Research Output Journal of Engineering and Scientific Research 5(1): 29-35, 2026

ROJESR Publications Online ISSN: 1115-9790

https://rojournals.org/roj-engineering-and-scientific-research/ Print ISSN: 1115-6155

https://doi.org/10.59298/ROJESR/2026/5.12935

SGLT2 Inhibitors for Diabetic Kidney Disease Prevention: Mechanisms, Clinical Evidence, and Guidelines

Nambi Namusisi H.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Diabetic kidney disease remained a leading cause of end stage renal disease globally, affecting approximately 40% of individuals with diabetes mellitus. Sodium glucose cotransporter 2 inhibitors represented a novel therapeutic class originally developed for glycemic control but have demonstrated profound renoprotective effects independent of glucose-lowering mechanisms. This review examined the biochemical mechanisms underlying the renoprotective effects of sodium glucose cotransporter 2 inhibitors, evaluated the clinical evidence supporting their use in diabetic kidney disease prevention, and synthesized current guideline recommendations for their implementation in clinical practice. A comprehensive synthesis of mechanistic studies, randomized controlled trials, meta-analyses, and international clinical practice guidelines published through early 2025 was conducted to evaluate sodium glucose cotransporter 2 inhibitor efficacy and safety in diabetic kidney disease. Sodium glucose cotransporter 2 inhibitors exerted renoprotection through multiple interconnected mechanisms, including restoration of tubuloglomerular feedback, reduction of intraglomerular pressure, attenuation of oxidative stress and inflammation, and modulation of renal energy metabolism. Recent evidence extended these benefits to patients with chronic kidney disease irrespective of diabetes status. Current guidelines recommend sodium glucose cotransporter 2 inhibitors as foundational therapy alongside renin angiotensin system blockade for patients with diabetic kidney disease and preserved ejection fraction. Sodium glucose cotransporter 2 inhibitors represented a paradigm shift in diabetic kidney disease management, offering robust renoprotection through pleiotropic mechanisms with an acceptable safety profile, though implementation barriers and knowledge gaps regarding optimal patient selection persist.

Keywords: Sodium glucose cotransporter 2 inhibitors, Diabetic kidney disease, Renoprotection, tubuloglomerular feedback, chronic kidney disease.

INTRODUCTION

Sodium glucose cotransporter 2 inhibitors constitute a class of antihyperglycemic agents that selectively inhibit the reabsorption of filtered glucose in the proximal convoluted tubule of the nephron [1]. These agents target the sodium glucose cotransporter 2 protein, which accounts for approximately 90% of renal glucose reabsorption under physiological conditions [2, 3]. By blocking this transporter, sodium glucose cotransporter 2 inhibitors induce glucosuria, thereby lowering plasma glucose concentrations in hyperglycemic states. Beyond their primary metabolic effects, these agents demonstrate remarkable pleiotropic properties affecting renal hemodynamics, systemic metabolism, and cardiovascular function. The class includes several approved agents such as empagliflozin, dapagliflozin, canagliflozin, and ertugliflozin, each with distinct pharmacokinetic profiles but similar mechanisms of action. Initial skepticism regarding the long term renal safety of inducing chronic glucosuria has been decisively refuted by accumulating evidence demonstrating substantial renoprotective benefits [4].

Diabetic kidney disease represents a microvascular complication of diabetes mellitus characterized by progressive albuminuria, declining glomerular filtration rate, and eventual progression to end-stage renal disease requiring

dialysis or transplantation [5, 6]. The pathophysiology involves a complex interplay of hemodynamic alterations, metabolic derangements, oxidative stress, inflammation, and fibrotic remodeling. Hyperglycemia-induced glomerular hyperfiltration, mediated through afferent arteriolar vasodilation and loss of tubuloglomerular feedback, contributes to intraglomerular hypertension and progressive nephron damage. Traditional management has centered on intensive glycemic control and renin angiotensin aldosterone system blockade, yet residual renal risk remains substantial, with approximately 30% to 40% of patients progressing despite optimal conventional therapy [7]. The emergence of sodium glucose cotransporter 2 inhibitors has fundamentally altered the therapeutic landscape by providing additive renoprotection through mechanisms largely independent of glycemic improvement. The objective of this review is to critically evaluate the biochemical mechanisms underlying sodium glucose cotransporter 2 inhibitor-mediated renoprotection, synthesize clinical evidence from major randomized controlled trials and real-world studies, and examine current guideline recommendations for their integration into diabetic kidney disease prevention and management strategies.

