UW PACC
Psychiatry and Addictions Case Conference
UW Medicine | Psychiatry and Behavioral Sciences

BIPOLAR DISORDER: UPDATES IN CLINICAL EPIDEMIOLOGY AND FROM A LARGE CLINICAL TRIAL

JOSEPH CERIMELE MD MPH
ASSOCIATE PROFESSOR
DEPT OF PSYCHIATRY AND BEHAVIORAL SCIENCES

OCTOBER 26TH, 2023

UW Medicine
UW SCHOOL OF MEDICINE

Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

SPEAKER DISCLOSURES

- None

UW PACC

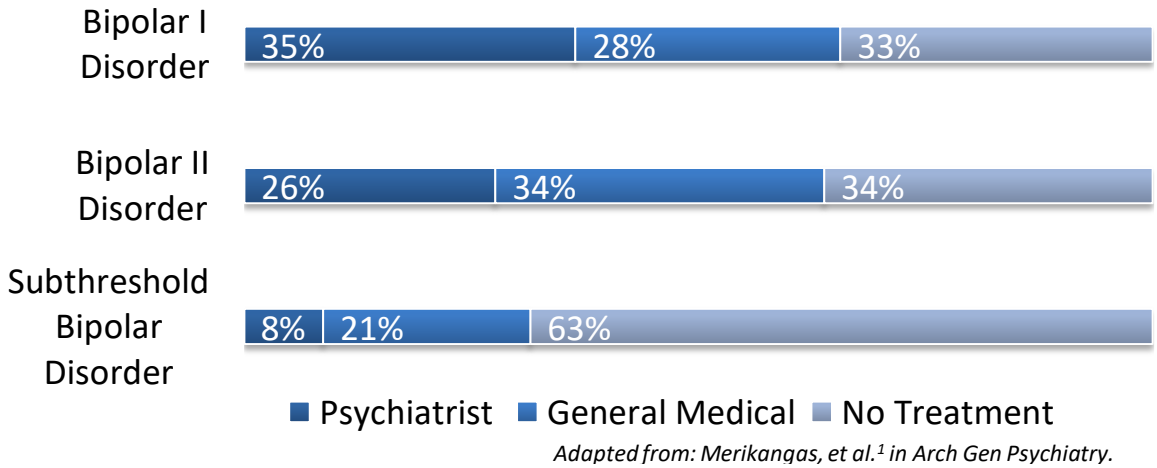
OBJECTIVES

- 1. Brief summary of bipolar disorder in primary care
  - 1a. Brief discussion of ‘mixed’ and concurrent symptoms
- 2. Results from a large clinical trial
- 3. A new symptom measure for use in clinical care

UW PACC

SUMMARY OF BIPOLAR DISORDER IN PRIMARY CARE – CLINICAL EPIDEMIOLOGY

- Twice the prevalence
- Where people go for care
- Difficulty in diagnosis
- Limited referral options

