Prevalence and 3-Year Psychiatric and Mental Health Outcomes of Primary and Secondary Mood Disorders

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Abstract

Background: Distinguishing between primary and secondary mood disorders (illness- or substance-induced) is important for appropriate treatment, yet their prevalence and outcomes in the general population remain understudied.

Aim: To compare psychiatric and mental health outcomes between primary and secondary mood disorders over a 3-year follow-up.

Methods: We used longitudinal data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative survey of the US adult population (Wave 1, 2001–2002; Wave 2, 2004–2005). Primary and secondary mood disorders were assessed following *DSM-IV* criteria. Outcomes assessed 3 years later included recurrence and persistence of mood disorders, suicide attempt, mental and physical health–related quality of life, and mental health help-seeking behavior. All analyses were adjusted for a wide range of sociodemographic and clinical characteristics.

Results: Among 3,602 participants with mood disorders during the 12 months before Wave 1, 298 (8.3%) had secondary and 3,304 (91.7%) primary mood diagnoses. Following adjustments, secondary mood disorders were associated with significantly poorer physical health–related quality of life (β = −2.75; 95% CI, −4.27 to −1.23) and lower 3-year recurrence (adjusted odds ratio [AOR] = 0.51; 95% CI, 0.36 to 0.72) and persistence rates (AOR = 0.49; 95% CI, 0.31 to 0.79) compared to primary mood disorders. Other outcomes showed no significant differences (all $P > .05$).

Conclusion: Secondary mood disorders were not rare and associated with poorer physical health–related quality of life than primary mood disorders. However, both groups showed similar risks of suicide attempts, impaired mental health–related quality of life, and rates of mental health help-seeking behavior. The findings for adults with secondary mood disorders align with efforts to integrate physical and mental health care.

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Mood disorders, particularly major depressive disorder and bipolar disorder, represent major public health concerns due to their high prevalence and their deleterious effects on social functioning and quality of life.[1] In addition to their substantial lifetime prevalence, 16% for major depressive disorder[2] and 5% for bipolar disorder,[3] these disorders are characterized by high recurrence rates,[4] increased risk of suicide attempt, suicide,[1] and all-cause mortality.[5,6]

The *DSM-5* delineates disorders based on their primary or secondary origin. Secondary mood disorders are defined as mood disturbances caused by general medical conditions, such as Cushing syndrome,[7] hypothyroidism,[8] neurological conditions,[9,10] or autoimmune disorders[11,12]; or by substances, such as alcohol,[13] cocaine,[14] or amphetamines[15]; or by medications such as corticosteroids[16] or interferons.[17] By contrast, primary mood disorders occur independently of any of these causes.

Distinguishing primary from secondary origin of mood disorders is important to guide appropriate management.[18,19] However, confounding factors and heterogeneity in most studies make it difficult to establish clear differences in the course of these groups. For example, the strong co-occurrence between mood disorders and substance use disorders[20] complicates the distinction between these 2 clinical conditions. Data regarding the prevalence of secondary mood disorders are scarce. Regarding substance-induced mood disorders, the lifetime prevalence of substance- or medication-induced depressive disorder has been estimated to be between 0.26% and 1% in a nationally representative survey of the US adult population.[21] As for mood disorders due to medical conditions, no studies have comprehensively

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Clinical Points

- Secondary mood disorders remain poorly understood in clinical practice, although they represent 8.3% of mood disorders.
- Lower relapse rates of secondary mood disorders at 3 years suggest a more favorable course when the underlying cause is identified and treated.
- Given their association with poorer physical health and a suicide risk similar to that of primary disorders, integrated medical and psychiatric care is essential.

evaluated their prevalence, and the few relevant findings demonstrate wide variation depending on the underlying medical condition. It also remains unclear whether certain characteristics or temporal patterns distinguish substance- or medical condition–induced mood disorders from primary mood disorders.[22] A 3-year prospective study[22] using National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) data showed that the incidence of mood disorders at follow-up was similar in individuals with an initially substance-induced depressive disorder and those with an independent depressive disorder. Moreover, most people initially classified as substance-induced were subsequently reclassified as primary major depressive disorder, highlighting the complexity of the diagnostic distinction over time. Another study[23] showed that patients meeting the criteria for poststroke major depression improved over a 2-year follow-up period, while those meeting the criteria for dysthymic depression had a less favorable prognosis, with lower remission rates.

To our knowledge, no population-based study has examined whether psychiatric and mental health outcomes differ from primary and secondary mood disorders. This knowledge would be important to clinicians and policy makers to help them anticipate and respond to the specific medical needs of these patients.

In this study, we compared primary and secondary mood disorders in relation to several critical outcomes, including recurrence and persistence of mood disorders, the occurrence of suicide attempts, and quality of life related to physical and mental health. Using longitudinal data from NESARC, we conducted a prospective cohort analysis to compare the frequency of these outcomes between adults with primary and secondary mood disorders, while adjusting for a wide range of potential sociodemographic and clinical confounders.

METHODS

Sample

Data were drawn from Wave 1 and Wave 2 NESARC, a nationally representative face-to-face survey of the US adult population, conducted in 2001–2002 (Wave 1) and 2004–2005 (Wave 2) by the National Institute on Alcoholism and Alcohol Abuse, as described in detail elsewhere.[24–27] The target population included the civilian, noninstitutionalized population, 18 years or older, residing in the US. The Wave 2 interview was conducted approximately 3 years after Wave 1 (mean interval of 36.6 months). The cumulative response rate at Wave 2 was 70.2%, resulting in 34,653 Wave 2 interviews[28] (Figure 1). Further details regarding data collection can be found in Supplementary Appendix 1.

Measures

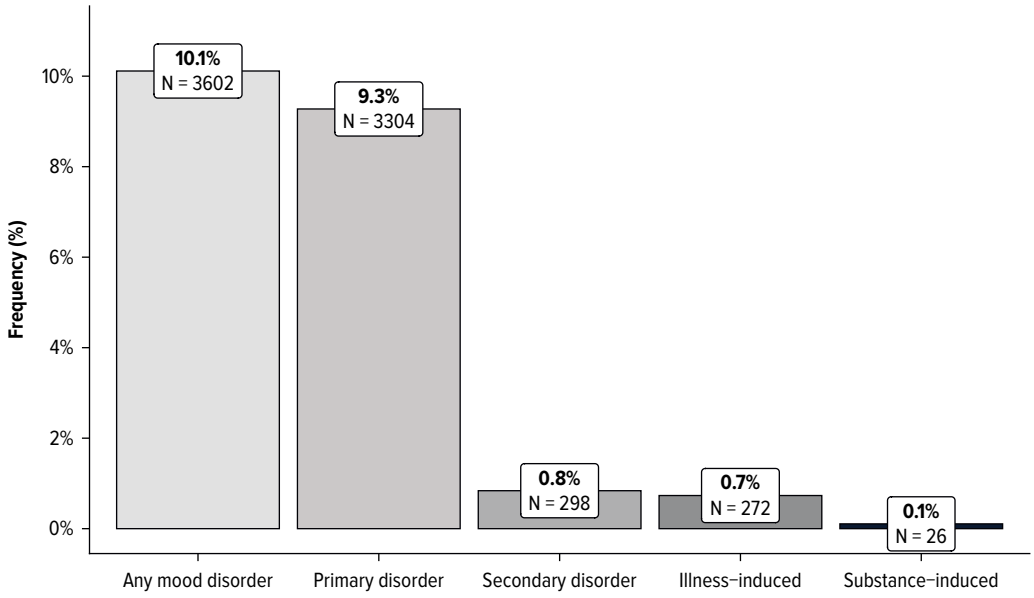
Current mood disorders. Psychiatric disorders were assessed using *DSM-IV* criteria with the Alcohol Use Disorder and Associated Disabilities Interview Schedule-*DSM-IV* Version (AUDADIS-IV). The AUDADIS-IV is a reliable and fully structured diagnostic interview, designed for professional interviewers. To meet the criteria for a psychiatric diagnosis, participants needed to meet diagnostic criteria at either or both NESARC waves. In this study, we examined several psychiatric disorders using the AUDADIS-IV, including mood disorders defined as manic episode, hypomanic episode, dysthymia, and major depressive disorder (defined as having at least 1 major depressive episode, without a lifetime history of mania or hypomania).

