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Meta-Analysis

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

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ABSTRACT

Chronic kidney disease (CKD) is a major complication of type 2 diabetes mellitus (T2DM) and a leading cause of end-stage renal disease (ESRD). Sodium-glucose co-transporter 2 (SGLT2) inhibitors have demonstrated renoprotective effects in clinical trials, but their precise impact on ESRD risk remains to be comprehensively quantified. This study aimed to evaluate the effectiveness of SGLT2 inhibitors in reducing ESRD risk in T2DM patients with CKD by synthesizing evidence from randomized controlled trials. A meta-analysis was conducted using data from eight randomized controlled trials involving 28,253 participants. Studies comparing SGLT2 inhibitors with placebo in T2DM patients with CKD were included. The primary outcome was the risk of ESRD, reported as a pooled risk ratio (RR) with 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic. The pooled analysis demonstrated a significant reduction in ESRD risk with SGLT2 inhibitors compared to placebo (RR, 0.73; 95% CI, 0.66–0.82), indicating a 27% risk reduction. Heterogeneity was low (I^2=0%; p=0.50), confirming consistency across trials. Subgroup analyses showed similar reductions across different CKD stages and follow-up durations. In conclusion, SGLT2 inhibitors significantly reduce the risk of ESRD in T2DM patients with CKD, highlighting their renoprotective potential. These findings support the integration of SGLT2 inhibitors into standard care for high-risk populations to delay CKD progression and prevent ESRD.

Keywords: SGLT2 inhibitors, CKD, T2DM, ESRD, Meta-analysis, Randomized controlled trials

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a global health burden, affecting millions of individuals and representing a significant risk factor for the development and progression of chronic kidney disease (CKD).[1] CKD is a leading cause of morbidity and mortality worldwide, often progressing to end-stage renal disease (ESRD), which necessitates dialysis or kidney transplantation. The interplay between diabetes and kidney disease is complex, with hyperglycemia-induced microvascular damage, inflammation, and oxidative stress contributing to structural and functional kidney deterioration. Managing this progression remains a critical challenge in the care of patients with T2DM and CKD.[2,3]

Conventional treatments for diabetic kidney disease have primarily focused on glycemic control, blood pressure management, and the use of renin-angiotensin-aldosterone system inhibitors. While these approaches slow CKD progression, they are often insufficient to prevent ESRD, highlighting the need for additional therapeutic options. In recent years, the discovery and development of sodium-glucose co-transporter 2 (SGLT2) inhibitors have transformed the management of T2DM, providing not only glycemic control but also cardiorenal benefits.[4,5]

SGLT2 inhibitors act by inhibiting glucose reabsorption in the proximal tubules of the kidneys, leading to increased urinary glucose excretion. This unique mechanism reduces blood glucose levels independently of insulin and is associated with additional benefits, including weight loss and reduced blood pressure. Beyond their role in glycemic control, SGLT2 inhibitors have demonstrated protective effects on the cardiovascular and renal systems, making them a valuable addition to the therapeutic arsenal for T2DM.[5-7]

The renal benefits of SGLT2 inhibitors extend beyond glucose-lowering mechanisms. They are thought to reduce intraglomerular pressure by modulating tubuloglomerular feedback, thereby alleviating hyperfiltration—a hallmark of diabetic nephropathy.[6] Furthermore, SGLT2 inhibitors exhibit anti-inflammatory, antifibrotic, and antioxidant properties, all of which contribute to the preservation of kidney function. These pleiotropic effects have been confirmed in large-scale randomized controlled trials (RCTs), where SGLT2 inhibitors consistently reduced the risk of kidney disease progression, including ESRD, in patients with T2DM and varying degrees of CKD.[5,8,9] Numerous landmark trials have evaluated the renal outcomes of SGLT2 inhibitors.[10-12] These studies underline the transformative potential of SGLT2 inhibitors in addressing the unmet need for effective strategies to halt CKD progression in T2DM patients.

