

Stemming the tide of chronic kidney disease: A focus on primary care prevention

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The prevalence of chronic kidney disease (CKD) among Singapore residents aged 18 to 74 years rose significantly from 8.8% in 2019–2020 to 13.8% in 2021–2022.^{1,2} Singapore ranks third globally for treated end-stage kidney disease (ESKD), with a median survival of 6 years post-dialysis.³ Diabetic nephropathy was the leading cause of stage 5 CKD, accounting for 64.6% of new dialysis patients in 2022.⁴ This is particularly concerning given Singapore's rapidly ageing population and rising lifestyle-related CKD risk factors. Notably, CKD prevalence is higher among those with pre-diabetes (21.8%), diabetes mellitus (DM) (42.3%) and hypertension (24.2%) compared to those without diabetes (10%).

Primary care plays a crucial role in CKD prevention, screening and diagnosis, particularly in managing risk factors such as DM and hypertension. Since 2017, the Holistic Approach in Lowering and Tracking Chronic Kidney Disease (HALT-CKD) programme has tracked polyclinic patients across all 3 public healthcare clusters with CKD stages G1–G3A to control risk factors and delay CKD progression.

In this issue of the *Annals*, Koh et al. present a retrospective cohort study evaluating the 5-year outcomes of 3800 CKD G1–G3A patients enrolled in the HALT-CKD programme across 5 polyclinics within 1 of the 3 healthcare clusters.⁵ Interventions included counselling and lifestyle modification, initiation and optimisation of angiotensin-converting enzyme inhibitors (ACEi)/angiotensin II receptor blockers (ARB), sodium-glucose cotransporter-2 inhibitors (SGLT2i) initiation, and optimisation of DM and hypertension control. The prevalence of DM and hypertension among the patients was 92.9% (median HbA1c 7.4%) and 92.4% (median blood pressure [BP] 132/73) respectively, reflecting relatively well-controlled conditions.

The study highlights the importance of addressing reasons behind ACEi/ARB discontinuation in CKD patients. Patients on the maximum dose of

ACEi/ARB rose from 35.7% to 49.2%, while those not on ACEi/ARB increased from 7.5% to 10.1%. Patients who had their ACEi/ARB dose reduced or stopped had an increased risk of progression to CKD stages G3B–G5 compared to those who maintained their doses (hazard ratio [HR] 1.92, 95% confidence interval [CI] 1.50–2.45). While the observational design of this study cannot establish causality, their findings are consistent with the robust evidence from randomised controlled trials (RCTs) and meta-analyses, and established clinical guidelines advocating for renin-angiotensin system blockade in CKD management.^{6,7} Notably, the study mentioned that ACEi/ARB cessations commonly occurred following hospital discharge for acute kidney injury, but the reasons were neither documented nor adjusted for in the study. Other common reasons for ACEi/ARB discontinuation encountered in clinical practice include hyperkalaemia and hypotensive events. Hyperkalaemia may be mitigated by reviewing concurrent drugs, moderating dietary potassium intake and considering the addition of diuretics, sodium bicarbonate and potassium binders. Resonium is available in public primary care clinics, but not lokelma, which is more palatable. Enhancing their availability and affordability in primary care, along with increasing physicians' confidence in their use, could help overcome barriers to continued ACEi/ARB use. Hypotension could be managed by switching to ARBs with weaker anti-hypertensive effects, such as losartan. Further research could investigate reasons for ACEi/ARB discontinuation, explore re-initiation, examine the duration of maximal-dose ACEi/ARB use and assess their impact on renal outcomes.

Increasing ACEi/ARB dosage did not significantly delay progression to CKD G3B–G5 (HR 1.01, 95% CI 0.77–1.32), contrasting with evidence and guidelines that support maximal tolerated doses.⁶ Baseline data show 35.7% of patients were already on maximal doses of ACEi/ARB, and a proportion

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not on maximal doses may have been on optimal or maximally-tolerated doses. Subgroup analyses restricted to patients not already on maximally-tolerated doses may provide further insights.

