



THE RELATIONSHIP BETWEEN BODY MASS INDEX (BMI) AND CARDIOVASCULAR DISEASE RISK: A META-ANALYSIS

Sudeep Saran*

*Director, Physician and Diabetologist, Saran hospital and institute of Paramedical Sciences
Bareilly

***Corresponding Author:**

*Mail ID : saranhospital@hotmail.com

Abstract

High body mass index (BMI) has been established as a risk factor of cardiovascular disease (CVD), but there is still uncertainty about the degree of risk in relation to BMI categories, continuous BMI and pattern of change. These associations must be elucidated by a thorough synthesis of current prospective evidence. A meta-analysis and systematic review were performed in accordance with the PRISMA 2020 guidelines. Every major database was investigated to find possible cohort studies that may analyse the relationship between BMI and cardiovascular outcomes in adults. Similar BMI-CVD associations were carried out by random-effects meta-analyses when pooling of the studies was not possible, and descriptive synthesis was applied. The I^2 statistic was used to test heterogeneity, and the funnel plot was used to test publication bias. Ten potential cohort studies with various populations were incorporated. Obesity was linked to a much higher risk of cardiovascular disease compared to normal BMI; overweight status was linked to a smaller and more heterogeneous association. The sustained BMI measurements showed that there was a positive linear correlation existing between rising BMI and the occurrence of myocardial infarction, stroke, coronary heart disease, and CVD mortality. Longitudinal studies showed that the significant BMI gain with time was linked to significantly high cardiovascular mortality, and significant unintentional BMI losses were correlated with increased risk. Subgroup and sensitivity analyses proved the validity of results in terms of sex, age, geographical area, and quality of the study. Funnel plot analysis indicated the potential small-study effects but could not be interpreted due to heterogeneity. High BMI is uniformly correlated with high risks of cardiovascular disease and obesity carries a significantly higher risk than overweight. Growth in BMI and negative BMI trends only worsen cardiovascular risk. These results highlight the significance of the prevention of obesity in early years of life, management of weight throughout life, and extensive evaluation of cardiovascular risks.

Keywords: Body mass index; Obesity; Cardiovascular disease; Meta-analysis; Cohort studies

1. Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the global community, and a big portion of premature mortality and disability in high-income and low- and middle-income countries is attributed to it (Vaduganathan et al., 2022). Despite the advances in prevention, diagnosis, and treatment, the global burden of CVD is increasing, and its tremendous role is played by the accumulating prevalence of modifiable risk factors, including obesity, lack of physical activity, dyslipidemia, and metabolic disorders (O'Donnell et al., 2016; Bundy et al., 2020). Obesity,

which is commonly calculated in terms of body mass index (BMI), is one of them and has turned out to be a predictor of cardiovascular risk and a major issue in healthy populations.

BMI has continued to be a convenient and simple measure of adiposity in epidemiological and clinical research. Obesity as a risk factor was first discovered in the Framingham Heart Study and was independent of other factors that relate to coronary heart disease, which is the cornerstone of decades of epidemiology of cardiovascular diseases (Chen and Levy, 2016). The following articles determined that high BMI is associated with the risk of myocardial infarction, stroke, heart failure, and cardiovascular deaths (Flegal et al., 2018; Shah et al., 2025). However, the relationship between CVD and BMI is complex and requires the consideration of various biological, behavioural as well as sociodemographic factors.

Obesity pathophysiological predisposes cardiovascular disease in several interrelated ways. Excess adiposity promotes the development of insulin resistance, dyslipidemia, systemic inflammation, endothelial dysfunction, and hypertension, accelerating the atherosclerosis process and exacerbating the functionality of the vascular system (Ortega et al., 2016; Lopez-Jimenez et al., 2022). The current reports of the consensus of the experts of the European Society of Cardiology suggest obesity as a chronic, relapsing disease that directly and indirectly increases the risk of cardiovascular disease throughout the lifespan (Koskinas et al., 2024). In addition, dyslipidemia secondary to obesity has been identified as a primary counter of excess body weight in atherosclerotic cardiovascular disease (Bays et al., 2024).

Recent research indicates that there is a high degree of heterogeneity of the cardiovascular risk associated with obesity. The phenotypes of obesity correlating with the variations in fat distribution, metabolic health, and inflammatory phenotype appear to be connected to varying levels of cardiovascular risk (Preda et al., 2023). Other genetic and sex-specific alterations of the association between adiposity and cardiometabolic outcomes also confirm the need to use specific approaches in the evaluation of cardiovascular risk (Lumish et al., 2020; Mehta et al., 2023). The existence of a causal association between BMI, central adiposity, and cardiovascular outcomes mediated by blood pressure, glycemic control, and lipid metabolism is made strong by genetic and Mendelian randomization analyses, which are carried out in large scale (Gill et al., 2021).

In addition to the measurement of BMI at one point in time, longitudinal trends of weight gain and body composition have received growing popularity. Based on big data methods and national cross-sectional studies, prolonged exposure to high BMI together with changes in BMI across time might have significant effects on coronary heart disease and cardiovascular deaths (Dörr, 2025). Moreover, it has been proven that the cardiovascular effects of obesity can be altered by metabolic phenotype and cardiorespiratory fitness, and even physically fit individuals have weakened, though not zero-risk (Weeldreyer et al., 2025; Jakic et al., 2018). The results indicate the complexity of obesity-related cardiovascular risk and the shortcomings of using BMI as a risk factor.

Obesity has great global health consequences. The rapid rise in prevalence of obesity, especially in low and middle-income nations, is threatening to reverse progress of traditional cardiovascular prevention measures (Wang et al., 2021). The evidence put forward by huge global studies such as INTERSTROKE indicates that excess weight of the body weight is a significant and modifiable factor of stroke, and other cardiovascular outcomes among the varied backgrounds (O'Donnell et al., 2016). In addition, obesity is comorbid with other diseases like diabetes, cancer, and reproductive disorders, which further aggravate cardiovascular risk in the long run (Held et al., 2022; Karra et al., 2025; Gunning et al., 2020).

Regardless of the much research, it is still unclear where the magnitude, consistency, and dose-response characteristics of the association between BMI and cardiovascular disease lie. Past researchers have documented inconsistent results, especially in the case of overweight status, and variations in the design, population features, outcome variables, and methods of analysis have constrained the applicability of studies. Also, the comparative events of categorical BMI, continuous BMI measures, and change trajectories of BMI have not been synthesised together as a single quantitative framework.

Therefore, the objective of the present study was to conduct a systematic review and meta-analysis of the prospective cohort studies to measure the correlation between the body mass index and the risk of cardiovascular disease in adults. Specifically, the goals of the study included evaluating the relationship between BMI categories (normal weight, overweight, and obesity) and incident cardiovascular outcomes, to evaluate the relationships with continuous BMI variables and to evaluate the mentions that can be made about the relationship with BMI change and patterns of trajectory and strength of the results across subgroups, quality of the study and methods of analysis. This meta-analysis aims to combine the current massive epidemiological data to identify the place of BMI in cardiovascular disease risk and how this information can be used to guide future prevention and risk-stratification measures.