Despite these promising results, gaps remain in understanding the consistency and magnitude of SGLT2 inhibitors' effects across diverse populations and clinical settings. Individual studies often have varying patient populations, intervention durations, and baseline kidney function, making it challenging to draw uniform conclusions.[7-10] Additionally, while the renal benefits of SGLT2 inhibitors are well-documented, their exact role in preventing ESRD in advanced stages of CKD requires further exploration. The available evidence necessitates a comprehensive synthesis to provide clarity on the long-term renal outcomes of these agents.

In this context, meta-analyses play a pivotal role in synthesizing evidence from individual studies to generate robust conclusions. By pooling data from multiple RCTs, meta-analyses can provide higher statistical power and greater precision in estimating treatment effects. This is particularly relevant for outcomes such as ESRD, which, despite their clinical importance, are relatively rare events in individual trials. The aim of this meta-analysis was to evaluate the effectiveness of SGLT2 inhibitors in reducing the risk of progression to ESRD among patients with T2DM and CKD.

METHODS

This meta-analysis was conducted to evaluate the impact of SGLT2 inhibitors on the progression to ESRD among patients with T2DM and CKD. The methodology followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines to ensure the rigor and transparency of the study design[14]. We performed a comprehensive literature search across PubMed, Web of Science, Scopus, MEDLINE, the Cochrane Library, and Google Scholar from inception until the present. Keywords included combinations of "SGLT2 inhibitors," "chronic kidney disease," "end-stage renal disease," "type 2 diabetes mellitus," and "randomized controlled trials." Boolean operators, truncation, and medical subject headings (MeSH) terms were utilized to refine the search strategy. The search was supplemented by scanning reference lists of relevant articles to identify additional eligible studies. This meta-analysis was conducted during the period from May 2024 to October 2024.

Eligibility criteria

Studies were included if they were RCTs comparing SGLT2 inhibitors with placebo in adults diagnosed with T2DM and CKD. Only studies that reported the progression to ESRD as a primary or secondary outcome were considered. The inclusion criteria also required the availability of sufficient data to calculate the pooled risk ratio (RR) and 95% confidence interval (CI). Exclusion criteria included observational studies, studies without a placebo control, and trials involving pediatric or non-diabetic populations.

Study selection

Following the removal of duplicates, titles and abstracts were screened independently by two reviewers to identify potentially relevant studies. Full-text articles of shortlisted records were retrieved and assessed for eligibility based on predefined criteria. Discrepancies between reviewers were resolved through discussion or consultation with a third reviewer.

Data extraction

Data were extracted independently by two reviewers using a standardized data collection form. Extracted information included study characteristics (author, year of publication, study setting), patient demographics (mean age, sex distribution, duration of diabetes), intervention details (SGLT2 inhibitor used, dose, follow-up duration), control agent, and outcomes (number of ESRD events in each group). Any discrepancies in data extraction were resolved through discussion or by involving a third reviewer.

Outcome measure

The primary outcome was the risk of progression to ESRD in patients with T2DM and CKD. ESRD was defined as the initiation of renal replacement therapy, including dialysis or kidney transplantation, or a sustained estimated glomerular filtration rate (eGFR) <15 ml/min/1.73 m².

Data synthesis and statistical analysis

The meta-analysis was conducted using RevMan 5.4 software. The pooled RR with 95% CI was calculated using a fixed-effects model, given the low heterogeneity observed. Statistical heterogeneity was assessed using the Chi^2 test and the I^2 statistic, with I^2 values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. A p value <0.10 in the Chi^2 test was considered significant for heterogeneity. Publication bias was evaluated using a funnel plot. Sensitivity analyses were performed to examine the robustness of the results by excluding studies with high risk of bias.

