Diagnostic Accuracy of Anthropometric Markers of Obesity for Prediabetes: A Systematic Review and Meta-Analysis

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Abstract: *Introduction*: Prediabetes is a significant public health concern due to its high risk of progressing to diabetes. Anthropometric measures of obesity, including body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR) have been demonstrated as key risk factors in the development of prediabetes. However, there is a lack of clarity on the diagnostic accuracy and cut-off points of these measures.

Objective: To determine the diagnostic accuracy of these anthropometric measures for their most effective use in identifying prediabetes.

Methodology: A systematic review (SR) with metanalysis of observational studies was carried out. The search was conducted in four databases: Pubmed/Medline, SCOPUS, Web of Science, and EMBASE. For the meta-analysis, sensitivity and specificity, together with their 95% confidence intervals (CI 95%) were calculated.

Results: Among all the manuscripts chosen for review, we had four cross-sectional studies, and three were classified as cohort studies.

The forest plots showed the combined sensitivity and specificity for both cross-sectional and cohort studies. For cross-sectional studies, the values were as follows: BMI had a sensitivity of 0.63 and specificity of 0.56, WC had a sensitivity of 0.59 and specificity of 0.58, and WHtR had a sensitivity of 0.63 and specificity of 0.73. In the cohort studies, the combined sensitivity and specificity were: BMI at 0.70 and 0.45, WC at 0.68 and 0.56, and WHtR at 0.68 and 0.56, respectively. All values are provided with 95% confidence intervals.

Conclusions: This systematic review and meta-analysis evaluated the diagnostic accuracy of BMI, WC, and WHtR in identifying prediabetes. The results showed variations in sensitivity and specificity, with WHtR having the highest specificity in cross-sectional studies and BMI having improved sensitivity in cohort studies.

Keywords: Prediabetic state, body weights and measures, body mass index, waist circumference, waist-height ratio, sensitivity and specificity (source: MeSH NLM).

INTRODUCTION

Prediabetes occurs when blood sugar levels are higher than normal, but not yet high enough to be diagnosed as diabetes. Patients with prediabetes are prone to developing diabetes, making it a significant public health issue [1]. Each year, it is estimated that 5% to 10% of patients with prediabetes will develop diabetes [2]. Additionally, about 70% of those diagnosed with prediabetes would present with diabetes at some point in their lives [3].

Globally, the prevalence of prediabetes varies: In China, it is 35.7% [4]. In a meta-analysis that included Caucasian and Asian populations, the prevalence of high glucose levels reached 53.1% [5]. In a study that processed data from 200 countries, in 2019, it was estimated that the global prevalence of prediabetes was 43.9% and, by 2030, it will increase to 52.0%; this equates to 850 million patients with prediabetes in 2019, with the potential to rise to 1.28 billion by 2030 [6].

Due to the increase in prediabetes, a growing diabetes epidemic is predicted if effective interventions are not implemented [7]. Exercise, diet, and weight loss are lifestyle changes that help prevent or delay the progression of diabetes in prediabetics. Medicine can also help. Intervention is necessary to address this issue and to stop this threat to global public health, especially in developing countries [8].

In many studies, it has been found that anthropometric measures of obesity, such as waist circumference (WC) [11, 12] or waist-to-height ratio

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(WHtR) [13, 14] and body mass index (BMI) [9, 10] play an important role as risk factors in the manifestation of prediabetes. These measures, derived from simple and accessible indicators, are crucial for identifying patients at risk; this allows for the implementation of strategies to preventively intervene to significantly halt the onset of diabetes.

Despite these findings, there is still no clarity regarding the precise cut-off points for these measures and their accurate diagnosis, which includes different values from each study, such as specificity and sensitivity [15-17]. This results in some ambiguity in their application, which potentially limits their effectiveness as detection tools. Given this, it is essential to carry out systematic reviews to definitively determine the diagnostic accuracy of these anthropometric measures and facilitate their use in identifying prediabetes more reliably.

METHODS

A systematic review (SR) with a meta-analysis of diagnostic test studies. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement was used to inform the structure of this work [18].

Search Strategy

A systematic search was conducted in the Web of Science (WOS), EMBASE, Scopus, and PubMed databases from February 1 to March 1, 2023. The following keywords were used: "prediabetes", "body mass index", "waist circumference", "waist-height ratio", "sensibility" and "specificity". The search strategy for each database is available in Supplementary Material 1.

