NIH Public Access
Author Manuscript
J Psychiatr Res. Author manuscript; available in PMC 2011 November 1.

Published in final edited form as:
J Psychiatr Res. 2010 November ; 44(15): 1010–1016. doi:10.1016/j.jpsychires.2010.04.007.

Psychotropic Medication Use Mediates the Relationship Between Mood and Anxiety Disorders and Obesity: Findings from a Nationally Representative Sample

Jasper A. J. Smits, Ph.D.[1], **David Rosenfield, Ph.D.**[1], **Amber A. Mather, B.A.**[2], **Candyce D. Tart, M.A.**[1], **Christine Henriksen, B.A.**[2], and **Jitender Sareen, M.D.**[2]

[1]Department of Psychology, Southern Methodist University

[2]Department of Psychiatry, University of Manitoba

Abstract

Growing evidence points to a relationship between obesity and both mood and anxiety disorders, but the question of what accounts for this association remains unanswered. The present study examined the use of psychotropic medications as a mediator of the mood/anxiety disorder-obesity relationship. Data came from the public use dataset of the Canadian Community Health Survey Cycle 1.2 (age 15 years and older, *N*=36,984). Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition psychiatric diagnoses of 12-month mood disorders (e.g., major depressive disorder, mania) and anxiety disorders (e.g., panic attacks, panic disorder, social phobia, agoraphobia) were examined as was use of psychotropic medications (e.g., antidepressants, antipsychotics, anxiolytics, hypnotics, mood stabilizers) and obesity (defined as body mass index ≥30). A series of multiple logistic regression analyses were completed to test study hypotheses. Covariates in these analyses included sociodemographic factors, physical activity, and physical illness burden. The use of two medication classes, namely antidepressants and antipsychotics, emerged as significant predictors of obesity as well as mediators of the psychiatric diagnosis-obesity relationship after evaluating all psychotropic medication classes simultaneously, while also controlling for other theoretically relevant variables. The use of these two medications accounted for 86% of the relationship between mood disorders and obesity and 32% of the relationship between anxiety disorders and obesity. The study findings guide advances in the theoretical conceptualization of the mechanisms involved in mood/anxiety disorder-obesity relations. Clinical implications are discussed.

Keywords

antidepressant; antipsychotic; anxiety disorders; medication; mood disorders; obesity

© 2010 Elsevier Ltd. All rights reserved.

Corresponding author: Jasper A. J. Smits, Ph.D. Department of Psychology Southern Methodist University Dedman College P.O. Box 750442 Dallas, TX 75275 Phone: (214) 768-4125 Fax: (214) 768-4191 jsmits@smu.edu.

Contributors

J.A.J.S. designed the study, conducted the literature searches, participated in the data analyses, and wrote a first draft of the manuscript. J.S. assisted with the development of the study design, interpretation of the data and the writing of the manuscript. D.S., A.A.M., C.D.T., and C.H., participated in the data analyses strategies, interpretation of data and writing of the manuscript. All authors contributed to and approved the final manuscript.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

INTRODUCTION

The rate of obesity has reached an epidemic level. Indeed, the 2005-2006 National Health and Nutrition Examination Survey estimated that approximately one-third of U.S. adults are obese (body mass index [BMI] $\geq$ 30 kg/m^2; Ogden et al., 2007). Prevalence rates of obesity in Canada and Europe are approximately 15% (Katzmarzyk & Mason, 2006; Seidell & Flegal. 1997) and the estimate of adults affected worldwide is approximately 250 million (WHO, 1998). These high rates are concerning, given that obesity is a major cause of morbidity and mortality (Flegal et al., 2007; Must et al., 1999).

Growing evidence points to a relationship between obesity and both mood and anxiety disorders. Specifically, several cross-sectional epidemiologic surveys have now documented that (lifetime and past year) prevalence rates of mood and anxiety disorders are increased among obese adults relative those who are in the normal weight range (Mather et al., 2009; Petry et al., 2008, Scott et al., 2008; Simon et al., 2006). This relationship appears robust, as it remains significant and meaningful after controlling for demographic factors (Mather et al., 2009; Petry et al., 2008, Scott et al., 2008; Simon et al., 2006) and physical health problems (Mather et al., 2009). Further, there is evidence suggesting that the association between obesity and mood and anxiety disorders may be stronger among women compared to men (Carpenter et al., 2000; Onyike et al., 2003; Scott et al., 2008; Mather et al., 2009), although the moderator effect of gender was not observed in the National Comorbidity Survey-Replication (NCS-R; Simon et al., 2006).

