The New Cardiovascular-Kidney-Metabolic (CKM) Syndrome: An Opportunity for CKD Detection and Treatment in Primary Care

Sara-Megumi Rumrill and Michael G. Shlipak

In October of 2023, the American Heart Association (AHA) published a scientific statement and advisory that defined a novel entity, cardiovascular-kidney-metabolic (CKM) syndrome.[1,2] The overall framework proposes that a substantial proportion of cardiovascular disease (CVD) burden is attributable to a syndrome that extends in stages from obesity (stage 1) to metabolic/kidney risk factors for CVD (diabetes mellitus, chronic kidney disease [CKD], hypertension, and dyslipidemia) (stage 2), subclinical CVD (state 3), and finally clinical CVD (stage 4). The report that describes the CKM paradigm documents the scientific justification for a syndrome; highlights the overlap in risk factors among individuals with obesity, diabetes, CKD, and CVD; and aligns the evidence and guideline statements that address screening, prevention, and management of these conditions. The CKM syndrome paradigm is an aspirational framework that pulls from a wide body of literature and disease-specific guidelines with an overall, shared goal of reducing CVD at a population level. But for clinicians at the front lines of CVD prevention, those of us in primary care, will the new syndrome enhance or complicate our practice?

Primary care providers (PCPs) are already buried under myriad recommendations and mandates. One reason for the epidemic of burnout in primary care is that clinicians have such a broad scope of responsibility and numerous metrics to grade our performance; these range from preventive care with vaccinations and cancer screening to chronic disease management across many organ systems.[3,4] And, regardless of our anticipated agenda of guideline-driven tasks for a specific patient visit, we are often shifted toward other priorities, such as pain control, mental health, or social support needs. In this context of a very full plate, any new syndrome or recommendation may feel like a hardship for PCPs. So, while PCPs may have initial curiosity for the CKM concept, we might also dread the consequences of the additional tasks assigned to us from any new "syndrome."

Why did AHA choose to propose and promote CKM syndrome now? Given AHA's prioritization of CVD prevention, the likely impetus for proposing CKM syndrome is the introduction of 2 new medication classes that have overlapping indications to prevent and treat diabetes, CKD, and heart disease. Along with renin-angiotensin-aldosterone system (RAAS) inhibitors, sodium/glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists have indications for at least 2 of the CKM conditions. Without a holistic CVD preventive framework, the various indications for these medications could seem confusing or even competing with one another, and the responsibility to prescribe them might be lost between PCPs and specialists.

From a primary care perspective, CKM syndrome has potential appeal. Generalists are trained to emphasize lifestyle first, and when prescribing medications, we naturally seek synergistic treatment benefits because we often negotiate with patients regarding their concerns about pill burden. Similarly, relative to managing specific recommendations for each of these disease conditions, a succinct syndrome that aligns recommendations and treatments has the potential to be *less* overwhelming. The CKM syndrome framework also has the potential to be patient centered and to make treatments easier for patients to understand. We have all experienced the challenge of motivating patients to take medications for asymptomatic conditions like hypertension and CKD, whereas CVD risk reduction is a familiar strategy for patients that could avoid focusing on individual diseases, like "stage 3 CKD."

CKM syndrome management could elevate estimated glomerular filtration rate (eGFR) and urinary albumin-creatinine ratio (UACR) testing and CKD diagnosis in primary care. The majority of primary and secondary prevention of CVD is embedded within primary care.[5] Most PCPs accept this responsibility and take ownership of managing obesity, diabetes, hypertension, and dyslipidemia, which comprise the CKM-related conditions aside from CKD. Unfortunately, CKD screening and treatment are not routine in primary care, and early CKD management has been relatively ignored. Recent KDIGO (Kidney Disease: Improving Global Outcomes) 2024 guidelines strongly endorse CKD case finding through routine eGFR and UACR testing in persons with diabetes, hypertension, or CVD, although current testing patterns are woefully inadequate even among persons with diabetes.[5,6] The CKM report adopts the KDIGO recommendations and advocates for routine testing of both eGFR and UACR for persons with obesity or any of the CKM conditions. If adopted as part of a CVD prevention paradigm, the CKM guidance could lead to tremendous advances in CKD detection.

