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Sibeprenlimab Poised to Shake Up IgA Nephropathy Care

By Bridget M. Kuehn

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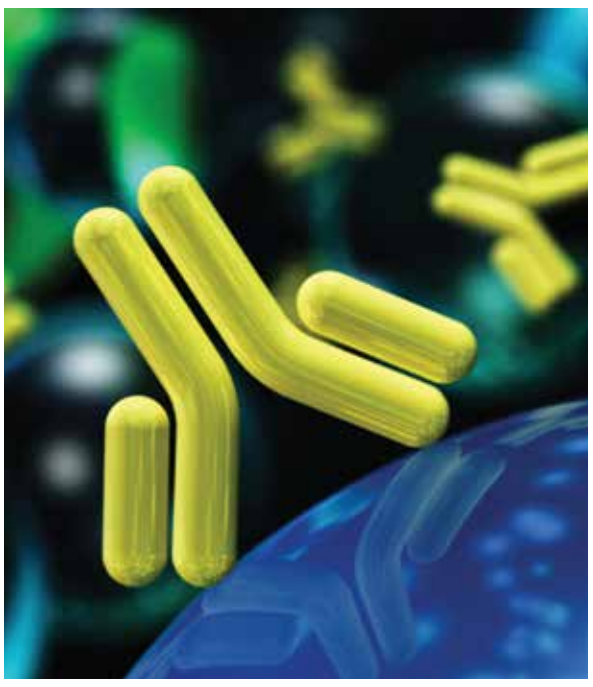

The experimental monoclonal antibody sibeprenlimab demonstrated a 51.2% reduction in proteinuria in people with immunoglobulin A nephropathy (IgAN) in an interim analysis of the phase III VISIONARY trial (NCT05248646) (1), helping bring the drug one step closer to approval.

The US Food and Drug Administration (FDA) granted priority review for the biologic's manufacturer, Otsuka Pharmaceutical Co., Ltd., in May and set a decision date of November 28, 2025. Other regulators around the world are also reviewing the therapy. If regulators authorize the drug as expected, the once-every-4-week injection could mark a sea change in IgAN care. The VISIONARY trial's principal investigator Vlado Perkovic, MBBS, PhD, FASN, a nephrologist and professor of medicine and provost at the University of New South Wales in Sydney, Australia, presented results of a prescheduled interim analysis at the European Renal Association Congress in Vienna, Austria, in June.

The analysis occurred after the first 320 patients who were enrolled in the trial had reached the 9-month mark. A total of 530 patients will be enrolled in the trial and followed for 2 years, a milestone that Perkovic expects to reach next year. Perkovic noted that achieving that degree of proteinuria reduction with a single drug is remarkable.

"Proteinuria is the single strongest marker that predicts how likely someone is to lose kidney function," Perkovic said. "By reducing proteinuria, the evidence we have suggests that we will dramatically slow the loss of kidney function with these therapies."

Targeted action

Sibeprenlimab has a novel mechanism of action targeting a key step in the development of the disease. It binds to and reduces the activity of a proliferation-inducing ligand (APRIL), which helps set off and maintain the cascade of events that leads to IgAN. It reduces the production of IgA and its pathogenic counterpart, galactose-deficient IgA1—and possibly also the corresponding anti-glycan

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Drug Companies Express Resurgence of Interest in AKI

By Karen Blum

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Because acute kidney injury (AKI) is a complex, heterogeneous condition, Steven Burke, MD, said he was surprised to identify about 15 companies working on new drugs for the prevention or treatment of AKI. "It's almost like there's a renaissance in AKI drug development," said Burke, senior vice president of Research and Development and chief medical officer at Akebia Therapeutics, a renal biopharmaceutical company in Cambridge, MA, during the Kidney Innovation Conference in May, held in Washington, DC. Many people who tested positive for SARS-CoV-2 during the COVID-19 pandemic also developed AKI, which may explain the renewed enthusiasm in this area, Burke said at the conference, which was sponsored by the Kidney Health Initiative, the Kidney Innovation Accelerator (KidneyX), and KidneyCure.

AKI is "a very deadly disease" with several confounding factors that impact clinical trial design and agreement on endpoints to measure, added Jorge Cerda, MD, MS, FASN, chief of medicine at St. Peter's Health Partners in Albany, NY. Another issue is that manufacturers do not have good enough feedback from patients, he said. "Patients ask questions about AKI that have little to do with creatinine or [the biomarker neutrophil gelatinase-associated lipocalin] and are all to do with whether [their] family member will be on dialysis forever and whether that person will or will not die."

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antibody—and, in doing so, reduces the immune onslaught that leads to kidney damage and proteinuria.

The drug is the first in a new class of IgAN therapies in the pipeline, often called APRIL/B cell activating factor (BAFF) inhibitors, said Richard Glassock, MD, FASN, emeritus professor at the David Geffen School of Medicine at the University of California, Los Angeles. He expects sibeprenlimab to become available by early 2026 and more examples of the general class of therapies to follow within the next year or two. "This will be a very transformative time for the treatment of IgA nephropathy because it is a whole new class of drugs, unlike all the other drugs on the market," Glassock said. "It seems to have the capability to stop disease progression entirely."

If the ongoing research confirms the expected long-term kidney-preserving benefits of sibeprenlimab, by showing stable estimated glomerular filtration rates over many months or years, it would represent a breakthrough for the field, Glassock remarked. "It will likely mean the paradigm of IgA nephropathy treatment will change very drastically, much to the benefit of patients," he said.

New treatment paradigm

Glassock explained that the arrival of the APRIL/BAFF inhibitors would likely lead to the reprioritization of which therapies to use for initial treatment of IgAN. Currently, FDA-approved and widely available drugs can reduce proteinuria, but patients often still experience progressive loss of nephrons. But sibeprenlimab and its classmates, which appear to stop the destruction of nephrons, could help patients avoid dialysis and would likely become the first-line choice for many people living with IgAN, he said. "It is a very special and rapidly changing time in the field of IgA nephropathy," Glassock said. "It has happened so quickly that it has been difficult for physicians to adapt."

Current treatment protocols begin with renin–angiotensin–aldosterone system (RAAS) inhibitors in mild cases with lifestyle changes and care for comorbid conditions, Glassock explained. Sodium-glucose cotransporter-2 inhibitors can be added to these baseline regimens as needed (2). In selected cases, sparsentan can also be used as a substitute for RAAS inhibitors or atrasentan added to ongoing RAAS inhibition. For those at high risk of progression, high- or low-dose corticosteroids (systemic or gastrointestinal-targeted), mycophenolate mofetil, or iptacopan may be added, Glassock noted.

Glassock said that, based on the data so far, sibeprenlimab combined with RAAS inhibition for blood pressure control may be sufficient to control IgAN for many people. Other medications like steroids, mycophenolate mofetil, iptacopan, atrasentan, or sparsentan may only be used for patients who do not respond to treatment with the APRIL/BAFF inhibitors. However, comparative data on these drugs will be needed to prove this, he noted.

Perkovic agreed that there is a need to determine how to best use the available therapies and emerging ones. Future studies should investigate how to match patients with the most beneficial therapies or combinations, as well as determine the optimal order of drug administration.

So far, sibeprenlimab's side-effect profile appears acceptable, Glassock said. Because the drug and its classmates reduce the production of immunoglobulins that help protect patients from infection, there may be an increased risk of infection, especially with long-term use, he said. The VISIONARY trial results so far indicate that the rate of adverse events, including infections, is lower in the sibeprenlimab group than in the placebo group. "There was no signal of an increased risk of infection of any meaningful type, suggesting that this drug appears to be quite safe as well as effective in patients with IgA nephropathy," Perkovic said.

There will also be a learning curve for patients who will have to administer the injections themselves at home or have a caregiver do so, Glassock said. In the VISIONARY trial, patients received the injections at the hospital. But Glassock noted that popular injectable anti-obesity medications have cleared this hurdle with a more frequent dosing schedule than once-monthly sibeprenlimab. "Many people find once-monthly injections more convenient than daily pills," Perkovic noted. Another potential challenge may be whether the medications will be affordable for patients worldwide, Perkovic said. He explained that the costs of the medications were not yet known.

Despite any potential challenges, both Glassock and Perkovic expressed optimism about the prospect that the growing number of drugs for IgAN will help change people's long-term trajectory and hopefully prevent kidney failure. "We do not have any idea how long the beneficial effects of these drugs will last, and it will be many years before we know just how many patients, despite treatment with these drugs, will end up with kidney failure," Glassock noted. "At the moment, it seems like that number will be dramatically lower."

Perkovic noted that until a few years ago, there were no proven therapies for IgAN. Nephrology as a whole has also seen a growing number of new kidney-preserving therapies in recent years. Perkovic called it a "golden age" for the field.

"We now have a number of approved therapies [for IgAN], and we have many, many more coming down the pipeline," Perkovic said. "It is a transformative moment for nephrology as a whole and for our patients, and it is very exciting to think about the [potential] to transform their disease and hopefully stop it in its tracks in the future." ■

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Drug Companies Express Resurgence of Interest in AKI

Continued from cover

There are only two US Food and Drug Administration-approved treatments for AKI, each for a limited patient population, Burke said. Terlipressin is used to improve kidney function in adults with hepatorenal syndrome and a rapid reduction in kidney function, and Quelimmune is a therapeutic device to treat AKI in pediatric patients with sepsis. The device can be integrated into the dialysis circuit used to treat people with AKI, where it targets highly activated proinflammatory neutrophils and monocytes and restores them to a reparative state.

In a breakout session at the conference, Burke shared results from a survey conducted by the Kidney Health Initiative, which sheds light on AKI product development. Nearly 70% of the respondents from the 12 companies that completed the survey indicated that they were actively developing products for AKI, and another 18% said that they were planning products, even though about half of the company respondents relayed that they anticipated this as having a low or negative return on investment. The company respondents expressed a range of concerns regarding clinical trial operations, including the rate of patient recruitment, study size, cost, history of prior failed trials, approvable endpoints to measure, and patient heterogeneity.

Replying to additional survey questions, company respondents reported that cardiac surgery, sepsis, and organ transplantation were the patient populations among which they would first plan to run clinical trials. Most respondents said that they have considered using patient-reported outcomes in AKI trials and that they plan to incorporate patient input into AKI trial design and reporting.

A majority of respondents said that they believed a composite of major adverse kidney events such as death, a new requirement for dialysis, or worsened kidney function (defined as 25% or greater decline in estimated glomerular filtration rate) was the universal approvable endpoint for AKI trials. Other adverse outcomes associated with AKI that company respondents expressed interest in were prolonged intensive care unit (ICU) stays or hospitalizations, pulmonary or circulatory failure, and heart failure and atrial fibrillation.

Additionally, the majority of respondents indicated that they would consider long-term outcomes such as death or change in chronic kidney disease stage when designing AKI trials and that they would benefit from having access to a data repository of completed AKI trials.

Although the survey indicated that most companies consider one endpoint for AKI, the condition occurs in multiple settings and has multiple etiologies, so the patient journey "is going to be very different depending upon the settings," said Aliza Thompson, MD, MS, director of the Division of Cardiology and Nephrology at the US Food and Drug Administration's Center for Drug Evaluation and Research, during a panel discussion following the breakout. Therapies for AKI may need to do more than help just the kidney, she added.

"There is not some one endpoint. The question is: What outcomes are we trying to prevent in particular settings?" Thompson said. "The endpoint should be defined around those—whether they're the hospitalization, the duration in the ICU, [or] the associated need to be ventilated, which may be appropriate in some settings. There may be other settings [in which] other endpoints should be used, but it really depends in part on the outcomes we're trying to prevent as well as what the therapy does."

AKI has so many different effects that "it becomes very difficult to think about how you design a trial with endpoints that are specific for AKI when the renal process of AKI is in some ways nonspecific," said John Kellum, MD, Distinguished Professor of Critical Care Medicine at the University of Pittsburgh in PA. Designing a trial for prevention of AKI, for example, is challenging because the intervention would have to be given to many people who will never develop the endpoint, which becomes a safety risk as well as a cost concern.

Trials need to be designed to be "fit for purpose, with real thought and clarity about what is the question you're answering, and what is the population, and what are the proposed mechanisms of action," said Meg Jardine, MBBS, PhD, director of the National Health and Medical Research Council Clinical Trials Centre at the University of Sydney in Australia. Every aspect of that lens must be considered, she said, especially in AKI, which is "more of a descriptive syndrome rather than a discrete [pathologic] process."

Bhupinder Singh, MD, FASN, FNKF, chief medical officer at Renibus Therapeutics, Southlake, TX, said he moved from private nephrology practice to pharmaceutical research after finding himself frustrated with designs of clinical trials in which his patients participated. One of the products that his company has been developing (RBT-1) is a preconditioning drug given intravenously before nonemergent cardiac surgery, with the goal of activating anti-inflammatory and antioxidant pathways to prevent AKI and other complications.

The company enrolled 423 patients in a phase 3 trial of RBT-1 (NCT06021457), using a novel composite endpoint of all-cause death, AKI requiring dialysis, 30-day cardiopulmonary hospital readmission, and time in the ICU, Singh said. Results are expected in the third quarter of 2025.

After the meeting, Burke noted, "In light of the survey results and the group discussion, it was clear there is a strong desire by stakeholders to explore the creation of a data repository of AKI trials. The data could help validate biomarkers and surrogate endpoints, increasing the efficiency and future success of clinical trials."

GLP-1 Receptor Agonist Use in Kidney Transplant Recipients

By Corey Joseph, Karela Herrera-Enriquez, and Daniel C. Brennan

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The retrospective cohort study by Orandi et al., recently published in *The Lancet Diabetes & Endocrinology*, offers compelling evidence on the effectiveness and safety of glucagon-like peptide-1 (GLP-1) receptor agonists in kidney transplant recipients with pre-existing type 2 diabetes (1). Using data from 18,016 kidney transplant recipients in the United States from 2013 to 2020, the study found that those prescribed GLP-1 receptor agonists post-transplant experienced a 49% reduction in death-censored graft loss and a 31% decrease in all-cause mortality compared with nonusers.

A significant strength of this study is its use of a large, nationally representative dataset, enhancing the generalizability of the results. The researchers used robust statistical methods, including inverse probability of treatment weighting to control for measured confounding; treated GLP-1 receptor agonist use as a time-varying exposure to preclude immortal time bias; and created matched cohorts based on post-transplant survival time to further test their findings against this bias. These methodologies bolster the credibility of the observed associations between GLP-1 receptor agonist use and improved transplant outcomes.

Despite these methodological strengths, several considerations warrant careful attention when interpreting these promising results. The study estimates the effects of treatment initiation rather than sustained GLP-1 receptor agonist therapy. Assessing sustained treatment effects is particularly challenging in a database like the US Renal Data System, in which detailed follow-up data on key clinical variables are limited for making the assessment of treatment initiation effects valid for this population. However, the authors report that 38.8% of patients discontinued therapy within 6 months, with a median duration of only 254 days. Given that GLP-1 receptor agonists require sustained exposure for cardiovascular and renal benefits (2, 3), understanding treatment initiation effects may have limited clinical use in this complex post-transplant milieu, in which multiple factors influence outcomes.

Beyond questions of treatment duration, the choice of comparison group presents interpretive challenges. The authors compare GLP-1 receptor agonist users with all nonusers. Although they appropriately used inverse probability of treatment weighting to control for confounding, this approach does not ensure clinical equipoise, limiting causal interpretation because the comparison includes patients who may never have been appropriate candidates for treatment. Alternative approaches such as overlap weights could restrict analyses to patients with genuine clinical equipoise (4, 5).

The study's temporal scope introduces another layer of complexity. During the study period, patients younger than 62 years at transplant lost Medicare eligibility 3 years post-transplant (6, 7). This policy creates a significant limitation: Whereas the study reports a 5-year follow-up, only older patients contributed meaningful long-term outcome data, restricting the understanding of treatment effects in younger transplant recipients.

These methodologic considerations gain particular clinical relevance when examining the study's safety findings. Although the study reports a 49% increased risk of diabetic retinopathy among GLP-1 receptor agonist users, an increase in diabetic retinopathy and reduction in hemoglobin A_{1c} have been reported in a meta-analysis of the cardiovascular trials of GLP-1 receptor agonists, as the authors cited (8). Both the study by Orandi et al. (1) and the meta-analysis (8) lack detailed information on the severity and progression of diabetic retinopathy. It is interesting, however, that pancreas transplantation, which is associated with improvement in hemoglobin A_{1c}, is also associated with progression of diabetic retinopathy in the first year after transplantation (9). Taken together, these findings suggest the need for careful ophthalmologic monitoring in transplant patients receiving GLP-1 receptor agonists.

Orandi et al.'s study (1) provides valuable insights into the potential benefits of GLP-1 receptor agonists for kidney transplant recipients with type 2 diabetes. The associations with improved graft and patient survival are promising, yet the increased risk of diabetic retinopathy warrants caution. Prospective randomized controlled trials are essential to confirm these findings and to further elucidate the risk-benefit profile of GLP-1 receptor agonists in this unique patient cohort. ■

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The authors report no conflicts of interest.

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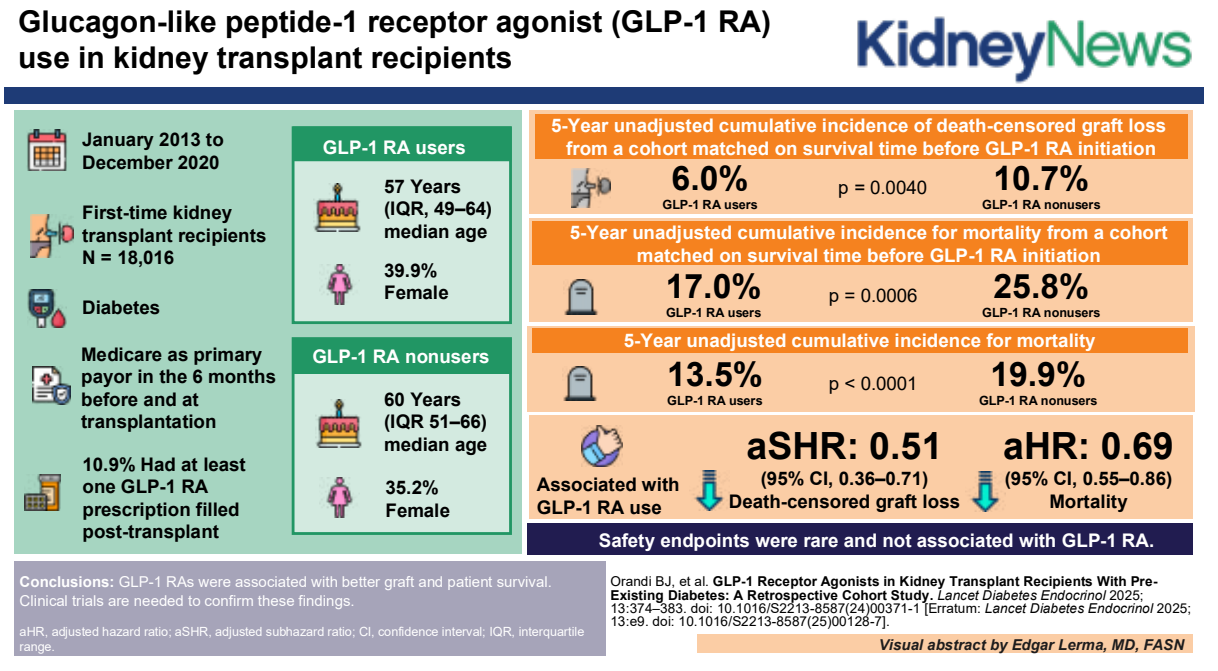

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ASN President's Update

We Must Grasp This Moment

By Prabir Roy-Chaudhury

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Despite a constantly changing world, the first 8 months of my 1-year tenure as ASN president have been the greatest privilege—and an absolute highlight—of my professional career. Above all else, this position has allowed me to engage with an extraordinary, diverse, and dedicated group of ASN members, often in their own communities. And when I say members, I truly mean *all* of the society's members.

