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Leveraging Real-World Patient Data Is Key to Kidney Care Innovation

By Bridget Kuehn

Reams of electronic data are generated during day-to-day care of patients with kidney diseases. Some data are entered by clinicians into electronic medical records; other data are collected by monitors or machines used in patient care. Experts who attended the Kidney Innovation Conference in June agree that the often-untapped data trove may hold the key to helping accelerate innovation in kidney health care.

The 2-day conference hosted by the Kidney Health Initiative, KidneyCure, and the Kidney Innovation Accelerator (KidneyX) brought together clinicians, patients, regulators, and industry representatives to discuss the best ways to rapidly improve care and outcomes for patients with kidney diseases. Across all sectors, experts agreed that better leveraging of the available data to discover new insights, personalize care, and make care more proactive is essential to progress. Some participants advocated for "pragmatic trials" conducted in real-world clinical care settings.

"We need to have more innovation; we need to be faster getting care to our patients, generating the evidence for the next step," said Miguel Vazquez, MD, FASN, clinical chief of nephrology and professor in the Department of Internal Medicine at The University of Texas Southwestern Medical Center, Dallas. "Pragmatic trials can offer an opportunity to do that using already available data or generating data with our partners in health systems."

Other speakers described how new technologies like artificial intelligence (AI) or machine learning could extract insights from large amounts of data to help clinicians predict when patients with chronic kidney disease (CKD) might progress, need dialysis, or develop vascular access difficulties and enable early interventions. The devices aim to help nephrologists work more efficiently and effectively by taking on tasks that they might otherwise not have time for, said Mandar Gori, MS, MBA, chief business officer at AWAK Technologies based in Singapore.

"The final decision [about what to do with the data] is still the clinician's," said Gori, whose medical technology company is developing AI-driven patient-monitoring software. "Taking on some of these other tasks frees up [clinicians'] time elsewhere that could lead to more improvement."

Real-world studies

Pragmatic trials are rigorous randomized trials carried out in everyday practice settings with more representative populations than are typically included in traditional randomized trials, which often exclude patients with comorbidities or

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More Research Needed on Menopause and the Kidneys

By Melanie Padgett Powers

Menopause is coming out of the shadows. Every person who has ovaries and lives to a certain age will go through the menopausal transition. And yet, until recently, there has not been much public discussion about perimenopause (the transitional time before menopause) and menopause. But as Generation X (those born between 1965 and 1980) and Millennials (those born between 1981 and 1996) reach the age of perimenopause, they are often baffled and shocked by the spectrum of symptoms, learning that it is not just hot flashes with which they must contend. These generations are more outspoken about the topic, and social media is filled with individuals in their 40s and 50s sharing their symptoms and quests for treatment.

"Menopause is such a normal part of female life, and females make up 51% of the population, so this is something we should be talking about," said nephrologist Sandra Dumanski, MD, MSc. "A lot of female-specific health concerns have been hushed for many years, and it's only lately that we're seeing a wave of renewed interest." Dumanski, an assistant professor in the Department of Medicine at the University of Calgary, Alberta, Canada, studies the impact of sex and gender on kidney and cardiovascular (CV) outcomes.

Not every individual with ovaries will become pregnant, but every individual with ovaries will eventually reach menopause. Yet, there are very little training or

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other conditions, Vazquez explained. The nature of pragmatic trials can make it easier to generalize the results of the studies to typical patient populations, and the studies help demonstrate the feasibility of implementing the intervention in day-to-day practice, he said. "Our patients already go to many, many appointments [whether they are undergoing dialysis or living with CKD or have undergone transplant]," Vazquez said. "[Pragmatic trials] don't add additional follow-ups."

Vazquez and his colleagues conducted a pragmatic trial to test an intervention designed to improve primary care for patients with co-occurring CKD, diabetes, and hypertension (1). The investigators randomized primary care clinics to implement the intervention or continue providing usual care. The study received a waiver of informed consent from the institutional review board overseeing it, but patients could opt out of having their data used by the study. Participating health systems included a local safety net hospital system in Dallas County, TX; a private hospital system in North Texas; the Veterans Affairs North Texas health care system; and an accountable care organization in Connecticut.

Participating practices updated patients' problem lists and implemented a suite of simple, evidence-based practices, including blood pressure and cholesterol management, diabetes care, immunizations, avoidance of medications harmful to the kidney, and education about kidney diseases.