The question of what accounts for the association between obesity and mood and anxiety disorders remains unanswered. It is possible that these co-occurring conditions have a common cause (e.g., negative early life experiences, genetic vulnerability, gene-environment interactions; cf. Stunkard et al., 2003). Alternatively, it is possible that obesity causes mood or anxiety disorders, perhaps through the negative social consequences of obesity (e.g., stigmatization), as suggested by Simon and colleagues (2006). A third explanation is that mood and anxiety disorders cause obesity. Support for this hypothesis comes from a recent prospective cohort study (Kivimaki et al., 2009), in which the authors repeatedly measured weight and height (through direct measurement) and common mental disorders (i.e., depression and anxiety) in a sample of 4,636 adults over the course of 19 years. The results were consistent with a temporal sequence of mental disorder to obesity but not vice versa.

One pathway by which mood and anxiety disorders may cause obesity is the use of psychotropic medications. The use of prescription psychotropic medications is common in the US adult population in general (Paulose-Ram et al., 2004; Olfson & Marcus, 2009) and particularly among persons who receive outpatient treatment for mood or anxiety disorders (Olfson et al., 2002, 2004). Importantly, evidence from efficacy trials indicates that the use of psychotropic medications, specifically antipsychotics, antidepressants, and mood stabilizers, are associated with significant weight gain (Allison et al., 1999; Babtista et al., 1995; Demyttenaere & Jaspers, 2008; Fava, et al., 2000; Stahl et al., 2009; Sussman et al., 2001; Taylor & McAskill, 2000). Data collected as part of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) provides initial support for the hypothesis that the relationship between obesity and mood or anxiety disorders is mediated by psychotropic medication use. Specifically, Petry and colleagues (2008) observed a reduction in the strength of the relationship between obesity and mood and anxiety disorders when medication information was entered as an additional covariate in the model. However, NESARC only asked respondents whether their doctor had ever prescribed medications for symptoms of each mood disorder assessed but did not collect information about specific classes and actual use of medications. Accordingly, as the authors aptly pointed out, the findings with respect to actual medication *use* in this study are difficult to interpret.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

The present study sought to build upon previous studies in three significant ways. First, we attempted to replicate and extend the findings from the Petry et al. (2008) study by investigating the relationship between the use of different classes of psychotropic medications (i.e., antidepressants, antipsychotics, anxiolytics, hypnotics, and mood stabilizers) and increased rates of obesity. Second, we tested for the specificity of the proposed mechanism by evaluating it after controlling for other theoretically relevant variables (e.g., sociodemographic factors, physical activity, physical illness burden). Finally, we explored the possibility that the proposed mechanism varied as a function of gender. These questions were examined using data collected as part of the Canadian Community Health Survey-Mental Health and Well-Being (CCHS 1.2).

MATERIALS AND METHODS

Sample

Specific information regarding the methodology of the CCHS 1.2 has been published previously (Gravel & Beland, 2005). In short, the CCHS 1.2 is a cross-sectional, nationally representative survey of residents of private dwellings in all 10 Canadian provinces. The CCHS 1.2 used a multistage stratified cluster design to select respondents and obtained an overall response rate of 77% to yield 36,984 individuals ages 15 and older. Statistics Canada interviewer training was completed with guidance from the Centre for Addiction and Mental Health and the Canadian Mental Health Association, and addressed the use of the Computer-Assisted Personal Interviewing application, survey content, as well as sensitivity to, and awareness of, mental health issues. Most interviews (86%) were conducted face to face; the remainder (14%) was conducted by telephone. The analyses conducted in this paper are based on the public use CCHS 1.2 dataset made available by Statistics Canada.

Obesity

Consistent with contemporary definitions, obesity was defined as a BMI of 30kg/m^2 or greater. BMI was calculated by dividing weight in kilograms by the square of height in meters. Height and weight data were obtained by self-report.

Psychotropic Medication Use

For each class of medication investigated in this study (antidepressants; antipsychotics, anxiolytics, hypnotics, and mood stabilizers), the CCHS 1.2 asked respondents to indicate if they had taken the medication in the past 12 months. For each medication class, the interviewer provided three example brands (antidepressants: Prozac, Paxil, or Effexor; antipsychotics: Haldol, Risperdol, or Seroquel; anxiolytics: Ativan, Valium, or Serax; hypnotics: Imovane, Nytol, or Starnoc; mood stabilizers: Lithium, Tegretol, or Epival). These five binary (i.e., yes, no) variables were used in the analyses.

