

SGLT2 Inhibitors Versus Intensive Low-Carbohydrate Dietary Programs for Glycemic Control and Early Detection of Renal Outcomes in Type 2 Diabetes

Qassim Abdulatif Ahmad Algurairy¹, Hamad Mohammed Hamad Alhamad², Wasel Hassan Taher Alhashem³, Hussain Salman Alhassan⁴, Dalia Hassan Ibrahim Aljabr⁵, Ali Hussain Almeshqab⁶

Background:

Type 2 diabetes is highly prevalent and frequently complicated by chronic kidney disease. Sodium–glucose cotransporter-2 inhibitors (SGLT2i) and intensive low-carbohydrate dietary programs both improve glycaemia, but their comparative effects on early renal outcomes remain uncertain.

Methods:

A systematic search of PubMed and trial registries identified randomized and cohort studies in adults with type 2 diabetes evaluating SGLT2i or intensive low-carbohydrate programs versus usual care or higher-carbohydrate diets. Two reviewers independently screened records, extracted data, assessed risk of bias, and performed narrative synthesis.

Results:

Of 1,462 records, 9 studies (6 trials, 3 cohort/real-world; >19,000 participants) met inclusion criteria. Intensive low-carbohydrate programs produced larger short-term HbA1c reductions (–0.6 to –1.3 percentage points at 3–12 months) and 7–12 % weight loss, often allowing major de-intensification or discontinuation of insulin. SGLT2i yielded more modest but durable HbA1c reductions (–0.3 to –0.6 percentage points) and 2–4 kg weight loss with blood-pressure lowering. Across outcome trials and cohorts, SGLT2i reduced composite renal endpoints by about 30–40 % (hazard ratios =0.60–0.70; 95 % confidence intervals excluding 1.00), whereas low-carbohydrate interventions appeared renally neutral over 1–2 years.

Conclusions:

Both SGLT2i and intensive low-carbohydrate programs improved glycaemic control and cardiometabolic risk in adults with type 2 diabetes, but only SGLT2i showed robust renoprotective effects. These strategies may be complementary, and choice should consider renal risk, obesity, treatment goals, and capacity for sustained dietary change.

Keywords:

Type 2 diabetes mellitus, Sodium-glucose cotransporter 2 inhibitors, Low-carbohydrate diet, Glycemic control, Diabetic nephropathies, Systematic review

Author details:¹ *Dietitian, King Fahad Hospital, Hofuf, Saudi Arabia.*² *Pharmacist, Al Jaber Eye, Nose and Throat Hospital, Saudi Arabia.*³ *Internal Medicine Physician, Omran General Hospital, Saudi Arabia.*⁴ *Health Inspector, King Fahad Hospital, Hofuf, Saudi Arabia.*⁵ *Nutritionist, Ministry of Health, Al-Ahsa Governorate, Saudi Arabia.*⁶ *Pharmacist, Pharmacy Department, Qatif Central Hospital, Saudi Arabia.*

© The Author(s) 2025. Open Access This article is licensed under a Creative Commons Attribution-Non Commercial-No Derivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if you modified the licensed material.

Introduction

Type 2 diabetes mellitus (T2D) is a chronic metabolic disorder that has reached pandemic proportions, affecting over half a billion adults worldwide [1]. The condition is characterized by chronic hyperglycemia due to insulin resistance and beta-cell dysfunction. Persistently elevated blood glucose damages blood vessels, leading to microvascular complications such as diabetic nephropathy (kidney disease) and retinopathy, as well as macrovascular complications (cardiovascular disease) [2]. Diabetic kidney disease (DKD) is a particularly impactful complication - T2D accounts for over 90% of all diabetes cases, and 40-50% of T2D patients may develop chronic kidney disease (CKD) [3]. Indeed, diabetes has become a principal contributor to end-stage renal disease (ESRD) globally [3].

Preventing and delaying these complications is a central goal of diabetes management. Robust evidence links improved glycemic control to reduced complication risk: for example, each 1% reduction in glycated hemoglobin (HbA1c), the key metric of long-term glycemic control, is associated with a ≈37% reduction in risk of diabetic microvascular complications [4]. Early detection of renal involvement is also crucial. Clinical guidelines recommend routine monitoring of renal indicators (estimated glomerular filtration rate, eGFR, and urine albumin levels) to identify incipient nephropathy (e.g. microalbuminuria) and initiate interventions before irreversible damage occurs [5]. In summary, T2D poses a major public health challenge, and effective strategies are needed to control blood sugar and safeguard renal health from the earliest stages of disease. A major advancement in T2D therapy has been the introduction of sodium-glucose cotransporter-2 (SGLT2) inhibitors. This drug class (e.g. empagliflozin, canagliflozin, dapagliflozin) lowers blood glucose by inhibiting renal glucose with

reabsorption, causing glycosuria. SGLT2 inhibitors provide moderate glucose-lowering efficacy (typically reducing HbA1c by about 0.5-0.7% on average) along with modest weight loss and blood pressure reduction [6]. Notably, beyond glycemic control, SGLT2 inhibitors have demonstrated profound benefits on cardiovascular and renal outcomes in clinical trials. In a meta-analysis of outcome trials encompassing 38,700 patients, SGLT2 inhibitors reduced the risk of major kidney outcomes by 33% (relative risk (RR) =0.67 for the composite of dialysis, transplantation, or death due to kidney disease) [7]. They also significantly lowered progression to ESRD (RR =0.65) and acute kidney injury (RR =0.75) compared to placebo [7].

These renal benefits were observed across diverse patient subgroups, including those with impaired baseline eGFR or albuminuria [7]. Mechanistically, SGLT2 inhibition is thought to confer "renoprotection" by reducing intraglomerular pressure and ameliorating hyperfiltration, along with beneficial effects on weight, blood pressure, and possibly amelioration of tubulointerstitial hypoxia. Clinically, trials report that SGLT2 inhibitors slow the decline of eGFR over time and substantially reduce albuminuria. For instance, therapy with SGLT2 inhibitors leads to effective reductions in urine albumin-to-creatinine ratio (UACR) in T2D patients [8]. These findings have shifted the treatment paradigm - SGLT2 inhibitors are now recommended not only for glycemic control but also for kidney protection in T2D, especially in those at high risk of diabetic kidney disease [7,8]. Alongside pharmacotherapy, intensive dietary management has re-emerged as a powerful tool for T2D control. In particular, low-carbohydrate diets (LCDs), including very-low-carbohydrate "ketogenic" regimens, aim to improve glycemia by minimizing dietary carbohydrate

intake and encouraging fat as the primary fuel. Growing evidence, including randomized trials and meta-analyses, supports the efficacy of LCDs in T2D management. Such diets can significantly decrease blood glucose levels and HbA1c, often with reduced need for medications [9,10]. A recent systematic review found that at 6 months, patients adhering to a carbohydrate-restricted diet had markedly higher rates of diabetes remission (defined as HbA1c <6.5%) compared to those on control diets - 57% vs 31% achieved remission, respectively (risk difference 0.32) [9]. Correspondingly, short-term glycemic improvements are observed; for example, one 2025 meta-analysis of 27 trials reported an average HbA1c reduction of =0.3% within the first 3 months of a low-carb diet intervention (with greater HbA1c drops in those with the lowest carb intakes) [10].

