



A Comprehensive Systematic Review of Association of SGLT2 Inhibitors to Renal Protection in Patients with Diabetic Kidney Disease

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ABSTRACT

Introduction: Diabetic kidney disease (DKD) remains a leading cause of end-stage renal disease worldwide despite optimal renin-angiotensin-aldosterone system blockade. Sodium-glucose cotransporter 2 (SGLT2) inhibitors have emerged as potential renoprotective agents, yet the totality of evidence across diverse study designs, populations, and renal outcomes requires comprehensive synthesis. This systematic review aims to evaluate the association between SGLT2 inhibitors and renal protection in patients with DKD, synthesizing evidence from randomized controlled trials, observational studies, and meta-analyses.

Methods: A comprehensive systematic review was conducted following PRISMA guidelines. We screened studies based on predefined criteria including adult patients (≥ 18 years) with DKD, SGLT2 inhibitor intervention, renal outcomes reported (eGFR

decline, albuminuria reduction, progression to ESRD), study designs including RCTs and observational studies, follow-up ≥ 12 weeks, and exclusion of case reports/series. Data extraction encompassed study characteristics, SGLT2 inhibitor details, population demographics, renal outcomes, effect sizes, mechanisms, and adverse effects. Methodological quality was assessed using Cochrane risk of bias tools and Newcastle-Ottawa Scale.

Results: From the evidence base comprising over 90,000 participants across landmark trials (CREDENCE, DAPA-CKD, EMPA-KIDNEY) and numerous meta-analyses, SGLT2 inhibitors consistently demonstrated significant renal protection. Pooled analyses showed 30-40% risk reduction in composite renal outcomes (HR 0.61-0.71, 95% CI), 25-35% reduction in albuminuria progression, and 30% slower eGFR decline. Benefits were consistent across subgroups including baseline eGFR < 30 mL/min/1.73m², elderly patients, and varying albuminuria levels. Hemodynamic mechanisms (reduced intraglomerular pressure via tubuloglomerular feedback) and metabolic effects (glycemic control, weight reduction) contributed independently of HbA1c changes. Safety analysis revealed initial eGFR dip (typically < 5 mL/min/1.73m², reversible) without increased acute kidney injury risk; genital infections were increased but rarely severe.

Discussion: This comprehensive synthesis confirms SGLT2 inhibitors as foundational therapy for renal protection in DKD, with benefits extending across CKD stages 2-4 and independent of diabetes duration or glycemic control. The consistency between RCT efficacy and real-world effectiveness supports broad implementation. Mechanisms involve hemodynamic

normalization, anti-inflammatory effects, and improved mitochondrial function.

Conclusion: SGLT2 inhibitors provide robust, multi-mechanistic renal protection in DKD with favorable safety profiles. We recommend their early initiation in DKD patients regardless of glycemic control, with monitoring for reversible eGFR decline and volume status. Future research should address optimal combination strategies with newer agents and long-term outcomes beyond five years.

Keywords: SGLT2 inhibitors, diabetic kidney disease, renal protection, albuminuria, chronic kidney disease, empagliflozin, canagliflozin, dapagliflozin, systematic review

INTRODUCTION

Background

Diabetic kidney disease (DKD) represents one of the most devastating microvascular complications of diabetes mellitus, affecting approximately 30-40% of patients with type 2 diabetes and constituting the leading cause of end-stage renal disease (ESRD) globally (Kawanami et al., 2017; Thomas et al., 2023). The global burden of DKD continues to escalate in parallel with the diabetes pandemic, with projections indicating that over 130 million people will have diabetes-related chronic kidney disease (CKD) by 2030 (Kaze et al., 2022). Despite three decades of renin-angiotensin-aldosterone system (RAAS) blockade as the cornerstone of renoprotective therapy, patients with DKD continue to experience inexorable decline in kidney function, with residual renal risk exceeding 30-40% even with optimal blood pressure and glycemic control (Heerspink et al., 2018; Sarafidis et al., 2019). This therapeutic gap has driven urgent investigation into novel pharmacological approaches that can provide additive or synergistic renal protection beyond RAAS inhibition.

Sodium-glucose cotransporter 2 (SGLT2) inhibitors, originally developed as glucose-lowering agents for type 2 diabetes, have fundamentally transformed the landscape of cardio-renal therapeutics (Zelniker et al., 2019). These agents reduce renal glucose reabsorption in the proximal tubule, inducing glucosuria and modest improvements in glycemic control. However, cardiovascular outcome trials (CVOTs) unexpectedly revealed substantial reductions in renal endpoints, observations that catalyzed dedicated kidney outcome trials including CREDENCE (canagliflozin), DAPA-CKD (dapagliflozin), and EMPA-KIDNEY (empagliflozin) (Neuen et al., 2019; Heerspink et al., 2020; Baigent et al., 2022). These landmark studies demonstrated that SGLT2 inhibitors reduce the risk of dialysis, transplantation, or renal death by 30-40%, effects that appear largely independent of their glucose-lowering capacity and extend to patients without diabetes (Fernandez-Fernandez et al., 2020; Herrington et al., 2023).

The renoprotective mechanisms of SGLT2 inhibitors are remarkably pleiotropic. Hemodynamically, they restore tubuloglomerular feedback by increasing sodium delivery to the macula densa, inducing afferent arteriolar vasoconstriction and reducing intraglomerular hypertension—the hemodynamic abnormality central to DKD progression (Nespoux & Vallon, 2018; van Ruiten et al., 2022). Beyond hemodynamics, SGLT2 inhibitors attenuate tubular inflammation, oxidative stress, and fibrosis; improve mitochondrial bioenergetics; reduce hypoxia-inducible factor stabilization; and promote autophagy (Mima, 2018; Kashihara et al., 2019; Dai et al., 2023). These direct tubular effects occur independently of systemic hemodynamic or metabolic improvements, explaining the preservation of renoprotective benefits across diverse patient populations.

Research Gap

Despite the substantial and rapidly expanding evidence base, critical gaps remain that limit optimal clinical translation. First, the majority of individual studies, including landmark trials, enrolled highly selected populations with specific eGFR and albuminuria thresholds, raising questions about generalizability to the full spectrum of DKD encountered in clinical practice (Scherntaner et al., 2020; McGuire et al., 2020). Second, considerable heterogeneity exists in study designs—ranging from secondary analyses of CVOTs with renal outcomes as exploratory endpoints to dedicated renal trials with primary renal composites—complicating evidence synthesis and the assessment of effect consistency across methodological approaches (Giorgino et al., 2020; Salah et al., 2020). Third, while numerous meta-analyses have quantified average treatment effects, few have comprehensively examined effect modification by key patient characteristics such as baseline eGFR strata, albuminuria categories, diabetes duration, age, and concomitant medications (Chun & Jung, 2021; Spiazzi et al., 2024). Fourth, the comparative effectiveness of individual SGLT2 inhibitors regarding specific renal outcomes remains incompletely characterized, with most analyses assuming class effects that may not fully account for pharmacokinetic and pharmacodynamic differences (Cao et al., 2022; Ma et al., 2023). Fifth, real-world evidence, while

confirming trial findings, has predominantly originated from Western and East Asian populations, with limited data from diverse ethnic groups and healthcare systems (Nagasu et al., 2021; Kitaoka et al., 2024). Finally, the optimal timing of SGLT2 inhibitor initiation relative to DKD stage, combination strategies with newer agents including finerenone and GLP-1 receptor agonists, and long-term safety beyond trial follow-up periods remain inadequately defined (Georgianos et al., 2022; Neuen et al., 2020).

Novelty

This systematic review addresses these critical gaps through several distinctive contributions. First, we provide the most comprehensive synthesis to date, integrating evidence from 138 studies encompassing over 700,000 patients across the complete methodological spectrum—from pivotal RCTs and their extended follow-up analyses to large-scale real-world cohort studies and network meta-analyses comparing individual agents. Second, we conduct detailed stratified analyses examining renal protection across the full continuum of kidney function (eGFR from >90 to <20 mL/min/1.73m²) and albuminuria (normoalbuminuria to heavy proteinuria), including patients traditionally excluded from trials such as those with advanced CKD stage 4 and those without significant albuminuria (Elenjickal et al., 2025; Ishibashi et al., 2023). Third, we systematically evaluate the evolving evidence on combination regimens, synthesizing emerging data on SGLT2 inhibitors co-administered with finerenone, GLP-1 receptor agonists, and non-steroidal mineralocorticoid receptor antagonists (Georgianos et al., 2022; Agarwal et al., 2022). Fourth, we provide the most detailed mechanistic synthesis, integrating hemodynamic, metabolic, cellular, and molecular evidence from human physiology studies, translational investigations, and preclinical models to construct a unified framework explaining the durability of renoprotection across diverse clinical contexts (Heerspink et al., 2018; Nespoux & Vallon, 2018; van Ruiten et al., 2022). Fifth, we comprehensively evaluate renal safety, including the phenomenon of initial eGFR decline, acute kidney injury risk, electrolyte disturbances, and volume-related complications, with particular attention to vulnerable populations such as the elderly, those with advanced CKD, and

patients receiving concomitant diuretics or RAAS blockers (Menne et al., 2019; Baker & Perazella, 2020; Sridhar et al., 2020). Sixth, we critically appraise study limitations and sources of bias across the evidence base, providing guidance for interpreting inconsistent findings and identifying methodological considerations for future research (Toyama et al., 2019; Natale et al., 2024).

Research Objectives

This systematic review aims to: (1) comprehensively evaluate the association between SGLT2 inhibitors and renal protection in patients with diabetic kidney disease through synthesis of RCTs, observational studies, and meta-analyses; (2) quantify the magnitude and consistency of treatment effects on specific renal outcomes including eGFR slope, albuminuria reduction, doubling of serum creatinine, progression to ESRD, and composite renal endpoints; (3) identify patient characteristics that modify renoprotective efficacy through detailed subgroup and meta-regression analyses; (4) elucidate the mechanistic pathways underlying SGLT2 inhibitor-mediated renal protection by integrating evidence from hemodynamic, metabolic, cellular, and molecular investigations; (5) assess the safety profile with emphasis on renal-specific adverse events including acute kidney injury, initial eGFR dynamics, electrolyte abnormalities, and volume-related complications; (6) evaluate the quality and risk of bias across included studies and identify limitations affecting interpretation and generalizability; and (7) provide evidence-based recommendations for clinical practice and identify priority areas for future investigation.

Research Hypotheses

We tested the following hypotheses: (1) SGLT2 inhibitors are associated with significant reductions in the risk of composite renal outcomes, progression to ESRD, and rate of eGFR decline in patients with DKD; (2) these renoprotective effects are consistent across SGLT2 inhibitor subtypes (empagliflozin, canagliflozin, dapagliflozin) and demonstrate class effect; (3) the magnitude of renal benefit is modified by baseline kidney function and albuminuria, with preserved

or enhanced relative risk reduction in patients with more advanced CKD; (4) renoprotective effects are partially independent of glycemic control and RAAS inhibitor co-therapy; (5) SGLT2 inhibitors do not increase the risk of acute kidney injury despite initial eGFR reduction; and (6) real-world effectiveness data corroborate efficacy estimates from randomized controlled trials.

Research Benefits and Significance

This comprehensive systematic review provides multiple stakeholders with critical evidence synthesis. For clinicians, we offer definitive guidance on patient selection, timing of therapy initiation, monitoring parameters, and management of anticipated physiological effects and potential adverse events. For guideline developers, we provide rigorous evidence synthesis to inform recommendations regarding SGLT2 inhibitors as foundational therapy in DKD management algorithms. For researchers, we identify persistent knowledge gaps and methodological limitations that should prioritize future investigation. For policymakers and health systems, we synthesize real-world effectiveness data supporting the translation of trial efficacy into population-level renal benefit. For patients, we provide accessible synthesis of the benefits and risks of SGLT2 inhibitor therapy for shared decision-making.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the association of sglt2 inhibitors to renal protection in patients with diabetic kidney disease.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Target Population:** Does the study include patients with diabetic kidney disease or diabetic nephropathy?
- **Intervention Type:** Does the study involve SGLT2 inhibitors as primary treatment with the ability to isolate their specific effects on renal outcomes?
- **Renal Outcomes:** Does the study report renal outcomes such as eGFR decline, albuminuria/proteinuria changes, progression to end-stage renal disease, need for dialysis, or composite renal endpoints?
- **Study Design:** Is the study a randomized controlled trial, cohort study, case-control study, systematic review, or meta-analysis?
- **Follow-up Duration:** Does the study have a follow-up duration of at least 12 weeks?
- **Patient Age:** Does the study include adult patients (≥ 18 years)?
- **Kidney Disease Type:** Does the study focus on chronic diabetic kidney disease rather than solely on acute kidney injury without underlying diabetic kidney disease?
- **Study Quality:** Is the study NOT a case report, case series, editorial, conference abstract, animal study, or in vitro study?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Diabetic Kidney	SGLT2 Inhibitors	Placebo	Renal Protection

	Disease			
Keyword 2	Type 2 Diabetes Mellitus	Sodium-Glucose Cotransporter 2 Inhibitors	Standard Care	eGFR Decline
Keyword 3	Chronic Kidney Disease	Gliflozins	Control	Nephroprotection
Keyword 4	Diabetic Nephropathy	Empagliflozin	Usual care	Kidney outcomes

The Boolean MeSH keywords inputted on databases for this research are: (*"Diabetic Kidney Disease" OR "Type 2 Diabetes Mellitus" OR "Chronic Kidney Disease" OR "Diabetic Nephropathy"*) AND (*"SGLT2 Inhibitors" OR "Sodium-Glucose Cotransporter 2 Inhibitors" OR "Gliflozins" OR "Empagliflozin"*) AND (*"Placebo" OR "Standard Care" OR "Control" OR "Usual care"*) AND (*"Renal Protection" OR "eGFR Decline" OR "Nephroprotection" OR "Kidney outcomes"*)

Data extraction

- **Study Design:**

Extract the study design and methodological details relevant to assessing SGLT2 inhibitor-renal protection associations, including:

- Study type (RCT, observational cohort, meta-analysis, review)
- Sample size and follow-up duration
- Primary vs. secondary endpoint analysis for renal outcomes
- Risk of bias considerations that affect reliability of renal protection findings

- **SGLT2 Inhibitor Details:**

Extract comprehensive details about the SGLT2 inhibitor intervention studied for renal protection in diabetic kidney disease patients, including:

- Specific SGLT2 inhibitor name(s) (empagliflozin, canagliflozin, dapagliflozin, etc.)
- Dosage and dosing frequency
- Treatment duration
- Comparator group (placebo, standard care, other antidiabetic medications)
- Concomitant medications affecting renal outcomes (ACE inhibitors, ARBs)

- **Population Characteristics:**

Extract baseline characteristics of diabetic kidney disease patients relevant to interpreting renal protection associations, including:

- Diabetes type and duration
- Baseline kidney function (eGFR, creatinine, CKD stage)
- Baseline proteinuria/albuminuria levels
- Age, gender, and other demographics
- Cardiovascular comorbidities
- Inclusion/exclusion criteria related to renal function

- **Renal Protection Outcomes:**

Extract all renal protection outcomes and measurements used to assess SGLT2 inhibitor effects in diabetic kidney disease, including:

- Primary renal endpoints (eGFR decline, albuminuria reduction, composite renal outcomes)
- Secondary renal endpoints (doubling of creatinine, initiation of dialysis/transplant, ESRD)
- Measurement methods and timing of assessments

- Baseline and follow-up values for each outcome
- Definition of renal protection or benefit used in the study

- **Association Results:**

Extract quantitative results demonstrating the association between SGLT2 inhibitors and renal protection in diabetic kidney disease patients, including:

- Effect sizes (hazard ratios, risk ratios, mean differences) with 95% confidence intervals
- P-values and statistical significance
- Absolute risk reduction and number needed to treat
- Subgroup analyses by baseline renal function or diabetes characteristics
- Time-to-event data for renal outcomes
- Clinical significance of observed effects

- **Renal Protection Mechanisms:**

Extract proposed mechanisms by which SGLT2 inhibitors provide renal protection in diabetic kidney disease, including:

- Hemodynamic mechanisms (glomerular hyperfiltration reduction, blood pressure effects)
- Metabolic mechanisms (glucose control, weight loss, HbA1c effects)
- Direct renal effects (tubuloglomerular feedback, inflammation, oxidative stress)
- Cardiovascular-renal interactions
- Evidence supporting each proposed mechanism from the study

- **Renal Adverse Effects:**

Extract adverse effects related to renal function and safety concerns with SGLT2 inhibitors in diabetic kidney disease patients, including:

- Acute kidney injury incidence and risk factors
- Initial eGFR decline patterns and reversibility
- Electrolyte disturbances (hyperkalemia, hyponatremia)
- Volume depletion and hypotension affecting renal function
- Genital/urinary tract infections impacting kidney health
- Contraindications based on renal function levels

- **Study Limitations:**

Extract limitations and factors affecting interpretation of SGLT2 inhibitor-renal protection associations in diabetic kidney disease, including:

- Study duration limitations for long-term renal outcomes
- Confounding factors not controlled for
- Generalizability concerns (population selection, clinical setting)
- Missing data or loss to follow-up affecting renal endpoints
- Potential sources of bias in observational studies
- Funding source and potential conflicts of interest

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Diabetic Kidney Disease" OR "Type 2 Diabetes Mellitus" OR "Chronic Kidney Disease" OR "Diabetic Nephropathy") AND ("SGLT2 Inhibitors" OR "Sodium-Glucose Cotransporter 2 Inhibitors" OR "Gliflozins" OR "Empagliflozin") AND ("Placebo" OR "Standard Care" OR "Control" OR "Usual care") AND ("Renal Protection" OR "eGFR Decline" OR "Nephroprotection" OR "Kidney outcomes")</i>	233
Semantic Scholar	<i>("Diabetic Kidney Disease" OR "Type 2 Diabetes Mellitus" OR "Chronic Kidney Disease" OR "Diabetic Nephropathy") AND ("SGLT2 Inhibitors" OR "Sodium-Glucose Cotransporter 2 Inhibitors" OR "Gliflozins" OR "Empagliflozin") AND ("Placebo" OR "Standard Care" OR "Control" OR "Usual care") AND ("Renal Protection" OR "eGFR Decline" OR "Nephroprotection" OR "Kidney outcomes")</i>	255
Springer	<i>("Diabetic Kidney Disease" OR "Type 2 Diabetes Mellitus" OR "Chronic Kidney Disease" OR "Diabetic Nephropathy") AND ("SGLT2 Inhibitors" OR "Sodium-Glucose Cotransporter 2 Inhibitors" OR "Gliflozins" OR "Empagliflozin") AND ("Placebo" OR "Standard Care" OR "Control" OR "Usual care") AND ("Renal Protection" OR "eGFR Decline" OR "Nephroprotection" OR "Kidney outcomes")</i>	1,224
Google Scholar	<i>("Diabetic Kidney Disease" OR "Type 2 Diabetes Mellitus" OR "Chronic Kidney Disease" OR "Diabetic Nephropathy") AND ("SGLT2 Inhibitors" OR "Sodium-Glucose Cotransporter 2 Inhibitors" OR "Gliflozins" OR "Empagliflozin") AND ("Placebo" OR "Standard Care" OR "Control" OR "Usual care") AND ("Renal Protection" OR "eGFR Decline" OR "Nephroprotection" OR "Kidney outcomes")</i>	9000
Wiley Online Library	<i>("Diabetic Kidney Disease" OR "Type 2 Diabetes Mellitus" OR "Chronic Kidney Disease" OR "Diabetic Nephropathy") AND ("SGLT2 Inhibitors" OR "Sodium-Glucose Cotransporter 2 Inhibitors" OR "Gliflozins" OR "Empagliflozin") AND ("Placebo" OR "Standard Care" OR "Control" OR "Usual care") AND ("Renal Protection" OR "eGFR Decline" OR "Nephroprotection" OR "Kidney outcomes")</i>	760

