

Accepted Manuscript

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PII: S0165-0327(17)32376-5
DOI: [10.1016/j.jad.2018.04.102](https://doi.org/10.1016/j.jad.2018.04.102)
Reference: JAD 9757



To appear in: *Journal of Affective Disorders*

Received date: 25 November 2017
Revised date: 23 February 2018
Accepted date: 8 April 2018

Please cite this article as: Nikolena Repousi , Maria Masana , Albert Sanchez-Niubo , Josep Maria Haro , Stefanos Tyrovolas , Depression and metabolic syndrome in the older population: a review of evidence, *Journal of Affective Disorders* (2018), doi: [10.1016/j.jad.2018.04.102](https://doi.org/10.1016/j.jad.2018.04.102)

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Highlights

- Depression seems to be associated with metabolic syndrome in people aged 60 years or over
- Mixed evidence was found on whether depression was related to the individual components of metabolic syndrome in older adults.
- Abdominal obesity was reported, among this Review studies, to be related more consistently with depression

Depression and metabolic syndrome in the older population: a review of evidence

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Abstract

Background Metabolic syndrome (MetS) has been shown to be associated with depression in older adults but the results are mixed. We summarized and evaluated the association between depression and MetS in people aged 60 years or over.

Methods Relevant published studies from January 1997 to July 2017 were identified by searching two electronic databases: PubMed/Medline and EMBASE. Observational studies were considered.

Results Twelve studies were included in the systematic review. Depression seemed to be related with MetS in the majority of the studies (10/12 = 83.3%). As far as the longitudinal studies are concerned, the onset of depression was related to MetS in 2 out of 3 studies (66.6%), while a relation between chronicity of depression and MetS was reported (1 study). Regarding cross-sectional studies, 7 out of 9 (77.7%) concluded that there was a positive association between depression and MetS. Mixed evidence was found among studies concerning the association between depression and the individual components of MetS. Four out of ten studies (40%) reported that depression was significantly associated with the waist circumference, a component of MetS.

Limitations There was a high degree of heterogeneity between studies regarding their design. Only studies written in English, from peer-reviewed journals were included.

Conclusions Depression seemed to be significantly associated with MetS in people aged 60 years or over. Among the components of MetS, abdominal obesity seemed to be associated more strongly and consistently with depression. The direction of the causality and mechanisms underlying the relationship are still largely unknown.

Keywords: metabolic syndrome; depression; older adults

1. Introduction

The number of older persons -60+ years old- has increased substantially in recent years in most countries and regions, and that growth is projected to accelerate in the coming decades (United Nations, 2015). Population ageing has many implications for nearly all sectors of society. Increasing life expectancy has been associated with increasing risk of aging-associated diseases and with an increased chronic disease burden (Prince et al., 2015). The leading contributors to disease burden in older people are cardiovascular diseases (CVDs). Also, depression is one of the main disorders that afflict older people (worldwide 7.5 million older adults suffer from major depressive disorder) (Prince et al., 2015).

The clustering of several metabolic and cardiovascular risk factors is a common phenomenon among older adults. Within this framework, metabolic syndrome (MetS), which is a combination of factors thought to predispose an individual to CVDs is considered to be a major public health issue in this age group. In particular, MetS is characterized by elevated abdominal obesity, high level of triglycerides, low level of high-density lipoprotein cholesterol (HDL-C), high blood pressure (BP) and elevated fasting plasma glucose (FPG) or diabetes. The prevalence of MetS peaks around the age of 60–75 years (Knut Borch-Johnsen, 2013). MetS is a heterogeneous disorder, with substantial variability in the prevalence of component traits within and across populations (Denys et al., 2009). The prevalence of MetS in older adults varies from 11% to 43% according to the World Health Organization (WHO), and 23% to 55% according to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III) (Denys et al., 2009).

Depression is one of the most common mental disorders during elderliness. The frequencies of depression and of subsyndromal depressive indications are reported 1-4% and 10-15% respectively (Sözeri-Varma, 2012). Unipolar depression occurs in 7% of older adults and it accounts for 5.7% of Years lived with disability (YLDs) among over 60 year olds (WHO, 2016). Depression is the leading cause of disability for both males and females (WHO, 2012). It is associated with increased risk of morbidity, increased risk of suicide, decreased physical, cognitive and social functioning, and greater selfneglect, all of which are in turn associated with increased mortality (Fiske et al., 2009). Older adults with depressive symptoms have poorer functioning compared to those with chronic medical conditions such as lung disease, hypertension or diabetes (WHO, 2016). Increase of morbidity and medicines consumption along with aging are related with depressive symptoms. Also, disability, as well as indispensable disconnections in social communication contribute to the late-life depression (Sözeri-Varma, 2012).

