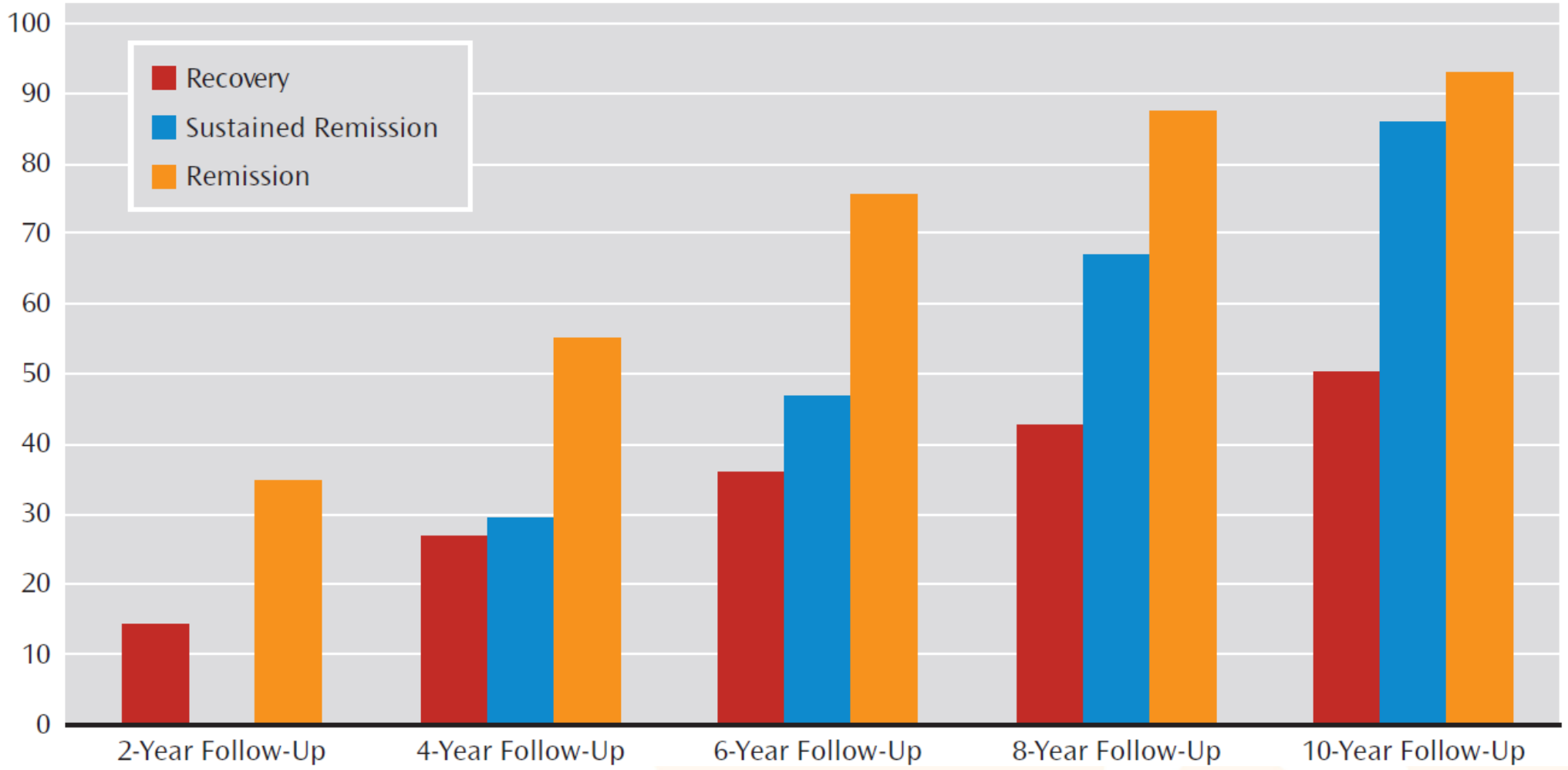
MSAD

- Sample
  - 290 inpatients at McLean Hospital with BPD age 18–35 years
  - 72 inpatient controls with other personality disorders
- Methods
  - Interview every 2 years with semi-structured interviews for up to 16 years
  - Follow-up success rate: 92% of surviving patients at 10 years
- Definitions
  - Remission: Not meeting BPD criteria for 2 years
  - Sustained remission: Not meeting BPD criteria for at least 4 years
  - Recovery: GAF ≥ 61
    - At least 1 emotionally sustaining relationship
    - Work or school consistently on a full-time basis

GAF = Global Assessment of Functioning.