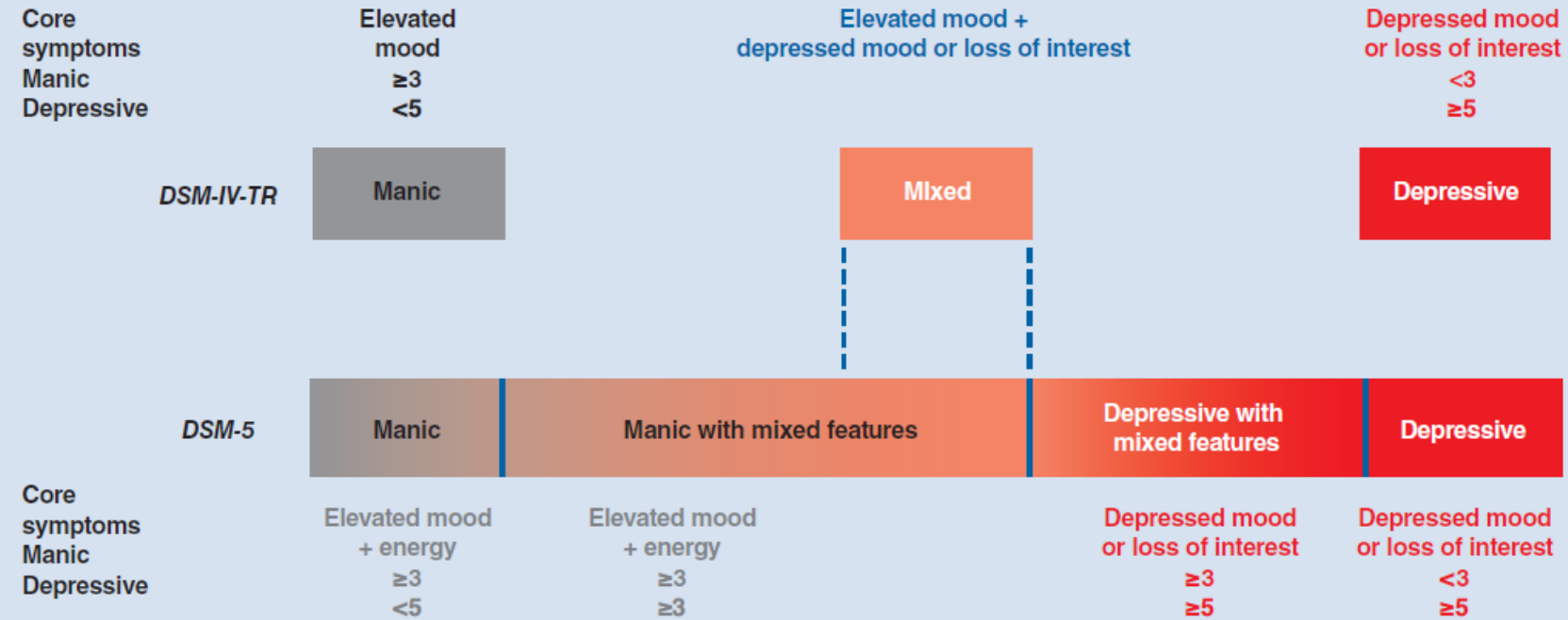


Adapted from: Merikangas, et al.[1] in Arch Gen Psychiatry.

UW PACC

FIGURE 2

Conceptualization of pure and mixed states in *DSM-IV-TR* and *DSM-5*[2-4]



Source: Hu J, Mansur R, McIntyre RS. Mixed specifier for bipolar mania and depression: highlights of DSM-5 changes and implications for diagnosis and treatment in primary care. *Prim Care Companion CNS Disord*. 2014;16(2):pii. Copyright 2014, Physicians Postgraduate Press. Reprinted by permission.

DIAGNOSIS IS DIFFICULT IN ANY SETTING

- Often seems like there isn't enough information
- Uncertainty/lack of clarity about accuracy of past experiences and diagnoses
- Clinicians try to balance uncertainty with knowing that many individuals with bipolar disorder go 8 yrs without accurate diagnosis
- How do you manage diagnostic uncertainty?

UW PACC

DEFINE THE TIME PERIOD

- Change in Mood (irritable or euphoric) and/or Energy (increased or restless)?
- When did that happen and was it for several days at least?
- When that happened did other things occur?

UW PACC

CIDI-based Bipolar Disorder Screening Scale

Stem Questions

Euphoria Stem Question

1. Some people have periods lasting several days when they feel much more excited and full of energy than usual. Their minds go too fast. They talk a lot. They are very restless or unable to sit still and they sometimes do things that are unusual for them, such as driving too fast or spending too much money.
   Have you ever had a period like this lasting several days or longer?

