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Review

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# Anti-obesity medications in people with kidney disease: a review

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Obesity accelerates progression of chronic kidney disease (CKD), worsens cardiovascular risk and limits access to kidney transplantation. This narrative review summarises current evidence for anti-obesity medications in CKD. Traditional therapies provide modest weight loss and carry safety limitations, whereas incretin-based agents, including glucagon-like peptide-1 receptor agonists and the dual GIP/GLP-1 agonist tirzepatide, achieve substantial weight reduction with emerging renal benefits. Evidence remains limited in advanced CKD and dialysis populations.

Obesity is a growing global health challenge with significant implications for individuals living with chronic kidney disease (CKD). The increasing prevalence of obesity has contributed not only to the rising incidence of CKD—through shared risk factors such as type 2 diabetes (T2D) and hypertension—but also to the complexity of its management[1]. In individuals with CKD, obesity exacerbates disease progression, worsens cardiovascular outcomes, and can limit access to kidney transplantation due to weight-related eligibility criteria[2,3,4]. Despite the well-recognised burden of obesity in this population, effective and safe treatment strategies remain underutilised[5].

Pharmacological management with anti-obesity medications (AOMs) has advanced in recent years, particularly with the emergence of incretin-based therapies such as glucagon-like peptide-1 (GLP-1) receptor agonists (GLP-1RAs) and dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 agonists. These agents, originally developed for glycaemic control in T2D, have demonstrated significant weight loss effects in people with or without diabetes[6–8]. Importantly, accumulating evidence from large cardiovascular and kidney outcome trials has demonstrated renoprotective effects alongside substantial weight loss, establishing incretin-based therapies as an attractive option for patients with coexisting obesity and CKD.

However, the use of AOMs in CKD remains complex. Altered pharmacokinetics, reduced renal clearance[9], and limited data in advanced stages of kidney disease—particularly in end-stage renal failure (ESRF)—present significant challenges[10,11]. Moreover, current clinical guidelines offer limited direction on how best to incorporate these therapies into the care of patients with CKD[12,13].

In this narrative review, we will explore the role of AOMs, with a focus on incretin-based therapies, in the management of obesity in people with CKD. It will highlight the burden of obesity in this population, summarise the available evidence for pharmacological treatment options, and discuss the clinical considerations and gaps in knowledge, particularly in those with ESRF.

## Methods

We undertook a focused, non-systematic, narrative review of the literature with searches of the published literature in PubMed (https://pubmed.ncbi.nlm.nih.gov/) and Google Scholar (https://scholar.google.com/) with a broad range of combinations of the medical subject headings (MeSH) terms: "Obesity", "Anti-Obesity Agents", 'Glucagon-Like Peptide 1 Receptor Agonists" AND "Chronic Kidney Disease", "End-Stage Renal Disease", and terms and phrases relevant to this review. To help identify recently published studies, we additionally used OpenEvidence (an AI-assisted literature mapping tool available from https://www.openevidence.com/) as a supplementary screening tool. English language articles retrieved up until March 2026 were included.

Evidence was selected based on its relevance to the scope of this review, with priority given to high-quality evidence including randomised controlled trials, cardiovascular and kidney outcome trials, systematic reviews, meta-analyses, major clinical practice guidelines including *Kidney Disease: Improving Global Outcomes* (KDIGO) and the *American Diabetes Association* (ADA), and landmark observational studies where randomised data were limited. Studies focusing on obesity pharmacotherapy in CKD, renal outcomes of incretin-based therapies, and clinical considerations relevant to patients with CKD or end-stage kidney disease were preferentially included. Case reports, conference abstracts, and studies not directly relevant to the review objectives were generally excluded unless they addressed important safety considerations or populations for whom higher-level evidence was unavailable. As a narrative review, formal quality assessment and risk-of-bias evaluation were not performed.

### Epidemiology of obesity and CKD

The global prevalence of obesity has increased over recent decades, contributing to the growing burden of non-communicable diseases, including CKD. Obesity is now recognised as both a risk factor for the development of CKD and an accelerator of its progression to ESRF. Epidemiological data