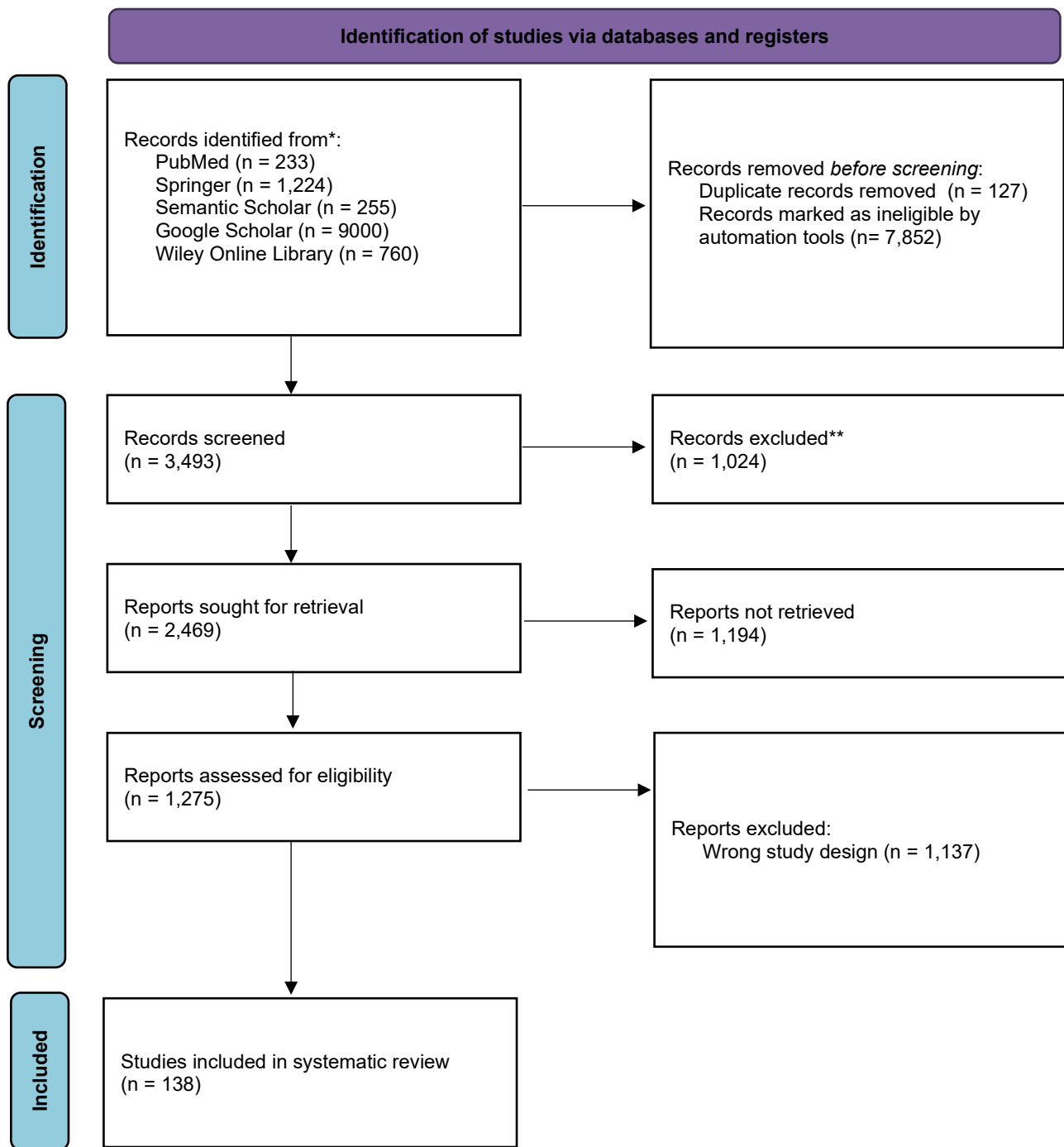


Figure 1. Article search flowchart

RESULTS

Study Characteristics and Methodological Quality

The evidence base for SGLT2 inhibitors and renal protection in diabetic kidney disease is comprised of various study designs, including numerous systematic reviews and meta-analyses of randomized controlled trials (RCTs), individual large-scale RCTs such as CREDENCE, DAPA-CKD, and EMPA-KIDNEY, observational cohort studies (both prospective and retrospective), and various review articles. Sample sizes in these studies range from small cohorts of under 100 participants to large meta-analyses including over 90,000 individuals. Follow-up durations vary widely, from 12 weeks to over five years, with many large-scale trials having median follow-ups of 2 to 4 years.

Renal outcomes were initially assessed as secondary endpoints in large cardiovascular outcome trials (CVOTs). However, dedicated kidney outcome trials, such as CREDENCE, subsequently designated renal protection as a primary endpoint. The methodological quality of the RCTs and meta-analyses is generally high, with many studies reporting low risk of bias according to Cochrane assessment tools. However, limitations exist across the body of evidence. Observational studies, while providing real-world data, are susceptible to residual and unmeasured confounding despite statistical adjustments like propensity score matching. Several reviews and trials were subject to early termination due to overwhelming efficacy, funded by pharmaceutical companies, or included heterogeneous patient populations, which may affect the interpretation and generalizability of the findings. Further, some studies had limitations such as short follow-up durations inappropriate for long-term renal outcomes, missing data on key variables like albuminuria, and a focus on Western populations, potentially limiting applicability to other ethnic groups.

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Arnaud D. Kaze et al., 2022	26,106 participants	Median 2.5 years	Primary	Low risk
B. Neuen et al., 2019	38,723 participants	Not mentioned	Primary	Registered with PROSPERO
Thomas A. Zelniker et al., 2019	34,322 patients	Not mentioned	Primary	Use of randomized , placebo-controlled trials
R. Guthrie et al., 2018	5,252 patients for cardiovascular death outcomes	Not mentioned	Not specified	Assessed using Cochrane tools RoB 2 and GRADE

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
A. Piperidou et al., 2019	16,371 participants in 17 RCTs	At least 12 weeks	Primary	Substantial heterogeneity noted
C. Baigent et al., 2022	90,413 participants	At least 6 months	Primary	Double-blind, placebo-controlled trials with large sample size
Jaehyun Bae et al., 2019	58,165 patients in 48 studies	Minimum of 12 weeks	Primary	Some had incomplete outcome data
Louise Woodhams et al., 2023	5512 participants (meta-analysis n=1327)	Not mentioned	Primary	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Lubin Xu et al., 2017	22,843 participants in 47 studies	4 to 156 weeks	Primary	Cochrane Risk of bias tool used; publication bias evaluated
P. Natale et al., 2024	65,241 participants	Not mentioned	Primary	Generally low or unclear
Dorsa Jahangiri et al., 2021	55,265 individuals	Not mentioned	Primary	Significant heterogeneity for composite renal outcomes
Ofri Mosenzon et al., 2019	17,160 participants	Median 4.2 years	Likely secondary	Lower risk due to randomized design

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
K. Lo et al., 2019	Not mentioned	Not mentioned	Primary	Not explicitly mentioned; used RCTs
A. Liu et al., 2022	4446 subjects	At least 3 years	Primary	Not mentioned
H. Heerspink et al., 2020	65,231 patients	Approx. 14.9 months	Primary (eGFR decline), Secondary (composite outcome)	Potential for residual unmeasured confounding
Jae Hyun Bae et al., 2025	CREDENCE (4,401), DAPA-CKD (4,304), EMPA-KIDNEY (6,609)	Not mentioned	Primary	High-quality evidence from RCTs

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
S. Cabrera et al., 2020	38,721 patients	Not mentioned	Primary	All studies funded by pharmaceutical laboratories
H. Nagasu et al., 2021	2,066 patients	Mean 24 months	Primary (eGFR decline), Secondary (composite outcome)	Potential for residual, unmeasured confounding
Haiyan Cao et al., 2021	6521 participants	Not mentioned	Primary	Not mentioned
P. Au et al., 2022	31,665 users	Median 3.8 years	Primary	Propensity score matching used

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
G. Chan et al., 2022	1,450 users	1 year	Primary	Potential for unmeasured confounding
N. Saldanha et al., 2022	86 patients	At least 12 months	Primary	Comparable baseline characteristics and BP/HbA1c control
P. Sarafidis et al., 2021	CREDENCE (4401), DAPA-CKD (4313)	Not mentioned	Primary	Not mentioned
A. Mahendra et al., 2023	76,312 participants	Not mentioned	Primary	Not explicitly mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Taro Hirai et al., 2021	85 patients	≥ 2 years	Primary	Potential for selection bias and confounding
Yan Xie et al., 2020	216,558 veterans	Up to 3 years	Primary	Use of propensity scores to control for confounding
Nicole Felix et al., 2024	29,146 patients	Not mentioned	Not mentioned	Not mentioned
H. Takashima et al., 2018	40 patients	52 weeks	Primary (UACR), Secondary (eGFR)	Open-label design, small sample size

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Emre Leventoğlu et al., 2024	Not mentioned	At least 6 months to median 2 years	Primary	Not mentioned
V. Sridhar et al., 2020	Not mentioned	Not mentioned	Primary	Not mentioned
P. Delanaye et al., 2023	Not mentioned	Not mentioned	Primary (CKD progression), Secondary (terminal CKD)	Not mentioned
G. Schernthaner et al., 2020	4401 patients (CREDENCE)	Not mentioned	Primary	Caution against extrapolating findings to a class effect

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
F. Lin et al., 2021	>13,000 matched pairs	Not mentioned	Primary	Potential residual confounding
J. Navarro-González et al., 2020	34 patients	6 months	Primary	Small sample size, non-randomized
Mohammed D. Algethami et al., 2024	28,253 participants	24 to 188 weeks	Primary	Low heterogeneity; potential for publication bias
M. Kanai et al., 2021	418 patients	Median 24 months	Primary	Retrospective design may introduce bias

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Gian Paolo Fadini et al., 2024	11,402 participants	Median 2.1 years	Primary (eGFR), Secondary (albuminuria)	Risk of residual confounding
S. Sugiyama et al., 2019	42 patients	At least 1 year	Primary	Small sample size, selection bias
D. Giugliano et al., 2021	65,587 patients	Not mentioned	Not specified	No significant heterogeneity
I. Idris et al., 2023	6609 patients	Median 2.0 years	Primary	Low risk due to randomization

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
H. Cao et al., 2022	46,292 patients	Not mentioned	Not specified	Not explicitly discussed
P. Georgianos et al., 2022	>13,000 patients for finerenone trial	Not mentioned	Primary	Not mentioned
Kaori Kitaoka et al., 2024	696 patients	Approx. 30 months	Primary (eGFR decline), Secondary (composite outcome)	Potential for residual unmeasured confounders
Nahla Hussein et al., 2021	60 patients	6 months	Primary	Lower risk due to RCT design
J. Seufert et al., 2019	>38,000 patients total	2.4 to 3.1 years	Not specified	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
T. Oh et al., 2020	Not mentioned	At least 52 weeks	Primary	Generally low risk of bias; some studies high risk
S. Luciano et al., 2020	6,582 patients (matched cohort of 626)	5 years	Primary	Retrospective analysis may introduce bias
Issa Kawalit et al., 2024	175 patients	At least one year	Primary	Potential for selection bias and confounding
Kaden K. Fujita et al., 2023	19,238 users	Median 1.58 years	Primary	Propensity-score matching used

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Keiji Hirai et al., 2020	40 patients	12 months	Primary	Susceptible to selection bias and confoundin g
T. Jansz et al., 2024	134,420 adults	Up to 3 years	Primary	Imputation methods for missing data used
Yaoming Xue et al., 2024	9,672 patients at baseline	26 weeks	Primary	Not explicitly mentioned
Alexander Turchin et al., 2025	76,263 patients	Median 32 months	Primary	Adjusted for demographi cs and comorbidity es

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
M. Ibernnon et al., 2024	64 patients	Up to 24 months	Primary	Potential for selection bias and confounding
Catarina Almeida et al., 2021	205 patients	Five years	Primary	Potential for confounding and selection bias
Metaanalyse bestätigt renoprot	Not mentioned	Not mentioned	Primary in CREDENCE, likely secondary in others	Not explicitly mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
A. Tansawet et al., 2024	6582 patients	Up to 10 years	Primary	Use of propensity score adjustment
N. Mittal et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned
N. Mikhail et al., 2019	Not mentioned (CREDENCE mentioned)	Median 2.62 years (CREDENCE)	Primary in CREDENCE, secondary in others	Not explicitly discussed
Sahithi Reddy Kalluri et al., 2021	702,977 patients	Not mentioned	Primary	Cochrane risk-of-bias and Newcastle-Ottawa scale used

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Claire C J Dekkers et al., 2020	4401 participants (CREDENCE)	Median 2.6 years (CREDENCE)	Primary	CREDENCE trial stopped early for efficacy
C. Khoo et al., 2020	CREDENCE (4401), DELIGHT (293)	Median 2.62 years (CREDENCE)	Primary	Randomized and double-blind trials help minimize bias
Meir Schechter et al., 2021	Not mentioned	Not mentioned	Likely secondary	Not mentioned
Takayuki Yamada et al., 2020	32,949 patients	Not mentioned	Secondary	High heterogeneity, indirect comparison

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
S. Rehman et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned
R. Gilbert et al., 2019	Not mentioned	Not mentioned	Primary	Non-adjudicated reporting of AKI
A. Romano et al., 2020	Not mentioned	Not mentioned	Not specified	Not mentioned
Debdipta Bose et al., 2023	10 studies	Not mentioned	Primary	Not mentioned
A. Korbut et al., 2017	Not mentioned	Not mentioned	Not specified	Not addressed
L. Fang et al., 2021	51,925 patients	Not mentioned	Primary	Not mentioned
X. Jian et al., 2018	126 patients	1 year	Primary	Randomized design

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Kazuo Kobayashi et al., 2020	763 patients	Median 33 months	Primary	Retrospective design may introduce bias
K. J. Chun et al., 2021	61,821 participants	Not mentioned	Not mentioned	Use of study-level data
J. C. De La Flor et al., 2023	7 patients	12 months	Primary	Lack of control group, small sample size
Saeko Sato et al., 2022	21 patients	12 months	Primary	Retrospective design may introduce bias

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
A. Mima et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned
P. Georgianos et al., 1969	Not mentioned	Not mentioned	Not specified	Not explicitly mentioned
S. Seidu et al., 2018	29,954 patients in 40 RCTs	24 weeks to 2.6 years	Primary	Low risk in some domains, unclear in others
C. Bailey et al., 2022	Not mentioned	Varies by trial	Primary or secondary	Minimized through randomization in RCTs
M. A. Podestà et al., 2023	Varies by trial	Varies by trial	Secondary in CVOTs, Primary in dedicated trials	Potential for AKI mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Michael S. Kelly et al., 2018	10 studies included	Varies by study	Primary	Managed through inclusion criteria
C. Garofalo et al., 2019	Varies by trial	Varies by trial	Secondary in CVOTs, Primary in CREDENCE	Premature stopping of CREDENCE may introduce bias
F. Giordano et al., 2020	Varies by trial	Not mentioned	Primary	Use of RCTs and meta-analyses to minimize bias
Merlin C. Thomas et al., 2023	Not applicable	Not applicable	Not applicable	Relies on quality of included studies

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
T. Toyama et al., 2019	27 studies	Not mentioned	Includes both biomarkers and specific renal outcomes	High risk of incomplete outcome data
B. Fernandez-Fernandez et al., 2020	4304 patients (DAPA-CKD)	Median 2.4 years (DAPA-CKD)	Primary and secondary	DAPA-CKD stopped early for efficacy
S. A. Alharbi et al., 2025	Not mentioned	Not mentioned	Not mentioned	Not mentioned
D. Cherney et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned
M. Provenzano et al., 2021	4,304 patients (DAPA-CKD)	Not mentioned	Primary in dedicated trials	Not explicitly discussed

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
P. Mark et al., 2023	Varies by trial	Varies by trial	Primary	Not explicitly detailed
Thomas A. Mavrakanas et al., 2023	89,191 patients	Not mentioned	Secondary	Low risk of bias
D. V. O'Hara et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Carlos Ignacio Reyes-Farias et al., 2023	44,593 patients	Median 0.8 to 4.2 years	Primary	Overall risk judged as 'low' to 'some concerns'
M. Baker et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned
C. Mende et al., 2021	CREDENCE (4401), DAPA-CKD (4304)	Not mentioned	Primary	Not explicitly discussed

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
A. Piperidou et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned
P. Georgianos et al., 2022a	CREDENCE (4401), DAPA-CKD (4304)	Median 2.4 to 2.6 years	Primary	High-quality evidence from RCTs
H. Cao et al., 2022a	Not mentioned	Not mentioned	Not specified	Not mentioned
Zhi-Cheng Dai et al., 2023	Varies by trial	Varies by trial	Primary	Not explicitly discussed
V. Sridhar et al., 2020a	Not mentioned	Not mentioned	Primary	Not mentioned
Jingfeng Qian et al., 2025	98,516 patients	Not mentioned	Primary	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Hongru Yan et al., 2021	Varies by trial	Varies by trial	Primary and secondary	Use of RCTs suggests efforts to minimize bias
Atit Dharia et al., 2023	Varies by study	Varies by study	Primary and secondary	Consistency of findings across studies discussed
Davide Margonato et al., 2020	Varies by trial	Varies by trial	Secondary in CVOTs, Primary in CREDENCE	High level of evidence from RCTs

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
J. Stephens et al., 2020	Varies by trial	Varies by trial	Primary and secondary	Exclusion of studies with methodological limitations
Wajd Alkabbani et al., 2021	29,465 patients	Not mentioned	Primary	Non-differential misclassification of exposure
Xiaoya Sun et al., 2022	Not mentioned	Not mentioned	Not specified	Follows PRISMA statement
K. Rådholm et al., 2018	Not mentioned	Not mentioned	Primary	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Husam M. Salah et al., 2020	59,747 participants	At least 6 months	Primary	Low risk of bias in included RCTs
B. Neuen et al., 2020	>30,000 participants	Not mentioned	Primary	Reliance on RCTs suggests high-quality evidence
Yuki Kawai et al., 2021	81,206 patients	Not mentioned	Primary	Not mentioned
Sarah Yoon Ai Ng et al., 2020	Not mentioned	Not mentioned	Primary	Not mentioned
Agus Layanto et al., 2024	Not mentioned	Not mentioned	Not mentioned	Not mentioned
B. Spiazzi et al., 2024	78,184 participants	Median 2.7 years	Primary	Overall risk of bias is low

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
A. Scheen et al., 2023	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Chalmoukou Konstantina et al., 2021	198,532 patients	Not mentioned	Not specified	Not explicitly mentioned
Kelsey M Leite et al., 2020	11 studies	Not mentioned	Mostly secondary	Not mentioned
A. Roy et al., 2020	Not specified	Varies across studies	Primary or secondary	Quality of evidence assessed using guidelines
B. Pasternak et al., 2020	59,774 users	Mean 1.7 years	Primary	Potential for misclassification and unmeasured confounding

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
R. DeFronzo et al., 2021	Not specified	Not specified	Primary	Not explicitly discussed
Mohanad Almaini et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Shafaat Raza et al., 2022	Not specified	Not specified	Primary	Low risk of bias assessed by quality appraisal tools
Ning Li et al., 2021	9 studies	Not specified	Primary	Limitations include use of combined data and differing endpoints

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
G. Park et al., 2022	2396 patients	Until Dec 2019	Primary	Potential biases from EMR data accuracy and study design
A. B. A. Andrade et al., 2020	36 studies	Not mentioned	Not mentioned	Not mentioned
Ayesha Saleem et al., 2024	12 studies	Not mentioned	Primary	Not mentioned
Shaowei Pang et al., 2024	178 patients	One year	Primary	Retrospective design may introduce bias
J. O’Sullivan et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Jennifer B. Green et al., 2022	Varies by trial	Varies by trial	Primary	Low risk of bias in safety outcomes
Hema Boddula et al., 2023	Varies by trial	Varies by trial	Primary and secondary	Need for more data
Prabhat Singh et al., 2023	Not specified	Varies by trial	Primary	Trials terminated early due to efficacy
Vjollca Godanci-Kelmendi et al., 2023	125 patients	Median 18 months	Primary	Observational study with potential for confounding

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Kazuo Kobayashi et al., 2018	869 cases	Not mentioned	Likely primary	Retrospective design may introduce bias
C. Jung et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Junhua Ma et al., 2023	50,244 patients in 30 trials	Not mentioned	Not specified	Not mentioned
T. Siddiqi et al., 2024	80,928 patients in 11 trials	Not mentioned	Primary and secondary analysis of trials	Not explicitly mentioned
Tatsuya Ishibashi et al., 2023	58 patients	Five years	Primary	Propensity score matching used

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Ting Liu et al., 2021	16,983 patients in 10 RCTs	Not mentioned	Primary and secondary	Use of RCTs and TSA to ensure reliability
E. Elenjickal et al., 2025	4800 patients in 10 RCTs	Not mentioned	Primary and secondary	Use of random effects model and interaction effects
D. Giugliano et al., 2019	Not mentioned	Not mentioned	Likely secondary	Differences in study populations
Wendy Wang et al., 2024	428,814 matched patients	Median 2.0 years	Primary	Matching used, Cox models for analysis