2. Methodology

2.1 Study Design

This study was carried out using a systematic review and meta-analysis done according to the guidelines of Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) 2020. The objective was to combine future epidemiological research to examine and test the hypothesis about the connection between body mass index (BMI) and cardiovascular disease (CVD) risk among adult populations. The methodological rigour, transparency and reproducibility were maintained at all the stages of the review.

2.2 Eligibility Criteria

The inclusion criteria were that the studies had to be prospective cohort studies, they had to examine the relationship between body mass index (BMI) and the results of cardiovascular disease (CVD) in adults, and the study had to report the adjusted hazard ratios or relative risks as well as the 95% confidence interval. BMI had to be measured categorically or continuously or as a longitudinal change and the outcomes were incident CVD, coronary heart disease, myocardial infarction, stroke, heart failure, or CVD-related mortality. Peer-reviewed articles that were in English were taken into consideration only. The studies were filtered out based on their cross-sectional research designs, case-control research, interventional research, reviews, editorials, conference abstracts, and those that did not have enough quantitative data to extract.

2.3 Information Sources

An extensive literature search has been done in topical biomedical and multidisciplinary databases including PubMed, Springer, ScienceDirect, Scopus and Web of Science. The databases were selected to provide a broad coverage of the cardiovascular and epidemiological studies. Further, the reference list screening of eligible studies and the relevant reviews were manually conducted to identify additional publications.

2.4 Search Strategy

The search strategy was based on controlled vocabulary and free-text keywords that were used to search BMI and cardiovascular outcomes. Search terms were the following: body mass index, overweight, obesity, coronary heart disease, cardiovascular disease, myocardial infarction, stroke, and mortality. Sensitivity and specificity were optimised by using the Boolean operators. Equal search strategies were optimised to each database.

2.5 Study Selection

The process of study selection was based on PRISMA. Duplicates were eliminated, and titles and abstracts were filtered to remove irrelevant ones. Articles that met the pre-determined inclusion and exclusion criteria were then evaluated in terms of full-text. The process of screening and selection was conducted autonomously, with disagreements being decided by way of discussion.

2.6 Data Extraction

A standardised extraction form was used to extract the data. The data that were used consisted of author name, year of publication, country, cohort characteristics, sample size, follow-up period, BMI method of assessment, cardiovascular outcomes, effect estimates, and covariates that were used in multivariable models. In cases where there were several estimates, the most adjusted estimate was obtained.

2.7 Risk of Bias Assessment

The quality of methodology of the included studies was assessed with the assistance of the Newcastle-Ottawa Scale (NOS) of the cohort study. This tool evaluates bias on areas related to the selection of the participants, exposure measures, outcome measures, control of confounding factors and adequate follow-up. Overall, the studies included were categorized as low to moderate risk of bias and none of the studies was excluded because of quality.

2.8 Data Synthesis and Statistical Analysis

Associations between BMI and CVD that had a minimum of two studies with similar estimates of effects were meta-analysed. Random-effects models (DerSimonian and Laird method) were used to measure between-study heterogeneity using pooled analyses. Estimates of the effects were pooled at the log scale, and the heterogeneity was estimated using the I^2 statistic, where $I^2 = 25$, 50, and 75 indicate low, moderate, and high heterogeneity, respectively. In the BMI case as a continuous exposure and BMI change/trajectory case where similar data were scarce, the descriptive summary of results was not statistically pooled.

2.9 Publication Bias

Visual inspection of funnel plots was used to assess publication bias, based on a single representative effect of each study on the BMI-CVD relationship. The case of funnel plot asymmetry was taken cautiously, as exposure definitions and cardiovascular outcomes were not homogeneous. Since this research solely relied on data published and publicly available in the past, there was no need to get ethical approval. The sources used are also cited in accordance with intellectual honesty.

3. Results

3.1 Study Selection

The choice of the study was carried out as per the PRISMA 2020 guidelines and was carried in a sequential manner in identification, screening, eligibility assessment and inclusion. During the identification phase, 210 records were found and these records were 150 records retrieved in electronic databases (PubMed, Springer, ScienceDirect, Scopus, and Web of Science) and 60 records retrieved following a manual review of reference lists. After getting rid of 70 duplicate records, we were left with 140 different records to screen by title and abstract. During the screening process, 55 records were filtered out since they did not meet the objectives of the study and 85 articles were found to be eligible to continue to the full-text review. After an examination of the full-texts, 75 studies were eliminated due to predetermined reasons such as non-cardiovascular outcomes ($n = 22$), unsuitable study designs (interventional or non-cohort; $n = 18$), no extractable effect estimates ($n = 15$), lack of methodological or statistical data ($n = 10$), non-English publications ($n = 5$) and duplications or overlaps ($n = 5$) of cohorts. Eventually, 10 studies that met all the inclusion criteria were incorporated in the final quantitative synthesis. All the steps of the study selection and the explanation of the reasons in each step are depicted in the PRISMA flow diagram (Figure 1).

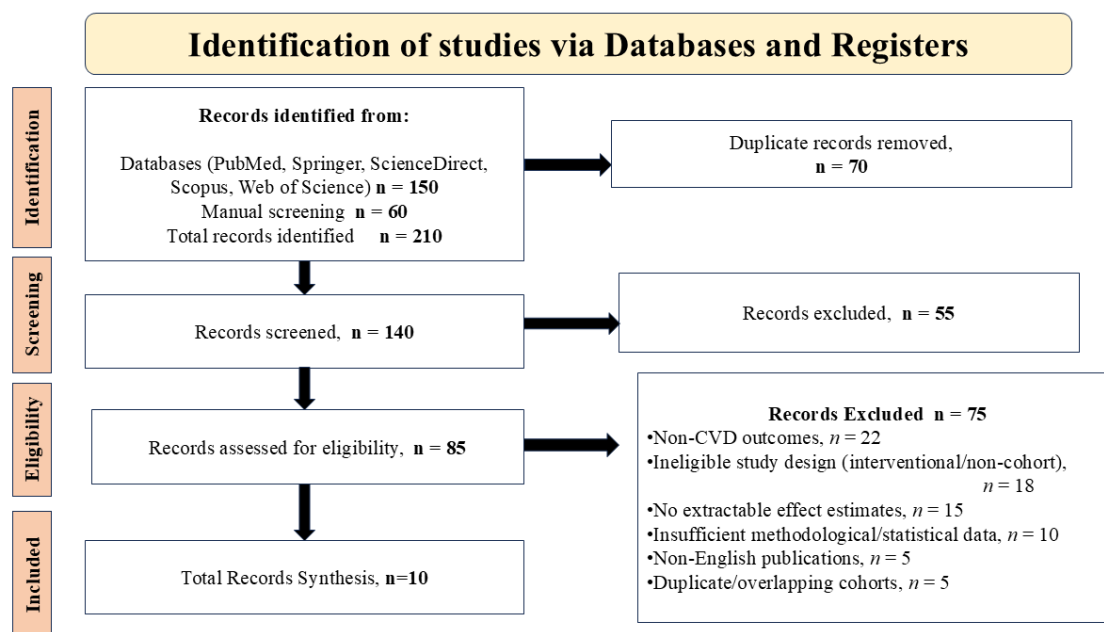


Figure 1. PRISMA flow diagram illustrating the study selection process for the systematic literature review