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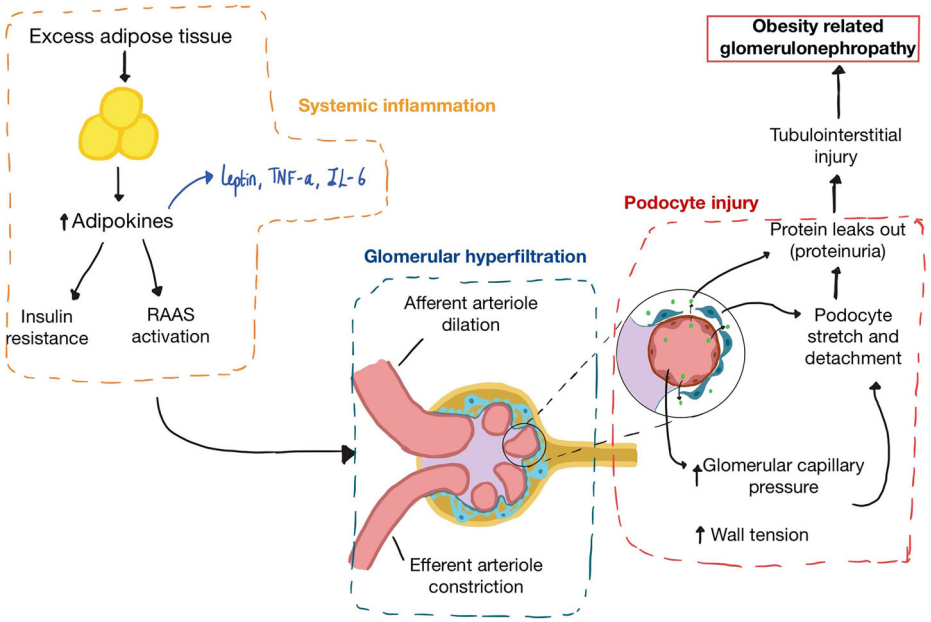


**Fig. 1 | Pathophysiology of Obesity-Related Glomerulopathy (ORG).** Adipose-derived inflammatory mediators promote insulin resistance and RAAS activation, leading to glomerular hyperfiltration and increased intraglomerular pressure. Podocyte stress and detachment result in proteinuria and progressive kidney injury. *TNF-α* tissue necrosis factor-alpha, *IL-6* interleukin 6, *RAAS* renin angiotensin aldosterone system.

suggest that approximately 14–25% of CKD cases in industrialised nations can be attributed directly to overweight and obesity. In the United States, over 42% of adults are classified as living with obesity[14], while in the United Kingdom approximately 29% of adults have obesity and a further 35% are overweight[15]. This high prevalence of obesity places a substantial public health burden with direct implications for CKD incidence and progression[16].

According to the World Health Organization (WHO) criteria, overweight is defined as a body mass index (BMI) of 25–29.9 kg/m², while obesity is defined as a BMI ≥ 30 kg/m²[17]. However, emerging expert consensus—including the 2025 *Lancet Diabetes & Endocrinology* Commission on Clinical Obesity[18]—contends that BMI alone is an insufficient measure of adiposity and health risk. The Commission redefines obesity as a chronic, systemic disease characterised by excess adiposity that causes organ dysfunction and impaired health, and recommends supplementing BMI with measures such as waist circumference, body fat distribution and clinical manifestations of adiposity-related organ dysfunction[18].

Obesity is highly prevalent among individuals with CKD. In the UK, the estimated prevalence of CKD stages 3–5 is around 3–4% of the adult population, with an upward trend in patients requiring renal replacement therapy (RRT)[19]. Up to 60% of individuals with CKD meet criteria for overweight or obesity[1], and among dialysis patients 30–40% are classified as living with obesity depending on region and modality. Importantly, CKD is often underdiagnosed in individuals with obesity, as reduced muscle mass and altered creatinine production may mask declines in estimated glomerular filtration rate (eGFR)[20,21].

Estimating kidney function in individuals with obesity is further complicated by the limitations of creatinine-based eGFR equations. Serum creatinine is influenced by muscle mass rather than total body weight; many individuals with obesity have disproportionate increases in adipose tissue relative to muscle mass, leading to deceptively low creatinine levels and overestimation of kidney function[22]. Additionally, commonly used eGFR algorithms such as the Modification of Diet in Renal Disease (MDRD) equation and CKD Epidemiology Collaboration (CKD-EPI) equation, index GFR to a standard body surface area of 1.73 m²—a convention based on early 20th-century Caucasian cohorts—and may not accurately reflect renal function in individuals with severe obesity or very small body size[23]. This artificial normalisation can mask clinically significant reductions in absolute GFR and result in delayed CKD diagnosis or misclassification of disease severity.

To address these limitations, KDIGO recommends the use of equations based on cystatin C or combined creatinine–cystatin C measurements, which are less influenced by muscle mass and have demonstrated superior accuracy in obese populations[24]. Furthermore, "de-indexing" eGFR by adjusting for actual body surface area is increasingly advocated when estimating drug clearance or determining eligibility for advanced CKD interventions[25]. Failure to account for these methodological issues contributes to under-recognition of CKD in individuals living with obesity and may compromise safe prescribing of renally excreted pharmacotherapies including AOMs.

