Published in final edited form as:
Int J Obes (Lond). 2012 April ; 36(4): 595–602. doi:10.1038/ijo.2011.111.

Bidirectional Association between Depression and Obesity in Middle-aged and Older Women

Dr. An Pan, PhD, **Dr. Qi Sun, MD, ScD**, **Dr. Sébastien Czernichow, MD, PhD**, **Dr. Mika Kivimaki, PhD**, **Dr. Olivia I. Okereke, MD, SM**, **Dr. Michel Lucas, PhD**, **Dr. JoAnn E. Manson, MD, DrPH**, **Dr. Alberto Ascherio, MD, DrPH**, and **Dr. Frank B. Hu, MD, PhD**
Department of Nutrition (Drs Pan, Sun, Lucas, Ascherio, Hu) and Epidemiology (Drs Okereke, Manson, Ascherio, and Hu), Harvard School of Public Health, 655 Huntington Avenue, Boston, MA 02115, United States; Channing Laboratory (Drs Sun, Okereke, Ascherio, and Hu) and Division of Preventive Medicine (Drs Manson), Department of Medicine, and Department of Psychiatry (Dr Okereke), Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, United States; Department of Public Health, Hôpital Avicenne and University Paris 13 (Dr Czernichow); Nutritional Epidemiology Research Unit – UMR (INSERM U557, INRA, CNAM, UP13), Faculté SMBH. 74, rue Marcel Cachin 93017 Bobigny, France; Department of Epidemiology and Public Health (Dr Kivimaki), University College London, London WC1E 6BT, United Kingdom

Abstract

Objective—Although it has been hypothesized that the depression-obesity relation is bidirectional, few studies have addressed this hypothesis in a prospective setting. We aimed to examine the bidirectional relationship in middle-aged and elderly women.

Subjects—A total of 65,955 women aged 54–79 years in the Nurses' Health Study were prospective followed from 1996 to 2006 with updated information on body weight, depression status and various covariates every two years. Depression was defined as self-report of physician-diagnosed depression and/or antidepressant use. Obesity was defined as a body mass index ≥30.0 kg/m^2. The first three waves (1996–2000) were used as the baseline period, and the last three waves (2002–2006) were used as the follow-up period.

Results—After adjusting for baseline age, physical activity, comorbidities, body mass index (BMI) and other covariates, depression at the baseline period was associated with an increased risk of obesity at the follow-up period in all women (multivariate-adjusted odds ratio [OR], 1.38; 95% CI, 1.24–1.53) and baseline non-obese women (OR, 1.51; 95% CI, 1.36–1.67). In the opposite direction, after adjusting for baseline age, physical activity, comorbidities, depression status and other covariates, obese women at baseline had a moderately increased risk of depression at the follow-up period compared with normal weight women (OR, 1.11; 95% CI, 1.03–1.18); and this association was similar for new onset of depression (OR for obese vs. normal weight women, 1.10; 95% CI, 1.02–1.20).

Conclusions—Our results suggest a bidirectional association between depression and obesity in middle-aged and elderly women. Future studies are needed to confirm our findings in different populations, and investigate the potential mechanisms underlying this association. Our results underscore the importance of early detection and proper behavioral modifications to lower the burden of both conditions.

*Corresponding Author: Frank B. Hu, MD, PhD., Phone: 617 432 0113; Fax: 617 432 2435. frank.hu@channing.harvard.edu.

Conflict of Interest
The authors declare no conflict of interest.

Keywords

obesity; depression; prospective cohort study

INTRODUCTION

Obesity has reached epidemic proportions globally. According to the World Health Organization estimation, approximately 1.5 billion adults (age 20 years or older) were overweight (body mass index [BMI] 25.0 to 29.9 kg/m^2), among which more than 200 million men and nearly 300 million women were obese (BMI ≥30 kg/m^2).[1] Depression is also a major public health problem globally and will rank the second of the disease burden by 2030.[2] The lifetime incidence of depression was over 16% in the general population.[3] Furthermore, recent prescription statistics suggest that antidepressant medication (ADM) is currently one of the most commonly prescribed classes of medications in outpatient medical practices.[4,5,6] Because both depression and obesity confer an increased risk for adverse health outcomes, such as type 2 diabetes,[7,8] cardiovascular disease[9,10] and premature death,[11,12] the association between the two conditions deserves careful examination.

Meta-analyses and systematic reviews of cross-sectional studies have suggested that depression and obesity are associated with each other.[13,14] However, cross-sectional evidence does not provide detailed insight into the temporal relationship between the two conditions. Recently, several longitudinal studies were conducted, and a meta-analysis suggested a reciprocal link between depression and obesity.[15] Nevertheless, this conclusion was based on unadjusted results. In addition, in most studies, assessments of depression were undertaken at only one point in time. Furthermore, only two studies have simultaneously investigated the bidirectional association between depression and obesity, with inconsistent results.[16,17] Therefore, we examined the bidirectional relationship between depression and obesity by taking advantage of repeated measurements of BMI and numerous lifestyle risk factors and health conditions (including depression) during 10 years of follow-up in the Nurses' Health Study (NHS) cohort.

