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Mental Disorders as a Risk Factor of Acute Coronary Syndrome
A Systematic Review and Meta-Analysis

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IMPORTANCE Mental disorders have been associated with traditional cardiovascular risk factors that may mediate the risk of acute coronary syndrome (ACS).

OBJECTIVE To estimate the association of ACS among patients with mental disorders, as compared with patients without mental disorders.

DATA SOURCES MEDLINE, Embase, and PubMed were searched for studies between July 1, 2025, and date of database inception.

STUDY SELECTION Study screening was performed in duplicates with conflicts resolved upon consensus. Inclusion criteria were as follows: (1) observational or randomized study, (2) measured association with ACS (incident events, risk ratio, odds ratio, hazard ratio [HR]), and (3) investigated any clinical mental disorder (based on *DSM* and *International Classification of Diseases*) before ACS events.

DATA EXTRACTION AND SYNTHESIS This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. Data extraction was performed in duplicate and resolved on consensus. Data were quantitatively synthesized through random-effects meta-analysis. The National Institutes of Health Study Quality Assessment Tools were used to assess the quality of included studies. Studies were analyzed from January 1966 to October 2021.

MAIN OUTCOMES AND MEASURES Association and/or risk of ACS.

RESULTS Among 3616 initially identified studies, 25 full-text articles met inclusion criteria with 22 048 504 participants of median (IQR) age 48.0 (34.5-56.1) years, with 13 019 897 males (59.1%). Depressive disorder (HR, 1.40; 95% CI, 1.11-1.78; $P = .01$; Grading of Recommendations Assessment, Development, and Evaluation [GRADE] certainty = very low), anxiety disorder (HR, 1.63; 95% CI, 1.40-1.89; $P < .001$; GRADE certainty = low), sleep disorder (HR, 1.60; 95% CI, 1.22-2.10; $P < .001$; GRADE certainty = low), and posttraumatic stress disorder (PTSD; HR, 2.73; 95% CI, 1.94-3.84; $P < .001$; GRADE certainty = moderate) were associated with increased risk of ACS. Bipolar (HR, 1.48; 95% CI, 0.47-4.61; $P = .28$; GRADE certainty = very low) and psychotic (HR, 0.97; 95% CI, 0.01-178.30; $P = .06$; GRADE certainty = very low) disorders were not significantly associated with increased risk of acute myocardial infarction, although they had similar point estimates to some other mental disorders.

CONCLUSIONS AND RELEVANCE Results of this systematic review and meta-analysis suggest that depressive disorders, anxiety disorders, PTSD, and sleep disorders were associated with an increased risk of ACS. Particularly, PTSD and sleep disorders emerged as significant risk factors for ACS, indicating the potential impact of sleep quality on cardiovascular outcomes. Future research addressing these limitations could provide more nuanced insights into the association between mental health and ACS.

Supplemental content

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Mental disorders are a putative risk factor for acute coronary syndromes (ACSs), including myocardial infarction (MI) and unstable angina. Nearly 1 in 5 patients hospitalized for ACS met diagnostic criteria for depression, with an even greater proportion having subclinical depression.[1] In fact, the American Heart Association concluded that depression may be predictive of nonfatal cardiac events, making it an important prognostic factor in populations with ACS.[2] Likewise, mental disorders may increase the risk of early cardiovascular disease, with studies observing acute myocardial infarction (AMI) among patients with schizophrenia 10 years earlier than nonpsychiatric controls.[3] Other mental disorders implicated in ACS include bipolar disorder, posttraumatic stress disorder (PTSD), and substance use disorders (SUDs).[4-6]

Mental disorders have been associated with traditional cardiovascular risk factors that may mediate the risk of ACS. For instance, patients with type 1 bipolar disorders have over 4-fold odds of having hypertension, compared with healthy counterparts.[7] Moreover, patients with multiepisode schizophrenia, irrespective of medications, were at higher odds of having diabetes, hypertension, dyslipidemia, and overall metabolic syndrome, as compared with the general population.[8] Independent of traditional risk factors, schizophrenia, bipolar disorder, and other mental disorders are associated with proinflammatory states (ie, vascular dysfunction, oxidative stress, accelerated aging), critical to the development of ACS.[9-16] For example, depression has been associated with higher platelet factor 4 and β-thromboglobulin levels, and reduced nitric oxide synthase levels, which may mediate increased thrombosis.[17] There may also be an association between mental disorders and biological hypersensitivity to acute stressors, as well as genetic predispositions to both mental and cardiovascular disorders.[18]

Despite significant progress in diagnosis and management, ischemic heart diseases remain the second most common contributors to mortality and disability-adjusted life-years worldwide.[4] Thus, it is important to recognize and treat at-risk populations in a timely fashion, as treatment of cardiovascular disease risk factors has been associated with reduced incidence of MI and subsequent mortality.[19] Despite investigations into the prevalence of mental disorders among patients with cardiovascular disease and the development of risk calculators incorporating mental disorders as a predictor (eg, QRISK3 [University of Nottingham]), to date, there are few systematic reviews investigating the impact of mental disorders on ACS.[2,3,20] Existing reviews often investigate mental disorders in isolation (eg, depression only and anxiety only), heterogeneously define mental disorders using older criteria (eg, *DSM-III*), pool heterogeneous effect sizes, and include subclinical mental disorders.[21,22] Therefore, to build on the existing literature, through systematic review and meta-analysis, this study intended to estimate the association of mental disorders with ACS, specifically in those with *International Classification of Diseases* (*ICD*) or *DSM* diagnosed mental disorders.

Key Points

Question What is the association between mental disorders and acute coronary syndrome (ACS)?

Findings In this systematic review and meta-analysis including 25 full-text articles with 22 048 504 participants, posttraumatic stress disorder (PTSD) and depressive, anxiety, and sleep disorders were generally associated with increased risk of ACS, with PTSD and sleep disorders underscoring the importance of sleep quality on cardiovascular outcomes. Meanwhile, bipolar and schizophrenia-spectrum disorders were unclearly associated with ACS.

Meaning Sleep and other mental disorder–driven behaviors may mediate ACS risk in this patient population; future research addressing these limitations could provide more nuanced insights into the association between mental health and ACS.

