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The association between mood and anxiety disorders with vascular diseases and risk factors in a nationally-representative sample

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Abstract

Objective—To investigate the association between mood and anxiety disorders and vascular diseases after controlling for vascular disease risk factors.

Methods—Using a nationally representative sample of adults (N=5,692) from the National Comorbidity Survey Replication (NCS-R), participants with mood disorders were hierarchically classified as having any lifetime history of mania, hypomania, or major depression. Anxiety disorders were also assessed. The reference group consisted of those without mental disorders. Vascular disease was determined by self-reported history of heart disease, heart attack, or stroke on the NCS-R survey. Vascular risk factors included diabetes, high blood pressure, and obesity.

Results—In multivariate logistic regression models that controlled for obesity, high blood pressure, smoking and diabetes, vascular disease was associated with bipolar disorder in women (OR 2.80, 95% C.I. 1.63–4.80), and major depressive disorder in men (OR 1.85, 95% C.I. 1.17–2.92). Controlling for anxiety disorders reduced the associations in both men and women, and in fact, anxiety disorders were more strongly associated with vascular diseases in men, whereas bipolar disorder continued to be an important correlate of vascular disease in women.

Conclusion—These findings demonstrate the importance of evaluation of sex differences, mood disorder subtype and co-occuring anxiety disorders in assessing the association between mood

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disorders and vascular diseases. Future research should investigate potential biologic mechanisms for these associations in order to define potential targets for intervention.

Keywords

anxiety disorders; diabetes mellitus; hypertension; obesity; mood disorders; vascular diseases

INTRODUCTION

Vascular disease is a leading cause of excess death in mood disorders [1]. Pooled data from studies estimating cardiovascular mortality in bipolar disorder [1–5] indicate that the risk is approximately twice that expected from general population estimates [6]. With respect to mood disorder subtypes, most [1,2,7] but not all [3] studies that examined polarity demonstrated a greater risk for bipolar disorder when compared with unipolar depression, with a particularly stronger association in women [1,8]. The aforementioned mortality studies, however, were based on cohorts identified following an inpatient admission and may not be representative of a general population, community sample. With some exceptions [9], excess cardiovascular mortality has also been associated with anxiety disorders [10–13], and even independent of depression in some studies [14].

Although a two-fold increase in heart disease among those with mood and anxiety disorders was found in the World Mental Health (WMH) surveys,[15] the impact of established risk factors for vascular disease was not included in the analyses. Several studies have estimated the prevalence of risk factors for vascular disease in mood disorders. Individuals with major depression and bipolar disorder have a greater prevalence of established risk factors for vascular disease, including diabetes mellitus,[16–21] obesity [18,22–28], smoking [29,30], and less consistently, hypertension [18,31–35]. Bipolar disorder also appears to be associated with a greater prevalence of hypertriglyceridemia [23,25]. The prevalence ratio for metabolic syndrome, which encompasses many of these risk factors, in bipolar disorder has been estimated at 1.4 in United States (U.S.) and 1.8 in other samples [36].

Increased obesity in mood disorders, particularly bipolar disorder, could also explain the links with cardiovascular diseases and mortality. A prior analysis from the National Comorbidity Survey Replication (NCS-R) demonstrated a higher odds ratio for obesity with lifetime bipolar disorder (OR 1.47, 95% C.I. 1.12–1.93) than major depression (OR 1.21, 95% C.I. 1.09–1.35) with greater differences by polarity for past year instead of lifetime diagnoses (OR 1.61 versus 1.09) [27]. However, this analysis did not include the data for the chronic physical diseases collected only from Part II respondents and reported herein. The associations between mood and anxiety disorders with obesity (ORs 1.2–1.5) were only significant for females in the WMH survey [37], as well as in two other previous studies [28,38].

Several prospective studies of people with vascular disease have suggested that the presence of depressive symptoms may independently predict adverse outcome including risk of death or cardiovascular events in individuals with stable coronary artery disease [39], unstable angina [40], acute coronary syndromes [41], suspected myocardial infarction [42], acute myocardial infarction [43], or following coronary artery bypass grafting [44]. Anxiety symptoms have predicted similar outcomes in individuals with coronary artery disease [39,45] or suspected coronary artery disease [46]. Because of their relative infrequency, mood elevation symptoms have not been as well studied. Results of a prospective cohort study of participants with bipolar disorder showed that (hypo)manic symptoms independently predicted cardiovascular mortality in a dose-dependent fashion[47]. These

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data suggest that mood disorders may mediate vascular disease through mechanisms independent of and distinct from traditional risk factors.