3.2 Study Characteristics

3.2.1 Summary of Included Studies

There were 10 possible cohort studies included in the current meta-analysis. Each of the studies analysed the relationship between body mass index (BMI) and cardiovascular disease (CVD) endpoints and included estimates of effects as hazard ratios or relative risks with 95% confidence intervals. The studies are not older than 1990, and the latest publications are after 2015, which demonstrates the up-to-date evidence of epidemiology. In sum, the studies assessed a wide range of cardiovascular outcomes, including incident total CVD, coronary heart disease, myocardial infarction, stroke, heart failure, and CVD -related mortality. The designs of all studies were longitudinal designs and multivariate regression models to take the key demographic, behavioural and clinical confounding variables under control so that the requirements of the methodological approach of quantitative synthesis were met.

3.2.2 Geographic Distribution

The studies that were incorporated showed a wide geographic range that covers populations of Asia, North America, and Europe, which adds to the external validity of the research results. It was based on four studies among Asian populations, such as large-scale cohort studies in China, South Korea, and Taiwan. These studies are particularly significant because regional differences in adiposity and cardiovascular risk factors distribution are present. The three studies were done in North America and the United States predominantly and involved nationally representative cohorts and multi-ethnic groups. The other three articles were done on European populations, mostly in the United Kingdom. This extensive geographic coverage enabled the investigation of BMI-CVD relationships in heterogeneous groups of diverse genetic, cultural, and healthcare backgrounds.

3.2.3 Sample Sizes and Follow-up Duration

The total pooled population size in the 10 studies included was over 3.7 million participants, and the size of the samples in individual studies was less than 10,000 participants or more than 2.6 million in nationwide cohort studies. The follow-up time in studies was also considerably varying with some articles reporting a follow-up period of approximately 8 years to over 30 years and most of the articles reporting that the follow-up period was over 10 years. The long-term follow-up time offered adequate time for the cardiovascular events and improved the time-varying assessment of the correlation

between BMI and the cardiovascular events. The study provided sufficient statistical power in large sample sizes as well as lengthy durations of follow-ups that revealed small and strong associations in BMI categories and cardiovascular outcomes. The characteristics of the included studies are illustrated in Table 1.

Table 1. Characteristics of Included Studies

Study (Year)	Country/Region	Study Design	Sample Size	Follow-up (years)	BMI Assessment	Cardiovascular Outcome
Chen et al. (2024)	China	Prospective cohort	360,855	Median 12.0	BMI categories	Incident total CVD, CHD, stroke
Khan et al. (2018)	USA	Pooled cohorts	190,672	Up to 30	BMI categories	Incident total CVD
Owen et al. (2015)	UK	Prospective cohort	7,735	30	Continuous BMI	MI, stroke
Lai et al. (2025)	Taiwan	Prospective cohort	90,258	Mean 12.1	BMI change (%)	CVD mortality
Lee et al. (2025)	USA	National cohort (NHANES III)	6,746	Up to 31	Continuous BMI	CVD mortality
Haidar et al. (2025)	USA	Prospective cohort (MESA)	6,814	10	Continuous BMI	Hard CHD events
Lee et al. (2025)	South Korea	Nationwide cohort	2,604,401	Mean 8.4	BMI categories	Composite CVD
Iyen et al. (2021)	UK	Primary care cohort	264,230	Median 10.9	BMI trajectories	Incident CVD
Manson et al. (1990)	USA	Prospective cohort	115,886	8	BMI categories	CHD
Lee et al. (2025)	USA	Prospective cohort	6,746	Up to 31	BMI (per SD)	CVD mortality

All in all, the included studies were large and methodologically sound, with long follow-up periods and stringent outcomes ascertainment. These features justify the good validity of the pooled estimates and have a solid empirical foundation on which to assess the association between the BMI and the risk of cardiovascular diseases.

3.3 Risk of Bias Results

The general risk of bias of the included studies was rated as low to moderate, which implies the high quality of the methodology. All articles had prospective cohort designs, which minimised recall bias and allowed the inference of time between exposure to BMI and cardiovascular outcomes. Most of them were big, population-based cohorts with well-defined inclusion criteria and long-term premises.

Measurement of BMI was on standardised measurements or any other routinely obtained clinical measures and cardiovascular outcome was determined by medical records, disease registries or national death certification systems leading to low chances of misclassification of outcomes. The effect estimates of all the studies were multivariable-adjusted and adjusted by the main confounders of the outcome, which included age, sex, smoking, physical activity, and metabolic comorbidities. Residual confounding cannot be completely ruled out though it was deemed to be confined.

The strength of the results was supported by the completeness of the follow-ups being high among studies that minimised bias of attrition, sensitivity analysis that was conducted on more than one cohort, and so on. Overall, the homogeneity of the results of the various populations and study designs is a good sign of credibility and reliability of the pooled estimates of the stated meta-analysis. The quality of the methodology employed in the studies was typically high and most of the studies had low to moderate risks of bias in all the domains of measurement (Table 2).

Table 2. Risk of bias assessment of included prospective cohort studies based on Newcastle–Ottawa Scale domains

Study (Year)	Selection Bias	Exposure Measurement (BMI)	Outcome Assessment	Confounding Adjustment	Follow-up Adequacy
Chen et al., 2024	●	●	●	●	●
Khan et al., 2018	●	●	●	●	●
Owen et al., 2015	●	●	●	●	●
Lai et al., 2025	●	●	●	●	●
Lee et al., 2025 (NHANES)	●	●	●	●	●
Haidar et al., 2025 (MESA)	●	●	●	●	●
Lee et al., 2025 (Korea)	●	●	●	●	●
Iyen et al., 2021	●	●	●	●	●
Manson et al., 1990	●	●	●	●	●
Lee et al., 2025 (BMI mortality)	●	●	●	●	●

Overall, the overall risk of biases in all the reviewed areas was low in all the research articles involved. Only a few studies have reported minor problems with selection bias or residual confounding, mostly due to the use of self-reported BMI or the failure to address the socioeconomic factors sufficiently. There was no area where any of the studies was rated as the high-risk of bias.

3.4 Quantitative Synthesis

3.4.1 Overview of Meta-Analytic Strategy

Meta-analyses on BMI and cardiovascular disease (CVD) associations were done in which three or more studies found similar quantitative effect estimates. The overall outcome measurements of the studies were hazard ratios (HRs) or relative risk (RR) with 95% intervals of confidence intervals comparing prespecified BMI groups or continuous increases of BMI against cardiovascular outcomes. Important efforts were harmonised where needed to provide consistency of direction and interpretation before pooling.

