

Prevalence of Bipolar Disorder Risk Among Antidepressant Non-Responders

David J. Muzina, M.D.¹; Robert M.A. Hirschfeld, M.D.²; Gary S. Sachs, M.D.³; Mark A. Frye, M.D.⁴; Thomas R. Thompson, M.D.⁵; Michael L. Reed, Ph.D.⁶; Joseph R. Calabrese, M.D.⁷

¹Bipolar Disorders Clinic, Cleveland Clinic Foundation, Cleveland, OH; ²Department of Psychiatry & Behavioral Sciences, University of Texas Medical Branch, Galveston, TX; ³Bipolar Disorder Clinic and Research Program, Massachusetts General Hospital, Boston, MA;

⁴University of California at Los Angeles, Los Angeles, CA; ⁵GlaxoSmithKline, Research Triangle Park, NC; ⁶Vedanta Research, Chapel Hill, NC; ⁷Department of Psychiatry, Case Western Reserve University, University Hospitals of Cleveland, Cleveland, OH

ABSTRACT (Revised)

Objective

The objective of this study was to assess the rate of bipolar disorder (BPD) risk among unipolar depression patients currently in treatment.

Method

Psychiatrists from community and private practice clinic settings randomly selected patients with unipolar depression who had one or more prior antidepressant (AD) medication failures. Patients with a diagnosis of BPD, OCD, or schizophrenia were excluded. Medical record abstraction obtained patient history as well as current and prior AD medication use. A self-administered patient survey collected demographics, current bipolar symptoms via the Mood Disorder Questionnaire (MDQ), and co-morbid health problems.

Results

Data were collected from 602 patients. A total of 18.6% of patients screened positive on the MDQ and this rate was not impacted by the number of prior AD failures or patient demographics. There were 74 patients (12.3%) who reported a prior history of BPD. The positive MDQ rate in this subgroup was 41.9%.

Conclusions

These data suggest that clinicians should carefully screen for BPD among their unipolar patients, regardless of AD treatment history or demographic subgroup. Further consideration should be given to identifying and evaluating those with prior BPD history.

INTRODUCTION

At least 30% of patients with depression fail to respond fully to adequate antidepressant therapy,¹ and remission rates in controlled clinical trials remain below 50%.²⁻³ More recent research suggests that a substantial subset of patients diagnosed with unipolar major depression who do not show an adequate response to antidepressants in fact suffer from bipolar disorder.⁴

This study was designed to estimate the prevalence of bipolar disorder (BPD) risk (based on the Mood Disorder Questionnaire – MDQ) among patients with unipolar depression who are not responding to antidepressant medication. The study hypothesized that a proportion of patients currently receiving antidepressant treatment actually suffer from BPD and the risk of BPD would increase with the number of antidepressant medication failures. Although the MDQ is not a diagnostic tool, its sensitivity (73%) and specificity (90%) in clinical settings suggest that a patient with a positive screen has a reasonable probability of being bipolar.⁵

METHODS

Selection of Subjects

- Psychiatrists from private practice and clinic settings (N=63) were asked to identify their next 10 patients with major depression who had experienced one or more prior medication failure (defined as a change in their depression medication or regimen).
- Eligible patients were 18 years of age and older, had a current diagnosis of major depression, and were currently in treatment for major depression, but not diagnosed with bipolar disorder, obsessive-compulsive disorder, schizophrenia, or schizoaffective disorder.
- Patients were eligible for this study if
 - They had received treatment for major depression for at least 3 months and had one or more medication changes during their current episode, or
 - Treated less than three months, they had changed medications at least three times.

Instruments

- Patient survey:** Demographic and family history form; the Center for Epidemiologic Studies Depression Scale (CES-D); a health care resource use form; the Mood Disorder Questionnaire (MDQ); a co-morbid health problems form; and legal problems were assessed with the legal status section of the Addiction Severity Index (ASI)
- A medical records abstraction form:** Patient and family health history; lifetime history of major depression; current episode of major depression; prescription drug treatment history; number of prior antidepressant medication failures; health care resource use; and outcomes of treatment