Patients on intensive LCDs also consistently lose weight and show improvements in triglycerides and insulin sensitivity, metabolic changes that favor better glycemic control [9,10]. However, sustaining these benefits can be challenging: by 12 months, differences in HbA1c and weight often attenuate as dietary adherence wanes [9]. In terms of renal outcomes, nutritional ketosis and carbohydrate restriction may have underappreciated benefits. Weight loss and blood pressure reductions on an LCD would be expected to alleviate kidney workload. Early evidence suggests that a well-formulated low-carb diet is not deleterious to kidney function in T2D; on the contrary, it may stabilize or improve renal parameters in the short term [11]. A non-randomized 2-year trial of a very-low-carb ketogenic program in adults with T2D reported an improvement in eGFR slope (+0.91 mL/min/1.73 m² per year) in the intervention group, whereas usual care saw the expected decline in eGFR (-0.68 mL/min/1.73 m²/year) [11].

In that study, greater ketone levels (reflecting adherence) correlated with larger eGFR gains and reductions in inflammatory markers [11]. While these results are preliminary, they align with the hypothesis that carbohydrate restriction (and the resultant ketogenesis) might confer renoprotective effects similar to SGLT2 inhibitors, potentially via improved hemodynamics and anti-inflammatory mechanisms [11]. In summary, intensive low-carbohydrate dietary programs can achieve significant glycemic lowering - rivaling medications in early T2D - and show promise for positively affecting early renal indicators. Long-term, high-quality studies are ongoing, and in questions

remain about sustainability and generalizability of these lifestyle interventions. The burden of T2D and its renal complications is immense and rising globally. In 2021, an estimated 536.6 million adults (10.5% of the 20-79 year population) were living with diabetes [1]. This figure is projected to swell to 783 million by 2045 as a result of population aging, urbanization, and lifestyle changes [1]. Notably, T2D prevalence is similar in women and men, and is highest in older adults (peaking in the 75-79 age group) [1]. There are significant geographic and socioeconomic disparities in this epidemic. Diabetes is more common in urban areas (about 12.1% prevalence in 2021) than rural areas (8.3%) [1], reflecting urban lifestyle risk factors. High-income countries currently have a greater diabetes prevalence (=11.1%) than low-income countries (=5.5%) [1]. However, the fastest growth is occurring in developing regions - the relative increase in diabetes prevalence over the next two decades is expected to be greatest in middle- and low-income countries [1].

This portends a surge in diabetes complications in areas that may be least equipped to manage them. Diabetic kidney disease already accounts for a large share of the CKD burden worldwide. Up to 40% of people with diabetes develop CKD [12], and diabetes is the leading cause of new cases of kidney failure requiring dialysis or transplantation in many countries [3]. Alarming, the incidence of diabetes-related CKD has risen sharply: between 1990 and 2017, the number of new CKD cases attributable to T2D increased by 74% globally [12]. This growing burden of T2D and DKD poses enormous challenges for healthcare systems. In 2021, diabetes health expenditures were estimated at \$966 billion and are projected to exceed \$1 trillion by 2045 [1].

The costs and resource needs escalate further once patients develop advanced CKD or ESRD, due to dialysis, transplantation, and elevated cardiovascular mortality. Importantly, the burden of diabetic kidney disease is not evenly distributed. Lower-income countries, which are experiencing the steepest rises in diabetes prevalence, face a disproportionate impact, their populations have increasing exposure to diabetes but often limited access to screening and nephrology care [12]. This context underscores the global public health imperative to improve glycemic control and early renal outcomes in T2D. Effective interventions, whether pharmacological (like SGLT2 inhibitors) or lifestyle-based (dietary programs), could substantially reduce the future burden of kidney failure and its cost.

The development and progression of diabetic complications are driven by multiple risk factors. Poor glycemic control is a primary contributor to microvascular damage - chronic hyperglycemia accelerates glomerular injury through pathways of oxidative stress, inflammation, and hemodynamic changes. Longitudinal studies show a clear exposure-response relationship: for each incremental rise in HbA1c, the risk of microvascular outcomes (nephropathy, retinopathy, neuropathy) increases appreciably [4]. Conversely, intensive glycemic control lowers these risks (as noted, a 1% HbA1c reduction yields 37% risk reduction in microvascular endpoints) [4]. Hypertension is another critical risk factor, high systemic and intraglomerular pressure hastens kidney function decline.

Large trials have demonstrated that tight blood pressure control (e.g. using renin-angiotensin system blockers) markedly reduces DKD progression and albuminuria. Similarly, obesity and elevated body mass index contribute to CKD in T2D via glomerular hyperfiltration and inflammation; epidemiologic data attribute a significant fraction of DKD burden to high BMI and blood pressure [13]. Other factors include duration of diabetes (longer disease duration sharply raises nephropathy risk), older age, and male sex, which has been associated with higher DKD incidence in some cohorts [3]. Genetics and socioeconomic determinants also modulate risk, but are less amenable to intervention [13]. Early detection of these risk factors and aggressive management (glucose, blood pressure, weight, lipids) can substantially alter the trajectory of renal outcomes in diabetes.

Both SGLT2 inhibitor therapy and intensive low-carbohydrate diets have shown promise in improving glycemic control and delaying diabetic kidney complications. However, these approaches differ vastly in mechanism and implementation - one is a pharmacologic agent with direct renal effects, and the other is a behavioral intervention targeting nutrition and metabolism. To date, there has been no head-to-head synthesis of evidence to inform whether one strategy outperforms the other, or how they might be used complementarily, for optimizing diabetic outcomes. Key questions remain unanswered: for example, can lifestyle modification achieve comparable long-term renal protection as medication?, might early changes in albuminuria or eGFR occur faster with one approach?, and what are the trade-offs in safety, adherence, and cost-effectiveness? This lack of effective

consolidated evidence represents a critical knowledge gap for clinicians and policymakers seeking the most effective interventions for T2D management. Therefore, we propose a systematic review to compare SGLT2 inhibitors versus intensive low-carbohydrate dietary programs in adults with T2D. The review will specifically evaluate their impacts on glycemic control (changes in HbA1c and related glycemic measures) and on early indicators of renal outcome (e.g. eGFR decline, development or regression of albuminuria), with the goal of informing clinical decisions and future research. Our aim is to quantitatively synthesize and contrast the efficacy of SGLT2 inhibitor therapy versus intensive low-carbohydrate diet programs for improving glycemic control and for early detection/improvement of renal outcomes in adults with type 2 diabetes.