Mood and Anxiety Disorder Diagnoses

The CCHS 1.2 employed the World Mental Health-Composite International Diagnostic Interview (WMH-CIDI; Kessler & Ustun, 2004) to assess the following DSM-IV lifetime and past-year mood and anxiety disorders: major depressive disorder, mania, panic attacks, panic disorder, agoraphobia, agoraphobia without panic disorder, and social phobia. Respondents were included the “mood disorders” category if they met criteria for major depressive disorder or mania, and in the “anxiety disorder” category if they met criteria for panic attacks, panic disorder, agoraphobia, agoraphobia without panic disorder, or social phobia. For the present study, we focused on the past-year diagnostic categories because the assessment of medication employed that same time frame.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Covariates

Sociodemographic factors—Based on previous findings from this sample (Mather et al., 2009), age, gender, and socioeconomic status, as indexed by educational attainment, were included as covariates in the present study.

Physical illness burden—As has been done previously, we used the scores on the Charlson Comorbidity Index (CCI) to adjust for physical health problems (Mather et al., 2009; Landi et al., 2000; Sareen et al., 2007). The CCI provides an estimate of 1-year relative risk of mortality by taking into account the seriousness and number of medical conditions an individual reports. The chronic medical conditions assessed in the CCHS 1.2 were based on participants' responses to explicit questions of whether they had been diagnosed with a particular condition by a health professional (e.g., "Do you have high blood pressure?"). Eighteen of these conditions were given a weight from 0 to 6, and these weights were then summed to arrive at a final CCI score for each respondent. This CCI score was used as a covariate in the present study.

Physical activity—Respondents were presented with a list of leisure-time activities and asked the number of times they had engaged in the activity and the average duration of the session in the past three months. These data were used in combination with the compendium of physical activities, which lists metabolic equivalency of tasks (MET; Ainsworth et al., 2000) to estimate a daily energy expenditure value (kilocalories per kilogram per day [KKD]) for each respondent (see also Bryan et al., 2006). This continuous variable was used as a covariate in the present study.

DATA ANALYSIS

Given that the dependent variables (obesity, medication usage) were dichotomous, data analyses were performed using multiple logistic regression analyses. All analyses included the following 5 covariates: gender, age, education, physical activity level, and Charlson Comorbidity Index scores. The predictors (including covariates and interactions) were entered simultaneously in the logistic regression analyses. To account for the complex sampling design of the CCHS 1.2, statistical analyses were carried out in SUDAAN version 9.0 (Research Triangle Institute, 2004), which allowed us to employ Taylor Series Linearization (TSL) as a variance estimation technique. To ensure representativeness of the sample, all statistical analyses were weighted using the information provided by Statistics Canada.

RESULTS

Sample Characteristics

Of the 36,984 participants in the survey, 54.6% were female. Median age was 44, and mean body mass index was 25.7 (SD = 4.82). Educational attainment varied widely, with 28.8% not completing high school, 17.7% with a high school degree but no post-secondary education, 8.3% with some post-secondary education, but no post-secondary degree, 30.5% with a trade school, community college, or other post-secondary, non Bachelor's degree, and 14.7% with a college degree or higher.

Mood and Anxiety Disorders Predicting Obesity

Consistent with previous findings, both mood and anxiety disorders were significantly related to obesity. After controlling for the covariates, increased odds of obesity were observed among people suffering from mood disorders (adjusted odds ratio [AOR] = 1.22, Wald $F = 4.26$, $p < 0.05$) and anxiety disorders (AOR = 1.28, Wald $F = 11.36$, $p < 0.001$) relative to those who did not report these conditions. The relationship between obesity and mood and anxiety disorders, respectively, did not vary as a function of gender (ps > .36 for the interaction of

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

gender with each disorder). Accordingly, the moderating effects of gender were dropped from subsequent analyses.

Psychotropic Medication Use Predicting Obesity

The relationship between medication usage and obesity was first examined for each psychiatric medication class (e.g., antidepressants, antipsychotics, anxiolytics, hypnotics, and mood stabilizers) separately (see Table 1). The only medications that were significantly related to obesity were antidepressants (AOR = 1.47, Wald $F = 28.76$, $p < 0.0001$) and antipsychotics (*AOR* = 3.03, Wald $F = 23.31$, $p < 0.0001$). Obesity rates were 14.8% vs. 21.9% for persons who did not report antidepressant medication use relative to those who did. For antipsychotic medication, the obesity rates among non-users and users were 15.1% and 36.6%, respectively.