Methods

This study was conducted from January 2024 to July 2025 and adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 reporting guidelines.[23] The protocol was uploaded to Open Science Framework a priori.[24]

Search Strategy and Inclusion Criteria

With the involvement of a research librarian, we searched MEDLINE, Embase, and PubMed for studies on December 1, 2024, investigating the influence of mental disorders on ACS (ie, AMI and/or acute unstable angina) with no restrictions based on the date of publication or language. Our search terms were related to AMI, unstable angina, ACS, and various mental disorders, with specifics highlighted based on frequency of appearance when collecting key articles. We included studies if they met the following criteria: (1) observational or randomized study, (2) measured association of ACS (incident events, risk ratio [RR], hazard ratio [HR], odds ratio [OR]) based on *ICD*, and (3) investigated any clinical mental disorder (based on *DSM* and *ICD*) before subsequent ACS event. In addition to the inverse of our inclusion criteria, we excluded studies if they (1) measured prevalence (eg, cross-sectional studies), (2) included other forms of MI (eg, type 2), (3) did not include mental disorders (eg, depressive symptoms instead of major depression), and (4) did not provide adjusted effect sizes. There were no sample size or language criteria.

Screening

We completed study screening on Covidence software. Reviewers screened titles and full texts in duplicate, with discrepancies resolved by a third independent reviewer. The references of all included studies were also systematically screened to identify any additional relevant articles.

Extraction

We independently and in duplicate extracted relevant data from the included studies into a Microsoft Excel spreadsheet that was designed a priori. The primary outcome was the association with ACS. We extracted the maximally adjusted effect sizes with corresponding 95% CIs. When 95% CI was not reported, we extracted the SE or *P* value to calculate the 95% CI. We collected information including study design (cohort, case-control), first author, year of publication, country, mental disorder, diagnostic criteria, sample size, and demographic data (age, sex, ethnicity). Race and ethnicity data were not reported for this study;

rather, we reported whether or not included studies adjusted for ethnicity in their respective analyses.

Quality Assessment

We used the National Institutes of Health (NIH) Study Quality Assessment Tools to assess the quality of included studies. Independent reviewers assessed each criterion of the checklist in duplicate, with discrepancies resolved by consensus.

Statistical Analysis

We used R, version 4.2.1 (R Foundation for Statistical Computing) for all statistical analyses. A meta-analysis was performed to calculate pooled HRs or ORs for dichotomous variables or a pooled standardized mean difference for continuous variables. We used the maximally adjusted effect sizes where possible. Where 1 outcome had multiple effect sizes (eg, HR and RR), we avoided combining heterogeneous effect sizes and opted to meta-analyze studies with the most commonly reported effect size among that group. We pooled HRs under the proportional hazards assumption, whereby we assumed risk is independent of time, and the point estimate reflected an average, instantaneous risk. Heterogeneity was considered substantial if $P < .10$ based on the χ^2 test and was considered high if I^2 >50%. We used random-effects models for a more conservative estimate of the effect size, acknowledging inherent heterogeneity across various study populations and methodologies. Forest plots were used to graphically present significant findings. Funnel plots were used to graphically represent the potential for publication bias, and statistics (intercept, SE, *t* value, *P* value) were reported where possible. We assessed certainty in pooled estimates using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) approach, where pooled data from observational studies started as low certainty evidence and were lowered if issues were identified in the domains of risk of bias, indirectness, inconsistency, imprecision or publication bias.[25] All *P* values were 2-sided, and a *P* value <.05 was considered significant. Studies were analyzed from January 2024 to July 2025.

Results

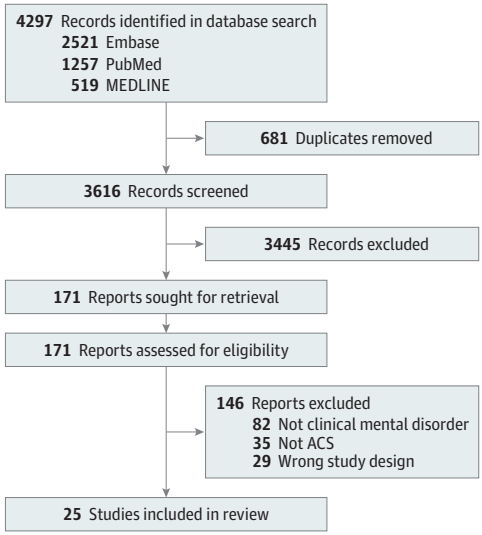
Study Characteristics

The **Figure** summarizes the screening process in the PRISMA flow diagram. The initial search yielded 4297 studies with 681 duplicates, of which 3445 studies were removed by title and abstract, leaving 171 full texts for review. Among 3616 initially identified studies, 25 full-text articles met inclusion criteria with 22 048 504 participants of median (IQR) age 48.0 (34.5-56.1) years, with 9 028 607 (40.9%) females and 13 019 897 males (59.1%). Information on search strategy, NIH Quality Assessment, GRADE analysis, and the PRISMA checklist can be found in eTables 1 to 4 in Supplement 1.

Table 1[26-50] summarizes individual study characteristics. Approximately, 18 studies (72%) were retrospective cohort studies,[27-32,37,39-46,48-50] 6 (24%) were prospective cohort studies,[33-36,38,47] and 1 (4%) were case-control studies.[26] Psychiatric disorders were mainly identified by *ICD* codes in 21 studies (84%)[26-33,35-41,43-45,48-50] or *DSM* criteria in 4 studies (16%).[34,42,46,47] The most commonly investigated disorders were anxiety (9 studies [36%]),[27,31,34,35,40,42,43,45,49] depressive (10 studies [40%]),[28,30,31,34,36-38,41,44,45] and substance use (4 studies [16%])[26,32,43,48] disorders. Among the various forms of ACS (ST-elevation MI [STEMI], non-STEMI [NSTEMI], unstable angina), included studies mainly investigated AMI (STEMI, NSTEMI) in 21 studies (84%),[26-33,35-44,46-50] any ACS in 2 studies (8%),[29,38] missed MI in 2 studies (8%),[30,45] and reinfarction in 2 studies (8%).[31,45]

Of the included sample of 22 048 504 participants, 2 853 773 (12.9%) were diagnosed with a mental disorder at baseline, and 317 780 (1.4%) fulfilled criteria for an incident ACS event.

Figure. PRISMA Flow Diagram



ACS indicates acute coronary syndrome.