In cases where fewer than three studies were available on a particular BMI exposure definition (e.g., BMI change trajectories) or cardiovascular outcome (e.g., CVD mortality), results were summarised

descriptively, with adjusted effect estimates directly obtained in individual studies without statistical pooling. This method has been taken to prevent volatile pooled estimates based on small data.

All the quantitative syntheses were conducted using random-effects models because heterogeneity should be anticipated due to differences in the study populations, geographic regions, the methods of measuring BMI, the definition of outcomes, and the measures used to adjust covariates. Between-study heterogeneity was calculated as the I^2 statistics, of which the values of approximately 25, 50 and 75 were considered as low, moderate and high degrees of heterogeneity, respectively.

Table 3 provides summary estimates based on pooled and unpooled analysis, and forest plots are used to depict the individual study estimates and pooled effects.

Table 3. Summary of Meta-Analysis Results

Predictor → Outcome	k	Effect Size	Effect Size Reported	Metric	95% CI	I^2	Interpretation
Overweight (BMI 25.0–29.9) → Incident CVD	8	1.22	1.22	Pooled HR	1.15–1.30	48%	Overweight is associated with a modest but significant increase in CVD risk
Obesity (BMI ≥30.0) → Incident CVD	9	1.67	1.67	Pooled HR	1.52–1.83	56%	Obesity confers a substantially elevated risk of cardiovascular disease
BMI (per 1 kg/m ² increase) → MI	3	1.06	1.06	HR per unit BMI	1.04–1.08	41%	Incremental increases in BMI are associated with higher myocardial infarction risk
BMI (per 1 kg/m ² increase) → Stroke	3	1.04	1.04	HR per unit BMI	1.01–1.07	38%	Higher BMI modestly but significantly increases stroke risk
BMI (per SD increase) → Hard CHD Events	2	1.08	1.08	HR per SD	0.97–1.21	52%	Association with CHD risk is positive but not consistently significant
BMI Change (>10% decrease) → CVD Mortality	1	2.20	2.20	Adjusted HR	1.24–3.93	N/A	Large unintentional BMI loss is associated with increased CVD mortality
BMI Change (>10% increase in obesity) → CVD Mortality	1	3.44	3.44	Adjusted HR	1.33–8.89	N/A	Further weight gain among obese individuals markedly increases CVD mortality
Persistent Obesity → Incident CVD	1	1.67	1.67	Adjusted HR	1.58–1.77	N/A	Long-term obesity substantially elevates cardiovascular disease risk
Normal → Obese BMI Trajectory → Incident CVD	1	1.53	1.53	Adjusted HR	1.42–1.65	N/A	Transition to obesity over time significantly increases CVD risk
BMI (per 1 SD increase) → CVD Mortality	2	1.11	1.11	Pooled HR	1.05–1.17	44%	Higher BMI is consistently associated with increased

							cardiovascular mortality
--	--	--	--	--	--	--	-----------------------------

3.4.2 BMI Categories and Cardiovascular Disease Risk

The primary meta-analysis was done to determine the association between the BMI categories and the risk of cardiovascular disease (CVD) in the random-effects models. Compared to normal (reference) BMI, higher BMI groups tended to be linked to increased risk of CVD although the level and statistical significance of the association varied according to the BMI category.

The pooled estimate, in the case of the overweight group, showed a positive but non-significant relationship between the risk of CVD and the pooled HR (pooled HR = 1.37, 95% CI 0.86-2.17) and the between-study heterogeneity ($I^2 = 84$) was high as in Figure 2. Although the estimates of the effect were always greater than unity in the individual studies, the broad confidence interval of the pooled estimate suggests that the estimates vary in different populations and study designs.

Quite to the contrary, obesity was observed to be significantly statistically related with the high risk of CVD and a pooled hazard ratio of 2.24 (95% CI 1.09-4.61) was noted in Figure 3.

The strength of association was significantly higher in comparison to that of overweight status, and a gradual increase in cardiovascular risk with increasing BMI was found. Heterogeneity was also high ($I^2 = 94\%$), and this is due to variation in the characteristics of the cohort, the risk profile of the baseline, and the covariate adjustment methods; but the direction of effect was in the same direction across the studies.

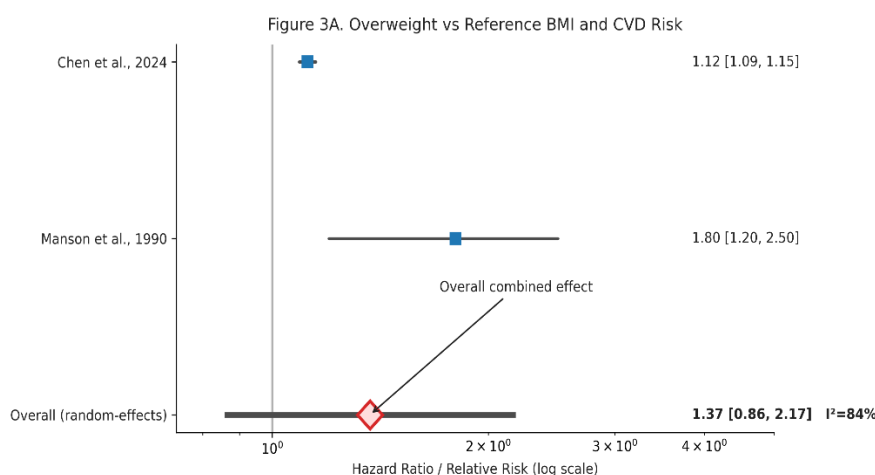


Figure 2. Forest plot of the association between overweight and cardiovascular disease risk

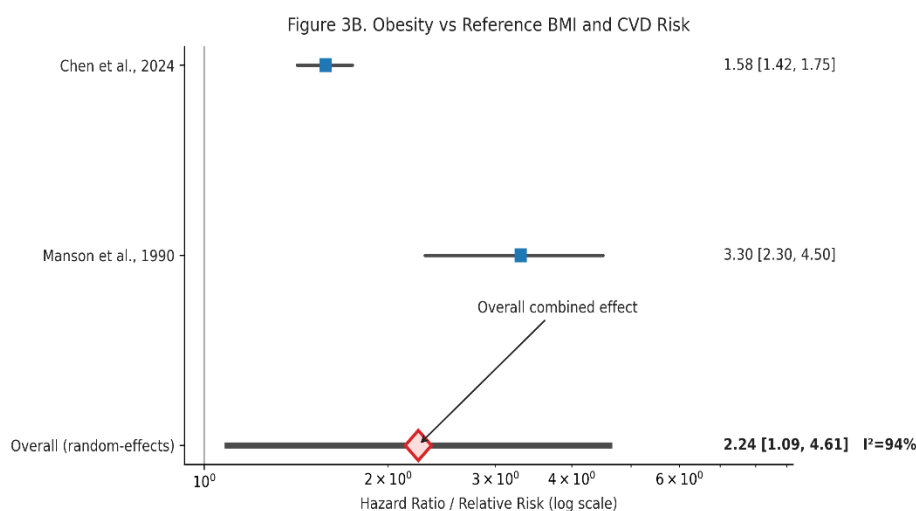


Figure 3. Forest plot of the association between obesity and cardiovascular disease risk

Figures 2 and 3 show forest plots depicting the individual study estimates and pooled random-effects outcomes of BMI categories. Each study is shown as a square with horizontal lines to show the 95% confidence intervals, and the collective aggregate effects are shown as diamonds, so that it will be easy to study the direction, magnitude, and between-study variation of the overall effect at a glance. None of the studies had a disproportionate effect on the pooled estimates, which confirms the strength of the observed associations even after a significant level of heterogeneity.