Using the nationally representative National Comorbidity Survey–Replication (NCS-R) sample, we examined the association between mood and anxiety disorders and vascular disease independent of established risk factors for vascular disease. In contrast to previous studies, we also controlled for the effect of anxiety disorders in examining the association between mood disorders and vascular diseases. We hypothesized that a history of mania or hypomania would be associated with a greater prevalence of vascular disease and vascular disease risk factors when compared to those with major depression without mood elevation, other mental disorders, and those without mental disorders. We further assessed whether mood disorders were associated with an increased risk independent of available cardiovascular risk factors and independent of co-occurring anxiety disorders. We also investigated links between anxiety disorders with vascular disease because of the well-established comorbidity with mood disorders and the lack of previous research on this association.

METHODS

Participants

Conducted between February 2001 and April 2003, the NCS-R was a face-to-face household survey of adults 18 years of age or older from a representative sample of the 48 contiguous United States. Internal sub-sampling was used to reduce respondent burden by dividing the interview into two parts. Part I included the core diagnostic assessment of mental disorders, whereas Part II included collection of additional information relevant to a wide range of survey aims, including assessment of chronic physical conditions. All respondents completed Part I. Part II oversampled the original 9,282 NCS-R respondents for mental disorders [48]. The sample was weighted to adjust for differential probabilities of selection within households and for differences in intensity of recruitment effort. As a result of weighting, sample distributions closely match the population of the United States on sociodemographic variables. For this analysis, our sample consisted of the 5,692 Part II NCS-R respondents.

Participants were initially mailed a letter and brochure, followed by an in-person visit. Interviewers obtained verbal informed consent prior to beginning the interview. Professional non-clinician interviewers from the Institute for Social Research at the University of Michigan conducted all interviews, after receiving 7 days of study-specific training. Interviews were administered with the assistance of laptop computer-assisted software with skip-logic, timing flags, and consistency checks. Supervisors recontacted a random sample of 10% of participants for quality control purposes. Participants received $50 for participating and the overall response rate was 70.9%. The protocol was approved by the human subjects committees at Harvard Medical School in Boston, MA and the University of Michigan in Ann Arbor, MI. Further details of the methods have been published elsewhere [48,49].

Diagnostic assessment

Diagnosis of mental disorders was made utilizing the WMH version of the World Health Organization Composite International Diagnostic Interview (CIDI version 3.0), a fully structured assessment developed for use by trained non-clinician interviewers from diverse communities [50]. For the analyses presented herein, mood disorder diagnoses considered include bipolar I disorder, bipolar II disorder, and major depressive disorder (MDD) with other mental disorders including all other diagnoses of mental disorders. The diagnosis of

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bipolar I was made for any respondent with a lifetime history of mania and bipolar II for any respondent with a lifetime history of hypomania without mania. The anxiety disorder diagnoses considered individually included panic disorder, generalized anxiety disorder (GAD), and post-traumatic stress disorder (PTSD). A broader category of any anxiety included panic disorder, GAD, PTSD, obsessive-compulsive disorder, social phobia, specific phobia, and separation anxiety disorder. Prior validity studies have demonstrated good concordance between NCS-R CIDI diagnoses and blind clinical diagnoses [50–52].

Covariates

Sociodemographic characteristics were obtained by self-report, including sex, age, income, smoking, marital status, race/ethnicity, employment, and urbanicity. Age was stratified into three groupings: less than 40 years, 40 to less than 60 years, or greater than or equal to 60 years. Age groupings were selected to facilitate comparison to contemporaneously published data from the National Health and Nutrition Examination Survey (NHANES) [53,54]. Ratio of family income to census poverty threshold (income) was divided into 4 groups: 0 to 1.5 (low), 1.6 to 3 (low-average), 4 to 6 (high-average), and greater than 6 (high). Education was classified as less than high school, high school graduate, some college, and college graduate or higher. Smoking status was categorized as current, former, or never. Marital status was classified as married/cohabitating, previously married, and never married. Race was categorized as Hispanic, Non-Hispanic Black, Other, and Non-Hispanic White. Employment was grouped as working, homemaker, student, retired, and other. Urbanicity was obtained by linking interview location records to information for urban-rural continuum of counties per the Department of Agriculture. It was categorized as major metropolitan counties, other urbanized counties, or rural counties. Family history of heart disease was determined by self-report of any first degree relative with serious heart problems.

Outcomes

Assessment of chronic medical conditions was performed only with Part II respondents, who were asked if they had ever had any stroke or heart attack at any time in their life. Part II respondents were further asked if a doctor or other health professional ever told them that they had: heart disease, high blood pressure, and diabetes or high blood sugar. Obesity was based on a body mass index greater than or equal to 30 kg/m^2 from self-reported height and weight. Vascular disease in the study was operationally defined as any self-report of heart attack, heart disease, or stroke.

