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Bold Investment Needed in Kidney Care Research to Deliver Prevention and Cures

By Bridget M. Kuehn

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About one in seven Americans lives with kidney disease—most completely unaware of this silent killer. Yet, the United States' annual investment in research to better prevent, treat, and cure kidney diseases is just $19 per patient annually, lagging other conditions like cancer or Alzheimer disease, which receive hundreds of dollars in funding per patient per year, according to the *Transforming Kidney Health Research* report (1).

To close this gap and spur further innovation in the field, ASN, in partnership with the American Association of Kidney Patients, the American Kidney Fund, the American Society of Pediatric Nephrology, and the National Kidney Foundation, assembled the Transforming Kidney Health Research (TKHR) Panel in September 2024. The panel comprised patients, clinicians, researchers, and policy experts and sought input from federal research agencies, therapeutic and device developers, and other kidney community stakeholders. Together, they developed a comprehensive roadmap for kidney research across the federal government, published in October 2025.

"The TKHR Panel and report unite many different stakeholders in the kidney advocacy community and will hopefully put wind in our sails as we use the report to advocate for change and a major transformative investment in kidney health research," said TKHR Panel Chair and ASN President Samir M. Parikh, MD, FASN, professor in the Department of Medicine and chief of the Division of Nephrology, The University of Texas Southwestern Medical Center, Dallas.

The report's executive summary includes the following: "The TKHR Panel envisions a future in which most patients never develop progressive kidney disease as a result of advances in preventive care. For those who do develop a progressive disease, this report describes bold research priorities that will lead to breakthrough cures. Finally, among

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Education Critical to Boosting Home Dialysis, Panel Says

By Karen Blum

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Far more people in the United States and in many other countries are eligible for home dialysis than those who pursue that route. By one estimate, 85% of patients in America could engage in home dialysis, but only 13% to 17% do so (1).

The key to further increasing the use of home dialysis may be education, according to panelists speaking on equity in home dialysis at Kidney Week 2025 in Houston, TX. "Home dialysis, be that peritoneal dialysis or home hemodialysis, really offers greater independence, better quality of life, comparable or even superior outcomes depending on the domains you analyze, and potentially lower costs," said Christopher Chan, MD, director of the Division of Nephrology at University Health Network in Toronto, Ontario, Canada. Yet, access to home dialysis remains inequitable across and within countries, he stated (2).

Australia (20% peritoneal dialysis, 9% hemodialysis), New Zealand (31% peritoneal dialysis, 19% hemodialysis), and Canada (17.5% peritoneal dialysis, 4.0% hemodialysis) are often viewed as potential exemplars of home dialysis penetration, Chan said, citing data from the US Renal Data System (3). However, at least in Canada, these percentages have not grown much, "so there's more to do in every single country," he said.

Patients who choose home dialysis do so for the freedom and lifestyle control, noted Chan, but usually only after they

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Bold Investment Needed in Kidney Care Research to Deliver Prevention and Cures

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those patients for whom a cure remains elusive, we envision transplantation and a future free of the burdens that come with today's heavy immune-suppressing medicines."

Kidney "moonshot"

Major advances in kidney care in recent years, including newly approved therapies to treat kidney diseases and prevent disease progression and xenotransplantation advancing into clinical trials, have built momentum in the field. Yet, there remains an urgent need for further innovation to prevent disease progression, develop cures, and improve care for people living with kidney diseases.

For those who provide kidney care or have loved ones with kidney disease, like Parikh, who, in addition to being a nephrologist, has multiple family members with kidney disease, it can be difficult to watch them progress through the disease stages and see it take a toll on their bodies and on their caregivers. "If you're a patient or someone who gives care to a patient, I think you recognize that that first visit you have with the nephrologist, what you're really hoping to hear is hope," Parikh said. "Hope takes the form of new therapies, of cures of transplantation. We need more hope."

TKHR Panel member Leonardo Riella, MD, PhD, FASN, the Harold and Ellen Danser Endowed Chair in Transplantation and Medical Director of Kidney Transplantation at Massachusetts General Hospital, Boston, has seen that sense of urgency firsthand in his work on ongoing xenotransplantation clinical trials. "What's striking is the overwhelming patient response; our team has received hundreds of messages from individuals on dialysis, eager to volunteer for xenotransplant trials," he explained. "Patients are clearly voicing that they want more than just dialysis," Riella said. "Investing now will allow us to build on early successes, address unanswered questions, and potentially offer a reliable transplant option for patients who would otherwise wait years or die on dialysis."

Living donor Anne Rohall, JD, who participated in the TKHR Panel as a patient advocate, noted that people with kidney diseases do not have cures for what is ultimately a fatal disease. She said that while other fields have seen transformative advances like improved pacemakers, continuous glucose monitors and insulin pumps, and curative cancer therapies, people with kidney diseases have been left behind with therapies that come with heavy care burdens.

"Patients and families, parents, and caregivers live with an enormous uncertainty and fear about life and death," Rohall said. "Innovation hasn't kept up with patient needs."

Policymakers have also recognized the need for urgent action. President Donald J. Trump's Executive Order on Advancing American Kidney Health in 2019 pushed for greater access to transplant and more person-centered kidney care (2). Several pieces of legislation aimed at strengthening the transplantation system, including the 2023 Securing the US Organ Procurement and Transplantation Network Act, have been enacted in recent years (3).

However, limited kidney research infrastructure and funding have stymied these efforts. The TKHR report aims to overcome this barrier to innovation and deliver more hope and better care options to patients through a bold investment in a comprehensive research plan. The plan is modeled after successful efforts like Cancer Moonshot, which provided a $1.6 billion investment in cancer research through the National Cancer Act, signed into law by former President Richard M. Nixon in 1971 (4). That project and subsequent investments in cancer research have yielded advances in cancer care, including targeted cancer therapies that have revolutionized care and dramatically improved patient survival and quality of life.

"We know that the model works," Parikh said. "If you can make bold investments in research, there will be payoffs." The potential return on investment from a large public investment in kidney care research could be substantial, given that the United States currently spends $150 billion a year on kidney disease care, including $50 billion on dialysis and transplantation for people with kidney failure, according to the TKHR report. The report notes, for example, that spending $1.8 billion per year for 10 years could lead to cures for kidney diseases that negate the need for dialysis and could be paid for with just 2 weeks of Medicare dialysis spending.

Ending kidney failure

The result of the panel's nearly year-long effort is a comprehensive roadmap for advancing kidney research. It includes recommendations to leverage advanced tools and technologies for kidney disease screening and diagnostics, promote early preventive care, expand access and improve outcomes for transplant patients, improve the quality of life for patients, and build the kidney research workforce and infrastructure necessary to achieve the report's ambitious goals.

"*The Transforming Kidney Health Research* report is a crucial step toward reshaping how we understand, study, and treat kidney disease," said panel member Benjamin Humphreys, MD, PhD, FASN, the Joseph Friedman Professor of Renal Diseases in Medicine and chief of the Division of Nephrology, John T. Milliken Department of Medicine, at Washington University in St. Louis, MO. "By prioritizing collaborative research, data-driven personalized medicine, and patient-centered innovation, it [the report] lays the groundwork for breakthroughs that could dramatically improve outcomes for millions affected by chronic kidney disease."

Parikh noted that the report addresses every part of the patient journey and the need for nephrologists to be proactive, shifting care to earlier disease stages—starting with prevention in those at risk, better screening and diagnostics, and use of kidney-preserving therapies. Rohall highlighted the report's emphasis on advancing precision medicine, including gene and cell therapies, especially for children with kidney diseases who have had limited care options. "That will move us from managing the disease to actually curing it," she said.

The report also addresses the need to overcome the shortage of clinicians and researchers necessary to deliver kidney care innovation, a need both Rohall and Parikh emphasized. Rohall noted that there is a critical shortage of clinicians in the entire kidney care team, especially in pediatric nephrology. Parikh also stressed the need for more cross-specialty research collaboration, more research consortia, sustainable career paths, and better use of technology and biomedical engineering to boost kidney research. "We have to attract more and different people to join the kidney research workforce," he said. "We also need more collaborations and work happening at the boundaries of our field."

The report also addresses the need to develop and refine existing therapies. It includes efforts to increase the pool of potential organs for transplant through the development of technologies, such as xenotransplantation and donor organ preservation techniques; to improve the quality of life for people living with a kidney allograft; and to implement policy innovations needed to deliver care.

> **"The TKHR Panel envisions a future in which most patients never develop progressive kidney disease as a result of advances in preventive care. For those who do develop a progressive disease, this report describes bold research priorities that will lead to breakthrough cures. Finally, among those patients for whom a cure remains elusive, we envision transplantation and a future free of the burdens that come with today's heavy immune-suppressing medicines."**

"The biggest impact we hope to see is a shift away from dialysis as the default long-term treatment of kidney failure," said Riella. "Kidney replacement therapy should prioritize transplantation, and dialysis should become the exception, not the rule. Every [person] with kidney failure deserves timely access to a transplant and a real chance at regaining health, independence, and dignity. The TKHR recommendations offer a roadmap to make that a reality." ■

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Education Critical to Boosting Home Dialysis, Panel Says

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have been educated about this option (4). "There are important barriers and fears to overcome, and it is our job to actually empower our patients through education to overcome these barriers."

A study identifying major hurdles to home dialysis found that perceived barriers by patients include fear of performing home dialysis, limited space for equipment and supplies, and insufficient home-based support; for clinicians, perceived barriers include inadequate patient education, limited home-based support staff, and insufficient experienced staff (5). The overall theme is a need for increased education, Chan explained.

Chan discussed some efforts at the University Health Network to improve home dialysis education. For one, the company uses a VARK (visual, aural, read/write, and kinesthetic) questionnaire to determine how individual patients learn best, and tailor their education accordingly. One study found that nonvisual learners were 4.35 times more likely to have an adverse event (6). "That doesn't mean we shouldn't teach nonvisual learners," he said. "It means that we need to empower them and personalize their programs." His team also has made use of the OSCE (objective structured clinical examination) to test for patients' competency in home dialysis skills during and after training before they initiate dialysis at home (7).

Simulation-based teaching is another means to improve education for patients, Chan said, and in his experience, this means that patients are less likely to need home dialysis nurse visits (8). His group also designed the Home Dialysis Virtual Ward study to evaluate potential gaps in care among patients being discharged from the hospital (9). The ward is simply a checklist or audit list that clinicians and nurses can use to check in with patients and ensure that they are prepared, including securing follow-up appointments and medications, he explained. Auditing patients for vascular access technique also can help catch errors and help prevent infections, he noted (10).

In additional education efforts, Chan discussed the importance of coaching, noting that nurses have taken on that role in his practice for patients who are discordant with their dialysis prescriptions, conducting weekly motivational interviews with patients via telephone, email, or in-clinic visits (11). "Patients may not always be looking after themselves, and you need to coach them back," he said. "Just like an elite athlete, they go up and down in terms of their psychology."

However, understanding workforce shortages, digital counseling programs for chronic kidney disease, and home dialysis can be used to offer education online, Chan said (12). To date, research from a program used at the University Health Network, called ODYSSEE Kidney Health, indicates that among patients using the application, the more engaged they are, the higher their quality-of-life scores and the higher improvement seen in burden and anxiety scores.

Nurse navigation

Empowering and educating nurses are also key to home dialysis expansion, said Ana Elizabeth Figueiredo, RN, MSc, PhD, a professor at the School of Nursing at the Pontifical Catholic University of Rio Grande do Sul in Porto Alegre, Brazil. "We have to make sure nurses and patients are well-educated. That will make the difference," she said.

Nurses play a central role in the home dialysis ecosystem, Figueiredo said (13). They provide patient coordination, ensuring seamless patient care. They provide training to patients and partners or caregivers; instructions on equipment operations and troubleshooting; and education on infection prevention, safety protocols, and recognition of potential complications. But nurses need to be competent in these areas to train patients, she said, and to incorporate a variety of materials for different learning styles.

Nurse navigation is a newer concept for most countries, said Figueiredo, and incorporates the nurse playing a role in coordinating patient care, conducting home assessments, managing supplies, and providing early detection of complications. However, she said, nurses are often overburdened and lack specialized training or institutional support to take ownership of complex home programs, which contributes to the stifled growth of home dialysis.

One potential solution would be to create certification programs for home dialysis nurse specialists, Figueiredo explained, as well as plans to assess competencies. Studies have indicated that training nurses on how to care for people living with chronic kidney disease can improve outcomes for nurses, which translates to higher quality patient care (14). "There's no way we're going to have our patients better empowered if we don't have the nurses empowered themselves—they're linked together," she said.

"There are important barriers and fears to overcome, and it is our job to actually empower our patients through education to overcome these barriers."

More efforts to enhance home dialysis equity

- The International Home Dialysis Consortium, launched in 2024, is bringing stakeholders together to drive home dialysis uptake globally, said Vivekanand Jha, MD, co-chair of the consortium and executive director of The George Institute for Global Health, India, and chair of Global Kidney Health, Faculty of Medicine, Imperial College London, England (15). It has four work streams: 1) empowering people needing dialysis, 2) educating the nephrology workforce, 3) developing workforce and resources, and 4) integrating care and payment policies. To date, more than 50 nephrology societies have signed the group's manifesto, a public declaration advocating for the promotion of home dialysis (16).
- The Veterans Health Administration (VHA), the largest provider of health care to US adults with kidney diseases, has undertaken several efforts to increase use of home dialysis, said Michael Fischer, MD, MSPH, FASN, nephrology section chief at the Jesse Brown Department of Veterans Affairs Medical Center in Chicago, IL. The VHA Home Dialysis Committee, created in 2019, conducted a survey of all VHA health care facilities in 2020 and came up with a number of solutions. Among them, the system has developed comprehensive kidney disease education that can be delivered via telehealth and enacted a directive that all veterans be provided an opportunity to choose any form of dialysis. The ongoing TEACH-VET study (NCT04064086) is evaluating the impact of comprehensive patient education on choosing home dialysis (17). Additional programs are using telehealth to connect VHA hub medical centers with physicians and patients in rural or community-based clinics or homes and are focusing on peer support programs for veterans with kidney failure. ■

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Thakar Sets Designs on Future Direction of *Kidney360*

By Karen Blum

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Charuhas Thakar, MD, FASN, likens his feelings about taking on the editor-in-chief role of *Kidney360*, ASN's online open-access journal, to the times he steps onto the tennis court for a match: "A little bit of butterflies is healthy."

"It's a big responsibility, and I would like to thank ASN in entrusting me with this role," said Thakar, director of the Wellcome-Wolfson Institute for Experimental Medicine at Queen's University in Belfast, Northern Ireland, United Kingdom. But he has a solid plan. His 6-year term as the first to lead an ASN journal from overseas began January 1st.

Novel clinical research will continue to be the primary driver of the journal, he said. "What is unique about the journal is that 70% of our published content is original research that comes from investigators, and 30% is invited content, but it's very carefully crafted, including special features such as Debates in Nephrology and Global Perspectives."

He looks forward to launching Case Reports in 2026 and is considering adding brief commentaries to the Case Reports, along with new clinical pathologic correlations.

"We want the best in nephrology to be published by ASN journals as much as possible," says Thakar, who has been meeting with the other ASN journal editors since June 2025 to prepare. "I look forward to working with Rajnish Mehrotra, MD, MS, FASN, the ASN Portfolio lead and editor-in-chief of *JASN*, and Connie Rhee, MD, MS, the editor-in-chief of *CJASN*. Together, we want to complement each other as a unified strong journal portfolio for the global kidney community."

Kidney360 will continue to have a global presence, Thakar said. Submissions have come from over 66 countries, with almost 40% of the content arising from outside of North America, which will remain to be important, he said.

In terms of original research to feature, he said, "We want to look at cost-effective analyses, real-world data, pharmaco-epidemiology studies, research design and methods, and qualitative and interdisciplinary research. We also want to focus on areas such as trial design and clinical trials with renal endpoints from other disciplines, such as critical care, cardio-metabolic, urology, and surgery."

He plans to boost basic and translational research, which currently constitutes 15% of the journal's content, to 25% of submissions. A carefully selected team of associate editors includes those with expertise in clinical research and with PhDs in biomedical sciences from the United States, Canada, and the United Kingdom. As the only online open-access ASN journal, *Kidney360* continuing to feature basic science is important for authors, Thakar said.

"The timeline from submission to publication is very efficient for the open-access journal of the ASN portfolio, and many authors want their ideas and scholarly work in the public domain as soon as it's possible," he noted. He also would like to raise the journal's impact factor, which currently resides within the top quartile of nephrology journals, to be within the top 10% within the next 3 to 5 years.

Thakar said the journal would like to capitalize on the Global Perspectives features that highlight kidney care in different parts of the world—"a very important feature for the entire portfolio," he said. He is looking to name an international ambassador to the editorial team, a role that could swap out on a 2- or 3-year rotating cycle. The person could serve as a reviewer and writer of related editorials, suggest content areas, and bring ideas from various regions, he said, as well as serve as a conduit or link between authors from their network and the journal.

He said he is looking forward to working with the journal's new editorial team. "We have been able to assemble immensely talented and accomplished individuals as deputy and associate editors of the journal. The journal has been purposeful in considering content expertise as well as geographic diversity while selecting this team," Thakar said.

For instance, one associate editor recruited by the journal (Rahul Chanchlani, MD, MBBS, MS, FASN, associate professor at McMaster Children's Hospital in Ontario, Canada) is an expert in pediatric nephrology and transplantation, a new area for the journal. "We want to make sure that our colleagues in pediatric nephrology, who want to publish high-quality work, look at us as one of their destination journals," Thakar said.

Additionally, former associate editors Neera Dahl, MD, PhD, FASN, a nephrologist with the Mayo Clinic in Rochester, MN, and Timmy Lee, MD, MPH, FASN, division director and vice chair for research in the Department of Medicine at The University of Alabama at Birmingham, will advance to become the two deputy editors of *Kidney360*.

"I'm a big believer in career development," he said. "So we are purposefully blending early-, mid-, and experienced professorial-level associate editors so we can all learn from each other. I think it bodes well for the journal," said Thakar, who previously served as editor-in-chief of *Advances in Kidney Disease and Health*, a National Kidney Foundation journal, since January 2020. He also has been an associate editor, guest editor, and contributor to several other prominent nephrology journals and textbooks.

It was Thakar's continued passion for professional education that propelled him to apply for the position.

"We live in a very critical time for research," he said. "On one hand, research funding is challenging all over the world for a variety of geopolitical reasons. Thus, the research that is going to be generated and the people who are accepting research as a career path are going to face a lot of challenges in the next 5 years. On the other hand, we are also living in the times where we are experiencing some major scientific breakthroughs in precision and personalized medicine in nephrology."

Additionally, he said, we live in an era in which both misinformation and disinformation can distort the truth. "We want to have a global impact of true, accurate research dissemination. Thus, we as journal editors will have to be real gatekeepers and ambassadors to publish the highest-quality content. There's a big onus on journals and editors to be able to invite, encourage, and maintain that quality, which is ultimately going to benefit our patients.

"Creative minds are thinking about what's going to be new and transformational in nephrology, what's going to benefit patients in the next 5 to 10 years from now, and we get to assess and read that firsthand, even before it gets into print," Thakar continued. "That's a very exciting prospect for anybody who works in this editorial profession."