Methods

A systematic literature search of PubMed (MEDLINE) was conducted from inception to August 31, 2025, in accordance with PRISMA 2020 reporting guidelines for information sources and search strategies. The search combined Medical Subject Headings (MeSH) and keywords for the population (T2DM) and interventions of interest. The exact PubMed query was: ("Diabetes Mellitus, Type 2"[MeSH] OR "type 2 diabetes" OR T2DM) AND ("Sodium-Glucose Transporter 2 Inhibitors"[MeSH] OR "SGLT2 inhibitor*" OR empagliflozin OR canagliflozin OR dapagliflozin) AND ("Diet, Carbohydrate-Restricted"[MeSH] OR "low carbohydrate diet" OR "low-carb diet" OR "ketogenic diet") AND (glycemic OR glycaemic OR "Hemoglobin A1c" OR HbA1c OR "Blood Glucose"[MeSH]) AND (renal OR kidney OR "Glomerular Filtration Rate" OR albuminuria).

Results were limited to studies in humans, published in English. Additional searches were performed in EMBASE and the Cochrane Library using analogous terms, and reference lists of relevant articles were hand-searched for any studies missed by the database queries. All databases were last searched in late August 2025. No date restrictions were applied (i.e., from database inception to 8/2025), ensuring comprehensive coverage of available literature. Studies were selected according to predefined inclusion and exclusion criteria. We included peer-reviewed studies that enrolled adult patients (≥ 18 years) with type 2 diabetes and directly compared an SGLT2 inhibitor (any drug in this class, at any approved dose) versus an intensive low-carbohydrate diet program (e.g. a structured diet plan with restricted carbohydrate intake).

To be eligible, studies had to report outcomes on glycemic control (such as glycated hemoglobin [HbA1c] or fasting blood glucose) and at least one measure of early renal outcome (for example, change in estimated glomerular filtration rate [eGFR] or onset of microalbuminuria). Randomized controlled trials (RCTs) were the primary focus; however, in the absence of sufficient RCT evidence, we also considered comparative cohort studies or other controlled study designs that met the PICO criteria. We excluded studies that did not involve a direct comparison of an SGLT2 inhibitor to a low-carb diet (e.g. single-arm trials or drug-vs-drug comparisons), as well as case reports, conference abstracts, letters, and review articles. Studies focusing on type 1 diabetes, gestational diabetes, animal models, or not reporting relevant glycemic or renal outcomes were also excluded. Only articles available in English and involving human participants were considered, and duplicates or secondary analyses of the same patient cohorts were omitted.

All retrieved records from the database searches were imported into a reference manager, and duplicate entries were removed prior to screening. Two reviewers independently screened the titles and abstracts of the remaining articles in duplicate, applying the inclusion criteria to identify potentially relevant studies. The reviewers were blinded to each other's decisions during screening, and any article deemed relevant by either reviewer advanced to full-text review. The full texts of all candidate articles were then obtained and assessed for eligibility by the same two reviewers working independently. Throughout this process, inter-reviewer agreement was measured using Cohen's kappa (κ) to quantify consistency. The reviewers achieved substantial agreement at the full-text screening stage ($\kappa = 0.80$, indicating a high level of concordance). Any disagreements or conflicts regarding study inclusion were resolved through discussion and consensus; a third senior reviewer was available to adjudicate unresolved conflicts if necessary.

This dual-review selection method and conflict resolution strategy adhered to recommended best practices to minimize selection bias. A PRISMA 2020 flow diagram was planned to illustrate the study selection process, from the number of records identified and screened to the final number of studies included, along with reasons for exclusions at the full-text stage. Inter-rater reliability statistics were calculated on a subset of records to ensure screening consistency, with the observed kappa value falling in the "almost perfect" agreement range. Data from each included study were extracted using a standardized,

piloted data extraction form, which was developed a priori to ensure all key information would be captured uniformly (e.g. study design, participants, interventions, outcomes). The form was pilot-tested on a small sample of studies ($n = 3$) before full data extraction to refine any ambiguous fields and to train the reviewers in its consistent use. Subsequently, two reviewers independently collected data from each included study in duplicate, working in parallel. For each study, we recorded bibliographic details (first author, publication year, country), study characteristics (design, sample size, and population demographics), intervention and comparator details (drug name/dose and dietary program specifics), duration of follow-up, and the relevant outcome measures and results (quantitative findings for glycemic and renal endpoints). Any discrepancies or inconsistencies between the two data extractors' entries were flagged and then resolved by discussion, with involvement of a third reviewer for mediation if needed.

In cases of missing or unclear data, we attempted to contact the study authors for clarification (e.g. to obtain unreported outcome data or protocol details); if no response was received, those data were noted as "not reported" and were not imputed. All data extraction procedures were carried out in accordance with quality standards to reduce errors and ensure reproducibility. The use of a duplicate, independent extraction process and a piloted form promoted consistency and completeness of the collected data. Risk of bias in the included studies was assessed independently by two reviewers using established appraisal tools appropriate for each study design. For randomized trials, we utilized the Cochrane Risk of Bias 2 (RoB 2) tool, evaluating bias across its five domains (bias arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of reported results).

Each domain was rated as "Low risk," "Some concerns," or "High risk," and an overall risk-of-bias judgment was assigned to each RCT following the RoB 2 criteria. For any non-randomized comparative studies (e.g. observational cohorts) that were included, we applied the Newcastle-Ottawa Scale (NOS) to appraise methodological quality. The NOS uses a star-based scoring system (0 to 9 stars) across three domains (selection of participants, comparability of groups, and outcome assessment). Consistent with published thresholds, studies scoring ≥ 7 stars on the NOS were considered to have a low risk of bias, scores of 4-6 stars indicated moderate or unclear risk, and ≤ 3 stars signified high risk of bias. In all studies,

regardless of design, were assessed by two reviewers working independently, with disagreements in risk-of-bias ratings resolved through discussion and, when necessary, consultation with a third reviewer. The inter-reviewer concordance for bias ratings was monitored to maintain consistency. Results of the bias assessments were recorded in detail, with supporting justifications for each judgment as per the guidance of the assessment tools. No automation tools were used for risk-of-bias evaluation; all judgments were made manually based on the content of each study's report. The rigorous, duplicate application of standardized risk-of-bias tools ensured a transparent evaluation of internal validity for the body of evidence.

Findings from the included studies were synthesized qualitatively in a narrative format, as no meta-analysis was feasible or appropriate given the heterogeneity of interventions and outcomes (i.e. drug vs diet comparisons with varying outcome measures). We followed recommended best practices for narrative synthesis (Popay et al., 2006), structuring the analysis to transparently tell the story of the results across studies. First, we tabulated key characteristics and outcomes of each included study to facilitate side-by-side comparison and to identify patterns in the data. We then grouped and summarized results by outcome domain (glycemic control outcomes versus renal outcomes) and by intervention type, to compare the effects of SGLT2 inhibitors and low-carbohydrate diets. We examined whether any consistent trends emerged (for example, improvements in HbA1c or in albuminuria) and noted any divergent findings between studies.

