Unlocking the potential: boosting SGLT2 inhibitor uptake to prevent the cardiorenal consequences of chronic kidney disease

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Chronic kidney disease (CKD) is projected to become the fifth leading cause of death worldwide by 2030.[1] Considering its severe health consequences, including renal and cardiovascular complications, it is imperative to adopt measures that mitigate these risks from both clinical and public health perspectives. The advent of SGLT2 inhibitors marks a significant advancement in therapeutic options to prevent the cardiorenal consequences of CKD. With robust evidence supporting their efficacy, the time is now to intensify implementation efforts to ensure that these life-saving drugs reach the patients who need them the most.

As a therapeutic class, the SGLT2 inhibitors have consistently demonstrated renal and cardiovascular protective effects. Meta-analyses of randomized clinical trials involving patients with CKD have shown significant reductions in the risks of kidney disease progression, end-stage kidney disease, acute kidney injury, heart failure hospitalizations, and cardiovascular mortality.[2] These protective effects have been observed across the CKD spectrum and are evident irrespective of the presence of diabetes. However, despite the compelling evidence of cardiorenal protection, data on the potential impact of these medications in the broader population are still relatively scarce.

In *The Lancet Regional Health—Western Pacific*,[3] Neuen and colleagues report on a comprehensive cross-sectional analysis conducted using MedicineInsight, a nationally representative individual-level dataset encompassing 392 primary care practices across Australia. The study aimed to quantify the absolute number of cardio-renal and kidney failure events potentially preventable through optimal SGLT2 inhibitor usage– defined in their study as 75% uptake among the Australian adult population.

The authors utilized the MedicineInsight dataset to identify patients with an eGFR < 60 ml/min/1.73 m^2 and/or a urinary albumin to creatinine ratio of >3.4 mg/mmol. These individuals were then matched to the inclusion criteria from three pivotal SGLT2 inhibitor trials in CKD: CREDENCE, DAPA-CKD, and EMPA-KIDNEY. Subsequently, they extrapolated the age- and sex-stratified CKD prevalence (using different eGFR and UACR definitions) to the Australian population using national census data. This allowed them to estimate the number of cardio-renal and kidney failure events potentially preventable across Australia, drawing on effectiveness data from these clinical trials.

Overall, during 2020–2021, 147,119 (12.1%) adults in MedicineInsight were found to have an eGFR < 60 and/or an UACR > 3.5 mg/mmol. Nearly half of these individuals (44%) met the inclusion criteria for EMPA-KIDNEY, 17% for DAPA-CKD, and 7% for CREDENCE.[4–6] Compared to these clinical trials, the MedicineInsight population was older, had a higher eGFR, and were less likely to have established cardiovascular disease. Notably, renin angiotensin system (RAS) blockade usage was substantially lower compared to the clinical trials where virtually all participants were randomized to SGLT2 on a background of RAS inhibition. Baseline use of SGLT2 inhibitors was very low ranging from 4.1% among EMPA-KIDNEY eligible patients to 14.4% in CREDENCE eligible patients.

Using strict criteria for CKD (eGFR < 60 ml/min/1.73 m^2 and/or UACR > 3.4 mgl/L on at least 2 occasions, 90 days apart), the study yielded numbers needed to treat (NNT) to prevent one cardio-renal event ranging from 14 to 25, and 15 to 27 to avert a kidney failure event over three years. These estimates translated into more than 3500 cardio-renal events and more than 1000 kidney failure events that could be potentially prevented annually with the optimal implementation of this therapy. These findings remained robust across various CKD definitions, thresholds for "optimal SGLT2 inhibitor use," and the presence or absence of diabetes.

This study provides a valuable glimpse into the tangible clinical impact that SGLT2 inhibitors could have in a real-world setting. It underscores three key points: a significant portion of primary care patients could benefit from SGLT2 inhibitors; the current uptake in eligible patients is disappointingly low, with only 15% of very high-risk CKD patients (eligible for CREDENCE) on this treatment; and, the optimal implementations of SGLT2 inhibitors could yield significant clinical and public health benefits, far outweighing their potential adverse effects.

This study's primary limitation is its reliance on projected rather than directly observed effects of SGLT2

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inhibitors, extrapolated from clinical trial data. Discrepancies often exist between the demographic and clinical characteristics of clinical trial participants and the broader population. Additionally, medication adherence in the real world may not reach the levels observed in clinical trials, potentially reducing the expected population-level benefits. Therefore, future studies should measure real-world adherence, side effects, and discontinuation rates of SGLT2 inhibitors to more accurately assess their impact in the general population.

Despite the compelling evidence of their benefits for individuals and society, the uptake of SGLT2 inhibitors remains strikingly low. Structural barriers to CKD care, such as inadequate testing for albuminuria and a treatment paradox where those with more severe albuminuria—and consequently higher cardiorenal risk—are less likely to receive preventive treatments,[7,8] are exacerbated by SGLT2-specific challenges. These include high costs, racial and ethnic disparities in prescriptions, and lack of comprehensive knowledge about their indications, benefits, and potential side effects.[9,10]

To address these barriers, coordinate multidisciplinary implementation efforts are critically needed. The substantial clinical and public health advantages that can be realized through proper implementation of SGLT2 inhibitors warrant immediate and concerted action.

Declaration of interests

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