During the last 8 months, I met or communicated with:

- community-based nephrologists from large value-based care organizations comprising more than 500 practitioners based all across the country to solo practitioners in rural Ohio and Kentucky;
- academic nephrologists leading kidney centers in large metropolitan areas with hundreds of faculty and staff, as well as five-member nephrology divisions in smaller cities and home to the only nephrology fellowship training program for hundreds of miles;
- early-career nephrologists working in storied nephrology divisions;
- nephrologists who are international medical graduates completing their J-1 visa waivers by providing vital care in rural or underserved areas;
- physician-scientists working across the nephrology continuum, from exploring the inner workings of subcellular organelles to defining new payment models;
- nephrologists and other health professionals committed to reducing kidney health disparities, from a focus on global health to the local impact of climate change on kidney health;
- nephrologists across the educational spectrum, from the first in their families to attend college to third-generation nephrologists;
- nephrologists who are administrators, educators, and entrepreneurs; and
- transplant nephrologists dedicated to ensuring patient access to the optimal therapy, improving transplant nephrology training, and demonstrating the value of transplant nephrology within health systems.

Regardless of role or location, every nephrologist, researcher or scientist, and health professional I meet is united in their passion for—and dedication and commitment to—kidney health, be it in the context of biology, the process of discovery and innovation, education and awareness, patient care, entrepreneurship, or policy and advocacy. While humbled by the depth and breadth of experience and expertise of our members, I also realize this incredible pool of talent and commitment is needed more than ever before.

As a specialty, nephrology is at an incredibly exciting time with a huge increase in innovation and investment in kidney health. Following a quarter century of therapeutic stagnation, promising new therapies are emerging for glomerular diseases, cardiovascular-kidney-metabolic (CKM) syndrome, and acute kidney injury.

The only way we can come closer to our vision of a world without kidney diseases is if all of us grasp this moment. Every nephrologist must be a part of this change, contribute to this change, drive this change, and deliver this change to the millions of people living with kidney diseases.

Changing kidney care

At a personal level but still wearing my nephrologist hat, I believe these advances mean that my standard of care for kidney diseases will now no longer be to start a patient on an angiotensin-converting enzyme/angiotensin receptor blocker, tell them that I will measure the slope of their estimated glomerular filtration rate over the next year, and then share with them whether they will reach kidney failure in 3 years, 7 years, or 10 years. I have always felt that this approach was pitiful, but no alternatives existed. Similarly, my hope is that within the next 5 years, the treatment of acute kidney injury will no longer be fluids on day 1, furosemide on day 2, and dialysis on day 3!

These new therapies, however, are only the beginnings of change for kidney care. So much more innovation and implementation are needed if we truly want to cure kidney diseases. Today, I want to throw down the gauntlet to every ASN member and challenge them: The only way we can come closer to our vision of a world without kidney diseases is if all of us grasp this moment. Every nephrologist must be a part of this change, contribute to this change, drive this change, and deliver this change to the millions of people living with kidney diseases.

If all of us become a part of this change, then, perhaps, we can also transform nephrology as a specialty. The new therapies could allow nephrology to break out of its small, comfortable bubble. Currently, the specialty is dominated by kidney failure and dialysis, but we have an opportunity to play in a much larger space—one that includes education and awareness, early diagnosis and treatment, and innovation and investment.

By creating innovation pathways, advocating for fair payment pathways, and establishing care pathways (including models based on centers of excellence), nephrologists can demonstrate the *value* that kidney care brings to health systems, insurers, and payors. Importantly, these steps would ensure that the new kidney drugs, devices, and biologics are appropriately reimbursed, an essential step toward patients benefiting from the therapeutic advances that these products bring.

Representing more than 21,000 nephrologists, researchers and scientists, and other health professionals, ASN is uniquely positioned to leverage the following three pathways to help nephrology grasp this moment.

1 Creating innovation pathways

Innovation pathways require transforming nephrology through new drugs, devices, and biologics. The first step is to champion current and future kidney health investigators across every career stage, accelerate the development of novel treatment options, and support groundbreaking potential from AI (artificial intelligence) to "Z" (xenotransplantation). Through KidneyCure, the Kidney Health Initiative, the Kidney Innovation Accelerator (KidneyX), and the forthcoming Transforming Kidney Health Research report, ASN is outlining the path to success for the kidney community.

These new therapies must also be available to clinicians, affordable to patients, and integrated into the delivery of care. As such, ASN and the kidney community must ensure that screening is performed for people who are at risk for kidney diseases (and are not currently being screened) as well as continue to support research around new, cost-effectiveness analyses, which can mitigate the costs of screening and treating broader segments of our population. The US Preventive Services Task Force must support screening to identify the millions of people living with kidney diseases, many of whom are not aware of their declining kidney function until it is too late.

In addition to restructuring the Medicare End-Stage Renal Disease (ESRD) Program's Prospective Payment System (PPS) to provide real payment for innovation, ASN and the community must design, support, and work with policymakers to continuously improve care delivery systems. In the future, payment systems must efficiently and effectively provide all people with access to new therapies to slow progression of kidney diseases and avoid kidney failure. ASN is partnering with economists to analyze how both investment in kidney research and the advent of new therapies—to treat CKM syndrome, for example—can reduce costs to the Medicare ESRD Program.

2 Advocating for payment pathways

By restructuring the Medicare ESRD PPS, ASN and the kidney community will likely accelerate efforts to pursue other payment pathways, such as:

- working with the Centers for Medicare & Medicaid Services Innovation Center to ensure the success of the Increasing Organ Transplant Access (IOTA) Model, a mandatory payment model intended to improve access to kidney transplants for Americans living with kidney failure;
- advocating for the development of a multipayor, multigenerational model on chronic kidney disease; and
- highlighting the need for a multispecialty emergency (and opportunity) model that includes obesity and the kidney, heart, and liver to prepare a report to Congress by 2027 identifying payment gaps.

Beyond IOTA and other models, ASN is focusing on improving compensation, reimbursement, and payment to nephrologists. Together, ASN and the community must change how nephrology is valued in current payment models, value-based care, and future payment approaches. As a first step, ASN is convening a task force with transplant nephrologists to develop the tactics needed—such as a toolkit—to improve outcomes for patients by appropriately valuing the contributions of transplant nephrology to the health system and ultimately increasing compensation for transplant nephrologists.

This effort is also well-timed with the likelihood that the Accreditation Council for Graduate Medical Education (ACGME) will start accrediting transplant nephrology fellowship

training programs in July 2026. As a reminder, ASN partnered with the American Society of Transplantation to urge ACGME to start accrediting transplant nephrology fellowship programs. Only ACGME-accredited residency and fellowship programs are eligible for the estimated $18 billion in Medicare funding for graduate medical education, which is also linked to a less-onerous review process for fellows training on J-1 visas (1).

For 3 years, ASN has partnered with Phairify on the ASN Benchmarking Compensation Survey to provide the society's members with exclusive access to nephrology-specific compensation and productivity data. After completing the Benchmarking Compensation Survey, ASN members gain access to the Physician Value Exchange, a powerful business intelligence application, in which they can filter data to see how they compare with their peers and define their ideal career opportunities. To learn more about the ASN Benchmarking Compensation Survey, powered by Phairify, please visit https://www.asn-online.org/phairify for a case study, article, and additional resources (2).

3 Establishing care pathways

Last year, ASN launched a Kidney Health Guidance series to promote "person-directed outcomes-oriented" kidney care (3). The ASN Kidney Health Guidance series is succinct, practical, and aimed at clinical practice, targeting emerging, urgent, or high-priority clinical issues facing nephrologists and other health professionals. For example, the forthcoming ASN Kidney Health Guidance on Conservative (Kidney) Management will define a pathway, provide tools, and offer resources to assist the nephrology community as well as help patients (and care partners) understand and choose how they want to experience advanced kidney disease and end of life.

To develop Kidney Health Guidance, ASN focuses on innovation, nimbleness, and flexibility to offer tools and resources that facilitate implementation and translation of current evidence while complementing clinical practice guidelines—such as Kidney Disease: Improving Global Outcomes (KDIGO)—albeit for clinicians who practice in the United States (4). Other leading specialty societies have been following suit with an interest in providing clinical decision support through publication of concise guidance with a narrow focus on clinical topics with evolving evidence (5).

Next year marks the 10th anniversary of ASN's partnership with the US Centers for Disease Control and Prevention (CDC) to initiate Nephrologists Transforming Dialysis Safety (NTDS). During the past decade, NTDS (now a part of ASN's Excellence in Patient Care initiative) has concentrated on ASN's "clinical priorities to provide high-quality care for people with kidney diseases" through 12 projects and initiatives (6). Focusing on three of these projects will help highlight how ASN and the kidney community can partner to establish care pathways that could change kidney care.

In response to "Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association" (AHA) in October 2023 (7), ASN has launched the "Saving Kidneys, Hearts, and Lives" initiative (8). Earlier this year, ASN held a workshop on "Nephrology in a New Era of Cardiovascular-Kidney-Metabolic Health." Funded in part with support from AHA, this workshop identified 10 "enabling opportunities" for community engagement in CKM care. These opportunities include early screening, education, economics, engagement, and effectiveness. ASN looks forward to continuing to partner with AHA as well as with other members of the kidney community—particularly the National Kidney Foundation and the American Kidney Fund—to implement these enabling opportunities.

To promote high-quality care for people living with glomerular diseases, the ASN Glomerular Diseases Collaborative is producing a compendium to provide a "one-stop shop" for nephrologists and other health professionals interested in learning more about this fast-moving area of nephrology. Additionally, ASN is working closely with the International Society of Glomerular Disease, GlomCon, and other stakeholders as they work to improve care for people living with glomerular diseases.

The ASN Home Dialysis Project has hosted 90 nephrology fellows in the ASN Home Dialysis University Home Dialysis Scholarship Program since 2023, with funding from CDC. Participants in the program attend the Home Dialysis University and participate in a virtual longitudinal education series. Sixty additional fellows will begin the program this month. Additionally, ASN is developing a program to recognize home dialysis centers that meet a set of criteria to be considered a center of excellence. ASN anticipates piloting the program in 2026 and seeking external comments for refinement prior to the official launch.

ASN also recognizes the importance of providing professional growth opportunities to its early-career members. The newly launched Fostering Innovative Leaders in Nephrology and Dialysis is a 1-year virtual leadership training program, providing mentorship, leadership skills development, and networking opportunities for early-career nephrology professionals (9). ASN plans to provide ongoing opportunities for these future kidney leaders to use their newly acquired skill sets within ASN, other professional kidney organizations, or their professional practice (academia, community practice, or other work settings).

If not us, then who?

I have been incredibly fortunate to have had a fulfilling career in nephrology. Before the last 5 years (since the results of the Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation [CREDENCE] trial), however, I did not realize how much we had been missing in the 25 years prior or how profoundly we were failing our patients. I personally never want to go back to the so-called "good old days" when all we could do was count the days, weeks, and months until we started patients on a 50-year-old treatment with a 3-year mortality of 50%.

On behalf of the more than 850 million people worldwide living with kidney diseases, we must grasp this opportunity to change kidney care for the better, leveraging the collective vision and action of our membership. As I continue to engage ASN members—diverse in backgrounds, expertise, and passions yet united by a common purpose to improve care—it is clearer to me than ever that the society's members are its greatest strength. To quote my mentor and friend, Ronald J. Falk, MD, FASN, from his ASN President's Address in 2012, "We must challenge each other, all of us who care for patients, to ask our patients how we may restore their health" (10). If not us, if not you, then who? ■

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The author thanks ASN Executive Vice President Tod Ibrahim and other members of ASN staff for their contributions to this editorial. To comment on Dr. Roy-Chaudhury's editorial, please contact email@asn-online.org.

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ASN Advocacy Efforts Facilitate Prevention, Early Detection, and Equitable Intervention

https://doi.org/10.62716/kn.001412025

New diagnosis code for APOL1-mediated kidney disease

The Centers for Disease Control and Prevention's (CDC's) *International Statistical Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) Coordination and Maintenance Committee recently approved the creation of a new diagnosis code specifically for apolipoprotein L1 (APOL1)-mediated kidney disease (AMKD). This important development represents a major step forward in recognizing and addressing a condition that disproportionately affects individuals of Sub-Saharan African ancestry and contributes significantly to health disparities in kidney disease outcomes. The new code, *ICD-10-CM* N07B: "Hereditary nephropathy, not elsewhere classified, with APOL1-mediated kidney disease (AMKD)," is scheduled to become effective for clinical use beginning in 2026.

In May 2024, ASN sent a formal letter to the CDC's *ICD-10-CM* Coordination and Maintenance Committee in support of the proposal to create this code (1). In the letter, ASN emphasized that establishing a specific *ICD-10-CM* code for AMKD is critical to improving care for people who are affected by this condition. It explained that a unique diagnostic code will enable health care practitioners to more precisely diagnose and document the condition, facilitate earlier intervention, and enhance clinical tracking and data-collection efforts. Furthermore, the letter relayed that the code will also increase disease visibility within health systems and among researchers, which is essential for understanding the epidemiology of AMKD and addressing its impact on vulnerable populations.

Moreover, ASN highlighted that the creation of a dedicated code will support ongoing and future research efforts, including the development and evaluation of targeted therapies. Currently, no treatment approved by the US Food and Drug Administration exists specifically for AMKD, but several promising candidates are under investigation. Having a specific code in place will assist in identifying eligible patients for clinical trials and help in the postmarket surveillance of new treatments once approved.

By supporting the adoption of this code, ASN reinforces its commitment to advancing kidney health equity and ensuring that individuals at increased genetic risk for kidney diseases receive the attention, resources, and care they need.

ASN receives Encoding Equity grant

ASN received a $100,000 grant to support its "Encoding Equity: ASN eGFR [Estimated Glomerular Filtration Rate] Toolkit 2.0" project (2), which aims to promote health equity by examining and improving the use of race in clinical kidney care. The grant is one of eight awarded by the Council of Medical Specialty Societies through its Encoding Equity Alliance, launched in 2024, with support from the Doris Duke Foundation. The initiative supports projects that assess and revise clinical guidelines and algorithms to ensure that they are evidence-based, equitable, and designed to improve outcomes for all patients.

The original ASN eGFR Toolkit (3), launched in 2024, serves as a key resource for kidney professionals on best practices for GFR testing, promoting early kidney disease detection, and advancing health equity. ASN's Health Care Justice Committee will lead the project to enhance the original toolkit's ability to identify and address persistent misconceptions about the removal of race from eGFR calculations.

With support from this grant, ASN will develop a comprehensive communications toolkit aimed at educating and engaging nephrologists, other health care professionals, and patients. The central goal of the project is to create messaging that is tailored to appropriate audiences, created by physicians, and delivered by trusted messengers to engage with people at all levels of awareness.

ASN underscores support for trusted, evidence-based preventive care

ASN has partnered with other health care groups to urge congressional leadership to protect the integrity of the US Preventive Services Task Force (USPSTF), which is an independent, volunteer panel of experts that is supported by the Agency for Healthcare Research and Quality (AHRQ). Since 1984, USPSTF has used rigorous methodologies and significant public input to formulate recommendations based on research, data, and evidence.

Senate and House leaders receiving the request for support of USPSTF are Senator Bill Cassidy, MD (R-LA), chair of the Senate Health, Education, Labor, and Pensions (HELP) Committee; Senator Bernie Sanders (I-VT), ranking member of the Senate HELP Committee; Congressman Brett Guthrie (R-KY-02), chairman of the House Committee on Energy and Commerce (E&C); and Congressman Frank Pallone (D-NJ-06), ranking member of the House Committee on E&C.

ASN and other groups underscored the value of USPSTF as a scientifically independent, volunteer panel of national experts in prevention and evidence-based medicine that has issued nearly 300 evidence-based recommendations across 90 different topics to support preventive care and help people live healthier, longer lives. The current panel of 16 members features experts in clinical medicine, scientific research, and public health, and members are appointed by the US Department of Health and Human Services (HHS) secretary to serve 4-year terms. All members are extensively vetted for conflicts of interest, and their service is completely voluntary and uncompensated.

Federal policymakers rely on USPSTF recommendations, including the Centers for Medicare & Medicaid Services, CDC, and the Health Resources and Services Administration. Notably, under the Affordable Care Act, insurers must provide cost-free coverage for preventive services that have been recommended by USPSTF, such as lung and colorectal cancer screenings, behavioral counseling, prevention of maternal depression, childhood vision screenings, adult diabetes screenings, and many more.

On June 27, the US Supreme Court upheld the requirement for cost-free coverage of preventive services recommended by USPSTF under the Affordable Care Act in *Kennedy v Braidwood*. In its ruling, the court affirmed the constitutionality of USPSTF and emphasized the long-standing authority of the secretary of HHS to appoint and remove task force members at will. In light of this decision, it is critical that Congress acts to protect the integrity of USPSTF from both intentional and unintentional political interference. The loss of trustworthiness in the rigorous and nonpartisan work of the task force would devastate patients, hospital systems, and payors, as misinformation creates barriers to accessing lifesaving and cost-effective care.

To maintain USPSTF's objectivity, effectiveness, and public trust, the following structures of the task force must remain intact:

- limited 4-year terms for members to ensure that the panel evolves alongside scientific developments;
- staggered membership rotation (about one-quarter of members rotate each year) to provide continuity and institutional knowledge;
- membership consisting of experienced primary care clinicians from institutions across the United States, ensuring both relevant expertise and broad geographic representation;
- volunteer service to eliminate financial incentives and reinforce independence;
- rigorous conflict-of-interest vetting conducted for all candidates and reviewed by AHRQ, both before appointment and as each new topic review begins;
- open-member nominations process announced annually in the *Federal Register*, encouraging broad public participation;
- scientific and public health input into appointments as USPSTF and AHRQ leadership reviews all nominations, interviews promising candidates, and then recommends to the secretary who should be appointed; and
- the secretary endorses and appoints all of USPSTF's recommended members, preserving scientific integrity across administrations.

ASN believes USPSTF's transparent, rigorous, and scientifically independent process is a national asset. ASN urges Congress to protect and preserve USPSTF's current structure and operations to ensure that everyone continues to benefit from trusted, evidence-based preventive care. ■

To keep track of ASN's policy efforts, follow coverage in *Kidney News* and the ASN podcast feed, and visit ASN's Kidney Health Advocacy webpage (https://www.asn-online.org/policy/kidney-health.aspx). For real-time updates from ASN Policy, follow @ASNAdvocacy on X.

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Steroid-Resistant Nephrotic Syndrome in Youths: Prognostic Implications

https://doi.org/10.62716/kn.001432025

Among children with nephrotic syndrome, steroid resistance is associated with substantially increased risks of kidney failure, chronic kidney disease (CKD), and death, according to a meta-analysis in *Nephrology Dialysis Transplantation*.

In a systematic review, the researchers identified 229 studies including 32,712 children with idiopathic nephrotic syndrome. Most were single-center, retrospective cohort studies and included patients with both steroid-resistant nephrotic syndrome (SRNS) and steroid-sensitive nephrotic syndrome (SSNS).

Outcome analyses included data on kidney failure in 20,699 patients; CKD, including kidney failure, in 2325 patients; and all-cause mortality in 13,779 patients. The median follow-up was 5.1 years.

Rates of all three adverse outcomes were sharply elevated in children with steroid-resistant disease. Pooled incidence of kidney failure was 2.65 per 1000 person-years in children with SSNS compared with 33.34 per 1000 person-years in those with SRNS. Steroid resistance was also associated with increased incidence of CKD (46.90 versus 3.80 per 1000 person-years) and death (12.52 versus 2.30 per 1000 person-years). Kidney failure and infections were the most common causes of death.

Rates of CKD and death associated with steroid resistance were lower in more recent years. On analysis of 899 children from 13 studies, only 16 cases of incident cancer were identified.

The study is the first systematic review of evidence on medium- to long-term outcomes in pediatric nephrotic syndrome. Children with SRNS have higher rates of kidney failure, CKD, and death, all of which occur at "very low" rates among patients with SSNS. The researchers emphasize the need for prospective studies to establish long-term kidney function and mortality in patients receiving modern immunosuppressive regimens [Robinson CH, et al. Kidney function and mortality in childhood nephrotic syndrome. *Nephrol Dial Transplant*, published online July 2, 2025. doi: 10.1093/ndt/gfaf118]. ■

Based on KRT Only, Registries Miss Many Cases of Kidney Failure

https://doi.org/10.62716/kn.001442025

Kidney failure registries, based solely on initiation of kidney replacement therapy (KRT), may miss up to two-thirds of patients with incident kidney failure, according to a report in *Kidney International*.

