

# The Relationship Between Depression and Metabolic Syndrome: Systematic Review and Meta-Analysis Study

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## Abstract

**Context:** Several studies have been conducted on the relationship between depression and metabolic syndrome, which have had conflicting results. The purpose of this study was a meta-analysis of studies that have examined the relationship between these two variables.

**Evidence Acquisition:** This meta-analysis systematically reviewed the relationship between depression and metabolic syndrome. Scientific databases including IranMedex, SID, Magiran, Scopus, PubMed, Google Scholar, and Science Direct were searched and 17 articles were extracted from 2000 to 2014. Selected studies data were analyzed using meta-analysis and random effects model. Heterogeneity between the studies was examined using I<sup>2</sup>. Data were analyzed using STATA software version 12.1.

**Results:** Seventeen studies were analyzed with a sample size of 31880 people. Analysis by the type of studies showed that the relationship between the two variables in cross-sectional studies (OR = 1.51, CI 95% = 1.36 - 1.68) and cohort studies (OR = 1.6, CI 95% = 1.23 - 2.08) was significant. In general, the heterogeneity test results among the studies was not significant (P for heterogeneity = 0.08, I<sup>2</sup> = 39.8%).

**Conclusions:** There is a relationship between depression and metabolic syndrome.

**Keywords:** Meta-Analysis, Depression, Metabolic Syndrome

## 1. Context

Metabolic syndrome includes a cluster of risk factors that ultimately increases the risk of developing cardiovascular diseases and diabetes (1). People with metabolic syndrome will be afflicted by cardiovascular disease and mortalities three to five times more than the non-afflicted ones (2, 3). Metabolic syndrome, for the first time, was defined as three conditions of high blood pressure, high blood glucose, and Gout disease by Kylin in 1920, and Reaven announced insulin resistance as a major feature of this disorder and called it X syndrome in 1988 (4). Several definitions have been proposed for metabolic syndrome, but the most practical definition is adult treatment panel (ATP3), the diagnosis of which is confirmed based on at least three of the five symptoms of high blood pressure, abdominal obesity, impaired fasting blood sugar, high triglycerides, and low HDL-C (5, 6). According to the World Health Organization report, metabolic syndrome is a new pandemic of the 21st century which will afflict over more than half of the people in the next 20 years (7). Currently, about one quarter of American adults and 30% of Iranian adults have metabolic syndrome (1, 8, 9). The simultaneous exis-

tence of several symptoms is more dangerous and harmful than any symptoms of metabolic syndrome alone (10). The importance of the issue will appear when in the case of being afflicted by metabolic syndrome, the overall mortality of people increases 20% to 80% (11). One of the factors that may be associated with metabolic syndrome is depression (12). Depression is one of the main causes of disability in the world and it is predicted that it will become the second important disease for causing economic and humanitarian damage by 2020 (13). Depression has increased the risk of metabolic syndrome in the general population by two times (14). People with depression are prone to metabolic syndrome due to poor health-related behaviors (15). Limited studies have examined the relationship between these two variables and reported conflicting results. In some studies, there was no relationship between depression and metabolic syndrome (16, 17), and in some studies, there was a relationship only between certain components of metabolic syndrome with depression (18), and in others, there was a relationship between the two variables (15, 19). Metabolic syndrome and depression are the important problems in the field of health and scattered re-

searches have reported conflicting results in the field of the relationship between these two problems. Therefore, summarizing and analyzing the performed studies are important to achieve a similar result.

The purpose of this study was conducting a systematic review and meta-analysis study to determine a relationship between depression and metabolic syndrome.

## 2. Evidence Acquisition

### 2.1. Data Source

The present study was a systematic review and meta-analysis that looked at the performed studies on the relationship between depression and metabolic syndrome. The study included the steps of determining the exact problem, collecting and analyzing data, and interpreting the findings. To search the published articles (Persian and English) from July 2000 to 2014, the databases of Scopus, Magiran, SID, IranMedex, Sciences Direct, and PubMed were investigated using the keywords of depression, metabolic syndrome, X syndrome, depressive, and their possible combinations.

### 2.2. Study Selection

He studies that had investigated the relationship between depression and metabolic syndrome were considered. Three reviewers independently reviewed the title and abstract of each article to eliminate duplicated, reviews, case studies, clinical trials, and those published in languages other than English. Studies that were observational were included. Disagreements among reviewers were resolved by consensus.