Quality Assessment

All 25 studies were of fair quality per the NIH Study Quality Assessment Tools. The most common weaknesses among studies included lack of repeat exposure measurements (24 studies [96%]),[27-50] lack of sample size justification (24 studies [96%]),[26-30,32-50] and lack of blinding (24 studies [96%]).[26-39,41-50]

Primary Outcomes

Table 2 summarizes pooled effect sizes and 95% CIs for all eligible analyses.

Anxiety Disorders

Anxiety disorders were significantly associated with increased AMI events in 5 studies[27,36,42,44,45] (HR, 1.63; 95% CI, 1.40-1.89; $P < .001$; GRADE certainty = low) (eFigure 1 in Supplement 1).

Mood Disorders

Depression was significantly associated with increased ACS events in 6 studies[28,36,38,41,44,45] (HR, 1.40; 95% CI, 1.11-1.78;

Table 1. Study Characteristics

Source	Study type	Country	Source	Mental disorder	Criteria	Age (SD), y	Total sample size, No.	Female, %	Mental disorder, %	Follow-up period	Adjusted factors
Ashraf et al,[26] 2021	CC	US	Medicare	Alcohol use disorder	*ICD*	NR	32 846	40.9	16.7	90 d	Age, sex, geographic region, Elixhauser comorbidity index
Chen et al,[27] 2009	RC	Taiwan	NHIRD	Panic disorder	*ICD*	NR	38 564	61.1	25.0	1 y	Age, sex, hyperlipidemia, kidney disease, coronary heart disease, monthly income, urbanization level
Cho et al,[28] 2019	RC	South Korea	NHIS	Depression	*ICD*	NR	2 705 900	50.3	64.0	10 y	Age, sex, socioeconomic status, hypertension, diabetes, dyslipidemia, smoking, alcohol use, physical activity, body mass index
Chung et al,[29] 2013	RC	Taiwan	NHIRD	Nonapnea sleep disorder	*ICD*	51.4 (16.7)	147 297	63.7	33.3	10 y	Age, sex, comorbidities
Daskalopoulou et al,[30] 2016	RC	UK	CALIBRE	Depression	*ICD*	47.6 (15.3)	1 723 695	50.8	23.6	13 y	Age, smoking, systolic blood pressure, diabetes, cholesterol, socioeconomic status
Flygare et al,[31] 2023	RC	Sweden	SWEDEHEART	Anxiety, depression	*ICD*	62.3 (8.4)	30 212	36.1	11.3	5 y	Age, sex, country of birth, highest attained education, annual income adjusted for family composition, occupational status, hospital size, hospital stay in days, admission year, diabetes, hypertension, asthma, bronchitis, emphysema, other chronic respiratory disease, peripheral artery disease, previous stroke, dementia, body mass index, smoking status, left ventricular ejection fraction, heart rate, systolic blood pressure, infarct type, reperfusion, revascularization, discharge angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, oral anticoagulants, other antiplatelets, β-blockers, aspirin, calcium antagonist, digitalis, statins, other lipid lowering agents
Gili et al,[32] 2014	RC	Spain	NR	Cocaine, tobacco use disorder	*ICD*	59.1 (NR)	5 475 325	54.4	22.1	NR	Age, sex, addictions, hospital group, comorbidities
Hsu et al,[33] 2015	PC	Taiwan	NHIRD	Insomnia	*ICD*	47.7 (15.7)	44 080	57.1	50.0	9 y	Age, sex, hypertension, diabetes, coronary artery disease, hyperlipidemia, chronic kidney disease, congestive heart failure, peripheral artery disease, chronic pulmonary disease
Iozzia et al,[34] 2020	PC	Netherlands	Lifelines	Anxiety, depression	*DSM*	44.3 (12.6)	125 988	58.8	16.0	NR	Age, sex, somatic disease related to myocardial infarction, smoking, physical health-related quality of life
Jakobsen et al,[35] 2017	PC	Denmark	Danish PCR	Affective disorder	*ICD*	64.0 (0.1)	12 102	61.7	3.8	NR	Age, sex, symptom duration
Janszky et al,[36] 2010	PC	Sweden	NR	Depression	*ICD*	NR	49 230	0.0	1.6	37 y	Smoking, diabetes, systolic blood pressure, alcohol consumption, physical activity, father's occupation, coronary heart disease, geographic area
Jung et al,[37] 2021	RC	South Korea	NHIS	Depression	*ICD*	NR	2 228 043	2.8	37.9	9 y	Age, sex, smoking, alcohol consumption, regular exercise, body mass index, hypertension, dyslipidemia, chronic kidney disease, fasting blood glucose, insulin use, prescription of 2 or more antidiabetic agents
Khambaty et al,[38] 2016	PC	US	VACS	Major depressive disorder, dysthymic disorder	*ICD*	48.0 (9.4)	26 144	2.8	27.3	6 y	Age, sex, race, hypertension, dyslipidemia, CD4 count, HIV-1 RNA, antiretroviral, hepatitis C virus, kidney disease, alcohol consumption, cocaine abuse or dependence, hemoglobin levels
Lee et al,[39] 2024	RC	South Korea	NHIS	Psychotic disorders	*ICD*	38.2 (13.9)	96 252	50.9	50.0	15 y	Age, sex, Charleston Comorbidity Index, household income, disability

(continued)

Table 1. Study Characteristics (continued)