The mechanisms linking obesity to CKD are both direct and indirect[19]. Obesity induces glomerular hyperfiltration, primarily through afferent arteriolar vasodilation and increased tubular sodium reabsorption, which eventually leads to glomerular injury and proteinuria. Obesity-related glomerulopathy (ORG) is characterised histologically by glomerulomegaly and focal segmental glomerulosclerosis (FSGS), typically in the perihilar region. Additionally, excess adipose tissue contributes to systemic inflammation, oxidative stress, insulin resistance, and activation of the renin-angiotensin-aldosterone system (RAAS) (Fig. 1), all of which contribute to renal damage[26,27].

Obesity further complicates the clinical course of CKD by increasing the risk of cardiovascular disease (CVD)—the leading cause of mortality in CKD and ESRF populations[28]. Adiposity is associated with dyslipidemia, endothelial dysfunction, and elevated levels of inflammatory cytokines, compounding CVD risk. From a practical perspective, obesity also poses challenges in dialysis, such as difficulty with vascular access, suboptimal dialysis clearance, and higher rates of peritonitis in peritoneal dialysis patients.

In the context of kidney transplantation, obesity can be a barrier to access, with many transplant programmes recommending BMI cutoffs of 35–40 kg/m², delaying or excluding otherwise eligible candidates. Obesity is also associated with worse post-transplant outcomes, including wound complications and delayed graft function.

Intriguingly, some studies have described an "obesity paradox" in dialysis populations, where higher BMI is associated with improved short-term survival[29]. This paradox is thought to reflect confounding factors such as higher body fat conferring survival advantage during periods of acute illness; persons with lower BMI may have lost weight due to more severe illness; BMI is an unsatisfactory indicator of body fat; and the paradox may be a statistical anomaly due to collider stratification bias[30]. Despite this, the

**Table 1 | Mechanisms, efficacy, and CKD considerations for commonly used AOMs**

| Drug/Class | Mechanism | Typical Weight Loss | Safety Notes | CKD Considerations |
|---|---|---|---|---|
| Orlistat | Lipase inhibitor | ~3–5% | GI side effects; non-systemic; risk of renal oxalate stones | Poorly tolerated; Risk of hyperoxaluria and renal oxalate stones |
| Naltrexone/Bupropion | Central appetite suppression | ~5–10% | May raise BP; seizure risk | Limited data; avoid in ESRF |
| Phentermine/Topiramate | Sympathomimetic (phentermine) + anticonvulsant (topiramate; enhances GABA, inhibits glutamate, alters taste) | ~10–12% | Cognitive effects; teratogenic | Avoid in ESRF; minimal safety data |
| GLP-1RAs (liraglutide, semaglutide) | Incretin mimetics | ~10–15% | GI effects; possible thyroid C-cell concerns | Fairly safe in CKD; some renoprotective data |
| Tirzepatide | Dual GIP/GLP-1 agonist | Up to ~20% | Similar GI side effects; more potent weight loss | Pharmacokinetics unaffected by renal function; early data promising |
| SGLT2 inhibitors (e.g.dapagliflozin, empagliflozin | Inhibit renal glucose reabsorption | ~2–3% | Genital yeast infections, risk of volume depletion | Strong renal & CV protective effects; effective in CKD even at lower eGFR |

*GLP-1RA* glucagon-like peptide-1 receptor agonist, *GIP* glucose-dependent insulinotropic polypeptide, *GI* gastrointestinal, *BP* blood pressure, *CKD* chronic kidney disease, *ESRF* end-stage renal failure, *CV* cardiovascular, *eGFR* estimated glomerular filtration rate.

long-term adverse consequences of obesity on cardiovascular and renal health are well established.

Taken together, obesity is a modifiable, yet under-addressed risk factor across the CKD spectrum. Its impact on both renal and cardiovascular outcomes highlights the importance of integrating weight management strategies—including pharmacological therapies—into nephrology care pathways.

## Treatment of obesity

The foundations of the management of obesity comprise lifestyle, dietary and behavioural modifications, AOMs, and metabolic/bariatric surgery. Lifestyle modifications are an essential component of obesity treatment. Dietary changes alone or combined with exercise can lead to clinically significant weight loss that can be enhanced further by integrating cognitive behavioural therapy[26]. Whilst lifestyle, dietary and behavioural changes are generally safe, they are complicated by poor sustainability and weight regain in the longer term[31].

## Anti-obesity medications

The pharmacological management of obesity has evolved significantly over the past decade, offering a broader and more effective range of treatment options for individuals in whom lifestyle modification alone is insufficient. For people with CKD, AOMs may facilitate clinically meaningful weight loss while also improving glycaemic control and reducing cardiovascular and kidney disease progression. In particular, sodium–glucose co-transporter-2 (SGLT2) inhibitors and GLP-1RAs have demonstrated robust cardiorenal protection in large randomised clinical trials and are now recommended by major international guidelines including KDIGO and the ADA. Nevertheless, important evidence gaps remain in individuals with advanced CKD and dialysis-dependent kidney failure. Current AOM options include gastrointestinal lipase inhibitors, centrally acting appetite suppressants, combination agents, incretin-based therapies including GLP-1RAs and dual GIP/GLP-1 agonists, and SGLT2 inhibitors (Table 1). Each class of these medications varies in efficacy, safety profile, and renal considerations.