"*What is the point in detecting early-stage CKD, when it doesn't change management?*" This oft-repeated question has been a barrier to efforts to improve CKD detection and diagnosis for decades. For many years, the best answer has been "*CVD risk reduction.*" The vast majority of patients with CKD are early stage and most will never meet criteria for nephrology referral. Yet, the potential benefits of

implementing CVD prevention strategies for patients at all stages of CKD could be enormous. One approach to closing the current treatment gap for those with diagnosed CKD would be to implement a CKD-focused intervention, but this would compete for attention and resources with many other primary care priorities. In contrast, implementing the CKM framework could accomplish appropriate CKD diagnosis and treatment in primary care without a specific CKD focus. Therefore, the CKM syndrome concept might be a great opportunity to accomplish CKD guideline–concordant treatment recommendations in the primary care setting.

Implementing the CKM paradigm in primary care would require substantial intervention and investment, and nephrologist engagement would be critically important. The CKM concepts might seem utopian and unrealistic in our current system, where health care is siloed and PCPs already cannot keep up with existing recommendations. For a multidisciplinary framework like CKM syndrome to succeed, it must be embraced and coordinated within primary care. But there would be minimal enthusiasm within primary care without substantial engagement from relevant specialists, including nephrology, endocrinology, and cardiology. Specialists in other fields have successfully partnered with primary care on topics including screening and surveillance for lung cancer[7] and preventive health related to cirrhosis.[8]

This is a tremendous opportunity for nephrologists to influence CKD prevention and early-stage treatment for large numbers of patients that they otherwise might never encounter. At a health systems level, nephrologists could serve as champions for the CKD detection and treatment strategies that would be implemented in primary care. Nephrologists could also advocate for removing prescribing barriers for PCPs, so they can easily order medications recommended within the CKM algorithm in health care plans that have restrictions. At the individual patient care level, nephrologists might find that CKM syndrome implementation leads to increased e-consults and other referrals; in these consultations, PCPs would appreciate having nephrologists initiate prescriptions and provide rationales that educate their PCP colleagues.

The new PREVENT (Predicting Risk of Cardiovascular Disease Events) CVD risk equation could be the first tool toward implementing the CKM syndrome paradigm and advancing CKD detection. AHA recently presented this updated and improved heart disease risk equation, which should replace the prior ASCVD Risk Calculator.[9] The PREVENT calculator catalyzes focus on CKM syndrome, as it has added measures of obesity (body mass index), prediabetes (hemoglobin A1c in addition to diagnosed diabetes mellitus), and kidney health testing with eGFR and UACR inputs (Fig 1). When PCPs adopt PREVENT as the primary tool for CVD risk assessment, we are beginning the CKM assessment, which can be used for subsequent treatment algorithms.

Major interventions will be required to translate testing and diagnosis of CKD into guideline-recommended treatments. There are 2 major categories of interventions that could facilitate evidence-based management: decision support and panel management. Decision support includes algorithm-informed, technology-driven recommendations and facilitators, which are embedded within the electronic health record. These automated implementation strategies often fail because PCPs lack the time and energy to address the recommended actions and the automated reminders may not seamlessly integrate into the clinical workflow.[10] Decision support tools can be enhanced when they are implemented by allied care providers embedded within primary care, who serve as "one-focus" providers dedicated to implementing a specific set of actions. A successful example of this within the US Department of Veterans Affairs (VA) health care system are the clinical pharmacy specialists based within the primary care practice who currently assist in managing diabetes, hypertension, and dyslipidemia. The same or similar providers in other health systems could facilitate implementation of CKM recommendations without much additional training or changes in scope of practice.

The second implementation strategy, panel management, is conducted by identifying patients within a primary care practice who have unmet diagnostic or treatment needs. A team then works systematically to close the gaps in care.[11] Panel management occurs proactively and typically outside of scheduled provider visits and would be a critical way that health systems optimize the care of a population of patients in CKM care.[12] PCPs need dedicated time and system collaboration to be effective at this work, but they are ideal providers for these tasks given their knowledge of the specific patients and potential barriers that may not be gleaned by chart review alone. There are also opportunities for other trained clinicians, including specialists, to conduct panel management in collaboration with a primary care team if resources are available. This helps a health system as a whole to "own" panel management related to CKM treatment while directly supporting primary care.