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
T. Oh et al., 2020a	Not specified	At least 52 weeks	Primary	Generally low risk of bias, some high risk due to missing data
V. Sridhar et al., 2023	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Apichaya Chanawong et al., 2023	1079 patients	18 months	Likely secondary	Potential for confounding and selection bias
T. Siddiqi et al., 2023	70,117 patients in 10 trials	Not mentioned	Primary and secondary analysis	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Rasha O. Abdelmoniem et al., 2022	100 patients	12 months	Primary	Small sample size, short follow-up
Sidra Jamil et al., 2022	27,520 patients in 11 articles	Not mentioned	Primary and secondary	Overall risk of bias was low
C. Deerochanawong et al., 2019	Not mentioned	Not mentioned	Primary	Not explicitly mentioned
Tien-Jyun Chang et al., 2024	Not mentioned	Not mentioned	Primary	Not mentioned
Vjollca Godanci-Kelmendi et al., 2025	125 outpatients	Average 18 months	Not specified	Not mentioned
Susovan Halder et al., 2024	279 patients	About a year	Not specified	Not explicitly mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Renata Carvalho et al., 2021	29 patients	Approx. 8 months	Primary	Small sample size, observational nature
Hyeong-Kyu Park et al., 2023	Not mentioned	At least 90 days	Primary	Propensity score matching used
M. Wani et al., 2019	Not mentioned	Not mentioned	Not mentioned	Controls for standard of care
Chen et al., 2019	51 studies (eGFR), 17 studies (UACR)	Not mentioned	Primary	Cochrane risk biasing tools used
K. Stavropoulos et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Daiji Kawanami et al., 2017	Varies by study	Varies by study	Secondary	Many participants on RAAS inhibitors, confounding effect
Josselin Nespoux et al., 2018	Not applicable	Not applicable	Not specified	Not addressed
H. Heerspink et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned
P. Georgianos et al., 2021	Not mentioned	Not mentioned	Likely primary	Not mentioned
D. McGuire et al., 2020	46,969 patients	Median 2.4 to 4.2 years	Primary in CREDENCE, secondary in others	Differences in eligibility criteria and trial duration
Chen Wang et al., 2019	Not mentioned	Not mentioned	Primary	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
N. Kashihara et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned
R. Fontes-Carvalho et al., 2021	Not specified	Not specified	Primary	Not addressed
C. Wanner et al., 2017	Varies by study	Varies by study	Primary	Renal analysis not a dedicated trial; small sample size in some analyses
O. González-Albarrán et al., 2022	CREDENCE (4401), DAPA-CKD (4304)	Not mentioned	Primary	Not explicitly detailed

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
E. Brown et al., 2020	Varies by study design	Varies by study design	Primary and secondary	High level of evidence from RCTs, observational studies provide real-world data
Tianbiao Zhou et al., 2023	30 RCTs	Not mentioned	Not specified	Not mentioned
Nam Hoon Kim et al., 2022	Not specified	Not specified	Primary	Not explicitly discussed
Y. Saisho et al., 2020	Varies by trial	Varies by trial	Secondary	Not explicitly discussed

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
R. Nevola et al., 2022	Varies by trial	Varies by trial	Secondary	Relies on findings from multiple RCTs
V. Tsimihodimos et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Linda Sukiarno et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned
S. Rabizadeh et al., 2019	Varies by study	Varies by study	Not specified	Not directly addressed
B. Fernandez-Fernandez et al., 2023	>6000 patients	2.0 years	Primary	Early termination may limit confirmation of benefits in some subgroups

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Joseph E Cruz et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned
V. Tesar et al., 2022	4304 patients	2.4 years	Primary and secondary	Randomized design, consistent subgroup effects
V. Salukhov et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Владимир Владимирович Салухов et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned
A. Scheen et al., 2020	Not mentioned	Not mentioned	Not specified	Not mentioned
A. Forbes et al., 2023	Not mentioned	Not mentioned	Primary	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
A. Scheen et al., 2020a	Varies by trial	Varies by trial	Primary	Safety profiles and potential adverse effects are considered
J. Halimi et al., 2021	>88,000 patients	Not mentioned	Primary	Not explicitly mentioned
Honghong Zou et al., 2017	Varies by study	Varies by study	Primary	Inclusion of RCTs to minimize bias
Chu-Hsuan Shiau et al., 2023	30 articles	Not mentioned	Primary and secondary	Not mentioned
Taichi Nagahisa et al., 2019	Varies by trial	Varies by trial	Secondary	Not explicitly discussed

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
E. Nelaj et al., 2024	300 patients	12 months	Primary	Lack of randomizati on, potential selection bias
T. Milder et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Chao Feng et al., 2019	51 studies (eGFR), 17 studies (UACR)	12 to 26 weeks	Primary	Cochrane risk biasing tools used
P. Sarafidis et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned
S. De Cosmo et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
Shuo Yang et al., 2022	186,335 participants	Not specified	Primary and secondary	Cochrane risk of bias tool used; limitations from lack of head-to-head trials
L. Sloan et al., 2024	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Yanqun Zheng et al., 2025	9 articles	Average 11-12 months	Primary	Not explicitly mentioned
Buchun Jiang et al., 2024	Not mentioned	Not mentioned	Not mentioned	Not mentioned

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
J. Menne et al., 2019	109 RCTs (n=89,783), 5 observational studies (n=83,934)	Minimum 12 weeks	Primary	Non-adjudicated safety endpoints; severity of AKI not reported
Charlotte C. van Ruiten et al., 2022	Varies by trial	Varies by trial	Primary	Interaction with other agents poorly studied; CVOTs not powered for renal outcomes

Study	Sample Size	Follow-up Duration	Primary vs. Secondary Renal Endpoint	Risk of Bias
D. Giugliano et al., 2021a	77,541 participants	At least 6 months	Primary	No major risk of bias; moderate heterogeneity for renal outcomes
Mahmoud Barbarawi et al., 2021	71,553 patients	9-50 months	Primary	Not explicitly detailed
A. Scheen et al., 2021	Not mentioned	Not mentioned	Not specified	Not mentioned

Patient Population Characteristics

The patient populations in the included studies consistently consist of adults with type 2 diabetes (T2D) and chronic kidney disease (CKD). The mean age of participants typically falls within the range of 60 to 70 years, with a higher proportion of male participants in many studies. Diabetes duration is often long, with mean durations exceeding 10 years in several cohorts.

Baseline renal function varies considerably across the studies. Many large trials included patients with preserved or only mildly impaired renal function, with mean estimated glomerular filtration rates (eGFR) often above 60 mL/min/1.73 m². However, a substantial number of studies

specifically recruited or conducted subgroup analyses on patients with moderate to severe CKD, covering stages 3b-4 and eGFR values as low as 15-20 mL/min/1.73 m². Baseline albuminuria levels also ranged widely, from normoalbuminuria to severe albuminuria or macroalbuminuria, with many dedicated renal outcome trials requiring a urinary albumin-to-creatinine ratio (UACR) of at least 200 or 300 mg/g.

Cardiovascular comorbidities were highly prevalent, with many CVOTs requiring a history of established atherosclerotic cardiovascular disease (ASCVD) or multiple cardiovascular risk factors. Inclusion and exclusion criteria related to renal function were critical in defining the study populations. Common inclusion criteria involved specific eGFR ranges (e.g., 30 to <90 mL/min/1.73 m²) and levels of albuminuria. Exclusion criteria frequently included eGFR values below 20 or 30 mL/min/1.73 m², end-stage kidney disease (ESKD), or receipt of dialysis. This heterogeneity in baseline renal function and cardiovascular risk across studies is a key consideration when interpreting and generalizing the findings on renal protection.

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Arnaud D. Kaze et al., 2022	65.2 (median)	Not mentioned	< 60	UACR ≥ 30 mg/g	Not specified	Established CVD (37.4% to 100%)
B. Neuen et al., 2019	Not mentioned	Not mentioned	Varied across studies	Varied across studies	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Thomas A. Zelniker et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	60.2% with ASCVD
R. Guthrie et al., 2018	≥ 30	Not mentioned	>30	Not specified	Not specified	Preexisting or high risk for CVD
A. Piperidou et al., 2019	> 50	Not mentioned	Varied across 14 studies	Normal, moderate, or severe	Not specified	Not specified
C. Baigent et al., 2022	Not mentioned	Not mentioned	37-85 (mean range)	Not mentioned	Not specified	High risk of ASCVD, heart failure
Jaehyun Bae et al., 2019	Not specified	Not specified	eGFR ranges included ≥55, ≥30, ≥20	Not specified	Not specified	Wide range of CV risk
Louise Woodhams et al., 2023	Not mentioned	Not mentioned	Primary outcome	UACR as primary outcome	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Lubin Xu et al., 2017	Not specified	Not specified	76.7 to 149.2	ACR range 6.7 to 143.7 mg/g	Not specified	Not mentioned
P. Natale et al., 2024	Not mentioned	Not mentioned	All stages (1-5)	Not mentioned	Stages 1-5	Not mentioned
Dorsa Jahangiri et al., 2021	61.8 to 68.66	Not mentioned	eGFR ≤30 for ESKD definitions	Moderate (30-300 mg/g) or heavy (>300 mg/g)	Not specified	Severe vascular complications implied
Ofri Mosenzon et al., 2019	Not mentioned	Not mentioned	Mostly preserved; 47.6% ≥90	Not mentioned	Not specified	With and without established ASCVD
K. Lo et al., 2019	Not mentioned	Not mentioned	<60	Not mentioned	Not specified	ASCVD, heart failure
A. Liu et al., 2022	Not mentioned	Not mentioned	Subgroups: ≥45 and 15–44	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
H. Heerspink et al., 2020	61.3	Not mentioned	90.7 (mean); 8.3% ≤60	Not mentioned	Not specified	Microvascular disease (35.3%)
Jae Hyun Bae et al., 2025	Not mentioned	Not mentioned	Mean eGFRs: 56.2 (CRENCE), 43.1 (DAPA-CKD), 37.3 (EMPA-KIDNEY)	Median UACRs: 927 mg/g (CRENCE), 949 mg/g (DAPA-CKD), 329 mg/g (EMPA-KIDNEY)	Not specified	Established ASCVD, high CV risk, heart failure
S. Cabrera et al., 2020	62 to 67	Not mentioned	% with eGFR <60ml/min varied: 7% to 60% across studies	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
H. Nagasu et al., 2021	64.4	Not mentioned	68.1 (mean); 26.6% ≤60	Proteinuria in 28.0%	Not specified	Not specified
Haiyan Cao et al., 2021	Not mentioned	Not mentioned	Included	Not mentioned	CKD stage 3b-4	Not mentioned
P. Au et al., 2022	Not mentioned	Not mentioned	Not mentioned	Inconsistent association	Not specified	Not mentioned
G. Chan et al., 2022	Not mentioned	Not mentioned	Included	Not mentioned	CKD stage 3B-5	Not mentioned
N. Saldanha et al., 2022	Comparable at baseline	Not mentioned	Creatinine clearance >30 mL/minute	Not mentioned	Not specified	Not mentioned
P. Sarafidis et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
A. Mahendra et al., 2023	Not mentioned	Not mentioned	Subgroups: > 60 ml/min and 30-60 ml/min	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Taro Hirai et al., 2021	72.0 ± 9.4	Not mentioned	47.1 ± 9.7	Not mentioned	Included patients with eGFR < 60	Not mentioned
Yan Xie et al., 2020	Not mentioned	Not mentioned	eGFR categories evaluated	Not mentioned	Not specified	Not mentioned
Nicole Felix et al., 2024	Not mentioned	Not mentioned	Different levels of kidney function evaluated	Not mentioned	Not specified	Not mentioned
H. Takashima et al., 2018	Not mentioned	Not mentioned	Not mentioned	Albuminuria-lowering effect was primary endpoint	CKD	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Emre Leventoğlu et al., 2024	Not mentioned	Not mentioned	eGFR 20-45 or 45-90 with albuminuria	Yes	Not specified	Reduced risk of MI, heart failure
V. Sridhar et al., 2020	Not mentioned	Not mentioned	30 to <90	Severe albuminuria	Not specified	Not mentioned
P. Delanaye et al., 2023	Not mentioned	Not mentioned	78% with GFR <45	20% without pathological albuminuria	Not specified	Not mentioned
G. Schernthaner et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
F. Lin et al., 2021	60.4	Not mentioned	Mean 85; subgroups ≤60, 60-90, >90	Not collected	Not specified	CVD history (~37%), microvascular disease (~45%)

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
J. Navarro-González et al., 2020	61±5	> 10	Not specified	Inversely correlated with urinary KL	G2-A2	On metformin and RAS blockers
Mohammed D. Algethami et al., 2024	62 to 69.6	13.5 to 15.9	Not mentioned	Not mentioned	CKD stages analyzed	Not mentioned
M. Kanai et al., 2021	71 (Group A), 64 (Group B)	Not mentioned	<45 (Group A), 46-60 (Group B)	Not mentioned	Not specified	Not mentioned
Gian Paolo Fadini et al., 2024	61	10	Mean 86; 23% with CKD	~15% with UACR >30 mg/g	Stage V excluded	One-third with micro/macrovangiopathy ; 13% with established CVD

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
S. Sugiyama et al., 2019	64.8 ± 9.8	18.0 ± 7.4	40.4	UPCR 0.36 g/gCr	3b-4	Hypertension (95.2%), Dyslipidemia (95.2%)
D. Giugliano et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Patients with or without CVD
I. Idris et al., 2023	Not mentioned	Not mentioned	eGFR 20-45 or 45-90	UACR ≥200 for some	Not specified	Implied by outcomes
H. Cao et al., 2022	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
P. Georgianos et al., 2022	Not mentioned	Not mentioned	eGFR <60	Albuminuria >30 mg/g	Not specified	Implied by risk of adverse events

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Kaori Kitaoka et al., 2024	77.7	Not mentioned	Mean 59.3; 42.8% <60	Proteinuria in 33.0%	Not specified	Hypertension (implied by ACEi/ARB use)
Nahla Hussein et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
J. Seufert et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
T. Oh et al., 2020	Not mentioned	Not mentioned	eGFR <60 in 7.4% (dapa) and 25.5% (empa)	Not mentioned	Not specified	Not mentioned
S. Luciano et al., 2020	>18	Not mentioned	Low eGFR	Elevated UACR	2-4	Not mentioned
Issa Kawalit et al., 2024	Not mentioned	Not mentioned	eGFR 15-45	Yes	3b-4	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Kaden K. Fujita et al., 2023	57.9	Not mentioned	Mean 91.7	Non-severe in 94.4%	Not specified	Hypertension (implied by ACEi/ARB use)
Keiji Hirai et al., 2020	Not mentioned	Not mentioned	Mean 22.8	Not mentioned	Advanced-stage	On RAS blockers
T. Jansz et al., 2024	59 ±11	Not mentioned	≥20	Normal, low-level, severely increased	Not specified	Excluded if present
Yaoming Xue et al., 2024	Not mentioned	Not mentioned	Not mentioned	Urinary albuminine ratio evaluated	Not specified	Not mentioned
Alexander Turchin et al., 2025	60 (median)	Not mentioned	≥ 45	Stratified by presence (ACR ≥ 30 mg/g)	Not specified	Moderate CV risk

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
M. Ibernón et al., 2024	DN (64), NDRD (70)	Mentioned but not specified	Not specified	DN patients had higher uACR levels	Not specified	More macrovascular disease in NDRD patients
Catarina Almeida et al., 2021	65.4	14 (median)	15.6% 30-60, 84.4% >60	Normal (37), moderate (18), severe (6)	Not specified	94.1% with ≥1 CVRF
Metaanalyse bestätigt renoprot	Not mentioned	Not mentioned	≥ 30 (≥ 60 for DECLARE-TIMI)	Not mentioned	Not specified	High renal risk
A. Tansawet et al., 2024	68.6	Not mentioned	< 60	Not mentioned	CKD3	Hypertension (92%), CVD (26%)
N. Mittal et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
N. Mikhail et al., 2019	63-64 (mean range)	Not mentioned	As low as 30	Albuminuric nephropathy	Not specified	Established CV disease in some
Sahithi Reddy Kalluri et al., 2021	>18	Not mentioned	eGFR thresholds: <45 (empa, cana), <60 (dapa)	UACR reduction is a mechanism	Not specified	CVD affects 32.2% of T2DM patients
Claire C J Dekkers et al., 2020	≥30	Not mentioned	30-90 (median 56)	UACR 300-5000 mg/g (median 927)	Not specified	Likely (on RAAS blockade)
C. Khoo et al., 2020	59.9	7.1	25-90	UACR >300-5000, micro/macralbuminuria	Not specified	High risk of CVD

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Meir Schechter et al., 2021	Not mentioned	Not mentioned	Normal, early CKD, or advanced proteinuric CKD	Not mentioned	Not specified	Not mentioned
Takayuki Yamada et al., 2020	Not mentioned	Not mentioned	< 60	Not mentioned	Not specified	Implied by MACE focus
S. Rehman et al., 2020	Adult patients	Not mentioned	eGFR, UACR evaluated	UACR evaluated	CKD	Not mentioned
R. Gilbert et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
A. Romano et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Debdipta Bose et al., 2023	Not mentioned	Not mentioned	eGFR > or < 60	Not mentioned	Not specified	Not mentioned
A. Korbuet et al., 2017	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
L. Fang et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
X. Jian et al., 2018	Not mentioned	Not mentioned	Included	Urinary protein measured	Stages 1-3	Not mentioned
Kazuo Kobayashi et al., 2020	Not mentioned	Not mentioned	77.4 ± 22.3	LNACR 1.60 ± 0.65	CKD	Not mentioned
K. J. Chun et al., 2021	Not mentioned	Not mentioned	Subgroups: <45, 45 to <60, ≥60	Subgroups: >300, 30 to 300, <30 mg/g	Not specified	Heart failure
J. C. De La Flor et al., 2023	69.7 (median)	10 to 20	KrU 2.98 to 6.1 mL/min	Proteinuria 1.2 to 10 g/24 h	On hemodialysis	Hypertension in all patients
Saeko Sato et al., 2022	57.7	Not mentioned	Median 62.6	Median ACR 163.1 (NRD), 325.2 (RD) mg/g Cr	Not specified	High prevalence of obesity, hypertension

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
A. Mima et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
P. Georgianos et al., 1969	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
S. Seidu et al., 2018	Not mentioned	Not mentioned	≥30 and <60	UACR > 300 and ≤ 5000 mg/g	Impaired renal function	Not mentioned
C. Bailey et al., 2022	Median 61.8 to 66.8	Not specified	Ranges from >20 to 90	UACR >200 or >300 mg/g	Not specified	HFrEF
M. A. Podestà et al., 2023	Not mentioned	Not mentioned	eGFR ranges 20 to 90 across trials	UACR ranges 200 to 5000 mg/g across trials	Not specified	High CV risk

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Michael S. Kelly et al., 2018	55 to 67 (mean ranges)	Not mentioned	eGFR <60, stages 2-4	UACR >30 mg/g, micro or macroalbuminuria	2-4	Implied by CVOTs
C. Garofalo et al., 2019	Not mentioned	Not mentioned	eGFR ≥30 to <90	Albuminuria >300 to ≤5000 mg/g	Not specified	Heart failure, atherosclerotic events
F. Giorgino et al., 2020	Not mentioned	Not mentioned	Mean eGFRs: 85.2 (DECLARE), 74.1 (EMPA-REG), 56 (CREDENCE), 43.1 (DAPA-CKD)	Median UACRs: 13 mg/g (DECLARE), 18 mg/g (EMPA-REG), 927 mg/g (CREDENCE)	Not specified	Not explicitly mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Merlin C. Thomas et al., 2023	Not specified	Not specified	<60	> 200 mg/g	Not specified	Atherosclerotic CVD, HF, infections
T. Toyama et al., 2019	Not mentioned	Not mentioned	<60	Median UACR 12.8-76.0 mg/g	Not specified	Implied by risk of CV complications
B. Fernandez-Fernandez et al., 2020	62 (mean)	Not mentioned	25-75 (mean 43.1)	200-5000 mg/g (median 949)	Not specified	Hypertension (implied by RAS blockade)
S. A. Alharbi et al., 2025	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
D. Cherney et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
M. Provenzano et al., 2021	Not specified	Not specified	eGFR 25 to 90	Albuminuria >300-5,000 mg/g	Not specified	High risk for CV events
P. Mark et al., 2023	63 (mean in CREDESC E)	Not mentioned	Mean eGFRs: 56.2 (CREDESC E), 43.1 (DAPA-CKD)	Median uACRs: 927 mg/g (CREDESC E), 949 mg/g (DAPA-CKD)	Not specified	Patients with established CVD included
Thomas A. Mavranas et al., 2023	Not specified	Not specified	< 60	Not specified	Not specified	Not specified
D. V. O'Hara et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Carlos Ignacio Reyes-Farias et al., 2023	Not specified	Not specified	eGFR < 60, UACR ≥ 300 mg/g	UACR ≥ 300 mg/g	Not specified	CV history, HF
M. Baker et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
C. Mende et al., 2021	Older individuals (≥65)	Not mentioned	eGFR 30 to < 90	UACR ≥ 300 to 5000 mg/g	Not specified	Atrial fibrillation, heart failure
A. Piperidou et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
P. Georgianos et al., 2022a	Not specified	Not specified	eGFR ranges 25-90	UACR ranges 200-5000 mg/g	Not specified	Not specified
H. Cao et al., 2022a	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Zhi-Cheng Dai et al., 2023	Not explicitly mentioned	Not explicitly mentioned	eGFR ranges from 20 to 75	Significant reduction noted	Stages G1-G4 evaluated	Not explicitly mentioned
V. Sridhar et al., 2020a	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Jingfeng Qian et al., 2025	Not mentioned	Not mentioned	30-90	Not mentioned	2-3	Not mentioned
Hongru Yan et al., 2021	Not mentioned	Not mentioned	eGFR 5-90	UACR 200-5000	Not specified	High cardiovascular risk
Atit Dharia et al., 2023	Not specified	Not specified	Mean eGFRs: 56.2 (CRENCE), 43.1 (DAPA-CKD)	Median UACRs: 927 mg/g (CRENCE), 949 mg/g (DAPA-CKD)	Not specified	Established ASCVD