   If this question is endorsed, the next question (the irritability stem question) is skipped and the respondent goes directly to the Criterion B screening question

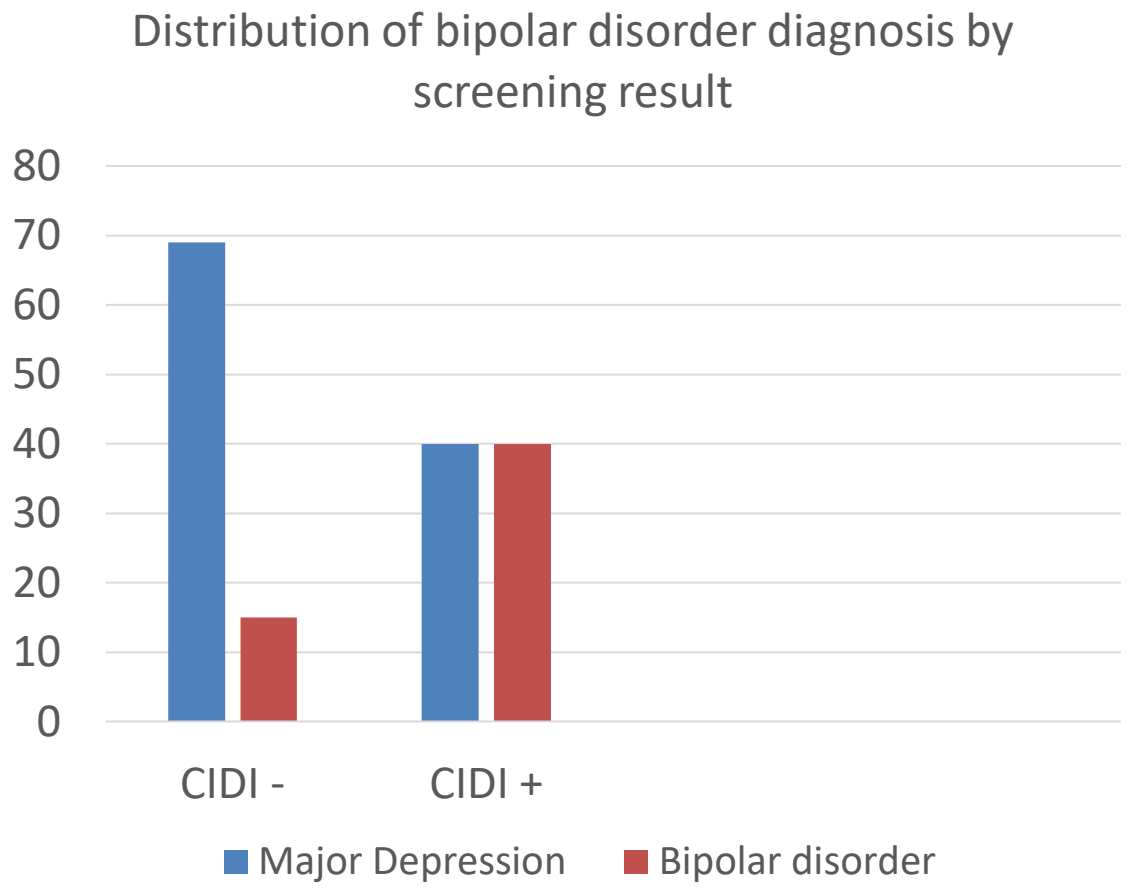
Irritability Stem Question

2. Have you ever had a period lasting several days or longer when most of the time you were so irritable or grouchy that you either started arguments, shouted at people or hit people?

Criterion B Screening Question

3. People who have episodes like this often have changes in their thinking and behavior at the same time, like being more talkative, needing very little sleep, being very restless, going on buying sprees, and behaving in many ways they would normally think inappropriate.
   Did you ever have any of these changes during your episodes of being excited and full of energy or very irritable or grouchy?