Next, all five psychotropic medication classes were used as simultaneous predictors (along with other covariates) of obesity to determine if any of the medication classes were related to obesity over and above concurrent usage of other medications. The results showed that the use of antidepressant and antipsychotic medications remained significantly related to higher rates of obesity when controlling for the use of the other psychiatric medications (antidepressants: AOR = 1.49, Wald $F = 23.80$, $p < 0.0001$; antispychotics: AOR = 2.63, Wald $F = 15.79$, $p < 0.001$).

Psychotropic Medication Use as a Mediator of the Relationship between Psychiatric Diagnosis and Obesity

Because the use of antidepressant and antipsychotic medications are related to higher rates of obesity, and since these medications are often prescribed for people with mood and/or anxiety disorders, it is possible that the use of these medications accounts for the relationship between certain psychiatric disorders (in this case, mood and anxiety disorders) and obesity. To examine this hypothesis, the use of antidepressant and antipsychotic medications were examined as simultaneous mediators of the relationship between (a) mood disorders and obesity and (b) anxiety disorders and obesity (see Figures 1 and 2).

We used the causal steps approach to mediation (see Baron & Kenny, 1986; MacKinnon et al., 2002). Although MacKinnon and colleagues demonstrated that this approach is more conservative than other approaches to mediation, the difference in power is small for large sample sizes (as in this study). Further, since these results could be important in decision-making concerning the treatment for some disorders, it is important that these findings have very low Type 1 error rates. The causal steps approach has the lowest Type 1 error rate of the major approaches to mediation (MacKinnon et al., 2002) and was therefore selected to evaluate mediation in the present study. In this approach, first, a relationship between the independent variable (mood or anxiety disorder diagnosis) and the dependent variable (obesity) must be established (the *c* path; see Table 3, Step 1). Second, a relationship between the independent variable (mood or anxiety disorder diagnosis) to the mediator(s) (i.e., antidepressant and antipsychotic medication use) must be present (the *a* paths; see Table 3, Step 2 and Figures 1 and 2). Thirdly, the mediators must be related to the DV (i.e., obesity) while controlling for the IV (the *b* paths; see Table 3, Step 3 and Figures 1 and 2). Finally, the relationship between the psychiatric disorder classes and obesity must be reduced by the addition of the mediators to the regression predicting obesity (*c*' path [Table 3, Step 3] < *c* path). For each mood disorder, we calculated the proportion of the overall effect of the disorder on obesity that was accounted for by the mediators. This proportion is the difference between the overall effect of the disorder on obesity (path *c*) and the effect of the disorder on obesity controlling for the mediators (path *c*'), divided by path *c* (i.e., proportion = $(c - c')/(c)$; MacKinnon, 2008).

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Mood Disorders—The results are presented in Table 2 and Figure 1. Our first set of analyses demonstrated that the relationship between mood disorders and obesity (controlling for the five covariates) was significant (i.e., the *c* path). Not surprisingly, mood disorders were also significantly related to use of both antidepressant (AOR = 14.91, Wald $F = 1081.64$, $p < 0.0001$) and antipsychotic medications (AOR = 18.06, Wald $F = 155.86$, $p < 0.0001$; i.e., the *a* paths). In addition, after controlling for the effect of mood disorder diagnosis, both antidepressant medication use (AOR = 1.41, Wald $F = 16.84$, $p < 0.0001$) and antipsychotic medication use (AOR = 2.50, Wald $F = 14.61$, $p < 0.001$) remained significant predictors of obesity (i.e., the *b* paths). Lastly, the effect of mood disorders on obesity (as measured by the AOR) was reduced by 86% and was no longer significant ($p = 0.77$) when adding these medications as mediators of the relation between mood disorders and obesity. Without accounting for mediators, the odds of being obese increased 22% for those with a mood disorder. After accounting for the mediators, the odds of obesity were increased only 3% for those with a mood disorder. Together, these results are consistent with full mediation.

Anxiety Disorders—The results are presented in Table 2 and Figure 2. Our first set of analyses had demonstrated that the relationship between anxiety disorders and obesity was significant (i.e., the *c* path). As expected, the diagnosis of an anxiety disorder was also related to use of both antidepressant medication (AOR = 5.51, Wald $F = 558.42$, $p < 0.0001$) and antipsychotic medication (AOR = 9.21, Wald $F = 88.65$, $p < 0.0001$; i.e., the *a* paths). After controlling for the effects of anxiety disorder diagnosis, the use of antidepressant medications (AOR = 1.37, Wald $F = 15.66$, $p < 0.001$) and antipsychotic medications (AOR = 2.33, Wald $F = 12.15$, $p < .001$) remained significant predictors of obesity (i.e., the *b* paths). These mediators accounted for 32% of the relationship between anxiety disorders and obesity (as measured by the AOR). Without considering the effect of the mediators, the odds of being obese increased 28% for those with an anxiety disorder. Accounting for the effects of the medications as mediators, the odds of being obese increased only 19% for those with an anxiety disorder. Together, these results are consistent with partial mediation.