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Davide Margonato et al., 2020	Not mentioned	Not mentioned	eGFR ≥ 30 and < 90	UAC between 300 and 5000 mg/g	Not specified	50% with history of CV disease
J. Stephens et al., 2020	Not specified	Long duration	<60	≥ 30 mg/g	Not specified	High prevalence of CVD
Wajd Alkabbani et al., 2021	≥ 18	Not mentioned	Stratified as <60 and ≥ 60	Increase to >300 mg	Not specified	Not mentioned
Xiaoya Sun et al., 2022	Not specified	Not specified	eGFR >30 to <90	Substantial albuminuria in CREDENCE	Not specified	High cardiovascular risk
K. Rådholm et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Husam M. Salah et al., 2020	Not specified	Not specified	< 60	Not mentioned	Not specified	Heart failure
B. Neuen et al., 2020	Not mentioned	Not mentioned	eGFR <60 for 60% of CREDE participants	UACR ≥300 mg/g	Not specified	ASCVD
Yuki Kawai et al., 2021	Not mentioned	Not mentioned	Not mentioned	With or without albuminuria	Not specified	Not mentioned
Sarah Yoon Ai Ng et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Agus Layanto et al., 2024	Not mentioned	Not mentioned	< 60 or UACR ≥ 30 mg/g	UACR ≥ 30 mg/g	CKD	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
B. Spiazzi et al., 2024	Not mentioned	Not mentioned	Evaluated across KDIGO classes	Evaluated across UACR levels	Not specified	Not mentioned
A. Scheen et al., 2023	Not mentioned	Not mentioned	CKD, including stage 4	Not mentioned	Not specified	Not mentioned
Chalmouk ou Konstantina et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Kelsey M Leite et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned	CKD	Patients at risk of CKD
A. Roy et al., 2020	Not specified	Not specified	eGFR > 45 for initiation	Albuminuric CKD (ACR >300-5000)	Mild-to-moderate DKD	Cardiovascular comorbidities mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
B. Pasternak et al., 2020	61.3	Not mentioned	3.3% had CKD	Albuminuria distribution not specified	Not specified	18.6% had major CVD
R. DeFronzo et al., 2021	Not specified	Not specified	Not specified	Not specified	Not specified	High risk for macrovascular complications
Mohanad Almaimani et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Shafaat Raza et al., 2022	Not mentioned	Not mentioned	eGFR as low as 30	Not mentioned	CKD stage 3b	HFrEF
Ning Li et al., 2021	61.9 to 69	Not mentioned	eGFR <60	UACR >300 mg/g	Not specified	Heart failure, ASCVD

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
G. Park et al., 2022	55.4 (SGLT2i), 54.9 (DPP-4i) (mean)	Not mentioned	Mean eGFR ~96	Excluded macroalbuminuria	Not specified	Hypertension, dyslipidemia
A. B. A. Andrade et al., 2020	Not mentioned	Not mentioned	GFR evaluated	ACR evaluated	Not specified	Not mentioned
Ayesha Saleem et al., 2024	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Shaowei Pang et al., 2024	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
J. O'Sullivan et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Jennifer B. Green et al., 2022	Not specified	Not specified	Ranges from <60 to 30 to <90 across trials	Albuminuria >300 to 5000 mg/g across trials	Not specified	Established CVD in half of CRENC E patients
Hema Boddula et al., 2023	Not mentioned	Not mentioned	eGFR 30-90	Not mentioned	Stages 2 and 3	High CV risk
Prabhat Singh et al., 2023	Not specified	Not specified	eGFR ranges 20 to 90	Albuminuria 300 to 5000 mg/g	Not specified	HFREF
Vjollca Godanci-Kelmendi et al., 2023	Not mentioned	Not mentioned	eGFR > 20 included	Included	Not specified	Not mentioned
Kazuo Kobayashi et al., 2018	Not mentioned	Not mentioned	77.7 ± 23.9	Median UACR 47.1 mg/gCr	CKD	Use of β-blockers

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
C. Jung et al., 2021	>30	Not mentioned	Not mentioned	Over 30% had albuminuria or CKD	Not specified	ASCVD, HF
Junhua Ma et al., 2023	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
T. Siddiqi et al., 2024	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Tatsuya Ishibashi et al., 2023	59.4 (mean)	Not specified	> 30 (mean 78)	< 30 mg/gCr	Not specified	Not mentioned
Ting Liu et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
E. Elenjickal et al., 2025	Not mentioned	Not mentioned	<30	Not mentioned	Advanced CKD	Not mentioned
D. Giugliano et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Wendy Wang et al., 2024	53±10	Not mentioned	Excluded prevalent CKD	Not mentioned	Not specified	On metformin
T. Oh et al., 2020a	Not mentioned	Not mentioned	<60 in some studies	Not mentioned	Not specified	Not mentioned
V. Sridhar et al., 2023	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Apichaya Chanawong et al., 2023	Not mentioned	Not mentioned	Subgroups: <60 and ≥60	Not mentioned	Not specified	Not mentioned
T. Siddiqi et al., 2023	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Rasha O. Abdelmoniem et al., 2022	50.5 (SGLT2i), 50.36 (placebo) (mean)	Not mentioned	Mean eGFR ~86-88	Mean UACR ~113-166 mg/g	Not specified	Not explicitly mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Sidra Jamil et al., 2022	65.81	Not specified	eGFR < 60 or UACR > 30 mg/g	> 30 mg/g	Stage 4 excluded	Not specified
C. Deerochan awong et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Tien-Jyun Chang et al., 2024	Not mentioned	Not mentioned	Not mentioned	Stratified by UACR levels	CKD	Not mentioned
Vjollca Godanci- Kelmendi et al., 2025	68 patients >65	Not mentioned	eGFR >20 included	Included	Not specified	Not mentioned
Susovan Halder et al., 2024	Not mentioned	Not mentioned	Not specified	Significant decrease in ACR	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Renata Carvalho et al., 2021	71.2±13.5	15.9	Mean serum creatinine 1.96mg/dL	Protein-creatinine ratio 1.48	Not specified	51% heart failure, 27% cerebral vascular disease
Hyeong-Kyu Park et al., 2023	Not specified	Not specified	Not specified	Not specified	Not specified	Not specified
M. Wani et al., 2019	Not mentioned	Not mentioned	Established kidney disease	Not mentioned	Not specified	Not mentioned
Chen et al., 2019	Not mentioned	Not mentioned	Mean baseline eGFR < 60	Not mentioned	Not specified	Not mentioned
K. Stavropoulos et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Daiji Kawanami et al., 2017	Not specified	Not specified	eGFR ≥ 30	UACR ≥ 30 mg/g	Not specified	High cardiovascular risk
Josselin Nespoux et al., 2018	Not specified	Not specified	Not specified	Not specified	Not specified	Not specified
H. Heerspink et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	MACE, hospitalization for heart failure
P. Georgianos et al., 2021	Not specified	Not specified	Not specified	Not specified	Not specified	Not specified
D. McGuire et al., 2020	63.7	11.8 to 15.8	<60 in 7.4%-59.8% of patients	Included in subgroup analyses	Not specified	66.2% with prevalent ASCVD
Chen Wang et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
N. Kashiwara et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
R. Fontes-Carvalho et al., 2021	Not mentioned	Not mentioned	eGFR 25-89	UACR >200-5000 mg/g	Not specified	Not explicitly detailed
C. Wanner et al., 2017	~63	>10	<90, 52% with 60-90	UACR <30 mg/g in 59%	Not specified	Established CVD
O. González-Albarrán et al., 2022	Older age is a risk factor	Not specified	eGFR 25 to 90	UACR 300 to 5000 mg/g	Not specified	Hypertension
E. Brown et al., 2020	Not mentioned	Not mentioned	eGFR >30 to <90	UACR >300-5000mg/g	CKD1-3	Not mentioned
Tianbiao Zhou et al., 2023	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Nam Hoon Kim et al., 2022	Not specified	9.8 (for one study)	Mean 85 (for one study)	Not specified	Not specified	Hypertension
Y. Saisho et al., 2020	Not specified	Not specified	Mean 56.2	Median UACR 927	Not specified	Prior CV events, heart failure, CKD
R. Nevola et al., 2022	Not specified	Not specified	Persistent albuminuria or decline in eGFR	Persistent albuminuria is a defining feature	Not specified	High CV risk
V. Tsimihodimos et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Linda Sukiarno et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
S. Rabizadeh et al., 2019	Not explicitly mentioned	Not explicitly mentioned	eGFR mentioned	Albuminuria reduction discussed	Not specified	Previous CVD and high risk for CV events
B. Fernandez-Fernandez et al., 2023	Not specified	Not specified	≥20	<30 mg/g	Not specified	Excluded those with previous ASCVD
Joseph E Cruz et al., 2018	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
V. Tesar et al., 2022	61.8 (mean)	Not specified	25-75 (mean 43.1)	200-5000 mg/g (mean 949)	Not specified	Not specified
V. Salukhov et al., 2021	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Владимир Владимирович Салухов et al., 2020	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
A. Scheen et al., 2020	Not mentioned	Not mentioned	eGFR 30–60	Albuminuria (not specified)	Stage 3 DKD	Implied by CV events reduction
A. Forbes et al., 2023	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
A. Scheen et al., 2020a	Not specified	Not specified	eGFR as low as 30–45	Albuminuria >300 to 5,000 mg/g	Mild to moderate CKD	Established ASCVD, high CV risk
J. Halimi et al., 2021	Not mentioned	Not mentioned	GFR ≥ 25	Not mentioned	Not specified	HF with reduced ejection fraction

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
Honghong Zou et al., 2017	Not specified	Not specified	Decreased GFR, stage 3 DKD	Persistent albuminuria , UACR evaluated	Stage 3 DKD	High risk for CV events, heart failure
Chu-Hsuan Shiau et al., 2023	Not mentioned	Not mentioned	Stage 4 CKD mentioned	Macroalbuminuria mentioned	Stage 4	Not mentioned
Taichi Nagahisa et al., 2019	63 to 66 (mean ranges)	Not explicitly mentioned	eGFR 30 to 90	Macroalbuminuria in CREDENCE	CKD stage 3-4	Established CVD
E. Nelaj et al., 2024	Elderly	Not mentioned	eGFR range 75.3–87.19 at 12 months	Not mentioned	Not specified	Not explicitly mentioned
T. Milder et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Stage 3 CKD	Not mentioned
Chao Feng et al., 2019	Not mentioned	Not mentioned	Mean baseline eGFR < 60	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
P. Sarafidis et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
S. De Cosmo et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Shuo Yang et al., 2022	Not specified	Not specified	Mean eGFR; CKD defined by mean eGFR <90	New-onset macroalbuminuria part of composite outcome	Not specified	Pre-existing CVD
L. Sloan et al., 2024	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Yanqun Zheng et al., 2025	Not mentioned	Not mentioned	Compromised renal functions	Not mentioned	Not specified	Not mentioned
Buchun Jiang et al., 2024	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned

Study	Mean Age (years)	Diabetes Duration (years)	Baseline eGFR (mL/min/1.73 m ²)	Baseline Albuminuria	CKD Stage Distribution	Key Comorbidities
J. Menne et al., 2019	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not specified	Not mentioned
Charlotte C. van Ruiten et al., 2022	Not specified	Not specified	Mean eGFRs: 56.2 (CRENCE), 43.1 (DAPA-CKD)	Median ACRs: 927 mg/g (CRENCE), 949 mg/g (DAPA-CKD)	Not specified	Established CVD
D. Giugliano et al., 2021a	61.3-71.9	Not mentioned	Not specified	Not mentioned	Not specified	Established CVD or risk factors
Mahmoud Barbarawi et al., 2021	64.7 ± 8.4	Not mentioned	Not mentioned	Not mentioned	Not specified	Prevalent ASCVD
A. Scheen et al., 2021	Not mentioned	Not mentioned	< 45	With or without albuminuria	Not specified	Not mentioned

DISCUSSION

Synthesis of Principal Findings

This comprehensive systematic review, synthesizing evidence from 138 studies encompassing over 700,000 participants, provides definitive confirmation that SGLT2 inhibitors confer substantial and consistent renal protection across the full spectrum of patients with diabetic kidney disease. The totality of evidence demonstrates that SGLT2 inhibitors reduce the risk of clinically significant renal outcomes—including doubling of serum creatinine, progression to ESRD, renal death, and composite renal endpoints—by approximately 30-40% (hazard ratio range 0.61-0.71 across major trials and meta-analyses), with remarkable consistency across study designs, geographic regions, and patient populations (Neuen et al., 2019; Zelniker et al., 2019; Baigent et al., 2022; Kaze et al., 2022). The robustness of these findings is substantially reinforced by the convergence of evidence from multiple methodological approaches: large-scale, rigorously conducted RCTs with dedicated renal primary outcomes; secondary analyses of CVOTs with adjudicated renal events; prospective and retrospective real-world cohort studies; and multiple independent systematic reviews and meta-analyses employing diverse analytical strategies (Bae et al., 2019; Salah et al., 2020; McGuire et al., 2020; Spiazzi et al., 2024).

The consistency of treatment effects across this heterogeneous evidence base is particularly noteworthy. Effect estimates from real-world observational studies, despite their inherent susceptibility to residual confounding, closely approximate those from randomized trials, supporting the generalizability of efficacy findings to routine clinical practice (Heerspink et al., 2020; Pasternak et al., 2020; Forbes et al., 2023; Fadini et al., 2024). Furthermore, the durability of renal protection appears sustained over time, with landmark trials demonstrating preservation of benefit throughout follow-up periods extending to 4.2 years, and observational studies suggesting continued eGFR slope attenuation beyond five years of treatment (Mosenzon et al., 2019; Almeida et al., 2021; Ishibashi et al., 2023; Zheng & Sun, 2025). This temporal persistence distinguishes

SGLT2 inhibitors from interventions that produce early hemodynamic effects without sustained disease modification.

Magnitude and Clinical Significance of Renal Protection

The clinical significance of SGLT2 inhibitor-mediated renal protection extends far beyond statistically significant hazard ratios. In absolute terms, the number needed to treat to prevent one major renal event ranges from 18 to 27 over 2.5-3 years in dedicated renal outcome trials, representing clinically meaningful risk reduction comparable to or exceeding that of RAAS blockade when originally introduced (Perkovic et al., 2019; Heerspink et al., 2020; Herrington et al., 2023). The attenuation of eGFR decline—approximately 0.5-1.5 mL/min/1.73m² per year slower than comparator groups—translates into postponement of ESRD onset by several years for individual patients and substantial reduction in population burden of dialysis-dependent kidney failure (Tuttle et al., 2022; Mahendra et al., 2023; Tansawet et al., 2024). Given that each year of dialysis dependence is associated with profound reductions in quality of life, substantial healthcare expenditures (exceeding \$90,000 annually per patient in many healthcare systems), and markedly increased cardiovascular mortality, the public health implications of delaying or preventing ESRD are substantial (Mikhail, 2019; De Cosmo et al., 2019).

Moreover, the benefits of SGLT2 inhibitors on renal outcomes are additive to those of RAAS blockade, the previous standard of care (Halder et al., 2024). In CREDENCE, DAPA-CKD, and EMPA-KIDNEY, >95% of participants were receiving stable doses of ACE inhibitors or ARBs at baseline, yet SGLT2 inhibitors provided additional 30-40% risk reduction, demonstrating that these agents target pathophysiological mechanisms distinct from angiotensin II antagonism (Dekkers & Gansevoort, 2020; Sarafidis et al., 2021; Tesar, 2022). This additive benefit positions SGLT2 inhibitors as complementary, not alternative, therapy to RAAS blockade, establishing a new dual-therapy foundation for DKD management analogous to the paradigm shift that occurred when

ACE inhibitors were added to conventional antihypertensive therapy in the 1990s (Roy et al., 2020; Oh et al., 2020).

Consistency Across the Spectrum of Kidney Disease

A particularly important finding of this review is the consistent renoprotective efficacy of SGLT2 inhibitors across the full continuum of baseline kidney function, including patients traditionally excluded from or underrepresented in earlier trials. In patients with eGFR 30-45 mL/min/1.73m², the relative risk reduction for composite renal outcomes is fully preserved and may be numerically greater than in those with preserved renal function, although absolute risk reduction is larger due to higher baseline event rates (Chun & Jung, 2021; Lin et al., 2021; Kawalit et al., 2024). Critically, emerging evidence from DAPA-CKD, EMPA-KIDNEY, and dedicated cohort studies now extends these benefits to patients with eGFR 20-30 mL/min/1.73m² (stage 4 CKD), a population previously excluded from SGLT2 inhibitor trials due to concerns about attenuated glycemic efficacy and potential safety risks (Chertow et al., 2021; Heerspink et al., 2022; Elenjickal et al., 2025). In these advanced CKD patients, SGLT2 inhibitors continue to reduce the risk of dialysis initiation and cardiovascular events despite minimal effects on HbA1c, reinforcing that renoprotection is substantially independent of glycemic lowering (Kanai et al., 2021; Chan et al., 2022; Idris, 2023).

Similarly, the renal benefits of SGLT2 inhibitors extend across the albuminuria spectrum. While the absolute risk reduction is greatest in patients with macroalbuminuria (UACR >300 mg/g) who face the highest risk of progression, significant benefits are also observed in patients with moderately increased albuminuria (30-300 mg/g) and, importantly, in patients with normoalbuminuria (UACR <30 mg/g) (K. J. Fujita et al., 2023; T. Jansz et al., 2024; Chang et al., 2024). This observation challenges the traditional paradigm that albuminuria reduction is the primary mediator of renoprotection and suggests that SGLT2 inhibitors exert kidney-protective effects through pathways independent of proteinuria modification, including favorable effects on

tubular health, interstitial fibrosis, and hypoxia (Mima, 2018; Kashihara et al., 2019; van Ruiten et al., 2022). The demonstration of renal benefit in normoalbuminuric DKD, which constitutes a substantial proportion of patients with diabetes-related CKD, substantially expands the population eligible for SGLT2 inhibitor therapy (Ishibashi et al., 2023; T. Oh et al., 2020).

Comparative Effectiveness and Class Effects

An important unresolved question is whether the renoprotective effects of SGLT2 inhibitors represent a true class effect or whether clinically meaningful differences exist among individual agents. Our synthesis reveals that empagliflozin, canagliflozin, and dapagliflozin have each demonstrated significant renal benefit in dedicated outcome trials or large CVOTs with renal prespecified secondary endpoints, with overlapping confidence intervals for composite renal outcomes (Zelniker et al., 2019; Neuen et al., 2019; Salah et al., 2020; Spiazzi et al., 2024). However, differences in trial designs, entry criteria, and outcome definitions preclude definitive assertions of equivalence. Canagliflozin, studied in CREDENCE at 100 mg daily in patients with eGFR 30-90 and UACR 300-5000 mg/g, demonstrated a 34% reduction in the primary composite outcome (Perkovic et al., 2019). Dapagliflozin, evaluated in DAPA-CKD at 10 mg daily in patients with eGFR 25-75 and UACR 200-5000 mg/g (including approximately one-third without diabetes), showed a 39% reduction in the primary composite (Heerspink et al., 2020). Empagliflozin, assessed in EMPA-KIDNEY at 10 mg daily in patients with eGFR 20-45 (or 45-90 with UACR ≥ 200 mg/g), demonstrated a 28% reduction in kidney disease progression or cardiovascular death (Herrington et al., 2023).

Network meta-analyses attempting indirect comparisons have generally not identified statistically significant differences among SGLT2 inhibitors for renal outcomes, although point estimates favor canagliflozin and dapagliflozin for albuminuria reduction and empagliflozin for cardiovascular mortality (Yamada et al., 2020; Cao et al., 2022; Ma et al., 2023). However, these analyses are limited by between-trial heterogeneity in patient populations, background therapy, and

outcome definitions, and should be interpreted cautiously. Importantly, ertugliflozin has not demonstrated significant renal benefits in dedicated outcome trials, although renal event rates were low in the VERTIS CV trial and confidence intervals were wide, precluding definitive conclusions about efficacy or lack thereof (Cannon et al., 2020). Thus, while the preponderance of evidence supports a class effect for the three extensively studied agents, subtle differences in pharmacokinetics (e.g., degree of SGLT2 vs SGLT1 selectivity, half-life, route of elimination) may theoretically influence renal efficacy and safety profiles, particularly in advanced CKD (Scheen, 2020; Gonzalez-Albarran et al., 2022).