## Orlistat

A gastrointestinal lipase inhibitor, orlistat reduces dietary fat absorption by irreversibly inhibiting pancreatic and gastric lipases. Its non-systemic mechanism—it is not systemically absorbed and is faecally excreted—makes it a theoretically safe option in CKD, including advanced stages, as it does not rely on renal clearance. However, weight loss efficacy is modest ( ≈ 3–5%), and gastrointestinal effects—such as steatorrhea and flatulence—often lead to poor tolerability and adherence[32]. Importantly, orlistat has been linked to enteric hyperoxaluria, whereby fat malabsorption increases intestinal oxalate absorption and may contribute to oxalate-mediated renal injury. Although oxalate nephropathy has primarily been described in case reports, population data demonstrate a higher incidence of acute kidney injury following initiation of orlistat[33], supporting a clinically relevant renal safety signal. Caution is therefore warranted when prescribing orlistat in patients with kidney vulnerability.

## Centrally acting agents

Centrally acting agents induce anorectic and satiating effects via appetite-regulating pathways in the hypothalamus and the mesolimbic reward system. Of currently approved AOMs from this class, the combination product naltrexone/bupropion has demonstrated moderate weight loss efficacy ( ≈ 6–7% over 28–56 weeks) but is associated with potential adverse effects including elevated blood pressure and seizure risk, which are of particular concern in CKD patients who may already be at elevated cardiovascular and neurologic risk[34,35]. Clinical data in individuals with moderate to severe CKD are scarce, and the combination is typically not recommended in ESRF. Due to uncertain cost effectiveness and unknown long-term clinical effectiveness, it is not recommended by the National Institute for Health and Care Excellence

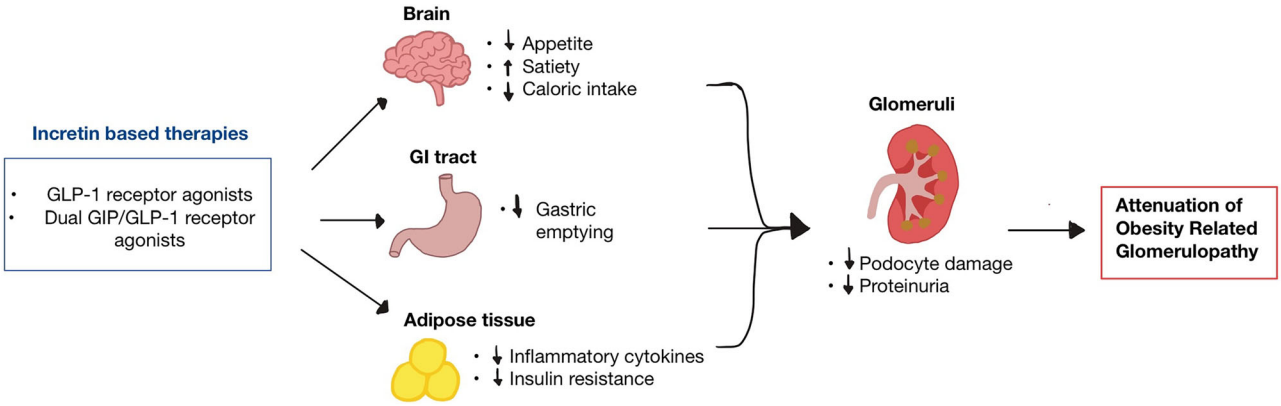


**Fig. 2 | Method of action of incretin based therapies.** Mechanisms of action of incretin-based therapies in obesity-related glomerulonephropathy. GLP-1 receptor agonists and dual GIP/GLP-1 receptor agonists act centrally to reduce appetite and caloric intake, slow gastric emptying, and improve adipose tissue inflammation and insulin resistance. These metabolic effects contribute to reduced podocyte injury and proteinuria, attenuating obesity-related glomerular damage. *GLP-1* glucagon-like peptide-1, *GIP* glucose-dependent insulinotropic polypeptide, *GI tract* Gastrointestinal tract.

(NICE) for clinical use in the publicly-funded National Health Service (NHS) in England[36].