ASN President's Update

Hope in Nephrology

By Samir M. Parikh

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Every person touched by kidney diseases carries a request we need to acknowledge at the outset and often thereafter: Give me hope. Hope that kidney function will hold steady a little longer; hope that dialysis will not define an entire life; hope that a transplant call will come; hope that new therapies are on the way.

But the need for hope does not stop with the patient. All of us in nephrology live by it. Caregivers hope for a normal day for their loved ones. Clinicians hope that medicine will keep pace with need. Researchers hope that the next study will open a new frontier. Trainees hope to pursue careers of impact. Policymakers hope that their efforts can bend the curve for Americans living with kidney diseases.

Hope is deeply personal but also profoundly professional. Hope calls us to clinic appointments, late nights in research, persistence in mentorship, and resilience in advocacy. Hope reaches us with a message of renewal: Our story in nephrology is just beginning.

My beginning

The desire for a better life brought my parents to the United States from India in the early 1970s. That same aspiration kept us here through the uncertainties of my childhood, including financial setbacks and a period of heightened racial tension in New Jersey during the 1980s. Opportunities guided my path: to Harvard for college; to Vanderbilt for medical training, and, more importantly, meeting my wife Amy. We subsequently returned to Boston, where I became a scientist because I was a physician.

Although I did not realize it then, shifting career paths so late in my training was an exercise in hope—namely, to do better one day in the future than I was doing today at the bedside. A life in research has conferred deep personal appreciation for the many steep challenges that commence with discovery and culminate with impact that transforms patients' lives. Joining the community of people seeking these transformations has given me a clear professional purpose.

After 20 years, this journey led me to Dallas, TX, drawn by the chance to serve a community whose forebears had shaped the field of nephrology and the very organization I now have the honor to lead. The hope and determination that brought my parents to this country a half-century ago not only fostered the innumerable prerequisites to yield my career but in truth, have been the well of inspiration from which I draw every day.

Action in 2025: ASN achievements

ASN is our collective aspiration embodied. Indeed, "a world without kidney diseases" is unapologetically ambitious. In 2025, ASN and our partners transformed this vision into major actions that make immediate progress for today and sow hope for the future. These efforts included:

- **Transforming Kidney Health Research** launched to unite the kidney advocacy community around a bold new agenda to increase federal research funding.
- **Saving Kidneys, Hearts, and Lives** commenced to prevent disease progression.
- **Kidney Health Guidance** provided clinicians with practical tools to care confidently for patients.
- **Humanitarian collaborations** expanded, ensuring access to care during crises.
- **KidneyCure**, already the largest foundation funder of kidney research training, provided $3 million in research funding to fuel discoveries that will change the future of kidney diseases and committed an additional $6 million to help scientists navigate these challenging times.
- **Legislative and regulatory efforts** were led to modernize transplant policy.
- **The Migration Policy Institute** partnership helped address myriad challenges faced by international medical graduates, who, like my parents, are seeking a better life.

A shared responsibility

ASN's mantra of a world without kidney diseases belongs to all of us:

- **Patients and caregivers**, who remind us why our work matters
- **Nephrologists, nurses, and the entire care team**, who dedicate their careers to patients
- **Researchers**, who pursue breakthroughs that once seemed impossible
- **Educators**, who try to make the next generation better than themselves
- **Trainees**, who will inherit and expand this field
- **Innovators**, who take risks to bring new therapies into practice
- **The National Institutes of Health and other federal research agencies**, which are the foundation of discovery
- **The Centers for Medicare & Medicaid Services and other payors**, which ensure that innovation translates into access, affordability, and sustainability
- **Legislators and policymakers,** who are responsible for protecting the public's health

The ASN Strategic Plan makes plain the urgency with which we must all act. Each stakeholder contributes a thread. As a result, the very fabric of nephrology is now changing dramatically: Once the forever-promised future, xenotransplantation now feels like a tractable scientific challenge. Our attention is now firmly on medicines that can prevent entry into kidney failure for millions of people worldwide.

As I begin 2026 as ASN's 59th president, I am humbled by the collective story of nephrology. My journey is one entwined thread in our great tapestry, woven by all who dedicate their lives to kidney health. Our responsibility is clear. We must carry purpose into every interaction: to lift patients with compassion, to mentor trainees with encouragement, to advocate relentlessly for policies that make care equitable and accessible, and to invest in research that can bring tomorrow's solutions into the present day.

When this vision permeates every corner of nephrology—clinic, laboratory, teaching rounds, dialysis unit, think-tank, government—it becomes tangible and enduring. People living with kidney diseases do not come to us only for medicine. They come for hope that progress is possible. And in that conviction lies the power to transform lives, communities, and our field itself.

Looking forward to 2026

Optimism is both a beginning and a compass. It guides action, shapes policy, fuels innovation, and strengthens every connection within our field. It carries the promise that tomorrow can be better, that challenges can be met, and that progress is achievable. At the end of this year, I will judge ASN's success based on accomplishing at least the following goals:

1. Execute ASN's new Strategic Plan.
2. Advance major priorities, including expanding access to kidney transplant and advocating for increased research funding.
3. Recognize that the only way to increase interest in nephrology careers is to compensate nephrologists fairly for the work they do.
4. Support the next-generation workforce by expanding KidneyCure and fostering international medical graduates.
5. Continue to implement recommendations for training and education from the ASN Task Force on the Future of Nephrology (1).

In 2026 and beyond, let us commit to fostering this outlook across every corner of nephrology. Let us strive to provide the best care possible, to innovate, and to teach. Together, we can turn hope into achievement and vision into reality. Because in nephrology, hope is not optional. It is essential. ■

Samir M. Parikh, MD, FASN, is a professor of internal medicine and pharmacology and the Chief of Nephrology at The University of Texas Southwestern Medical School, Dallas, and ASN president.

To comment on Dr. Parikh's editorial, please contact email@asn-online.org.

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ASN STRATEGIC PLAN (2026–2027)

Vision

A world without kidney diseases

Mission

ASN transforms kidney care and improves lives through science, education, advocacy, and collective action.

Values

- Excellence: setting high standards to achieve outstanding results
- Community: advancing common interests, standards, and goals
- Creativity: introducing innovative ideas, methods, and actions
- Integrity: emphasizing honesty and transparency
- Inclusivity: providing equal access to opportunities and resources

Pillars

- Advance kidney care
- Foster kidney science and innovation
- Enhance nephrology education and professional growth
- Assert the value of nephrology to health care
- Lead kidney policy and advocacy

Goals

1 Advance kidney care

- Prioritize screening, diagnosis, and interventions to prevent, cure, or slow kidney diseases
- Produce guidance, and promote best practices for preventing and treating all stages of kidney diseases
- Educate other specialties engaged in the care of people living with kidney diseases

2 Foster kidney science and innovation

- Accelerate development, translation, and dissemination of scientific breakthroughs
- Increase interest in careers in kidney research
- Leverage scientific, medical, and patient advocacy organizations to transform kidney health research

3 Enhance nephrology education and professional growth

- Meet the diverse educational needs of the kidney community
- Support nephrology fellowship training programs as well as clinical and research trainees
- Address challenges faced by internationally trained physicians and researchers

4 Assert the value of nephrology to health care

- Define integrated pathways (clinical and financial) for the delivery of high-value kidney care, including access to new therapies
- Articulate the importance of kidney diseases to health systems and value-based care
- Cultivate leaders to enhance the specialty and its influence

5 Lead kidney policy and advocacy

- Champion kidney care, research, and education goals outlined in “STAND for Kidney Health”
- Advocate for a permanent US Department of Health and Human Services Officer of Kidney Health and Transplant
- Advance patient access and optimal outcomes by modernizing payment systems and aligning the economics of kidney care

Making Dialysis Brain- and Heart-Friendly: Lessons From Multiparametric MRI

By Sourabh Sharma, Tapas Sahoo, and J. S. K. Chaitanya

https://doi.org/10.62716/kn.001982025

Cognitive decline and dementia are increasingly acknowledged as significant complications in individuals undergoing maintenance hemodialysis (HD), affecting nearly two-thirds of individuals (1). In contrast to cardiovascular outcomes, which have been the focus of extensive research over decades, the "silent epidemic" of brain aging in HD remains mainly unexamined and ignored.

The research conducted by Cox and colleagues represents a pivotal advancement on the association of brain aging with HD by offering mechanistic insights through multiparametric magnetic resonance imaging (MRI) (2). For the first time, to our knowledge, the researchers reveal a sudden increase in white matter (WM) T1 relaxation time during HD, which aligns with elevated cerebral water content. The most probable reason for this intradialytic alteration is the osmotic imbalance across the blood-brain barrier due to the slow diffusion of urea and organic osmolytes. This alteration is a crucial mechanistic link between acute HD sessions and the accelerated brain-aging phenomenon. Repeated occurrence of such incidents three times each week, over several years, may lead to cumulative WM damage, explaining the increased cognitive burden in patients undergoing HD compared with their age-matched counterparts (2).

Table. Neuro-cardio-protective strategy for brain- and heart-friendly HD

Domain	Mechanistic concern	Potential interventions	Supporting evidence
Osmotic stability	Rapid solute removal creates an osmotic gradient across the blood-brain barrier, causing cerebral water influx and micro-edema (5).	· Isonatremic/isotonic prescriptions · Slower urea kinetics (incremental or more frequent HD) · Adjusted dialysate Na	· Acute increase in WM T1 relaxation time, consistent with brain water accumulation during HD (2) · Prior small studies confirm osmotic shifts linked to DDS (5, 6).
Hemodynamic optimization	Intradialytic hypotension causes cerebral hypoperfusion and WM injury.	· UF profiling, biofeedback · Dialysate cooling · Continuous blood pressure and cerebral oximetry	· Cox et al. documented hemodynamic alterations without evidence of accelerated cardiac aging; findings support selective brain vulnerability (2). · Eldehni et al. showed WM protection with cooled dialysate (7).
Cognitive surveillance	Cognitive decline often subclinical until advanced (1)	· MoCA, TMT testing · Digital cognitive assessment · Incorporation into HD adequacy	· WM microstructural changes are associated with accelerated brain aging, validating the need for early cognitive monitoring (2). · A cohort study supports feasibility (8).
Neuroprotective environment	Sedentary intradialytic routine and CKD milieu amplify brain aging.	· Intradialytic exercise · Cognitive training programs · Sleep-optimization strategies	· WM integrity deteriorates faster in patients on HD versus healthy aging, underscoring the need for lifestyle-based neuroprotection (2). · RCTs support exercise and engagement interventions (9).
Individualized prescription	Interpatient variability in susceptibility to brain injury	· MRI/DTI-guided risk stratification · Bioimpedance for precise volume status · Wearable NIRS for cerebral perfusion	· Multiparametric MRI is shown to be feasible to monitor acute and chronic brain changes; could guide personalization of HD (2). · Emerging imaging-led studies reinforce individualized prescription (10).
Collaborative care	Brain health is under-recognized in routine HD care.	· Nephrology–neurology joint clinics · Family education on cognitive risk · Early rehabilitation referral	· Cox et al. highlight the unique vulnerability of the brain versus the heart, calling for interdisciplinary management (2). · Aligns with calls for brain–heart teams in CKD

CKD, chronic kidney disease; DDS, dialysis disequilibrium syndrome; DTI, diffusion tensor imaging; MoCa, Montreal Cognitive Assessment; Na, sodium; NIRS, near-infrared spectroscopy; RCTs, randomized clinical trials; TMT, Trail Making Test; UF, ultrafiltration.

Nevertheless, the susceptibility of different organ systems to this alteration associated with HD is varied; although HD caused expected hemodynamic alterations and structural changes in the heart, the study did not reveal any signs of accelerated cardiac aging. This discrepancy highlights the brain's unique vulnerability to osmotic and microvascular stress. This increased vulnerability may be due to its high metabolic requirements, fragile water-solute balance, and dependence on intact WM pathways for cognitive functioning (2, 3). Also, in contrast to HD, peritoneal dialysis might protect brain aging by more physiologic removal of solutes and fluids and more gradual osmotic fluctuations (4). Further research could help determine if peritoneal dialysis offers a neuroprotective benefit.

The implications of the Cox et al. study are significant: The traditional adequacy measures for HD, focused on urea kinetics and fluid management, are no longer sufficient (2). HD adequacy needs to be redefined, keeping neuroprotection as an essential outcome. Safeguarding cognitive function is not a peripheral concern; it is vital for sustaining patients' independence, functional capacity, and quality of life, and it is fundamental to patient-centered dialysis (1).

Based on these observations, we suggest a neuro-cardio-protective strategy (Table) designed to make dialysis beneficial for brain and heart health. This comprehensive approach incorporates established cardioprotective measures and includes innovative methods for osmotic stabilization, cognitive assessment, and collaborative care. The current challenge lies in translating these strategies into practical application, validating them through clinical trials, and shifting policies toward results that prioritize what is most important to patients—not just survival but survival with cognitive function, autonomy, and dignity. ■

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The authors report no conflicts of interest.

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Gene-Edited Islet Cell Transplant Offers Hope for Type 1 Diabetes, Eliminating Need for Immunosuppression

By Everly Faith P. Ramos and Daniel C. Brennan

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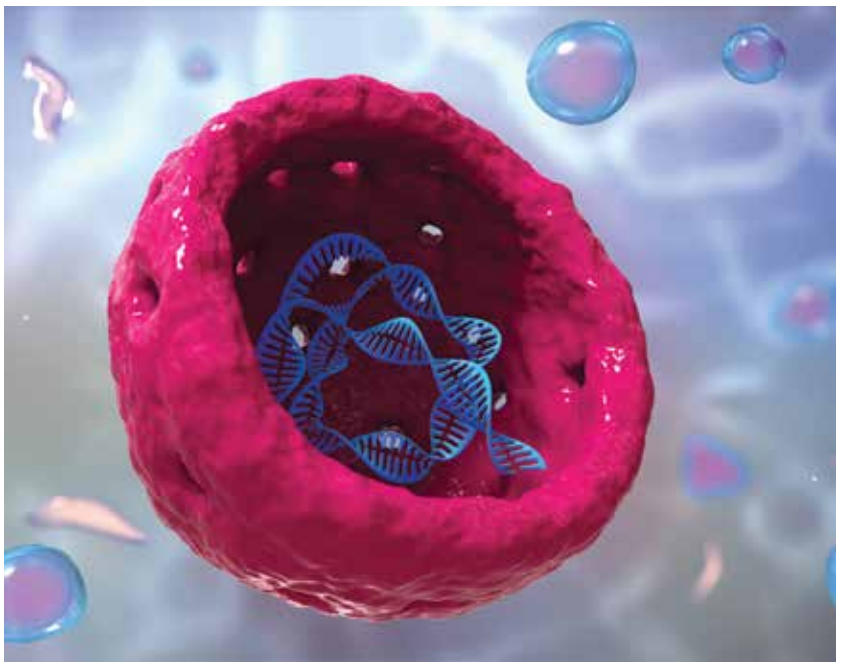

In a groundbreaking proof-of-concept study published in *The New England Journal of Medicine*, researchers report the successful transplant of gene-edited islet cells into a person with type 1 diabetes (T1D), without the need for immunosuppressive drugs (1).

In this study, researchers used CRISPR-Cas12b (CRISPR-associated protein 12b) gene-editing technology to modify donor islet cells to make them "hypoimmune." The modified cells were designed to evade T cell rejection by inactivating histocompatibility leukocyte antigen (HLA) class I and II genes and to resist innate immunity cell attack from macrophages and natural killer cells by overexpressing CD47, a "don't eat me" signal. The final therapeutic product, called UP421, is comprised of three cell populations: 1) fully-edited, HLA-depleted, CD47-overexpressing, hypoimmune platform (HIP) islet cells; 2) HLA class I and II double-knockout cells with endogenous CD47 levels; and 3) wild-type cells. UP421 was then transplanted into the forearm muscle of a 42-year-old man with a 37-year history of T1D, a hemoglobin A_{1c} (HbA_{1c}) of 10.9%, and an undetectable C-peptide. The patient did not receive any immunosuppressive drugs.

Results of the study at 12 weeks after transplant showed survival and function of the HIP cells. Cytotoxicity assays showed that T cells killed the wild-type cells, and donor-specific antibodies developed. Natural killer cells and macrophages killed the double-knockout cells. No cytotoxicity was demonstrated against the HIP islet cells, and no donor-specific antibodies developed. When incubated with the recipient's peripheral blood mononuclear cells and serum, both the wild-type and double-knockout cells were killed, but the HIP cells survived by evading the immune cells in the participant. Post-transplant, the participant exhibited measurable, meal-responsive C-peptide, with a 42% reduction in HbA_{1c}, although this was attributed to peri-transplant insulin optimization. Four nonserious adverse effects occurred, including paresthesia in the left lower arm.

The usual implantation site for islet cells is in the liver through the portal vein. However, portal vein islet cell transplant can cause postoperative bleeding, vascular emboli formation, portal hypertension, periportal fatty degeneration, and a blood-mediated acute inflammatory response that can result in massive graft loss (2). The choice of intramuscular implantation addresses some of these complications, although forearm muscle capacity and vulnerability remain concerns.

The islet cell dose used was intentionally lower, estimated to be 7% of the dose found to produce insulin independence in clinical practice. Nevertheless, it was sufficient to demonstrate the differences in immune reaction to the different cell populations, as well as C-peptide production in the participant. Importantly, C-peptide production is clinically relevant and has been linked to lower risks of complications such as retinopathy, nephropathy, neuropathy, and cardiovascular disease (3–6).

These results highlight the growing recognition of innate immune cells as critical therapeutic targets in both transplantation and autoimmune diseases (7–13). Most notably, the study represents the first demonstration of survival and function of genetically modified allogeneic islet cell transplants without immunosuppression. This technology can be applied to islet cells derived from pluripotent stem cells that can potentially provide an inexhaustible supply of islet cells, as recently successfully demonstrated by Reichman et al. (14). Together, these findings offer new hope for the long-sought goal of safe and effective islet transplant in people with T1D. ■

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The authors report no conflicts of interest.

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Siglec-E Pathway as Key Immune "Brake" That Protects Against Transplant Rejection

By Ryo Matsuura and Hamid Rabb

https://doi.org/10.62716/kn.002502025

T Cell-mediated rejection is a major cause of acute and chronic rejection in kidney transplantation, and its treatment remains an opportunity to improve care (1). Although cytotoxic T cells are the primary effector of allograft dysfunction, and the extent of their infiltration in kidney grafts is correlated with graft survival (2–4), innate immunity is also a critical mediator of T cell-mediated rejection (5, 6). Damage-associated molecular patterns, released in the donor organ during the process of brain death or as a result of ischemia reperfusion, can activate innate immune cells including dendritic cells, leading to the stimulation of allogeneic T cells and graft rejection (6). However, how innate immune cells regulate cytotoxic T cells in allografts is less well understood.