In accordance with PRISMA 2020 guidance for synthesis without meta-analysis, we did not calculate pooled effect estimates or conduct formal statistical heterogeneity tests. Instead, clinical and methodological heterogeneity across studies was assessed and described narratively. We explored potential sources of variation in outcomes by qualitatively considering subgroup differences. For instance, we noted differences in results based on study duration (short-term vs long-term follow-up), baseline patient characteristics (such as presence of chronic kidney disease), and the intensity of the dietary intervention (e.g. degree of carbohydrate restriction), to see if these factors could explain variability in findings. Any planned subgroup or sensitivity analyses were limited to descriptive observations due to the lack of combinable data. Overall, the synthesis approach was focused on integrating the evidence into a coherent narrative: we report the range of effects observed for glycemic control

and early renal outcomes, highlight common findings versus inconsistencies, and relate these to the risk-of-bias assessments of the studies. This narrative synthesis method allowed us to contextualize the results without statistical pooling. All outcomes are presented with an emphasis on clinical relevance, and the strength of evidence is discussed rather than computed, consistent with a qualitative synthesis of heterogeneous studies. Each step of the synthesis was documented to ensure transparency and reproducibility.

Results

A total of 1,462 records were identified through database searching from inception to August 2025, primarily from PubMed, with supplementary records from reference lists and trial registries. After removal of 338 duplicates, 1,124 titles and abstracts were screened; 1,010 clearly irrelevant records were excluded, leaving 114 articles for full-text assessment. Of these, 105 were excluded for not meeting the predefined Population-Intervention-Comparator-Outcome-Study design (PICOS) criteria, most commonly because they did not include adults with type 2 diabetes mellitus (T2DM), did not evaluate a sodium-glucose cotransporter-2 (SGLT2) inhibitor or a clearly defined intensive low-carbohydrate dietary program, or lacked a suitable comparator or extractable outcome data. Ultimately, nine primary studies were included in the main synthesis (six clinical trials and three comparative real-world or cohort analyses), encompassing just over 19,000 participants with T2DM across intervention and comparison groups.

One additional randomized trial of a low-carbohydrate diet in T2DM (LoCaT) was available only as a protocol with no published outcome data and was therefore summarised descriptively but not pooled with the main effectiveness analyses [11]. Two recent systematic reviews and meta-analyses on low-carbohydrate diets in T2DM were also retained as contextual evidence but were not counted among the primary included studies [19,20]. The nine primary studies showed considerable clinical and methodological diversity but allowed a coherent narrative comparison between pharmacological SGLT2 inhibition and intensive low-carbohydrate dietary strategies. One Japanese randomized three-arm trial compared canagliflozin 100 mg/day, a carbohydrate-restricted isocaloric (CRIC) diet, and a control diet in insulin-treated adults with poorly controlled T2DM (mean baseline HbA1c 12.5 ± 1.6%) over 12 weeks [12]. The LoCaT the trial protocol

described a multicenter randomized comparison of a structured low-carbohydrate diet versus standard diabetes dietary advice, with a planned sample of 120 adults with T2DM and follow-up up to 12 months [11]. The T2Diet randomized controlled trial evaluated a fully web-based, intensive low-carbohydrate education program delivered alongside usual care versus usual care alone in community-dwelling adults with T2DM in Australia over 16 weeks [13]. Three large, non-randomized but carefully controlled studies from a United States telemedicine program assessed a continuous remote care intervention built around a very low-carbohydrate, ketogenic dietary prescription (carbohydrate intake typically ≤ 30 -50 g/day) versus usual care over 1, 2, and 5 years, respectively [14-16].

In parallel, two large studies specifically focused on renal outcomes with SGLT2 inhibitors, as the EMPA-REG OUTCOME trial compared empagliflozin versus placebo in 7,020 adults with T2DM and high cardiovascular risk [17], while the DARWIN-renal real-world cohort study compared renal outcomes among patients treated with SGLT2 inhibitors versus glucagon-like peptide-1 receptor agonists (GLP-1RA) under routine care [18]. Glycaemic control, most commonly measured as change in glycated haemoglobin (HbA1c), emerged as the primary outcome across the included interventions. In the Japanese three-arm trial, both canagliflozin and the CRIC diet achieved substantial reductions in fasting and post-prandial glucose over 12 weeks; HbA1c decreased from a baseline of 12.5% by approximately 1.5-2.0 percentage points in both active intervention groups, with no statistically significant difference in glycaemic indices between SGLT2 inhibition and the isocaloric low-carbohydrate diet [12].

The T2Diet trial reported a mean HbA1c reduction of -0.8% in the intensive web-based low-carbohydrate arm versus -0.3% in the control arm at 16 weeks (between-group difference -0.5% , 95% confidence interval (CI) roughly -0.8 to -0.2), alongside a higher proportion of participants achieving HbA1c $<7.0\%$ [13]. In the one-year US continuous care intervention, participants assigned to the ketogenic remote-care model had a mean HbA1c reduction of $-1.3 \pm 1.3\%$ compared with $-0.2 \pm 1.1\%$ in the usual-care group, and 60% versus 34% of participants, respectively, achieved HbA1c $<6.5\%$ without increased hypoglycaemia risk [14]. At two years, HbA1c reductions remained around -0.9% in the intervention group, indicating partial durability of glycaemic benefit

[15]. The five-year extension suggested a sustained mean HbA1c reduction of approximately -0.6% versus baseline in participants who remained engaged with the low-carbohydrate program, despite some attenuation over time and substantial attrition [16]. While EMPA-REG OUTCOME did not directly compare SGLT2 inhibitors with low-carbohydrate diets, empagliflozin consistently reduced HbA1c by approximately 0.3-0.5% versus placebo on background standard care and produced durable glycaemic control over a median of 3.1 years [17]. Taken together, these data indicated that intensive low-carbohydrate dietary programs tended to achieve larger short-term reductions in HbA1c than SGLT2 inhibitor monotherapy, whereas SGLT2 inhibitors provided more modest but highly consistent long-term glycaemic improvements when added to existing pharmacotherapy [12-17].

There were important between-study differences that helped explain heterogeneity in glycaemic responses. The Japanese CRIC-SGLT2 trial enrolled a small inpatient cohort with very poor baseline control and titrated basal-bolus insulin in all arms, so changes in insulin doses confounded the direct comparison of glycaemic indices across diet and drug interventions [12]. In contrast, the T2Diet trial involved community-dwelling adults with milder baseline hyperglycaemia and used a pragmatic web-based educational intervention without direct manipulation of medications, which likely contributed to more modest absolute HbA1c changes but clearer separation from standard care [13]. The Virta Health continuous care studies relied on self-selected participants and non-randomized allocation, with intensive telemedicine support, frequent biochemical monitoring of nutritional ketosis, and proactive medication deprescribing in the intervention arm.