### 2.3. Data Extraction

At first, a list of titles and abstracts of all available articles in above databases was prepared by the researchers. After the initial search of articles, the abstracts were studied and cases related to the research topic were selected. A checklist of required information for the research, including the first author's name, year of publication, the total sample size, place of the study, and frequency of people with depression and metabolic syndrome were prepared, as recommended by the corresponding author (the number of cases and controls or participants). Relevant articles were entered for meta-analysis and irrelevant articles were excluded from the study. The lists of references used in all the searched articles were evaluated for the possibility of entering other references in the study as well. In this study, only observational studies (cross-sectional, case-control and cohort) were selected.

### 2.4. Statistical Analysis

Since in the studies the effect size of the depression on metabolic syndrome was a qualitative dichotomy (yes-no), odds ratio (OR) was used. To combine the results of the studies, logarithm was used in each study and using random-effects model, the ORs were combined. For variables that were presented as percentage (prevalence of depression and metabolic syndrome), at first, variance and standard deviation were calculated for each study using binomial distribution formula. Then, fixed or random effects model was used to combine the results. Cochran test and DerSimonian-Laird were used to determine the heterogeneity between the studies. If there was heterogeneity among the studies, the random effects model would be used to combine the studies. Using this model, the accumulation diagram (forest plot) was drawn and meta-regression method was used to investigate the relationship among the sample size, effect size, and year of the study. Sensitivity analysis was used to investigate the effect of each study on the overall OR and subgroups analyses were carried out based on the type of study and continent. Data analyses were conducted using STATA software version 12.

## 3. Results

The summary of 17 articles that were entered in the meta-analysis is presented in [Table 1](#). The total sample size was 31880 people with the mean of 1875 samples per study. Just one study was on females and two were on males. General characteristics and data for each of the studies are presented in [Table 1](#).

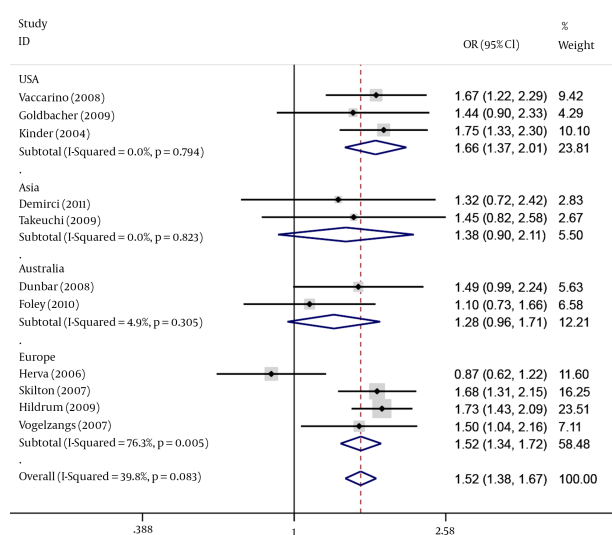
The results showed that the relationship between depression and metabolic syndrome was significant (OR = 1.52; CI 95% = 1.38 - 1.67). Most of the studies have been conducted in Europe. In an analysis of different continents, the results of studies conducted in America (OR = 1.66, CI 95% = 1.37 - 2.01) and Europe (OR = 1.52, CI 95% = 1.34 - 1.72) were significant ([Figure 1](#)).

The relationship between depression and metabolic syndrome was not significant in six studies, because the OR point estimates for those studies were above 1, and in five studies this relationship was significant ([Figure 2](#)). The overall OR indicated that the risk of metabolic syndrome in people with depression was 1.5 times more than non-depressed people, and this value was statistically significant. The accumulation diagram showed the relationship between depression and metabolic syndrome based on the type of studies; in cross-sectional (OR = 1.51, CI 95% = 1.36 - 1.68) and cohort (OR = 1.6, CI 95% = 1.32 - 2.08) studies, the correlations between the two variables were significant.