A few review studies have been conducted that focus on the association between depression and MetS in the general population (Pan et al., 2012; Marazziti et al., 2013; Goldbacher et al., 2007; Gheshlagh et al., 2016; Foley et al., 2010; Vancampfort et al., 2013). However, data on the aforementioned association in the group of older individuals is sparse. It is of special interest to examine the relationship between depression and MetS in people aged 60 years or over, because both these conditions increase with age and have adverse consequences on quality of life. In addition, since it has been suggested that cerebrovascular disease may predispose, precipitate, or perpetuate some geriatric depressive syndromes (vascular subtype of depression), it is of paramount importance to investigate the association between depression and MetS in

older adults. Therefore, this review study aims to provide an overview of the literature assessing the relation between depression and MetS in people aged 60 years or over.

2. Methods

This systematic review was written following the general principles published in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) Statement (Liberati et al., 2009).

2.1. Eligibility criteria

The studies were eligible for inclusion if they examined the association between depression and MetS in older adults. Original peer-reviewed observational studies (longitudinal studies, cross-sectional and case-control studies) published between January 1997 and July 2017, written in English, were considered. Letters, reviews, symposia, comments, editorials, case reports and randomized clinical trials (RCTs) were excluded.

Studies were included if they published quantitative empirical research examining the association between depression or depressive symptoms and MetS. There was no restriction in the methodology used for measuring depression/depressive symptoms and MetS. Thus, depression status/depressive symptoms could be assessed by self-reported symptom scales [e.g. Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS)], physician/clinician diagnosis, or structured clinical diagnostic interview, while MetS could be defined by using NCEP ATP-III criteria (Grundy et al., 2005), International Diabetes Federation (IDF) criteria (Alberti et al., 2005), other organizations' criteria (Balkau and Charles, 1999; Alberti and Zimmet, 1998) or modified versions.

Only individuals, who were aged 60 years or over were considered. Due to the bias introduced when designating particular target groups as participants, only studies involving community samples were included. Studies with inpatients or individuals living in long-term care facilities were excluded. Studies not employing probability or random sampling were excluded. Studies that examined the association between depression and MetS only in women or only in men were not considered. Due to the focus on older adults, published studies on infants, children, adolescents, young adults and middle-aged adults were also excluded. Studies that investigated the association of bipolar disorder and recurrent depressive disorder with MetS were excluded. Moreover, studies that examined the relationship between depression and only some of the components of the MetS were not considered.

2.2. Information sources and search

Relevant studies were identified by searching two electronic data bases: PubMed/Medline (January 1997 to 10 July 2017) and EMBASE (January 1997 to 10 July 2017). In order to conduct a comprehensive systematic literature search, Medical Subject Headings (MeSH), which is the national library of medicine's controlled vocabulary to index journal articles in an hierarchical structure permitting a search at various levels of specificity, were used. The search strategy involved combining key words for depression ("depression", "depressive symptoms", "depressive disorder") and MetS ("metabolic syndrome", "syndrome X") [Table 1]. Two authors independently reviewed potential articles to be included based on the aforementioned criteria. Disagreements were resolved subsequently by consensus.

2.3 Data collection process

A data extraction sheet was developed and the information from the studies included in the review were extracted and tabulated. Extracted information comprised characteristics of the included studies, such as study name, authors, publication year and journal, country where the study was conducted, study design, aims of the study, number of participants, population age, female to male ratio, data collection methods, key measures, main findings and information about potential sources of bias.

2.4. Study quality and risk of bias

The study quality and risk of bias of each included study were assessed using the guidelines of the Effective Public Health Practice Project (EPHPP) (Thomas et al., 2004) for observational studies. The EPHPP, which was identified as one of the most useful tools for assessing methodological quality of non-randomized studies (Deeks et al., 2003), consists of six components: (a) selection bias, (b) study design, (c) confounders, (d) blinding, (d) data-collection, and (e) withdrawals and drop-outs. Each individual component received the rating weak, moderate or strong based on EPHPP guidelines. Finally the study received a total rating of strong, if there was no weak rating in any of the six components, moderate if there was one weak rating and weak if there were two or more weak ratings [Table 2].

3. Results

3.1. Study selection

The search of PubMed/Medline and EMBASE provided a total of 256 unduplicated citations at initial screening. Of these records, 211 were excluded because these articles clearly did not meet the predetermined eligibility criteria after reviewing the abstracts. Further inspection of the full-texts of the remaining 45 articles revealed

that 33 studies did not meet the eligibility criteria. Thus, a total of 12 studies were included in this review. See flow diagram in [Figure 1].

