



# Obesity and Depression: Its Prevalence and Influence as a Prognostic Factor: A Systematic Review

Beatriz Villagrasa Blasco<sup>1</sup>, Jesús García-Jiménez<sup>2</sup>, Isabel Bodoano<sup>3</sup>, and Luis Gutiérrez-Rojas<sup>4,5,6</sup> ✉

<sup>1</sup>Psychogeriatrics Area, Benito Menni CASM, Barcelona, Spain

<sup>2</sup>Psychiatry Service, Hospital General Básico Santa Ana, Motril, Granada, Spain

<sup>3</sup>Psychiatry Service, Virgen de las Nieves Hospital, Granada, Spain

<sup>4</sup>Department of Psychiatry, University of Granada, Granada, Spain

<sup>5</sup>CTS-549 Research Group, Institute of Neurosciences, University of Granada, Granada, Spain

<sup>6</sup>Psychiatry Service, San Cecilio University Hospital, Granada, Spain

**Objective** Depression and obesity are two conditions with great impact over global health. This is mainly due to their high prevalence and the morbidity and mortality associated to both. The main aim of the present systematic review is to study the association between obesity and depression and the prognostic implications derived from it.

**Methods** A literature review was performed in the PUBMED database. 18 articles were found (9 cross-sectional studies, 6 longitudinal studies and 3 clinical trials), which were reviewed by critical reading after which a summary of the main conclusions was written.

**Results** These selected articles confirmed that there is indeed a link between depression and obesity, although there are doubts as to the significance of this relationship. Depression is a risk factor for obesity, especially atypical depression and in African-American adolescent males. Obesity is a risk factor for depression, especially in women and for recurrent depressive disorder. The comorbidity between obesity and depression is a risk factor for a bad prognosis illness.

**Conclusion** The relationship between both disorders has been analysed in scientific literature, obtaining significant associations but also contradictory results. The most current data demonstrates that there is a relationship between both entities, although there is no unanimity when it comes to establishing the meaning of this association.

**Psychiatry Investig 2020;17(8):715-724**

**Key Words** Depressive disorder, Obesity, Prevalence, Atypical depression.

## INTRODUCTION

Obesity and depression are considered notorious health problems, not only because of their significant prevalence but also because of their high morbidity mortality rates. According to recent data from the World Health Organization (WHO) in 2014 it was estimated that more than 600 million people were affected with obesity whilst at least 2.6 million people die from obesity every year. 44% of global cases of diabetes, 23% of ischemic heart diseases and 7–41% of certain cancers are attributable to overweight and obesity.<sup>1</sup> When it comes to depression

the figures are no less alarming, it is estimated that depression affects 350 million people in the world, making it one of the main causes of disability and morbidity worldwide. In addition, depression is also an important cause of premature mortality, primarily due to suicide.<sup>2</sup>

The probable association between obesity and depression has been studied repeatedly over time in scientific literature. This is mainly due to the fact that they both carry a high prevalence and an increased risk of cardiovascular disease.<sup>3</sup> While many cross-sectional studies have documented this relationship its significance still remains unclear.

Prospective studies have revealed inconsistent findings regarding the sequence in the onset of depression and obesity.<sup>4</sup> This discrepancy could be due to the methodological variation of the different studies (including variations in the sample selection) the duration of the follow-up and/or the evaluation and diagnosis of depression and obesity. The relationship between obesity and depression has also been studied in childhood and adolescence. A prospective study<sup>5</sup> determined that adolescent

Received: March 15, 2020 Revised: April 30, 2020

Accepted: May 9, 2020

✉ Correspondence: Luis Gutiérrez-Rojas, MD

Department of Psychiatry, University of Granada, Faculty of Medicine-tower A, floor 9. Avenida de la Investigación nº 11. E-18016 Granada, Spain

Tel: +34 958 240711, Fax: +34 958 240730, E-mail: gutierrezrojasl@hotmail.com

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

women affected with obesity predicted an increased risk of major depression (up to almost 4 times more). However this risk was not significant for men. A meta-analysis that included 8 longitudinal studies,<sup>6</sup> concluded that there was a bidirectional relationship between depression and obesity. Thus he determined that people with obesity had a 55% increased risk of developing depression over time, and that depressed people had a 58% increased risk of obesity. In addition, the relationship between obesity and depression was stronger than the relationship between overweight and depression, which reflected a dose-response gradient.

The main objectives of this review will be three; 1) to define the methodological quality of those more recent studies that analysed the association between depression and obesity, 2) to determine whether there is indeed an association between both conditions and 3) to clarify what influence they may have over each other. Additionally it will examine the importance of certain socio-demographic, clinical and therapeutic variables in the relation between obesity and depression.

## METHODS

A literature review was conducted of those articles published in the PUBMED database with an inclusion deadline from January 1, 2012 to December 31, 2017, using the following MeSH terms: “obesity” AND “depressive disorder.” The filters applied were those of studies published in the last 6 years and carried out in humans. 179 articles were obtained and the main researcher (BV) made an exhaustive reading of the abstracts, selected the publications based on the inclusion criteria and was responsible for the successive stages. We follow the international recommendations for systematic reviews as Preferred Items for Reporting of Systematic Reviews and Meta-Analyses (PRISMA).<sup>7</sup>

The following inclusion criteria was applied: available abstract, English written articles, already established diagnostic criteria for both conditions (obesity according to body mass index (BMI) and depression according to major depression criteria in the DSM IV or ICD-10, studies of prevalence in both pathologies and finally, the evaluation of the possible prognostic association between these conditions when they affect the same person simultaneously. The exclusion criteria were the following: no available abstract, articles written in a non-English language, articles of very low quality according to the GRADE system (Grading of Recommendations, Assessment, Development and Evaluation),<sup>8,9</sup> and the failure to fulfil the objectives of the study.

