TITLE PAGE

- ✓ Title: The effect of abdominal obesity on depression in general population: a systematic review and meta-analysis

- ✓ Authors: Mrs Qunyan Xu[1](corresponding author, PhD candidate); Professor Debra Anderson[1]; Dr. Janine Lurie-Beck[2]
  [1]: Institute of Health and Biomedical Innovation, Queensland University of Technology
  [2]: School of Psychology and Counseling, Faculty of Health, Queensland University of Technology

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- ✓ Contacting information of corresponding author: Qunyan Xu
  - o Postal address: N Block, QUT Kelvin Grove Campus, Victoria Park Road, Kelvin Grove, QLD, 4059, Australia
  - o Email: qunyan.xu@student.qut.edu.au
  - o Telephone: +61 07 31385953
  - o Fax number: +61 07 3138 3814

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Abstract

Obesity has been widely regarded as a public health concern because of its adverse impact on individuals' health. Systematic reviews have been published in examining the effect of obesity on depression, but with major emphasis on general obesity as measured by the body mass index. Despite stronger effect of abdominal obesity on individuals' physical health outcomes, to our best knowledge, no systematic review was undertaken with regard to the relationship between abdominal obesity and depression. This paper reports the results of a systematic review and meta-analysis of cross-sectional studies examining the relationship between abdominal obesity and depression in a general population. Multiple electronic databases were searched until the end of September 2009. 15 articles were systematically reviewed and meta-analyzed. The analysis showed that the odds ratio of having depression for individuals with abdominal obesity was 1.38 (95%CI, 1.22-1.57), as compared to those who are not obese. Furthermore, it was found that this relationship did not vary with potential confounders including gender, age, measurement of depression and abdominal obesity, and study quality.

Introduction

It is widely accepted that obesity is strongly correlated with a variety of medical conditions such as cardiovascular diseases, Type 2 diabetes and some types of cancer (1-3). Two types of obesity are presented among literature, which are general obesity, estimated by the body mass index (BMI); and abdominal obesity, commonly evaluated by waist circumference (WC) or waist hip ratio (WHR). A review article by Shoelson and colleagues suggests that adiposity increases the risk of diseases by promoting a chronic, subacute status of inflammation, for which the adiposity accumulated on abdomen is particularly a main contributor (4). By definition, BMI indicates overall fat distribution, thus is not as effective as WC in reflecting abdominal fat (5). Corresponding to the statement of the role abdominal obesity played in inflammatory pathogenesis, other researchers have observed that BMI combined with WC did not increase the predictive value to health risk compared to WC alone (6), suggesting a greater emphasis to be placed on WC (7).

As much the same way of the causal linkage to physical diseases, the mechanism of the relationship between abdominal obesity and depression is associated with inflammatory markers and dysregulation of the hypothalamic-pituitaty-adrenocortical (HPA) axis (8, 9). Impaired feedback regulation of HPA axis is commonly presented in patients with depression (9) and is thought responsible for inducing sickness behaviors that are indistinguishable from human major depression (e.g. sleep disturbance, social isolation, feeling down) (10). At biological level, dysfunction of HPA feedback regulation is believed to be mediated by reduced number of glucocoticoid receptors (GR), which result in elevated concentration of cortisol, ultimately interrupt normal regulation (11). Meanwhile, decreased level of GR is found to be inhibited by a variety of cytokines (12, 13). In the immune system, adipose tissue is an endocrine organ that releases cytokines and other molecules, which

influence on immune activation by mechanisms stated earlier and eventually lead to or exacerbate symptoms of depression. Of particular importance to the current research is that abdominal adiposity produces a greater effect on systemic inflammation than other sites of adiposity (4); therefore, in relation to depression, the role of abdominal fat should be underlined.

Last decade witnessed an increasing number of studies examining the relationship between obesity and depression among general population, which is evidenced by emerging publications of systematic reviews for both cross-sectional and prospective relationships of these two constructs (14-17). Despite of the well detailed description of the relationship between obesity and depression, obesity in these reviews is commonly defined by BMI (14-17), an indicator of general fat distribution. Given the stronger effect of abdominal fat on immune system and greater ability to predict health outcomes, summarizing the relationship between abdominal obesity and depression is clearly a necessity. Meanwhile, although the relationship between abdominal obesity and depression is discussed when reviewing the correlation between metabolic syndrome and depression (18, 19), no systematic review and meta-analysis have been conducted to systematically assess the relationship between abdominal obesity and depression. The purpose of this review is to quantify the relationship between depression and abdominal obesity. Previous systematic reviews for cross-sectional (14) and longitudinal (15) relationships between general obesity and depression have examined the potential moderating effect of gender, age, measurement of depression and study quality indicator. These factors together with the measurement of abdominal obesity were also to be examined in subgroup analysis to enable comparison.

