GLP-1 Receptor Agonists in Non-Diabetic Chronic Kidney Disease: A Systematic Review

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Abstract

Introduction: Glucagon-like peptide-1 receptor agonists have demonstrated cardiovascular and kidney benefits in type 2 diabetes, but their role in non-diabetic chronic kidney disease remains uncertain.

Methodology: A systematic review following PRISMA 2020 guidelines was conducted, in which MEDLINE (PubMed), Cochrane Library, TRIP and NICE databases were used. Search strategies combined MeSH terms and free-text strategies. Eligible studies included randomized controlled trials, observational studies, systematic reviews, meta-analyses and clinical practice guidelines published in English, Portuguese or Spanish. A thorough examination of reference lists was conducted to identify additional studies. Evidence was graded using the Strength of Recommendation Taxonomy.

Results: The final synthesis included two placebo-controlled randomized trials. In the SELECT trial, non-diabetic adults with overweight or obesity and established cardiovascular disease who received semaglutide 2.4 mg once weekly showed a slower decline in estimated glomerular filtration rate and approximately 22% fewer composite kidney events compared with placebo, with a greater benefit in those with baseline estimated glomerular filtration rate below 60 mL/min/1.73 m². In the SMART trial, adults with non-diabetic chronic kidney disease and overweight or obesity experienced a 52% reduction in albuminuria at 24 weeks with semaglutide, while measured and estimated glomerular filtration rate remained stable.

Conclusion: These findings suggest potential benefits of glucagon-like peptide-1 receptor agonists on albuminuria and kidney function trajectories independent of diabetes, but effects on long-term kidney outcomes remain unknown. Use in this population should be individualized and further studies are required to validate this use.

Keywords: Glucagon-Like Peptide-1 Receptor Agonists/therapeutic use; Kidney Failure, Chronic/drug therapy; Renal Insufficiency, Chronic/drug therapy

INTRODUCTION

Chronic kidney disease (CKD) affects approximately 14% of the global adult population and remains a major cause of morbidity, premature mortality, and healthcare burden worldwide.[1] Among patients with type 2 diabetes (T2D), glucagon-like peptide-1 receptor agonists (GLP-1a) have become well-established agents with proven cardiovascular and renal benefits extending beyond glycemic control.[2–5]

Large randomized controlled trials such as LEADER (liraglutide),[2] SUSTAIN-6 (semaglutide),[3] and REWIND (dulaglutide)[4] demonstrated significant reductions in new or worsening nephropathy, mainly driven by decreased albuminuria and a slower decline in estimated glomerular filtration rate (eGFR). These renal findings were corroborated by the dedicated FLOW trial, [5] in which semaglutide significantly reduced the risk of kidney failure, substantial loss of kidney function, and cardiovascular death among patients with T2D and CKD. Collectively, these studies have established GLP-1a as a renoprotective agent in diabetic kidney disease, complementing the benefits of sodium–glucose cotransporter-2 inhibitors (SGLT2i) and renin–angiotensin system (RAS) blockers.

The underlying mechanisms appear to be multifactorial, involving improvements in glycemic control, weight reduction, blood-pressure lowering, natriuresis, and anti-inflammatory as well as anti-atherogenic effects.[6] These pleiotropic pathways provide a biological rationale for potential kidney benefits independent of diabetes status.

Although dedicated evidence in non-diabetic populations remains limited, subgroup analyses suggest that the renoprotective effects of GLP-1a may extend beyond diabetes itself.[7,8]

Despite these advances, current guidelines recommend GLP-1a only for patients with T2D and CKD, particularly

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when SGLT2 inhibitors are contraindicated or insufficient for glycemic or cardiovascular control.[9] No formal recommendation currently supports their use in non-diabetic CKD, underscoring the need to systematically appraise the available evidence in this population.

Therefore, this evidence-based systematic review aims to identify, critically appraise, and synthesize the available data on the effectiveness of GLP-1a in adults with non-diabetic CKD, and to contextualize these findings within current guideline recommendations.