A new study published in *Science Translational Medicine* highlights the critical role of the innate immune system in driving rejection (7). Researchers at Massachusetts General Hospital identified sialic acid-binding immunoglobulin-like lectin-E (Siglec-E), a myeloid cell-expressed inhibitory receptor, as a key suppressor of dendritic cell activation and T cell-mediated rejection in murine kidney, heart, and skin allografts. This study found that Siglec-E is upregulated when dendritic cells are treated with damage-associated molecular patterns like heat shock protein 70 and lipopolysaccharide and that knockout of Siglec-E led to more severe allograft rejection with an increased number of infiltrating cytotoxic CD8 T cells. Conversely, Siglec-E overexpressing dendritic cells stimulated allogeneic T cells to a lesser degree. These findings demonstrated that Siglec-E expressed on dendritic cells controls allogeneic T cell responses. In addition, loss of Siglec-E led to accelerated graft loss through heightened nuclear factor-κB signaling and tumor necrosis factor-κ production in dendritic cells, resulting in stimulating allogeneic T cells and causing graft rejection. The effects of Siglec-E on graft rejection were also correlated in humans. In human heart and kidney allograft biopsies, increased transcript expression of Siglec-7 and Siglec-9 (human homologs of Siglec-E) was associated with improved graft outcomes over 15 years.

This exciting research has many important findings. First, the study demonstrated a mechanism in which dendritic cells can regulate allogeneic T cells in preclinical models. Although innate immunity involves various immune cells, dendritic cells are identified as key effector cells controlling T cell activity. Second, the researchers identified Siglec-E as a key molecule to prevent innate immunity activation and allograft rejection. The Siglec-E pathway can control the production of inflammatory cytokines that activate allogeneic T cells. Third, the investigators demonstrated the effects of Siglec-E in three types of organ transplantation: heart, kidney, and skin. This finding suggests that Siglec-E expressed on dendritic cells can be a potential therapeutic target broadly across various organ transplantation.

This carefully performed study extends our understanding of the mechanisms by which innate immune cells control allogeneic T cells through the Siglec-E pathway, a promising biomarker and therapeutic target in transplantation. ■

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The authors report no conflicts of interest.

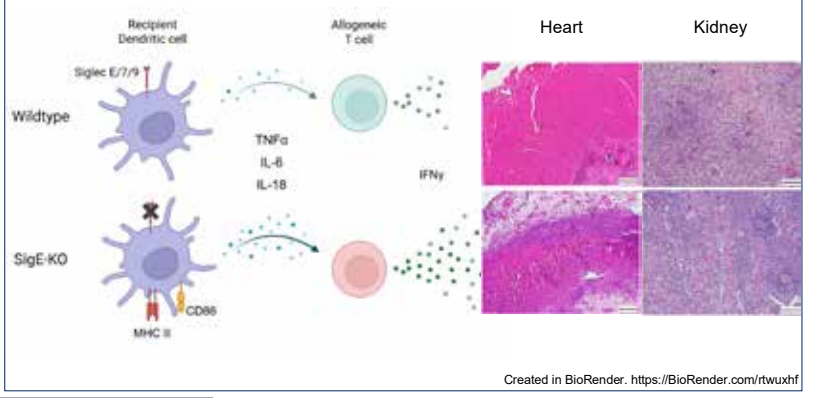
Siglec-E: A key immune "brake" that protects against transplant rejection

KidneyNews

Methods

- In vivo: Hearts or kidneys from BALB/cJ or CB6F1/J mice were transplanted to wildtype or Siglec-E-KO C57BL/6 mice.
- In vitro: Syngeneic or allogeneic T cells were cocultured with wildtype or Siglec-E (SigE) KO dendritic cells, and IFNγ production was measured.
- Human study: Investigating the association with graft survival and the expression of Siglec-7/9 in the transplanted organ.

Findings



Conclusions: The Siglec-E pathway inhibits the production of inflammatory cytokines and the activation of allogeneic T cells, resulting in transplant tolerance.
IFN, interferon; IL, interleukin; KO, knockout; MHC, major histocompatibility complex; TNF, tumor necrosis factor.

Borges TJ, et al. **The Inhibitory Receptor Siglec-E Controls Antigen-Presenting Cell Activation and T Cell-Mediated Transplant Rejection.** *Sci Transl Med* 2025; 17:eads2694. doi: 10.1126/scitranslmed.ads2694

Visual abstract by Matsuura R, Rabb H

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CREATIVE CORTEX

Echoes of Silence

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The “Echoes of Silence” resonates with the rhythm of life, where kidney strings echo resilience. The guitar—an abstract kidney—sings an unspoken melody, vibrant yet fragile. Swirling red mimics flowing blood, entwining the organ in waves of harmony and distortion. Geometric fragments mirror the fragmented struggles of kidney health, yet the silent chords persist. This piece is an ode to unseen battles, a visual symphony of vitality and vulnerability, where silence speaks louder than sound. ■

Artwork by AnilzArt. Anil Saxena, MD, FASN, is a digital artist based in Dubai, United Arab Emirates. His abstract artwork blends trained medical expertise with vibrant color palettes, creating visually captivating landscapes of human identity and transformation. Saxena's work has been exhibited internationally and featured on the covers of medical journals.

KIDNEY WATCH 2026

Every year, members of the *Kidney News* editorial board outline what they think will be the key topics to watch across nephrology in the upcoming year based on the latest research, presentations, and advancements in the field of kidney health. Explore this year's top areas to watch, from new drug therapies to trends in onconephrology, artificial intelligence, transplantation, and more.

Read past Kidney Watch editorials: https://www.kidneynews.org/page/kidney-watch

Navigating New Therapies for IgA Nephropathy in 2026

By Ayman Al Jurdi

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This is an exciting time for the treatment of immunoglobulin A nephropathy (IgAN). Just a few years ago, we managed IgAN largely with supportive measures. Now, we have an expanding armamentarium of disease-modifying therapies. At ASN Kidney Week 2025, phase 3 clinical trial interim data were presented for sibeprenlimab, atacicept, and telitacicept, all of which showed significant proteinuria reduction. It is becoming difficult to keep up with all of the new treatments—and even harder to know when to use each one. This is a good problem to have.

A simplified way to categorize the new treatments is to assess whether they are immunosuppressive. The nonimmunosuppressive options include renin-angiotensin-aldosterone system (RAAS) blockers, sodium-glucose cotransporter-2 (SGLT2) inhibitors, and endothelin receptor blockers. Immunosuppressive therapies include glucocorticoids, a proliferation-inducing ligand (APRIL)/B cell activating factor (BAFF) inhibitors, anti-CD38 antibodies, antimetabolites, and complement inhibitors. The approval of APRIL/BAFF inhibitors has been highly anticipated for several reasons. First, they target the disease pathophysiology proximally at the level of reducing galactose-deficient IgA1 production (1, 2). Second, phase 3 clinical trial data have shown promising results with impressive proteinuria reduction (1, 2). Third, they do not have glucocorticoid side effects or the encapsulated organism infection risk associated with complement pathway blockade.

The main question that remains now is how to decide between these treatment options: Which ones do we use up front? Do we use them as monotherapy or in combination? And for how long do we treat people? The way to move the field of IgAN forward is for us to conduct studies to answer these important questions.

At this time, we do not have the answers to these questions, but we do know some things. First, we know that dual endothelin and RAAS blockade with sparsentan results in lower proteinuria levels and slower estimated glomerular filtration rate decline at 2 years (3). The limited data available from an atrasentan trial also suggest that the magnitude of proteinuria reduction from endothelin blockade is consistent whether or not patients are receiving SGLT2 inhibitors (4). Therefore, it is clear that the optimal nonimmunosuppressive therapy for people with IgAN and persistent proteinuria is a combination of RAAS, endothelin, and SGLT2 blockade.

Second, we know that the proteinuria-reducing effect of several immunosuppressive therapies studied so far (sibeprenlimab, atacicept, and iptacopan) is independent of SGLT2 inhibitor use (1, 2, 5). This independence suggests that these drug classes may have additive benefits—a key consideration when designing combination regimens. Many of these trials were conducted before endothelin blocker approval, and therefore, we do not know whether their benefits are independent of endothelin blockade. I suspect they are independent due to their different mechanisms of action, but this will need to be confirmed. Newer trials have included individuals receiving endothelin blockade as well as RAAS and SGLT2 inhibitors (e.g., NCT06291376).

Third, we know that MEST-C scoring (mesangial hypercellularity, endocapillary hypercellularity, segmental glomerulosclerosis, tubular atrophy/interstitial fibrosis, and cellular/fibrocellular crescents) alone should not dictate the choice of initial therapy. Trials have shown that iptacopan and sibeprenlimab are effective regardless of biopsy MEST-C scores, although some trials excluded those with C2 and T2 scores (2, 5). Therefore, in clinical practice, individuals with IgAN do not need repeat biopsies to assess "disease activity" before deciding on initiating an immunosuppressive IgAN treatment. What probably matters more is the aggressiveness of the disease. People with rapidly progressive glomerulonephritis from IgAN are unlikely to respond to supportive therapies alone, which is why guidelines recommend immunosuppressive therapies for these individuals (2, 5). However, we do not know the optimal treatment for this subgroup, as they were excluded from all of the IgAN clinical trials. Future trials need to study the efficacy of new IgAN treatments in this group of patients.

We know that lower time-averaged proteinuria is associated with a lower risk of kidney failure for people with IgAN (6). So, should we be starting combination therapy up front? If so, should the combination be an immunosuppressive "disease-modifying" agent and a supportive treatment? It makes pathophysiologic sense to use at least one agent that targets the immunopathogenesis of the disease. Otherwise, if we just use combinations of nonimmunosuppressive agents, we are not affecting the early drivers of disease pathogenesis. Does the mechanism of action of treatment matter if we achieve the same level of proteinuria control? Are the long-term outcomes different if we achieve the same level of proteinuria control with APRIL/BAFF inhibitors compared with combinations of supportive therapies? Real-world data using well-designed cohort studies will be critical to answer these questions.

In summary, we have made much progress in the treatment of IgAN, but there is more to be done. We must now determine whether combination therapy up front yields better outcomes than sequential escalation. We need to better phenotype people with IgAN to identify who is more likely to benefit from one treatment versus another up front, as opposed to a trial-and-error strategy. We also need to investigate the efficacy of the new treatments in clinical trials for groups excluded from trials. These include individuals with rapidly progressive glomerulonephritis and recurrent IgAN after kidney transplantation. Accomplishing these goals will require coordinated trials, registries, and biomarker research. ■

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Practicing Precision Medicine: Onconephrology Innovations From ASN Kidney Week 2025

By Paul Hanna and Prakash Gudsoorkar

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Onconephrology, the interface of nephrology and oncology, continues to evolve as cancer therapies expand in scope and complexity. The ASN Kidney Week 2025 oral abstract session (Figure) on "Onconephrology: Updates, Therapies, and Mechanisms" showcased a spectrum of studies addressing acute kidney injury (AKI), metabolic derangements, and renal protection strategies in cancer care. This editorial synthesizes pivotal findings across these investigations, spanning plasma exchange in myeloma-related nephropathy, metabolic interventions in tumor lysis syndrome (TLS), immune checkpoint inhibitor nephritis, and biomarker-driven precision nephrology. Collectively, these studies refine our understanding of kidney injury mechanisms in patients with cancer and offer key suggestions to optimize clinical management in this vulnerable population.

Plasma exchange in light-chain cast nephropathy: Re-evaluating the evidence

Chewcharat et al. reported a multicenter target trial emulation (TTE) evaluating plasma exchange (PLEX) in 500 patients with light-chain cast nephropathy (LCCN) treated between 2010 and 2024 (1). Historically, randomized trials failed to show benefit, but these predated modern clone-directed myeloma therapy. In this rigorously adjusted analysis, no difference in renal recovery was observed between PLEX and non-PLEX groups (odds ratio, 0.66; 95% confidence interval [CI], 0.09–4.68). Subgroup analysis suggested a modest benefit in newly diagnosed myeloma cases but not in relapsed disease. *Clinical impact*: Despite methodologic sophistication, this large TTE reaffirms that PLEX should not be routinely used in LCCN, except in select cases with newly diagnosed high free light-chain burden and rapid AKI progression. The study emphasizes prioritizing rapid initiation of clone-directed therapy, such as bortezomib and supportive measures, over extracorporeal interventions.

Uricase therapies in tumor lysis syndrome: Optimizing efficacy and timing

Pegloticase as a novel option

Mandayam et al. investigated pegloticase, a long-acting PEGylated uricase, as an alternative to rasburicase in more than 30 patients with severe TLS (2). A single intravenous dose reduced serum uric acid from 8.7 to less than 0.4 mg/dL within 6 hours and maintained suppression (<3.5 mg/dL) for 30 days, accompanied by a mean serum creatinine reduction of 3.5 mg/dL by day 7. No major adverse events, such as the need for dialysis, occurred in this small cohort. *Clinical impact*: These findings suggest that pegloticase could offer durable urate control in TLS, potentially obviating the need for repeated rasburicase dosing, reducing drug costs, and serving as an alternative for those with glucose-6-phosphate dehydrogenase deficiency. Its extended half-life may particularly benefit patients with hematologic malignancies who have delayed cell lysis or ongoing uric acid production.

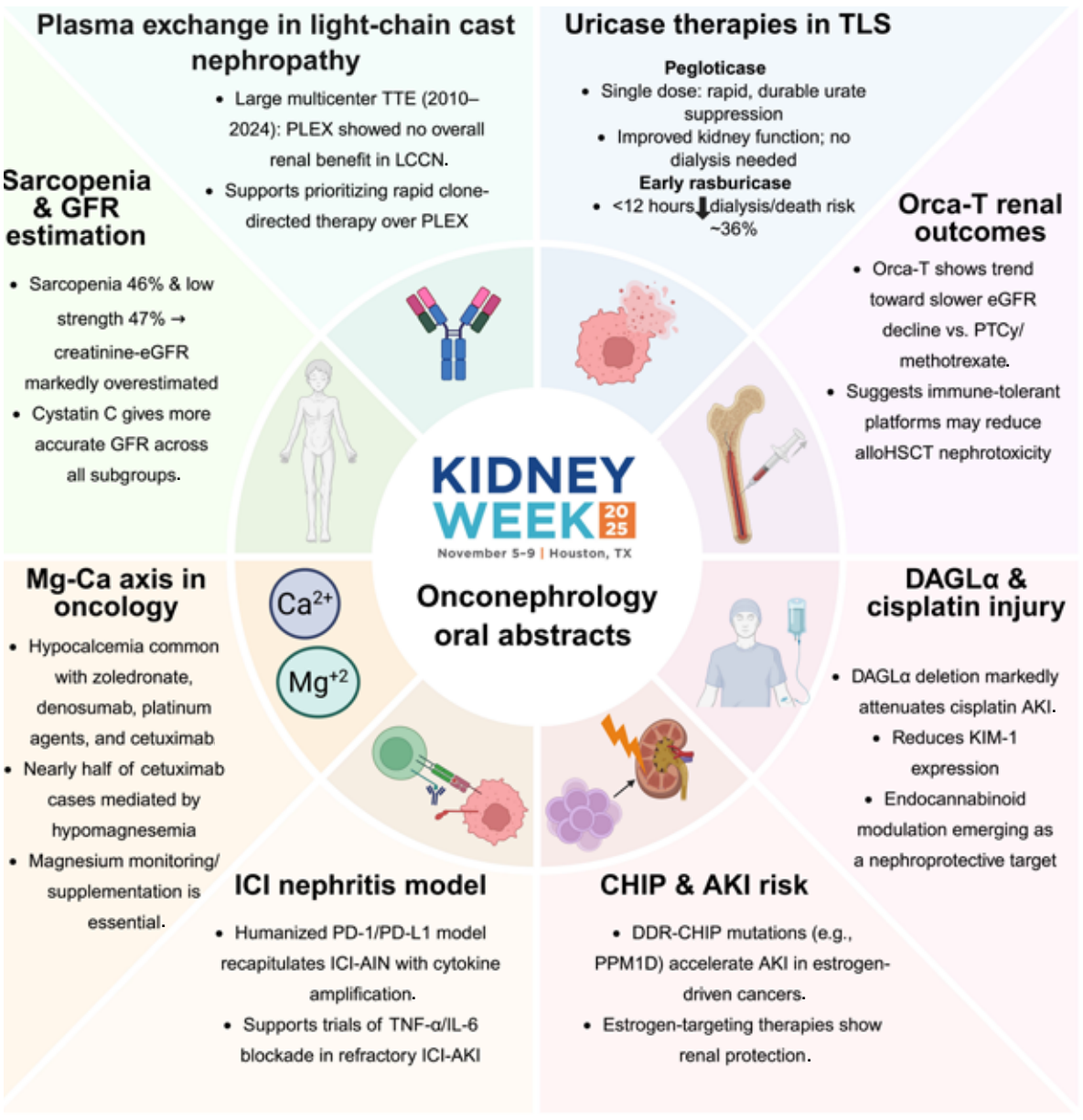
Early rasburicase use and survival

In a complementary study, Shenoy and Leaf (STOP-TLS [Stop Tumor Lysis Syndrome] investigators) analyzed data from over 1000 patients with TLS treated across 26 hospitals (3). Early rasburicase administration (within 12 hours of TLS onset) was associated with a 36% reduction in the composite outcome of AKI requiring dialysis or in-hospital death (adjusted odds ratio, 0.64; 95% CI, 0.47–0.87) compared with later administration. The benefit is extended to both AKI prevention and mortality reduction. *Clinical impact*: The data validate time-sensitive uric acid lowering as a key determinant of outcomes in TLS, urging institutions to integrate early recognition protocols and standardized rasburicase order sets within oncology pathways.

Post-transplant kidney function: The Orca-T paradigm

Orca-T is an investigational allogeneic T-cell immunotherapy developed by the biotechnology company, Orca Bio (4). Ziolkowski et al. compared renal trajectories after allogeneic hematopoietic stem cell transplantation (alloHSCT) using Orca-T, post-transplant cyclophosphamide (PTCy), or methotrexate for graft-versus-host disease prophylaxis (5). Among 240 recipients, Orca-T recipients exhibited a slower estimated glomerular filtration rate (eGFR) decline (difference-in-differences = 7 mL/min/1.73 m^2 per year; 95% CI, –9 to 23) and an 80% posterior probability of renal preservation compared with methotrexate. In contrast, the eGFR declined faster with PTCy (difference-in-differences = –8 mL/min/1.73 m^2 per year; 95% CI, –28 to 11), with only a 23% posterior probability of slower decline. However, none of these differences in the eGFR slope reached statistical significance. *Clinical impact*: By promoting immune tolerance and reducing graft-versus-host disease, Orca-T may indirectly mitigate transplant-associated nephrotoxicity. These results lay the groundwork for incorporating renal endpoints into alloHSCT trials, bridging immunotherapy and nephrology.

Figure. Summary of oral presentations on onconephrology at Kidney Week 2025



AIN, acute interstitial nephritis; Ca/Ca^{2+}, calcium; DDR, DNA damage response; KIM-1, kidney injury molecule-1; Mg/Mg^{2+}, magnesium; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1.

Mechanistic insights: Endocannabinoid pathway in cisplatin nephrotoxicity

Wang et al. examined diacylglycerol lipase-κ (DAGLκ)-knockout mice treated with cisplatin (6). Deletion of DAGLκ markedly attenuated kidney injury: Blood urea nitrogen fell from 101 to 45 mg/dL and serum creatinine from 1.04 to 0.41 mg/dL compared with wild-type controls. Tubular injury scores and kidney injury molecule-1 expression were also substantially reduced. *Clinical impact*: These preclinical findings highlight DAGLκ as a potential therapeutic target to prevent chemotherapy-induced nephrotoxicity, specifically cisplatin. Modulating renal endocannabinoid synthesis may complement strategies like hydration, magnesium supplementation, and dose optimization in patients with high-risk cancer.