RESULTS

Patients Demographics	N (%)	MDQ Positive %
Total	602 (100%)	18.60
Gender		
Males	140 (23.26)	17.86
Females	462 (76.74)	18.83
Age (Mean = 47.9, Median = 48.0)		
18-24	22 (3.67)	27.27
25-44	212 (35.33)	22.64
45-64	316 (52.67)	16.46
65+	50 (8.33)	12.00
Ethnic Background		
African American	51 (8.5)	17.65
Caucasian	512 (86.39)	17.69
Other	31 (4.8)	37.9
Of Spanish or Hispanic Heritage	20 (3.4)	15.00
Marital Status		
Single	102 (17.0)	20.59
Married	298 (49.67)	21.14
Divorced	128 (21.33)	16.41
Separated	29 (4.83)	13.79
Widowed	43 (7.17)	6.98
Schooling		
8 Grades or Less	15 (2.49)	6.67
Some High School	49 (8.14)	14.29
High School Graduate or GED	129 (21.43)	19.38
Some College or Technical School	243 (40.37)	21.4
College Grad (bachelor's degree)	115 (19.1)	13.04
Graduate Degree	51 (8.47)	23.53
Income		
<\$20,000	254 (43.2)	15.75
\$20,000 to \$39,999	130 (22.11)	26.15
\$40,000 to \$59,999	104 (17.69)	13.46
\$60,000 to \$79,999	46 (7.82)	26.09
\$80,000 to \$99,999	16 (2.72)	6.25
\$100,000 to \$119,999	11 (1.87)	9.09
\$120,000+	27 (4.59)	25.93
Employment Status		
Currently Employed	254 (42.83)	18.90
Retired	58 (9.78)	17.24
Homemaker	44 (7.42)	18.18
Student	9 (1.52)	33.30
Disabled	165 (27.82)	19.39
Unemployed	58 (9.78)	13.79
Other	5 (0.84)	20.00

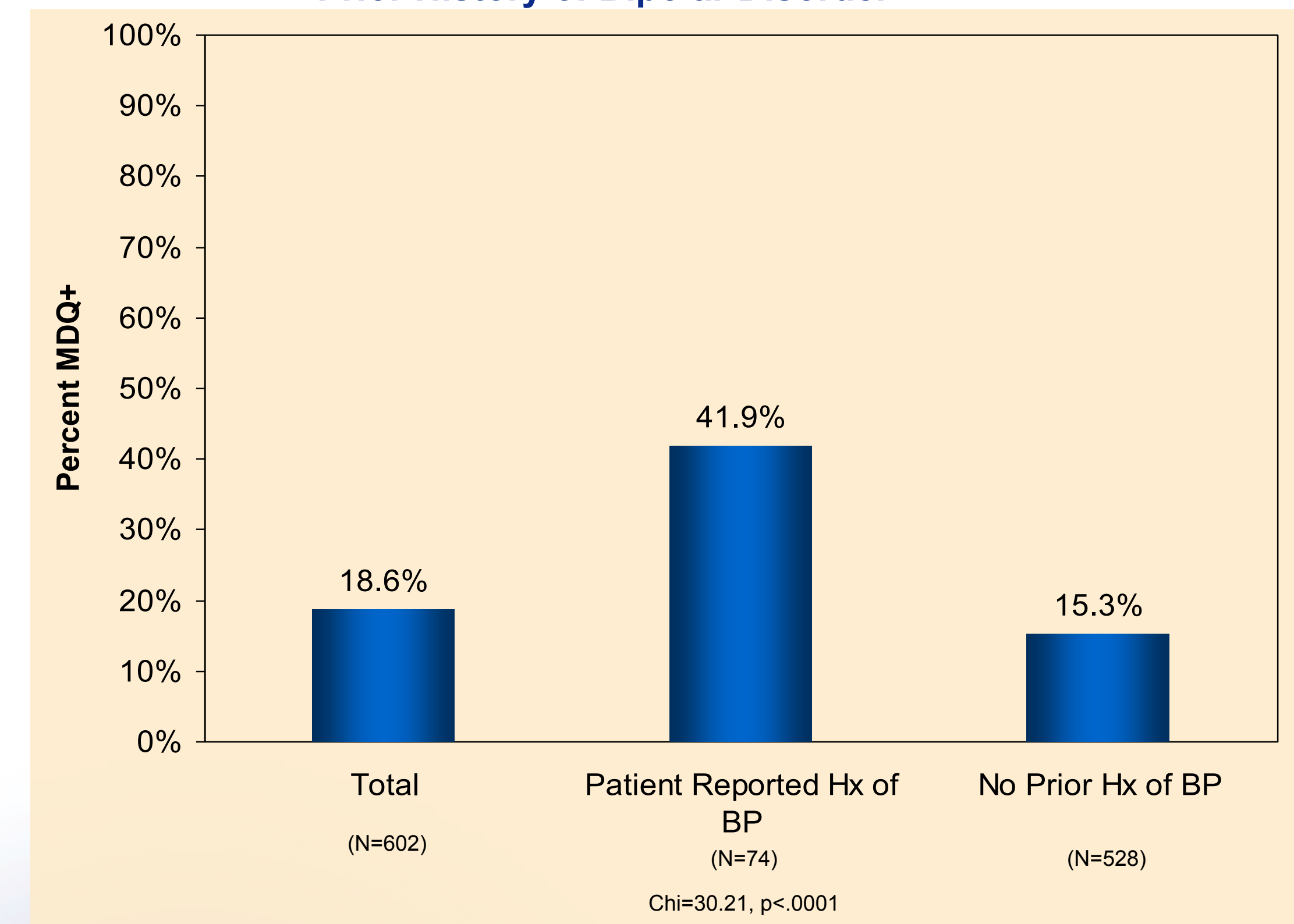
Results by Number of Antidepressant Medication Failures (changes in individual AD medications)