Statistical Analysis

Cross-tabulations were used to calculate prevalence and comorbidity. Logistic regression analysis was used to examine the effects of mood disorders on dichotomous dependent variables, i.e. vascular disorder and risk factors for vascular disease including obesity, high blood pressure and diabetes. Odds ratios (ORs) were calculated from the logistic regression coefficients to provide an estimate of the likelihood of vascular disease or risk factors for vascular disease controlling for individual's demographic characteristics. The reference group for all comparisons represented individuals without mental disorders. The mutually exclusive, hierarchical mood disorders were first assessed: mania, hypomania, major depression, and other mental disorders. Variances and 95% confidence intervals (CIs) of ORs were estimated using Taylor series linearization method implemented in the SUDAAN version 9. Significance tests were performed using Wald χ^2 tests that were adjusted for design effects using Taylor series method to accommodate sampling weights and account for stratification and clustering of the multistage sampling design. Statistical significance was based on 2-sided design-based tests evaluated at the 0.05 level of significance. In a separate analysis, odds ratios were similarly calculated for panic disorder, GAD, PTSD, and any anxiety disorder.

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RESULTS

The sociodemographic characteristics of those with mania, hypomania, MDD, other mental disorders, or without mental disorders are detailed in Table 1. Individuals with mood disorders were more likely to be female than those without mental disorders. Those with any mental disorders tended to be younger than those without. Individuals with mania and hypomania were more likely to be low income and current smokers though less likely to be married or cohabitating.

Comorbidity of vascular disease and vascular risk factors are reported for each of the hierarchical mood disorder categories by sex and age group in Table 2. The odds ratios for each of these conditions after modeled in multivariate logistic regression are further reported in Table 3. When adjusted for age, urbanicity, income, education, smoking, marital status, race/ethnicity, employment, and family history of heart disease; the risk of vascular disease was elevated for women (OR 3.12, 95% C.I. 1.85–5.25) but not men (OR 1.70, 95% C.I. 0.61–4.77) with bipolar disorder (mania or hypomania). After additionally controlling for the presence of obesity, high blood pressure, and diabetes in the full models, the risk remained elevated for women with bipolar disorder (OR 2.80, 95% C.I. 1.63–4.80) and men with MDD (OR 1.85, 95% C.I. 1.17–2.92). The greatest risk was seen for women with a history of mania (OR 4.14 95% C.I. 1.42–12.02); adjusted for obesity, high blood pressure, diabetes, and demographic characteristics (OR 3.87 95% CI 1.42–10.56). The odds ratios for vascular disease, obesity, high blood pressure, and diabetes were qualitatively higher for women with mania and hypomania than those with MDD or other mental disorders. When the interaction of sex and mood disorder on vascular disorder was assessed, no evidence of positive synergistic effects was found.

The associations between selected anxiety disorders and vascular disease were also assessed. The presence of any anxiety disorder was associated with high blood pressure in both men (OR 1.37, 95% C.I. 1.05–1.79) and women (OR 1.62, 95% C.I. 1.22–2.14). Likewise, anxiety disorders were associated with vascular disease in men (OR 1.86, 95% C.I. 1.35–2.57) and women (OR 1.62, 95% C.I. 1.14–2.29). The association between anxiety disorder and vascular disease in men (OR 1.77, 95% C.I. 1.24–2.51) and women (OR 1.50, 95% C.I. 1.07–2.12) occurred independent of the risk factors obesity, high blood pressure, and diabetes.

When including both anxiety and mood disorders in the model controlling for all demographic characteristics and risk factors of vascular disease, the association between anxiety disorder and vascular disease was significant for both men and women, but it was more pronounced in men than in women (OR=1.62, 95% C.I. 1.19–2.21 for men; OR 1.36, 95% C.I. 1.04–1.79 for women). When anxiety was included in the model, the association between mood disorder and vascular disease was not significant for men, and was attenuated but remained statistically significant for mania and hypomania in women.

DISCUSSION

The results from this nationally representative sample of U.S. adults confirm that vascular disease equivalents and risk factors are more common among those with co-occurring mood and anxiety disorders and anxiety disorders alone in both men and women. The greatest risk was seen for women with bipolar disorder, particularly mania, although severity of the mood disorder is one possible explanation for this finding. These associations could not be explained by the confounding effects of a number of sociodemographic and clinical variables and further appeared independent of the assessed traditional risk factors for vascular disease: diabetes mellitus, family history of heart disease, high blood pressure,

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obesity, and smoking. Anxiety disorders were associated with excess vascular risk in both genders, independent of mood, and mood disorders did not contribute to any significant elevations in risk in the presence of an anxiety disorder in men.