3.2. *Study characteristics*

All 12 studies included in this review were published in English and comprised 12 observational studies in total, 9 cross-sectional studies (Ruas et al., 2016; Hildrum et al., 2009; Morikawa et al., 2013; Park et al., 2014; Roriz-Cruz et al., 2007; Viscogliosi et al., 2012; Vogelzangs et al., 2007a; Vogelzangs et al., 2007b; Vogelzangs et al., 2009) and 3 longitudinal studies (Akbaraly et al., 2011; Mast et al., 2008; Vogelzangs et al., 2011). The range of the follow-up period for the cohort studies was 2 years (Ruas et al., 2016; Mast et al., 2008) to 6 years (Vogelzangs et al., 2011). Of these 12 studies, 3 were from Italy (Viscogliosi et al., 2012; Vogelzangs et al., 2006; Vogelzangs et al., 2011), 1 was from France (Akbaraly et al., 2011), 1 was from Norway (Hildrum et al., 2009), 1 was from the Netherlands (Vogelzangs et al., 2011), 2 were from the United States of America (USA) (Vogelzangs et al., 2007; Mast et al., 2008), 2 were from Brazil (Ruas et al., 2016; Roriz-Cruz et al., 2007), 1 from Japan (Morikawa et al., 2013) and 1 from Korea (Park et al., 2014). The sample size ranged from 60 (Park et al., 2014) to 4496 individuals (Akbaraly et al., 2011). The number of participants in the other studies included in this review was respectively, 1,469 (Ruas et al., 2016), 823 (Vogelzangs et al., 2011), 2,483 (Hildrum et al., 2009), 2,959 (Mast et al., 2008), 3,796 (Morikawa et al., 2013), 2,017 (Vogelzangs et al., 2007b), 867 (Vogelzangs et al., 2007a), 422 (Roriz- Cruz et al., 2007), 133 (Viscogliosi et al., 2012) and 1,212 (Vogelzangs et al., 2009). All the studies included both sexes.

3.3. *MetS*

Most studies (Akbaraly et al., 2011; Ruas et al., 2016; Mast et al., 2008; Roriz-Cruz et al., 2007; Viscogliosi et al., 2012; Vogelzangs et al., 2011; Park et al., 2014; Vogelzangs et al., 2007a; Vogelzangs et al., 2007b; Vogelzangs et al., 2009; Hildrum et al., 2009) defined MetS according to the NCEP ATP-III as having three or more of the following criteria: abnormal waist circumference (in men > 102 cm, and in women > 88 cm), low HDL-C (< 40 in men, 50 in women), high triglycerides (> 150), high FPG (> 110 or taking diabetic medication), high BP ($> 130/85$ or taking antihypertensive medication). Roriz-Cruz and colleagues used body mass index (BMI) of 30 kg/m^2 and higher and BP of $140/90$ mmHg or higher to diagnose the obesity and hypertensive component of the syndrome, respectively. The cut-off for high BP was raised at $160/90$ in 2 studies (Vogelzangs et al., 2007a; Vogelzangs et al., 2009). Also, in 1 study fructosamine $> 247 \text{ } \mu\text{mol/L}$ (or antidiabetic medication) was used as proxy for FPG (Vogelzangs et al., 2009). Park and colleagues used a modified version of NCEP ATP-III definition as well. Morikawa and colleagues and Hildrum and colleagues defined MetS according to the International Diabetes Federation (IDF) definition, as having central obesity (defined as waist circumference with ethnicity specific values) plus any two of the following four factors: 1) raised triglycerides $\geq 150 \text{ mg/dL}$ or specific treatment for this lipid abnormality 2) reduced HDL-C (HDL-C $< 40 \text{ mg/dL}$ in males $< 50 \text{ mg/dL}$ in females or specific treatment for this lipid abnormality), 3) raised BP (systolic BP ≥ 130 or diastolic BP $\geq 85 \text{ mm Hg}$ or treatment of previously diagnosed hypertension), 4) FPG $\geq 100 \text{ mg/dL}$. Hildrum and colleagues defined MetS according to the IDF definition, and secondarily according to NCEP ATP-III criteria.

3.4. Depression

The majority of the studies (Akbaraly et al., 2011; Mast et al., 2008; Vogelzangs et al., 2011; Vogelzangs et al., 2007a; Vogelzangs et al., 2007b; Vogelzangs et al., 2009; Park et al., 2014) used the CES-D (Radloff, 1977) to assess depressive symptoms. A cut-off point of 16/60 on the 20 item version CES-D was used by 2 studies (Akbaraly et al., 2011; Vogelzangs et al., 2009), a cut-off of 20/60 was used by another study (Vogelzangs et al., 2007a), while 1 study used both cut-offs (Vogelzangs et al., 2011). A cut-score of 8/30 on the 10-item CES-D was used by 1 study (Mast et al., 2008) to indicate incident elevated depressive symptoms). Vogelzangs and colleagues performed analyses with both the continuous CES-D score (referred to as depressive symptoms) as well as a dichotomous indicator for clinically relevant depressed mood (Vogelzangs et al., 2009). Some studies (Roriz-Cruz et al., 2007; Viscogliosi et al., 2012, Morikawa et al., 2013), used the 15-item GDS (Almeida and Almeida, 1999), while 1 study (Ruas et al., 2016) used the 12-item version of the General Health Questionnaire (GHQ-12) (Costa et al., 2006). Morikawa and colleagues used a cut-off score of 6/15 while Viscogliosi and colleagues, according to the score, identified normal subjects (score: 0–5), subjects with low probability of depression (score: 6–10) and subjects with high probability of depression (score: 11–15). For statistical models Ruas and colleagues stratified depressive symptoms in tertiles (each tertile was added as an ordinal variable in statistical analysis). Hildrum and colleagues used the 7 items for depression of Hospital Anxiety and Depression Scale (HADS-D) (Zigmond and Snaith, 1983) to assess depressive symptoms and they used a cut-off of the score of 8/21. In addition to the use of the aforementioned scales, in 3 studies depressive symptoms were assessed through a psychiatric interview (3rd ed.; DSM-III; American Psychiatric Association, 1980; 4th ed., text rev.; DSM-IV-TR; American Psychiatric Association, 2000) as well (Vogelzangs et al., 2009; Roriz-Cruz et al., 2007; Park et al. 2014).

