INPLASY

Effects of Lifestyle and GLP-1RA based Interventions on Waist Circumference: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 August 2025 and was last updated on 23 August 2025.

INTRODUCTION

Review question / Objective Using the PICOS framework, this systematic review and meta-analysis was designed to address the following question:

Population (P): Adults (≥18 years) with overweight, obesity, or central adiposity, including those with and without type 2 diabetes.

Intervention (I): Lifestyle interventions (diet, exercise, or diet + exercise) and glucagon-like peptide-1 receptor agonist (GLP-1RA) therapy.

Comparator (C): Placebo, standard care, or active comparator interventions (e.g., alternative diet/exercise regimens or other pharmacological agents).

Outcomes (O): Primary outcome was change in waist circumference (WC, cm) as a surrogate for visceral adipose tissue (VAT). Secondary outcomes included correlation between WC and %VAT change, as well as exploration of baseline moderators (age, BMI, WC, weight, and prevalence of type 2 diabetes).

Study design (S): Randomized controlled trials (RCTs) published between January 2010 and August 2025.

Objective:
To systematically evaluate and synthesize evidence from RCTs assessing the effects of lifestyle interventions and GLP-1RA therapy on waist circumference, and to explore baseline characteristics that may modify intervention response.

Rationale Visceral adiposity, reflected by increased waist circumference (WC), is a key determinant of cardiometabolic health. Unlike body mass index (BMI), which does not distinguish between fat and lean mass or fat distribution, WC is a practical clinical measure that correlates strongly with visceral adipose tissue (VAT) volume. Excess VAT contributes to insulin resistance,

systemic inflammation, dyslipidemia, and hypertension, thereby accelerating the development of type 2 diabetes mellitus (T2DM), cardiovascular disease, and non-alcoholic fatty liver disease.

Interventions targeting weight reduction are known to reduce VAT; however, the magnitude of WC reduction achieved by different strategies, including lifestyle modification (diet, exercise, or both) and pharmacotherapy, remains incompletely characterized. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have emerged as highly effective agents for weight reduction and metabolic improvement, with several cardiovascular outcome trials demonstrating broader benefits. Lifestyle interventions, such as calorie-restricted diets, Mediterranean diet, structured exercise, and combined programs, remain foundational to obesity and metabolic syndrome management.

Despite growing trial evidence, few systematic reviews have specifically synthesized WC outcomes across both lifestyle and GLP-1RA interventions. Prior meta-analyses have often focused on body weight or BMI, without adequately addressing WC as a surrogate marker of VAT and cardiometabolic risk. Furthermore, potential effect modifiers, such as age, BMI, baseline WC, body weight, and T2DM prevalence, have not been systematically evaluated.

This review therefore aims to fill this evidence gap by synthesizing randomized controlled trial (RCT) data on WC outcomes across lifestyle and GLP-1RA interventions, and by exploring baseline characteristics that may explain heterogeneity of response. By doing so, it provides clinicians and researchers with clearer insights into the role of these interventions in targeting central adiposity, a modifiable driver of cardiometabolic disease.

Condition being studied The condition of interest is visceral adiposity, commonly referred to as central obesity. Visceral adipose tissue (VAT) is metabolically active fat located within the abdominal cavity, surrounding internal organs such as the liver, pancreas, and intestines. Excess VAT is strongly associated with increased risk of type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, chronic kidney disease, and non-alcoholic fatty liver disease. Unlike subcutaneous fat, VAT contributes disproportionately to insulin resistance, systemic inflammation, and adverse cardiometabolic outcomes.

Waist circumference (WC) is widely used in both clinical practice and research as a surrogate marker for VAT. Elevated WC is a core diagnostic criterion for metabolic syndrome and has been independently linked to cardiovascular and all-cause mortality, even after adjusting for BMI. The reduction of WC is therefore considered an important therapeutic goal, both as a marker of improved body fat distribution and as a proxy for reduced long-term cardiometabolic risk.

The present review focuses on adults with overweight, obesity, or central adiposity, with or without type 2 diabetes. These individuals represent a population at particularly high risk of cardiometabolic complications, and interventions that effectively reduce WC are expected to have substantial health benefits. By assessing the effects of lifestyle and GLP-1RA interventions on WC, this review directly addresses a clinically relevant condition that underpins multiple chronic diseases.

