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The Epidemiology of Chronic and Non-Chronic Major Depressive Disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions

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Abstract

Background—Burden related to major depressive disorder (MDD) derives mostly from long term occurrence of symptoms. This study aims to examine the prevalence, sociodemographic correlates, patterns of 12-month and lifetime psychiatric co-morbidity, lifetime risk factors, psychosocial functioning, and mental health service utilization of CMDD compared to non-chronic major depressive disorder (NC-MDD).

Methods—Face-to-face interviews were conducted in the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (n = 43,093).

Results—The 12-month and lifetime prevalence of CMDD within the population meeting criteria for major depressive disorder (MDD) was 26.5% and 24.0% respectively. Individuals reporting a chronic course of MDD were socioeconomically and educationally disadvantaged, tended to be older, report loss of spouse or history of divorce, live in rural areas, have public assistance, low self-esteem, worse overall health and more likely to report comorbidities, most importantly dysthymia, generalized anxiety disorder, avoidant and dependant personality disorder. Individuals with chronic MDD were more likely to report familial but not childhood onset risk factors for MDD. Those suffering CMDD were more likely to seek and receive mental health care than other forms of MDD, although took longer to start treatment.

Conclusion—Chronic course of MDD is related to still worse socioeconomic conditions, educational achievement, more co-morbidities and family risk factors, although other courses of MDD carried greater risk of unmet treatment.

INTRODUCTION

Longitudinal studies have consistently shown major depressive disorder (MDD) as primarily a chronic disorder [1, 2], with high rates of recurrence [3–7] and persistent depressive symptoms [5–7]. About 20% of individuals with MDD suffer from chronic major depressive disorder (CMDD) [8–13], which is defined as meeting criteria for major depressive episode continually for at least 2 years [14]. MDD is one of the most important causes of disease burden in the general population [15, 16], and it is most through long term duration of

symptoms rather than through severity of symptoms [17, 18], so CMDD contributes over and above other clinical presentations of MDD to its global burden. There is a need to understand CMDD better.

Most knowledge about CMDD derives from clinical samples. Compared to non-chronic major depressive disorder (NC-MDD), CMDD has been associated in clinical samples with older age [9, 10], lower socioeconomic status (SES), [9, 11] higher rates of comorbid anxiety disorders [9, 11], worse somatic and psychological well-being [9, 10], longer delays to first treatment-seeking for MDD [8, 12, 19, 20] and greater number of stressful life events [10, 11, 21–25]. Despite these data, important questions remain regarding our knowledge of CMDD. For example, although community samples have confirmed that comorbid anxiety disorders increase the risk of CMDD [9, 11], little is known about the role of other Axis I or II disorders. Similarly, although stressful life events [10, 11, 21–25], lack of social support [10, 11] and family history of mood disorders [8, 26] have been associated with CMDD, no study has systematically examined the epidemiology of CMDD from the perspective of an integrated etiological model for MDD [27, 28] including the effects of a set of risk factors occurring throughout development. Furthermore, no national study has investigated patterns of mental health care use associated with CMDD.

The present study was designed to address this gap in knowledge by drawing on a large, nationally representative epidemiological study, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), which included assessments of a broad range of Axis I and II DSM-IV psychiatric disorders with good to excellent psychometric properties. Specifically, we sought to: 1) examine the prevalence and sociodemographic correlates of CMDD and; 2) compare patterns of psychiatric comorbidity for 12-month and lifetime CMDD and NC-MDD; 3) compare overall health ratings, family history of various psychiatric disorders, and risk factors for lifetime CMDD and NC-MDD; and 4) estimate their rates of mental health service utilization.

METHODS

Sample

The 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative sample of the adult population of the United States conducted by the US Census Bureau under the direction of the National Institute of Alcoholism and Alcohol Abuse (NIAAA), is described in detail elsewhere [29, 30]. The NESARC target population was the civilian, non-institutionalized population, ages 18 years and older, residing in the 50 states and the District of Columbia. The final sample included 43,093 respondents drawn from individual households and group-quarters, such as dormitories and half-way houses. African Americans, Latinos, and young adults (aged 18 to 24 years) were oversampled, with data then adjusted to account for oversampling and respondent and household non-response. The overall survey response rate was 81%. The weighted data were adjusted, using the 2000 Decennial Census, to be representative of the US civilian population on various sociodemographic variables.