METHODS

Study Design

A systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement[10] was performed. The protocol was not registered in PROSPERO because the available evidence was limited to a small and well-defined set of eligible studies, with minimal scope for analytical flexibility.

Search Strategy

A comprehensive literature search was conducted up to 1 November 2025 across MEDLINE (via PubMed), Cochrane Library, TRIP and NICE databases. For MEDLINE, the following MeSH-based query was used: ((“Kidney Diseases”[Mesh] OR “Kidney Failure, Chronic”[Mesh] OR “Renal Insufficiency, Chronic”[Mesh] OR “Chronic Kidney Diseases of Uncertain Etiology”[Mesh]) NOT (“Diabetes Mellitus”[Mesh] OR “Diabetes Mellitus, Type 2”[Mesh] OR “Diabetes Mellitus, Type 1”[Mesh])) AND (“Glucagon-Like Peptide-1 Receptor Agonists”[Mesh] OR “Liraglutide”[Mesh] OR “semaglutide” [Supplementary Concept] OR “dulaglutide” [Supplementary Concept] OR “Exenatide”[Mesh] OR “rGLP-1 protein” [Supplementary Concept] OR “efpeglenatide” [Supplementary Concept] OR “lixisenatide” [Supplementary Concept]). To ensure broader coverage, an additional free-text search was performed using: ((“chronic kidney disease” OR CKD OR “renal insufficiency” OR “kidney failure” OR eGFR OR albuminuria OR UACR) NOT (diabetes OR diabetic OR “type 2” OR T2D OR “Type 1” OR T1D)) AND (semaglutide OR liraglutide OR dulaglutide OR exenatide OR lixisenatide OR “GLP-1 receptor agonist*” OR “GLP1 receptor agonist*” OR GLP1). The search was limited to human studies and to Portuguese, English, and Spanish languages, with no time restriction. Original studies were accepted including randomized controlled trials, observational studies, systematic reviews and meta-analyses.

Potentially eligible studies were first screened by title and abstract. Articles considered potentially relevant underwent full-text review. A thorough examination of reference lists was conducted to identify any additional eligible publications. A separate search for clinical practice guidelines and practice recommendations was also conducted.

Eligibility Criteria

Only studies that allowed the evaluation of the effect of GLP-1a on renal function of non-diabetic patients, following the predefined acronym PICO framework, were included in the systematic review:

Population: non-diabetic adults with CKD (any stage, as defined by KDIGO criteria).

Intervention: exposure to a GLP-1a.

Comparison: non-exposure to GLP-1a or placebo/ other active treatment.

Outcomes: kidney-related outcomes (e.g., eGFR slope, kidney failure, composite renal events, albuminuria).

Studies that did not meet the aim of the review, lacked a control group, or did not report kidney-related outcomes were excluded.

The Strength of Recommendation Taxonomy (SORT) scale was applied to evaluate the level of evidence (LE) and strength of recommendation for the included studies.[11]

RESULTS

Literature Search

The database search across four electronic sources (MEDLINE via PubMed, Cochrane Library, TRIP and NICE) yielded 60 records after applying predefined filters. After removal of duplicates and screening of titles and abstracts, 56 records were excluded for not meeting the predefined criteria. Four full-text articles were assessed for eligibility. One full-text article was excluded for not meeting the inclusion criteria. Two systematic reviews with meta-analyses were excluded because, for non-diabetic CKD, they provided only indirect data derived from a single trial already included in our review. Then, only one randomized controlled trial fulfilling the defined PICO was included. One additional randomized controlled trial was eligible and included in the present review after a thorough examination of reference lists.

In total, two placebo-controlled randomized controlled trials met the eligibility criteria and were evaluated. The literature selection process is illustrated in Fig. 1 (PRISMA flow diagram).