Modeling immune checkpoint inhibitor-associated nephritis

Cuenca Narvaez et al. used a humanized programmed cell death protein-1/programmed death-ligand 1 mouse model to study immune checkpoint inhibitor (ICI) nephrotoxicity (7). Pembrolizumab plus anti-cytotoxic T-lymphocyte-associated protein 4, with or without tumor necrosis factor (TNF)-κ/interferon-κ coadministration, induced acute interstitial nephritis marked by $CD4^+$ infiltration, elevated interleukin (IL)-6, monocyte chemoattractant protein 1, and TNF-κ levels, and enrichment of T/natural killer cell and macrophage clusters on single-cell RNA sequencing. *Clinical impact*: The model reproduces the immunopathology of ICI nephritis, confirming cytokine amplification loops as mechanistic drivers. This work supports trials of cytokine blockade (e.g., TNF-κ or IL-6 inhibitors) for steroid-refractory ICI-AKI and provides a translational platform for testing nephroprotective interventions.

Personalizing AKI risk: CHIP mutations and estrogen signaling in cancer care

Won and colleagues explored whether clonal hematopoiesis of indeterminate potential (CHIP) increases the risk of AKI in patients with estrogen-sensitive cancers independent of other known cancer-related risk factors (8). Using data from nearly 25,000 patients with solid tumors, they analyzed trends in serum creatinine alongside genetic sequencing and treatment histories. Their findings revealed that mutations in DNA damage response genes, particularly PPM1D, were linked to a faster onset of AKI in breast, endometrial, ovarian, and non-small cell lung cancers. Interestingly, therapies targeting estrogen signaling, such as estrogen receptor antagonists and selective modulators, were associated with a lower risk of AKI, suggesting a protective effect. *Clinical impact:* This study identifies specific CHIP mutations as potential prognostic markers for AKI in estrogen-driven cancers. It also highlights the role of estrogen signaling in modulating kidney injury risk, opening the door to more personalized nephrology care in oncology settings.

Electrolyte disorders in oncology: The magnesium–calcium axis

Suzuki et al. analyzed 5474 patients receiving antineoplastic therapy to identify drug-related hypocalcemia and the mediating roles of serum magnesium (9). Hypocalcemia occurred in 7.5% of patients, predominantly with zoledronate, denosumab, carboplatin, cisplatin, and cetuximab. Notably, 46.6% of cetuximab-associated hypocalcemia was mediated by hypomagnesemia, whereas denosumab-induced hypocalcemia was independent of magnesium. *Clinical impact*: The findings underscore the centrality of magnesium monitoring in patients receiving epidermal growth factor receptor inhibitors or platinum compounds. Preventive magnesium supplementation could reduce secondary hypocalcemia, minimizing neuromuscular and cardiac complications during therapy.

Body composition and GFR estimation in older patients with cancer

Costa e Silva et al. examined 213 older patients with cancer to assess how muscle mass and strength affect GFR estimation (10). Sarcopenia (46%) and low muscle strength (47%) led to significant overestimation of eGFR based on creatinine clearance, whereas cystatin C-based equations improved accuracy across all subgroups. *Clinical impact*: This is the first study, to our knowledge, to show that reduced muscle strength can lead to significant bias and poor accuracy in creatinine-based eGFRs even in patients with normal muscle mass. Assessing muscle strength is simple to incorporate into routine clinical care. It can help identify individuals who may benefit from more reliable methods of kidney function assessment, such as cystatin C-based equations or directly measured GFR.

Conclusion

Collectively, these studies reshape the field of onconephrology, offering a fresh perspective on mechanisms, diagnostics, and treatments for patients with onconephrologic needs. A unifying theme across all accepted research is the critical role of precision medicine, whether it is timing interventions in TLS, targeting specific pathways like DAGLκ or cytokines, or tailoring assessments based on patient characteristics such as muscle mass. As advanced oncologic treatments move toward personalized treatments, onconephrologists must integrate new insights to anticipate, prevent, and mitigate renal complications in cancer care. ■

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Artificial Intelligence and Technology in Nephrology

By Jing Miao, Charat Thongprayoon, and Wisit Cheungpasitporn

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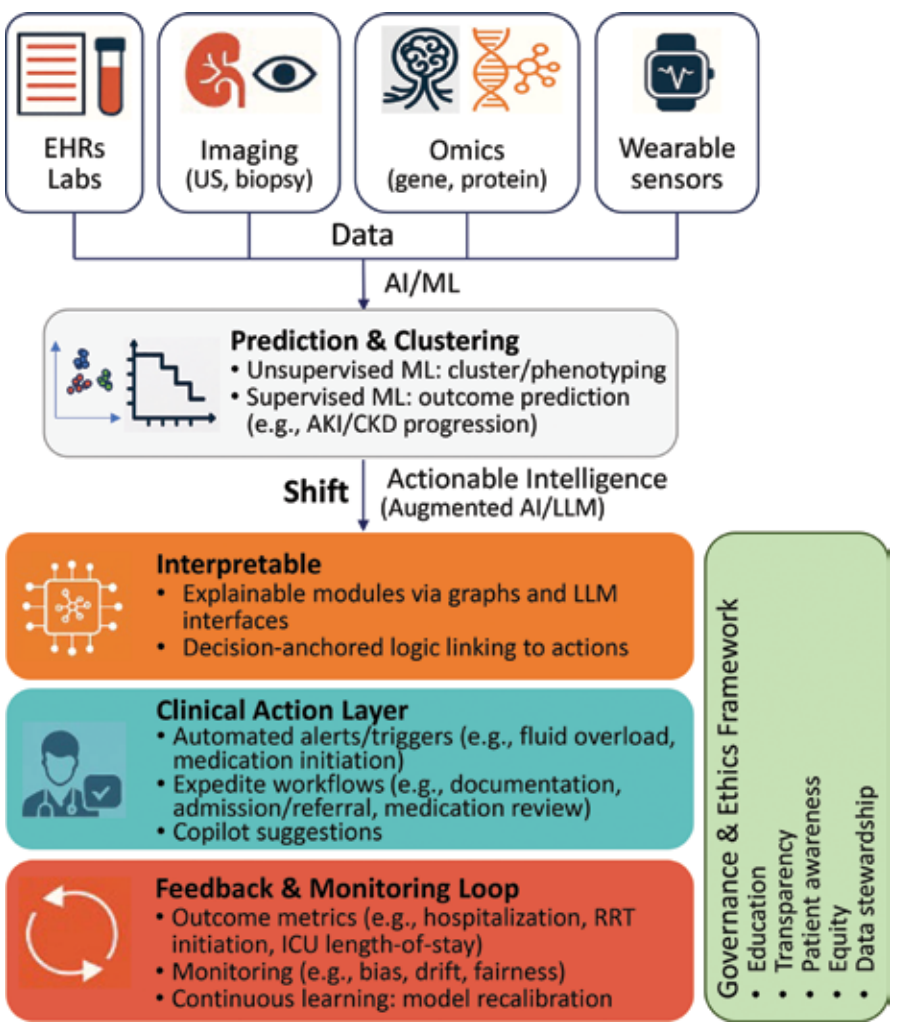
Artificial intelligence (AI) has shifted from proof of concept to core infrastructure within kidney care delivery, influencing how clinicians interpret data, make decisions, and engage patients. A landmark statement, "Responsible Use of Artificial Intelligence to Improve Kidney Care," written by the ASN AI Workgroup, outlines foundational principles to guide AI development: prioritizing patient benefit, ensuring clinician oversight, and advancing innovation in high-burden disease areas (1). This ethical and operational framework delineates the boundaries within which innovation must evolve, emphasizing that AI should augment rather than substitute physician judgment. The challenge, therefore, extends beyond technical achievement; it involves integrating AI in ways that enhance diagnostic precision, streamline workflows, and individualize therapy, while preserving the human judgment and empathy that remain central to effective kidney care (Figure).

From prediction to actionable intelligence

Early nephrology-AI applications were largely retrospective: models to forecast acute kidney injury (AKI) or chronic kidney disease (CKD) progression (2, 3). Increasingly, the paradigm is shifting to *decision-anchored* intelligence: Predictive outputs are immediately tied to evidence-based actions. Examples include automated triggers to initiate sodium-glucose cotransporter-2 inhibitors, to expedite transplant referral, or to optimize ultrafiltration rates in dialysis (4). Analytics without a tangible clinical consequence are no longer sufficient.

Complementing this shift is the adoption of rapid-cycle validation methodologies: Embedded monitoring loops of 30 to 60 days measure not only model performance (area under the curve, calibration) but real-world outcomes such as hospitalization reduction, referral shortening, or dialysis-free survival (1, 4). This closes the loop between insight and impact.

Figure. From algorithm to action: AI in nephrology workflow



This schematic illustrates the progressive integration of AI into kidney care. Data from electronic health records (EHRs), imaging, and biosensors feed into interpretable AI and machine learning (ML) engines that generate clinically actionable insights. These insights trigger decision-support interventions such as medication optimization, transplant referral, or dialysis management, which are reviewed by the clinician within a "physician-in-the-loop" framework. Continuous feedback loops monitor outcomes, bias, and data drift, ensuring adaptive learning and sustained clinical value. Governance and ethics layers reinforce transparency, patient awareness, and equitable deployment across health care settings. RRT, renal replacement therapy; US, ultrasound.

From algorithms to action: Global translation

At ASN Kidney Week 2025 in Houston, TX, the session "Artificial Intelligence and Data Science Transforming Kidney Care: From Algorithms to Action" showcased international initiatives ranging from intensive care unit (ICU) temporal risk modeling and dialysis phenotyping to pathomic evaluation in transplantation and organoid-based nephrology experimentation (5). Five recurrent themes emerged:

1) Predictive precision in dialysis and critical care settings
2) Explanation via knowledge graphs and large language model (LLM)-driven interfaces
3) A pathology revolution integrating histology, proteomics, and imaging
4) Translational integration bridging computational output and biologic validation
5) Global collaboration in building interoperable, ethical AI ecosystems

These themes reflect a maturing field: The focus is not merely "Can we build a model?" but rather, "How do we embed it responsibly into care pathways across continents?"

Augmented intelligence at the frontline

Clinicians increasingly interact with AI in their everyday workflows. Ambient-documentation tools and nephrology-specific "copilots" now:

- Synthesize labs and trends
- Propose structured notes
- Suggest treatment-plan options within secure electronic health record environments

These systems reduce the documentation workload while preserving clinician oversight, thereby fulfilling the ASN mandate for a "physician in the loop" (4, 6).

In critical care, interpretable models now forecast AKI up to 48 hours ahead, and prototype systems guide continuous renal replacement therapy decisions on ultrafiltration rate and anticoagulation (7, 8). Outpatient applications include CKD risk engines that trigger referrals and medication reviews, dialysis analytics forecasting admissions/fluid overload, and "virtual-biopsy" algorithms refining donor-organ evaluation (9). Success metrics have shifted from abstract model metrics to clinically meaningful endpoints: shorter ICU stays, improved survival, fewer admissions, and faster transplant listing (8).

Ethics, education, and governance

The ASN statement codifies practical principles for responsible implementation:

- Local validation across demographic subgroups
- Transparent documentation of clinician responses to AI recommendations
- Continuous postdeployment monitoring for bias, drift, and fairness
- Clear patient content or awareness when key decisions are AI-influenced

Educational imperatives have followed. Fellowship programs in nephrology now incorporate AI literacy, bias detection, and regulatory context. LLMs are emerging as interactive teachers, generating case simulations and feedback loops that accelerate clinical reasoning and knowledge retention.

Outlook: Toward responsible precision

As nephrology enters 2026, the challenge is no longer "invent the next algorithm" but rather "integrate responsibly at scale." The Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference on Technological Advancements to Support Guideline-Informed Care (November 20–23, 2025, in Madrid, Spain) emphasized this shift: interoperability, real-world validation, explaining AI, and embedding in continuous learning health systems (10).

In effect, the alignment of the ASN framework and KDIGO deliberations defines what "good AI" in nephrology looks like:

- Decision-anchored and clinically actionable
- Ethically governed and transparent
- Locally validated, monitored, and fair
- Human-centered, enabling precision care while safeguarding trust

AI in nephrology is no longer "on the horizon"; it is becoming the backbone of modern kidney medicine. The task ahead is one of stewardship: ensuring that technologic progress actually advances patient outcomes, clinician empowerment, and global equity. Responsible adoption requires harmonized standards, continuous validation, and transparency in how AI influences clinical decisions. It also demands investment in education so that nephrologists understand, critique, and guide these systems rather than passively use them. In both resource-rich and resource-limited settings, the goal remains the same: to use AI not as a replacement for human judgment but as a multiplier of human insight, bridging data and compassion to deliver more precise, timely, and just kidney care for all. ■

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The authors report no conflicts of interest.

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Board Certification Without a US Residency: An Option Under New ABIM Pilot

By Katherine Kwon

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The American Board of Internal Medicine (ABIM) has started a pilot program that allows international medical graduates (IMGs) who completed their internal medicine residency abroad to become board eligible after fellowship training in the United States (1). The pilot is available to fellows in training across all internal medicine subspecialties. Prior to this pilot, such physicians could complete a US nephrology fellowship program but were then required to complete an internal medicine residency program in the United States in order to be eligible for both the internal medicine and nephrology board examinations. The one exception was Pathway A, for doctors who had held full-time faculty positions abroad for at least 3 years. This new pilot does not have that requirement. Practices that are now hiring may encounter participants in this pilot program. They should understand the guardrails that exist to ensure that these physicians have adequate training to practice medicine in the United States, as well as potential challenges with state licensing.

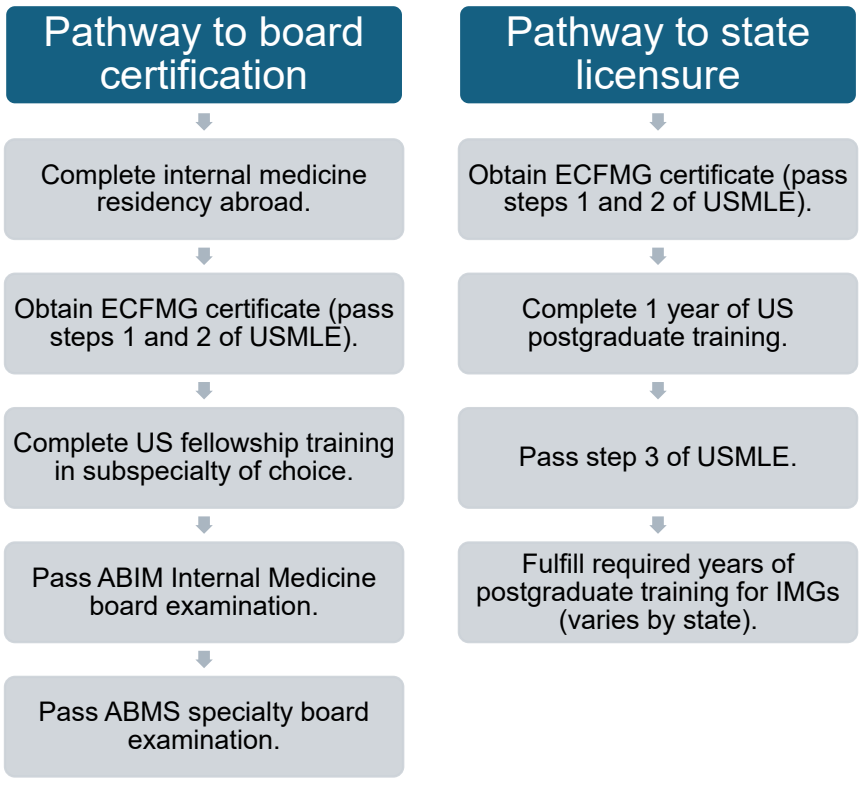
To be eligible for the pilot, physicians need to have successfully completed a 3-year postgraduate training program outside the United States or Canada. The candidate needs to have also demonstrated exceptional qualifications as described by the Accreditation Council for Graduate Medical Education (ACGME). These could include additional scholarships or leadership positions beyond the training program requirements. While ACGME provides examples, it is up to the local education committee to determine what counts as an exceptional qualification for an individual applicant. Pilot participants must also obtain their certificate from the Educational Commission for Foreign Medical Graduates (ECFMG), which in turn requires them to have passed steps 1 and 2 of the US Medical Licensing Examination (USMLE) (2). Fellows admitted under exceptional qualifications, like all IMGs admitted to US training programs, must be evaluated for clinical competence in the first 12 weeks of their program (3).

After completing fellowship training, physicians in the pilot are then eligible to take the ABIM Internal Medicine initial certification examination. A physician must pass this examination to be allowed to sit for a subspecialty examination, which includes the nephrology boards. These physicians are not eligible to sit for the internal medicine boards until after their fellowship training is done. Given the timing of when the internal medicine and nephrology boards are offered, participants in this pilot project will not be able to take their nephrology boards the first year after graduating fellowship (4), but they will be considered "board eligible."

It is important to note that board certification, while required by many hospitals and payors, is separate from state licensure, which allows a physician to practice independently. All states require physicians to pass step 3 of USMLE, which can be taken after a year of postgraduate medical training. Many states have additional requirements for the training of IMGs. There is some ambiguity in how these requirements have been written into state law, which may pose problems for participants in this pilot. For example, Maine and North Dakota both require IMGs to complete more than 2 years of ACGME accredited training and therefore may not be able to license an IMG after 2 years in a US nephrology fellowship (5).

This pilot pathway to board certification will run for the next 5 years. Those considering hiring physicians who proceed through this pathway should carefully check their state licensing requirements, and make sure the candidate and the practice both understand the multiple steps that will be required before full board certification (Figure). ABIM will be monitoring the results of the pilot program to determine participants' long-term practice patterns. If successful, the pilot may be converted to a permanent pathway. ■

Figure. New pilot pathway to board certification versus pathway to state licensure for an IMG



ABMS, American Board of Medical Specialties.

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Beyond Dialysis: The Growing Evidence Base for Conservative Kidney Management

By Annie Liu

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People with advanced chronic kidney disease (CKD) experience high mortality rates, particularly among older adults (1). The majority of people living with stages 4 and 5 CKD are over age 65 years, and fewer than 20% ultimately receive a kidney transplant (1, 2). Frailty, multimorbidity, cognitive impairment, and functional limitations remain major barriers to transplant eligibility (3). As kidney failure progresses, dialysis is often positioned as the default life-sustaining treatment. However, hemodialysis carries well-known challenges: thrice-weekly travel to dialysis centers, complications related to volume shifts or infections, and the cumulative time demands of treatment. Although dialysis may prolong survival, it can also negatively impact quality of life and may introduce symptoms such as intradialytic hypotension or postdialysis malaise that further impair physical and emotional well-being (4–6). Yet for many older adults, especially those with frailty or diminishing functional reserve, the burdens of dialysis can be substantial, and the net benefit may be uncertain (7, 8). These trade-offs prompt consideration of alternative approaches to align more with values, goals, and preferences.