SUBJECTSAND METHODS

Study Population

The NHS cohort was established in 1976 when 121,700 female registered nurses aged 30–55 years residing in 11 states of the U.S. responded to a mailed questionnaire regarding their medical history and health practices. The cohort has been followed every 2 years with mailed questionnaires that update exposure information and inquire about newly diagnosed medical illnesses. Details have been published elsewhere.[18,19] Total follow-up rate for the cohort exceeds 90%. In the current analysis, data as of the year 2000 questionnaire in NHS (n=94,793) was used as the baseline, because physician-diagnosed depression information was available from this year. Participants were excluded if they had missing information on depression measures (n=28,546) or BMI (n=292) throughout the study (1996–2006). After exclusion, a total of 65,955 women were included in the current analysis. Participants excluded from the analysis had similar BMI levels, but were more likely to have comorbidities (diabetes, heart disease and stroke) compared with women included in the analysis (Supplemental Table 1). The study flow is shown in Supplemental Figure 1. The study protocol was approved by the institutional review boards of Brigham and Women's Hospital and Harvard School of Public Health.

Depression Measurement

ADM use and physician-diagnosed depression were used as measures of depression. Regular ADM use during the past two years was first assessed in 1996. This information was updated biennially. The nurses were also asked whether they ever (1996 or before, 1997–1998, 1999, 2000 or after) had physician-diagnosed depression in year 2000 questionnaire. This information was also updated biennially. Therefore, depression was defined as reporting a physician-diagnosed depression and/or using ADM.

Assessment of Overweight and Obesity

Weight and height were collected on the questionnaire in 1976, and weight was further requested every two years thereafter. Self reported weight was highly correlated (r= 0.96) with measured weight in a previous validation study in 184 participants.[20] We calculated the BMI as weight in kilograms divided by the square of height in meters (kg/m^2) to measure overall obesity, and used 25.0 and 30.0 kg/m^2 as the cut-off points to define normal weight, overweight and obesity, respectively.[21]

Covariates

In the biennial follow-up questionnaires, we inquired and updated information on menopausal status and menopausal hormone use, lifestyle factors, such as cigarette smoking and physical activity, as well as a history of chronic diseases, including diabetes, hypertension, hypercholesterolemia, cardiovascular disease and cancer. Dietary information (including alcohol intake) was assessed using a validated semi-quantitative food frequency questionnaire every four years,[22] and a western dietary pattern was derived by using factor analysis to characterize the usual dietary pattern.[23] Marital status and living status were updated every four years.

Statistical Analysis

Information from the first three waves (1996–2000) was used as the baseline period, and information from the last three waves (2002–2006) was used as the follow-up period. Because our two objectives required different population samples, we hereby described analytic samples and procedures separately.

Baseline Depression Status and Risk of Overweight/Obesity (Analysis 1)— Average BMI of the three waves during the follow-up period was used as the outcome, and missing data were replaced by available BMI value in the follow-up period. Women were excluded if they did not report their body weights in any of the three waves. Depression status during the baseline period was used as the exposure, and it was defined as currently reporting or having a history of physician-diagnosed depression and/or regular use of ADMs at least in one of the baseline questionnaires. We further classified participants into four groups: no depression; physician-diagnosed depression without ADM use; ADM use but without reporting physician-diagnosed depression; physician-diagnosed depression and ADM use. Multinomial logistical regression models with their 95% confidence intervals (95% CIs) were used with BMI as a categorical variable (normal weight, overweight, and obesity). To evaluate the temporal association between depression and obesity, we also restricted the analysis to participants with normal weight or overweight at baseline.

Baseline BMI Status and Risk of Depression (Analysis 2)—Average BMI during the baseline period was used as the exposure, and depression status during the follow-up period was used as the outcome. A participant was defined as a case if she reported physician-diagnosed depression or ADM use at least in one of the follow-up questionnaires. Logistical regression models (95% CIs) were used with depression (yes/no) as the dependent

variable, and BMI was used as the independent variable and modeled as a categorical variable (normal weight, overweight, and obesity). We also restricted the analysis to participants free of depression at baseline to assess the association between overweight/obesity with new onset of depression.

