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Prevalence, correlates, comorbidity and treatment-seeking among individuals with a lifetime major depressive episode with and without atypical features: Results from the National Epidemiologic Survey on Alcohol and Related Conditions

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Abstract

Objective—To examine prevalence, correlates, comorbidity and treatment-seeking among individuals with a lifetime major depressive episode (MDE) with and without atypical features.

Methods—Data were derived from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions, a large cross-sectional survey of a representative sample (N = 43,093) of the U.S. population, which assessed psychiatric disorders using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV). Comparison groups were defined based on the presence or absence of hypersomnia or hyperphagia in individuals who meet criteria for lifetime DSM-IV MDE.

Results—The presence of atypical features during a MDE was associated with greater rates of lifetime psychiatric comorbidity, including alcohol abuse, drug dependence, dysthymia, social anxiety disorder, specific phobia and any personality disorder (PD), except antisocial PD, than MDE without atypical features. Compared with the later group, MDE with atypical features was associated with female gender, younger age of onset, more MDEs, greater episode severity and disability, higher rates of family history of depression, bipolar I disorder, suicide attempts, and larger mental health treatment-seeking rates.

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Conflict of Interest

The authors have no conflicts of interest to report. The funding sources had no role or involvement in this study.

Disclaimer

The Views and opinions expressed in this report are those of the authors and should not be construed to represent the views of sponsoring organizations, agencies, or the U.S. government.

Corresponding Author Statement

Dr. Bridget Grant attests that all authors had access to the study data, take responsibility for the accuracy of the analyses, and had authority over manuscript preparation and the decision to submit the manuscript for publication.

Conclusions—Our data provide further evidence for the clinical significance and validity of this depressive specifier. Based on the presence of any of the two reversed vegetative symptoms during an MDE most of the commonly cited validators of atypical depression were confirmed in our study. MDE with atypical features may be more common, severe, and impairing than previously documented.

Keywords

Major depression; atypical features; vegetative symptoms

Preparations for the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), have brought to the forefront of the research agenda the need to reexamine the classification of depressive disorders and their subtypes.¹ In the study of depressive disorders, few questions have generated more controversy than the validity of atypical depression as an independent nosological entity. Despite decades of research, debate continues regarding its clinical presentation, associated characteristics, and prognostic value.^{2–27} DSM-IV classifies as atypical major depressive episodes (MDE) those in which the subject experiences mood reactivity plus two or more of the following features: increased appetite or weight gain, hypersomnia, leaden paralysis, and interpersonal rejection sensitivity.²⁸

In recent years, community^{29–31} and clinical studies^{32–33} have provided some support for the validity of a simplified diagnostic approach that emphasizes reversed vegetative symptoms to identify of major depression with atypical features. This approach, which identifies cases of major depression with atypical features based on the presence of hypersomnia and hyperphagia, has been shown in previous studies^{29–33} to identify this depressive subtype with reasonable accuracy. Further support for the reversed vegetative approach is provided by data from those samples which suggest that the reverse vegetative symptom diagnostic approach allows for identification of a depressed group of individuals who closely resemble those with DSM-IV atypical depression, including younger age of onset, female gender, higher rates of comorbid anxiety disorders, greater disability and higher rates of health care service utilization.

Clinical studies have suggested that the depressive phase of bipolar disorder is characterized by atypical symptoms, but few studies have examined the prevalence of reversed vegetative symptoms in a nationally representative sample of depressed bipolar individuals. The present study was designed to address previous limitations and to present data on the epidemiology of major depression with atypical features using the 2001–2002 National Institute on Alcohol Abuse and Alcoholism's (NIAAA) National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

METHOD

NESARC Sample

The 2001–2002 NESARC is a survey of a representative sample of the United States sponsored by the NIAAA.³⁴ The target population was individuals age 18 years and older in the civilian non-institutional population residing in households and group quarters. The survey included those residing in the continental United States, District of Columbia, Alaska and Hawaii. Face-to-face personal interviews were conducted with 43,093 respondents. The survey response rate was 81%. Blacks, Hispanics, and young adults (aged 18-to-24) were oversampled with adjustments for nonresponse and oversampling. Weighted data were then adjusted to be representative of the US civilian population based on the 2000 Census.

