Diabetes, Metabolic Syndrome and Obesity

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REVIEW

Relation Between Obesity, Normal-Weight Obesity, and Risk of Diabetes Among Youth and Females - A Systematic Review and Meta-Analysis

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Background: Obesity is a significant modifiable risk factor for the development of diabetes. While this relationship is well established, the strength of association and its variation across age, sex, and body composition remains insufficiently understood.

Objective: This systematic review and meta-analysis aimed to assess the association between obesity, as measured by body mass index (BMI), and the risk of developing diabetes, with additional focus on subgroups by age, sex, and obesity phenotype, including normal-weight obesity (NWO).

Methods: A Total of 1243 studies were screened using PRISMA guidelines and PICOS criteria across five major databases between 1994 and 2022. After rigorous screening, 10 studies comprising over 1.7 million participants met the inclusion criteria. Meta-analysis used a random-effects model to calculate pooled hazard ratios (HRs).

Results: The pooled hazard ratio (HR) was 2.40 (95% CI: 2.07–2.79, $I^2 = 77\%$, $\tau^2 = 0.0339$, $p < 0.01$), indicating that obese individuals had more than twice the risk of developing diabetes compared with their nonobese counterparts. Subgroup analyses revealed that younger individuals (HR: 3.45, 95% CI: 2.90–4.10) and females (HR: 2.90, 95% CI: 2.35–3.55) presented greater diabetes risk than older individuals (HR: 2.95, 95% CI: 2.55–3.45) and males (HR: 2.60, 95% CI: 2.10–3.20). Normal weight obesity NWO was associated with an elevated risk in females (HR: 3.10, 95% CI: 1.37–7.01) but not males (HR: 1.16, 95% CI: 0.31–4.30).

Conclusion: Obesity is strongly linked with an increased risk of diabetes, with significant effects in younger individuals, females, and those with high body fat despite an abnormal BMI. There is a need for comprehensive obesity assessments, including body composition analysis, in clinical practice and managing diabetes risk.

Keywords: obesity, body mass index, normal weight obesity, diabetes risk, high body fat, youth diabetes risk, female diabetes risk

Introduction

Diabetes is a chronic metabolic disorder characterized by abnormally high blood glucose levels due to defects in insulin production, insulin action, or both.[1,2] It is becoming increasingly prevalent worldwide and is a significant public health problem with important implications for morbidity, mortality, and healthcare costs.[3] Obesity, defined as excessive fat accumulation that presents a health risk, is a major modifiable risk factor for T2DM.[4] Obesity is not only a significant risk factor for type 2 diabetes, but its role in the development of other types of diabetes, including autoimmune and other less common forms, is becoming increasingly recognized.[5,6]

The parallel raise in the global obesity epidemic and increasing incidence of diabetes have prompted the possibility of a link between these two conditions beyond the well-established mechanism of insulin resistance[7] Excess adiposity is known to result in systemic inflammation, metabolic stress, and dysregulated immune responses, which may contribute to the pathogenesis and progression of diabetes[8,9] Emerging evidence suggests that obesity may accelerate or exacerbate the underlying processes leading to various forms of diabetes, previously considered distinct from metabolic dysfunction.[10]

https://doi.org/10.2147/DMSO.S547743
Received: 23 June 2025
Accepted: 21 August 2025
Published: 24 May 2026

The evidence is growing that obesity, especially in early life, may accelerate the onset of diabetes.[11] Obesity-induced metabolic stress is a dysfunction that increases the likelihood of diabetes in those predisposed to the disease.[12] Since childhood and adolescent obesity rates are increasing, understanding the possible role of excess weight in diabetes development has become increasingly urgent.[13,14]

Although research in this area is expanding, the relationship between obesity and diabetes remains complex and poorly understood.[15] Discrepancies arise due to variations in study design, population characteristics, and definitions of obesity.[16] However, some studies have shown a direct relationship between higher body mass index (BMI) and increased diabetes risk. In contrast, others have indicated that age, sex, and genetic predisposition may complicate this relationship.[17,18] This is complicated by the recognition of normal weight obesity (NWO), wherein individuals have a normal BMI but elevated body fat, suggesting that traditional BMI-based classifications may omit overweight individuals at elevated metabolic risk.[19,20]

Obesity and diabetes are two growing public health concerns. According to Global Burden of Disease estimates, global obesity rates have nearly doubled since 1980, contributing significantly to the rising prevalence of type 2 diabetes worldwide.[21] This dual epidemic, often referred to as "diabesity", is driven by sedentary lifestyles, urbanization, and dietary changes.[22]

Body Mass Index (BMI) is commonly used to define obesity; however, it does not reflect fat distribution or composition. Alternative measures such as waist circumference, waist-to-hip ratio, and body fat percentage may better capture visceral adiposity and its metabolic impact. These tools, though less frequently used in clinical settings, offer valuable insight, particularly in populations at risk despite an abnormal BMI.[23]

Normal Weight Obesity (NWO) is one such phenotype, characterized by a normal BMI (18.5–24.9 kg/m^2) but elevated body fat percentage, typically above 24% in men and 33% in women.[23] Individuals with NWO, especially women, are at increased risk of developing type 2 diabetes despite having BMI values in the normal range.[23,24] This makes NWO a critical but often underrecognized contributor to diabetes risk.