Our findings are consistent with and extend prior findings from the WMH and NCS-R. However, the lower associations in our study than those in earlier analyses of the NCS-R and the WMH survey [15,37,55] are likely attributable to our inclusion of more covariates or our more broadly defined vascular disease variable, which self-reported heart disease, heart attacks, and stroke. Our analysis was unique in assessing whether vascular disease risk was independent of available vascular risk factors or co-occurring mental disorders.

The prevalence of vascular disease and risk factors for vascular disease in our sample was comparable to data from other U.S. community and clinical studies. In our analysis, obesity was seen in 36% of those with a history of mania and 32% of those with a history of hypomania compared to data from U.S. clinical samples ranging from 32–50% [22–25,56]. Associations between mood and anxiety disorders with high blood pressure and diabetes mellitus from the present study are comparable to those from other population surveys including the Department of Veterans Affairs national study [17] and NHANES [54]. In our study, heart attack was reported by 3.2% of respondents, somewhat fewer than the 4.1% reported in NHANES [57], although our sample over-represents those with mental disorders who tended to be younger. An analysis of data from the National Epidemiologic Survey on Alcohol and Related Conditions demonstrated a slightly stronger association between major depression and coronary heart disease (OR 2.05) though, contrary to our findings did not find an independent association with anxiety disorders [58]. Our analysis controlled for several vascular risk factors and demonstrated anxiety disorders (independent of mood), bipolar disorders in women (independent of anxiety), and major depressive disorder in men to be independently associated with vascular disease.

There are a number of important limitations of this study. Height and weight were self-reported, which may underestimate of the overall prevalence of obesity [59]. Indeed, our overall estimates of obesity are somewhat lower than would be expected from published data from NHANES for the same period, 2001–2002 [53]. Despite this underestimation, the prevalence of obesity in certain subgroups remained much higher than expected. For instance, the prevalence of obesity for individuals 40–59 year of age with mania was 49% compared to the expected 34% from NHANES and the 33% observed among those without mental disorders. Differential misclassification of reported height and weight is possible in a direction that may be difficult to predict though under-reporting of weight does not appear to differ between the depressed and non-depressed [60,61]. The determination of vascular disease equivalents and risk factors represents another important limitation of the study. The observed frequency of vascular disease in less common conditions, such as mania and hypomania, reduces confidence in the precision of the estimates. These diagnoses were also limited to self-report of clinician diagnoses. Self-reporting of medically diagnosed vascular disease has acceptable validity [62–64] and has been used for related research [15,37,55,65–69]. Those in treatment for mental disorders may also have greater surveillance for metabolic and vascular conditions. The potential bias for this is reduced because our sample includes those identified with mental disorders from the CIDI assessment and not simply a sample of those already diagnosed. Further, evidence suggests that individuals with serious mental disorders may be less likely to be screened for these conditions [25,70], reducing this potential bias. Another limitation relates to the cross-sectional study design, which is not well suited for causal inference. As part of our design, we controlled for the presence of high blood pressure, diabetes mellitus, or obesity to determine whether the risk of vascular disease occurred independent of these traditional risk factors. These variables are considered categorically and without the presence of other established risk factors, such as those

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provided in a lipid profile. Subsequently, inference about associations independent of traditional risk factors leaves the possibility of residual confounding.

The NCS-R poses several advantages over prior studies of vascular disease and vascular risk factors in those with mood and anxiety disorders. The sample was designed to be representative of the non-institutionalized population of the contiguous United States and the results are thus readily generalizable to this population. Prior clinical and non-representative community samples may not be representative of the general population with mental disorders, potentially exaggerating estimates of vascular co-morbidity. Our representative sample reduces the likelihood that the associations seen in prior studies can be merely dismissed due to selection or Berkson's bias. This may particularly apply to our findings with obesity, determined form self-reported height and weight and not requiring clinician diagnosis. Thus, the nature of our sample and the magnitude and robustness of the associations observed suggests our findings are neither spurious nor biased.

The assessment of mental disorders with the structured CIDI represents another notable strength of the study. Participants underwent a rigorous, reliable and validated evaluation for mental disorders. The CIDI also facilitates the use of lifetime diagnoses, which are preferable for study of vascular disease, which would be expected to result from more long-term biobehavioral mechanisms. The size of the NCS-R dataset further allows for stratification by sex and diagnosis, allowing us to identify or confirm gender or sex as a potential moderator of observed associations.

Our findings strongly support prior studies suggesting greater vascular morbidity with mental disorders and further identify a sub-group at particular risk – women with bipolar disorder, and underscore the importance of appropriate screening for vascular disease in these at risk populations. The association between anxiety disorders and vascular disease independent of mood also highlights the importance of evaluating the role of anxiety disorders in vascular disease. Given that this risk cannot entirely be accounted for by sociodemographic and other clinical risk factors, including available risk factors for vascular disease, research into potential shared mechanisms between vascular disease and mood/anxiety disorders is warranted. Given the magnitude and robustness of the associations observed, women with bipolar disorder may represent a particularly relevant target population for further study.