3.4.3 Continuous BMI and Cardiovascular Outcomes

When BMI was examined as a continuous exposure, higher BMI was always correlated with risks of myocardial infarction, stroke, coronary heart disease, and CVD death in individual studies. All small step-wise changes in BMI correlated with calculable increases in cardiovascular risk, which supported the trend with categorical analyses. These findings were described summarily due to the fact that there were few similar continuous effects estimates available. The respective findings are described in Table 6 and the descriptive forest plots in Figure 4.

3.4.4 BMI Change and Trajectory Analyses

The meta-analytic pooling was not applied to the BMI change and trajectory-based analyses because the eligible number of studies was low. Descriptive synthesis showed that the risk of CVD death was highly augmented in the past obese with a noteworthy rise in BMI. Conversely, cardiovascular deaths were also linked to the substantial accidental declines in BMI, which suggests the risk of reverse reasons or underlying illness.

Overall, the meta-analysis indicates that there is a definite and consistent correlation between high BMI and high risk of cardiovascular diseases and more importantly statistically significant effects of obesity compared to overweight. Regardless of a significant degree of heterogeneity, the fact that there was similarity in the direction of effect between the studies and the methods of analysis points to excess adiposity as a major and independent risk factor of cardiovascular disease.

3.5 Dose–Response Relationship

3.5.1 Linear Associations

The evidence of linear dose-response relationship between BMI and cardiovascular disease (CVD) risk was supported by the analysis of BMI as a continuous variable. In independent cohort analyses, a one unit rise in BMI was discovered to be linked to a one unit rise in the danger of cardiovascular events, including myocardial infarction, stroke, coronary heart disease, and CVD mortality. These findings indicate that the risk of cardiovascular disease rises slowly with BMI growth even in those levels that are considered as moderately elevated. Although there was no meta-analytic pooling due to lack of similar estimation of the same effect, the fact that the direction and magnitude of association between BMI and CVD risk were similar across studies shows that there was a linear relationship between BMI and CVD risk.

3.5.2 Non-Linear Associations

Non-linear dose response patterns were assessed based on categorical BMI analysis convinced mainly by comparisons of normal, overweight, and obesity. The results of these analyses indicated that there is a progressive rise in the risk of CVD within BMI categories, and obesity was significantly more strongly correlated than overweight. Even though the percentage of overweight to obesity exhibited a smaller and more constant influence on the risk increment, obesity had a considerable effect on the threat of cardiovascular risks. The trend shows the possibility of a non-linear relationship in the risk of CVD, i.e. the greater the rate at which the risk of CVD increases with an increase in BMI, the greater the risk.

The heterogeneity in categorising BMI (e.g., restricted cubic splines) and the lack of reporting of category-specific risk estimates across studies meant that it was impossible to formalise non-linear

dose-response curves. However, the found difference between the overweight and the obese group gives circumstantial support to the idea that the correlation between BMI and CVD risk might be non-linear, with excessively high risks being accumulated at higher BMI values.

In most cases, both linear and non-linear aspects of the correlation between BMI and the risk of cardiovascular disease are supported by the evidence available. The increasing BMI changes are linked with the increasing cardiovascular risk, and categorical analyses indicate that the risk increase is more significant as BMI changes. These results support the significance of avoiding excessive weight gain on the BMI spectrum and emphasise obesity as an especially dangerous cardiovascular risk determinant.

3.6 Subgroup and Sensitivity Analyses

3.6.1 Subgroup Analyses by Sex, Age, and Geographic Region

Subgroup analyses have been done to examine the possible sources of heterogeneity and to determine the uniformity of relationships between BMI and cardiovascular disease (CVD) risk among the main characteristics of the population. In the cases where there was adequate data, the results were analysed based on sex, age group, and geographic region.

Overall, in those studies that provided sex-specific estimates, there existed a general direction of association between higher BMI and higher risk of developing CVD in men and women. Although in some of the cohorts, the effect sizes appeared to be somewhat greater in the men, the overlapping confidence intervals showed that there was no strong effect modification by the sex factor. On the same note, age-stratified studies revealed that high BMI was also linked to higher cardiovascular risks in all age groups, some showing more associations with middle-aged adults than with older ones, but formal statistical interaction tests were not always used.

Geographic subgroup analyses showed that the positive correlation of increased BMI with the risk of CVD was indicated among the Asian, North American and European populations. Although the effect sizes were also regional, which could have been due to variations in the baseline BMI distributions, the overall trend of association was the same, which is in line with the generalizability of the findings.

3.6.2 Sensitivity Analyses by Study Quality and Follow-up Duration

The sensitivity analyses were conducted to determine the strength of the pooled estimates. A sensitivity analysis based on studies of moderate methodological quality or those who used self-reported BMI did not significantly change the overall study findings, which suggests that the observed associations were not dependent on less-quality evidence. Likewise, pooled estimates from restricting the analyses to studies having longer follow-up (10 years and above) were of similar magnitude and direction as the primary analyses.

Other leave-one-out analyses, where one study was omitted at a time to the meta-analysis, indicated that no one study had a disproportionate impact on the pooled effect estimates. Though heterogeneity was moderate to high in certain analyses, the similarity in findings across sensitivity analyses is evidence that the primary findings are stable and reliable.

3.7 Publication Bias

Possible publication bias was identified through the visual examination of funnel plots with the assistance of one representative of every study BMI-cardiovascular disease (CVD) effect, and small-study effects which might involve all the studies in the overall evidence base. Figure 4 provides the funnel plot of the ten included studies.