The test-retest reliability of the AUDADIS-IV is good for major depressive disorder ($\kappa = 0.65–0.73$),[29] fair to good for other mood disorders ($\kappa = 0.40–0.60$),[26,29,30] and good to excellent for substance use disorders ($\kappa > 0.74$).[29,31,32] Consistent with *DSM* classification, the term "primary" refers to mental disorders that are neither substance-induced nor caused by a general medical condition (illness-induced).[33] Respondents with mood disorders induced by a general medical condition (illness-induced) or a substance were considered as having a secondary mood disorder.[20] To identify secondary disorders, the AUDADIS-IV included structured questions for each episode, asking about illness timing and substance use context, following a computer-assisted script without physical examination.[34] Participants were classified as having a mood disorder if they met mood disorder criteria during the 12 months before the Wave 1 interview. This classification was considered fixed throughout the 3-year study period. While we refer to *DSM-5* framework for clarity with recent literature, this study uses *DSM-IV* criteria, which maintain equivalent distinctions between primary and secondary mood disorders.

Assessments of major mood disorders outcomes. Outcomes included recurrence and persistence of mood disorders, suicide attempt, physical and mental health–related quality of life, and mental health help-seeking behavior.

Recurrence and persistence of mood disorders were assessed separately for each specific mood disorder.

Figure 1.
Twelve-Month Rates of Any Mood Disorder by Cause (N = 33,687)[a]



[a]Percentages are weighted.

Recurrence was defined as meeting mood disorder criteria at both waves but not during the first 24 months postinterview. Persistence was defined as meeting criteria continuously from Wave 1 through the entire 3-year follow-up.

Suicide attempts between the 2 waves were based on self-reports. Physical and mental health–related quality of life was assessed using the 12-item Short-Form Health Survey (SF-12).[35] Two numeric scores are derived: the physical component summary (PCS) and mental component summary (MCS), reflecting overall physical and mental quality of life, respectively. Higher scores indicate better quality of life and functioning. The SF-12 was administered at both waves.

Mental health help-seeking behavior was classified as meeting any of the following: (1) visiting a doctor, counselor, therapist, or psychologist to get help for a specific mental disorder; (2) psychiatric hospitalization for at least 1 night; (3) emergency room visits to get help for the disorder; or (4) being prescribed medications to alleviate related symptoms.

Covariates. Sociodemographic factors included sex, age, race/ethnicity, education, marital status, and annual personal income. We also assessed several potential confounders regarding past-year presence of comorbidities including any medical condition, any personality disorder, any substance use disorder, any substance use outside substance use disorders, and any anxiety disorders, as well as physical and mental quality of life.

To reduce bias related to potential differences in mood disease severity between primary and secondary mood disorders, we further adjusted for age at onset of the first episode of the first mood disorder, the lifetime number of mood disorders, the age at first search for help for mood disorder, and the type of past-year mood disorders (ie, major depressive disorder, manic episode, hypomanic episode, and dysthymia).

Complete descriptions of all study variables, including detailed categorizations of sociodemographic factors, the full list of medical conditions, and psychiatric diagnoses criteria, are provided in Supplementary Appendix 2.

Statistical analyses. We calculated weighted percentages or means of all covariates described above, along with their standard error, using the study's Wave 2 sampling weights.

To examine the 3-year association of secondary versus primary mood disorders and versus no mood disorder with the outcomes, we performed univariate and multivariable logistic (ie, recurrence and persistence of the disorder, suicide attempt, and mental health–seeking behavior) and linear (ie, physical and mental health–related quality of life) regression models, adjusting for potential confounders assessed at Wave 1 (listed in Supplementary Table 1). As a sensitivity analysis, we examined the 3-year outcomes by separately comparing illness-induced mood disorders and substance-related mood disorders with primary mood disorders.

For all analyses, weighted estimates were considered significant if their 95% CIs did not include 1.00. We performed residual analyses to assess goodness of fit, checked for multicollinearity using the generalized variance inflation factor (GVIF), and examined potential outliers. All analyses were performed using R version 4.3.0 and accounted for the NESARC's complex sampling design.[36]

The reporting of this study follows the STROBE guidelines (see Supplementary Appendix 3).

RESULTS

Out of the 34,653 participants who were interviewed in both waves, we excluded 119 (0.3%) participants due to missing information on any of the outcomes and 847 (2.5%) respondents due to missing data on at least 1 covariate. Among the remaining 33,687 participants, 3,602 had a *DSM-IV* diagnosis of mood disorder in the last 12 months (10.1%) (Supplementary Figure 1). Among those with a mood disorder, 3,304 (91.7%) had a primary (major) mood disorder, whereas 298 (8.3%) had a secondary mood disorder, including 26 (1.1%) participants with a substance-induced mood disorder and 272 (7.2%) an illness-induced mood disorder (Figure 1; Table 1). The prevalence of 12-month rates at Wave 1 specific mood disorders is shown in Supplementary Figure 2. The frequency distributions of baseline characteristics stratified by type of mood disorder (any cause, primary diagnosis, secondary diagnosis, and absence of mood disorder) are presented in Supplementary Table 1. The frequency distributions of baseline characteristics stratified by outcome and the multivariable associations of each covariate with the outcomes are presented in Supplementary Tables 2 and 3, respectively.

Compared with individuals with primary mood disorders, those with secondary mood disorders were older, more frequently married, and demonstrated higher rates of medical comorbidities and past-year dysthymic disorder. They also exhibited later onset of mood disorders and initiated mood-related care at a more advanced age. Conversely, individuals with primary mood disorders attained higher levels of education, reported greater personal income, and showed increased prevalence of past-year personality disorders and substance use. They also demonstrated higher scores in both mental and physical quality of life and exhibited greater frequency of past-year manic or hypomanic episodes compared with those with secondary mood disorders (Supplementary Table 1).

Following adjustments, we found that participants with secondary mood disorders experienced significantly lower rates of recurrence (adjusted odds ratio [AOR] = 0.51; 95% CI, 0.36 to 0.72) and persistence (AOR = 0.49; 95% CI, 0.31 to 0.79) of mood disorders compared to participants with primary mood disorders. No significant differences were found in suicide attempt occurrence, mental health–related quality of life, and mental health help-seeking behavior between the two groups. Secondary mood disorders were associated with lower physical health–related quality of life (adjusted β [Aβ] = −2.75; 95% CI, −4.27 to −1.23) than primary mood disorders (Table 2). Sensitivity analyses examining illness-induced mood disorders separately yielded similar results, while analyses for substance-related mood disorders could not be computed due to the small sample size (n = 26) (Supplementary Table 4).

Both primary and secondary mood disorders were significantly associated with greater rates of occurrence of mood disorder (AOR = 2.51; 95% CI, 2.24 to 2.82 and AOR = 1.52; 95% CI, 1.03 to 2.22, respectively) and lower mental health–related quality of life (Aβ = −2.38; 95% CI, −2.9 to −1.87 and Aβ = −2,59; 95% CI, −4.12 to −1.06, respectively) as compared with having neither diagnosis (Table 3).

DISCUSSION

In our study, the physical quality of life at 3 years was lower for adults with a diagnosis of secondary mood disorders compared to those with a primary disorder, and the same results were observed when comparing them to individuals without mood disorders. These results are consistent and support consideration of secondary mood disorders as a distinct clinical and nosological entity, as they affect different populations.

Adults with secondary mood disorders were less likely than those with primary mood disorders to relapse within 3 years or to progress to persistent mood disorder, after adjusting for confounding factors. This suggests that secondary disorders have a distinctive clinical trajectory with a lower tendency to relapse. This could be due to the efficacy of addressing underlying factors. For instance, reducing or abstaining from alcohol[37,38] or normalizing calcium levels after parathyroidectomy[39] have been shown to improve depressive symptoms and lower the risk of relapse for relevant patients with secondary mood disorders.

The literature on the prognosis of secondary mood disorders remains limited. This is likely because studies often focus on a narrow subset of secondary disorders, frequently limited to substance-induced disorders, or they use outdated definitions of "secondary" that do not align with the current *DSM* criteria. Regarding substance-induced disorders, mood disorder symptoms typically resolve within about 1 month following withdrawal, cessation of intoxication,[38] or treatment of the substance use disorder.[40] A 24-week clinical trial[37] revealed that patients with alcohol-induced depression showed greater improvement compared to those with primary depression, which the authors attributed to a greater reduction in alcohol consumption, a finding consistent with other studies.[41]

Interestingly, despite a lower relapse rate, the risk of suicidal behavior was not significantly different between primary and secondary mood disorders. Similarly, mental health–related quality of life did not significantly differ,

Table 1.