RESULTS

The systematic search of six databases, including PubMed, Web of Science, Scopus, Medline, the Cochrane Library, and Google Scholar, yielded 781 records. After removing 388 duplicates, 393 studies underwent title and abstract screening. From these, 351 records were excluded for reasons such as irrelevant outcomes, non-RCT design, or ineligible populations. Subsequently, 42 articles were sought for full-text retrieval; however, 2 were unavailable. Of the 40 studies assessed for eligibility, 32 did not meet the inclusion criteria due to incomplete data on ESRD outcomes or inadequate follow-up durations. Ultimately, 8 studies were included in the meta-analysis, all meeting the criteria for evaluating the effects of SGLT2 inhibitors on ESRD progression in patients with T2DM and CKD. The details of the selection process are presented in the PRISMA flow diagram (Figure 1).

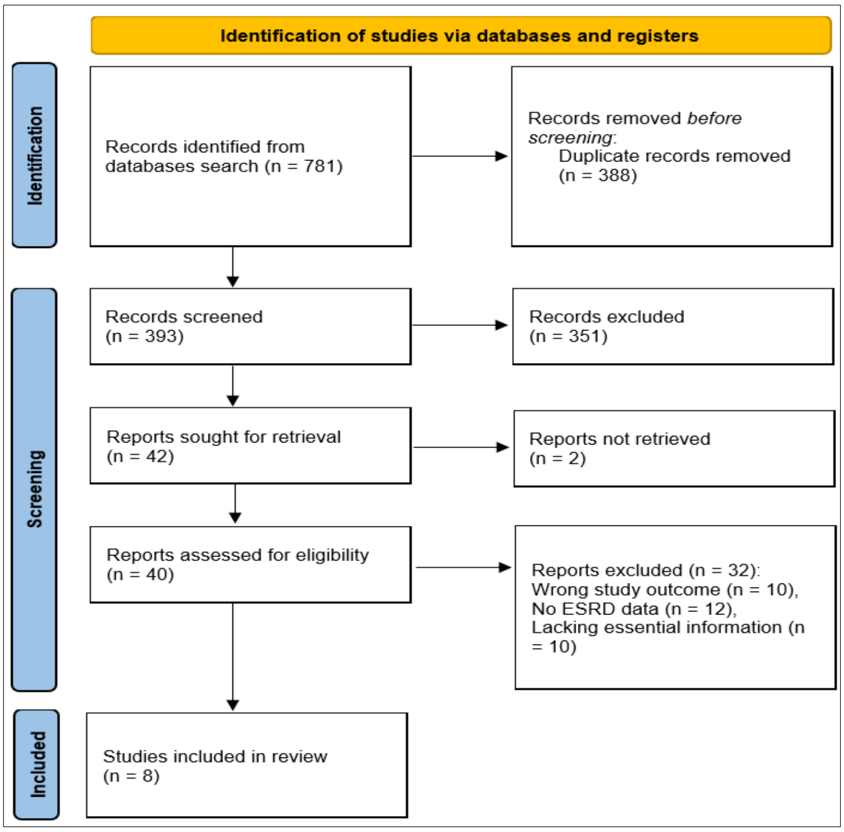

Figure 1: PRISMA flow diagram for the summary of the search and screening processes.

Characteristics and findings of the included studies

The eight included studies were all RCTs that assessed the efficacy of various SGLT2 inhibitors in reducing ESRD risk compared to placebo among patients with T2DM and CKD. These studies encompassed a total of 28,253 participants, reflecting the robust evidence base for the analysis.[16-23]

The age of participants ranged from a mean of 62 years in Wheeler et al to 69.6 years in Allegretti et al, suggesting a predominantly older population affected by advanced diabetic nephropathy.[16,23] Four studies reported mean ages between 62 and 69 years, while the others did not specify age data.[17,19,22] The proportion of male participants was consistently higher, ranging from 56.7% in Fioretto et al to 71.4% in Wanner et al.[17,22] This demographic reflects the higher prevalence of T2DM and CKD among men in clinical trial cohorts.