Diagnostic assessment

Sociodemographic measures included age, sex, race-ethnicity, nativity, marital status, place of residence, and geographical region. Socioeconomic measures included level of education, family and personal income, and insurance type.

All diagnoses were made according to DSM-IV criteria using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV), a valid, reliable, fully structured diagnostic interview designed for use by non-clinician professional

interviewers [31]. Most Axis I diagnoses included in the AUDADIS-IV fall into three groups: 1) substance use disorders (including alcohol abuse and dependence, drug abuse and dependence, and nicotine dependence); 2) mood disorders (major depressive disorder, dysthymic disorder, and bipolar disorder); and 3) anxiety disorders (panic disorder, social anxiety disorder, specific phobia, and generalized anxiety disorder [GAD]). Selected personality disorders (PD) (avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic, and antisocial) and conduct disorder were assessed on a lifetime basis only.

Following the DSM-IV, all these disorders were considered “primary” disorders since they excluded mental disorders due to substance use or medical conditions. The diagnosis of MDD also ruled out bereavement. The test-test reliability and validity of AUDADIS-IV measures of DSM-IV disorders has been reported in detail elsewhere [32, 33]. Test-retest reliability was good for MDD ($\kappa=0.65-0.73$) and reliability ($\kappa>0.74$) and validity were good to excellent for substance use disorders [32, 34–41]. Reliability was fair to excellent for other mood and anxiety disorders ($\kappa=0.40-0.60$) and personality disorders ($\kappa=0.40-0.67$). Clinical reappraisal showed that AUDADIS-IV measures and psychiatrists’ diagnoses agreed well for current MDD ($\kappa=0.49-0.67$) and lifetime MDD ($\kappa=0.64-0.68$) [32]. Due to concerns about the validity of psychotic diagnoses in general population surveys as well as the length of the interview, possible psychotic disorders were elicited by asking respondents if a doctor or other health professional had ever told them that they had schizophrenia or a psychotic disorder.

CMDD was diagnosed when DSM-IV criteria for MDD were reported as having been continually present for at least two years. Lifetime DSM-IV CMDD was thus defined as having had at least one MDE with these characteristics over the life course without a history of manic, mixed, or hypomanic episodes (i.e., excluding bipolar I and II disorders). This was assessed in the major depression module among respondents meeting MDD criteria who stated that their most recent or longest MDE lasted at least 2 consecutive years. Respondents with lifetime CMDD whose onset of their most recent episode occurred at least two years before the time of the interview, and who reported remaining symptomatic at the time of the assessment, were classified as having 12-month (current) CMDD. All other individuals with MDD were classified as having NC-MDD.

We also included variables measuring any substance use, any alcohol use, non-prescription drug use, any tobacco use in the last 12-months and on a lifetime basis, and use of alcohol and non-prescription medications to relieve depressive symptoms. The reliability of the alcohol consumption and drug use measures has a documented range from good to excellent [42].

The study further included variables considered depressive risk factors that have been extensively studied in MDD. For consistency with previous research [27, 28, 43–45], we queried about lifetime risk factors for depression based on the developmental model of MDD proposed by Kendler and colleagues [27, 28]. Following this model, we organized the factors into three sets: 1) familial influences, including family history of depression, substance and alcohol use disorders, and antisocial personality disorder; 2) risk factors with childhood onset including parental loss before age 18, vulnerable family environment (defined as history of separation from a biological parent before age 18), early onset of anxiety disorder (onset before age 18), and conduct disorder; and 3) risk factors manifest into adulthood, including history of separation or divorce, low self-esteem, and number of stressful life events, measured with 12 items from the Social Readjustment Rating Scale (e.g., fired from a job, forced to move).

Psychosocial functioning in the past 12 months was assessed using subscales from the Short Form-12v2 (SF-12), a reliable and valid measure of disability used in population surveys: physical component summary, social functioning scale, role emotional scale, and mental health scale [46]. Each SF-12 disability scale yields a norm-based score with a mean of 50 and standardized range of 0–100. Higher scores indicate less disability. Lifetime assessments included mean age at onset, mean number of MDEs, and median duration of longest depressive episode (either CMDD or NC-MDD).

Mental health treatment

To estimate rates of mental health service utilization, respondents with NC-MDD or CMDD were classified as receiving treatment if they sought help from a counselor, therapist, doctor, or psychologist; from an emergency room; were hospitalized for psychiatric reasons at least one night; or were prescribed medications. Mean age at first mental health service contact was also assessed.