A comprehensive literature synthesis is needed to clarify the impact of obesity on type 2 diabetes risk, its role in other forms of diabetes, and its impact across different age groups, sexes, and geographic populations remains less clear. This systematic review and meta-analysis examine diabetes risk across BMI categories (normal weight, overweight, and obese) and explore variations by age, sex, and geographic location. It also assesses the effects of the NWO and missing data on body composition and the development of diabetes. This review aims to provide evidence-based insights for clinical practice and public health strategies focused on weight management and early identification of at-risk individuals.

Methodology

Study Design and Framework

We carried out this systematic assessment and meta-analysis in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to enhance methodological transparency, rigor, and reproducibility. The main goal of this review was to summarize existing findings on the relationship between obesity, as measured by body mass index (BMI), and susceptibility to diabetes, including demographic variations and obesity phenotypes, such as Normal Weight Obesity (NWO). The review used PICOS (Population, Intervention, Comparison, Outcome, and Study Design) format to outline eligibility criteria and inform a somewhat organized data collection and synthesis process.

Eligibility Criteria

The following inclusion criteria applied: (1) answered the study questions, (2) peer-reviewed articles written in English; (3) investigated the association between obesity (measured by BMI) and risk of diabetes; (4) included human participants of various populations and age groups; (5) applied validated measures of both exposures (BMI) and outcomes (incident type1 diabetes); (6) utilized an observational or an experimental study, including cohort studies, case-cohort studies, cross-sectional designs, randomized controlled trials (RCTs) and systematic reviews with original data; and (Follow-up duration was not reported, but only studies that had a clearly described follow-up were analyzed; (7) durations ranging from 5 years to 24 years, and 8) Studies between 1994 to 2022. Research articles that did not include BMI information, or studies that specialized in either gestational diabetes or type 2 diabetes, studies with a sample size of less than 50, research that was not published in English, or research involving human experimentation were not included.

Search Strategy

We conducted a comprehensive literature search across five major electronic databases: PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar. Search queries were constructed using a combination of Boolean operators (AND, OR) and Medical Subject Headings (MeSH) terms. The search terms included "obesity", "body mass index", "BMI", "diabetes", "type 2 diabetes", "T2D", "risk", and "incidence." The search was limited to studies involving human participants and written in English, with publication dates ranging from database inception to November 2023. To ensure thoroughness, we screened manually reference lists of all selected articles and relevant systematic reviews for potentially eligible studies not captured in the database searches.

Study Selection Process

The selection of studies followed the four-phase PRISMA process: identification, screening, eligibility assessment, and inclusion. Initially, 1243 records were identified through the database search. After removing 382 duplicates, 861 unique titles and abstracts were screened for relevance. Of these, 753 were excluded based on title and abstract review. The remaining 108 articles underwent full-text review for eligibility against predefined inclusion criteria. Ultimately, 10 studies met all inclusion criteria and were included in the qualitative synthesis and meta-analysis. Two investigators independently and blindly performed title and abstract screening to minimize selection bias. Disagreements were resolved through discussion and consensus.

Study Questions

We used the PICOS framework to determine the guiding question for this systematic review: "What is the relationship between obesity and the risk of developing diabetes?" **Table 1 shows a structured approach to evidence retrieval and appraisal.**

Data Extraction and Quality Assessment

We extracted the records using standardized data extraction forms to facilitate uniformity and precision. The extract variables involved titles of the study, the author or authors; the year of publication, the country of origin, the way the study was conducted, the sample size used in the study, age and sex proportion of the participants involved in the study, the measurements of the BMI, how obesity was defined, the results of the development of diabetes (the type, the way it was diagnosed) and the time which was covered in studying the given results. Mismatches in data extraction were overcome by collective review and discussion among the reviewers.

We used two standardized tools to evaluate the methodological quality and risk of bias of the studies used. The quality of observational studies has been assessed using the Newcastle-Ottawa Scale (NOS), which ranks studies based on their

Table 1 PICOS Framework for Research Questions of the Recent Study

Parameter	Description
Population (P)	Diverse human populations, including children, adolescents, and adults, across the United States, Denmark, Israel, Sweden, Japan, and China.
Intervention (I)	Obesity as measured by Body Mass Index (BMI), including subtypes such as Normal Weight Obesity (NWO).
Comparison (C)	Individuals with normal weight or non-obese BMI classifications.
Outcomes (O)	Incidence and risk of developing diabetes, particularly type 2 diabetes.
Study Design (S)	Observational studies (cohort, cross-sectional, case-control), RCTs, and systematic reviews.

https://doi.org/10.2147/DMSO.S547743

methods of participant selection, group comparison, and outcome measurement. The grades were 6 (moderate quality), 7 (good quality), 8 (excellent quality), and 9 (high quality). We used the Cochrane Risk of Bias Tool to evaluate randomized controlled trials by considering random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting. The quality of all included studies was moderate to good, and no studies at high risk were used in the meta-analysis.