DISCUSSION

The present study sought to extend previous work on the relationship between obesity and mood/anxiety disorders by examining the potential mediating effects of psychotropic medication use. Using a representative sample of Canadian men and women ages 15 and older, we demonstrated that the increased odds of obesity in mood disorders are fully mediated by medication use, whereas the relationship between anxiety disorder diagnosis and obesity is partially mediated by medication use. Interestingly, the effects of medication use in this context were specific to antidepressants and antipsychotics. That is, the use of these two medication classes emerged as significant predictors of obesity and mediators of the psychiatric diagnosis-obesity relationship after evaluating all psychotropic medication classes simultaneously, while also controlling for other theoretically relevant variables (e.g., sociodemographic factors, physical health problems, and physical activity). Finally, our analyses revealed that the psychiatric diagnosis-obesity relationship did not vary as a function of gender.

The present study findings are in line with efficacy trials that have demonstrated the weight-gaining properties of antidepressants and antipsychotics (e.g., Allison et al., 1999; Demyttenaere & Jaspers, 2008; Fava et al., 2000; Sussman et al., 2001). Indeed, even after controlling for theoretically relevant variables, the obesity rate among persons taking antidepressants over the past 12 months was over one and a half times the rate observed among persons who did not take this medication; for antipsychotics this ratio was greater than two. We did not observe a relationship between mood stabilizers and obesity, which appears at odds with findings of clinical trials that have consistently shown that the prescription of this medication class is associated with significant weight gain (e.g., Baptista et al., 1995).

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

The principal limitation of this study is that the data are cross-sectional. Accordingly, we cannot make any inferences regarding the directionality of the observed relationships. Although our data are consistent with the hypothesis that mood/anxiety disorders cause obesity through the use of psychotropic medications, we cannot rule out alternative explanations. Here, we would like to note that it seems unlikely that the directionality of the relationships would be reversed. Reverse directionality in this case would imply that a prescription of antidepressant or antipsychotic medication would lead to a diagnosis of a mood or anxiety disorder, rather than vice versa. It would also mean that becoming obese would lead to the prescription of antidepressant or antipsychotic medication, rather than vice versa. Thus, although cross-sectional data cannot rule out the possibility of reverse causation, reverse causation in the present model seems unlikely. Our attempts to rule our spuriousness involved controlling for a number of third variable candidates, including age, socioeconomic status, physical illness burden and physical activity. Unfortunately, true experimentation is not an option given that it is difficult (practically and ethically) to manipulate the variables of interest, and therefore eliminating third variable explanations may not be possible.

Our work can be extended by examining the variables of interest, along with possible third variable candidates, repeatedly over the course of time. Such future research should also incorporate direct measures of height and weight instead of relying on self-report. People tend to underreport weight and overreport height (Roberts, 1995), which may have influenced the effect sizes in the present study. Likewise, the inclusion of diaries to track dose and duration of medication use instead of merely asking about past medication use, as was done in the current study, can help determine whether the relationships are dose dependent. Finally, future work would benefit from including measures of possible mechanisms underlying the observed effects, such as maladaptive eating behaviors (Dallman et al., 2003), dysregulation of the hypothalamic-pituitary-adrenocortical axis (Bornstein et al., 2006), or clinical improvement and the associated increase in appetite (Czobor et al., 2002).

If replicated, the study findings offer a clear target for reducing obesity rates among people suffering from mood or anxiety disorders. The use of psychotropic medication is often indicated for these psychiatric disorders and therefore termination and switching to nonpharmacological treatments is not always an option. One alternative is to augment pharmacological interventions for mood and anxiety disorders with strategies aimed at reducing weight gain. A growing body of work points to behavioral weight management programs as efficacious adjuncts to antipsychotic treatments. Alvarez-Jimenez and colleagues (2008) meta-analytically reviewed randomized controlled trials ($N = 10$) of the efficacy of nonpharmacological interventions (e.g., cognitive–behavioral intervention strategies; nutritional counseling interventions; and combined nutritional and exercise interventions) to control antipsychotic-induced weight gain in patients with first-episode or chronic schizophrenia and found significant reduction in mean body weight gain for participants in the nonpharmacological intervention groups compared with those receiving treatment as usual. Other alternative strategies may include adjunctive weight loss pharmacotherapy or bariatric surgery (McElroy, 2009).