Selection Criteria

First, two independent reviewers conducted a review of titles and abstracts. Subsequently, potentially relevant studies for full-text review were identified. Articles with unclear titles were read in their entirety. Discrepancies were resolved through agreement with the third reviewer. The following inclusion criteria were used: 1) Primary observational studies published in peer-reviewed journals: cross-sectional or cohort design, 2) studies in humans aged ≥18 years, 3) anthropometric indices used: BMI, WC, and WHtR, 4) investigations aimed at evaluating the predictive value of BMI, WC, and WHtR for prediabetes, and 5) studies reporting predictive measures: sensitivity and specificity. Meanwhile, studies meeting any of the following criteria were excluded: 1) letters to the editor or abstracts of conference proceedings, protocols, and review studies, and 2) articles without abstracts and full text in Spanish or English.

Prediabetes was established as an anomaly in fasting glucose according to the standards of the World Health Organization (WHO) (6.1 to 6.9 mmol/L) [19] or the definition of the American Diabetes Association (ADA) (5.6 to 6.9 mmol/L) [20], an alteration in glucose tolerance (7.8 to 11.0 mmol/L during an oral glucose tolerance test, after two hours) [20] or an elevated HbA1c according to ADA criteria (5.7 to 6.4%) [20].

Study Selection

The Rayyan online software (https://rayyan.qcri.org) was used to save the articles found in each of the databases explored. Three researchers independently reviewed the titles and abstracts of the manuscripts. If both agreed that a manuscript should be included, it was included; otherwise, it was excluded. In the case of discrepancy, the co-authors met to reach a consensus on the manuscript. Subsequently, the full text of the included articles was reviewed. Whether the study should be included or not was recorded in an Excel sheet. This process was carried out in the same way as the previous methodology process.

Data Extraction and Qualitative Analysis

The remaining articles moved on to data extraction, using a Microsoft Excel 2022 form. For cross-sectional studies, the summary table included: First author, year, country, study design, population (selection criteria), sample, sex (% female), mean (SD) or median (IQR), prediabetes prevalence, and gold standard for prediabetes diagnosis. Meanwhile, for cohort studies: First author, year, country, study design, follow-up time, population (selection criteria), sample, sex (% female), mean (SD) or median (IQR), prediabetes incidence, and gold standard for prediabetes diagnosis.

Additionally, a summary table was created, detailing the sensitivity, specificity, cut-off point, true positives, false negatives, true negatives, and false positives.

Risk of Bias Assessment

Two independent evaluators analyzed the methodological integrity of the involved studies, applying the guidelines of the newly revised version 2 of the Quality Assessment of Diagnostic Accuracy

Studies (QUADAS) [23]. Each criterion was scored as "yes", "no", or "uncertain" when there were not enough data to make a definitive decision. Any conflict was resolved through consensus among the co-authors. The Rev-Man 5.2 software was used to visually represent the quality of the included studies.

Quantitative Analysis

For the diagnostic precision meta-analysis, we used the number of true positives (TP), false negatives (FN), true negatives (TN), and false positives (FP), alongside the number of prediabetic patients, to calculate sensitivity and specificity. The positive and negative likelihood ratios, along with their 95% confidence intervals (CI 95%), for each anthropometric marker were extracted for both cross-sectional and cohort design studies. Six tables were developed: one for each marker, according to the type of study. All statistical analyses were performed using the STATA MP 16.0 statistical program (Stata Corp LP, College Station, Texas).

RESULTS

Eligible Studies

A total of 5367 publications were identified. Of these, 2850 duplicates were removed, resulting in 2,517 manuscripts being assessed via title and abstract. From these, 2,506 studies were excluded, leaving 11 manuscripts to be evaluated in full text. Finally, 7 manuscripts [15-17, 24-27] were selected (Figure **1**).

Characteristic of the Studies

Among all the manuscripts chosen for review, we had four cross-sectional studies [15, 24-26], and three were classified as cohort studies [16, 17, 27]. Each article included in this comprehensive review was disseminated to the public from the year 2018 through to 2021. The summary of the cross-sectional studies are found in Table **1**, as well as the cohort studies in Table **2**.