Zanarini MC, et al. *Am J Psychiatry*. 2010;167(6):663-667.

Time to Attainment of Remission, Sustained Remission, and Recovery from BPD



Zanarini MC, et al. *Am J Psychiatry*. 2010;167(6):663-667.

MSAD:
Cumulative Recovery Rates over 16 Years of Follow-up

	Recovery
Year 2	27%
Year 4	36%
Year 8	43%
Year 10	47%
Year 12	50%
Year 14	56%
Year 16	60%

Zanarini MC, et al. *Am J Psychiatry*. 2012;169(5):476-483.

CLPS

- Sample
  - 175 patients with BPD at 4 sites (Brown, Columbia, Harvard, Yale)
  - Age 18–45 years
- Methods
  - Interview every 2 years with semi-structured interviews for up to 10 years
  - Follow-up success rate: 63% of surviving patients at 10 years
- Definitions
  - Remission: ≤ 2 BPD criteria for 1 year

Gunderson JG, et al. *Arch Gen Psychiatry*. 2011;68(8):827-837.

CLPS:
Cumulative Remission Rates

	Remission (< BPD criteria)	Functional Remission (GAF > 70 for 2 months)
Year 2	29%	5%
Year 4	51%	10%
Year 6	66%	13%
Year 10	85%	21%

Gunderson JG, et al. *Arch Gen Psychiatry*. 2011;68(8):827-837.

Conclusions

1. The longitudinal course of BPD is heterogeneous
2. The rate of remission depends, in part, on how remission is defined
3. The vast majority of patients with BPD remit symptomatically. Thus, there is cause for optimism
4. Functional remission is less likely than symptomatic remission. However, many patients with BPD achieve satisfactory–good functional remission during a 10-year follow-up

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

Treatment of BPD: Psychotherapy

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

- Variables examined
  - Type of therapy
  - Stand-alone vs add-on treatment
  - Treatment developer
  - Risk of bias in trial
    - Random assignment
    - Concealing treatment assignment
    - Blind assessment (or self-report)
    - Intent to treat with imputing missing values

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

Meta-Analysis of Efficacy of Psychotherapy for BPD

- 33 trials
  - 2256 participants
- 22 stand-alone, 11 add-on
- 12 DBT, 8 psychodynamic, 5 CBT
- Control group: 21 TAU, 10 manualized
- Treatment developer involvement: 20 trials

TAU = treatment as usual.

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

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

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

Meta-Analysis of Efficacy of Psychotherapy for BPD: Subgroup Analyses

- Type of therapy
  - CBT: Hedges *g*=.24 (ns)
  - DBT: Hedges *g*=.34
  - Psychodynamic therapy: Hedges *g*=.41
- Control group manualized—no difference between active treatment and controls
- Treatment developer as co-author—no effect
- Risk of bias
  - Lower risk: Hedges *g*=.11
  - Higher risk: Hedges *g*=.48

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.

The Cost of Therapy for BPD

- Review of 30 economic evaluations of therapy for BPD
- Mean cost-saving per patient per year: $2987.82
- Mean cost-saving compared to treatment as usual: $1551

Meuldijk D, et al. *PLoS One*. 2017;12(3):e0171592.

Recent Progress in Psychotherapy for BPD: Considering PTSD

- Patients with BPD and PTSD
  - High frequency of PTSD in patients with BPD
  - Comorbidity associated with increased depression, anxiety, impulsiveness, suicidality
  - Lower likelihood of remission over 10-year follow-up
- Development of treatments of both disorders
  - Incorporating exposure strategies improves PTSD symptoms
  - No increase in suicidality or self-injury

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

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.

Limitation with the Treatment Literature

- Little attention given to improving functional outcome
  - Almost all research focuses on symptom improvement

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

Treatment of BPD: Medication

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.