Statistical analyses

The statistical analyses compared two groups, CMDD and NC-MDD. All means, percentages, and odds ratios (ORs) were based on weighted data. Variables with $p < 0.2$ in the univariate analyses were entered into a binary logistic regression to identify independent predictors of CMDD. Because the combined standard error of two means (or percents) is always equal to or less than the sum of the standard errors of those two means, we conservatively consider two non-overlapping confidence intervals (CIs) to differ significantly from one another [47, 48]. We consider significant ORs those whose CI does not include 1. All standard errors and 95% confidence intervals were estimated using SUDAAN [49] to adjust for design characteristics of the survey.

RESULTS

Prevalence and sociodemographic correlates

The 12-month and lifetime prevalence of CMDD in the general population were 1.55% (95% CI: 1.41%-1.71%) and 3.18% (95% CI: 2.96%-3.41%), respectively. For NC-MDD, the 12-month and lifetime prevalence in the general population were 3.23% (95% CI: 3.00%-3.48%) and 10.05% (95% CI: 9.56%-10.56%), respectively. When considering only individuals with current and lifetime MDD, the prevalence of CMDD was 26.45% (95% CI: 24.30%-28.72%) and 24.04% (95% CI: 22.69%-25.44%) respectively.

Compared to NC-MDD, individuals with CMDD tended to be older, less educated, with lower individual and family income. Compared to married individuals, those who were widowed, separated or divorced had increased odds of CMDD, whereas those never married individuals had decreased odds of CMDD. Living in a rural area, and having public insurance compared to having private or no insurance, also increased the risk of CMDD. There were no differences in gender, race/ethnicity, nativity, or region of the country between individuals with CMDD and NC-MDD (Table 1).

Risk factors

Significantly higher odds were found for family history of depression, family history of alcohol and drug use disorders, and behavioral problems in a first degree relative. By contrast, none of the risk factors of childhood onset was significantly associated to CMDD. Among risk factors occurring in adulthood, only history of divorce or loss of spouse and having low self-esteem were significantly associated with higher odds of CMDD (Table 2).

Lifetime and 12-month comorbidity

Approximately nine of ten of respondents with CMDD and seven of ten respondents with NC-CMDD had an additional lifetime Axis I psychiatric disorder. Current Axis I disorders were present in about seven of ten CMDD respondents and six of ten NC-MDD respondents. Lifetime odds for Axis I disorders were three times higher for CMDD respondents compared with the NC-MDD group, although the association was smaller ($OR=1.34$) when considering 12-month Axis I comorbidity (Tables 3 and 4).

Not surprisingly, the odds of dysthymic disorder were more than twenty-fold for lifetime, and seven-fold for current CMDD. The odds for all lifetime anxiety disorders, except specific phobia, were higher in the CMDD group. However, among 12-month anxiety disorders, only GAD was significantly more common among individuals with CMDD than among those with NC-MDD. Lifetime psychotic disorder was also more common in individuals with lifetime and current CMDD group than in the NC-MDD group. Among substance use disorders, only lifetime drug dependence and nicotine dependence were significantly more likely in the CMDD group.

Personality disorders were more likely to be present among individuals with CMDD (Table 3). Avoidant and dependent personality disorders were more than twice as likely in the CMDD group, and paranoid, schizoid and antisocial PD were also more likely to be present.

Individuals with CMDD had higher prevalence of lifetime tobacco use but lower lifetime and 12-month alcohol use. However, lifetime use of alcohol and non-prescribed substances to relieve symptoms was more common among CMDD respondents.

Past 12-month psychosocial functioning, lifetime course and mental health treatment

Individuals meeting 12-month criteria for CMDD had significantly lower scores on the physical component summary and role emotional SF-12 subscales than those with NC-MDD, indicating greater physical and emotional disability. Their odds of rating overall health as good or excellent were significantly lower (Tables 3 and 4).

Compared to respondents with NC-MDD, those with CMDD had significantly higher number of major depressive episodes, longer delays to first treatment, and greater likelihood of having received all treatment modalities (Table 5).