The study found that SGLT2i, prescribed to 39.6% of patients, did not significantly delay progression to CKD stages G3B–G5. This contrasts sharply with multiple RCTs (EMPA-REG OUTCOME, CANVAS Program, CREDENCE and DECLARE-TIMI 58) as well as a meta-analysis which demonstrated substantial risk reduction for ESKD as well as dialysis, transplantation or death due to kidney disease.⁸ Additionally, Koh et al.'s finding is inconsistent with Liu et al.'s local real-world study, which showed that SGLT2i reduced the risk of CKD progression and ESKD.⁹ Given the robust evidence from renal outcome trials, the utilisation of SGLT2i has been incorporated as a key performance indicator for the HALT-CKD programme, with empagliflozin included in the Ministry of Health's standard medication list since November 2023. Since Koh et al.'s study predates these changes, the lack of observed benefit may reflect delayed SGLT2i initiation for patients with poorer HbA1c control, more significant albuminuria or later CKD stages. Additionally, the relatively shorter exposure of SGLT2i use towards the end of a 5-year follow-up may have limited the detection of its long-term benefits. The findings underscore that an "absence of evidence is not evidence of absence."

Other medications, such as mineralocorticoid receptor antagonists (MRAs) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs), could further reduce albuminuria and delay CKD progression if included in HALT-CKD. Spironolactone is available in public primary care clinics, but not finerenone, a non-steroidal MRA with fewer side effects. GLP-1 RAs have shown significant benefits in HbA1c control, weight management and cardiovascular risk reduction. Incorporating these medications into primary care practice would enhance the armamentarium for slowing CKD progression.

Albuminuria improvements were noted, with an increase in patients with albuminuria stage A1 from baseline ($P<0.001$). Although there were statistically significant improvements in HbA1c (from 7.4% to 7.3%), systolic BP (from 132 to 130 mmHg) and diastolic BP (73 to 70 mmHg), these changes were less clinically significant. Overall, 12.6% of patients progressed to advanced CKD (stages 3B and above). Comparable figures for CKD progression using similar definitions are not available, but pre-HALT-CKD analyses may enable comparisons. Additionally, subgroup analyses might reveal differing progression rates, particularly between

CKD G1 and CKD G3A. HALT-CKD is a nationwide programme, while this study focused on patients from 5 polyclinics within 1 cluster. Future studies across other public healthcare clusters could provide comparative data. While major interventions, such as ACEi/ARB therapy, are consistent across clusters, differences in counselling approaches and care models can affect the programme outcomes. Some study variables might reach statistical significance with a larger study population.

Despite 92.9% of patients receiving CKD counselling and lifestyle modification advice, progression to advanced CKD stages was not delayed. It is unclear if this is due to the high percentage receiving counselling, resulting in insufficient variation to detect a difference, or the nature of the counselling, typically limited to 1 or 2 sessions. Effective patient education programmes should be tailored to their specific needs, should enhance CKD knowledge, teach strategies to prevent CKD progression, empower self-management and focus on improving health literacy.¹⁰ Ho et al. found limited health literacy and male gender correlated with poorer self-care in CKD among Singaporean patients.¹¹ Hwang et al. identified limited CKD awareness and ineffective patient-physician communication in a qualitative study exploring perceived barriers and facilitators to CKD care among patients in Singapore.¹² A suggested solution is the use of "health coaches" who can spend more time to provide education and support behaviour change. Another qualitative study exploring healthcare professionals' perspectives highlighted knowledge and practice gaps, systemic constraints for nephrology referrals, short consultation times, suboptimal care coordination, and patients' lack of CKD awareness and self-management skills as barriers.¹³ CKD training for primary care physicians, structured CKD care protocols, multidisciplinary team-based care and prioritising nephrology referrals based on risk assessment were identified as key facilitators.

Koh et al.'s study is one of the first to assess the real-world effectiveness of the HALT-CKD programme. While findings, such as the importance of maintaining ACEi/ARB therapy, align with existing literature, the limited impact of SGLT2i and counselling and lifestyle modifications highlights areas for primary care improvement to better align clinical outcomes with the promising results observed in controlled trials.

Healthier SG will further strengthen existing preventive care efforts through healthy lifestyle promotion, increased screening and improved management of chronic conditions, including DM, hypertension and CKD. Starting in January 2025, the HSG CKD Care Protocol will further empower

primary care in managing CKD stages G1–G3A.¹⁴ This protocol recommends (1) patient education, (2) optimising management of risk factors and comorbidities, (3) initiating workup for complications and (4) initiating and titrating ACEi/ARB to maximally tolerated dose in CKD patients with DM or albuminuria, as well as initiating SGLT2i for persistent albuminuria. Aligned with Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, this protocol bridges critical knowledge and implementation gaps, enabling primary care to play a central role in delivering comprehensive CKD management to stem the tide of CKD.

Declaration

The authors declare there are no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript.

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