Molecular and Biochemical Mechanisms of Renoprotection

The renoprotective effects of sodium glucose cotransporter 2 inhibitors arise from multiple interconnected molecular pathways that extend beyond simple glucose lowering [8]. Restoration of tubuloglomerular feedback represents a primary mechanism whereby reduced proximal tubular sodium and glucose reabsorption increases distal sodium delivery to the macula densa, triggering afferent arteriolar vasoconstriction through adenosine-mediated signaling [9]. This hemodynamic correction reduces intraglomerular capillary pressure and single-nephron hyperfiltration, thereby attenuating mechanical stress on the glomerular filtration barrier. Studies in experimental diabetes models demonstrate that sodium glucose cotransporter 2 inhibition normalizes the suppressed tubuloglomerular feedback response characteristic of early diabetic kidney disease, with measurable reductions in glomerular capillary pressure within days of treatment initiation.

Beyond hemodynamic effects, sodium glucose cotransporter 2 inhibitors modulate intrarenal metabolism and reduce cellular stress pathways [10, 11]. Proximal tubular cells in diabetic kidneys exhibit increased workload due to enhanced sodium glucose reabsorption, elevating oxygen consumption and generating oxidative stress. By reducing this reabsorptive burden, sodium glucose cotransporter 2 inhibitors decrease tubular oxygen demand, improve the cortical oxygen tension gradient, and attenuate hypoxia inducible factor activation [12, 13]. This metabolic reprogramming shifts cellular energy utilization toward more efficient ketone body oxidation while reducing reliance on glycolysis and fatty acid metabolism, pathways implicated in lipotoxicity and mitochondrial dysfunction. Furthermore, these agents demonstrate anti-inflammatory and antifibrotic properties through suppression of nuclear factor kappa B signaling, reduced transforming growth factor beta expression, and decreased extracellular matrix accumulation in both tubular and glomerular compartments.

Emerging evidence indicates that sodium glucose cotransporter 2 inhibitors favorably influence systemic metabolic parameters relevant to renal health [14]. Modest reductions in body weight, blood pressure, and uric acid levels contribute to overall cardiorenal risk reduction. The natriuretic effect, while transient during initiation, promotes volume contraction and reduces cardiac preload, indirectly benefiting renal hemodynamics. Additionally, erythropoietin stimulation and improved iron homeostasis may enhance renal oxygen delivery. The integration of these pleiotropic mechanisms produces a comprehensive renoprotective phenotype that substantially exceeds predictions based on glycemic control alone [15]. However, the relative contribution of each mechanism remains debated, and individual patient responses likely reflect genetic, environmental, and disease stage variability. Future mechanistic studies employing advanced imaging, omics profiling, and computational modeling will refine the understanding of these complex pathways and identify potential biomarkers for treatment response prediction.

Clinical Evidence from Randomized Controlled Trials

Landmark cardiovascular outcome trials initially revealed the unexpected renoprotective potential of sodium glucose cotransporter 2 inhibitors when examining secondary renal endpoints [16, 17]. The EMPA REG OUTCOME trial demonstrated that empagliflozin reduced the composite outcome of doubling of serum creatinine, initiation of renal replacement therapy, or death from renal causes by 46% compared with placebo in patients with type 2 diabetes and established cardiovascular disease [18, 19]. Similarly, the CANVAS program showed that canagliflozin decreased albuminuria progression and the composite renal outcome by 40% [20]. The DECLARE TIMI 58 trial confirmed that dapagliflozin reduced the composite of sustained estimated glomerular filtration rate decrease of 40% or more, end-stage renal disease, or renal death by 47% [21]. These consistent findings across different agents and diverse patient populations established sodium glucose cotransporter 2 inhibitors as a renoprotective drug class, prompting dedicated renal outcome trials.

The CREDENCE trial represented the first prospective study specifically designed to evaluate renal outcomes, enrolling patients with type 2 diabetes, albuminuria, and estimated glomerular filtration rate between 30 and 90 milliliters per minute per 1.73 square meters [22, 23]. Canagliflozin reduced the primary composite endpoint of end stage kidney disease, doubling of serum creatinine, or renal or cardiovascular death by 30%, with early separation

of Kaplan Meier curves suggesting rapid onset of benefit. Importantly, renoprotective effects persisted across baseline estimated glomerular filtration rate subgroups, including those with advanced chronic kidney disease. The DAPA CKD trial extended these findings by enrolling patients with chronic kidney disease with or without type 2 diabetes, demonstrating a 39% reduction in the composite of sustained estimated glomerular filtration rate decline of 50% or more, end-stage kidney disease, or renal or cardiovascular death [24, 25]. This landmark study established efficacy in nondiabetic chronic kidney disease, fundamentally expanding the therapeutic indication for sodium glucose cotransporter 2 inhibitors.