Data Synthesis and Statistical Analysis

We carried out a narrative synthesis to summarize the findings across the studies included. We used a meta-analysis using R software to carry out a quantitative synthesis. We employed a random-effects model (DerSimonian and Laird method) to estimate pooled hazard ratios (HRs), accounting for heterogeneity across studies. We used the I2 statistic and its value to determine heterogeneity. Subgroup analysis was conducted to assess whether the obesity-diabetes association was moderated by age, sex, and NWO. Then, we performed a sensitivity analysis by removing studies with short follow-ups and small sample sizes to assess robustness.

Assessment of Publication Bias

We used funnel plots and Egger's regression test to assess publication bias. The funnel plots were visually inspected to detect any possible asymmetry that may indicate small-study effects. The Egger test statistically confirmed the presence of publication bias, and a slight overall bias was observed.

Protocol Registration

Admittedly, this systematic review was not registered in PROSPERO or other international protocol registry, which can be considered a limitation. To improve transparency and methodological responsibility, future reviews must embrace preregistration.

Results

Figure 1 shows the PRISMA flow chart, which represents the selection process that included 10 studies.

Summary of Findings From Included Studies

Table 2 shows the characteristics and outcomes of the selected 10 studies, and Table 3 determines their quality and the related risk of bias.

Summary of Findings From Included Studies

Many studies have used a prospective cohort design, whereas others have used population-based or case–cohort methodologies. Longitudinal studies, such as,[35] were complemented with prevalence data from cross-sectional studies, such as.[31] There is significant variation in the age range of participants, with some studies studying adolescents[27] and others studying middle-aged adults.[28,29]

Across all studies, the primary measure of obesity was BMI, with definitions ranging from BMI ≥ 25 kg/m² to BMI ≥ 35 kg/m². BMI was stratified into quintiles for a dose-response analysis.[35] Normal weight obesity (NWO), defined as participants with a normal BMI but >24% body fat in men and >33% body fat in women, was considered obese.[23]

Fasting plasma glucose levels, oral glucose tolerance tests (OGTTs), or self-reported diabetes diagnoses were used to determine diabetes outcomes. The incidence of diabetes varies widely depending on population demographics, follow-up durations, and baseline obesity levels.

Individuals with higher BMI levels exhibited greater diabetes risk, but significantly, those with NWO—despite having a normal BMI—also showed elevated risk due to high body fat percentage. These results underscore that reliance solely on BMI may overlook individuals at metabolic risk. The findings have direct implications for improving screening criteria and tailoring public health interventions.[22–24]