In both analyses 1 and 2, we adjusted for age (5-year category), ethnicity (whites, non-whites), marital status (currently having spouse or not), living status (living alone or not), menopausal status (premenopausal or postmenopausal) and postmenopausal hormone use (never, past or current use), smoking status (never, past, or current smoking of 1–14, 15–24, or ≥25 cigarettes/d), alcohol intake (0, 0.1–4.9, 5.0–14.9, ≥15 g/d), physical activity (<3, 3–8.9, 9–17.9, 18–26.9, ≥27 Metabolic Equivalent-hours/week), and quintile of total energy intake and Western dietary pattern. We further adjusted for major comorbidities (diabetes, hypertension, hypercholesterolemia, heart disease, stroke and cancer). In the final model, we further adjusted for baseline average BMI (analysis 1) or baseline depression status (analysis 2). These factors can be categorized as personal characteristics, lifestyle information, and comorbidities, and these factors are widely considered to be important determinants of risks for depression and/or obesity. In both analyses, BMI was also used as a continuous instead of a categorical variable to examine whether the results were sensitive to the predetermined BMI cut-off point. The statistical analysis was performed with SAS version 9.1 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Baseline Depression Status and Risk of Overweight/Obesity

Table 1 summarizes the characteristics of the participants in NHS by baseline depression status as of 2000. At baseline, 18.0% participants reported a history of depression. Compared with participants free of depression, those with depression were slightly younger, more likely to have a higher BMI level, to have a history of smoking or menopausal hormone use, to adopt a western dietary pattern, to live alone and be unmarried, and less likely to be physically active. Participants with depression had a higher prevalence of comorbidities (diabetes, hypertension, hypercholesterolemia, heart disease, stroke and cancer) compared with their non-depressed counterparts.

Depression was associated with increased odds of overweight and obesity (Table 2). Compared with non-depressed women, the age-adjusted ORs (95% CIs) were 1.19 (1.13–1.24) for overweight, and 1.82 (1.73–1.92) for obesity. The ORs were attenuated after adjustment for covariates including comorbidities, and the ORs were 1.09 (1.03–1.14) for overweight, and 1.44 (1.36–1.53) for obesity, respectively. The associations did not materially change with further adjustment for baseline obesity status. When treating BMI as a continuous variable, the mean difference of BMI between women with and without depression during the follow-up period was 0.74 (95% CI, 0.65–0.84) kg/m^2 before controlling for baseline BMI category, and was 0.29 (95% CI, 0.24–0.35) kg/m^2 after including baseline BMI category in the model.

We further categorized the participants with depression into three groups: women with only reported physician-diagnosed depression, women with only ADM use, and women with both physician-diagnosed depression and ADM use. In the fully adjusted multinomial logistical model, the combination of both physician-diagnosed depression and ADM use was associated with an increased risk of overweight (OR, 1.14; 95% CI, 1.03–1.26) and obesity (OR, 1.61; 95% CI, 1.40–1.85).

We further investigated the temporal association between depression and incident overweight or obesity in this cohort (Table 3). In non-obese women at baseline, the

multivariate-adjusted OR of becoming obesity during the follow-up was 1.51 (95% CI, 1.36–1.67). Among normal weight women at baseline, the multivariate-adjusted OR of becoming overweight/obesity during the follow-up was 1.20 (95% CI, 1.15–1.26).

Baseline BMI and Risk of Depression

Table 1 also summarizes the characteristics of the participants by baseline BMI categories. The prevalence of overweight and obesity was 35.2% and 21.4%, respectively. Compared to women with normal weight, overweight or obese individuals were less likely to be physically active and to have a history menopausal hormone use, and more likely to be unmarried, to show a western dietary pattern and to have a higher prevalence of comorbidities (hypertension, hypercholesterolemia, diabetes, and heart disease) and depression.

Overweight and obesity were associated with an increased risk of reporting depression during the follow-up period in age-adjusted model (Table 4). The age-adjusted ORs (95% CIs) of depression were 1.16 (1.11–1.21) for overweight and 1.63 (1.56–1.71) for obesity compared with normal weight. The ORs were attenuated after adjustment for covariates including comorbidities, and were 1.04 (1.00–1.09) for overweight, and 1.28 (1.22–1.35) for obesity, respectively. Further adjustment for baseline depression status attenuated the association with overweight (OR, 1.00; 95% CI, 0.95–1.06), and obesity (OR, 1.11; 95% CI, 1.03–1.18). When treating BMI as a continuous variable in analysis 2, a 5 kg/m^2 increase of BMI was associated with an 11% (95% CI, 9%–13%) and 4% (95% CI, 2%-7%) increased risk of depression before and after including baseline depression status in the model, respectively.

We further analyzed the association between overweight/obesity and new-onset depression (Table 4). In women without history of depression at baseline, obesity was associated with a moderately increased risk of depression onset at follow-up (OR, 1.10; 95% CI, 1.02–1.20), but overweight was not associated with depression risk (OR, 1.00; 95% CI, 0.94–1.07).

DISCUSSION

Results from this well-characterized cohort of about 66,000 U.S. women provide evidence that the association between depression and obesity is bidirectional. Depression was associated with a significant increased risk of being obese at follow-up, and this association was more remarkable in women with both physician-diagnosed depression and ADM use. The converse analysis showed that baseline obesity was also associated with a moderately increased risk of being depressed at follow-up. Both associations were only partially explained by lifestyle factors and baseline comorbidities.