More recently, the EMPA KIDNEY trial enrolled a broad chronic kidney disease population, including patients with estimated glomerular filtration rate as low as 30 milliliters per minute per 1.73 square meters and varying albuminuria levels [26]. Empagliflozin reduced the primary outcome of kidney disease progression or cardiovascular death by 28%, with benefits observed regardless of diabetes status, baseline estimated glomerular filtration rate, or albuminuria severity [27, 28]. Meta-analyses incorporating these major trials consistently demonstrate hazard ratios between 0.60 and 0.70 for composite renal outcomes, with number needed to treat estimates of approximately 20 to 30 patients over two to four years to prevent one renal event. Safety analyses reveal acceptable tolerability with increased genital mycotic infections but no excess risk of acute kidney injury, diabetic ketoacidosis rates remaining low, and volume depletion manageable through appropriate patient selection and monitoring. These robust data establish sodium glucose cotransporter 2 inhibitors as evidence-based renoprotective therapy with applicability across the chronic kidney disease spectrum.

Pathophysiological Considerations and Clinical Implications

The clinical benefits of sodium glucose cotransporter 2 inhibitors in diabetic kidney disease reflect their impact on fundamental pathophysiological processes driving disease progression [29, 30]. The early reduction in intraglomerular pressure addresses the hemodynamic injury hypothesis central to diabetic nephropathy pathogenesis. Traditional renin angiotensin system inhibitors preferentially dilate efferent arterioles, while sodium glucose cotransporter 2 inhibitors restore physiological afferent arteriolar tone, creating complementary mechanisms when used in combination. This dual approach to pressure reduction may explain the additive benefits observed when sodium glucose cotransporter 2 inhibitors are added to background renin angiotensin system blockade, the current standard of care. The hemodynamic effects manifest clinically as a transient estimated glomerular filtration rate dip during treatment initiation, typically 3 to 5 milliliters per minute per 1.73 square meters, which stabilizes within weeks and is followed by a slower rate of subsequent decline compared with placebo. Beyond hemodynamics, sodium glucose cotransporter 2 inhibitors address metabolic and inflammatory contributors to diabetic kidney disease [31]. The reduction in proximal tubular workload and improved oxygenation may prevent tubular cell senescence and epithelial to mesenchymal transition, processes implicated in tubulointerstitial fibrosis. Attenuation of oxidative stress reduces reactive oxygen species-mediated damage to podocytes and endothelial cells, preserving glomerular filtration barrier integrity. The anti-inflammatory effects, evidenced by reduced urinary and circulating inflammatory biomarkers, may interrupt feed-forward cycles of immune cell infiltration and tissue injury. Clinically, these mechanistic effects translate to consistent reductions in urinary albumin to creatinine ratio, often by 30% to 50% within three to six months of therapy initiation. Albuminuria reduction correlates with long-term renal protection and represents an important surrogate endpoint in clinical practice.

The cardiovascular benefits of sodium glucose cotransporter 2 inhibitors complement their renoprotective effects, addressing the bidirectional relationship between cardiac and renal dysfunction [32, 33]. Heart failure with preserved ejection fraction, highly prevalent in diabetic kidney disease populations, responds favorably to sodium glucose cotransporter 2 inhibition with reduced hospitalization rates and improved quality of life. This cardiorenal protection creates a clinical imperative for early initiation before advanced kidney disease develops. However, implementation challenges persist, including delayed prescribing due to outdated concerns regarding estimated glomerular filtration rate thresholds, inadequate awareness among nonspecialists, cost and access barriers in resource-limited settings, and incomplete integration into multidisciplinary care pathways. Optimal patient selection requires consideration of contraindications, including type 1 diabetes without appropriate protocols, recurrent genitourinary infections, and volume-depleted states requiring correction before initiation.