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

Diagnostic Assessment

DSM Diagnostic Interview—The Alcohol Use Disorder and Associated Disabilities Interview Schedule—DSM-IV Version (AUDADIS-IV), a structured diagnostic interview designed for lay interviewers, was used to generate diagnoses.³⁵

Lifetime Major Depressive Episode with and without Atypical Features—The assessment of mood disorders in the NESARC has been described in detail elsewhere.^{36–38} Consistent with DSM-IV diagnostic rules, individuals who endorsed depressed mood or anhedonia completed the major depressive episode module, whereas all other individuals skipped out of that module. A major depressive episode (MDE) was diagnosed when at least 2 weeks of persistent depressed mood or anhedonia were present, accompanied by a total of at least 5 or more of the 9 DSM-IV symptoms of major depression during the episode. Lifetime DSM-IV MDE was defined as having at least 1 MDE over the life course (including major depressive disorder and bipolar 1 and bipolar 2 disorders). To minimize respondents' burden, the assessment of MDE focused on the most severe episode.

MDD was defined as having at least 1 major depressive episode over the life course without history of manic, mixed, or hypomanic episodes. In contrast, bipolar depression was defined as having one lifetime MDE among respondents with history of manic or hypomanic episodes. Among respondents with a lifetime MDE thus defined, and consistent with previous epidemiological studies,^{29–31} respondents with the presence of reversed vegetative symptoms, i.e., hyperphagia or hypersomnia (or both), were classified as having MDE with atypical features. Hyperphagia was defined as: (1) gain of at least 2 pounds a week, or 10 pounds altogether, during the major depressive episode; or, (2) desire to eat a lot more than usual for no special reason, most days for at least 2 weeks. Hypersomnia was defined as sleeping more than usual nearly every day for at least 2 weeks.

Individuals were classified as having MDE with atypical features if they reported at least one reversed (i.e., atypical) vegetative symptoms, regardless of whether or not they also reported any typical vegetative symptom. Respondents who met criteria for lifetime MDE but did not report any atypical features were classified as having MDE without atypical features. In summary, the main two groups in these analyses are mutually exclusive, since a MDE with atypical features include only respondents who endorsed hypersomnia, or hyperphagia or both during a lifetime a MDE, whereas the comparison group MDE without atypical features, includes those respondents that endorsed neither hyperphagia, nor hypersomnia, during a lifetime MDE.

To examine the robustness of our findings, we considered several operationalizations of the definition of atypical depression, based on the number of reversed vegetative symptoms (one versus two) and the presence or absence of typical vegetative symptoms during an MDE with atypical features (see Table 1 for a summary of the operationalizations). Individuals with atypical symptoms and no typical vegetative symptoms were considered to have MDE with strict atypical features, whereas those with atypical vegetative symptoms and at least one typical vegetative symptoms were considered to have broad atypical features.

Combining the number of symptoms and whether atypical features were broad or strict, resulted in four mutually exclusive groups: 1) MDE with broad atypical features with only one reversed vegetative symptom; 2) MDE with broad atypical features with both reversed

vegetative symptoms; 3) MDE with strict atypical features with only one reversed vegetative symptom; and, 4) MDE with strict atypical features with both reversed vegetative symptoms. The first two groups considered together comprised the “MDE with broad atypical features (one or two symptoms)” group, whereas the other two groups considered jointly constituted the “MDE with strict atypical features (one or two symptoms)” group.

We focused our main analyses on individuals with “MDE with broad atypical features (one or two symptoms)”, because previous studies included in their analyses all individuals with atypical symptoms, regardless of whether or not they also had any typical symptoms. However, to guard against the possibility of variations in the results due to different definitions of the MDE with atypical features group, we conducted identical analyses separately using alternative operationalizations of atypical depression (see Table 1). The following additional comparisons were conducted: (1) Each of the four subgroups of MDE with atypical features separately (i.e. broad and strict with one or both atypical symptoms) versus “MDE without atypical features”; and, (2) Individuals with one atypical feature MDE versus those with both atypical features, regardless of whether they belonged to the “broad” or “strict” atypical groups.

Furthermore, to examine whether MDE with atypical features is different in individuals with bipolar disorder than in those with major depressive disorder (MDD), we compared individuals with “MDE with broad atypical features group (one or two symptoms)” versus individuals with “MDE without atypical features” stratified by whether individuals had MDD or bipolar disorder. In addition, we directly compared individuals with bipolar depression with atypical features versus individuals with MDD with atypical features.

We present the results of the main analyses comparing the “MDE with broad atypical features group (one or two symptoms)” versus “MDE without atypical features” groups, and indicate the main differences from all other comparisons. Results from the direct comparisons between bipolar depression with atypical features and MDD with atypical features are presented in supplementary tables. All other results are available upon request.

As reported in detail elsewhere, the test-retest reliability^{38–39} and validity^{36, 40–42} of AUDADIS-IV measures of major depressive disorder and major depressive episode³⁹ are good (0.64–0.67), and a clinical reappraisal study⁴⁰ of major depression diagnoses showed good agreement between AUDADIS-IV and psychiatrist’s diagnoses ($\kappa=0.64–0.68$).