In sum, the present study provides evidence suggesting that psychotropic medication use, and antidepressant and antipsychotic medication use specifically, account for the association between mood disorders and obesity and account, in part, for the relationship between anxiety disorders and obesity. The implications of these findings are clear when considering the high prevalence rates of mood and anxiety disorders (Kessler et al., 2005) and the observation that the rates of antidepressant use alone and the combination of antidepressant and antipsychotic use have nearly doubled between 1996-2005 (Olfson and Marcus, 2009).

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Acknowledgments

Role of Funding Source

Dr. Smits receives support from NIH grants R01DA027533 and R01MH075889 and a research grant from Schering-Plough/Merck. Dr. Sareen receives support from Canadian Institutes of Health Research New Investigator Award (#152348) and a Manitoba Health Research Council Chair Award. These funding sources had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

References

Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DV Jr, Schmitz KH, Emplaincourt PO, Jacobs DR Jr, Leon AS. Compendium of physical activites: an update of activity codes and MET intensities. Medicine and Science in Sports and Exercise 2000;32:498–516.

Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infante MC, Weiden PJ. Antipsychotic-induced weight gain: a comprehensive research synthesis. The American Journal of Psychiatry 1999;156:1686–1696. [PubMed: 10553730]

Alvarez-Jimenez M, Hetrick SE, Gonzalez-Blanch C, Gleeson JF, McGorry PD. Non-pharmacological management of antipsychotic-induced weight gain: systematic review and meta-analysis of randomized controlled trials. The British Journal of Psychiatry 2008;193:101–107. [PubMed: 18669990]

Baptista T, Teneud L, Contreras Q, Alastre T, Burguera JL, de Burguera M, et al. Lithium and body weight gain. Pharmacopsychiatry 1995;28:35–44. [PubMed: 7624385]

Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. Journal of Personality and Social Pscyhology 1986;51:1173–1182.

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. Molecular Psychiatry 2006;11:892–902. [PubMed: 16880826]

Bryan SN, Tremblay MS, Pérez CE, Ardern CI, Katzmarzyk PT. Physical activity and ethnicity: evidence from the Canadian Community Health Survey. Canadian Journal of Public Health 2006;97(4):271–6.

Carpenter KM, Hasin DS, Allison DB, Faith MS. Relationships between obesity and DSM-IV major depressive disorder, suicide ideation, and suicide ideation and suicide attempts: results from a general population study. American Journal of Public Health 2000;90:251–257. [PubMed: 10667187]

Czobor P, Volavka J, Sheitman B, Lindenmayer JP, Citrome L, McEvoy J, Cooper TB, Chakos M, Lieberman JA. Antipsychotic-induced weight gain and therapeutic response: a differential association. Journal of Clinical Psychopharmacology 2002;22:244–51. [PubMed: 12006893]

Dallman MF, Pecoraro NC, Akana SF, la Fleur SE, Gomez F, Houshyar H, Bell ME, Bhatnagar S, Luagero KD, Manalo S. Chronic stress and obesity: a new view of “comfort food”. Proceedings of the National Academy of Sciences 2003;100:11696–11701.

Demyttenaere K, Jaspers L. Bupropion and SSRI-induced side effects. Journal of Psychopharmacology 2008;22:792–804. [PubMed: 18308785]

Fava M, Judge R, Hoog SL, Milsson ME, Koke SC. Fluoxetine versus sertraline and paroxentine in major depressive disorder: changes in weight with long-term treatment. Journal of Clinical Psychiatry 2000;61:863–867. [PubMed: 11105740]

Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and Trends in Obesity Among US Adults, 1999-2000. Journal of the American Medical Association 2002;288:1723–1727. [PubMed: 12365955]

Flegal KM, Graubard BI, Williamson DF, Gail MH. Cause-specific excess deaths associated with underweight, overweight, and obesity. Journal of the American Medical Association 2007;298:2028–2037. [PubMed: 17986696]

Gravel R, Beland Y. The Canadian Community Health Survery: Mental Health and Well-Being. Canadian Journal of Psychiatry 2005;50:573–579.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Katzmarzyk PT, Mason C. Prevalence of class I, II and III obesity in Canada. Canadian Medical Association Journal 2006;174:156–157. [PubMed: 16415457]

Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distribution of DSM-IV disorders in the National Comorbidity Survey replication. Archives of General Psychiatry 2005;62:593–602. [PubMed: 15939837]

