Advancing American Kidney Health and the Role of Sodium-Glucose Cotransporter-2 Inhibitors

A Missed Opportunity

Jiahua Li,[1] *Sri Lekha Tummalapalli*,[2] *and Mallika L. Mendu*[1,3]

CJASN 16: 1584–1586, 2021. doi: https://doi.org/10.2215/CJN.05450421

[1]Division of Renal Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts
[2]Division of Healthcare Delivery Science and Innovation, Department of Population Health Sciences, Weill Cornell Medicine, New York, New York
[3]Center for Population Health, Mass General Brigham, Boston, Massachusetts

Correspondence:
Dr. Jiahua Li, 4 Blackfan Circle 550, Boston, MA 02115. Email: jli54@bwh.harvard.edu

On July 10, 2019, the Trump administration signed an Executive Order titled the "Advancing American Kidney Health" (AAKH) Initiative, which primarily aims to reduce the incidence of kidney failure by 25% by 2030 and shift kidney care from treating kidney failure to maximizing kidney health (1). AAKH includes optional Kidney Care First and Comprehensive Kidney Care Contracting payment models that incentivize nephrologists to delay CKD progression to kidney failure in patients with an eGFR<30 ml/min per 1.73 m^2. With the recent advancement in new therapies, such as sodium-glucose cotransporter-2 inhibitors (SGLT2is), that slow CKD progression beyond traditional angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use, there is a novel opportunity to stem CKD progression and maximize kidney health significantly. AAKH encourages the "adoption of evidence-based interventions to delay or stop progression to kidney failure" (1). For the AAKH initiative to achieve its goals and maximize the benefit for patients, payors, and providers, there should be an investment in and incentivization of the most evidence-based risk reduction therapies, which result in the best clinical outcomes for the patients (avoiding kidney failure) and the payors (mitigating dialysis and lowering health care cost). In this perspective, we outline why the AAKH optional models should include patients with an eGFR of 30–59 ml/min per 1.73 m^2 and severely increased albuminuria (urinary albumin-creatinine ratio [UACR] >300 mg/g; CKD G3A3) and detail how systemic implementation of SGLT2i therapy in this subgroup can substantially increase health care value. We offer recommendations regarding actionable policy changes.

In 2020, the United States Renal Data System estimated that 37 million people in the United States and 24.6 million Medicare fee-for-service beneficiaries have CKD (2). The prevalence of CKD stratified by eGFR and albuminuria in the Medicare fee-for-service beneficiaries is estimated in Figure 1 using the 2009–2018 National Health and Nutrition Examination Survey (3). The prevalence of CKD G3A3 is approximately two times that of CKD G4A1 among Medicare-aged patients; as a result, patients with CKD G3A3 account for more cases of incident kidney failure than those with CKD G4A1 (Figure 1) (2,4). In addition, patients with CKD G3A3 have similar, if not higher, relative risks of CKD progression, AKI, and all-cause mortality compared with patients with CKD stage 4 without albuminuria (CKD G4A1) (4). The AAKH optional models focus on patients with advanced CKD, which misses the opportunity to fully address patients who have intervenable CKD progression. Early identification and treatment of patients with CKD G3A3 are of utmost importance in preventing kidney failure.

The dedicated kidney outcome trials CREDENCE and DAPA-CKD showed that SGLT2is are safe and efficacious in preventing kidney failure, lowering risk by approximately 30%–40% in patients with eGFR≥25 ml/min per 1.73 m^2 and with UACR≥200 mg/g. Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend initiating an SGLT2i when the eGFR is >30 ml/min per 1.73 m^2, and SGLT2i can be continued for kidney protection when the eGFR drops below 30 ml/min per 1.73 m^2 (5). KDIGO does not recommend using SGLT2i in patients with eGFR below 30 ml/min per 1.73 m^2, meaning that patients currently eligible for the AAKH optional models are not recommended for SGLT2i. Although ongoing clinical trials are testing the efficacy and safety of SGLT2is in advanced CKD, there is a clear opportunity to incentivize SGLT2i use in patients with CKD G3A3, among whom the number needed to treat to prevent one kidney failure in 2.6 years is 27 according to the CREDENCE trial (6). If the 294,850 Medicare fee-for-service beneficiaries with CKD G3A3 were treated with an SGLT2i for 2.6 years, 10,920 cases (294,850/27) of kidney failure could be prevented. Recent cost-effectiveness analyses estimate that SGLT2i is cost saving by preventing kidney failure as well as cardiovascular events, and the incidence and related costs of adverse events are minimal, further establishing the lifetime benefits and value of SGLT2is (7).

The clinical benefit demonstrated in clinical trials will not translate to improved clinical outcomes and value creation in the real-world setting without successful and practical implementation in the appropriate population. Given demonstrated gaps in routine proteinuria measurement (2), one major barrier is the

