






Prevalence of Metabolically-Obese Normal-Weight Worldwide: Systematic Review and Meta-Analysis

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Abstract

Background: Obesity causes the loss of body homeostasis and predisposes to the development of disease; some individuals present alterations described even having a normal body mass index (BMI), and these are called thin metabolically obese. The objective was to carry out a systematic review with meta-analysis to determine the prevalence of metabolically-obese normal-weight (MONW) worldwide.

Methods: The search for studies was conducted from May to June 2022 in the EMBASE, PubMed, WOS, and Scopus databases. The purification and ordering of data were carried out using the Excel 2016 program, later a meta-analysis with the Stata version 17 program.

Results: A total of 408,251 people with normal BMI were identified, of whom 78,054 had a metabolic disorder, and the prevalence after the meta-analysis was 26.78% (95% confidence interval: 18.45 - 36.03) with high heterogeneity ($I^2 = 99.86\%$).

Conclusion: The findings of the systematic review confirm a high prevalence of MONW worldwide.

Keywords: Systematic review; Metabolically-obese normal-weight; Obesity; Prevalence

Introduction

The prevalence of obesity has doubled in the last four decades

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in more than 70 countries [1]. According to the World Health Organization (WHO), in 2016, 650 million adults worldwide were obese [2]. While in Latin America, it is estimated that about 58% of the region's inhabitants live with overweight [3]. In Peru, according to a report prepared at the national level, the prevalence of obesity increased by 6.3%, since it went from 18.3% in 2013 to 24.6% in 2020 [4].

Obesity causes loss of body homeostasis and predisposes to developing some diseases such as type 2 diabetes mellitus, hypertension, liver disease, cancer, allergies, osteoporosis and sarcopenia [5]. Nevertheless, despite the relationship between obesity and its comorbidities, some individuals present alterations described even having a body mass index (BMI) within normal values, and these are called metabolically-obese normal-weight (MONW) [6].

Due to the absence of excess body weight, MONW people easily mask their condition, creating the need for screening and consequently delaying diagnosis and treatment [7]. The prevalence of MONW in adults has inadvertently increased over the years. Taking a study carried out in Iran in 1996 [8] as an example, the prevalence was 16.06%, but 20 years later, another study conducted in the same country found a prevalence of 34.82%.

Currently, it is estimated that the prevalence of MONW is approximately 30.04% worldwide [9]; however, up to the time of this review, no study was found that scrupulously classified the samples of the included manuscripts. Therefore, due to the challenge it represents to public health and all of those mentioned above, the objective of this article was to carry out a systematic review with meta-analysis of the prevalence of MONW worldwide.

Materials and Methods

Study design

This study was a systematic review with meta-analysis that synthesizes the current information on the prevalence of MONW worldwide. For this, the manuscript was carried out following the PRISMA method.

Definition of MONW

Metabolically healthy people are those without metabolic al-

terations and any associated disease, although the definition varies according to the author [10]. Likewise, the WHO defines a person of normal weight as those with a BMI of 18.5 to 24.9. Therefore, for this review, we considered MONW in subjects with a normal BMI, but with metabolic alterations.

Selection criteria

Studies were included that 1) had a probability sample; 2) included the total number of MONW of patients with normal BMI; 3) participants were ≥ 18 years of age; 4) cross-sectional studies; 5) if they used a criterion to define the MONW patient; 6) if they used the BMI as a criterion to define whether the patient was obese. We excluded 1) systematic reviews and letters to the editor; 2) studies whose total population had a BMI above or below the normal range; 3) studies whose participants had a prior diagnosis of any communicable or non-communicable disease.

Search strategy

The search for studies was carried out from May to June 2022 in the EMBASE, PubMed, WOS, and Scopus databases. The search formula can be found in Supplementary Material 1 (www.jofem.org). No distinction was made regarding the language or the date on which the studies were prepared. Additionally, references of the included studies were checked for additional relevant articles.

Synthesis and analysis

Data filtering and ordering was carried out using the Excel 2016 program, and later a meta-analysis for prevalence was carried out with the program Stata version 17. Two analyses were done, one with all studies and then only with those that met the criteria according to the Newcastle-Ottawa Scale [11] for a truly representative sample.

Ethical compliance with human

The article was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Selection of studies

After the search was carried out, duplicates were removed. The results were downloaded. Two authors (VJVP and ITR) screened the title and abstract of each manuscript, selecting those consistent with the review theme, and then two researchers (ITR and GZZT) reviewed the full texts in order to define whether the manuscripts complied, in effect, with the selection criteria. In the case of any discrepancy, it was resolved by a

third researcher (VJVP). For both stages, the Rayyan online software was used (Fig. 1).