Conservative kidney management (CKM)—also referred to as conservative care—is an active, patient-centered approach to managing advanced kidney failure without dialysis (9). Importantly, CKM is not synonymous with "doing nothing." Rather, it involves comprehensive medical management to control symptoms of uremia, fluid overload, pruritus, pain, sleep disturbances, and other common CKD-related concerns. CKM also emphasizes minimizing hospitalizations, aligning care with patient goals, and integrating psychosocial and palliative care support—all of which require active management, interdisciplinary support, and close communication with the patient and/or caregiver.

At ASN Kidney Week 2025, I was encouraged by the growing body of rigorous work in the CKM space. I found it both humbling and energizing to witness how clinicians and investigators across the country are pushing the boundaries of what conservative care can look like for people with advanced CKD. While important research continues in related areas—such as "palliative dialysis," symptom-focused dialysis strategies, and broader integration of specialty palliative care in nephrology—CKM is receiving attention as a meaningful care pathway for older adults.

One notable oral presentation came from Connie Rhee, MD, MS, and coauthors' prediction model estimating survival among people with advanced CKD who pursue conservative, nondialytic care versus dialysis among a Veterans Affairs cohort and externally validated with a separate dataset (10). This model fills an important gap by offering clinicians and patients additional tools to weigh the expected benefits of dialysis against the potential burdens. They identified several factors associated with higher mortality among veterans with advanced CKD including older chronological age, rapid estimated glomerular filtration rate decline, albuminuria, frailty markers, recent hospitalization, and specific comorbidities. These findings align with what practicing nephrologists observe clinically, yet the ability to quantify risk in a validated model would strengthen our capacity to engage in more transparent and empathetic conversations with people with advanced CKD and their family members about their future. In the future, it will be helpful to note how the model is incorporated into a clinical setting and implemented.

A central theme emerging from the presentations at Kidney Week was the growing recognition that quality of life be considered a research outcome for people with kidney diseases. CKM-centered research is uniquely positioned to focus on these patient-reported outcomes and ensure that they are central to treatment planning. Important challenges remain—many clinicians lack training in symptom management or structured decision-making conversations for nondialytic pathways. Reimbursement structures are still needed for supportive care. Future work must address these barriers to ensure access to conservative care options. I am hopeful that CKM will occupy a larger and more clearly defined role in our treatment options. Kidney Week showcased the momentum, but these efforts must be accompanied by sustained research, funding, training, and system-level support. Ultimately, our responsibility is to help people navigate the uncertainty of advanced CKD with compassion and a comprehensive range of options, including CKM, so they can live the life that aligns most closely with their goals and values. ■

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New Horizons in C3 Glomerulopathy: Targeted Complement Inhibition Arrives

By Sungsoo Kim, Krishna Mohita Kuruvada, and Kenar D. Jhaveri

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For decades, C3 glomerulopathy (C3G) remained a frustrating disorder, as our pathophysiologic clarity far outpaced therapeutic options. With the recent US Food and Drug Administration (FDA) approvals of Fabhalta (iptacopan) and Empaveli (pegcetacoplan), nephrologists finally have agents that directly target the complement pathways driving disease progression (Figure) (1).

The APPEAR-C3G phase 3 study (NCT04817618) enrolled 74 adults with biopsy-proven C3G, low serum C3, and persistent proteinuria despite standard therapy. Patients were randomized to receive oral iptacopan (200 mg twice a day) or placebo for 6 months, followed by open-label extension. At 6 months, iptacopan reduced proteinuria by 35% relative to placebo ($p = 0.0014$) while stabilizing the estimated glomerular filtration rate (eGFR) and normalizing complement activity markers. Most adverse events were mild to moderate, and notably, no meningococcal infections occurred. This trial provided the first robust, placebo-controlled evidence, to our knowledge, that targeted inhibition of the alternative pathway confers measurable kidney benefit in C3G (2).

The subcutaneous C3 inhibitor pegcetacoplan received FDA approval in 2025 for C3G and immune-complex membranoproliferative glomerulonephritis (IC-MPGN) in patients aged 12 years or older. By blocking complement C3, it prevents the cascade of glomerular injury characteristic of these diseases. The VALIANT study (NCT05067127)—a phase 3 randomized, double-blind, placebo-controlled trial across 122 global centers (the largest to date, to our knowledge, in these conditions)—enrolled 124 patients (69 adults and 55 adolescents) with native or transplanted kidneys and C3G or IC-MPGN (3). Participants received pegcetacoplan twice weekly or placebo, in addition to angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, sodium-glucose cotransporter-2 inhibitors, or steroids. Pegcetacoplan achieved a 68% relative reduction in proteinuria compared with placebo at 26 weeks (–67.2% versus +2.9%), meeting the primary endpoint. Secondary endpoints strongly favored pegcetacoplan: 49% achieved the composite renal response (eGFR preservation; i.e., ≤15% decline plus ≥50% proteinuria reduction) compared with 3% with placebo, and 60% achieved 50% or more proteinuria reduction compared with 5% with placebo. Remarkably, C3 staining cleared to 0 intensity in 71% of patients compared with 9% receiving placebo, demonstrating a true reversal of complement deposition. Safety was comparable with placebo, with no meningococcal infections reported. The effects were consistent across age, sex, race and ethnicity, transplant status, and concomitant immunosuppression. These findings establish pegcetacoplan as the first therapy to produce robust clinical, biochemical, and histologic improvement in complement-mediated MPGN.

Together, these studies herald a new era in the study of complement-mediated kidney disease. Iptacopan suppresses the complement amplification loop at factor B; pegcetacoplan blocks the central C3 hub (Table). Appropriate vaccination and infection precautions are still required with both agents, even though they modulate the upstream drivers of disease rather than the downstream inflammatory response. Although the long-term data on durability, eGFR trajectory, and cost-effectiveness are still required, the path forward is finally mechanism-based.

We believe the time has come to move beyond steroids, mycophenolate, and perhaps even eculizumab and to embrace the true disease-modifying agents to treat these rare conditions. Future guidelines should consider iptacopan and pegcetacoplan as first-line therapeutic options for C3G and idiopathic IC-MPGN. ■

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Drs. Kim and Kuruvada report no conflicts of interest. Dr. Jhaveri reports serving as a consultant for Apellis and Novartis.

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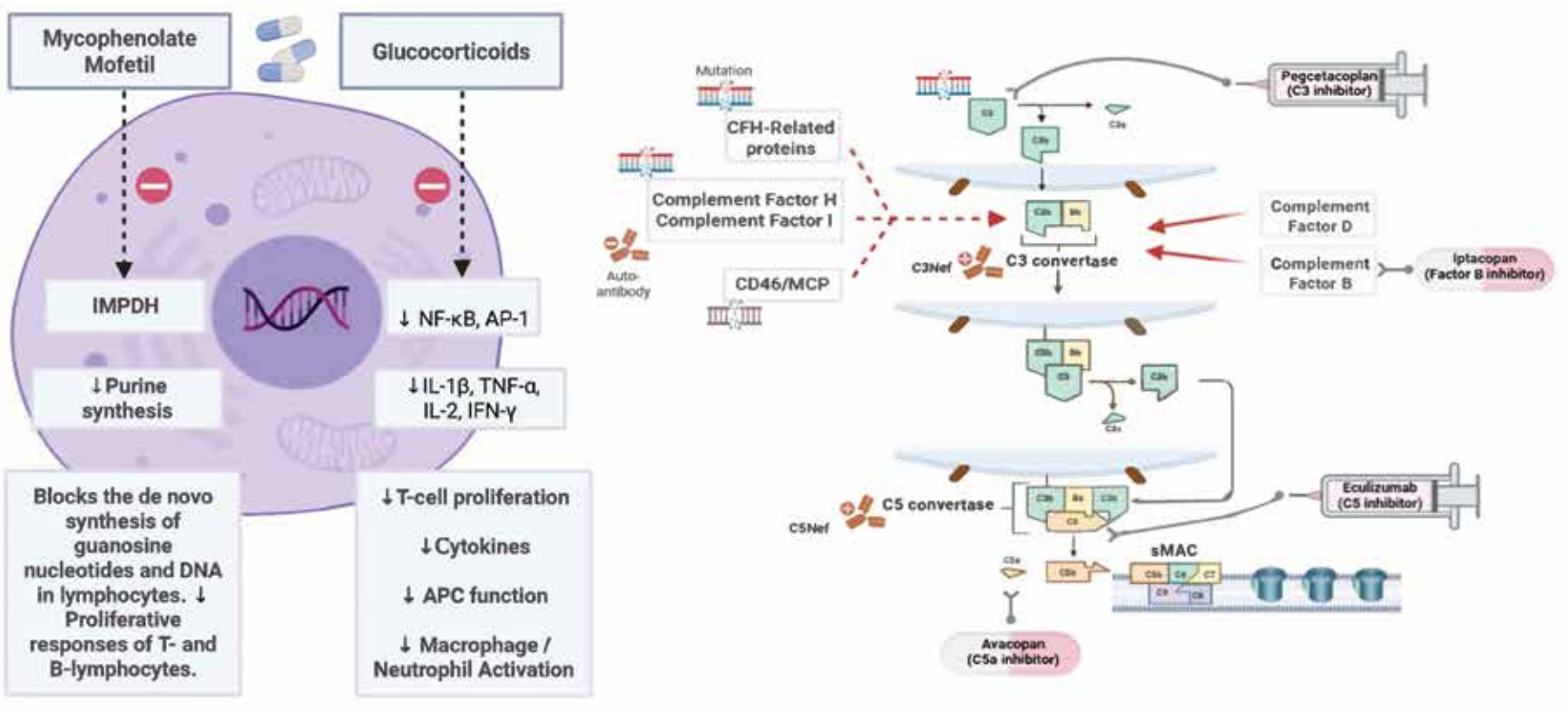
Figure. Therapeutic targets in C3G



This schematic illustrates the major immunosuppressive and complement-directed therapeutic strategies used in C3G. *Left*: Conventional immunosuppressive agents, including mycophenolate mofetil, which inhibits inosine monophosphate dehydrogenase (IMPDH) and blocks de novo guanine nucleotide synthesis, thereby suppressing T- and B-lymphocyte proliferation, and glucocorticoids, which downregulate nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and activator protein-1 (AP-1), reduce proinflammatory cytokines (interleukin [IL]-1κ, tumor necrosis factor [TNF]-κ, IL-2, and interferon [IFN]-γ), and inhibit T-cell activation, antigen-presenting cell (APC) function, and macrophage/neutrophil activation. *Right:* The complement pathway dysregulation characteristic of C3G, driven by genetic mutations (e.g., complement factor H [CFH] or factor I), CD46/membrane cofactor protein (MCP) defects, and autoantibodies such as C3 nephritic factor (C3Nef), which stabilize the alternative pathway C3 convertase (C3bBb). Therapeutic inhibitors target multiple steps: pegcetacoplan, a C3 inhibitor; iptacopan, a factor B inhibitor; avacopan, a C5a receptor antagonist; and eculizumab, a terminal complement C5 inhibitor that prevents soluble membrane attack complex (sMAC) formation. Together, these agents aim to reduce uncontrolled complement activation and downstream inflammatory injury characteristic of C3G.

Table. Comparison of iptacopan and pegcetacoplan in C3G

Feature	Iptacopan (Fabhalta)	Pegcetacoplan (Empaveli)
Mechanism of action	Selective factor B inhibitor; blocks formation of the alternative pathway C3 convertase, reducing amplification of complement activation	C3/C3b inhibitor; prevents activation of all classical, lectin, and alternative complement pathways; inhibits both C3 and C5 convertases
Complement target	Alternative pathway	Central complement component C3
Route/dosing	Oral, twice daily	Subcutaneous, twice weekly
eGFR cutoff	eGFR ≥30 mL/min/1.73 m^2	eGFR ≥30 mL/min/1.73 m^2
Pivotal trial	APPEAR-C3G (phase 3, randomized, double-blind, placebo-controlled)	VALIANT (phase 3, double-blind, placebo-controlled)
Study population	74 Adults (aged ≥18 years) with biopsy-proven C3G, low serum C3, proteinuria despite standard therapy	124 Patients (69 adults, 55 adolescents; aged ≥12 years) with C3G or IC-MPGN, including post-transplant recurrence
Primary endpoint	Percent change in urine protein at 6 months	Percent change in urine protein at 26 weeks
Efficacy highlights	35% Relative reduction in proteinuria versus placebo; eGFR stabilization	68% Relative reduction in urine protein creatinine ratio (UPCR) versus placebo; ≥50% UPCR reduction in 60% versus 5% in placebo; C3 staining clearance to 0 intensity in 71%; eGFR reduction: −1.5 versus 7.8 mL/min/1.73 m^2 (consistent across subgroups: age, sex, race and ethnicity, transplant status, and immunosuppression)
Safety profile	Tolerated well through 6 months; mild to moderate adverse events; no meningococcal infections	Injection-site reactions most common; mild to moderate adverse events similar to placebo; no meningococcal infections; one COVID-19–related death; no allograft rejection or loss
Approved indication (FDA 2025)	C3G in adults	C3G and IC-MPGN in adults and adolescents aged ≥12 years
Monitoring/precautions	Vaccinate against encapsulated bacteria; monitor kidney function and complement markers	Vaccination against encapsulated bacteria; monitor kidney function and complement markers
Unresolved questions	Duration of remission, eGFR preservation, efficacy in dense-deposit disease, use in kidney transplantation	Long-term safety, relapse prevention, pediatric use aged <12 years, cost/accessibility; limited transplant data; optimal treatment duration

From Variant to Bedside, Making Genetics Routine in Nephrology

By Zohreh Gholizadeh Ghozloujeh, Sayna Norouzi, and Edgar Lerma

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Genetic testing is evolving from a send-out curiosity into a tool that can inform frontline clinical care. The Kidney Disease: Improving Global Outcomes (KDIGO) Genetics in Kidney Health Summit in 2025 signaled that the question is no longer whether to integrate genetic testing in nephrology but how to do so in a sustainable and meaningful way. This article explores key domains in genetics that will shape nephrology in 2026 and beyond (Figure).

Implementation, not aspiration

The summit's dominant message was implementation. Genetic testing must be woven into routine nephrology practice through clear referral pathways, embedded variant boards, and kidney-genetics clinics that link nephrologists, genetic counselors, and laboratorians (1, 2). KDIGO called for measurable "value metrics": diagnostic yield, change in management, and cost-effectiveness, rather than publication counts. Such infrastructures allow genetics to inform daily decisions from clinic triage to transplant donor screening without creating new inequities.

The VUS decade

Variants of uncertain significance (VUS) remain common in kidney gene testing, and classifications evolve as new data accrue. This reality requires explicit policies for periodic reinterpretation, careful documentation, and, when clinically relevant, possibly recontact of patients (2–4). While genetic testing interpretation requires a multidisciplinary approach and close collaboration with genetic counselors, nephrologists cannot outsource genetic literacy. They should be able to explain uncertainty, integrate updated classifications into care, and coordinate cascade testing when a VUS is upgraded. The American College of Medical Genetics and Genomics/Association for Molecular Pathology 2015 standards still provide the basic framework for variant interpretation, but kidney-specific work, such as autosomal dominant polycystic kidney disease (ADPKD) VUS approaches and recognition of COL4-related cystic phenotypes, shows how nephrologists are adapting these rules in practice (3, 4).

Education as infrastructure

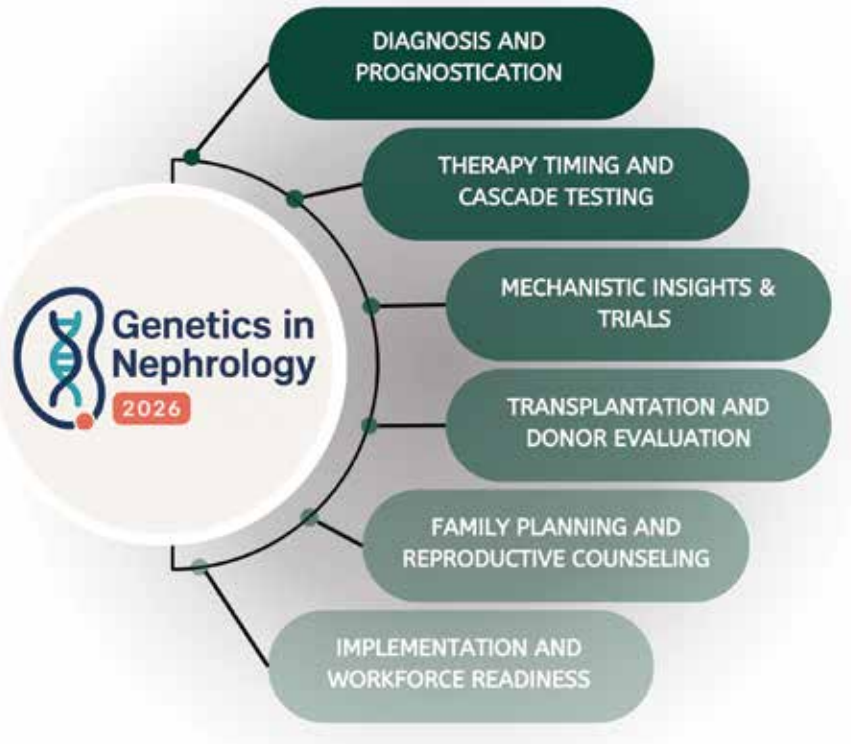
KDIGO and the National Kidney Foundation Working Group both underscored that implementation will fail without workforce readiness. Core competencies now include basic variant interpretation, familiarity with consent language, and knowledge of privacy protections under the Genetic Information Nondiscrimination Act (1, 5). Fellowship curricula and continuing medical education programs must embed genetic modules, whereas e-consults and telegenetics services can extend expertise to smaller centers (2). Education is not an accessory; it is the infrastructure that makes interpretation credible.

Where testing changes care

Genetic testing is already reshaping day-to-day nephrology. For example, in ADPKD, genotype can refine prognosis, support donor evaluation, and guide family counseling (6). In Fabry disease, combining enzyme activity, lyso-Gb3, and α-Gal A gene sequencing improves diagnostic accuracy, particularly in females and nonclassic presentations, and enables earlier cascade testing (7, 8). In glomerular diseases, genomic data are clarifying disease mechanisms and helping define more precise trial populations (9). These applications show that genetics is not theoretical; it is influencing decisions across inherited cystic, metabolic, and immune-mediated kidney diseases.

Continued on page 22

Figure. Key domains in which genetics is reshaping nephrology in 2026



From Variant to Bedside

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Reproductive nephrology and PGT-M

Preimplantation genetic testing for monogenic disease (PGT-M) now achieves analytic accuracies of approximately 98%–99% for most couples, with some condition-specific variation. Its use is increasing in monogenic kidney diseases, particularly in late-onset disorders such as ADPKD, in which many families consider PGT-M as an alternative to prenatal diagnosis when counseling is available (10). KDIGO 2025 recommends that nephrologists introduce the option early, ideally before conception, and do so in collaboration with reproductive-genetics specialists to address procedural, legal, and ethical considerations. Early and nondirective counseling supports informed and autonomous decision-making and brings reproductive planning into the core of precision nephrology.

Transplant

Genetic testing has become an integral part of pretransplant evaluation, for instance, including apolipoprotein L1 (APOL1) on kidney disease gene panels and offering testing when APOL1-associated nephropathy is clinically suspected, regardless of race or ethnicity, with structured counseling about uncertainty (2). In donor evaluation, adopt policy-driven, optional testing with informed consent while awaiting APOLLO (NCT03615235) results, aiming for informed choice rather than exclusion. Incorporating genetic information into donor evaluation, without weaponizing it, exemplifies the summit's implementation ethos.