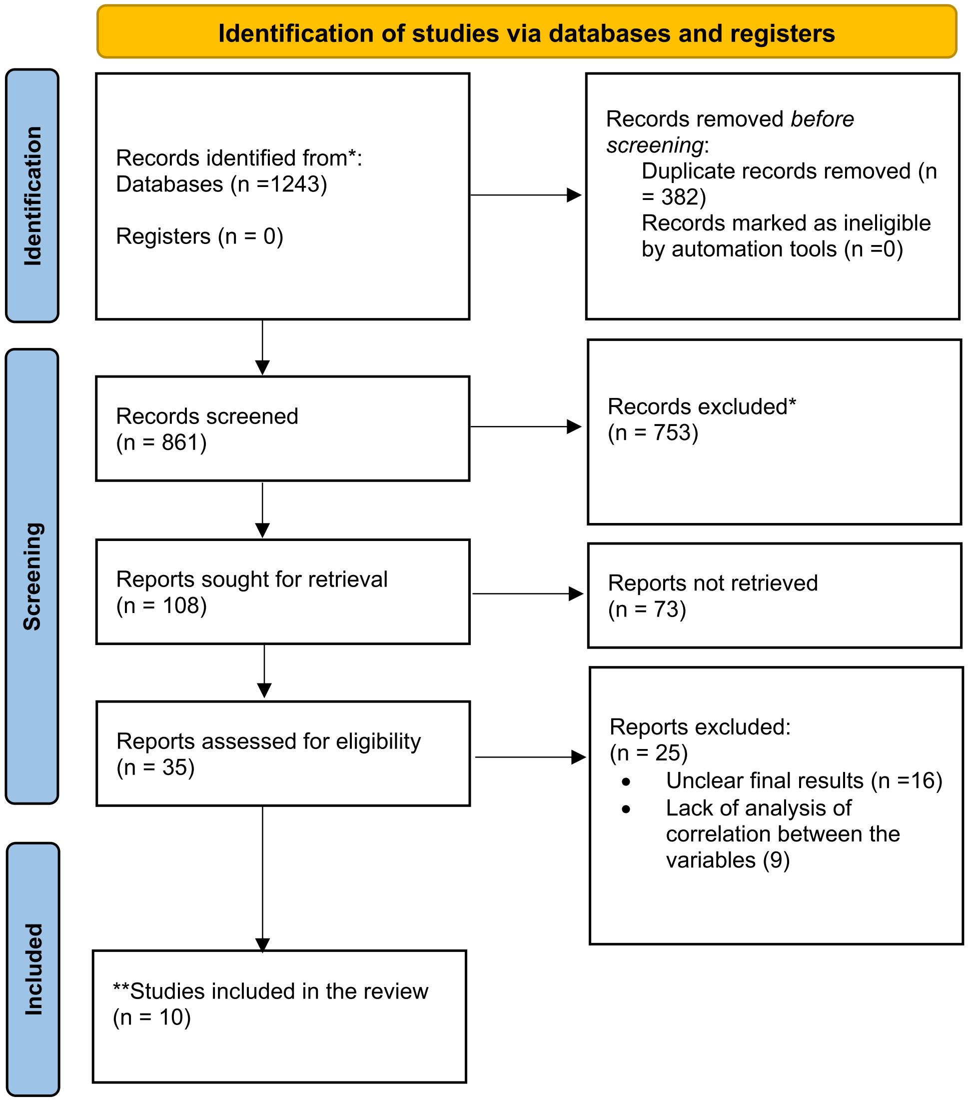

Figure 1 PRISMA flow diagram.
Notes: PRISMA figure adapted from Page MJ, McKenzie JE, Bossuyt PM et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. Creative Commons.[25] *All exclusions performed by human reviewers; no automation tools used. **Each study corresponds to one report (no multiple reports per study).

Key Findings From Included Studies

A systematic review revealed consistent evidence for an association between obesity and increased risk for diabetes. In nearly all the studies, participants who were obese (BMI ≥ 30 kg/m²) had a greater incidence of diabetes than nonobese participants did.

A precise dose–response relationship between BMI and diabetes risk in adolescents was reported, and it was demonstrated that severe obesity (BMI ≥ 35) was associated with a significantly increased incidence of diabetes.[27] Middle-aged men in the highest BMI stratum (≥35 kg/m²) had a markedly elevated risk for developing diabetes over a 5-year follow-up.[28]

In another study, metabolome-defined obesity (BMI ≥ 30) was shown to be associated with a two-to-threefold increase in diabetes risk during 18 years of follow-up.[29] This finding agrees with other findings of Lee et al, who reported that type 2 diabetes incidence correlated strongly with predicted fat mass and obesity indicators in both men and women. [30]

 https://doi.org/10.2147/DMSO.S547743

Table 2 Study Characteristics and Outcomes

Study Title	Study ID (Author, Year)	Study Design	Sample Size	Age (Mean ± SD or Range)	Sex (M/F %)	Location	BMI (Mean ± SD or Categories)	Obesity Definition (BMI Cutoff)	Type 2 Diabetes Cases (n)	Non-Diabetes Cases (n)	Follow-Up (Years or Duration)
Obesity, Unfavorable Lifestyle, and Genetic Risk of Type 2 Diabetes: A Case-Cohort Study	(Schnurr et al, 2020)[26]	Case-Cohort Study	9556	56.1 ± 4.3	49.6% Female	Denmark	27.1 ± 4.5	BMI ≥ 30 (Obese), 25–29.9 (Overweight)	4729	4827	14.7 (Median)
Adolescent Obesity and Early-Onset Type 2 Diabetes	(Twig et al, 2020)[27]	Population-Based Cohort Study	1,462,362	17.4 (Mean)	59% Male	Israel	BMI Percentiles (Overweight, Obese)	Severe Obesity: BMI ≥ 35	2177	1,460,185	11.3 (Median)
Obesity, Fat Distribution, and Weight Gain as Risk Factors for Clinical Diabetes in Men	(Chan et al, 1994)[28]	Prospective Cohort Study	27,983	40-75	100% Male	United States	BMI Categories (9 strata)	BMI ≥ 35 kg/m²	272	27,711	5 years
Metabolome-Defined Obesity and the Risk of Future Type 2 Diabetes and Mortality	(Ottosson et al, 2022)[29]	Population-Based Cohort	7663	41.6 (MOS), 57.6 (MDC)	52.4% Female	Sweden, Italy	26.0 ± 4.6	BMI >30 kg/m²	491	7172	18.2 (Median)
Association of Predicted Fat Mass and Obesity Indicators with Type 2 Diabetes Risk	(Lee et al, 2018)[30]	Prospective Cohort Study	97,111	40-75 (HPFS), 30–55 (NHS)	37.3% Male (HPFS)	United States	BMI Quintiles	BMI ≥ 30 kg/m²	7993	89,118	24 (Median)
Relationship Between Obesity and Diabetes in US Adults: NHANES 1999–2006	(Nguyen et al, 2011)[31]	Cross-Sectional Study	21,205	59 (Mean for diabetics)	50.5% Male	United States	BMI Classes (Normal, Overweight, Obese)	BMI ≥ 30 kg/m²	2894	18,311	N/A
Ectopic Fat Obesity and Diabetes Risk	(Okamura et al, 2018)[32]	Longitudinal Cohort Study	15,464	44.1 ± 9.0	54.5% Male	Japan	23.0 ± 3.0	BMI ≥ 25 kg/m²	373	15,091	5.8 (Men), 5.1 (Women)
Diabetes Risk Among Overweight and Obese Metabolically Healthy Young Adults	(Twig et al, 2014)[33]	Longitudinal Cohort Study	33,939	30.9 ± 5.2	100% Male	Israel	BMI ≥ 25 (Overweight), BMI ≥ 30 (Obese)	BMI ≥ 30 kg/m²	734	33,205	6.1 (Median)
Comparison of Abdominal Adiposity and Obesity in Predicting Diabetes Risk	(Wang et al, 2005)[34]	Prospective Cohort Study	27,270	40-75	100% Male	United States	BMI Quintiles	BMI ≥ 30 kg/m²	884	26,386	13 years
Normal Weight Obesity and the Risk of Diabetes in Chinese People	(Xu et al, 2021)[23]	Population-Based Cohort Study	1128	43.89 ± 12.35	42.3% Male	China	23.65 ± 3.29	BMI < 24 kg/m² with BF% ≥ 24% (men) or ≥ 33% (women)	113	1015	9 years