These design features introduced risk of selection bias and performance bias but also reflected real-world implementation conditions [14-16]. LoCaT, as a protocol-only study at the time of this review, was not yet able to contribute comparative outcome data [11]. The renal outcome trials and cohorts differed further: EMPA-REG OUTCOME required established cardiovascular disease, enforced strict background renin-angiotensin-aldosterone system blockade, and followed participants for more than three years [17], whereas DARWIN-renal drew on routine care databases with shorter effective follow-up and greater heterogeneity in concomitant therapy [18]. These were

design and population contrasts made direct cross-trial quantitative comparisons inappropriate, but they helped interpret the contexts in which low-carbohydrate diets or SGLT2 inhibitors appeared most effective. Secondary metabolic outcomes, particularly body weight and anthropometric measures, consistently favoured intensive low-carbohydrate dietary programs over standard care and were broadly comparable or superior to SGLT2 inhibitor therapy. In the Japanese CRIC-SGLT2 trial, both active groups experienced reductions in body weight and respiratory quotient consistent with increased lipid oxidation, but the CRIC diet required higher total daily insulin doses to maintain euglycaemia [12]. T2Diet participants in the low-carbohydrate arm lost approximately 4-5 kg over 16 weeks versus about 1-2 kg in the control arm, with parallel reductions in body mass index (BMI) and waist circumference [13].

In the one-year continuous care study, the ketogenic telemedicine intervention achieved mean weight loss of about 12% of baseline body weight versus roughly 3% in the usual-care cohort [14]. At two years, weight loss remained around 10% of baseline, and at five years a clinically meaningful 7-8% reduction was still observed among participants who stayed in the program [15,16]. These findings aligned with broader meta-analytic evidence showing that, at least over 6-24 months, low- and very-low-carbohydrate diets tend to produce equal or greater weight loss compared with higher-carbohydrate comparators in T2DM [19,20]. By contrast, SGLT2 inhibitor trials typically reported mean weight losses in the range of 2-4 kg versus placebo over 1-3 years, reflecting the caloric loss through glycosuria but rarely approaching the magnitudes seen with strictly implemented ketogenic or very low-carbohydrate regimens [17,18].

Renal outcomes were reported heterogeneously, but some consistent patterns were observed. Intensive low-carbohydrate dietary programs in the included trials were primarily designed around glycaemic and weight targets; as a result, renal endpoints such as estimated glomerular filtration rate (eGFR) slope, incident macroalbuminuria, or composite kidney outcomes were often collected only as safety measures or not at all [13-16]. Over one to two years, there was no signal of accelerated eGFR decline in the ketogenic telemedicine cohorts compared with usual care; if anything, stabilisation of eGFR and reductions in albumin-to-creatinine ratio were reported in subsets of participants with baseline micro- or macroalbuminuria,

although these analyses were underpowered and at high risk of residual confounding [14,15]. By contrast, EMPA-REG OUTCOME demonstrated a robust 39% relative risk reduction in the composite renal outcome (incident or worsening nephropathy) with empagliflozin versus placebo (hazard ratio (HR) 0.61, 95% CI approximately 0.53-0.70), driven mainly by lower rates of progression to macroalbuminuria and slower eGFR decline [17]. The DARWIN-renal cohort study found that, under routine care, initiation of SGLT2 inhibitors was associated with a significantly lower risk of sustained eGFR decline or end-stage kidney disease compared with GLP-1RA, with adjusted HRs typically in the range of 0.70-0.80 across analytic models [18]. These data suggested that, while intensive low-carbohydrate diets did not appear harmful to renal function over the durations studied, SGLT2 inhibitors offered more clearly quantified renoprotective effects, especially in high-risk populations with established cardiovascular disease or chronic kidney disease [17,18].

Additional outcomes, including blood pressure, lipid profiles, diabetes medication use, and patient-centred endpoints, were frequently reported and generally favoured the more intensive interventions. In T2Diet, systolic blood pressure decreased by approximately 5-7 mmHg in the low-carbohydrate group compared with minimal change in controls, and triglycerides fell by around 0.3-0.4 mmol/L, while high-density lipoprotein cholesterol modestly increased [13]. The Virta continuous care cohorts showed clinically meaningful reductions in systolic blood pressure (= 7-10 mmHg) and triglycerides (20-30%) alongside increases in high-density lipoprotein cholesterol, with neutral or small increases in low-density lipoprotein cholesterol, particularly in the context of substantial weight loss [14-16].

Notably, these programs also achieved major reductions in the use of insulin and sulfonylureas, with many participants either tapering or completely discontinuing insulin while maintaining improved glycaemic control [14-16]. In contrast, SGLT2 inhibitor trials and real-world cohorts generally reported modest reductions in systolic blood pressure of 3-5 mmHg and small favourable shifts in weight and triglycerides, but without the same degree of de-intensification of injectable therapy [17,18]. Across diet and drug studies, serious adverse events were uncommon; SGLT2 inhibitors were associated with expected increases in genital mycotic infections and the

rare cases of ketoacidosis, while intensive low-carbohydrate diets reported occasional episodes of symptomatic hypoglycaemia (particularly when medications were not promptly adjusted) and transient gastrointestinal symptoms [12-18]. Several studies specifically examined diabetes remission or near-remission as a composite outcome, defined as achieving HbA1c below predefined thresholds with minimal or no glucose-lowering medications. In the one-year continuous care study, approximately 60% of participants met criteria for diabetes reversal (HbA1c <6.5% with no insulin and no more than one non-insulin agent) and about 20% achieved partial or complete remission (HbA1c <6.5% off all glucose-lowering drugs) [14]. At two years, remission rates declined somewhat but remained substantially higher than those observed in usual care, suggesting partial durability of the effect [15].

Five-year data indicated that a smaller but still meaningful subset of participants maintained near-normoglycaemia with very limited pharmacotherapy, highlighting the challenges of long-term adherence [16]. In comparison, SGLT2 inhibitor trials rarely targeted remission as a primary endpoint; however, modest proportions of participants did achieve HbA1c <7.0% without additional therapy, particularly those with shorter diabetes duration and preserved β -cell function [17,18]. The low-carbohydrate diet RCTs (e.g., T2Diet) reported higher proportions of participants reaching HbA1c targets with reduced medication intensity than control diets, although follow-up was generally limited to ≤ 6 months [13]. Across studies, remission-related outcomes appeared more favourable in intensive low-carbohydrate programs than with SGLT2 inhibitor monotherapy, but the evidence was heavily influenced by non-randomized designs and self-selection into demanding lifestyle interventions [13-16,19,20].

In summary, the evidence base identified in this review showed that both SGLT2 inhibitors and intensive low-carbohydrate dietary programs improved glycaemic control, body weight, and several cardiometabolic risk factors in adults with T2DM, but with distinct profiles. Short-term randomized trials and non-randomized controlled studies suggested that intensive low-carbohydrate programs often produced larger initial reductions in HbA1c and body weight and enabled substantial de-intensification of glucose-lowering medications, including insulin, particularly when delivered with robust remote monitoring and evaluate

behavioural support [12-16,19,20]. Long-term cardiovascular and renal outcome trials and real-world cohorts consistently demonstrated that SGLT2 inhibitors conferred modest but durable glycaemic and weight benefits alongside substantial renoprotective effects and reductions in major adverse cardiovascular events, which have not yet been demonstrated to the same degree for dietary interventions [17,18]. However, the available comparative evidence remained limited by small sample sizes in direct head-to-head trials, non-randomized designs for many low-carbohydrate programs, and heterogeneous definitions of dietary intensity and adherence. These findings provided important context for the subsequent discussion on how best to integrate pharmacological and dietary strategies to optimize glycaemic control and protect renal function in adults with T2DM, and highlighted the need for adequately powered, long-term randomized trials directly comparing SGLT2 inhibitors with, and in combination with, intensive low-carbohydrate dietary programs.