Source	Study type	Country	Source	Mental disorder	Criteria	Age (SD), y	Total sample size, No.	Female, %	Mental disorder, %	Follow-up period	Adjusted factors
Lin et al,[40] 2010	RC	Taiwan	NHIRD	Schizophrenia	*ICD*	NR	29 412	61.6	25.0	6 y	Age, sex, comorbidities
Lin et al,[41] 2014	RC	Taiwan	NHIRD	Depression	*ICD*	NR	54 355	43.9	20.0	9 y	Age, sex, level of urbanization, geographic location, monthly income
Martens et al,[42] 2010	RC	US	VACS	Generalized anxiety disorder	*DSM*	67.2 (11.0)	1015	17.9	10.0	9 y	Age
McGuiness et al,[43] 2021	RC	US	NIS	Cannabis use disorder	*ICD*	69.2 (10.0)	4684	39.0	50.0	9 y	Disorders of lipid metabolism, hypertension, diabetes, history of coronary artery disease, history of cerebrovascular disease, chronic kidney disease, COPD, congestive heart failure, liver disease, alcohol-related disorders, malignancy, non–skin cancer, hematologic malignancy, metastatic cancer, schizophrenia, personality disorders, mood disorders, asthma
Nakada et al,[44] 2023	RC	UK	UK Biobank	Anxiety, depression	*ICD*	56.1 (8.1)	431 971	55.1	0.7	NR	Age, sex, ethnicity, sleep deprivation level, alcohol consumption, smoking, sleep duration, television viewing, physical activity, body mass index
Park et al,[45] 2023	RC	South Korea	NHIS	Anxiety, bipolar, depression, insomnia, PTSD, schizophrenia	*ICD*	30.8 (5.0)	6 557 727	59.5	13.1	10 y	Age, sex, hypertension, diabetes, dyslipidemia, metabolic syndrome, chronic kidney disease, smoking, alcohol consumption, physical activity, low income level
Prieto et al,[46] 2016	RC	US	REP	Bipolar 1	*DSM*	NR	688	52.0	50.0	17.3 to 20.9 y	Hypertension, smoking, diabetes, alcohol use disorder
Remch et al,[47] 2018	PC	US	WTCHP	PTSD	*DSM*	51.3 (NR)	5971	18.3	20.9	4 y	Age, sex, blood pressure, total cholesterol, body mass index, tobacco use
Sharp et al,[48] 2022	RC	US	KPSC	Substance use disorder	*ICD*	48.9 (20.7)	325 088	57.2	16.6	30 d	Age, sex, race, coronary artery disease, hypertension, diabetes, hyperlipidemia, stroke, peripheral vascular disease, and medical center
Um et al,[49] 2023	RC	South Korea	NHIS	Panic disorder	*ICD*	54.3 (12.1)	1 624 718	68.0	0.4	10 y	Age, sex, income, smoking, drinking, exercise, body mass index, depression, fasting blood glucose, insulin use, prescription of three or more antidiabetic agents
Wu et al,[50] 2015	RC	Taiwan	NHIRD	Bipolar, schizophrenia	*ICD*	40.7 (15.3)	277 817	46.9	20.9	NR	Age, sex, income level, urbanization, hypertension, diabetes, hyperlipidemia, psychotropic use

Abbreviations: CC, case-control; COPD, chronic obstructive pulmonary disease; *ICD*, *International Classification of Diseases*; KPSC, Kaiser Permanente Southern California; NHIRD, National Health Insurance Research Database; NHIS, National Health Insurance System; NIH, National Institutes of Health Quality Assessment; NR, not reported; PC, prospective cohort; Danish PCR, Danish Psychiatric Central Research Register; PTSD, posttraumatic stress disorder; REP, Rochester Epidemiology Project; RC, retrospective cohort; SWEDEHEART, The Swedish Web System for Enhancement and Development of Evidence-Based Care in Heart Disease; VACS, Veterans Aging Cohort Study; WTCHP, WTC Health Program.

P = .01; GRADE certainty = very low). However, bipolar disorders were not significantly associated with AMI in 3 studies[45,46,50] (HR, 1.48; 95% CI, 0.47-4.61; *P* = .28; GRADE certainty = very low) (eFigures 2 and 3 in Supplement 1).

Psychotic Disorders

Psychotic disorders were not significantly associated with AMI in 2 studies[39,50] (HR, 0.97; 95% CI, 0.01-178.30; *P* = .06; GRADE certainty = very low) (eFigure 4 in Supplement 1).

Sleeping Disorders

Sleeping disorders were associated with increased ACS events in 3 studies[29,33,45] (HR, 1.60; 95% CI, 1.22-2.10; *P* < .001; GRADE certainty = low) (eFigure 5 in Supplement 1).

PTSD

PTSD was associated with increased incidence of AMI in 2 studies[45,47] (HR, 2.73; 95% CI, 1.94-3.84; *P* < .001; GRADE certainty = moderate) (eFigure 6 in Supplement 1).

SUD

SUD was associated with an increased odds of AMI in 3 studies[26,32,43] (OR, 2.41; 95% CI, 1.45-3.99; *P* = .01; GRADE certainty = very low) (eFigure 7 in Supplement 1).

Recurrent ACS Events

Severe mental illness was not associated with increased reinfarction events in 2 studies[31,45] (HR, 1.14; 95% CI, 0.98-1.33; *P* = .06; GRADE certainty = very low) (eFigure 8 in Supplement 1).

Table 2. Summary of Meta-Analyses

Mental disorder	Outcome	Measure	ES (95% CI)	*P* value	k[a]	I^2	χ^2	GRADE certainty
Anxiety	AMI	HR	1.63 (1.40-1.89)	<.001	5	41.0	0.14	Low
Bipolar	AMI	HR	1.48 (0.47-4.61)	.28	3	90.4	<0.0001	Very low
Depressive	ACS	HR	1.40 (1.11-1.78)	.02	6	93.7	<0.0001	Very low
Any mood	ACS	HR	1.42 (1.14-1.77)	.006	9	92.1	<0.0001	Very low
Psychotic	AMI	HR	0.97 (0.01-178.30)	.95	2	97.9	<0.0001	Very low
Sleeping	ACS	HR	1.60 (1.22-2.10)	<.001	3	75.5	0.02	Low
PTSD	AMI	HR	2.73 (1.94-3.84)	<.001	2	0.0	0.33	Moderate
SUD	AMI	OR	2.41 (1.45-3.99)	.01	3	84.1	0.0003	Very low
Severe mental illness	Reinfarction	HR	1.14 (0.98-1.33)	.06	2	0.0	0.73	Very low

Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; ES, effect size; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; HR, hazard ratio; OR, odds ratio; PTSD, posttraumatic stress disorder; SUD, substance use disorder.

[a] Represents number of studies.

Discussion

This systematic review and meta-analysis of over 22 million patients investigating the association of mental disorders with ACS found that depressive, anxiety, posttraumatic, and sleeping disorders were associated with an increased risk of ACS. The included studies were primarily retrospective cohorts with large sample sizes and moderate quality of evidence. Although bipolar and psychotic disorders failed to reach statistical significance, previous results suggest that they may still be associated with cardiovascular disease and mortality.[51]

Building on existing literature, our review reaffirms mental disorders as a potential risk factor for cardiovascular disease, namely ACS and AMI. Mental disorders likely mediate ACS through traditional vascular risk factors, a genetic link to coronary artery disease, proinflammatory states, exaggerated physiologic responses to acute stressors (eg, increased sympathoadrenal hyperactivity), and their sequelae (eg, increased plasma catecholamines, vasoconstriction, platelet activation).[22,52-54] Disorder-driven behaviors (eg, avoidant coping strategies in anxiety disorders) may predispose and augment unhealthy behaviors (eg, reduced smoking cessation) among individuals with mental disorders.[55,56] These behaviors may be conceptualized as confounders, mediators, or both with mediation related to the extent that they are driven by the underlying disorder. Nevertheless, this meta-analysis was limited by significant statistical heterogeneity, and future studies may benefit from separately adjusting for behaviors to facilitate interpretation.