Problems with the Treatment Literature

- Lack of generalizability

Generalizability of Medication Treatment Studies of BPD

8 criteria used in > 10% medication trials

Exclusion Criterion	Excluded (%)
Psychosis	5.2
Current substance use disorder	29.9
Lifetime bipolar disorder	29.7
Current major depressive disorder	19.2
Significant suicidal risk	2.2
Significant medical condition	32.5
Pregnancy/breastfeeding	1.2
Current psychotropic medication	NA
Any criterion	**75.9%**

Hoertel N, et al. *Personal Disord*. 2015;6(1):81-87.

Generalizability of Psychotherapy Treatment Studies of BPD

5 criteria used in > 10% psychotherapy trials

Exclusion Criterion	Excluded (%)
Psychosis	5.2
Current substance use disorder	29.9
Lifetime bipolar disorder	29.7
Currently in therapy	NA
Intellectual disability	NA
Any criterion	**51.3%**

Hoertel N, et al. *Personal Disord*. 2015;6(1):81-87.

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.

European Drug Safety Project Results:
Changes over Time

Medication	2001–2003	2009–2011
Quetiapine	7.5%	32.9%
Aripiprazole	5.8%	7.2%
Olanzapine	13.3%	3.6%
Risperidone	5.4%	5.4%
SSRIs	39.2%	39.2%
SNRIs	6.6%	18.2%

SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin-norepinephrine reuptake inhibitor.

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

Real World Pharmacologic Treatment of BPD: Barcelona Study

- Patients
  - 226 inpatients
  - Evaluated with semi-structured interviews
  - 83.1% had comorbid affective (37%), anxiety (43%), eating (38%), or substance use disorder (39%)
  - Cross-sectional analysis

Pascual JC, et al. *Int Clin Psychopharmacol*. 2010;25(6):349-355.

Barcelona Study of Psychopharmacology of BPD: Results

Rates of Polypharmacy

- Mean number of medications = 2.7
- 57% on 3+ psychoactive medications

Medications used

- Antidepressants 79.2%
- Antipsychotics 34.5%
- Mood stabilizers 44.2%
- Benzodiazepines 73.5%

Pascual JC, et al. *Int Clin Psychopharmacol*. 2010;25(6):349-355.

Barcelona Study of Psychopharmacology of BPD: Changes over Time

Medication	2001–2002	2007–2008
Mood stablizers	21%	52%
Atypical antipsychotics	7%	40%
SSRIs	52%	54%
Benzodiazepines	75%	62%

Pascual JC, et al. *Int Clin Psychopharmacol*. 2010;25(6):349-355.

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Pascual JC, et al. *Int Clin Psychopharmacol*. 2010;25(6):349-355.

Cochrane Review of Pharmacotherapy of BPD

- Search up to June 2008
- 27 RCTs (26 placebo-controlled, 1 active vs active)
- Total of 1714 participants (2 studies > 300 patients, most of small N)
- Most common exclusion criteria
  - Bipolar disorder, psychosis, current MDD, substance use disorder, suicidal ideation

RCT = randomized controlled trial.

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

Cochrane Review of Pharmacotherapy of BPD

Medication	# Studies
Olanzapine	6
Aripiprazole	1
Ziprasidone	1
First-generation Antipsychotics	5
Carbamazepine	2
Topiramate	3
Valproate	2
Lamotrigine	1

Medication	# Studies
Fluoxetine	2
Fluvoxamine	1
Mianserin	1
Omega-3 Fatty Acids	2
Phenelzine	1

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

Cochrane Review of Pharmacotherapy of BPD: Results of Meta-Analysis

- First-generation antipsychotics
  - Haloperidol: Anger
- Second-generation antipsychotics
  - Aripiprazole: Anger, impulsivity, interpersonal relationships, depression, anxiety
  - Olanzapine: Anger, affective instability
  - Ziprasidone: No benefit

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

Cochrane Review of Pharmacotherapy of BPD: Results of Meta-Analysis

- Antidepressants
  - No benefit
- Mood stabilizers
  - Valproate: Anger, interpersonal relationships
  - Lamotrigine: Anger, impulsivity
  - Topiramate: Anger, interpersonal problems, impulsivity
- Omega-3 fatty acids
  - Suicidality, depression

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

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.