Other Psychiatric Disorders—AUDADIS-IV assessments of DSM-IV lifetime anxiety disorders (generalized anxiety disorder, panic disorder, social anxiety disorder, and specific phobia), substance use disorders, and personality disorders (PDs), including avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic and antisocial personality disorders, have been described in detail previously.^{35, 39, 43–44} Reliability ($\kappa>0.74$) and validity were good to excellent for substance use disorders,^{39, 43, 45–46} fair to good for anxiety disorders ($\kappa = 0.40–0.60$), and personality disorders ($\kappa = 0.40–0.67$).^{39–40}

Other measures—Age of onset, number of episodes, duration of only or longest episode (if more than one), and use of alcohol or drugs to help relieve symptoms of depression were assessed. To be consistent with previous research,^{47–48} the study also incorporated measures of known risk factors for MDE, including: (1) family history of depression; (2) parental absence or separation from a biological parent before age 18; (3) parental loss due to death before age 18; (4) early-onset anxiety, operationalized as onset of any anxiety disorder before age 18; (5) conduct disorder; and (6) history of divorce or loss of spouse. Although it was not used to classify individuals as having atypical symptoms, we assessed the presence

of lifetime rejection sensitivity regardless of whether depressed or not, defined as avoiding getting involved with people unless the respondent was certain of being liked.

Overall health status was assessed by self-report by asking respondents: “in general, would you say your health is excellent, very good, fair, or poor?”. Individuals were classified as having received mental health treatment for MDE if they: (1) visited a counselor, therapist, doctor, or psychologist; (2) were a patient in a hospital for at least one night; (3) visited an emergency room; or (4) were prescribed any psychotropic medications for the treatment of MDE.

Statistical Analysis—Weighted cross-tabulations were used to calculate prevalence rates for each study group. A series of logistic regression analyses, adjusting for sociodemographic characteristics and total number of criteria, yielded adjusted odds ratios, indicating associations between MDE subtype and: (1) sociodemographic characteristics; (2) each specific 12-month and lifetime psychiatric disorder; (3) course, clinical symptoms, psychopathological correlates and disability; and (4) 12-month and lifetime mental health service utilization. In these sets of analyses, the group without atypical features served as the reference group. We consider two percentages to differ significantly if the 95% confidence interval (95% CI) of their OR does not include 1.⁴⁹ Standard errors and 95% confidence limits for all analyses were estimated using SUDAAN.⁵⁰

RESULTS

Prevalence and Sociodemographic Correlates

The prevalence of lifetime MDE with atypical features was 10.23%, while the prevalence of MDE without atypical features was 6.31%. Among individuals with atypical features 43.54% had only hypersomnia, 23.88% only hyperphagia and 32.58% had both features.

Individuals with MDE with atypical features were significantly more likely than those without atypical features to be female, US-born, younger than age 29 and never married, to live in urban areas, and to have an income lower than \$19,000 and no insurance (Table 2).

Rates of DSM-IV disorders

Lifetime rates of any Axis I psychiatric disorder, except alcohol dependence, drug abuse, nicotine dependence, panic disorder and generalized anxiety disorder, and pathological gambling, were significantly higher among individuals with lifetime MDE with atypical features than among those without atypical features. Furthermore all personality disorders, except antisocial personality disorder, were significantly more common among individuals with MDE with atypical features than among those without them (Table 3).

Course and Clinical Correlates

Individuals with MDE with atypical features were significantly younger at the time of their first MDE, had significantly more episodes, and reported a higher total number of criteria than those without atypical features. They were also significantly more likely than those without atypical features to use drugs or medications to help relieve symptoms of depression, to have family history of depression and early-onset anxiety, and to report subjective sensitivity to rejection. They were less likely than individuals without atypical features to report childhood parental loss or history of divorce/loss of spouse. Individuals with bipolar I (but not II) disorder were more likely than those with MDD to experience atypical features (Table 4).

Symptoms and Health Status

In addition, individuals with MDE with atypical features were significantly more likely to endorse anhedonia, fatigue, psychomotor agitation, worthlessness, guilt, indecisiveness, and irritability, and less likely to report motor retardation. The former group was also more likely to report thoughts of suicide and of own death, and also reported significantly poorer overall health than individuals without atypical features (Table 5).

Treatment Seeking

Individuals with atypical features had significantly higher rates of mental health care utilization than those without atypical features (Table 6).

Analyses of Alternative Operationalizations of MDE with Atypical Features

Across all operationalizations of MDE with atypical features shown in Table 1, only minor differences arose when comparing MDE with atypical features to MDE without atypical features across sociodemographic, comorbidity, clinical characteristics and rates of treatment-seeking. The overall pattern of results remained the same. Similarly, the pattern of results of the main analyses held true when the analyses of MDE with atypical features versus MDE without atypical features were stratified by whether the individuals had MDD or bipolar disorder (all results available upon request).