Using population-based health data from Alberta, Canada, the researchers identified a cohort of 6995 patients who initiated KRT between 2008 and 2019. Of these, approximately one-half (3475 patients) started KRT with no previous documentation of kidney failure based on the estimated glomerular filtration rate (eGFR). In a cohort of 9691 patients who developed kidney failure during the same period, nearly two-thirds (6216 patients) were identified on the basis of eGFR.

Patients in the kidney failure cohort were older and more likely to be female compared with the KRT cohort. The kidney failure cohort had lower rates of hospitalizations, emergency department visits, and nephrology consultations compared with the KRT cohort.

The annual incidence rate of KRT was 212 cases per million population compared with 293 per million for kidney failure. Thirty-four percent of patients who met eGFR criteria died within 5 years without initiating KRT. In both sexes, the incidence of eGFR-based kidney failure increased significantly with age. Women were less likely to receive KRT and more likely to die without receiving KRT.

Most kidney failure registries enroll patients only after they initiate KRT, potentially missing those who never receive KRT. The new findings suggest that using KRT as the sole criterion captures only one-third of incident kidney failure cases.

Current registries may over-represent healthier survivors who meet eGFR criteria before starting KRT while under-representing women and older patients. The researchers conclude: "Incorporating eGFR measurements to expand kidney failure data collection initiatives can potentially improve early disease identification, equity of [health care] planning, and outcome reporting for all affected individuals" [Liu P, et al. Integrating estimated glomerular filtration rate and kidney replacement therapy criteria within the definition of kidney failure. *Kidney Int,* published online July 4, 2025. doi: 10.1016/j.kint.2025.06.015]. ■

Diet and Nutrition in Children With Chronic Kidney Disease

More on diet, nutrition, and exercise starting on page 21

By Kanwal Ojha and Anuradha Gajjar

https://doi.org/10.62716/kn.000912025

People with kidney diseases have myriad needs that require a multidisciplinary approach to address. A suboptimal diet continues to be one of the top causes of deaths globally, which is why nutrition is one of the key pillars in optimizing the health of people with kidney diseases. Dietary intervention is a key component of therapy, specifically for people living with chronic kidney disease (CKD), in an attempt to reduce the symptoms and metabolic complications that characterize various kidney diseases (1). In particular, children with CKD often experience growth failure due to growth hormone resistance and thus have even more of a need for key nutrients that are not sufficiently met by most diets (2). Recent studies have shown that despite increased patient education on the importance of nutrition, there continues to be a gap between the actual consumption of sodium, phosphorus, protein, and calories and what is recommended for these individuals, highlighting a need for more robust nutritional counseling and monitoring. It is essential for health care professionals to approach patient encounters as an opportunity to offer and educate families on evidence-based food and nutritional interventions.

Although the initiation of a kidney-friendly diet often starts with limiting salt and protein intake, as disease progresses to advanced stages or kidney failure, a full kidney-friendly diet requires intentional nutritional changes that can be a stark difference from what many people are used to consuming (3). Emerging studies suggest that a plant-based diet or Dietary Approaches to Stop Hypertension (DASH) diet can slow the progression of CKD. Plant-based diets can help lower blood pressure, manage blood sugar levels, assist in weight management, and reduce metabolic acidosis, all of which are key factors in kidney diseases (4). A DASH diet, on the other hand, focuses more specifically on normalizing blood pressure (Figure).

Barriers to access

There are numerous notable barriers that patients have in accessing adequate nutrition. These barriers include, but are not limited to, distance to grocery stores, lack of transportation, hours of grocery store opening, price of nutritious foods, selection of items available at grocery stores, quality of items available at grocery stores, physical disabilities, and time available to go grocery shopping (5). Encountering barriers to healthy food is associated with more frequent use of convenience foods, many of which are highly processed and high in calories, fat, sugar, and salt.

Special considerations for children with CKD

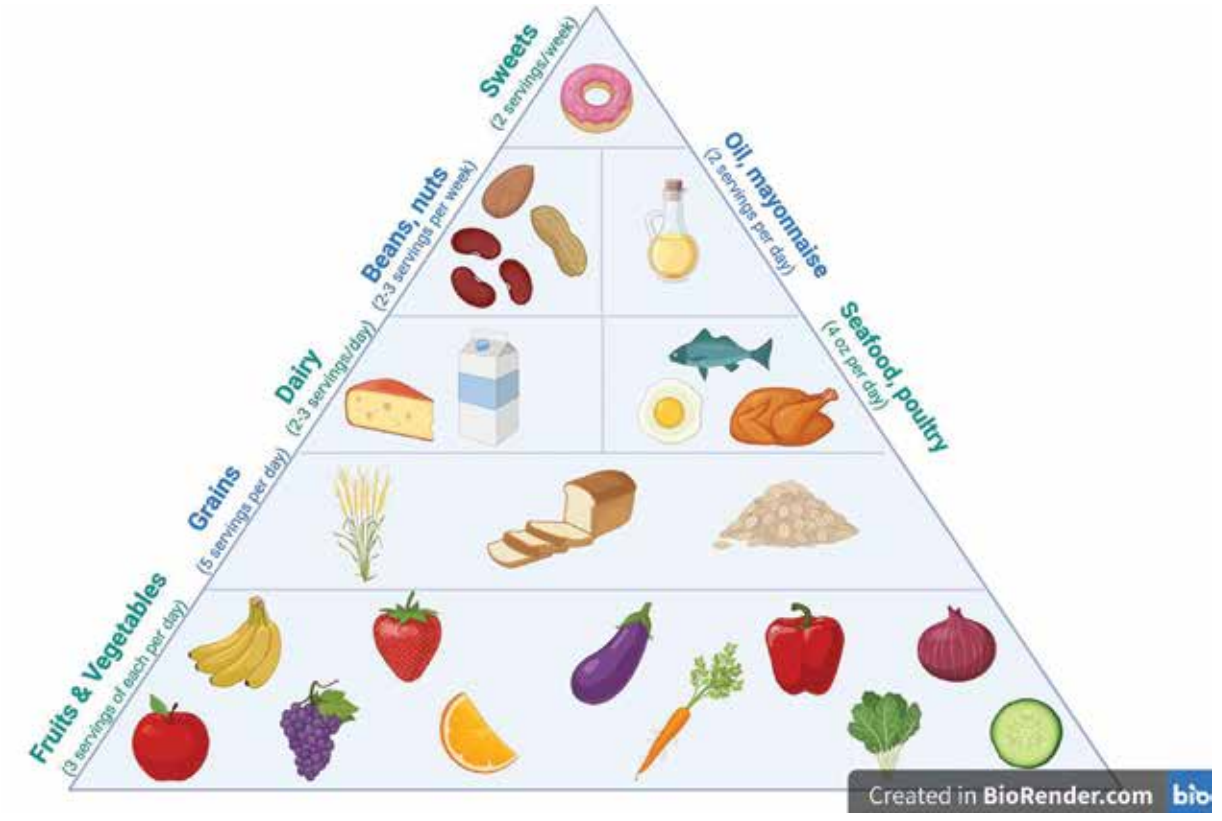
Factors such as body weight, length, waist circumference, skinfold thickness, bone composition, serum albumin and prealbumin, and creatinine index are objective measurements that can be monitored in people with CKD to assess nutritional status. Children, however, are unique, due to the rapid changes that their bodies experience as they develop through childhood and into young adulthood (6). Assessing and addressing the complete nutritional status of this patient population requires comprehensive care, including expertise from an experienced pediatrician dietitian in tandem with a pediatric nephrologist (7). Comprehensive care for people with CKD, but specifically children with CKD, must include renal dietitians available at clinic visits who can create sustainable and individualized plans for children and their families that are updated as they grow and their kidney function changes.

Continued comprehensive interventions are essential in the care of people with CKD. Multidisciplinary, resourceful, and equitable interventions must be taken to address the unique needs of children with CKD and their families to provide opportunities for optimal and sustainable health outcomes. ■

Kanwal Ojha, MD, is a resident physician, and Anuradha Gajjar, MD, is a pediatric nephrologist at Children's National Hospital, Washington, DC.

The authors reports no conflicts of interest.

Figure. Sample DASH diet provided to patients aged 9–11



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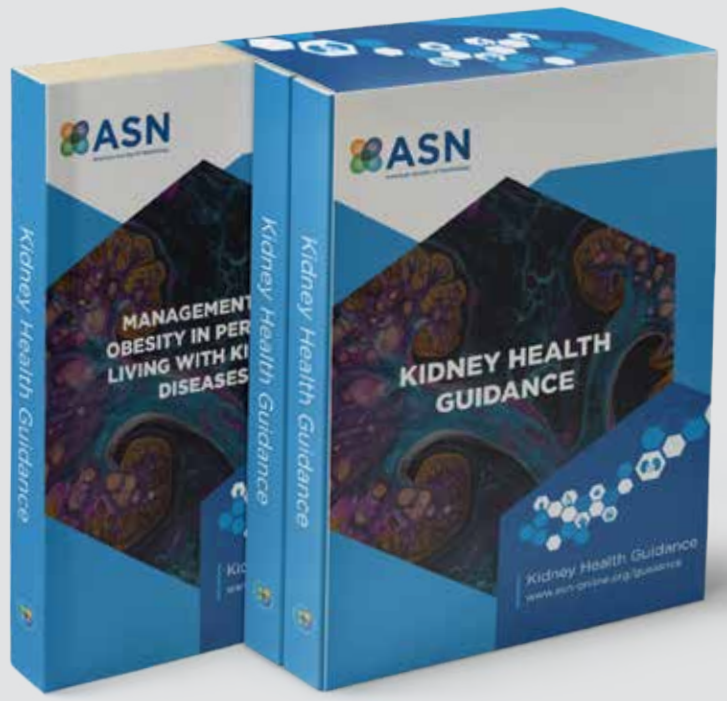
PRACTICE RESOURCE

ASN Kidney Health Guidance

ASN Kidney Health Guidance emphasizes offering succinct, practical, clinical information focused on emerging and challenging issues facing the nephrology community. Developed with a focus on person-centered care, this collection of resources promotes improved outcomes and aims to enhance care across the spectrum of kidney health and diseases.



Access Today

https://journals.lww.com/asnjournals/Pages/ASN-Kidney-Health-Guidance.aspx.

For additional information, please visit the ASN website.

ASN American Society of Nephrology | JASN Journal of the American Society of Nephrology

Business Round-Up: Q1–Q2 2025 Activity in the Nephrology Industry

By Melissa West

https://doi.org/10.62716/kn.001392025

To best understand the evolving landscape of health care, ASN staff regularly monitors leading news and media outlets for developments related to the business of health care. This ongoing review captures updates on regulatory approvals, scientific advancements from industry, investments, mergers and acquisitions, and more. The resulting inventory is compiled into a quarterly report, published biannually in *Kidney News*, to keep the nephrology community informed about the latest changes and innovations in the industry.

Beyond identifying key advancements in kidney care, this activity supports ASN's efforts to track and understand trends across health care and other medical specialties—ultimately, helping advance the society's work toward a world without kidney diseases.

The following summaries are generated from over 800 data points collected from January 1 to June 30, 2025. In addition to the summaries presented, several additional areas of focus are worth highlighting from the first half of 2025:

Artificial intelligence

As we end the first half of the year, it is imperative that leaders think about the impact and adoption of artificial intelligence (AI) on their business. Advancing at record speed and said to be the biggest change on humankind since the advent of the internet, many AI articles discuss regulation, validation of tools, and frameworks to ensure safety of patient data. Additionally, the incoming National Institutes of Health director and US Food and Drug Administration (FDA) commissioner have prioritized the adoption of AI to enhance efficiency and meet their chronic disease agenda. In kidney care, large companies and academic centers are leaning into AI with strategic planning and hiring of experts to help their businesses adapt as AI evolves.

To support the kidney community in this regard, ASN launched an online discussion community, *AI-Powered Kidney Care Network*, which provides regular posts on notable articles covering AI tools or research. You can join this community as an ASN member through the ASN Communities page (https://community.asn-online.org/home), and remember to set your ASN Communities notifications to receive new posts.

Cell and gene therapy

With the approval of gene therapies for sickle cell disease in December 2024, journalists have been tracking cell and gene therapy in 2025. Autoimmune diseases seem to be the priority outside of cancer treatments, especially for chimeric antigen receptor T cell therapies. Several companies are advancing products for kidney-related diseases, including Kyverna Therapeutics and Cabaletta Bio. Other large pharmaceutical companies are acquiring or partnering with companies to incorporate the techniques into their development programs. As cell and gene therapies are advancing, key leaders at FDA's Center for Biologics Evaluation and Research have resigned, leading some to wonder what comes next for the cell and gene therapy pipelines and programs.

Cardiovascular, kidney, and metabolic health

It has become clear that companies are prioritizing obesity and cardiovascular pipelines through research and development as well as acquisitions. A core pillar in these strategic decisions is slowing the progression of kidney diseases. ASN, along with the National Kidney Foundation, DaVita, and the American Kidney Fund, has partnered with the American Heart Association's Cardiovascular-Kidney-Metabolic Health 4-year initiative, ensuring that kidney care remains a priority, and the role of the nephrologist and kidney care team is considered and remains important to the care of people with these complex conditions.

Xenotransplantation

The last 6 months have been incredible for the field of xenotransplantation. Individuals on dialysis have volunteered to be pioneers in receiving pig kidney transplants, with support from many in the kidney community. Additionally, the companies approved for xenotransplantation trials have begun work, with the first 50-patient, 3-year trial to begin later this year or in early 2026.

Policy and advocacy

Nearly 20% of the articles collected during this time relate to priorities of the Trump Administration, including but not limited to updates on the appointment of agency leaders, federal research funding, vaccine recommendations, and drug-pricing strategy. For the latest information on ASN advocacy and public policy, visit the Kidney Health Advocacy page (https://www.asn-online.org/policy/kidney-health.aspx). ■

Summary: Biologic, drug, and device approvals and label extensions

Approval	Category: Type	Product	Company	Reference
Label extension	Drug: Chronic kidney disease indication	Ozempic (semaglutide)	Novo Nordisk	FDA approves Ozempic® (semaglutide) as the only GLP-1 RA to reduce the risk of worsening kidney disease and cardiovascular death in adults with type 2 diabetes and chronic kidney disease (January 28, 2025). https://www.prnewswire.com/news-releases/fda-approves-ozempic-semaglutide-as-the-only-glp-1-ra-to-reduce-the-risk-of-worsening-kidney-disease-and-cardiovascular-death-in-adults-with-type-2-diabetes-and-chronic-kidney-disease-302362466.html
Approval	Drug: C3 Glomerulopathy	Fabhalta® (iptacopan)	Novartis	Novartis receives third FDA approval for oral Fabhalta® (iptacopan)—the first and only treatment approved in C3 glomerulopathy (C3G) (March 21, 2025). https://www.novartis.com/news/media-releases/novartis-receives-third-fda-approval-oral-fabhalta-iptacopan-first-and-only-treatment-approved-c3-glomerulopathy-c3g
510(k) Clearance	Device: Dialysis	X-1 Automated Peritoneal Dialysis (APD) Cycler	Byonyks	Byonyks receives 510(k) clearance for new dialysis machine (May 21, 2025). https://byonyks.com/fda-510k-clearance/

Summary: Biologic, drug, and device development

Activity	Category	Product	Company	Reference
Phase 2 failure	Drug	Monlunabant	Novo Nordisk	Novo flunks kidney disease trial, again linking obesity prospect to neuropsychiatric side effects (February 5, 2025). https://www.fiercebiotech.com/biotech/novo-flunks-kidney-disease-trial-again-linking-obesity-prospect-neuropsychiatric-side
Termination	Drug	Vemircopan	AstraZeneca (acquired through Alexion)	AstraZeneca takes $753M charge on abandoned complement drug from Alexion deal (February 6, 2025). https://endpts.com/astrazeneca-takes-753m-charge-on-abandoned-complement-drug-from-alexion-deal
Interim phase 2 readout	Drug	Glucosylceramide synthase (GCS) inhibitor AL01211	AceLink Therapeutics	AceLink's Fabry hopeful shows potential in mid-stage study (February 10, 2025). https://www.biospace.com/drug-development/acelinks-fabry-hopeful-shows-potential-in-mid-stage-study
Supplemental new drug application (sNDA) submission	Drug	Sparsentan	Travere Therapeutics	Travere Therapeutics to submit sNDA for FILSPARI® (sparsentan) in FSGS (February 11, 2025). https://ir.travere.com/news-releases/news-release-details/travere-therapeutics-submit-snda-filsparir-sparsentan-fsgs
Phase 1/2a results	Drug	ARO-C3	Arrowhead Pharmaceuticals	Arrowhead Pharmaceuticals announces topline results from part 2 of phase 1/2 study of ARO-C3 in patients with IgA nephropathy (March 10, 2025). https://arrowheadpharma.com/news-press/arrowhead-pharmaceuticals-announces-topline-results-from-part-2-of-phase-1-2-study-of-aro-c3-in-patients-with-iga-nephropathy
Phase 3 plan	Drug	Vafseo	Akebia Therapeutics	Amid Vafseo's US launch, Akebia plots phase 3 study to grow CKD anemia med's reach (March 13, 2025). https://www.fiercepharma.com/pharma/amid-vafseos-us-debut-akebia-plots-late-stage-study-push-ckd-anemia-med-wider-nondialysis

Activity	Category	Product	Company	Reference
Shortage	Device	8-mm FMC Streamline bloodline, with part number SL-2000M2095	B. Braun	FDA warns hemodialysis tubing shortage could continue into autumn (March 17, 2025). https://www.fiercebiotech.com/medtech/fda-warns-hemodialysis-tubing-shortage-could-continue-autumn
FDA alert	Device	Rotarex Atherectomy System	Bard	Update on alert: Atherectomy Catheter System issue from Bard Peripheral Vascular (March 20, 2025). https://www.fda.gov/medical-devices/medical-device-recalls/update-alert-atherectomy-catheter-system-issue-bard-peripheral-vascular
Phase 3 results	Drug	Atacicept	Vera Therapeutics	Vera Therapeutics announces Atacicept achieved 46% proteinuria reduction in ORIGIN phase 3 trial in adults with IgA nephropathy (June 2, 2025). https://ir.veratx.com/news-releases/news-release-details/vera-therapeutics-announces-atacicept-achieved-46-proteinuria
Phase 3 results	Drug	Finerenone	Bayer	Finerenone with empagliflozin in chronic kidney disease and type 2 diabetes (June 5, 2025). https://www.nejm.org/doi/abs/10.1056/NEJMoa2410659
Phase 3 results	Drug	Sibeprenlimab	Otsuka	Otsuka sibeprenlimab phase 3 data show a statistically significant and clinically meaningful proteinuria reduction for the treatment of immunoglobulin A nephropathy (IgAN) (June 6, 2025). https://www.otsuka-us.com/news/otsuka-sibeprenlimab-phase-3-data-show-statistically-significant-and-clinically-meaningful
Phase 2/3 results	Cell therapy	Resecabtagene autoleucel (rese-cel), previously known as CABA-201	Cabaletta Bio	Cabaletta Bio announces new rese-cel safety and efficacy data in patients with myositis, lupus and scleroderma to be presented at the EULAR 2025 Congress (June 11, 2025). https://www.cabalettabio.com/news-media/press-releases/detail/130/cabaletta-bio-announces-new-rese-cel-safety-and-efficacy
Phase 2 results	Drug	Lorundrostat	Mineralys Therapeutics	Mineralys Therapeutics announces positive topline results from phase 2 Explore-CKD trial of lorundrostat for the treatment of hypertension in subjects with CKD and albuminuria (June 17, 2025). https://ir.mineralystx.com/news-events/press-releases/detail/73/mineralys-therapeutics-announces-positive-topline-results
Phase 2/3 results	Drug	Isaralgagene civaparvovec, or ST-920	Sangamo Therapeutics	Sangamo Therapeutics announces positive topline results from registrational STAAR study in Fabry disease (June 24, 2025). https://investor.sangamo.com/news-releases/news-release-details/sangamo-therapeutics-announces-positive-topline-results
Complete response letter	Drug	Oxylanthanum carbonate	Unicycive Therapeutics	Unicycive Therapeutics announces receipt of complete response letter for oxylanthanum carbonate for the treatment of hyperphosphatemia in patients with chronic kidney disease on dialysis (June 30, 2025). https://ir.unicycive.com/news/detail/104/unicycive-therapeutics-announces-receipt-of-complete