https://doi.org/10.2147/DMSO.S547743

Table 3 Newcastle–Ottawa Scale (NOS) Quality and Risk of Bias Assessment of Included Studies

Study ID (Author, Year)	Selection (4)	Comparability (2)	Outcome (3)	Total Score (Max 9)	Quality Interpretation
(Schnurr et al, 2020)[26]	4	2	3	**9**	High
(Twig et al, 2020)[27]	4	2	3	**9**	High
(Chan et al, 1994)[28]	4	1	2	**7**	Moderate
(Ottosson et al, 2022)[29]	4	2	3	**9**	High
(Lee et al, 2018)[30]	4	2	3	**9**	High
(Nguyen et al, 2011)[31]	3	1	2	**6**	Moderate
(Okamura et al, 2018)[32]	4	2	3	**9**	High
(Twig et al, 2014)[33]	4	2	3	**9**	High
(Wang et al, 2005)[34]	4	2	3	**9**	High
(Xu et al, 2021)[23]	3	1	2	**6**	Moderate

Most notably, Xu et al[23] reported increased diabetes risk in individuals with normal weight obesity (NWO). Participants with a normal BMI but a high body fat percentage had an HR of 2.11 for developing diabetes. In contrast, participants with a normal BMI and body fat percentage had an HR of 2.11. This emphasizes the danger of relying on BMI alone to predict diabetes risk and highlights the importance of body composition.[23]

Using data from Nguyen et al,[31] we present a steep gradient in diabetes prevalence across BMI categories. The prevalence of diabetes increased from 8% in normal weight individuals to 43% in class III obese individuals (BMI $\geq$ 40).

Furthermore, longitudinal analyses by Wang et al[34] strengthened the predictive value of BMI for diabetes risk, with a follow-up period of 13 years resulting in 884 new cases of diabetes among 27,270 participants.

Subgroup and Sensitivity Analyses

Several studies have performed subgroup analyses stratified by sex, age, and BMI category. Men seem to have a higher obesity-related diabetes risk than women do, as reported by Twig et al,[33] and men with ectopic fat obesity have a higher diabetes incidence than women do, as reported by.[32] However, Xu et al[23] reported that women with normal weight obesity had a threefold greater risk for diabetes than men did. Similar results were obtained when sensitivity analyses were performed, excluding studies with short follow-up durations or small sample sizes, suggesting the robustness of the findings.

In summary, this review indicates that obesity is strongly and consistently associated with diabetes risk in a wide range of populations and age groups. These data broadly support the need for targeted interventions to reduce obesity and diabetes risk.

Data Synthesis

The meta-analysis of ten studies assessing the association between obesity and diabetes risk yielded a pooled hazard ratio (HR) of 2.40 (95% CI: 2.07–2.79). The heterogeneity among studies was substantial, with an I^2 value of 77% (τ^2 = 0.0339, $p < 0.01$), indicating significant variability in effect estimates across the included studies (Figure 2).