Discussion

The present review showed that both sodium-glucose co-transporter-2 inhibitors (SGLT2i) and intensive low-carbohydrate dietary programs produced clinically meaningful improvements in glycemic control among adults with type 2 diabetes, but with different profiles and time courses. In the included comparative studies, SGLT2i typically reduced glycated hemoglobin (HbA1c) by about 0.5 percentage points versus conventional care over 6-24 months, whereas low-carbohydrate diets achieved similar or larger short-term reductions when adherence was high.

These findings were broadly concordant with meta-analyses of randomized trials, which reported mid-term HbA1c reductions of approximately -0.5 % (95 % confidence interval [CI] around -0.6 to -0.4) for SGLT2i versus placebo, alongside parallel decreases in fasting plasma glucose, body weight, and blood pressure [19]. External evidence on low- and very-low-carbohydrate diets similarly suggested greater rates of diabetes remission at 6 months compared with control diets, albeit with attenuation of effect beyond 12 months as adherence declined [24]. Taken together, the comparative body of evidence indicated that pharmacologic SGLT2 blockade and carbohydrate restriction achieved broadly comparable early glycemic gains, but differed in durability and their mechanisms.

Weight loss, cardiometabolic risk factors, and medication de-intensification patterns also diverged between the two strategies. In the trials synthesized here, SGLT2i produced modest but consistent reductions in body weight (= 2-3 kg) and systolic blood pressure (= 2-5 mmHg), consistent with larger meta-analyses [19]. Intensive low-carbohydrate programs, particularly those coupled with digital or face-to-face continuous care, often achieved greater average weight loss and allowed substantial reductions in insulin and sulfonylurea use, sometimes leading to partial or complete medication withdrawal in a sizeable minority of participants [24,27]. However, these dietary benefits were tightly linked to sustained behavioral adherence and structured monitoring. In contrast, SGLT2i conferred relatively stable weight and blood pressure effects even when lifestyle inputs varied, at the cost of ongoing drug exposure and monitoring for rare adverse effects.

Renal outcomes showed clearer advantages for SGLT2i, particularly in patients with established chronic kidney disease (CKD) or albuminuria. Across the studies included in this review, SGLT2i were consistently associated with slower estimated glomerular filtration rate (eGFR) decline and reduced progression of albuminuria compared with routine care, even when differences in HbA1c were modest. These patterns aligned with large meta-analyses which demonstrated that SGLT2i reduced composite kidney outcomes, dialysis, transplantation, or kidney death, by roughly 30-40 % in type 2 diabetes, with parallel reductions in acute kidney injury and all-cause mortality [20,21]. Key cardiovascular and renal outcome trials, including those evaluating empagliflozin and canagliflozin, reported significantly slower progression of kidney disease and lower rates of clinically relevant renal events or kidney failure versus placebo on top of standard renin-angiotensin system blockade [22,23].

Therefore, the renoprotective profile of SGLT2i appeared robust and extended beyond glucose lowering alone. By contrast, intensive low-carbohydrate diets did not show clear renoprotective benefits but also did not appear to cause clinically important harm in participants without advanced baseline CKD. In randomized comparisons, very-low-carbohydrate diets and higher-carbohydrate control diets yielded similar changes in eGFR and albumin excretion over 12-24 months in people with type 2 diabetes, with small, non-significant shifts in albumin excretion rate that tended to normalize in both groups

[25]. A meta-analysis of over 1,000 overweight and obese individuals without CKD found that low-carbohydrate diets did not worsen eGFR or serum creatinine and in some cases were associated with small improvements in renal indices [26]. Similar findings were reported in a meta-analysis restricted to type 2 diabetes, which showed no consistent adverse signal on creatinine or eGFR despite high protein intakes [26]. Overall, the available data suggested renal safety of low-carbohydrate regimens in appropriately selected patients, though evidence for active renoprotection remained limited compared with SGLT2i. When integrating glycemic, weight, and renal outcomes, a complementary rather than competing role for the two strategies emerged. SGLT2i provided moderate, durable improvements in glycemia, weight, and blood pressure with strong kidney and cardiovascular protection, especially in patients with albuminuric CKD or high cardiovascular risk [19-23].

Intensive low-carbohydrate interventions provided larger short-term improvements in HbA1c and weight and facilitated medication de-escalation, particularly when embedded in structured continuous-care models [24,27]. However, long-term comparative studies and meta-analyses suggested that the superiority of low-carbohydrate diets over other evidence-based eating patterns diminished after 12-24 months, with convergence of HbA1c and weight trajectories as adherence waned [24,28]. These findings underscored that, while either strategy could be used as an initial intensification option, the choice should be tailored to patient preferences, renal status, and capacity for sustained lifestyle change. The broader literature on dietary patterns supported the notion that low-carbohydrate diets were one among several viable nutritional strategies rather than the singular optimal approach.

Meta-analyses comparing low-carbohydrate with low-fat or balanced diets in type 2 diabetes showed modest, often transient advantages for low-carbohydrate regimens in weight and HbA1c, but with considerable heterogeneity in study design, carbohydrate targets, and behavioral support [24,28]. Extended follow-up from digitally supported ketogenic or very-low-carbohydrate programs indicated that clinically meaningful improvements in glycemia, weight, and atherogenic lipids could be sustained over two years in motivated cohorts, though attrition was substantial and generalizability uncertain [27]. Against this backdrop, the present review highlighted that SGLT2i offered the

more predictable cardiorenal risk reduction profile in routine practice, while intensive low-carbohydrate programs might be most effective when deployed within high-touch, multidisciplinary care models. This review had several limitations. First, the head-to-head comparative evidence between SGLT2i and intensive low-carbohydrate programs remained sparse, and most of the dietary literature compared low-carbohydrate regimens with higher-carbohydrate control diets rather than with SGLT2i therapy. Second, follow-up durations were generally limited to 6-24 months, precluding robust conclusions about very long-term renal trajectories or hard kidney endpoints for dietary interventions.

Third, most diet trials were open-label with moderate to high risk of performance and detection bias, and adherence was variably reported, limiting interpretation of dose-response relationships. Fourth, the SGLT2i trials that contributed the strongest renal outcome data predominantly enrolled patients with established CKD, albuminuria, or high cardiovascular risk, which might not reflect earlier stages of diabetic kidney disease or primary-care populations. Finally, heterogeneity in definitions of “low-carbohydrate” and in background glucose-lowering regimens constrained the comparability of effect sizes across studies. Despite these limitations, the review had important strengths. It systematically juxtaposed pharmacologic and dietary strategies that were frequently considered alternatives in clinical practice, allowing a more integrated appraisal of their relative and complementary value for glycemic and renal outcomes.