We found that bipolar disorder had a nonsignificant association with ACS, coinciding with conflicting literature. For instance, although Lin and colleagues[57] found bipolar disorder not to be significantly associated with AMI, a meta-analysis[58] of 27 studies showed that bipolar disorder was associated with an elevated RR of cardiovascular mortality of 1.76 (95% CI, 1.53-2.01). A greater burden of mood symptoms over the long-term course of illness has been associated with bipolar disorder.[59,60] Our nonsignificant result likely reflects our included sample's younger age and likely use of psychotropic medications. As extended course of mental disorder is associated with increased cardiovascular mortality, accelerated aging likely mediates ACS and AMI among patients with bipolar disorder.[61] The lower prevalence of these markers in younger patients, combined with the higher incidence of atherosclerosis-driven cardiovascular mortality in those older than 65 years, likely reduces the impact of course of illness as a mediator and nullifies the association between bipolar disorder and ACS.[61] Many studies did not report age; therefore, this systematic review cannot assess whether age differences in samples moderated the association. Finally, with smaller sample sizes, these meta-analyses were likely subject to methodological heterogeneity across studies.

Our review observed the largest risk of ACS and AMI among patients with PTSD and sleep disorders. Augmenting traditional mechanisms, we hypothesize sleep disturbances to be a significant driver of coronary heart disease in both disorders, coinciding with previous findings of PTSD-associated disturbances being most firmly associated with history of MI.[62] Poor sleep is associated with poor glycemic control and increased oxidative stress, which may augment PTSD symptoms and mediate risk for AMI.[62] To the extent that poor sleep is due to the disorder, it would represent a proximal mediator to the resultant distal mediators (eg, glycemic control, oxidative stress). As our meta-analyses' primary studies adjusted for traditional vascular risk factors, positive signals seen in sleep disorders reinforce their potential impact on ACS incidence. Well-designed prospective studies could estimate to what extent sleep mediates the association between PTSD or other mental disorders on ACS, especially as sleep symptoms are underreported in primary settings.[62] However, especially as PTSD is associated with depression, anxiety, and other psychiatric comorbidities, without adjustment for other psychiatric comorbidities, it may be difficult to ascertain the true independent impact of sleep on ACS events.

Notably, psychotic disorders were not associated with increased AMI risk, directly contrasting with previous studies suggesting otherwise.[50,57] This was likely driven by Wu and colleagues,[50] as depending on degree of adjustment (ie, omitting adjustment for medications), the effect size varied. Antipsychotic drugs are associated with traditional vascular risk factors including weight gain, lipid abnormalities, insulin resistance, and direct cardiac adverse effects.[63] Regressions adjusting for both vascular risk factors and antipsychotic medications likely introduce some collinearity, which could lead to

underestimation of illness effects. Thus, in addition to acceleration of coronary atherosclerosis, schizophrenia likely confers additional risk to AMI. However, without multiple models adjusting for different clusters of variables (eg, vascular risk factors, medications, behavior), it is difficult to discern in what ways and with what results coronary atherosclerosis may mediate or confound psychotic disorders' association with ACS.

Among the included studies, anxiety and depressive disorders accounted for the majority of investigated mental disorders. This finding is reflected in the meta-analysis by Zeng and colleagues[64] in which a high prevalence of coronary heart disease was seen among this population; through mendelian randomization, Zeng and colleagues[64] postulated a strong causal link between depression and coronary heart disease. Patients with mood disorders are thought to experience greater mood-induced release of glucocorticoids leading to altered amygdala function and hyperalgesia from the heart. Subsequently, patients with depressive and anxiety disorders are more likely to report physical symptoms.[63] An increased tendency to report physical symptoms concerning for angina may lead to more investigation among patients with mental disorders and subsequently reduce chance of unrecognized MIs.[56] However, the importance of diagnostic overshadowing cannot be overstated as Solmi and colleagues[65] recognized in their meta-analysis, with significant disparities in screening between patients with and without mental disorders, namely for schizophrenia and bipolar disorders. Although our results do not warrant changes in diagnostic strategies for patients with mental disorders, it is imperative that physicians remain objective and continue to provide high-quality physical health care to patients with mental disorders.

Strengths and Limitations

Our study's strengths include its inclusion of cohort studies with large sample sizes from multiple databases, use of a broad search strategy, and use of adjusted effect size. Our a priori protocol minimized reporting bias, and our screening, extraction, and quality assessment in duplicate reduced interrater errors. Furthermore, included studies in this meta-analysis were mainly of fair quality of evidence, which allowed for synthesis of generally reliable evidence.

However, our study has some limitations, which include underreporting of baseline characteristics, including precise follow-up duration (precluding meta-regression), the type of AMI (ie, STEMI, NSTEMI), or the type of psychotropic medications. Augmented by the predominance of studies investigating AMI over unstable angina, it is difficult to comment to what extent the severity of coronary heart disease correlates with mental disorder. Moreover, heterogeneity likely stemmed from diverse samples, varied study designs, different follow-up periods, and inconsistent adjustment of covariates. For instance, among included studies for depression, the mean age ranged from 30.8 years to as high as 62.3 years, thereby introducing varying vascular risk profiles. Likewise, although most included studies adjusted for age and sex, adjustment of different degrees of vascular risk factors or socioeconomic factors likely further introduced heterogeneity. Additionally, by using *ICD* codes, data were subject to administrative-based claims and, thus, misclassification bias due to heterogeneity in diagnostic criteria. As severe cases are more likely to be captured, milder and prevalent cases may be missed; thus, the association of mental disorders with ACS may be exaggerated. Despite analyses with substantial heterogeneity, as our aim was to summarize the overall direction and magnitude of associations rather than to derive a single precise estimate, we used a random-effects meta-analysis to account for the substantial heterogeneity among studies. The findings should be interpreted with caution, as the observed variability underscores the need for more standardized and methodologically consistent research in this area. Finally, we acknowledge that meta-analyses including only 2 studies provide limited statistical power and do not allow for robust assessment of heterogeneity or publication bias. However, given the scarcity of available data on this topic, we included these analyses to provide a preliminary quantitative summary and to highlight areas where further research is needed. Thus, future studies should perform multistaged regressions adjusting for different clusters of variables (eg, vascular risk factors, behaviors and coping mechanisms, medications) to help estimate impacts of both confounders and mediators affecting the relationship of mental disorders and ACS (and outcomes including mortality or hospitalizations).

