Temporal Relationships Between Overweight and Obesity and *DSM-IV* Substance Use, Mood, and Anxiety Disorders: Results From a Prospective Study, the National Epidemiologic Survey on Alcohol and Related Conditions

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ABSTRACT

Objective: To present nationally representative findings on the prospective relationships between overweight and obesity and *DSM-IV* substance use, mood, and anxiety disorders.

Method: A nationally representative sample of 34,653 US adults was interviewed in Wave 1 (2001–2002) and Wave 2 (2004–2005) of the National Epidemiologic Survey on Alcohol and Related Conditions. The target population was the civilian population residing in households and group quarters, with gathered data adjusted to be representative of the civilian population of the United States on the basis of the 2000 Decennial Census. The main outcome measures were the incidence of *DSM-IV* substance use, mood, and anxiety disorders and changes in body mass index status during the 3-year follow-up period.

Results: Regression analyses that controlled for a wide array of covariates showed that overweight and obese women were at increased risk ($P < .05$) for incident major depressive disorder during the follow-up period (adjusted OR [AOR] = 1.3 [95% CI, 1.02–1.56] and AOR = 1.2 [95% CI, 1.02–1.51], respectively). Overweight men and obese men were at decreased risk ($P < .05$) of incident drug abuse and alcohol dependence (AOR = 0.7 [95% CI, 0.44–0.96] and AOR = 0.7 [95% CI, 0.52–0.97]), respectively. Obese women had a decreased risk ($P < .05$) of incident alcohol abuse and drug dependence (AOR = 0.6 [95% CI, 0.45–0.88] and AOR = 0.4 [95% CI, 0.21–0.91], respectively). Men with drug dependence and women with specific phobia had a decreased risk ($P < .05$) of becoming overweight or obese during the follow-up period (AOR = 0.4 [95% CI, 0.19–0.99] and AOR = 0.8 [95% CI, 0.66–0.95], respectively).

Conclusions: Increased risk of major depressive disorder among overweight and obese women could be attributed to stigma and greater body dissatisfaction among women in Western cultures. Overweight and obesity may serve as protective factors against developing incident substance use disorders, possibly due to shared neural functions in the brain underlying addictions to numerous substances. Results are discussed in terms of their clinical implications, including the need to update treatment guidelines for the management of overweight, obesity, and major depressive disorder.

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From 1976–1980 to 2003–2004, the prevalence of obesity (body mass index [BMI] ≥ 30.0) in the United States doubled from 15.1% to 32.2%.[1] During the same period, the prevalence of overweight and obesity (BMI ≥ 25.0) markedly increased from 45.0% to 66.3%.[2,3] Although associations between overweight and obesity and major medical conditions[4,5] and their associated disabilities[6] and excess and premature mortality,[7] including diabetes mellitus, cardiovascular diseases, and degenerative joint disease, have been extensively studied, evidence concerning their relationships to psychiatric disorders is limited.

To date, 16 cross-sectional and 9 prospective surveys using standardized psychiatric assessment interviews have examined relationships between BMI status and psychopathology. Most cross-sectional studies[8–24] found modest associations[8,10,11,14–23] between overweight and/or obesity and any mood disorder or major depressive disorder (MDD), with some finding the relationship only among women.[8,11,14–17,19,20] Six studies also found associations between overweight and/or obesity and any anxiety disorder,[9,21,23] including panic disorder,[15,19,20,23] specific phobia,[8,19,20,22] generalized anxiety disorder,[15,19] and social phobia.[8,15,22]

Most prospective studies[25–33] on obesity and psychopathology have focused on MDD. Longitudinal surveys among cohorts of children or adolescents spanning about 20 years have consistently shown that MDD is associated with an increased risk of later obesity,[25–27] although only among women in 1 study.[30] In contrast, 1 long-term longitudinal survey of women of an average age of 27 years at baseline[28] found that baseline obesity predicted MDD 30 years later.[28] Prospective studies of much shorter durations (2 to 5 years) conducted among adults aged 50 years and older found the same result.[31–33]

Studies examining relationships between substance use disorders and overweight and/or obesity have been mixed. Except for 2 studies,[19,24] no associations were observed between alcohol abuse, alcohol dependence, or any alcohol use disorder and overweight and obesity.[10,15,20–22] Most studies also found no associations with drug abuse,[19,20] drug dependence,[15,19] any drug use disorder,[22] or overall substance use disorders.[9,12,13] One study found an inverse relationship between drug dependence and obesity among men,[20] while another found a positive association between substance use disorders and obesity among men.[17]

Although much has been learned about relationships between overweight and obesity and psychopathology from

prior epidemiologic work, none of these studies were without limitations. For example, some previous studies were restricted by age and/or geography; failed to exclude pregnant women and underweight individuals; did not analyze data by sex or present data on specific psychiatric disorders; or failed to differentiate between overweight and obesity and between MDD and bipolar disorder and, by definition, could not discern temporal relationships between BMI status and psychopathology. Prospective studies have also been limited by long follow-up periods with sporadic measurement of BMI and psychopathology, an exclusive focus on child or adolescent cohorts or on individuals over the age of 50 years, and failure to measure a broad range of specific psychiatric disorders that are highly comorbid with one another. The latter limitation, also shared by most cross-sectional studies, is important, as psychiatric comorbidity, a potentially critical confounder of BMI-psychopathology associations, could not be controlled. Other critical factors, eg, substance use, medical conditions, stress and psychotropic medication use, have also not been controlled.