By contrast, direct comparisons between bipolar depression with atypical features and MDD with atypical features yielded several significant differences. First, the odds of any lifetime Axis I psychiatric disorder, except alcohol abuse, and any PD, were significantly greater among bipolar depression with atypical features than among MDD with atypical features. Secondly, bipolar depression with atypical features had a significantly stronger association than MDD with atypical features to younger age of onset, higher number of criteria for MDE and total number of episodes. Bipolar depression with atypical features was also more strongly associated than MDD with atypical features to greater rates of alcohol and drug use to help relieve symptoms of depression, higher rates of family history of depression, early-onset anxiety, and rejection sensitivity. Third, individuals with bipolar depression with atypical features were significantly more likely to report any DSM-IV symptom of depression, and thoughts of suicide and suicide attempts, than individuals with MDD with atypical features. Finally, individuals with bipolar depression with atypical features exhibited a longer time to treatment-seeking and had higher rates of any lifetime and 12-month treatment seeking, than the later group (Supplementary tables 1–5).

DISCUSSION

In a large, nationally representative sample, individuals with lifetime MDE with atypical features could be distinguished from those without atypical features by the presence of either reverse vegetative symptom (hypersomnia or hyperphagia). Individuals with atypical features exhibited higher rates of psychiatric comorbidity, greater symptom severity and disability, and higher rates of treatment-seeking than those without them. Furthermore, MDE with atypical features had more severe manifestations in the context of bipolar disorder than among individuals with MDD.

Confirming previous epidemiologic studies,^{29, 31} individuals with MDE with atypical features could be distinguished from those without them based on the presence of reversed vegetative symptoms. Across a broad range of operationalizations, the diagnosis of MDE with atypical features had significant associations with the prevalence of lifetime psychiatric comorbidity, the course and severity of the disorder, its degree of functional impairment, the association with bipolar I disorder, and the rates of mental health treatment-seeking. Those

differences held regardless of whether one or both reversed vegetative symptoms were endorsed, suggesting that there are no significant differences between individuals with one versus two atypical features. Furthermore, depressed individuals with broad versus strict atypical features had similar patterns across all dimensions examined, with even greater severity and disability in the group with broad atypical features. Our findings suggest that the presence of just one reversed vegetative symptom during a MDE establishes a threshold that clinically distinguishes depressed individuals with atypical features from those without them, regardless of the presence or absence of typical vegetative symptoms.

Using this new threshold, we found that, although the prevalence of individuals with both atypical features is similar to that documented in prior studies, the overall prevalence of MDE with atypical features is much higher than previously documented.^{29–31} Differences in the criteria used to define atypicality (i.e. one vs. both reversed vegetative symptoms of hypersomnia or hyperphagia), exclusion of individuals with bipolar disorder or with typical vegetative symptoms, and changing diagnostic DSM criteria, may partially account for the higher prevalence estimates found in our study.^{29, 31} Nevertheless, these findings highlight the public health significance of a diagnostic group that, possibly due to its name, may have been assumed to be rare and, consequently, insufficiently studied.

Consistent with prior studies, MDE with atypical features was associated with female gender,³¹ earlier age of onset of MDE,^{29–31, 51} family history of depression,^{31, 51} higher rates of comorbid anxiety and drug use disorders,^{29–31} higher number of depressive symptoms and rates suicidal ideation and attempts,^{29, 31} and greater disability and use of mental health services.³¹ Our study extends previous findings by documenting the association of MDE with atypical features with (1) greater overall rates of lifetime psychiatric disorders; (2) bipolar I disorder; (3) any PD, antisocial personality disorder; (3) higher total number of MDE symptoms (5) early-onset anxiety; (6) increased use of drug or medications to help relieve depressive symptoms; (6) higher rates of rejection sensitivity; and, (7) worse overall health. These findings remained significant in models adjusting for several sociodemographic covariates.

The current study also examined the relationship between reversed vegetative symptoms and bipolar disorder in a general population sample. In contrast with data from clinical samples,^{52–55} individuals with MDE with atypical features had significantly higher rates of bipolar I disorder than those without atypical features. Data from clinical samples^{53, 55–56} may not generalize to the community. Alternatively, this discrepancy may be partially explained by the use of different definitions of MDE with atypical features across studies, or the exclusion of bipolar I patients from most clinical studies.^{53, 55} In our study, even after controlling for total number of criteria, individuals with bipolar depression with atypical features were more likely than individuals with MDD with atypical features to have higher rates of any Axis I and II disorders. The two groups also differed significantly in sociodemographic characteristics, clinical course, symptomatology, disability and treatment-seeking behavior. These findings are consistent with previous clinical data.⁵⁶ Overall, these differences parallel those between major depression with and without atypical features and suggest that the characteristics of atypical depression, although common in both disorders, are even more accentuated in bipolar depression than in MDD with atypical features.