Extraction of information

For the extraction of information, a file created by the authors was elaborated (Table 1). The data extraction was carried out by JMCT and GZZT to be later verified by VJVP in order to verify their accuracy.

Risk of bias

An adaptation of the Newcastle-Ottawa Scale for descriptive cross-sectional studies was used (Supplementary Material 2, www.jofem.org). The evaluation was done in duplicate to avoid any bias. Finally, only those manuscripts with a representative or random sample of the population (classification A or B, according to the Newcastle-Ottawa Scale) were selected [11].

The most used criteria to diagnose MONW in the studies included in this review are summarized in Table 1.

Results

Study characteristics

Of the 920 manuscripts identified, 26 were selected (Fig. 1). The oldest study was published in 1987, while the most current ones were carried out in 2018. It was found that 23 studies used one of these three criteria: the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), the International Diabetes Federation (IDF), and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) or Joint Interim Statement (JIS) (Table 1); while three manuscripts used others (Supplementary Material 2, www.jofem.org). The characteristics of the included studies are shown in Table 2 [8, 9, 12-35].

A total of 408,251 people with normal BMI were identified, of which 78,054 had a metabolic disorder, therefore the prevalence of MONW worldwide according to the present review would be 19.11%.

The data were collected from 26 studies; 26.92% of the studies were conducted in China ($n = 7$) [9, 17, 20, 21, 23, 28, 33], 19.23% ($n = 5$) [8, 15, 29-31] in Iran, and 11.53% ($n = 3$) [13, 16, 25] in Korea. In addition, it was reviewed three countries with the same number of studies ($n = 2$), representing 7.69% each: United States [12, 19], Spain [14, 18], and Poland [22, 35]; finally another five countries [24, 26, 27, 32, 34] (Peru, Italy, The Netherlands, Iceland and Palestine) represented 15.36% of the total manuscripts (3.84% each, $n = 1$) (Fig. 2). In Asia, the total MONW sample represented 80.65% ($n = 62,954$) of cases worldwide; in America, it was 3.99% ($n = 3,120$), and in Europe 5.34% ($n = 11,980$).

Finally, the prevalence of MONW recorded each year has been increasing progressively, going from 9.18% in 1987 to 52.46% in 2012.