Methods

Study selection

The search strategy was constructed in consultation with a qualified university librarian, and was considered comprehensive enough to capture all relevant sources of information. Electronic databases were searched for publications up to the end of September 2009. These included PubMed, Cumulative Index to Nursing and Allied Health (CINAHL), PsycINFO, PsychoARTICLE, SPORTDiscus, and ProQuest Psychological Journal. Evidence Based Medicine Reviews Multi-file was also searched including ACP Journal Club (ACP) and Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and Database of Abstract of Reviews of Effects. Searches were conducted using keywords that included central adiposity, abdominal obesity, visceral obesity, adiposity, WC, WHR, metabolic syndrome, syndrome X, body fat distribution, affective disorder, depression, psychiatric disorder, mood, psychological distress, mental health and combinations of these. No limitations were included in the search strategy. Relevant review articles were hand searched to maximize the number of potentially eligible studies. The current review was limited to observational studies (cross-sectional & prospective) that measured the direct association between abdominal obesity on depression. Studies reporting the relationship between weight gain and depression were not included in this review. Experimental studies were excluded, as were commentaries and narrative reviews without statistical results. Studies examining the relationship between abdominal obesity and depression in a cohort limited to those with a specific disease (e.g. hypertension) or in an adolescent population were excluded. No inclusion criteria were specified regarding the measurement of abdominal obesity and depression; instead, the difference in effect size relating to the

measurement of depression and abdominal obesity was analyzed (20). No restriction was applied on language to reduce selection bias and enable exploration of the heterogeneity of English and non-English written articles. Odds ratio (OR) was chosen as the estimate for the relationship between depression and abdominal obesity. Research studies using OR as an effect size, or reporting other statistics that allow transformation of effect size to OR were included. A manual search of reference lists of review articles was conducted to maximize the number of studies identified. A total of 6039 articles were returned in total.

Coding process & author contact

A coding protocol was developed for eligible studies, and comprised of study level and effect size level information. The study descriptors coded were publication type and year, mean age of sample, percentage of females, country, measurement of depression and abdominal obesity; and the effect size. The coding process was undertaken by one researcher, but was conducted repeatedly to minimize coding error. It is not uncommon to find multiple publications from one study. In this review, coding process is study unit based, which is defined by study sample. Author contact was initiated when presented data were incomplete or unusable for analysis.

Quality assessment

A checklist of different aspects of study quality was adapted from the Newcastle-Ottawa Scale (21), whose content validity and interrater reliability have been established. The evaluated aspects of study quality included representative sampling strategy, sampling sources of both obese and non-obese groups, response rate, measurement of abdominal

obesity and depression, and control of confounders. A response rate of 60% was used as a cutoff point in the current study, which has been used in the previous systematic reviews (22). The use of sum scoring in meta-analysis of observational studies has been controversial (23), therefore, not attempted here. Studies quality assessment was conducted by two authors independently. The results of both authors were compared and the disagreement was solved after discussion. An appendix table was attached.

Data analyses

The analysis was conducted using statistical software of Statistical Package for the Social Sciences 16.0 in combination with the meta-analysis macros provided by Lipsey and Wilson (24). Prior to the analysis of the overall effect size and its relationship with sample characteristics, a homogeneity test (Q test) was performed to determine the usage of random or fixed effect model (24). A random effect model would be chosen if Q test was shown to be significant (defined as a p value of less than .05), and if not, a fixed effect model was selected. An outlier in the current meta-analysis was defined as any observation that is more than 3 standard deviations from the mean. If an outlier is presented, overall effect sizes with and without excluding outlier were both calculated. Publication bias was evaluated using funnel plot (25, 26), where standard normal deviate is regressed on precision, defined as the inverse of the standard error. In testing bias in meta-analysis, a *p* value less than 0.1 is considered as significant, which has been applied in previous analysis (25).