Cochrane Review of Pharmacotherapy of BPD: Update (2015)

- Antidepressants
  - No new placebo-controlled studies since 2004
- Antipsychotics
  - Placebo-controlled study of quetiapine
    - 8-week study comparing quetiapine 150 mg, 300 mg, and placebo
    - Efficacy found for Zanarini Rating Scale for BPD (ZAN-BPD), interpersonal symptoms, affective symptoms, cognitive symptoms
- Mood stabilizers
  - Small study of divalproex sodium as add-on to DBT (no effect)

Stoffers JM, et al. *Curr Psychiatry Rep*. 2015;17(1):534.

Cochrane Review of Pharmacotherapy of BPD: Update (2015)

- Omega-3 fatty acids
  - Placebo-controlled augmentation study of valproic acid
  - 12-week study
  - Augmentation group had lower BPD severity, impulsivity, affective instability, and anger

Stoffers JM, et al. *Curr Psychiatry Rep*. 2015;17(1):534.

LABILE Study

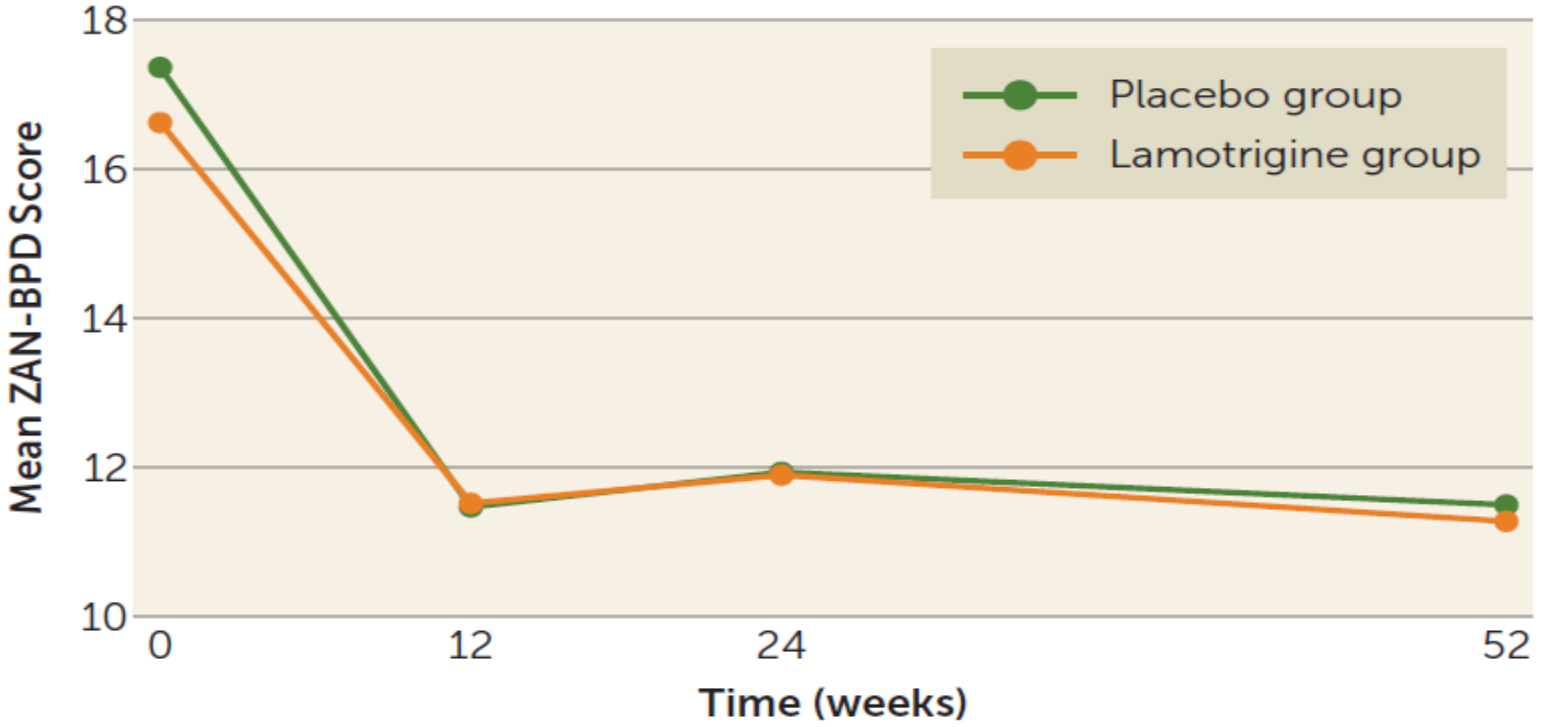
- Placebo-controlled study of lamotrigine
- Exclusion
  - Bipolar disorder; Psychotic disorder
  - On mood stabilizer in past month
- Sample
  - 137 lamotrigine, 139 placebo
- Dose
  - Up to 200 mg of lamotrigine (400 mg for women on oral contraceptives)
- Duration
  - 52 weeks
  - Outcome assessed at 3 months and every 3 months thereafter