Summary: Investments

Company	Amount, $	Type	Reference
Evergreen Nephrology	130 Million	Capital	Evergreen Nephrology raises $130 million to transform and expand access to value-based kidney care (January 7, 2025). https://www.prnewswire.com/news-releases/evergreen-nephrology-raises-130-million-to-transform-and-expand-access-to-value-based-kidney-care-302344770.html
Maze Therapeutics	140 Million	Initial public offering (IPO)	Maze Therapeutics reports fourth quarter and full-year 2024 financial results and recent highlights (March 31, 2025). https://ir.mazetx.com/news-releases/news-release-details/maze-therapeutics-reports-fourth-quarter-and-full-year-2024
Merida Biosciences	121 Million	Series A	Merida Biosciences launches with $121M to create therapeutics for multiple autoimmune and allergic diseases (April 8, 2025). https://meridabio.com/news/merida-biosciences-launches-with-121m-to-create-therapeutics-for-multiple-autoimmune-and-allergic-diseases/
Vantive	1 Billion	Company investment	Former Baxter kidney unit Vantive to invest $1B in digitally enabled therapies (June 2, 2025). https://www.massdevice.com/vantive-invest-1b-digitally-enabled-therapies/

Summary: Mergers, acquisitions, and partnerships

Company	Amount, $	Type	Reference
Vera Therapeutics	Undisclosed	Exclusive license agreement with Stanford University	Vera Therapeutics acquires global rights to novel, next generation dual BAFF/APRIL inhibitor (January 13, 2025). https://ir.veratx.com/news-releases/news-release-details/vera-therapeutics-acquires-global-rights-novel-next-generation
Boston Scientific	540 Million	Acquisition of SoniVie	Boston Scientific snags renal denervation developer SoniVie for $540M (March 3, 2025). https://www.fiercebiotech.com/medtech/boston-scientific-snags-renal-denervation-developer-sonivie-540m
Mallinckrodt	6.7 Billion	Merger with Endo	Mallinckrodt, Endo look to carve out brighter future through $6.7B merger (March 13, 2025). https://www.fiercepharma.com/pharma/mallinckrodt-endo-look-carve-out-brighter-future-through-67b-merger
OPKO Health	60%/40% Agreement	Partnership with Entera Bio	OPKO Health and Entera Bio enter into collaboration agreement to advance oral GLP-1/glucagon tablet candidate into the clinic to treat obesity and metabolic disorders (March 17, 2025). https://www.opko.com/investors/news-events/press-releases/detail/517/opko-health-and-entera-bio-enter-into-collaboration-agreement-to-advance-oral-glp-1glucagon-tablet-candidate-into-the-clinic-to-treat-obesity-and-metabolic-disorders
Amicus Therapeutics	30 Million, up to 560 million milestone payments	Acquisition of Dimerix Limited	Dimerix and Amicus Therapeutics announce exclusive license agreement for DMX-200 in the United States (April 30, 2025). https://ir.amicusrx.com/news-releases/news-release-details/dimerix-and-amicus-therapeutics-announce-exclusive-license
Novartis	800 Million	Acquisition of Regulus Therapeutics	Novartis to acquire Regulus Therapeutics and farabursen, an investigational microRNA inhibitor to treat ADPKD, the most common genetic cause of renal failure (April 30, 2025). https://www.novartis.com/news/media-releases/novartis-acquire-regulus-therapeutics-and-farabursen-investigational-microrna-inhibitor-treat-adpkd-most-common-genetic-cause-renal-failure
Eli Lilly and Company	1.3 Billion	Acquisition of Verve Therapeutics	Lilly to acquire Verve Therapeutics to advance one-time treatments for people with high cardiovascular risk (June 17, 2025). https://investor.lilly.com/news-releases/news-release-details/lilly-acquire-verve-therapeutics-advance-one-time-treatments

Summary: Value-based kidney care (VBC)

Organization	Type	VBC relationship	Reference
Humana	Insurer	Monogram Health	Humana and Monogram Health announce expansion of comprehensive kidney care program (February 13, 2025). https://www.monogramhealth.com/press/humana-and-monogram-health-announce-expansion-of-comprehensive-kidney-care-program/
Memorial Hermann Health System	Nonprofit health system	Monogram Health	Monogram Health and Memorial Hermann launch joint venture (March 4, 2025). https://www.monogramhealth.com/press/monogram-health-and-memorial-hermann-launch-joint-venture/
Zing Health	Insurer	Strive Health	Strive Health expands partnership with Zing Health to provide value-based kidney care to chronic disease population (March 11, 2025). https://strivehealth.com/news/strive-health-expands-partnership-with-zing-health-to-provide-value-based-kidney-care-to-chronic-disease-population/

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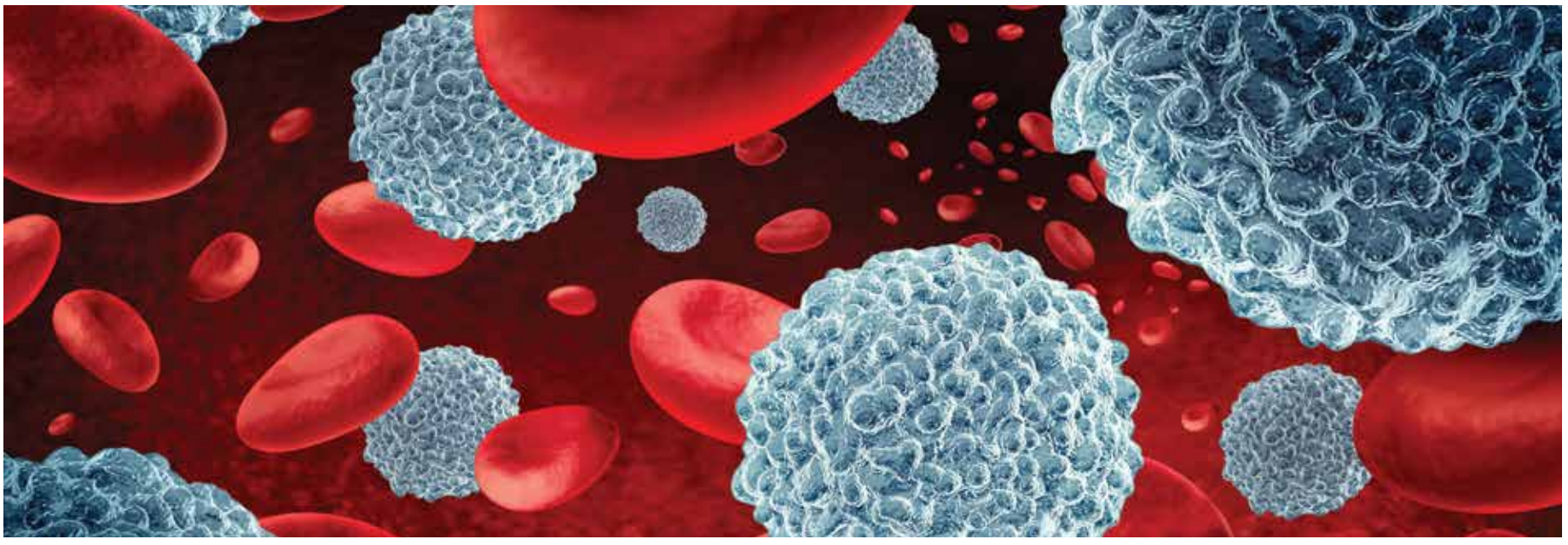

Clonal Hematopoiesis Accelerates CKD Progression

By Mihai Dumbrava and Raad Chowdhury

https://doi.org/10.62716/kn.001022025

Clonal hematopoiesis of indeterminate potential (CHIP) is an age-related expansion of hematopoietic cells carrying leukemia driver mutations harbored by nearly one in five adults aged over 60 years (1). Currently, CHIP is detected through next-generation sequencing as part of hereditary cancer panels and cytopenia evaluations due to its association with hematologic malignancies (2). Beyond the hematologic impact of CHIP, there is growing evidence suggesting downstream cardiovascular and kidney effects through various inflammatory pathways (3, 4). Recent studies have linked CHIP to a higher risk of acute kidney injury and estimated glomerular filtration rate (eGFR) decline (5). However, the effects of CHIP on people with pre-existing chronic kidney disease (CKD), which is characterized by the accumulation of inflammatory infiltrates within the renal interstitium, are unclear to date. Here, we summarize the major renal effects of CHIP driver mutations on CKD.

In a multicohort analysis by Vlasschaert et al. of 5654 individuals with CKD, it was found that CHIP—specifically mutations outside of *DNMT3A*—is associated with CKD progression (6). This comprehensive study examined the effects of CHIP on CKD in four cohorts including the Chronic Renal Insufficiency Cohort; the African American Study of Kidney Disease; individuals with CKD from the BioVU Biorepository; and the Canadian Study of Prediction of Death, Dialysis and Interim Cardiovascular Events. Overall, about one-quarter of the people with CKD had CHIP variants. Carriers of the most common driver mutation, *DNMT3A*, were not at higher risk of CKD progression compared with individuals without CHIP variants. By contrast, patients with non-*DNMT3A* mutations—most often in *TET2*, *ASXL1*, or *JAK2*—had a 64% higher risk of a 50% eGFR decline or kidney failure (hazard ratio [HR], 1.64; 95% confidence interval [CI], 1.00–2.68). Furthermore, the risk of CKD progression was greater among those patients with non-*DNMT3A* CHIP with better baseline kidney function (CKD stage G3 versus G4), suggesting that the effect of CHIP is less pronounced when it is superimposed on already advanced CKD.

Mechanistic work using a CKD mouse model engrafted with the *Tet2* mutant marrow validates the findings of the patient cohort. *Tet2*$^{-/-}$ CHIP mice were associated with a significantly lower eGFR compared with wild-type only upon induction of CKD with dietary adenine administration (57 ± 10 versus 98 ± 13 µL/minute). The renal parenchyma of these mice had increased inflammatory cell infiltration, especially macrophages and neutrophils; expression of proinflammatory cytokines such as interleukin (IL)-6 and IL-1ß; and signs of tubule injury and fibrosis. Together, this suggests that a proinflammatory cytokine blockade with agents such as canakinumab (a monoclonal antibody against IL-1ß) may represent a viable therapeutic strategy to mitigate kidney injury secondary to CHIP-related dysregulated inflammatory activity (7).

Going forward, further mechanistic studies are needed with correlation to human histopathology to elucidate whether CHIP is renally significant. For patients, the screening CHIP status could refine risk stratification in CKD, explain unexpectedly steep declines in eGFR, and identify candidates for anti-inflammatory treatments—representing a new therapeutic avenue in CKD. ■

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The authors report no conflicts of interest.

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3. Jaiswal S, et al. Clonal hematopoiesis and risk of atherosclerotic cardiovascular disease. *N Engl J Med* 2017; 377:111–121. doi: 10.1056/NEJMoa1701719
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5. Vlasschaert C, et al. Clonal hematopoiesis of indeterminate potential is associated with acute kidney injury. *Nat Med* 2024; 30:810–817. doi: 10.1038/s41591-024-02854-6
6. Vlasschaert C, et al.; Chronic Renal Insufficiency Cohort (CRIC) Study Investigators. Clonal hematopoiesis of indeterminate potential and progression of CKD. *J Am Soc Nephrol* (published online April 9, 2025). doi: 10.1681/ASN.0000000680
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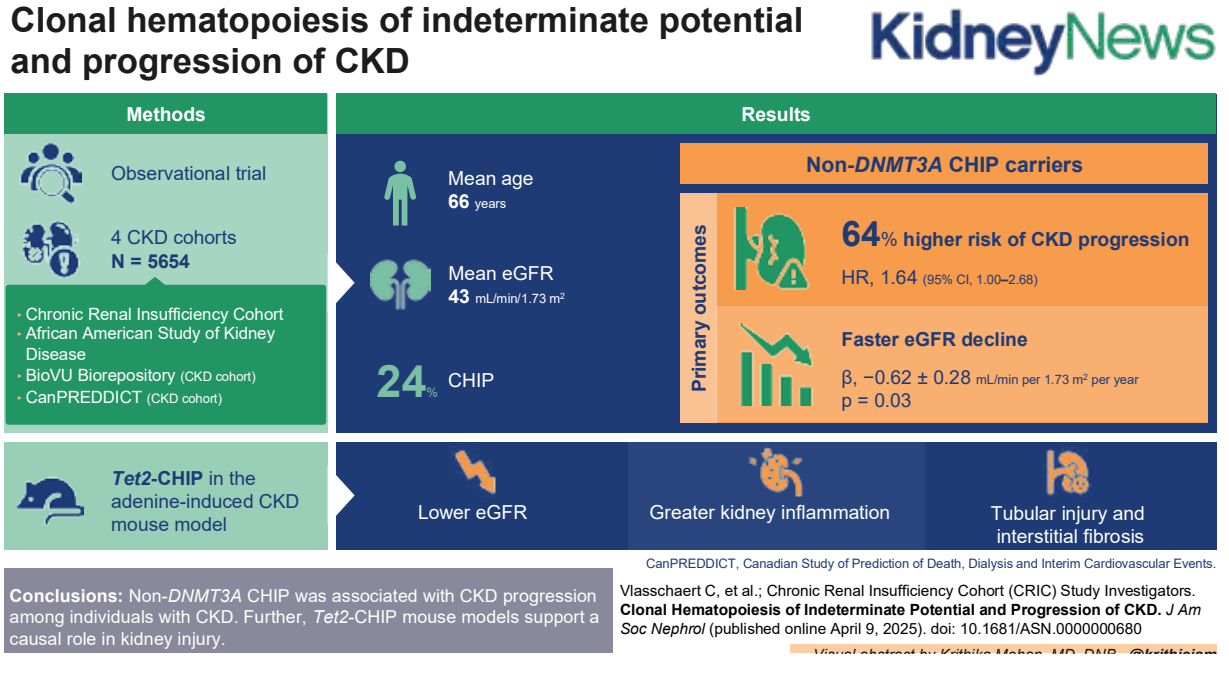


Patient, Advocate, and Inspirational Voice Calls for a Kidney Care Revolution

By Lisa Schwartz

https://doi.org/10.62716/kn.001322025

Diagnosed with autosomal dominant polycystic kidney disease (ADPKD) in 2017, Arnold Davis has since emerged as a powerful patient advocate and motivating voice for reshaping the future of nephrology. Davis has set out to inspire the next generation of nephrologists as he speaks around the country, encouraging physicians and researchers to lead a revolution in kidney care. His call for innovation in kidney disease treatment has been fueling a renewed passion for reform and ingenuity.

Through social media, public speaking, and national committee roles, Davis is inspiring the kidney community to lead boldly and think differently. *Kidney News* (*KN*) spoke with Davis about his path from diagnosis to advocacy and his urgent call for change.

KN: Tell us how your journey with ADPKD began.

Davis: My father had PKD and was told it wouldn't impact his life expectancy. But in his 60s, his health deteriorated, and he ended up on dialysis before receiving a kidney transplant from my aunt. He lived another 10 years, thanks to the care from his doctors and my mother. After he passed away, I began to suspect my own high blood pressure was a sign of a similar kidney disease. I got tested and was soon after diagnosed with ADPKD.

KN: How have clinicians influenced your journey with ADPKD? What specific qualities make an exceptional nephrologist, in your view?

Davis: Great kidney doctors see the whole person. They make you feel like you have a partner in this lifelong journey. I have been very fortunate to have Arlene Chapman, MD, The University of Chicago Medicine—an exceptional clinician and pioneer in ADPKD—as my physician. Very early in my diagnosis, I had the good fortune of encountering Rebecca Frazier, MD, Duke University School of Medicine, who was a nephrology fellow at Northwestern University at the time. I remember attending my first clinic appointment with a list of drugs in clinical trials, determined to find a treatment, and she had already reviewed the major ADPKD trial website before our second visit. She encouraged me, made me feel heard, and was incredibly generous with her time.

Five years later, at the STARS [ASN Kidney Students and Residents] luncheon at ASN Kidney Week 2023, a student asked me when I felt most human as a patient. Knowing that in a few short years they too would be fellows, I told them about Dr. Frazier's incredible ability to connect with patients and how her care made all the difference to me. These were qualities they, too, should aspire to possess.

KN: You have described yourself as "the over-the-top patient." What was going through your mind when you were first diagnosed?

Davis: My diagnosis and seeing the limited treatments for PKD made me dive deep into the field of nephrology to find answers. I was shocked by how little progress had been made in treating kidney diseases. I couldn't believe that dialysis had not fundamentally changed in decades. The pool of new nephrologists and students interested in the field has been waning. And, I was frustrated to learn that the only drug to treat or slow down the progression of ADPKD—tolvaptan—had been initially rejected by a US Food and Drug Administration panel that included nephrologists. I felt helpless, as I had to wait for this drug to finally be approved in the United States. I realized that I had to advocate for myself, for other people living with kidney diseases, and for the future of nephrology, which led me to an incredible community of kidney care professionals on Twitter [now X].

KN: How did discovering the kidney community on social media help launch your advocacy work?

Davis: Social media gave me a platform to speak directly to the nephrology community. I needed an outlet for my frustrations and questions, and I found it through #NephTwitter, an ecosystem of kidney professionals and researchers on X. I started sharing my perspective and challenged this community to envision a future of continuously improving kidney care. The response was overwhelming. I started engaging with nephrologists, researchers, and students who wanted to hear more.

That led to invitations to join advisory boards at The University of Chicago, Northwestern University, and the National Institutes of Health (NIH). Today, my following in this community has grown to over 1600 nephrology professionals who share the desire for change and progress.

KN: You have spoken at major events like Kidney Week, Kidney TREKS [Tutored Research and Education for Kidney Scholars], a National Kidney Foundation Fellows' Night, and to NIH. What is your core message to future and new nephrologists?

Davis: Create a future for nephrology that is unrecognizable from today so that every 5 years, we can look back and see how dramatically this field has changed and grown. I want kidney professionals to keep going forward and never give up; demonstrate a relentless drive to return to nephrology's founding values, in which interdisciplinary thinking combines with technologic advances and a fierce ambition to improve the lives of the 850 million people with kidney diseases.

KN: Why are you so passionate about this idea of an "unrecognizable future" for nephrology?

Davis: Because we have stagnated for too long. Despite decades of care, patients today still face many of the same barriers as my father did. Especially now with potential cuts to NIH funding, our voices need to be heard so that research and development and innovation are not slowed or stopped. The most urgent need within the kidney care community is a shift in mindset. We must believe nephrology can be the most innovative branch of medicine.

I have seen signs of real progress, however. Advances in xenotransplantation and artificial intelligence-powered insights from patient data, new medications like sodium-glucose cotransporter-2 inhibitors and glucagon-like peptide-1 agonists, and policy reforms show that the promise of a brighter future is within our reach.

KN: What is your message to the next generation of nephrologists and kidney professionals?

Davis: Don't play it safe. Do not let impostor syndrome or your insecurities stand in your way. Use the power of your voice. Be the clinician who uses their interest in public policy to influence lawmakers. Believe you will create a better future for kidney care. Advocate for patients.

The field of nephrology is at a crossroads. We can wait and hope someone else will innovate, or we can lead and redefine the future. Imagine if every nephrologist contributed one "mediocre" idea to improve dialysis every year; the compounding effect would be a revolution.

And finally, believe that you are the person who can help make that revolution happen.

For more inspiration, follow Arnold Davis on X (@kidneyrebel) and on Bluesky (@kidneyrebel.bsky.social), where all kidney professionals are encouraged to join the conversation around innovation and bold thinking.

Are you a fellow and have a tip or idea you'd like to share with your fellow peers and the broader kidney community?