Phentermine/topiramate, another combination product, integrates a sympathomimetic (phentermine) and an anticonvulsant (topiramate) to suppress appetite and prolong satiety. It achieves relatively higher weight loss ( ≈ 10–12%) in the general population but is limited by risks of cognitive impairment, mood changes, and teratogenicity. Furthermore, phentermine's stimulatory effects raise concerns about hypertension and tachycardia, rendering it unsuitable for patients with advanced CKD or cardiovascular disease. It is also not recommended for clinical use by NICE[37].

### SGLT2 inhibitors

By inhibiting sodium–glucose co-transporter-2 in the proximal renal tubules, SGLT2 inhibitors promote urinary glucose excretion and modest reductions in body weight. The average weight loss achieved is ≈2–3 kg, primarily due to caloric loss through glycosuria. Beyond their glycaemic effects, SGLT2 inhibitors reduce intraglomerular pressure, mitigate hyperfiltration, and confer substantial cardiovascular and renal protection, with robust evidence from large outcome trials in people with T2D and CKD[38]. These benefits have led to widespread adoption of SGLT2 inhibitors in nephrology and cardiology guidelines[39]. Importantly, although their efficacy for weight reduction is less pronounced than that of GLP-1RAs or tirzepatide, their proven renoprotective profile and cardiovascular benefits have established SGLT2 inhibitors as an essential component of CKD management. Current FDA (U.S. Food and Drug Administration) prescribing information for empagliflozin does not specify an eGFR threshold for initiation in CKD, although evidence remains limited in patients receiving dialysis[40].

### Incretin-based AOMs

Incretin-based therapies, including GLP-1RAs such as liraglutide and semaglutide, and dual GIP/GLP-1 agonists such as tirzepatide, have emerged as the most effective AOMs to date, achieving average weight loss of up to 20% alongside improvements in glycaemic control and cardiovascular outcomes[26]. Unlike most other AOMs, they have been studied in CKD populations and appear safe for use in moderate renal impairment. Given their unique metabolic and renal benefits, these therapies warrant more detailed examination.

GLP-1RAs function by mimicking the incretin hormone GLP-1, which is released postprandially and enhances glucose-dependent insulin secretion while suppressing glucagon release. They also delay gastric emptying and modulate satiety through central pathways (Fig. 2).

### Liraglutide

Liraglutide was the first GLP-1RA approved specifically for chronic weight management and established the clinical foundation for incretin-based anti-obesity pharmacotherapy. At a dose of 3.0 mg daily, liraglutide produces sustained weight loss of approximately 5–8% and improves glycaemic and cardiometabolic risk markers, as demonstrated in the SCALE programme across populations with and without diabetes[41]. Beyond weight reduction, liraglutide has demonstrated cardiovascular benefit in outcome trials and has been studied in individuals with moderate chronic kidney disease, where it appears safe without the need for dose adjustment[42,43]. These findings positioned GLP-1 receptor agonism as a viable strategy for obesity management and paved the way for newer, more potent incretin-based AOMs.

### Semaglutide

In major trials such as STEP-1[6] and STEP-2[44], semaglutide at doses up to 2.4 mg weekly has consistently produced weight loss of ≈15% in non-diabetic individuals with obesity and ≈10% in individuals with T2D. It has shown similar benefits in the SELECT cardiovascular outcomes study, which reported a 20% reduction in major adverse cardiovascular events among individuals with obesity without diabetes[45].

Beyond weight reduction, several cardiovascular outcome trials of GLP-1RAs including LEADER[42], SUSTAIN-6[46], EXSCEL[47], REWIND[48], and AMPLITUDE-O[49], have collectively demonstrated a 21–22% reduction in composite kidney outcomes—such as macroalbuminuria, sustained eGFR decline, need for renal replacement therapy, or kidney-related death —among patients with T2D[50]. In non-diabetic CKD populations, post-hoc analyses from SUSTAIN 6[13] and the SELECT trial[51] revealed both preservation of eGFR and reductions in albuminuria regardless of baseline CKD stages 1–3.

The FLOW trial[52], focused specifically on diabetic CKD, reinforced these findings by demonstrating that semaglutide reduced the risk of the primary composite kidney outcome by 24%, alongside an 18% reduction in major adverse cardiovascular events (MACE) over a median follow-up of 3.4 years, with consistent benefits across KDIGO-defined risk categories. Semaglutide also slowed the annual eGFR decline by approximately 1.16 mL/min/1.73 $m^2$ and reduced albuminuria by approximately 32%, effects that appeared to exceed what could be explained by blood pressure or glycaemic changes alone[52].

Collectively, these studies provide robust evidence that GLP-1 receptor agonists confer cardiovascular and renal protection in patients with T2D and CKD, culminating in the FLOW trial, which provided the first dedicated randomised evidence of kidney protection with semaglutide. It should be recognised, however, that the renal benefits reported in earlier cardiovascular outcome trials were

derived largely from secondary or exploratory endpoints, with composite outcomes often driven by reductions in albuminuria rather than hard renal endpoints such as kidney failure or dialysis initiation. Furthermore, although the evidence is now strong for patients with CKD stages 3–4, individuals with advanced CKD, dialysis-dependent kidney failure and kidney transplant recipients remain substantially underrepresented in pivotal trials, limiting the generalisability of these findings to these high-risk populations.

