

## **Supplementary Material**

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

Mood Disorders

**Authors:** Antoine Lathiere, MD; Pierre Lavaud, MD; Marina Sánchez-Rico, PhD;

Mark Olfson, MD, MPH; Katayoun Rezaei, MPH; Frédéric Limosin, MD, PhD; and

Nicolas Hoertel, MD, MPH, PhD

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#### **DISCLAIMER**

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# 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. <sup>1-4</sup> 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 <sup>5</sup> (**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.<sup>3,6,7</sup>

#### **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 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.<sup>8</sup>

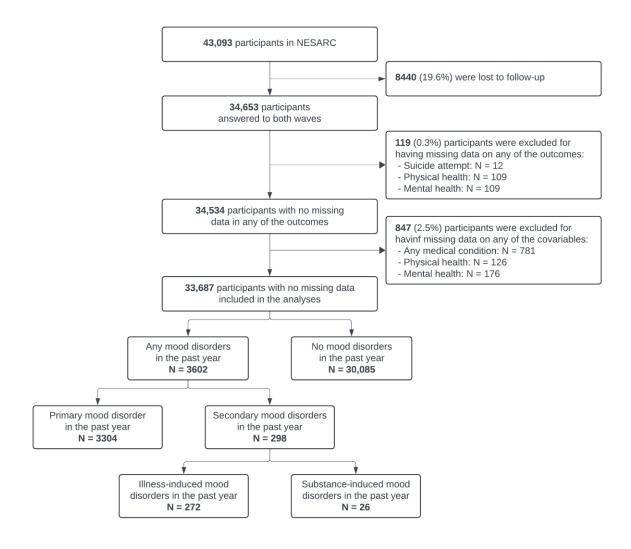
All psychiatric diagnoses, including drug use disorders (related to alcohol, nicotine, cannabis, amphetamines, hallucinogens, cocaine, heroin, opioids, sedatives, tranquilizers, and inhalants), anxiety disorders (panic disorder, social phobia, specific phobia, generalized anxiety disorder) and personality disorders (antisocial, avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic), were made according to DSM-IV criteria. 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).

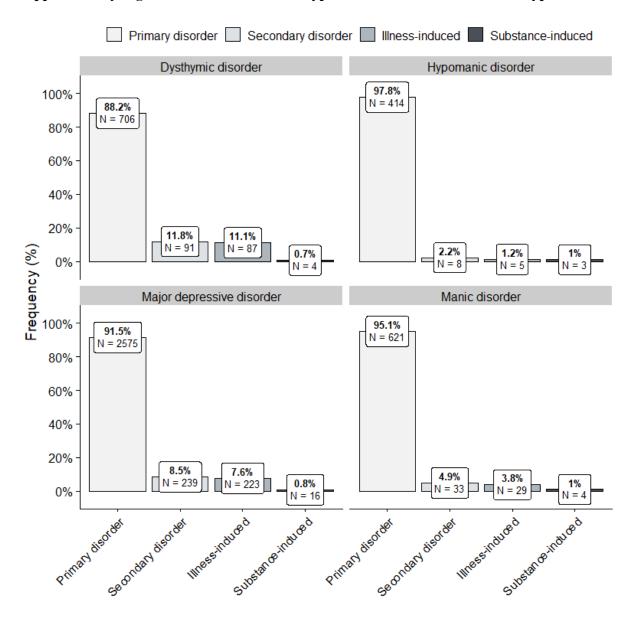
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#### Supplementary Figure 1. Flowchart.



### 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	Primary diagnosis	Secondary diagnosis	No mood disorder	Primary diagnosis vs. secondary diagnosis	
	N (%) <sup>a</sup> /	N (%) <sup>a</sup> /	N (%) <sup>a</sup> /	N (%) <sup>a</sup> /	SMD	
	Mean (SE) <sup>a</sup>	Mean (SE) <sup>a</sup>	Mean (SE) <sup>a</sup>	Mean (SE) <sup>a</sup>	אואוט	
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

<sup>&</sup>lt;sup>a</sup> 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	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
	N (%) <sup>a</sup> / Mean (SE) <sup>a</sup>	N (%) <sup>a</sup> / Mean (SE) <sup>a</sup>	N (%) <sup>a</sup> / Mean (SE) <sup>a</sup>	Mean (SE) <sup>a</sup>	Mean (SE) <sup>a</sup>	N (%) <sup>a</sup> / Mean (SE) <sup>a</sup>
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%)

<sup>&</sup>lt;sup>a</sup> 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] <sup>a</sup>	AOR [95%CI] <sup>a</sup>	AOR [95%CI] <sup>a</sup>	AOR [95%CI] <sup>a</sup>	AOR [95%CI] <sup>a</sup>	AOR [95%CI] <sup>a</sup>
Sociodemographic characteristics						
Sex						
Male	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
emale	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]***
∖ge	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]***
thnicity						
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 ndian/Alaska native Asian/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]
lawaiian/Pacific slander	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]**
lispanic/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]***
ducation level						
ess than high school	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
ligh 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]*
ome college or igher	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.
Vidowed/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]
lever 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]***
ersonal income						
12K	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
.2K-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						

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]***

<sup>&</sup>lt;sup>a</sup> 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 (%) <sup>a</sup>	OR (95%CI) p-value	AOR (95%CI) p-value <sup>b</sup>
Recurrence of mood disorders <sup>c</sup>	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) <sup>a</sup>	Mean (SE) <sup>a</sup>	β (95%CI) p-value	Aβ (95%CI) p-value $^{\pi}$
Physical health-related quality of life Mental 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*
	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 disord	
	Events / N (%) a	Events / N (%) <sup>a</sup>	OR (95%CI) p-value	AOR (95%CI) p-value b
Recurrence of mood disorders <sup>c</sup>	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) <sup>a</sup>	Mean (SE) <sup>a</sup>	β (95%CI) p-value	Aβ (95%CI) p-value $^{\pi}$
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

<sup>&</sup>lt;sup>a</sup> Weighted percentages and means.

Abbreviations: SE, standardized error; OR, odds ratio; CI, confidence interval; AOR, adjusted odds ratio, Aβ, adjusted β coefficient.

<sup>&</sup>lt;sup>b</sup> 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).

<sup>&</sup>lt;sup>c</sup> Defined as the occurrence of any mood disorder during the follow-up (i.e., incidence or recurrence or chronicity)

<sup>\*</sup> p-value is statistically significant (p<0.05).

## 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
Title and 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/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement).	4-5
measurement		Describe comparability of assessment methods if there is more than one group	
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
		(a) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	-
Statistical methods	12	(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			
	1.01	(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
Participants	13*	(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	FigureS1
	4.47	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
Descriptive data	14*	(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
Main results	16	(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			<u> </u>
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

<sup>\*</sup>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.