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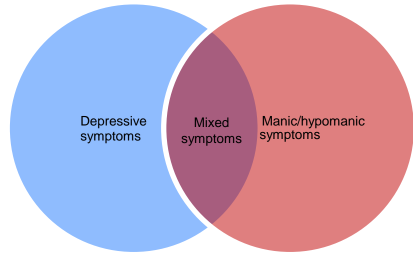
The Contribution of Depressive, Manic, and Mixed Symptoms to Suicidal Ideation and Behavior in the National Network of Depression Centers Mood Outcomes Program

Jane E. Persons,[a] Jess G. Fiedorowicz,[a] Michael J. Ostacher,[b] William H. Coryell[a]
from the NNDC Bipolar Disorders Interest Group

[a] University of Iowa, Iowa City, Iowa; [b] Stanford University, Palo Alto, CA

BACKGROUND



Mixed Symptoms

- Occur in ~24% of individuals with major depressive disorder[1]
- Occur in as many as 38% of individuals with bipolar disorder[1,2,3]

While mixed symptoms have long been considered a high-risk state for suicide, it is not established that this risk is any greater than that of the component depressive symptoms.

This question has been addressed by Persons et al. using a cohort of 429 individuals with bipolar disorder prospectively followed through the Collaborative Depression Study,[3] and subsequently by Fiedorowicz et al. in a cohort of 290 individuals with bipolar disorder followed through the National Network of Depression Centers Clinical Care Registry.[4] Both determined that the risk of suicidal behavior in mixed states is not increased beyond the risk attributable to the depressive component.

This current study aims to address this question in a larger sample and extend the analysis to major depressive disorder.

Aim: To assess whether mixed symptoms increase suicide risk beyond that attributable to the manic or depressive components of mood symptoms alone.

METHODS

Study sample: National Network of Depression Centers Mood Outcomes Program

- 6105 patients (bipolar disorder: 988; major depression: 5117)
- 17,179 total visits
- Mean visits per patient: 2.8 (SD 3.3)
- Mean length of follow-up: 197.7 days (up to 1425 days)

*Exposure: **Mood state***

Depressive symptoms: Primary: continuous Patient Health Questionnaire-8 (PHQ-8) score
Secondary: PHQ-8 ≥ 10

Manic symptoms: Primary: continuous Altman Self-Rating Mania (ASRM) Scale score
Secondary: ASRM > 5

Mixed symptoms: Primary: PHQ-8*ASRM interaction term
Secondary: ASRM >5 and PHQ-8 ≥ 10

*Primary Outcome: **Suicidal ideation or behavior*** reported on Columbia-Suicide Severity Rating Scale (C-SSRS) coinciding with visit for mood ratings.

Statistical Analysis: Generalized linear mixed models (binomial distribution, logit link (canonical)) with a random intercept term for repeated observations within patients

RESULTS

Figure 1:

Relative to patients with bipolar disorder, patients with major depressive disorder were younger, more likely to be female, and more likely to be diagnosed with a co-occurring anxiety disorder

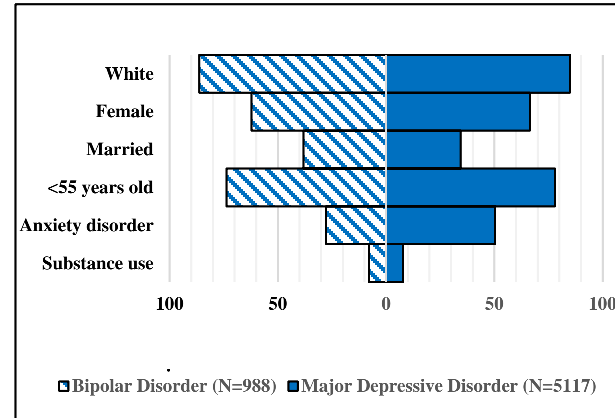


Table 1: Depressive symptoms are strongly associated with suicidal ideation or behavior, but mixed symptoms convey no excess risk of suicidal ideation or behavior beyond the depressive or manic components. Results from the primary analysis using generalized linear mixed models demonstrate a robust effect of PHQ-8 score, but not of mixed symptoms, on suicidal ideation and behavior. Patients with major depression additionally demonstrated a protective effect of higher ASRM score on suicidal ideation and behavior.

Bipolar Disorder Subsample[1]				
	β	SE	95% CI	*p*-value
Mixed symptoms[2]	0.00078	0.0038	-0.0066-0.0082	0.84
PHQ-8 score	0.23	0.017	0.20-0.26	**<0.0001**
ASRM score	0.015	0.024	-0.031-0.062	0.52
Major Depression Subsample[1]				
	β	SE	95% CI	*p*-value
Mixed symptoms[2]	0.0017	0.0019	-0.0021-0.0055	0.39
PHQ-8 score	0.25	0.0076	0.24-0.27	**<0.0001**
ASRM score	-0.042	0.013	-0.067- -0.016	**0.0013**

[1]Adjusted for gender, age, race, marital status, and comorbid substance use or anxiety disorders
[2]Modeled as an interaction term between PHQ-8 and ASRM scores

SUMMARY

Prospective real-world evidence from 6105 members of the National Network of Depression Centers Mood Outcomes Program

Exposure: Mood symptoms, captured by PHQ-8 and ASRM scores
Outcome: Suicidal ideation or behavior

Highlights:

- High occurrence of suicidal ideation and behavior during depression
- Mixed symptoms convey no greater risk for suicidal ideation/behavior than depressive symptoms alone

Takeaway Message:

Mixed states do not appear to convey additional suicide risk beyond that attributable to depressive or manic symptoms alone. Depressive symptoms appear to have the strongest influence on suicidal ideation and behavior. Clinical focus should be placed on depressive symptoms in the assessment and management of suicide risk.

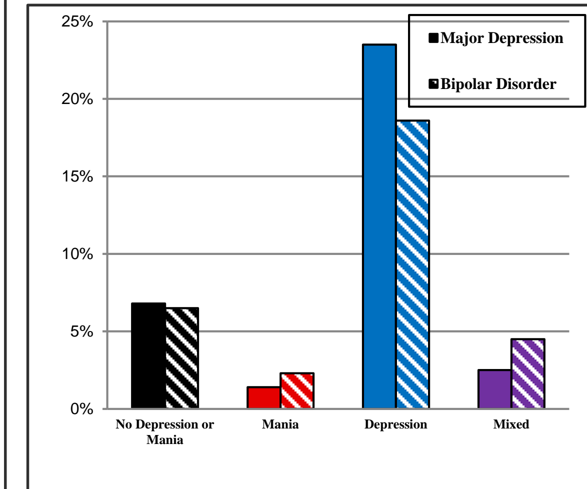


Figure 2. Depression is a high-risk mood state for suicidal ideation or behavior. This figure illustrates the percentage of visits among patients in each categorically-defined and mutually-exclusive mood state during which suicidal behavior or ideation was observed. A given patient could provide multiple data points in this presentation of raw data. In total, there were 5839 visits with suicidal ideation or behavior (34.0% of visits).

REFERENCES

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4. Fiedorowicz, J. G., Persons, J. E., Assari, S., Ostacher, M., Zandi, P., Wang, P., . . . Coryell, W. (2018). Mixed symptoms do not carry an increased risk for suicidal ideation and behavior beyond that attributable to depressive symptoms in bipolar disorder. *Journal of Affective Disorders*, 2018.