3.4 The association between depression and MetS

Overall, depression was significantly associated with MetS people aged 60 years or over in 10 out of 12 studies (10/12 = 83.3%) (Akbaraly et al., 2011; Ruas et al., 2016; Mast et al., 2008; Morikawa et al., 2013; Park et al., 2014; Roriz-Cruz et al., 2007; Viscogliosi et al., 2012; Vogelzangs et al., 2007a; Vogelzangs et al., 2007b; Vogelzangs et al., 2011).

3.4.1 Longitudinal studies

Depression was associated with MetS in older adults in all the longitudinal studies included in this review study (3/3 = 100%) (Vogelzangs et al., 2011; Mast et al., 2008; Akbaraly et al., 2011). However, Akbaraly and colleagues reported that MetS was associated with a 1.8-fold odds ratio for new-onset depressive symptoms in individuals aged 65-70 years [OR = 1.82; 95%CI (1.12-2.95); p = 0.04], but not in octogenarians group (70-91 years old). In addition, Vogelzangs and colleagues reported that the onset of depression was not significantly associated with MetS [adjusted OR = 1.20; 95%CI (0.8-1.78); p = 0.38, fully adjusted OR = 1.01; 95%CI (0.66-1.54); p = 0.96], but they also showed that MetS strongly predicted the chronicity of depression [adjusted OR = 2.93; 95%CI (1.18-7.26); p = 0.02, fully adjusted OR = 2.66; 95%CI (1.01-7.00); p = 0.05]. More specifically, Vogelzangs and colleagues showed that although persons depressed at baseline, both those with and those without MetS tended to show a decline in CES-D score over 6 years, those with the MetS continued to have high scores at the 3 years follow-up and declined only thereafter. [Table 3]

3.4.2 Cross-sectional studies

A positive association between depression and MetS in older adults was found in 7 out of 9 cross-sectional studies included in this review study ($7/9 = 77.8\%$) (Ruas et al., 2016; Morikawa et al., 2013; Park et al., 2014; Roriz-Cruz et al., 2007; Viscogliosi et al., 2012; Vogelzangs et al., 2007a; Vogelzangs et al., 2007b). No association between depression and MetS was found in 2 studies ($2/9 = 22.3\%$) (Hildrum et al., 2009; Vogelzangs et al., 2009). It is noteworthy, that one cross-sectional study reported a relationship between depressive symptoms and MetS mediated by racial effect (Vogelzangs et al., 2007b). Specifically the relation was significant only in white [OR = 1.11; 95%CI (1.01–1.23); $p = 0.03$], but not in black persons [OR = 0.97; 95%CI (0.86–1.11); $p = 0.67$], while no association was found after additional adjustment for other psychological risk factors (anxiety symptoms, negative life events, inadequate emotional support) either in blacks [OR = 0.91; 95%CI (0.79–1.05); $p = 0.21$] or whites [OR = 1.10; 95%CI (0.98–1.23); $p = 0.11$]. Moreover, it should be mentioned that another cross-sectional study reported that there was a significant association between the severity of depressive symptoms and MetS [OR = 1.20; 95%CI (1.02–1.41); $p = 0.03$], despite the fact that the association between depressed mood and the MetS was not statistically significant [OR = 1.30; 95%CI (0.88–1.90); $p = 0.19$] (Vogelzangs et al., 2007a).[Table 4]

3.5 Other findings

The relation between depression and the components of MetS in adults aged 60 years old or over was examined in 10 out of 12 studies ($10/12 = 83\%$) [Table 5]. Overall, results varied across studies, possibly due to causes related to the methodological and operational choices of studies. Four studies ($4/10 = 40\%$) (Park et al., 2014; Vogelzangs et al., 2007a; Vogelzangs et al., 2010; Vogelzangs et al., 2009)

presented a significant association between waist circumference and depressive symptomatology. Three studies (3/10 = 30%) (Akbaraly et al., 2011; Mast et al., 2008; Vogelzangs et al., 2009) reported that HDL-C was associated with depression. In addition, two studies (2/10 = 20%) (Mast et al., 2008; Viscogliosi et al., 2012) showed that FPG was associated with depression, while 1 study reported a relationship between BP and depressive symptoms (Vogelzangs et al., 2007b). Ruas and colleagues concluded that no graded association between increasing number of MetS components and depressive symptoms existed, while they showed that only high triglyceride levels were significantly associated with depressive symptoms [OR = 1.47; 95%CI (1.19-1.81); $p < 0.0001$]. Roriz-Cruz and colleagues reported no relation between depression and components of MetS.

