Breaking the Barriers to Innovation in Kidney Care
The Time is Now

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> "Individual commitment to a group effort—that's what makes a team work, a company work, a society work, a civilization work."
>
> Vince Lombardi

The kidney care community has made stunning progress in the past decade developing and disseminating innovative drugs, diagnostics, devices, and care models. One superb example is the application of sodium-glucose cotransporter 2 inhibitors to attenuate progression of CKD, an intervention already transforming the lives of patients with CKD, preventing or delaying the need for dialysis or kidney transplantation (1,2). In laboratories around the world, ongoing work targeting the mechanisms of kidney disease will likely yield more specific, novel therapeutic agents in the next decade (3). The future for tens of millions of patients worldwide with CKD is optimistic, and the path forward has been illuminated through great creativity and collaboration. In 2012, the Kidney Health Initiative (KHI) was launched by the American Society of Nephrology (ASN) in partnership with the US Food and Drug Administration (FDA) (4). In parallel, the Kidney X innovation accelerator, a partnership of ASN and the Department of Health and Human Services, has provided funds to help innovators advance their creative ideas (5). In June 2019, the American Association of Kidney Patients (AAKP) launched The Decade of the Kidney, a global effort to mobilize kidney patients in support of consumer care choice and innovation-friendly policies (6). In July 2019, former President Trump issued the Executive Order on Advancing American Kidney Health, specifically targeting earlier intervention, increased home dialysis and transplantation, and accelerated development of artificial (implantable) kidneys (7). Kidney Care Partners (KCP) made driving innovation a key policy pillar in 2019 in its Kidney Care First: A Framework for Improving Renal Disease Support & Treatments report and highlighted multiple barriers to real progress (8).

Barriers inhibiting innovation are better understood within a conceptual kidney disease framework, similar to the patient-centered quality pyramid that has been applied in kidney failure and pharmacy services for patients with kidney diseases (9). In the process of innovation, as in the development of approaches to optimize quality of care, patient engagement is essential and requires framing innovation in the context of the overall patient journey. The framing process starts with early identification (*e.g.*, new approaches to home/point-of-care diagnosis of kidney disease); it proceeds with interventions to slow CKD progression. Then, it addresses complications of CKD as they develop, such as anemia or metabolic bone disease (*e.g.*, hypoxia-inducible factor prolyl hydroxylase inhibitor and phosphate-lowering therapies), and proactively plans and ensures optimal availability of preemptive transplantation (*e.g.*, transplant evaluation/listing software) or home dialysis (*i.e.*, remote monitoring and patient-friendly/safe delivery equipment) as preferred approaches to kidney failure or deceased donor kidney transplantation (*e.g.*, early diagnosis of rejection and tolerance induction) and in-center hemodialysis (*e.g.*, more efficient, safer, and smarter dialysis equipment). Innovation, fueled by patient engagement, is required at each stage of the journey, and incorporation of patient insight data is essential to understanding which innovations prove most valuable to patient consumers.

With such intense interest and activity already underway, questions remain. When will kidney care innovation meet the full expectations of patients, taxpayers, providers, health care systems, and payers? When will their value proposition be embraced by payers and policy makers as well as investors, patients, health care systems, and physicians? What are the remaining barriers to accelerated progress and results, and can individuals, such as the readers of *CJASN*, help accelerate the pace of innovation and drive the care that the patients need and deserve?

In kidney care, the key areas of innovation include pharmaceutical discovery and development, device development, and design and implementation of new care delivery models. There are certain barriers to success that are common to all three, but each has its own unique barriers. For example, the regulatory barriers to success are particularly noteworthy, although somewhat different, for devices and pharmaceuticals and less important for care delivery innovation. Nuances and policies about reimbursement, whether by public or private payers, are relevant for all three types of innovation. For many developing drugs or

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devices, there is a bias toward traditional approaches to innovation. Innovators or founders of new companies identify a clinical (or financial) need, develop an innovative product, create an investor pitch, sometimes modify the idea to fit investor's interests, raise finance *via* capital markets, work aggressively for FDA approval, and then, hope a strategic partner will acquire the company/asset and see that it enters the market so that, finally, it finds its way to patients. Unfortunately, this approach often fails because of a fundamental gap in insights about the complex terrain, key stakeholders, the role of typical strategic partners (large pharmaceutical or device manufacturers or care providers), evolving patient consumer expectations, and challenges to successful commercialization. It is worth pointing out that the approach described and its frequent failures are not unique to innovation in kidney care; similar issues exist in biomedical innovation in a variety of disease states. In the case of kidney care, however, there is frequently an underestimation of the complexity posed by the numerous and sometimes disparate interests among stakeholders, including payers, Medicare, patient advocates, nephrologists, and others. Finally, there is inexperience in execution of a clinical development or business plan that focuses on patient needs versus investor and regulator demands, underestimation of the cash required to power success, and the challenge of engaging dialysis organizations, particularly when the innovation involves drugs and devices or might be caught up in policy disagreements about reimbursement approaches. The small number of organizations in the United States that are the major customers, or in some cases, the manufacturers of equipment, and also oversee the clinical care represents a significant barrier to entry for new products. Lack of acceptance of new drugs and/or devices by these organizations is seen by innovators and potential investors as a massive barrier to success that clearly discourages entrepreneurialism. Current product commitments, contractual obligations, and the need to continue to optimize shareholder value or fund nonprofit activities make risk taking for these organizations unpalatable and the *status quo* safer. In addition, even the best innovations only bring value to patients when they are accepted by physicians and adopted by patients.