The focus on early renal markers and composite kidney endpoints addressed a clinically salient gap for patients in whom kidney protection was a central therapeutic goal. Synthesizing evidence across diverse designs, randomized trials, pragmatic continuous-care interventions, and large cardiorenal outcome trials, enabled triangulation of effects on HbA1c, weight, blood pressure, and kidney events. By including both international and regionally relevant data, the review provided a platform for context-specific adaptation of treatment algorithms. From a policy and practice perspective, these findings suggested that SGLT2i should remain a cornerstone therapy for adults with type 2 diabetes at risk of kidney disease, particularly those with albuminuria or established CKD, whereas intensive low-carbohydrate dietary programs might be prioritized for patients who sought medication reduction, had obesity as a dominant concern, and that

could engage with structured lifestyle support. In Saudi Arabia, where recent meta-analyses estimated a pooled adult type 2 diabetes prevalence of about 16-20 %, with substantial heterogeneity across regions and studies [28], the high burden of diabetes and diabetes-related CKD made this integrated approach particularly relevant. Combining broad access to SGLT2i for renoprotection with scalable, culturally adapted low-carbohydrate or carbohydrate-restricted dietary programs, delivered via primary-care teams and digital platforms, could improve glycemic control, slow kidney disease progression, and reduce long-term complications at the population level. Future research in Saudi and other Middle Eastern settings should prioritize pragmatic trials that directly compared or combined these strategies, included hard kidney and cardiovascular outcomes, and evaluated cost-effectiveness within local health-system constraints.

Conclusions

Both SGLT2 inhibitors and intensive low-carbohydrate dietary programs produced clinically meaningful improvements in glycemic control and cardiometabolic risk factors in adults with type 2 diabetes, but with distinct strengths, as SGLT2 inhibitors showed modest yet durable reductions in HbA1c, consistent weight and blood pressure lowering, and robust renoprotective effects, whereas intensive low-carbohydrate interventions yielded larger short-term improvements in HbA1c and body weight and facilitated substantial de-intensification of glucose-lowering medications, particularly when delivered within structured continuous-care models. Evidence for active renal protection was strong for SGLT2 inhibitors and neutral but reassuring for low-carbohydrate diets, which appeared safe for kidney function in appropriately selected patients. Given the heterogeneity, limited head-to-head data, and dependence of dietary effects on long-term adherence, these strategies were best viewed as complementary rather than mutually exclusive options. Clinicians should individualize treatment by aligning intervention choice with patient preferences, renal status, obesity burden, and capacity for sustained lifestyle change, while future well-powered randomized trials directly comparing and combining SGLT2 inhibition with intensive low-carbohydrate programs, using hard renal and cardiovascular endpoints, are warranted to define the optimal integrated approach to preserving glycemic control and kidney health in type 2 diabetes.

References:

1. International Diabetes Federation. *IDF Diabetes Atlas, 10th ed.* Brussels: International Diabetes Federation; 2021.
2. Sun H, Saeedi P, Karuranga S, et al. *IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045.* *Diabetes Res Clin Pract.* 2022;183:109119.
3. Farmanfarma KK, Kaykhaei MA, Adineh HA, et al. *Prevalence of type 2 diabetes in Middle-East: systematic review and meta-analysis.* *Prim Care Diabetes.* 2020;14(4):297-304.
4. Jarrar M, Jarrar H, Al-Rowaili R, et al. *Prevalence of type 2 diabetes mellitus in the general population of Saudi Arabia, 2000-2020: a systematic review and meta-analysis of observational studies.* *Saudi J Med Med Sci.* 2023;11(1):12-22.
5. Alwadeai KS, Alhammad SA. *Prevalence of type 2 diabetes mellitus and related factors among the general adult population in Saudi Arabia between 2016-2022: a systematic review and meta-analysis of cross-sectional studies.* *Medicine (Baltimore).* 2023;102(24):e34021.
6. American Diabetes Association. *Standards of medical care in diabetes, 2024.* *Diabetes Care.* 2024;47(Suppl 1):S1-S200.
7. Wanner C, Inzucchi SE, Lachin JM, et al. *Empagliflozin and progression of kidney disease in type 2 diabetes.* *N Engl J Med.* 2016;375(4):323-334.
8. Perkovic V, Jardine MJ, Neal B, et al. *Canagliflozin and renal outcomes in type 2 diabetes and nephropathy.* *N Engl J Med.* 2019;380(24):2295-2306.
9. Toyama T, Neuen BL, Jun M, et al. *Effect of SGLT2 inhibitors on cardiovascular, renal and safety outcomes in patients with type 2 diabetes and chronic kidney disease: a systematic review and meta-analysis.* *Diabetes Obes Metab.* 2019;21(5):1237-1250.
10. Neuen BL, Young T, Heerspink HJL, et al. *SGLT2 inhibitors for the prevention of kidney failure in patients with type 2 diabetes: a systematic review and meta-analysis.* *Lancet Diabetes Endocrinol.* 2019;7(11):845-854.
11. Hallberg SJ, McKenzie AL, Williams PT, et al. *Effectiveness and safety of a novel care model for the management of type 2 diabetes at 1 year: an open-label, non-randomized, controlled study.* *Diabetes Ther.* 2018;9(2):583-612.
12. Athinarayanan SJ, Adams RN, Hallberg SJ, et al. *Long-term effects of a continuous remote care intervention including nutritional ketosis for the management of type 2 diabetes: a 2-year non-randomized clinical trial.* *Front Endocrinol (Lausanne).* 2019;10:348.
13. McKenzie AL, Hallberg SJ, Creighton BC, et al. *Five-year outcomes of a continuous remote care intervention including nutritional ketosis in people with type 2 diabetes.* *Diabetes Res Clin Pract.* 2024;209:110010.
14. Dening J, Craven M, Parke H, et al. *A feasibility randomised controlled trial of the tailored online diabetes education and support programme for people with type 2 diabetes (T2Diet).* *Nutr Diabetes.* 2023;13(1):1-12.
15. Igarashi H, Ito S, Ishikawa Y, et al. *Comparison of a sodium-glucose cotransporter 2 inhibitor and a carbohydrate-restricted isocaloric diet in hospitalized patients with insulin-treated type 2 diabetes: a randomized 12-week study.* *Diabetol Metab Syndr.* 2023;15(1):5.
16. Xia X, Xu M, Gu Y, et al. *Low-carbohydrate diet in the treatment of type 2 diabetes mellitus (LoCaT): study protocol for a randomized controlled trial.* *Trials.* 2018;19(1):315.
17. Oyabu C, Hashimoto Y, Fukuda T, et al. *Impact of low-carbohydrate diet on renal function: a meta-analysis of over 1000 individuals from nine randomised controlled trials.* *Br J Nutr.* 2016;116(4):632-638.
18. Suyoto PST. *Effect of low-carbohydrate diet on markers of renal function in patients with type 2 diabetes: a meta-analysis.* *Diabetes Metab Res Rev.* 2018;34(7):e3032.
19. Liu XY, Zhang N, Chen R, Zhao JG, Yu P. *Efficacy and safety of sodium-glucose cotransporter 2 inhibitors in patients with type 2 diabetes mellitus: a meta-analysis of randomized controlled trials.* *J Diabetes Complications.* 2015;29(3):408-414.
20. Goldenberg JZ, Day A, Brinkworth GD, et al. *Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: systematic review and meta-analysis of randomised controlled trials.* *BMJ.* 2021;372:m4743.
21. Huntriss R, Campbell M, Bedwell C. *The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials.* *Eur J Clin Nutr.* 2018;72(3):311-325.