**Table 1.** Conducted Studies Characteristics to Investigate the Relationship Between Depression and Metabolic Syndrome

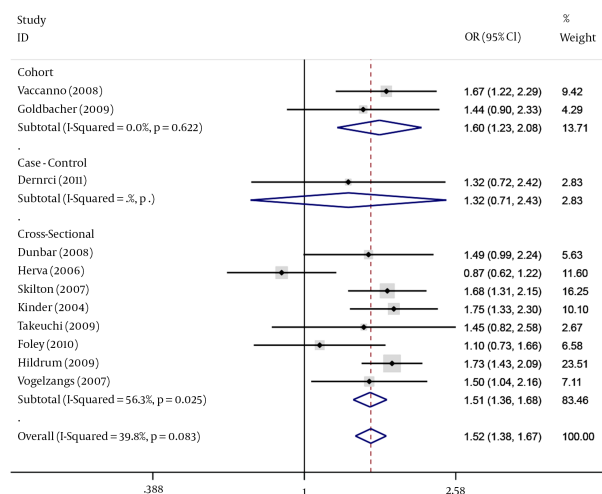
Number	First Author	Country	Date of Publishing	Sample Size	All Depression	All MetSyn	Case		Control	
							MetSyn+	MetSyn-	MetSyn+	MetSyn-
1	Butnorieni et al. (20)	Lithuania	2014	1115	412	334				
2	Vargas et al. (21)	Brazil	2014	342	25	101				
3	Marijnissen et al. (22)	Netherlands	2013	1277	213	425				
4	Demirci et al. (16)	Turkey	2011	250	52	121	28	24	93	105
5	Akbaraky et al. (23)	France	2011	4446	827	574				
6	Foley et al. (14)	Australia	2010	2525	486	145	30	456	115	1924
7	Takeuchi et al. (24)	Japan	2009	1215	92	148	15	77	133	990
8	Goldbacher et al. (25)	USA	2009	429	151	88	37	114	51	227
9	Hildrum et al. (26)	Norway	2009	9571	468	2716	187	281	2529	6574
10	Dunbar et al. (27)	Australia	2008	1345	936	409	41	65	368	871
11	Vaccarino et al. (12)	USA	2008	652	347	391	228	119	163	142
12	Miettola et al. (18)	Finland	2008	416	43	153	20	23	133	240
13	Skilton et al. (27)	France	2007	1598	392	983	276	116	707	499
14	Herva et al. (17)	Finland	2007	5691	768	325	39	729	286	4637
15	Vogelzang et al. (28)	Italy	2007	867	179	212	55	124	157	531
16	Kinder et al. (15)	USA	2004	6189	545	478	66	479	412	5232
17	McCaffery et al. (29)	USA	2003	149						

**Figure 1.** The Dispersion Studies Based on the Separation of the Continents



The CI 95% for each study is drawn in the form of horizontal lines around the main mean. The diamond sign is the result of combining all the studies with 95% CI.

In general, heterogeneity test among the studies was not significant ( $P$  for heterogeneity = 0.08,  $I^2 = 39.8\%$ ), and this was also consistent with the cross-sectional studies ( $P$  for heterogeneity = 0.025,  $I^2 = 56.3\%$ ). Fixed effects model was used to combine the studies, because the heterogeneity test among the studies was not significant (Figure 2).

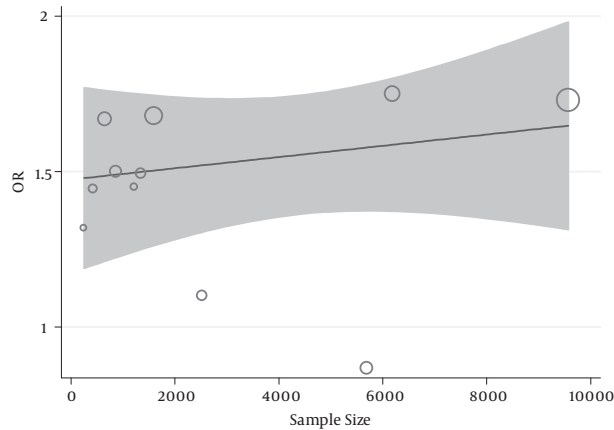


**Figure 2.** Forest Plot of Correlation Between Depression and Metabolic Syndrome According to Types of Studies

Figure 3 shows the relationship between depression and metabolic syndrome according to sample size using meta-regression. Meta-regression showed that the relationship between depression and metabolic syndrome was estimated lower in studies with larger samples, although this reduction was not significant ( $P = 0.06$ ). In Figure 3, the positive slope of the meta-regression line showed that the relationship between depression and metabolic syndrome had an increasing trend with slow slope, but it

was not significant ( $P = 0.06$ ).