UW PACC



UW PACC

Table 1.1. **Symptoms of bipolarity across the mood spectrum**

Symptom	Point A	Point B	Point C	Point D	Point E
Distractability	No manic symptoms	Slightly unfocused	Notable difficulty staying on task	ADD could be invoked	Nonfunctional
Insomnia	No disturbance	6 hours or less, sometimes broken	4 hours or less, frequent awakenings	2 hours or less, waking too early	Nights of no sleep at all
Grandiosity	No extremes of self-esteem	Pleased with accomplishments, abilities, prospects	"Life of the party," charismatic	Intrusively self-confident, irritating	Grandiose; "narcissistic," unshakeable beliefs in self
Flight of ideas	Nothing unusual	Many ideas about many things	Highly creative, making rapid connections	Experiencing many unrelated ideas at high speed	Psychotic disconnection of thought (highly tangential to loose)
Activity level	Unremarkable	Highly energetic, engaged	Multiple projects at quick pace	So many projects, not completing them, bouncing one to another	Constant motion, ineffectual
Speech	Normal prosody	Quick but not otherwise remarkable	Rapid speech, occasionally difficult to follow	Very rapid speech, losing most listeners	The proverbial "fire hose"
Impulsive risk	Safe or minimally risky behavior	Some choices regrettable and not thought through in advance	Increased risk taking, impulsive	Spending hundreds of dollars, increased "sex, drugs and rock-and-roll"	Spending sprees far beyond means; illegalities, dangerous choices

Of course there are no real Points B or C. These merely indicate

What questions do you ask?

ORIGINAL ARTICLE

Prevalence and Characteristics of Undiagnosed Bipolar Disorders in Patients With a Major Depressive Episode

The BRIDGE Study

Jules Angst, MD; Jean-Michel Azorin, MD; Charles L. Bowden, MD; Giulio Perugi, MD; Eduard Vieta, MD, PhD; Alex Gamma, PhD; Allan H. Young, MD, PhD; for the BRIDGE Study Group

Arch Gen Psychiatry. 2011;68(8):791-799

521 psychiatrists in 18 countries resulting in **5635 patients** with major depressive episode

Routine clinical consultation

903 diagnosed with DSM-IV-TR bipolar disorder (16%) (685 BP-I, 218 BP-II)

Variables associated with bipolar disorder diagnosis:

family history of bipolar disorder, >2 past mood episodes, current substance use

mixed states, prior activation/hypomania during antidepressant treatment

Table 2. Presence of Lifetime Bipolar Symptoms in Patients Fulfilling the 2 Definitions of Bipolar Disorder and the Complete Sample of All Subjects With MDEs

	No. (%)[a]		
	MDE	Bipolar Disorder	
Symptom	Total (N=5635)	*DSM-IV-TR* (n=903)	Bipolar Specifier (n=2647)
Elevated mood	2544 (45.3)	830 (92.2)	2174 (82.5)
Irritable mood	2573 (45.8)	689 (76.6)	1906 (72.3)
Increased activity	2656 (47.3)	808 (89.9)	2223 (84.4)
Inflated self-esteem	2071 (37.6)	736 (81.6)	1855 (70.2)
Decreased sleep	2573 (46.8)	813 (90.1)	2227 (84.3)
More talkative	2777 (50.5)	829 (92.0)	2369 (89.6)
Nonstop ideas	1820 (33.1)	638 (70.8)	1653 (62.6)
Distractibility	2381 (43.3)	715 (79.3)	1954 (73.9)
Goal-directed activity	2620 (47.6)	781 (86.6)	2187 (82.7)
Psychomotor agitation	1951 (35.5)	602 (66.7)	1608 (60.8)
Pleasurable activities	1614 (29.3)	628 (69.5)	1516 (57.3)
Unequivocal change	2434 (44.2)	840 (93.1)	2173 (82.2)
Marked impairment	1768 (32.1)	670 (74.2)	1540 (58.2)
Observable by others	2714 (49.3)	855 (94.7)	2346 (88.6)
Hospitalization	916 (16.7)	431 (47.8)	850 (32.2)

Abbreviation: MDE, major depressive episode.
[a] Denominators vary for some analyses.

What proportion had 'bipolar specifier' of
---Irritable or elevated mood, OR increased activity, plus 3 symptoms (ie racing thoughts).