The GRADE system initially classifies the evidence into high or low, coming from experimental or observational studies; subsequently and following a series of considerations (risk/

benefit balance, values and preferences of the patients and professionals, and the use of resources or costs), the evidence is classified into high, moderate, low or very low.<sup>9</sup> In comparison with other systems, the advantages of GRADE classification includes a clear separation between quality of evidence and strength of recommendations, provide comprehensive criteria and acknowledgment of values and preferences and explicit evaluation of the importance of outcomes of alternative management strategies.<sup>8</sup> Finally studies which main objective was the evaluation of interventions aimed at reducing the frequency of these conditions were also excluded.

By reading the abstracts, a total of 39 articles were selected, which were then thoroughly revised, eventually discarding 21 of them for not complying with the inclusion criteria. Most of these articles were discarded for failing to adapt to the international diagnostic standards rendering it difficult to draw clear conclusions. The third stage corresponded to the critical reading of the 18 selected articles. Figure 1 summarizes each of these stages. Subsequently, the methodological quality of the 18 selected works was evaluated, for which the GRADE classification was used.<sup>8,9</sup> This system is a rigorous and transparent instrument that classifies scientific publications according to their level of evidence and determines the strength of their conclusions. There are 4 levels of quality, so that initially the publications are classified as high or low quality, depending on whether they are experimental or observational studies. In the final phase, a series of characteristics are analysed (limitations, biases and possible confusion biases among others) that allow us to sort the final classification in high, moderate, low or very low evidence level.

## RESULTS

### Different types of studies and methodological quality

Of the 18 selected studies, 15 were observational and 3 were experimental clinical trials. Within the observational group (15), 6 had a longitudinal design (one retrospective and five prospective) and the other 9 were cross-sectional. The main features as well as the evaluation of the quality of these studies are summarized in Tables 1, 2 and 3. The heterogeneity in the ages of the selected samples should be noted, so that four of the studies were performed in adolescents aged 11 to 17 years<sup>10-13</sup> and the other two<sup>14,15</sup> in patients aged 65 and over.

Methodological quality of the studies (Tables 1, 2 and 3) varied between the low gradation (in the observational studies) and the moderate gradation (in the experimental ones), none of these studies reached the maximum score for they contained important methodological errors.

### Depression as a risk factor for obesity

In this section we will focus on those 10 studies that studied depression as a risk factor for obesity. The conclusions here obtained were not uniform. Three of these studies<sup>15-17</sup> concluded that only atypical depression (DSM subtype) was a risk factor

for obesity. However, there was no correlation between the other subtypes such as classic or melancholic depression and obesity. Others studies found an association between depressive symptoms and obesity. A higher OR was found for abdominal obesity compared to BMI >30<sup>18</sup> whilst there was a higher OR

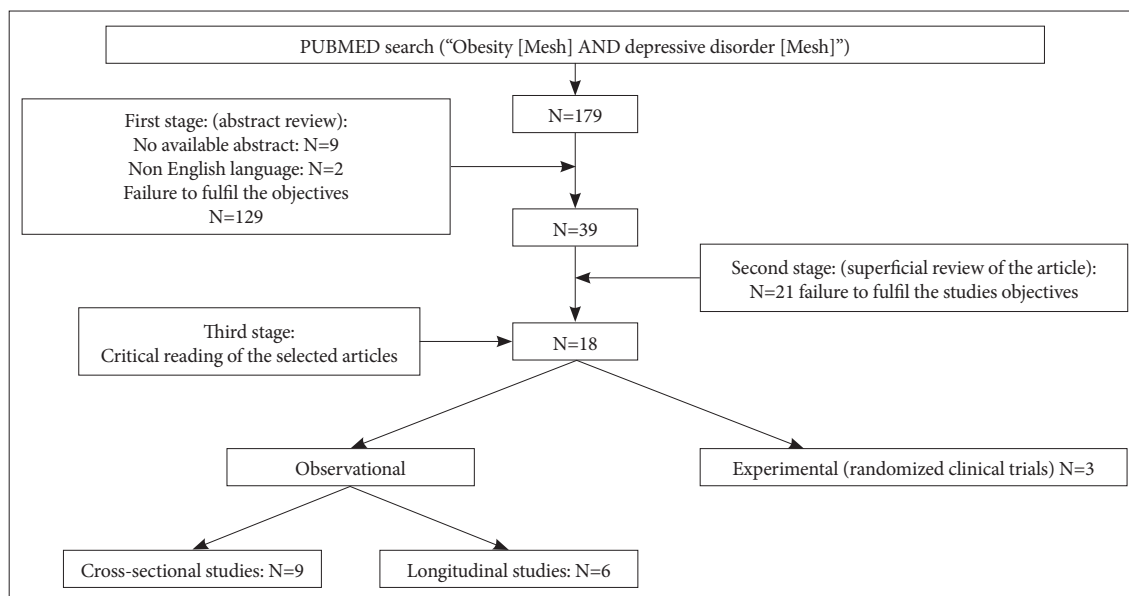


Figure 1. Flow chart of the literature search.