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Table 1

Mood disorders by demographic characteristics (NCS-R, n=5,692)

			Mania		Hypomania		MDD		Other MI		No MI		Wald F (df) [p]
Variable	**Category**	**N**	**%**	**SE**	**%**	**SE**	**%**	**SE**	**%**	**SE**	**%**	**SE**	
		5692	**(n=101)**		**(n=243)**		**(n=1573)**		**(n=2,004)**		**(n=1,771)**		
Sex	Male	2382	0.8	0.1	2.5	0.3	13.4	0.9	29.5	1.0	53.8	1.5	16.99 (4) [<.001]
	Female	3310	1.1	0.2	2.8	0.2	20.0	0.6	24.4	0.9	51.8	1.2	
Age	<40yrs	2558	1.4	0.2	3.3	0.4	17.4	0.9	32.3	1.3	45.6	1.5	24.91 (8) [<.001]
	40–59yrs	2160	1.0	0.2	3.0	0.3	20.0	1.0	26.8	1.0	49.3	1.6	
	60+yrs	974	0.2	0.1	0.8	0.2	10.4	0.9	15.9	1.2	72.7	1.7	
Urbanicity	Metropolitan	2350	1.1	0.2	2.3	0.3	16.9	0.9	27.5	1.5	52.3	1.8	3.44 (8) [.004]
	Other urban	2028	1.4	0.3	2.8	0.3	17.1	0.8	28.5	1.3	50.1	1.9	
	Rural	1314	0.5	0.2	3.1	0.6	16.6	1.7	24.2	1.5	55.6	2.9	
Education	Less than high school	849	1.2	0.3	3.4	0.6	13.4	1.2	27.7	2.3	54.3	2.9	7.33(12) [<.001]
	High school grad	1715	1.1	0.2	3.1	0.5	16.1	0.7	26.9	1.4	52.8	1.8	
	Some college	1710	1.2	0.3	2.5	0.3	18.8	1.0	27.6	1.3	49.9	1.6	
	College grad or higher	1418	0.4	0.1	1.7	0.3	18.3	1.1	24.8	1.5	54.8	1.8	
Income	Low	1177	1.5	0.3	3.8	0.6	16.1	0.9	26.1	1.3	52.5	1.7	9.01 (12) [<.001]
	Low-average	1267	1.3	0.3	2.6	0.4	15.1	1.1	29.7	1.4	51.4	2.2	
	High-average	1885	0.8	0.2	2.5	0.4	17.4	1.0	27.6	1.5	51.7	1.8	
	High	1363	0.6	0.2	1.9	0.3	18.5	1.0	23.5	1.3	55.6	1.9	
Smoking	Current	1638	2.3	0.4	4.9	0.7	20.6	1.1	33.3	1.4	38.9	1.8	13.87 (8) [<.001]
	Former	1569	0.7	0.2	2.0	0.4	16.8	1.3	27.3	1.2	53.3	1.3	
	Never	2485	0.5	0.1	1.9	0.2	14.9	0.8	22.9	1.1	59.8	1.6	
Marital Status	Married/Cohabiting	3236	0.8	0.1	2.1	0.2	15.4	0.7	26.1	0.8	55.7	1.2	9.72 (8) [<.001]
	Previous Married	1239	1.0	0.3	3.3	0.4	20.9	1.3	24.2	1.5	50.6	2.3	
	Never married	1217	1.6	0.3	3.5	0.6	16.8	1.1	30.6	1.7	47.5	2.1	
Race/Ethnicity	Hispanic	527	1.5	0.4	2.8	1.0	14.0	1.5	25.7	3.0	56.1	4.0	2.77 (12) [.007]
	Non-Hispanic Black	717	1.2	0.3	3.7	0.5	10.9	1.2	25.0	2.1	59.1	2.8	
	Other	268	1.0	0.5	3.6	1.2	19.5	2.6	29.5	3.7	46.5	4.1	