Send your idea to the ASN *Kidney News* Fellows First column at kidneynews@asn-online.org

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION

TAVNEOS (avacopan) is indicated as an adjunctive treatment of adult patients with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with standard therapy including glucocorticoids. TAVNEOS does not eliminate glucocorticoid use.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

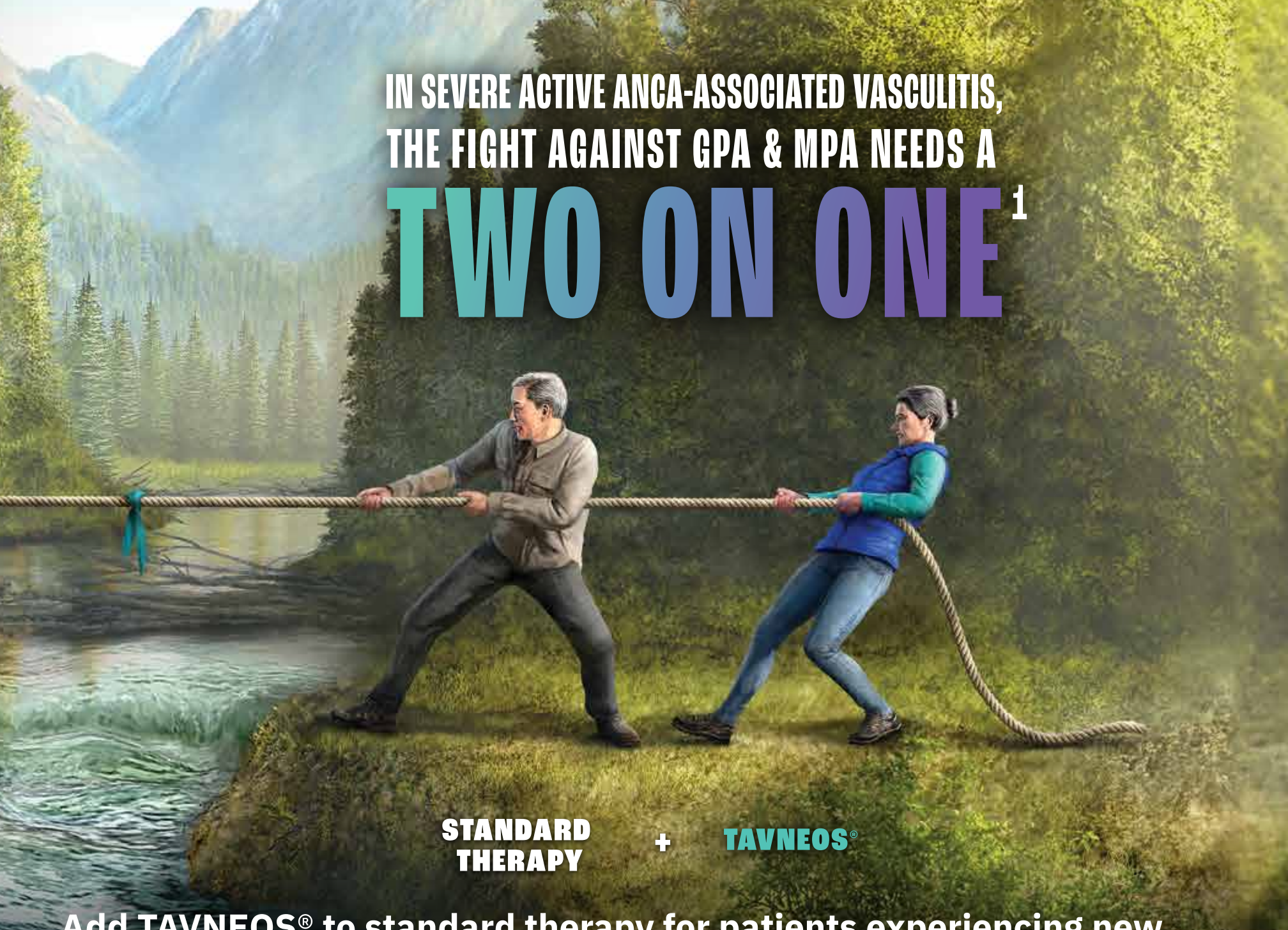
Serious hypersensitivity to avacopan or to any of the excipients.

WARNINGS AND PRECAUTIONS

Hepatotoxicity: Serious cases of hepatic injury have been observed in patients taking TAVNEOS, including life-threatening events. Obtain liver test panel before initiating TAVNEOS, every 4 weeks after start of therapy for 6 months and as clinically indicated thereafter. Monitor patients closely for hepatic adverse reactions, and consider pausing or discontinuing treatment as clinically indicated (refer to section 5.1 of the Prescribing Information). TAVNEOS is not recommended for patients with active, untreated, and/or uncontrolled chronic liver disease (e.g., chronic active hepatitis B, untreated hepatitis C, uncontrolled autoimmune hepatitis) and cirrhosis. Consider the risks and benefits before administering this drug to a patient with liver disease.

Serious Hypersensitivity Reactions: Cases of angioedema occurred in a clinical trial, including 1 serious event requiring hospitalization. Discontinue immediately if angioedema occurs and manage accordingly. TAVNEOS must not be readministered unless another cause has been established.

Hepatitis B Virus (HBV) Reactivation: Hepatitis B reactivation, including life-threatening hepatitis B, was observed in the clinical program. Screen patients for HBV. For patients with evidence of prior infection, consult with physicians with expertise in HBV and monitor during TAVNEOS therapy and for 6 months following. If patients develop HBV reactivation, immediately discontinue TAVNEOS and concomitant therapies associated with HBV reactivation, and consult with experts before resuming.



Add TAVNEOS® to standard therapy for patients experiencing new, relapsing, or persistent disease activity[1,2]

Serious Infections: Serious infections, including fatal infections, have been reported in patients receiving TAVNEOS. The most common serious infections reported in the TAVNEOS group were pneumonia and urinary tract infections. Avoid use of TAVNEOS in patients with active, serious infection, including localized infections. Consider the risks and benefits before initiating TAVNEOS in patients with chronic infection, at increased risk of infection, or who have been to places where certain infections are common.

ADVERSE REACTIONS

The most common adverse reactions (≥5% of patients and higher in the TAVNEOS group vs. prednisone group) were nausea, headache, hypertension, diarrhea, vomiting, rash, fatigue, upper abdominal pain, dizziness, blood creatinine increased, and paresthesia.

DRUG INTERACTIONS

Avoid co-administration of TAVNEOS with strong and moderate CYP3A4 enzyme inducers. Reduce TAVNEOS dose when co-administered with strong CYP3A4 enzyme inhibitors to 30 mg once daily. Consider dose reduction of CYP3A4 substrates when co-administering TAVNEOS. Co-administration of avacopan and 40 mg simvastatin increases the systemic exposure of simvastatin. While taking TAVNEOS, limit simvastatin dosage to 10 mg daily (or 20 mg daily for patients who have previously tolerated simvastatin 80 mg daily for at least one year without evidence of muscle toxicity). Consult the concomitant CYP3A4 substrate product information when considering administration of such products together with TAVNEOS.

TAVNEOS is available as a 10 mg capsule.

To report a suspected adverse event, call 1-833-828-6367. You may report to the FDA directly by visiting www.fda.gov/medwatch or calling 1-800-332-1088.

References: 1. TAVNEOS [package insert]. Cincinnati, OH: Amgen Inc. **2.** Chung SA, Langford CA, Maz M, et al. *Arthritis Rheumatol*. 2021;73(8):1366-1383.

Please see Brief Summary of Prescribing Information for TAVNEOS® on the following pages.

05/25 USA-569-81131

AMGEN

BRIEF SUMMARY OF PRESCRIBING INFORMATION
TAVNEOS® (avacopan) capsules, for oral use
Please see package insert for full Prescribing Information.

INDICATIONS AND USAGE

TAVNEOS is indicated as an adjunctive treatment of adult patients with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with standard therapy including glucocorticoids. TAVNEOS does not eliminate glucocorticoid use.

CONTRAINDICATIONS

TAVNEOS is contraindicated in patients with serious hypersensitivity reactions to avacopan or to any of the excipients *[see Warnings and Precautions (5.2)]*.

WARNINGS AND PRECAUTIONS

Hepatotoxicity

Serious cases of hepatic injury have been observed in patients taking TAVNEOS. During controlled trials, the TAVNEOS treatment group had a higher incidence of transaminase elevations and hepatobiliary events, including serious and life-threatening events *[see Adverse Reactions (6.1)]*.

Obtain liver test panel (serum alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase, and total bilirubin) before initiating TAVNEOS, every 4 weeks after start of therapy for the first 6 months of treatment and as clinically indicated thereafter.

If a patient receiving treatment with TAVNEOS presents with an elevation in ALT or AST to >3 times the upper limit of normal, evaluate promptly and consider pausing treatment as clinically indicated.

If AST or ALT is >5 times the upper limit of normal, or if a patient develops transaminases >3 times the upper limit of normal with elevation of bilirubin to >2 times the upper limit of normal, discontinue TAVNEOS until TAVNEOS-induced liver injury is ruled out *[see Adverse Reactions (6.1)]*.

TAVNEOS is not recommended for patients with active, untreated and/or uncontrolled chronic liver disease (e.g., chronic active hepatitis B, untreated hepatitis C, uncontrolled autoimmune hepatitis) and cirrhosis. Consider the risk and benefit before administering TAVNEOS to a patient with liver disease. Monitor patients closely for hepatic adverse reactions *[see Use in Specific Populations (8.7)]*.

Hypersensitivity Reactions

TAVNEOS may cause angioedema *[see Adverse Reactions (6.1)]*. In clinical trials, two cases of angioedema occurred, including one serious event requiring hospitalization. If angioedema occurs, discontinue TAVNEOS immediately, provide appropriate therapy, and monitor for airway compromise. TAVNEOS must not be re-administered unless another cause has been established. Educate patients on recognizing the signs and symptoms of a hypersensitivity reaction and to seek immediate medical care should they develop.

Hepatitis B Virus (HBV) Reactivation

Hepatitis B virus (HBV) reactivation, including life threatening hepatitis B, was observed in the clinical program.

HBV reactivation is defined as an abrupt increase in HBV replication, manifesting as a rapid increase in serum HBV DNA levels or detection of HBsAg, in a person who was previously HBsAg negative and anti-HBc positive. Reactivation of HBV replication is often followed by hepatitis, i.e., increase in transaminase levels. In severe cases, increase in bilirubin levels, liver failure, and death can occur.

Screen patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with TAVNEOS. For patients who show evidence of prior hepatitis B infection (HBsAg positive [regardless of antibody status] or HBsAg negative but anti-HBc positive), consult physicians with expertise in managing hepatitis B regarding monitoring and consideration for HBV antiviral therapy before and/or during TAVNEOS treatment.

Monitor patients with evidence of current or prior HBV infection for clinical and laboratory signs of hepatitis, or HBV reactivation during and for six months following TAVNEOS therapy.

In patients who develop reactivation of HBV while on TAVNEOS, immediately discontinue TAVNEOS and any concomitant therapy associated with HBV reactivation, and institute appropriate treatment. Insufficient data exist regarding the safety of resuming TAVNEOS treatment in patients who develop HBV reactivation. Resumption of TAVNEOS treatment in patients whose HBV reactivation resolves should be discussed with physicians with expertise in managing HBV.

Serious Infections

Serious infections, including fatal infections, have been reported in patients receiving TAVNEOS. The most common serious infections reported in the TAVNEOS group were pneumonia and urinary tract infections.

Avoid use of TAVNEOS in patients with an active, serious infection, including localized infections. Consider the risks and benefits of treatment prior to initiating TAVNEOS in patients:

- with chronic or recurrent infection
- who have been exposed to tuberculosis
- with a history of a serious or an opportunistic infection
- who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or
- with underlying conditions that may predispose them to infection.

Closely monitor patients for the development of signs and symptoms of infection during and after treatment with TAVNEOS. Interrupt TAVNEOS if a patient develops a serious or opportunistic infection. A patient who develops a new infection during treatment with TAVNEOS should undergo prompt and complete diagnostic testing appropriate for an immunocompromised patient; appropriate antimicrobial therapy should be initiated, the patient should be closely monitored, and TAVNEOS should be interrupted if the patient is not responding to antimicrobial therapy. TAVNEOS may be resumed once the infection is controlled.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Hepatotoxicity *[see Warnings and Precautions (5.1)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.2)]*
- Hepatitis B Virus (HBV) Reactivation *[see Warnings and Precautions (5.3)]*
- Serious Infections *[see Warnings and Precautions (5.4)]*

Clinical Trials Experience

Because the clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The identification of potential adverse drug reactions was based on safety data from the phase 3 clinical trial in which 330 patients with ANCA-associated vasculitis were randomized 1:1 to either TAVNEOS or prednisone *[see Clinical Studies (14)]*. The mean age of patients was 60.9 years (range of 13 to 88 years), with a predominance of men (56.4%) and Caucasians (84.2%). The cumulative exposure to TAVNEOS was 138.7 patient-years. Additionally, two phase 2 trials were conducted in ANCA-associated vasculitis. The cumulative clinical trial exposure from the phase 2 and 3 trials equals 212.3 patient-years.

The most frequent serious adverse reactions reported more frequently in patients treated with TAVNEOS than with prednisone were pneumonia (4.8% TAVNEOS vs. 3.7% prednisone), GPA (3.0% TAVNEOS vs. 0.6% prednisone), acute kidney injury (1.8% TAVNEOS vs. 0.6% prednisone), and urinary tract infection (1.8% TAVNEOS vs. 1.2% prednisone). Within 52 weeks, 4 patients in the prednisone treatment group (2.4%) and 2 patients in the TAVNEOS group (1.2%) died. There were no deaths in the phase 2 trials.

In the phase 3 trial, seven patients (4.2%) in the TAVNEOS treatment group and 2 patients (1.2%) in the prednisone treatment group discontinued treatment due to hepatic-related adverse reactions, including hepatobiliary adverse reactions and liver enzymes abnormalities. The most frequent adverse reaction that led to drug discontinuation reported by > 1 patient and more frequently reported in patients treated with TAVNEOS was hepatic function abnormal (1.8%).

The most common adverse reactions that occurred in ≥5% of patients and higher in the TAVNEOS group as compared with the prednisone group are listed in Table 1.

Table 1: Adverse Reactions Reported in ≥5% of Patients and Higher in TAVNEOS Group vs. Prednisone Group in Phase 3 Trial

Adverse Reaction	Prednisone (N=164) n (%)	TAVNEOS (N=166) n (%)
Nausea	34 (20.7)	39 (23.5)
Headache	23 (14.0)	34 (20.5)
Hypertension	29 (17.7)	30 (18.1)
Diarrhea	24 (14.6)	25 (15.1)
Vomiting	21 (12.8)	25 (15.1)
Rash	13 (7.9)	19 (11.4)
Fatigue	15 (9.1)	17 (10.2)
Upper abdominal pain	10 (6.1)	11 (6.6)
Dizziness	10 (6.1)	11 (6.6)
Blood creatinine increased	8 (4.9)	10 (6.0)
Paresthesia	7 (4.3)	9 (5.4)

N=number of patients randomized to treatment group in the Safety Population; n=number of patients in specified category.

Hepatotoxicity and Elevated Liver Function Tests

In the phase 3 trial, a total of 19 patients (11.6%) in the prednisone group and 22 patients (13.3%) in the TAVNEOS group had hepatic-related adverse reactions, including hepatobiliary adverse reactions and liver enzyme abnormalities. Study medication was paused or discontinued permanently due to hepatic-related adverse reactions in 5 patients (3.0%) in the prednisone group and 9 patients (5.4%) in the TAVNEOS group. Serious hepatic-related adverse reactions were reported in 6 patients (3.7%) in the prednisone group and 9 patients (5.4%) in the TAVNEOS group. A serious hepatic-related adverse reaction was reported in 1 patient in the TAVNEOS group in the phase 2 studies.

Angioedema

In the phase 3 trial, 2 patients (1.2%) in the TAVNEOS group had angioedema; one event was a serious adverse reaction requiring hospitalization.

Elevated Creatine Phosphokinase

In the phase 3 trial, 1 patient (0.6%) in the prednisone group and 6 patients (3.6%) in the TAVNEOS group had increased creatine phosphokinase. One TAVNEOS-treated patient discontinued treatment due to increased creatine phosphokinase.

DRUG INTERACTIONS

CYP3A4 Inducers

Avacopan exposure is decreased when co-administered with strong CYP3A4 enzyme inducers such as rifampin *[see Clinical Pharmacology (12.3)]*. Avoid co-administration of strong and moderate CYP3A4 inducers with TAVNEOS.

CYP3A4 Inhibitors

Avacopan exposure is increased when co-administered with strong CYP3A4 enzyme inhibitors such as itraconazole *[see Clinical Pharmacology (12.3)]*. Administer TAVNEOS 30 mg once daily when co-administered with strong CYP3A4 inhibitors.

CYP3A4 Substrates

Avacopan is a moderate CYP3A4 inhibitor. Co-administration of avacopan and 40 mg simvastatin increases the systemic exposure of simvastatin. While taking TAVNEOS, limit simvastatin dosage to 10 mg daily (or 20 mg daily for patients who have previously tolerated simvastatin 80 mg daily for at least one year without evidence of muscle toxicity). Consider dose reduction of CYP3A4 substrates when co-administering TAVNEOS with CYP3A4 substrates. Consult the concomitant CYP3A4 substrate product information when considering administration of such products together with TAVNEOS *[see Clinical Pharmacology (12.3)]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no adequate and well-controlled studies with TAVNEOS in pregnant women to inform a drug-associated risk. In animal reproduction studies, oral administration of avacopan to pregnant hamsters and rabbits during the period of organogenesis produced no evidence of fetal harm with exposures up to approximately 5 and 0.6 times, respectively, the exposure at the maximum recommended human dose (MRHD) of 30 mg twice daily (on an area under the curve [AUC] basis). Avacopan caused an increase in the number of abortions in rabbits at an exposure 0.6 times the MRHD *(see Animal Data)*.

The background risk of major birth defects and miscarriage for the indicated population are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In an embryo-fetal development study with pregnant hamsters dosed by the oral route during the period of organogenesis from gestation days 6 to 12, avacopan produced an increase in the incidence of a skeletal variation, described as supernumerary ribs, at an exposure that was 5 times the MRHD (on an AUC basis with a maternal oral dose of 1000 mg/kg/day). No structural abnormalities were noted with exposures up to 5 times the MRHD (on an AUC basis with maternal oral doses up to 1000 mg/kg/day).

In an embryo-fetal development study with pregnant rabbits dosed by the oral route during the period of organogenesis from gestation days 6 to 18, avacopan caused an increase in the number of abortions at an exposure 0.6 times the MRHD (on an AUC basis with a maternal oral dose of 200 mg/kg/day), however, no evidence of fetal harm was observed with such exposures. Maternal toxicity, as evidenced by decreased body weight gains, was observed at exposures 0.6 times and higher than the MRHD (on an AUC basis with maternal oral doses of 30 mg/kg/day and higher).

In a prenatal and postnatal development study with pregnant hamsters dosed by the oral route during the periods of gestation and lactation from gestation day 6 to lactation day 20, avacopan had no effects on the growth and development of offspring with exposures up to approximately 5 times the MRHD (on an AUC basis with maternal oral doses up to 1000 mg/kg/day).

Lactation

Risk Summary

There are no available data on the effects of avacopan on the breastfed child or on milk production. It is unknown whether avacopan is secreted in human milk. Avacopan was detected in the plasma of undosed hamster pups nursing from drug-treated dams *(see Animal Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TAVNEOS and any potential adverse effects on the breast-fed infant from TAVNEOS or from the underlying maternal condition.

Animal Data

Avacopan has not been measured in the milk of lactating animals; however, it was detected in the plasma of nursing offspring in a pre- and post-natal development study with hamsters at a pup to maternal plasma ratio of 0.37. This finding suggests that avacopan is secreted into the milk of lactating hamsters *[see Nonclinical Toxicology (13.1)]*.

Pediatric Use

The safety and effectiveness of TAVNEOS in pediatric patients have not been established.

Geriatric Use

Of the 86 geriatric patients who received TAVNEOS in the phase 3 randomized clinical trial for ANCA-associated vasculitis *[see Clinical Studies (14)]*, 62 patients were between 65-74 years and 24 were 75 years or older. No overall differences in safety or effectiveness were observed between geriatric patients and younger patients.

Patients With Renal Impairment

No dose adjustment is required for patients with mild, moderate, or severe renal impairment *[see Clinical Pharmacology (12.3)]*. TAVNEOS has not been studied in patients with ANCA-associated vasculitis who are on dialysis.