### Tirzepatide

A dual GIP/GLP-1 agonist, Tirzepatide delivered greater average weight loss of ≈20% in the SURMOUNT-1[7] and SURPASS-2[53] trials, alongside potent improvements in glycaemic control. Post-hoc analysis from SURPASS-4[54], which enroled high cardiovascular-risk individuals with CKD, documented significant decreases in albuminuria and slower eGFR decline compared to insulin glargine. Moreover, pharmacokinetic studies reveal that tirzepatide does not accumulate in severe renal impairment or dialysis, supporting its safety across CKD stages[55,56].

Meta-analyses aggregating data from over 85,000 participants further affirm that GLP-1RAs significantly reduce the risk of kidney failure ( −16%), worsening renal function ( −22%), cardiovascular events ( −14%), and all-cause mortality ( −13%)—effects consistent across CKD and non-CKD populations[57].

Although tirzepatide has demonstrated greater weight loss and glycaemic improvement than currently available GLP-1RAs, evidence supporting direct renoprotective effects remains comparatively limited. Most renal findings have been derived from secondary analyses of diabetes or obesity trials rather than dedicated kidney outcome studies. Consequently, while early reductions in albuminuria and slower eGFR decline are encouraging, confirmation of long-term renal protection awaits the results of ongoing CKD-specific randomised trials.

### Challenges in obesity management in CKD/ESRF

Despite the established cardiovascular and renal benefits of GLP-1RAs in patients with diabetic CKD, several important uncertainties remain regarding their use in advanced CKD, dialysis-dependent kidney failure and kidney transplant recipients, as these populations have largely been excluded from pivotal clinical trials.

### Altered pharmacokinetics and dosing concerns

Renal impairment can significantly alter drug metabolism and clearance. Although most GLP-1RAs (e.g., liraglutide, dulaglutide, semaglutide) and tirzepatide are primarily catabolised and do not require renal dose adjustments, certain agents such as exenatide demonstrate increased plasma concentrations and reduced clearance in severe CKD and dialysis patients, contraindicating their use in these populations[58].

### Gastrointestinal effects and risk of AKI

Gastrointestinal (GI) side effects such as nausea, vomiting and diarrhoea are common with incretin-based therapies and may lead to volume depletion, increasing the risk of acute kidney injury (AKI) in vulnerable CKD patients[59]. Rare case reports have also associated GLP-1RAs with acute interstitial nephritis, likely immune-mediated, underscoring the need for ongoing renal monitoring[60,61].

### Limited trial data for severe CKD and dialysis

Landmark trials (FLOW, SURPASS-4) predominantly enroled patients with eGFR ≥25–30 mL/min/1.73 m², with under-representation of those with more advanced renal disease or those on dialysis[7,56,62]. Emerging real-world data and small observational studies suggest that tirzepatide is pharmacokinetically stable and metabolically effective in haemodialysis patients[63], yet the lack of randomised evidence limits clear guidance for those with eGFR <30 mL/min.

### Non-pharmacologic limitations: lifestyle and access barriers

Obesity management extends beyond medications. Individuals with CKD often adhere to dietary restrictions—such as low potassium or low phosphate diets—which can conflict with calorie reduction goals. Uremic symptoms and fatigue reduce exercise capacity, while the cost and need for injectable administration pose access barriers, especially in public health systems. Additionally, socioeconomic disadvantage and lack of specialist support may further limit treatment engagement[64–66].

### Clinical considerations and guidelines

Guideline organisations, including KDIGO and the ADA, are now recognising incretin-based therapies as integral to managing T2D, obesity, and CKD. The 2024 KDIGO guideline emphasises lifestyle intervention as the foundation of CKD management, encouraging weight loss in individuals with obesity and identifying an optimal BMI of <27 kg/m² as a treatment target where appropriate[24]. When lifestyle measures alone are insufficient, KDIGO advocates a layered treatment strategy in which GLP-1RAs are recommended as preferred pharmacologic agents—especially in patients with obesity, T2D, and CKD—due to their demonstrated benefits for weight reduction, glycaemic control, and cardiovascular and renal outcomes[67]. Recent expert reviews have further highlighted the evolving evidence base and the need for clearer guidance on the use of GLP-1RAs for obesity in CKD, particularly outside the context of diabetes[68].