METHODS

Search strategy A comprehensive literature search was conducted to identify randomised controlled trials (RCTs) reporting waist circumference (WC) or visceral adipose tissue (VAT) as primary or secondary outcomes. The following electronic databases were searched from January 2010 to August 2025: PubMed
The search strategy combined controlled vocabulary (MeSH/Emtree terms) and free-text keywords, structured around the Population, Intervention, Comparator, and Outcomes (PICO) framework. Search terms included, but were not limited to:

Population terms: “overweight”, “obesity”, “central obesity”, “visceral adiposity”, “abdominal fat”, “waist circumference”

Intervention terms: “diet”, “exercise”, “physical activity”, “lifestyle intervention”, “calorie restriction”, “low calorie diet”, “very low energy diet”, “Mediterranean diet”, “GLP-1 receptor agonist”, “liraglutide”, “semaglutide”, “exenatide”, “tirzepatide”

Comparator terms: “placebo”, “usual care”, “standard care”, “active comparator”

Outcome terms: “waist circumference”, “visceral adipose tissue”, “VAT”, “central adiposity”

Study design terms: “randomized controlled trial”, “RCT”

Search strings were adapted for each database, using Boolean operators ("AND", "OR"), truncation, and field tags. For example, the PubMed strategy included: (waist circumference OR visceral adipose tissue OR VAT OR central obesity) AND
(diet OR exercise OR lifestyle OR calorie restriction OR Mediterranean OR GLP-1 OR liraglutide OR semaglutide OR exenatide OR tirzepatide) AND
(randomized controlled trial OR RCT). The search was restricted to English-language publications and adult human populations (≥18 years). Reference lists of included studies and relevant reviews were also screened manually for additional eligible trials.

Participant or population This review focuses on adult participants (≥18 years) with overweight, obesity, or central adiposity, as defined by study authors. Both individuals with and without type 2 diabetes mellitus (T2DM) were eligible, reflecting the broader clinical population at risk of cardiometabolic complications from visceral fat accumulation.

Inclusion: Adults with overweight/obesity (BMI ≥25 kg/m², or equivalent criteria by ethnicity), increased waist circumference (sex-specific thresholds), or documented central adiposity/VAT excess by imaging. Studies recruiting mixed populations (e.g., diabetic and non-diabetic) were included if subgroup data were available or overall WC/VAT data were reported.

Exclusion: Studies involving children/adolescents (<18 years), individuals with type 1 diabetes, latent autoimmune diabetes of adults (LADA), gestational diabetes, pregnancy, or those with advanced organ failure (renal, hepatic, cardiac) or transplant recipients.

This broad population definition captures individuals most representative of clinical practice, where both lifestyle interventions and GLP-1 receptor agonist therapy are applied to address excess central adiposity and its cardiometabolic consequences.

Intervention Lifestyle interventions including diet (low-calorie, very low energy, Mediterranean, or other structured dietary regimens), structured exercise (aerobic, resistance, or combined training), or diet + exercise programs. Pharmacological interventions include GLP-1 receptor agonist (GLP1RA)-based therapies such as liraglutide, semaglutide, exenatide, or tirzepatide.

Comparator Placebo, usual care, standard care, or active comparator interventions (e.g., alternative dietary strategies, exercise regimens, or pharmacological comparators such as insulin or SGLT2 inhibitors).

Study designs to be included Randomised controlled trials.

Eligibility criteria Inclusion: Adult participants (≥18 years) with overweight, obesity, or central adiposity; RCTs reporting WC or VAT outcomes; studies with ≥12 weeks follow-up; sample size ≥30 (≥15 per arm).

Exclusion: Non-randomized studies, observational designs, studies in children/pregnant women, type 1 diabetes or LADA, and interventions <12 weeks.

Information sources Electronic databases: PubMed/MEDLINE will be searched systematically. Manual searches will include reference lists of included trials and relevant reviews. Grey literature (conference abstracts, trial registries such as ClinicalTrials.gov and WHO ICTRP) will be screened to identify additional eligible trials. Authors may be contacted if essential outcome data (WC/VAT) are missing from published reports.