Results

As shown in Figure 1, out of the 150 potentially relevant articles selected for further screening, 96 articles were excluded due to no measures of abdominal obesity or depression, use of a clinical population, investigation of weight gain, not available, not relevant to the topic or were commentaries without statistics. The reference lists of the 13 identified review articles were manually searched before exclusion, and no new studies were found. Further, 4 longitudinal studies examining the effect of depression on abdominal obesity were excluded.

This procedure resulted in 37 potentially eligible articles to be coded. During the subsequent coding procedure, authors of 16 articles that had incomplete or unusable data were contacted. Six authors then provided the data requested. As a result of the coding process, a further 15 articles were excluded. These included 1 study that examined the longitudinal effect of abdominal obesity on depression among adolescents(27), 1 article was a conference poster which did not provide author contact details(28), the other 9 articles were those for which the authors did not respond to the request for further data(29-37), 1 article reporting gender-stratified correlation coefficients only and a pooled result could not be calculated due to heterogeneity between subsamples (38), and 3 articles that were multiple reports from one study sample (39-41). Among the 22 articles left from this procedure, it was decided the 3 prospective studies (42-44) were not included for review due to the small number and heterogeneity among them. Furthermore, 4 studies that did not have relevant data to convert correlation coefficient to OR were excluded (45-48). The effect size of two studies (49, 50) using mean differences and one study (51) with correlation coefficient was transformed into OR. As a result, 15 studies were systematically reviewed and meta-analyzed.

Pooled effect size of the relationship between depression and abdominal obesity

Data from the 15 cross-sectional studies using OR as an effect size were meta-analyzed to examine the association between abdominal obesity on depression. Prior to the calculation of pooled effect size, presence of outlier was examined. The mean OR of studies in this review was 1.49 ± .59; therefore, an outlier was any observation beyond the range of -.28 to 3.26 in the current review. The range of effect size was from .75 to 2.86, thus, no outlier was identified based on the above criteria. The homogeneity test of 15 studies showed a Q value of 39.589, *df* = 14, *p* = .0003; therefore, a random effect model was applied. With this model, it was shown that the pooled OR was 1.38 (95% CI, 1.22-1.57). A forest plot of studies were displayed in Figure 2.

Subgroup analysis

The moderate effect of gender, measurement of depression and abdominal obesity, confounder control and age on the association between depression and abdominal obesity was investigated.

Seven studies reported the prevalence of depression for women and men separately, two studies used a women exclusive sample, and one studied a male exclusive sample. Therefore, the number of female studies could be utilized were nine, and the number of male studies was eight. As shown in Table 1, the pooled OR for women was 1.50 (95% CI, 1.10-2.04), and the OR for men was 1.43 (95% CI, 1.00-2.03). Both estimates showed an elevated risk of having depression among individuals with abdominal obesity; however, gender was not believed to be a moderator for the association of interest given the nearly

identical 95% confidence intervals of the two estimates (Cochrane handbook of systematic reviews of interventions).

Regarding the measurement of depression, the current study found three studies used a clinical interview and twelve studies applied self-report psychometric scales. The OR of having major depression that was diagnosed with clinical interview was 1.30 (95%CI, 0.96-1.75), suggesting no difference in clinical depression between obese and non-obese groups. In contrast, the OR for depressive symptoms as measured by psychometric scales was statistically significant, with an OR being 1.41 (95% CI, 1.22-1.64). Comparing the two estimates found that the 95%CI of depression symptoms subgroup was included in that of clinical depression subgroup, suggesting no statistical difference between these two groups.

For the measurement of abdominal obesity, fourteen studies used WC as a measurement of abdominal obesity and one used WHR (50). Because there was only one study using WHR, examining the difference of effect size between studies using WHR and WC was not attempted. Rather, studies using the NCEP-ATPIII's standard of WC were compared with those adopted conservative cutoff points. As can be seen from Table 1, nine studies used the NCEP-ATPIII's standard, which defines abdominal obesity as having a WC greater than 88 cm for women and 102 cm for men. The other five studies used lower cutoff points of WC, such as having a waist circumference ≥ 90 cm in a Japanese men study (52) or a waist girth ≥ 88 cm in an Australian middle aged women study (53). The pooled OR for studies using a conservative threshold of WC was 1.24 (95%CI, 1.00-1.53), and the corresponding value for those using the NCEP-ATPIII standard was 1.40 (95%CI, 1.19-1.65). Again, it was believed that there was no statistical difference between these two subgroups, given the considerable overlap between two 95% confidence intervals.