To our knowledge, only two previous studies investigated the bidirectional association between depression and obesity in a prospective setting, and the results were inconsistent. Roberts et al.[16] found in a sample of 1,886 US middle-aged and elderly men and women that obesity at baseline was associated with an increased risk of depressed mood 5 years later (OR, 1.53; 95% CI, 0.99–2.38), while the other temporal direction of this association was not significant (OR, 1.17; 95% CI, 0.64–2.15). However, Kivimaki et al.[17] found in 4,154 British men and women with 19 years of follow-up that common mental disorders, measured by the 30-item General Health Questionnaire (which focuses on self-reported symptoms of anxiety and depression), were associated with an increased risk of future obesity, but obesity at baseline did not predict onset of these disorders among participants free of them at baseline. Both studies relied on self-reported questionnaires to define mental health status, and the sample sizes were relatively small. In addition, the first study

contained two waves of measurements, the second study included four waves, while neither of them defined mental health outcome based on repeated measurements.

Overall, our results are consistent with a recent meta-analysis on the bidirectional association between depression and obesity. Luppino et al.[15] pooled unadjusted data from 15 cohorts and found that baseline depression was associated with an increased risk of developing obesity (OR, 1.58; 95% CI, 1.33–1.87), baseline obesity increased the risk of depression occurrence (OR, 1.55; 95% CI, 1.22–1.98), and the association between depression and overweight was null. A subanalysis found the effect of obesity on the development of depression was stronger in the U.S. than non-U.S. studies, and was stronger for depressive disorder than for depressive symptoms.[15] However, only 4 studies in the meta-analysis adjusted for various covariates, and the association was attenuated for the adjusted association between depression and overweight in either direction,[15] which was consistent with our findings. Nevertheless, some of the covariates could be on the causal pathway of the association between depression and obesity, such as physical activity and comorbidities; therefore, the adjusted results might underestimate the true relation. Notably, our sample size (n=65,955) was larger than all the previous cohorts combined (total n= 7196 for analysis of obesity as the outcome and 55,387 for analysis of depression as the outcome).[15] Therefore, our results provide further evidence that this reciprocal association was partially explained by lifestyle factors and comorbidities. The present analysis is also consistent with our previous publication in the same cohort, where we found a reciprocal association between depression and type 2 diabetes,[18] a condition strongly related to elevated BMI levels.

There are several plausible explanations for the association between depression and an increased risk of overweight and obesity. Depression may be associated with poor health behaviors (*i.e.*, poor diet or over-eating, physical inactivity, sleep disturbance), which might increase the risk of obesity. Moreover, depressed women had a higher prevalence of various comorbidities, and these physical limitations might also be associated with weight gain and obesity. Although we controlled for a large number of health behavior factors and other medical conditions, unmeasured and residual confounding is still possible. Furthermore, weight gain is a common side effect in long-term treatment with most ADMs.[24,25] In a large nested case-control study with a 4-year follow-up,[26] users of ADMs (different types) were found to gain significantly more weight than non-users. Finally, depression is associated with dysregulation of the hypothalamic–pituitary–adrenal axis, which may be involved in the link between depression and obesity.[27]

In the analysis of the opposite temporal association, we found that obesity was associated with a moderately increased risk of depression. This is in agreement with a recent Mendelian Randomization study which found the fat mass and obesity-associated *FTO* genotype to be positively associated with obesity and common mental disorders and that long-term obesity, based on gene-instrumented analysis, was associated with increased likelihood of symptoms of depression and anxiety.[28] However, that finding was not replicated by another Mendelian randomization analysis on obesity and psychological distress.[29]

There are several plausible explanations for the association of obesity with future depression. First, the stigma toward obese may cause obese individuals to suffer from lower self-esteem and negative images, potentially leading to higher levels of depression.[30] Ross also proposed the “fitting-appearance-norms hypothesis”, and argued that “for those who are obese, fitting the norm for weight is stressful because dieting is stressful rather than obesity *per se*”.[30] This may be particularly true when weight control is not successful, which is commonly the case.[31,32] Furthermore, obesity was associated with physical inactivity and various chronic disorders, which could also increase the risk of depression.[33]

Strengths and Limitations

Strengths of the current study include the large sample size, long-term follow-up, and biennially updated information on the exposure and outcome, disease onset and lifestyle risk factors. We used information from three separate repeated measures as the baseline period and three repeated measurements as the follow-up period, which is likely to decrease substantially the potential measurement error and misclassification associated with single measure. A sensitivity analysis of using only one single measure as baseline (2000) or follow-up (2006) revealed similar results (data not shown).

