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Comparative Efficacy of Anti-Obesity Medications on Cardiovascular and Renal Outcomes in Non-Diabetic Patients: A Network Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - This study received no financial support.

Review Stage at time of this submission - Other - Completed but not published. We are intended to be transparent, and we were unaware of the pre-registration requirement for systematic reviews, and are registering now to uphold quality standards.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202650054

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

INTRODUCTION

Review question / Objective Among non-diabetic patients with obesity, how do different classes of anti-obesity medications (SGLT2 inhibitors, GLP-1 receptor agonists, and GLP-1/GIP dual agonists) compare in their effects on cardiovascular and renal outcomes?

Rationale Non-diabetic obesity in adults using the different classes of anti-obesity medications, while evaluating associated cardiovascular and renal outcomes.

Condition being studied Adult patients with non-diabetic obesity receiving different classes of anti-obesity medications, with evaluation of associated cardiovascular and renal outcomes.

METHODS

Search strategy A multi-step literature search was performed, beginning with a broad initial search using generic terms across PubMed, Scopus, and Embase. Then, a comprehensive strategy was developed incorporating relevant keywords and MeSH terms, which was applied to PubMed, Scopus, ClinicalTrials, and Web of Science. The final search was conducted on November 2025 and used the specific query: ((SGLT2 AND inhibitor*) OR (Gliflozin*) OR (dapagliflozin*) OR (BMS AND 512148) OR Farxiga OR Forxiga OR Qtern OR Xigduo OR Qternmet OR Canagliflozin* OR Invokana OR empagliflozin OR (BI AND 10773) OR Jardiance OR (Dipeptidyl AND Peptidase AND Inhibitor*) OR (DDP-4 AND inhibitor*) OR Gliptin* OR Tirzepatide OR LY3298176 OR Zepbound OR Mounjaro OR Liraglutide OR (NN AND 2211) OR Victoza OR Saxenda OR dulaglutide OR (LY AND

2189265) OR Trulicity OR (Glucagon Like Peptide) OR GLP* OR Sitagliptin* OR (MK AND 0413) OR Januvia OR Saxagliptin* OR (BMS AND 477118) OR Galvus) AND (cardiovascular OR cardiacMACE OR "heart failure" OR renal OR "total death") AND (trial*).

Participant or population Adult patients with non-diabetic obesity receiving different classes of anti-obesity medications.

Intervention Different classes of anti-obesity medications (AOMs).

Comparator Other anti-obesity medication classes or placebo/control groups.

Study designs to be included Randomized controlled trials (RCTs) evaluating the effects of anti-obesity medications on cardiovascular and renal outcomes in non-diabetic adults with obesity were included.

Eligibility criteria Inclusion Criteria: RCTs of AOMs with non-diabetic individuals, Articles written in English, Articles could be retrieved in full text. Exclusion Criteria: Articles without outcomes of interest, Abstracts, letters to editors, comments, opinions, case reports, and reviews, Articles written in languages other than English.

Information sources PubMed, Scopus, Embase, Scopus, ClinicalTrials, and Web of Science.

Main outcome(s) The Effect on Cardiac Parameters:
The effects of various AOMs on cardiac parameters were compared, such as SBP, HR, arrhythmia, and ACS, to determine whether one drug had superior cardioprotective properties.
The Effect on Renal Parameters:
Renal parameters, such as the incidence of AKI or nephrolithiasis, were documented, and comparisons were drawn among all drugs, and between each drug and placebo.
Complications:
The safety profiles of tirzepatide, semaglutide, mazdutide, empagliflozin, and dapagliflozin were pooled in the form of 'any adverse events,' serious adverse events,' and 'adverse events leading to drug discontinuation.'

Quality assessment / Risk of bias analysis Two different reviewers assessed the quality of all full-text articles, and conflicts were resolved by a third reviewer. The reviewers evaluated the methodological quality of all RCTs using the Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) provided by Cochrane.

Strategy of data synthesis The study adhered to the outlined principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Cochrane Handbook for Systematic Reviews of Interventions.

Subgroup analysis Subgroups included age, gender, BMI, NYHA functional class, lipid profile parameters (LDL and HDL), and specific cardiorenal outcomes, including systolic blood pressure (SBP), heart rate (HR), arrhythmia, acute coronary syndrome (ACS), acute kidney injury (AKI), and nephrolithiasis.

Sensitivity analysis Sensitivity analyses were performed by sequentially excluding studies with high risk of bias, small sample sizes, short follow-up periods, or substantial heterogeneity to assess the stability and consistency of the pooled estimates.

Language restriction Only studies published in the English language were included.

Country(ies) involved Saudi Arabia - Clinical Pharmacy Department, College of Pharmacy, Taif University, Taif, Saudi Arabia.

Other relevant information Studies conducted worldwide were eligible for inclusion.

Keywords Nondiabetic Obesity; Obesity; Anti-Obesity Medications; Systematic Review; Network Meta-Analysis.

Dissemination plans The findings of this study will be disseminated through publication in a peer-reviewed journal and presentation at relevant scientific conferences.

Contributions of each author

Author 1 - Fahad H. Baali - The author contributed substantially to all stages of the study, including study design, data collection, analysis, interpretation, and manuscript preparation.
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