Regarding study quality control as indicated by confounder control (see Table 1), the average OR of adequately adjusted studies was 1.30 (95%CI, 0.99-1.72), whereas the corresponding value of non-adjusted studies was 1.42 (95%CI, 1.21 -1.67). Although the OR for the uncontrolled studies was statistically significant and higher than that for the controlled studies, there was no statistical difference between them.

The impact of age on the effect of abdominal obesity and depression was evaluated, too. Studies were categorized into two groups based on the mean age of samples: less than 60 years and 60 years or older. As indicated from Table 1, the mean OR was 1.37 (95%CI, 1.18-1.59) for the younger population, and 1.44 (95%CI, 1.09 -1.90) for the elderly. No significant difference was suggested as can be seen from the overlap of 95% of the two estimates.

Publication bias

The Eggers' test revealed that the measure of funnel plot asymmetry was not significant, $p = .258$. This result suggested no publication bias.

Discussion

The analysis of 15 cross-sectional studies based on a general population showed a moderate magnitude relationship between abdominal obesity and depression (OR, 1.38; 95%CI, 1.22-1.57), which is stronger than that between general obesity and depression as revealed by previous study (OR, 1.26) (14). The observed greater association confirmed the hypothesized the important role abdominal obesity played in relation to depression. This finding stresses a clear need to place more emphasis on abdominal obesity than general obesity for health practice. None of the potential factors including age, gender, measurement of depression and abdominal obesity and confounder control had a moderate

effect on the studied association. Despite of the non-significant finding, it needs to be noted that the number of studies are generally small, particularly in some subgroups such as clinical depression subgroup (N = 3), which may limit the statistical power to detect the real difference.

The current review found an approximately 50% increased risk of having depression among both men and women with abdominal obesity. This finding is consistent with a previous systematic review (14), where a relationship between BMI measured obesity and depression was examined among community based studies. Similarly, in the review by De Wit et al. (14) only a trend for a more marked association in women than men was found. Overall, our and the previous systematic review suggest that gender itself may not increase the risk of depression for those with abdominal obesity. Of interest is that both the ORs for male (OR, 1.43) and female subgroups (OR, 1.50) were higher than the overall effect size (OR, 1.38). This was because when contrasting estimates of genders, five studies in the review that did not report usable gender specific data were excluded from comparative analysis. The overall effect size for the rest ten studies included in the gender comparative analysis was 1.44 (95%CI, 1.21-1.71), which was in between the two estimates of genders.

Subgroup analysis regarding measurement of depression found that individuals with abdominal obesity have no increased risk of major depression, whereas they are more likely to experience depressive symptoms. This finding collaborates with a previous systematic review on depression and diabetes, where a non-significant OR was found for depression defined by structured interview and a larger and significant OR for self-report scales measured depression (54). Despite this, it needs to be noticed is that subgroup analysis is observational and no potential confounder was controlled. Hence, the non-significant

relationship between major depression and abdominal obesity may be a result of inadequate statistical power and/or failure to control for confounders. Alternatively, such result may have indicated that clinical interview diagnosed major depression is a more severe condition that takes more than abdominal obesity to occur. As compared to major depression, depressive symptoms are minor and temporary, which is more likely to be experienced by individuals with abdominal obesity considering the pervasive stigma and discrimination toward these people (55).

A few limitations of the current review should be acknowledged. First, the number of studies is generally small and the majority of them were undertaken in developed countries. Since being overweight is an index of wealth in many developing countries, the association between abdominal obesity and depression may vary according to country of origin. Unfortunately, this cannot be proved by the current review due to a shortage of studies from developing countries. Second, the estimate of the relationship between abdominal obesity and depression may be inflated, as the majority of the studies did not adjust for potential confounders such as socio-demographic factors and chronic conditions. In addition, the effect size of controlled studies also was smaller and statistically non-significant.

Overall, it is concluded that there is moderate relationship between abdominal obesity and depression in general population. Given the fact that, abdominal obesity has a stronger association with depression than general obesity and even mild depressive symptoms increase the risk of cardiac mortality (56), it is essential for health professionals to pay more attention to clients' abdominal fat distribution.

Xu, Q.