The individual hazard ratios ranged from 1.75 (95% CI: 1.42–2.09) to 3.12 (95% CI: 2.67–3.65). The study with the smallest effect size reported an HR of 1.75 (95% CI: 1.42–2.09), whereas the most significant effect size was 3.12 (95% CI: 2.67–3.65). The weight assigned to each study ranged from 2.8% to 11.8%, reflecting differences in sample size and variance.

https://doi.org/10.2147/DMSO.S547743

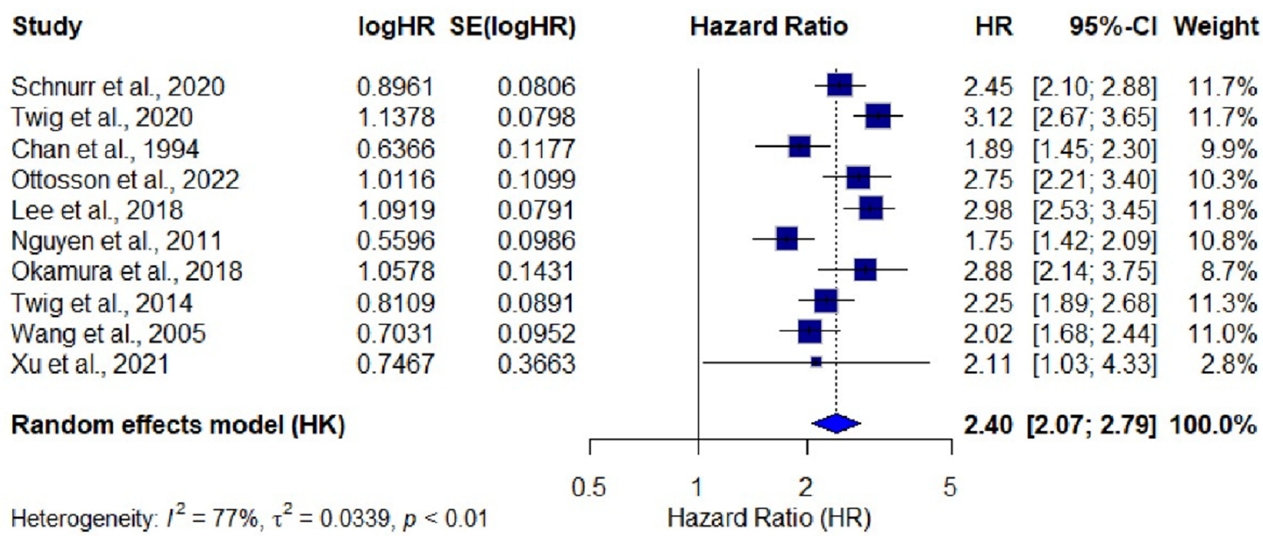

Figure 2 Forest plot of hazard ratios (HR) 95% confidence intervals (CI) from the overall meta-analysis of obesity and diabetes risk (pooled HR: 2.40, I^2 = 77%).

The random-effects model, which was applied via the DerSimonian and Laird (DL) method, confirmed the association's robustness despite the observed heterogeneity. The Hartung-Knapp (HK) adjustment further ensured reliable estimation of the pooled effect, as indicated by the summary diamond in the forest plot (Figure 2).

We used the funnel plot to evaluate publication bias. The distribution appeared symmetrical around the pooled estimate, suggesting limited evidence of publication bias. The slight asymmetry reflects potential small-study effects, which may have contributed to the overall heterogeneity.

Subgroup Analysis

We conducted a subgroup analysis to explore potential sources of heterogeneity, stratifying studies by age, sex, and BMI categories as shown in Figure 3. The pooled HR across subgroups was 2.58 (95% CI: 2.07–3.21), with heterogeneity reduced to I^2 = 75% (τ^2 = 0.0429, $p < 0.01$).