Prevalence of Past-Year Mood Disorders at Baseline (N = 33,687)

	Any cause N (%)[a]	Primary diagnosis N (%)[a]	Secondary diagnosis N (%)[a]	Illness induced N (%)[a]	Substance induced N (%)[a]
Any mood disorder	3,602/33,687 (10.1%)	3,304/3,602 (91.7%)	298/3,602 (8.3%)	272/3,602 (7.2%)	26/3,602 (1.1%)
Major depressive disorder	2,814/33,687 (7.9%)	2,575/3,304 (77.9%)	239/298 (79.6%)	223/272 (82.4%)	16/26 (60%)
Manic episode	654/33,687 (1.8%)	621/3,304 (18.7%)	33/298 (10.6%)	29/272 (9.6%)	4/26 (17.5%)
Hypomanic episode	422/33,687 (1.3%)	414/3,304 (13.5%)	8/298 (3.4%)	5/272 (2.1%)	3/26 (12.4%)
Dysthymia	797/33,687 (2.1%)	706/3,304 (20.1%)	91/298 (29.7%)	87/272 (32.1%)	4/26 (13.2%)

[a]Weighted percentages. "Any cause" column: prevalence in total sample (N = 33,687). Other columns: distribution among participants with any mood disorder (N = 3,602) for the first row and distribution within each mood disorder category (primary, secondary, illness-induced, substance-induced) for subsequent rows.

Table 2.

Psychiatric and Mental Health Outcomes of Participants With a 12-Month Diagnosis of Primary and Secondary Mood Disorders

	Any primary mood disorder at baseline	Any secondary mood disorder at baseline (ref)	Secondary mood disorders vs primary mood disorders	
	Events/N (%)[a]	Events/N (%)[a]	OR (95% CI) *P* value	AOR (95% CI) *P* value[b]
Recurrence of mood disorders[c]	1,181/3,304 (35.2%)	71/298 (21.5%)	0.50 (0.35–0.71) <.001*	0.51 (0.36–0.72) .001*
Persistence of mood disorders	653/3,304 (18.8%)	37/298 (12.3%)	0.60 (0.38–0.95) .034*	0.49 (0.31–0.79) .005*
Suicide attempt	110/3,304 (3.2%)	12/298 (4.7%)	1.50 (0.67–3.36) .326	1.54 (0.66–3.58) .326
Mental-health help-seeking behavior	881/3,304 (25.7%)	71/298 (33.1%)	1.43 (1.05–1.94) .027*	1.16 (0.84–1.61) .370
	Mean (SE)[a]	Mean (SE)[a]	β (95% CI) *P* value	Aβ (95% CI) *P* value[b]
Physical health–related quality of life	48.55 (0.28)	38.54 (1.16)	−10.0 (−12.1 to −7.91) <.001*	−2.75 (−4.27 to −1.23) .001*
Mental health–related quality of life	45.0 (0.27)	42.24 (0.97)	−2.75 (−4.53 to −0.97) .004*	0.020 (−1.61 to 1.65) .981

[a]Weighted percentages and means.
[b]Adjusted for sex, age, ethnicity, education level, marital status, personal income, any medical condition, any personality disorder, any substance use in the past year, any anxiety disorder in the past year, physical and mental quality of life, age at onset of the first episode of the first mood disorder, lifetime number of mood disorder types, age at first help-seeking behavior for mood disorder, and past-year history of MDD, mania, hypomania, and dysthymia (*df* = 25; all GVIF <2.5).
[c]Defined as the occurrence of any mood disorder during the follow-up (ie, incidence or recurrence or chronicity).
**P* value is statistically significant (*P* < .05).
Abbreviations: Aβ = adjusted β coefficient, AOR = adjusted odds ratio, CI = confidence interval, GVIF = Generalized Variance Inflation Factor, MDD = major depressive disorder, OR = odds ratio, SE = standardized error.

suggesting that mood disorder relapse is not the sole determinant of overall mental health. Given that secondary disorders are often associated with potentially reversible external factors, one might expect an improvement in psychiatric outcomes following treatment of the underlying cause. However, our findings do not support this expectation. Furthermore, these individuals frequently exhibit a high burden of medical comorbidities, which may contribute to sustained mental health risks, even in the absence of psychiatric relapse. Supporting this hypothesis, a study conducted among patients with a history of mood disorders revealed that respiratory diseases, hypertension, and the number of physical comorbidities were associated with suicidal behavior, independently of sociodemographic factors and psychiatric or addictive comorbidities.[42] Furthermore, another study reported an increase in suicidal ideation among patients with pulmonary disease, even after adjusting for these same factors.[43,44]

While some associations between primary and secondary mood disorder and outcomes were observed in univariate analyses, they lost statistical significance after adjustment for multiple covariates, with no evidence of multicollinearity (all GVIF <2.5). This highlights the role of confounding factors, such as age at onset or medical comorbidities, in shaping the relationship between mood disorder type and prognosis.

Compared to adults with primary mood disorders, those with secondary mood disorders have a tendency to relapse less frequently and become less persistent, though they had poorer physical health–related quality of life. These findings clinically and nosologically distinguishing primary and secondary mood disorders. Despite this reduction in relapse rates, our results did not reveal significant differences between primary and secondary mood disorders in terms of suicide attempt risk and mental health–related quality of life, suggesting that mood disorder relapse is not the sole determinant of overall mental health. The findings highlight that integrated approaches aimed at better coordinating the management of psychiatric disorders and physical health could prove beneficial, as already shown by prior studies,

Table 3.

Psychiatric and Mental Health Outcomes of Participants With and Without a 12-Month Diagnosis of Primary and Secondary Mood Disorders

	Any primary mood disorder at baseline	No mood disorder at baseline (ref)	Primary mood disorders vs no mood disorder at baseline	
	Events/N (%)[a]	Events/N (%)[a]	OR (95% CI) *P* value	AOR (95% CI) *P* value[b]
Occurrence of mood disorders[c]	1,321/3,304 (39.2%)	2,838/30,085 (9.1%)	6.37 (5.80–7.00) <.001*	2.51 (2.24–2.82) <.001*
Suicide attempt	110/3,304 (3.2%)	116/30,085 (0.35%)	8.45 (6.15–11.6) <.001*	1.99 (1.41–2.82) <.001*
Mental-health help-seeking behavior	881/3,304 (25.7%)	1,527/30,085 (4.8%)	6.45 (5.79–7.18) <.001*	2.41 (2.12–2.74) <.001*
	Mean (SE)[a]	Mean (SE)[a]	β (95% CI) *P* value	Aβ (95% CI) *P* value[b]
Physical health–related quality of life	48.55 (0.28)	50.56 (0.11)	−1.90 (−2.46 to −1.34) <.001*	0.18 (−0.31–0.66) .481
Mental health–related quality of life	44.99 (0.27)	52.22 (0.08)	−7.14 (−7.69 to -6.6) <.001	−2.38 (−2.9 to −1.87) <.001*
	Any secondary mood disorder at baseline	No mood disorder at baseline (ref)	Secondary mood disorders vs no mood disorder at baseline	
	Events/N (%)[a]	Events/N (%)[a]	OR (95% CI) *P* value	AOR (95% CI) *P* value[b]
Occurrence of mood disorders[c]	75/298 (22.2%)	2,838/30,085 (9.1%)	2.11 (1.5–2.96) <.001*	1,52 (1.03–2.22) .039*
Suicide attempt	12/298 (4.7%)	116/30,085 (0.35%)	8.01 (3.63–17.71) <.001*	2.18 (0.97–4.87) .064
Mental-health help-seeking behavior	100 /298 (33.1%)	1,527/30,085 (4.8%)	6.78 (5.02–9.18) <.001*	2.17 (1.55–3.05) <.001*
	Mean (SE)[a]	Mean (SE)[a]	β (95% CI) *P* value	Aβ (95% CI) *P* value[b]
Physical health–related quality of life	38.54 (1.16)	50.56 (0.11)	−11.8 (−13.9 to −9.77) <.001*	−3.91 (−5.47 to −2.35) <.001*
Mental health–related quality of life	42.24 (0.97)	52.22 (0.08)	−9.3 (−11.03 to −7.58) <.001*	−2.59 (−4.12 to −1.06) .002*

[a]Weighted percentages and means.
[b]Adjusted for sex, age, ethnicity, education level, marital status, personal income, any medical condition, any personality disorder, any substance use disorder in the past year, any anxiety disorder in the past year, and physical and mental quality of life (*df* = 18; all GVIF <2.5).
[c]Defined as the occurrence of any mood disorder during the follow-up (ie, incidence or recurrence or chronicity).
*P value is statistically significant (*P* < .05).
Abbreviations: AOR = adjusted odds ratio, CI = confidence interval, GVIF = Generalized Variance Inflation Factor, OR = odds ratio, ref = reference, SE = standardized error.

for this population.[45–47] Although our study does not permit an evaluation of the effect of such approaches, collaborative care models, whose main objective is to improve access and quality of care in the general population, could help to meet the complex needs of these patients, particularly in primary care. Moreover, our findings also indicate that healthcare-seeking behavior was low in both groups and not significantly higher in the secondary than primary group, despite their greater burden of physical comorbidities. This suggests substantial room for improvement, particularly for patients with secondary mood disorders. Furthermore, other studies have shown that psychiatric treatment and support can be a good prognostic factor for maintaining abstinence from alcohol[48] and for reducing morbidity and mortality risks of patients with medical comorbidities.[49]