Conclusions

In conclusion, in this systematic review and meta-analysis, we found depressive, anxiety, traumatic, and sleeping disorders to be associated with an increased incidence of ACS, highlighting the importance of mental health in cardiovascular outcomes. These associations are likely mediated through genetic predispositions, traditional vascular risk factors, proinflammatory processes, and illness-driven behaviors. PTSD and sleep disorders emerged as notable factors, likely reflecting the importance of sleep on cardiovascular outcomes. Meanwhile, bipolar and psychotic disorders failed to reach statistical significance; however, they are likely associated with ACS, albeit more dependent on traditional vascular risk factors. Understanding these mechanisms can guide targeted interventions to mitigate the risk of ACS in individuals with mental disorders. However, the meta-analysis also acknowledges limitations, such as statistical heterogeneity, and potential biases in study designs. Future research addressing these limitations could provide more nuanced insights into the association between mental health and ACS outcomes. Ultimately, integrating mental health screening and management into cardiovascular care could significantly improve outcomes and reduce the burden of ACS among individuals with mental health disorders.

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REFERENCES

1. Thombs BD, Bass EB, Ford DE, et al. Prevalence of depression in survivors of acute myocardial infarction. *J Gen Intern Med*. 2006;21(1):30-38. doi:10.1111/j.1525-1497.2005.00269.x

2. Lichtman JH, Froelicher ES, Blumenthal JA, et al; American Heart Association Statistics Committee of the Council on Epidemiology and Prevention and the Council on Cardiovascular and Stroke Nursing. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American Heart Association. *Circulation*. 2014;129(12):1350-1369. doi:10.1161/CIR.0000000000000019

3. Goldstein BI, Carnethon MR, Matthews KA, et al; American Heart Association Atherosclerosis; Hypertension and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young. Major depressive disorder and bipolar disorder predispose youth to accelerated atherosclerosis and early cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2015;132(10):965-986. doi:10.1161/CIR.0000000000000229

4. Vos T, Lim SS, Abbafati C, et al; GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1204-1222. doi:10.1016/S0140-6736(20)30925-9

5. Bodén R, Molin E, Jernberg T, Kieler H, Lindahl B, Sundström J. Higher mortality after myocardial infarction in patients with severe mental illness: a nationwide cohort study. *J Intern Med*. 2015;277(6):727-736. doi:10.1111/joim.12329

6. Edmondson D, von Känel R. Posttraumatic stress disorder and cardiovascular disease. *Lancet Psychiatry*. 2017;4(4):320-329. doi:10.1016/S2215-0366(16)30377-7

7. Goldstein BI, Fagiolini A, Houck P, Kupfer DJ. Cardiovascular disease and hypertension among adults with bipolar I disorder in the US. *Bipolar Disord*. 2009;11(6):657-662. doi:10.1111/j.1399-5618.2009.00735.x

8. Vancampfort D, Wampers M, Mitchell AJ, et al. A meta-analysis of cardiometabolic abnormalities in drug naive, first-episode and multiepisode patients with schizophrenia versus general population controls. *World Psychiatry*. 2013;12(3):240-250. doi:10.1002/wps.20069

9. Najjar S, Pahlajani S, De Sanctis V, Stern JNH, Najjar A, Chong D. Neurovascular unit dysfunction and blood-brain barrier hyperpermeability contribute to schizophrenia neurobiology: a theoretical integration of clinical and experimental evidence. *Front Psychiatry*. 2017;8:83. doi:10.3389/fpsyt.2017.00083

10. Oral E, Halici Z, Cinar I, Ozcan E, Kutlu Z. Evaluation of endothelial dysfunction in bipolar affective disorders: serum endocan and urotensin II levels. *Clin Psychopharmacol Neurosci*. 2019;17(2):211-221. doi:10.9758/cpn.2019.17.2.211

11. Więdłocha M, Zborowska N, Marcinowicz P, et al. Oxidative stress biomarkers among schizophrenia inpatients. *Brain Sci*. 2023;13(3):490. doi:10.3390/brainsci13030490

12. Tam To B, Roy R, Melikian N, Gaughran FP, O'Gallagher K. Coronary artery disease in patients with severe mental illness. *Interv Cardiol*. 2023;18:e16. doi:10.15420/icr.2022.31

13. Caspi A, Shireby G, Mill J, Moffitt TE, Sugden K, Hannon E. Accelerated pace of aging in schizophrenia: 5 case-control studies. *Biol Psychiatry*. 2024;95(11):1038-1047. doi:10.1016/j.biopsych.2023.10.023

14. Lima CNC, Kovács EHC, Mirza S, et al. Association between the epigenetic lifespan predictor GrimAge and history of suicide attempt in bipolar disorder. *Neuropsychopharmacology*. 2023;48(6):954-962. doi:10.1038/s41386-023-01557-9

15. Sodhi SK, Linder J, Chenard CA, Miller D, Haynes WG, Fiedorowicz JG. Evidence for accelerated vascular aging in bipolar disorder. *J Psychosom Res*. 2012;73(3):175-179. doi:10.1016/j.jpsychores.2012.06.004

16. Goldstein BI, Baune BT, Bond DJ, et al. Call to action regarding the vascular-bipolar link: a report from the Vascular Task Force of the International Society for Bipolar Disorders. *Bipolar Disord*. 2020;22(5):440-460. doi:10.1111/bdi.12921

17. Laghrissi-Thode F, Wagner WR, Pollock BG, Johnson PC, Finkel MS. Elevated platelet factor 4 and β-thromboglobulin plasma levels in depressed patients with ischemic heart disease. *Biol Psychiatry*. 1997;42(4):290-295. doi:10.1016/S0006-3223(96)00345-9