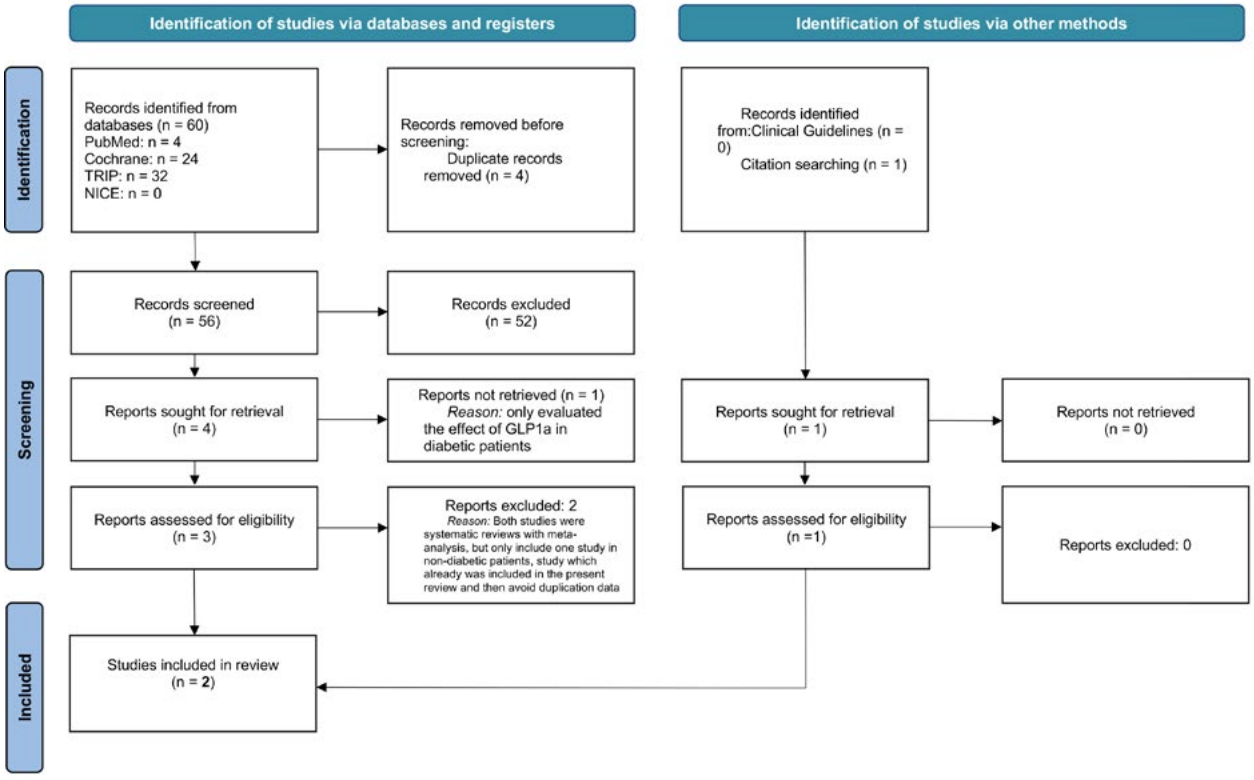

Figure 1. PRISMA flow diagram of the literature selection process for the present review.

Characteristics and Main Findings of the Included Trials

Table 1 shows the characteristics of the studies included in the systematic review.