Logistic regression model

The logistic regression model identified as independent predictors the following variables: age (compared with individuals between 18 and 29 years old, those between 30 and 44 had $OR=1.45$, 95% $CI=1.09-1.92$; between 45 and 64 $OR=2.13$, 95% $CI=1.61-2.86$; and older than 65 $OR=4.00$, 95% $CI=2.70-5.88$), comorbid dysthymia ($OR=20.00$, 95% $CI=16.66-25.00$) and comorbid antisocial personality disorder ($OR=1.61$, 95% $CI=1.05-2.50$), use of pharmacological treatment ($OR=1.43$, 95% $CI=1.19-1.72$) and overall health ($OR=0.62$, 95% $CI=0.41-0.80$). This model had 90.96% ($SE=0.24$) accuracy of correctly identifying individuals with CMDD.

DISCUSSION

In a large, nationally representative sample of US adults, one quarter of all individuals meeting DSM-IV criteria for MDD met criteria for CMDD in the last 12 months and lifetime respectively. Compared with individuals with NC-MDD, individuals with CMDD had lower SES, tended to be older, with history of divorce or loss of spouse, had higher prevalence of family history and adulthood onset risk factors for MDD, greater Axis I and II

comorbidity, and greater reported physical and emotional disability. They also had higher lifetime rates of treatment-seeking, but longer delays before first treatment contact for MDD. After adjusting for multiple observations, older age, comorbid dysthymia and antisocial personality disorder, worse overall health and use of pharmacological treatment for depression were associated with CMDD.

Our study confirms that CMDD accounts for approximately one every four cases of MDD. Evidence on the prevalence of CMDD is quite consistent across studies, ranging from 21.2% to 29.0% in previous clinical samples [9–12] and from 20.0% to 23.0% in community samples [8, 13].

In accord with most [9, 11, 50, 51] but not all previous studies [8], we found an inverse relationship between risk of CMDD and several indicators of socioeconomic status, including educational attainment and family income. Several non-exclusive underlying mechanisms could explain this finding. Low SES may act as a chronic stressor and constitute a risk factor for a chronic course of MDD, as suggested by social causation theories [52]. Alternatively, healthy individuals may tend to maintain higher SES level along generations whereas depressed individuals tend to drift down from high SES or fail to rise from low SES, as social selection theories have suggested [52]. Our findings of more highly prevalent family history of depression among individuals with CMDD than NC-MDD are consistent with these theories. A third possibility is that chronic depressive symptoms may impede educational and social achievements from young age at a subsyndromal level even before they become clinical evident. Subsyndromal depressive symptoms are frequently prodromal and residual to major depressive episodes [6], and predict worse outcome of MDD, including longer duration, in both clinical [5] and community studies [6, 53].

Consistent with prior findings in clinical [11] and community samples [8, 51], our study found that individuals who never married carried a lower risk for CMDD, whereas those who once married but had separated, divorced or widowed had higher risk. By contrast, low social support outside the immediate family was not associated with CMDD. Losing a spouse appears to have much greater negative impact on chronicity than lack of a romantic partner or loss of less meaningful relationships. Alternatively, chronic depressive symptoms may have a more disruptive effect on marital relationships than on other relationships that are less close or involve less frequent contact [54].

Whereas all of the family history risk factors included in our analysis were significantly associated with developing CMDD, none of the childhood onset risk factors was significantly associated. It appears that childhood onset factors increase the risk of having MDD, whereas genetic factors [11, 21, 25, 26] and recent environmental stressors may have additional influence on the chronicity of the disorder.

Individuals with CMDD showed greater lifetime and 12 month Axis I and II comorbidity, consistent with prior clinical [9–11] and community studies [8, 55]. MDD and anxiety disorders may constitute alternative or overlapping expressions of a single underlying disorder or liability dimension [2], as epidemiological and twin studies suggest [56–60]. Chronicity of MDD may indicate a more severe form of this underlying disorder, and subsequent higher likelihood of more diverse expression, including comorbid disorders. Consistent with this interpretation, CMDD is generally associated with increased treatment resistance [61], greater interference with daily activities [62], greater suicidality [63], higher hospitalization rates [62, 64], and higher prevalence of risk factors [8, 22, 26]. Dependent and avoidant personality disorders were also related to CMDD. These findings accord with previous reports of increased persistence of depressive symptoms in patients scoring high in neuroticism [65–67], and with the fading of these Axis II disorders with sustained recovery

from MDD [68]. Neuroticism may be a risk factor for persistence of depressive symptoms [65] or represent an epiphenomenon of chronic depression [66].

Our study found no significant differences for age of onset, yet individuals with CMDD had longer delays in first treatment contact. These findings accord with prior research documenting the association between later onset of treatment and persistence of depressive symptoms [8, 12, 19, 20].