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Nil

Table 1 Results of pooled effect size and subgroup analysis for the association between depression and abdominal obesity

Subgroups	No. of studies	Effect size	95% CI
OR			
Overall	15	1.38	1.22-1.57
Gender			
Men	8	1.43	1.00-2.03
Women	9	1.50	1.10-2.05
Depression measurement			
Clinical interview	3	1.30	0.96-1.75
Self-report scale	12	1.41	1.22-1.64
Abdominal obesity measurement			
NCEP-ATPIII	9	1.40	1.19-1.65
Lower than NCEP-ATPIII	5	1.24	1.00-1.53
No. of confounders controlled			
More than three	3	1.30	0.96-1.75
Less than three	12	1.41	1.22-1.64
Age			
Under 60 years	12	1.37	1.18-1.59
60 years and older	3	1.44	1.09-1.90

Table 2 Summary of cross-sectional studies examining the relationships between abdominal obesity and depression

Study description	Country	Sample size	% female	Mean age (SD)	Assessment of abdominal obesity	Assessment of depression	Confounders	Effect size estimate		
								Overall	Male	Female
Viinamaki et al., 2009(57)	Finland	219	57.8	54.15 (9.81)	NCEP-ATPIII	Clinical interview	No	0.79 (0.35-1.79)	0.84 (0.27-2.63)	0.97 (0.28-3.36)
Takeuchi, et al. 2009(52)	Japan	1215	0.0	42.5 (10.3)	≥ 90 cm§	POMS	age, prior history of cardiovascular disease, type 2 diabetes, life habits (smoking, alcohol consumption, exercise, sleep) and job situation	1.65 (1.02-2.70)	-	-
Herva, et al., 2006(58)	Finland	5648	50.3	31 (0)	NCEP-ATPIII	HSCL	gender, smoking, alcohol consumption, marital status, level of education and physical activity	1.06 (0.85-1.33)	-	-
Gil, et al.,2006(59)	Poland	795	58.0	55.5 (5.0)	NCEP-ATPIII	BDI	No	1.13 (0.83-1.55)		
Vogelzangs, et al. 2007(60)	USA	2917	51.5	73.6 (2.9)	NCEP-ATPIII	CESD-20	No	2.42 (1.66-3.54)	1.49 (0.85-2.60)	1.26 (0.72-2.21)
William et al., 2009(53)	Australia	979	100.0	51.5 (17.22)	≥ 88 cm (obtained from author)	Clinical interview	No*	1.24 (0.94-1.64)	-	-
Hildrum, et al., 2009(61)	Norway	9571	49.6	50.3 (15.94)	NCEP-ATPIII (obtained from author)	HADS	No*	1.27 (1.09-1.47)	1.35 (1.06-1.73)	1.24 (1.01-1.51)
Kinder et al., 2004(62)	USA	6189	48.5	28.71 (0.29)	NCEP-ATPIII	Clinical interview	No*	1.50 (1.23-1.83)	1.14 (0.75-1.73)	1.33 (1.06-1.69)
Vogelzangs, et al. 2007(63)	Italy	867	55.0	74.1 (6.6)	NCEP-ATPIII	CESD-20	No*	1.50 (1.08-2.09)	-	-
Ma & Xiao, 2010(64)	USA	1829	100.0	47.8 (0.8)	NCEP-ATPIII	PHQ	Age, BMI	1.61 (1.07-2.43)	-	-
Miettola, et al., 2008(65)	Finland	411	52.6	50.4 (10.5)	NCEP-ATPIII	BDI	No^	2.13 (1.13-4.01)	1.73 (0.70-4.30)	2.64 (1.08-6.45)
Ho, et al., 2008(66)	Singapore	2601	60.4	67.8 (8.6)	≥90cm men ≥80cm women	GDS	No^	0.98 (0.78-1.22)	-	-
Dunbar et al., 2008(49)	Australia	1317	52.4	55.0 (13.1)	≥102 cm men ≥88 cm women	HADS	Age, sex, smoking, alcohol intake, physical activity, marital status and education	1.38 (1.14-1.68)		
Ahlberg, et al.,2002(50)	USA	59	0.0	52.5 (3.5)	WHR>1.0 vs. <1.0	BDI	No	2.86 (1.11-7.61)		
Muhtz, et al., 2009(51)	Germany	215	50.0	48.6 (10.81)	≥94cm men ≥80cm women	PHQ	age, education, physical activity, smoking, cortisol	0.75 (0.21-2.68)		