Kessler R, Ustun TB. The World Mental Health (WMH) survey initiative version of the World Health Organization (WHO) composite. International Diagnostic Interview (CIDI). International Journal of Methods in Psychiatric Research 2004;13:93–121. [PubMed: 15297906]

Kivimäki M, Lawlor DA, Singh-Manoux A, Batty GD, Ferrie JE, Shipley MJ, Nabi H, Sabia S, Marmot MG, Jokela M. Common mental disorder and obesity: insight from four repeat measures over 19 years: prospective Whitehall II cohort study. BMJ 2009;339:b3765. [PubMed: 19808765]

Landi F, Onder G, Gambassi G, Pedone C, Carbonin P, Bernabei R. Body mass index and mortality among hospitalized patients. Archives of Internal Medicine 2000;160:2641–2644. [PubMed: 10999978]

Mather A, Cox B, Enns B, Sareen J. Associations of obesity with psychiatric disorders and suicidal behaviors in a nationally representative sample. Journal of Psychosomatic Research 2009;66:277–285. [PubMed: 19302884]

MacKinnon, DP. Introduction to Statistical Mediation Analysis. Lawrence Erlbaum Associates; New York: 2008.

MacKinnon DP, Lockwood CM, Hoffman JM, West SG, Sheets V. A comparison of methods to test mediation and other intervening variable effects. Psychological Methods 2002;7:83–104. [PubMed: 11928892]

McElroy SL. Obesity in patients with severe mental illness: overview and management. Journal of Clinical Psychiatry 2009;70(Suppl 3):12–21. [PubMed: 19570497]

Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. Journal of American Medical Association 1999;282:1523–11529.

Ogden CL, Carroll MD, McDowell MA, Flegal KM. Obesity among adults in the United States—no statistically significant change since 2003-2004. NCHS Data Brief 2007;1:1–8. [PubMed: 19389313]

Olfson M, Marcus S, Druss B, Pincus H. National trends in the use of outpatient psychotherapy. American Journal of Psychiatry 2002;159:1914–1920. [PubMed: 12411228]

Olfson M, Marcus SC. National patterns in antidepressant medication treatment. Archives of General Psychiatry 2009;66:848–856. [PubMed: 19652124]

Olfson M, Marucs S, Wan G, Geissler E. National trends in the outpatient treatment of anxiety disorders. Journal of Clinical Psychiatry 2004;65:1166–1173. [PubMed: 15367042]

Onyike CU, Crum RM, Lee HB, Constantine GL, Eaton WW. Is obesity associated with major depression? Results from the Third National Health and Nutrition Examination Survey. American Journal of Epidemiology 2003;158:1139–1147. [PubMed: 14652298]

Paulose-Ram R, Jonas BS, Orwig D, Safran MA. Prescription psychotropic medication use among the U.S. adult population: results from the third National Health and Nutrition Examination Survey, 1988-1994. Journal of Clinical Epidemiology 2004;57:309–317. [PubMed: 15066692]

Petry NM, Barry D, Pietrzak RH, Wagner JA. Overweight and obesity are associated with psychiatric disorders: results from the National Epidemiologic Survey on alcohol and related conditions. Psychosomatic Medicine 2008;70:288–97. [PubMed: 18378873]

Sareen J, Cox BJ, Stein MB, Afifi TO, Fleet C, Asmundson GJ. Physical and mental comorbidity, disability, and suicidal behavior associated with posttraumatic stress disorder in a large community sample. Psychosomatic Medicine 2007;69:242–8. [PubMed: 17401056]

Schwartz TL, Nihalani N, Jindal S, Virk S, Jones N. Psychiatric medication-induced obesity: a review. Obesity Research 2004;5:115–121.

Scott KM, Bruffaerts R, Simon GE, Alonso J, Angermeyer M, et al. Obesity and Mental Disorders in the General Population: Results from the World Mental Health Surveys. International Journal of Obesity 2008;32:192–200. [PubMed: 17712309]

Seidell JC, Flegal KM. Assessing obesity: classification and epidemiology. British Medical Bulletin 2007;53:238–252. [PubMed: 9246834]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Simon GE, Von Korff M, Saunders K, Miglioretti DL, Crane PK, van Belle G, Kessler RC. Association between obesity and psychiatric disorders in the US adult population. Archives of General Psychiatry 2006;63:824–30. [PubMed: 16818872]

Stahl SM, Mignon L, Meyer JM. Which comes first: atypical antipsychotic treatment or cardiometabolic risk? Acta Psychiatrica Scandinavica 2009;119:171–179. [PubMed: 19178394]

Stunkard A, Faith M, Allison K. Depression and obesity. Biological Psychiatry 2003;54:330–337. [PubMed: 12893108]

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

Taylor DM, McAskill R. Atypical antipsychotics and weight gain: a systematic review. Acta Psychiatrica Scandinavica 2000;101:416–432. [PubMed: 10868465]

World Health Organization. Obesity: Preventing and Managing the Global Epidemic: Report of the WHO Consultation of Obesity. World Health Organization; Geneva: 1998.