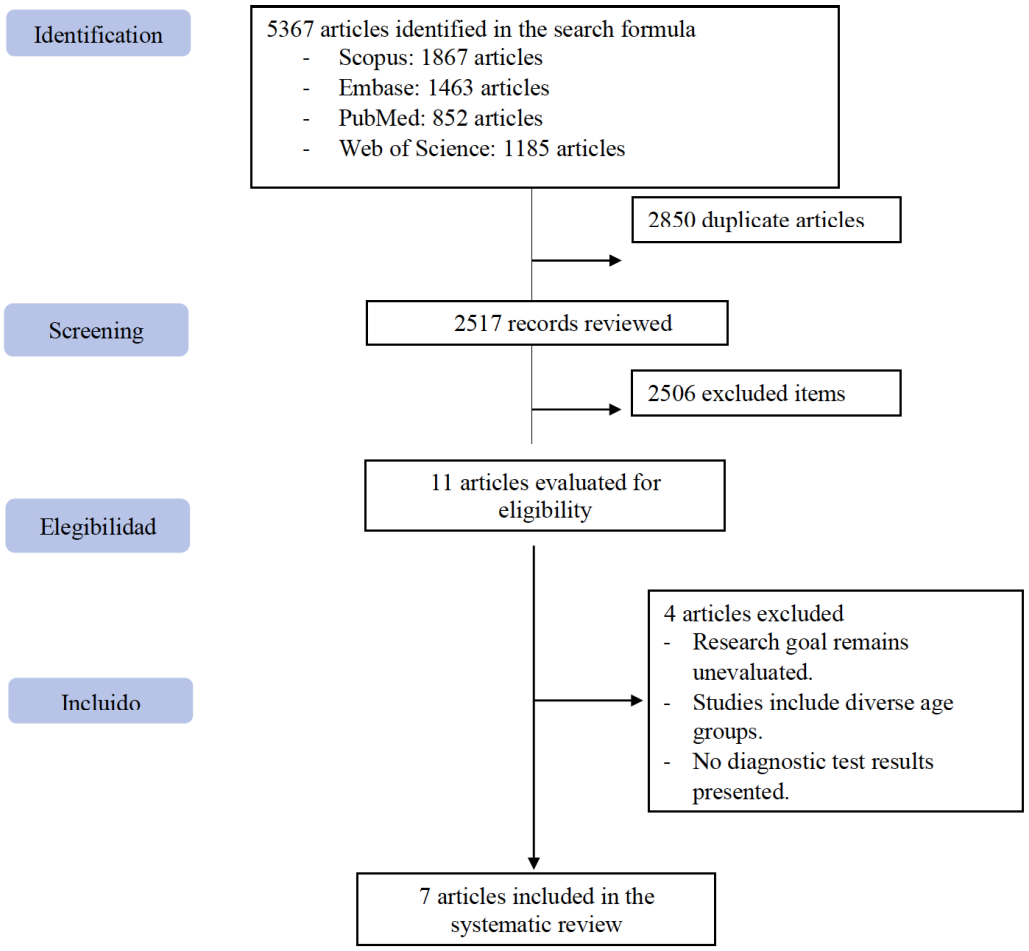


Figure 1: Flowchart.

Table 1: Characteristics of the Studies with a Cross-Sectional Design Included in the Review

First author, year	Country	Study design	Population (selection criteria)	Sample	Sex (% female)	Mean (SD) or Median (ICR) age	Prevalence of prediabetes (%)	Gold standard for prediabetes
Sánchez, 2021	Spain	Cross-sectional	The study included patients aged 45 to 70 years who had no history of cardiovascular disease but had at least one risk factor such as dyslipidemia, hypertension, obesity, smoking habit, or a first-degree relative with early onset cardiovascular disease (men below 55 years old, women below 65). However, patients with any type of diabetes, kidney disease, active cancer, life expectancy of less than 18 months, or who were pregnant were excluded from the study.	8188	50.89	Without prediabetes 56 (52–62) With prediabetes 59 (54–64)	33.35%	HbA1c: 5.7 – 6.4%
Chu, 2020	China	Cross-sectional	They recruited non-pregnant women (aged 18−45 years. The study did not include women who had a prior diagnosis of Type 1 or Type 2 diabetes mellitus before recruitment. Women were also omitted from the study if they were using oral or implanted contraception, undergoing assisted fertility treatment, taking systemic steroids, anticonvulsants, HIV or Hepatitis B or C medication within the last month. No participant was on metformin during the enrolment period, and all had a negative urinary pregnancy test at the time of enrolment.	971	100%	30.8 ± 3.7	10.90%	FPG 6.1 – 6.9 mmol/L and/or 2hPG ≥ 7.8 – <11.1 mmol/L
Hernandez, 2021	Mexico	Cross-sectional	Subjects aged ≥ 18 years old Women who agreed to sign an informed consent form, had fasted for 8 to 10 hours, and were enrolled in the program. Pregnant women and those with any disability were excluded, as well as those lacking 90% of the necessary information.	130	100%	—	35.40%	FPG 5.6 – 6.9 mmol/L
Zhao, 2018	China	Cross-sectional	Subjects aged 18-79 years old. Using a multistage stratified random cluster sampling method	15 078	54.57	46 (37–56) without prediabetes 51 (42–59) with prediabetes	8.47%	FPG 6.1 – 7.0 mmol/L