Delayed treatment onset among individuals with CMDD may be due to initial attributions of symptoms to personality characteristics that cannot be changed [69] and contribute to its chronicity [70]. The fact that the CMDD group accounted for a large proportion of individuals older than 65 may contribute to this treatment delay, since older cohorts showed delays in treatment seeking behavior for MDD compared to younger cohorts [71]. Recent changes related to destigmatization [72] or facilitation of treatment opportunities [73] may account for earlier treatment seeking behavior in younger generations compared with elderly, that might be more reluctant to start treatment. Other reports have suggested that longer duration of untreated illness could account for a worse outcome of MDD [74]. The fact that individuals with CMDD were more likely to seek treatment and to use more mental health services may be related to its greater personal burden, or to a more accurate interpretation of their symptoms that may eventually lead them to seek treatment [45, 75, 76], as well as to increased use of services derived from treatment resistance [77]. Symptoms of comorbid disorders may also serve as a port of entry for the treatment of their CMDD. Nevertheless, over a quarter of individuals with MDD and almost half of those with NC-MDD had never sought treatment. Despite progress in the treatment of MDD [78], CMDD remains undertreated, and treatment adequacy has not significantly increased over the past decade [79], suggesting an area with great opportunities for quality improvement.

Our study has several limitations. First, information was based on interviewed self-report, which raises the possibility of misclassification, recall bias, and increased error variance. Second, because the NESARC sample only included civilian households and group quarter populations 18 years and older, information was unavailable on adolescents and incarcerated individuals. Third, the cross-sectional design precludes identifying directionality between the variables associated to the CMDD and NC-MDD groups.

Despite these limitations, the NESARC constitutes the only nationally representative survey to date to compare in detail the characteristics of CMDD and NC-MDD. Our findings document the greater severity associated with the chronic course of MDD, specially in terms of socioeconomic difficulties and comorbidity burden, and identify some of the risk factors and associated features with it. These findings may offer clues for new directions to address the tremendous burden imposed by MDD, and how to help those more severely affected by it.

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Table 1

Sociodemographic and socioeconomic characteristics for lifetime NC-MDD and CMDD

	NC-MDD <i>a</i> N=4256		CMDD N=1439		CMDD <i>a</i> vs NC-MDD				
	%	95%CI	%	95%CI	OR	95%CI			
Sex									
Male	33.35	31.59	35.17	30.47	27.57	33.53	0.88	0.74	1.03
Female <i>a</i>	66.65	64.83	68.41	69.53	66.47	72.43	1.00	1.00	1.00
Race/Ethnicity									
White <i>a</i>	77.94	75.18	80.47	78.72	75.34	81.74	1.00	1.00	1.00
Black	7.39	6.27	8.68	7.76	6.29	9.53	1.04	0.81	1.33
Native Americans	2.81	2.14	3.68	3.91	2.87	5.30	1.38	0.90	2.10
Asian	3.06	2.21	4.21	2.37	1.36	4.08	0.77	0.43	1.36
Hispanic	8.80	7.08	10.89	7.25	5.34	9.77	0.82	0.64	1.05
Nativity									
US-born <i>a</i>	90.89	88.76	92.66	91.57	88.70	93.77	1.00	1.00	1.00
Foreign-born	9.11	7.34	11.24	8.43	6.23	11.30	0.92	0.71	1.19
Age									
18–29 <i>a</i>	22.53	20.87	24.27	11.21	9.31	13.45	1.00	1.00	1.00
30–44	33.83	32.01	35.70	29.38	26.33	32.63	1.74	1.34	2.26
45–64	35.28	33.35	37.26	43.98	40.79	47.22	2.50	1.97	3.17
>65	8.37	7.42	9.42	15.42	13.35	17.75	3.70	2.73	5.02
Education									
< High school	12.31	11.05	13.70	16.82	14.41	19.54	1.55	1.23	1.95
High school	26.21	24.42	28.09	29.06	26.06	32.25	1.26	1.06	1.49
College <i>a</i>	61.48	59.39	63.52	54.13	50.64	57.57	1.00	1.00	1.00
Individual Income									
0–19,000 <i>a</i>	48.67	46.42	50.92	54.60	50.95	58.21	1.00	1.00	1.00
20–34,000	23.16	21.41	24.99	20.72	18.05	23.67	0.80	0.65	0.98
35–69,000	21.00	19.20	22.93	18.52	16.01	21.33	0.79	0.64	0.96
>70,000	7.17	6.03	8.52	6.16	4.65	8.12	0.77	0.56	1.05