Patients With Hepatic Impairment

No dosage adjustment is recommended for patients with mild or moderate (as indicated by the Child-Pugh method) hepatic impairment *[see Clinical Pharmacology (12.3)]*. TAVNEOS has not been studied in patients with severe hepatic impairment (Child-Pugh Class C).

The risk information provided here is not comprehensive. The FDA-approved product labeling can be found at www.tavneospro.com or contact Amgen Medical Information at 1-800-772-6436.

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Fueling Kidney Health: Diet, Nutrition, and Exercise

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Getting an appropriate amount of exercise, and eating a balanced, kidney-friendly diet are the cornerstones of managing various kidney diseases. From prescribing the proper amount of protein to preventing the metabolic acidosis and calcium-phosphorus disorders associated with kidney diseases, diet is a major factor in kidney health. Beyond promoting general well-being, regular exercise helps prevent cardiovascular complications, control weight, and keep blood pressure in check. In this special section of *Kidney News*, we discuss the role of diet, nutrition, and exercise—important yet often overlooked aspects of kidney disease management. *Kidney News* thanks Dr. Mayuri Trivedi and Dr. Keiichi Sumida for selecting and coediting these articles.

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The Role of Exercise in CKD Care

By Thomas J. Wilkinson and Hannah M. L. Young

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Physical activity and exercise are key components of a healthy lifestyle. Yet, people living with chronic kidney disease (CKD) are profoundly physically inactive, increasing the risk of adverse clinical events such as premature mortality, morbidity, functional impairment, and an inability to complete activities of daily living (1, 2). Exercise has emerged as a promising nonpharmacologic intervention for people with CKD, with evidence suggesting that it can improve myriad physical and psychological health outcome parameters (3, 4). The inclusion of exercise is endorsed by the management of many major international kidney disease organizations (2, 5), including the Global Renal Exercise Network, an international collaborative of researchers, patients, and clinicians (2, 6).

Clinical benefits and disease modification

Physical activity confers extensive benefits across the spectrum of kidney diseases, including among those on dialysis and those who have undergone kidney transplant (5). Exercise exhibits robust evidence for reducing inflammatory markers and for enhancing functional performance, cognitive function, psychosocial aspects, and cardiorespiratory fitness. In addition, resistance training improves skeletal muscle health, including hypertrophy and strength. Combining aerobic and resistance training is key to achieving an optimized benefit in this population (3, 7). Despite improvements in vascular function, glucose metabolism, and blood pressure, the role of exercise on kidney function itself is still unclear and inconsistent, likely due to small, underpowered, and short-term trials (4).

Safely prescribing exercise for people with CKD

Despite the evidence, patients remain inactive, partly driven by a lack of knowledge and confidence from health care practitioners involved in their management (2). Potential key elements in improving exercise in people with CKD include better education, tools, and training resources among kidney health professionals on exercise recommendations, counseling, prescriptions, and referrals to appropriate professionals for assessment, implementation, and monitoring (6).

Although the risks associated with exercise are low, even in people with long-term conditions, those living with CKD might feel otherwise. An understanding of patients' current health status, derived from discussion and review, is often enough to identify any contraindications to exercise (6). Once cleared, health care professionals should consider how comorbidities and, where applicable, forms of kidney replacement therapy might impact the selection of safe and appropriate exercise.

Patients with a history of falls, or at high risk of falling, should be cautioned against brisk walking because it may increase exposure to factors that can cause falls (8). Instead, these patients should focus on strength and balance training, which have been shown to reduce the incidence of falls in frailer populations. In people undergoing hemodialysis, resistance training is essential; these patients should be counseled that there are no known contraindications to upper-limb training and that it is important to maintain upper-limb function (9). However, they should avoid exercising the limb with a temporary or healing arteriovenous fistula and refrain from upper-limb exercise following dialysis (6). Intradialytic exercise is an effective and convenient option for this population (7). Sit-ups and activities involving full hip flexion should be avoided for those undergoing peritoneal dialysis. Instead, abdominal strengthening may be achieved by performing isometric contractions (10). In kidney transplant recipients, exposure to infectious environments should be avoided (6). In cases of rejection, activity should be decreased in intensity and duration, rather than eliminated. Contact sports or extreme sports are high risk for traumatic damage to the kidney allograft. Health care professionals encountering patients for whom these activities are essential should engage in a shared decision-making process to carefully weigh the benefits and risks of the activity for the individual and explore whether adaptations can be made to reduce the risks. Similarly, prolonged extreme exercise should be considered carefully.

Time to walk the walk

There remains an urgent global need to get people living with CKD to move more. Despite the numerous benefits, exercise remains under-resourced and underappreciated by many. Exercise plays a vital role for people living with kidney diseases, and researchers and clinicians must act strategically to take action. Advancing exercise implementation in CKD care is no longer a question of why but of how—and the time to act is now.

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Boosting Plant-Based Diets in Kidney Disease Management

By Nimrit Goraya and Paula A. Duran

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Chronic kidney disease (CKD) has emerged as a silent epidemic, posing significant challenges to health care systems across the globe. Diet is gaining traction as a major CKD-related risk factor for death and disability (1). The role of plant-based diets (PBDs) is being increasingly explored as a preventative and therapeutic measure. A recent meta-analysis of 31 observational studies involving 176,625 participants showed that the most promising diets for CKD prevention are those low in salt, high in fruits and vegetables, and high in potassium. These diets were associated with 22% reduced odds for risk for CKD, supporting that adherence to a healthy as opposed to an unhealthy diet is associated with reduced risk for CKD (2).

By shifting the paradigm from protein restriction to a proactive inclusion of plant-based foods, clinicians and patients alike can move toward a more comprehensive and sustainable approach to kidney health.

PBD is used to describe eating patterns that include a large proportion of plant-rich foods. These include the Mediterranean diet, modified kidney diet, Dietary Approaches to Stop Hypertension (DASH), and Plant-Dominant Low-Protein Diet (PLADO), which are described in the Table. High in fiber, with a high ratio of fiber-to-animal–based protein, these PBDs are associated with reduced CKD risk (3). A major advantage of PBDs lies in their ability to address critical metabolic disturbances associated with kidney diseases.

PBDs also foster a healthier gut microbiome, which reduces the production of uremic toxins such as p-cresyl sulfate and indoxyl sulfate (4). Diets with a higher animal-based protein-to-fiber ratio are associated with higher serum levels of such uremic toxins (3). This modulation of gut health not only alleviates markers of kidney stress, such as serum creatinine and blood urea nitrogen levels, but also enhances the overall quality of life for patients by addressing fatigue, inflammation, and other debilitating symptoms of CKD.

By significantly reducing dietary acid load, PBDs help combat metabolic acidosis, a common complication in CKD that accelerates disease progression and contributes to bone demineralization. Additionally, potassium derived from plant-based foods is largely bound to nonchloride citrate anions, which facilitate its renal excretion, thereby reducing the likelihood of hyperkalemia while still offering the benefits of potassium's heart-protective qualities (5, 6). Phosphate in PBDs is in the form of phytates (phytic acid) that have much lower gastrointestinal tract absorption than the elemental phosphate in food additives, thereby lowering cardiovascular risk and vascular calcifications (7).

By shifting the paradigm from protein restriction to a proactive inclusion of plant-based foods, clinicians and patients alike can move toward a more comprehensive and sustainable approach to kidney health. Because of the described benefits of PBDs, investigators have studied these diets in people with CKD and have shown similar nutritional status in such patients compared with those ingesting similar amounts of a primarily animal-sourced protein diet (8, 9). Further studies are needed to consider the character (plant vs animal protein) in addition to the amount of daily dietary protein recommended for people living with CKD.

PBDs, however, are not without challenges in their practical application. Limited access to fresh, plant-based ingredients; cultural preferences; and economic disparities might hinder adherence. We suggest following medical nutrition therapy-guided endorsements of kidney-friendly diets and particularly stress the benefits of Mediterranean dietary patterns. Leveraging digital health tools, such as apps that track dietary intake and provide tailored feedback, could further empower patients in managing their conditions effectively. Community initiatives aimed at improving food accessibility can also play a transformative role (10). For example, programs that support urban gardening, provide subsidies for fresh produce, and introduce culturally relevant plant-based recipes can alleviate economic and logistic barriers, encouraging wider adoption of PBDs.

Well-designed and well-conducted randomized controlled trials are needed to provide data for evidence-based guidelines. In conclusion, the results from observational studies, meta-analyses, and clinical reviews by authors highlight the pivotal role of PBDs in kidney disease prevention and management. This lifestyle intervention aligns with the principles of patient empowerment that will translate into improved clinical outcomes and better quality of life. ■

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The authors report no conflicts of interest.

Table. Composition of predominant plant-based diets

Food	Mediterranean diet	Modified kidney diet	DASH	PLADO
Cereals and whole grains	Every meal	Every meal	7–8 Servings/day	Every meal
Fruits and vegetables	3–4 Servings/day	Potassium friendly	4–5 Servings/day	3–5 Servings/day
Olive oil	Every meal	Every meal	2–3 Servings/day	2–3 Servings/day
Fish and seafood	5–6 Times/week	5–6 Times/week	0–2 Servings/day	Minimal
Meat: Poultry	0–2 Times/week	0–2 Times/week	0–2 Servings/day	Minimal
Meat: Red, lean	<4 Times/month	<4 Times/month	0–2 Servings/day	Minimal
Nuts and seeds	1–2 Times/day	1–2 Times/day	1–2 Servings/day	3–4 Servings/day
Sweets	<3 Times/week	<3 Times/week	<5 Times/week	3–5 Times/week
Dairy	2 Servings/day	2 Servings/day	2–3 Servings/day	2–3 Servings/day

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Rooted in Diversity: Rethinking Plant-Based Diets and Gut Microbes for Kidney Health

By Jordan Stanford and Matthew Snelson

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"Beans, beans, they're good for your heart…" is the starting refrain of a song that is sung across schoolyards worldwide. Purported health benefits of beans are partly due to raffinose, a carbohydrate that humans cannot digest because we lack the enzyme α-galactosidase. Instead, raffinose passes through into the colon, where it is fermented by our resident gut microbes (1). Many vegetables contain carbohydrates that are not digestible by human digestive enzymes, collectively referred to as "dietary fiber," which are potent dietary modulators of the gut microbial consortium. Increasingly, the ability to target the microbiome with nutrition interventions is being recognized as important in many diseases, including chronic kidney disease (CKD).

In CKD, communication between the gut and kidneys, referred to as the gut-kidney axis, becomes increasingly disrupted as kidney function declines. Accumulating urea and other waste products can translocate into the gut lumen, where they alter the gut environment, raising colonic pH and shifting the composition of the microbial community (2). CKD has been associated with a loss of beneficial bacteria that produce short-chain fatty acids, combined with an increase in species that produce urease and protease enzymes (3), and convert the dietary amino acids tryptophan and tyrosine into indole and p-cresol, respectively (4). These compounds are subsequently transformed by either the liver or colonic mucosal cells into indoxyl sulfate (IS) and p-cresyl sulfate (PCS) (4). The levels of these uremic toxins in the blood have been linked with accelerated kidney disease progression and higher cardiovascular mortality (5), underscoring the potential clinical significance of these microbial metabolites.

Epidemiologic studies consistently associate higher dietary fiber intakes with improved CKD outcomes, including slower disease progression and improved gut health. Clinical trials using isolated resistant starches and other prebiotic fibers have demonstrated reductions in circulating levels of IS and PCS, along with increases in beneficial gut bacteria such as *Roseburia* and *Ruminococcus*, particularly among participants with more advanced CKD (6).

Vegetables, fruits, legumes, and whole grains are key food groups that naturally provide not only dietary fiber but also plenty of other gut-loving compounds like polyphenols. Plant-based diets, which emphasize these foods, are increasingly being considered in the management of CKD. The Plant-Dominant Low-Protein Diet, which combines moderate protein restriction (0.6–0.8 g/kg/day) primarily from plant sources, has gained traction as a practical, balanced dietary compromise (7). Beyond traditional endpoints like blood pressure or acid-base balance, plant-based diets are increasingly valued for their potential to modulate the gut microbiome. A notable example is the Medika crossover trial, which compared a plant-based very low-protein diet supplemented with keto-analogues and a Mediterranean-style, plant-focused diet with a free diet. Both the very low-protein and Mediterranean diets resulted in statistically significant reductions in uremic toxins and beneficial shifts in the gut microbiota compared with the free diet (8).

Historically, there were concerns that plant-based diets may increase hyperkalemia in people with CKD, yet a majority of studies have not shown a relationship between increased plant food intake and hyperkalemia (9). Although those following plant-based diets do have increased dietary potassium intake, these foods have higher alkalinity, higher fiber content, and low potassium bioavailability, which limit their effects on serum potassium levels (9).

An emerging approach focuses on increasing plant diversity through small, manageable dietary changes, rather than promoting strict veganism or vegetarianism approaches. Examples include adding an extra vegetable (a new "color") to meals, topping salads with nuts or seeds, or incorporating legumes into stews and salads. Supporting this concept, a newly published randomized crossover trial evaluated this approach, comparing a pragmatic, high-diversity plant-based diet (30 or more unique plant types per week) with a low-diversity plant diet (15 or fewer types) (10). The high-diversity diet significantly improved diet quality, reduced dietary acid load, and alleviated symptoms such as constipation. A microbiome analysis showed an increase in beneficial gut microbes, including those with genes involved in producing anti-inflammatory short-chain fatty acids like butyrate or isobutyrate, which was supported by higher plasma concentrations. In contrast, the low-diversity diet led to a loss of 27 microbial species and 33 functional genes. While reductions in IS and PCS were not seen uniformly across all participants, notable improvements were observed in individuals with more advanced CKD and higher baseline toxin levels (10). These findings point to two critical unanswered research questions: 1) Who benefits most from microbiome-targeted dietary strategies? and 2) When (what stage of disease intervention is likely to be most effective)?

As the evidence base grows, it is becoming increasingly clear that flexible, fiber-rich, and diverse plant-based diets offer promising benefits for individuals with CKD, not only in terms of gut microbiome modulation and symptom relief but also in their practicality and sustainability. Moving forward, research focused on a personalized approach that considers individual disease stage, microbiome profile, and dietary preferences may be key to optimizing outcomes. Perhaps in the future, school children of the world will be singing: "Plants, plants, they're good for your kidneys…." ■

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Advancing Potassium Management for Kidney Health: Restricting the Restrictions

By Maryanne Zilli Canedo Silva, Alice Sabatino, and Carla Maria Avesani

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Potassium disorders are common in chronic kidney disease (CKD) due to impaired potassium homeostasis, including altered redistribution and reduced renal excretion. Hyperkalemia (HK), defined as serum potassium above 5.5 mEq/L, is associated with adverse outcomes and increased use of hospital resources (1). In CKD, potassium intake is only one of the potential causes of HK; other contributing factors include diabetes mellitus, gut dysbiosis, constipation, the use of medications that affect potassium balance, impaired renal excretion, and metabolic acidosis (2).

Despite its multifactorial nature, diet has historically been considered one of the main culprits of HK, although available evidence does not support this view (3, 4). With this in mind, dietary counseling for potassium management would benefit from a paradigm shift, focusing on an individualized approach with less restriction of healthy potassium-rich food sources.

Dietary restrictions versus dietary patterns

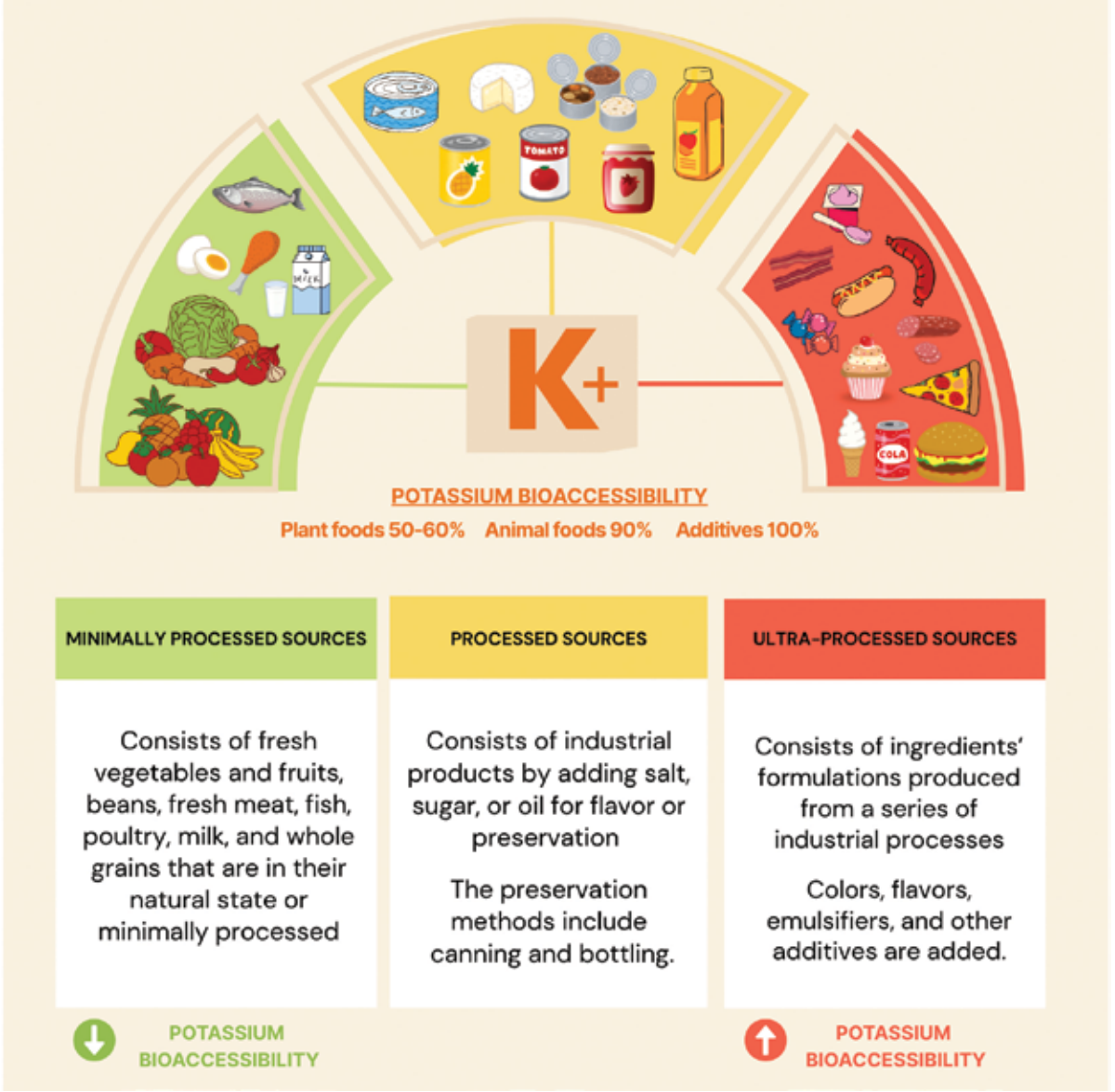
Traditionally, nutritional recommendations for potassium management in people with CKD have focused on restricting intake of fruits, vegetables, legumes, nuts, and whole grains. Consequently, dietary sources of vitamins and minerals, bioactive components, antioxidants, and fiber are reduced, and overall dietary quality worsens. Moreover, the practice of restricting healthy potassium-rich foods is not evidence-based.

First, observational studies have failed to demonstrate an association between potassium intake and serum or plasma levels in people with CKD, both those not on dialysis and on dialysis, as shown in a narrative review (4). Second, to date, the only clinical trial known to us did not show that potassium intake leads to HK. In a randomized crossover trial involving people with stage 3 CKD without HK, the effects of high- and low-potassium diets (3.9 versus 1.6 g/day, respectively) on serum potassium were compared. After 2 weeks on the high-potassium diet, serum potassium increased significantly but not to the level of HK. Moreover, the two participants who developed HK during the trial had medical conditions unrelated to diet that explained the HK episodes (5).