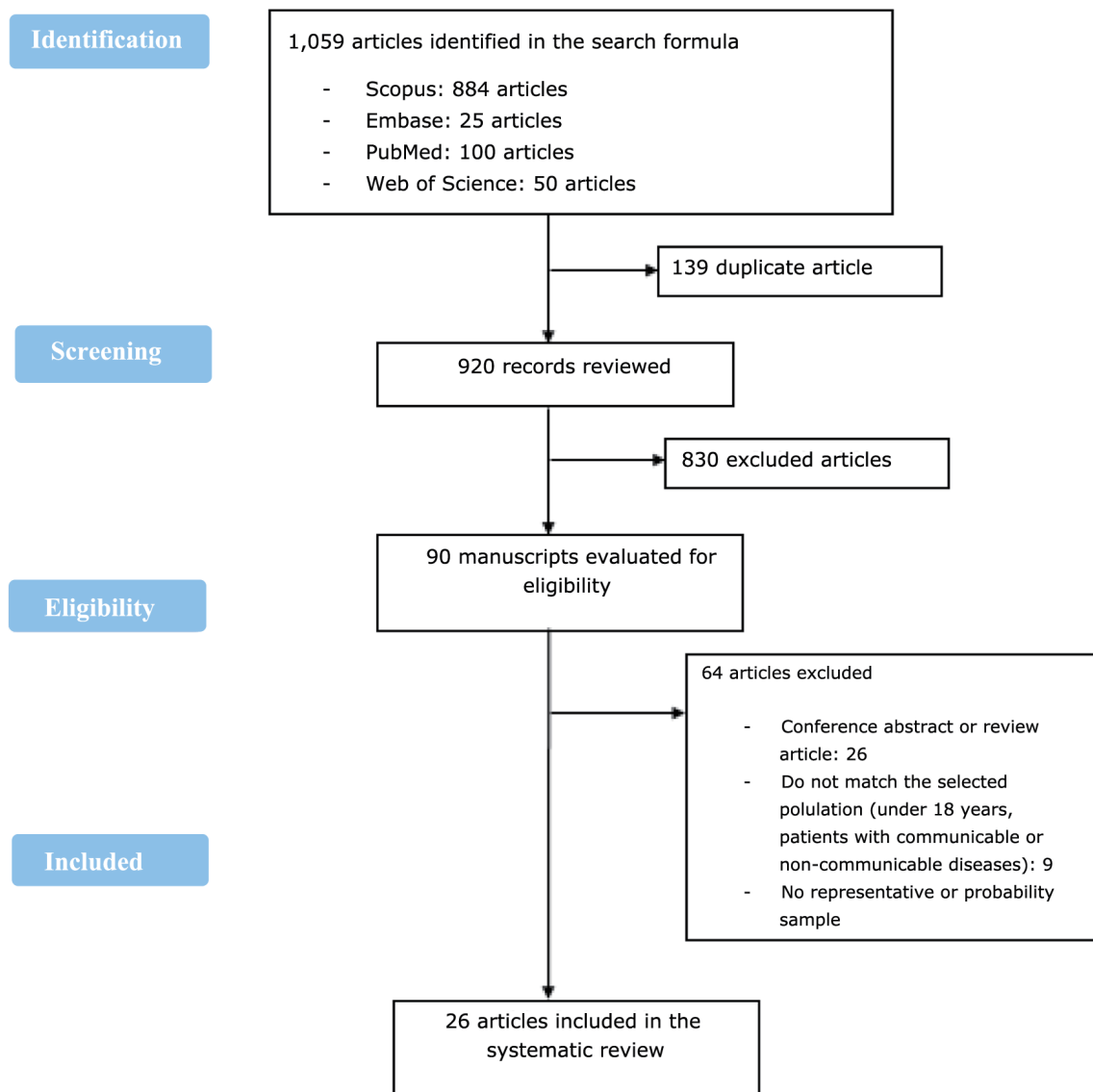


Figure 1. Flow chart.

Table 1. Criteria Used to Define Metabolic Disorders

	ATP III	IDF	AHA/NHLBI	JIS
Absolutely required	None	Increased waist circumference	None	None
Criterion	At least three criteria	At least two criteria in addition to waist circumference	At least three criteria	At least three criteria
Waist circumference	> 102 cm (men); > 89 cm (women)	≥ 94 cm (men); ≥ 80 cm (women)	>102 cm (men); > 89 cm (women)	> 85 cm (men); > 80 cm (women)
Blood pressure	≥ 130/85 mm Hg	≥ 130/85 mm Hg	≥ 130/85 mm Hg	≥ 130/85 mm Hg
Fasting triglycerides	≥ 150 mg/dL	≥ 150 mg/dL	≥ 150 mg/dL	≥ 150 mg/dL
HDL cholesterol	< 40 mg/dL (men); < 50 mg/dL (women)	< 40 mg/dL (men); < 50 mg/dL (women)	< 40 mg/dL (men); < 50 mg/dL (women)	< 40 mg/dL (men); < 50 mg/dL (women)
Higher fasting blood sugar	≥ 100 mg/dL	≥ 100 mg/dL	≥ 100 mg/dL	≥ 100 mg/dL

HDL: high-density lipoprotein.

Table 2. Characteristics of the Studies Included in the Review

Authors (year ^a)	Country	Metabolic disorder criteria	Sample with normal BMI	MONW	MONW prevalence	Age range
Bradshaw et al (1987) [12]	United States	ATP III	4,823	443	9.18%	45 - 64
Amouzegar et al (1996) [8]	Iran	JIS	666	107	16.06%	≥ 20
Lee et al (2003) [13]	South Korea	AHA/NHLBI	753	216	28.68%	≥ 40
Goday et al (2004) [14]	Spain	ATP III	202,265	4,419	2.18%	34 - 55
Hadaegh et al (2006) [15]	Iran	ATP III	3,444	361	10.48%	≥ 20
Lee et al (2007) [16]	South Korea	Presence of diabetes mellitus, hypertension or dyslipidemia	18,524	8,711	27.9%	40 - 69
Jia et al (2007) [17]	China	JIS	9,988	2,877	28.80%	≥ 20
Gomez-Huelgas et al (2007) [18]	Spain	IDF	841	179	21.28%	18 - 80
Moazzami et al (2009) [19]	United States	AHA/NHLBI	11,680	2,294	19.64%	≥ 18
Wang et al (2009) [9]	China	ATP III	6,973	2,099	30.1%	≥ 18
Tian et al (2009) [20]	China	ATP III	5,453	1,678	30.77%	18 - 85
Zheng et al (2010) [21]	China	WGOC	17,876	6,097	34.1%	≥ 20
Suliga et al (2010) [22]	Poland	IDF	13,172	6,217	47.2%	37 - 66
Zhang (2010) [23]	China	IDF	11,884	968	8.14%	≥ 39
Benziger et al (2010) [24]	Peru	IDF	890	383	43.03%	≥ 35
Kim et al (2011) [25]	South Korea	At least one of six metabolic disorders	79,012	36,178	45.78%	≥ 35
Buseemi et al (2011) [26]	Italy	At least two of four metabolic disorders	284	97	34.15%	18 - 90
Perini et al (2011) [27]	The Netherlands	ATP III	6,910	1,060	15.34%	18 - 70
Li et al (2011) [28]	China	ATP III	2,911	1,018	34.97%	≥ 40
Hajian-Tilaki, Heidari (2012) [29]	Iran	ATP III	324	170	52.46%	20 - 70
Tabatabaei-Malazy et al (2016) [30]	Iran	ATP III	6,082	2,118	34.82%	> 25
Zoghi et al (2016) [31]	Iran	ATP III	1,414	74	5.23%	35 - 70
Olafsdottir et al (2016) [32]	Iceland	JIS	182	1	0.54%	18
Zhu et al (2017) [33]	China	ATP III	1,293	253	19.56%	> 18
Damiri et al (2018) [34]	Palestine	IDF	346	29	8.38%	18 - 65
Placzkowska et al (2018) [35]	Poland	IDF	261	7	2.68%	18 - 31