Despite its prospective design, our study has several limitations. First, diagnoses were based on the AUDADIS interview, administered by trained non-clinician Census Bureau interviewers, and not on psychiatric and non-psychiatric medical assessments. Information on the specific medical conditions and substances linked to mood disorders was not available. Additionally, certain psychiatric disorders, such as psychotic disorders and borderline personality disorders, were not recorded in the follow-up, preventing us from accounting for these confounders in our analyses. Second, generalizability of our findings may be limited by several factors. The NESARC survey excluded the population of adolescents and institutionalized participants, who are particularly at risk of substance use disorders. It is noteworthy that, although our analysis covered a range of mood disorders, major depressive disorder was the most common diagnosis in our sample. Therefore, it is likely that our overall results are primarily influenced by the characteristics of this disorder. Furthermore, the heterogeneous nature of secondary mood disorders, which can present with varying clinical trajectories depending on the specific underlying medical condition or substance involved, combined with the unbalanced distribution in our sample (with a marked predominance of illness-induced disorders) limit the generalizability of our results. Our findings regarding the "secondary" group are therefore mainly driven by the characteristics of illness-related disorders. Future studies with larger samples of substance-induced mood disorders would be needed to examine their specific trajectories. Third, the age of the NESARC data may not reflect current access to and effectiveness of treatments for mood disorders. Fourth, despite the large overall sample size, analyses of less common outcomes may have been statistically underpowered. Fifth, while our study examined on the 3-year evolution of primary and secondary mood disorders, their course may differ over longer or shorter periods. Finally, residual confounding in observational

studies prevents causal inferences from the observed associations.

In a nationally representative sample, we found that secondary mood disorders are not rare and associated with poorer physical health–related quality of life than primary mood disorders, though with lower risk of recurrence and persistence. The risks of suicide attempt, impaired mental health–related quality of life, and prevalence of mental health help-seeking behavior of adults with secondary mood disorders did not significantly differ from those of primary mood disorders. These findings may help inform future research or clinical strategies to better address the physical health burden in patients with secondary mood disorders.

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References

1. Grande I, Berk M, Birmaher B, et al. Bipolar disorder. *Lancet*. 2016;387(10027):1561–1572.
2. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003;289(23):3095–3105.
3. Merikangas KR, Akiskal HS, Angst J, et al. Lifetime and 12-Month prevalence of bipolar spectrum disorder in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2007;64(5):543–552.
4. Solomon DA, Keller MB, Leon AC, et al. Multiple recurrences of major depressive disorder. *Aust J Pharm*. 2000;157(2):229–233.
5. Crump C, Sundquist K, Winkleby MA, et al. Comorbidities and mortality in bipolar disorder: a Swedish national cohort study. *JAMA Psychiatry*. 2013;70(9):931–939.
6. Cuijpers P, Smit F. Excess mortality in depression: a meta-analysis of community studies. *J Affect Disord*. 2002;72(3):227–236.
7. Andela CD, Van Haalen FM, Ragnarsson O, et al. Mechanisms in endocrinology: cushing's syndrome causes irreversible effects on the human brain: a systematic review of structural and functional magnetic resonance imaging studies. *Eur J Endocrinol*. 2015;173(1):R1–R14.
8. Bode H, Ivens B, Bschor T, et al. Hyperthyroidism and clinical depression: a systematic review and meta-analysis. *Transl Psychiatry*. 2022;12(1):362.
9. Santos CO, Caeiro L, Ferro JM, et al. Mania and stroke: a systematic review. *Cerebrovasc Dis*. 2011;32(1):11–21.
10. Schwarz J, Odin P, Buhmann C, et al. Depression in Parkinson's disease. *J Neurol*. 2011;258(S2):336–338.
11. Carta MG, Moro MF, Lorefice L, et al. The risk of bipolar disorders in multiple sclerosis. *J Affect Disord*. 2014;155:255–260.
12. Meszaros ZS, Perl A, Faraone SV. Psychiatric symptoms in systemic lupus erythematosus: a systematic review. *J Clin Psychiatry*. 2012;73(7):993–1001.
13. Boden JM, Fergusson DM. Alcohol and depression. *Addiction*. 2011;106(5):906–914.
14. Fonseca F, Mestre-Pintó JI, Gómez-Gómez À, et al. The tryptophan system in cocaine-induced depression. *JCM*. 2020;9(12):4103.
15. Peet M, Peters S. Drug-induced Mania. *Drug Saf*. 1995;12(2):146–153.
16. Patten SB, Barbui C. Drug-Induced depression: a systematic review to inform clinical practice. *Psychother Psychosom*. 2004;73(4):207–215.
17. Loftis JM, Hauser P. The phenomenology and treatment of interferon-induced depression. *J Affect Disord*. 2004;82(2):175–190.
18. Bell V, Wilkinson S, Greco M, et al. What is the functional/organic distinction actually doing in psychiatry and neurology? *Wellcome Open Res*. 2020;5:138.
19. Harrison PJ. The neuropathology of primary mood disorder. *Brain*. 2002;125(Pt 7):1428–1449.
20. Grant BF, Stinson FS, Dawson DA, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2004;61(8):807–816.
21. Blanco C, Alegría AA, Liu SM, et al. Differences among major depressive disorder with and without co-occurring substance use disorders and substance-induced depressive disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry*. 2012;73(6):865–873.
22. Magidson JF, Wang S, Lejuez CW, et al. Prospective study of substance-induced and independent major depressive disorder among individuals with substance use disorders in a nationally representative sample. *Depress Anxiety*. 2013;30(6):538–545.
23. Robinson RG, Bolduc PL, Price TR. Two-year longitudinal study of poststroke mood disorders: diagnosis and outcome at one and two years. *Stroke*. 1987;18(5):837–843.
24. Blanco C, Hoertel N, Wall MM, et al. Toward understanding sex differences in the prevalence of posttraumatic stress disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry*. 2018;79(2):16m11364.
25. Blanco C, Wall MM, Hoertel N, et al. Psychiatric disorders and risk for multiple adverse outcomes: a national prospective study. *Mol Psychiatry*. 2021;26(3):907–916.
26. Grant BF, Dawson DA, Stinson FS, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. *Drug Alcohol Depend*. 2003;71(1):7–16.
27. Hoertel N, Franco S, Wall MM, et al. Mental disorders and risk of suicide attempt: a national prospective study. *Mol Psychiatry*. 2015;20(6):718–726.
28. Blanco C, Hasin DS, Wall MM, et al. Cannabis use and risk of psychiatric disorders: prospective evidence from a US national longitudinal study. *JAMA Psychiatry*. 2016;73(4):388–395.
29. Canino G, Bravo M, Ramírez R, et al. The Spanish Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability and concordance with clinical diagnoses in a Hispanic population. *J Stud Alcohol*. 1999;60(6):790–799.
30. Cottler LB, Grant BF, Blaine J, et al. Concordance of DSM-IV alcohol and drug use disorder criteria and diagnoses as measured by AUDADIS-ADR, CIDI and SCAN. *Drug Alcohol Depend*. 1997;47(3):195–205.
31. Grant B, Harford TC, Dawson DA, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability of alcohol and drug modules in a general population sample. *Drug Alcohol Depend*. 1995;39(1):37–44.
32. Ruan WJ, Goldstein RB, Chou SP, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of new psychiatric diagnostic modules and risk factors in a general population sample. *Drug Alcohol Depend*. 2008;92(1-3):27–36.
33. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. American Psychiatric Association; 2013.