The SELECT trial (Colhoun HM *et al*, 2024)[12] enrolled 17 604 adults with overweight or obesity and established cardiovascular disease but without diabetes (eGFR ≥30 mL/min/1.73 m²). Participants were randomly assigned to once-weekly subcutaneous semaglutide 2.4 mg or placebo and followed for a mean of 3.5 years. In a prespecified kidney analysis, semaglutide significantly slowed the annual decline in eGFR (−0.75 *vs* −1.17 mL/min/1.73 m² per year with placebo; $p<0.001$) and reduced the composite kidney outcome of ≥50% eGFR decline, kidney failure, or renal death by approximately 22%. The greatest benefit was observed in participants with baseline eGFR <60 mL/min/1.73 m², who experienced a treatment difference of 2.19 mL/min/1.73 m² in eGFR at 104 weeks. Semaglutide also reduced albuminuria, with larger relative reductions among participants with higher baseline urinary albumin-to-creatinine ratio (UACR). The SMART trial (Apperloo *et al*, 2025)[13] was the first randomized, double-blind, placebo-controlled clinical trial specifically designed to evaluate the renal effects of a GLP-1 receptor agonist in adults with non-diabetic chronic kidney disease and overweight or obesity. A total of 101 participants were randomized to semaglutide 2.4 mg once weekly or placebo for 24 weeks. CKD was defined according to KDIGO criteria, requiring an eGFR ≥25 mL/min/1.73 m² and moderate-to-severe albuminuria (UACR 30–3.500 mg/g) at baseline. CKD etiologies included chronic glomerulonephritis, hypertensive nephropathy, and obesity-related glomerulopathy. The primary renal endpoint, percentage change in UACR from baseline to week 24, was significantly reduced with semaglutide compared with placebo (52.1% placebo-corrected reduction; 95% CI –65.2 to –34.1; $p<0.0001$). Secondary outcomes, including eGFR based on creatinine, cystatin C, and measured GFR by iohexol clearance, showed no significant between-group differences over 24 weeks. An early, transient decrease in creatinine-based eGFR was observed at week eight in the semaglutide arm, but values subsequently returned to baseline, and no sustained change in kidney filtration was detected. Semaglutide also led to clinically meaningful reductions in body weight, systolic blood pressure, high-sensitivity C-reactive protein (hsCRP), and N-terminal pro B-type natriuretic peptide (NT-proBNP), with a safety profile consistent with previous GLP-1a trials, dominated by gastrointestinal adverse events.

Table 1. Characteristics and main kidney-related findings of the randomized controlled trials evaluating GLP-1 receptor agonists in non-diabetic chronic kidney disease.

Study/ Year	Study Design	Study Populations	Selection Criteria	Definition of CKD	Intervention Treatment	Control Treatment	Evaluated Kidney Outcomes	Main Kidney Findings	SORT Evidence Level
Colhoun HM *et al*, 2024[12]	Randomized, double-blind, placebo-controlled trial	17 604 non-diabetic adults with overweight/obesity and established cardiovascular disease; approximately one-fifth had CKD (eGFR <60 mL/min/1.73 m² or UACR ≥30 mg/g at baseline)	Adults ≥ 45 years; BMI ≥ 27 kg/m²; established CVD; no history of diabetes	Baseline eGFR < 60 mL/min/1.73 m² or UACR ≥ 30 mg/g	Semaglutide 2.4 mg weekly	Placebo	eGFR slope; composite kidney outcome	Semaglutide slowed eGFR decline and reduced composite kidney events; clear benefit in non-diabetic CKD subgroup	1
Apperloo *et al*, 2025[13]	Randomized, double-blind, placebo-controlled clinical trial	101 adults with non-diabetic CKD; BMI ≥27 kg/m²; CKD etiologies included chronic glomerulonephritis, hypertensive CKD, and obesity-related CKD	Adults ≥ 18years without diabetes, with CKD and with a BMI of ≥27kgm²	eGFR ≥ 25 mL/min/1.73 m² and UACR ≥ 30mg/g and ≤3.500mg/g	Semaglutide 2.4 mg weekly	Placebo	Primary: % change UACR; Secondary: eGFR (Cr), eGFR (CysC), measured GFR (iohexol)	52% placebo-corrected UACR reduction; no change in estimated or measured GFR; early transient dip in eGFR.	1

CKD = chronic kidney disease; CVD = cardiovascular disease; BMI = body mass index; eGFR = estimated glomerular filtration rate; UACR = urine albumin-to-creatinine ratio; GFR = glomerular filtration rate; SORT = Strength of Recommendation Taxonomy