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			Mania		Hypomania		MDD		Other MI		No MI		Wald F (df) [p]
Variable	**Category**	**N**	**%**	**SE**	**%**	**SE**	**%**	**SE**	**%**	**SE**	**%**	**SE**	
		5692	**(n=101)**		**(n=243)**		**(n=1573)**		**(n=2,004)**		**(n=1,771)**		
	Non-Hispanic White	4180	0.9	0.2	2.4	0.2	18.2	0.8	27.1	0.8	51.4	1.3	
Employment	Other	609	2.2	0.5	6.8	1.1	22.5	2.1	28.5	2.2	39.9	3.2	14.43 (16) [<.001]
	Working	3918	0.9	0.2	2.6	0.3	17.9	0.8	28.9	0.9	49.6	1.3	
	Student	143	1.5	0.7	2.1	0.7	11.1	2.4	33.4	5.1	51.9	4.7	
	Homemaker	340	1.2	0.4	1.2	0.5	14.9	1.6	23.0	3.0	59.8	3.3	
	Retired	682	0.3	0.2	1.0	0.3	10.5	1.1	16.0	1.6	72.2	2.1	
Family history of Heart disease	No	5334	1.0	0.1	2.7	0.3	16.7	0.6	26.9	0.7	52.8	1.1	0.79 (4) [.536]
	Yes	358	1.3	0.5	2.7	0.7	19.5	2.2	24.5	2.8	52.1	3.8	

MDD = Major depressive disorder, MI = Mental illness

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Table 2

Sex-specific adjusted rates of vascular disorders and risk factors by lifetime mood disorder subtypes (NCS-R)

Outcome	Age Group	Male					Female				
		Mania/Hypomania n=135 % (95%CI)	MDD n=524 % (95%CI)	Other MI n=953 % (95%CI)	No MI n=770 % (95%CI)	Wald F [p][1] (df=3)	Mania/Hypomania n=209 % (95%CI)	MDD n=1,049 % (95%CI)	Other MI n=1,051 % (95%CI)	No MI n=1,001 % (95%CI)	Wald F [p][1] (df=3)
Vascular Disorder[2]	**Total**	**8.8 (4.0 – 18.1)**	**10.9 (8.4 – 14.1)**	**9.7 (7.6 – 12.4)**	**10.5 (7.7 – 14.1)**	**3.89 [.015]**	**11.7 (8.8 – 15.5)**	**7.3 (5.6 – 9.7)**	**6.9 (5.6 – 8.6)**	**7.6 (6.0 – 9.7)**	**13.15 [.000]**
	<40yrs	6.8 (2.0 – 21.0)	3.2 (1.6 – 6.3)	1.6 (0.8 – 3.1)	1.4 (0.5 – 3.9)	1.39 [.140]	3.3 (1.2 – 9.0)	1.9 (0.9 – 4.2)	2.4 (1.4 – 4.1)	0.5 (0.1 – 2.2)	1.65 [.192]
	40–59yrs	8.9 (3.6 – 20.5)	11.4 (7.3 – 17.3)	11.3 (7.6 – 16.4)	5.4 (2.9 – 9.7)	1.88 [.148]	19.1 (13.3 – 26.7)	8.8 (5.7 – 13.3)	7.6 (5.1 – 11.2)	4.4 (2.7 – 7.0)	7.83 [<.001]
	60yrs+	28.7 (3.9 – 80.0)	44.4 (29.7 – 60.2)	38.4 (30.5 – 47.0)	30.8 (21.8 – 41.5)	1.51 [.225]	36.6 (16.4 – 62.9)	18.5 (12.6 – 26.4)	22.5 (14.4 – 33.3)	18.6 (14.0 – 24.3)	1.30 [.286]