34. National Institute on Alcohol Abuse and Alcoholism. *National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III): Data Notes*. National Institute on Alcohol Abuse and Alcoholism; 2014.
35. Robins LN, Helzer JE, Croughan J, et al. National Institute of Mental Health Diagnostic Interview Schedule: its history, characteristics, and validity. *Arch Gen Psychiatry*. 1981;38(4):381–389.
36. Lumley T. Analysis of complex survey samples. *J Stat Soft*. 2004;9(8):1–19.
37. Foulds JA, Douglas Sellman J, Adamson SJ, et al. Depression outcome in alcohol dependent patients: an evaluation of the role of independent and substance-induced depression and other predictors. *J Affect Disord*. 2015; 174:503–510.
38. Myrick H, Cluver J, Swavely S, et al. Diagnosis and treatment of co-occurring affective disorders and substance use disorders. *Psychiatr Clin North Am*. 2004; 27(4):649–659.
39. Parks KA, Parks CG, Onwuameze OE, et al. Psychiatric complications of primary hyperparathyroidism and mild hypercalcemia. *Aust J Pharm*. 2017;174(7): 620–622.
40. Gallagher C, Radmall Z, O'Gara C, et al. Anxiety and depression among patients with alcohol dependence: co-morbid or substance-related problems? *Ir J Psychol Med*. 2018;35(2):121–126.
41. Brown SA, Inaba RK, Gillin JC, et al. Alcoholism and affective disorder: clinical course of depressive symptoms. *Am J Psychiatry*. 1995;152(1):45–52.
42. MacLean J, Kinley DJ, Jacobi F, et al. The relationship between physical conditions and suicidal behavior among those with mood disorders. *J Affect Disord*. 2011;130(1–2):245–250.
43. Goodwin RD, Kroenke K, Hoven CW, et al. Major depression, physical illness, and suicidal ideation in primary care. *Psychosom Med*. 2003;65(4): 501–505.
44. Qin P, Webb R, Kapur N, et al. Hospitalization for physical illness and risk of subsequent suicide: a population study. *J Intern Med*. 2013;273(1):48–58.
45. Doherty AM, Gaughran F. The interface of physical and mental health. *Soc Psychiatry Psychiatr Epidemiol*. 2014;49(5):673–682.
46. Uga A, Kulkarni S, Heeramun V, et al. Evaluation of a model of integrated care for patients with chronic medical and psychiatric illness. *Psychosomatics*. 2017;58(4): 437–440.
47. Van Eck Van Der Sluijs JF, Castelijns H, Eijsbroek V, et al. Illness burden and physical outcomes associated with collaborative care in patients with comorbid depressive disorder in chronic medical conditions: a systematic review and meta-analysis. *Gen Hosp Psychiatry*. 2018;50:1–14.
48. Kodl MM, Fu SS, Willenbring ML, et al. The impact of depressive symptoms on alcohol and cigarette consumption following treatment for alcohol and nicotine dependence. *Alcohol Clin Exp Res*. 2008;32(1):92–99.
49. Gold SM, Köhler-Forsberg O, Moss-Morris R, et al. Comorbid depression in medical diseases. *Nat Rev Dis Primers*. 2020;6(1):69.

The Journal of Clinical Psychiatry

Supplementary Material

Article Title: Prevalence and 3-Year Psychiatric and Mental Health Outcomes of Primary and Secondary Mood Disorders

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

DISCLAIMER

This Supplementary Material has been provided by the authors as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Appendix 1. National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

Data were drawn from Wave 1 and Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative face-to-face survey of the US adult population, conducted in 2001–2002 (Wave 1) and 2004–2005 (Wave 2) by the National Institute on Alcoholism and Alcohol Abuse (NIAAA), as described in detail elsewhere.[1–4] The target population included the civilian, noninstitutionalized population, aged 18 years or older, residing in the US. The Wave 2 interview was conducted approximately 3 years after Wave 1 (mean interval of 36.6 months). The cumulative response rate at Wave 2 was 70.2%, resulting in 34,653 Wave 2 interviews[5] (**Figure 1**).

Participants provided written informed consent, and all procedures received full human subjects review and approval from the U.S. Census Bureau and U.S. Office of Management and Budget.
The NESARC was administered by approximately 1,800 experienced U.S. Census Bureau interviewers using computer-assisted software. Interviewers received standardized training supervised by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and several quality control measures were put in place, including random follow-up checks on 10% of respondents by regional supervisors.[3,6,7]

Supplementary Appendix 2. Covariates.

Sociodemographic factors included sex, age, race/ethnicity (i.e., White, Black, American Indian/Alaska native, Asian/Native Hawaiian/Pacific Islander, and Hispanic/Latino), education (less than high school, high school graduate and college or higher), marital status (married, widowed/divorced, and never married), and annual personal income (<12K, 12K-30K, >30K). We also assessed several potential confounders regarding past-year presence of comorbidities including any medical condition, any personality disorder, any substance use disorder, any substance use outside substance use disorders, and any anxiety disorders, as well as physical and mental quality of life.

The presence of any medical condition was evaluated using information from the NESARC Wave 1 and 2 interviews, which collected data on 18 chronic medical conditions diagnosed by doctors in the past year, including arteriosclerosis, hypertension, diabetes, high cholesterol, liver diseases, myocardial infarction, other minor heart conditions, stomach ulcer, stroke, gastritis, arthritis, HIV (Human immunodeficiency virus), AIDS (Acquired immunodeficiency syndrome), and any other sexually transmitted diseases. For this analysis, having any medical condition was defined as the presence of at least one of these conditions in the year before the Wave 2 interview.[8]

All psychiatric diagnoses, including drug use disorders (related to alcohol, nicotine, cannabis, amphetamines, hallucinogens, cocaine, heroin, opioids, sedatives, tranquilizers, and inhalants), anxiety disorders (panic disorder, social phobia, specific phobia, generalized anxiety disorder) and personality disorders (antisocial, avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic), were made according to DSM-IV criteria.[9] Diagnoses for all Axis I disorders were made for the 12 months prior to Wave 1.

To reduce bias related to potential differences in mood disease severity between primary and secondary mood disorders, we further adjusted for age-at-onset of the first episode of the first mood disorder, the lifetime number of mood disorders, the age at first search for help for mood disorder, and the type of past-year mood disorders (i.e., major depressive disorder (MDD), manic disorder, hypomanic disorder and dysthymic disorder).

References

1. Blanco C, Hoertel N, Wall MM, et al. Toward Understanding Sex Differences in the Prevalence of Posttraumatic Stress Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry*. 2018;79(2):16m11364. doi:10.4088/JCP.16m11364

2. Blanco C, Wall MM, Hoertel N, et al. Psychiatric disorders and risk for multiple adverse outcomes: a national prospective study. *Mol Psychiatry*. 2021;26(3):907-916. doi:10.1038/s41380-019-0459-4

3. Grant BF, Dawson DA, Stinson FS, Chou PS, Kay W, Pickering R. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. *Drug and Alcohol Dependence*. 2003;71(1):7-16. doi:10.1016/S0376-8716(03)00070-X

4. Hoertel N, Franco S, Wall MM, et al. Mental disorders and risk of suicide attempt: a national prospective study. *Mol Psychiatry*. 2015;20(6):718-726. doi:10.1038/mp.2015.19

5. Blanco C, Hasin DS, Wall MM, et al. Cannabis Use and Risk of Psychiatric Disorders: Prospective Evidence From a US National Longitudinal Study. *JAMA Psychiatry*. 2016;73(4):388. doi:10.1001/jamapsychiatry.2015.3229

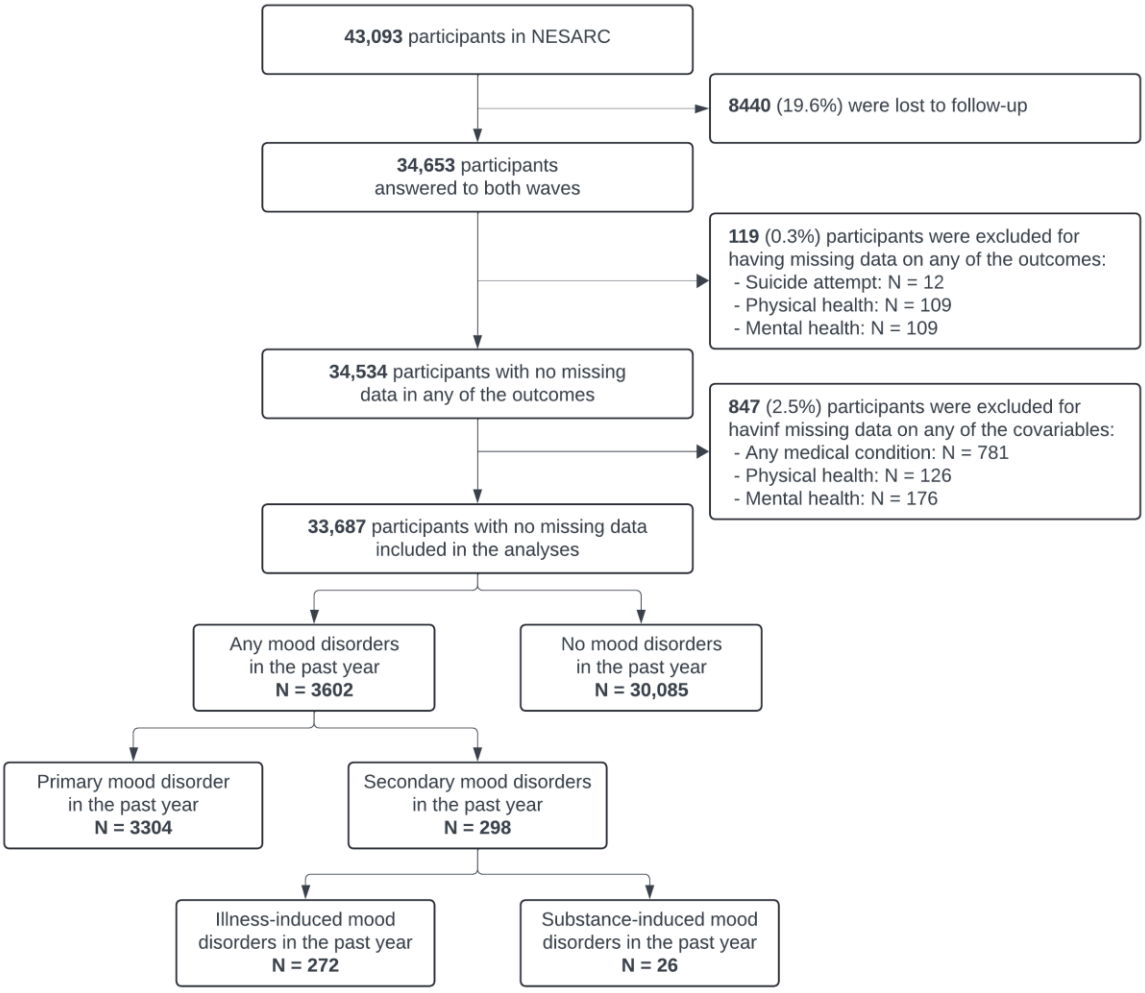
6. Goodwin RD, Lipsitz JD, Keyes K, Galea S, Fyer AJ. Family history of alcohol use disorders among adults with panic disorder in the community. *J Psychiatr Res*. 2011;45(8):1123-1127. doi:10.1016/j.jpsychires.2011.01.017