The study yielded a few surprises. One was that many patients at participating institutions were already well-managed for their co-occurring conditions. The intervention also did not reduce hospitalization rates compared with usual care, the primary study endpoint. It also did not improve 30-day readmissions, emergency department visits, or cardiovascular events. However, a manual chart review did find improvements in the care that patients received at clinics implementing the intervention.

The study is ongoing, and although it did not find a reduction in hospitalizations, it did demonstrate that it is possible to implement an intervention with high fidelity across a diverse set of health systems, Vazquez said. He thinks that investigators can replicate this model to study interventions to slow CKD progression, prevent acute kidney injury, improve transplant, or smooth care transitions.

Gary Curhan, MD, ScD, FASN, a professor at Harvard Medical School in Boston, MA, cautioned that real-world studies cannot answer every question but may be more informative or more practical than randomized trials in some situations. For example, if a large sample size is needed, or patients must be followed for years or decades, randomized trials may be too costly or logistically challenging. He noted that real-world datasets like electronic health records' systems may have data on millions of patients over many years.

The real-world studies may also help study rare diseases or unusual disease presentations. For example, Curhan noted an AI study examining Fabry disease, a rare kidney disease with a heterogeneous presentation, in 5000 patients (2). The study provided valuable data on the wide variation in symptom presentation and allowed the team to test a method to identify patients who may be undiagnosed. Similarly, a large study using data in the Geisinger Health System found that patients who have one allele for the recessive genetic condition Alport syndrome were more likely to have blood in their urine and reduced estimated glomerular filtration rates and proteinuria than people with no copies of the syndrome-linked allele (3). But these individuals did not have hearing loss like individuals with two copies of the allele. The study suggested that these individuals may also have Alport syndrome, but clinicians may not diagnose them because they do not have two alleles or hearing loss, Curhan said.

"Many of these real-world studies are opportunistic, but if you can take advantage of the data, [these studies may be the] only way to answer some of these questions." He cited another study that linked elevated 24-hour urine oxalate levels with a higher risk of incident CKD (4).

Big data to solve big problems

Patients on hemodialysis often struggle not knowing when potential complications might arise, said Samit Gupta, PhD, chief scientific officer and cofounder of Alio.ai. He noted that access failures, fluid overload, or cardiac problems caused by potassium abnormalities can all crop up unexpectedly. "There's a whole host of challenges that your care team and your clinic are trying to help you manage as best they can, but you are living in a constant state of existential dread," Gupta said. "That sense of frustration and lack of control also exists on the [practitioner] side."

Gupta and his colleagues at Alio.ai are trying to leverage AI to solve this problem. They have received US Food and Drug Administration (FDA) clearance to use their technology to monitor hemoglobin, hematocrit, and potassium levels and for signs of access failure. Patients wear a peel-and-stick patch that uses sensors to capture acoustic, mechanical, and thermal data. For example, the company uses the sensors to monitor the patient's pulse and for sounds that clinicians would usually capture with a stethoscope that may indicate disruptions in blood flow or stenosis associated with access failure to provide early warnings. Physicians can view their patients' data in a portal that tracks patients' trends and alerts them to signs of trouble. Gupta said some clinicians use the technology to check the portal daily to monitor patients, whereas others rely on notifications. "We are actively working on moving upstream to [monitor patients during] earlier stages of kidney disease[s] and peritoneal dialysis," Gupta said.

Another potential application for AI is identifying patients whose kidney disease is progressing before they "crash into dialysis," said Gori. He noted that more than 60% of patients crash into dialysis, which leads to higher costs, fewer options for patients, and poorer outcomes. He said only about 12% of patients in the United States are on home dialysis, a substantially lower rate than in other countries. AWAK Technologies is currently testing a wearable dialysis device that would provide patients with another option for peritoneal dialysis. "Many patients are going into in-center dialysis when we know that quality of life is much better when the patient is dialyzed at home," he said. "We wanted to go upstream and capture patients [who are progressing toward kidney failure] earlier on."

The company has developed a monitoring device for use with AWAK's wearable dialysis device, which may also help identify patients with later-stage CKD progressing toward kidney failure and predict the need for dialysis. The device can classify patients as low, medium, or high risk of progression or needing dialysis. To do this, the company uses evidence-based guidelines and adds additional patient information to improve its prediction accuracy. "It's a decision support tool, which helps [clinicians] to save time and focus on [the patients who need more attention]," Gori explained.