The mean duration of diabetes was reported in three studies, ranging from 13.5±7.8 years in Neal et al to

15.9±9.1 years in Allegretti et al and Perkovic et al.[16,20,21] These figures underscore the inclusion of a population with long-standing disease, predisposing them to advanced renal complications. In contrast, four studies did not provide specific data on diabetes duration.[17-19,23]

Sample sizes varied substantially, ranging from 252 participants in Kohan et al to 10,142 in Neal et al.[19,20] Larger studies, such as those by Herrington et al, Neal et al, and Wanner et al, provided strong statistical power to detect clinically meaningful differences in ESRD progression rates.[18,20,22] Smaller studies, such as Allegretti et al and Kohan et al, contributed valuable data despite their limited scope.[16,19]

The interventions evaluated across studies included dapagliflozin, empagliflozin, canagliflozin, and bexagliflozin.[16-23] Each trial utilized placebo as a control, ensuring consistent comparative data. Follow-up durations ranged widely, from 24 weeks in Allegretti et al to a maximum of 188 weeks in Neal et al.[16,20] Extended follow-up periods, such as those in Herrington et al and Perkovic et al, were critical for assessing long-term renal outcomes, including the development of ESRD.[18,21] Table 1 summarizes the characteristics of the included studies.

Quantitative data synthesis

The meta-analysis included 28,253 participants across all studies, with 587 ESRD events occurring in the SGLT2 inhibitor groups compared to 745 in the placebo groups. The pooled RR for ESRD with SGLT2 inhibitor use was 0.73 (95% CI, 0.66–0.82), demonstrating a significant 27% risk reduction. Heterogeneity was low (I^2=0%; p=0.50), indicating consistency across studies (Figure 2). These results strongly support the protective effects of SGLT2 inhibitors against ESRD progression in this high-risk population.

Table 1: Characteristics of the included studies (n=8).

Study	Age (years)	Males (%)	Duration of diabetes	Setting	Intervention agent	Control agent	Sample size	Follow up duration (weeks)
Allegretti et al, 2019[16]	69.6±8.3	62.80	15.9±9.1	Multicentre	Bexagliflozin	Placebo	320	24
Fioretto et al, 2018[17]	NR	56.70	NR	Multicentre	Dapagliflozin	Placebo	321	27
Herrington et al, 2024[18]	63±14	65.90	NR	Multicentre	Empagliflozin	Placebo	4891	144
Kohan et al, 2014[19]	NR	65.10	NR	Multicentre	Dapagliflozin	Placebo	252	104
Neal et al, 2017[20]	63.3±8.3	64.20	13.5±7.8	Multicentre	Canagliflozin	Placebo	10142	188
Perkovic et al, 2019[21]	63.0±9.2	67.10	15.8±8.6	Multicentre	Canagliflozin	Placebo	4401	137
Wanner et al, 2016[22]	NR	71.40	NR	Multicentre	Empagliflozin	Placebo	7020	136