4. Discussion

4.1 Depression and MetS

The majority of the studies (10/12 = 83.3%) reported a positive association between depression and MetS in older adults. Two studies (2/12 = 16.6%) concluded that there was no association between major depression and MetS in people aged 60 years or over.

As far as the longitudinal studies are concerned, the onset of depression was related to MetS in 2 out of 3 studies (66.6%), while a relation between chronicity of depression and MetS was reported (1 study). Regarding cross-sectional studies, 7 out of 9 (77.7%) concluded that there was a positive association between depression and MetS. This contradiction may be explained at least in part by methodological differences, particularly concerning the definition of depression cases, assessment of depressive symptoms, the type of the study and the size of the sample. Another possible

explanation is the use of different diagnostic criteria for MetS (NCEP-ATP III, 2005 IDF), the statistical method employed and the fact that studies were carried out in different countries.

The positive association between depression and MetS in the general population regardless of age has been emphasized in previous reviews (Gheshlagh et al., 2016; Goldbacher et al., 2007; Pan et al., 2012). Moreover, until now depressive symptoms/MetS interrelation has been evidenced in many observational studies targeting middle-aged individuals (Akbaraly et al., 2009; Koponen et al., 2008; Gil et al., 2006; Butnorienė et al., 2014) as well as adults of all ages (Skilton et al., 2007; Dunbar et al., 2008; Takeuchi et al., 2009; Vanhala et al., 2009).

4.2 Depression and components of MetS

The evidence was mixed among studies concerning the association between depression and the components of MetS -waist circumference, HDL-C, triglycerides, systolic BP and FPG-. Depression was reported to be associated with MetS components following different pathways. Depression was appeared to be associated mainly with waist circumference and HDL-C. These results are partially in line with recently published results. Specifically it was reported that central obesity, high triglycerides, and low HDL-C were the main contributing factors to the association of depression and MetS (Akbaraly et al., 2009).

It seemed that among all the features of MetS, depression was more consistently related with waist circumference. Indeed, abdominal obesity is often regarded as a key component of the MetS (Després et al., 2008; Després, 2006) and previous reports have suggested that it is the most important MetS feature in relation to depression (Dunbar et al., 2008; Takeuchi et al., 2009). In the literature an association between depression and

obesity has been shown in older adults (Luppino et al., 2010) as well as in people of different ages (Vaccarino et al., 2008 , Herva et al., 2006; McCaffery et al., 2003; Pulkki-Råback et al., 2009).

Furthermore, across studies included in this review, HDL-c was the second most commonly associated component of metabolic syndrome with depression. A positive association between depression and HDL-c has also been suggested in a previous meta-analysis and review study (Shin et al., 2008), as well as in a few observational studies (Vanhala et al., 2009; Dunbar et al., 2008; Igna et al., 2008). However, a review research highlighted a negative association between depression and HDL-c (Papakostas et al., 2004).

Two studies in this review pointed out a significant association between depression and FPG. Besides, numerous previous studies have established a positive association between depression and diabetes mellitus (Anderson et al., 2001; Bădescu et al., 2016; Roy et al., 2012; Gale et al., 2010).

Triglycerides were related to depressive symptoms only in one study in this review. Literature data related with the aforementioned association are contradictory. Specifically recent studies have reported that there is no association between triglyceride levels and depression (Sheich et al., 2004; Liaw et al., 2015), while other have presented significant relations (Akbaraly et al., 2009; Pulkki-Råback et al., 2009; Vaccarino et al., 2008; Kinder et al., 2004; McCaffery et al., 2003).

Regarding BP, it appeared not to play a principal role in the incidence or severity of depressive symptoms, given that a relation with depression was observed only in one study. This result is in accordance with previous research (Denys et al., 2009; Shen et al., 2003).

The results of our study imply that associations between depression and MetS are more consistent than the association among depression and isolated components of MetS. However, more research is needed on the association between depression and MetS in older adults.