Table 1. Clinical trials studying treatment of patients with obesity and depression

Author (year)	Participants	Objectives	Results	Quality of the study
Kiecolt-Glasser et al. <sup>26</sup> (2015)	N=58 women (38 breast cancer survivors and 20 controls)	To study the impact of daily stressors and major depression over metabolic responses related to obesity in the presence of high-calorie food	Stress and depression alter the metabolic response to rich in fat foods increasing obesity (up to 104 kcal more per meal)	Moderate
Lin et al. <sup>10</sup> (2014)	N=131 (126 of them included in the analysis) patients admitted into acute hospitalization ward diagnosed with major depression	Changes in the Hamilton and functional scale based on body weight and BMI in those patients treated with 20 mg of fluoxetine for 6 weeks	Patients who did not achieve remission had a higher BMI and greater weight before commencing the treatment High weight and BMI are correlated with a slower improvement in both symptoms and functionality at the end of treatment	Moderate
Toups et al. <sup>24</sup> (2013)	N=662 patients with chronic or recurrent major depression, randomized into 3 treatment groups (28 weeks duration, with open phase and single blind phase) BMI was measured before and after the treatment	To assess if BMI has any influence over the response to antidepressant treatment or in its comorbidities	Depression in obesity was common (46.2%) compared to the 25.5% of the sample with normal weight There were no significant differences in the response to treatment in the different groups The comorbidities did vary depending on the weight BMI is associated with the clinical presentation and the prevalence of comorbidities, but not to the response in antidepressant treatment	Moderate

**Table 2.** Longitudinal studies in patients suffering from depression and obesity

Author (year)	Participants	Objectives	Results	Quality of the study
Nigatu et al. <sup>20</sup> (2015)	N=1,094, follow up for an average of 2.17 years. Ages between 33 and 79	To examine the significance of the relationship between major depression and obesity, depending on whether it is a single or recurrent episode of depression	In individuals with obesity there was no increased risk of single major depressive episode (OR=0.75, 95% CI 0.25–2.30), but there was risk of major depression with recurrent episodes (OR=11.63; 95% CI 1.05–128.60) There was no association found between a single depressive episode or depression with recurrent episodes and the development of obesity in the future	Low
Laserte et al. <sup>16</sup> (2014)	N=3,054 (51.3% women, ages from 35 to 66) 5.5 follow-up years	To determine whether the subtypes of major depressive disorder (melancholic, atypical, combined and non-specific) are predictive of adiposity in terms of obesity incidence and changes in BMI	Only patients with atypical depression subtype had an increased risk of obesity with an OR of 3.75 (95% CI 1.24–11.35) The subtype of atypical depression is a strong predictor of obesity	Low
Angstmann et al. <sup>25</sup> (2013)	Retrospective N=1,111 with major depressive disorder (including dysthymia). BMI was measured. 75% of the sample were women, average age around 40 (18–92.3)	To assess whether obesity can have a negative effect over the response to multimodal treatment for depression (6 months)	Treatment results after six months were not significantly affected by patients BMI	Low
Roberts and Duong <sup>11</sup> (2013)	N=4,175 adolescents from 11 to 17 years of age. 1 follow-up year. Cohort study. DISC-IV (Diagnostic Interview Schedule for Children) questionnaire. Measure of height and weight. Classification according to BMI	To examine whether obesity increases the risk of developing depression, if depression increases de risk of obesity or if there is a reciprocal effect	Initial weight did not predict major depression or depressive symptoms (non-significant OR and adjusted OR). Major depression increased the risk of future obesity by more than two [OR between obesity in phase 2 and major depression in phase 1 was 2.87 (95% CI 1.34–6.18)] Young people who are obese are not more likely to be depressed than non-obese people. However, depressed youth are more likely to become obese	Low
Godin et al. <sup>14</sup> (2012)	N=3,090 people over 65 years of age (without depression). 10 years of cohort follow-up. 1,744 people complete de study. 478 cases of depression. The diagnosis of depression was made with MINI (International Psychiatric Structural Interview) or also if the patient was still taking anti-depressive treatment	To investigate the association of BMI and the risk of developing depression in an older population (this study also took blood pressure into account)	Obese subjects (BMI larger than 30) had an increased risk of developing depression when compared to subjects with a normal BMI (RR=1.60 95% CI 1.03–2.51) BMI is prospectively associated with the risk of depression	Low
Pickering et al. <sup>22</sup> (2011)	N=34,653 adults from the USA. Ages 18 and over. 3 years follow up Rating of depression with AUDADIS-IV (Alcohol Use Disorder and Associated Disabilities Interview Schedule) and obesity with BMI	The aim was to determine the incidence in mood disorders, anxiety and substance abuse (DSM IV) and the changes in BMI during the follow-up period	Women who are overweighted, have a higher risk of depression than those with normal weight OR=1.3 CI 95% (1.02–1.56); obese women, also had a higher risk of depression than those with a normal weight OR=1.2 CI 95% (1.02–1.51)	Low