7. Grant BF, Stinson FS, Hasin DS, Dawson DA, Chou SP, Anderson K. Immigration and Lifetime Prevalence of DSM-IV PsychiatricDisorders Among Mexican Americans and Non-Hispanic Whites in the United States: Results From the National Epidemiologic Survey on Alcohol and RelatedConditions. *Arch Gen Psychiatry*. 2004;61(12):1226. doi:10.1001/archpsyc.61.12.1226

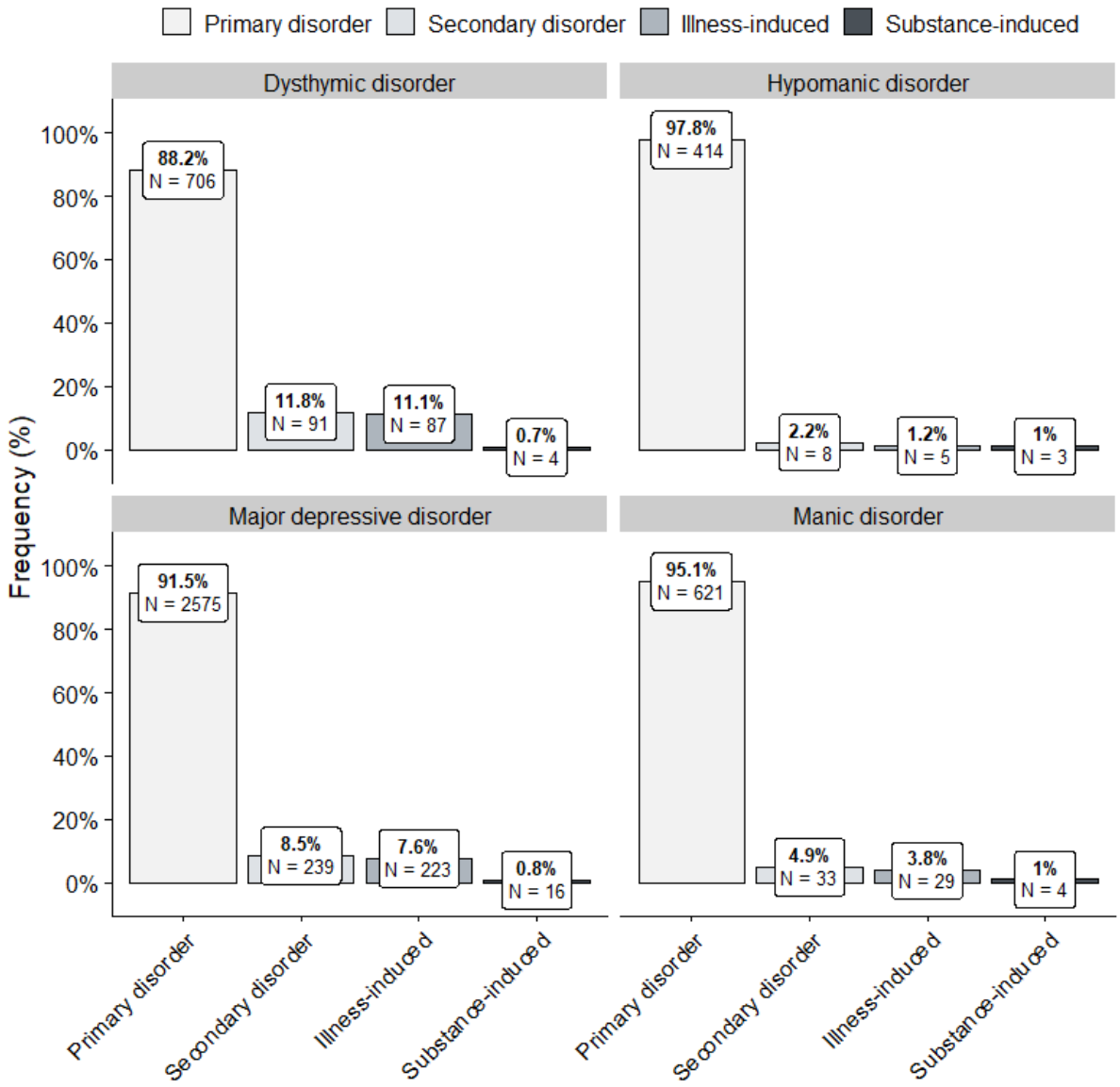
8. Udo T, Purcell K, Grilo CM. Perceived weight discrimination and chronic medical conditions in adults with overweight and obesity. *Int J Clin Pract*. 2016;70(12):1003-1011. doi:10.1111/ijcp.12902

9. Airagnes G, Sánchez-Rico M, Deguilhem A, et al. Nicotine dependence and incident psychiatric disorders: prospective evidence from US national study. *Mol Psychiatry*. Published online September 11, 2024. doi:10.1038/s41380-024-02748-6

Supplementary Figure 1. Flowchart.



Supplementary Figure 2. 12-month rates of types of mood disorder and their types.



Note. Weighted percentages were calculated based on the total number of patients on each subgroup of mood disorder (dysthymic disorder, N=796; hypomanic disorder, N=422; major depressive disorder, N = 2811; manic disorder, N=654).

Supplementary Table 1. Baseline characteristics by type of mood disorders.

	Any cause mood disorder N (%) [a] / Mean (SE) [a]	**Primary diagnosis** N (%) [a] / Mean (SE) [a]	**Secondary diagnosis** N (%) [a] / Mean (SE) [a]	**No mood disorder** N (%) [a] / Mean (SE) [a]	**Primary diagnosis vs. secondary diagnosis** SMD
Sociodemographic characteristics					
Sex					0.090
Male	1133 (37%)	1055 (38%)	78 (33%)	12987 (49%)	
Female	2469 (63%)	2249 (62%)	220 (67%)	17098 (51%)	
Age	39.38 (15.38)	38.72 (15.17)	46.68 (15.74)	45.69 (17.45)	**0.515**
Ethnicity					0.096
White	2171 (73%)	1998 (73%)	173 (73%)	17475 (71%)	
Black	609 (10%)	557 (10%)	52 (8.5%)	5753 (11%)	
American Indian/Alaska native	104 (3.7%)	95 (3.7%)	9 (3.1%)	455 (2.0%)	
Asian/Native Hawaiian/Pacific Islander	72 (3.2%)	63 (3.1%)	9 (3.6%)	856 (4.4%)	
Hispanic/Latino	646 (10%)	591 (10.0%)	55 (12%)	5546 (12%)	
Education level					**0.184**
Less than high school	210 (4.9%)	181 (4.6%)	29 (7.5%)	2066 (5.6%)	
High school graduate	1483 (41%)	1359 (40%)	124 (46%)	11451 (38%)	
Some college or higher	1909 (54%)	1764 (55%)	145 (47%)	16568 (57%)	
Marital Status					**0.250**
Married	1436 (49%)	1292 (48%)	144 (60%)	16584 (65%)	
Widowed/Divorced	1083 (22%)	1000 (22%)	83 (18%)	7203 (16%)	
Never married	1083 (29%)	1012 (30%)	71 (22%)	6298 (19%)	
Personal income					**0.151**
<12K	1625 (46%)	1470 (45%)	155 (52%)	9905 (32%)	
12K-30K	1127 (31%)	1043 (31%)	84 (29%)	9757 (31%)	
>30K	850 (24%)	791 (24%)	59 (19%)	10423 (36%)	
Past-year presence of comorbidities					
Any medical condition	2040 (55%)	1805 (53%)	235 (77%)	12685 (40%)	**0.523**