The absence of a large national prospective survey of US adults on the temporal relationships between BMI status and psychiatric disorders represents a gap in our knowledge in terms of etiology, prevention, intervention, and economic costs for each of these conditions. The present study was the first to examine temporal relationships between overweight and obesity and *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*)-specific[34] substance use, mood, and anxiety disorders within a 3-year national prospective survey of the US population, the Waves 1 and 2 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).[35,36] The analyses importantly controlled for comorbidity at Wave 1 and concurrent comorbidity during the follow-up period, in addition to a battery of sociodemographic and clinical covariates shown to influence BMI-psychopathology associations, including sex.

METHOD

Sample

The 2001–2002 Wave 1 of the NESARC is described in detail elsewhere.[35,36] The Wave 1 NESARC surveyed a representative sample of the adult US population 18 years of age and older, oversampling blacks, Hispanics, and young adults aged 18–24 years. The target population was the civilian population residing in households and group quarters. Face-to-face interviews were conducted with 43,093 respondents, with a response rate of 81.0%.

The 2004–2005 Wave 2 NESARC attempted face-to-face reinterviews with all Wave 1 participants.[37] Excluding respondents ineligible for the Wave 2 interview, the Wave 2 response rate was 86.7%, reflecting 34,653 completed interviews. The cumulative response rate at Wave 2 was 70.2%. The mean interval between the 2 interviews was 36.6 months. Wave 2 NESARC data were weighted to reflect design characteristics of the NESARC and to account for oversampling. Wave 2 NESARC weights included a component that adjusted for nonresponse, sociodemographic factors, and psychiatric diagnosis to ensure that the Wave 2 sample approximated the target population, that is, the original sample minus attrition between the 2 waves. There were no significant differences between the Wave 2 respondents and the target population on sociodemographic characteristics, BMI status, or the presence of any lifetime psychiatric disorder.[34] Weighted data were then adjusted to be representative of the civilian population of the United States on the basis of the 2000 Decennial Census.

The research protocol, including informed consent procedures, received ethical review and approval from the US Census Bureau and the US Office of Management and Budget.

Body Mass Index

Body mass index (calculated as the weight in kilograms divided by height in meters squared) was defined using standards developed by the National Heart, Lung, and Blood Institute: healthy weight, BMI of 18.5–24.9; overweight, BMI of 25.0–29.9; and obesity, BMI of ≥ 30.0. Similar to previous studies, height and weight were self-reported in the NESARC. Self-reported weight correlates highly with measured weight ($r = 0.86$) and is largely independent of height ($r \approx -0.03$).[38] Validation studies suggest that any bias in self-reported BMI is unlikely to affect conclusions about associations in epidemiologic studies, especially those conducted over time.[39–42] In ancillary analyses, correlation coefficients were computed to examine associations between the Wave 1 NESARC BMI data and comparable data from the combined 1999–2002 National Health and Nutrition Examination Survey,[43] which measured actual height and weight by sex, by 5 racial/ethnic groups, and by 4 age groups. Correlations of BMI were 0.76 for healthy weight, 0.85 for overweight, and 0.84 for obesity.

Psychiatric Disorders

The diagnostic interview was the Alcohol Use Disorder and Associated Disabilities Interview Schedule–*DSM-IV* Version (AUDADIS-IV).[44,45] Axis I disorders were assessed identically in the Wave 1 and Wave 2 versions of the AUDADIS-IV except for the time frames. In Wave 1, these time frames were (1) the year preceding the interview and (2) the past, including all but the year preceding the interview. In Wave 2, the time frames were (1) the year preceding the Wave 2 interview and (2) the intervening period, about 2 years, between the Wave 1 interview and the year preceding the Wave 2 interview. Thus, in the Wave 2 interview, the entire time between Waves 1 and 2 was covered for each respondent.

In Waves 1 and 2, *DSM-IV*–specific drug abuse and dependence diagnoses were aggregated to yield diagnoses of any drug abuse and any drug dependence. Mood disorders included *DSM-IV* MDD and bipolar I disorder. Anxiety disorders included *DSM-IV* panic disorder (with and without agoraphobia), social and specific phobias, and generalized anxiety disorder. The AUDADIS-IV methods

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to diagnose these disorders are described in detail elsewhere.[46–51] All AUDADIS-IV mood and anxiety disorder diagnoses excluded disorders that were substance-induced or due to general medical conditions.

Past-year and prior-to-past-year diagnoses of attention-deficit/hyperactivity disorder and posttraumatic stress disorder were assessed in Wave 2 and served only as control variables in the analyses. Lifetime personality disorders (*DSM-IV*) also served as control variables. Personality disorders measured at Wave 1 (described in detail elsewhere[52]) included avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic, and antisocial. Borderline, schizotypal, and narcissistic personality disorders were measured at Wave 2. The importance of controlling for Wave 1 and 2 *other* psychiatric disorders was to adjust for their comorbidity effects with the target psychiatric disorder.