4.3 Strengths and limitations

To our knowledge this is the first systematic review to address the relationship between depression and MetS in older adults. Nevertheless, there are some limitations that should be borne in mind when interpreting the results of this systematic review. First, there was a high degree of heterogeneity between studies regarding their design. Different methods for assessing depression and different diagnostic criteria for defining MetS were used, limiting comparability and increasing the risk of misclassification bias. The fact that we included studies in which case ascertainment was established by a validated screening tool with a pre-established cut-off, may limit the credibility of the association between depression and MetS (Levis et al., 2017). Also, since this review included studies from wide cultural and national contexts, cultural differences may also exist. The fact that only studies from peer-reviewed journals were included may limit our findings. Exclusion of non-English studies might bias the results as well.

5. Conclusion

Depressive symptoms seem to be related with MetS in the older population. All the included prospective studies reported that older adults with MetS had higher odds to present a depressive symptomatology in comparison with older adults not having MetS. The majority of cross-sectional studies confirmed the positive association between depression and MetS in older adults. Data was contradictory regarding the relationship

between the components of MetS (such as diabetes, obesity etc.) and depression. Therefore, more longitudinal studies need to be carried out in order to elucidate the association between depression and MetS in older adults. Considering the dramatic raise of older population, studies targeting to these subjects need to be conducted, as the implementation of public health services in specific age groups seems more necessary than ever.

Conflict of interest

The authors report no conflict of interest.

Contributors

Nikolena Repousi and Stefanos Tyrovolas contributed to the concept and design of the study, analysis and interpretation of data, and preparation of the manuscript. Maria Masana, Albert Sanchez-Niubo, Stefanos Tyrovolas and Josep Maria Haro contributed to interpretation of data, critical review and revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

Role of funding source

None declared.

Acknowledgments

Stefano Tyrovolas's work was supported by the Foundation for Education and European Culture (IPEP), the Sara Borrell postdoctoral programme (reference no. CD15/00019 from the Instituto de Salud Carlos III (ISCIII - Spain) and the Fondos Europeo de Desarrollo Regional (FEDER).

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Table 1. List of sources searched and search items used for systematic review.

Electronic databases

Pubmed/Medline

EMBASE

Search terms

MetS (MeSH terms) OR Syndrome X (MeSH terms)

AND

Depression (MESH terms) OR Depressive symptoms (MeSH terms) OR Depressive disorder (MeSH terms)

AND

Adults aged 60 years or over (MeSH terms)

AND

Year: 1997 TO 2017

AND

Humans (MeSH terms)

AND

English

Figure 1. Selection of studies for systematic review

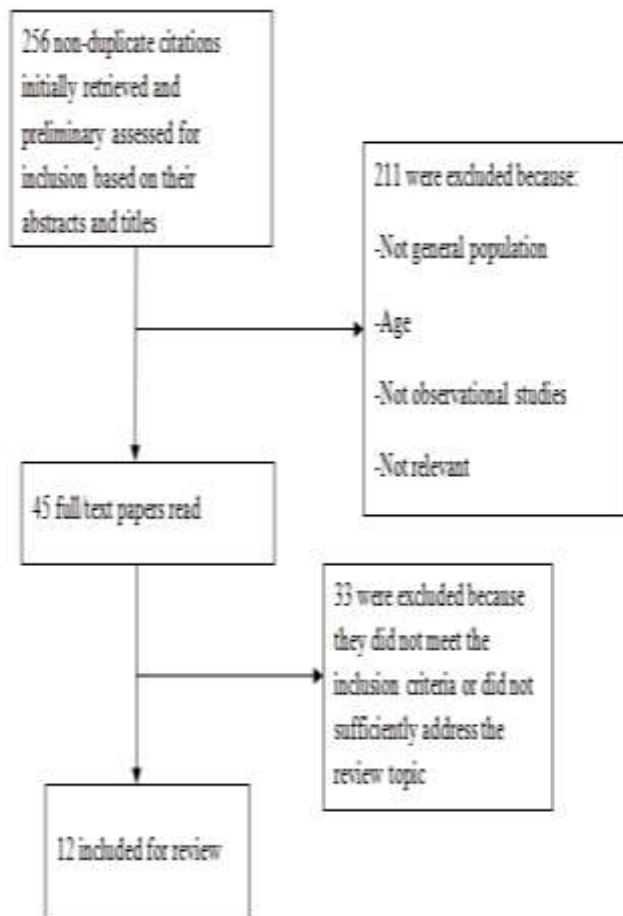


Table 2. Quality assessment of observational studies for each component using Effective Public Health Practice Project (EPHPP) tool.