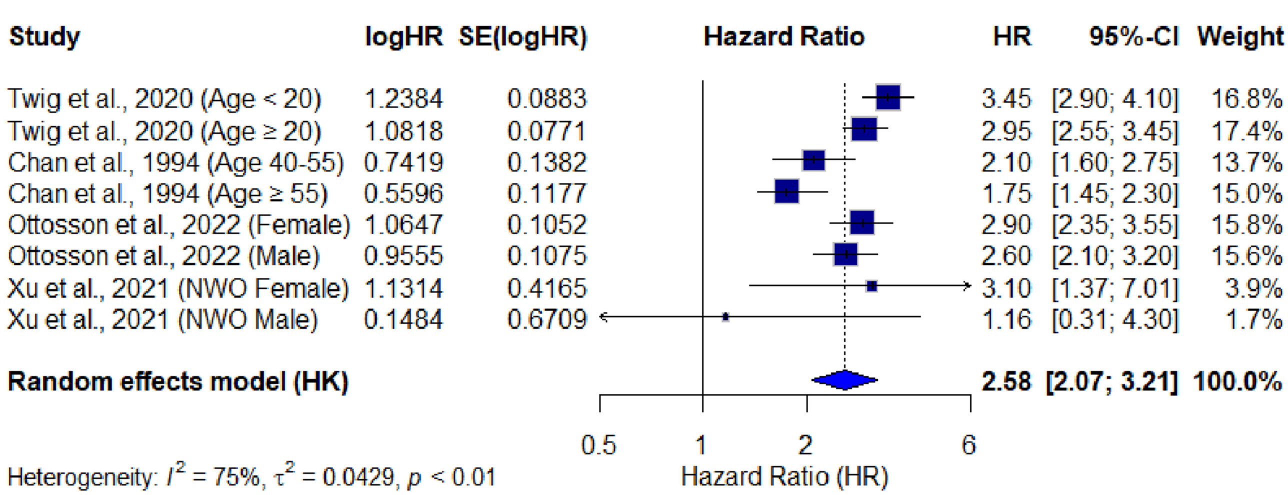

Figure 3 Forest plot of subgroup analyses. Including age, sex, and BMI categories (pooled HR: 2.58, I^2 = 75%).

- Age: Individuals aged <20 years had a greater hazard ratio (HR) of 3.45 (95% CI: 2.90–4.10) than those aged ≥20 years (HR: 2.95, 95% CI: 2.55–3.45).
- Sex: Females had a pooled HR of 2.90 (95% CI: 2.35–3.55), whereas males had a slightly lower HR of 2.60 (95% CI: 2.10–3.20).
- Normal weight obesity (NWO): The HR for NWO females was 3.10 (95% CI: 1.37–7.01), which was significantly greater than that for NWO males (HR: 1.16, 95% CI: 0.31–4.30).

Discussion

We considered high-quality studies in our review that included 10 studies with more than 1.7 million participants/cases, selecting them from various study designs, including longitudinal cohorts and population-based data, to present a comprehensive review. The included studies demonstrated a strong positive association between obesity and the risk of developing type 2 diabetes. Any reported weakness or nonsignificant association is attributed to differences in study populations, follow-up duration, diagnostic criteria, and obesity measures used to define obesity.[18,28]

Obesity and Diabetes Mechanisms

This systematic review confirms the close association between obesity and type 2 diabetes mellitus (T2DM), and this relationship is biologically supported by insulin resistance, adipokine imbalance, and chronic inflammation. Compared with subcutaneous adiposity, visceral adiposity is positively associated with metabolic disruption, owing to the release of inflammatory cytokines, such as IL-6 and TNF-alpha, that disrupt insulin receptor signaling.[36] Moreover, the decreased insulin sensitivity due to lower adiponectin levels in obese patients contributes to the 8-cell dysfunction.[37]

Obesity also precipitates ectopic fat deposition in other important organs, like the liver and pancreas. Fat accumulation in the liver can further manifest as insulin resistance, and fat in the pancreas will affect the insulin-secreting capacity of the two cells.[38,39] These organ-specific outcomes underline the point that not only total fat volumes but also fat distribution contribute to the metabolic risk.

Genetics, Epigenetics, and Microbiota

In addition to physiology, genetics and epigenetics contribute to the risk of developing diabetes among obese people. An association was found between genomic polymorphism (FTO and TCF7L2), increased BMI, and poor glucose metabolism.[40] Epigenetic alterations, such as DNA methylation patterns in response to early-life exposures, also mediate insulin signaling and adipocyte differentiation. [41]

Further, the gut microbiome is shaping up as a key factor in the metabolic imbalance of obesity. Obese people have low microbial diversity and altered relationships between Firmicutes and Bacteroidetes that influence energy acquisition and promote bowel permeability. This leads to the release of bacterial endotoxins, such as LPS, into the blood, which promotes insulin resistance and a generalized inflammatory process. [42,43]

Population-Level Trends and Risk Profiles

The emergence of diabetes and obesity has been synergistic around the globe. According to the Global Burden of Disease (GBD) study, the number of people with obesity has almost doubled since 1980 and has contributed to the increase in the number of cases of T2DM in the global population.[44] The underlying factors in this double epidemic are urbanization, sedentary lifestyles, and consumption of processed foods, which are sometimes referred to as diabesity. [45]

Risk is also dependent on age and sex. Obese adolescents are more likely to develop diabetes at an early age, and, as a result, its course is more aggressive, and cardiovascular outcomes are more significant.[46] Conditions like polycystic ovary syndrome (PCOS) in females add to insulin resistance without associating it with BMI, and sex-specific programs should be used in this case.[47]

Beyond BMI: The NWO Phenotype

Among the most significant lessons of this review is the danger of Normal Weight Obesity (NWO), a condition in which a person has a normal BMI but a high body fat percentage. The incidence of this phenotype is most evident in Asian communities, where the risk of diabetes emerges at a lower BMI level.**24 According to Oh etal,48 persons with NWO were susceptible to developing diabetes by almost a fortnight compared to their counterparts, with women posing a higher risk than men.** These facts discourage the use of BMI as the sole diagnostic parameter and encourage the addition of body composition assessment using DXA or BIA to periodic screening.