Table 2: Characteristics of the Studies with a Cohort Design Included in the Review

First autor, year	Country	Study design	follow-up time	Population (selection criteria)	Sample	Sex (% female)	Mean (SD) or Median (ICR) age	Incidence of prediabetes (%)	gold standar for prediabetes
Zhang, 2018	China	Cohort	3 years	40 to 49 years Subjects with a history of diabetes, incident diabetes or prediabetes verified by an oral glucose tolerance test (OGTT), those missing values or any parameter, or having any of the other conditions, were excluded.	1885	65.57%	56 (IQR: 48–61)	34.64% 104.9 per 1000 person-years	FPG 5.6 – 6.9 mmol/L and/or 2hPG ≥ 7.8 – <11.1 mmol/L
Ding, 2020	China	Cohort	8 years	40 to 49 years Subjects with with IFG, diabetes, or cancer or without glucose information, were excluded.	30 649	34.48%	Average age of 45.6 years (± 13.3 years) in men and 45.5 years (± 11.1 years) in women	25.2% 99.6 and 78.4 per 1000 person-years in men and women, respectively	FPG 5.6 – 6.9 mmol/L
Xia, 2018	China	Cohort	3 years	Aged over 45 years	2558	61.49%	59 (55-66) without prediabetes 62 (56-70) with prediabetes	21.30%	FPG 6.1 – 7.0 mmol/L and/or 2hPG ≥ 7.8 – 11.1 mmol/L

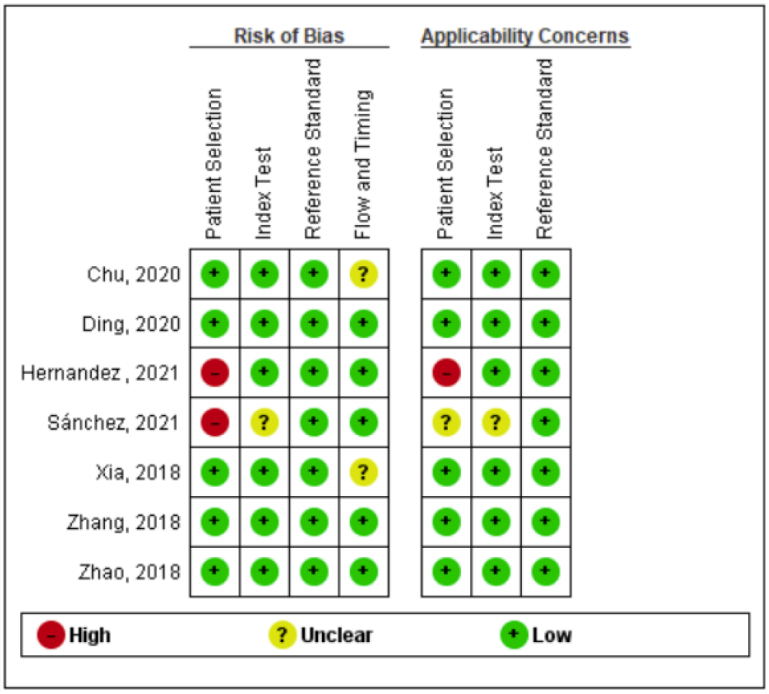


Figure 2: Quality assessment of included diagnostic studies, according to the QUADAS-2 tool.

The selected studies were conducted in nine countries: Spain (n=1) [15], China (n=5) [16, 17, 24, 25, 27] and Mexico (n=1) [26]. The sample reached a total of 24,367 in cross-sectional studies, ranging from 130 to 15,078. In the case of cohort studies, a total of 35,092 was worked with, ranging from 1,858 to 30,649. In all cross-sectional studies, subjects over the age of 18 participated, except for the work by Sánchez *et al*. [15], while in cohort studies, subjects over the age of 40 were recruited. The follow-up time ranged from three to eight years.