Studies	Selection bias	Study Design	Confounders	Blinding	Data collection method	Withdrawals and drop-outs
Akbaraly et al., 2011	Strong	Moderate	Strong	Weak	Strong	Moderate
Ruas et al., 2016	Strong	Weak	Strong	Strong	Strong	Strong
Mast et al., 2008	Moderate	Moderate	Moderate	Weak	Strong	Weak
Park et al., 2014	Moderate	Weak	Weak	Moderate	Strong	Strong
Roriz-Cruz et al., 2007	Strong	Weak	Moderate	Weak	Strong	Strong

Viscogliosi et al., 2012	Moderate	Weak	Strong	Weak	Strong	Moderate
Vogelzangs et al., 2007b	Moderate	Weak	Strong	Weak	Strong	Moderate
Vogelzangs et al., 2007a	Strong	Weak	Moderate	Weak	Strong	Moderate
Vogelzangs et al., 2011	Strong	Moderate	Moderate	Weak	Strong	Moderate
Vogelzangs et al., 2009	Strong	Weak	Moderate	Weak	Strong	Weak
Morikawa et al., 2013	Strong	Weak	Strong	Weak	Strong	Strong
Hildrum et al., 2009	Strong	Weak	Moderate	Weak	Strong	Strong

Table 3. Results of the association between depression and MetS in older adults aged 60 years or over in the cross-sectional studies included in this review.

Studies	MetS	Depression	Methods	Adjustments	Results
Ruas et al., 2016	NCEP-ATP III	GHQ	Logistic regression	Sociodemographic variables (gender, age, schooling, and monthly family income), lifestyle characteristics (current smoking, alcohol consumption, and no exercise), cognitive functioning, biological variables, current use of psychoactive drugs	MetS was associated with depressive symptoms [OR = 1.31; 95%CI (1.05-1.63); p = 0.014]
Hildrum et al. 2009	2005 IDF NCEP-ATP III	HADS	Logistic regression Age-stratified association	Age, gender, education, physical activity, pulse rate, smoking	No association between depression and MetS in people aged 60-89 years old [OR = 0.59; 95%CI (0.69-1.21); p = 0.280]

Morikawa et al., 2013	2005 IDF	GDS	Logistic regression	Age, gender, MetS, sleep status, smoking, alcohol use, social supports, visual, hearing, walking, cognitive function, and life events.	MetS was statistically associated with depressive symptoms [OR = 1.32; 95%CI (1.03–1.68); p < 0.05]
Park et al., 2014	Modified NCEP-ATP III	DSM-IV CES-D	Logistic regression	Sex and age matching	The newly-diagnosed depression group showed a significantly increased risk of MetS [OR = 4.75; 95%CI (1.58–14.25); p = 0.039] compared with the control group.
Roriz-Cruz et al., 2007	Modified NCEP-ATP III	GDS	Logistic regression	Age, sex, ischemic heart disease, all MetS components	MetS was associated with higher likelihood of depression [OR = 2.02; 95%CI (1.11-3.68); p < 0.05]
Viscogliosi et al., 2012	NCEP-ATP III	GDS	Multiple regression	Sex, age, education, smoke, MMSE, components of MetS, hypertension, diabetes, medications, ESR, and hsCRP	A significant association between depressive symptoms and MetS [β = 1.446; 95%CI (0.184–2.709); p = 0.025].

Vogelzangs et al., 2007b	NCEP-ATP III	CES-D	Logistic regression	Age, sex, race, educated, income, smoking status, alcohol use, physical activity, other psychosocial risk factors (anxiety symptoms, negative life events, inadequate emotional support)	An association of depressive symptoms with the MetS was found only in whites [OR = 1.11; 95%CI (1.01-1.23); p = 0.03] and not in blacks [OR = 0.97; 95%CI (0.86-1.11); p = 0.67]. No association either in blacks [OR = 0.91; 95%CI (0.79-1.05); p = 0.21] or whites [OR = 1.10; 95%CI (0.98-1.23); p = 0.11] with additional adjustment.
Vogelzangs et al., 2007a	Modified NCEP-ATP III	CES-D	Logistic Regression	Age, sex, education, smoking, alcohol use, number of chronic diseases	Significant association between the severity of depressive symptoms and MetS [OR per SD increase=1.20; 95%CI (1.02-1.41); p = 0.03]
Vogelzangs et al., 2009	Modified NCEP-ATP III	CES-D DSM-III	Logistic regression	Age, sex, educational level, smoking, alcohol use, physical activity, diabetes, CVD, number of other chronic diseases.	Sub threshold depression decreased odds of MetS [OR = 0.55; 95%CI (0.37-0.82), p = 0.004], whereas major depression did not change probability of MetS [OR 1.16; 95%CI (0.54-2.49); p = 0.71]

OR = odds ratio; CI = confidence interval; NCEP-ATP III = National Cholesterol Education Program Adult Treatment Panel III; IDF = International Diabetes Foundation; GHQ = General Health Questionnaire; HADS = Hospital Anxiety and Depression; BMI = Body Mass Index; CES-D = Center for Epidemiologic Studies Depression Scale; GDS = Geriatric Depression Scale; CVD = cardiovascular disease; DSM =

Diagnostic and Statistical Manual of Mental Disorders; MMSE = mini mental state examination; ESR = erythrocyte sedimental rate; hsCRP = high sensitivity C-reactive protein; MetS = metabolic syndrome

Table 4. Results of the association between depression and MetS in older adults aged 60 years or over in the longitudinal studies included in this review.