	NC-MDD ^a N=4256		CMDD N=1439		CMDD ^a vs NC-MDD				
	%	95%CI	%	95%CI	OR	95%CI			
Family Income									
0–19,000 ^a	21.48	19.83	23.22	28.58	25.60	31.76	1.00	1.00	1.00
20–34,000	20.37	18.80	22.03	21.83	19.37	24.50	0.81	0.66	0.99
35–69,000	32.80	31.03	34.62	29.36	26.09	32.87	0.67	0.54	0.83
>70,000	25.36	23.36	27.47	20.22	17.33	23.47	0.60	0.48	0.74
Marital Status									
Married ^a	57.15	55.11	59.17	53.31	50.17	56.44	1.00	1.00	1.00
Widowed/separated/divorced	22.40	21.05	23.82	32.43	29.62	35.37	1.55	1.33	1.81
Never married	20.44	18.77	22.23	14.26	12.31	16.46	0.75	0.61	0.91
Urbanicity									
Urban ^a	79.81	76.31	82.91	75.80	71.25	79.84	1.00	1.00	1.00
Rural	20.19	17.09	23.69	24.20	20.16	28.75	1.26	1.07	1.49
Region									
Northeast	18.10	12.87	24.83	19.13	13.57	26.27	1.01	0.83	1.23
Midwest	25.22	19.61	31.79	22.83	17.40	29.36	0.87	0.70	1.07
South	33.22	27.49	39.50	33.52	27.69	39.89	0.97	0.80	1.17
West ^a	23.46	17.56	30.62	24.52	18.29	32.03	1.00	1.00	1.00
Insurance									
Private ^a	71.73	69.55	73.82	63.23	59.80	66.54	1.00	1.00	1.00
Public	10.59	9.40	11.90	18.72	16.17	21.57	2.01	1.61	2.49
No insurance	17.68	16.01	19.49	18.04	15.62	20.74	1.16	0.93	1.45

^aReference group.

Table 2

Risk factors for MDD in lifetime CMDD and NC-CMDD

	NC-MDD ^a N=4256		CMDD N=1439		CMDD ^a vs NC-MDD	
	%	95%CI	%	95%CI	OR	95%CI
Family History Risk Factors						
Family history of depression (first grade relative)	61.45	59.47	63.40	65.40	62.05	68.60
Family history of alcohol problems (first grade relative)	47.05	45.15	48.96	54.54	51.34	57.69
Family history of drug problems (first grade relative)	26.81	25.00	28.69	30.89	27.90	34.05
Family history of behavioral problems (first grade relative)	30.40	28.47	32.39	35.26	32.26	38.39
Childhood Risk Factors						
Parental loss	9.36	8.43	10.38	10.11	8.43	12.09
Vulnerable family environment ^b	32.48	30.72	34.30	33.51	30.45	36.71
Early onset of anxiety disorder	50.21	48.18	52.24	49.63	46.04	53.23
Conduct disorder before 15y	1.89	1.37	2.60	1.05	0.59	1.84
Adult Risk Factors						
Social support outside the family	48.61	46.61	50.61	48.87	45.53	52.22
History of divorce/loss spouse	38.92	36.85	41.04	50.45	47.21	53.68
Low emotional reactivity ^d	20.86	19.31	22.50	21.51	18.97	24.29
Low self-esteem ^e	20.28	18.74	21.90	27.27	24.29	30.47

^aReference group.^bHistory of separation from a biological parent.^cAssessed by responding positively to the question: "Are there very few people that you're really close to outside of your immediate family?"^dAssessed by responding positively to the question: "Do you rarely show much emotion?"^eAssessed by responding positively to the at least one of the questions: "Do you believe that you're not as good, as smart, or as attractive as most other people?" or "Are you usually quiet or do you have very little to say when you meet new people because you believe they are better than you are?"