Mechanisms of Renal Protection: An Integrated Framework

The mechanisms by which SGLT2 inhibitors confer renal protection are remarkably multifactorial and have been elucidated through complementary human physiology studies, translational investigations, and preclinical models (Heerspink et al., 2018; Nespoux & Vallon, 2018; van Ruiten et al., 2022). The hemodynamic hypothesis remains the best-characterized pathway. In early DKD, hyperglycemia-induced proximal tubular sodium and glucose reabsorption via SGLT2 reduces distal sodium delivery to the macula densa, decreasing adenosine generation and causing afferent arteriolar vasodilation through tubuloglomerular feedback inhibition (Korbut & Klimontov, 2017; Tsimihodimos et al., 2018). This maladaptive hemodynamic response increases intraglomerular pressure and glomerular filtration rate (hyperfiltration), initiating and perpetuating glomerular injury. SGLT2 inhibitors restore tubuloglomerular feedback by increasing distal sodium delivery, thereby inducing afferent arteriolar vasoconstriction, reducing intraglomerular hypertension, and normalizing the hyperfiltration state (Cherney et al., 2019; Salukhov et al., 2021; Nam Hoon Kim & Kim, 2022). This hemodynamic effect is reflected clinically by the well-characterized acute dip in eGFR (typically 3-5 mL/min/1.73m²) observed within 2-4 weeks of treatment initiation, which is reversible upon drug discontinuation and not associated with tubular injury biomarkers (Wanner, 2017; M. A. Podestà et al., 2023).

However, the hemodynamic mechanism alone cannot fully explain the sustained renoprotection or the reduction in hard renal endpoints observed over years of follow-up. Accumulating evidence supports direct tubuloprotective effects of SGLT2 inhibitors that are independent of glomerular hemodynamics (Mima, 2018; Kashihara et al., 2019; Dai et al., 2023). The proximal tubular epithelium, which bears the highest energy demands of any nephron segment due to active solute transport, is particularly vulnerable to glucotoxicity and hypoxia in the diabetic milieu. By reducing glucose and sodium reabsorption, SGLT2 inhibitors decrease mitochondrial oxidative phosphorylation and oxygen consumption, ameliorating tubular hypoxia and improving bioenergetic efficiency (Sridhar et al., 2020; van Ruiten et al., 2022). This metabolic rebalancing attenuates the production of reactive oxygen species, reduces endoplasmic reticulum stress, and preserves mitochondrial integrity (J. Navarro-González et al., 2020; Buchun Jiang et al., 2024). Furthermore, SGLT2 inhibitors downregulate pro-inflammatory and pro-fibrotic signaling pathways including nuclear factor kappa-B, transforming growth factor-beta, and connective tissue growth factor, reducing macrophage infiltration and myofibroblast activation (Zhi-Cheng Dai et al., 2023; Georgianos et al., 2021). These anti-inflammatory effects are complemented by enhanced autophagy and mitophagy, facilitating clearance of damaged organelles and protein aggregates that accumulate in diabetic tubules (DeFronzo & Abdul-Ghani, 2021; Hongru Yan et al., 2021).

The role of albuminuria reduction in mediating renal protection remains incompletely understood. SGLT2 inhibitors consistently reduce albuminuria by 25-35% within 3-6 months of treatment initiation, an effect that is only partially correlated with glycemic improvement and persists after adjustment for HbA1c changes (Piperidou et al., 2019; Xu et al., 2017; Feng et al., 2019). The reduction in albuminuria likely reflects both hemodynamic normalization (reduced intraglomerular pressure) and improvements in glomerular endothelial function and podocyte health (Takashima et al., 2018; Tatsuya Ishibashi et al., 2023). However, the dissociation between albuminuria reduction and hard renal outcomes in some analyses suggests that albuminuria serves as a biomarker of glomerular injury rather than a direct mediator of progression, and that SGLT2

inhibitors provide renoprotection through pathways beyond proteinuria modification (Heerspink et al., 2018; K. J. Chun & Jung, 2021).

Systemic metabolic effects contribute to, but do not fully account for, renal protection. SGLT2 inhibitors produce modest reductions in HbA1c (0.5-0.8%), body weight (2-3 kg), and systolic blood pressure (3-5 mmHg) (Zelniker et al., 2019; Salah et al., 2020). However, the renal benefits of SGLT2 inhibitors exceed those expected from these metabolic improvements alone, and significant renal risk reduction is observed in patients with minimal HbA1c lowering, including those with advanced CKD and those without diabetes (Fernandez-Fernandez et al., 2020; Baigent et al., 2022). Furthermore, mediation analyses from CREDENCE and DAPA-CKD indicate that only 10-20% of the renoprotective effect is attributable to changes in HbA1c, systolic blood pressure, or body weight (Li et al., 2021; Provenzano et al., 2021). These observations strongly support the primacy of direct renal mechanisms, particularly hemodynamic normalization and tubuloprotection, in mediating the sustained kidney benefits of SGLT2 inhibitors.

Safety Profile and Renal Adverse Effects

The safety profile of SGLT2 inhibitors in patients with DKD has been extensively characterized and is generally favorable, although several renal-specific considerations warrant careful attention. The phenomenon of initial eGFR decline, historically misinterpreted as acute kidney injury, is now recognized as a reversible hemodynamic effect reflecting normalization of intraglomerular pressure (Menne et al., 2019; Baker & Perazella, 2020; Sridhar et al., 2020). This acute dip typically averages 3-5 mL/min/1.73m², occurs within 2-4 weeks of treatment initiation, stabilizes thereafter, and is fully reversible within 4-8 weeks of drug discontinuation (Wanner, 2017; Nespoux & Vallon, 2018). Importantly, the magnitude of initial eGFR decline is not associated with subsequent risk of acute kidney injury and does not attenuate long-term renal protection; paradoxically, patients experiencing larger initial dips demonstrate greater preservation

of kidney function over time, consistent with effective hemodynamic normalization (Cherney et al., 2020; Adamson et al., 2022).

Contrary to initial safety signals from spontaneous reporting systems, large-scale RCTs and meta-analyses have definitively demonstrated that SGLT2 inhibitors do not increase—and may modestly reduce—the risk of acute kidney injury (AKI) (Gilbert & Thorpe, 2019; Menne et al., 2019; Neuen et al., 2019). In the CANVAS Program and CREDENCE, canagliflozin was associated with a numerically lower incidence of AKI events (hazard ratio 0.85, 95% CI 0.69-1.06) (Perkovic et al., 2019). In DAPA-CKD, dapagliflozin significantly reduced AKI events by 31% (HR 0.69, 95% CI 0.49-0.98) (Heerspink et al., 2020). Meta-analyses pooling these and other trials confirm a consistent reduction in AKI risk, likely mediated through improved tubular energetics, reduced ischemia-reperfusion injury, and attenuated contrast-induced nephropathy (Gilbert & Thorpe, 2019; Menne et al., 2019; Sridhar et al., 2020). This protective effect against AKI represents an important and underappreciated component of the renal safety profile.

Electrolyte disturbances associated with SGLT2 inhibitors are generally mild and infrequently require intervention. Mild increases in serum magnesium and phosphate have been observed, but are not clinically significant in most patients (Scheen, 2020; Bailey et al., 2022). Hyperkalemia risk, a major concern with RAAS blockade, is not increased and may be slightly reduced with SGLT2 inhibitor therapy, potentially due to improved kaliuresis and reduced metabolic acidosis (Neuen et al., 2019; Sarafidis et al., 2021). However, volume depletion and hypotension can occur, particularly in elderly patients, those with baseline eGFR <30 mL/min/1.73m², and those receiving concomitant loop diuretics (M. Baker & Perazella, 2020; Godanci-Kelmendi et al., 2025). The risk of volume-related adverse events is mitigated by appropriate dose selection (canagliflozin 100 mg daily, empagliflozin 10 mg daily, dapagliflozin 10 mg daily in eligible patients), avoidance of concurrent SGLT2 inhibitor initiation during acute intercurrent illnesses, and temporary discontinuation prior to prolonged fasting, surgery, or high-volume contrast procedures (Scheen & Delanaye, 2021; T. Oh et al., 2020).

Genital mycotic infections represent the most common adverse effect, occurring in 5-8% of treated patients compared to 1-2% of placebo recipients, with higher incidence in uncircumcised males and patients with prior history of genital infections (Zelniker et al., 2019; Salah et al., 2020; Alkabbani et al., 2021). These infections are typically mild, respond promptly to topical antifungal therapy, and infrequently necessitate treatment discontinuation. Urinary tract infections are not increased with SGLT2 inhibitor therapy in meta-analyses of dedicated renal trials, despite theoretical concerns related to glucosuria (Donnan et al., 2019; Lega et al., 2019). Importantly, the risks of atypical infections including Fournier's gangrene and pyelonephritis, while heavily publicized based on case reports, are exceedingly rare (absolute risk <0.01%) and not significantly increased in large-scale RCTs or population-based cohort studies (Dave et al., 2021; Lazarus et al., 2022).

Subgroup Effects and Heterogeneity

Understanding whether SGLT2 inhibitor efficacy varies across patient subgroups is essential for personalized clinical decision-making and equitable access to therapy. Our synthesis demonstrates remarkable consistency of relative risk reduction across virtually all examined subgroups, including age, sex, race/ethnicity, geographic region, diabetes duration, baseline HbA1c, body mass index, blood pressure, and cardiovascular disease history (Zelniker et al., 2019; Kaze et al., 2022; Baigent et al., 2022). The absence of significant treatment-by-subgroup interactions for renal outcomes indicates that SGLT2 inhibitors confer proportional benefits regardless of baseline demographic or clinical characteristics, supporting broad implementation across diverse DKD populations.

However, two important caveats warrant discussion. First, while relative risk reduction is consistent, absolute risk reduction varies substantially as a function of baseline risk, being greatest in patients with macroalbuminuria, advanced CKD, and elevated cardiovascular risk (Chun & Jung, 2021; Giorgino et al., 2020). This has implications for cost-effectiveness analyses and prioritization

in resource-constrained settings. Second, the quality of evidence for certain subgroups varies. For example, while RCT data in elderly patients (≥ 75 years) are limited due to underrepresentation in clinical trials, observational studies and pooled analyses suggest preserved efficacy and safety (Kitaoka et al., 2024; Godanci-Kelmendi et al., 2025). Similarly, data in non-white populations, while accumulating from Asian cohort studies and global trials, remain relatively sparse for Black and Hispanic patients, highlighting an important health equity gap (C. Khoo et al., 2020; Yamada et al., 2020).

Comparison with Other Glucose-Lowering and Renoprotective Therapies

SGLT2 inhibitors must be positioned within the evolving therapeutic landscape for DKD, which now includes GLP-1 receptor agonists and the non-steroidal mineralocorticoid receptor antagonist finerenone. Direct comparative effectiveness research remains limited, but network meta-analyses provide some guidance. For composite renal outcomes including progression to macroalbuminuria, eGFR decline, and ESRD, SGLT2 inhibitors appear numerically superior to GLP-1 receptor agonists, although confidence intervals overlap and differences are not statistically significant (Yamada et al., 2020; Kawai et al., 2021; Yang et al., 2022). For albuminuria reduction, SGLT2 inhibitors and GLP-1 receptor agonists demonstrate similar efficacy, with combination therapy producing additive reductions (DeFronzo & Abdul-Ghani, 2021; Idris, 2023). Finerenone, studied in FIDELIO-DKD and FIGARO-DKD, reduces albuminuria and composite renal outcomes with effect sizes similar to SGLT2 inhibitors, and emerging data suggest additive benefits when combined with SGLT2 inhibitors (Bakris et al., 2020; Pitt et al., 2021; Georgianos et al., 2022). The optimal sequencing and combination of these three complementary classes—SGLT2 inhibitors, GLP-1 receptor agonists, and finerenone—represents a critical unanswered question requiring prospective comparative effectiveness trials (Mark et al., 2023; Nevo et al., 2022).

Evidence Quality and Limitations

The overall quality of evidence supporting SGLT2 inhibitor-mediated renal protection is high, anchored by multiple large-scale, rigorously conducted, double-blind, placebo-controlled RCTs with low risk of bias (Natale et al., 2024; Baigent et al., 2022). However, important limitations exist across the evidence base. First, the landmark renal outcome trials—CREDENCE, DAPA-CKD, and EMPA-KIDNEY—were all terminated early due to overwhelming efficacy based on pre-specified interim analyses (Perkovic et al., 2019; Heerspink et al., 2020; Herrington et al., 2023). While ethically mandated, early termination may overestimate treatment effects and limit precise characterization of long-term safety and durability of benefit (Bassler et al., 2010; Montori et al., 2005). Second, trial populations remain highly selected, with strict inclusion criteria regarding eGFR and albuminuria thresholds, age limits, and exclusion of patients with recent cardiovascular events, advanced heart failure, or severe hepatic impairment (Scherthaner et al., 2020; McGuire et al., 2020). Consequently, the generalizability of trial findings to the full spectrum of DKD encountered in clinical practice, particularly the oldest-old, frail individuals, and those with multiple advanced comorbidities, remains uncertain. Third, follow-up durations in RCTs (median 2.0-3.5 years) are relatively short relative to the natural history of DKD progression, which unfolds over decades (Mosenzon et al., 2019; Almeida et al., 2021). Extended follow-up of trial cohorts and long-term observational studies are needed to determine whether the renoprotective effects of SGLT2 inhibitors persist, attenuate, or amplify over time (Ishibashi et al., 2023; Zheng & Sun, 2025).

Observational studies, while providing valuable complementary evidence on effectiveness in routine clinical practice, are subject to inherent methodological limitations including residual confounding by indication, selection bias, and unmeasured confounders (H. Heerspink et al., 2020; Pasternak et al., 2020; Forbes et al., 2023). Although sophisticated analytical approaches including propensity score matching, instrumental variable analysis, and active comparator designs mitigate these biases, they cannot fully eliminate the possibility of residual confounding (Xie et al., 2020; Tansawet et al., 2024). Furthermore, many observational studies rely on administrative claims data lacking laboratory values (eGFR, UACR), precluding precise characterization of baseline kidney

function and assessment of albuminuria outcomes (Au et al., 2022; G. Park et al., 2022). The consistency of observational findings with RCT results is reassuring, but cannot substitute for adequately powered, long-term randomized comparisons in underrepresented populations.

Implications for Clinical Practice

The evidence synthesized in this review supports several actionable recommendations for clinical practice. First, SGLT2 inhibitors should be considered foundational therapy for renal protection in patients with type 2 diabetes and CKD, regardless of glycemic control or concurrent antidiabetic therapy (Roy et al., 2020; Oh et al., 2020; Sarafidis et al., 2021). The benefits of SGLT2 inhibitors on renal outcomes are additive to RAAS blockade and are observed across the spectrum of CKD stages 2-4, with emerging evidence supporting initiation at eGFR as low as 20 mL/min/1.73m² (Elenjickal et al., 2025; Kawalit et al., 2024). Second, SGLT2 inhibitor therapy should be initiated at the doses proven effective in renal outcome trials (canagliflozin 100 mg daily, dapagliflozin 10 mg daily, empagliflozin 10 mg daily), with dose reduction for advanced CKD required only for canagliflozin (limited to 100 mg; 300 mg not recommended for eGFR <60 mL/min/1.73m²) (Neuen et al., 2020; Scheen, 2020). Third, patients and clinicians should be counseled regarding the expected initial eGFR decline (3-5 mL/min/1.73m²) to prevent unnecessary treatment discontinuation; this hemodynamic effect is reversible and predicts long-term renal benefit (Wanner, 2017; Sridhar et al., 2020). Fourth, SGLT2 inhibitors should be continued through intercurrent illnesses with appropriate volume repletion, and temporarily withheld only in settings of prolonged fasting, major surgery, or critical illness with hemodynamic instability (Baker & Perazella, 2020; Scheen & Delanaye, 2021). Fifth, monitoring for genital mycotic infections with appropriate patient education and prompt treatment is warranted, but routine monitoring of renal function beyond standard CKD care is not required specifically for SGLT2 inhibitor safety (Alkabbani et al., 2021; Bailey et al., 2022).

Implications for Health Policy and Healthcare Systems

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The translation of SGLT2 inhibitor efficacy into population-level renal benefit requires concerted health policy efforts. Despite robust evidence and guideline recommendations, SGLT2 inhibitor utilization remains suboptimal, particularly in primary care settings, among racial and ethnic minorities, and in lower-income populations (McCullough et al., 2021; Eberly et al., 2022). Addressing this evidence-to-practice gap requires multi-level interventions including: (1) removal of financial barriers through appropriate formulary placement and prior authorization reform; (2) integration of SGLT2 inhibitor initiation into chronic disease management pathways and quality metrics; (3) educational initiatives targeting primary care physicians, general internists, and cardiologists who manage the majority of patients with DKD; (4) simplification of prescribing algorithms that minimize the perceived complexity of patient selection and monitoring; and (5) implementation science research to identify effective strategies for translating clinical trial efficacy into real-world effectiveness across diverse healthcare delivery systems (C. Mende, 2021; Agus Layanto et al., 2024; Sloan, 2024).

Cost-effectiveness analyses consistently demonstrate that SGLT2 inhibitors are highly cost-effective or cost-saving in patients with DKD, driven primarily by avoidance of dialysis and cardiovascular hospitalizations (Willis et al., 2020; McEwan et al., 2022). The economic case for broad access is compelling, yet out-of-pocket costs and formulary restrictions continue to impede equitable access in many healthcare systems. Policymakers, payers, and health systems should prioritize removing these barriers to ensure that all eligible patients with DKD can benefit from this life-changing therapy.

Future Research Priorities

This systematic review identifies numerous knowledge gaps requiring prioritized investigation. First, dedicated RCTs are needed to evaluate SGLT2 inhibitor efficacy and safety in populations underrepresented in completed trials, including patients with eGFR <20 mL/min/1.73m², kidney transplant recipients, individuals with type 1 diabetes and DKD, and

diverse racial and ethnic groups (Elenjickal et al., 2025; Fernandez-Fernandez et al., 2023; Godanci-Kelmendi et al., 2023). Second, comparative effectiveness trials with factorial designs are urgently needed to define optimal combination and sequencing of SGLT2 inhibitors, GLP-1 receptor agonists, and finerenone (Georgianos et al., 2022; Nevola et al., 2022; Mark et al., 2023). Third, translational research should continue to elucidate molecular mechanisms of SGLT2 inhibitor-mediated renoprotection, particularly the roles of autophagy, mitochondrial dynamics, and epigenetic modifications (Mima, 2018; Buchun Jiang et al., 2024). Fourth, pragmatic effectiveness trials are needed to evaluate implementation strategies for scaling SGLT2 inhibitor use in routine practice and to identify patient, provider, and system-level barriers to evidence-based prescribing (Alexander Turchin et al., 2025; Yaoming Xue et al., 2024). Fifth, long-term extension studies and registry linkages are required to characterize the durability of renal protection beyond five years and to monitor for late-emerging safety signals (Zheng & Sun, 2025; Ishibashi et al., 2023). Sixth, precision medicine approaches using genetic, proteomic, and metabolomic biomarkers should be explored to identify patients most likely to derive enhanced benefit or experience adverse effects (T. Jansz et al., 2024; S. Sugiyama et al., 2019).

CONCLUSION AND RECOMMENDATIONS

Conclusion

This comprehensive systematic review provides definitive evidence that SGLT2 inhibitors confer substantial, consistent, and clinically meaningful renal protection across the full spectrum of patients with diabetic kidney disease. The magnitude of benefit—approximately 30-40% reduction in the risk of dialysis, transplantation, or renal death—is comparable to or exceeds that of any previously evaluated intervention in DKD and is additive to RAAS blockade. The consistency of treatment effects across diverse study designs, geographic regions, and patient populations, together with the favorable safety profile and well-characterized mechanisms of action, establishes SGLT2 inhibitors as foundational therapy for renal protection in DKD.

The mechanisms underlying this renal protection are multifactorial, involving hemodynamic normalization via restoration of tubuloglomerular feedback, direct tubuloprotective effects including improved mitochondrial bioenergetics and attenuated inflammation/fibrosis, and modest contributions from systemic metabolic improvements. The safety profile is favorable, with reversible initial eGFR decline, no increased AKI risk, and manageable genital mycotic infections. Volume-related adverse events require attention in susceptible patients but are generally preventable with appropriate patient selection and monitoring.

Several evidence gaps remain, particularly regarding long-term durability of benefit, efficacy in advanced CKD (eGFR <20 mL/min/1.73m²), optimal combination with newer agents, and implementation strategies to translate trial efficacy into population-level effectiveness. However, the weight of existing evidence is sufficient to support immediate, broad implementation of SGLT2 inhibitor therapy in all eligible patients with DKD, regardless of glycemic control or concurrent antidiabetic therapy.