With either strategy, performance metrics are required to monitor the progress and motivate behavioral change in CKM implementation. For CKM-related conditions, current metrics encompass testing (eg, eGFR and UACR), achieved physiological targets (eg, hemoglobin A1c <9%, blood pressure <140/90), and prescribed medications (statins for secondary CVD prevention). To optimize care and implement CKM, we need more sophisticated metrics that measure treatment expectations, such as adding SGLT2 inhibitors for patients on RAAS inhibitors who have UACR >300 mg/g. We think the ultimate power of the CKM framework would be to unify the diagnosis and treatment of CKD, along with management of hypertension, diabetes, and dyslipidemia, and to facilitate panel management for guideline-directed care. Successful implementation would certainly lead to reductions of CVD events.

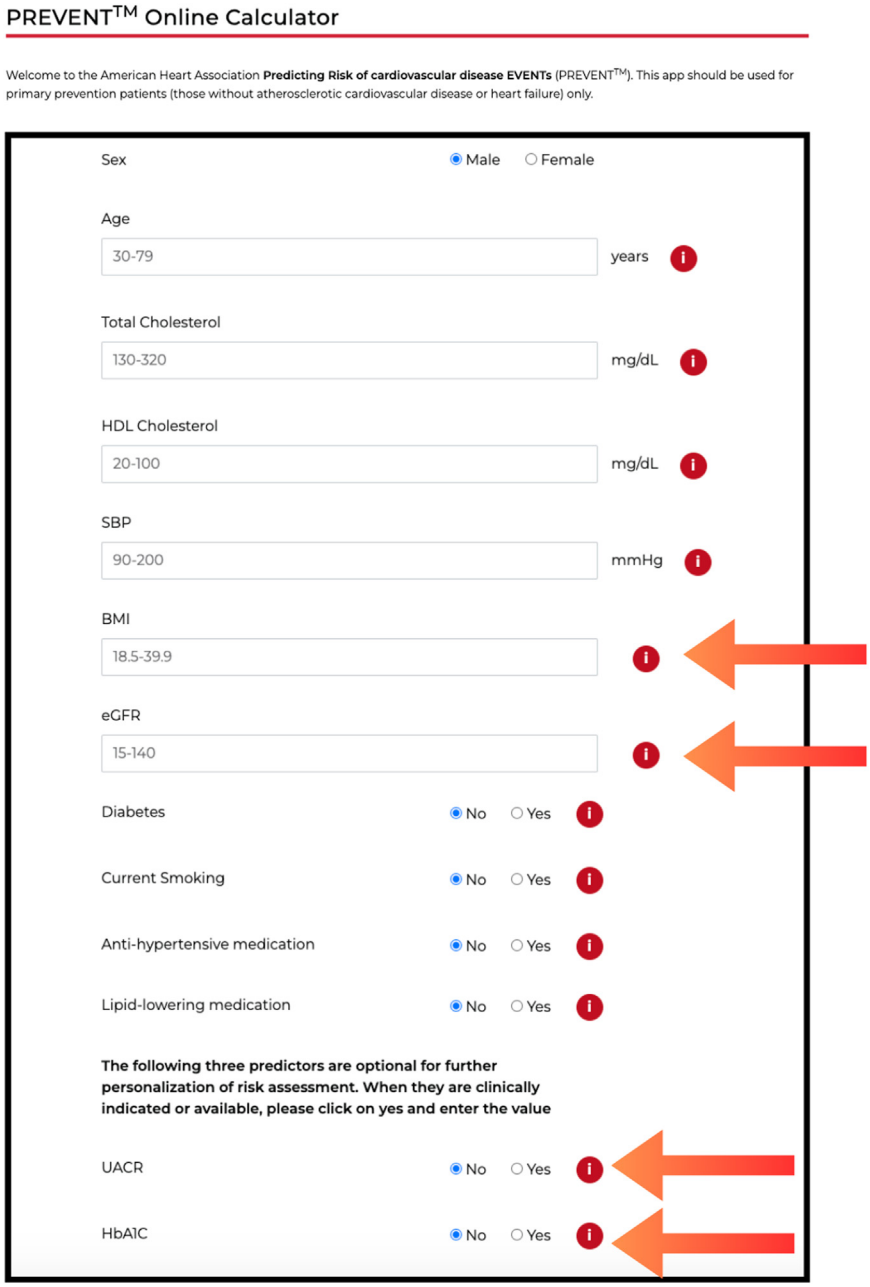

Figure 1. Cardiovascular disease (CVD) risk in persons with chronic kidney disease (CKD). A screenshot from the online PREVENT risk calculator (https://professional.heart.org/en/guidelines-and-statements/prevent-calculator) that adds estimated glomerular filtration rate (eGFR) and urinary albumin-creatinine ratio (UACR) to CVD risk calculations. The arrows indicate the new inputs to CVD risk prevention that are specifically relevant to cardiovascular-kidney-metabolic syndrome screening and CKD detection.