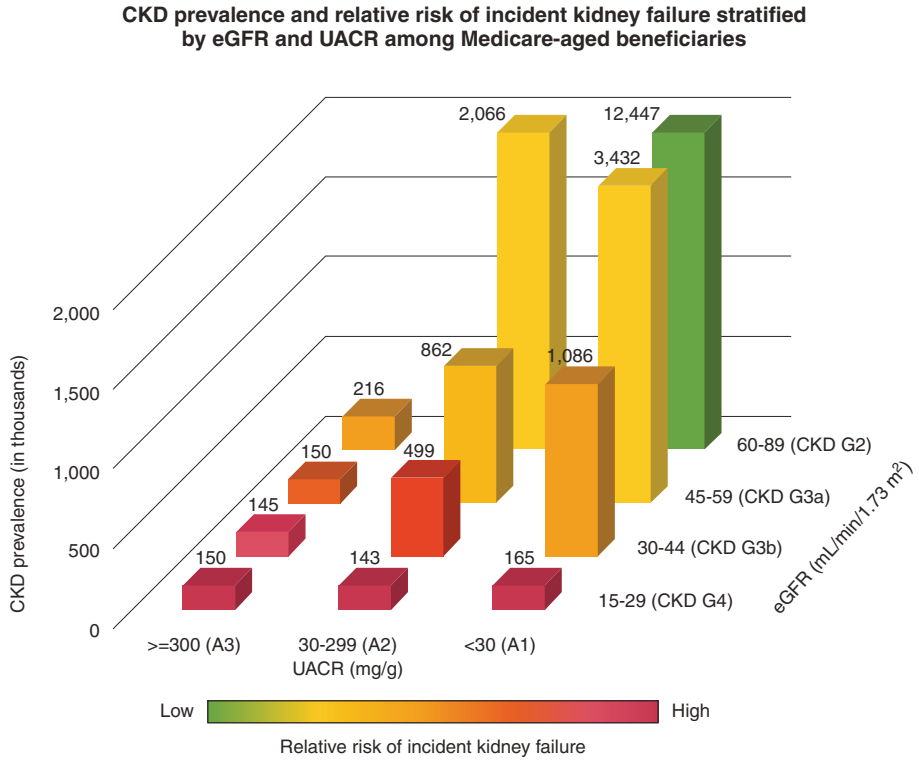

Figure 1. | **CKD prevalence and relative risk of incident kidney failure stratified by eGFR and UACR among Medicare-aged beneficiaries.** The reference group for relative risks of kidney failure is eGFR≥60 ml/min per 1.73 m^2 and urine albumin-creatinine ratio (UACR) <30 mg/g (green). CKD stage 5 was omitted due to small numbers. The relative risks of incident kidney failure are reproduced from Levey *et al.* (4) from pooled meta-analyses of general population cohorts (3). G, eGFR category.

identification of high-risk patients and widespread implementation of SGLT2i therapy. A population health approach like CardioCompass, a remote, algorithm-driven disease management system leveraging care navigators and clinical pharmacists supported by specialists for BP and lipid management (8), is suitable for implementing SGLT2i across large health care systems, yet it requires upfront investment in infrastructure and multidisciplinary care team building. Nephrologists and health systems should be incentivized to prevent kidney failure using SGLT2i, similar to the Merit-Based Incentive Payment System approach to promoting quality and lower cost, yet the current AAKH optional models lack this mechanism in patients with CKD G3A3. We suggest that policy makers consider the following actions. First, the Center for Medicare & Medicaid Innovation (CMMI) could expand the beneficiary list of the AAKH optional models to include CKD G3A3. CMMI could work with model participants to identify these patients using UACR results, in the absence of dedicated ICD-10 coding for albuminuria. Second, measure developers can create and test an SGLT2i therapy quality measure to be incorporated in national quality measurement, including the AAKH optional models and the Merit-Based Incentive Payment System. Third, Medicare can develop programs to increase coverage and affordability of SGLT2i. Currently, only 53% and 64% of Medicare Part D plans cover canagliflozin and dapagliflozin, respectively, without prior authorization or step therapy requirements. Empagliflozin is the most covered SGLT2i in Medicare Part D plans, with an annual retail price of $6048 and a median out-of-pocket expense of $1097, representing substantial barriers to adoption (9). The initiation rate of SGLT2i therapy was <10% for Medicare-aged beneficiaries in 2019 (10), compared with 56% for angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (2). Integrating SGLT2i affordability programs within the AAKH optional models where pharmaceutical manufacturers offer price discounts in the coverage gap, similar to the Part D Senior Savings Model for insulin, could lower patient out-of-pocket costs and increase SGLT2i utilization.

In summary, AAKH is a major step forward in reducing kidney failure in the United States. As part of this policy initiative, there is alignment between providers, patients, and payors in stemming CKD to prevent kidney failure. If the AAKH payment models include patients with CKD G3A3 and if there is broader incentivization of the use of novel kidney protective therapies, like SGLT2i, it would enable nephrologists and health systems to invest resources in screening patients for albuminuria, identifying patients with high kidney failure risk at an early stage, and implement kidney protective therapies systemically, which will translate into improved outcomes for patients and value for payors.

Disclosures

J. Li has been employed as a full-time employee by Akebia Therapeutics, Inc. since April 5, 2021 and continues to be employed as a part-time employee by Brigham and Women's Hospital. J. Li

reports ownership interest in Akebia Therapeutics, Inc. M.L. Mendu reports consultancy agreements with Bayer AG. S.L. Tummalapalli reports consultancy agreements with Bayer AG and receiving research funding from Scanwell Health. S.L. Tummalapalli is supported by the National Kidney Foundation Young Investigator grant.

Funding

None.

Acknowledgments

The content of this article reflects the personal experience and views of the author(s) and should not be considered medical advice or recommendation. The content does not reflect the views or opinions of the American Society of Nephrology (ASN) or *CJASN*. Responsibility for the information and views expressed herein lies entirely with the author(s).

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Published online ahead of print. Publication date available at www.cjasn.org.