This study also has limitations. First, our study population primarily consisted of middle-aged and elderly white nurses. Although the homogeneity of our study participants led to less confounding by socioeconomic status, the generalizability to other populations, particularly men, and other racial/ethnic minorities, may be limited. However, a previous meta-analysis did not find a significant gender difference in either direction of associations.[15] Second, information of physician-diagnosed depression and antidepressants use was self-reported. However, using this joint information on self-reported diagnosis and ADMs to classify depression status, we identified lifetime prevalence of depression in our cohort that was highly comparable to the age/gender-specific prevalence reported in a population-based study that used face-to-face diagnostic interviews.[34] Nevertheless, the self-reported depression measure, if under-reported, was more likely to attenuate the observed association between obesity and depression. Moreover, antidepressants can be used for other conditions, such as anxiety disorders, insomnia, neuropathic pain,[3] and premenstrual syndrome[35] and hot flushes[36] in women, and we did not have information on dose and duration of ADM use. Thus, although including ADM use as a component of depression definition increased the sensitivity of case detection, the specificity may be slightly lower. However, the results did not change if we only used physician-diagnosed depression as the case definition (data not shown). Finally, a large proportion of participants were excluded from the analysis because of missing information on ADM use. Although baseline characteristics between women who remained in the analysis and those who were excluded did not differ appreciably (Supplemental Table 1), selection bias and surveillance bias could not be fully excluded.

CONCLUSIONS

The results from this large well-established long-term cohort study suggest a bidirectional association between depression and obesity in middle-aged and elderly women. Given that both conditions are highly prevalent in the U.S. and globally, and that they are major risk factors for chronic diseases and premature death, our findings have significant public health importance. In the clinical settings, care providers need to monitor the body weight in depressed patients and also mood status in obese individuals. For the general public, individuals with depression need to pay attention to their body weight changes, and people with obesity should be watchful for depressive symptoms. The reciprocal association between depression and obesity calls for early detection and the development of prevention and treatment strategies that can eventually lower the risk of both conditions. In addition, future studies are still needed to confirm our findings in different populations, and to investigate specific mechanisms through which depression and obesity may interact.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding/Support

The study was supported by the National Institutes of Health grant (DK58845). Dr Ascherio received a grant from the National Alliance for Research on Schizophrenia & Depression (Project ID: 5048070-01). Dr. Sun was supported by a career development award K99HL098459 from the National Heart, Lung, and Blood Institute. Dr Lucas received a postdoctoral fellowship from the Fonds de recherche en santé du Québec (FRSQ). Dr Kivimaki is supported by the NIH (HL036310-20A2 from National Heart, Lung, and Blood Institute and AG034454 from National Institute of Aging) and the BUPA Foundation, UK. Dr. Okereke was supported by the NIH (career development award K08AG029813 from National Institute of Aging, and R01MH091448 from the National Institute of Mental Health). The funding sources did not involve in the data collection, data analysis, manuscript writing and publication.

We are indebted to the participants in the Nurses' Health Study for their continuing outstanding support and colleagues working in these studies for their valuable help.

References

1. World Health Organisation. [Accessed March 9, 2011] Obesity and overweight. WHO Fact Sheet No 311. Available from: http://www.who.int/mediacentre/factsheets/fs311/en/
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 2006; 3:e442. [PubMed: 17132052]
3. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003; 289:3095–3105. [PubMed: 12813115]
4. Olfson M, Marcus SC. National Patterns in Antidepressant Medication Treatment. Arch Gen Psychiatry. 2009; 66:848–856. [PubMed: 19652124]
5. Cherry DK, Woodwell DA, Rechtsteiner EA. National Ambulatory Medical Care Survey: 2005 summary. Advance Data. 2007; 387:1–39. [PubMed: 17703793]
6. Middleton K, Hing E, Xu J. National Hospital Ambulatory Medical Care Survey: 2005 outpatient department summary. Advance Data. 2007; 389:1–34. [PubMed: 17784724]
7. Mezuk B, Eaton WW, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: a meta-analysis. Diabetes Care. 2008; 31:2383–2390. [PubMed: 19033418]
8. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001; 345:790–797. [PubMed: 11556298]
9. Van der Kooy K, van Hout H, Marwijk H, Marten H, Stehouwer C, Beekman A. Depression and the risk for cardiovascular diseases: systematic review and meta analysis. Int J Geriatr Psychiatry. 2007; 22:613–626. [PubMed: 17236251]
10. Bogers RP, Bemelmans WJ, Hoogenveen RT, Boshuizen HC, Woodward M, Knekt P, et al. Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels: a meta-analysis of 21 cohort studies including more than 300 000 persons. Arch Intern Med. 2007; 167:1720–1728. [PubMed: 17846390]
11. Cuijpers P, Smit F. Excess mortality in depression: a meta-analysis of community studies. J Affect Disord. 2002; 72:227–236. [PubMed: 12450639]
12. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess Deaths Associated With Underweight, Overweight, and Obesity. JAMA. 2005; 293:1861–1867. [PubMed: 15840860]
13. Atlantis E, Baker M. Obesity effects on depression: systematic review of epidemiological studies. Int J Obes (Lond). 2008; 32:881–891. [PubMed: 18414420]
14. de Wit L, Luppino F, van Straten A, Penninx B, Zitman F, Cuijpers P. Depression and obesity: a meta-analysis of community-based studies. Psychiatry Res. 2010; 178:230–235. [PubMed: 20462641]
15. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry. 2010; 67:220–229. [PubMed: 20194822]