All psychopathology covariates were entered into each model as any mood, any anxiety, or any personality disorder dichotomous variables. The good to excellent test-retest reliability and validity of AUDADIS-IV substance use, mood, anxiety, personality, and attention-deficit/hyperactivity disorder diagnoses are documented in clinical and general population samples.[47–63]

Table 1. Number of Respondents at Risk for Substance Use Disorders, Mood Disorders, and Anxiety Disorders at Wave 1 and 3-Year Incidence of BMI Status During the Follow-Up Period by Sex

Disorder	Number of Respondents at Risk at Wave 1	Incidence During 3-Year Follow-Up Period		
		Healthy Weight, % (SE)	Overweight, % (SE)	Obese, % (SE)
Men				
Substance use disorder				
Alcohol abuse	8,391	8.7 (0.67)	9.0 (0.62)	3.1 (0.20)
Alcohol dependence	11,853	6.1 (0.46)	3.9 (0.30)	3.7 (0.44)
Drug abuse	12,275	3.5 (0.36)	1.6 (0.24)	1.8 (0.35)
Drug dependence	13,777	1.8 (0.29)	0.9 (0.15)	0.8 (0.20)
Mood disorder				
Major depressive disorder	12,893	3.5 (0.30)	2.7 (0.29)	3.5 (0.44)
Bipolar I disorder	13,792	2.0 (0.29)	1.7 (0.22)	1.8 (0.27)
Anxiety disorder				
Panic disorder	13,760	1.4 (0.21)	1.0 (0.16)	1.4 (0.23)
Social phobia	13,631	1.5 (0.22)	1.1 (0.14)	1.5 (0.22)
Specific phobia	13,312	2.2 (0.29)	1.6 (0.20)	1.7 (0.24)
Generalized anxiety disorder	13,836	2.2 (0.26)	1.7 (0.18)	2.5 (0.34)
Women				
Substance use disorder				
Alcohol abuse	15,020	3.9 (0.32)	2.8 (0.32)	2.0 (0.24)
Alcohol dependence	16,772	2.6 (0.25)	1.6 (0.23)	1.8 (0.26)
Drug abuse	16,922	1.4 (0.15)	1.2 (0.19)	1.0 (0.20)
Drug dependence	17,840	0.7 (0.14)	0.6 (0.15)	0.3 (0.11)
Mood disorder				
Major depressive disorder	15,028	5.8 (0.33)	7.0 (0.55)	7.5 (0.50)
Bipolar I disorder	17,535	2.0 (0.20)	1.8 (0.23)	2.8 (0.29)
Anxiety disorder				
Panic disorder	16,991	2.6 (0.26)	2.1 (0.26)	3.0 (0.31)
Social phobia	17,166	1.9 (0.18)	1.6 (0.22)	2.2 (0.28)
Specific phobia	15,951	3.1 (0.30)	3.0 (0.31)	3.1 (0.37)
Generalized anxiety disorder	17,181	4.3 (0.31)	4.1 (0.37)	5.6 (0.48)
Total				
Substance use disorder				
Alcohol abuse	23,411	5.6 (0.33)	6.0 (0.37)	3.9 (0.31)
Alcohol dependence	28,625	4.0 (0.24)	3.0 (0.20)	2.7 (0.25)
Drug abuse	29,197	2.2 (0.18)	1.4 (0.16)	1.4 (0.20)
Drug dependence	31,617	1.1 (0.14)	0.8 (0.11)	0.6 (0.11)
Mood disorder				
Major depressive disorder	27,921	4.8 (0.23)	4.3 (0.27)	5.4 (0.33)
Bipolar I disorder	31,327	2.0 (0.17)	1.7 (0.15)	2.3 (0.20)
Anxiety disorder				
Panic disorder	30,751	2.1 (0.19)	1.4 (0.14)	2.2 (0.19)
Social phobia	30,797	1.7 (0.12)	1.3 (0.13)	1.8 (0.19)
Specific phobia	29,263	2.7 (0.19)	2.2 (0.18)	2.4 (0.21)
Generalized anxiety disorder	31,017	3.4 (0.22)	2.6 (0.19)	4.0 (0.29)

Abbreviation: BMI = body mass index.

Other Covariates

Sociodemographic variables included age, race/ethnicity, marital status, education, income, urbanicity, and region of the country, all of which have been associated with both BMI and psychiatric disorders in past research. Fourteen stressful life events occurring during the year prior to the Wave 1 interview were summed to produce a scale of 0, 1, and 2+ events. Respondents were asked whether a doctor or other health care professional had told them that they had any of 11 medical conditions in the year preceding the Wave 1 interview. The number of medical conditions was summed into a scale of 0, 1, or 2+ conditions.

When substance use and substance use disorders served as covariates, 3-level mutually exclusive variables were constructed for respondents' lifetimes and for the year preceding the Wave 1 interview: (1) no alcohol use/disorder, alcohol use/no alcohol use disorder, and alcohol use disorder; (2) no drug use/disorder, drug use/no drug use disorder, and drug use disorder; and (3) no nicotine use/dependence, nicotine use/no nicotine dependence, and nicotine dependence. For the period between Wave 1 and 2, we used *any* alcohol use, *any other* drug use, and *any* nicotine use as covariates. Whether the respondents were prescribed medication for the target mood or anxiety disorder of interest and for any other mood or anxiety disorder during the follow-up period were also covariates in the multivariable analyses.