Therapeutic Integration and Guideline Recommendations

International clinical practice guidelines have rapidly incorporated sodium glucose cotransporter 2 inhibitors into diabetic kidney disease management algorithms based on the strength of accumulated evidence [34]. The Kidney Disease Improving Global Outcomes 2022 guideline update recommends sodium glucose cotransporter 2 inhibitors as first-line therapy alongside renin angiotensin system inhibitors for adults with type 2 diabetes and chronic kidney disease, irrespective of baseline glycemic control or hemoglobin A1c levels [35]. This represents a conceptual shift from viewing these agents purely as antihyperglycemic medications to recognizing them as renoprotective therapies with glucose-lowering as a secondary benefit. The American Diabetes Association Standards of Care similarly position sodium glucose cotransporter 2 inhibitors as preferred agents in patients with diabetic kidney disease,

particularly when estimated glomerular filtration rate exceeds 20 milliliters per minute per 1.73 square meters, and albuminuria is present.

European Society of Cardiology and European Renal Association Best Practice Position Statement extends recommendations to patients with chronic kidney disease without diabetes, reflecting evidence from DAPA CKD and EMPA KIDNEY trials. Specific agent selection considerations include approved indications, which vary by jurisdiction and estimated glomerular filtration rate thresholds, with newer labels permitting initiation at lower estimated glomerular filtration rate values than historical restrictions. For example, empagliflozin and dapagliflozin are now approved for chronic kidney disease patients with estimated glomerular filtration rate as low as 20 milliliters per minute per 1.73 square meters, whereas earlier approvals required higher thresholds [36, 37]. Guidelines emphasize continuation of therapy even as estimated glomerular filtration rate declines below initiation thresholds, as trial data demonstrate persistent benefit and acceptable safety during progressive chronic kidney disease. Temporary discontinuation is advised during acute illnesses, surgical procedures, or circumstances that increase the risk of ketoacidosis.

Practical implementation requires systematic approaches to patient identification, initiation protocols, and ongoing monitoring. Clinical decision support tools integrated into electronic health records facilitate the identification of eligible patients who might otherwise be overlooked. Initiation checklists should verify adequate volume status, review concurrent medications for potential drug interactions, and establish baseline estimated glomerular filtration rate and electrolyte values. Patient education addressing transient estimated glomerular filtration rate decline, mycotic infection prevention, sick day management, and euglycemic ketoacidosis recognition enhances adherence and safety. Follow-up monitoring at four to six weeks post initiation assesses tolerability and confirms the expected estimated glomerular filtration rate trajectory. Quality improvement initiatives demonstrate that systematic implementation protocols increase prescribing rates from less than 20% to over 60% in eligible populations. Addressing disparities in access, particularly in underserved populations disproportionately affected by diabetic kidney disease, remains an urgent priority requiring advocacy for reimbursement, generic availability, and global health initiatives extending access beyond high-income countries.

Knowledge Gaps, Controversies, and Future Research Directions

Despite robust evidence supporting sodium glucose cotransporter 2 inhibitor efficacy in diabetic kidney disease prevention, important knowledge gaps and controversies persist. The optimal timing of therapy initiation remains debated, particularly regarding whether earlier intervention in normoalbuminuric patients or those with preserved estimated glomerular filtration rate provides incremental benefit compared with initiation after albuminuria emerges [38]. Post hoc analyses suggest benefits across albuminuria categories, but prospective trials specifically targeting early-stage diabetic kidney disease could refine preventive strategies. Similarly, the role of sodium glucose cotransporter 2 inhibitors in type 1 diabetes associated kidney disease remains uncertain, as regulatory approvals exclude this indication due to ketoacidosis concerns, despite a mechanistic rationale and limited observational data suggesting potential benefit with appropriate safeguards.

Mechanistic uncertainties include the relative importance of hemodynamic versus metabolic mechanisms, which has implications for predicting individual treatment responses and identifying patients most likely to benefit. Emerging biomarkers, including urinary inflammatory mediators, metabolomic signatures, and genetic polymorphisms in sodium glucose cotransporter genes may enable precision medicine approaches [39]. The phenomenon of acute estimated glomerular filtration rate decline upon initiation, while generally reversible and not associated with adverse outcomes, requires better characterization to distinguish expected hemodynamic responses from pathological acute kidney injury. Additionally, long term safety data extending beyond four-to-five-year trial durations would strengthen confidence regarding fracture risk, observed with canagliflozin in some but not all studies, and potential unanticipated effects of chronic glucosuria on renal and systemic homeostasis.