Some limitations of the current study should be considered in interpreting our findings. First, we identified individuals with MDE with atypical features based on the presence of reversed vegetative symptoms, rather than the full DSM-IV criteria. However, our approach is consistent with that of previous epidemiologic surveys^{29–31} and clinical studies,³² which has consistently identified a clinically meaningful group of individuals characterized by greater rates of comorbidity, severity of illness, risk of suicide attempt and overall disability similar

to the group identified in clinical samples using the full DSM-IV criteria. Furthermore, our results were robust across multiple operationalizations of atypical depression. Indirect evidence of the validity of our approach is provided by the higher rates of rejection sensitivity among individuals with atypical features. Second, our assessment was limited to clinical features and did not any include neurobiological assessments or examination of treatment response. Third, the duration of depressive episodes may have impact on the likelihood that the individual will experience a period of atypical symptoms. However, the duration MDE episodes did not differ significantly among individuals with and without atypical features, suggesting that duration of the episode is unlikely to be a major determinant of the presence of atypical symptoms. Fourth, the cross-sectional nature of this survey limits the examination of lifetime comorbidity between “typical” and “atypical” features in depressed individuals.

Despite these limitations, our data provide further evidence for the clinical significance and validity of the atypical features specifier. Based on the presence of any of the two reversed vegetative symptoms during an MDE most of the commonly cited validators of atypical depression were confirmed in our study. MDE with atypical features may be, in fact, more common, severe, and impairing than MDE without atypical features. Given its prevalence, and high risk for suicide and disability, early detection, targeted interventions and development of more effective treatments for individuals with atypical features are important.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1Definitions of major depressive episode (MDE) with atypical features. ^a

DEFINITIONS	Reversed Vegetative Symptoms ^b	Typical Vegetative Symptoms ^c
1. MDE without atypical features (reference group for all analyses)	No reversed vegetative symptoms present	One or both typical vegetative symptom may be present but are not required
2. MDE with atypical features ^d	At least one reversed vegetative symptom present	One or both typical vegetative symptom may be present but are not required
3. MDE with <u>Broad</u> atypical features with only one reversed vegetative symptom	One reversed vegetative symptom is present, but not both	At least one typical vegetative symptom is present
4. MDE with <u>Broad</u> atypical features with two reversed vegetative symptoms	Both reversed vegetative symptoms present	At least one symptom typical vegetative symptom is present
5. MDE with <u>Strict</u> atypical features with one reversed vegetative symptom	One symptom reversed vegetative is present, but not both	No typical vegetative symptoms present
6. MDE with <u>Strict</u> atypical features with two reversed vegetative symptoms	Both reversed vegetative symptoms are present	No typical vegetative symptoms present
7. MDE with <u>Broad</u> atypical features (one or two reversed vegetative symptoms) ^e	One or both reversed vegetative symptom are present	At least one typical vegetative symptom is present
8. MDE with <u>Strict</u> atypical features (one or two reversed vegetative symptoms) ^f	One or both reversed vegetative symptom are present	At least one typical vegetative symptom is present

^aRefer to the methods section for reference.^bReversed Vegetative Symptoms = Hypersomnia or Hyperphagia.^cTypical Vegetative Symptoms = Insomnia or Loss of weight/appetite.^dIndividuals were classified as having MDE with atypical features if they reported *one or both* reversed vegetative symptoms: hyperphagia or hypersomnia. This was done regardless of whether or not respondents also reported at least one typical vegetative symptom during the MDE.^eComprises all individuals in groups 3 and 4.^fComprises all individuals in groups 5 and 6.

Table 2

Prevalence and sociodemographic characteristics of individuals with lifetime MDE with and without atypical features