Statistical Analyses

To determine the temporal relationship between BMI status and psychopathology, 3 sets of multivariable analyses were conducted separately for men and women. In the first set of multivariable linear logistic regression analyses, BMI status (normal weight, overweight, or obese) was the major exposure variable predicting each first-onset or incident-specific psychiatric disorder occurring during follow-up, controlling for mood, anxiety, and personality disorder comorbidity and alcohol, drug, and nicotine use and disorders at Wave 1 and during the follow-up period, and Wave 1 sociodemographic characteristics, past-year medical conditions, and stressful life events. Incidence rates of first onset were also calculated for each psychiatric disorder, that is, those disorders developing for the first time during the 3-year follow-up across

Table 2. Adjusted Odds Ratios[a] of BMI Status at Wave 1 Predicting Incident *DSM-IV* Substance Use, Mood, and Anxiety Disorders During the Follow-Up Period by Sex

	Men		Women		Total	
Disorder	Overweight vs Healthy Weight, AOR (95% CI)	Obese vs Healthy Weight, AOR (95% CI)	Overweight vs Healthy Weight, AOR (95% CI)	Obese vs Healthy Weight, AOR (95% CI)	Overweight vs Healthy Weight, AOR (95% CI)	Obese vs Healthy Weight, AOR (95% CI)
Substance use disorder[b]						
Alcohol abuse	**1.3 (1.04–1.64)**[c]	0.9 (0.63–1.14)	0.9 (0.72–1.23)	**0.6 (0.45–0.88)**[c]	1.2 (1.00–1.39)	**0.8 (0.61–0.93)**[c]
Alcohol dependence	0.9 (0.70–1.10)	**0.7 (0.52–0.97)**[c]	0.7 (0.50–1.02)	0.7 (0.49–1.06)	0.8 (0.68–1.00)	**0.7 (0.55–0.91)**[c]
Drug abuse	**0.7 (0.44–0.96)**[c]	0.7 (0.41–1.03)	1.1 (0.76–1.63)	0.8 (0.51–1.35)	0.8 (0.59–1.03)	**0.7 (0.51–0.96)**[c]
Drug dependence	0.8 (0.48–1.20)	0.6 (0.30–1.03)	1.2 (0.64–2.07)	**0.4 (0.21–0.91)**[c]	0.8 (0.58–1.22)	**0.5 (0.30–0.80)**[c]
Mood disorder						
Major depressive disorder	0.8 (0.58–1.08)	1.0 (0.69–1.39)	**1.3 (1.02–1.56)**[c]	**1.2 (1.02–1.51)**[c]	1.1 (0.90–1.24)	1.1 (0.95–1.33)
Bipolar I disorder	1.0 (0.66–1.68)	0.9 (0.59–1.40)	0.9 (0.63–1.25)	1.0 (0.71–1.37)	0.9 (0.73–1.23)	0.9 (0.72–1.20)
Anxiety disorder						
Panic disorder	0.8 (0.52–1.26)	1.0 (0.64–1.52)	0.8 (0.60–1.13)	1.0 (0.72–1.37)	0.8 (0.63–1.07)	1.0 (0.75–1.30)
Social phobia	0.8 (0.51–1.32)	1.0 (0.62–1.63)	0.9 (0.67–1.30)	1.0 (0.69–1.38)	0.9 (0.66–1.15)	1.0 (0.72–1.27)
Specific phobia	0.8 (0.55–1.25)	0.8 (0.53–1.29)	1.1 (0.84–1.42)	1.1 (0.79–1.49)	1.0 (0.79–1.17)	1.0 (0.74–1.24)
Generalized anxiety disorder	0.9 (0.65–1.32)	1.9 (0.80–1.80)	0.9 (0.75–1.20)	1.1 (0.83–1.39)	0.9 (0.74–1.13)	1.1 (0.88–1.33)

[a]Odds ratios adjusted for the following: Wave 1 sociodemographic characteristics; other lifetime psychiatric disorders; alcohol, drug, and nicotine use and disorders at Wave 1 and during follow-up; Wave 1 past-year health care provider–diagnosed medical conditions; and past-year stressful life events: moving or acquiring a new roommate; fired/laid off from a job; unemployed and looking for a job for more than a month; trouble with a boss/coworker; changing jobs; separated, divorced, or breaking off a serious relationship; serious problems with neighbor/friend/relative; major financial crisis including bankruptcy; serious trouble with police or the law; something stolen or property intentionally damaged; death of a close friend/family member; physical attack on family member/close friend; and any family member's/close friend's serious trouble with the police or law.
[b]For substance use disorders, Wave 1 lifetime use of the specific target substance is not included as a covariate (eg, lifetime alcohol consumption for incident alcohol abuse and dependence).
[c]Boldface type indicates significance ($P < .05$).
Abbreviations: AOR = adjusted odds ratio, BMI = body mass index.

BMI status categories. Each of these analyses was restricted to individuals at risk for each incident target disorder (ie, those who never had the target psychiatric disorder at Wave 1).

Multinomial logistic regression analyses were also conducted in which each Wave 1 past-year psychiatric disorder served as the major exposure variable, with transitions in BMI status over follow-up as the outcome, controlling for Wave 1 sociodemographic characteristics and Wave 1 past-year mood and anxiety disorders, alcohol and drug use and disorders, medical conditions, and stressful life events, in addition to alcohol and drug use disorder comorbidity, anxiety and mood disorder comorbidity, use of alcohol or drugs, being prescribed medications for the target anxiety or mood disorder, and being prescribed medications for other mood and anxiety disorders during the follow-up period, as well as lifetime personality disorders. The categorical outcome variable, transition in BMI status, was categorized as (1) remaining in the same BMI category from Wave 1 to Wave 2; (2) moving into a lower BMI category; and (3) moving into a higher BMI category. These analyses were also repeated, substituting continuous BMI change variables for the categorical ones, that is, BMI at Wave 2 minus BMI at Wave 1, and conducting multivariable linear regression analyses.