Other Obesity Measures

BMI is a commonly used identifier and measure of obesity, but it does not capture the visceral fat or fat distribution. Other measures, such as waist circumference, waist-to-hip ratio, and body fat percentage, can offer a better assessment of the visceral adiposity, which is directly linked to metabolic disorders and diabetes risk. The findings show that even individuals with normal BMI but a high percentage of body fat (NWO) are at risk of getting diabetes, which indicates that BMI alone may underestimate the risk in specific subgroups.[15,33,45]

Limitations and Future Directions

Although the included studies showed a consistent body of evidence, the heterogeneity, especially in obesity and diabetes definitions, is a limitation. Risk estimates could vary with different diagnostic thresholds and measurement methodologies, and may be confounded by unmeasured lifestyle factors.[41] Nevertheless, the reliability of the conclusions is strengthened with the application of high-quality studies and a huge cumulative sample size. The studies included were limited to articles published only in English and those with clearly defined follow-up periods, as mentioned in the selection criteria, which may have introduced selection bias by excluding potentially relevant studies published in other languages or with different study designs, thereby constraining the comprehensiveness of the findings[17,38.] The review primarily focuses on studies from Western countries, which may limit the generalizability of the findings to populations in Asia, Africa, or low- and middle-income countries. We used BMI as a direct obesity indicator, regardless of other obesity measures such as waist circumference, which may be considered a considerable limitation.[45]

Future research should address the gaps and limitations identified in this systematic review, focusing on longitudinal studies to establish the global applicability of the findings. Future exploration of NWO and individuals with normal BMI but unhealthy metabolisms is essential to understand how these subgroups respond to preventive strategies. Discussing different measures of obesity, such as waist circumference, waist-to-hip ratio, and body fat percentage, remains a critical direction for future investigation.

Clinical Practices Recommendations

As discussed above, BMI alone may not be sufficient for assessing diabetes risk, particularly in NWO individuals. Incorporating waist circumference or body fat percentage into routine screening may help for earlier identification of high-risk individuals,[23,24,45] also providing lifestyle counseling and metabolic monitoring, even for those with normal BMI, is considered essential.[14,41]

Public Health Strategy

Following a systematic review demonstrating a strong relationship between obesity and diabetes risk, this review highlights essential implications for public health. Specifically, efforts to prevent diabetes should prioritize early intervention among high-risk individuals, including those with a normal BMI but high visceral fat. Strategies such as implementing front-of-package food labeling, promoting physical activity in schools, allocating a gym area in the workplace, and investing in community weight management programs have shown a promising impact in reducing obesity and metabolic risk.[18,36] In the other hand, tailored interventions for specific regional's cultural and contexts is essential and effective for controlling diabetes risk.[24]

Conclusion

This systematic review affirms a strong association between obesity and increased risk of diabetes. However, the strength and consistency of the findings vary across studies due to differences in study populations, definitions of obesity, and follow-up durations. Some studies have demonstrated weaker or non-significant associations, indicating that additional factors, such as genetics, fat distribution, and unmeasured confounders, may influence diabetes risk. This underscores the importance of applying findings cautiously across diverse populations.

Subgroup analyses identified specific high-risk populations, particularly younger adults, females, and individuals with normal weight obesity (NWO), who may carry elevated metabolic risk despite not being classified as obese by traditional BMI cutoffs. This defines a critical gap in routine clinical screening, which may overlook individuals at risk due to reliance on BMI alone, and highlights the need for more nuanced obesity assessment tools that go beyond BMI, incorporating waist circumference, body fat percentage, and potentially metabolic biomarkers, to recognize the subgroups at risk of diabetes for earlier interventions, which may delay or prevent diabetes onset.

Further research is needed to clarify the gaps and limitations discussed in this systematic review, to establish causality, and to refine risk-stratification strategies, especially in underrepresented populations.

Author Contributions

Yan He: Conceptualization, Methodology, Formal analysis, Project administration, and Writing- original draft. Wei Xu: Data curation, Formal analysis, Investigation, writing-review & editing. Yi Wang: Formal analysis, Investigation, Visualization, and Writing- original draft. Lihua Wang: Supervision, Investigation, Validation, and writing-review & editing. Dongchuan Ran: Data curation, Formal analysis, Resources, and writing-review & editing. All authors, Yan He, Wei Xu, Yi Wang, Lihua Wang, and Dongchuan Ran, have agreed on the journal to which the article has been submitted and agree to be accountable for all aspects of the work.

All authors reviewed the final draft and have approved it for publication.

Data Sharing Statement

All authors confirm that no new data were produced in this paper.

Funding

This work did not receive any funds.

Disclosure

The authors declare no conflict of interest.

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