Obesity	**Total**	**29.4 (19.8 – 41.2)**	**28.7 (24.7 – 33.1)**	**22.4 (19.4 – 25.7)**	**26.5 (22.0 – 31.6)**	**1.29 [.290]**	**36.1 (28.8 – 44.1)**	**27.8 (25.4 – 30.2)**	**25.3 (22.6 – 28.3)**	**24.5 (20.9 – 28.5)**	**3.18 [.034]**
	<40yrs	29.7 (14.4 – 51.3)	25.5 (20.3 – 31.5)	19.8 (16.1 – 24.1)	23.7 (17.9 – 30.6)	1.32 [.282]	28.7 (21.5 – 37.1)	24.9 (21.2 – 29.0)	20.5 (16.3 – 25.6)	19.4 (14.5 – 25.6)	1.90 [.145]
	40–59yrs	31.1 (19.3 – 45.9)	30.4 (23.6 – 38.1)	26.9 (20.6 – 34.4)	35.0 (26.8 – 44.2)	0.88 [.460]	47.4 (35.8 – 59.2)	31.4 (27.0 – 36.1)	29.9 (24.7 – 35.7)	31.2 (26.4 – 36.5)	3.01 [.041]
	60yrs+	12.6 (1.7 – 54.6)	35.5 (24.5 – 48.2)	19.0 (11.7 – 29.4)	19.1 (12.9 – 27.4)	1.98 [.132]	29.4 (8.9 – 64.0)	25.7 (19.8 – 32.7)	30.8 (23.2 – 39.7)	22.7 (16.7 – 30.2)	1.35 [.270]
High Blood Pressure	**Total**	**28.5 (22.9 – 34.8)**	**27.5 (21.6 – 34.2)**	**24.3 (21.0 – 28.0)**	**24.8 (22.2 – 27.5)**	**5.54 [.003]**	**22.9 (17.1 – 30.1)**	**23.3 (20.9 – 26.0)**	**22.1 (18.5 – 26.1)**	**23.5 (20.5 – 26.9)**	**5.34 [.003]**
	<40yrs	22.2 (14.0 – 33.4)	16.0 (9.7 – 25.4)	9.2 (6.4 – 13.2)	8.0 (4.9 – 12.8)	9.75 [<.001]	16.3 (10.8 – 23.8)	10.1 (7.4 – 13.5)	8.5 (5.4 – 13.1)	4.0 (2.5 – 6.4)	7.87 [<.001]
	40–59yrs	40.1 (26.7 – 55.2)	34.5 (27.7 – 42.0)	34.6 (28.1 – 41.8)	26.7 (21.9 – 32.2)	1.96 [.134]	29.0 (18.7 – 42.1)	26.6 (22.2 – 31.4)	25.9 (20.8 – 31.8)	24.1 (18.4 – 30.8)	0.42 [.740]
	60yrs+	0.0 (. -.)	46.3 (27.5 – 66.3)	55.2 (43.7 – 66.2)	46.7 (37.5 – 56.2)	0.50 [.683]	41.1 (16.4 – 71.3)	51.4 (43.9 – 58.8)	63.5 (55.1 – 71.2)	43.6 (36.9 – 50.6)	5.27 [.004]
Diabetes	**Total**	**5.6 (2.7 – 11.2)**	**8.9 (6.2 – 12.7)**	**5.0 (3.8 – 6.7)**	**7.7 (5.8 – 10.1)**	**1.69 [.184]**	**11.3 (8.6 – 14.7)**	**6.4 (5.0 – 8.2)**	**6.3 (4.5 – 8.7)**	**8.0 (6.0 – 10.5)**	**8.35 [<.001]**
	<40yrs	0.6 (0.1 – 4.6)	3.4 (1.5 – 7.3)	1.9 (0.9 – 4.0)	0.5 (0.1 – 3.1)	1.61 [.201]	8.9 (5.1 – 15.1)	3.7 (2.2 – 6.4)	4.4 (2.2 – 8.8)	0.3 (0.1 – 0.9)	6.33 [<.001]
	40–59yrs	12.8 (6.2 – 24.8)	10.7 (6.5 – 17.2)	7.2 (4.9 – 10.5)	9.1 (5.8 – 13.8)	0.97 [.415]	14.3 (8.8 – 22.6)	7.6 (5.3 – 10.7)	6.3 (4.2 – 9.4)	9.1 (6.8 – 12.1)	2.89 [.047]
	60yrs+	0.0 (. -.)	25.7 (13.8 – 42.9)	11.5 (6.4 – 20.0)	16.4 (10.9 – 23.9)	1.26 [.300]	12.9 (3.2 – 39.7)	10.8 (7.6 – 15.0)	13.3 (9.0 – 19.1)	14.8 (10.4 – 20.6)	0.65 [.585]