NR: Not reported

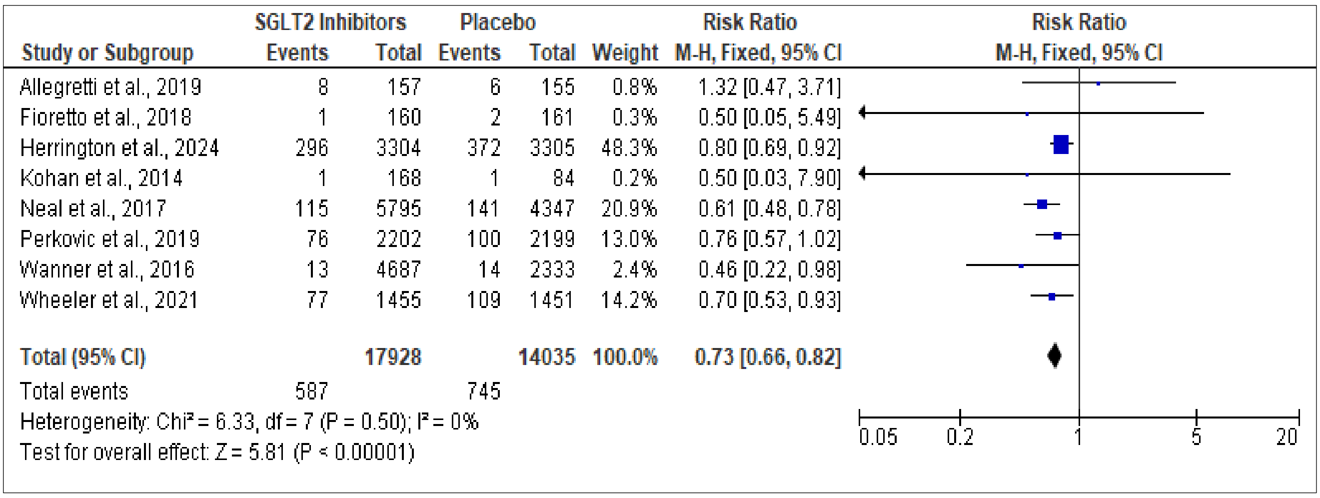

Figure 2: Forest plot of the risk of developing ESRD among T2DM patients using SGLT2 inhibitors versus placebo.

Several large trials contributed substantial weight to the pooled estimate. Herrington et al, which had the largest sample size of 4,891 participants, reported an RR of 0.80 (95% CI, 0.69–0.92) and contributed 48.3% of the overall weight.[18] Similarly, Neal et al with 10,142 participants, showed an RR of 0.61 (95% CI, 0.48–0.78) and contributed 20.9% weight to the analysis.[20] Wheeler et al also provided significant evidence, with an RR of 0.70 (95% CI, 0.53–0.93) and a weight of 14.2%.[23] Smaller studies, such as Fioretto et al and Kohan et al, demonstrated wide confidence intervals due to limited sample sizes and low event rates, but their findings did not contradict the overall effect.[17,19]

The symmetrical funnel plot (Figure 3) indicated no significant publication bias, as evidenced by the absence of asymmetry. This suggests that the results are robust and unlikely to be influenced by selective reporting or publication practices.

The findings highlight the efficacy of SGLT2 inhibitors as a therapeutic strategy for long-term kidney protection in T2DM patients with CKD, with consistent benefits observed across diverse patient populations and trial designs. These results have significant implications for clinical practice and the management of this high-risk group.

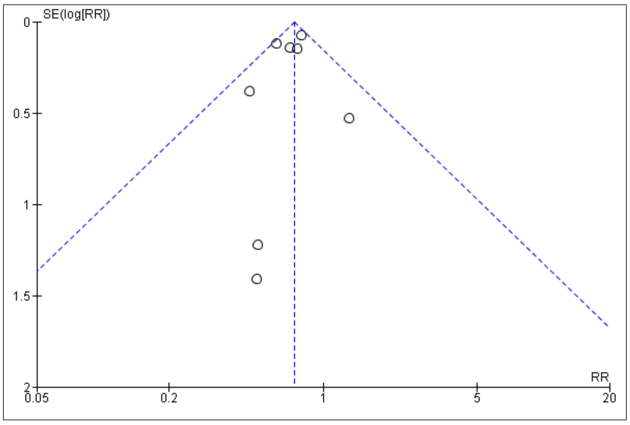

Figure 3: Funnel plot for assessment of publication bias.

DISCUSSION

CKD is a major complication of T2DM and is a leading cause of ESRD worldwide.[2,3] The progression to ESRD in T2DM patients not only reduces life expectancy but also increases healthcare costs and burden. SGLT2 inhibitors, initially developed as glucose-lowering agents, have emerged as promising therapies for delaying CKD progression and reducing the risk of ESRD.[5,8] These inhibitors exert renoprotective effects beyond glycemic control, likely mediated by hemodynamic and anti-inflammatory mechanisms. Despite individual trials demonstrating their efficacy in preventing renal outcomes, no previous meta-analysis has systematically quantified their impact on ESRD risk. Our study addresses this gap by synthesizing evidence from eight randomized controlled trials to evaluate the long-term effectiveness of SGLT2 inhibitors in T2DM patients with CKD.[7,8]

