

Association Between Body Composition Measures and Cardiometabolic Outcomes: A Systematic Review Protocol

INPLASY202640036

doi: 10.37766/inplasy2026.4.0036

Received: 10 April 2026

Published: 10 April 2026

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ADMINISTRATIVE INFORMATION

Support - Eli Lilly and Company.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202640036

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 April 2026 and was last updated on 10 April 2026.

INTRODUCTION

Review question / Objective Primary objective: To explore the association of body composition measures (BCMs) with risk of cardiometabolic events in people with obesity/overweight.

Additional objectives:

To assess whether BCMs are more strongly associated with the risk of cardiometabolic complications than body mass index (BMI).

To evaluate the association of different BCMs with each other and with BMI.

Rationale The World Obesity Federation (WOF) defines obesity as "a chronic, relapsing disease wherein excess body fat can result in health impairments" and the World Health Organization (WHO) defines obesity and overweight as "abnormal or excessive fat accumulation that presents a risk to health". Body mass index (BMI), a measure of weight relative to height, is a widely

used metric for screening and classification of obesity. BMI has been identified as a predictor of the risk and severity of obesity-related complications such as type 2 diabetes (T2D) and cardiovascular disease (CVD). Moreover, BMI has also been used to predict the morbidity and mortality burden in people with obesity. While BMI is useful as a screening tool for identifying people with obesity, BMI may not accurately reflect the actual distribution or quantification of body fat at an individual level. Additionally, there is a growing body of evidence that suggests that BMI is inconsistently associated with health risks. In this context, the imprecise nature of BMI as an indicator of body fat weakens the utility of BMI as a successful predictor of cardiometabolic risk. These observations highlight an unmet need for the development of direct measures of adiposity that can predict the risk of cardiometabolic complications among people with obesity. A variety of body composition metrics and assessments have been developed to overcome some of the limitations of BMI. These methods shift the emphasis from overall body mass to body

composition in obesity evaluations. Tools for body composition measures can provide data on total adiposity through indicators such as total body fat mass, percent body fat (PBF), and fat mass index (FMI). These can be assessed using imaging techniques like dual-energy X-ray absorptiometry (DEXA) or bioelectrical impedance analysis (BIA). However, the association between adiposity quantified through BCMs and the risk of cardiometabolic complications remain understudied. This systematic literature review aims to identify published evidence on the relationship of BCMs with risk of adverse cardiometabolic outcomes (CMO).

Condition being studied The Obesity Medicine Association (OMA) defines obesity as "A chronic, relapsing, multifactorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences." Obesity is now recognized as a global epidemic with significant individual and societal impacts. The most common method for screening and classification of obesity leverages BMI. In addition to BMI, tools for measurement of body composition can provide data on total body adiposity and in some cases also body fat distribution through indicators such as total body fat mass, PBF, FMI, waist circumference (WC), appendicular lean mass, waist to height ratio (WHtR), fat-free mass index (FFMI), visceral adipose tissue area, android to gynoid ratio. These can be assessed using imaging techniques like DEXA or BIA. In addition to being associated with an increased risk of mortality, obesity is also associated with increased risk of other complications including musculoskeletal pain, hypertension, psychiatric disorders, T2D, dyslipidemia, and CVD.

METHODS

Search strategy A two-phase search strategy will be employed. The initial search will capture literature published between 2015 and 2025. Subsequently, an updated search will be conducted to identify publications from 2025 to 2026.

Medline: Date of publication from 2014 to 2026*

1. Overweight/ Obesity, Morbid/ or Obesity/ or Obesity, Abdominal/ or exp *Body mass/ or "Body Weights and Measures"/ or exp *body weight/ or ((obes* or over?weigh* or overweight body mass ind*" or BMI or body mass or hyper\$adiposity or

adiposity or weight) Or (obes* or over?weigh* or overweight or "overweight" or "body mass ind*" or BMI or body mass or hyper\$adiposity or adiposity or weight)).ti,ab.

2. Waist-Height Ratio/ or Absorptiometry, Photon/ or Anthropometry/ or Body Composition/ or Adiposity/ or Body Fat Distribution/ Waist-Hip Ratio/ or Waist Circumference/ or Adipose Tissue/ or Subcutaneous Fat/ or Abdominal Fat/ or ('Percent body fat' or 'Fat mass index' or 'Fat?free mass index' or 'Appendicular Lean mass' or 'Waist-Height ratio' or 'Visceral adipose tissue area' or 'VAT volume' or 'Android?gynoid ratio' or 'DEXA' or 'WHR' or 'WtHR' or '' or 'FMI' or 'FFMI' or 'ALM' or 'WtHR' or 'VAT Area' or 'Visceral Adipose Tissue Volume').mp.