OR: odds ratio, CI: confidence interval, BMI: body mass index, RR: relative risk

**Table 3.** Cross-sectional studies performed in patients with obesity and depression

Author (year)	Participants	Objectives	Results	Quality of the study
Kinley et al. <sup>21</sup> (2015)	N=4,181 Ages from 18 to 65	To examine the association between cardiac and metabolic conditions including obesity, anxiety and depression	Among depressed individuals (N=699) 130 were obese (16.9%). It calculated the OR of obesity for people with depression adjusted to various confounding factors obtaining an OR of 0.85 (95% CI, 0.66 to 1.09) It concluded that depression was not associated either with cardiac or metabolic conditions, but rather with the deterioration of self-care which had an impact on these health problems	Low
Ul-Haq et al. <sup>30</sup> (2014)	N=140,564 Ages from to 40 to 69 (average age of 57)	To examine the probable relationship between major depression and various measurements of adiposity (BMI, waist circumference, waist-hip index and percentage of body fat)	The OR adjusted for obese participants was of 1.16 (1.12–1.20) using the BMI; 1.15 (1.11–1.19) applying the waist circumference and 1.18 (1.12–1.25) when applying the waist-hip index There was a significant association between adiposity and gender. Overweight women were at an increased risk of depression with a dose-response effect. However, in men, there was only a significant risk of depression for those with obesity type III Adiposity has been associated with probable major depression, regardless of the used measurements. The association is stronger in women than in men	Low
Rottenberg et al. <sup>19</sup> (2014)	N=210 people with depression, 195 siblings and 161 healthy controls The average age was of 17 in the first group 15.9 in the second one and 15.8 in the third one 63.3% were men	To assess whether there is an association between depression and cardiovascular risk factors (including obesity) in adolescents with depression which started during their childhood. To do this, he compares them with adolescent siblings of depressed patients (without depression) and with healthy controls	Major depression in childhood is associated with an unfavourable profile for cardiovascular risk factors. For overweight patients the OR (depressed/controls) was 2.13 (1.0–4.56) and for obese patients the OR (depressed/controls) was 3.67 (1.42–9.52)	Low
Yu et al. <sup>18</sup> (2014)	N=4,511 (1,382 men and 3,129 women). Ages varied between 35 and 69 (average age 53). BMI was measured and the questionnaire PHQ-9 was passed, based on DSM-IV criteria. They considered major depression if the score was equal to or greater than 10	To investigate the association between depressive symptoms and diet quality, physical activity and body composition	Compared with healthy individuals, those with mild and major depression have significantly higher ORs for obesity (BMI) and abdominal obesity. Thus, the OR of obesity (BMI>30) in major depression is 1.56 with a 95% CI of (1.30–1.87) and for abdominal obesity the OR is 1.88 with a 95% CI of (1.58–2.24)	Low
Vannucchi et al. <sup>23</sup> (2014)	Multicenter N=571 Ages vary from 18 to 75	To investigate the relationship between obesity and the history of manic or hypomanic symptoms in a sample of patients with major depression	Obese patients belonged more frequently to the bipolar group than non-obese patients. They reported more often an HCL scale of over 14. There were 27 people with bipolar disease in the obese patient group (31.4%) and 92 people in the non-obese group (19.0%). There were significant differences between both groups. In addition, the difference was greater in favour of patients with a BMI of over 35. The more obese a patient was the higher risk he had of suffering from bipolar disorder. Obesity in this sample of patients with a major depressive episode is associated with bipolar disorder	Low

**Table 3.** Cross-sectional studies performed in patients with obesity and depression (continued)

Author (year)	Participants	Objectives	Results	Quality of the study
Roberts and Duong <sup>12</sup> (2013)	N=4,175 adolescents with ages between 11 and 17. The population sample is taken from adolescents living in Houston homes, only 66% of them took part in this study. BMI is measured as well as, depression according to Diagnostic Schedule of Interviews for Children and Adolescents (DSM-IV), weight perception and body satisfaction	To examine the association between major depression, obesity and body image among adolescents	Obesity was associated with an increased risk of depression OR=2.51, 95% CI (1.47-4.29) However, when the association was examined in models that included weight, major depression and body image and covariates, there was no significant association between major depression and weight, or between body satisfaction and major depression. The real significant association was the relationship with perceived weight and depression Thus, even with normal weight, the OR for major depression was greater when the perceived weight was higher	Low
Chou and Yu <sup>15</sup> (2013)	N=10,557 adults over 70 years of age	To reveal the conclusion in the obesity rate associated with classic, atypical and undifferentiated depression compared with those subjects without depression in a representative sample of the population in the USA It measured obesity according to BMI (BMI>30), major depression based on AUDASDIS-IV score, and criteria of major depression according to DSM-IV	It was revealed that after adjusting for sex, age, marital status, race and personal income, the obesity rate was significantly higher for those who had atypical depression than for the rest of the subtypes including controls. The same results were concluded for people that had already passed depression, with current depression and depression throughout their life OR (obesity in atypical depression versus obesity control): Lifetime: 4.03; current: 5.53; past: 3.53, all of them significant The rest (classic and indifference vs. control) were not significant These findings suggest that the heterogeneity of depression should be considered when examining the effect of depression over obesity in the elderly	Low
Levitan et al. <sup>17</sup> (2012)	The group identified 5,092 American adults with past or current depression based on the DSM-IV criteria and 1,500 controls matched by gender. They were divided into three subgroups, depending on the subtype of major depression: classic, atypical and undifferentiated. Those who were both classical and undifferentiated were removed (266)	To examine whether the increased risk of obesity is significant for the basic subtypes of major depression or if it is limited to the atypical subtype	Subjects with atypical depression had noticeably elevated rates of obesity compared to controls and other depressed subjects. OR (atypical vs control); 2.61; 95% CI (2.16-3.16). OR (classic vs. atypical); 0.38; 95% CI (0.32-0.45). OR (atypical versus undifferentiated); 2.27 95% CI (1.90-2.71) Only atypical depression is associated with a high risk of obesity	Low
Merikangas et al. <sup>13</sup> (2012)	N=4,150 adolescents with ages between 12 and 19 from the USA. 76% of the initial sample (2001-2004). The study measured weight and height (BMI) subjects were considered obese if IMC was over 95% for their age	To study the association between obesity and depression in this sample of adolescents	After adjusting for sex, race or ethnicity, age and poverty, major depression was not significantly associated with obesity among adolescents in general (depressed obesity/non-depressed obesity) OR=1.6; 95% CI (0.9-2.9). However there was a significant increased risk among men suffering from depression [OR=2.7, 95% CI (1.1-7.1)] and among depressed non-Hispanic blacks [OR=3.1 with a 95% CI (1.1-8.3)]	Low