^aThe year in which the population was studied. MONW: metabolically-obese normal-weight; BMI: body mass index.

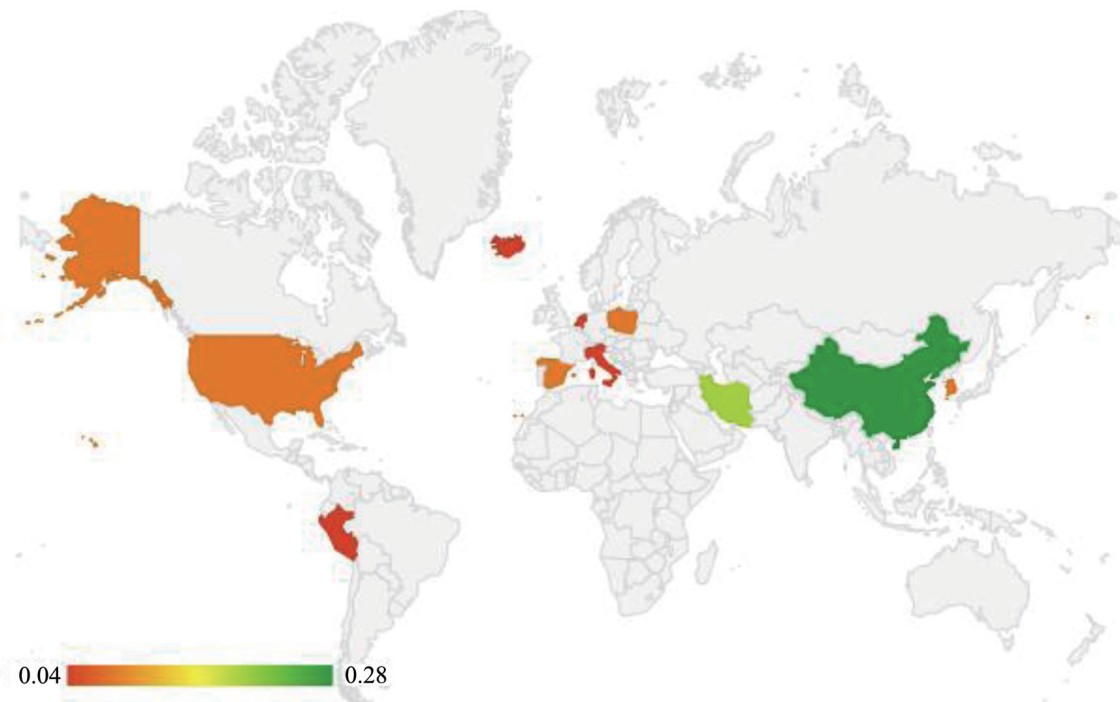


Figure 2. Regional prevalence of the studies selected for the review.

Meta-analysis

Of the studies included in the systematic review, those with a truly representative sample according to the New Castle-Ottawa Scale (all subjects or random sampling) were selected for meta-analysis. The study carried out by Suliga et al [22] was the one with the highest prevalence with 47.20% (95% confidence interval (CI): 46.35 - 48.05), while the manuscript by Hadaegh et al [15] had the lowest prevalence with 10.48% (95% CI: 9.50 - 11.55). Thus, the joint prevalence was 26.78% (95% CI: 18.45 - 36.03); however, it should be noted that there was high heterogeneity ($I^2 = 99.86\%$) (Fig. 3).

In order to prove if heterogeneity may have been secondary to the different criteria used for metabolic disorder, meta-analyses were performed between studies that used the same criteria (Figs. 4-7).