Analyses were conducted on weighted data, and standard errors and 95% confidence intervals were estimated using SUDAAN, Version 10,[64] a software package that adjusted for the design characteristics of the NESARC. All analyses excluded respondents who were pregnant at either Wave 1 or Wave 2 and those who were underweight at Wave 1. Separate analyses were conducted among men and women to (importantly) allow the impact of covariates to vary by gender, a phenomenon observed frequently in other empirical research.

RESULTS

Table 1 shows the numbers of respondents at risk at Wave 1 for each psychiatric disorder during the follow-up and the 3-year incidence of each disorder by Wave 1 BMI status. Incidence rates mirror their prevalence rate counterparts, with substance use disorder incidence being greater among men and mood and anxiety disorders incidences being much greater among women, regardless of BMI status. Table 2 shows prediction of incident substance use, mood, and anxiety disorders during the follow-up period by Wave 1 BMI status, controlling for all covariates. Among men, obesity at baseline decreased the risk of incident alcohol dependence, and being overweight at baseline decreased the risk of incident drug abuse over follow-up. Overweight men at baseline were at increased risk of incident alcohol abuse. Women who were obese at baseline were at decreased risk of incident alcohol abuse and drug dependence. In contrast, overweight or obesity at baseline increased the risk of incident MDD during the follow-up among women.

Table 3 shows percentages of respondents moving into each BMI category during the follow-up. Table 4 shows prediction of BMI categorical transitions over follow-up by Wave 1 past-year *DSM-IV* substance use, mood, and anxiety disorders, controlling for all covariates. Drug dependence at baseline decreased the risk of overweight and obesity among men, whereas specific phobia at baseline decreased the risk of overweight and obesity among women. When the continuous BMI change variables were substituted for the categorical transition variables, drug dependence at baseline predicted a decrease in BMI among men, consistent with the categorical results (Table 5). However, the association

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Table 3. Prevalences of Wave 1 Past-Year *DSM-IV* Substance Use, Mood, and Anxiety Disorders Predicting BMI Transition During the Follow-Up Period by Sex

	Percentages of Respondents With and Without Each Disorder Who…					
	Remained in Same BMI Category, % (SE)		Moved Into Lower BMI Category, % (SE)[a]		Moved Into Higher BMI Category, % (SE)[b]	
Disorder	With Disorder	Without Disorder	With Disorder	Without Disorder	With Disorder	Without Disorder
Men						
Substance use disorder						
Alcohol abuse	76.5 (1.66)	75.8 (0.51)	7.7 (0.96)	8.6 (0.32)	15.8 (1.50)	15.6 (0.40)
Alcohol dependence	72.9 (1.78)	76.0 (0.52)	10.0 (1.26)	8.4 (0.32)	17.1 (1.51)	15.6 (0.41)
Drug abuse	72.9 (3.44)	75.9 (0.51)	10.8 (2.14)	8.4 (0.31)	16.3 (2.85)	15.6 (0.40)
Drug dependence	77.8 (4.79)	75.9 (0.49)	13.9 (4.13)	8.4 (0.30)	8.4 (3.00)	15.7 (0.39)
Mood disorder						
Major depressive disorder	74.4 (2.50)	75.9 (0.51)	7.4 (1.20)	8.5 (0.31)	18.2 (2.23)	15.6 (0.40)
Bipolar I disorder	75.9 (3.31)	75.9 (0.50)	9.4 (2.38)	8.5 (0.31)	14.7 (2.69)	15.7 (0.39)
Anxiety disorder						
Panic disorder	70.6 (3.62)	75.9 (0.50)	8.2 (2.55)	8.5 (0.31)	21.2 (3.45)	15.6 (0.40)
Social phobia	77.8 (2.57)	75.8 (0.50)	8.4 (1.63)	8.5 (0.31)	13.8 (1.99)	15.7 (0.40)
Specific phobia	77.1 (1.95)	75.8 (0.50)	8.3 (1.35)	8.5 (0.31)	14.6 (1.53)	15.7 (0.40)
Generalized anxiety disorder	74.8 (3.59)	75.9 (0.50)	10.7 (2.39)	8.5 (0.31)	14.5 (2.97)	15.7 (0.40)
Women						
Substance use disorder						
Alcohol abuse	78.1 (2.08)	74.9 (0.43)	7.2 (1.52)	9.4 (0.28)	14.8 (1.64)	16.7 (0.40)
Alcohol dependence	73.1 (2.84)	74.0 (0.43)	9.0 (1.65)	9.4 (0.28)	17.9 (2.50)	16.6 (0.39)
Drug abuse	75.8 (5.19)	74.0 (0.42)	10.8 (4.78)	9.4 (0.27)	13.5 (3.47)	16.7 (0.39)
Drug dependence	81.5 (5.08)	74.0 (0.42)	5.2 (2.85)	9.4 (0.28)	13.4 (4.35)	16.6 (0.39)
Mood disorder						
Major depressive disorder	75.7 (1.51)	73.9 (0.45)	9.5 (0.96)	9.4 (0.30)	14.8 (1.33)	16.8 (0.41)
Bipolar I disorder	76.4 (2.47)	73.9 (0.43)	10.2 (1.68)	9.4 (0.28)	13.5 (2.07)	16.7 (0.40)
Anxiety disorder						
Panic disorder	73.7 (2.28)	74.0 (0.43)	9.9 (1.61)	9.4 (0.28)	16.5 (1.97)	16.6 (0.40)
Social phobia	77.0 (2.14)	73.9 (0.43)	9.6 (1.41)	9.4 (0.28)	13.4 (1.60)	16.7 (0.41)
Specific phobia	77.5 (1.16)	73.6 (0.45)	8.9 (0.85)	9.4 (0.29)	13.7 (0.99)	16.9 (0.41)
Generalized anxiety disorder	75.1 (2.50)	74.0 (0.43)	9.5 (1.62)	9.4 (0.29)	15.4 (2.22)	16.7 (0.39)
Total						
Substance use disorder						
Alcohol abuse	76.9 (1.31)	74.8 (0.37)	7.5 (0.79)	9.0 (0.23)	15.6 (1.17)	16.2 (0.29)
Alcohol dependence	73.0 (1.43)	75.0 (0.36)	9.7 (0.98)	8.9 (0.23)	17.3 (1.36)	16.1 (0.29)
Drug abuse	73.8 (2.68)	75.0 (0.36)	10.8 (1.95)	8.9 (0.23)	15.4 (2.21)	16.2 (0.28)
Drug dependence	78.8 (3.66)	74.9 (0.35)	11.3 (3.04)	8.9 (0.22)	9.8 (2.49)	16.2 (0.28)
Mood disorder						
Major depressive disorder	75.3 (1.25)	74.9 (0.38)	8.8 (0.76)	8.9 (0.23)	16.0 (1.13)	16.2 (0.29)
Bipolar I disorder	76.2 (2.08)	74.9 (0.36)	9.8 (1.45)	8.9 (0.23)	14.0 (1.76)	16.2 (0.29)
Anxiety disorder						
Panic disorder	72.7 (1.91)	75.0 (0.36)	9.3 (1.31)	8.9 (0.22)	18.0 (1.72)	16.1 (0.29)
Social phobia	77.3 (1.59)	74.9 (0.36)	9.1 (1.07)	8.9 (0.22)	13.5 (1.20)	16.2 (0.29)
Specific phobia	77.3 (1.03)	74.8 (0.37)	8.7 (0.70)	9.0 (0.24)	14.0 (0.88)	16.3 (0.29)
Generalized anxiety disorder	75.0 (2.02)	74.9 (0.36)	9.9 (1.26)	8.9 (0.23)	15.2 (1.79)	16.7 (0.28)