OR: odds ratio, CI: confidence interval, BMI: body mass index, RR: relative risk

in patients with obesity in comparison than those with overweight.<sup>19</sup>

Another study focused on age and ethnicity,<sup>13</sup> concluding that in the selected sample (African-American adolescent males), depression was a risk factor for the development of obesity. It found no association between obesity and the rest of the sample. Finally, 3 of the studies in this first section<sup>13,20,21</sup> did not obtain significant differences, concluding that depression was not a risk factor for obesity in the selected sample (Figure 2).

### Obesity as a risk factor for depression

In this second section, we discovered 5 studies that concluded that obesity was a risk factor for depression. Only one of the articles could not establish a relationship between both disorders, although the conclusions must be adjusted.<sup>11</sup> The group of Nigatu et al.<sup>20</sup> selected a sample with recurrent depressive disorder and another group of participants who had suffered a single depressive episode. They found that that obesity acted as a risk factor for depression only for the group with re-

current depressive episodes. Another group analysed the association between obesity, body image and depression in a sample of more than 4,000 adolescents.<sup>12</sup> Although it was initially established that obesity and depression were indeed associated, this was not maintained when adjusting the results for other factors such as sociodemographic and clinical variables. Regarding sex, there is data that suggests a different obesity-depression relationship between men and women, since it was only in woman that obesity increased the risk of depression.<sup>22</sup> Finally, in a different work on the same sample of 4,000 adolescents,<sup>11</sup> the authors concluded that adolescents affected with obesity did not have higher depression rates, although they did detect an increased risk of future obesity in the group of adolescents with depression (Figure 3).

### Obesity-depression association.

#### Prognostic implications

An overall of four articles viewed this subject. The first article,<sup>10</sup> studied the response to fluoxetine in patients admitted to

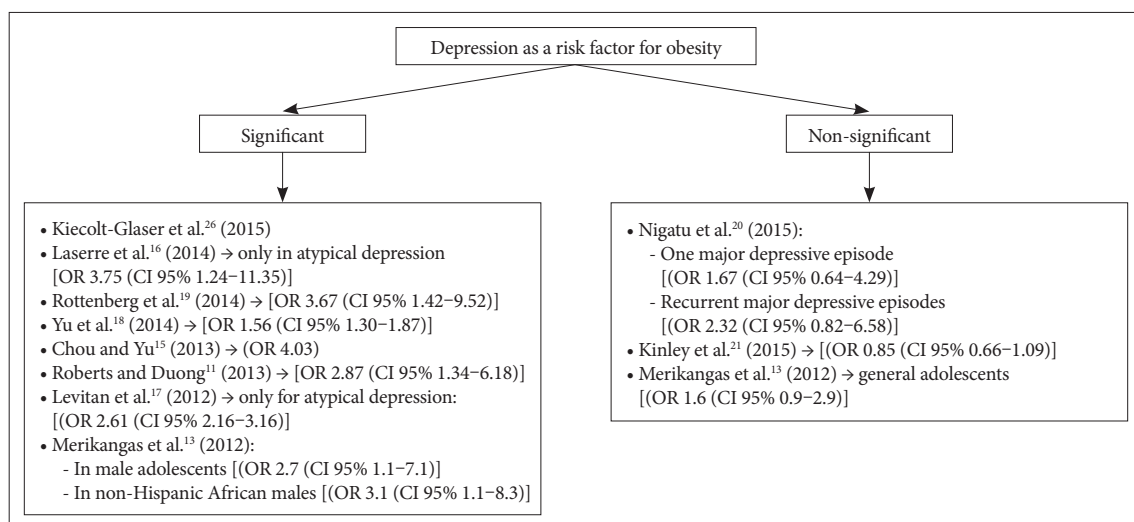


Figure 2. Depression as a risk factor for obesity.