Despite the forest plots carried out, we still point out a high heterogeneity, with the exception of the studies that used the AHA/NHLBI as criteria (Fig. 4).

Discussion

In this article, the prevalence of MONW in people with normal BMI has been reviewed. Of the 26 selected studies, only 38.46% ($n = 10$) were considered for the meta-analysis.

The present review addressed the prevalence of MONW in the adult population worldwide. The overall prevalence and post-meta-analysis prevalence were 21.92% (95% CI: 12.79 - 32.69) (Supplementary Material 2, www.jofem.org) and

26.78% (95% CI: 18.45 - 36.03), respectively. These results agree with those found in a meta-analysis conducted by Wang et al [9], in which the general prevalence of MONW in people with normal weight was 30.04% (95% CI: 25.59 - 35.57).

However, unlike the previously mentioned article, in which populations of European origin had the highest prevalences [9], in this study, a higher prevalence of MONW people was found in Asian populations. There is evidence [36] that Asian populations are less obese, but with greater susceptibility to metabolic disorders compared to Caucasians. This could be because they have higher visceral adipose tissue with similar levels of obesity.

There are some limitations that should be considered in our review. An important limitation of this review is that the sample was only collected from 11 countries, which limits the generalization to the worldwide prevalence. Furthermore, most of the Asian studies were conducted in China, only three were conducted in South Korea, and none were conducted in Japan, so they were not representative of the entire Asian population. In addition, it is important to point out that in this study, factors that influence the development of a metabolically unhealthy phenotype in subjects with normal weight were not considered [37] such as physical activity, genetics, lifestyle, tobacco and alcohol consumption; the latter two, according to the meta-analysis prepared by Wang et al, significantly increase the prevalence of MONW since they significantly impair metabolic health [9]. Finally, the heterogeneity between the vast majority of studies that used the same diagnostic criterion (ATP III, IDF, and JIS) reflects that this is mainly due to the relationship between metabolic disorders and lifestyles rather than using different criteria.