[a]Moving between Wave 1 and Wave 2 from healthy weight to underweight; overweight to healthy weight or underweight; or obese to overweight, healthy weight, or underweight.
[b]Moving between Wave 1 and Wave 2 from healthy weight to overweight or obese, or from overweight to obese.
Abbreviation: BMI = body mass index.

between specific phobia at baseline and decreased risk of overweight and obesity among women at follow-up was not confirmed.

DISCUSSION

The major finding of this prospective study was that overweight and obesity at baseline predicted an increased risk of incident MDD among women, after controlling for a wide array of covariates. These results are consistent with prior shorter-term prospective studies[31–33] but are at variance with longer-term longitudinal studies.[25–27,30] Two psychosocial models have been posited to explain the temporal relationship from overweight and obesity to subsequent MDD. The self-appraisal perspective posits that stigma toward overweight and obese individuals (especially women) promotes low self-esteem and negative self-image, leading to MDD.[65] Alternatively, the fitting-norms-of-appearance perspective argues that fitting the norm for weight is stressful among the obese because dieting is often unsuccessful, resulting in MDD. Women in Western cultures are generally under more pressure to be thin than are men and experience greater body dissatisfaction, factors that may increase their vulnerability to MDD.[66,67] Other factors explaining the observed directionality of the relationship among women could also, in part, reflect gender differences in access to

Table 4. Adjusted Odds Ratios[a] of Wave 1 Past-Year *DSM-IV*–Specific Substance Use, Mood, and Anxiety Disorders Predicting BMI Transition During the Follow-Up Period by Sex[b]