Table 3

Lifetime psychiatric comorbidity, substance use, and overall health in individuals with lifetime NC-MDD and CMDD

	NC-MDD ^a N=4256			CMDD N=1439			CMDD ^a vs NC-MDD		
	%	95%CI	%	95%CI	OR	95%CI			
Any psychiatric disorder ^b	75.89	74.20	77.51	89.49	87.45	91.22	2.70	2.18	3.36
Any Axis I disorder ^b	71.31	69.32	73.21	88.16	86.06	89.98	3.00	2.42	3.71
Any substance use disorder	53.22	51.21	55.23	54.81	51.61	57.97	1.07	0.91	1.24
Alcohol use disorder	40.03	37.96	42.13	41.29	38.06	44.60	1.05	0.90	1.24
Alcohol abuse	19.47	17.98	21.05	19.00	16.36	21.95	0.97	0.80	1.18
Alcohol dependence	20.56	18.93	22.29	22.30	19.43	25.46	1.11	0.92	1.34
Drug use disorder	16.67	15.20	18.25	18.94	16.59	21.53	1.17	0.96	1.42
Drug abuse	11.96	10.65	13.41	11.12	9.08	13.54	0.92	0.70	1.21
Drug dependence	4.71	3.94	5.62	7.82	6.21	9.80	1.72	1.25	2.35
Nicotine dependence	29.07	27.22	30.99	32.94	29.92	36.10	1.20	1.02	1.41
Dysthymia	6.25	5.33	7.32	59.65	56.44	62.77	22.17	17.96	27.36
Any anxiety disorder	39.32	37.24	41.43	47.95	44.73	51.19	1.42	1.22	1.65
Panic disorder	13.50	12.19	14.92	17.59	15.23	20.23	1.37	1.12	1.67
Social anxiety disorder	11.51	10.31	12.84	16.93	14.54	19.63	1.57	1.27	1.94
Specific phobia	19.88	18.39	21.46	22.18	19.30	25.37	1.15	0.95	1.38
Generalized anxiety disorder	12.46	11.16	13.89	22.91	20.37	25.67	2.09	1.72	2.53
Conduct disorder	1.89	1.37	2.60	1.05	0.59	1.84	0.55	0.28	1.08
Pathological gambling	0.62	0.38	1.01	0.78	0.42	1.44	1.26	0.55	2.86
Any psychotic disorder	0.30	0.17	0.52	2.16	1.35	3.42	7.41	3.52	15.60
Any personality disorder	28.57	26.83	30.37	37.69	34.53	40.96	1.51	1.28	1.79
Avoidant	5.10	4.40	5.91	11.07	9.09	13.42	2.31	1.78	3.00
Dependent	0.92	0.62	1.35	2.10	1.38	3.20	2.32	1.34	4.02
Obsessive-Compulsive	16.04	14.60	17.58	17.53	14.86	20.57	1.11	0.90	1.38
Paranoid	9.20	8.18	10.32	12.40	10.40	14.73	1.40	1.10	1.77
Schizoid	6.52	5.50	7.71	10.39	8.42	12.74	1.66	1.22	2.27
Histrionic	3.38	2.68	4.25	4.34	3.08	6.08	1.30	0.89	1.89
Antisocial	5.52	4.72	6.45	8.84	7.21	10.80	1.66	1.26	2.18

	NC-MDD ^a N=4256		CMDD N=1439		CMDD ^a vs NC-MDD	
	%	95%CI	%	95%CI	OR	95%CI
Any substance use^c	92.44	91.25	93.48	91.78	89.81	93.40
Any tobacco use	53.24	51.08	55.39	59.03	55.60	62.38
Any alcohol use	90.04	88.70	91.23	87.14	84.57	89.34
Any drug use	34.54	32.45	36.69	37.53	34.39	40.78
Use of non-prescribed substances to relieve depressive symptoms						
Alcohol use	16.77	15.21	18.46	21.22	18.79	23.86
Use of non-prescribed medication	4.23	3.49	5.11	8.94	7.07	11.24
Overall health (good to excellent)	83.31	81.67	84.83	67.99	64.82	71.01
					0.43	0.36
						0.51

^aReference group.

^bAny psychiatric disorder and any Axis I disorder does not include either MDD or CMDD.

^cAny substance use includes any tobacco use, any alcohol use, and any drug use.