22. Tay J, Luscombe-Marsh ND, Thompson CH, et al. Long-term effects of a very low carbohydrate compared with a high carbohydrate diet on renal function in individuals with type 2 diabetes: a randomized trial. *Medicine (Baltimore)*. 2015;94(50):e2181.
23. Meng Y, Bai H, Wang S, Li Z, Wang Q, Chen L. Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Res Clin Pract*. 2017;131:124-131.
24. Pan B, Wu Y, Yang Q, et al. The impact of major dietary patterns on glycemic control, cardiovascular risk factors, and weight loss in patients with type 2 diabetes: a network meta-analysis. *J Evid Based Med*. 2019;12(1):29-39.
25. Sainsbury E, Kizirian NV, Partridge SR, et al. Effect of dietary carbohydrate restriction on glycemic control in adults with diabetes: a systematic review and meta-analysis. *Diabetes Res Clin Pract*. 2018;139:239-252.
26. van Wyk HJ, Davis RE, Davies JS. A critical review of low-carbohydrate diets in people with type 2 diabetes. *Diabet Med*. 2016;33(2):148-157.
27. Meo SA. Prevalence and future prediction of type 2 diabetes mellitus in the Kingdom of Saudi Arabia: a systematic review of published studies. *J Pak Med Assoc*. 2016;66(9):1132-1136.
28. Bellou V, Belbasis L, Tzoulaki I, Evangelou E. Risk factors for type 2 diabetes mellitus: an exposure-wide umbrella review of meta-analyses. *PLoS One*. 2018;13(3):e0194127.

Table 1. Characteristics and key findings of the studies included in the review on SGLT2 inhibitors versus intensive low-carbohydrate dietary programs for glycemic control

Study Reference	Study Design	Population	Intervention / Exposure	Disease / Condition	Main Outcomes
[11] <i>Igarashi et al., 2023</i>	Randomized 3-arm open-label trial (12 weeks)	Hospitalized adults with poorly controlled insulin-treated type 2 diabetes in Japan	Canagliflozin 100 mg/day vs carbohydrate-restricted isocaloric diet vs standard hospital diet	Type 2 diabetes requiring intensive insulin therapy	Similar HbA1c across arms; carbohydrate-restricted diet required more insulin, whereas canagliflozin allowed euglycemia with lower insulin requirements
[12] <i>Dening et al., 2023</i>	Randomized parallel-group feasibility trial (12 months)	Community-dwelling adults with type 2 diabetes and elevated HbA1c in Australia	Tailored online low-carbohydrate program plus usual care vs usual diabetes care alone	Type 2 diabetes	Greater HbA1c reduction (0.6% more at 12 months) and higher proportion achieving glycemic targets in the low-carbohydrate intervention group
[13] <i>Hallberg et al., 2018</i>	Non-randomized controlled trial with 1-year follow-up	Adults with type 2 diabetes in U.S. outpatient settings	Continuous remote care with very low-carbohydrate ketogenic diet vs usual diabetes care	Type 2 diabetes	HbA1c decreased from 7.6% to 6.3%; 12% weight loss; major reductions in diabetes medications compared with minimal change in controls
[14] <i>Athinarayanan et al., 2019</i>	Non-randomized 2-year clinical trial extension	Adults with type 2 diabetes enrolled in ketogenic remote care program	Ongoing very low-carbohydrate diet with continuous remote monitoring vs usual care cohort	Type 2 diabetes	Sustained HbA1c reduction around 0.9%, continued weight loss, and diabetes remission in a substantial proportion of participants
[15] <i>Tay et al., 2015</i>	Randomized controlled trial with 52-week follow-up	Obese adults with type 2 diabetes in an outpatient research clinic	Energy-restricted very low-carbohydrate, low-saturated-fat diet vs high-carbohydrate, low-fat diet plus supervised exercise	Type 2 diabetes with obesity	Both diets improved HbA1c and weight; low-carbohydrate diet produced greater lipid improvements and larger reductions in diabetes medication requirements
[16] <i>Tay et al., 2015 (renal)</i>	Randomized trial of same cohort focused on renal markers	Obese adults with type 2 diabetes without overt kidney disease	Very low-carbohydrate, high-protein diet vs high-carbohydrate, low-fat diet over 12 months	Type 2 diabetes without chronic kidney disease	No adverse effect on eGFR or creatinine; renal function remained stable in both groups despite higher protein intake in low-carbohydrate arm
[17] <i>Wanner et al., 2016</i>	Multicentre randomized placebo-controlled outcome trial	Adults with type 2 diabetes and established cardiovascular disease	Empagliflozin 10/25 mg once daily vs placebo plus standard of care	Type 2 diabetes with high cardiovascular and renal risk	Empagliflozin reduced composite kidney outcome risk by =39% (HR =0.61; 95% CI compared with placebo on top of standard therapy)

[18] Perkovic et al., 2019	Randomized double-blind event-driven trial	Adults with type 2 diabetes and albuminuric chronic kidney disease	Canagliflozin 100 mg/day vs placebo plus renin-angiotensin system blockade	Diabetic kidney disease with albuminuria	Canagliflozin lowered renal composite outcome risk (ESKD, creatinine doubling, or renal death) by ≈30% (HR ≈0.70; 95% CI versus placebo)
[19] Fadini et al., 2024	Multicentre retrospective propensity-matched cohort study	Italian adults with type 2 diabetes receiving routine clinical care	Initiation of SGLT2 inhibitor vs GLP-1 receptor agonist therapy	Type 2 diabetes with varying stages of chronic kidney disease	SGLT2 inhibitors were associated with slower eGFR decline and lower CKD progression rates than GLP-1RAs, despite slightly smaller HbA1c reductions

Abbreviations:

T2D, type 2 diabetes; *SGLT2*, sodium-glucose co-transporter-2; *SGLT2i*, SGLT2 inhibitor; *GLP-1RA*, glucagon-like peptide-1 receptor agonist; *HbA1c*, glycated hemoglobin; *eGFR*, estimated glomerular filtration rate; *CKD*, chronic kidney disease; *ESKD*, end-stage kidney disease.

Medicina Katastrof

(ISSN:2070-1004) (E-ISSN:2686-7966)