3. Cardiovascular Diseases/ or Myocardial Infarction/ or Stroke/ or Death/ or Mortality/ or Percutaneous Coronary Intervention/ or Heart Failure/ or Angina Pectoris/ or Diabetes Mellitus, Type 2/ or Prediabetic State/ or ('myocardial infarction' or 'heart failure' or 'angina' or 'ischemia' or 'stroke' or 'type 2 diabetes' or mortality' or 'atherosclerotic cardiovascular disease' or 'ASCVD' or 'CVD' or 'Coronary revascularization ' or 'Pre? diabet*' or 'CVOT' or 'cardiovascular outcome*' or 'MACE' or 'Percutaneous coronary interventio' or 'PCI' or 'CABG').mp.

4. randomized controlled trial/ or Epidemiologic Studies/ or clinical trial/ or Pragmatic Clinical Trials/ or (random*or controlled trial or Clinical Trial or random* or "phase" or "placebo" or "controlled" or case?control* or observational stud* or "retrospective stud* or longitudinal?stud* or cross? section*").ti,ab.

5. 1 AND 2 AND 3 AND 4

6. limit 5 to (English language and humans)

Embase: Date of publication from 2014 and 2026*

1. Obesity/ or Obesity, Morbid/ or Obesity, Abdominal/ or Overweight/ or (obes* or over? weigh* or overweight or "body mass ind*" or BMI).ti,ab.

2. Waist-Height Ratio/ or Absorptiometry, Photon/ or Anthropometry/ or Body Composition/ or Body Fat Distribution/ or Sarcopenia/ or Waist-Hip Ratio/ or Waist Circumference/ or Adipose Tissue/ or Subcutaneous Fat/ or Abdominal Fat/ or Muscle, Skeletal/ or ('Percent body fat' or 'Fat mass index' or 'Fat?free mass index' or 'Appendicular Lean mass' or 'Waist-Height ratio' or 'Visceral adipose tissue area' or 'VAT volume' or 'Android?gynoid ratio' or 'DEXA' or 'WHR' or 'WtHR' or '' or 'FMI' or 'FFMI' or 'ALM' or 'WtHR' or 'VAT Area' or 'Visceral Adipose Tissue Volume').mp.

3. cardiovascular disease/ or heart infarction/ or cerebrovascular accident/ or death/ or mortality/ or

percutaneous coronary intervention/ or heart failure/ or angina pectoris/ or diabetes mellitus/ or ('myocardial infarction' or 'coronary disease' or 'heart failure' or 'angina' or 'ischemia' or 'stroke' or 'type 2 diabetes' or 'diabetes' or mortality' or 'atherosclerotic cardiovascular disease' or 'ASCVD' or 'CVD' or 'Coronary revascularization ' or 'Pre? diabet*' or 'CVOT' or 'cardiovascular outcome*' or 'cv outcome*' or 'MACE' or 'Major adverse cardiovascular events' or 'Percutaneous coronary interventio' or 'PCI' or 'Coronary artery bypass grafting' or 'CABG').mp.

4. randomized controlled trial/ or Epidemiologic Studies/ or clinical trial/ or Pragmatic Clinical Trials/ or (randomized controlled trial or Clinical Trial or random* or "phase" or "placebo" or "controlled" or case?control* or observational stud* or "retrospective stud* or longitudinal?stud* or cross?section*").ti,ab.

5. 1 AND 2 AND 3 AND 4

6. limit 5 to (human and English language)

Cochrane Central Register: Date of publication from 2014 and 2026*

1. Obesity/ or Obesity, Morbid/ or Obesity, Abdominal/ or Overweight/ or (obes* or over? weigh* or overweight or "overweight" or "body mass ind*" or BMI or body mass).ti,ab.

2. Waist-Height Ratio/ or Absorptiometry, Photon/ or Anthropometry/ or Body Composition/ or Body Fat Distribution/ or Sarcopenia/ or Waist-Hip Ratio/ or Waist Circumference/ or Adipose Tissue/ or Subcutaneous Fat/ or Abdominal Fat/ or Muscle, Skeletal/ or ('Percent body fat' or 'Fat mass index' or 'Fat?free mass index' or 'Appendicular Lean mass' or 'Waist-Height ratio' or 'Visceral adipose tissue area' or 'VAT volume' or 'Android?gynoid ratio' or 'DEXA' or 'WHR' or 'WtHR' or '' or 'FMI' or 'FFMI' or 'ALM' or 'WtHR' or 'VAT Area' or 'Visceral Adipose Tissue Volume').mp.