	Men		Women		Total	
Disorder	Moved Into Lower BMI Category[c] vs Remained in Same BMI Category, AOR (95% CI)	Moved Into Higher BMI Category[d] vs Remained in Same BMI Category, AOR (95% CI)	Moved Into Lower BMI Category[c] vs Remained in Same BMI Category, AOR (95% CI)	Moved Into Higher BMI Category[d] vs Remained in Same BMI Category, AOR (95% CI)	Moved Into Lower BMI Category[c] vs Remained in Same BMI Category, AOR (95% CI)	Moved Into Higher BMI Category[d] vs Remained in Same BMI Category, AOR (95% CI)
Substance use disorder[e]						
Alcohol abuse	1.0 (0.74–1.34)	0.9 (0.75–1.20)	0.8 (0.51–1.35)	0.8 (0.59–1.03)	0.9 (0.74–1.21)	0.9 (0.73–1.07)
Alcohol dependence	1.4 (0.99–1.95)	1.0 (0.78–1.25)	1.1 (0.72–1.69)	1.0 (0.72–1.50)	1.3 (0.98–1.63)	1.0 (0.83–1.26)
Drug abuse	1.4 (0.83–2.22)	0.9 (0.57–1.46)	1.3 (0.47–3.77)	0.7 (0.38–1.25)	1.4 (0.87–2.10)	0.9 (0.59–1.23)
Drug dependence	1.6 (0.78–3.28)	**0.4 (0.19–0.99)**[f]	0.5 (0.16–1.80)	0.8 (0.34–1.69)	1.2 (0.67–2.25)	**0.5 (0.30–0.97)**[f]
Mood disorder						
Major depressive disorder	0.9 (0.60–1.24)	1.1 (0.81–1.57)	1.0 (0.79–1.34)	0.9 (0.68–1.09)	1.0 (0.79–1.21)	0.9 (0.79–1.13)
Bipolar I disorder	1.0 (0.57–1.82)	0.9 (0.58–1.42)	1.1 (0.75–1.71)	0.8 (0.54–1.14)	1.1 (0.76–1.52)	0.8 (0.62–1.14)
Anxiety disorder						
Panic disorder	1.0 (0.48–2.22)	1.4 (0.88–2.12)	1.1 (0.72–1.55)	1.0 (0.77–1.41)	1.0 (0.74–1.45)	1.2 (0.89–1.48)
Social phobia	1.0 (0.63–1.54)	0.8 (0.56–1.16)	1.0 (0.73–1.45)	0.9 (0.64–1.20)	1.0 (0.76–1.30)	0.8 (0.67–1.06)
Specific phobia	1.0 (0.67–1.39)	0.9 (0.69–1.15)	0.9 (0.73–1.16)	**0.8 (0.66–0.95)**[f]	0.9 (0.77–1.14)	**0.8 (0.70–0.96)**[f]
Generalized anxiety disorder	1.3 (0.76–2.23)	1.0 (0.57–1.60)	1.0 (0.67–1.53)	1.0 (0.70–1.47)	1.1 (0.79–1.49)	1.0 (0.73–1.32)

[a]Odds ratios adjusted for Wave 1 sociodemographic characteristics; other Wave 1 past-year psychiatric disorders; Wave 1 past-year alcohol, drug, and nicotine use and disorders; Wave 1 past-year health care provider–diagnosed medical conditions and stressful life events; and any other psychiatric disorder, any alcohol use, any nicotine use, any drug use, and any prescribed medication for the target mood or anxiety disorder or other mood or anxiety disorder during the follow-up period.
[b]Results derived from multinomial logistic regression analyses.
[c]Moving between Waves 1 and 2 from healthy weight to underweight; overweight to healthy weight or underweight; or obese to overweight, healthy weight, or underweight.
[d]Moving between Waves 1 and 2 from healthy weight to overweight or obese, or from overweight to obese.
[e]For analyses of substance use disorders, Wave 2 past-year use of the substance of interest is not included as a covariate (eg, past-year alcohol consumption for prediction of change in BMI status by past-year alcohol abuse and dependence).
[f]Boldface type indicates significance ($P < .05$).
Abbreviations: AOR = adjusted odds ratio, BMI = body mass index.

Table 5. Adjusted[a] Associations of Wave 1 Past-Year *DSM-IV*–Specific Substance Use, Mood, and Anxiety Disorders With Change in BMI During the Follow-Up Period by Sex[b]

Disorder	Adjusted Change in BMI for Men, β (95% CI)	Adjusted Change in BMI for Women, β (95% CI)	Adjusted Change in BMI for Total Group, β (95% CI)
Substance use disorder[c]			
Alcohol abuse	−0.03 (−0.25 to 0.18)	−0.09 (−0.41 to 0.24)	−0.07 (−0.24 to 0.11)
Alcohol dependence	−0.29 (−0.57 to 0.02)	0.31 (−0.07 to 0.70)	−0.09 (−0.31 to 0.13)
Drug abuse	−0.32 (−0.81 to 0.17)	−0.07 (−0.75 to 0.60)	−0.22 (−0.61 to 0.16)
Drug dependence	**−0.62 (−1.18 to −0.06)**[d]	−0.32 (−1.45 to 0.81)	−0.50 (−1.02 to 0.01)
Mood disorder			
Major depressive disorder	0.19 (−0.09 to 0.48)	−0.10 (−0.36 to 0.17)	0.01 (−0.19 to 0.21)
Bipolar I disorder	−0.09 (−0.52 to 0.34)	−0.21 (−0.63 to 0.21)	−0.15 (−0.47 to 0.17)
Anxiety disorder			
Panic disorder	0.34 (−0.16 to 0.84)	−0.15 (−0.53 to 0.22)	0.01 (−0.29 to 0.30)
Social phobia	−0.08 (−0.35 to 0.18)	−0.23 (−0.55 to 0.09)	−0.17 (−0.39 to 0.06)
Specific phobia	−0.10 (−0.32 to 0.13)	−0.04 (−0.22 to 0.14)	−0.06 (−0.21 to 0.08)
Generalized anxiety disorder	−0.16 (−0.56 to 0.25)	−0.23 (−0.61 to 0.15)	−0.20 (−0.49 to 0.08)