DISCUSSION

This systematic review identified only two randomized placebo-controlled trials evaluating semaglutide in adults without diabetes and with increased kidney risk. The KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of CKD recognizes the expanding evidence base for GLP-1a but currently recommends their use only in adults with T2D and CKD.[9] Specifically, long-acting GLP-1a are recommended (grade 1B) for adults with T2D and CKD who have not achieved individualized glycemic targets despite metformin and SGLT2 inhibitor therapy, or who are unable to use these medications. The guideline advises prioritizing GLP-1a with proven cardiovascular benefit and explicitly notes the lack of evidence to support their use in non-diabetic CKD. Taken together, these data suggest that GLP-1a exert favorable effects on albuminuria and eGFR trajectories beyond glycemic control, but they also highlight important limitations that constrain their application to non-diabetic CKD in routine practice.[9]

Evidence from large cardiovascular outcome trials in T2D, including LEADER,[2] SUSTAIN-6,[3] REWIND[4] and FLOW,[5] has firmly established GLP-1a as effective in slowing kidney disease progression and reducing renal events, with benefits that extend beyond HbA1c lowering. However, these trials predominantly enrolled patients with diabetes, and kidney outcomes were often secondary or exploratory endpoints. The SELECT trial[12] represents a critical step toward understanding GLP-1a effects outside diabetes: in adults with overweight or obesity and established cardiovascular disease but no diabetes, semaglutide 2.4 mg weekly reduced composite kidney events and attenuated eGFR decline, with the largest effect in those with baseline CKD. Nonetheless, SELECT trial[12] was designed as a cardiovascular, not a kidney, outcome trial. Only a minority of participants had CKD at baseline (one-fifth of the population), the overall rate of eGFR decline was low (reflecting the low-risk population), and not all participants were receiving guideline-directed RAS blockade. Consequently, the observed kidney benefits may partly reflect indirect mechanisms such as weight loss, blood-pressure reduction, improved cardiac function and decongestion, rather than a direct nephroprotective effect.

The SMART trial, by Apperloo *et al*,[13] provides the first high-quality, disease-specific evidence in adults with non-diabetic CKD and overweight/obesity. Semaglutide 2.4 mg produced a striking 52% placebo-corrected reduction in UACR over 24 weeks, a magnitude comparable to that achieved with SGLT2 inhibitors and non-steroidal mineralocorticoid receptor antagonists in diabetic CKD. Albuminuria reduction was consistent across CKD etiologies and baseline albuminuria strata and occurred early, shortly after reaching the target semaglutide dose, preceding maximal weight loss.[13] Moreover, UACR remained substantially lower than baseline four weeks

after treatment discontinuation, suggesting a sustained or structural effect on kidney tissues rather than a purely hemodynamic change. Parallel reductions in hsCRP and NT-proBNP support anti-inflammatory and cardio-renal hemodynamic mechanisms.[6,13] Importantly, the albuminuria response was observed on top of contemporary background therapy, including SGLT2 inhibitors for a substantial proportion of participants, indicating that GLP-1a may offer additive renoprotective effects.[13] In contrast, semaglutide did not significantly change measured or estimated GFR over the 24-week follow-up in SMART trial, despite an early reversible dip in creatinine-based eGFR. This pattern resembles the acute hemodynamic response seen with other nephroprotective therapies, but the short duration and limited sample size preclude conclusions regarding longer-term kidney function preservation.[13] The trial population was also restricted to individuals with overweight or obesity, and most participants were White, so the generalizability of these findings to leaner or more ethnically diverse non-diabetic CKD populations remains uncertain. Additionally, not all participants received RAS blockade, in part due to intolerance and in part reflecting weaker guideline recommendations for RAS inhibition in non-diabetic CKD with preserved blood pressure and microalbuminuria.[13]