3. Cardiovascular Diseases/ or Myocardial Infarction/ or Stroke/ or Death/ or Mortality/ or Percutaneous Coronary Intervention/ or Heart Failure/ or Angina Pectoris/ or Diabetes Mellitus, Type 2/ or Prediabetic State/ or ('myocardial infarction' or 'coronary disease' or 'heart failure' or 'angina' or 'ischemia' or 'stroke' or 'type 2 diabetes' or mortality' or 'atherosclerotic cardiovascular disease' or 'ASCVD' or 'CVD' or 'Coronary revascularization ' or 'Pre? diabet*' or 'CVOT' or 'cardiovascular outcome*' or 'cv outcome*' or 'MACE' or 'Major adverse cardiovascular events' or 'Percutaneous coronary interventio' or 'PCI' or 'Coronary artery bypass grafting' or 'CABG').mp.

4. (random*or randomized controlled trial or Clinical Trial or Double Blind Method or Single

Blind Method or random* or "phase" or "placebo" or "controlled").mp.

5. 1 AND 2 AND 3 AND 4

6. limit 5 to English language

*The search strategy presented above is representative in nature

Participant or population Individuals aged 18 years and older with normal weight, overweight, or obesity—as reported by the authors—based on the following measures may be included. Individuals with normal weight will serve as the reference group but will not be considered an exclusive inclusion criterion.

Intervention Intervention – Not applicable

The following anthropometric and BCMs may be considered as exposures:

Percent body fat (PBF), including total fat mass

Fat mass index (FMI)

Fat-free mass index (FFMI)

Appendicular lean mass (ALM)

Waist-to-height ratio (WHtR)

Visceral adipose tissue (VAT) area and volume

Android-to-gynoid fat ratio.

Comparator Comparator – Not applicable.

Study designs to be included Randomized controlled or pragmatic trials; Observational studies.

Eligibility criteria Publications dated between 2014 and January 2026, and the latest available date will be included; those published prior to 2014 will be excluded.

Information sources Electronic databases

Grey literature search, including hand searching and conference abstract screening.

Main outcome(s) Associations between BCMs (PBF, total fat mass, FMI, FFMI, ALM, WHtR, VAT area and volume, android-to-gynoid fat ratio), and the following CMOs presented as a risk measurement (absolute risk, risk ratio, hazard ratio, relative risk, odds ratio):

Any major adverse cardiovascular event (MACE)

Myocardial infarction

Stroke

Cardiovascular (CV) death

All-cause mortality

Coronary revascularization

Heart failure

Angina
T2D
Progression from pre-diabetes to diabetes.

Additional outcome(s) The prognostic performance of anthropometric and BCMs for predicting CMOs evaluated using discrimination metrics such as the area under the receiver operating characteristic curve (AUC), c-statistic, and related performance indices.

Data management Records retrieved from database searches will be imported into a reference management tool and deduplicated. Two reviewers will independently screen records and extract data using a standardised extraction form. Discrepancies will be resolved through discussion or by a third reviewer.

Quality assessment / Risk of bias analysis All RCTs included in this systematic literature review will be assessed for bias using The Cochrane Risk of Bias (ROB2) tool and all observational studies will be assessed for bias using the Newcastle-Ottawa Scale (NOS) tool.

Strategy of data synthesis The following variables will be extracted: study design, sample size, sex distribution, subgroup descriptions, age, effect estimates for the association of BCMs with CMOs (reported as RR, OR, and HR), prognostic performance of BCMs for predicting CMOs (reported as AUC, c-stats), effect estimates for correlations among different BCMs (reported as correlation coefficients), study conclusions, reported limitations, and funding sources.

Where data are sufficiently homogeneous in terms of study design, population, exposures, and outcomes, a quantitative synthesis (meta-analysis) will be considered. However, based on the preliminary assessment of the available literature, substantial variability across studies is anticipated, which may limit the feasibility of meta-analysis.

In such cases, findings will be summarized using a narrative synthesis. The synthesis will be structured around study characteristics and organized for each BCM-CMO pair in terms of the direction and magnitude of associations and the consistency of findings across studies. To aid interpretation, results will be presented using tables and figures. In particular, we plan to employ non-pooled forest plots to visually display effect estimates across studies without statistically combining them. This approach will allow readers to compare effect sizes and confidence intervals across different studies, while accounting for anticipated heterogeneity.

Subgroup analysis N/A.

Sensitivity analysis N/A.

Language restriction Only articles published in English will be included; publications in any other language will be excluded.

Country(ies) involved USA, UK, and India.

Other relevant information This protocol was developed in accordance with PRISMA-P guidelines.

Keywords Obesity; Overweight; Cardiometabolic outcomes; Systematic literature review; BMI; Body composition measures; Fat mass.

Dissemination plans Findings may be submitted for publication in a peer-reviewed journal and/or presented at relevant scientific conferences.

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