47% of patients

Treatment implications?

UW PACC

ONLINE FIRST

Association Between Bipolar Spectrum Features and Treatment Outcomes in Outpatients With Major Depressive Disorder

Roy H. Perlis, MD, MSc; Rudolf Uher, PhD, MRCPsych; Michael Ostacher, MD; Joseph F. Goldberg, MD; Madhukar H. Trivedi, MD; A. John Rush, MD; Maurizio Fava, MD

Table 1. Prevalence of Possible Bipolar Spectrum Features in the STAR*D Cohort

Feature	Present, No. (%)	Assessed, No.[a]
Family history of bipolar disorder	351 (8.8)	4001
Episode duration ≤3 mo	872 (21.6)	4040
≥3 Prior episodes	1275 (36.5)	3495
Onset before 25 y of age	2315 (57.9)	3996
Atypical depression (*DSM-IV* diagnosis)	635 (17.0)	3740
Manialike symptoms, No.		
≥1	1524 (38.1)	3999
≥2	821 (20.5)	3999
≥3	444 (11.1)	3999
Psychosislike symptoms, No.		
≥1	1198 (30.0)	3999
≥2	526 (13.2)	3999
≥3	217 (5.4)	3999
Bipolar spectrum illness[b]	870 (27.5)	3166

Presence of bipolar spectrum classification in this sample NOT associated with worse outcomes (HR 0.93 [0.84-1.04])

3 or more: Irritability, motor activity, hypersomnia, hyperphagia, >3episodes, family history

UW PACC

SUMMARY OF BIPOLAR DISORDER IN PRIMARY CARE – OBSERVATIONAL DATA

Bipolar Disorder in Primary Care: Clinical Characteristics of 740 Primary Care Patients With Bipolar Disorder

Joseph M. Cerimele, M.D.
Ya-Fen Chan, Ph.D.
Lydia A. Chwastiak, M.D.
Marc Avery, M.D.
Wayne Katon, M.D.
Jürgen Unützer, M.D., M.P.H.

Summary:
High symptom severity,
High psychosocial impairment

Specifics:

1. High burden of depressive symptoms measured by PHQ9 (mean 18) (60% 1 or more on item 9)
2. Majority had past specialty mental health care; 1/3 had prior hospitalization
3. 15% homeless, 25% lack of support person, 33% lack of depen. transportation
4. 30% of patients experienced significant reduction in depression (PHQ9 < 10)
5. 25% of patients were referred from primary to specialty mental health care

BIPOLAR DISORDER IN PRIMARY CARE – RESULTS FROM A CLINICAL TRIAL - I

Two arm RCT, n=191, 12 months of treatment
--Collaborative care
--Co-located referral care

Effectiveness of Collaborative Care and Colocated Specialty Care for Bipolar Disorder in Primary Care: A Secondary Analysis of a Randomized Clinical Trial

Joseph M. Cerimele, M.D., M.P.H., Brittany E. Blanchard, Ph.D., Morgan Johnson, M.S., Joan Russo, Ph.D., Amy M. Bauer, M.D., M.S., Richard C. Veith, M.D., Jürgen Unützer, M.D., M.P.H., John C. Fortney, Ph.D.

Outcomes:

Clinical, N=190	Baseline CC (n=111)	Baseline Co-loc (n=80)	12mo CC	12mo Co-loc
VR-12 MCS	**21.99 (10.78)**	**24.15 (12.05)**	**30.63 (13.33)**	**34.16 (12.65)**
SCL-20	2.48 (0.73)	2.41 (0.72)	1.76 (0.89)	1.63 (0.78)
GAD-7	15.5 (4.94)	14.71 (6.5)	11.95 (6.46)	10.09 (6.57)

Process of care / 'intensity':

	Collaborative Care	Co-located care
Psychiatrist visits (100%)	1.6 (1.0)	4.8 (3.3)
Behavioral health care manager visits (99%)	11.8 (7.8)	----------
Systematic Case review (97%)	6.7 (4.0)	--------
Psychologist visits (63%)	----------	6.7 (4.6)