Polygenic scores: Promise with guardrails

Large biobanks have now identified hundreds of loci associated with kidney-function traits, and polygenic risk scores can stratify chronic kidney disease risk at a population level (11). Yet clinical utility remains unproven, with limited prospective validation and persistent ancestry bias. Current expert guidance is that polygenic metrics should be used alongside, rather than in place of, monogenic testing and standard clinical assessment until robust, ancestry-diverse outcome data emerge (2, 11).

Equity and the patient voice

Equitable access requires both coverage and communication. Telegenetics models reduce geographic disparity, while inclusion of patient-reported outcomes ensures that "genetic value" reflects lived experience (1, 2). KDIGO emphasized that success will be measured not by variant counts but by trust, with patients understanding, consenting, and benefiting from their results.

A call to action

By 2026, the nephrology community should aim to implement clinic-level interpretation and embed genetics education across training and continuing medical education pathways (2, 5). The message from the summit was clear: Genetics is no longer a niche add-on; it is part of core clinical nephrology, and nephrologists need to take ownership of it. ■

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The authors report no conflicts of interest.

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Three Steps Forward and Three to Come: An Evolution Continues

By Jenny Kinane, Reanna Ramlogan, and Sam Kant

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Kidney transplant medicine continues its evolution in the realms of furthering our understanding of immunology, bettering immunosuppression, and addressing the organ shortage. In this editorial, we highlight three remarkable new breakthroughs that have emerged during the past year, as well as three promising developments on the horizon (Figure).

Firstly, this past year saw a major breakthrough in desensitization medicine, namely the ConfIdeS trial (NCT04935177), which evaluated the use of imlifidase for 12 months in 64 highly sensitized individuals receiving kidney transplants versus a control group (1). Imlifidase is an enzyme derived from *Streptococcus pyogenes* that breaks down immunoglobulin G antibodies, thereby blocking immunoglobulin G-driven immune reactions. The trial met its primary endpoint by demonstrating a higher estimated glomerular filtration rate in the treatment group (difference in the estimated glomerular filtration rate of 32 mL/min/1.73 m^2; $p < 0.001$). The drug, which is due to be assessed by the US Food and Drug Administration in the coming months, has the potential to reduce transplant wait times and reduce the risk of antibody-mediated rejection in this cohort of patients who are human leukocyte antigen-sensitized.

Secondly, notable progress has been made in normothermic machine perfusion, particularly when combined with Doppler organ assessment. Normothermic machine perfusion (37°C), as opposed to hypothermic machine perfusion (4°C), allows metabolic activity within the kidney, meaning that organs can be assessed before transplantation (2). Assessment of marginal donor kidneys at Cornell University, Ithaca, NY, last year, using power Doppler imaging compared with renal blood flow during normothermic machine perfusion in porcine kidneys, has proven very successful (3). Results demonstrate the ability to distinguish functional from nonfunctional kidneys with a diagnostic accuracy of 82%. This technology will hope to increase the number of expanded criteria for deceased donor kidney transplants.

Possibly the most fascinating breakthrough last year relates to Massachusetts General Hospital successfully carrying out its second genetically edited pig kidney transplant into a living human (4). Development of genetic editing tools, advancements in immunosuppression, and herd infection reduction or elimination have led to this point of seemingly successful xenotransplant (5), offering a possible solution to the global organ shortage.

There are numerous groundbreaking innovations and treatments on the horizon. At present, methods of achieving drug-free tolerance are being thoroughly investigated from many different angles, including mixed chimerism, nanotechnology, and T regulatory cell therapies, to name a few. A phase 3 randomized controlled trial published in the *American Journal of Transplantation* in July 2025 reported the use of mixed chimerism to produce immune tolerance (6). Participants received a kidney from 2-haplotype human leukocyte antigen-matched living siblings. The treatment group (n = 20) received cellular product (MDR-101) from the same kidney donor following a nonmyeloablative conditioning protocol. A control group (n = 10) received standard of care. Of the 20 recipients who received MDR-101, none developed graft-versus-host disease, and 75% (n = 15) reached the primary study endpoint of being immunosuppression-free for over 2 years.

Development and integration of artificial intelligence (AI) and machine-learning tools in medicine are gaining momentum. Technologies that will assist with clinical decision-making, risk stratification, prediction of graft survival, and more are being developed. Previous research comparing machine-learning models with traditional statistical modeling for predicting allograft failure have not shown any clear prediction advantages (7, 8); however, AI tools are strengthening when it comes to discriminative and calibration power. One example is the UK Deceased Donor Kidney Transplant Outcome Prediction (UK-DTOP), a model that incorporates donor and recipient variables using data from almost 30,000 transplant cases and has demonstrated superiority compared with other predictive tools (9). When assessing potential outcomes, UK-DTOP achieved an area under the curve statistical score consistently above 0.72, in comparison with the Kidney Donor Risk Index, which achieved an area under the curve of 0.64. Overall, AI holds significant promise for supporting clinical decision-making in transplantation.

Regeneration and bioengineering of kidneys have taken a major step forward, as scientists in multiple sites have successfully grown miniature kidney-like structures in the laboratory by using pluripotent stem cells (10). These organoids exhibit remarkable kidney architectures and mimic human fetal kidney development. To date, stem cell-derived kidney organoids have lacked a ureter, hindering urine drainage. Last year saw the development of stem cell-derived ureteric tissue in vivo, which represents progress toward functional kidney organoids with urine flow (11). Developing full-sized therapeutic organs from these organoids will require further investigation, but the outcome could provide an inexhaustible source of organs and could be used as a research tool in drug development.

The past year has helped to advance the evolution of kidney transplant medicine by potentially addressing long-term issues such as waitlists and inadequacies of immunosuppression. The promise that these developments hold will not just further the specialty but also the cause that we all are working toward—the well-being of our patients. ■

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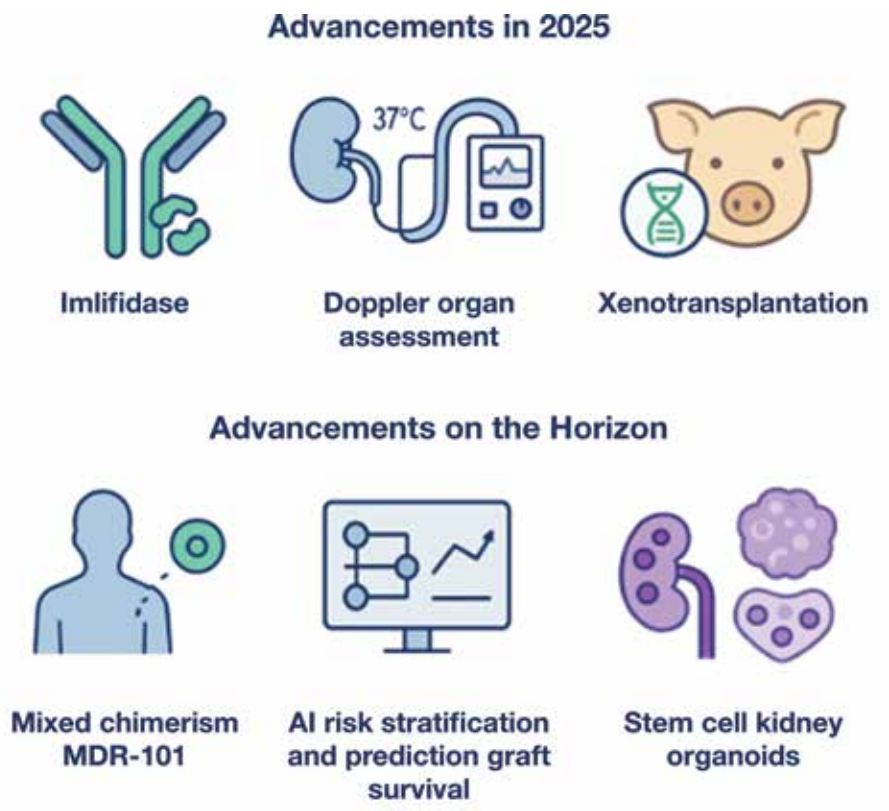
Figure. Kidney transplantation advancements in 2025 and ahead



Kidney Care Faces a Rapidly Evolving Policy Landscape Adaptation and New Strategies to Embrace Innovative Therapies and Tools Needed

By Bridget M. Kuehn

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For ASN Policy and Advocacy Committee member Ankur Shah, MD, MPH, FASN, associate chief for research, nephrology fellowship program director, and medical director for peritoneal dialysis in the Davita North-Providence program, Division of Kidney Disease and Hypertension, at The Warren Alpert Medical School of Brown University, Providence, RI, the last year of US policy changes affecting kidney diseases has felt like 10 years' worth.

He and his colleagues on the committee have worked with ASN policy staff to stay abreast of a raft of changes, including terminations of National Institutes of Health (NIH) grants and programs, caps on indirect research costs, frozen grant disbursements, changes in NIH grant funds disbursement, and new travel and immigration policies impacting the workforce. Shah joined a panel detailing the changes during an ASN Kidney Week 2025 session called "Two Years of Change in the United States: Congress, the White House, and the Policies Impacting Kidney Care for Private Practice and Academia Alike." Panelists described the impact of recent changes in government organization, payment policies, transplant system modernization, and funding. They also explained some of the policy challenges ahead in embracing growing innovation in kidney care.

Disruption and uncertainty

Those who rely on NIH grant funding faced a rollercoaster of ups and downs in 2025. Shah noted that in June and July, it looked likely that NIH grant funding would be drastically slashed, but thanks to Herculean efforts by the reduced staff at NIH, the total amount of funding released in 2024 pulled even with 2025 by the end of last year. However, the number of R01 grants awarded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has shrunk from 431 in 2024 to 261 in 2025, as the agency has shifted to a lump-sum grant-funding approach rather than spreading payments over years. The Agency for Healthcare Research and Quality, which plays a vital role in dialysis quality research, had no new projects launched last year, he said.

NIH is also facing a reorganization that would fold NIDDK into a National Institute on Body Systems and cut its budget from $7 to $4 billion under a "skinny budget" proposal from earlier last year, Shah said. However, at press time, the US House of Representatives and the Senate were debating budget proposals that will ultimately determine funding levels for 2026.

"We are seeing really big impacts on our research infrastructure," Shah said. He noted that the changes come at a time when the field is just starting to see past research-yield dividends in innovation, such as a growing number of therapies for immunoglobulin A nephropathy and new dialysis tools, and that the ongoing research cuts could have a "worrisome" impact on future innovation. About 5400 grants were also terminated in 2025, although NIH later reinstated 2860 of them, Shah said.

"This roller coaster is not good for science," he said. Training grants and equity-focused grants have been disproportionately affected by cancellations. Additionally, he noted that some fields, such as race and ethnicity, had been removed from the Centers for Medicare & Medicaid Services' 2728 forms, potentially reducing the amount of demographic information available about patients on dialysis. ASN and other members of the kidney community have advocated for the change to be reversed (1).

Tightened immigration restrictions are also likely to affect the kidney care workforce. Shah noted that a pause on visa interviews last summer led to some internal medicine residencies not filling their intern slots. "Today's internal medicine interns are tomorrow's nephrology fellows and next week's nephrologists," Shah explained. "It is a problem, and it is getting worse."

Additional changes would reduce the duration of J-1 visas to 4 years, in the middle of a nephrology fellowship. A proposed $100,000 fee for H-1B visas could also have a detrimental impact on the health care system. Shah explained that 11,000 to 12,000 people on J-1 and H-1B visas are in accredited residency and fellowship programs in the United States, totaling about 7.5% of the trainees and fellows in those programs (2). The impact could be even larger in nephrology, in which 31% of fellows hold one of these visa types, according to the 2024 ASN Nephrology Fellow Survey Report (3). The restrictions could also affect other members of the kidney care team. A study by the Texas Department of State Health Services, for example, found that nephrology had the highest proportion of internationally trained nurses representing about one in four of all nurses in the field, and about one in five dialysis nurses are internationally trained (4). "If we start seeing a reduction in our workforce, it is going to be very impactful," he said. He noted that the field is already facing a workforce crisis.

The domestic kidney care workforce could also be affected by new student loan restrictions. Federal student loans will be capped at $100,000 for graduate students and $200,000 over 4 years for professional students, with a $265,000 lifetime cap. Some professions would be reclassified as "nonprofessional," including nursing, and would see even lower annual loan caps of $20,500 (5). "We already face limitations in nephrology nurses and nephrologists," Shah said. "This is going to get worse."

Shifts have also occurred in value-based payment models, with the termination of the End-Stage Renal Disease Treatment Choices model by the end of 2025 and major revisions to the Kidney Care Choices (KCC) model in 2026. Shah noted that the KCC model led to a 31% increase in optimal dialysis starts, a 29% reduction in catheter use, a 10% increase in home dialysis, a 69% increase in pre-emptive transplants, and a 22% increase in living donor transplants, according to the Lewin report (6). However, those care improvements came at a cost of $304.8 million to Medicare. More than half of patients on dialysis have shifted to Medicare Advantage plans, and that proportion is expected to grow, heralding further payment changes on the horizon, Shah noted.

Cuts to nondiscretionary spending in the One Big Beautiful Bill, signed into law last summer, are also likely to affect kidney care. Shah noted that under the law, patients covered by Medicaid will now have $35 copays per visit, some will be required to work up to 80 hours per month to remain eligible, and eligibility will be determined every 6 months, which could lead to approximately 11.8 million people losing coverage over the next decade. The law also prevents new Medicaid taxes on clinicians and gradually lowers existing ones. Cuts to the Affordable Care Act subsidies are expected to lead to an additional 3 million people losing health coverage, unless Congress extends the subsidies. Supplemental food assistance benefits will also be cut by $300 billion over 10 years.

Shah noted that the changes will affect patients on dialysis with low incomes, as well as rural hospitals that serve larger proportions of uninsured or Medicaid-covered patients. "They are going to see an increase in uncompensated care," he said. The $50 billion Rural Health Transformation Program included in the law serves as a buffer but will not offset the full impact, he noted. "Disruption and uncertainty are the rule," he said.

Advocacy and adaptation

Yet, Shah also highlighted the resilience and ongoing advocacy by the kidney community on each of these issues and urged his fellow nephrologists to keep up to date on ASN's advocacy efforts (https://www.asn-online.org/policy/) and policy updates from Kidney Care Partners, a coalition of more than 25 organizations representing patients, kidney care clinicians, researchers, therapeutic developers, and manufacturers (https://kidneycarepartners.org/news/). "There is a lot of advocacy and adaptation," he said.

Scheduled speaker Tom Duvall, MBA, division director of the Center for Medicare and Medicaid Innovation (CMMI), was unable to attend Kidney Week due to the federal government shutdown at the time, so David White, senior regulatory and quality officer at ASN, provided an update on changes in federal payment programs. He noted that federal policies, such as President Donald J. Trump's 2019 Advancing American Kidney Health Initiative, aim to reduce progression to kidney failure; improve access to high-quality, person-centered

care; and increase access to transplantation. He noted that there has already been substantial progress toward increasing transplant access through the Health Resources and Services Administration (HRSA) Organ Procurement and Transplantation Network (OPTN) modernization initiative and CMMI's Increasing Organ Transplant Access (IOTA) Model. ASN's Transplant Policy Committee has been working with HRSA to help shape those initiatives and to advance legislation that supports patients undergoing transplant, such as the Living Donor Protection Act and the Honor Our Living Donors Act.

Panelist Yue-Harn Ng, MD, MPH, a member of ASN's Transplant Policy Committee and clinical professor of medicine at the University of Washington in Seattle, also highlighted the importance of these policy measures and the Securing the US (SUS) OPTN Act passed in 2023, which laid the groundwork for the modernization initiative. "Hopefully, there will be increased transparency and accountability by providing more funding and support [through SUS OPTN] to create a more efficient organ procurement and allocation system," she said. "The IOTA model will hopefully improve the quality of transplant care through an incentive payment model, and finally, the two living donor acts will hopefully remove disincentives and ensure financial neutrality for living donation."

White also highlighted the progress toward preventing kidney failure through stable rates of chronic kidney disease and progress made in delayed progression and home dialysis through KCC. He said to expect changes in CMMI's value-based care programs, based on the CMMI Pillars released in May 2025. These include a greater focus on upstream preventive care for people with chronic kidney disease and greater participation by private payors in value-based payment plans, he said. Additionally, the pillars call for better alignment between patient outcomes and financial incentives and for a focus on helping patients achieve their health goals. He also noted that CMMI has committed to protecting taxpayers by ensuring fiscally sound models, requiring clinicians or health care institutions to bear downside financial risks, reducing state governments' role in rate setting, and refining and simplifying benchmarks.

Pranav Garimella, MD, MPH, FASN, chief medical officer at the American Kidney Fund and associate professor of medicine at the University of California, San Diego, said another challenge moving forward will be resolving how to pay for innovations in kidney care. He highlighted the emergence of novel kidney disease risk-stratification tools and kidney disease progression biomarkers; therapies that slow disease progression; emerging targeted immune therapies and gene-based therapies; ongoing xenotransplant trials; novel organ preservation techniques; and even new drugs and devices for patients undergoing dialysis. But he noted that payment models have often unintentionally discouraged the adoption of new tools and therapies in kidney care due to cost-saving measures. "We have innovation in nephrology that is really being squeezed by several factors," Garimella said. "It is really going to take an act of Congress to fix."

Garimella noted that the Kidney Care Access Protection Act, introduced in September 2025, aims to create sustainable pathways for innovation and parity in Medicare Advantage payments for kidney care, which may lead to improvements in payments for innovative drugs and technologies. The Chronic Kidney Disease Improvement in Research and Treatment Act also aims to make it easier for outpatient dialysis centers to adopt hemofiltration devices and other new technologies. He noted that clinical trials for xenotransplantation are now underway, suggesting widespread adoption could be possible within 5 to 10 years. He suggested that regulatory pathways used to approve left ventricular assist devices as a bridge to transplantation may offer a model for advancing xenotransplantation. He encouraged the field to engage patients in how they would like to see this new technology used and work to consider how xenotransplants might fit into care paradigms and how they might be financed. "Innovation is outpacing us," Garimella explained. "What we need to do is find actual ways to pay for that innovation to bring it to patients."

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Suboptimal Dialysis Initiation

By Nupur Gupta and Srinath Yadlapalli

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A recent article in *Kidney360*, "Risk Factors for Suboptimal Dialysis Initiation: A Prospective Cohort Study," investigated risk factors for suboptimal dialysis among people with advanced chronic kidney disease (CKD) (1). The study found that suboptimal dialysis initiation was common despite close nephrology follow-up. Key risk factors identified were lower hemoglobin levels and a higher comorbidity index. Interestingly, people with suboptimal dialysis starts had more kidney replacement therapy (KRT) preparation at 6 months and a greater number of nephrologist visits in the past 6 months. While the study did not identify any readily modifiable patient-related risk factors, it did highlight the significant complexity of the topic (1).