### Case vignette

**Patient profile**. A 51-year-old woman with type 2 diabetes and chronic kidney disease stage G3b-A2 due to diabetic nephropathy was referred for weight management in anticipation of potential renal transplantation. Her eGFR was 25 mL/min, urine albumin 32.8 mg/L and urine albumin-to-creatinine ratio (ACR) 8.41 mg/mmol, with a 20% estimated five-year risk of kidney failure. She weighed 136.2 kg (BMI 53.2 kg/m²). As severe obesity precluded kidney transplantation, home haemodialysis was advised as the first-line option when clinically necessary. Medications included insulin glargine and insulin aspart (basal-bolus regimen), atorvastatin, furosemide, sodium bicarbonate, gabapentin and venlafaxine.

**Management**. The patient was commenced on tirzepatide alongside lifestyle and dietary modifications. The dose of tirzepatide was gradually titrated up to a maximum of 15 mg once a week which was well tolerated without any adverse effects. She achieved a significant weight loss (from 137 kg to 102.8 kg) over the course of GLP-1/GIP agonist therapy (Fig. 3).

**Renal outcomes**. There was significant improvement in renal function (from the lowest eGFR of 13 mL/min to 32 mL/min), reduction in albuminuria (urine albumin 47.1 mg/L, urine ACR 5.89 mg/mmol) and a considerable reduction in the risk of kidney failure (decreased to 8% over the next 5 years). The dose of furosemide was reduced to a quarter of her previous dose.

**Extra-renal outcomes**. Weight reduction and renal outcomes were accompanied by improved blood pressure control (135/88 mm Hg at presentation to recent reading of 106/74 mm Hg) and reduction in insulin requirement (HbA1c 105 mmol/mol at presentation to HbA1c 44 mmol/mol); she was gradually taken off insulin.

**Conclusion**. The substantial benefits of tirzepatide therapy in this patient, particularly in terms of weight reduction, glycaemic control, and renal function, has mitigated the need for renal transplantation for the foreseeable future.

The ADA's current Standards of Care similarly endorse GLP-1RAs like semaglutide and tirzepatide in CKD patients, emphasising their multifaceted benefits beyond blood glucose control. In ADA's treatment algorithm, these agents are prioritised for individuals with high cardiovascular

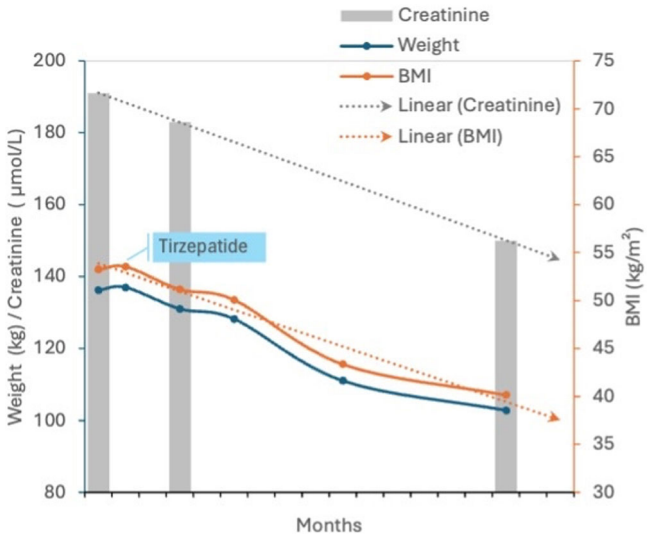


**Fig. 3 | Case vignette.** The patient described in the case vignette was treated with Tirzepatide and achieved significant weight loss accompanied by reduction in serum creatinine. Weight (kg) is depicted by solid blue line, body mass index (BMI, kg/m$^2$) by solid orange line, linear forecast of BMI by broken orange line, serum creatinine (µmol/L) by grey columns and linear forecast of serum creatinine by broken grey line.

or renal risk, regardless of glycated haemoglobin (HbA1c) levels, and are recognised for intentional weight reduction[69]. Both ADA and KDIGO stress the importance of individualised planning in advanced CKD, where pharmacokinetic changes and limited clinical trial evidence necessitate cautious application.

Regulatory approvals worldwide reflect this growing utility: liraglutide, semaglutide and tirzepatide are widely approved for chronic weight management in adults with obesity or overweight with comorbidities. Their use in CKD patients who meet the prescribing criteria aligns with approved indications. However, prescribing these therapies solely for weight loss in non-diabetic individuals with CKD remains off-label in many regions, where licenses are restricted to diabetes or cardiovascular applications—highlighting the importance of clinician awareness regarding local regulatory and reimbursement policies.

Shared decision-making is vital when initiating incretin therapies in patients with CKD. Patients should understand their weight loss potential, cardiac and renal benefits, and risks such as gastrointestinal side effects that may be exacerbated in advanced CKD. Practical considerations—including injectable delivery, dosing schedules, and gradual titration—should be discussed transparently. Additionally, high costs and varying coverage policies often limit access, particularly for those in underserved populations.