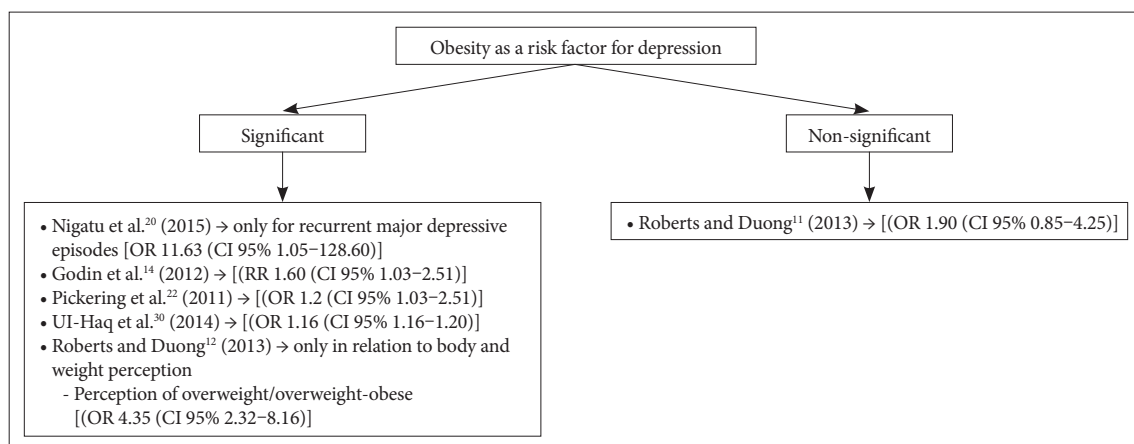


Figure 3. Obesity as a risk factor for depression.

an acute care unit when diagnosed with a depressive episode. The results concluded that those participants who did not reach symptomatic remission had a higher BMI at the beginning of the treatment. A second article<sup>23</sup> analysed the association between obesity, depression and bipolar disorder in a population sample. They observed that patients affected with obesity that had suffered a mayor depressive episode were more likely to suffer from bipolar disorder in the future than those patients that had depression but did not suffer from obesity. The association between obesity and the response to antidepressant treatment was also studied in one of the clinical trials.<sup>24</sup> Patients with depression were randomly assigned to take different therapeutic options. All patients had their BMI calculated at the beginning and end of the clinical trial. There were no significant differences in the response to treatment when classified by BMI yet there was disparity in the relationship between the BMI and comorbidities. This association was studied leading to the conclusion that BMI in this sample was related to the clinical presentation of depression, with those patients with higher BMI being more prone to suffer from comorbid pathologies (medical and psychiatric, such as social phobia and bulimia). Finally, the results of a multidisciplinary and intensive treatment for depression were not related to the BMI baseline of participants according to data from another study.<sup>25</sup>

## DISCUSSION

Our chief aim when undertaking this systematic review has been to clarify the association between obesity and depression, two diseases with great impact over global health. In none of the three sections in which the selected articles have been divided (depression>risk factor>obesity, obesity>risk factor>depression and prognosis when depression and obesity are associated) have we observed unanimity in the conclusions.

In the first group (depression as risk factor for obesity) 8 out of the 11 selected articles presented data in favour of this association. We highlight the results of a clinical trial<sup>26</sup> in which patients with depression who took a high-fat diet had higher rates of obesity than those patients with the same diet but without depressive disorder diagnosis. However, the subtype of depression must be taken into account in order to be able to relate it to obesity. Data derived from this clinical trial revealed that it is only the subtype of atypical depression that has been statistically associated. These findings support the current trends that suggest that within the depressive syndrome there would be different entities with different features that would be influenced in different ways by other variables. Regarding this subject, one of the selected articles<sup>13</sup> analysed if there was an association between depression and obesity in adolescents when divided according to ethnic group and sex. They found

that it was only in African-American males that depression was a risk factor for obesity; however this did not occur in the rest of the sample.

We also analysed articles that could not demonstrate a correlation between obesity and depression.<sup>20</sup> However, here we must point out that the methodological quality of these studies was not very high, for they did not take into account, for example, the considerable number of losses. They also failed to monitor the influence of certain important variables such as the antidepressant treatment.

In the second section there is a greater consensus when it comes to affirming that obesity increases the risk of depression. Out of the six selected articles, five concluded that there is an association between both factors. Once again, the depressive subtype, the average age of the sample and sex are variables that influenced the results. For example, according to Nigatu et al.<sup>20</sup> obesity would only act as a risk factor for depression in case of recurrent major depressive disorder, however for a sample of adolescents that were followed in time, there was no association between both factors.<sup>11</sup>

In the third section we analysed the influence on the prognosis of the obesity-depression combination in the same patient. We found two clinical trials<sup>10,24</sup> that analysed this issue. There was no homogeneity in the samples, since Lin selected hospitalized patients whilst Toups worked with an ambulatory sample with comorbid anxiety disorder. While in the first article the results show that in patients affected with obesity the response to the antidepressant treatment was significantly worse, in the second article no significant associations were obtained.