16. Roberts RE, Deleger S, Strawbridge WJ, Kaplan GA. Prospective association between obesity and depression: evidence from the Alameda County Study. Int J Obes Relat Metab Disord. 2003; 27:514–521. [PubMed: 12664085]

17. Kivimaki M, Lawlor DA, Singh-Manoux A, Batty GD, Ferrie JE, Shipley MJ, et al. Common mental disorder and obesity: insight from four repeat measures over 19 years: prospective Whitehall II cohort study. BMJ. 2009; 339:b3765. [PubMed: 19808765]

18. Pan A, Lucas M, Sun Q, van Dam RM, Franco OH, Manson JE, et al. Bidirectional association between depression and type 2 diabetes mellitus in women. Arch Intern Med. 2010; 170:1884–1891. [PubMed: 21098346]

19. Pan A, Lucas M, Sun Q, van Dam RM, Franco OH, Willett WC, et al. Increased mortality risk in women with depression and diabetes mellitus. Arch Gen Psychiatry. 2011; 68:42–50. [PubMed: 21199964]

20. Willett W, Stampfer MJ, Bain C, Lipnick R, Speizer FE, Rosner B, et al. Cigarette smoking, relative weight, and menopause. Am J Epidemiol. 1983; 117:651–658. [PubMed: 6859020]

21. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organization Technical Report Series. 1995; 854:1–452. [PubMed: 8594834]

22. Feskanich D, Rimm EB, Giovannucci EL, Colditz GA, Stampfer MJ, Litin LB, et al. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. J Am Diet Assoc. 1993; 93:790–796. [PubMed: 8320406]

23. Fung TT, Schulze M, Manson JE, Willett WC, Hu FB. Dietary patterns, meat intake, and the risk of type 2 diabetes in women. Arch Intern Med. 2004; 164:2235–2240. [PubMed: 15534160]

24. Zimmermann U, Kraus T, Himmerich H, Schuld A, Pollmacher T. Epidemiology, implications and mechanisms underlying drug-induced weight gain in psychiatric patients. J Psychiatr Res. 2003; 37:193–220. [PubMed: 12650740]

25. Sussman N, Ginsberg DL, Bikoff J. Effects of nefazodone on body weight: a pooled analysis of selective serotonin reuptake inhibitor- and imipramine-controlled trials. J Clin Psychiatry. 2001; 62:256–260. [PubMed: 11379839]

26. Kivimaki M, Hamer M, Batty GD, Geddes JR, Tabak AG, Pentti J, et al. Antidepressant Medication Use, Weight Gain and Risk of Type 2 Diabetes Mellitus: A Population-based Study. Diabetes Care. 2010; 33:2611–2616. [PubMed: 20823343]

27. Bornstein SR, Schuppenies A, Wong ML, Licinio J. Approaching the shared biology of obesity and depression: the stress axis as the locus of gene-environment interactions. Mol Psychiatry. 2006; 11:892–902. [PubMed: 16880826]

28. Kivimäki M, Jokela M, Hamer M, Geddes J, Ebmeier K, Kumari M, et al. Examining Overweight and Obesity as Risk Factors for Common Mental Disorders Using Fat Mass and Obesity-Associated (FTO) Genotype-Instrumented Analysis. Am J Epidemiol. 2011; 173:421–429. [PubMed: 21248310]

29. Lawlor DA, Harbord RM, Tybjaerg-Hansen A, Palmer TM, Zacho J, Benn M, et al. Using genetic loci to understand the relationship between adiposity and psychological distress: a Mendelian Randomization study in the Copenhagen General Population Study of 53,221 adults. J Intern Med. 2011 e-pub ahead of print 6 January 2011. 10.1111/j.1365-2796.2011.02343.x

30. Ross CE. Overweight and depression. Journal of Health and Social Behavior. 1994; 35:63–79. [PubMed: 8014430]

31. Brownell KD, Wadden TA. Etiology and treatment of obesity: understanding a serious, prevalent, and refractory disorder. J Consult Clin Psychol. 1992; 60:505–517. [PubMed: 1506499]

32. Jeffery RW, Drewnowski A, Epstein LH, Stunkard AJ, Wilson GT, Wing RR, et al. Long-term maintenance of weight loss: current status. Health Psychol. 2000; 19:S5–S16.