Nevertheless, we emphasize the need for a common defi-

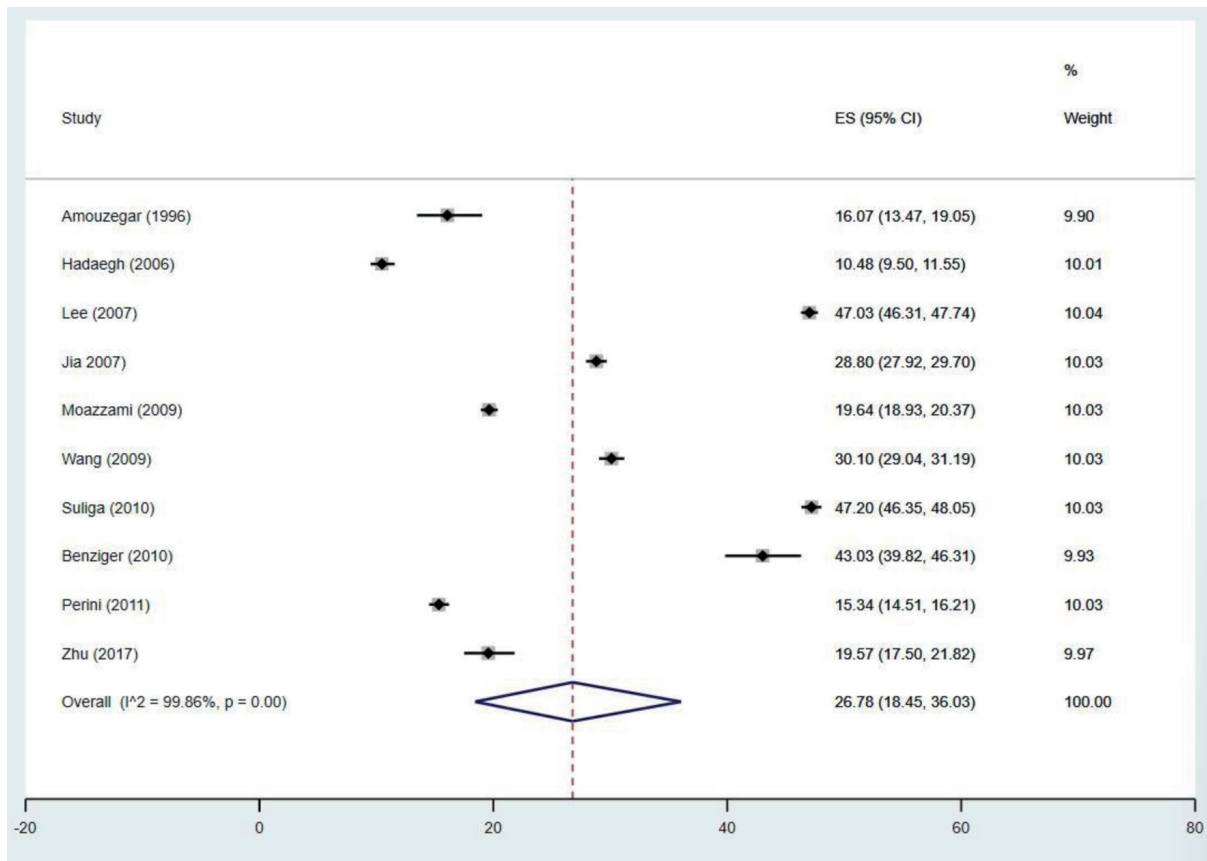


Figure 3. Forest plot of the prevalence of studies with truly representative samples.

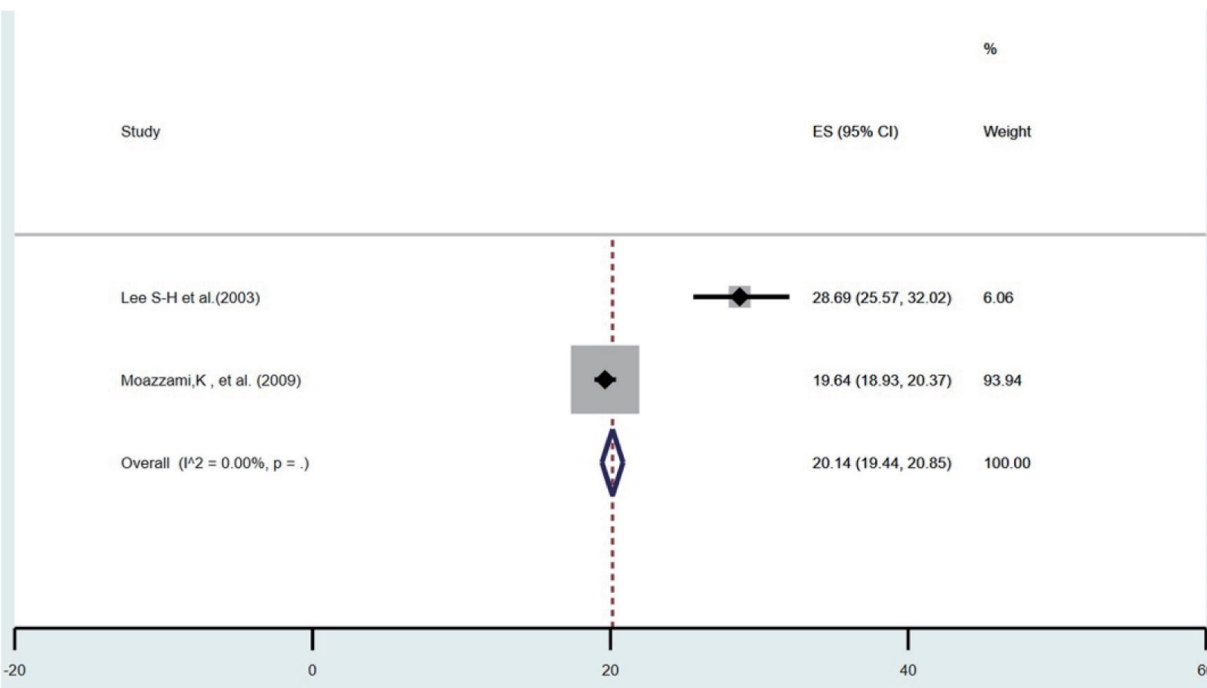


Figure 4. Forest plot of the studies that consider the AHA/NHLBI criteria for the diagnosis of metabolic disorder.