Alio.ai's technology relies on an artificial neural network to parse the data, but it has designed the program to explain the basis of its predictions to clinicians. The intention is to help avoid problems arising when previous technology was a "black box" for clinicians, preventing them from catching errors. That is part of a trend in the field—to create "explainable AI" to help avoid problems associated with poor transparency.

Gori and his colleagues trained their computer algorithm using data on more than 10,000 patients from five hospitals in Taiwan. Then, 10 nephrologists from another hospital tested the monitoring tool built using the algorithm for about 3 months. AWAK Technologies received a "breakthrough device" designation from FDA based on the data (5).

Pros and cons of AI

Brad Keller, MS, PhD, who leads the clinical development group at Baxter Healthcare, agreed that remote patient monitoring is one promising application for AI in kidney diseases. He noted that effective early management of adverse events could cut costs and improve outcomes. He said that remote cyclers for peritoneal dialysis capture large amounts of data on patients' therapy and adherence that could be paired with other patient data to monitor their condition. But the volume is so great that it would be difficult and time-consuming for a human to parse. AI could potentially help detect emerging problems. However, Keller warned that there are pitfalls that developers and clinicians need to be careful to avoid.

"With big data comes big problems because the more you assess people, the more you might find something that is or is not real," Keller said. He explained that assessing whether such anomalies are a real concern could require additional clinical care and evaluation and tax both the health system and patients, who already have a high care burden. He noted that frequent false positives can also cause patients and clinicians to ignore alerts.

He also noted that having the "right data" up front is vital to troubleshooting downstream. For example, many medical datasets have a survivor bias and may only include patients whose data were suspicious, leading to intervention. Those who did not have adverse events or whose adverse events went undetected may be missing from the data. Using such flawed datasets can lead to flawed tools. For example, recent studies have shown that pulse oximeters inaccurately reported oxygenation—leading to underdiagnosis of low oxygen—in people with dark skin who were under-represented in the datasets used to train the tools (6).

Keller emphasized the importance of using an iterative process to assess and improve the tools and troubleshoot problems. He also said that it is important to work together across sectors to collect data and ensure the right questions are being asked. "It's important to learn from the past so that we can accelerate to the future," he advised.

Ongoing improvement

FDA has authorized more than 500 AI- or machine learning-based devices across a wide range of medical specialties, said Sivakami Venkatachalam, MS, Gastroenterology and Endoscopy technical lead in FDA's Center for Devices and Radiological Health. The agency is working with developers to promote good practices and transparency in the development of devices and ways to make the process more efficient. "We are continuously looking at new ways to evolve the regulatory approach to enable fast-moving innovation," she said.

Gupta noted that beyond devices that require long developmental processes and FDA approval, AI may also be useful in gleaning insights from clinical data. He said there is likely other "low-hanging" fruit in patient care data that could be used to improve patient care. "There are opportunities for learning that are faster and not gated by technology development and approval," he added. ■

References

1. Vazquez MA, et al.; ICD-Pieces Study Group. Pragmatic trial of hospitalization rate in chronic kidney disease. *N Engl J Med* 2024; 390:1196–1206. doi: 10.1056/NEJMoa2311708
2. Jefferies JL, et al. A new approach to identifying patients with elevated risk for Fabry disease using a machine learning algorithm. *Orphanet J Rare Dis* 2021; 16:518. doi: 10.1186/s13023-021-02150-3
3. Solanki KV, et al. The phenotypic spectrum of COL4A3 heterozygotes. *Kidney Int Rep* 2023; 8:2088–2099. doi: 10.1016/j.ekir.2023.07.010
4. Puurunen M, et al. Twenty-four-hour urine oxalate and risk of chronic kidney disease. *Nephrol Dial Transplant* 2024; 39:788–794. doi: 10.1093/ndt/gfad221
5. AWAK Technologies Pte Ltd. AWAK Technologies announces FDA breakthrough device designation for their artificial intelligence enabled kidney disease prediction tool. PR Newswire. November 27, 2023. Accessed June 24, 2024. https://www.prnewswire.com/news-releases/awak-technologies-announces-fda-breakthrough-device-designation-for-their-artificial-intelligence-enabled-kidney-disease-prediction-tool-301997423.html
6. Gudelunas MK, et al. Low perfusion and missed diagnosis of hypoxemia by pulse oximetry in darkly pigmented skin: A prospective study. *Anesth Analg* 2024; 138:552–561. doi: 10.1213/ANE.0000000000006755