It has been suggested that the association between depression and obesity is probably due to the action of certain genes involved in both pathologies. For example the genes that encode glucocorticoids, leptin and dopamine receptors. The role of environmental factors should also be noted, especially all those situations that contribute to maintaining a situation of chronic stress. The results of a study conducted on twins by Afari et al.<sup>27</sup> concluded that only 12% of the genetic component of depression was shared by obesity, so that environmental factors are fundamental to understand how both pathologies are related.<sup>28</sup> The current etiopathogenic model states that chronic stress sets in motion a series of mechanisms involving the central nervous system, the hypothalamic-pituitary-adrenal axis and the autonomic nervous system.<sup>29</sup> These mechanisms would then generate a pro-inflammatory state through peripheral resistance to the glucocorticoid action, intestinal bacterial translocation, increase of catecholamines and the secretion of cytokines (TNF- $\alpha$  and IL-6). This pro-inflammatory environment would act over white fat adipocytes leading to an inappropriate local activation, with an increase in the pro-



duction of leptin and a decrease of adiponectin, causing inflammation and the accumulation of fatty tissue.<sup>30</sup> In addition to these local changes, inflammatory cytokines act over the central nervous system, inducing changes in synaptic plasticity and in neurogenesis that would be similar to those that occur in depression.

As previously explained, the wide methodological variety of the studies included in this review hampered the conclusion of unequivocal results. This is seen in the heterogeneity of the sample size, the design of the studies or the different instruments used to measure obesity and depression, all which could significantly influence the results. However, it can be stated that a high percentage of the analysed bibliography, demonstrates that both pathologies are associated, although in some cases it is difficult to determine the significance of this association.

Another strong point in this study is that it highlights the importance of the subtypes of depression, a feature that is not generally taken into account although there is increasing evidence that depressive disorder will bring different entities together, each with their own clinical and therapeutic characteristics. Furthermore, the influence of age, sex or ethnicity over depressive symptomatology validates the change in diagnostic manuals towards a more dimensional perspective, as well as the inclusion of sub-threshold forms of presentation associated with clinical and functional discomfort. These results highlight that the reality of the great psychiatric syndromes is probably much more complex than what it was initially believed to be.

The current systematic review has several limitations. Firstly, the articles were only reviewed by a single researcher and most of these studies were cross-sectional, rendering it impossible to obtain causality relationships from them. Following the type of design, a high percentage of the studies presented a low to moderate methodological quality according to the GRADE scale.<sup>8,9</sup> Finally, the search was carried out only in Pubmed, and although it is one of the most powerful databases to day, it is possible that additional publications collected in other bibliographic sources were not detected.

## CONCLUSIONS

Obesity and depression are disorders with a high prevalence and an extraordinary effect over global morbidity and mortality. The relationship between both disorders has been analysed in scientific literature, obtaining significant associations but also contradictory results. The most current data demonstrates that there is a relationship between both entities, although there is no unanimity when it comes to establishing the meaning of this association. Certain variables such as the subtype of atypical depression, female sex, and African-American ethnicity could influence the relationship between depres-

sion and obesity thus it is advised that they be examined in future studies. The limited methodological quality of the articles included in this review, with a large proportion of cross-sectional studies that are very heterogeneous in their design has influence the difficulty to draw clear conclusions. In the future it is recommended to include a larger number follow up of studies that are based on unified criteria.

## Acknowledgments

The authors would like to gratefully acknowledge the collaboration of Department of Psychiatry members in the University of Granada.

## Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

## Author Contributions

Conceptualization: Luis Gutiérrez-Rojas, Beatriz Villagrasa Blasco. Data curation: Luis Gutiérrez-Rojas, Beatriz Villagrasa Blasco. Formal analysis: Luis Gutiérrez-Rojas, Beatriz Villagrasa Blasco. Funding acquisition: Luis Gutiérrez-Rojas, Beatriz Villagrasa Blasco. Investigation: Luis Gutiérrez-Rojas, Beatriz Villagrasa Blasco. Methodology: Luis Gutiérrez-Rojas, Beatriz Villagrasa Blasco. Project administration: all authors. Resources: all authors. Software: all authors. Supervision: all authors. Validation: all authors. Visualization: all authors. Writing—original draft: all authors. Writing—review & editing: all authors.

## ORCID iDs

Beatriz Villagrasa Blasco	<a href="https://orcid.org/0000-0002-8858-6717">https://orcid.org/0000-0002-8858-6717</a>
Jesús García-Jiménez	<a href="https://orcid.org/0000-0002-3976-8776">https://orcid.org/0000-0002-3976-8776</a>
Isabel Bodoano	<a href="https://orcid.org/0000-0001-5552-9647">https://orcid.org/0000-0001-5552-9647</a>
Luis Gutiérrez-Rojas	<a href="https://orcid.org/0000-0003-0082-2189">https://orcid.org/0000-0003-0082-2189</a>

## REFERENCES

1. WHO. Organización Mundial de la Salud. 2015. Obesidad y sobrepeso. Available at: <http://www.who.int/mediacentre/factsheets/fs311/es/>. Accessed June 26, 2020.
2. WHO. Organización Mundial de la Salud. 2016. La depresión. Available at: <http://www.who.int/mediacentre/factsheets/fs369/es/>. Accessed June 26, 2020.
3. Pennix BW, Beekman AT, Honig A, Deeg DJ, Schoevers RA, Van Eijk JT, et al. Depression and cardiac mortality: results from a community-based longitudinal study. *Arch Gen Psychiatry* 2001;58:221-227.
4. Faith MS, Butryn M, Wadden TA, Fabricatore A, Nguyen AM, Heymsfield SB. Evidence for prospective associations among depression and obesity in population-based studies. *Obes Rev* 2011;12:e438-e453.
5. Anderson SE, Cohen P, Naumova EN, Jaques PF, Must A. Adolescent obesity and risk for subsequent major depressive disorder and anxiety disorder: prospective evidence. *Psychosom Med* 2007;69:740-747.
6. 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.
7. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg* 2010;8:336-341.
8. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924-926.
9. Aguayo-Albasini JL, Flores-Pastor B, Soria-Aledo V. GRADE system: classification of quality of evidence and strength of recommendation. *Cir Esp* 2014;92:82-88.