Comparative effectiveness research examining sodium glucose cotransporter 2 inhibitors versus mineralocorticoid receptor antagonists, newer nonsteroidal mineralocorticoid receptor antagonists, or combination strategies would inform optimal therapeutic sequencing [40, 41]. Real-world effectiveness studies complement randomized controlled trial evidence by providing data on diverse populations, adherence patterns, and pragmatic implementation outcomes. Cost-effectiveness analyses, while generally favorable in high-income countries, require contextualization to different healthcare systems and incorporation of societal perspectives. Future research priorities include mechanistic studies employing kidney biopsy analysis, advanced imaging to assess renal oxygenation and perfusion, and multi-omics approaches to define molecular pathways and treatment response biomarkers. Trials evaluating sodium glucose cotransporter 2 inhibitors in special populations, including kidney transplant recipients, patients receiving immunosuppression, and those with advanced chronic kidney disease approaching dialysis, would address critical evidence gaps. Ultimately, translating trial efficacy into real-world effectiveness requires continued focus on implementation science, health equity, and system-level interventions to ensure all eligible patients benefit from this transformative therapeutic class.

CONCLUSION

Sodium glucose cotransporter 2 inhibitors represent a paradigm shift in diabetic kidney disease prevention and management, offering robust renoprotection through pleiotropic mechanisms that extend beyond glycemic control. The convergence of mechanistic understanding, consistently positive randomized controlled trial results, and updated clinical guidelines establishes these agents as foundational therapy alongside renin angiotensin system blockade. The restoration of tubuloglomerular feedback and reduction of intraglomerular hypertension address core hemodynamic drivers of diabetic nephropathy, while metabolic reprogramming, anti-inflammatory effects, and antifibrotic properties target multiple pathophysiological pathways. Large-scale trials including CREDENCE, DAPA CKD, and EMPA KIDNEY demonstrate substantial reductions in clinically meaningful renal endpoints with hazard ratios consistently between 0.60 and 0.70, translating to prevention of end-stage kidney disease in a significant proportion of treated patients. The expansion of evidence to include patients with chronic kidney disease without diabetes broadens the therapeutic population and reinforces the kidney protective effects as distinct from antihyperglycemic properties. Despite an acceptable safety profile, implementation challenges, including prescriber inertia, access barriers, and knowledge gaps regarding optimal patient selection, temper the translation of trial efficacy into population-level benefit. Future research addressing mechanistic uncertainties, long-term safety, predictive biomarkers, and comparative effectiveness will further refine therapeutic strategies and enable precision medicine approaches to maximize individual patient benefit. Healthcare systems should implement systematic identification and treatment protocols incorporating sodium glucose cotransporter 2 inhibitors for all eligible patients with diabetic kidney disease and chronic kidney disease, prioritizing early initiation and addressing access disparities to achieve equitable cardiorenal protection.