The broader literature, although excluded from the quantitative synthesis of this review, supports the biological plausibility of glycemia-independent renoprotection of GLP-1a. Meta-analyses by Chen *et al*[7] and Mendonça *et al*[8] consistently showed that GLP-1a reduces kidney failure, eGFR decline and all-cause mortality in populations largely composed of patients with T2D, with treatment effects persisting after adjustment for HbA1c. Badve *et al*[14] further demonstrated that GLP-1a reduces a composite of kidney failure, substantial eGFR loss and kidney death, with treatment effects that appeared similar irrespective of diabetes status, although the only non-diabetic data came from SELECT and could not be analyzed separately. These findings, while indirect, support a class effect extending across the spectrum of cardiovascular–kidney–metabolic risk.

Additional support for glycemia-independent renoprotection comes from studies of dual incretin agonists and obesity-focused semaglutide trials. Secondary analyses of the SUMMIT programme in heart failure with preserved ejection fraction and obesity showed that tirzepatide improved eGFR trajectories and reduced albuminuria in patients with and without CKD.[15,16] A meta-analysis by Wu *et al*[17] suggested that semaglutide reduces major cardiovascular and some renal events in overweight or obese adults without diabetes. Furthermore, Skibicka and Małgorzewicz[18] highlighted the potential of metabolic therapies, including GLP-1a and dual agonists, to modify the course of obesity-related kidney disease and IgA nephropathy by targeting visceral adiposity, inflammation and endothelial dysfunction. These data reinforce the concept that incretin-based therapies exert multisystem protective effects in high cardiometabolic risk populations, including those with CKD.

Mechanistic insights are also emerging. Experimental and clinical studies suggest that GLP-1a may improve kidney outcomes through a combination of weight loss, blood-pressure reduction, natriuresis, improved renal hemodynamics, reduced oxidative stress and downregulation of pro-inflammatory pathways.[6,19,20] The REMODEL trial[19] is evaluating the effects of semaglutide on kidney oxygenation, perfusion and inflammation by magnetic resonance imaging in people with T2D and CKD, aiming to clarify pathways underpinning the FLOW results.[5] In addition, a meta-analysis has shown that interventions achieving >25% reductions in albuminuria are strongly associated with a lower risk of kidney failure, supporting albuminuria as a valid surrogate endpoint in CKD trials.[20] When viewed through this lens, the robust albuminuria reduction observed in Apperloo *et al*[13] provides a compelling, albeit still surrogate, signal of potential long-term renoprotection in non-diabetic CKD.

Despite these encouraging data, several limitations of the current evidence must be acknowledged. First, only two RCTs have evaluated GLP-1a in adults without diabetes and with increased kidney risk, and only one trial specifically targeted non-diabetic CKD as the primary disease state. Second, both SELECT and SMART trials focused on patients with overweight or obesity, leaving uncertainty about the applicability to normal-weight individuals with non-diabetic CKD. Third, follow-up in the dedicated CKD trial was short, and hard kidney endpoints such as sustained eGFR decline, kidney failure or renal death were not assessed. Fourth, most of the mechanistic and meta-analytic evidence arises from T2D populations, and subgroup analyses of non-diabetic participants are either absent or underpowered. Finally, safety data in non-diabetic CKD remain limited, although the available trials suggest that the adverse event profile of semaglutide is consistent with that seen in other indications, dominated by gastrointestinal symptoms without new kidney safety signals.[12,13]

Within this context, the KDIGO 2024 guideline, by restricting recommendations for GLP-1a to adults with T2D and CKD who have not achieved glycemic targets despite metformin and SGLT2 inhibitors, reflects both the strength of the diabetes-related evidence and the persisting uncertainty in non-diabetic CKD.[9] Taken together, the available data support the biological plausibility and clinical potential of GLP-1a therapy in non-diabetic CKD, particularly in patients with obesity and high cardiovascular risk, but they fall short of justifying routine use for kidney protection in this population.