Note: NCEP-ATPIII, abdominal obesity: > 88 cm for women; > 102 cm for men,

Abbreviations: HADS = Hospital Anxiety and Depression Scale. HSL = Hopkins Check List. BDI = Beck's Depression Inventory. POMS = Profile of mood states. PHQ = Patient Health Questionnaire. HDS = Hamilton Depression Scale. CESD= Center for Epidemiologic Studies Depression Scale. § Authors confirmed that cutoff score of waist circumference was ≥90 cm (typo in publication). *confounder control only refers to the effect of obesity on depression. ^original studies adjusted series of confounders, yet data were not comparable to other studies. Retrieved raw data, not adjusted.

Table 3 Summary of quality assessment of studies (cross-sectional & prospective)

Authors, year	Selection bias			Information bias		Confounding	
	representative sampling procedure of participants in	Non-obese drawn from same community as obese participants	overall participation rate of study ≥ 60%	obesity assessed from measured anthropometry	Depression measured being validated scale or structured interview	depression and obesity assessed in the same way for entire study	controlled for at least three important confounders
Viinamaki, et al. 2009(57)	Yes	Yes	No	Yes	Yes	Yes	No
Takeuchi, et al. 2009(52)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Herva, et al., 2006(58)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gil, et al.,2006(59)	Yes	Yes	Not reported	Yes	Yes	Yes	No
Vogelzangs, et al. 2007(60)	Yes	Yes	Yes	Yes	Yes	Yes	No
William et al., 2009(53)	Yes	Yes	Yes	Yes	Yes	Yes	No*
Hildrum, et al., 2009(61)	Yes	Yes	Yes	Yes	Yes	Yes	No*
Kinder et al., 2004(62)	Yes	Yes	Yes	Yes	Yes	Yes	No*
Vogelzangs, et al. 2007(63)	Yes	Yes	Yes	Yes	Yes	Yes	No*
Ma & Xiao, 2010(64)	Yes	Yes	Yes	Yes	Yes	Yes	No
Miettola, et al., 2008(65)	Yes	Yes	No	Yes	Yes	Yes	No^
Ho, et al., 2008(66)	Yes	Yes	Yes	Yes	Yes	Yes	No^

Authors, year	Selection bias			Information bias			Confounding
	representative sampling procedure of participants in	Non-obese drawn from same community as obese participants	overall participation rate of study ≥ 60%	obesity assessed from measured anthropometry	Depression measured being validated scale or structured interview	depression and obesity assessed in the same way for entire study	controlled for at least three important confounders
Muhtz, et al., 2009(51)	Yes	Yes	Not reported	Yes	Yes	Yes	Yes
Dunbar, et al.,2008(49)	Yes	Yes	No	Yes	Yes	Yes	Yes
Ahlberg, et al., 2002(50)	Yes	Yes	No	Yes	Yes	Yes	No

*confounder control only refers to the effect of obesity on depression. ^original studies adjusted series of confounders, yet data were not comparable to other studies. Retrieved raw data, not adjusted.

Appendix Study quality assessment criteria

Criteria	Response	
	Yes	No
Representative sampling procedure of participants in community base	Random sampling or consecutive strategy, sample drawn from the community	sample source is not community based, e.g. clinics
Non-obese drawn from same community as obese participants	The sampling populations of non-obese and obese participants are the same	Obese and non-obese samples were drawn from different populations
Overall participation rate of study ≥ 60%	The response rate of the study is 60% or over	Less than 60%
Obesity assessed from measured anthropometry	Waist circumference or waist hip ratio were measured by trained professionals, rather than self-reported.	Self-reported
Depression measured using validated scale or structured interview	Depression has to be measured by well-established psychometric scales like CESD, BDI et al., or a clinical interview. Both measurements were regarded as valid and accurate to reflect depression	Self-reported depression history
Depression and obesity assessed in the same way for entire study	Same measurement tools were used across the entire study population, and entire follow up period if it is prospective study	Measurements of depression and obesity varies by subgroups of study sample or time waves if it is prospective study
Controlled for at least three important confounders	Reported three or more confounders belonging to the following three categories: sociodemographic factors (age, sex, education, marital status, et al.), physical health condition (number of comorbidities, or single physical condition like heart disease), and lifestyle factors (physical activity, alcohol intake, smoking, or diet)	Reported less than three confounders (2 or no)

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