For the diagnosis of prediabetes, the manuscripts were based on the diagnosis based on IFG (5.6 – 6.9 mmol/L) [17, 24-26], except for the study by Zhao *et al*. [25] and Xia *et al*. [27], who used the WHO criteria (FPG: 6.1 – 7.0 mmol/L); the IGT (7.8 – 11 mmol/L) [16, 24, 27] and the HbA1c (5.7 – 6.4 %) [15]. The prevalence of prediabetes ranged from 8.47% to 35.49%. While the incidence ranged from 21.30% to 34.64% Table **1**.

In cross-sectional studies, the cut-off point for BMI varied from 22.6 to 31.5; for WC from 97.5 to 101.5 cm; and the WHtR from 0.65. For the cohort, the BMI changed from 21.36 to 24.4, the WC from 77.1 to 89.5 cm; while the WHtR was around 0.5.

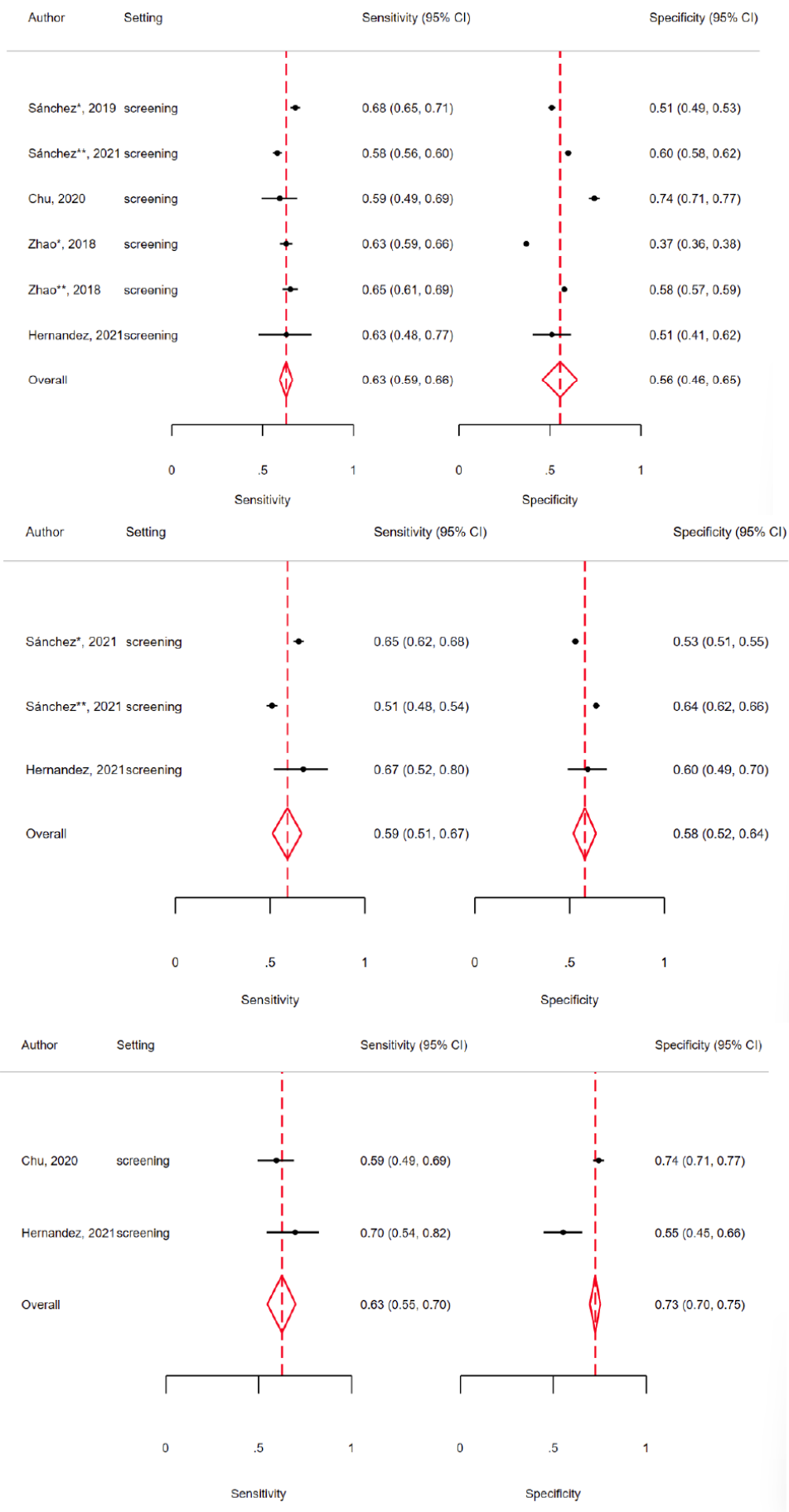
Risk of Bias Assessment

Seven studies were assessed using QUADAS-2. For the domain of patient selection, the studies by Hernandez *et al*. (26) and Sanchez *et al*. (15) presented a high level of risk of bias, because they did not use a probabilistic sampling and the first only recruited women. Therefore, the first mentioned study was considered as a high concern of bias, while the second was uncertain, as the sample size used was high. With respect to the application of the index test, in the work of Hernandez *et al*. (26) they do not clarify the results of the index test without knowledge of the results of the reference one, so an uncertain risk of bias was placed on it.