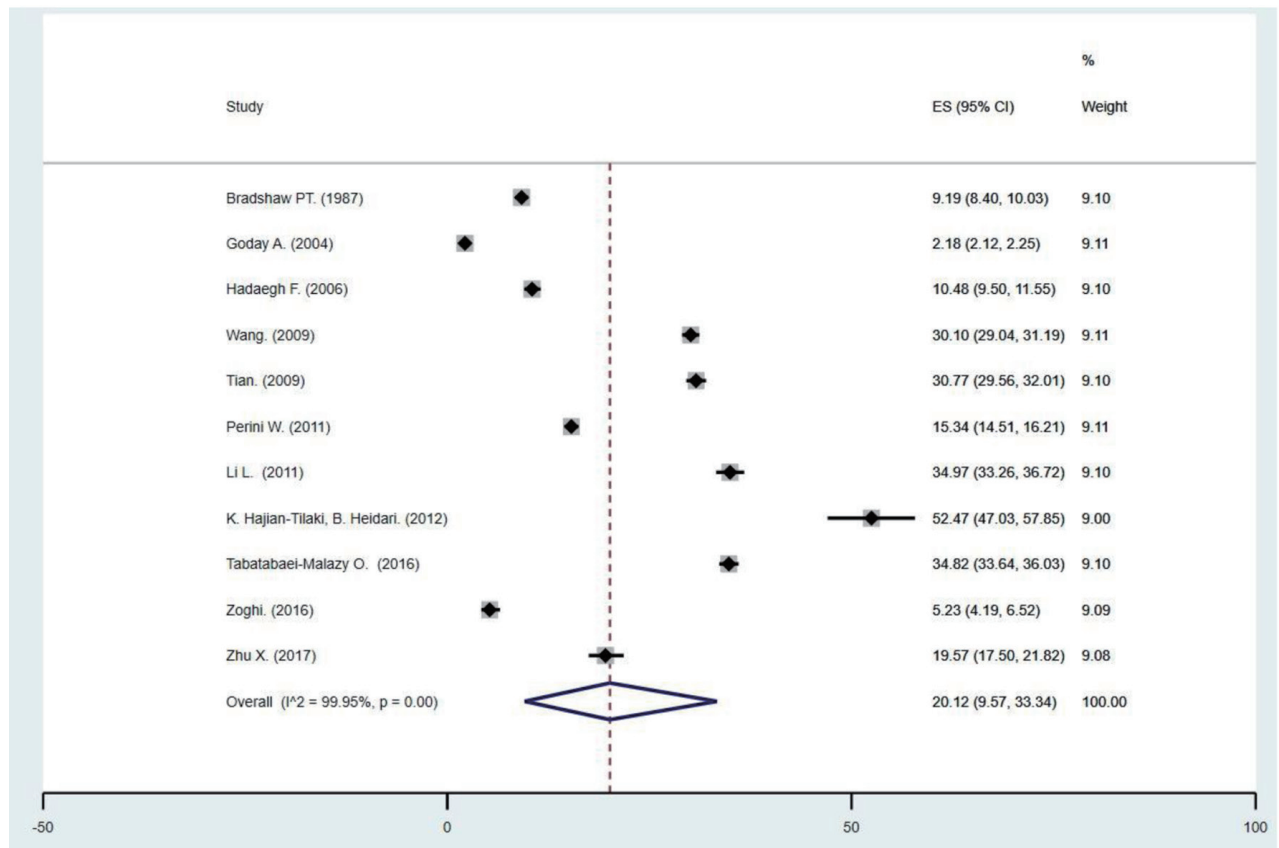


Figure 5. Forest plot of the studies that consider ATP III criteria for the diagnosis of metabolic disorder.