10. Lin CH, Chen CC, Wong J, McIntyre RS. Both body weight and BMI predicts improvement in symptom and functioning for patients with major depressive disorder. *J Affect Disord* 2014;161:123-126.
11. Roberts RE, Duong HT. Obese youths are not more likely to become depressed, but depressed youths are more likely to become obese. *Psychol Med* 2013;43:2143-2151.
12. Roberts RE, Duong HT. Perceived weight, not obesity, increases risk for major depression among adolescents. *J Psychiatr Res* 2013;47:1110-1117.
13. Merikangas AK, Mendola P, Pastor PW, Reuben CA, Cleary SD. The association between major depressive disorder and obesity in US adolescents: results from the 2001-2004 National Health and Nutrition Examination Survey. *J Behav Med* 2012;35:149-154.
14. Godin O, Elbejjani M, Kaufman JS. Body mass index, blood pressure, and risk of depression in the elderly: a marginal structural model. *Am J Epidemiol* 2012;176:204-213.
15. Chou KL, Yu KM. Atypical depressive symptoms and obesity in a national sample of older adults with major depressive disorders. *Depress Anxiety* 2013;30:574-579.
16. Laserre AM, Glaus J, Vanderleur CL, Marques-Vidal P, Vaucher J, Bastardot F, et al. Depression with atypical features and increase in obesity, body mass index, waist circumference, and fat mass: a prospective, population-based study. *JAMA Psychiatry* 2014;71:880-888.
17. Levitan RD, Davis C, Kaplan AS, Arenovich T, Phillips DI, Ravindran AV. Obesity comorbidity in unipolar major depressive disorder: refining the core phenotype. *J Clin Psychiatry* 2012;73:1119-1124.
18. Yu ZM, Parker L, Dummer TJ. Depressive symptoms, diet quality, physical activity, and body composition among populations in Nova Scotia, Canada: report from the Atlantic Partnership for Tomorrow's Health. *Prev Med* 2014;61:106-113.
19. Rottenberg J, Yaroslavsky I, Carney RM, Freedland KE, George CJ, Bajj I, et al. The association between major depressive disorder in childhood and risk factors for cardiovascular disease in adolescence. *Psychosom Med* 2014;76:122-127.
20. Nigatu YT, Bültmann U, Reijneveld SA. The prospective association between obesity and major depression in the general population: does single or recurrent episode matter? *BMC Public Health* 2015;15:350.
21. Kinley DJ, Lowry H, Katz C, Jacobi F, Jassal DS, Sareen J. Depression and anxiety disorders and the link to physician diagnosed cardiac disease and metabolic risk factors. *Gen Hosp Psychiatry* 2015;37:288-293.
22. Pickering RP, Goldstein RB, Hasin DS, Blanco C, Smith SM, Huang B, et al. 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. *J Clin Psychiatry* 2011;72:1494-1502.
23. Vannucchi G, Toni C, Marenmani I, Perugi G. Does obesity predict bipolarity in major depressive patients? *J Affect Disord* 2014;155:11-18.
24. Toups MS, Myers AK, Wisniewski SR, Kurian B, Morris DW, Rush AJ, et al. Relationship between obesity and depression: characteristics and treatment outcomes with antidepressant medication. *Psychosom Med* 2013;75:863-872.
25. Angstmann KB, Wade TW, Dejesus RS, Rundell JR, Atrichter PM. Patient body mass index does not predict six-month clinical outcome of depression managed under collaborative care. *J Prim Care Community Health* 2013;4:119-123.
26. Kiecolt-Glaser JK, Habash DL, Fagundes CP, Andridge R, Peng J, Malarkey WB, et al. Daily stressors, past depression, and metabolic responses to high meals: a novel path to obesity. *Biol Psychiatry* 2015;77:653-660.
27. Afari N, Noonan C, Goldberg J, Roy-Byrne P, Schur E, Golnari G, et al. Depression and obesity: do shared genes explain the relationship? *Depress Anxiety* 2010;27:799-806.
28. Wurtman JJ, Wurtman RJ. Depression can beget obesity can beget depression. *J Clin Psychiatry* 2015;76:e1619-e1621.
29. Ouakinin SRS, Barreira DP, Gois CJ. Depression and obesity: integrating the role of stress, neuroendocrine dysfunction and inflammatory pathways. *Front Endocrinol (Lausanne)* 2018;9:431.
30. Ul-Haq Z, Smith DJ, Nicholl BI, Cullen B, Martin D, Gill JM, et al. Gender differences in the association between adiposity and probable major depression: a cross-sectional study of 140,564 UK Biobank participants. *BMC Psychiatry* 2014;14:153.