Recently, healthy dietary patterns emphasizing plant-based diets (PBDs) have been proposed as a beneficial approach in CKD due to the synergistic effects of nutrients and associated health benefits (2, 4). Indeed, in two randomized clinical trials prescribing healthy plant-based foods to people with stages 3–4 CKD without HK at baseline, metabolic benefits were observed compared with usual care (6, 7). These benefits included improvements in markers of metabolic acidosis, body weight, lipidemia, systolic blood pressure, and proteinuria, along with reduced medication burden and health care costs—all without inducing HK (6, 7). Even for patients with HK, novel drugs show promise in managing serum potassium, enabling safer, less restrictive dietary recommendations (2, 3). This was recently tested in a feasibility clinical trial including people with stages 4–5 CKD who are not on dialysis and with HK at baseline. Patients were treated with potassium binders plus a PBD without potassium restriction. This combined approach maintained normokalemia during the study (8). Finally, among patients on hemodialysis, adherence to a healthy PBD was not associated with serum potassium levels or HK risk, while improving nutritional status (9).

Based on these findings, the concept of "restricting the restrictions" by promoting an individualized and healthy PBD appears to be the preferred approach, as endorsed by clinical guidelines from Kidney Disease: Improving Global Outcomes (KDIGO) and the Kidney Disease Outcomes Quality Initiative (KDOQI) (2, 3).

Figure 1. Food processing and potassium bioaccessibility



Colors represent different food categories based on processing level. Lower potassium bioaccessibility is found in minimally processed foods, whereas higher bioaccessibility is present in ultra-processed sources.

Beyond food processing: Potassium additives as hidden sources

Potassium bioaccessibility varies by food source (Figure 1). Plant-based foods, recommended as part of a healthy dietary pattern, have potassium bioaccessibility of approximately 50%–60%, lower than that of animal-based foods (~90%) (4, 10).

However, more important than natural sources is the consideration of food additives present in ultra-processed foods. Potassium additives have nearly 100% bioaccessibility, and because they are difficult to identify on food labels, they may represent a significant hidden source of potassium. Thus, food additives may pose a risk for HK (11), although further studies are needed to confirm this hypothesis. Beyond dietary factors, some medications contain potassium salts, such as losartan potassium, which is often prescribed for people with CKD. However, each tablet contains a very small amount of potassium and likely does not significantly affect serum potassium for most people.

Dietary approaches aiming to restore potassium homeostasis

Considering current evidence, we recommend that dietary approaches to managing potassium homeostasis in CKD be individualized and less restrictive. The first step is to assess the intake of ultra-processed foods containing potassium additives and encourage patients to replace them with healthier alternatives, emphasizing minimally processed foods. If necessary, replacing high-potassium with low-potassium healthy foods can be a secondary strategy (Figure 2). Additionally, home-cooked meals using methods such as boiling can help reduce the potassium content of foods (3, 4, 11). ■

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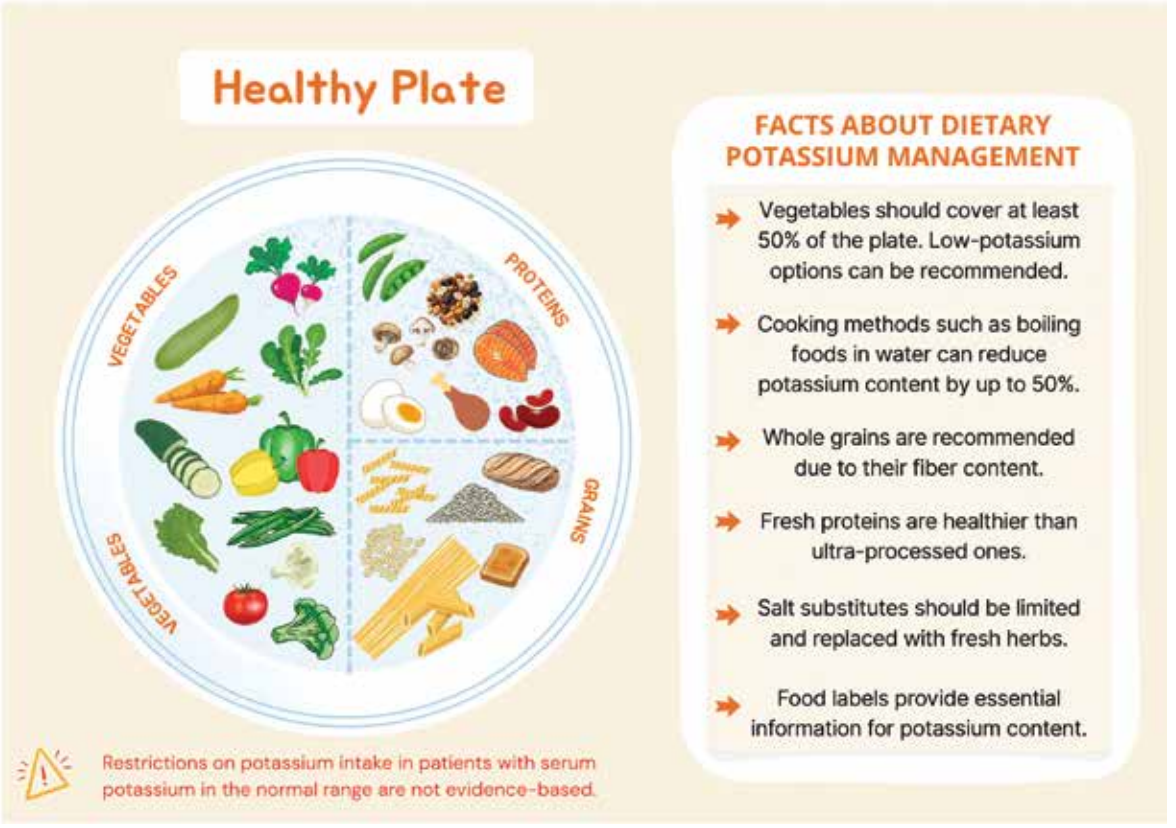
Dr. Silva reports no conflicts of interest. Dr. Sabatino reports participation in the development of The European Society for Clinical Nutrition and Metabolism 2021 clinical guidelines, which contain statements regarding the dietary management of people with chronic and acute kidney failure. Dr. Avesani reports receiving speaker honorarium from Fresenius Medical Care, Abbott Laboratories, and Baxter Healthcare and honorarium as an advisory board member from Fresenius Kabi and Dr. Schär.

Figure 2. Healthy plate and key facts about potassium management in CKD



A visual guide to a kidney-friendly healthy plate, highlighting food choices as part of an individualized strategy management to support potassium balance.

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Optimizing Phosphate Control for Kidney Health: Novel Dietary and Pharmacologic Interventions

By Annabel Biruete and Brandon Kistler

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Phosphorus management is a cornerstone of the treatment for individuals with chronic kidney disease (CKD) (1). The approach depends on the stage of kidney dysfunction but primarily includes limiting dietary phosphorus (1). Once an individual transitions to kidney replacement therapy, additional strategies such as phosphorus-lowering medications (i.e., phosphorus binders and agents that inhibit intestinal phosphorus absorption) and dialysis become essential (2). Effective phosphorus control is critical because hyperphosphatemia plays a central role in the development of CKD-mineral and bone disorder (CKD-MBD) (3). This disorder contributes to biochemical disturbances—most notably, elevated phosphorus, parathyroid hormone, and fibroblast growth factor-23—which lead to impaired bone metabolism, increased fracture risk, and cardiovascular calcification (2).

Dietary phosphorus management has shifted from broad restrictions to a more nuanced approach that emphasizes phosphorus bioaccessibility and bioavailability (4). Bioaccessibility refers to the portion of phosphorus available for intestinal absorption, whereas bioavailability describes the amount that is absorbed and used by the body (4). This paradigm shift moves away from the indiscriminate avoidance of all phosphorus-rich foods and instead considers the impact of the food matrix (4). Plant-based foods high in phytate (e.g., nuts, seeds, and whole grains) generally have low phosphorus bioaccessibility, animal-based foods have moderate bioaccessibility, and foods containing phosphate additives have the highest bioaccessibility (4). As a result, dietary recommendations now aim to limit phosphorus intake from sources with high bioaccessibility—particularly phosphate additives—while allowing more flexibility with plant-based foods (Figure) (4).

Focusing on limiting foods with phosphate-containing additives has been shown to improve biochemical endpoints in individuals with CKD, including those undergoing dialysis. In a recent feeding study, 11 adults with and 39 adults without CKD were fed a phosphate additive-enhanced diet for 2 weeks that provided 1940 ± 419 mg of phosphorus, followed by a low-phosphate additive diet providing 1327 ± 187 mg of phosphorus (5). After the low-phosphate additive diet, participants with CKD had significantly lower concentrations of circulating intact and C-terminal fibroblast growth factor-23, parathyroid hormone, and urinary phosphorus. In a cluster randomized controlled trial conducted in 14 in-center hemodialysis clinics, providing education on label-reading to avoid phosphate additives in grocery stores and fast-food restaurants resulted in a 0.6-mg/dL difference between the control group after 3 months (6). Together, these two studies, conducted in individuals at different grades of CKD, suggest that limiting foods with high phosphorus bioaccessibility by limiting phosphate additives may be an effective strategy for managing CKD-MBD.

Beyond diet, pharmacologic therapies to limit intestinal phosphate absorption are commonly used in individuals undergoing dialysis (Figure). These include phosphate binders and the sodium-hydrogen exchanger type 3 inhibitor, tenapanor. Phosphate binders act by binding dietary phosphate in the gastrointestinal tract to reduce absorption. However, their effectiveness is limited, especially when compared with the reported dietary phosphate intakes of people on dialysis (7). In contrast, tenapanor inhibits paracellular phosphate absorption, a pathway thought to contribute substantially to phosphorus uptake at usual dietary intake levels in this population (8). In the OPTIMIZE (NCT04549597) trial, tenapanor effectively lowered serum phosphorus concentrations both as monotherapy and when used in combination with phosphate binders (9). An additional benefit of tenapanor was a significant reduction in pill burden—from an average of nine pills per day to four pills per day in those that switch to tenapanor. Finally, a novel pan-inhibitor of intestinal phosphate transporters is currently under investigation. In a phase 1b trial (NCT02965053) involving patients undergoing hemodialysis, it was shown to be safe and well tolerated (10).

Targeting dietary sources of highly bioaccessible phosphorus, particularly those foods with phosphate-containing additives, coupled with pharmacologic agents to limit intestinal phosphate absorption, offers a complementary and effective approach to managing hyperphosphatemia and CKD-MBD. Dietary interventions focused on reducing foods with phosphate additives can improve key biochemical parameters, whereas newer pharmacologic agents such as tenapanor not only enhance phosphorus control but also reduce pill burden—an important factor for adherence in populations undergoing dialysis. Together, these strategies represent a shift toward more nuanced and patient-centered phosphorus management in CKD. ■

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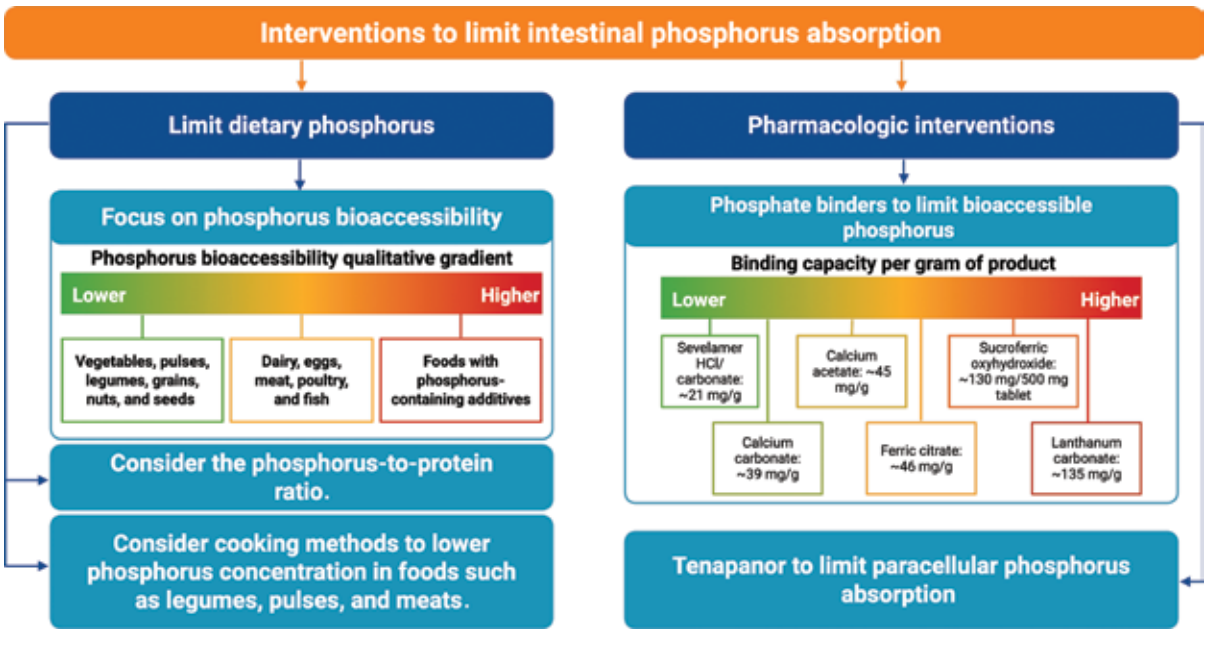
The authors report no conflicts of interest.

Figure. Dietary and pharmacologic interventions to limit intestinal phosphorus absorption



Adapted from Gutekunst (7) and created with BioRender.com.

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Nutritional Management in Children With CKD: The Path Forward

By Robert H. Mak and Arpana Iyengar

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Nutrition evaluation of children with chronic kidney disease (CKD) is important for guiding therapy and early detection of comorbidities such as protein energy wasting (PEW). Appetite assessments, both qualitative and quantitative, are essential. Important anthropometric parameters include percentiles for dry weight, height and length, weight-for-height, head circumference, and body mass index for height and age. Biochemical markers like serum albumin and prealbumin offer insights, but they should not be considered in isolation (1).

For children with CKD, including those on dialysis, the Paediatric Renal Nutrition Taskforce (PRNT) has provided dietary intake guidelines on energy, protein, calcium-phosphorus, sodium, potassium, and other nutrients, but they are mostly opinion-based (2). Anorexia is prevalent and an important contributor to the development of PEW in children with CKD. Enteral or gastrostomy feeding may benefit growth in infants with anorexia, but high rates of overweight and obesity among older children on maintenance peritoneal dialysis (19.7%) are not associated with normal linear growth (3). Growth hormone therapy, which has been approved by the US Food and Drug Administration for treating short stature in children with CKD, has recently been shown to improve appetite and prevent PEW in CKD mice (4). Emerging research underscores the association of inflammatory cytokines such as interleukin-1 (IL-1) in CKD PEW, with the IL-1 receptor antagonist anakinra demonstrating potential in preclinical models (5) and warranting further investigation in children.

Low-protein diets do not promote growth nor slow CKD progression in children with CKD. PRNT recommends protein intakes at the higher end of the standard range for children with CKD stages 2–5. Dietary fat intake should be restricted to less than 25%–30% of total calories, with an emphasis on encouraging complex carbohydrates and dietary fiber consumption (2).

Meticulous management of secondary hyperparathyroidism improves growth in children with CKD. Achieving the suggested dietary intake for calcium and strict control of serum phosphate by restricting phosphorus intake and phosphate binders have long been the standard of care (1, 2). Minimizing dairy products and ultraprocessed foods are thoughtful choices. A new phosphate binder—ferric citrate—is under evaluation for mitigating complications from elevated fibroblast growth factor (FGF)-23 levels in children with CKD and may slow kidney function decline (6). Early optimization of vitamin D concentrations, especially 25-hydroxy vitamin D and appropriate supplementation, promotes positive health outcomes in this population. Recently, vitamin D supplementation has been shown to improve muscle wasting and PEW in experimental CKD (7). Recognizing the clinical signs of vitamin deficiency or excess is paramount for effective management in children with CKD, particularly those on dialysis who experience losses of water-soluble vitamins and trace elements (1, 2).

Dietary sodium restriction is a fundamental strategy for managing blood pressure and preventing fluid retention in children with CKD. Current recommendations advise limiting sodium intake to less than 2 g per day for children over the age of 2 years, with potentially lower targets for younger children. Children with congenital anomalies of the kidneys and urinary tract often present with salt wasting and may require sodium supplementation. Guidelines for dietary potassium vary according to the stage of CKD, with more significant restrictions necessary in later stages and for patients on hemodialysis (1, 2).

A high-protein diet, particularly one rich in red meat, results in increased loads of sodium, phosphorus, and saturated fats, as well as induction of metabolic acidosis, potentially straining kidneys and worsening cardiovascular health in people with CKD. Metabolic acidosis is a known modifiable risk factor for poor growth. A balanced approach, such as plant-based diets, may be beneficial, ensuring sufficient protein while minimizing risks such as metabolic acidosis. Gut microbiota-derived metabolites, including trimethylamine N-oxide, p-cresol, and indoxyl sulfate, are associated with adverse outcomes. Strategies aimed at reducing these uremic toxins may lead to slowing CKD progression and improving cardiovascular complications (8). Gut microbiota-targeted strategies, including fermented foods, phytochemicals, prebiotics, probiotics, synbiotics, and oral absorbents, are exciting novel options (9).

Cardiorespiratory fitness in children with CKD is lower than that of age-matched healthy controls and contributes to frailty and poor quality of life. Muscle function tests should be part of routine nutritional assessment in CKD. Exercise intervention improves muscle function and should be included in the care of children with CKD (10).

The future of pediatric CKD nutrition management is geared toward establishment of evidence-based recommendations, promotion of healthy diets, and innovative strategies targeting anorexia, inflammation, nutrient deficiencies, and the burden of uremic toxins. Exercise is important to improve fitness and quality of life. Ferric citrate is under evaluation for treating iron deficiency, mitigating elevated FGF-23 levels, and slowing progression in children with CKD. Growth hormone therapy improves appetite and prevents PEW in experimental CKD. The IL-1 receptor antagonist anakinra has demonstrated potential in preclinical models of CKD PEW, thus warranting further investigation in children. Plant-based diets and gut microbiota-targeted strategies are interesting novel options in reducing uremic toxins and could lead to slowing CKD progression and improving cardiovascular complications. Collectively, these promising developments offer significant opportunities to advance nutritional care, with emphasis on promoting growth and delaying CKD progression in children. ■

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The authors report no conflicts of interest.

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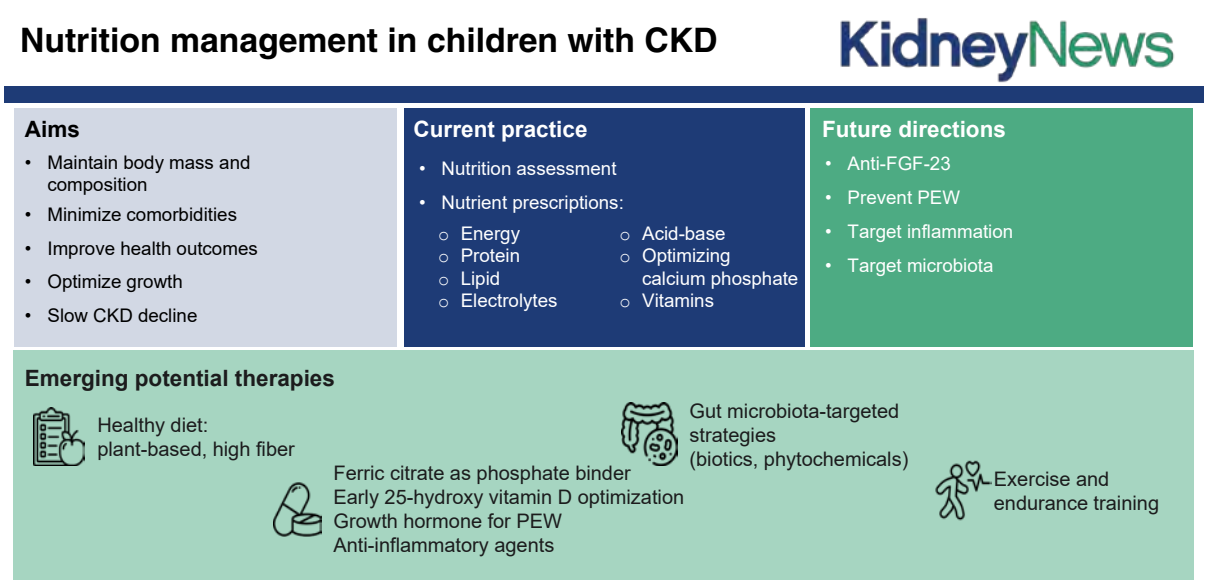

Post-Transplant Nutrition for Kidney Health: Balancing Graft Longevity, Metabolic Health, and Dietary Considerations

By Ekamol Tantisattamo and Kamyar Kalantar-Zadeh

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Kidney transplant is a current treatment of choice for suitable people with advanced chronic kidney disease (CKD) or kidney failure, offering improved survival and quality of life by reversing the uremic milieu (1). Whereas advancements in maintenance immunosuppressive therapies have significantly enhanced short-term kidney allograft outcomes, long-term outcomes remain variable and uncertain due to a combination of immunologic and nonimmunologic factors (2). Although preventing allograft rejection is a central focus for transplant practitioners to improve long-term graft survival, an often overlooked aspect is diet. Diet plays a potential role in mitigating the progression of CKD, yet it receives limited attention in the care of kidney transplant recipients (KTRs) (3).