UW PACC

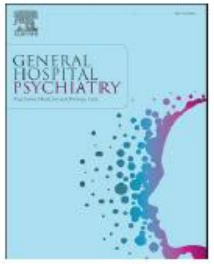
BIPOLAR DISORDER IN PRIMARY CARE – RESULTS FROM A CLINICAL TRIAL - II

- Similar across arms.
- Unchanged AD
- LMG incr in CC
- SGA incr
- Low lithium

Bipolar disorder in primary care: Medication treatment by co-located psychiatrists versus primary care clinicians supported by psychiatrists

Joseph M. Cerimele [a,*], Morgan Johnson [a], Brittany E. Blanchard [a], Joan Russo [a], Jürgen Unützer [a], John C. Fortney [a,b]

[a] University of Washington School of Medicine, Department of Psychiatry & Behavioral Sciences, United States of America
[b] Department of Veterans Affairs, HSR&D Center of Innovation for Veteran-Centered and Value-Driven Care, VA Puget Sound Health Care System, United States of America



General Hospital Psychiatry 78 (2022) 108–110

Medication	CC – Initial	CC- Last	Co-loc – Initial	Co-loc- Last
None	39%	17%	29%	11%
SGA	20%	49%	23%	36%
Anticonvulsant	23%	36%	36%	39%
Lithium	6%	7%	10%	4%
Any antidepressant	40%	40%	48%	50%
Antidepressant alone	24%	11%	13%	9%
2+ medications	20%	36%	41%	53%

- MEASUREMENT BASED CARE

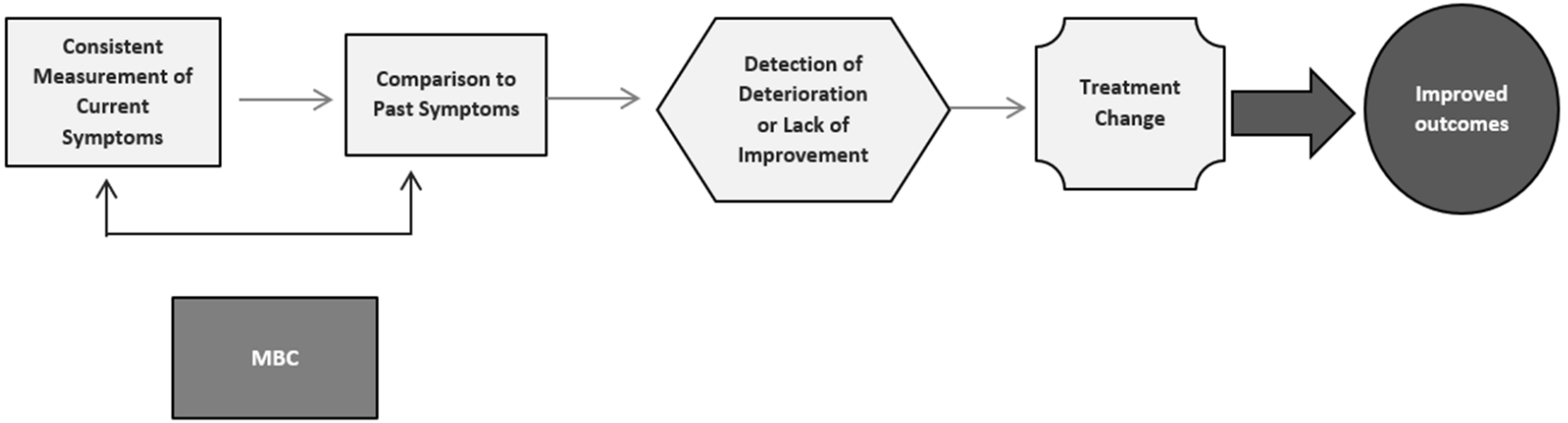


Figure 2. MBC (measurement-based care) promotes consistent symptom measurement and comparison of current to past symptoms