Various terms have been used for suboptimal dialysis initiation, including *unplanned*, *urgent*, and *crash dialysis* (2). Definitions of suboptimal dialysis vary, but they generally include the following three components: starting dialysis with a central venous catheter (CVC), acutely as inpatient, or on a modality that was not the patient's choice (3). Beyond the emotional toll that initiating KRT takes on many people (4), a suboptimal start has been shown to have significant clinical and economic consequences. Patients who have an optimal KRT start have a greater survival rate than those with a nonoptimal start (5), and suboptimal initiation also leads to higher costs and increased hospital utilization (6).

Identifying the factors that lead to suboptimal KRT initiation has been the subject of numerous studies. A combination of clinical, logistic, and patient-related issues contributes to this problem. These include timely nephrology referral, acute kidney injury (AKI) in advanced CKD, a high prevalence of cardiovascular events in people living with kidney diseases, patient delays in decision-making, surgical referral delays, and the primary failure of arteriovenous fistulas (AVFs) (7).

We will delve into the three main individual components of suboptimal dialysis.

1) Permanent vascular access

Optimal vascular access is the cornerstone of a planned dialysis start. A suboptimal start is often characterized by using a CVC rather than a permanent access such as an AVF or an arteriovenous graft (AVG). In the 1990s, the United States saw a surge in vascular access-related hospitalizations, with an estimated morbidity cost nearing $1 billion per year. This was partly due to the increasing use of polytetrafluoroethylene grafts instead of AVFs. Although AVGs could be used sooner, their secondary failure rate was much higher. Additionally, CVCs had complications, with infection being the most common (8). In 2003, the Centers for Medicare & Medicaid Services (CMS), along with End Stage Renal Disease Network Organizations, initiated the Fistula First Breakthrough Initiative with the goal of improving the use of AVFs in people undergoing hemodialysis in the United States. The initial targets were to achieve 40% AVF use in incident patients and 50% in prevalent patients. After these goals were met in 2005, a new target of 66% AVF use was set for 2009. The Fistula First Breakthrough Initiative had a significant impact, leading to a substantial increase in AVF use across the country, from 26% in 1998 to 63% in 2015 (9). The increase in AVF use was largely a result of a decline in AVG use, not a substantial decrease in dialysis catheter use. This trend spurred the "Fistula First, Catheter Last" initiative. However, with more older patients starting dialysis and a high mortality rate in their first year, this approach has been questioned. Consequently, a "Right Access for the Right Patient" philosophy has been suggested, especially for those with a limited life expectancy (10). The CMS End Stage Renal Disease Quality Incentive Program 2025 measure excludes patients with a catheter who have limited life expectancy (hospice care, metastatic cancer in the past 12 months, end stage liver disease in the past 12 months, or coma or anoxic brain injury in the past 12 months) so not to penalize centers for using CVCs in patients with limited life expectancy (11).

The Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guideline for Vascular Access, updated in 2019, recommends that people with progressive CKD and/or an estimated glomerular filtration rate of 15 to 20 mL/min/1.73 m^2 or those already on KRT should have an individualized End-Stage Kidney Disease (ESKD) (or kidney failure) Life Plan that is regularly reviewed, updated, and documented.

KDOQI considers it reasonable for people undergoing hemodialysis to have an AV access (AVF or AVG) that is consistent with their life plan and overall goals of care. It also outlines specific clinical circumstances for which tunneled CVCs are reasonable for both short-term and long-term use.

The work group recommended a patient-first approach, followed by an individualized plan for dialysis access. This plan includes four key components:

- vessel preservation
- insertion/creation
- contingency plan
- succession plans

This can be remembered by the mnemonic "VIP access plans," which stands for: Vessel Important Preservation, Access Creation, Contingency, and ESKD Access Success Plans (12).

2) Starting dialysis as an inpatient

Many factors lead to starting dialysis as an inpatient among people with CKD; some are modifiable, and some are not. The most common reasons are AKI and cardiovascular issues like acute myocardial infarction or congestive heart failure. Preventing AKI in people with CKD is challenging, and close follow-up with nephrologists has not always been shown to decrease suboptimal starts (1). Identifying subgroups of people who are at high risk of AKI or CKD worsening is critical. One such group would be people with kidney disease and heart failure who were found to have high rates of suboptimal dialysis initiation and higher rates of inpatient initiation (13, 14). Another high-risk group is comprised of people with high-risk variants of the *APOL1* gene. The African American Study of Kidney Disease and Hypertension and the Chronic Renal Insufficiency Cohort Study have shown that these variants are associated with higher rates of CKD progression and kidney failure (15). In early clinical trials of drugs like Inaxaplin, which target *APOL1*, results have been promising (16).

The recent study by Molnar et al. (1) reported a mean hemoglobin level of 10.7 g/dL in patients with suboptimal dialysis initiation. This is an acceptable value, considering that erythropoietin-stimulating agents are not typically used when hemoglobin is above 10 g/dL, due to the increased risk of thromboembolic and cardiovascular events (17).

Preventing cardiovascular disease in populations with CKD is easier said than done. This is mainly due to multiple contributing factors: People with CKD have a high incidence of hypertension and diabetes, which in turn increase cardiovascular disease, as well as issues with bone mineral metabolism, a high prevalence of anemia, and volume overload, to name a few. This complexity makes collaboration among different specialties, such as nephrologists, cardiologists, and primary care physicians, very important (18).

3) Patients' modality of choice

People currently have three choices for KRT: in-center hemodialysis, home dialysis modalities (including home hemodialysis or peritoneal dialysis), and kidney transplant. Of these options, kidney transplant is the best in terms of survival and cost-effectiveness (19, 20). However, with approximately 90,000 patients waiting for a kidney transplant in the United States, this may not be achievable. Additionally, 11 patients die every day while waiting for a kidney transplant (21).

Beyond the significant impact on health outcomes, the financial burden of kidney failure is immense. Although people with kidney failure make up less than 1% of the total Medicare population, they are responsible for 7% of total Medicare Fee-for-Service spending, as reported in the *2018 USRDS Annual Data Report* (22). In 2019, Advancing American Kidney Health was signed by President Trump. One of its goals is that 80% of people newly experiencing kidney failure in 2025 receive dialysis at home or receive a transplant. Aligned with these goals, the CMS Innovation Center has four kidney care models: One is Kidney Care First for nephrology practices, and the other three are payment options, including graduated, professional, and global, as part of Comprehensive Kidney Care Contracting. These models incentivize physicians for pre-emptive transplants, improving transition to dialysis with peritoneal dialysis or hemodialysis with a permanent vascular access and ensuring dialysis initiation is appropriately timed (23, 24).

Two important interventions, which could potentially improve outcomes with regard to suboptimal dialysis initiation, are patient education and a multidisciplinary approach. Predialysis education programs have been shown to increase patients' knowledge, involving them in the decision-making process, with some studies showing concordance between chosen and definitive modalities (25). These programs have also been associated with reduced patient anxiety, a delay in the need for dialysis, and a reduced number of emergency department visits and hospitalizations (26, 27). In line with this, Medicare covers up to six kidney disease education sessions starting from stage 4 CKD, for which people may require transplant or dialysis (28).

For people who have already started dialysis, transitional care units have been found to be a vital source for patient education. People starting KRT at a transitional care unit were found to have increased transplant referrals, high rates of permanent vascular access, and a higher use of home dialysis modalities (29, 30).

People living with kidney diseases are complex, and their care requires a multidisciplinary approach. This begins with the diagnosis of CKD, early detection of proteinuria, and early referral to nephrology by primary care physicians. It also involves the care team avoiding nephrotoxic agents and managing coexisting conditions such as hypertension, diabetes, and heart disease to better control CKD progression. As CKD progresses, other team members should be involved, including dietitians, vascular surgeons for AVFs, general surgeons, interventional nephrology and radiology colleagues for peritoneal dialysis catheters, social workers, case managers, and predialysis education teams. The patient's support system, including family members, should also be an integral part of this process (31). ■

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Retained Deep Luer Lock Microbial Contamination as a Potential Underappreciated Cause of IHD/CRRT Central Line-Associated Bloodstream Infections

By Terrence Jay O'Neil

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In 2020, there were 9548 central line-associated bloodstream infections (CLABSIs) reported to the National Healthcare Safety Network from 6849 hemodialysis facilities reporting 12 months of data (1). These occurred despite adoption of and adherence to a bundle of catheter-care protocols including use of gloves, "scrub the hub" protocols, and various needleless and disinfecting connector technologies for intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT) (2). Although the bloodstream infection incidence rate dropped by half between 2014 and 2020, in large part because of these protocols, there is a significant residual number of CLABSIs that seem to be irreducible despite these efforts. CLABSIs have an increased in-hospital mortality risk of between 1.51 and 1.64 (3).

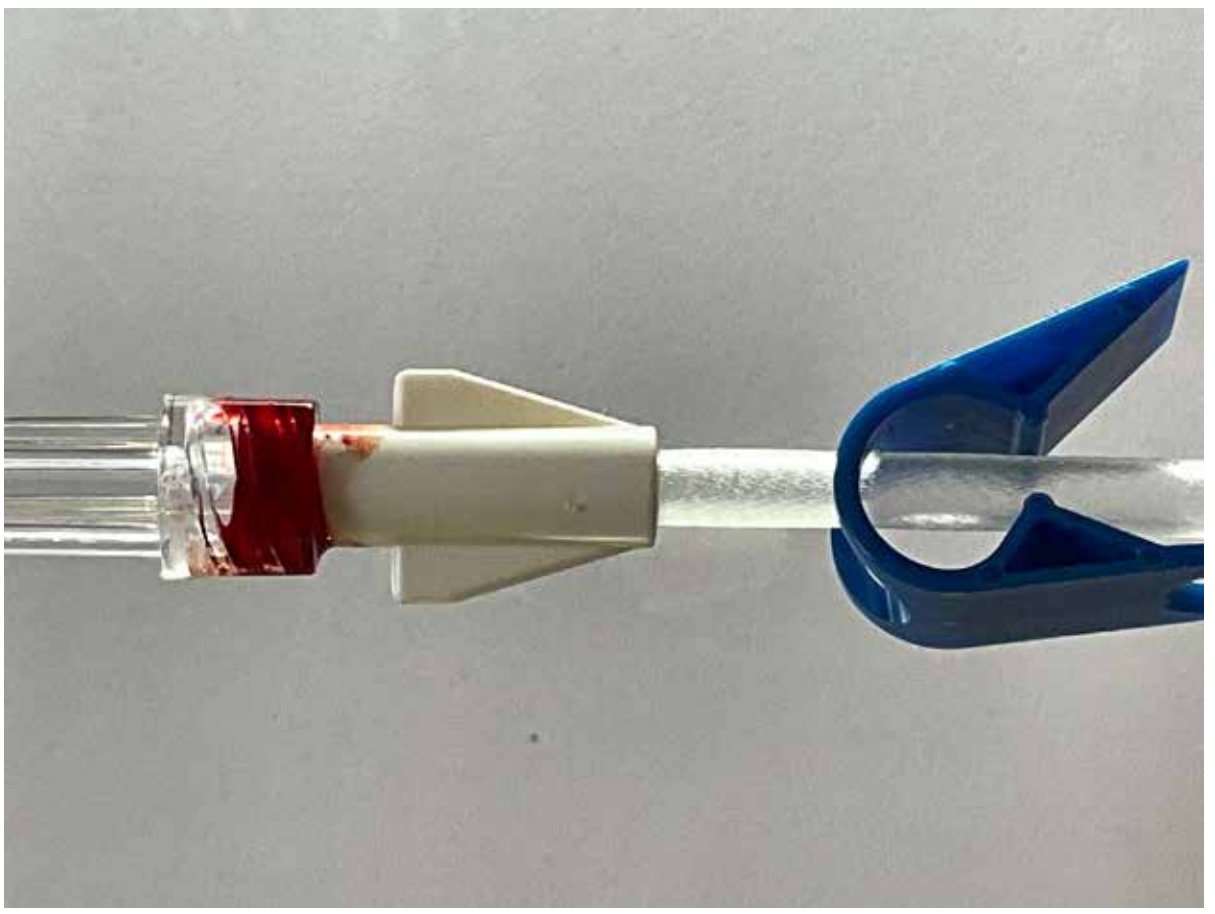
The prevailing hypothesis for most CLABSIs is that staff touch the bloodstream-facing parts of the central venous catheter/bloodline connection during disconnection and reconnection, resulting in bacterial inoculation into the open lumen when handling the catheter. Whereas human error and breaks in sterile technique are undeniably a large part of the problem, the inherent physical characteristics of the connectors have not been fully considered.

The device in general used to make connections between medical tubing segments is the Luer lock, which secures two lengths of tubing using screw threads. One under-appreciated characteristic of screw threads is that the approximation of the thread surfaces is very close but not uniformly occlusive, leading to gaps that exert a powerful capillary action, drawing fluids even against gravity.

Figure 1. Vertically oriented connector

Vertical orientation of a clear Leur lock connector after 5 minutes following the application of three drops of colored liquid, simulating microbially contaminated liquid. Image taken by author.

Figure 2. Horizontally oriented connector



Horizontal orientation of a Leur lock connector after 5 minutes following the application of three drops of colored liquid, simulating microbially contaminated liquid. Image taken by author.

Dialysis catheters are usually inserted either in the internal jugular venous position, where they are in close approximation to oral secretions, or in the femoral venous position, where they are easily contaminated by fecal material or urogenital fluid contamination. Because dialysis bloodline connectors are opaque and color coded to give strong visual cues for correct connection polarity, it is not possible to see the deep accumulation of microbially contaminated material resulting from even minimal fluid exposure. To date, there is no literature explicitly showing this, resulting in underappreciation of the role of unprotected Luer lock connectors in the blood circuit harboring an irreducible level of latent contamination not reached by practical disinfection protocols. It is easy to foresee that this contamination can gain access to the bloodstream with ongoing disconnection and reconnection cycles.

A simple demonstration was performed by the author at the home office of HD Clean LLC, using a clear Luer lock connector to which three to five drops of a colored aqueous solution were administered as surrogate for microbially contaminated fluid. Within 5 minutes, whether the connector was vertically oriented (as it would be in an internal jugular insertion) (Figure 1) or horizontally oriented (as it would be in a femoral insertion) (Figure 2), the fluid had penetrated deep into the female connector, creating a persistent contamination reservoir out of reach of feasible cleaning prior to disconnection and reconnection. Even a needleless device with Luer lock fitting must be replaced periodically. These are expected to accumulate sufficient microbial contamination to risk bloodstream introduction during change-outs.

Further efforts to characterize the quantitative aspects of this phenomenon using different contaminated fluids would seem warranted. Protection of exposed Luer locks within a fluid-resistant accessory may prove necessary to further reduce the incidence of health- and life-threatening dialysis CLABSIs. ■

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To Infuse or Not to Infuse: That Is the (Diagnostic) Question

By Basheer Kummangal and Nayan Arora

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Few things in medicine generate more angst than hyponatremia. The word alone is sufficient to transform confident medical residents into trembling puddles of saline, imagining endless calculations of osmolality. Distinguishing hypovolemic hyponatremia from the syndrome of inappropriate antidiuresis (SIAD) is particularly challenging yet represents the most common diagnostic predicament encountered in patients with hyponatremia. Traditional algorithms incorporate assessment of volume status to distinguish between these two entities; however, clinical volume assessment lacks sensitivity and specificity (1). Clinical practice guidelines suggest using a urine sodium threshold of less than 30 mmol/L to diagnose hypovolemic hyponatremia; however, this was developed from a small cohort of 58 patients (1) and lacks specificity (1–3).

In *Scientific Reports,* Chienwichai et al. (4) present a prospective cohort study to evaluate whether post-saline infusion urine sodium improves diagnostic accuracy. The investigators recruited 181 adults who were hospitalized at two Thai medical centers. The participants had nonedematous hypotonic hyponatremia, defined as a serum osmolarity of less than 275 mOsm/kg and serum sodium less than 130 mmol/L. All participants were required to receive at least 2 L of 0.9% saline, unless they experienced worsening symptoms of hyponatremia or a further decline in serum sodium levels. Participants who experienced serum sodium overcorrection (>10 mmol/L at 24 hours or >18 mmol/L at 48 hours) and those who received active treatment for hyponatremia during the evaluation phase were excluded. Additional exclusion criteria included diuretic use within the preceding 7 days, adrenal insufficiency, hypothyroidism, and metabolic alkalosis with bicarbonaturia. Ultimately, 113 participants were included in the final analysis. Asymptomatic patients received 500 mL of 0.9% saline at a rate of 1 to 2 mL/kg per hour, while patients who were symptomatic were administered 150 mL of 3% saline over 20 minutes. Baseline and postinfusion plasma and urine chemistries were obtained, followed by additional crystalloid administration, up to 4 L, until discontinuation criteria were met. SIAD and hypovolemic hyponatremia were distinguished based on achieving a serum sodium threshold of 135 mmol/L and/or a dynamic serum sodium response to infused fluid. SIAD was diagnosed if serum sodium decreased by more than 3 mmol/L after 1 L of 0.9% saline, decreased by less than 5 mmol/L after 2 L, or failed to reach 135 mmol/L or more after 4 L.

Urine sodium obtained at "time 1" (within 6 hours of 0.9% saline or 1 hour of 3% saline administration) had higher discriminatory accuracy compared with preinfusion values (area under the curve, 0.75 versus 0.61; p = 0.01). A urinary sodium cutoff of 24.5 mmol/L at time 1 achieved 75.2% accuracy (95% confidence interval [CI], 66.2%–82.9%), with 62.5% sensitivity (95% CI, 45.8%–77.3%) and 82.2% specificity (95% CI, 71.5%–90.2%). In comparison, a preinfusion urinary sodium of less than 30 mmol/L had a diagnostic accuracy of 63.7% (95% CI, 54.1%–72.6%), with a 57.5% sensitivity (95% CI, 40.9%–73.0%) and 67.1% specificity (95% CI, 55.1%–77.7%).

The authors should be commended on leveraging renal physiology to improve diagnostic yield for a common diagnostic dilemma. In patients with hypovolemia, saline infusion restores the effective circulating volume, suppressing arginine vasopressin release, which increases free water excretion and thereby reduces urinary sodium concentration. Conversely, in SIAD, saline infusion fails to suppress arginine vasopressin, and the resultant volume expansion could conceivably trigger the release of atrial natriuretic peptide, further increasing urinary sodium (5). Thus, saline infusion functions as a diagnostic test, unmasking divergent kidney responses, based on a dynamic, rather than static, measure.

If nothing else, this should give us the confidence not only to stop dismissing but to embrace urine studies postcrystalloid administration in patients with hyponatremia, which is frequently encountered in clinical practice.

However, certain limitations bear mentioning. First, clinicians were not blinded to urine chemistry results, which has the potential to introduce bias. Additionally, the exclusion of patients with the above comorbidities, in addition to rapid correctors, although only including participants who were deemed able to receive 2 L of saline, may limit generalizability. The fact that approximately 25% of patients were still misclassified despite the improved diagnostic yield supports the fact that SIAD physiology may often coexist with hypovolemia, making it difficult to categorize patients neatly into binary groups. Although only one patient in this study—with pre-existing left ventricular dysfunction—developed clinical heart failure, widespread implementation could certainly lead to more frequent hypervolemic events. Additionally, although the authors cite mathematical modeling (6), suggesting that isotonic saline rarely worsens SIAD-associated hyponatremia, caution would be prudent, particularly in those patients with very high urine osmolalities.