This meta-analysis included data from 28,253 participants across eight randomized controlled trials, all of which compared SGLT2 inhibitors with placebo in reducing the risk of ESRD in T2DM patients with CKD. The pooled RR for developing ESRD with SGLT2 inhibitor use was 0.73 (95% CI, 0.66–0.82), reflecting a significant 27% risk reduction compared to placebo. The results were consistent across studies, with low heterogeneity (I^2=0%; p=0.50), underscoring the robustness of the findings. Notably, large-scale trials such as Herrington et al and Neal et al demonstrated significant ESRD risk reductions of 20% to 39%, further validating the protective role of SGLT2 inhibitors.[18,20]

Our findings confirm the renoprotective effects of SGLT2 inhibitors in a high-risk population. The significant reduction in ESRD risk likely stems from the unique mechanisms of these drugs. SGLT2 inhibitors reduce intraglomerular pressure by restoring tubuloglomerular feedback and lowering glomerular hyperfiltration, key drivers of CKD progression. Additionally, their anti-inflammatory and antifibrotic properties may mitigate the structural damage to the kidneys, thereby delaying the onset of ESRD.[24-26]

The findings of our meta-analysis align with those of individual trials. For example, Herrington et al demonstrated a significant ESRD risk reduction (RR, 0.80; 95% CI, 0.69–0.92) over a 144-week follow-up period in patients treated with empagliflozin.[18] Neal et al which assessed canagliflozin in the CANVAS program, reported a risk reduction of 39% (RR, 0.61; 95% CI, 0.48–0.78) over 188 weeks.[20] Similarly, Wheeler et al observed a significant 30% ESRD risk reduction (RR, 0.70; 95% CI, 0.53–0.93) with dapagliflozin over a median follow-up of 2.4 years.[23] These results are consistent with our pooled analysis, which reflects the broad efficacy of SGLT2 inhibitors across diverse populations and clinical settings.

In contrast, smaller trials such as Allegretti et al and Fioretto et al reported nonsignificant risk reductions due to limited sample sizes and low event rates.[16,17] While their findings contribute to the overall evidence base, their lower weight in the meta-analysis highlights the importance of larger, longer-duration trials for detecting clinically meaningful differences.

The results of our meta-analysis are consistent with existing literature demonstrating the renoprotective effects of SGLT2 inhibitors. A prior meta-analysis by Neuen et al reported similar findings, showing that SGLT2 inhibitors reduce the risk of major kidney outcomes, including ESRD, by approximately 30%.[27] However, our study provides a more focused analysis on ESRD as the primary endpoint, offering a granular perspective on the benefits of SGLT2 inhibitors in delaying kidney failure.[28]

Furthermore, our findings align with those of real-world observational studies, such as the CREDENCE trial, which demonstrated a 32% reduction in ESRD risk with canagliflozin.[29] These studies corroborate the efficacy of SGLT2 inhibitors in routine clinical practice and highlight their potential to transform CKD management in T2DM patients.

The pooled RR of 0.73 (95% CI, 0.66–0.82) in our analysis underscores the consistent renoprotective benefits of SGLT2 inhibitors across trials. Importantly, the low heterogeneity (I^2=0%) enhances confidence in the generalizability of these findings. This consistency is likely attributable to the uniform mechanisms of action of SGLT2 inhibitors, which transcend variations in study populations, interventions, and follow-up durations.

The implications of our findings are significant. A 27% reduction in ESRD risk translates to fewer patients requiring dialysis or kidney transplantation, improving quality of life and reducing healthcare costs. These benefits are particularly relevant in populations with advanced CKD, where therapeutic options are limited, and ESRD prevention is paramount.

Despite the robust evidence from our meta-analysis, several limitations warrant consideration. First, some included trials, such as Fioretto et al and Kohan et al, had small sample sizes and short follow-up periods, limiting their power to detect significant effects.[17,19] Second, not all trials reported baseline characteristics such as diabetes duration or CKD stage, which may influence treatment response. Third, publication bias, while not evident in the funnel plot, cannot be entirely excluded, especially given the dominance of industry-funded trials in this field.