	MDE with Atypical Features ^a n=4,420				MDE without Atypical Features n=2,704			
	%	CI	%	CI	%	CI	OR	CI
Sex								
Male	30.70	28.94	32.52	37.64	39.92	42.25	0.67	0.58 0.76
Female	69.30	67.48	71.06	57.75	60.08	62.36	1.00	1.00 1.00
Race/Ethnicity								
White	76.91	74.07	79.53	75.23	77.86	80.29	1.00	1.00 1.00
Black	8.46	7.27	9.81	6.56	7.68	8.97	1.11	0.95 1.31
Native Americans	3.47	2.72	4.40	2.29	3.10	4.18	1.13	0.77 1.67
Asian	2.44	1.59	3.70	2.27	3.16	4.39	0.78	0.49 1.25
Hispanic	8.73	6.88	11.01	6.60	8.20	10.16	1.08	0.92 1.27
Nativity								
US-Born	91.93	89.75	93.68	87.14	89.68	91.76	1.31	1.09 1.58
Foreign-born	8.07	6.32	10.25	8.24	10.32	12.86	1.00	1.00 1.00
Age								
18–29	26.47	24.82	28.20	15.39	17.33	19.46	1.00	1.00 1.00
30–44	33.93	32.33	35.56	29.87	32.05	34.32	0.69	0.59 0.82
45–64	33.32	31.73	34.96	35.81	38.09	40.43	0.57	0.49 0.68
65+	6.28	5.52	7.13	11.06	12.52	14.15	0.33	0.26 0.41
Education								
< High School	13.64	12.26	15.14	13.76	15.53	17.48	0.84	0.70 1.02
High School	27.27	25.42	29.21	25.51	27.66	29.91	0.95	0.83 1.09
College	59.09	56.88	61.26	54.46	56.81	59.13	1.00	1.00 1.00
Individual Income								
0–19K	54.41	52.18	56.63	46.40	48.84	51.27	1.00	1.00 1.00
20–34K	22.04	20.30	23.89	20.37	22.33	24.42	0.89	0.75 1.04
35–69K	18.42	16.70	20.27	19.02	20.95	23.02	0.79	0.68 0.92
>70K	5.12	4.15	6.31	6.49	7.88	9.54	0.58	0.45 0.76
Family Income								

	MDE with Atypical Features ^a n=4,420			MDE without Atypical Features n=2,704					
	%	CI	%	CI	OR	CI			
0–19K	25.46	23.68	27.33	24.17	22.09	26.38	1.00	1.00	1.00
20–34K	21.50	20.01	23.06	20.55	18.81	22.41	0.99	0.85	1.15
35–69K	31.91	30.14	33.73	31.21	29.11	33.39	0.97	0.83	1.14
>70K	21.13	19.23	23.17	24.07	21.72	26.59	0.83	0.70	1.00
Marital Status									
Married	53.27	51.33	55.20	56.57	54.08	59.03	1.00	1.00	1.00
Widowed	22.31	21.00	23.67	26.85	24.93	28.87	0.88	0.78	1.00
Never Married	24.42	22.77	26.15	16.57	14.62	18.73	1.56	1.31	1.87
Urbanicity									
Urban	79.63	76.07	82.78	77.26	73.28	80.79	1.00	1.00	1.00
Rural	20.37	17.22	23.93	22.74	19.21	26.72	0.87	0.76	0.99
Region									
Northeast	18.87	13.58	25.61	17.35	12.21	24.07	1.08	0.89	1.30
Midwest	24.68	19.16	31.18	25.20	19.68	31.67	0.97	0.82	1.14
South	32.39	26.81	38.51	33.67	28.14	39.68	0.95	0.81	1.11
West	24.06	17.94	31.47	23.78	18.01	30.70	1.00	1.00	1.00
Insurance									
Private	66.02	64.04	67.94	68.90	66.37	71.33	1.00	1.00	1.00
Public	13.77	12.42	15.25	13.52	11.88	15.36	1.06	0.88	1.28
No insurance	20.21	18.65	21.87	17.57	15.77	19.53	1.20	1.03	1.39

^aMDE with Atypical Features defined as presence of *one or both* reversed vegetative symptoms (hyperphagia or hypersomnia), regardless of presence of at least one typical vegetative symptom during the MDE.

Table 3

Lifetime prevalence of comorbid psychiatric disorders in individuals with lifetime MDE with and without atypical features