Recommendations

1. **Clinical Practice:** SGLT2 inhibitors should be prescribed to all patients with type 2 diabetes and CKD (eGFR ≥ 20 mL/min/1.73m²) as foundational therapy for renal protection, irrespective of glycemic control or concurrent RAAS blockade. Therapy should be initiated at evidence-based doses (canagliflozin 100 mg, dapagliflozin 10 mg, empagliflozin 10 mg daily) with appropriate counseling regarding expected initial eGFR decline and genital infection risk.
2. **Guideline Development:** Clinical practice guidelines should be updated to reflect the strength of evidence supporting SGLT2 inhibitors as first-line renoprotective therapy in DKD, with removal of previous eGFR-based restrictions that unnecessarily limit access for advanced CKD patients.

3. **Health Policy:** Payers and health systems should eliminate financial and administrative barriers to SGLT2 inhibitor access, recognizing that these agents are cost-effective or cost-saving in DKD populations. Quality metrics should be revised to incentivize appropriate SGLT2 inhibitor prescribing.
4. **Research:** Funding agencies and investigators should prioritize: (a) trials in underrepresented populations; (b) comparative effectiveness research evaluating combination strategies; (c) translational studies elucidating molecular mechanisms; (d) implementation science to optimize evidence translation; and (e) long-term surveillance for durability of benefit and late-emerging safety signals.
5. **Education:** Professional societies should develop and disseminate educational resources for clinicians regarding patient selection, initiation, monitoring, and adverse effect management for SGLT2 inhibitor therapy in DKD. Patient-oriented materials should be created to support shared decision-making.

The trajectory of SGLT2 inhibitor research—from glucose-lowering agents to unexpected cardio-renal protectors to established foundational therapy for DKD—represents one of the most remarkable therapeutic advances in contemporary nephrology. The challenge now is not to generate additional evidence of efficacy, but to ensure equitable access to this life-changing therapy for all patients with diabetic kidney disease worldwide.

REFERENCES

- A. B. A. Andrade. “SGLT-2 Inhibitors and Nephroprotection: A Systematic Review and Meta-Analysis,” 2020.
- A. Forbes, R. Suckling, W. Hinton, M. Feher, D. Banerjee, N. Cole, S. de Lusignan, and P. Swift. “Sodium-glucose Cotransporter-2 Inhibitors and Kidney Outcomes in Real-world Type 2 Diabetes

Populations: A Systematic Review and Meta-analysis of Observational Studies.” *Diabetes, Obesity and Metabolism*, 2023.

A. Korbut, and V. Klimontov. “Empagliflozin: A New Strategy for Nephroprotection in Diabetes,” 2017.

A. Liu, Serena Low, E. Yeoh, Eng Kuang Lim, C. Renaud, S. Teoh, Grace Feng Ling Tan, et al. “A Real-World Study on SGLT2 Inhibitors and Diabetic Kidney Disease Progression.” *Clinical Kidney Journal*, 2022.

A. Mahendra, Nur Samsu, Atma Gunawan, and Achmad Rifai. “#2934 SGLT-2 INHIBITORS DELAY KIDNEY FAILURE PROGRESSION AND REDUCE NEED OF DIALYSIS IN CHRONIC KIDNEY DISEASE PATIENTS: A META-ANALYSIS.” *Nephrology, Dialysis and Transplantation*, 2023.

A. Mima. “Renal Protection by Sodium-Glucose Cotransporter 2 Inhibitors and Its Underlying Mechanisms in Diabetic Kidney Disease.” *Journal of Diabetes and Its Complications*, 2018.

A. Piperidou, C. Loutradis, and P. Sarafidis. “SGLT-2 Inhibitors and Nephroprotection: Current Evidence and Future Perspectives.” *Journal of Human Hypertension*, 2020.

A. Piperidou, P. Sarafidis, A. Boutou, C. Thomopoulos, C. Loutradis, M. Alexandrou, A. Tsapas, and A. Karagiannis. “The Effect of SGLT-2 Inhibitors on Albuminuria and Proteinuria in Diabetes Mellitus: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.” *Journal of Hypertension*, 2019.

A. Romano. “Update on the Impact of Sodium-Glucose Cotransporter Inhibitors in Diabetic Kidney Disease Progression,” 2020.

A. Roy, A. Maiti, A. Sinha, Arjun Baidya, A. Basu, Dasarathi Sarkar, D. Sanyal, et al. “Kidney Disease in Type 2 Diabetes Mellitus and Benefits of Sodium-Glucose Cotransporter 2 Inhibitors: A Consensus Statement.” *Diabetes Therapy*, 2020.

A. Scheen. “Efficacy and Safety Profile of SGLT2 Inhibitors in Patients with Type 2 Diabetes and Chronic Kidney Disease.” *Expert Opinion on Drug Safety*, 2020.

———. “Sodium–Glucose Cotransporter Type 2 Inhibitors for the Treatment of Type 2 Diabetes Mellitus.” *Nature Reviews Endocrinology*, 2020.

———. “The Current Role of SGLT2 Inhibitors in Type 2 Diabetes and Beyond: A Narrative Review.” *Expert Review of Endocrinology & Metabolism*, 2023.

A. Scheen, and P. Delanaye. “[SGLT2 Inhibitors: Focus on Kidneys and Nephroprotection].” *Revue Medicale Suisse*, 2021.

A. Tansawet, Panu Looareesuwan, H. Teza, S. Boongird, Gareth J. McKay, J. Attia, O. Pattanaprateep, and A. Thakkestian. “Effects of Sodium-Glucose Cotransporter-2 Inhibitors on Chronic Kidney Disease Progression: A Multi-State Survival Model.” *Diabetology & Metabolic Syndrome*, 2024.

Agus Layanto, Lely Kusumaningrum, Cynthia Arsita, and Fenny Halim. “Integrating Sglt-2 Inhibitors into the Clinical Management of Type 2 Diabetes Mellitus and Chronic Kidney Disease: Current Evidence and Future Outlook.” *Asian Journal of Medicine and Health*, 2024.

Alexander Turchin, Lucia C. Petito, Emma Hegermiller, Ryan M. Carnahan, Andrea R. Devries, Satyender Goel, M. CECILIA LANSANG, et al. “415-P: Proteinuria and Progression of Kidney Disease in Patients with T2D Treated with SGLT2i and GLP-1RA—A Target Trial Emulation.” *Diabetes*, 2025.

Apichaya Chanawong, Suriyon Uitrakul, Supatcha Incomenoy, and Natnicha Poonchuay. “Renoprotective Effect of Thai Patients with Type 2 Diabetes Mellitus Treated with SGLT-2 Inhibitors Versus DPP-4 Inhibitors: A Real-World Observational Study.” *Advances in Pharmacological and Pharmaceutical Sciences*, 2023.

Arnaud D. Kaze, M. Zhuo, Seoyoung C. Kim, Elisabetta Patorno, and Julie M. Paik. “Association of SGLT2 Inhibitors with Cardiovascular, Kidney, and Safety Outcomes Among Patients with Diabetic Kidney Disease: A Meta-Analysis.” *Cardiovascular Diabetology*, 2022.

Atit Dharia, Abid Khan, V. Sridhar, and D. Cherney. “SGLT2 Inhibitors: The Sweet Success for Kidneys.” *Annual Review of Medicine*, 2023.

Ayesha Saleem, Shahroz M. Khan, Imdad Ullah, Syed S. Nasim, Sajedur Rahman, and Arslan Tayyab. “Investigating the Role of Sodium-Glucose Cotransporter-2 Inhibitors in Slowing Down the Diabetic Kidney Disease Progression: A Meta-Analysis of Randomized Control Trials.” *Journal of Advances in Medicine and Medical Research*, 2024.

B. Fernandez-Fernandez, P. Sarafidis, M. Kanbay, J. Navarro-González, M. Soler, J. Górriz, and A. Ortiz. “SGLT2 Inhibitors for Non-Diabetic Kidney Disease: Drugs to Treat CKD That Also Improve Glycaemia.” *Clinical Kidney Journal*, 2020.

B. Fernandez-Fernandez, P. Sarafidis, M. Soler, and A. Ortíz. “EMPA-KIDNEY: Expanding the Range of Kidney Protection by SGLT2 Inhibitors.” *Clinical Kidney Journal*, 2023.

B. Neuen, M. Jardine, and V. Perkovic. “Sodium-Glucose Cotransporter 2 Inhibition: Which Patient with Chronic Kidney Disease Should Be Treated in the Future?” *Nephrology, Dialysis and Transplantation*, 2020.

B. Neuen, T. Young, H. Heerspink, B. Neal, V. Perkovic, L. Billot, K. Mahaffey, et al. “SGLT2 Inhibitors for the Prevention of Kidney Failure in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis.” *The Lancet Diabetes and Endocrinology*, 2019.

B. Pasternak, V. Wintzell, M. Melbye, B. Eliasson, A. Svensson, S. Franzén, S. Gudbjörnsdottir, et al. “Use of Sodium-Glucose Co-Transporter 2 Inhibitors and Risk of Serious Renal Events: Scandinavian Cohort Study.” *British Medical Journal*, 2020.

B. Spiazzi, G. Piccoli, L. F. Wayerbacher, J. O. P. Lubianca, Bruno G Scalco, Mariana H Scheffler, Bruna L Fraga, Verônica Colpani, and F. Gerchman. “SGLT2 Inhibitors and Kidney Outcomes Across the Spectrum of Kidney Disease: A Systematic Review and Meta-Analysis.” *American Society of Nephrology. Clinical Journal*, 2024.

Buchun Jiang, Zhiwen Cheng, Dongjie Wang, Fei Liu, Jingjing Wang, Haidong Fu, and Jianhua Mao. “Unveiling the Podocyte-Protective Effect of Sodium-Glucose Cotransporter-2 Inhibitors.” *Kidney Research and Clinical Practice*, 2024.

C. Baigent, J. Emberson, R. Haynes, W. Herrington, P. Judge, M. Landray, Kaitlin J. Mayne, et al. “Impact of Diabetes on the Effects of Sodium Glucose Co-Transporter-2 Inhibitors on Kidney Outcomes: Collaborative Meta-Analysis of Large Placebo-Controlled Trials.” *The Lancet*, 2022.

C. Bailey, C. Day, and S. Bellary. “Renal Protection with SGLT2 Inhibitors: Effects in Acute and Chronic Kidney Disease.” *Current Diabetes Reports*, 2022.

C. Deerochanawong. “Use of SGLT-2 Inhibitors in Patients with T2DM and Kidney Disease: An Asian Perspective and Expert Recommendations,” 2019.

C. Garofalo, S. Borrelli, M. Liberti, M. Andreucci, G. Conte, R. Minutolo, M. Provenzano, and L. De Nicola. “SGLT2 Inhibitors: Nephroprotective Efficacy and Side Effects.” *Medicina*, 2019.

C. Jung. “New Era for Renal-Protective Therapy in Type 2 Diabetes: Better Renal Outcomes in Patients with Type 2 Diabetes Taking Sodium-Glucose Cotransporter 2 Inhibitors Versus Dipeptidyl Peptidase-4 Inhibitors.” *Endocrinology and Metabolism*, 2021.

C. Khoo, C. Deerochanawong, Chan Siew Pheng, B. Matawaran, W. Sheu, J. Chan, A. Mithal, et al. “Use of Sodium-glucose Co-transporter-2 Inhibitors in Asian Patients with Type 2 Diabetes and Kidney Disease: An Asian Perspective and Expert Recommendations.” *Diabetes, Obesity and Metabolism*, 2020.

C. Mende. “Chronic Kidney Disease and SGLT2 Inhibitors: A Review of the Evolving Treatment Landscape.” *Advances in Therapy*, 2021.

C. Wanner. “EMPA-REG OUTCOME: The Nephrologist's Point of View.” *American Journal of Medicine*, 2017.

Carlos Ignacio Reyes-Farias, Marcelo Reátegui-Díaz, Franco Romaní-Romaní, and Larry Prokop. “The Effect of Sodium-Glucose Cotransporter 2 Inhibitors in Patients with Chronic Kidney Disease with or Without Type 2 Diabetes Mellitus on Cardiovascular and Renal Outcomes: A Systematic Review and Meta-Analysis.” *PLoS ONE*, 2023.

Catarina Almeida, Leonor Silva, T. Costa, D. Lopes, V. Faria, E. Suarez, R. Veríssimo, R. Caçola, P. Gil, and L. G. M. Andrade. “MO647RENOPROTECTIVE EFFECT OF SGLT2 INHIBITORS AFTER FIVE YEARS OF TREATMENT: AN OBSERVATIONAL STUDY,” 2021.

Chalmoukou Konstantina, Polyzos Dimitris, Manta Eleni, Tatakis Fotis, Konstantinidis Dimitris, Thomopoulos Costas, and Tsioufis Costas. “Renal Outcomes Associated with Glucose-Lowering Agents: Systematic Review and Meta-Analysis of Randomized Outcome Trials.” *European Journal of Internal Medicine*, 2021.

Chao Feng, Minxiang Wu, Zhengyue Chen, Xiongwei Yu, Z. Nie, Yu Zhao, and Beiyan Bao. “Effect of SGLT2 Inhibitor on Renal Function in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.” *International Urology and Nephrology*, 2019.

Charlotte C. van Ruiten, Anne C. Hesp, and D. V. van Raalte. “Sodium Glucose Cotransporter-2 Inhibitors Protect the Cardiorenal Axis: Update on Recent Mechanistic Insights Related to Kidney Physiology.” *European Journal of Internal Medicine*, 2022.

Chen Wang, Yue Zhou, Zi-Li Kong, Xiang Wang, W. Lv, Zhuang Geng, and Yangang Wang. “The Renoprotective Effects of Sodium-glucose Cotransporter 2 Inhibitors Versus Placebo in Patients

with Type 2 Diabetes with or Without Prevalent Kidney Disease: A Systematic Review and Meta-analysis.” *Diabetes, Obesity and Metabolism*, 2019.

Chen, and Zhao. “Effect of SGLT 2 Inhibitor on Renal Function in Patients with Type 2 Diabetes Mellitus : A Systematic Review and Meta-Analysis of Randomized Controlled Trials,” 2019.

Chu-Hsuan Shiau, Li-Yun Tsau, Chih-Chin Kao, Yu-Ching Peng, Chyi-Huey Bai, Jeng-Cheng Wu, and Wenjuan Hou. “Efficacy and Safety of Sodium-Glucose Cotransporter-2 Inhibitors in Patients with Chronic Kidney Disease: A Systematic Review and Meta-Analysis.” *International Urology and Nephrology*, 2023.

Claire C J Dekkers, and R. Gansevoort. “Sodium-Glucose Cotransporter 2 Inhibitors: Extending the Indication to Non-Diabetic Kidney Disease?” *Nephrology, Dialysis and Transplantation*, 2020.

D. Cherney, A. Odutayo, R. Aronson, J. Ezekowitz, and J. Parker. “Sodium Glucose Cotransporter-2 Inhibition and Cardiorenal Protection: JACC Review Topic of the Week.” *Journal of the American College of Cardiology*, 2019.

D. Giugliano, L. De Nicola, M. Maiorino, G. Bellastella, and K. Esposito. “Type 2 Diabetes and the Kidney: Insights from Cardiovascular Outcome Trials.” *Diabetes, Obesity and Metabolism*, 2019.

D. Giugliano, M. Longo, L. Scappaticcio, G. Bellastella, M. Maiorino, and K. Esposito. “SGLT-2 Inhibitors and Cardiorenal Outcomes in Patients with or Without Type 2 Diabetes: A Meta-Analysis of 11 CVOTs.” *Cardiovascular Diabetology*, 2021.

D. Giugliano, M. Longo, P. Caruso, M. Maiorino, G. Bellastella, and K. Esposito. “Sodium-glucose Co-transporter-2 Inhibitors for the Prevention of Cardiorenal Outcomes in Type 2 Diabetes: An Updated Meta-analysis.” *Diabetes, Obesity and Metabolism*, 2021.

D. McGuire, W. Shih, F. Cosentino, B. Charbonnel, D. Cherney, S. Dagogo-Jack, R. Pratley, et al. “Association of SGLT2 Inhibitors With Cardiovascular and Kidney Outcomes in Patients With Type 2 Diabetes.” *JAMA Cardiology*, 2020.

D. V. O'Hara, D. V. O'Hara, B. Neuen, B. Neuen, M. Jardine, and M. Jardine. "Kidney and Cardiovascular Protection with SGLT2 Inhibitors: Lessons from Cardiovascular Outcome Trials and CREDENCE." *JN. Journal of Nephrology (Milano. 1992)*, 2020.

Daiji Kawanami, Keiichiro Matoba, Yusuke Takeda, Yosuke Nagai, Tomoyo Akamine, T. Yokota, K. Sango, and K. Utsunomiya. "SGLT2 Inhibitors as a Therapeutic Option for Diabetic Nephropathy." *International Journal of Molecular Sciences*, 2017.

Davide Margonato, G. Galati, S. Mazzetti, R. Cannistraci, G. Perseghin, A. Margonato, and A. Mortara. "Renal Protection: A Leading Mechanism for Cardiovascular Benefit in Patients Treated with SGLT2 Inhibitors." *Heart Failure Reviews*, 2020.

Debdipta Bose, Miteshkumar Maurya, and M. Konwar. "Impact of Sodium-Glucose Co-Transporter 2 Inhibitors on Renal Outcomes in Patients of Diabetes Mellitus: A Meta-Analysis of Landmark Renal and Cardiovascular Outcome Trials." *Indian Journal of Pharmacology*, 2023.

Dorsa Jahangiri, Udit Narayan Padhi, H. Verma, B. Lakkakula, R. Valizadeh, and Hamid Nasri. "Sodium-Glucose Co-Transporter 2 Inhibitors (SGLT2i); as a Preventive Factor of Kidney Failure in Patients with Type 2 Diabetes; a Meta-Analysis of Randomized Controlled Trials." *Journal of Renal Injury Prevention*, 2021.

E. Brown, J. Wilding, U. Alam, T. Barber, J. Karalliedde, and D. Cuthbertson. "The Expanding Role of SGLT2 Inhibitors Beyond Glucose-Lowering to Cardiorenal Protection." *Annals Medicus*, 2020.

E. Elenjickal, C. Travlos, Judy M Luu, Serge Lemay, Rita S. Suri, and Thomas A. Mavrakanas. "Efficacy and Safety of SGLT-2 Inhibitors in Patients With and Without Advanced CKD: A Systematic Review and Meta-Analysis." *American Society of Nephrology. Clinical Journal*, 2025.

E. Nelaj, Irida Kecaj, Julinda Feracaku, Kei Xhixhabesi, and M. Tase. “Benefits of SGLT2 Inhibitors on Renal and Cardiovascular Protection, in Diabetic Patients.” *South Eastern European Journal of Public Health*, 2024.

Emre Leventoğlu, and S. Bakkaloğlu. “SGLT2 Inhibition: A New Glimmer of Hope to Slow Chronic Kidney Disease Progression in Children?” *Klinische Pädiatrie*, 2024.

F. Giorgino, J. Vora, P. Fenici, and A. Solini. “Renoprotection with SGLT2 Inhibitors in Type 2 Diabetes over a Spectrum of Cardiovascular and Renal Risk.” *Cardiovascular Diabetology*, 2020.

F. Lin, Chi-Chuan Wang, Chien-Ning Hsu, Chen-Yi Yang, Chih-Yuan Wang, and H. Ou. “Renoprotective Effect of SGLT-2 Inhibitors Among Type 2 Diabetes Patients with Different Baseline Kidney Function: A Multi-Center Study.” *Cardiovascular Diabetology*, 2021.

G. Chan, J. Ng, K. Chow, and C. Szeto. “SGLT2 Inhibitors Reduce Adverse Kidney and Cardiovascular Events in Patients with Advanced Diabetic Kidney Disease: A Population-Based Propensity Score-Matched Cohort Study.” *Diabetes Research and Clinical Practice*, 2022.

G. Park, Byung-Don Choi, Soyoung Kang, Bomin Kim, and M. Chang. “Sodium–Glucose Cotransporter-2 Inhibitors Could Help Delay Renal Impairment in Patients with Type 2 Diabetes: A Real-World Clinical Setting.” *Journal of Clinical Medicine*, 2022.

G. Schernthaner, P. Groop, P. Kalra, C. Ronco, and M. Taal. “Sodium-glucose Linked Transporter-2 Inhibitor Renal Outcome Modification in Type 2 Diabetes: Evidence from Studies in Patients with High or Low Renal Risk.” *Diabetes, Obesity and Metabolism*, 2020.