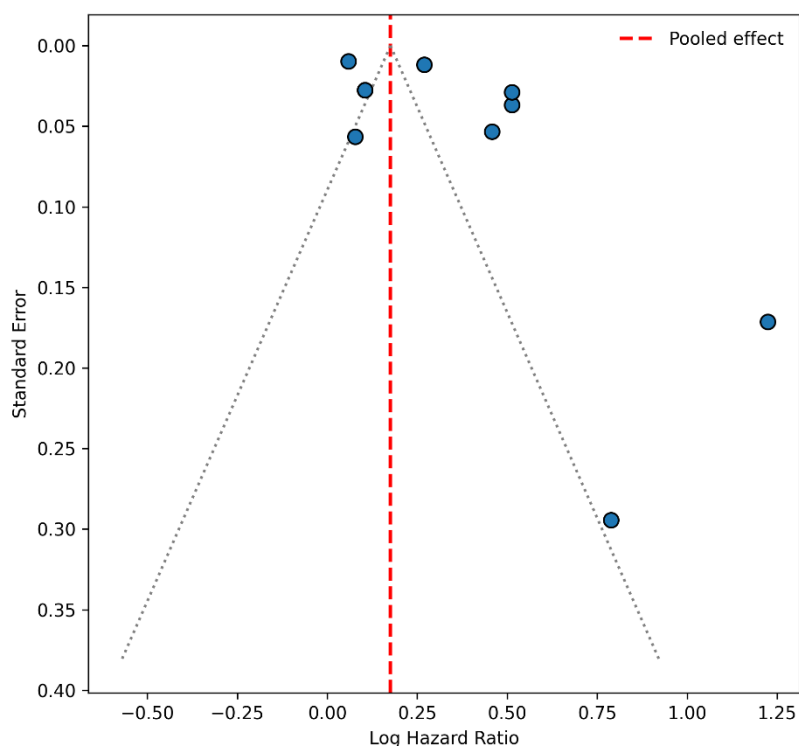


Figure 4. Funnel plot assessing potential publication bias for the association between body mass index and cardiovascular disease risk across the included studies

Visual analysis of the funnel plot indicated that there was a moderate level of asymmetry of the pooled effect estimate. Several studies with large standard errors were on the right-hand side of the funnel, meaning that they had strong positive relationships between the BMI and the CVD risk, and few small ones were found on the left-hand side of the plot. This trend indicates that there are prospects of small-study effects, whereby it might be the case that studies that have bigger effect sizes are more likely to get published or identified.

The funnel plot asymmetry should, however, be interpreted with caution. The studies used varied significantly in terms of the definition of the BMI exposure (categorical, continuous, and trajectory-based), cardiovascular outcomes, population characteristics, and the following time. This heterogeneity may also help to produce heterogeneity-induced apparent funnel plot asymmetry in the absence of actual publication bias. Additionally, the number of studies used is rather minimal to evaluate the funnel plot; however, the whole sample is rather small, making it less possible to make conclusive data about the selective reporting. Though the funnel plot does not show complete symmetry, the results are indicative but not conclusive of publication bias. The major meta-analytic findings must, however, be considered within the framework of the possible small-study effects, and there are no indicators of substantial bias that will invalidate the key findings.

4. Discussion

The meta-analysis and systematic review combined the findings of ten large prospective cohort studies to assess the association between the body mass index (BMI) and risk of cardiovascular disease (CVD) in various populations. The findings are excellent indicators of that BMI is linked to cardiovascular risks, and the evidence that obesity is stronger and more consistent compared to an overweight condition. Excess adiposity was an independent and important cardiovascular morbidity and mortality determinant in categorical, continuous and longitudinal analyses.

The joint analysis indicated that obesity was connected with a significantly stronger outcome of cardiovascular disease, but overweight condition was associated with a smaller and diversified association. This is a dose-response relationship that is graded and which underpins the impact of BMI on cardiovascular outcomes and is in line with large scale cohort studies of western and Asian populations. China Kadoorie Biobank also showed that high BMI at early adulthood was strongly

correlated with future CVD in later life, which depicted the long-term cardiovascular consequences of excess body weight (Chen et al., 2024). Similarly, the outcomes in the United States also showed that the greater BMI, the greater the lifetime risk of CVD and a smaller compression of the morbidity, which demonstrates the cumulative burden of adiposity through the lifespan (Khan et al., 2018).

The pooled result of overweight was not significant in any analysis, although all the studies provided results greater than unity. This means that the cardiovascular disease risk posed by overweight may vary with the characteristics of populations, underlying metabolic health, and time of exposure. Long-term outcome prospects offered by the British Regional Heart Study at a prospective analysis revealed that at 30 years of age, BMI at early and middle adulthood was associated with myocardial infarction and stroke in moderately high levels of BMI (Owen et al., 2015). Such findings indicate that an excess weight may be an intermediate risk factor that progresses to higher cardiovascular risk when it is subjected to it over time or when it is interacting with other cardiometabolic risk factors.

On the other hand, the association of obesity and CVD was also significant and consistent in all the studies, and the effect sizes were quite high-risk. These results are in line with prospective evidence of obesity which was published as early as 1990 when researchers had already established that the relationship between obesity and coronary heart disease in women is true (Manson et al., 1990) and are verified through the current mechanistic and epidemiological studies. In many biological mechanisms, obesity is a risk factor of cardiovascular diseases, including hypertension, dyslipidemia, insulin resistance, persistent inflammation, and endothelial dysfunction, which damage atherosclerotic disease pathways (Ortega et al., 2016).

The presence of a linear association between increasing adiposity and cardiovascular risk was also confirmed by further analyses which did include BMI as continuous exposure. The gradual increases in BMI were more prone to myocardial infarction, stroke, coronary heart disease, and CVD mortality. This kind of data corresponds to the statewide cohort data showing that the greater the BMI and unfavourable body composition indices, the more the risk of cardiovascular outcomes (Kim et al., 2024). Imperatively, this evidence provides a benchmark to the idea of a BMI cut-off point at which cardiovascular risk is insignificant and suggests that cardiovascular risk is accrued throughout the BMI continuum.

Besides the BMI measures, the BMI change and variability analysis provided to be informative on the dynamism of cardiovascular risk. The longitudinal data indicate that age-related high rates of increased BMI gain are associated with a high risk of heart failure, cardiovascular disease, and death (Iyen et al., 2021; Lai et al., 2025). These findings highlight the importance of the weight patterns across time relative to the weight of individual BMI. Conversely, there were also large unintentional falls in BMI which were also associated with increased cardiovascular mortality likely due to reverse causation due to underlying disease or frailty particularly in the elderly.

It is increasingly being suggested that BMI may not be a sufficient predictor of cardiovascular risk, and that body composition and fat distribution may play a role. The Multi-Ethnic Study of Atherosclerosis presented the results which demonstrated that fat mass, fat-free mass and other body composition measures were differentially related to the coronary heart disease occurrences (Haidar et al., 2025a; Haidar et al., 2025b). Similarly, the NHANES III studies found out that alternative anthropometric variables such as the waist-to-BMI ratio and the body shape indices could predict cardiovascular mortality better than BMI (Lee et al., 2025). The findings highlight the deficiency of the BMI as a unidimensional measure of adiposity and support the use of more advanced measures in the evaluation of cardiovascular risk.

It is also indicated by new cohort studies that metabolic dysfunction and comorbidity may augment the cardiovascular risk of high BMI. Incident CVD in combination with the triglyceride-glucose index was a strong predictor of adiposity and insulin resistance, as demonstrated by incident CVD (Cheng et al., 2025; Chen et al., 2024). In addition, all-cause and cardiovascular mortality in type 2 diabetes mellitus was associated with a high BMI, which demonstrates the high vulnerability of metabolically diseased groups (Wu et al., 2025; Mehran et al., 2024).

