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PatientVoice

Advancing American Kidney Health (AAKH): Catalyst for Investment in Kidney Diseases Clinical Trials and Precision Medicine

An Opportunity to Advance Upstream Interventions and the Importance of Nephrology

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Introduction

On July 10, 2019, President Trump issued the Executive Order (EO) on Advancing American Kidney Health (AAKH). I was invited to this historic announcement in Washington, DC, along with my Kidney Health Initiative, Patient Family Partnership Council colleagues. I never imagined that I would witness such a profound and hopeful moment with the potential to transform the system of care for people living with kidney diseases and, finally, disrupt the status quo. Although the dialysis entitlement benefit was created with the best of intentions, the system of kidney care did not evolve to meet the needs of patients with kidney disease. For the most part, the majority of patients with kidney disease faced the same patient journey. People wait for their kidneys to fail and be placed on hemodialysis. If they are fortunate to survive hemodialysis, they receive a kidney transplant. To be clear, the interests of the in-center hemodialysis ecosystem have been rewarded rather than the promotion of kidney health.

The EO states in Section 2 Policy that it is the policy of the United States to

1. prevent kidney failure whenever possible through better diagnosis, treatment, and incentives for preventive care;
2. increase patient choice through affordable alternative treatments for ESKD by encouraging higher-value care, educating patients on treatment alternatives, and encouraging the development of artificial kidneys; and
3. increase access to kidney transplants by modernizing the organ recovery and transplantation systems and updating outmoded and counterproductive regulations.

After the EO was issued, I paid close attention to how the US media reported this story. The majority of news coverage centered on objectives (*2*) and (*3*).

Although I fully support both of those goals, I believe the media missed an opportunity to report on objective (*1*): reducing the risk of kidney failure. Specifically, this objective plans on achieving the following:

1. by 2030, reduce patients with ESKD by 25%;
2. improve identification of populations at risk and in early stages of kidney disease; and
3. encourage adoption of treatments to retard or stop progression of kidney disease (1).

To achieve the first aim, the National Kidney Foundation (NKF) and the American Society of Nephrology (ASN) formed a partnership with the US Department of Health and Human Services (HHS) to collaborate on the Public Awareness Initiative outlined in the EO on AAKH. This collaborative partnership among the HHS, NKF, and ASN will provide education about the risks of kidney diseases and promote the early detection, treatment, and management of kidney diseases to improve patient outcomes. This initiative will also share information to enhance awareness of the causes and consequences of kidney disease. Although it is hard to comprehend, 90% of patients with CKD 3 are unaware of their kidney impairment.

NKF and CVS Kidney Care formed a partnership and launched their public awareness campaign in March 2020. In support of this campaign, I have two recommendations to accelerate the shift from treating the complications of kidney disease to earlier intervention: (*1*) increased risk-benefit patient conversations, and (*2*) increased use of angiotensin-converting enzyme/angiotensin receptor blockers.

Risk-Benefit Patient Conversations

The current system of kidney care has been ineffective at communicating the risk of kidney disease, including when patients experience kidney failure.

When asked to guess how long people of their age with similar health conditions usually live, 11.2% of hemodialysis survey participants responded <5 years, 15.1% responded 5–10 years, 33.1% responded >10 years, and 40.6% were not sure. These prognostic estimates contrast with the 60.3% 5-year mortality rate observed in the overall US in-center hemodialysis population. Payment and incentive structures for nephrologists and dialysis facilities have not traditionally encouraged, and may have even discouraged, honest conversations about health status (2).

The Kidney Risk Factor Equation (KFRE; https://kidneyfailurerisk.com/) tool is available for risk-benefit conversations (3). It is not clear if this patient engagement enabler has been disseminated and used by health care providers. Now is the time to increase the use of this tool with primary care physicians, nephrologists, and patient organizations. CVS Kidney Care offers a new provider, and hopefully, this will result in accountability for the detection of kidney diseases. This provides an opportunity to benchmark use of the KRFE tool among the different providers, including CVS Kidney Care.

Increased Use of Angiotensin-Converting Enzyme/Angiotensin Receptor Blockers

Although the evidence is well established that angiotensin-converting enzyme/angiotensin receptor blockers provide kidney protection, the use of these medications remains quite low, even with generic availability. In a study conducted by Tuttle *et al.* (4) at the University of Washington, kidney protective agents (*i.e.*, renin-angiotensin system inhibitors) were prescribed to approximately one fifth of adults with CKD, whereas potential nephrotoxins (*i.e.*, nonsteroidal anti-inflammatory drugs and proton pump inhibitors) were prescribed to more than one third of adults with CKD. Albuminuria and proteinuria testing for CKD assessment was rarely reported.