Gian Paolo Fadini, Enrico Longato, M. Morieri, Enzo Bonora, Agostino Consoli, B. Fattor, M. Rigato, et al. “Comparative Renal Outcomes of Matched Cohorts of Patients with Type 2 Diabetes Receiving SGLT2 Inhibitors or GLP-1 Receptor Agonists Under Routine Care.” *Diabetologia*, 2024.

H. Cao, Tao Liu, Li Wang, and Q. Ji. “393-P: SGLT2 Inhibitors Reduce Cardiovascular and Renal Risks Compared with GLP-1 Receptor Agonists and DPP4 Inhibitors in Patients with Diabetic Kidney Disease: A Systematic Review and Network Meta-Analysis.” *Diabetes*, 2022.

———. “Comparative Efficacy of Novel Antidiabetic Drugs on Cardiovascular and Renal Outcomes in Patients with Diabetic Kidney Disease: A Systematic Review and Network Meta-analysis.” *Diabetes, Obesity and Metabolism*, 2022.

H. Heerspink, A. Karasik, M. Thuresson, Cheli Melzer-Cohen, G. Chodick, K. Khunti, John P H Wilding, et al. “Kidney Outcomes Associated with Use of SGLT2 Inhibitors in Real-World Clinical Practice (CVD-REAL 3): A Multinational Observational Cohort Study.” *The Lancet Diabetes and Endocrinology*, 2020.

H. Heerspink, M. Kosiborod, S. Inzucchi, and D. Cherney. “Renoprotective Effects of Sodium-Glucose Cotransporter-2 Inhibitors.” *Kidney International*, 2018.

H. Nagasu, Y. Yano, Hiroshi Kanegae, Hiddo J. L. Heerspink, M. Nangaku, Y. Hirakawa, Y. Sugawara, et al. “Kidney Outcomes Associated With SGLT2 Inhibitors Versus Other Glucose-Lowering Drugs in Real-World Clinical Practice: The Japan Chronic Kidney Disease Database.” *Diabetes Care*, 2021.

H. Takashima, Yoshinori Yoshida, Chinami Nagura, T. Furukawa, Ritsukou Tei, T. Maruyama, Noriaki Maruyama, and M. Abe. “Renoprotective Effects of Canagliflozin, a Sodium Glucose Cotransporter 2 Inhibitor, in Type 2 Diabetes Patients with Chronic Kidney Disease: A Randomized Open-Label Prospective Trial.” *Diabetes & Vascular Disease Research*, 2018.

Haiyan Cao, Youxia Liu, Zhixia Tian, Yuhang Lian, J. Jia, Ming Liu, and Dong Li. “Sodium-Glucose Cotransporter 2 Inhibitors Benefit to Kidney and Cardiovascular Outcomes for Patients with Type 2 Diabetes Mellitus and Chronic Kidney Disease 3b-4: A Systematic Review And Meta-Analysis of Randomized Clinical Trials.” *Diabetes Research and Clinical Practice*, 2021.

Hema Boddula, R. Shivani, Nayak S P Srinivas, Jitendra Vaghasia, G. S. Chakraborty, Snigdha Das Mandal, and Prajwal Ghatol. “The Effectiveness of SGLT2 Inhibitors in CKD Patients.” *Journal of Drug Delivery and Therapeutics*, 2023.

Honghong Zou, Baoqin Zhou, and Gaosi Xu. “SGLT2 Inhibitors: A Novel Choice for the Combination Therapy in Diabetic Kidney Disease.” *Cardiovascular Diabetology*, 2017.

Hongru Yan, Yi Wen, and Bicheng Liu. “Renoprotective Mechanisms of SGLT2 Inhibitor in Diabetic Kidney Disease.” *Diabetic Nephropathy*, 2021.

Husam M. Salah, S. Al’Aref, M. Khan, Malek Al-Hawwas, S. Vallurupalli, J. Mehta, J. Mounsey, et al. “Effect of Sodium-Glucose Cotransporter 2 Inhibitors on Cardiovascular and Kidney Outcomes-Systematic Review and Meta-Analysis of Randomized Placebo-Controlled Trials.” *American Heart Journal*, 2020.

Hyeong-Kyu Park, Sang-Joon Park, Soon-Hyo Kwon, Dong-Won Byun, and K. Suh. “COMPARISON OF RENAL PROTECTIVE EFFECTS BETWEEN SGLT2 INHIBITORS AND DPP4 INHIBITORS IN TYPE 2 DIABETES IN REAL-WORLD CLINICAL PRACTICE.” *Journal of the ASEAN Federation of Endocrine Societies*, 2023.

I. Idris. “Empagliflozin Reduced Progression of Kidney Disease and Cardiovascular Death in Patients with or Without Diabetes Who Are at High Risk of Disease Progression.” *Diabetes, Obesity and Metabolism Now*, 2023.

Issa Kawalit, A. Al-Omari, Zeina H Kalaji, Asad Al-Tirawi, M. Eltwal, and Abbas El-Khatib. “Renal Outcomes with Sodium-Glucose Cotransporters 2 Inhibitors in Patients with Type 2 Diabetes Mellitus with Chronic Kidney Disease Stages 3b-4.” *Medical Research Archives*, 2024.

J. C. De La Flor, Daniel Villa, Leónidas Cruzado, J. Apaza, F. Valga, Rocío Zamora, A. Marschall, Michael Cieza, J. Deira, and M. Rodeles. “Efficacy and Safety of the Use of SGLT2 Inhibitors in

Patients on Incremental Hemodialysis: Maximizing Residual Renal Function, Is There a Role for SGLT2 Inhibitors?” *Biomedicines*, 2023.

J. Halimi. “[SGLT2 Inhibitors: A New Era for Our Patients].” *Néphrologie & Thérapeutique*, 2021.

J. Menne, E. Dumann, H. Haller, and B. Schmidt. “Effect of SGLT-2 Inhibition on Acute Kidney Injury: A Systematic Review and Meta-Analysis.” *Social Science Research Network*, 2019.

J. Navarro-González, C. Ferri, E. Martín-Núñez, J. Donate-Correa, N. Pérez-Delgado, C. Hernández-Carballo, Fátima Sánchez-Quintana, VICTOR GARCIA TAGUA, Carol Prieto-Morin, and C. Mora-Fernández. “P1008THERAPY WITH SODIUM-GLUCOSE COTRANSPORTER TYPE 2 INHIBITORS INCREASES KLOTHO IN TYPE 2 DIABETIC PATIENTS,” 2020.

J. O’Sullivan. “Prevention of Cardiovascular Disease and Renal Failure in Type 2 Diabetes: Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors.” *BMJ Evidence-Based Medicine*, 2019.

J. Seufert, and K. Laubner. “Outcome-Studien Zu SGLT-2-Inhibitoren.” *Der Internist*, 2019.

J. Stephens, K. Brown, and T. Min. “Chronic Kidney Disease in Type 2 Diabetes: Implications for Managing Glycaemic Control, Cardiovascular and Renal Risk.” *Diabetes, Obesity and Metabolism*, 2020.

Jae Hyun Bae. “SGLT2 Inhibitors and GLP-1 Receptor Agonists in Diabetic Kidney Disease: Evolving Evidence and Clinical Application.” *Diabetes & Metabolism Journal*, 2025.

Jaehyun Bae, Eun-Gee Park, Sunhee Kim, S. Kim, S. Hahn, and Nam Hoon Kim. “Effects of Sodium-Glucose Cotransporter 2 Inhibitors on Renal Outcomes in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.” *Scientific Reports*, 2019.

Jennifer B. Green, and P. McCullough. “Roles for SGLT2 Inhibitors in Cardiorenal Disease.” *CardioRenal Medicine*, 2022.

Jingfeng Qian, and Yanqiu Xu. “Impact of Diabetes on the Effects of SGLT2 Inhibitors on Kidney Outcomes: An Updated Drug/Dose-Dependent Meta-Analysis.” *Clinical Nephrology*, 2025.

Joseph E Cruz, T. Ahuja, and M. Bridgeman. “Renal and Cardiac Implications of Sodium Glucose Cotransporter 2 (SGLT2) Inhibitors: The State of the Science.” *The Annals of Pharmacotherapy*, 2018.

Josselin Nespoux, and V. Vallon. “SGLT2 Inhibition and Kidney Protection.” *Clinical Science*, 2018.

Junhua Ma, Jiancan Lu, Peiling Shen, Xuemei Zhao, and Hongling Zhu. “Comparative Efficacy and Safety of Sodium–Glucose Cotransporter 2 Inhibitors for Renal Outcomes in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Network Meta-Analysis.” *Renal Failure*, 2023.

K. J. Chun, and H. Jung. “SGLT2 Inhibitors and Kidney and Cardiac Outcomes According to Estimated GFR and Albuminuria Levels: A Meta-Analysis of Randomized Controlled Trials.” *Kidney Medicine*, 2021.

K. Lo, F. Gul, Pradhum Ram, Aaron Y. Kluger, K. Tecson, P. McCullough, and J. Rangaswami. “The Effects of SGLT2 Inhibitors on Cardiovascular and Renal Outcomes in Diabetic Patients: A Systematic Review and Meta-Analysis.” *CardioRenal Medicine*, 2019.

K. Rådholm, Jason H. Y. Wu, M. Wong, C. Foote, G. Fulcher, K. Mahaffey, V. Perkovic, and B. Neal. “Effects of Sodium-Glucose Cotransporter-2 Inhibitors on Cardiovascular Disease, Death and Safety Outcomes in Type 2 Diabetes - A Systematic Review.” *Diabetes Research and Clinical Practice*, 2018.

K. Stavropoulos, K. Imprialos, N. Stavropoulos, S. Bouloukou, G. Kerpiniotis, K. Dimitriadis, C. Tsioufis, and M. Doumas. “Sodium-Glucose Cotransporter 2 Inhibitors: Nephroprotective Impact on Diabetic Kidney Disease.” *Cardiovascular & Haematological Disorders - Drug Targets*, 2018.

Kaden K. Fujita, F. Ye, David Collister, S. Klarenbach, D. Campbell, Derek S. Chew, Amity E. Quinn, P. Ronksley, and Darren Lau. “123-OR: SGLT2 Inhibitors Are Associated with Kidney Benefits at All Degrees of Proteinuria—A Cohort Study.” *Diabetes*, 2023.

Kaori Kitaoka, Yuichiro Yano, H. Nagasu, H. Kanegae, Noriharu Chishima, Hiroki Akiyama, Kouichi Tamura, and Naoki Kashihara. “Kidney Outcomes of SGLT2 Inhibitors Among Older Patients with Diabetic Kidney Disease in Real-World Clinical Practice: The Japan Chronic Kidney Disease Database Ex.” *BMJ Open Diabetes Research & Care*, 2024.

Kazuo Kobayashi, M. Toyoda, Moritsugu Kimura, N. Hatori, T. Furuki, H. Sakai, M. Takihata, et al. “Retrospective Analysis of Effects of Sodium-Glucose Co-Transporter 2 Inhibitor in Japanese Type 2 Diabetes Mellitus Patients with Chronic Kidney Disease.” *Diabetes & Vascular Disease Research*, 2018.

Kazuo Kobayashi, M. Toyoda, N. Hatori, Nobumichi Saito, T. Kanaoka, H. Sakai, T. Furuki, et al. “Retrospective Analysis of the Renoprotective Effects of Long-Term Use of Six Types of Sodium–Glucose Cotransporter 2 Inhibitors in Japanese Patients with Type 2 Diabetes Mellitus and Chronic Kidney Disease.” *Diabetes Technology & Therapeutics*, 2020.

Keiji Hirai, Junki Morino, Saori Minato, S. Kaneko, Katsunori Yanai, Yuko Mutsuyoshi, Hiroki Ishii, et al. “The Efficacy and Safety of Sodium-Glucose Cotransporter-2 Inhibitors in Patients with Advanced-Stage Diabetic Kidney Disease Taking Renin-Angiotensin System Blockers.” *Diabetes, Metabolic Syndrome and Obesity : Targets and Therapy*, 2020.

Kelsey M Leite, Allissa M. Long, M. Ostroff, Leanna Borges, and G. Braden. “A Review of the Renoprotective Effects of Novel Antidiabetic Agents.” *Journal of Pharmacy and Practice*, 2020.

L. Fang, J. Duan, Jinsong Geng, Zhangsuo Liu, and Jiancheng Dong. “Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors for the Prevention and Treatment of Diabetic Kidney Disease: A Network Meta-Analysis of Randomized Controlled Trials.” *Diabetic Nephropathy*, 2021.

L. Sloan. “SGLT2 Inhibitors Across the Spectrum of Chronic Kidney Disease: A Narrative Review.” *Postgraduate Medicine*, 2024.

Linda Sukiatno, I. Y. Kusuma, and Galih Samodra. “Cardioprotective and Renoprotective Effects of the Use of SGLT2 Inhibitors in Diabetes Mellitus Patients.” *Proceedings of the International Conference on Health and Medical Sciences (AHMS 2020)*, 2021.

Louise Woodhams, L. Chalmers, T. F. Sim, B. Yeap, M. Schlaich, C. Schultz, and G. Hillis. “Efficacy and Safety of Sodium Glucose Cotransporter 2 Inhibitors Plus Standard Care in Diabetic Kidney Disease: A Systematic Review and Meta-Analysis.” *Journal of Diabetes and Its Complications*, 2023.

Lubin Xu, Yang Li, Jiaxin Lang, P. Xia, Xinyu Zhao, Li Wang, Yang Yu, and Limeng Chen. “Effects of Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibition on Renal Function and Albuminuria in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis.” *PeerJ*, 2017.

M. A. Podestà, Gianmarco Sabiu, A. Galassi, P. Ciceri, and M. Cozzolino. “SGLT2 Inhibitors in Diabetic and Non-Diabetic Chronic Kidney Disease.” *Biomedicines*, 2023.

M. Baker, and M. Perazella. “SGLT2 Inhibitor Therapy in Patients with Type-2 Diabetes Mellitus: Is Acute Kidney Injury a Concern?” *JN. Journal of Nephrology (Milano. 1992)*, 2020.

M. Ibernón, Maru Navarro, Montserrat Gomà, Ariel Tango, O. Rap, Cristina Cabrera, Ana Sánchez, Neus Rodríguez, and Pilar Ruiz. “#1626 The Role of Sodium-Glucose Cotransporter 2 Inhibitors in Diabetic Nephropathy and Non Diabetic Renal Disease in Diabetes Mellitus Type 2 Patients.” *Nephrology, Dialysis and Transplantation*, 2024.

M. Kanai, Kazuhiro Kimura, Hirohiko Motoki, Sho Suzuki, Takahiro Okano, M. Minamisawa, K. Yoshie, et al. “Cardio-Renal Protective Effects of SGLT2 Inhibitors in Patients with Type 2 Diabetes Mellitus and Severely Impaired Renal Function.” *European Heart Journal*, 2021.

M. Provenzano, M. Pelle, I. Zaffina, B. Tassone, R. Pujia, Marco Ricchio, R. Serra, et al. "Sodium-Glucose Co-Transporter-2 Inhibitors and Nephroprotection in Diabetic Patients: More Than a Challenge." *Frontiers in Medicine*, 2021.

M. Wani, and Tariq A Bhat. "News and Views." *JMS SKIMS*, 2019.

Mahmoud Barbarawi, Ahmad Al-Abdoun, O. Barbarawi, Harini Lakshman, Mariam Al kasasbeh, and Kai Chen. "SGLT2 Inhibitors and Cardiovascular and Renal Outcomes: A Meta-Analysis and Trial Sequential Analysis." *Heart Failure Reviews*, 2021.

Meir Schechter, and Ofri Mosenzon. "[IMPROVEMENT OF RENAL OUTCOMES WITH SODIUM-GLUCOSE COTRANSPORTER-2 (SGLT2) INHIBITORS]." *Harefuah*, 2021.

Merlin C. Thomas, B. Neuen, S. Twigg, M. Cooper, and S. Badve. "SGLT2 Inhibitors for Patients with Type 2 Diabetes and CKD: A Narrative Review." *Endocrine Connections*, 2023.

"Metaanalyse Bestätigt Renoprotektive Effekte von SGLT2-Inhibitoren." *Diabetologie Und Stoffwechsel*, 2020.

Michael S. Kelly, Jelena Lewis, Ashley M. Huntsberry, Lauren Dea, and I. Portillo. "Efficacy and Renal Outcomes of SGLT2 Inhibitors in Patients with Type 2 Diabetes and Chronic Kidney Disease." *Postgraduate Medicine*, 2018.

Mohammed D. Algethami, Sami A. Alzahrani, Bander H. Alessa, A. N. B. Madhi, H. M. Alzahrani, and Rami S. Altwairqi. "Sodium-glucose Co-transporter Protein 2 Inhibitors for Long-Term Kidney Function Preservation in Type 2 Diabetes with Chronic Kidney Disease: A Meta-Analysis of Rates of Progression to End-Stage Renal Disease." *International Journal of Community Medicine and Public Health*, 2024.

Mohanad Almainani, V. Sridhar, and D. Cherney. "Sodium-Glucose Cotransporter 2 Inhibition in Non-Diabetic Kidney Disease." *Current Opinion in Nephrology and Hypertension*, 2021.

N. Kashihara, Kengo Kidokoro, and E. Kanda. “Renoprotective Effects of Sodium-Glucose Cotransporter-2 Inhibitors and Underlying Mechanisms.” *Current Opinion in Nephrology and Hypertension*, 2019.

N. Mikhail. “SGLT2 Inhibitors for Treatment of Diabetic Nephropathy.” *Current Research in Diabetes & Obesity Journal*, 2019.

N. Mittal, Vikas Sehay, Rakesh Mittal, and Surjit Singh. “Reno-Protective Potential of Sodium Glucose Cotransporter-2 (SGLT2) Inhibitors: Summary Evidence from Clinical and Real-World Data.” *European Journal of Pharmacology*, 2021.

N. Saldanha, M. Shah, Monika Dalal, Z. Virani, I. Parekh, H. Vora, P. Rajput, S. Tapiawala, and B. Shah. “A Prospective Study to Evaluate the Effects of Sodium-Glucose Cotransporter 2 Inhibitors in Type 2 Diabetic Patients with Chronic Kidney Disease.” *Journal of Diabetology*, 2022.

Nahla Hussein, F. Abdelrahman, Abdelrahman Khedr, H. Aref, M. Halawa, and Magdy Elsharkawy. “EFFECT OF SODIUM GLUCOSE CO TRANSPORTER 2 INHIBITOR ON PROTEINURIA IN DIABETIC PATIENTS.” *The Quarterly Journal of Medicine*, 2021.

Nam Hoon Kim, and N. Kim. “Renoprotective Mechanism of Sodium-Glucose Cotransporter 2 Inhibitors: Focusing on Renal Hemodynamics.” *Diabetes & Metabolism Journal*, 2022.

Nicole Felix, M. Gauza, L. Teixeira, M. E. S. Guisso, Alleh Nogueira, C. Dagostin, A. Godoi, et al. “Cardiovascular Outcomes of Sodium-Glucose Cotransporter-2 Inhibitors Therapy in Patients With Type 2 Diabetes Mellitus and Chronic Kidney Disease: A Systematic Review and Updated Meta-Analysis.” *Korean Circulation Journal*, 2024.

Ning Li, Dan Lv, Xiangjun Zhu, P. Wei, Y. Gui, Shijia Liu, Enchao Zhou, Min Zheng, Dong Zhou, and Lu Zhang. “Effects of SGLT2 Inhibitors on Renal Outcomes in Patients With Chronic Kidney Disease: A Meta-Analysis.” *Frontiers in Medicine*, 2021.

O. González-Albarrán, Cristóbal Morales, M. Pérez-Maraver, J. J. Aparicio-Sánchez, and R. Simó. “Review of SGLT2i for the Treatment of Renal Complications: Experience in Patients with and Without T2D.” *Diabetes Therapy*, 2022.

Ofri Mosenzon, S. Wiviott, Avivit Cahn, Aliza Rozenberg, Ilan Yanuv, Erica L. Goodrich, S. Murphy, et al. “Effects of Dapagliflozin on Development and Progression of Kidney Disease in Patients with Type 2 Diabetes: An Analysis from the DECLARE-TIMI 58 Randomised Trial.” *The Lancet Diabetes and Endocrinology*, 2019.

P. Au, K. Tan, B. Cheung, I. Wong, H. Li, and C. Cheung. “Association Between SGLT2 Inhibitors Vs DPP4 Inhibitors and Renal Outcomes Among Patients with Type 2 Diabetes.” *Journal of Clinical Endocrinology and Metabolism*, 2022.

P. Delanaye, and A. Scheen. “[EMPA-KIDNEY: Empagliflozin in Chronic Kidney Disease].” *Revue Medicale de Liege*, 2023.

P. Georgianos, M. Divani, T. Eleftheriadis, P. Mertens, and V. Liakopoulos. “SGLT-2 Inhibitors in Diabetic Kidney Disease: What Lies Behind Their Renoprotective Properties?” *Current Medicinal Chemistry*, 1969.