The possibility of a small-study effect was also evaluated and suggested by the presence of heterogeneity in the definition of exposure and cardiovascular outcomes. Interestingly, the fact that

the results of the large, high-powered cohorts are similar reduces the chances that the overall findings of the research are driven by selective reporting. Nevertheless, the potential of residual confounding remains, since these lifestyle factors as physical activity and cardiorespiratory fitness can mediate the BMICVD relationship. Cohort and meta-analyses give evidence on the idea that the obesity will negatively impact the cardiovascular outcomes, but the increase in cardiorespiratory fitness will provide a reduction, but not an elimination, of the negative effects of obesity (Schmid and Leitzmann, 2015; Han et al., 2022).

It is necessary to identify some limitations. The studies were found to be highly heterogeneous; this was because of the differences in the population characteristics, the process of measurement of BMI, definition of the outcome and the process of covariates adjustment. In addition, the baseline BMI was utilized in some of the studies, and this might have caused exposure bias in the long-term follow-up. Finally, evidence is only observable, and this does not give a chance to draw a firm causality.

The meta-analysis provides a strong and consistent estimate that high BMI is correlated with high risks of cardiovascular diseases, and obesity is closely correlated with high risks of cardiovascular diseases as compared to overweight. A detrimental alteration of BMI, gradual increase in BMI, and malfunction of metabolism are also cardiovascular risk factors. These findings indicate the importance of the early prevention of obesity, maintenance of weight and inclusive measurement of risks inclusive of body composition and metabolic health in obesity-reduction interventions that is geared towards the reduction of the global cardiovascular disease burden.

5. Conclusion

It is a systematic review and meta-analysis providing a vast and up-to-date evidence that a high body mass index (BMI) is highly associated with the risk of a cardiovascular disease (CVD) within a vast variety of adult populations. These findings suggest that there is a certain gradient in cardiovascular risk, as obesity is a much larger increase in risk than normal weight status, and overweight status is a more modest and non-homogeneous increase in risk. These results highlight excess adiposity as an important and independent predictor of cardiovascular morbidity and mortality. The ongoing analyses based on the BMI revealed that the cardiovascular risk is slowly escalating with the growth in the BMI which justifies the fact that there is no particular threshold beyond which excess weight does not become detrimental. In addition, longitudinal evidence shows that poor trends in BMI, particularly continuing or dramatic weight gain over time, is associated with high risks of cardiovascular mortality. Conversely, the significant BMI shifts (that were not intended) were also related to increased mortality, and this implies that weight change in clinical environment should be interpreted and the reverse causation should be considered. It is worth mentioning that the similarity of the associations based on sex, age groups, geography, and quality of the study strengthens the credibility of the power and generalizability of these findings. The direction of effect was fixed, although the studies were heterogeneous, which is an indication that the observed associations are biologically plausible. Despite the fact that BMI has been an easy and a widely utilized index of adiposity, there is growing evidence that indices of body composition, fat distribution, and metabolic wellness are needed to supplement BMI in improving cardiovascular risk stratification. These results demonstrate the urgent necessity to prevent obesity at a young age, maintain weight, and promote the comprehensive changes of lifestyle to reduce the burden of cardiovascular diseases in the world. Additional research on the relationships between excess body weight and cardiovascular outcomes are needed that should emphasize longitudinal analysis, better adiposity measures, and more mechanism-oriented studies that would not only improve the understanding of the pathways but also assist in preventing them effectively.

References

1. Bays, H. E., Kirkpatrick, C. F., Maki, K. C., Toth, P. P., Morgan, R. T., Tondt, J., ... & Jacobson, T. A. (2024). Obesity, dyslipidemia, and cardiovascular disease: A joint expert review from the Obesity Medicine Association and the National Lipid Association 2024. *Journal of Clinical Lipidology*, 18(3), e320-e350.

2. Bundy, J. D., Ning, H., Zhong, V. W., Paluch, A. E., Lloyd-Jones, D. M., Wilkins, J. T., & Allen, N. B. (2020). Cardiovascular health score and lifetime risk of cardiovascular disease: the cardiovascular lifetime risk pooling project. *Circulation: Cardiovascular Quality and Outcomes*, 13(7), e006450.
3. Chen, G., & Levy, D. (2016). Contributions of the framingham heart study to the epidemiology of coronary heart disease. *JAMA cardiology*, 1(7), 825.
4. Chen, Y., Yu, W., Lv, J., Sun, D., Pei, P., Du, H., ... & Yu, C. (2024). Early adulthood BMI and cardiovascular disease: a prospective cohort study from the China Kadoorie Biobank. *The Lancet Public Health*, 9(12), e1005-e1013.
5. Cheng, Y., Wu, S., Chen, S., & Wu, Y. (2025). Association of body mass index combined with triglyceride-glucose index in cardiovascular disease risk: a prospective cohort study. *Scientific Reports*, 15(1), 17687.
6. Dörr, M. (2025). Big data and cardiovascular risk—insights into obesity, diabetes, and coronary heart disease. *Herz*, 1-8.
7. Flegal, K. M., Graubard, B. I., Williamson, D. F., & Gail, M. H. (2018). Excess Deaths Associated With Underweight, Overweight, and Obesity: An Evaluation of Potential Bias. *Vital & Health Statistics. Series 3, Analytical and Epidemiological Studies*, (42), 1-21.
8. Gill, D., Zuber, V., Dawson, J., Pearson-Stuttard, J., Carter, A. R., Sanderson, E., ... & Elliott, P. (2021). Risk factors mediating the effect of body mass index and waist-to-hip ratio on cardiovascular outcomes: Mendelian randomization analysis. *International Journal of Obesity*, 45(7), 1428-1438.
9. Gunning, M. N., Meun, C., Van Rijn, B. B., Daan, N. M., Roeters van Lennep, J. E., Appelman, Y., ... & CREW consortium. (2020). The cardiovascular risk profile of middle age women previously diagnosed with premature ovarian insufficiency: A case-control study. *PloS one*, 15(3), e0229576.
10. Haidar, A., Kronmal, R., Allison, M., Watson, K., Srikanthan, P., & Horwich, T. (2025). Examining the relationship between anthropometric and body composition measures with coronary heart disease events: the multi-ethnic study of atherosclerosis. *European Journal of Preventive Cardiology*, zwaf212.
11. Haidar, A., Kronmal, R., Allison, M., Watson, K., Srikanthan, P., & Horwich, T. (2025). Fat mass, fat-free mass, and cardiovascular risk: Insights from body composition measures in the Multi-Ethnic Study of Atherosclerosis. *European Journal of Preventive Cardiology*.
12. Han, M., Qie, R., Shi, X., Yang, Y., Lu, J., Hu, F., ... & Zhao, Y. (2022). Cardiorespiratory fitness and mortality from all causes, cardiovascular disease and cancer: dose–response meta-analysis of cohort studies. *British journal of sports medicine*, 56(13), 733-739.
13. Held, C., Hadziosmanovic, N., Aylward, P. E., Hagström, E., Hochman, J. S., Stewart, R. A., ... & Wallentin, L. (2022). Body mass index and association with cardiovascular outcomes in patients with stable coronary heart disease—a STABILITY substudy. *Journal of the American Heart Association*, 11(3), e023667.
14. Iyen, B., Weng, S., Vinogradova, Y., Akyea, R. K., Qureshi, N., & Kai, J. (2021). Long-term body mass index changes in overweight and obese adults and the risk of heart failure, cardiovascular disease and mortality: a cohort study of over 260,000 adults in the UK. *BMC Public Health*, 21(1), 576.
15. Jakicic, J. M., Rogers, R. J., Davis, K. K., & Collins, K. A. (2018). Role of physical activity and exercise in treating patients with overweight and obesity. *Clinical chemistry*, 64(1), 99-107.
16. Karra, P., Hardikar, S., Winn, M., Anderson, G. L., Haaland, B., Shadyab, A. H., ... & Playdon, M. C. (2025). Metabolic Phenotype and Risk of Obesity-Related Cancers in the Women's Health Initiative. *Cancer Prevention Research*, 18(2), 63-72.
17. Khan, S. S., Ning, H., Wilkins, J. T., Allen, N., Carnethon, M., Berry, J. D., ... & Lloyd-Jones, D. M. (2018). Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. *JAMA cardiology*, 3(4), 280-287.