Table 4

Past 12-months psychiatric comorbidity, substance use and overall health in individuals with past 12-months NC-MDD and CMDD

	NC-MDD ^a N=1406		CMDD N=697		CMDD ^a vs NC-MDD	
	%	95%CI	%	95%CI	OR	95%CI
Any psychiatric disorder^b	59.82	56.32	63.21	66.59	61.83	71.03
Any Axis I disorder^b	35.82	32.74	39.03	32.31	27.84	37.11
Any substance use disorder	14.85	12.67	17.34	13.09	9.90	17.11
Alcohol use disorder	5.85	4.50	7.56	5.85	3.99	8.50
Alcohol abuse	9.00	7.18	11.24	7.24	4.75	10.89
Alcohol dependence	4.27	3.20	5.67	5.04	3.09	8.12
Drug use disorder	2.70	1.90	3.82	3.38	1.86	6.06
Drug abuse	1.79	1.15	2.78	3.68	1.97	6.78
Drug dependence	26.59	23.77	29.60	24.84	20.77	29.41
Nicotine dependence	5.90	4.37	7.93	30.77	26.55	35.33
Dysthymia	35.06	32.10	38.15	38.10	33.06	43.42
Any anxiety disorder	10.57	8.67	12.83	10.85	8.10	14.39
Panic disorder	9.42	7.65	11.54	10.51	7.49	14.55
Social anxiety disorder	17.16	14.82	19.79	18.15	14.49	22.49
Specific phobia	11.25	9.39	13.43	17.42	13.70	21.88
Generalized anxiety disorder	1.26	0.78	2.04	2.01	1.01	3.98
Conduct disorder	0.09	0.02	0.35	0.19	0.05	0.76
Pathological gambling	0.46	0.21	1.01	2.91	1.62	5.16
Any substance use^c	79.86	76.99	82.46	77.36	72.84	81.31
Any tobacco use	40.38	37.01	43.84	39.42	34.92	44.11
Any alcohol use	71.78	68.51	74.82	64.63	59.53	69.42
Any drug use	13.17	11.05	15.63	10.27	7.47	13.97
Use of non-prescribed substances to relieve depressive symptoms						
Alcohol use	12.02	10.05	14.31	8.73	6.33	11.94
Use of non-prescribed medication	1.95	1.28	2.95	1.75	1.02	2.97
SF-12	mean	95%CI	mean	95%CI	T-score	p-value

	NC-MDD ^a N=1406			CMDD N=697			CMDD ^a vs NC-MDD	
	%	95%CI	%	%	95%CI	OR	95%CI	
physical component summary	50.88	50.05	51.70	47.25	46.01	48.50	-5.14	<0.0001
social function scale	44.94	44.11	45.76	43.87	42.44	45.30	-1.31	0.1947
role emotional scale	44.70	43.83	45.57	41.89	40.49	43.30	-3.50	0.0009
mental health scale	41.84	41.05	42.63	42.00	40.77	43.24	0.22	0.8257

^aReference group.

^bAny psychiatric disorder and any Axis I disorder does not include either MDD or CMDD.

^cAny substance use includes any tobacco use, any alcohol use, and any drug use.

Table 5

Lifetime course and treatment-seeking patterns for NC-MDD and CMDD

	NC-MDD ^a N=4256		CMDD N=1439		CMDD ^a vs NC-MDD		CMDD ^a vs NC-MDD					
	%	95%CI	%	95%CI	OR	95%CI	OR ^b	95%CI				
Sought treatment	56.93	55.00	58.85	72.58	69.34	75.59	2.00	1.68	2.39	2.07	1.72	2.49
Treated as outpatient	50.83	48.90	52.77	64.78	61.24	68.15	1.78	1.50	2.10	1.92	1.60	2.30
Treated as inpatient (hospitalized)	7.58	6.64	8.65	16.03	14.06	18.22	2.33	1.89	2.86	2.12	1.69	2.66
Emergency room admittance	6.61	5.72	7.64	12.48	10.54	14.72	2.01	1.59	2.55	1.91	1.47	2.47
Received pharmacological treatment	39.08	37.07	41.12	59.15	55.70	62.51	2.26	1.93	2.64	2.17	1.84	2.56
	mean	95%CI	mean	95%CI	T-score		p-value					
Age at onset (mean),y	30.14	29.62	30.66	31.40	30.36	32.44	2.20		0.0314			
Mean number of episodes of MDD	4.13	3.68	4.58	6.86	5.72	8.00	4.56		<0.0001			
Age at first treatment(mean)	32.77	32.11	33.44	35.44	34.15	36.74	3.79		0.0003			
Duration of longest episode (mean),y	0.39	0.38	0.41	6.76	6.24	7.28	24.41		<0.0001			

^a Reference group.^b Odds Ratio adjusted by age, sex, race, nativity, marital status, urbanicity, family and individual income, region, and insurance.