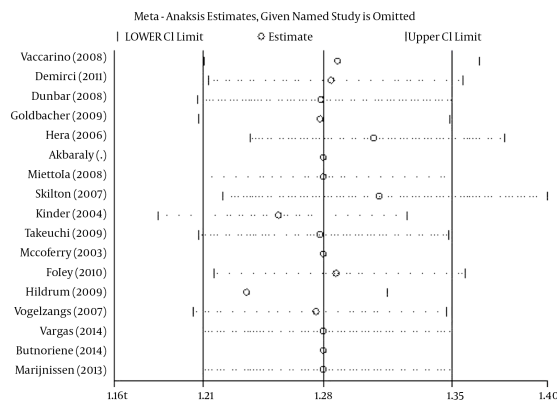
**Figure 3.** Meta-Regression of the Correlation Between Depression and Metabolic Syndrome According to Sample Size



Each of the circles represents the sample size; the larger circles represent greater and smaller circles represent a less statistical sample.

The meta-regression diagram shows the correlation between depression and metabolic syndrome based on the year of study; there was no publication bias in this study (Figure 5).

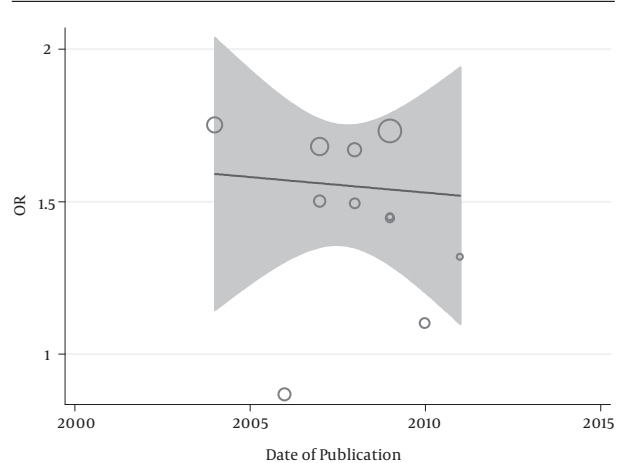
**Figure 4.** Sensitivity Analysis (effect of each study on OR)



In general, OR was significant.

#### 4. Conclusions

Different studies with contradictory results in different countries led to this study. This study aimed to investigate the relationship between metabolic syndrome and depression by systematic review and meta-analysis of 17 observational studies. The result of this study showed that



**Figure 5.** Meta-Regression Diagram and Correlation Between Depression and Metabolic Syndrome, According to the Year of Study

there was a significant relationship between depression and metabolic syndrome. Akbaraly wrote that the relationship between two the variables (depression and metabolic syndrome) was bilateral; this means that metabolic syndrome leads to depression and vice versa (23). Depression can activate the hypothalamus-pituitary-adrenal axis and by increasing the release of hydro-corticotrophin, adrenocorticotrophic and cortisol hormones lead to the depositing of visceral adipose tissue (27). Depression can also lead to metabolic syndrome by inducing unhealthy behaviors such as alcohol consumption, smoking, poor diet, a sedentary lifestyle, sleeping disorder and poor adherence to treatment (12, 19, 30, 31) Antidepressants may also have an impact on indicators of metabolic syndrome (31). On the other hand, patients with metabolic syndrome are prone to depression due to obesity and its social stigma, raising the level of inflammatory cytokines such as IL-6, CRP and leptin resistance (12, 31)

During the analysis according to the continents under the study, it was observed that the relationship between these two variables in studies in America and Europe was significant, but in the study of Dimirci, in Turkey (Asia), there was no correlation between depression and metabolic syndrome (16) and in the study of Takeuchi, a weak correlation was observed (24). Meta-regression showed that the relationship between depression and metabolic syndrome in the studies with larger sample sizes were estimated lower, although this decrease was not significant. For example, in the study of Kinder et al. the relationship between the two variables was only found in females (15). In these studies, interview and various tools were used to determine depression. It seems that using various tools to determine depression, racial differences

in samples, predisposing factors and methodological limitations are contradictory reasons for the above studies. Lack of access to some articles in databases and exclusion of non-English studies were the most important limitations of this study. The results of this study showed that there was a relationship between depression and metabolic syndrome and to investigate patients with depression, metabolic syndrome and its components must also be considered.

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### Footnotes

**Authors' Contribution:** Reza Ghanei Gheshlagh: data Collection and study design; Naser Parizad: final revision and grammar editing; Kouros Sayehmiri: biostatistical analysis.

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