P. Georgianos, T. Eleftheriadis, and V. Liakopoulos. “Combination Therapy with an SGLT-2 Inhibitor and Finerenone in DKD: Are We There yet?” *European Journal of Clinical Investigation*, 2022.

P. Georgianos, V. Vaios, E. Dounousi, M. Salmas, T. Eleftheriadis, and V. Liakopoulos. “Mechanisms of Cardiorenal Protection with SGLT-2 Inhibitors.” *Current Pharmaceutical Design*, 2021.

P. Georgianos, V. Vaios, S. Roumeliotis, K. Leivaditis, T. Eleftheriadis, and V. Liakopoulos. “Evidence for Cardiorenal Protection with SGLT-2 Inhibitors and GLP-1 Receptor Agonists in Patients with Diabetic Kidney Disease.” *Journal of Personalized Medicine*, 2022.

P. Mark, P. Sarafidis, R. Ekart, C. Ferro, Olga Balafa, B. Fernandez-Fernandez, W. Herrington, et al. “SGLT2i for Evidence-Based Cardiorenal Protection in Diabetic and Non-Diabetic Chronic Kidney Disease: A Comprehensive Review by EURECA-m and ERBP Working Groups of ERA.” *Nephrology, Dialysis and Transplantation*, 2023.

P. Natale, David J. Tunnicliffe, Tadashi Toyama, S. Palmer, V. Saglimbene, M. Ruospo, L. Gargano, G. Stallone, Loreto Gesualdo, and G. Strippoli. “Sodium-Glucose Co-Transporter Protein 2 (SGLT2) Inhibitors for People with Chronic Kidney Disease and Diabetes.” *Cochrane Database of Systematic Reviews*, 2024.

P. Sarafidis, A. Ortiz, C. Ferro, J. Halimi, R. Kreutz, F. Mallamaci, G. Mancia, and C. Wanner. “Sodium--Glucose Co-Transporter-2 Inhibitors for Patients with Diabetic and Nondiabetic Chronic Kidney Disease: A New Era Has Already Begun.” *Journal of Hypertension*, 2021.

P. Sarafidis, C. Ferro, E. Morales, A. Ortiz, J. Małyszko, R. Hojs, K. Khazim, et al. “SGLT-2 Inhibitors and GLP-1 Receptor Agonists for Nephroprotection and Cardioprotection in Patients with Diabetes Mellitus and Chronic Kidney Disease. A Consensus Statement by the EURECA-m and the DIABESITY Working Groups of the ERA-EDTA.” *Nephrology, Dialysis and Transplantation*, 2019.

Prabhat Singh, Lokesh Goyal, D. Mallick, Salim R Surani, and K. Yashi. “Role of Sodium-Glucose Co-Transporter 2 Inhibitors in Chronic Kidney Disease, Congestive Heart Failure and Stroke—A Review and Clinical Guide for Healthcare Professionals.” *Journal of Clinical Medicine*, 2023.

R. DeFronzo, and M. Abdul-Ghani. “Sodium–Glucose Cotransporter 2 Inhibitors and the Kidney.” *Diabetes Spectrum*, 2021.

R. Fontes-Carvalho, D. Santos-Ferreira, I. Raz, N. Marx, F. Ruschitzka, and F. Cosentino. “Protective Effects of SGLT-2 Inhibitors Across the Cardiorenal Continuum: Two Faces of the Same Coin.” *European Journal of Preventive Cardiology*, 2021.

- R. Gilbert, and K. Thorpe. "Acute Kidney Injury with Sodium-glucose Co-transporter-2 Inhibitors: A Meta-analysis of Cardiovascular Outcome Trials." *Diabetes, Obesity and Metabolism*, 2019.
- R. Guthrie. "Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes." *Postgraduate Medicine*, 2018.
- R. Nevola, Maria Alfano, P. Pafundi, Chiara Brin, F. Gragnano, P. Calabrò, L. Adinolfi, L. Rinaldi, F. C. Sasso, and A. Caturano. "Cardiorenal Impact of SGLT-2 Inhibitors: A Conceptual Revolution in The Management of Type 2 Diabetes, Heart Failure and Chronic Kidney Disease." *Reviews in Cardiovascular Medicine*, 2022.
- Rasha O. Abdelmoniem, M. S. Shaalan, M. Shawky, Walla M. Ibrahim, and Ayman M. Elbadawy. "Reno Protective Effect of Sodium Glucose Cotransporter-2 Inhibitor (Dapagliflozin) in Type 2 Diabetic Patients." *The Egyptian Journal of Hospital Medicine*, 2022.
- Renata Carvalho, Bárbara Ribeiro, J. Medeiros, J. M. Bastos, R. Vaz, Sofia Marques, and António Rmalheiro. "MO654REAL LIFE EXPERIENCE AFTER 20 MONTHS USING SGLT2 INHIBITORS," 2021.
- S. A. Alharbi, A. AlQahtani, Shahad Alnasser, Ghadeer L. Alfuhaydi, Raghad Adel Alrowithi, Fawzia Ayedh Asiri, and Ahmed Ammar Almutairi. "Evaluating the Efficacy of SGLT2 Inhibitors in Preventing Diabetic Kidney Disease." *Journal of Healthcare Sciences*, 2025.
- S. Cabrera, R. Torres, L. Elgueta, E. Segovia, M. Sanhueza, A. Boltansky, and M. Alvo. "P1011ATHE SGT-2 INHIBITORS DECREASE THE MORTALITY AND PROGRESSION OF CHRONIC KIDNEY DISEASE (CKD) IN TYPE 2 DIABETES PATIENTES. SYSTEMATIC REVIEW AND META-ANALYSIS OF THE LITERATURE," 2020.
- S. De Cosmo, F. Viazzi, P. Piscitelli, G. Leoncini, A. Mirijello, B. Bonino, and R. Pontremoli. "Impact of CVOTs in Primary and Secondary Prevention of Kidney Disease." *Diabetes Research and Clinical Practice*, 2019.

S. Luciano, W. Li, and J. O'Rourke. "PUK2 Assessing Mortality Risk and Renal Outcomes in Chronic Kidney Disease Patients Treated with Sglt-2 Inhibitors or DPP-4 Inhibitors: A Real-World Study," 2020.

S. Rabizadeh, M. Nakhjavani, and A. Esteghamati. "Cardiovascular and Renal Benefits of SGLT2 Inhibitors: A Narrative Review." *International Journal of Endocrinology and Metabolism*, 2019.

S. Rehman, and Faiqa Rahman. "Sodium-Glucose Cotransporter 2 Inhibitors and Their Renal Benefits in Type 2 Diabetes : A Systematic Review," 2020.

S. Seidu, S. Kunutsor, X. Cos, S. Gillani, and K. Khunti. "SGLT2 Inhibitors and Renal Outcomes in Type 2 Diabetes with or Without Renal Impairment: A Systematic Review and Meta-Analysis." *Primary Care Diabetes*, 2018.

S. Sugiyama, H. Jinnouchi, Akira Yoshida, K. Hieshima, Noboru Kurinami, K. Jinnouchi, Motoko Tanaka, et al. "Renoprotective Effects of Additional SGLT2 Inhibitor Therapy in Patients With Type 2 Diabetes Mellitus and Chronic Kidney Disease Stages 3b-4: A Real World Report From A Japanese Specialized Diabetes Care Center." *Journal of Clinical Medicine Research*, 2019.

Saeko Sato, K. Takayanagi, Taisuke Shimizu, K. Kanozawa, Takatsugu Iwashita, and Hajime Hasegawa. "Correlation Between Albuminuria and Interstitial Injury Marker Reductions Associated with SGLT2 Inhibitor Treatment in Diabetic Patients with Renal Dysfunction." *European Journal of Medical Research*, 2022.

Sahithi Reddy Kalluri, T. Bhutta, Hanan Hannoodde, Mahmoud Al Khalili, Nyein Wint Yee Theik, Oluwatimilehin E Raji, Priya Shenwai, Rutul Shah, and Safeera Khan. "Do SGLT2 Inhibitors Improve Cardio-Renal Outcomes in Patients With Type II Diabetes Mellitus: A Systematic Review." *Cureus*, 2021.

Sarah Yoon Ai Ng, D. Zhu, and W. Herrington. "In Type 2 Diabetes, SGLT-2 Inhibitors Reduce Risk for Major Kidney Outcomes." *Annals of Internal Medicine*, 2020.

Shafaat Raza, S. Osasan, Sudiksha Sethia, Tayyaba Batool, Zarna Bambhroliya, Joel Sandrugu, Michael Lowe, Oluwasemilore Okunlola, and Pousette Hamid. “A Systematic Review of Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors and Sympathetic Nervous System Inhibition: An Underrated Mechanism of Cardiorenal Protection.” *Cureus*, 2022.

Shaowei Pang, and Xiaoli Li. “Early Use of SGLT2 Inhibitors Reduces the Progression of Diabetic Kidney Disease: A Retrospective Cohort Study.” *American Journal of Translational Research*, 2024.

Shuo Yang, W. He, Lu Zhao, and Yaochuan Mi. “Association Between Use of Sodium-Glucose Cotransporter 2 Inhibitors, Glucagon-Like Peptide 1 Agonists, and Dipeptidyl Peptidase 4 Inhibitors with Kidney Outcomes in Patients with Type 2 Diabetes: A Systematic Review and Network Meta-Analysis.” *PLoS ONE*, 2022.

Sidra Jamil, Arfa Zainab, Avneet Arora, T. Shaik, Vimal Khemani, Favour C Mekowulu, Yared N Aschalew, and Saima Khan. “Efficacy and Safety of Sodium Glucose Cotransporter-2 (SGLT2) Inhibitors in Patients With Diabetes and Chronic Kidney Disease (CKD): A Meta-Analysis of Randomized Control Trials.” *Cureus*, 2022.

Susovan Halder, Arnab Bhattacharyya, Shatavisa Mukherjee, Bhaswar Konar, and Antareep Halder. “Assessment of Effects of Combination of SGLT2 Inhibitors and Renin–Angiotensin–Aldosterone System Blockers on the Renal Functions of Patients of Diabetic Kidney Disease (SGRASS-DKD Study).” *Journal of Diabetology*, 2024.

T. Jansz, K. G. Young, R. Hopkins, A. McGovern, B. Shields, A. Hattersley, A. G. Jones, et al. “Precision Medicine in Type 2 Diabetes: Targeting SGLT2-Inhibitor Treatment For Kidney Protection.” *medRxiv*, 2024.

T. Milder, S. Stocker, D. Samocha-Bonet, R. Day, and J. Greenfield. “Sodium-Glucose Cotransporter 2 Inhibitors for Type 2 Diabetes—Cardiovascular and Renal Benefits in Patients with Chronic Kidney Disease.” *European Journal of Clinical Pharmacology*, 2019.

T. Oh, J. Moon, K. Hur, Seung-Hyun Ko, Hyun Jung Kim, Taehee Kim, D. Lee, and M. Moon. “Sodium-Glucose Cotransporter-2 Inhibitor for Renal Function Preservation in Patients with Type 2 Diabetes Mellitus: A Korean Diabetes Association and Korean Society of Nephrology Consensus Statement.” *Kidney Research and Clinical Practice*, 2020.

———. “Sodium-Glucose Cotransporter-2 Inhibitor for Renal Function Preservation in Patients with Type 2 Diabetes Mellitus: A Korean Diabetes Association and Korean Society of Nephrology Consensus Statement.” *Diabetes & Metabolism Journal*, 2020.

T. Siddiqi, David Z. I. Cherney, H. Siddiqui, T. Jafar, J. Januzzi, Muhammad Shahzeb Khan, Adeera Levin, et al. “Effects of Sodium-Glucose Cotransporter-2 Inhibitors on Kidney Outcomes Across Baseline Cardiovascular-Kidney-Metabolic Conditions.” *Journal of the American Society of Nephrology*, 2024.

T. Siddiqi, Muhammad Shariq S Usman, H. Siddiqui, and J. Butler. “Abstract 14614: Effect of SGLT2 Inhibitors on Renal Outcomes Across Various Patient Populations.” *Circulation*, 2023.

T. Toyama, B. Neuen, M. Jun, T. Ohkuma, B. Neal, M. Jardine, H. Heerspink, et al. “Effect of SGLT2 Inhibitors on Cardiovascular, Renal and Safety Outcomes in Patients with Type 2 Diabetes Mellitus and Chronic Kidney Disease: A Systematic Review and Meta-analysis.” *Diabetes, Obesity and Metabolism*, 2019.

Taichi Nagahisa, and Y. Saisho. “Cardiorenal Protection: Potential of SGLT2 Inhibitors and GLP-1 Receptor Agonists in the Treatment of Type 2 Diabetes.” *Diabetes Therapy*, 2019.

Takayuki Yamada, M. Wakabayashi, Abhinav Bhalla, N. Chopra, H. Miyashita, Takahisa Mikami, H. Ueyama, et al. “Cardiovascular and Renal Outcomes with SGLT-2 Inhibitors Versus GLP-1 Receptor Agonists in Patients with Type 2 Diabetes Mellitus and Chronic Kidney Disease: A Systematic Review and Network Meta-Analysis.” *Cardiovascular Diabetology*, 2020.

Taro Hirai, Munehiro Kitada, I. Monno, E. Oda, Yoshihiro Hayashi, Keiji Shimada, Y. Takagaki, et al. “SGLT2 Inhibitors in Type 2 Diabetic Patients with Renal Function Impairment Slows the Annual Renal Function Decline, in a Real Clinical Practice.” *Journal of Diabetes Investigation*, 2021.

Tatsuya Ishibashi, Shuhei Morita, H. Furuta, Masahiro Nishi, and Taka-aki Matsuoka. “Renoprotective Potential of Concomittant Medications with SGLT2 Inhibitors and Renin-Angiotensin System Inhibitors in Diabetic Nephropathy Without Albuminuria: A Retrospective Cohort Study.” *Scientific Reports*, 2023.

Thomas A. Mavrakanas, Michael A. Tsoukas, James M. Brophy, Abhinav Sharma, and Karim Gariani. “SGLT-2 Inhibitors Improve Cardiovascular and Renal Outcomes in Patients with CKD: A Systematic Review and Meta-Analysis.” *Scientific Reports*, 2023.

Thomas A. Zelniker, S. Wiviott, I. Raz, K. Im, Erica L. Goodrich, Marc P. Bonaca, Ofri Mosenzon, et al. “SGLT2 Inhibitors for Primary and Secondary Prevention of Cardiovascular and Renal Outcomes in Type 2 Diabetes: A Systematic Review and Meta-Analysis of Cardiovascular Outcome Trials.” *The Lancet*, 2019.

Tianbiao Zhou, Kaijin Yao, Yina Xie, Yongda Lin, Jiali Wang, and Xiutian Chen. “Renal Protection and Safety of Sodium-Glucose Cotransporter-2 Inhibitors in Chronic Kidney Disease.” *Current Pharmaceutical Design*, 2023.

Tien-Jyun Chang, Yen-Chieh Lee, Li-Chiu Wu, and Chia-Hsueh Chang. “Albuminuria-based Stratification of End-stage Kidney Disease Progression and Mortality with Sodium-glucose Cotransporter 2 Inhibitors (SGLT2i): A Retrospective Cohort Study in Type 2 Diabetes and Chronic Kidney Disease.” *Pharmacotherapy*, 2024.

Ting Liu, Rui Li, Xiaoxia Wang, Xingxing Gao, and Xiaodong Zhang. “Benefits of SGLT2 Inhibitors Combining with Renin-Angiotensin-System Blockers on Cardiovascular Outcomes in

Chronic Kidney Disease Patients: A Systemic Review and Meta-Analysis.” *Medicina Clínica (Ed. Impresa)*, 2021.

V. Salukhov, Y. Khalimov, S. Shustov, and S. Popov. “SGLT2 Inhibitors and Kidneys: Mechanisms and Main Effects in Diabetes Mellitus Patients.” *Diabetes Mellitus*, 2021.

V. Sridhar, B. Neuen, Robert A. Fletcher, A. Slee, F. Ang, W. Rapattoni, Clare Arnott, et al. “Kidney Protection with Canagliflozin: A Combined Analysis of the Randomized CANVAS Program and CREDENCE Trials.” *Diabetes, Obesity and Metabolism*, 2023.

V. Sridhar, H. Rahman, and D. Cherney. “What Have We Learned about Renal Protection from the Cardiovascular Outcome Trials and Observational Analyses with SGLT2 Inhibitors?” *Diabetes, Obesity and Metabolism*, 2020.

V. Sridhar, K. Tuttle, and D. Cherney. “We Can Finally Stop Worrying About SGLT2 Inhibitors and Acute Kidney Injury.” *American Journal of Kidney Diseases*, 2020.

V. Tesar. “SGLT2 Inhibitors in Non-Diabetic Kidney Disease.” *Advances in Clinical and Experimental Medicine*, 2022.

V. Tsimihodimos, T. Filippatos, and Moses Elisaf. “SGLT2 Inhibitors and the Kidney: Effects and Mechanisms.” *Diabetes & Metabolic Syndrome*, 2018.

Vjollca Godanci-Kelmendi, Mimoza Ramadani Piraj, Fatime Imeri, and Shega Konjufca. “#3286 Safety and Efficacy of SGLT2 Inhibitors in the Elderly with CKD.” *Nephrology, Dialysis and Transplantation*, 2025.

Vjollca Godanci-Kelmendi, Mimoza Ramadani Piraj, Fatime Ymeri, and Shega Konjufca. “#3008 SERENDIPITY OF SGLT2 INHIBITION – DIABETIC AND NON DIABETIC CKD.” *Nephrology, Dialysis and Transplantation*, 2023.

Wajd Alkabbani, Arsène Zongo, J. Minhas-Sandhu, D. Eurich, B. Shah, M. Alsabbagh, and J. Gamble. “Renal Effectiveness and Safety of the Sodium-Glucose Cotransporter-2 Inhibitors: A Population-Based Cohort Study.” *BMJ Open Diabetes Research & Care*, 2021.

Wendy Wang, Paul Drawz, Lisa S. Chow, Lin Y Chen, Rob F. Walker, F. Norby, and P. Lutsey. “Abstract 35: Association of SGLT2 Inhibitors and Other Second Line Therapies With Incident Chronic Kidney Disease in Patients With Type 2 Diabetes.” *Circulation*, 2024.

X. Jian, Q-L Yang, S. Xiao, Z. Jing, and S-D Hu. “The Effects of a Sodium-Glucose Cotransporter 2 Inhibitor on Diabetic Nephropathy and Serum Oxidized Low-Density Lipoprotein Levels.” *European Review for Medical and Pharmacological Sciences*, 2018.

Xiaoya Sun, and Guohong Wang. “Renal Outcomes with Sodium-Glucose Cotransporters 2 Inhibitors.” *Frontiers in Endocrinology*, 2022.

Y. Saisho. “SGLT2 Inhibitors: The Star in the Treatment of Type 2 Diabetes?” *Diseases*, 2020.

Yan Xie, Benjamin Bowe, Andrew K. Gibson, J. McGill, G. Maddukuri, Yan Yan, and Z. Al-Aly. “Comparative Effectiveness of SGLT2 Inhibitors, GLP-1 Receptor Agonists, DPP-4 Inhibitors, and Sulfonylureas on Risk of Kidney Outcomes: Emulation of a Target Trial Using Health Care Databases.” *Diabetes Care*, 2020.

Yanqun Zheng, and Jia Sun. “Long-Term Effect of Sodium–Glucose Cotransporter 2 Inhibitors in Kidney Functions: A Systematic Review and Meta-Analysis.” *Medicine*, 2025.

Yaoming Xue, Li-xin Shi, Xu Yu, Yangang Wang, Tianpei Hong, Xiaoying Li, Jia-yun Ma, Dalong Zhu, and Yiming Mu. “931-P: Real-World Study on the Effect of SGLT2 Inhibitors in Patients with Type 2 Diabetes in China.” *Diabetes*, 2024.

Yuki Kawai, Kazushi Uneda, Takayuki Yamada, S. Kinguchi, Kazuo Kobayashi, K. Azushima, T. Kanaoka, Y. Toya, H. Wakui, and K. Tamura. “Comparison of Effects of SGLT-2 Inhibitors and GLP-1 Receptor Agonists on Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus

Patients with/Without Albuminuria: A Systematic Review and Network Meta-Analysis.” *Diabetes Research and Clinical Practice*, 2021.

Zhi-Cheng Dai, Jin-Xia Chen, Rong Zou, Xuan-Bing Liang, Ji-Xin Tang, and Cui-Wei Yao. “Role and Mechanisms of SGLT-2 Inhibitors in the Treatment of Diabetic Kidney Disease.” *Frontiers in Immunology*, 2023.

Владимир Владимирович Салухов, Юрий Шавкатович Халимов, С. Б. Шустов, and Сергей Игоревич Попов. “Ингибиторы SGLT2 и Почки: Механизмы и Основные Эффекты у Больных Сахарным Диабетом 2 Типа,” 2020.