	MDE with Atypical Features ^a n=4,420			MDE without Atypical Features n=2,704			AOR ^c (CI)		
	%	95% CI	%	95% CI	%	95% CI			
Any Psychiatric Disorder	83.43	82.10	84.68	77.91	75.88	79.82	1.35	1.17	1.57
Any Axis I Disorder	78.88	77.28	80.40	73.81	71.55	75.96	1.30	1.13	1.49
Any Substance Use Disorder ^b	58.81	56.90	60.70	53.92	51.46	56.37	1.22	1.07	1.39
Alcohol Use Disorder	45.36	43.37	47.36	40.90	38.40	43.44	1.28	1.13	1.45
Alcohol Abuse	20.21	18.60	21.92	17.33	15.60	19.21	1.31	1.12	1.54
Alcohol Dependence	25.15	23.44	26.93	23.57	21.33	25.96	1.09	0.94	1.27
Drug Use Disorder	22.46	20.69	24.35	17.95	16.14	19.92	1.28	1.07	1.52
Drug Abuse	13.57	12.17	15.11	12.28	10.81	13.91	1.07	0.88	1.31
Drug Dependence	8.89	7.83	10.08	5.67	4.64	6.91	1.55	1.21	1.99
Nicotine Dependence	33.83	31.83	35.90	31.91	29.79	34.11	1.06	0.94	1.20
Dysthymia	16.35	15.04	17.75	13.50	11.86	15.32	1.33	1.11	1.59
Any Anxiety Disorder	46.94	44.87	49.02	41.82	39.28	44.42	1.16	1.01	1.33
Panic Disorder	18.30	16.90	19.79	15.64	13.99	17.45	1.13	0.95	1.34
Social Anxiety Disorder	16.94	15.47	18.52	11.95	10.43	13.66	1.43	1.19	1.73
Specific Phobia	24.23	22.52	26.02	19.38	17.38	21.55	1.20	1.02	1.41
Generalized Anxiety Disorder	18.26	16.79	19.82	16.09	14.33	18.03	1.18	1.00	1.40
Pathological Gambling	0.83	0.59	1.16	1.14	0.70	1.85	0.83	0.48	1.45
Psychotic Disorder	1.47	1.06	2.03	0.81	0.51	1.29	1.93	1.05	3.58
Any Personality Disorder	40.12	38.37	41.90	32.10	29.76	34.53	1.32	1.16	1.51
Avoidant Personality Disorder	10.56	9.52	11.69	6.52	5.35	7.93	1.52	1.20	1.93
Dependent Personality Disorder	2.66	2.11	3.36	0.78	0.50	1.22	3.20	1.93	5.30
Obsessive-Compulsive Disorder	21.55	19.90	23.29	17.27	15.61	19.07	1.29	1.11	1.50
Paranoia Personality Disorder	16.04	14.70	17.49	11.53	9.99	13.27	1.32	1.09	1.60
Schizoid Personality Disorder	10.62	9.47	11.89	7.90	6.64	9.38	1.31	1.06	1.62
Histrionic Personality Disorder	6.90	5.96	7.97	4.15	3.35	5.13	1.52	1.18	1.97
Antisocial Personality Disorder	9.42	8.32	10.64	8.29	7.00	9.79	1.12	0.88	1.43

^aMDE with Atypical Features defined as presence of *one or both* reversed vegetative symptoms (hyperphagia or hypersomnia), regardless of presence of at least one typical vegetative symptom during the MDE.

^bAny Substance Use Disorder: including alcohol use disorder, drug use disorder, and nicotine dependence.

^cAdjusted for sex, US born, age, annual income, marital status, region, urbanicity, and number of criteria.

Table 4
Clinical characteristics and symptoms associated with Lifetime MDE with atypical features and MDE without atypical features

	MDE with Atypical Features ^a n=4,420			MDE without Atypical Features n=2,704			Wald F	p-value
	Mean	95% CI	Mean	95% CI	Mean	95% CI		
Age of Onset	27.45	26.99	27.92	31.71	30.95	32.47	18.19	0.0001
Number of Episodes	6.01	5.44	6.58	4.30	3.75	4.85	18.76	0.0001
Total number of criteria	8.14	8.10	8.19	7.61	7.54	7.68	147.04	<0.0001
	%	95% CI	%	95% CI	AOR ^b	95% CI		
Use of alcohol to help relieve symptoms	21.09	19.55	22.72	20.23	18.34	22.25	1.09	0.93
Self-medication to help relieve symptoms	8.61	7.49	9.88	5.27	4.30	6.45	1.66	1.26
Family History of depression (only 1st degree relatives)	66.82	64.88	68.70	60.49	58.08	62.86	1.28	1.13
Separation from a biological parent (before age 18)	95.69	94.98	96.30	95.94	95.08	96.65	1.03	0.80
Childhood parental loss due to death (before age 18)	8.60	7.65	9.66	11.41	10.11	12.85	0.79	0.65
Conduct Disorder	2.01	1.53	2.63	1.38	0.90	2.10	1.45	0.88
Early onset anxiety (before age 18) ^c	46.77	44.04	49.53	40.58	37.12	44.13	1.24	1.06
History of Divorce/loss of spouse	36.78	34.80	38.81	46.13	43.41	48.88	0.81	0.68
Rejection Sensitivity ^d	13.92	12.72	15.21	9.58	8.19	11.17	1.41	1.15
Bipolar I	13.99	12.64	15.47	8.51	7.28	9.92	1.61	1.32
Bipolar II	6.56	5.77	7.45	6.77	5.55	8.23	0.85	0.66

^a MDE with Atypical Features defined as presence of *one or both* reversed vegetative symptoms (hyperphagia or hypersomnia), regardless of presence of at least one typical vegetative symptom during the MDE.