33. Huang CQ, Dong BR, Lu ZC, Yue JR, Liu QX. Chronic diseases and risk for depression in old age: A meta-analysis of published literature. Ageing Res Rev. 2010; 9:131–141. [PubMed: 19524072]

34. Steffens DC, Skoog I, Norton MC, Hart AD, Tschanz JT, Plassman BL, et al. Prevalence of Depression and Its Treatment in an Elderly Population: The Cache County Study. Arch Gen Psychiatry. 2000; 57:601–607. [PubMed: 10839339]

35. Brown J, PM OB, Marjoribanks J, Wyatt K. Selective serotonin reuptake inhibitors for premenstrual syndrome. Cochrane Database Syst Rev. 2009; 2:CD001396. [PubMed: 19370564]

36. Stearns V, Ullmer L, Lopez JF, Smith Y, Isaacs C, Hayes D. Hot flushes. Lancet. 2002; 360:1851–1861. [PubMed: 12480376]

Table 1

Age-adjusted baseline characteristics according to history of depression status (analysis 1) or body mass index category (analysis 2) in the Nurses' Health Study (NHS).[a]

Characteristics	Analysis 1		Analysis 2		
	No depression	Depression	Normal Weight	Overweight	Obesity
N (%)	54059 (82.0)	11896 (18.0)	28624 (43.4)	23206 (35.2)	14125 (21.4)
Age (years, mean)	66.0	64.7	66.1	65.9	64.8
History of depression (%)	NA	NA	15	18	24
Body mass index (kg/m^2, mean)	26.4	27.7	22.4	27.2	34.3
Race (white, %)	98	98	98	98	98
Physical activity (MET-hrs/wk, mean)	18.7	14.4	21.6	17.1	12.0
Smoking status (%)					
Current smoker	8	10	10	7	5
Past smoker	46	51	45	48	49
Never smoked	46	39	45	45	46
Marital status (with spouse, %)	75	65	74	74	71
Living status (alone, %)	19	23	19	19	20
Total energy intake (KCal/d, mean)	1734	1752	1725	1734	1762
Western dietary score, mean	−0.02	0.05	−0.14	0.02	0.22
Fruit and vegetables (servings/d)	5.4	5.2	5.4	5.3	5.3
Whole grain (grams/d)	26.3	27.4	27.4	26.1	25.2
Cereal fiber (grams/d)	6.3	6.4	6.5	6.2	6.1
Glycemic load	115.9	117.0	117.4	115.4	11.4
Red meat (servings/d)	0.9	0.9	0.8	0.9	0.9
Fish (servings/d)	0.3	0.3	0.2	0.3	0.3
Soft drinks (servings/d)	0.7	0.9	0.6	0.8	1.0
Coffee (cups/d)	2.2	2.1	2.2	2.2	2.1
Polyunsaturated to saturated fat ratio	0.6	0.6	0.7	0.6	0.6
Trans fat (% of energy)	1.6	1.6	1.5	1.6	1.7
Alcohol (g/day, mean)	5.1	4.4	6.2	4.8	3.0
Premenopausal, %	1	1	1	1	1

Characteristics	Analysis 1		Analysis 2		
	No depression	Depression	Normal Weight	Overweight	Obesity
Ever menopause hormone use (%)[b]	71	82	76	71	67
Hypertension (%)	47	56	37	51	69
Hypercholesterolemia (%)	60	69	55	66	68
Diabetes (%)	7	13	3	8	19
Heart disease (%)	10	16	9	11	15
Stroke (%)	2	4	2	2	3
Cancer (%)	15	18	15	15	16

Abbreviations: MET-hrs/wk, Metabolic Equivalent-hours/week.

[a] Depression was defined as currently reporting or having a history of physician-diagnosed depression and/or antidepressant medication use as of 2000.

[b] Current plus past hormone use.

Table 2

Multinomial logistical models of association between depression and subsequent body mass index category in the Nurses' Health Study.[a]

Outcome (body mass index category)	Depression Status		Depression category		
	No depression	With depression	Only diagnosed depression	Only antidepressant medication	Diagnosed depression and antidepressant medication
No. of participants	54059	11896	1609	4340	5947
Overweight					
Age-adjusted model	1.00	1.19 (1.13–1.24)	1.07 (0.96–1.20)	1.17 (1.09–1.26)	1.24 (1.16–1.32)
Multivariate model 1[b]	1.00	1.15 (1.09–1.21)	1.05 (0.94–1.18)	1.13 (1.05–1.21)	1.20 (1.12–1.28)
Multivariate model 2[c]	1.00	1.09 (1.03–1.14)	1.03 (0.91–1.15)	1.06 (0.98–1.14)	1.14 (1.07–1.22)
Multivariate model 3[d]	1.00	1.09 (1.02–1.18)	1.22 (1.03–1.45)	0.99 (0.88–1.10)	1.14 (1.03–1.26)
Obesity					
Age-adjusted model	1.00	1.82 (1.73–1.92)	1.21 (1.07–1.38)	1.74 (1.61–1.89)	2.08 (1.95–2.23)
Multivariate model 1[b]	1.00	1.63 (1.54–1.72)	1.13 (0.98–1.29)	1.57 (1.44–1.70)	1.84 (1.71–1.97)
Multivariate model 2[c]	1.00	1.44 (1.36–1.53)	1.08 (0.94–1.24)	1.37 (1.25–1.49)	1.67 (1.55–1.80)
Multivariate model 3[d]	1.00	1.38 (1.24–1.53)	1.21 (0.94–1.57)	1.15 (0.99–1.35)	1.61 (1.40–1.85)