Ultimately, Chienwichai and colleagues have presented a compelling study that improves the diagnostic yield when differentiating etiologies of hypo-osmolar hyponatremia by shifting the paradigm from a static preinfusion urine sodium to a dynamic test grounded in physiology (4). The next step will require external validation across a broader patient population, better representing common comorbidities. If nothing else, this should give us the confidence not only to stop dismissing but to embrace urine studies postcrystalloid administration in patients with hyponatremia, which is frequently encountered in clinical practice. In other words, let the kidneys do the work. ■

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The authors report no conflicts of interest.

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The DIY Route to Altering Kidney Disease Through Nutrition

By Karen Blum

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When Sara Karjoo, MD, visited a nephrologist in 2022 to be evaluated for a kidney transplant, her surgeon looked at her glomerular filtration rate of 17 and said, "Sara, I will guarantee you will be on dialysis within a year. If you are not, we are going to dance together."

But by listening to her body and speaking with nutritionists, Karjoo gradually adopted a plant-based, ovo-pescatarian diet that helped her stay off dialysis for 2 years until her November 2024 kidney transplant. "She still owes me a dance," said Karjoo, a pediatric gastroenterologist at Johns Hopkins All Children's Hospital in St. Petersburg, FL.

Karjoo was one of four people with kidney disease who discussed how dietary changes helped keep their conditions in check, in a presentation at ASN Kidney Week 2025. They found dietary advice inconsistent across medical centers so went the do-it-yourself (DIY) route. They are working together on a kidney cookbook.

"The renal diet is incredibly limited, and it has inherently a high risk of malnutrition," Karjoo said. Most patients are told to limit protein intake, but that carries a risk of sarcopenia that increases morbidity and mortality before and after transplant, she explained. Karjoo had proteinuria and was "dumping protein" despite being on medications.

Patients also are told to avoid excess sodium, phosphorus, potassium, magnesium, and calcium, Karjoo said, which can avoid many vitamins and nutritious foods. Additionally, people with later-stage kidney diseases are unable to filter out hormones (which impacts the risk of obesity) and may become unable to tolerate processed foods, vitamins, or nutritional shakes, she said.

Karjoo focused on implementing a diet to preserve cardiac health. First, she set out to fix her electrolytes. She eliminated dairy to reduce phosphorus and later avoided natural flavors in items like sparkling drinks and breads. She avoided canned and processed foods to lessen sodium intake. She ate small amounts of mulberries for calcium and dark chocolate for magnesium.

Karjoo also adopted a strategy from one of her patient's families: to generally eat foods from the trees and avoid foods from the ground. She ate foods like berries, apples, pears, and clementines while avoiding foods such as legumes and bananas. She kept hydrated through water-dense foods such as cucumbers, lemon water, and watermelon, which reduced her gout symptoms and brain fog. She studied her lab results as feedback to tweak the diet. As her kidney disease worsened, she ate more fresh foods, rotating them to get a variety of vitamins and nutrients.

To preserve muscle mass, Karjoo, working with a nutritionist, limited herself to 0.8 g/kg/day of protein from peas, fish like branzino and salmon, eggs, and whole grains. She also boosted exercise—swimming, walking, or pilates. As her disease worsened, she reduced her exercise times. "Food and lifestyle [are] truly medicine and can be used to really enhance your patients' outcomes, as it did for me," she said.

Duane Sunwold, a chef with Inland Northwest Culinary Academy in Spokane, WA, was diagnosed at age 40, in 2001, with minimal change disease and focal segmental glomerulosclerosis. He had stage 4 chronic kidney disease (CKD) and was rapidly heading toward stage 5. Sunwold met with five nephrologists that year, but only one discussed dietary changes with him. By adopting a plant-based diet, Sunwold "ate his way" out of kidney disease and has been in remission for over 20 years. His estimated glomerular filtration rate went from 13 to 94.

"One thing I'd like all doctors to tell patients is, 'If you change your diet, there's a chance you can feel better. There's a chance you can enhance your quality of life,'" Sunwold urged. But, he said, "You can't just give us a list of foods we can't eat—it doesn't work. We need practical strategies."

Sunwold was given minimal input by a dietitian: Increase plant protein, reduce animal protein, and add more fruits and vegetables. He embraced the challenge. Now, he heads straight to the produce section of supermarkets, where he selects foods that are fresh, in season, and at their lowest price to build meals, and embraces salt-free herb blends from spice companies to boost flavor. He finds the diet portable and brings frozen vegetables with him each summer when he spends time on a tribal reservation, 45 miles from the closest grocery store with fresh produce.

Biologist Andrew Storfer, PhD, also has experimented with diet to stay healthy. He was diagnosed with lupus nephritis and stage 2 CKD at aged 15 years. Later, as an adult with stage 4 CKD, he tried a plant-based diet but too often relied on processed meat substitutes that were high in sodium and saturated fat. Then, he suffered a heart attack in 2022, when he also had progressed to stage 5 CKD, and was forced to start dialysis.

He was determined to try to alter his disease through diet. "Even having a PhD in biology and having been a professor for 26 years, it really takes an effort to find a great diet," said Storfer, the Eastlick Distinguished Professor at Washington State University in Pullman.

He tried to have fun with dialysis-friendly cooking, including seitan and kidney-friendly vegetables, and finding simple meals he could prepare in 20 minutes but struggled to find consistent information. "There's great agreement on low-protein, plant-based foods, but where do we go from there?" he asked. "People are overwhelmed."

Following a transplant in February 2024, Storfer found that his food preferences changed; he craved sweets and beef. When his A_{1c} levels approached prediabetic status, he altered his diet again. Today, he follows his own post-transplant diet that includes foods like chicken, beef, and fish from sustainable farms; organic produce; unprocessed foods; nuts; fruits; and chia seeds.

Nutrition "is the cornerstone of kidney transplant success, yet approaches to training and guidance differ widely across institutions," said kidney transplant recipient Shamekka Marty, chief executive officer and founder of Beyond the Game Health. Too often, clinicians are scientific about it and do not involve patients, she said. She called on clinicians to develop an evidence-based core nutrition curriculum for all transplant centers and shared the following advice:

- Nutrition training for patients must be practical, culturally sensitive, and accessible across literacy levels.
- Resources should be consistent for all patients, regardless of geography, socioeconomic status, or institution. Incorporate patient testimonials, cooking demonstrations, and culturally relevant meal planning.
- Move beyond one-time handouts at discharge to offer workshops, support groups, and nutrition coaching in person or via telehealth.

Eating healthy or organic does not have to break the bank, speakers said. Karjoo said she likes to help her patients learn where they can find fresh produce in their region or to suggest local farmers' markets or farms where people can pick their own. "Sometimes it's a matter that they feel disempowered," she said. "If you're there Googling it with them, they get an idea, and then they get inspired."

Patients can grow their own produce in indoor or outdoor gardens, Marty added. And they can think outside of the box for shopping. She has seen the same packaging of one organic food brand at Walmart and Whole Foods. "The only thing different is you buy it at Walmart for $2, and Whole Foods takes that same thing and marks it at $5. It's all about looking." ■

Findings

Albuminuria Outperforms Proteinuria as Kidney Risk Marker

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The urinary albumin-creatinine ratio (UACR) is more strongly associated with kidney failure than the urinary protein-creatinine ratio (UPCR)—particularly in groups with other strong risk factors, concludes a meta-analysis in the *Annals of Internal Medicine*.

The researchers performed a meta-analysis of individual-level data to assess the relative performance of UACR and UPCR as markers of chronic kidney disease (CKD)-related outcomes. The analysis included 148,994 participants who underwent same-day measurements of both markers, drawn from 38 clinical and research cohorts. Outcomes of interest included kidney failure, myocardial infarction, stroke, heart failure, and death from cardiovascular causes. Further analyses included subgroups defined by proteinuria severity, type 2 diabetes, an estimated glomerular filtration rate less than 60 mL/min/1.73 m^2, and glomerular disease.

In the pooled cohorts, 9773 kidney failure events occurred over a median follow-up of 3.8 years. Elevated values for both UACR and UPCR were associated with increased risk of kidney failure in log-linear fashion. However, the association with kidney failure was somewhat stronger for UACR compared with UPCR: adjusted hazard ratio, 2.55 versus 2.40 per one standard deviation increase, respectively.

The association of UACR with kidney failure was stronger for patients with high risk—particularly those with a higher baseline UACR, a lower estimated glomerular filtration rate, diabetes, or glomerulonephritis. Cardiovascular outcomes generally showed similar associations with both markers. On analysis of 21 cohorts with relevant data, adjusted hazard ratios were about the same for percentage change in UACR and UPCR.

Both UACR and UPCR are widely used for diagnosis and monitoring of CKD. Previous studies have not rigorously compared these two tests for association with kidney and cardiovascular outcomes, leading to variability in clinical practice, research, and guidelines.

This recent meta-analysis finds "strong and consistent" associations of both UACR and UPCR with CKD-related outcomes. However, the association with kidney failure appears stronger for UACR, especially among the groups with highest risk. "These results support the routine measurement of albuminuria to diagnose and risk-stratify patients," the investigators conclude [Heerspink HJL, et al.; CKD Prognosis Consortium. Proteinuria or albuminuria as markers of kidney and cardiovascular disease risk. *Ann Intern Med*, published online November 4, 2025. doi: 10.7326/ANNALS-25-02117]. ■

Deceased Donor Kidney Transplant: What's the Survival Benefit?

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Deceased donor kidney transplantation is associated with improved survival compared with dialysis, although the survival benefit is greatly affected by donor and recipient characteristics, concludes a study in *JAMA Internal Medicine*.

The researchers designed an emulated randomized clinical trial using data from the Australia and New Zealand Dialysis and Transplant Registry from 2010 through 2021. The analysis included 8011 patients waitlisted in Australia during this time. The median patient age was 53 years, and 63.8% were men.

Of the waitlisted patients, 56.5% underwent transplantation of kidneys with a Kidney Donor Risk Index (KDRI) under the 90th percentile, whereas 6.1% received a high KDRI-scoring kidney. The remaining 37.4% of patients did not undergo transplantation over a 3-year grace period.

Median wait times were 0.77 and 0.55 years for the high and low KDRI-scoring groups, respectively. Ten-year all-cause mortality was compared between groups by inverse probability-weighted pooled logistic regression.

Estimated 10-year mortality was 22.4% in the low KDRI group, 30.6% in the high KDRI group, and 39.1% for waitlisted patients receiving dialysis. Compared with waitlisting, mean survival gains were 6.6 months in the low KDRI group and 3.6 months in the high KDRI group.

Patients aged 60 years or older who received a low KDRI-scoring kidney had the largest survival benefit: a 35.8% reduction in mortality. In contrast, younger patients receiving high KDRI-scoring kidneys showed no survival benefit compared with waitlisting on dialysis.

Transplantation is regarded as the "optimal treatment" for people with kidney failure, but the true survival benefit is difficult to determine. This emulated randomized clinical trial finds a significant survival benefit of deceased donor kidney transplantation compared with waitlisting only.

The gain in survival, however, is affected by the quality of the donor kidney and the characteristics of the recipient. In particular, high KDRI-scoring kidneys appear to have limited survival benefits in younger patients. The researchers conclude, "These findings highlight the need for tailored counseling and shared decision-making to align treatment choices with individual risks and expected outcomes" [Zhu L, et al. Survival benefits of deceased donor kidney transplant vs waitlisting. *JAMA Intern Med* 2025; 185:1471–1478. doi: 10.1001/jamainternmed.2025.5624]. ■

Fish Oil Lowers Cardiovascular Risks in Patients on Dialysis

https://doi.org/10.62716/kn.002652025

Supplementation with n-3 polyunsaturated fatty acids reduces the risk of serious cardiovascular events in patients receiving maintenance dialysis, according to a randomized clinical trial in *The New England Journal of Medicine*.

The Protection Against Incidences of Serious Cardiovascular Events With Daily Fish Oil Supplementation in Dialysis Patients (PISCES) trial included 1228 adult patients undergoing hemodialysis, enrolled at 26 centers in Canada and Australia between 2013 and 2019. The patients' mean age was 64 years, and mean time on dialysis was 3.7 years. More than one-third (35.3%) had a previous cardiovascular event.

Patients were assigned to receive daily fish oil supplements—4 g of n-3 polyunsaturated fatty acids, including 1.6 g of eicosapentaenoic acid and 0.8 g of docosahexaenoic acid—or corn oil placebo. At 3.5 years' follow-up, the two groups were compared on a composite outcome of serious cardiovascular events along with secondary outcomes.

The rate of cardiovascular events was reduced by nearly one-half among patients assigned to fish oil: 0.31 versus 0.61 per 100 patient-days (hazard ratio [HR], 0.57). An analysis of an extended primary outcome including noncardiac causes of death also favored fish oil supplementation (HR, 0.77).

The fish oil group had lower rates of cardiac death (HR, 0.55), fatal or nonfatal myocardial infarction (HR, 0.56), and peripheral vascular disease leading to amputation (HR, 0.57). Fish oil was also associated with lower rates of fatal or nonfatal stroke (HR, 0.37) and first cardiovascular event or death from any cause (HR, 0.73). Treatment adherence and adverse events were similar between groups.

Previous evidence suggests that fish oil supplementation, especially with eicosapentaenoic acid and docosahexaenoic acid, has cardiovascular benefits in the general population. The PISCES results indicate that n-3 fatty acid supplements may help to lower the high risk of cardiovascular disease in patients on maintenance hemodialysis.

Other potential benefits include reductions in a wide range of secondary outcomes, including all-cause mortality. The researchers plan further studies to assess the mechanisms and cost-effectiveness of fish oil supplementation [Lok CE, et al.; PISCES Investigators. Fish-oil supplementation and cardiovascular events in patients receiving hemodialysis. *N Engl J Med*, published online November 7, 2025. doi: 10.1056/NEJMoa2513032]. ■

GLP-1 RAs Linked to Lower Cardiovascular Risks in CKD

https://doi.org/10.62716/kn.002662025

Among individuals with chronic kidney disease (CKD), treatment with glucagon-like peptide-1 receptor agonists (GLP-1 RAs) is associated with a reduced risk of cardiovascular events compared with dipeptidyl peptidase-4 (DPP-4) inhibitors, reports a study in the *American Journal of Kidney Diseases*.

Using Ontario, Canada, health care data from 2019 to 2021, the researchers identified 24,576 patients initiating treatment with GLP-1 RAs and 44,367 starting treatment with DPP-4 inhibitors. All patients had an estimated glomerular filtration rate less than 90 mL/min/1.73 m^2. In the GLP-1 RA group, the mean age was 69 years. Forty-one percent of patients had stages 3 to 5 CKD, and 92% had diabetes.

Ninety-eight percent of patients in the GLP-1 RA group received semaglutide. Patient characteristics were similar between groups. Major adverse cardiovascular adverse events (MACE) were compared between groups, along with secondary outcomes. The mean follow-up was 1.7 years.

New users of GLP-1 RAs were at lower risk of MACE compared with patients treated with DPP-4 inhibitors. Incidence rates were 31.6 versus 36.5 per 1000 person-years: subdistribution hazard ratio (sHR), 0.88 in the GLP-1 RA group. The reduction in primary outcomes mainly reflected a reduced risk of death from cardiovascular causes: sHR, 0.72.

On analysis of secondary outcomes, GLP-1 RA treatment was associated with lower rates of peripheral vascular disease revascularization (sHR, 0.85) and health care visits or hospitalization for heart failure (sHR, 0.58 at 0.5 years). The benefits of GLP-1 RA therapy were apparent across a range of estimated glomerular filtration rate values.

Treatment with GLP-1 RAs can lower the risk of MACE, whether prescribed for diabetes or obesity. This population-based study addresses the lack of real-world outcomes' data on the cardiovascular benefits of GLP-1 RA therapy across the spectrum of CKD.

The findings suggest reductions in MACE and cardiovascular deaths among people with CKD who initiate treatment with GLP-1 RAs. The study also finds a reduction in other outcomes, including heart failure. The researchers call for further studies to clarify the benefits of GLP-1 RA therapy in people with more advanced CKD [Yau K, et al. Glucagon-like peptide-1 receptor agonists and risk of major adverse cardiovascular events in patients with CKD. *Am J Kidney Dis*, published online November 12, 2025. doi: 10.1053/j.ajkd.2025.09.010]. ■

Suboptimal Dialysis Initiation

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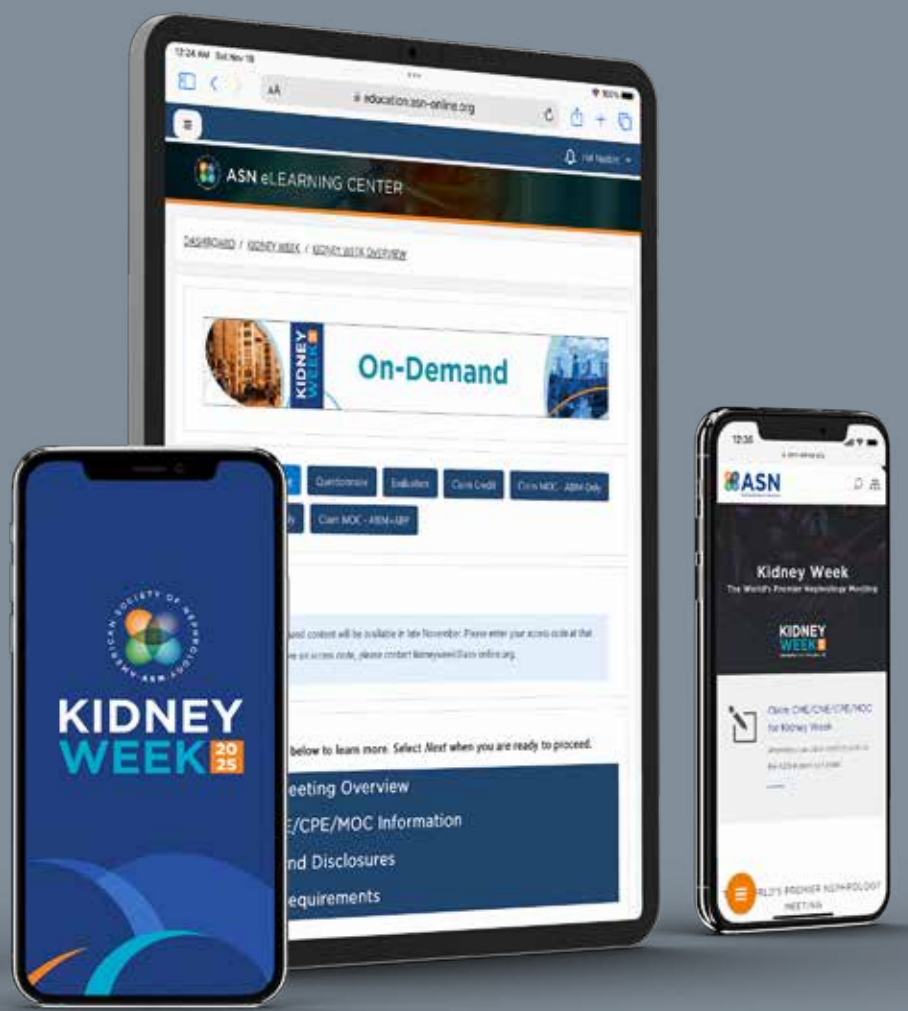

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