Main outcome(s) Change in waist circumference (WC, cm) from baseline to follow-up, expressed as mean difference (MD) with standard error (SE) or 95% confidence intervals (CI). WC was chosen as the primary outcome given its role as a surrogate for visceral adipose tissue (VAT) and cardiometabolic risk.

Additional outcome(s) Change in visceral adipose tissue (VAT) where available (measured by MRI, CT, or DXA).

Correlation between WC change and %VAT change.

Exploration of moderators: baseline BMI, WC, weight, age, and type 2 diabetes prevalence.

Risk of bias profiles of included studies.

Data management Search results will be imported into a reference management software (Zotero) for de-duplication. Screening (title/abstract, full-text) will be performed independently by two reviewers. Data extraction will be conducted in Excel using a piloted extraction sheet, capturing study design, population, intervention, comparator, outcomes, and baseline covariates. Any discrepancies will be resolved through consensus. Extracted data will be

cross-checked before analysis in R (version 4.4.3) and Python (version 3.11.9, matplotlib 3.9.2 for figures).

Quality assessment / Risk of bias analysis Risk of bias will be assessed independently by two reviewers using the Cochrane Risk of Bias 2 (ROB 2) tool, across domains: randomization, deviations from intended interventions, missing data, outcome measurement, and selective reporting. Results will be summarized using traffic-light and bar plots. Disagreements will be resolved by discussion.

Strategy of data synthesis Random-effects meta-analysis (DerSimonian–Laird) will pool mean differences (MD) in WC change with 95% CI. Heterogeneity will be assessed using prediction intervals. Subgroup analyses will be presented visually (forest plots) without statistical comparison across groups. Meta-regression will explore moderators (age, BMI, WC, weight, T2DM prevalence). Funnel plots and Egger's test will assess small-study effects. Analyses will be performed in R (meta, metafor packages).

Subgroup analysis Planned subgroups:

Intervention category (diet, exercise, diet + exercise, GLP1RAs)

Diabetes status (T2DM vs non-diabetic, if available)

Baseline BMI (≥30 vs <30 kg/m²)

Duration of intervention (<24 vs ≥24 weeks).

Sensitivity analysis Sensitivity analyses will exclude:

Arms with active comparators (e.g., diet vs diet, drug vs drug)

Studies with high risk of bias (ROB 2)

Small sample-size arms (<50 participants)
Analyses will be repeated with and without these exclusions to test robustness of pooled estimates.

Language restriction English language.

Country(ies) involved India.

Other relevant information This review adheres to the PRISMA 2020 guidelines for systematic reviews and meta-analyses. The analytical plan, including correlation analyses, meta-regression, subgroup analyses, and sensitivity analyses, was prespecified and is transparently documented in the Supplementary Appendix. Figures were generated primarily using R (version 4.4.3; meta, metafor, and ggplot2 packages), with the correlation scatterplot prepared in Python (version 3.11.9; matplotlib version 3.9.2). Deviations from the protocol, if any, will be reported in the final manuscript. No conflicts of interest are declared. Funding and author contributions will be fully disclosed at the manuscript submission stage.

Keywords Waist circumference; visceral adipose tissue; GLP-1 receptor agonist; lifestyle intervention; diet; exercise; obesity; meta-analysis.

Dissemination plans The findings of this review will be submitted for publication in a peer-reviewed journal specializing in endocrinology, metabolism, or obesity research. Results will also be presented at relevant national and international conferences to reach clinicians, researchers, and policymakers. To promote accessibility, a lay summary and graphical abstract will be made available via institutional and professional social media channels. All extracted data and supplementary materials will be shared in a publicly accessible repository upon acceptance for publication, ensuring transparency and reproducibility.

Contributions of each author

Author 1 - Samit Ghosal - Conceived the study, designed the search strategy, extracted and analyzed data, and drafted the manuscript.
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Author 2 - Anuradha Ghosal - Performed independent screening and data extraction, cross-checked analyses, and contributed to manuscript drafting and critical revision.
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