As for the time, the cross-sectional studies were considered an adequate time between the application of the test and the gold standard. However, the studies by Zhang *et al*. [16] and Xia *et al*. [27], due to the proposed objective, had little time (about three years) for the development of the event, which is why the risk level is considered uncertain. The risk of bias and applicability ratings for each outcome with justification are provided in Figure **2**.

Meta-Analysis of BMI, WC and WHtR and Prediabetes

Figure **3** summarizes the diagnostic test values of BMI, WC and WHtR for prediabetes, for both cross-sectional and cohort studies. The forest plots revealed that the combined sensitivity and specificity for cross-sectional studies were for BMI: 0.63 (95% CI 0.59, 0.66) and 0.56 (95% CI 0.46, 0.65), for WC: 0.59


Author
Setting
Sensitivity (95% CI)
Specificity (95% CI)
Sánchez*, 2019 screening 0.68 (0.65, 0.71) 0.51 (0.49, 0.53)
Sánchez**, 2021 screening 0.58 (0.56, 0.60) 0.60 (0.58, 0.62)
Chu, 2020 screening 0.59 (0.49, 0.69) 0.74 (0.71, 0.77)
Zhao*, 2018 screening 0.63 (0.59, 0.66) 0.37 (0.36, 0.38)
Zhao**, 2018 screening 0.65 (0.61, 0.69) 0.58 (0.57, 0.59)
Hernandez, 2021 screening 0.63 (0.48, 0.77) 0.51 (0.41, 0.62)
Overall 0.63 (0.59, 0.66) 0.56 (0.46, 0.65)
0 .5 1
Sensitivity
0 .5 1
Specificity
Author
Setting
Sensitivity (95% CI)
Specificity (95% CI)
Sánchez*, 2021 screening 0.65 (0.62, 0.68) 0.53 (0.51, 0.55)
Sánchez**, 2021 screening 0.51 (0.48, 0.54) 0.64 (0.62, 0.66)
Hernandez, 2021 screening 0.67 (0.52, 0.80) 0.60 (0.49, 0.70)
Overall 0.59 (0.51, 0.67) 0.58 (0.52, 0.64)
0 .5 1
Sensitivity
0 .5 1
Specificity
Author
Setting
Sensitivity (95% CI)
Specificity (95% CI)
Chu, 2020 screening 0.59 (0.49, 0.69) 0.74 (0.71, 0.77)
Hernandez, 2021 screening 0.70 (0.54, 0.82) 0.55 (0.45, 0.66)
Overall 0.63 (0.55, 0.70) 0.73 (0.70, 0.75)
0 .5 1
Sensitivity
0 .5 1
Specificity

(Figure 3). Continued.