The CKM syndrome paradigm proposes CKD detection and monitoring as a core component of CVD prevention, and a potential catalyst would be the recently developed PREVENT CVD equation, which includes CKD testing. This novel framework has great potential to elevate CKD detection and treatment within primary care, but only if the broad recommendations are implemented with multidisciplinary engagement and proven strategies such as decision support and panel management. As PCP leaders who struggle to encourage practice change to our already overburdened colleagues, we urge nephrologists to partner in the development of CKM education, quality improvement, and care coordination strategies. Under the banner of CVD prevention, the CKM framework is a welcome advance toward reducing the burden of CKD.

Article Information

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References

1. Ndumele CE, Neeland IJ, Tuttle KR, et al; American Heart Association. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic (CKM) syndrome: a scientific statement from the American Heart Association. *Circulation*. 2023;148(20):1636-1664. doi:10.1161/CIR.0000000000001186
2. Khan SS, Coresh J, Pencina MJ, et al; American Heart Association. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. *Circulation*. 2023;148(24):1982-2004. doi:10.1161/CIR.0000000000001191
3. Dillon EC, Tai-Seale M, Meehan A, et al. Frontline perspectives on physician burnout and strategies to improve well-being: interviews with physicians and health system leaders. *J Gen Intern Med*. 2020;35(1):261-267. doi:10.1007/s11606-019-05381-0
4. Privett N, Guerrier S. Estimation of the time needed to deliver the 2020 USPSTF Preventive Care Recommendations in Primary Care. *Am J Public Health*. 2021;111(1):145-149. doi:10.2105/AJPH.2020.305967
5. Kidney Disease: Improving Global Outcomes CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int*. 2024;105(4S):S117-S314. doi:10.1016/j.kint.2023.10.018
6. Chu CD, Xia F, Du Y, et al. Estimated prevalence and testing for albuminuria in US adults at risk for chronic kidney disease. *JAMA Netw Open*. 2023;6(7):e2326230. doi:10.1001/jamanetworkopen.2023.26230
7. Wiener RS, Gould MK, Arenberg DA, et al; ATS/CHEST Committee on Low-Dose CT Lung Cancer Screening in Clinical Practice. An official American Thoracic Society/American College of Chest Physicians policy statement: implementation of low-dose computed tomography lung cancer screening programs in clinical practice. *Am J Respir Crit Care Med*. 2015;192(7):881-891. doi:10.1164/rccm.201508-1671ST
8. El-Gohary M, Moore M, Roderick P, et al. Local care and treatment of liver disease (LOCATE) - a cluster-randomized feasibility study to discover, assess and manage early liver disease in primary care. *PLoS One*. 2018;13(12):e0208798. doi:10.1371/journal.pone.0208798
9. Khan SS, Matsushita K, Sang Y, et al; Chronic Kidney Disease Prognosis Consortium, American Heart Association Cardiovascular-Kidney-Metabolic Science Advisory Group. Development and validation of the American Heart Association's PREVENT equations. *Circulation*. 2024;149(6):430-449. doi:10.1161/CIRCULATIONAHA.123.067626
10. Ge J, Fontil V, Ackerman S, Pletcher MJ, Lai JC. Clinical decision support and electronic interventions to improve care quality in chronic liver diseases and cirrhosis. *Hepatology*. 2023. doi:10.1097/HEP.0000000000000583. Epub ahead of print.
11. Dulay M, Bowen JL, Weppner WG, et al. Interprofessional population health advocacy: developing and implementing a panel management curriculum in five Veterans Administration primary care practices. *J Interprof Care*. 2023;37(sup1):S75-S85. doi:10.1080/13561820.2018.1469476
12. Kaminetzky CP, Nelson KM. In the office and in-between: the role of panel management in primary care. *J Gen Intern Med*. 2015;30(7):876-877. doi:10.1007/s11606-015-3310-x