^b Adjusted for sex, US born, age, annual income, marital status, region, urbanicity, and number of criteria.

^c Early onset anxiety defined as onset of any anxiety disorder before age 18.

^d Lifetime rejection sensitivity defined as avoiding getting involved with people unless the respondent was certain of being liked.

Table 5
Clinical characteristics and symptoms associated with Lifetime MDE with atypical features and MDE without atypical features

	MDE with Atypical Features ^a n=4,420			MDE without Atypical Features n=2,704			AOR (CI) ^b		
	%	95% CI	%	95% CI					
Clinical Symptoms									
Lack of interest or pleasure	89.89	88.72	90.95	86.81	84.98	88.45	1.30	1.07	1.58
Fatigue	90.62	89.50	91.64	76.70	74.76	78.55	2.93	2.50	3.43
Motor retardation	49.87	47.96	51.79	63.49	60.93	65.98	0.58	0.51	0.66
Motor agitation	42.41	40.46	44.40	37.93	35.45	40.46	1.21	1.06	1.39
Worthlessness	66.82	65.00	68.60	60.28	58.13	62.38	1.32	1.16	1.50
Guilt	62.22	60.50	63.91	57.04	54.68	59.36	1.20	1.06	1.36
Trouble concentrating	85.71	84.29	87.02	86.24	84.54	87.78	0.90	0.77	1.06
Trouble making decisions	78.17	76.62	79.65	75.39	73.37	77.30	1.18	1.03	1.36
Irritability	56.51	54.84	58.16	46.66	44.20	49.13	1.32	1.18	1.48
Attempt suicide	13.29	12.13	14.53	8.78	7.52	10.24	1.45	1.17	1.81
Thoughts of suicide	42.64	40.87	44.42	34.84	32.64	37.10	1.32	1.18	1.48
Thoughts of own death	58.59	56.85	60.31	54.14	51.91	56.37	1.15	1.03	1.29
Overall Health excellent to good	68.44	66.22	70.59	71.00	68.28	73.57	0.84	0.75	0.94
Overall health fair to poor	31.56	29.41	33.78	29.00	26.43	31.72	1.00	1.00	1.00
	Mean	95% CI	Mean	95% CI	Wald F	p-value			
Physical component summary ^c	49.64	49.16	50.12	49.69	49.10	50.28	9.80	0.0026	
Mental component summary ^c	45.33	44.93	45.73	47.33	46.81	47.86	29.52	<0.0001	
Social Functioning Scale Score ^c	46.74	46.29	47.19	48.24	47.67	48.80	21.83	<0.0001	
Role of Emotional Functioning Scale Score ^c	46.08	45.63	46.53	47.73	47.16	48.30	33.51	<0.0001	
Mental Health Scale Score ^c	44.95	44.52	45.39	46.49	45.96	47.01	16.52	0.0001	

^aMDE with Atypical Features defined as presence of *one or both* reversed vegetative symptoms (hyperphagia or hypersomnia), regardless of presence of at least one typical vegetative symptom during the MDE.

^bAdjusted for sex, US born, age, annual income, marital status, region, urbanicity, and number of criteria.

Table 6

Treatment-seeking rates in individuals with lifetime MDE with atypical features and MDE without atypical features

	MDE with Atypical Features ^a n=4,420		MDE without Atypical Features n=2,704		AOR ^b (CI)				
	%	95% CI	%	95% CI					
Any Lifetime Treatment	64.80	62.92	66.63	56.01	53.75	58.25	1.43	1.27	1.61
Lifetime Outpatient treatment seeking	58.73	56.81	60.62	49.42	47.02	51.82	1.39	1.24	1.56
Lifetime Emergency Room/Hospital	10.96	9.79	12.26	8.41	7.16	9.86	1.25	1.01	1.56
Lifetime use of medication	49.73	47.52	51.94	37.83	35.69	40.01	1.67	1.49	1.88
Treatment seeking in the past 12 months	28.65	26.82	30.57	18.27	16.42	20.27	1.68	1.44	1.96
	Mean	95% CI	Mean	95% CI	Wald F	p-value			
Age when first sought treatment	31.04	30.41	31.67	33.95	35.98	1.6	0.211		
Time to Treatment Seeking (years)	3.68	3.37	3.99	3.09	4.01	1.5	0.2253		

^a MDE with Atypical Features defined as presence of *one or both* reversed vegetative symptoms (hyperphagia or hypersomnia), regardless of presence of at least one typical vegetative symptom during the MDE..

^b Adjusted for sex, US born, age, annual income, marital status, region, urbanicity, and number of criteria.