The horizon of clinical research in this area is expanding, with some randomized trials currently underway to

evaluate the impact of GLP-1a and dual agonists in specific non-diabetic kidney disease etiologies. For instance, the NCT06582875 trial is currently assessing the efficacy of a GLP-1a in reducing total kidney volume growth in patients with autosomal dominant polycystic kidney disease (ADPKD).[21] Furthermore, dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonists, such as tirzepatide, are being investigated in overweight or obese individuals with CKD (including cohorts without type 2 diabetes) to evaluate their effects on renal oxygenation and cardio-renal outcomes (NCT04777409 trial).[22] Although these trials are still in progress and their findings cannot yet be extrapolated to routine practice, they will be instrumental in determining whether the pleiotropic benefits observed in exploratory analyses translate into robust, etiology-specific clinical recommendations.

Overall, the present review underscores the need for longer-term, adequately powered randomized trials of GLP-1a and dual incretin agonists in non-diabetic CKD, using hard kidney outcomes alongside mechanistic and imaging endpoints. Such trials will be essential to determine whether the observed improvements in albuminuria and eGFR trajectories translate into meaningful reductions in kidney failure and mortality.

CONCLUSION

Current evidence suggests that GLP-1a may offer renoprotective benefits in non-diabetic CKD, likely mediated through weight loss, anti-inflammatory pathways, and improved cardiorenal hemodynamics. While significant reductions in albuminuria have been demonstrated, the evidence base remains limited to a small number of trials, and the long-term impact on hard clinical endpoints, such as kidney failure, remains unestablished in this specific population. At present, no clinical guidelines endorse GLP-1a therapy solely for kidney protection in the absence of type 2 diabetes. Adequately powered, long-term randomized clinical trials are essential to validate these findings and determine the role of GLP-1a in the routine management of non-diabetic CKD.

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IRA and MRM: Literature review, manuscript design, writing and approval the final version to be published.

REFERENCES

1. GBD 2023 Chronic Kidney Disease Collaborators. Global, regional, and national burden of chronic kidney disease in adults, 1990–2023, and its attributable risk factors: a systematic analysis for the Global Burden of Disease Study 2023. Lancet. 2025;406:2461-82. doi:10.1016/S0140-6736(25)01853-7
2. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2016;375:311-22. doi:10.1056/NEJMoa1603827
3. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2016;375:1834-44. doi:10.1056/NEJMoa1607141
4. Gerstein HC, Colhoun HM, Dagenais GR, Diaz R, Lakshmanan M, Pais P, et al. Dulaglutide and renal outcomes in type 2 diabetes: an exploratory analysis of the REWIND randomised, placebo-controlled trial. Lancet. 2019;394:131-8. doi:10.1016/S0140-6736(19)31150-X
5. Perkovic V, Tuttle KR, Rossing P, Mahaffey KW, Mann JFE, Bakris G, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. N Engl J Med. 2024;391:109-21. doi:10.1056/NEJMoa2403347
6. Muskiet MHA, Tonneijck L, Smits MM, an Baar MJ, Kramer MH, Hoorn EJ, et al. GLP-1 and the kidney: from physiology to pharmacology and outcomes in diabetes. Nat Rev Nephrol. 2017;13:605-28. doi:10.1038/nrneph.2017.123
7. Chen JY, Hsu TW, Liu JH, Pan HC, Lai CF, Yang SY, et al. Kidney and cardiovascular outcomes among patients with CKD receiving GLP-1 receptor agonists: a systematic review and meta-analysis of randomized trials. Am J Kidney Dis. 2025;85:555-69.e1. doi:10.1053/j.ajkd.2024.11.013
8. Mendonça L, Moura H, Chaves PC, Neves JS, Ferreira JP. The impact of glucagon-like peptide-1 receptor agonists on kidney outcomes: a meta-analysis of randomized placebo-controlled trials. Clin J Am Soc Nephrol. 2024;20:159-68. doi:10.2215/CJN.0000000584
9. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int. 2024;105:S117-S314. doi:10.1016/j.kint.2023.10.018
10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:71. doi:10.1136/bmj.n71
11. Ebell MH, Siwek J, Weiss BD, Woolf SH, Susman J, Ewigman B, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. J Am Board Fam Pract. 2004;17:59-67. doi:10.3122/jabfm.17.1.59
12. Colhoun HM, Lingvay I, Brown PM, Deanfield J, Brown-Frandsen K, Kahn SE, et al. Long-term kidney outcomes of semaglutide in obesity and cardiovascular disease in the SELECT trial. Nat Med. 2024;30:2058-66. doi:10.1038/s41591-024-03015-5