18. Herrmann-Lingen C. Mental disorders and cardiovascular disease: not just an issue of older age. *Eur J Prev Cardiol*. 2023;30(15):1580-1581. doi:10.1093/eurjpc/zwad118

19. Bittner V, Bertolet M, Barraza Felix R, et al; BARI 2D Study Group. Comprehensive cardiovascular risk factor control improves survival: the BARI 2D trial. *J Am Coll Cardiol*. 2015;66(7):765-773. doi:10.1016/j.jacc.2015.06.019

20. Hippisley-Cox J, Coupland C, Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. *BMJ*. 2017;357:j2099. doi:10.1136/bmj.j2099

21. Nicholson A, Kuper H, Hemingway H. Depression as an etiologic and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies. *Eur Heart J*. 2006;27(23):2763-2774. doi:10.1093/eurheartj/ehl338

22. Roest AM, Zuidersma M, de Jonge P. Myocardial infarction and generalized anxiety disorder: 10-year follow-up. *Br J Psychiatry*. 2012;200(4):324-329. doi:10.1192/bjp.bp.111.103549

23. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372(71):n71. doi:10.1136/bmj.n71

24. OSF. Protocol page. Accessed December 1, 2025. https://osf.io/ezhrj/overview

25. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64(4):383-394. doi:10.1016/j.jclinepi.2010.04.026

26. Ashraf AM, Swiggett SJ, Golub IJ, et al. The association of alcohol use disorder with perioperative outcomes after primary total shoulder arthroplasty for glenohumeral osteoarthritis: a retrospective matched cohort study. *Semin Arthroplasty*. 2021;32:327-333. doi:10.1053/j.sart.2021.11.005

27. Chen YH, Tsai SY, Lee HC, Lin HC. Increased risk of acute myocardial infarction for patients with panic disorder: a nationwide population-based study. *Psychosom Med*. 2009;71(7):798-804. doi:10.1097/PSY.0b013e3181ad55e3

28. Cho Y, Lim TH, Kang H, Lee Y, Lee H, Kim H. Socioeconomic status and depression as combined risk factors for acute myocardial infarction and stroke: A population-based study of 2.7 million Korean adults. *J Psychosom Res*. 2019;121:14-23. doi:10.1016/j.jpsychores.2019.01.016

29. Chung WS, Lin CL, Chen YF, et al. Sleep disorders and increased risk of subsequent acute coronary syndrome in individuals without sleep apnea: a nationwide population-based cohort study. *Sleep*. 2013;36(12):1963-1968. doi:10.5665/sleep.3240

30. Daskalopoulou M, George J, Walters K, et al. Depression as a risk factor for the initial presentation of 12 cardiac, cerebrovascular, and peripheral arterial diseases: data linkage study of 1.9 million women and men. *PLoS One*. 2016;11(4):e0153838. doi:10.1371/journal.pone.0153838

31. Flygare O, Boberg J, Rück C, et al. Association of anxiety or depression with risk of recurrent cardiovascular events and death after myocardial infarction: a nationwide registry study. *Int J Cardiol*. 2023;381:120-127. doi:10.1016/j.ijcard.2023.04.023

32. Gili M, Ramírez G, Béjar L, López J, Franco D, Sala J. Cocaine use disorders and acute myocardial infarction, excess length of hospital stay and overexpenditure. *Rev Esp Cardiol (Engl Ed)*. 2014;67(7):545-551. doi:10.1016/j.recesp.2013.11.009

33. Hsu CY, Chen YT, Chen MH, et al. The association between insomnia and increased future cardiovascular events: a nationwide population-based study. *Psychosom Med*. 2015;77(7):743-751. doi:10.1097/PSY.0000000000000199

34. Iozzia G, de Miranda Azevedo R, van der Harst P, Rosmalen JGM, de Jonge P, Roest AM. Association of recognized and unrecognized myocardial infarction with depressive and anxiety disorders in 125 988 individuals: a report of the Lifelines cohort study. *Psychosom Med*. 2020;82(8):736-743. doi:10.1097/PSY.0000000000000846

35. Jakobsen L, Terkelsen CJ, Christiansen EH, et al. Severe mental illness and clinical outcome after primary percutaneous coronary intervention. *Am J Cardiol*. 2017;120(4):550-555. doi:10.1016/j.amjcard.2017.05.021

36. Janszky I, Ahnve S, Lundberg I, Hemmingsson T. Early-onset depression, anxiety, and risk of subsequent coronary heart disease: 37-year follow-up of 49 321 young Swedish men. *J Am Coll Cardiol*. 2010;56(1):31-37. doi:10.1016/j.jacc.2010.03.033

37. Jung I, Kwon H, Park SE, et al. Increased risk of cardiovascular disease and mortality in patients with diabetes and coexisting depression: a nationwide population-based cohort study. *Diabetes Metab J*. 2021;45(3):379-389. doi:10.4093/dmj.2020.0008

38. Khambaty T, Stewart JC, Gupta SK, et al. Association between depressive disorders and incident acute myocardial infarction in human immunodeficiency virus-infected adults: Veterans Aging Cohort Study. *JAMA Cardiol*. 2016;1(8):929-937. doi:10.1001/jamacardio.2016.2716

39. Lee YB, Kim H, Lee J, et al. Psychotic disorders and the risk of type 2 diabetes mellitus, atherosclerotic cardiovascular diseases, and all-cause mortality: a population-based matched cohort study. *Diabetes Metab J*. 2024;48(1):122-133. doi:10.4093/dmj.2022.0431

40. Lin HC, Chen YH, Lee HC, Lin HC. Increased risk of acute myocardial infarction after acute episode of schizophrenia: 6-year follow-up study. *Aust N Z J Psychiatry*. 2010;44(3):273-279. doi:10.3109/00048670903487209

41. Lin YN, Lin CL, Chang YJ, et al. Increased subsequent risk of acute coronary syndrome for patients with depressive disorder: a nationwide population-based retrospective cohort study. *Psychiatry Clin Neurosci*. 2014;68(4):263-269. doi:10.1111/pcn.12125

42. Martens EJ, de Jonge P, Na B, Cohen BE, Lett H, Whooley MA. Scared to death—generalized anxiety disorder and cardiovascular events in patients with stable coronary heart disease: the Heart and Soul Study. *Arch Gen Psychiatry*. 2010;67(7):750-758. doi:10.1001/archgenpsychiatry.2010.74

