INPLASY

INPLASY202650012

doi: 10.37766/inplasy2026.5.0012

Received: 4 May 2026

Published: 4 May 2026

Corresponding author:
Bing Wang

18782937150@163.com

Author Affiliation:
Quality Control Department, Chengdu Qingbaijiang District Center for Disease Control and Prevention, Chengdu, China.

Effect of GLP-1 Receptor Agonists on Body Weight and Albuminuria in Patients With and Without Type 2 Diabetes: A Protocol for a Systematic Review and Meta-Analysis

Huang, R; Wang, B.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published - The systematic review and meta-analysis has been completed and the manuscript is under revision. Prospective registration was not performed because the authors were unaware of the registration requirement at the time the study was initiated. This registration is being completed post-study in accordance with the journal's requirement.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202650012

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 4 May 2026 and was last updated on 4 May 2026.

INTRODUCTION

Review question / Objective The aim of this systematic review and meta-analysis is to quantify the overall effect of GLP-1 receptor agonists on urinary albumin-to-creatinine ratio (UACR) and body weight, and to investigate whether these effects are consistent in patient subgroups with and without type 2 diabetes.

Rationale GLP-1 receptor agonists are established for weight management and cardiovascular risk reduction, with emerging evidence for kidney protection. However, whether albuminuria-lowering effects extend to non-diabetic chronic kidney disease remains uncertain. Previous meta-analyses have primarily focused on diabetic populations, leaving a gap in understanding the drug class's effects across the full glycemic spectrum. This systematic review aims to address this gap by including both T2DM and non-T2DM populations.

Condition being studied Chronic kidney disease (CKD) and albuminuria in patients with and without type 2 diabetes mellitus.

METHODS

Search strategy A comprehensive search of PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) was performed from inception to October 2025. The search strategy combined MeSH terms and free-text keywords for "GLP-1 Receptor Agonists" (semaglutide, liraglutide, dulaglutide, exenatide) and terms related to renal outcomes (albuminuria, urine albumin-to-creatinine ratio, UACR, chronic kidney disease, renal function). Boolean operators (AND, OR) were used to combine search terms. Reference lists of included articles and relevant systematic reviews were manually screened.

Full search strategy is available in Supplementary Table S1.

Participant or population Adults (≥18 years) with CKD or at high risk for renal/cardiovascular events, including both patients with type 2 diabetes mellitus and those without diabetes. No restrictions were applied based on age, sex, or ethnicity.

Intervention GLP-1 receptor agonists (including semaglutide, liraglutide, dulaglutide, and exenatide) at any dose, administered via any route.

Comparator Placebo or standard care (including active comparators where GLP-1RA was added to background therapy).

Study designs to be included Randomized controlled trials (RCTs) only.

Eligibility criteria Inclusion criteria:
(1) Randomized controlled trial design
(2) Adult participants with CKD or at high risk for renal/cardiovascular events
(3) GLP-1 receptor agonist compared to placebo or standard/active care
(4) Change in UACR reported as an outcome

Exclusion criteria:
(1) Non-randomized or observational studies
(2) Case reports, reviews, or animal studies
(3) Studies not reporting UACR data
(4) Duplicate publications

No language restrictions were applied.

Information sources PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL). Additional sources: manual screening of reference lists of included articles and relevant systematic reviews.

Main outcome(s) Co-primary outcomes:
(1) Mean difference (MD) in body weight (kg)
(2) Percentage change in urinary albumin-to-creatinine ratio (UACR).

Additional outcome(s) Secondary outcomes: MD in estimated glomerular filtration rate (eGFR), systolic blood pressure (SBP), and glycated hemoglobin (HbA1c).

Data management Two independent reviewers (Jun Xu and Zhen Wang) screened all retrieved titles and abstracts. Full texts were assessed against pre-defined criteria. Disagreements were resolved by consensus or consultation with a third reviewer (Qingshen Gao). Data extraction was performed independently by two reviewers using a standardized form. Study selection and data management were conducted using reference management software. Statistical analyses were performed using R (metafor package).

Quality assessment / Risk of bias analysis Methodological quality was assessed using the Cochrane Risk of Bias tool (RoB 2.0). Certainty of evidence was graded using the GRADE framework (domains: risk of bias, inconsistency, indirectness, imprecision, publication bias).

Strategy of data synthesis Random-effects meta-analysis using restricted maximum likelihood (REML) was performed to pool mean differences with 95% confidence intervals. Heterogeneity was quantified by τ^2 and I^2, and 95% prediction intervals were reported. Prespecified subgroup analyses tested interaction by glycemic status, drug class, treatment duration, ethnicity, baseline eGFR, baseline UACR, and concomitant therapies. Random-effects meta-regression (REML with Knapp-Hartung adjustment) evaluated study-level moderators. Small-study effects were assessed via funnel plots and trim-and-fill. Sensitivity analyses included leave-one-out diagnostics, restriction to low-risk-of-bias studies, and exclusion of T2DM trials. Two-sided α=0.05 was used throughout.

Subgroup analysis Prespecified subgroup analyses were conducted for: glycemic status (T2DM vs non-T2DM), drug class (semaglutide vs exenatide), treatment duration, ethnicity proportion, baseline eGFR (>60 vs ≤60 mL/min/1.73 m^2), baseline UACR (>300 vs ≤300 mg/g), and prevalence of lipid-lowering or antihypertensive therapy.

Sensitivity analysis Sensitivity analyses included: (1) leave-one-out influence diagnostics, (2) restriction to studies with low risk of bias, and (3) exclusion of T2DM trials to verify the non-diabetic signal.

Language restriction No language restrictions were applied.

Country(ies) involved China.

Other relevant information Not applicable.

Keywords GLP-1 receptor agonist; albuminuria; UACR; chronic kidney disease; semaglutide; exenatide; meta-analysis; non-diabetic CKD.

Dissemination plans The results of this systematic review will be submitted for publication in a peer-reviewed journal.

Contributions of each author

Author 1 - Rong Huang - Literature search, data extraction, quality assessment, writing the manuscript.
Email: huangrong5511@126.com
Author 2 - Bing Wang - Supervision, resolution of disagreements, review and approval of final manuscript.
Email: 18782937150@163.com