Of course, the "elephant in the room" in kidney failure is the current federal bundled payment system, which discourages investors who see little chance of realizing a favorable return on their investment, at least in the United States. Even an innovation that significantly improves patient outcomes and lowers total care and taxpayer costs is seen as an up-front cost, one that investors fear will not be borne by Medicare or potential provider customers. Uncertainty about Medicare policy and criteria for innovations and ongoing concern over the bundled payment system are also viewed as unacceptable risks among potential investors.

The substantial groundwork for future innovations that FDA, KHI, and Kidney X have laid underscores the powerful effect that small, diverse teams of patients and professionals can have on the future of *status quo* care. Yet, more must be done to bring solutions to consumer markets. This requires the energy and bold voices of more professionals willing to demonstrate the same sense of urgency as patient advocates.

As with most challenges, there is a path forward despite the barriers, and the promise to patients with kidney diseases of better clinical outcomes and lower costs of care can be realized. What are the concrete steps that can be undertaken now?

(1) Engage the general public as well as patients with kidney diseases and their insights in all aspects of innovation.
(2) Articulate the narrative of the clinical journey of patients with kidney disease as the framework for understanding current gaps in kidney care innovation. Emphasize early diagnosis and treatment of kidney diseases as a key to avoiding severe and costly CKD or kidney failure.
(3) Identify executable innovations, at each step along the journey, that will make a difference for patients (meaning in the marketplace and accessible) within the next 3–5 years.
(4) Educate key health sciences investors about opportunities in kidney care that both improve patients' lives and result in a fair investment. Articulate the financial rewards of such opportunities along with intangibles, such as name recognition, to cultivate angel investors in this sector.
(5) Collaborate with key advocacy organizations (ASN, the National Kidney Foundation, KCP, AAKP, and others) to create legislation that authorizes reimbursement for new devices and pharmaceuticals with payments outside the dialysis care bundle.
(6) Widen efforts with other key federal health agencies, including the Veteran's Administration and the Department of Defense, to leverage their history and expertise in accelerating innovations in care for patients with kidney diseases.
(7) Hammer home the message that new care models on the basis of patient care choice, value-based care, and fair reimbursement are innovations as important as new drugs and devices.

Interest in kidney innovation, on the basis of the number of applications to the Kidney X prize competitions alone, is at a record level. KHI and Kidney X, quite rapidly, captured the imagination of what the future holds, forged a consensus and pathways for change, and injected a greater sense of urgency into our shared mission to save more patient lives. This represents the tip of the iceberg required to transcend the *status quo*. The presence of KHI and Kidney X alone cannot guarantee that innovations will reach patient consumers within their lifetimes; we each need to contribute to complete the long arc of innovation. The kidney community has the momentum, passion, and will to act now to take kidney care to the next level, and we must embrace the challenge to win. We must broaden our base, include more diverse disciplines, educate investors on opportunities and unmet needs, and support policies that help innovators get transformative therapies to patients. Patients with kidney diseases, and our society, deserve nothing less.

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G.M. Chertow reports consultancy agreements with Akebia, Amgen, Ardelyx, AstraZeneca, Baxter, Cricket, DiaMedica, Gilead,

Miromatrix, Reata, Sanifit, Unicycive, and Vertex; ownership interest in Ardelyx, CloudCath, Durect, DxNow, Eliaz Therapeutics, Outset, Physiowave, and PuraCath; research funding from the National Institute of Allergy and Infectious Diseases and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); serving in an advisory or leadership role as coeditor of *Brenner & Rector's The Kidney* (Elsevier) and as a member of the board of directors of Satellite Healthcare; and DSMB service for Angion, Bayer, NIDDK, and ReCor. P.T. Conway reports employment with AAKP (uncompensated position); honoraria from 2018 to 2021 from (nominal stipend) the American Board of Internal Medicine, (nominal stipend) ASN, (travel/nominal stipend) AZ ADVICE Collaborative/AZ Department of Health Services, (travel/nominal stipend) Bayer, (nominal stipend) the External Expert Panel of the Kidney Precision Medicine Project of the National Institutes of Health (NIH)/NIDDK, and (speaker fee) UC Irvine Grand Rounds; and serving as a patient voice editor for *CJASN*. P.T. Conway also serves as BOD, chair of policy & global affairs, immediate past president, AAKP; board, ABIM nephrology specialty board; liaison, Centers for Disease Control and Prevention/HICPAC; reviewer, DOD/CDRMP; patient rep. program, FDA; panelist, FDA/CRDAC; panelist, FDA/MDAC circulatory devices panel; chair, FDA PEAC; board, KHI; external expert panel, NIH/NIDDK/KPMP; contract mgt. board, NIH/NIDDK/United States Renal Data System; adv. board, Novartis, Global Transplant PRO; chair, PAPR; and member, TEP, CMS/home dialysis quality measures. P.T. Conway serves on the speakers bureau for AAKP and has other interests/relationships as cochair, AAKP/George Washington University School of Medicine & Health Sciences Global Summit on Kidney Disease Innovation; stakeholder adv. council, GWU PCORI/highway study; member, patient adv. board, Kidney Research Institute/Center for Dialysis Innovation, University of Washington/NW Kidney Centers; member, Transplant Roundtable; participant on the adv. board, University of Pittsburgh NIH/COPE-AKI study; and focus grp, WHO/lived experience advocacy research NCDs & mental health conditions. A.R. Nissenson reports consultancy agreements with Nephroceuticals; ownership interest in Angion, Nephrian, Nephroceuticals, Oxidien, Rockwell, Diality and Sentien; serving as a scientific advisor or member of Angion, Nephroceuticals, Renal Care Innovation Holdings, and Rockwell; and other interests/relationships as cofounder of Renal Care Investment Holdings.

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Author Contributions

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