43. McGuinness B, Goel A, Elias F, Rapanos T, Mittleman MA, Ladha KS. Cannabis use disorder and perioperative outcomes in vascular surgery. *J Vasc Surg*. 2021;73(4):1376-1387.e3. doi:10.1016/j.jvs.2020.07.094

44. Nakada S, Ho FK, Celis-Morales C, Jackson CA, Pell JP. Individual and joint associations of anxiety disorder and depression with cardiovascular disease: a UK Biobank prospective cohort study. *Eur Psychiatry*. 2023;66(1):e54. doi:10.1192/j.eurpsy.2023.2425

45. Park CS, Choi EK, Han KD, et al. Increased cardiovascular events in young patients with mental disorders: a nationwide cohort study. *Eur J Prev Cardiol*. 2023;30(15):1582-1592. doi:10.1093/eurjpc/zwad102

46. Prieto ML, Schenck LA, Kruse JL, et al. Long-term risk of myocardial infarction and stroke in bipolar I disorder: a population-based cohort study. *J Affect Disord*. 2016;194:120-127. doi:10.1016/j.jad.2016.01.015

47. Remch M, Laskaris Z, Flory J, Mora-McLaughlin C, Morabia A. Posttraumatic stress disorder and cardiovascular diseases: a cohort study of men and women involved in cleaning the debris of the World Trade Center complex. *Circ Cardiovasc Qual Outcomes*. 2018;11(7):e004572. doi:10.1161/CIRCOUTCOMES.117.004572

48. Sharp AL, Pallegadda R, Baecker A, et al. Are mental health and substance use disorders risk factors for missed acute myocardial infarction diagnoses among chest pain or dyspnea encounters in the emergency department? *Ann Emerg Med*. 2022;79(2):93-101. doi:10.1016/j.annemergmed.2021.08.016

49. Um YH, Han KD, Kim TW, Jeong JH, Hong SC, Seo HJ. Does panic disorder increase the risk of cardiovascular diseases in diabetics: a nationwide population-based study. *J Affect Disord*. 2023;325:604-610. doi:10.1016/j.jad.2023.01.066

50. Wu SI, Chen SC, Liu SI, et al. Relative risk of acute myocardial infarction in people with schizophrenia and bipolar disorder: a population-based cohort study. *PLoS One*. 2015;10(8):e0134763. doi:10.1371/journal.pone.0134763

51. Correll CU, Solmi M, Veronese N, et al. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3 211 768 patients and 113,383,368 controls. *World Psychiatry*. 2017;16(2):163-180. doi:10.1002/wps.20420

52. Lu Y, Wang Z, Georgakis MK, Lin H, Zheng L. Genetic liability to depression and risk of coronary artery disease, myocardial infarction, and other cardiovascular outcomes. *J Am Heart Assoc*. 2021;10(1):e017986. doi:10.1161/JAHA.120.017986

53. Halaris A. Inflammation-Associated Co-morbidity Between Depression and Cardiovascular Disease. In: Dantzer R, Capuron L, eds. *Inflammation-Associated Depression: Evidence, Mechanisms, and Implications*. Springer International Publishing; 2016:45-70. doi:10.1007/7854_2016_28

54. Gustad LT, Laugsand LE, Janszky I, Dalen H, Bjerkeset O. Symptoms of anxiety and depression and risk of acute myocardial infarction: the HUNT 2 study. *Eur Heart J*. 2014;35(21):1394-1403. doi:10.1093/eurheartj/eht387

55. Strik JJ, Honig A, Maes M. Depression and myocardial infarction: relationship between heart and mind. *Prog Neuropsychopharmacol Biol Psychiatry*. 2001;25(4):879-892. doi:10.1016/S0278-5846(01)00150-6

56. Benninghoven D, Kaduk A, Wiegand U, Specht T, Kunzendorf S, Jantschek G. Influence of anxiety on the course of heart disease after acute myocardial infarction—risk factor or protective function? *Psychother Psychosom*. 2006;75(1):56-61. doi:10.1159/000089227

57. Lin HC, Tsai SY, Lee HC. No higher risk of myocardial infarction among bipolar patients in a 6-year follow-up of acute mood episodes. *Psychosom Med*. 2008;70(1):73-76. doi:10.1097/PSY.0b013e31815c1e93

58. Biazus TB, Beraldi GH, Tokeshi L, et al. All-cause and cause-specific mortality among people with bipolar disorder: a large-scale systematic review and meta-analysis. *Mol Psychiatry*. 2023;28(6):2508-2524. doi:10.1038/s41380-023-02109-9

59. Fiedorowicz JG, Jancic D, Potash JB, Butcher B, Coryell WH. Vascular mortality in participants of a bipolar genomics study. *Psychosomatics*. 2014;55(5):485-490. doi:10.1016/j.psym.2014.02.001

60. Fiedorowicz JG, Solomon DA, Endicott J, et al. Manic/hypomanic symptom burden and cardiovascular mortality in bipolar disorder. *Psychosom Med*. 2009;71(6):598-606. doi:10.1097/PSY.0b013e3181acee26

61. Fiedorowicz JG. Depression and cardiovascular disease: an update on how course of illness may influence risk. *Curr Psychiatry Rep*. 2014;16(10):492. doi:10.1007/s11920-014-0492-6

62. Akosile W, Young R, Lawford B, Voisey J, Colquhoun D. PTSD symptoms associated with myocardial infarction: practical clinical implications. *Australas Psychiatry*. 2018;26(1):60-64. doi:10.1177/1039856217734738

63. Loerbroks A, Bosch JA, Mommersteeg PMC, Herr RM, Angerer P, Li J. The association of depression and angina pectoris across 47 countries: findings from the 2002 World Health Survey. *Eur J Epidemiol*. 2014;29(7):507-515. doi:10.1007/s10654-014-9926-z

64. Zeng J, Qiu Y, Yang C, et al. Cardiovascular diseases and depression: a meta-analysis and mendelian randomization analysis. *Mol Psychiatry*. 2025;30(9):4234-4246. doi:10.1038/s41380-025-03003-2

65. Solmi M, Fiedorowicz J, Poddighe L, et al. Disparities in screening and treatment of cardiovascular diseases in patients with mental disorders across the world: systematic review and meta-analysis of 47 observational studies. *Am J Psychiatry*. 2021;178(9):793-803. doi:10.1176/appi.ajp.2021.21010031