BIPOLAR DISORDER IN PRIMARY CARE – A NEW PATIENT REPORTED MANIC SYMPTOM MEASURE

- In context of trial developed a new patient-reported manic symptom measure
- Widely-used
- Widely-interpreted

Table 1 Patient Mania Questionnaire-9 (PMQ-9) Scale

Over the past week, how often have you …	Not at all	Several Days	More Than Half of the Days	Nearly Every Day
1. Had little or no sleep, and still felt energized	0	1	2	3
2. Felt easily irritated	0	1	2	3
3. Felt overactive	0	1	2	3
4. Acted impulsively or done things without thinking about consequences	0	1	2	3
5. Felt sped up or restless	0	1	2	3
6. Been easily distracted	0	1	2	3
7. Felt pressure to keep talking or been told by someone you are more talkative	0	1	2	3
8. Felt argumentative	0	1	2	3
9. Had racing thoughts	0	1	2	3

Score = ___ + ___ + ___ + ___

Cerimele, et al. J Gen Intern Med. 2022;37:1380-1387.

UW PACC

• PMQ-9 AND PHQ-9 TOGETHER

- PMQ-9 Psychometric evaluation (two samples)
- Sample A (n=114)
  - Test-retest reliability – Pearson correlation coefficient – 0.85
  - Concurrent validity – with Internal State Scale – 0.70
  - Concurrent validity – with Altman Mania Rating Scale – 0.26
- Sample B (n=179)
  - Internal Consistency - α=0.88
  - Sensitivity to change - next

Over the last *week*, how often have you...(Please check appropriate box)	Not At All (0)	Several Days (1)	More Than Half the Days (2)	Nearly Every Day (3)
1. Had little or no sleep, and still felt energized	☐	☐	☐	☐
2. Felt easily irritated	☐	☐	☐	☐
3. Felt overactive	☐	☐	☐	☐
4. Acted impulsively or done things without thinking about consequences	☐	☐	☐	☐
5. Felt sped up or restless	☐	☐	☐	☐
6. Been easily distracted	☐	☐	☐	☐
7. Felt pressure to keep talking or been told by someone you are more talkative	☐	☐	☐	☐
8. Felt argumentative	☐	☐	☐	☐
9. Had racing thoughts	☐	☐	☐	☐
10. Little interest or pleasure in doing things	☐	☐	☐	☐
11. Feeling down, depressed, or hopeless	☐	☐	☐	☐
12. Trouble falling or staying asleep, or sleeping too much	☐	☐	☐	☐
13. Feeling tired or having little energy	☐	☐	☐	☐
14. Poor appetite or overeating	☐	☐	☐	☐
15. Feeling bad about yourself or that you are a failure or have let yourself or your family down	☐	☐	☐	☐
16. Trouble concentrating on things, such as reading the newspaper or watching television	☐	☐	☐	☐
17. Moving or speaking so slowly that other people could have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	☐	☐	☐	☐
18. Thoughts that you would be better off dead, or of hurting yourself	☐	☐	☐	☐