Among dietary strategies aimed at preserving kidney function, protein intake and plant-based diets are among the most studied. Overall low dietary protein intake (DPI) appears to be beneficial for kidney allograft function (4). Similar to non-KTRs, high protein intake can lead to hemodynamic changes, which among KTRs, occur in the allograft, including afferent arteriolar dilatation and increased intraglomerular pressure, leading to glomerular hyperfiltration. In the long term, chronically elevated intraglomerular pressure may lead to glomerular damage, often manifesting as secondary focal segmental glomerulosclerosis (4, 5). Although several clinical studies demonstrated improved allograft function among KTRs who consumed a low-protein diet, there were several limitations to concluding the amount of DPI that can be universally implemented in KTRs. This is because the daily dietary protein requirement for KTRs can vary widely based on several factors, including periods after kidney transplant, metabolic status, level of kidney allograft function, and medical comorbidities. For instance, the recommended DPI is in the range of 0.8–1.0 g/kg/day in KTRs with stable kidney allograft function and up to 1.0–1.3 g/kg/day in those with increased catabolic needs or during the early post-transplant period (4). It is important to note that the Recommended Dietary Allowance of protein intake in the United States is 0.8 g/kg/day, whereas most Americans eat 1.1–1.3 g/kg/day. The Recommended Dietary Allowance was established by the US Food and Nutrition Board within the Dietary Reference Intakes framework.

In addition to the quantity of DPI, the quality of dietary protein may have a bearing on kidney allograft function. In the United States and most other countries, more than two-thirds of the daily protein intake is from animal sources. The intake in the Plant-Dominant Low-Protein Diet, also known as PLADO, reverses the proportion of animal- versus plant-based protein and is theoretically and clinically advantageous for the longevity of kidney allograft function; however, its potential unintended consequences may lead to concerns and barriers to implementing it in KTRs. Protein-energy wasting and skeletal muscle-mass loss or sarcopenia are common in people with CKD as one of the consequences of the uremic milieu and chronic inflammatory process (6). Although improved uremia and inflammation after successful kidney transplant should maintain or even improve muscle mass in KTRs, multiple factors increase the risk of muscle wasting after transplant, including chronic inflammation, acute kidney allograft rejection, opportunistic infections, and glucocorticoid therapy.

There is no consistent evidence of skeletal muscle-mass loss in KTRs who follow a moderately low-protein diet compared with those with a normal protein diet (4). However, one longitudinal cohort study revealed that DPI was inversely associated with graft failure and mortality mediated by skeletal muscle mass (7), and a recent single-center prospective study demonstrated a positive association between DPI and the skeletal muscle index (8). Other studies showed that high DPI was associated with a lower risk of obesity in KTRs due to early satiety (9).

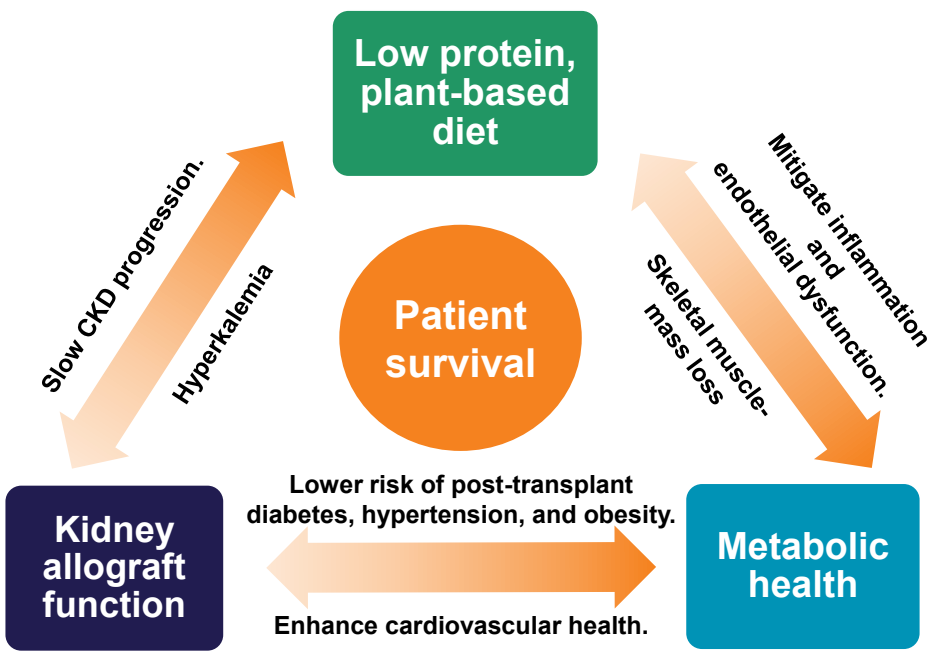
Nevertheless, the potential benefit of a moderate-protein, plant-dominant diet, specifically a Mediterranean diet, is the lower risk of post-transplant inflammation and endothelial dysfunction, which are associated with decreased cardiovascular disease, diabetes, hypertension, and obesity (3) (Figure).

Given the high potassium content of many fruits and vegetables, hyperkalemia is another commonly stated concern of PLADO in the setting of other potential risk factors for hyperkalemia post-transplant, such as type 4 renal tubular acidosis, calcineurin inhibitors, and trimethoprim, among others. However, PLADO is less likely to be the major contributor to post-transplant hyperkalemia unless there are concomitant risk factors or low kidney allograft function.

Although there is evidence demonstrating the benefits of low DPI and a plant-based diet on kidney allograft function, there were several heterogeneities of those studies, including study population, design, and duration of follow-up to guide transplant practitioners on the amount and type of DPI and plant-based diet. Although clinical trials have demonstrated the benefits of cardio-metabolic outcomes of plant-based diets such as the Dietary Approaches to Stop Hypertension (DASH) diet, the Mediterranean diet, PLADO, and other vegetarian diets in KTRs, similar to all other dietary intervention trials, the long-term outcomes—including kidney allograft function as well as allograft and patient survival, which unlikely occur in a short term—are lacking. This may be because of the challenge in the nature of the dietary behavioral changes that require dietary adherence of the study participants. One way to overcome this limitation is to design dietary intervention studies as type 1 hybrid effectiveness-implementation trials to mainly evaluate the efficacy of the dietary intervention on the clinical outcomes of interest, whereas also assessing implementation outcomes, especially acceptability, adoption, feasibility, and fidelity of the dietary intervention (10). Therefore, a multidisciplinary team approach for these hybrid trials needs to involve all relevant stakeholders, such as registered dietitian nutritionists and nursing educators, to reach the study population, who indeed need dietary intervention.

Implementing evidence from the trials to real-world clinical practice should ultimately mitigate the inequity among patients in accessing nonpharmacologic interventions to enhance the longevity of kidney allograft survival, while receiving the most benefits of a kidney-healthy diet, such as PLADO, in high-risk populations like KTRs. ■

Figure. Relationship among post-transplant nutrition, kidney allograft longevity, and metabolic health with benefits and potential unintended consequences of low-protein, plant-based diets



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Strategies for Fellows to Maximize Their Nephrology Fellowship Experience

By James D. Alstott

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Nephrology fellowship is rigorous and transformative. Fellows must simultaneously learn to balance clinical and educational activities all while caring for the most medically complex patients (1). The focus of nephrology fellowship educational literature has largely been on improving recruitment; the role of procedures in training; and innovations in educational content, delivery, and evaluation. Yet, little has been written on ways for the nephrology trainee to optimize the fellowship experience to meet future career goals. There exists a body of literature in medical subspecialty journals devoted to mentoring, education, and training outside of nephrology that imparts generalizable wisdom that nephrology fellows can draw from to make the most of their fellowship (Table 1) (2–8). Four common themes emerge and are expanded on in this editorial, with application to nephrology fellowship: 1) career planning, 2) active learning, 3) mentorship, and 4) scholarship.

Career planning

Fellows should practice early on in fellowship the second habit of *The 7 Habits of Highly Effective People*: "Begin with the end in mind" (9). Self-reflection on individual values and circumstances, self-assessment of strengths and weaknesses, and discussion with mentors are potential methods to elucidate a clear vision for a career in nephrology. A key distinction among careers in nephrology is between a private or an academic practice setting. For those planning on pursuing a private practice position, understanding practice structure, duties of the medical director, and available private nephrology employment opportunities is beneficial for future practice (10).

A survey of recent nephrology fellowship graduates found that the vast majority of fellows reported feeling less competent with the business and leadership aspects of clinical practice despite these competencies being identified as important in their current position (11). Membership with organizations such as ASN (https://www.asn-online.org/education/training/fellows/) and the Renal Physicians Association (https://www.renalmd.org/page/membership) is free for fellows. Both organizations provide fellow-centered workshops and resources, and their annual meetings have opportunities for career development and planning. Programs such as the Nephrology Business Leadership University course (https://nbluniv.org/) can teach trainees the financial aspects of practice management, and ASN's Fostering Innovative Leaders in Nephrology and Dialysis (https://epc.asn-online.org/projects/fostering-innovative-leaders-in-nephrology-and-dialysis-find-growing-future-generations-of-leaders/) can provide trainees with comprehensive training, mentorship, and networking.

For fellows pursuing a career in academics, finding an area of focus in clinical, research, or education that aligns with one's passions and strengths is critical. Aspiring clinician educators may participate in local or national teaching skills-building activities as well as create a teaching portfolio. Clinician scientists planning to have a research career should consider additional training in grant funding and writing, running a laboratory, and completing a research project from inception to dissemination. Another important consideration for career planning during fellowship is the option for further subspecialization (Table 2). Fellows interested in subspecialization can use local experts as mentors and tailor elective experiences, research, or quality improvement projects to cultivate expertise applicable to future careers.

Table 1. Fellow-focused articles with recommendations for success during and after training

Reference	Specialty	Recommendations
Lewis (2)	Gastroenterology	· Find a mentor. · Make yourself unique. · Get formal training in research methods. · Hone your writing skills. · Take advantage of speaking opportunities. · Pick your first research project carefully. · Keep a list of potential research ideas. · Learn to set priorities, and allocate your time as needed to achieve your goals. · Start looking for funding if you plan to do research. (It is never too early.) · Pick your first job carefully.
Morrow (3)	Oncology	· Choose an institution that values clinical research and has a research infrastructure. · Get prepared. · Find a mentor. · Seize opportunities when they arise.
Mehta and Forde (4)	Gastroenterology	· Consider intrinsic and extrinsic motivators for a career. · Identify an area of focus for specialization. · Create a mentorship team with a plan for engagement. · Follow a self-assessment plan.
Adams et al. (5)	Gastroenterology	· Acquire new skills. · Maximize efficiency. · Master effective consult communication. · Find a clinical focus. · Build clinical knowledge. · Identify a mentor. · Focus research/electives to career objectives. · Plan a career throughout fellowship.
Daily and Guerrier (6)	Cardiology	· Capitalize on learning opportunities. · Become a self-directed, lifelong learner. · Supplement clinical activities with didactic learning. · Read regularly. · Seek out guided practice. · Choose to live a balanced life. · Seek mentorship. · Perform a meaningful research project. · Review primary data for all studies. · Seek feedback regularly.
Ashton et al. (7)	Pulmonary/critical care	· Take responsibility for learning. · Keep an eye on the future. · Have a mentor. · Engage in scholarship. · Get involved. · Invest in wellness.
Essien et al. (8)	General medicine	· Find your purpose or passion. · Find the right mentor(s). · Identify and pursue funding opportunities. · Secure an academic job.

Active learning

Active learning refers to behaviors that are trainee-driven to enhance learning experiences, accomplish goals, and support professional development. Fellows can take responsibility for self-directed learning by identifying learning needs, setting educational goals, and tailoring these to available learning opportunities and professional interests (7). Feedback is an important part of active learning (6, 7). Explicitly seeking feedback from faculty on learning goals helps trainees discover areas for improvement. A useful tool to define goals and seek feedback longitudinally is the use of an individual development plan.

Self-assessment allows the learner to objectively analyze strengths and weaknesses for self-improvement. In nephrology fellowship, the ASN In-Training Examination is one of the ways that fellowship programs and fellows can objectively assess nephrology knowledge. Data from the In-Training Examination can be useful for generating learning goals, feedback, and assessment of progress in learning gaps on repeat examinations. Review of documentation, teaching activities, dialysis practice panel metrics, and even curriculum vitae are other sources for self-assessment and feedback. As a fellow gains competence and autonomy over time, active learning remains ever important as new learning gaps and professional goals are generated.

Mentorship

Effective mentorship in fellowship has the capacity to truly transform the fellowship experience. Mentorship in academic medicine has been found to favorably impact mentees' personal development, career planning, and scholarship (12). Because of the pleiotropic effects of mentorship, fellows should be vigilant upon starting fellowship to identify possible mentors. General traits of good mentors include availability, empathy, trustworthiness, honesty, and consistency. Fellows should consider having multiple mentors (formal and/or informal) to capitalize on the mentee's varied needs as well as the strengths of individual mentors. For example, a fellow may have a mentor in the division with

similar research interests while simultaneously seeking mentorship from another faculty member who demonstrates excellence at the bedside or admirable work–life integration. Both parties in the mentorship relationship should set goals and expectations for the partnership, have a timeline for future meetings, and provide mutual respect for the other party's uniqueness and time. ASN has composed a robust collection of resources related to mentorship, which is freely accessible on ASN's mentoring resources webpage (https://www.asn-online.org/education/training/mentors/).

Scholarship

Scholarly activities described by the Accreditation Council for Graduate Medical Education (ACGME) include publication of articles, book chapters, abstracts, case reports in peer-reviewed journals, quality improvement or educational research, and peer-reviewed funding and presentation of peer-reviewed abstracts at local, state, or national specialty meetings (13). The value of scholarship goes beyond the achievement of a publication. A scholarly project can serve as an area of expertise in employment after fellowship. Idea generation, project design, data analysis, manuscript writing, and navigating the peer-review process impart vital experience necessary for those intending on academic careers. More generally, a scholarly project bestows all trainees with a more refined critical analysis of the evidence used in practice. Optimal projects are ones that the fellow finds interesting rather than projects given to the fellow by faculty. Mentors can help fellows refine research questions, choose projects that can be completed during training, and share local resources (databases, informatics and statistics support, grant-writing courses, and funding for projects) (8).

As nephrology training continues to evolve, fellows can capitalize on their fellowship experience by identifying future career goals and mentors. Adopting a more active role in learning and participation in scholarly efforts will also promote professional development necessary for a successful career after training.

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Table 2. Opportunities for additional training and nephrology subspecialization

Area	Length of training, year	Number of US programs
Transplant	1	66[a]
Interventional	1	13[b]
Critical care–nephrology	1 For additional critical care fellowship; 3 for combined critical care–nephrology	45[c]
Palliative care–nephrology	1 For palliative care; 2 for combined palliative care–nephrology	197 Palliative care/hospice fellowships; 3 ACGME AIRE combined programs
Glomerular disease	1	10
Onconephrology	1	5
Home-based dialysis	1	3
Uronephrology	N/A	N/A
Obstetric nephrology	N/A	N/A
Cardionephrology	N/A	N/A

AIRE, Advancing Innovation in Residency Education; N/A, not applicable.
[a]Number of programs accredited through the Transplant Nephrology Fellowship Training Accreditation Program.
[b]Number of American Society of Diagnostic and Interventional Nephrology Hemodialysis Vascular Access accredited US programs.
[c]Number of ACGME accredited 1-year critical care fellowships.

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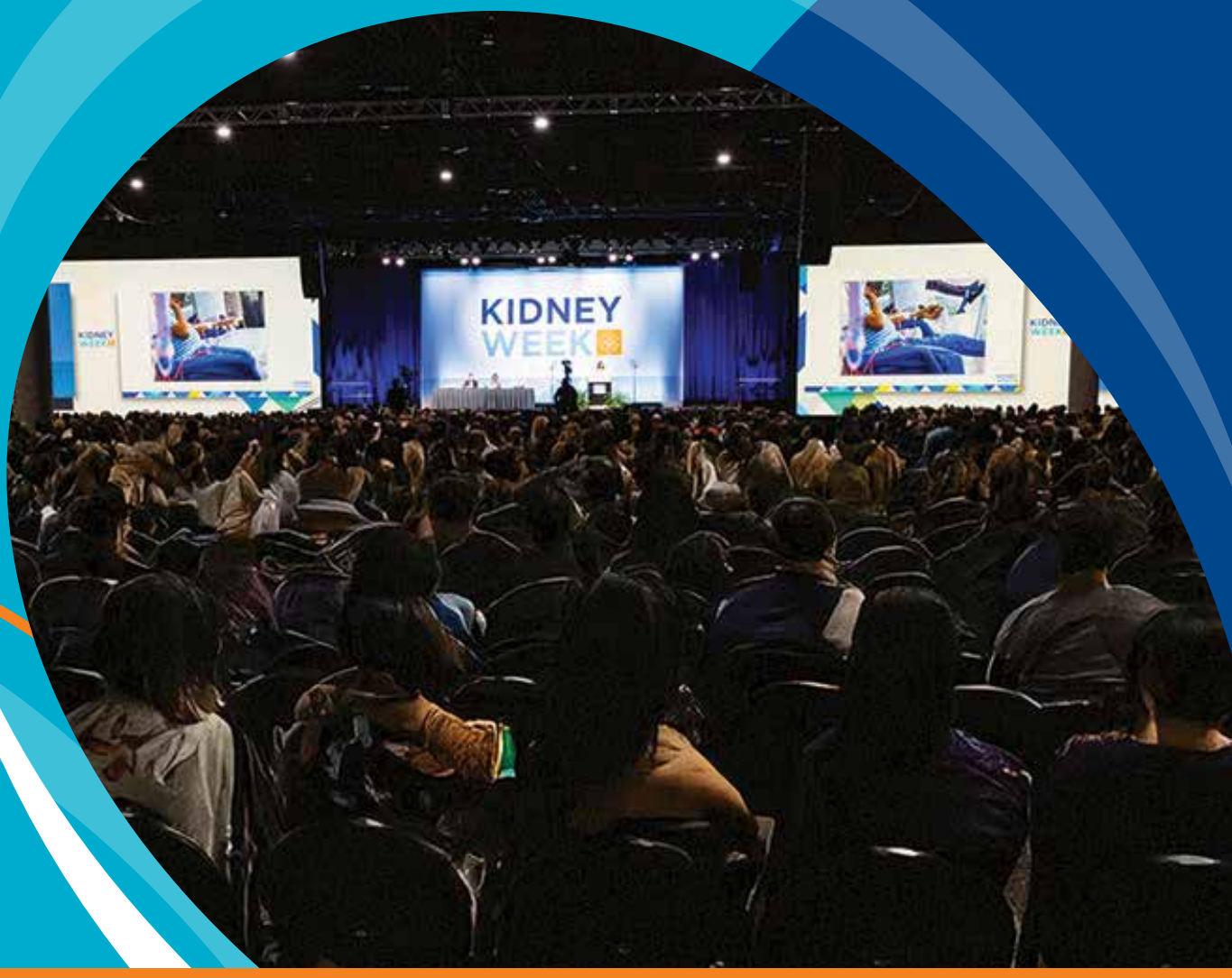

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