Number of Unique Antidepressant Medication Failures	Current Episode	
	N (%)	MDQ Positive (%)
One Antidepressant Medication Failure	18 (3.0)	35.3
Two Antidepressant Medication Failures	237 (39.4)	18.5
Three Antidepressant Medication Failures	189 (31.4)	17.9
Four Antidepressant Medication Failures	90 (15.0)	16.7
Five Antidepressant Medication Failures	55 (9.1)	21.8
Six or More Antidepressant Medication Failures	13 (2.2)	8.3
Mean # of Unique AD Medications	2.9	

Results by Number of Antidepressant Regimen Failures (changes in combination of AD medications)

Number of Unique Antidepressant Regimen (2+ Medications) Failures	Current Episode	
	N (%)	MDQ Positive (%)
One Antidepressant Regimen Failure	27 (4.49)	25.9
Two Antidepressant Regimen Failures	330 (54.91)	17.8
Three Antidepressant Regimen Failures	152 (25.29)	16.5
Four Antidepressant Regimen Failures	53 (8.82)	26.4
Five Antidepressant Regimen Failures	39 (6.49)	17.9
Mean # of Unique AD Regimens	2.6	

MDQ+ Rates Among Patients Reporting Prior History of Bipolar Disorder



A similar pattern of results was seen for males (chi square=7.17, p<.007) and for females (chi square=23.04, p<.0001).

SUMMARY

- Among this sample of patients with depression with one or more prior antidepressant medication failures:
 - More than 60% were severely depressed (based on CES-D) at the time of the study.
 - They were taking an average of three antidepressant medications for their current episode of depression.
 - Nearly one in five (18.6%) screened positive for BPD on the MDQ.
 - 12% reported a prior history of BPD that was unknown to the clinician.
- The rate of BPD risk (MDQ positive screens) did not vary significantly across demographic subgroups.
- The rate of BPD risk also did not vary by the number of antidepressant medication failures or the number of past medication regimens.
- Patients reporting a prior history of BPD disorder were three times more likely to screen positive on the MDQ (41.9%) versus those with no prior history (15.3%).

CONCLUSION

- This study found that one in five patients (18.6%) with difficult to treat depression screened positive on the MDQ, suggesting that clinicians should carefully screen for BPD among their unipolar patients regardless of AD treatment history or demographic characteristics.
- Study entry criteria excluded patients with a prior history of bipolar disorder. However 12% of patients reported a history of bipolar disorder that was unknown to the clinician. Given the significantly higher bipolar disorder risk among this group (41.9%), further consideration should be given to identifying and carefully evaluating those patients with a prior history bipolar disorder.

REFERENCES

- Stimpson N, Agrawal N, Lewis G. Randomised controlled trials investigating pharmacological and psychological interventions for treatment-refractory depression. Systematic review. Br J Psychiatry. 2002 Oct; 181:284-94.
- Entsuah AR, Huang H, Thase ME. Response and remission rates in different subpopulations with major depressive disorder administered venlafaxine, selective serotonin reuptake inhibitors, or placebo. J Clin Psychiatry. 2001 Nov;62(11):869-77.
- Thase ME, Entsuah AR, Rudolph RL. Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. Br J Psychiatry. 2001 Mar;178:234-41.
- Hirschfeld RM, Calabrese JR, Weissman MM, Reed M, Davies MA, Frye MA, Keck PE Jr, Lewis L, McElroy SL, McNulty JP, Wagner KD. Screening for bipolar disorder in the community. J Clin Psychiatry. 2003 Jan;64(1):53-9.
- Hirschfeld RMA, Williams JB, Spitzer RL, Calabrese JR, Flynn L, Keck PE Jr, Lewis L, McElroy SL, Post RM, Rappaport DJ, Russell JM, Sachs GS, Zajecka J. Development and Validation of a Screening Instrument for Bipolar Spectrum Disorder: The Mood Disorder Questionnaire. Am J Psychiatry. 2000; 157(11): 1873-1875.