Studies	MetS	Depression	Methods	Adjustments	Results
Akbaraly et al., 2011	NCEP-ATP III	CES-D	Logistic regression	Age, sex, study center, marital status, education, smoking habits, alcohol consumption, BMI categories, cognitive impairment, disability, MetS treatment, self-reported history of CVD at baseline	MetS was associated with new-onset of depressive symptoms in participants aged 65-70 years at 4 year follow-up [OR = 1.82; 95%CI (1.12-2.95); p = 0.04] but no association was found for older participants.
Mast et al., 2008	NCEP-ATP III	CES-D	Logistic regression	Age, race, gender, education, recruitment site, physical and cognitive functioning	MetS was associated with increased risk for incident elevated depressive symptoms at 2 year follow-up[OR = 1.70; 95%CI (1.17-2.45); p < 0.01]

Vogelzangs et al., 2011	NCEP-ATP III	CES-D	Logistic regression	Age, sex, years of education, smoking, alcohol intake, physical activity, number of chronic diseases	MetS does not predict the onset of depression [OR = 1.01; 95%CI (0.66-1.54); p = 0.96]. Once a person is depressed MetS increases the odds of that person is remaining depressed or having recurrent episodes [OR = 2.66; 95%CI (1.01-7.00); p = 0.05].
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OR = odds ratio; CI = confidence interval; NCEP-ATP III = National Cholesterol Education Program Adult Treatment Panel III; BMI = Body Mass Index; CES-D = Center for Epidemiologic Studies Depression Scale; CVD = cardiovascular disease; MetS = metabolic syndrome

Table 5. Association between depression and components of MetS in older adults aged 60 years or over.

Studies	Analysis	Adjustment	Results
Akbaraly et al., 2011	Logestic regression	Age, sex, study center, MetS treatment, educational attainment, marital status, smoking, alcohol consumption, cognitive deficit, disability, self-reported history of CVD at baseline	Only the low HDL-C component was significantly associated with new onset of depressive symptoms in the age group 65-70 years old [OR = 1.81; 95%CI (1.04-3.17); p = 0.03].
Ruas et al., 2016	Logestic regression	Sociodemographic variables(gender, age, schooling, and monthly family income), lifestyle characteristics (current smoking, alcohol consumption, and no exercise), cognitive functioning, biological variables, current use of psychoactive drugs	High triglyceride level was the individual component that showed the strongest association with depressive symptoms [OR = 1.47; 95%CI (1.19-1.8); p < 0.0001].
Mast et al., 2008	Logestic regression	Age, gender, education, race, recruitment size, Teng Modified Mini-Mental State Exam, walking ability	Significant association between depression and HDL-C [OR = 1.66; 95%CI (1.13-2.44); p < 0.05] and FPG [OR = 1.52; 95%CI (1.03-2.26); p < 0.05]

Park et al., 2014	Logistic regression	Age and sex matched controls	Only waist circumference was found to be significantly associated with newly-diagnosed depression in elder patients [OR = 4.33; 95%CI(1.20-15.61); p < 0.05]
Roriz-Cruz et al., 2007	Logistic regression	-	No one of components of MetS was significantly associated with depression
Viscogliosi et al., 2012	Multiple regression	Sex, age, education, smoke, MMSE, MetS and its single components, hypertension, diabetes, medications, ESR, hsCRP	FPG was the only component of MetS that was significantly associated with depressive symptoms [β = 0.039; 95%CI (0.012-0.067); p = 0.005]
Vogelzangs et al., 2007b	Linear regression	Age, race, sex, education, income, smoking status, alcohol use, physical activity	Depressive symptoms were significantly associated only with BP (p < 0.05)
Vogelzangs et al., 2007a	Linear regression	Age, sex, smoking, alcohol use, number of chronic diseases	Higher depressive symptoms were associated with larger waist circumference (β = 0.864; p = 0.07) and lower HDL-C (β = -0.07; p = 0.05)
Vogelzangs	Logistic	Age, sex, years of education, smoking status,	Waist circumference was associated with increased odds

et al., 2011	regression	alcohol intake, physical activity, number of chronic diseases	of depression onset follow-up [OR = 1.28; 95%CI (1.05-1.56); p = 0.01]
Vogelzangs et al., 2009	Linear regression	Age, sex, educational level, smoking, alcohol use, physical activity, diabetes, cardiovascular disease, other chronic diseases	Only waist circumference (β =-0.063, p = 0.03) and HDL-C (β = 0.089; p = 0.001) were significantly associated with depressive symptoms

OR = odds ratio; CI = confidence interval; CVD =cardiovascular disease; HDL-C = high-density lipoprotein cholesterol; MMSE = mini-mental state exam; ESR = erythrocyte sedimental rate; hsCRP = high sensitivity C-reactive protein; MetS = metabolic syndrome