Any personality disorder	1797 (50%)	1668 (51%)	129 (40%)	4791 (15%)	**0.230**
Any substance use disorder	1285 (38%)	1187 (38%)	98 (35%)	4589 (16%)	0.055
Any substance use in the past year(outside disorder)	2773 (79%)	2573 (79%)	200 (70%)	20749 (71%)	**0.216**
Any anxiety disorder in the past year	1413 (40%)	1290 (40%)	123 (39%)	3063 (9.8%)	0.022
Quality of life					
Physical	45.41 (14.07)	46.38 (13.58)	34.66 (14.96)	51.63 (11.24)	**0.820**
Mental	42.31 (12.07)	42.61 (12.08)	38.91 (11.42)	53.44 (9.34)	**0.315**
Only for patients with any mood disorder					
Age at onset of first episode of the first mood disorder	27.89 (15.35)	27.09 (14.91)	36.73 (17.26)	43.40 (18.17)	**0.598**
Lifetime number of mood disorder types	8.73 (20.07)	8.81 (20.09)	7.80 (19.75)	0.47 (3.13)	0.051
Age at first help-seeking behavior for mood disorder	34.00 (15.20)	33.37 (14.93)	40.92 (16.42)	44.68 (17.69)	**0.481**
Past year history of MDD	2814 (78%)	2575 (78%)	239 (80%)	0 (0%)	0.041
Past year history or mania	654 (18%)	621 (19%)	33 (11%)	0 (0%)	**0.232**
Past year history of hypomania	422 (13%)	414 (13%)	8 (3.4%)	0 (0%)	**0.369**
Past year history of dysthymia	797 (21%)	706 (20%)	91 (30%)	0 (0%)	**0.223**

[a] Weighted percentage

Standarized mean differences (SMD) > 0.1 (in bold) are considered substantial.

Supplementary Table 2. Baseline characteristics by outcome assessed 3 years later.

	Recurrence of mood disorders N (%) [a] / Mean (SE) [a]	**Persistence of mood disorders** N (%) [a] / Mean (SE) [a]	**Suicide attempt since last interview** N (%) [a] / Mean (SE) [a]	**Physical health-related quality of life** Mean (SE) [a]	**Mental health-related quality of life** Mean (SE) [a]	**Mental-health help-seeking behavior** N (%) [a] / Mean (SE) [a]
Sociodemographic characteristics						
Sex						
Male	860 (33%)	445 (33%)	71 (33%)	50.97 (10%)	52.56 (8.9%)	615 (29%)
Female	2221 (67%)	1116 (67%)	167 (67%)	49.64 (11%)	50.47 (9.9%)	1,893 (71%)
Age	39.62 (15.10)	40.91 (15.51)	34.86 (11.86)	45.05 (17.4)	45.05 (17.4)	42.46 (15.08)
Ethnicity						
White	1853 (72%)	865 (69%)	119 (64%)	50.23 (10.7%)	51.58 (9.3%)	1,627 (78%)
Black	558 (11%)	286 (11%)	36 (8.5%)	49.08 (11%)	50.46 (10.3%)	365 (7.9%)
American Indian/Alaska native	72 (3.2%)	37 (3.0%)	10 (5.5%)	47.12 (12.7%)	50.92 (10.9%)	56 (2.8%)
Asian/Native Hawaiian/Pacific Islander	57 (2.7%)	41 (3.8%)	9 (4.3%)	52.66 (8.4%)	51.53 (9%)	33 (2.1%)
Hispanic/Latino	541 (10%)	332 (13%)	64 (18%)	51.38 (9.2%)	51.78 (9.8%)	427 (9.2%)
Education level						
Less than high school	172 (4.2%)	118 (5.7%)	21 (6.8%)	43.41 (13.2%)	50.29 (11.4%)	148 (4.3%)
High school graduate	1272 (41%)	677 (44%)	111 (42%)	48.7 (11.3%)	50.8 (10.2%)	977 (39%)
Some college or higher	1637 (55%)	766 (50%)	106 (51%)	52.01 (9.3%)	52.03 (8.7%)	1,383 (57%)
Marital Status						
Married	1332 (52%)	700 (54%)	90 (47%)	50.65 (10.2%)	52.02 (9.1%)	1,223 (60%)
Widowed/Divorced	858 (20%)	438 (20%)	80 (23%)	45.41 (12.7%)	50.13 (10.9%)	746 (21%)
Never married	891 (28%)	423 (26%)	68 (30%)	53.02 (8.5%)	50.81 (9.4%)	539 (19%)
Personal income						
<12K	1374 (44%)	747 (46%)	141 (58%)	48.08 (12.1%)	49.88 (10.7%)	1,125 (45%)
12K-30K	968 (31%)	499 (32%)	61 (27%)	50.01 (10.4%)	51.52 (9.5%)	742 (29%)
>30K	739 (25%)	315 (21%)	36 (15%)	52.62 (8.5%)	52.94 (7.9%)	641 (26%)

Past-year presence of comorbidities						
Any medical condition	1635 (51%)	865 (53%)	139 (56%)	45.95 (12.3%)	50.32 (10.6%)	1,453 (56%)
Any personality disorder	1470 (47%)	755 (48%)	136 (55%)	49.34 (11.3%)	47.77 (11.1%)	1,040 (41%)
Any substance use disorder	941 (33%)	462 (31%)	109 (47%)	50.14 (11%)	49.27 (10.6%)	734 (32%)
Any substance use in the past year(outside disorder)	2307 (78%)	1128 (74%)	190 (84%)	51.14 (10%)	51.41 (9.4%)	1,855 (77%)
Any anxiety disorder in the past year	1040 (34%)	538 (35%)	85 (39%)	48.4 (12%)	47.44 (11.1%)	864 (35%)
Quality of life						
Physical	46.86 (13.33)	45.15 (14.14)	42.23 (15.16)	51 (11.7)	51 (11.7)	45.50 (14.20)
Mental	45.15 (11.65)	43.59 (13.00)	40.78 (14.08)	52.31 (10.2)	52.31 (10.2)	44.54 (11.95)
Only for patients with any mood disorder						
Age at onset of first episode of the first mood disorder	29.97 (15.93)	32.35 (17.13)	26.66 (13.25)	41.83 (18.5)	41.83 (18.5)	33.60 (17.05)
Lifetime number of mood disorder types	6.26 (18.00)	6.78 (21.10)	11.21 (30.16)	1.31 (7.5)	1.31 (7.5)	5.62 (17.81)
Age at first help-seeking behavior for mood disorder	34.64 (15.27)	35.99 (16.06)	29.84 (11.75)	43.6 (17.8)	43.6 (17.8)	37.26 (15.94)
Past year history of MDD	1040 (33%)	591 (37%)	102 (45%)	47.54 (12.8%)	43.98 (12.1%)	846 (33%)
Past year history or mania	288 (9.6%)	176 (11%)	43 (19%)	47.45 (12.3%)	43.11 (12%)	207 (8.2%)
Past year history of hypomania	125 (3.9%)	42 (2.5%)	7 (3.6%)	51.6 (9.9%)	48.41 (10.8%)	54 (2.1%)
Past year history of dysthymia	332 (9.8%)	250 (15%)	61 (24%)	42.72 (14%)	39.67 (12.9%)	327 (13%)

[a] Weighted percentages and means.

Supplementary Table 3. Multivariable associations of baseline characteristics with the outcomes assessed 3 years later.