13. Apperloo EM, Gorriz JL, Soler MJ, Cigarrán Guldris S, Cruzado JM, Puchades MJ, et al. Semaglutide in patients with overweight or obesity and chronic kidney disease without diabetes: a randomized double-blind placebo-controlled clinical trial. Nat Med. 2025;31:278-85. doi:10.1038/s41591-024-03327-6
14. Badve SV, Bilal A, Lee MMY, et al. Effects of GLP-1 receptor agonists on kidney and cardiovascular disease outcomes: a meta-analysis of randomised controlled trials. Lancet Diabetes Endocrinol. 2025;13:15-28. doi:10.1016/S2213-8587(24)00271-7
15. Borlaug BA, Zile MR, Kramer CM, Baum SJ, Hurt K, Litwin SE, et al. Effects of tirzepatide on circulatory overload and end-organ damage in heart failure with preserved ejection fraction and obesity: a secondary analysis of the SUMMIT trial. Nat Med. 2025;31:544-51. doi:10.1038/s41591-024-03374-z
16. Packer M, Zile MR, Kramer CM, Murakami M, Ou Y, Borlaug BA, et al. Interplay of chronic kidney disease and the effects of tirzepatide in patients with heart failure, preserved ejection fraction, and obesity: the SUMMIT trial. J Am Coll Cardiol. 2025;85:1721-35. doi:10.1016/j.jacc.2025.03.009
17. Wu R, Xing B, Zhou Z, Yu L, Wang H. Effect of semaglutide on arrhythmic, major cardiovascular, and renal outcomes in patients with overweight or obesity: a systematic review and meta-analysis. Eur J Med Res. 2025;30:835. doi:10.1186/s40001-025-03124-y
18. Skibicka A, Małgorzewicz S. Visceral obesity and metabolic dysfunction in IgA nephropathy: nutritional and metabolic perspectives on disease progression. Nutrients. 2025;17:3307. doi:10.3390/nu17203307
19. Bjornstad P, Cherney D, Lawson J, Møntegaard C, Pruijm M, Tuttle K,et al. Remodel: a mechanistic trial evaluating the effects of semaglutide on the kidneys in people with type 2 diabetes and chronic kidney disease. Nephrol Dial Transplant. 2022;37:i290-i291. doi:10.1093/ndt/gfac070.013
20. Heerspink HJL, Greene T, Tighiouart H, Gansevoort RT, Coresh J, Simon AL,et al. Change in albuminuria as a surrogate endpoint for progression of kidney disease: a meta-analysis of treatment effects in randomised clinical trials. Lancet Diabetes Endocrinol. 2019;7:128-39. doi:10.1016/S2213-8587(18)30314-0
21. ClinicalTrials.gov. Efficacy and Safety of a GLP-1 Receptor Agonist in Patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD). Identifier: NCT06582875. [accessed Oct 2025] Available at: https://clinicaltrials.gov/study/NCT06582875
22. ClinicalTrials.gov. A Study of Tirzepatide on Renal Oxygenation and Cardio-Renal Outcomes in Patients with Overweight or Obesity and Chronic Kidney Disease. Identifier: NCT04777409. [accessed Oct 2025] Available at: https://clinicaltrials.gov/study/NCT05536804