Although it is not clear why these medications are not being used, the consequences of underutilization are very clear. Approximately 40% of patients with ESKD crash on dialysis (5), thereby limiting patient choice to in-center hemodialysis and preventing the opportunity to have home dialysis or a preemptive kidney transplant. It is important to note that there is some ambiguity to this percentage. Speaking from my own personal experience, I chose to ignore the symptoms of my kidney disease on the basis of fear. I was extremely fortunate that I had 3 years to prepare for my eventual kidney failure. The underutilization of cost-effective kidney protective treatments requires immediate answers. These answers should result in increased use, especially in CKD 3 when these medications offer the greatest benefit in slowing down the progression of kidney disease.

After people engage in risk-benefit conversations, I expect that people with the highest-risk progression are fully informed of the potential downstream complications of kidney disease. For people with genetic forms of kidney disease (FSGS and autosomal dominant polycystic kidney disease), the consequences of progression are very clear. In turn, these patient populations are motivated to intervene earlier and also participate in clinical trials that may improve their patient journeys. However, there are patient populations, such as Blacks, Hispanics, and Native Americans, that are at high risk for kidney failure and disproportionately shoulder the burden of ESKD. Blacks are only 13% of the US population, but they represent 35% of the people on dialysis (6). Although the APOL1 project has provided evidence on understanding the causes of progression of kidney diseases in Blacks, the knowledge of all kidney diseases remains not well understood.

In May 2016, the first Kidney Precision Medicine Project (KPMP) meeting was conducted. The KPMP was launched on the basis of community feedback that, despite significant effort from industry and academia, development of pharmacologic therapies for AKI and CKD has been hampered by

- nonpredictive animal models;
- the inability to identify and prioritize human targets;
- the limited availability of human kidney biopsy tissue; and
- a poor understanding of AKI and CKD heterogeneity (7).

Historically, AKI and CKD have been described as single, uniform diseases. However, growing consensus suggests that different disease pathways lead to different subgroups of AKI and CKD.

Access to human kidney biopsy tissue is a critical first step to defining disease heterogeneity and determining the precise molecular pathways that will facilitate identification of specific drug targets and, ultimately, enable individualized care for people with AKI and CKD. Ultimately, I believe that increased knowledge of kidney diseases will result in increased pharmaceutical investment in upstream interventions.

Coupled with National Institutes of Health investment in the KPMP, there has been an upsurge in pharma investment in kidney diseases. On the horizon, there are potential treatments for autosomal dominant polycystic kidney disease, FSGS, IgA nephropathy, lupus nephritis, and Alport syndrome. Because of emerging models of care that support earlier intervention of kidney diseases, the timing is right for these treatments to emerge. Hopefully, the pharma research will shed more light on the knowledge of kidney diseases, and this information will be shared with the nephrology community.

Amid this hopeful future exists the troubling state of the nephrology profession. Only six of every ten nephrology training positions were filled in Appointment Year 2018, down from nine in ten filled in 2010, 2011, and 2012 (8). This declining interest in nephrology takes on greater significance when you consider the growing prevalence of kidney diseases. When ten residents were interviewed on their chosen specialty, four of the residents stated that lack of innovation in nephrology was a major factor in choosing to not become a nephrologist. A specific contributing factor was dialysis treatment itself. One quote in particular resonated deeply with me: "What I don't like about it is. . .a lot of your patients are undergoing dialysis and are just there kind of living their life on dialysis. You're not really doing much for them. You're just basically acting as their kidneys every other day" (9). I see investment in clinical trials serving dual interests:

- advancing earlier interventions for people living with kidney diseases; and
- bringing innovation to nephrology, thereby increasing the attractiveness of nephrology as a career.

On the basis of my professional experience recruiting for clinical trials, the overwhelming majority of people living with diseases are unaware of clinical trials. They have expected their physicians to inform them of the available trials and how the trials may improve their patient journey. These patients are looking for hope, and a clinical trial is a tangible measure of hope. Risk-benefit conversations in kidney diseases must include the availability of clinical trials and the role that they have in bringing hope to patients' lives. Upstream interventions will bring innovation to nephrologists, increase their value to the people they serve, and expand patients' choices.

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