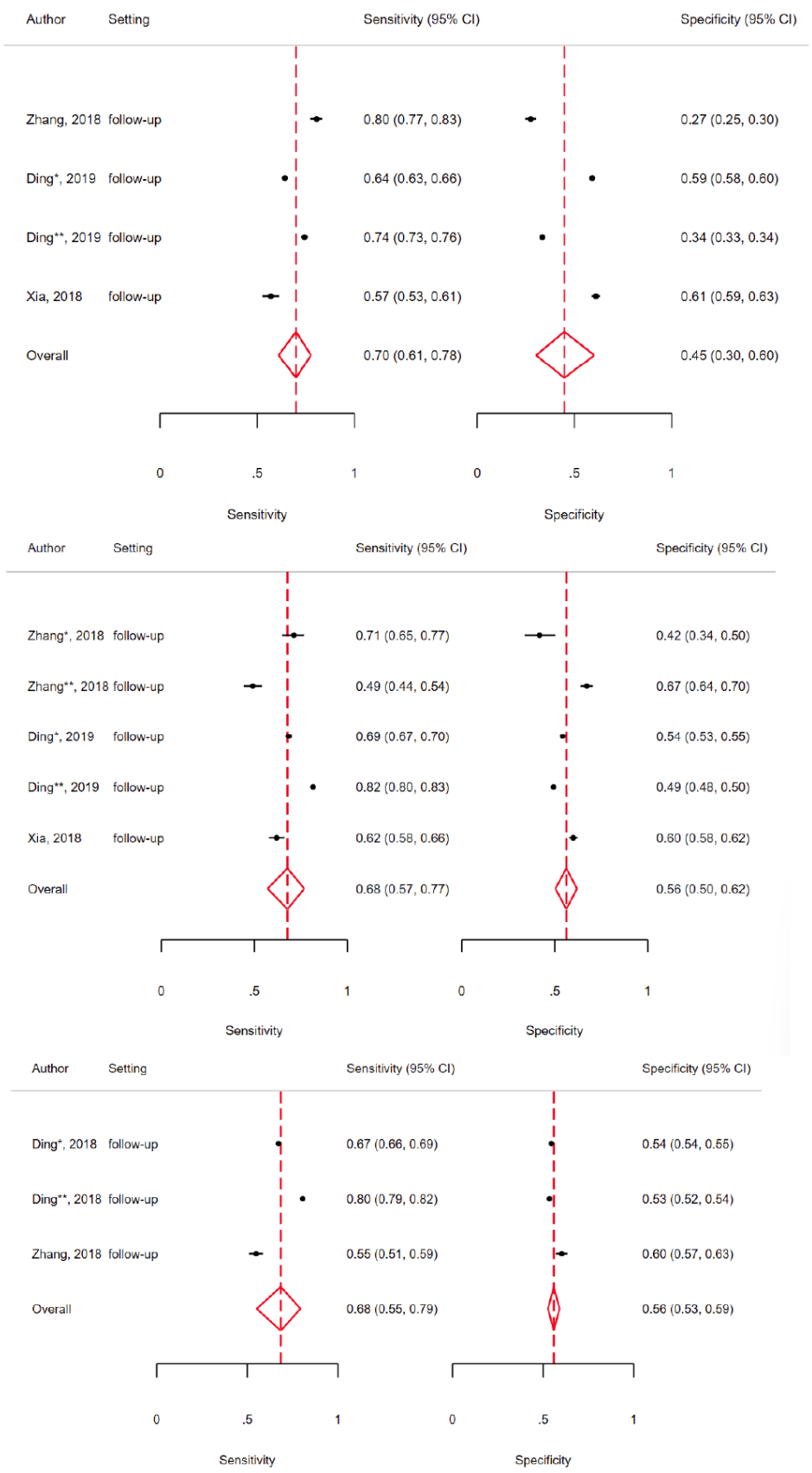


Figure 3: Forest plots of pooled sensitivity and specificity of BMI (**a**), WC (**b**) and WHtR (**c**) as a screening marker of prediabetes; and sensitivity and specificity of BMI (**d**), WC (**e**) and WHtR (**f**) as a prognostic marker of prediabetes.

(95% CI 0.51, 0.67) and 0.58 (95% CI 0.52, 0.64), and for WHtR: 0.63 (95% CI 0.55, 0.70) and 0.73 (95% CI 0.70, 0.75), respectively. In the case of the cohort, combined sensitivity and specificity to fulfill their prognostic role were, for BMI: 0.70 (95% CI 0.61, 0.78) and 0.45 (95% CI 0.30, 0.60), for WC: 0.68 (95% CI 0.57, 0.77) and 0.56 (95% CI 0.50, 0.62), and for WHtR 0.68 (95% CI 0.55, 0.79) and 0.56 (95% CI 0.53, 0.59), respectively.

DISCUSSION

In our meta-analysis, both in cross-sectional and cohort studies, it was found that anthropometric measurements such as BMI, WC, and WHtR have a modest ability to identify patients at risk of prediabetes. The WHtR had higher combined sensitivity and specificity among the cross-sectional studies, while BMI and WC maintained similar performance. In the cohort studies, all three markers had comparable sensitivity, however, there is moderate specificity in order to predict the development of prediabetes.

The association of these measurements and prediabetes is due to the fact that the accumulation of visceral fat is closely related to insulin resistance and inflammation [28]. Visceral fat releases free fatty acids that could interfere with the action of insulin in the liver and muscle. In addition, visceral fat secretes pro-inflammatory adipokines that contribute to low-grade systemic chronic inflammation [29, 30]. Abdominal obesity, as measured by WHtR, could be a slightly better predictor of visceral fat; this explains its better performance [31].