	Recurrence of mood disorders	Persistence of mood disorders	Suicide attempt since last interview	Physical health-related quality of life	Mental health-related quality of life	Mental-health help-seeking behavior
	AOR [95%CI] [a]	AOR [95%CI] [a]	AOR [95%CI] [a]	AOR [95%CI] [a]	AOR [95%CI] [a]	AOR [95%CI] [a]
Sociodemographic characteristics						
Sex						
Male	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Female	1.03 [1.03 - 1.04]***	1.02 [1.01 - 1.02]***	1.00 [1.00 - 1.00]	1.02 [1.00 - 1.05]	0.88 [0.86 - 0.91]***	1.04 [1.03 - 1.05]***
Age	1.08 [1.06 - 1.10]***	0.99 [0.99 - 0.99]***	1.00 [0.99 - 1.00]***	0.81 [0.8 - 0.82]***	1.07 [1.05 - 1.08]***	0.98 [0.98 - 0.99]***
Ethnicity						
White	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Black	0.99 [0.98 - 1.00]	0.99 [0.98 - 1.00]**	1.00 [0.99 - 1.00]*	0.97 [0.95 - 1.00]	0.98 [0.95 - 1.02]	0.97 [0.96 - 0.97]***
American Indian/Alaska native	1.00 [0.97 - 1.03]	1.00 [0.98 - 1.02]	1.01 [0.99 - 1.02]	0.91 [0.82 - 1.00]	1.12 [1.02 - 1.24]*	0.99 [0.96 - 1.01]
Asian/Native Hawaiian/Pacific Islander	0.98 [0.96 - 1.01]	1.00 [0.99 - 1.02]	1.00 [1.00 - 1.01]	1.09 [1.03 - 1.15]**	0.94 [0.86 - 1.01]	0.97 [0.96 - 0.99]**
Hispanic/Latino	0.99 [0.98 - 1.00]*	1.00 [1.00 - 1.01]	1.00 [1.00 - 1.01]	1.05 [1.01 - 1.09]**	1.05 [1.01 - 1.10]*	0.98 [0.97 - 0.99]***
Education level						
Less than high school	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High school graduate	1.01 [0.99 - 1.02]	1.01 [1.00 - 1.02]	1.00 [0.99 - 1.00]	1.09 [1.03 - 1.16]**	1.00 [0.93 - 1.07]	1.01 [1.00 - 1.03]*
Some college or higher	1.01 [0.99 - 1.02]	1.00 [0.99 - 1.02]	1.00 [1.00 - 1.01]	1.12 [1.05 - 1.20]**	1.02 [0.96 - 1.09]	1.02 [1.01 - 1.04]***
Marital Status						
Married	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Widowed/Divorced	1.01 [1.00 - 1.02]**	1.00 [1.00 - 1.01]	1.00 [1.00 - 1.01]*	0.87 [0.84 - 0.89]***	0.95 [0.92 - 0.98]**	1.01 [1.00 - 1.02]
Never married	1.02 [1.00 - 1.03]**	1.00 [1.00 - 1.01]	1.00 [1.00 - 1.00]	0.94 [0.92 - 0.97]***	0.97 [0.94 - 1.00]	0.98 [0.97 - 0.99]***
Personal income						
<12K	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
12K-30K	0.99 [0.99 - 1.00]	1.00 [0.99 - 1.01]	1.00 [0.99 - 1.00]*	1.09 [1.06 - 1.12]***	1.05 [1.02 - 1.08]**	0.99 [0.98 - 1.00]*
>30K	0.99 [0.98 - 1.00]*	0.99 [0.98 - 1.00]*	1.00 [0.99 - 1.00]*	1.19 [1.16 - 1.22]***	1.08 [1.04 - 1.12]***	0.99 [0.98 - 1.00]*
Past-year presence of comorbidities						

Any medical condition	1.01 [1.00 - 1.02]*	1.01 [1.00 - 1.01]	1.00 [1.00 - 1.00]	0.85 [0.83 - 0.87]***	0.99 [0.96 - 1.01]	1.01 [1.01 - 1.02]***
Any personality disorder	1.09 [1.07 - 1.10]***	1.06 [1.04 - 1.07]***	1.01 [1.00 - 1.01]***	0.97 [0.94 – 1.00]*	0.79 [0.76 - 0.81]***	1.06 [1.05 - 1.07]***
Any substance use disorder	1.02 [1.01 - 1.03]**	1.01 [1.00 - 1.02]	1.01 [1.00 - 1.01]**	0.98 [0.95 - 1.01]	0.93 [0.90 - 0.97]***	1.02 [1.01 - 1.03]***
Any substance use in the past year(outside disorder)	1.00 [1.00 - 1.01]	1.00 [0.99 - 1.00]	1.00 [1.00 - 1.00]	1.05 [1.02 - 1.08]**	0.98 [0.95 - 1.01]	1.00 [1.00 - 1.01]
Any anxiety disorder in the past year	1.07 [1.05 - 1.08]***	1.05 [1.04 - 1.06]***	1.01 [1.00 - 1.01]**	0.98 [0.95 - 1.01]	0.87 [0.84 - 0.90]***	1.08 [1.07 - 1.1]***
Quality of life						
Physical	0.99 [0.98 - 0.99]***	0.99 [0.98 - 0.99]***	1.00 [0.99 - 1.00]**	1.53 [1.51 - 1.56]***	1.19 [1.17 - 1.21]***	0.98 [0.98 - 0.98]***
Mental	0.97 [0.97 - 0.98]***	0.98 [0.97 - 0.98]***	1.00 [0.99 - 1.00]***	1.02 [1.01 - 1.03]**	1.29 [1.27 - 1.31]***	0.97 [0.96 - 0.97]***

[a] Adjusted for sex, age, ethnicity, education level, marital status, personal income, any medical condition, any personality disorder, any substance use in the past year, any anxiety disorder in the past year, physical and mental quality of life (df=17; all GVIF < 2.5).

* p<0.05; ** p<0.01; *** p<0.001

Abbreviations: AOR, adjusted odds ratio, CI, confidence interval

Supplementary Table 4. Psychiatric and mental health outcomes of participants with a 12-month diagnosis of primary mood disorders versus illness-induced and substance-related mood disorders.

	Any primary mood disorder at baseline	**Any illness-induced mood disorder at baseline (ref.)**	**Illness-induced mood disorders vs. primary mood disorders**	
	Events / N (%) [a]	Events / N (%) [a]	OR (95%CI) p-value	AOR (95%CI) p-value [b]
Recurrence of mood disorders [c]	1181 / 3304 (35.2%)	65 / 272 (22.6%)	0.54 (0.37; 0.77) 0.001*	0.52 (0.36; 0.76) 0.002*
Persistence of mood disorders	653 / 3304 (18.8%)	33 / 272 (13.1%)	0.65 (0.40; 1.05) 0.081	0.49 (0.30; 0.81) 0.009*
Suicide attempt	110 / 3304 (3.2%)	12 / 272 (5.4%)	1.73 (0.78; 3.88) 0.185	1.66 (0.69; 3.96) 0.262
Mental-health help-seeking behavior	881 / 3304 (25.7%)	97 / 272 (36.9%)	1.69 (1.23; 2.32) 0.002*	1.26 (0.89; 1.80) 0.202
	Mean (SE) [a]	Mean (SE) [a]	β (95%CI) p-value	Aβ (95%CI) p-value [π]
Physical health-related quality of life	48.55 (0.28)	36.38 (1.14)	-12.17 (-14.20; -10.14) <0.001*	-3.35 (-5.02; -1.68) <0.001*
Mental health-related quality of life	45.0 (0.27)	41.35 (1.01)	-3.63 (-5.42; -1.84) <0.001*	-0.16 (-1.95; 1.62) 0.859
	Any primary mood disorder at baseline	**Any substance-related mood disorder at baseline (ref.)**	**Substance-related mood disorders vs. primary mood disorders**	
	Events / N (%) [a]	Events / N (%) [a]	OR (95%CI) p-value	AOR (95%CI) p-value [b]
Recurrence of mood disorders [c]	1181 / 3304 (35.2%)	6 / 26 (13.9%)	0.30 (0.10; 0.84) 0.026*	NA
Persistence of mood disorders	653 / 3304 (18.8%)	4 / 26 (6.8%)	NA	NA
Suicide attempt	110 / 3304 (3.2%)	0 / 26 (0.0%)	NA	NA
Mental-health help-seeking behavior	881 / 3304 (25.7%)	3 / 26 (6.9%)	NA	NA
	Mean (SE) [a]	Mean (SE) [a]	β (95%CI) p-value	Aβ (95%CI) p-value [π]
Physical health-related quality of life	48.55 (0.28)	53.40 (1.63)	4.85 (2.01; 7.70) 0.001*	NA
Mental health-related quality of life	45.0 (0.27)	48.33 (2.93)	3.35 (-1.62; 8.32) 0.192	NA

[a] Weighted percentages and means.

[b] Adjusted for sex, age, ethnicity, education level, marital status, personal income, any medical condition, any personality disorder, any substance use in the past year, any anxiety disorder in the past year, physical and mental quality of life, age at onset of the first episode of the first mood disorder, lifetime number of mood disorder types, age at first help-seeking behavior for mood disorder, and past-year history of MDD, mania, hypomania, and dysthymia (df=25; all GVIF < 2.5).
[c] Defined as the occurrence of any mood disorder during the follow-up (i.e., incidence or recurrence or chronicity)
* p-value is statistically significant ($p<0.05$).
Abbreviations: SE, standardized error; OR, odds ratio; CI, confidence interval; AOR, adjusted odds ratio, Aβ, adjusted β coefficient.

Supplementary Appendix 3. STROBE Statement - Checklist of items that should be included in reports of *cohort studies.*

	Item No	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	7
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	FigureS1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7
		(c) Summarise follow-up time (eg, average and total amount)	7

Outcome data	15*	Report numbers of outcome events or summary measures over time	7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.