REFERENCES

1. De Nicola, L., Gabbai, F.B., Liberti, M.E., Sagliocca, A., Conte, G., Minutolo, R.: Sodium/Glucose Cotransporter 2 Inhibitors and Prevention of Diabetic Nephropathy: Targeting the Renal Tubule in Diabetes. American Journal of Kidney Diseases. 64, 16–24 (2014). https://doi.org/10.1053/j.ajkd.2014.02.010
2. Brown, E., Rajeev, S.P., Cuthbertson, D.J., Wilding, J.P.H.: A review of the mechanism of action, metabolic profile and haemodynamic effects of sodium-glucose co-transporter-2 inhibitors. Diabetes, Obesity and Metabolism. 21, 9–18 (2019). https://doi.org/10.1111/dom.13650
3. Brown, E., Rajeev, S.P., Cuthbertson, D.J., Wilding, J.P.H.: A review of the mechanism of action, metabolic profile and haemodynamic effects of sodium-glucose co-transporter-2 inhibitors. Diabetes, Obesity and Metabolism. 21, 9–18 (2019). https://doi.org/10.1111/dom.13650
4. Padda, I.S., Mahtani, A.U., Parmar, M.: Sodium-Glucose Transport 2 (SGLT2) Inhibitors. In: StatPearls. StatPearls Publishing, Treasure Island (FL) (2025)
5. Alum, E.U., Ikpozu, E.N., Offor, C.E., Igwenyi, I.O., Obaroh, I.O., Ibiam, U.A., Ukaidi, C.U.A.: RNA-based diagnostic innovations: A new frontier in diabetes diagnosis and management. Diabetes & Vascular Disease Research. 22, 14791641251334726 (2025). https://doi.org/10.1177/14791641251334726
6. Hussain, S., Chand Jamali, M., Habib, A., Hussain, M.S., Akhtar, M., Najmi, A.K.: Diabetic kidney disease: An overview of prevalence, risk factors, and biomarkers. Clinical Epidemiology and Global Health. 9, 2–6 (2021). https://doi.org/10.1016/j.cegh.2020.05.016
7. Galindo, R.J., Beck, R.W., Scioscia, M.F., Umpierrez, G.E., Tuttle, K.R.: Glycemic Monitoring and Management in Advanced Chronic Kidney Disease. Endocr Rev. 41, 756–774 (2020). https://doi.org/10.1210/endrev/bnaa017
8. Heerspink, H.J.L., Kosiborod, M., Inzucchi, S.E., Cherney, D.Z.I.: Renoprotective effects of sodium-glucose cotransporter-2 inhibitors. Kidney International. 94, 26–39 (2018). https://doi.org/10.1016/j.kint.2017.12.027
9. Koh, E.S., Kim, G.-H., Chung, S.: Intrarenal Mechanisms of Sodium-Glucose Cotransporter-2 Inhibitors on Tubuloglomerular Feedback and Natriuresis. Endocrinol Metab. 38, 359–372 (2023). https://doi.org/10.3803/EnM.2023.1764
10. Sen, T., Heerspink, H.J.L.: A kidney perspective on the mechanism of action of sodium glucose co-transporter 2 inhibitors. Cell Metabolism. 33, 732–739 (2021). https://doi.org/10.1016/j.cmet.2021.02.016
11. Brown, E., Rajeev, S.P., Cuthbertson, D.J., Wilding, J.P.H.: A review of the mechanism of action, metabolic profile and haemodynamic effects of sodium-glucose co-transporter-2 inhibitors. Diabetes, Obesity and Metabolism. 21, 9–18 (2019). https://doi.org/10.1111/dom.13650
12. Salvatore, T., Galiero, R., Caturano, A., Rinaldi, L., Di Martino, A., Albanese, G., Di Salvo, J., Epifani, R., Marfella, R., Docimo, G., Lettieri, M., Sardu, C., Sasso, F.C.: An Overview of the Cardiorenal Protective Mechanisms of SGLT2 Inhibitors. International Journal of Molecular Sciences. 23, 3651 (2022). https://doi.org/10.3390/ijms23073651
13. Hesp, A.C., Schaub, J.A., Prasad, P.V., Vallon, V., Laverman, G.D., Bjornstad, P., van Raalte, D.H.: The role of renal hypoxia in the pathogenesis of diabetic kidney disease: a promising target for newer renoprotective agents