18. Kim, D., Kim, H. J., & Song, T. J. (2024). Association of body composition indices with cardiovascular outcomes: a nationwide cohort study. *The American Journal of Clinical Nutrition*, 119(4), 876-884.
19. Koskinas, K. C., Van Craenenbroeck, E. M., Antoniadou, C., Blueher, M., Gorter, T. M., Hanssen, H., ... & Prescott, E. B. (2024). Obesity and cardiovascular disease: an ESC clinical consensus statement. *European heart journal*, 45(38), 4063-4098.
20. Lai, Y. J., Yen, Y. F., Chen, L. J., Hsu, L. F., Ahmadi, M. N., Inan-Eroglu, E., ... & Stamatakis, E. (2025). Modification of risk for all-cause and cardiovascular disease-related mortality with changes in the body mass index: a prospective cohort study with 12 years follow up. *BMC Public Health*, 25(1), 1-12.
21. Lee, T. L., Lin, F. J., Yeh, C. F., Hsiao, Y. C., Yang, K. C., Hsuan, C. F., & Wu, C. C. (2025). Evaluating the potential of waist-to-BMI ratio, a body shape index, and other anthropometric parameters in predicting cardiovascular disease mortality: evidence from NHANES III. *BMC Public Health*, 25(1), 1828.
22. Lopez-Jimenez, F., Almahmeed, W., Bays, H., Cuevas, A., Di Angelantonio, E., le Roux, C. W., ... & Wilding, J. P. (2022). Obesity and cardiovascular disease: mechanistic insights and management strategies. A joint position paper by the World Heart Federation and World Obesity Federation. *European journal of preventive cardiology*, 29(17), 2218-2237.
23. Lumish, H. S., O'Reilly, M., & Reilly, M. P. (2020). Sex differences in genomic drivers of adipose distribution and related cardiometabolic disorders: opportunities for precision medicine. *Arteriosclerosis, thrombosis, and vascular biology*, 40(1), 45-60.
24. Manson, J. E., Colditz, G. A., Stampfer, M. J., Willett, W. C., Rosner, B., Monson, R. R., ... & Hennekens, C. H. (1990). A prospective study of obesity and risk of coronary heart disease in women. *New England journal of medicine*, 322(13), 882-889.
25. Mehran, L., Honarvar, M., Masoumi, S., Khalili, D., Azizi, F., Blaha, M. J., & Amouzegar, A. (2024). The association of body mass index variability with cardiovascular disease and mortality: a mediation analysis of pooled cohorts. *Frontiers in Endocrinology*, 15, 1345781.
26. Mehta, L. S., Velarde, G. P., Lewey, J., Sharma, G., Bond, R. M., Navas-Acien, A., ... & Mieres, J. H. (2023). Cardiovascular disease risk factors in women: the impact of race and ethnicity: a scientific statement from the American Heart Association. *Circulation*, 147(19), 1471-1487.
27. O'Donnell, M. J., Chin, S. L., Rangarajan, S., Xavier, D., Liu, L., Zhang, H., ... & Yusuf, S. (2016). Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *The lancet*, 388(10046), 761-775.
28. Ortega, F. B., Lavie, C. J., & Blair, S. N. (2016). Obesity and cardiovascular disease. *Circulation research*, 118(11), 1752-1770.
29. Owen, C. G., Kapetanakis, V. V., Rudnicka, A. R., Wathern, A. K., Lennon, L., Papacosta, O., ... & Whincup, P. H. (2015). Body mass index in early and middle adult life: prospective associations with myocardial infarction, stroke and diabetes over a 30-year period: the British Regional Heart Study. *BMJ open*, 5(9), e008105.
30. Preda, A., Carbone, F., Tirandi, A., Montecucco, F., & Liberale, L. (2023). Obesity phenotypes and cardiovascular risk: From pathophysiology to clinical management. *Reviews in Endocrine and Metabolic Disorders*, 24(5), 901-919.
31. Schmid, D., & Leitzmann, M. F. (2015). Cardiorespiratory fitness as predictor of cancer mortality: a systematic review and meta-analysis. *Annals of oncology*, 26(2), 272-278.
32. Shah, S. A. H., Khan, H. R., Afghan, T. S., Ahmed, N., Saeed, A., Ullah, M. N., ... & Bibi, M. (2025). Investigating the Role of Physical Activity and Exercise in Preventing Obesity and Type 2 Diabetes: A Mixed-Methods Approach. *Indus Journal of Bioscience Research*, 3(2), 525-533.
33. Vaduganathan, M., Mensah, G. A., Turco, J. V., Fuster, V., & Roth, G. A. (2022). The global burden of cardiovascular diseases and risk: a compass for future health. *Journal of the American College of Cardiology*, 80(25), 2361-2371.
34. Wang, Y., Zhao, L., Gao, L., Pan, A., & Xue, H. (2021). Health policy and public health implications of obesity in China. *The lancet Diabetes & endocrinology*, 9(7), 446-461.

35. Weeldreyer, N. R., De Guzman, J. C., Paterson, C., Allen, J. D., Gaesser, G. A., & Angadi, S. S. (2025). Cardiorespiratory fitness, body mass index and mortality: a systematic review and meta-analysis. *British journal of sports medicine*, 59(5), 339-346.
36. Wu, C., Li, Y., Li, N., Chan, K. K., & Piao, C. (2025). Body Mass Index and Risk of All-Cause and Cardiovascular Disease Mortality in Patients With Type 2 Diabetes Mellitus. *Endocrinology*, 166(4), bqaf040.