It should be noted that these markers have limitations in identifying users with prediabetes, specifically with obesity. Many with excess body fat remain sensitive to insulin, while some lean individuals develop insulin resistance and hyperglycemia. Other factors such as genetics, aging, and lifestyle usually also affect metabolic risk [32].

On the other hand, our systematic review included data from nine countries, such as Asia and Latin America, with a total of 24,367 people in cross-sectional studies and 35,092 in cohort studies [15-17, 24-27]. In most studies, middle-aged or older adults were recruited, so our findings apply more to this population. Meanwhile, the average follow-up of the cohort studies was three to eight years in general; it could give a first preamble to evaluate the progression to prediabetes from normoglycemia [16, 17, 27].

Thus, more work is needed in other parts of the world: Africa and the Middle East, where diabetes rates are rising very quickly. The inclusion of younger people is also important, due to the alarming increase in obesity in children and adolescents [33]. It is likely that anthropometric measures do not work adequately for the prediction of metabolic complications in the younger ones, given the hormonal differences and other age influences with respect to body fat distribution [34].

Future longitudinal works should be carried out over longer periods, such as 10 years or more, to give a more complete picture of how these markers could predict the development not only to prediabetes but to diabetes. Well-designed prospective research is important in various populations in order to strengthen clinical recommendations regarding the use of simple anthropometric measures to preventively detect patients at high risk of metabolic diseases associated with obesity [35, 36].

There was substantial variability in the cut-off points used for anthropometric measures between cross-sectional and cohort studies. For example, the BMI cut-off point ranged from 21.36 to 31.5 kg/m2, while the WC cut-off point ranged from 77.1 cm to 101.5 cm. This heterogeneity makes it difficult to compare findings between works and the determination of precise thresholds for the prediction of prediabetes. These differences may or may not identify users at risk. Furthermore, it is necessary to have well-designed validations that use objective tests of insulin resistance and other cardiometabolic risk markers in order to establish optimal cut-off points for these measures in different social groups.

In view of the above, subsequent works should report multiple cut-off points together with their diagnostic performance measures. This would allow clinicians and public health officials to select appropriate thresholds according to the priorities of their target population, to maximize specificity or sensitivity. Also, it would provide more evidence on how the cut-off points can be applied to initiate interventions at the levels of primary versus secondary care.

Our research has some essential limitations that should be considered. First, the substantial heterogeneity in the design of the works, the populations of people, and the cut-off points used makes direct comparison of the findings and

determination of conclusions difficult. The lack of geographical and ethnic diversity among the studies also limits the generalization of our results. Secondly, longer follow-up periods are needed to understand more about the long-term predictive capacity of these measures. Therefore, appropriately designed pragmatic trials are necessary to determine whether these could predict the risk of those in the highest percentiles of BMI, WC, and WHtR distributions.

In accordance with the results found, where anthropometric measures such as BMI, WC, and WHtR have a modest capacity for the prediction of prediabetes in isolation, they remain useful tools for initial risk stratification in clinical practice. They are non-invasive, low-cost, and easy to obtain measures that could provide information about a patient's overall and abdominal adiposity. Moreover, it can help physicians to decide whether additional tests such as blood analysis or glucose tolerance tests are justified.

In addition to other clinical data such as family history, these markers can provide a comprehensive assessment of the risk of prediabetes and other related comorbidities. Also, long-term monitoring of these markers could motivate users to adhere to lifestyle interventions by objectively demonstrating their progress towards fat loss or redistribution goals. Even though they are not sufficient, simple anthropometric measures still have a place in the primary and secondary prevention of chronic diseases such as type 2 diabetes.

CONCLUSIONS

BMI, WC, and WHtR have a moderate capacity to identify prediabetes. More rigorous and well-designed longitudinal studies are needed in different demographic groups to confirm these findings. However, despite their probable limited accuracy, these simple and economical tools are of great value to healthcare systems with scarce resources.

Despite the existing doubts, anthropometric measurements represent an invaluable first step towards personalized disease prevention. The correlation of individual trends in these indicators with lifestyle choices allows patients to gain a meaningful understanding of their modifiable risks and favor motivation to make lasting changes to their health. This patient-centered approach in primary care can generate a substantial impact on the metabolic risk profile.

COMPETING INTEREST

The authors declared they do not have a potential conflict of interest and have not received financial funding from public or non-public institutions.

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AUTHORSHIP CONTRIBUTIONS

The authors participated in the genesis of the idea, project design, data collection and interpretation, analysis of results, and preparation of the manuscript of this research work.

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