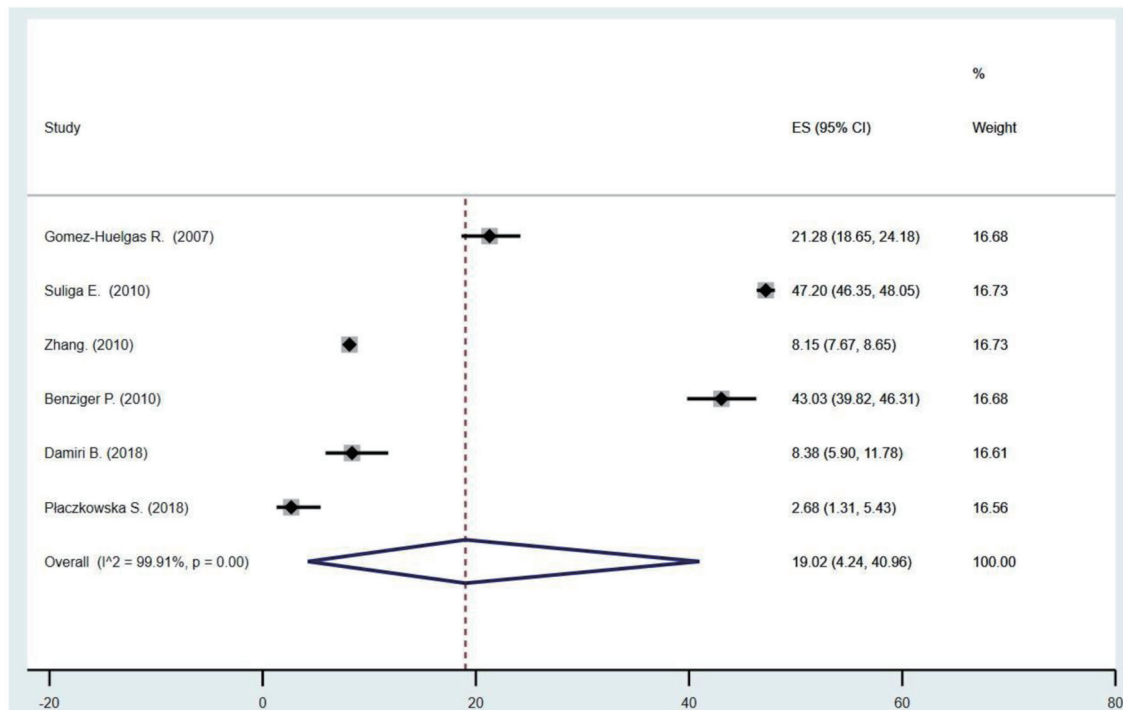


Figure 6. Forest plot of the studies that consider IDF criteria for the diagnosis of metabolic disorder.

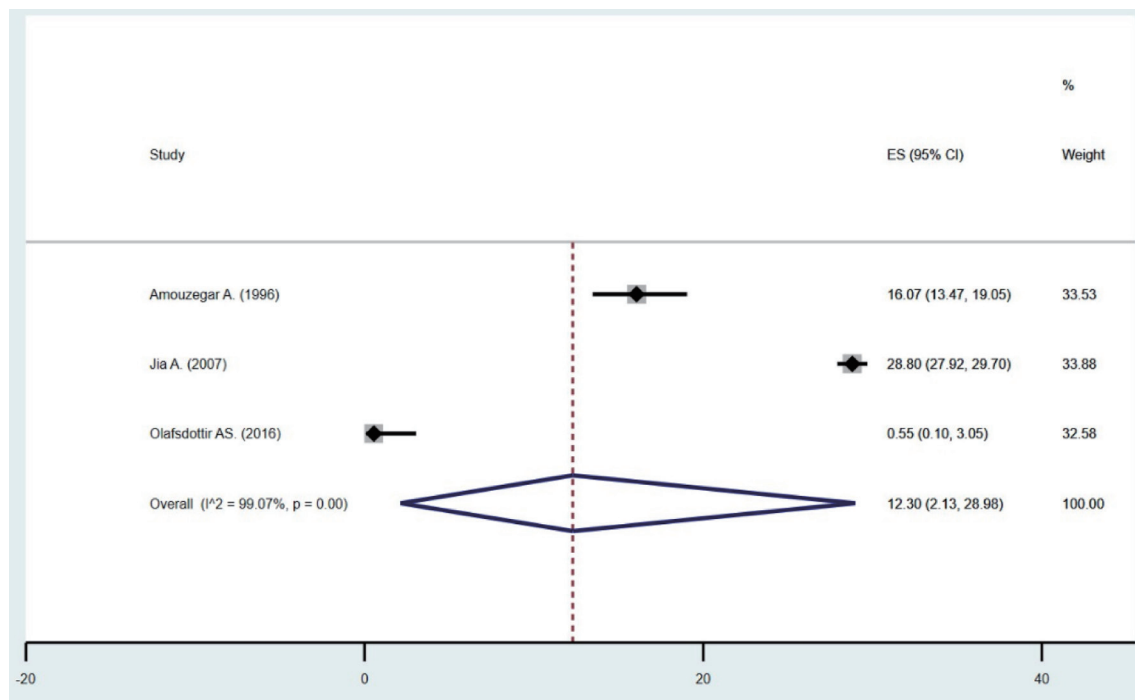


Figure 7. Forest plot of the studies that consider JIS criteria for the diagnosis of metabolic disorder.

dition because we found two studies carried out in different countries and years that diagnosed metabolic disorders with the same criterion (AHA/NHLBI) did not have heterogeneity.

Conclusion

This systematic review and meta-analysis confirm a high prevalence of MONW worldwide. Likewise, the need to develop a uniform criterion that can be used by clinical and research groups to diagnose MONW is highlighted.

Supplementary Material

Suppl 1. Different terms that were used to search for manuscripts in different databases.

Suppl 2. Studies truly representative and with a justified sample size according to the Newcastle-Ottawa Scale; other criteria used to define metabolic alterations; forest plot of the prevalence of all the studies.

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None to declare.

Financial Disclosure

This study did not receive any funding in any form.

Conflict of Interest

The authors declare no conflict of interest.

Informed Consent

Not applicable.

Author Contributions

GZZT and VJVP participated in the genesis of the idea, project design, development. The authors JMCT, REAM and ITR participated in collection and interpretation of data, analysis of the results and preparation of the manuscript.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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