Implementation is most effective within a multidisciplinary framework involving nephrology, endocrinology, pharmacy, and dietetics to optimise drug choice, dosing, and monitoring. Initiation should be accompanied by close surveillance of renal function, volume status, and tolerability, particularly in individuals with eGFR below 30 mL/min/1.73 m$^2$[70]. Continuous patient education and support are key to overcoming adherence challenges and achieving treatment goals.

### Future directions

The FLOW trial has substantially strengthened the evidence supporting incretin-based therapies in CKD, marking an important milestone in the field[52]. However, several important questions remain unanswered, and further research is needed to define the role of these agents across the full spectrum of kidney disease. The role of anti-obesity medications in CKD is likely to expand as evidence from ongoing clinical trials becomes available.

The SURPASS programme has provided robust data on tirzepatide. Across these trials, tirzepatide achieved reductions in HbA1c of up to 2.3% and weight loss of nearly 10 kg[71]. In SURPASS-2, tirzepatide was superior to semaglutide for both glycaemic and weight outcomes, while SURPASS-3 demonstrated superiority over insulin degludec[53,72]. Importantly, in SURPASS-4, tirzepatide slowed the annual rate of eGFR decline and reduced urinary albumin-to-creatinine ratio compared with insulin glargine, suggesting possible renoprotective properties[73]. The ongoing SURPASS-CVOT trial will provide further insight into its cardiovascular and renal safety profile[74].

Future directions must also consider populations underrepresented in existing trials, including patients with ESRF and kidney transplant recipients. Preliminary observational studies suggest that incretin-based therapies, including tirzepatide, may be feasible in dialysis settings, but prospective, high-quality evidence is required before widespread adoption[75].

Overall, the strength of evidence varies considerably across incretin-based therapies and CKD populations. Robust randomised trial data now support the use of GLP-1 receptor agonists for cardiovascular and renal protection in patients with T2D and CKD, with semaglutide providing the strongest evidence following publication of the FLOW trial. By contrast, evidence supporting the use of tirzepatide in CKD, particularly among individuals with advanced CKD, dialysis-dependent kidney failure or kidney transplantation, remains comparatively immature and is largely based on subgroup analyses, observational studies and small pilot cohorts. Future studies should therefore prioritise dedicated renal outcome trials and the inclusion of populations traditionally excluded from landmark obesity trials.

Ultimately, the integration of these therapies into nephrology will require an individualised approach, recognising heterogeneity in metabolic risk, comorbidities, and treatment priorities. Addressing gaps in trial representation, ensuring cost-effectiveness, and aligning therapy with patient preferences will be essential to optimising their use in CKD and ESRF populations[26,76].

## Conclusion

Obesity represents a significant and modifiable risk factor in the progression of CKD yet remains under-recognised and undertreated within nephrology. Its contribution to glomerular hyperfiltration, proteinuria, and systemic inflammation, as well as its impact on cardiovascular morbidity and transplant access, highlights the critical importance of effective weight management strategies in the CKD population.

Incretin-based therapies—particularly GLP-1 receptor agonists and dual GIP/GLP-1 receptor agonists—have emerged as promising agents in this domain. Their capacity to induce substantial weight loss, improve glycaemic control, and potentially slow renal decline offers a unique therapeutic opportunity for patients with coexisting obesity and CKD. The evidence to date, drawn from both cardiovascular outcome trials and kidney-specific analyses, suggests that these medications may exert renoprotective effects that extend beyond glucose lowering.

However, the field is still evolving. Many pivotal trials have underrepresented patients with advanced CKD or those on dialysis, leaving important questions about safety, efficacy, and optimal dosing unanswered in these populations. As new data emerge from ongoing studies—including SURPASS-CVOT—there is a need to translate these findings into real-world nephrology practice.

Future research must prioritise the inclusion of diverse CKD populations, explore long-term renal endpoints, and examine outcomes in special groups such as transplant recipients and individuals on renal replacement therapy. Personalised treatment plans that account for comorbidity profiles, treatment goals, and patient preferences will be essential to optimising the use of incretin-based therapies in this high-risk group.

Integrating obesity management into CKD care offers a timely and necessary opportunity to mitigate renal and cardiovascular complications, while improving both clinical outcomes and quality of life in this underserved population.

## Data availability

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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## Author contributions

Nikita.J. developed the search strategy, literature review and led the writing of the manuscript. Neil.J. contributed to development of the manuscript. F.A. prepared the case vignette. A.A.S. conceived the review and supervised the project, including development of the search strategy and oversight of manuscript preparation and revision. All authors contributed to revision of the manuscript and approved the final version.

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## Additional information

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