[1] adjusted for age for 'total' rows

[2] included stroke, heart disease and heart attack

MDD = Major depressive disorder, MI = Mental illness

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Table 3

Sex-specific associations between mood and anxiety disorders with vascular diseases, adjusting for vascular risk factors (NCS-R, n=5,692)

Mood Disorder	Male						Female					
	aOR (95% CI) [1]				aOR (95% CI)[2] Vascular Dx[4]	aOR (95% CI)[3,5] Vascular Dx[4]	aOR (95% CI)[1]				aOR (95% CI)[2] Vascular Dx[4]	aOR (95%CI)[3,5] Vascular Dx[4]
	Vascular Dx[4]	Obesity	High BP	Diabetes			Vascular Dx[4]	Obesity	High BP	Diabetes		
Mania	0.90 (0.18–4.60)	1.70 (0.79–3.66)	1.28 (0.46–3.60)	1.40 (0.39–5.05)	0.91 (0.16–5.15)	0.69 (0.13–3.79)	4.14 (1.42–12.02)	2.00 (1.20–3.34)	1.82 (0.86–3.84)	2.50 (1.17–5.33)	3.87 (1.42–10.56)	3.45 (1.19–9.95)
Hypomania	2.05 (0.63–6.72)	1.18 (0.67–2.09)	2.22 (1.55–3.19)	0.78 (0.29–2.07)	1.89 (0.58–6.23)	1.44 (0.41–5.06)	2.84 (1.59–5.06)	1.61 (0.93–2.78)	1.71 (1.05–2.77)	1.79 (1.06–3.04)	2.51 (1.35–4.66)	2.26 (1.06–4.83)
MDD	1.90 (1.23–2.95)	1.16 (0.89–1.51)	1.52 (1.01–2.29)	1.49 (0.88–2.53)	1.85 (1.17–2.92)	1.48 (0.88–2.50)	1.52 (0.93–2.49)	1.29 (1.01–1.65)	1.63 (1.23–2.15)	1.12 (0.71–1.76)	1.45 (0.87–2.42)	1.33 (0.74–2.41)
Other MI	1.52 (1.04–2.21)	0.84 (0.60–1.16)	1.37 (1.02–1.84)	0.82 (0.55–1.24)	1.47 (1.00–2.17)	1.19 (0.75–1.89)	1.51 (1.05–2.18)	1.10 (0.87–1.39)	1.65 (1.20–2.27)	1.16 (0.69–1.93)	1.41 (0.97–2.04)	1.26 (0.71–2.22)
No MI	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Wald F[p-value]	10.4 [0.034]	6.6 [0.156]	26.2 [<0.001]	6.0 [0.198]	8.3 [0.080]	2.5 [0.642]	22.7 [<0.001]	10.2 [0.037]	18.5 [0.001]	12.8 [0.012]	17.6 [0.001]	9.1 [0.060]
Mania/Hypomania vs. No MI	1.70 (0.61–4.77)	1.12 (0.77–1.65)	1.95 (1.36–2.80)	0.94 (0.42–2.08)	1.61 (0.57–4.56)	1.22 (0.41–3.65)	3.12 (1.85–5.25)	1.71 (1.09–2.69)	1.73 (1.12–2.68)	1.95 (1.24–3.04)	2.80 (1.63–4.80)	2.50 (1.27–4.95)
Mania/Hypomania/MDD vs. No MI	1.87 (1.22–2.86)	1.18 (0.93–1.50)	1.59 (1.12–2.27)	1.40 (0.87–2.25)	1.80 (1.16–2.82)	1.43 (0.86–2.40)	1.72 (1.12–2.66)	1.36 (1.06–1.75)	1.64 (1.28–2.11)	1.25 (0.83–1.89)	1.63 (1.04–2.55)	1.42 (0.81–2.50)
Mood & Anxiety[5]	2.06 (1.21–3.52)	1.06 (0.78–1.44)	1.79 (1.24–2.58)	1.57 (0.83–2.98)	1.91 (1.10–3.33)	-	1.78 (1.12–2.80)	1.40 (1.06–1.84)	1.71 (1.33–2.21)	1.26 (0.82–1.93)	1.67 (1.04–2.68)	-
Mood alone	1.51 (0.94–2.42)	1.62 (1.10–2.39)	1.17 (0.75–1.81)	1.42 (0.83–2.43)	1.56 (0.96–2.54)	-	1.66 (1.03–2.70)	1.32 (0.99–1.76)	1.38 (1.03–1.84)	1.14 (0.70–1.83)	1.61 (0.97–2.65)	-
Anxiety alone	1.86 (1.35–2.57)	1.02 (0.71–1.45)	1.37 (1.05–1.79)	1.06 (0.69–1.61)	1.77 (1.24–2.51)	-	1.62 (1.14–2.29)	1.16 (0.90–1.49)	1.62 (1.22–2.14)	1.07 (0.66–1.73)	1.50 (1.07–2.12)	-
No mood or Anxiety	Reference	Reference	Reference	Reference	Reference	-	Reference	Reference	Reference	Reference	Reference	-
Wald F [p-value]	21.4 [<0.001]	6.8 [0.083]	15.62 [0.001]	3.77 [0.288]	16.1 [0.001]	-	11.5 [0.009]	7.02 [0.071]	20.7 [<0.001]	1.33 [0.721]	8.52 [0.036]	-

[1] Adjusted for demographics including age, urbanicity, income, education, smoking, marital status, race, employment & family history of heart disease

[2] Adjusted for demographics, obesity, high blood pressure and diabetes

[3] Adjusted for demographics, obesity, high blood pressure, diabetes, and any anxieity disorder

[4] Vascular disease includes stroke, heart disease or heart attack

[5] Mood disorder included any of mania, hypomania and MDD; Anxiety disorder Included any of panic disorder, generalized anxiety disorder, post-tramatic stress disorder, obsessive compulsive disorder, agoraphobia, social phobia, specific phobia, separation anxiety disorder

BP = Blood pressure, CI = Confidence interval, MDD = Major depressive disorder, MI = Mental illness