[a] Depression was defined as currently reporting or having a history of physician-diagnosed depression and/or antidepressant medication use as of 2000. Overweight was defined as a body mass index of 25.0 to 29.9 kg/m^2, and obesity was defined as a body mass index of 30.0 kg/m^2 or greater. The outcome was assessed in 2002–2006.

[b] Model 1: adjusted for age, ethnicity, marital status, living status, physical activity level, smoking status, alcohol consumption, menopausal status, postmenopausal hormone therapy, and quintiles of total energy intake and Western dietary score.

[c] Model 2: model 1 plus a history of comorbidities (diabetes, hypertension, hypercholesterolemia, cardiovascular disease, and cancer).

[d] Model 3: model 2 plus baseline body mass index category (normal weight, overweight, or obesity).

Table 3

Multinomial logistical models of association between depression and incident overweight or obesity in the Nurses' Health Study.[a]

Baseline normal weight women			Baseline normal weight or overweight women		
Outcome	**No depression (n=24275)**	**With depression (n=4349)**	**Outcome**	**No depression (n=43392)**	**With depression (n=8438)**
Overweight/obesity			Obesity		
Age-adjusted model	1.00	1.41 (1.36–1.47)	Age-adjusted model	1.00	1.73 (1.57–1.91)
Multivariate model 1[b]	1.00	1.31 (1.26–1.37)	Multivariate model 1[b]	1.00	1.60 (1.45–1.77)
Multivariate model 2[c]	1.00	1.20 (1.15–1.26)	Multivariate model 2[c]	1.00	1.51 (1.36–1.67)

[a] Depression was defined as currently reporting or having a history of physician-diagnosed depression and/or antidepressant medication use as of 2000. Overweight was defined as a body mass index of 25.0 to 29.9 kg/m^2, and obesity was defined as a body mass index of 30.0 kg/m^2 or greater. The outcome was assessed in 2002–2006.

[b] Model 1: adjusted for age, ethnicity, marital status, living status, physical activity level, smoking status, alcohol consumption, menopausal status, postmenopausal hormone therapy, and quintiles of total energy intake and Western dietary score.

[c] Model 2: model 1 plus a history of comorbidities (diabetes, hypertension, hypercholesterolemia, cardiovascular disease, and cancer).

Table 4

Odds ratios (95% confidence intervals) of depression according to baseline body mass index category in the Nurses' Health Study.[a]

	Prevalent depression			New-onset depression		
	Normal weight	**overweight**	**Obesity**	**Normal weight**	**overweight**	**Obesity**
No. of participants	28624	23206	14125	24275	19117	10667
Age-adjusted model	1.00	1.16 (1.11–1.21)	1.63 (1.56–1.71)	1.00	1.08 (1.02–1.15)	1.30 (1.21–1.40)
Multivariate model 1[b]	1.00	1.12 (1.07–1.17)	1.48 (1.41–1.56)	1.00	1.06 (1.00–1.13)	1.24 (1.15–1.34)
Multivariate model 2[c]	1.00	1.04 (1.00–1.09)	1.28 (1.22–1.35)	1.00	1.00 (0.94–1.07)	1.10 (1.02–1.20)
Multivariate model 3[d]	1.00	1.00 (0.95–1.06)	1.11 (1.03–1.18)	NA	NA	NA

[a] Overweight was defined as a body mass index of 25.0 to 29.9 kg/m^2, and obesity was defined as a body mass index of 30.0 kg/m^2 or greater. Depression was defined as currently reporting or having a history of physician-diagnosed depression and/or antidepressant medication use. The outcome was assessed in 2002–2006.

[b] Model 1: adjusted for age, ethnicity, marital status, living status, physical activity level, smoking status, alcohol consumption, menopausal status, postmenopausal hormone therapy, and quintiles of total energy intake and Western dietary score at baseline.

[c] Model 2: model 1 plus a history of comorbidities (diabetes, hypertension, hypercholesterolemia, cardiovascular disease, and cancer).

[d] Model 3: model 2 plus baseline depression status (1996–2000, yes or no).