LABILE = Lamotrigine and Borderline Personality Disorder: Investigating Long-Term Effects

Crawford MJ, et al. *Am J Psychiatry*. 2018 Apr 6;[Epub ahead of print].

LABILE Study: Results

FIGURE 2. Change in Score on the Zanarini Rating Scale for Borderline Personality Disorder at 12, 24, and 52 Weeks in a Placebo-Controlled Study of Lamotrigine for People With Borderline Personality Disorder



Crawford MJ, et al. *Am J Psychiatry*. 2018 Apr 6;[Epub ahead of print].

LABILE Study: Results

TABLE 3. Primary and Secondary Outcome Measures at 52 Weeks in a Placebo-Controlled Study of Lamotrigine for People With Borderline Personality Disorder

Measure	Lamotrigine Group (N=137)		Placebo Group (N=139)		Adjusted Difference[a]	95% CI	p
	Mean	SD	Mean	SD			
Zanarini Rating Scale for Borderline Personality Disorder	11.3	6.6	11.5	7.7	0.1	−1.8, 2.0	0.906
Beck Depression Inventory	28.8	16.1	28.7	15.5	−0.2	−4.5,4.1	0.937
Social Functioning Questionnaire	12.4	4.3	12.3	4.9	0.0	−1.2, 1.2	0.987
Alcohol use[b]	28	31	22	25	1.4	0.7, 2.7	0.354
Any other substance use[b]	27	30	23	26	1.2	0.6, 2.3	0.598
Quality-adjusted life-years	0.467	0.300	0.511	0.269	−0.012	−0.057, 0.034	0.612
	N	%	N	%			
Deliberate self-harm in past 6 months	45	46	8	39	1.25	0.68, 2.28	0.464

[a] Adjusted by site and other stratification factors. The estimate is the difference in means for continuous outcomes, and odds ratio for binary outcomes. Severity was not included in the model for self-harm, alcohol use, and any other substance use because of collinearity.

[b] For these measures, Ns were 83 for the lamotrigine group and 77 for the placebo group.

Crawford MJ, et al. *Am J Psychiatry*. 2018 Apr 6;[Epub ahead of print].

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

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, 2018.

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, 2018.

Conclusions

So, What Should I Do?

Practical Approach to Diagnosing and Treating BPD

1. Screen for the diagnosis
2. Tell patients if you make the diagnosis
3. Educate patients about the diagnosis (and prognosis)
4. Don’t let patients define themselves by their disorder
5. Be collaborative
6. Set limits
7. Don’t be rigid
8. Be willing to be wrong
9. Think long-term
10. Refer for therapy
    - Possibly require it

Practical Approach to Diagnosing and Treating BPD

11. Be an island of stability and predictability
12. Set expectations regarding medication
13. Understand the downside of prescribing medication
14. Remember, improvement may be the placebo effect
15. Try to avoid medicating crises
16. Try to avoid polypharmacy (or poly, polypharmacy)
17. Switching is preferred to augmenting
18. Adequate duration and dosage
19. Involve the family
20. Focus on functioning and symptom management rather than symptom elimination

Practical Approach to Diagnosing and Treating BPD

21. Acceptance
22. Promote healthy lifestyle
23. Talk to colleagues about your frustrations and concerns