Zimmerman U, Kraus T, Himmerich H, Schuld A, Pollmacher T. Epidemiology, implications and mechanisms underlying drug-induced weight gain in psychiatric patients. Journal of Psychiatric Research 2003;37:193–220. [PubMed: 12650740]

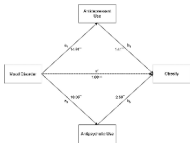

Figure 1.
Medication Use as a Mediator of the Relationship between Mood Disorders and Obesity.
Note: Path coefficients are AORs; $^{**}p < .01$

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

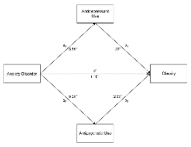

Figure 2.
Medication Use as a Mediator of the Relationship between Anxiety Disorders and Obesity.
Note: Path coefficients are AORs; *$p < .05$; **$p < .01$.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Table 1

Medication Use Predicting Obesity

	Obese	
Medication	**%**	**AOR (CI)**
Antidepressants		
Yes	21.85	1.47**
No	14.79	(1.28-1.69)
Antipsychotics		
Yes	36.61	3.03**
No	15.12	(1.92-4.76)
Anxiolytics		
Yes	18.44	1.09
No	15.01	(.93-1.27)
Hypnotics		
Yes	16.96	.99
No	15.02	(.87-1.14)
Mood Stabilizers		
Yes	20.19	1.35
No	15.14	(.99-1.82)

Note. AORs, CIs, and percentages adjusted for age, gender, education, and Charlson Comorbidity Index (CCI); Percentages are weighted to be representative of the Canadian population

** $p < .01$.

NIH-PA Author Manuscript NIH-PA Author Manuscript NIH-PA Author Manuscript

Table 2

Medication Use as a Function of Past-Year Mood or Anxiety Disorders

	Medication									
	Antidepressants		Antipsychotics		Anxiolytics		Hypnotics		Mood Stabilizers	
Disorder	**%**	**AOR (CI)**	**%**	**AOR (CI)**	**%**	**AOR (CI)**	**%**	**AOR (CI)**	**%**	**AOR (CI)**
Mood										
Yes	39.19	14.91**	3.36	18.06**	25.43	7.82**	32.03	4.90**	10.55	17.64**
No	3.97	(12.69-17.51)	.19	(11.47-28.45)	4.35	(6.57-9.32)	8.99	(4.17-5.76)	.58	(12.70-24-51)
Anxiety										
Yes	20.19	5.51**	1.70	9.21**	18.49	6.17**	21.02	2.91**	4.52	5.89**
No	4.08	(4.79-6.35)	.19	(5.80-14.62)	3.90	(5.29-7.19)	8.82	(2.55-3.34)	.69	(4.38-7.92)

Note. AORs, CIs and percentages adjusted for age, gender, education, and Charlson Comorbidity Index (CCI); Percentages are weighted to be representative of the Canadian population

** $p < .01$

J Psychiatr Res. Author manuscript; available in PMC 2011 November 1.

NIH-PA Author Manuscript NIH-PA Author Manuscript NIH-PA Author Manuscript

Table 3

Logistic Regressions for the Mediation Analyses

				Mood Disorder		Anxiety Disorder	
Step	**Path**	**Independent Variable**	**Dependent Variable**	**AOR**	**Wald F**	**AOR**	**Wald F**
1	*c*	Disorder	Obesity	1.22	4.26*	1.28	11.36**
2	a_1	Disorder	Antidepressant Use	14.91	1081.64**	5.51	558.42**
	a_2	Disorder	Antipsychotic Use	18.06	155.86**	9.21	88.65**
3	*c'*	Disorder	Obesity	1.03	.09	1.19	5.20*
	b_1	Antidepressant Use		1.41	16.84**	1.37	15.66**
	b_2	Antipsychotic Use		2.50	14.61**	2.33	12.15**

Note.

AOR = adjusted odds ratio; all 5 covariates (gender, age, education, physical activity, and CCI) were included as additional predictors in each analysis. Step 2 includes 2 regressions; one for each dependent variable (mediator). See Figures 1 and 2.

* $p < .05$

** $p < .01$.