including SGLT2 inhibitors? Kidney International. 98, 579–589 (2020). https://doi.org/10.1016/j.kint.2020.02.041
14. Heerspink, H.J.L., Perkins, B.A., Fitchett, D.H., Husain, M., Cherney, D.Z.I.: Sodium Glucose Cotransporter 2 Inhibitors in the Treatment of Diabetes Mellitus. Circulation. 134, 752–772 (2016). https://doi.org/10.1161/CIRCULATIONAHA.116.021887
15. Takata, T., Isomoto, H.: Pleiotropic Effects of Sodium-Glucose Cotransporter-2 Inhibitors: Renoprotective Mechanisms beyond Glycemic Control. International Journal of Molecular Sciences. 22, 4374 (2021). https://doi.org/10.3390/ijms22094374
16. Heerspink, H.J.L., Kosiborod, M., Inzucchi, S.E., Cherney, D.Z.I.: Renoprotective effects of sodium-glucose cotransporter-2 inhibitors. Kidney International. 94, 26–39 (2018). https://doi.org/10.1016/j.kint.2017.12.027
17. Vasquez-Rios, G., Nadkarni, G.N.: SGLT2 Inhibitors: Emerging Roles in the Protection Against Cardiovascular and Kidney Disease Among Diabetic Patients. International Journal of Nephrology and Renovascular Disease. 13, 281–296 (2020). https://doi.org/10.2147/IJNRD.S268811
18. Mayer, G.J., Wanner, C., Weir, M.R., Inzucchi, S.E., Koitka-Weber, A., Hantel, S., von Eynatten, M., Zinman, B., Cherney, D.Z.I.: Analysis from the EMPA-REG OUTCOME® trial indicates empagliflozin may assist in preventing the progression of chronic kidney disease in patients with type 2 diabetes irrespective of medications that alter intrarenal hemodynamics. Kidney International. 96, 489–504 (2019). https://doi.org/10.1016/j.kint.2019.02.033
19. Empagliflozin and Cardio-renal Outcomes in Patients with Type 2 Diabetes and Cardiovascular Disease – Implications for Clinical Practice. 1. (2018)
20. Neuen, B.L., Ohkuma, T., Neal, B., Matthews, D.R., de Zeeuw, D., Mahaffey, K.W., Fulcher, G., Li, Q., Jardine, M., Oh, R., Heerspink, H.L., Perkovic, V.: Effect of Canagliflozin on Renal and Cardiovascular Outcomes across Different Levels of Albuminuria: Data from the CANVAS Program. Journal of the American Society of Nephrology. 30, 2229 (2019). https://doi.org/10.1681/ASN.2019010064
21. Mosenzon, O., Wiviott, S.D., Cahn, A., Rozenberg, A., Yanuv, I., Goodrich, E.L., Murphy, S.A., Heerspink, H.J.L., Zelniker, T.A., Dwyer, J.P., Bhatt, D.L., Leiter, L.A., McGuire, D.K., Wilding, J.P.H., Kato, E.T., Gause-Nilsson, I.A.M., Fredriksson, M., Johansson, P.A., Langkilde, A.M., Sabatine, M.S., Raz, I.: 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 & Endocrinology. 7, 606–617 (2019). https://doi.org/10.1016/S2213-8587(19)30180-9
22. de Boer, I.H., Khunti, K., Sadusky, T., Tuttle, K.R., Neumiller, J.J., Rhee, C.M., Rosas, S.E., Rossing, P., Bakris, G.: Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). Diabetes Care. 45, 3075–3090 (2022). https://doi.org/10.2337/dci22-0027
23. Jardine, M.J., Mahaffey, K.W., Neal, B., Agarwal, R., Bakris, G.L., Brenner, B.M., Bull, S., Cannon, C.P., Charytan, D.M., de Zeeuw, D., Edwards, R., Greene, T., Heerspink, H.J.L., Levin, A., Pollock, C., Wheeler, D.C., Xie, J., Zhang, H., Zinman, B., Desai, M., Perkovic, V., on behalf of the CREDENCE study investigators: The Canagliflozin and Renal Endpoints in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) Study Rationale, Design, and Baseline Characteristics. Am J Nephrol. 46, 462–472 (2017). https://doi.org/10.1159/000484633
24. Heerspink, H.J.L., Stefánsson, B.V., Correa-Rotter, R., Chertow, G.M., Greene, T., Hou, F.-F., Mann, J.F.E., McMurray, J.J.V., Lindberg, M., Rossing, P., Sjöström, C.D., Toto, R.D., Langkilde, A.-M., Wheeler, D.C., DAPA-CKD Trial Committees and Investigators: Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 383, 1436–1446 (2020). https://doi.org/10.1056/NEJMoa2024816
25. Nashar, K., Khalil, P.: Clinical Evaluation of Dapagliflozin in the Management of CKD: Focus on Patient Selection and Clinical Perspectives. IJNRD. 15, 289–308 (2022). https://doi.org/10.2147/IJNRD.S234282
26. The EMPA-KIDNEY Collaborative Group: Empagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 388, 117–127 (2023). https://doi.org/10.1056/NEJMoa2204233
27. Fernández-Fernandez, B., Sarafidis, P., Soler, M.J., Ortiz, A.: EMPA-KIDNEY: expanding the range of kidney protection by SGLT2 inhibitors. Clin Kidney J. 16, 1187–1198 (2023). https://doi.org/10.1093/ckj/sfad082
28. Levin, A., Perkovic, V., Wheeler, D.C., Hantel, S., George, J.T., von Eynatten, M., Koitka-Weber, A., Wanner, C., Investigators, on behalf of the E.-R.O.: Empagliflozin and Cardiovascular and Kidney Outcomes across KDIGO Risk Categories: Post Hoc: Analysis of a Randomized, Double-Blind, Placebo-Controlled, Multinational Trial. Clinical Journal of the American Society of Nephrology. 15, 1433 (2020). https://doi.org/10.2215/CJN.14901219
29. DeFronzo, R.A., Reeves, W.B., Awad, A.S.: Pathophysiology of diabetic kidney disease: impact of SGLT2 inhibitors. Nat Rev Nephrol. 17, 319–334 (2021). https://doi.org/10.1038/s41581-021-00393-8