[a]Mean change in BMI between Waves 1 and 2 associated with Wave 1 past-year prevalence of index disorder, adjusted for Wave 1 sociodemographic characteristics; other Wave 1 past-year psychiatric disorders; Wave 1 past-year alcohol, drug, and nicotine use and disorders; Wave 1 past-year health care provider–diagnosed medical conditions and stressful life events; and any other psychiatric disorder, any alcohol use, any nicotine use, any drug use, and any prescribed medication for the target mood or anxiety disorder or other mood or anxiety disorder during the intervening period between Waves 1 and 2.
[b]Results derived from multiple linear regression analyses.
[c]For analyses of substance use disorders, Wave 2 past-year use of the substance of interest is not included as a covariate (eg, past-year alcohol consumption for prediction of change in BMI status by past-year alcohol abuse and dependence).
[d]Boldface type indicates significance ($P < .05$).
Abbreviation: BMI = body mass index.

health care and treatment preferences,[68] differential reporting of atypical features (eg, increased appetite, weight gain) of MDD, and biological factors, including genetic variation in susceptibility to both overweight and obesity and MDD.[69] Furthermore, these results could be due to gender differences in high-fat dietary intake, sedentary lifestyle, sleep deprivation, and vulnerability to stress that could contribute to the development of obesity, possibly through alterations in the hypothalamic-pituitary-adrenal axis.[70]

Although this study's results on BMI status and MDD are not conclusive regarding mechanisms underlying the relationships, these findings do suggest a unidirectional

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relationship between overweight and obesity and subsequent MDD among women. However, the disparity in results between prospective studies of child and adolescent samples that found unidirectional relationships between MDD and overweight and obesity, and short-term studies of older samples in which baseline obesity predicted later MDD, is intriguing in suggesting that the directionality of the relationship may vary over the life course. In many respects, both overweight and obesity and psychiatric disorders are results of life-long interactions between biological and psychological risk and protective factors, and long-term studies beginning in childhood are warranted.

With respect to substance use disorders, overweight men had a decreased risk of drug abuse and obese men had a decreased risk of alcohol dependence at follow-up, whereas obese women had a decreased risk of alcohol abuse and drug dependence during the follow-up. Among men, drug dependence lowered the odds of transitioning into a higher BMI category. The finding that overweight and obesity at baseline generally appear protective, decreasing the risk of later substance use disorders, has been observed in several cross-sectional studies.[21,22] These findings are consistent with research suggesting that neural circuits in the brain serving the functions of desiring, seeking, procuring, and consuming food, ethanol, and other psychoactive substances may overlap.[71] Overeating may compete with substances of abuse for brain reward sites, resulting in reduced substance intake and lower probabilities of developing substance use disorders among the overweight and obese.[72,73]

In this study, drug dependence at baseline lowered the risk of overweight and obesity during follow-up among men. Drug-dependent individuals may neglect their physical health, including appropriate caloric intake, while procuring, using, and recovering from the adverse effects of substances.[74] Drug dependence may disrupt eating habits, nutrient absorption, and metabolism through associated physical morbidities including gastritis, pancreatitis, and hepatitis.[75,76] Why this relationship was observed only among men may reflect the much greater prevalences of drug dependence among men relative to women in the general population.

With 1 exception, anxiety disorders did not predict later overweight or obesity, and baseline overweight and obesity did not predict any anxiety disorders during follow-up, results at variance with the few cross-sectional epidemiologic surveys[8,14,18–22] that examined anxiety disorders. Also inconsistent with prior research[19,20,22] was the puzzling relationship observed among women between specific phobia at baseline and decreased risk of overweight or obesity during follow-up, a result not replicated when continuous BMI change served as the outcome measure. Nonetheless, the extraordinary fear, anxiety, and avoidance of phobic stimuli among individuals with specific phobia can significantly interfere with social and occupational functioning and eating habits, including undereating.[34] However, the cardinal feature of excessive anxiety is common to most anxiety disorders, all of which were not shown to reduce the risk of overweight or obesity during the follow-up. Future research is warranted to determine what, if any, characteristics of specific phobia confer protection against subsequent overweight or obesity among women.

This study has limitations common to most large-scale surveys. First, because NESARC samples only households and group quarters and those 18 years of age and older, information on adolescents and the homeless was unavailable. Second, the BMI measure was self-reported. However, self-reported BMI has been shown to yield valid results in epidemiologic surveys, and correlations between the NESARC and NHANES BMI data were strong.

Despite these limitations, the observed temporal relationships between overweight and obesity and MDD among women and between drug dependence and overweight and obesity among men have strong clinical and public health implications. The temporal relationship between overweight and obesity and MDD may presage increases in MDD among women, given that the epidemics of overweight and obesity are predicted to increase in the United States. Accordingly, overweight and obese women should be monitored for MDD by primary care physicians and other health professionals and targeted for weight reduction interventions to prevent incident MDD. Given the lack of effective treatments for obesity, however, more research is needed to test specific interventions targeting overweight and obesity among women, especially those with MDD. Foremost, there is an urgent need to update treatment guidelines for MDD to address the management of overweight and obesity. Similarly, nutritional counseling may be warranted for men with drug dependence.

With regard to research implications, this study revealed important gender differences in the temporal relationships between overweight and obesity and specific psychiatric disorders. Identification of additional psychosocial and biological factors impacting on these relationships within a long-term longitudinal study commencing in early childhood is urgently needed.

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