INDIVIDUAL

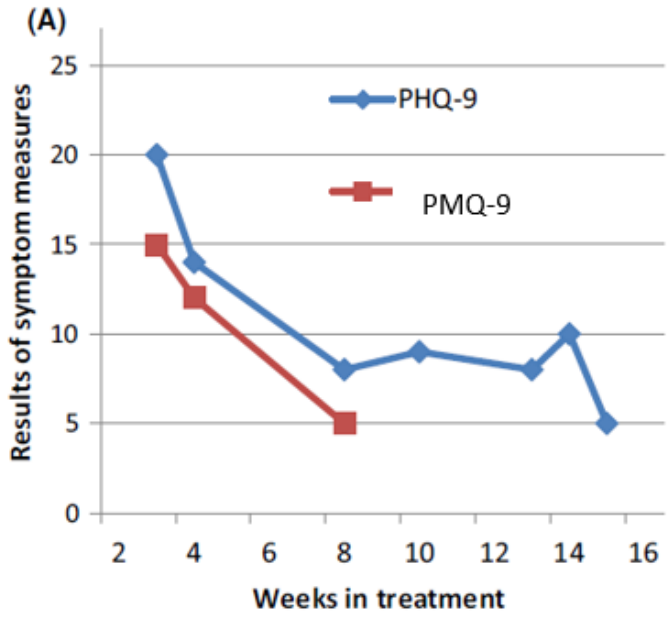
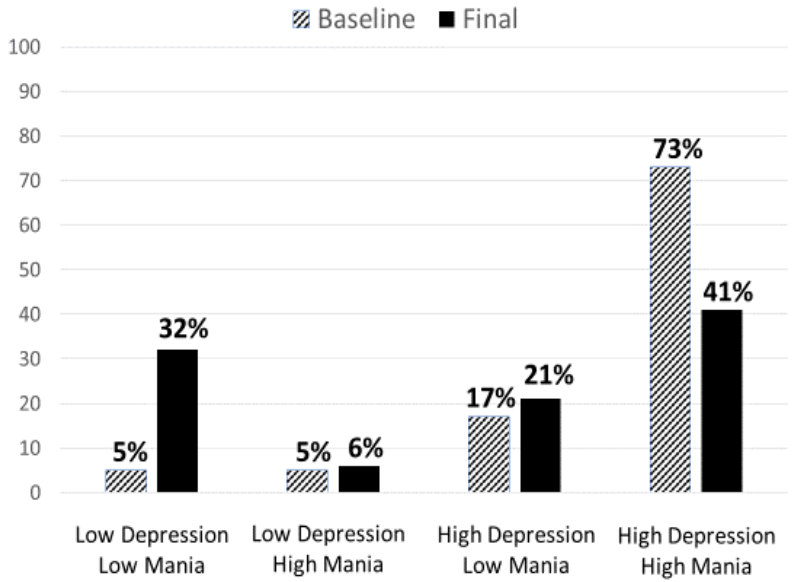


Figure 3. Results of two patient reported symptom measures (PHQ-9 for depressive, and PMQ-9 for manic) over time

Cerimele and Lostutter.
Bipolar Disord. 2020;22:97-100

POPULATION

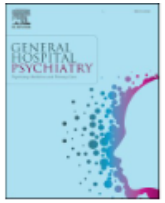


UW PACC

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: www.elsevier.com/locate/genhospsych



Letter to the editor

Clinician preferences for using bipolar disorder symptom severity and quality of life scales for measurement-based care

Joseph M. Cerimele[a,*], Brittany E. Blanchard[a], Jared M. Bechtel[a], John C. Fortney[a,b]

[a] *Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA, United States*

[b] *Department of Veterans Affairs, HSR&D Center of Innovation for Veteran-Centered and Value-Driven Care, VA Puget Sound Health Care System, Seattle, WA, United States*

109 clinicians (51 psychiatrists, 36 psychologists, 11 PCPs, 5 SWs)

Clinical setting: 39% general mental health clinic, 38% primary care, 20% hospital, 7% bipolar disorder specialty

Web-based survey

Reviewed 4 out of 8 measures.

Significantly preferred symptom over quality-of-life measures
PMQ-9 + PHQ-9 top-rated overall and in both categories,

- CONCLUSION

- 1. Individuals with bipolar disorder present for treatment in primary care
- 2. Two models of care are effective
- 3. The PMQ-9 can be used with the PHQ-9 to monitor treatment, which is a combination preferred by clinicians
- 4. Current steps ----

Current Steps:

1. Views/opinions on symptom measures among individuals diagnosed with bipolar disorder

2. Putting PMQ-9 and PHQ-9 into use in primary care

3. Clinical trial of use of PMQ-9 and PHQ-9 in individuals diagnosed with bipolar disorder in primary care

4. Prospective symptom assessment in young adults with elevated risk for bipolar disorder

UW PACC