Future research should focus on head-to-head comparisons of different SGLT2 inhibitors to determine whether specific agents offer superior renoprotective effects. Additionally, longer-term studies are needed to assess the durability of ESRD risk reductions and explore potential benefits in earlier CKD stages.

The findings of our meta-analysis support the integration of SGLT2 inhibitors into standard care for T2DM patients with CKD. Given their consistent efficacy in reducing ESRD risk, these drugs should be prioritized as first-line therapy in this population. Moreover, their cardiovascular benefits, which were not the focus of our study, further strengthen their utility in managing multimorbidity in T2DM patients.

CONCLUSION

In conclusion, our meta-analysis demonstrates that SGLT2 inhibitors significantly reduce the risk of ESRD in T2DM patients with CKD by 27% (RR, 0.73; 95% CI, 0.66–0.82). These findings, supported by consistent results across trials and low heterogeneity, highlight the renoprotective potential of SGLT2 inhibitors. By delaying ESRD progression, these agents offer a valuable therapeutic option for improving renal outcomes and reducing the burden of kidney failure in high-risk populations. Future studies should aim to address remaining knowledge gaps and optimize the use of SGLT2 inhibitors for kidney preservation.

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REFERENCES

1. Nanda M, Sharma R, Mubarik S, Aashima A, Zhang K. Type-2 diabetes mellitus (T2DM): spatial-temporal patterns of incidence, mortality and attributable risk factors from 1990 to 2019 among 21 world regions. Endocrine. 2022;77(3):444-54.
2. Liu B, Li L, Cui H, Zhao Q, Chen S. Analysis of the global burden of CKD-T2DM in young and middle-aged adults in 204 countries and territories from 2000 to 2019: A systematic study of the global burden of disease in 2019. Diabetes Res Clin Pract. 2024;217:111884.
3. Fenta ET, Eshetu HB, Kebede N, Bogale EK, Zewdie A, Kassie TD, et al. Prevalence and predictors of chronic kidney disease among type 2 diabetic patients worldwide, systematic review and meta-analysis. Diabetol Metab Syndrome. 2023;15(1):245.
4. Wheeler DC, James J, Patel D, Viljoen A, Ali A, Evans M, et al. SGLT2 inhibitors: slowing of chronic kidney disease progression in type 2 diabetes. Diabetes Therapy. 2020;11:2757-74.
5. DeFronzo RA, Reeves WB, Awad AS. Pathophysiology of diabetic kidney disease: impact of SGLT2 inhibitors. Nat Rev Nephrol. 2021;17(5):319-34.
6. Wright EM. SGLT2 inhibitors: physiology and pharmacology. Kidney360. 2021;2(12):2027-37.
7. Oe Y, Vallon V. The pathophysiological basis of diabetic kidney protection by inhibition of SGLT2 and SGLT1. Kidney Dialysis. 2022;2(2):349-68.
8. Davidson JA. SGLT2 inhibitors in patients with type 2 diabetes and renal disease: overview of current evidence. Postgrad Med. 2019;131(4):251-60.
9. Cowie MR, Fisher M. SGLT2 inhibitors: mechanisms of cardiovascular benefit beyond glycaemic control. Nat Rev Cardiol. 2020;17(12):761-72.
10. Seidu S, Kunutsor SK, Cos X, Gillani S, Khunti K. SGLT2 inhibitors and renal outcomes in type 2 diabetes with or without renal impairment: a systematic review and meta-analysis. Prim Care Diabetes. 2018;12(3):265-83.
11. Kelly MS, Lewis J, Huntsberry AM, Dea L, Portillo I. Efficacy and renal outcomes of SGLT2 inhibitors in patients with type 2 diabetes and chronic kidney disease. Postgrad Med. 2019;131(1):31-42.