30. Heerspink, H.J.L., Perkins, B.A., Fitchett, D.H., Husain, M., Cherney, D.Z.I.: Sodium Glucose Cotransporter 2 Inhibitors in the Treatment of Diabetes Mellitus. Circulation. 134, 752–772 (2016). https://doi.org/10.1161/CIRCULATIONAHA.116.021887
31. Heerspink, H.J.L., Perkins, B.A., Fitchett, D.H., Husain, M., Cherney, D.Z.I.: Sodium Glucose Cotransporter 2 Inhibitors in the Treatment of Diabetes Mellitus. Circulation. 134, 752–772 (2016). https://doi.org/10.1161/CIRCULATIONAHA.116.021887
32. Heerspink, H.J.L., Kosiborod, M., Inzucchi, S.E., Cherney, D.Z.I.: Renoprotective effects of sodium-glucose cotransporter-2 inhibitors. Kidney International. 94, 26–39 (2018). https://doi.org/10.1016/j.kint.2017.12.027
33. Vasquez-Rios, G., Nadkarni, G.N.: SGLT2 Inhibitors: Emerging Roles in the Protection Against Cardiovascular and Kidney Disease Among Diabetic Patients. International Journal of Nephrology and Renovascular Disease. 13, 281–296 (2020). https://doi.org/10.2147/IJNRD.S268811
34. Roddick, A.J., Wonnacott, A., Webb, D., Watt, A., Watson, M.A., Staplin, N., Riding, A., Lioudaki, E., Kuverji, A., Kossi, M.E., Holmes, P., Holloway, M., Fraser, D., Carvalho, C., Burton, J.O., Bhandari, S., Herrington, W.G., Frankel, A.H.: UK Kidney Association Clinical Practice Guideline: Sodium-Glucose Co-transporter-2 (SGLT-2) Inhibition in Adults with Kidney Disease 2023 UPDATE. BMC Nephrol. 24, 310 (2023). https://doi.org/10.1186/s12882-023-03339-3
35. Rossing, P., Caramori, M.L., Chan, J.C.N., Heerspink, H.J.L., Hurst, C., Khunti, K., Liew, A., Michos, E.D., Navaneethan, S.D., Olowu, W.A., Sadusky, T., Tandon, N., Tuttle, K.R., Wanner, C., Wilkens, K.G., Zoungas, S., De Boer, I.H.: KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney International. 102, S1–S127 (2022). https://doi.org/10.1016/j.kint.2022.06.008
36. Dapagliflozin and empagliflozin for treating chronic kidney disease: a multiple prescribing statement.
37. Dapagliflozin for treating chronic kidney disease. National Institute for Health and Care Excellence (NICE), London (2025)
38. Rivara, M.B., Mehrotra, R.: Timing of Dialysis Initiation - What Has Changed Since IDEAL? Semin Nephrol. 37, 181–193 (2017). https://doi.org/10.1016/j.semnephrol.2016.12.008
39. Tye, S.C., Provenzano, M., Heerspink, H.J.L.: Biomarkers and Precision Medicine in Diabetes. In: Textbook of Diabetes. pp. 414–428. John Wiley & Sons, Ltd (2024)
40. Nguyen, B.-N., Nguyen, L., Mital, S., Bugden, S., Nguyen, H.V.: Comparative efficacy of sodium-glucose co-transporter-2 inhibitors, glucagon-like peptide-1 receptor agonists and non-steroidal mineralocorticoid receptor antagonists in chronic kidney disease and type 2 diabetes: A systematic review and network meta-analysis. Diabetes, Obesity and Metabolism. 25, 1614–1623 (2023). https://doi.org/10.1111/dom.15009
41. Nguyen, B.N.: Comparative efficacy and cost-effectiveness of sodium-glucose co-transporter 2 inhibitors, glucagon-like peptide 1 receptor agonists, and nonsteroidal mineralocorticoid receptor antagonists in type 2 diabetes and chronic kidney disease, https://hdl.handle.net/20.500.14783/14361, (2023)

CITE AS: Nambi Namusisi H. (2026). SGLT2 Inhibitors for Diabetic Kidney Disease Prevention: Mechanisms, Clinical Evidence, and Guidelines. Research Output Journal of Engineering and Scientific Research 5(1): 29-35. https://doi.org/10.59298/ROJESR/2026/5.12935