12. Spiazzi BF, Piccoli GF, Wayerbacher LF, Lubianca JP, Scalco BG, Scheffler MH, et al. SGLT2 inhibitors and kidney outcomes across the spectrum of kidney disease: a systematic review and meta-analysis. Clin J Am Soc Nephrol. 2024;10:2215.
13. McGuire DK, Shih WJ, Cosentino F, Charbonnel B, Cherney DZ, Dagogo-Jack S, et al. Association of SGLT2 inhibitors with cardiovascular and kidney outcomes in patients with type 2 diabetes: a meta-analysis. JAMA Cardiol. 2021;6(2):148-58.
14. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;29:372.
15. Review Manager (RevMan). Version 5.4. The Cochrane Collaboration. Available at: revman.cochrane.org. Accessed on 12 August 2024.
16. Allegretti AS, Zhang W, Zhou W, Thurber TK, Rigby SP, Bowman-Stroud C, et al. Safety and effectiveness of bexagliflozin in patients with type 2 diabetes mellitus and stage 3a/3b CKD. Am J Kidney Dis. 2019;74(3):328-37.
17. Fioretto P, Del Prato S, Buse JB, Goldenberg R, Giorgino F, Reyner D, et al, DERIVE Study Investigators. Efficacy and safety of dapagliflozin in patients with type 2 diabetes and moderate renal impairment (chronic kidney disease stage 3A): The DERIVE Study. Diabetes Obesity Metabolism. 2018;20(11):2532-40.
18. Herrington WG, Staplin N, Agrawal N, Wanner C, Green JB, Hauske SJ, et al. Long-Term Effects of Empagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2024;25:10-56.
19. Kohan DE, Fioretto P, Tang W, List JF. Long-term study of patients with type 2 diabetes and moderate renal impairment shows that dapagliflozin reduces weight and blood pressure but does not improve glycemic control. Kidney Int. 2014;85(4):962-71.
20. Neal B, Perkovic V, Mahaffey KW, De Zeeuw D, Fulcher G, Erondu N, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med. 2017;377(7):644-57.
21. Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJ, Charytan DM, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med. 2019;380(24):2295-306.
22. Wanner C, Inzucchi SE, Lachin JM, Fitchett D, von Eynatten M, Mattheus M, et al. Empagliflozin and progression of kidney disease in type 2 diabetes. N Engl J Med. 2016;375(4):323-34.
23. Wheeler DC, Stefánsson BV, Jongs N, Chertow GM, Greene T, Hou FF, et al. Effects of dapagliflozin on major adverse kidney and cardiovascular events in patients with diabetic and non-diabetic chronic kidney disease: a prespecified analysis from the DAPA-CKD trial. Lancet Diabetes Endocrinol. 2021;9(1):22-31.
24. Geng S, Li Y, Ge J, Liu Y, Li Q, Chen X, et al. Nephroprotective effect of SGLT2 inhibitors in elderly patients with type 2 diabetes mellitus and hypertension: a real-world population-based cohort study. Postgrad Med. 2024;136(8):855-63.
25. Garofalo C, Borrelli S, Liberti ME, Andreucci M, Conte G, Minutolo R, et al. SGLT2 inhibitors: nephroprotective efficacy and side effects. Medicina. 2019;55(6):268.
26. Yaribeygi H, Simental-Mendía LE, Banach M, Bo S, Sahebkar A. The major molecular mechanisms mediating the renoprotective effects of SGLT2 inhibitors: An update. Biomed Pharmacotherapy. 2019;120:109526.
27. Neuen BL, Young T, Heerspink HJ, Neal B, Perkovic V, Billot L, et al. SGLT2 inhibitors for the prevention of kidney failure in patients with type 2 diabetes: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2019;7(11):845-54.
28. Scheen AJ, Delanaye P. Understanding the protective effects of SGLT2 inhibitors in type 2 diabetes patients with chronic kidney disease. Exp Rev Endocrinol Metabolism. 2022;17(1):35-46.
29. Giorgino F, Vora J, Fenici P, Solini A. Renoprotection with SGLT2 inhibitors in type 2 diabetes over a spectrum of cardiovascular and renal risk. Cardiovasc Diabetol. 2020;19:1-9.

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