

## ASN and ABIM Reach Out to Accrediting Agency about Training Deficiencies

*Organizations tell ACGME that some fellowship programs are falling short*

By Eric Seaborg



Some nephrology fellowship programs are not providing all fellows the required training in several procedures, ASN and the American Board of Internal Medicine (ABIM) charge in a letter to the programs' accrediting agency.

The two organizations sent a formal letter to the Accreditation Council for Graduate Medical Education (ACGME) expressing concern that some accredited nephrology training programs provide little or no experience in performing kidney biopsies, placing temporary vascular access for hemodialysis, and placing dialysis catheters for continuous renal replacement therapy.

"Despite the debates in recent years about the need to retain requirements for competency in biopsies and temporary hemodialysis catheter placement, they are current requirements," according to the May 16, 2019, letter addressed to Thomas J. Nasca, MD, president and CEO of ACGME. The letter was signed by ASN President Mark E. Rosenberg, MD, FASN, and Jeffrey S. Berns, MD, FASN, chair of the ABIM Nephrology Board. "Both published lit-

erature during the last decade as well as substantial anecdotal evidence have made it abundantly clear that some nephrology fellowship programs accredited by the ACGME provide little or no experience" with the procedures.

The concern has been a topic of discussion at ASN Nephrology Training Program Retreats and is widely acknowledged within the nephrology training community, Drs. Rosenberg and Berns state.

ASN Councilor David H. Ellison, MD, FASN, who serves as liaison to the ASN Workforce and Training Committee, said he expects the next step will be for ASN, ABIM, and ACGME to meet and begin a dialog on the issues.

### ACGME to respond

"The ACGME has received the letter and is taking the questions seriously," Susan White, director of external communications at ACGME said in an email to *Kidney News*. "The ACGME will provide the recommendations to the

*Continued on page 3* >

## Both Kidney Function and Albumin Predict Outcomes in Type 2 Diabetes

By Timothy O'Brien

Independently and together, changes in estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (UACR) predict the risk of kidney and cardiovascular events and death in patients with type 2 diabetes, reports a study in a recent issue of *CJASN*.

"Our overall results suggest that a combined approach of determining clinically meaningful magnitudes of earlier change in both eGFR and UACR in type 2 diabetes may add substantial prognostic value to that associated with eGFR or albuminuria change alone," concludes the report by John Chalmers, MD, PhD, of The George Institute for

Global Health, University of New South Wales, Camperdown, Australia.

Based on 10-year follow-up data of nearly 9000 patients from an international randomized trial, the study suggests that assessing kidney function and albuminuria in combination might not only provide valuable information for risk stratification. "These are very simple and very good markers," Chalmers said. "The combination should be a more potent predictor of major outcomes, especially renal outcomes, than either marker alone."

*Continued on page 5* >

## Inside

### Findings

Does early dialysis benefit children?



### Allograft failure

An opportunity for collaborative care and improved outcomes



### Children with Kidney Diseases

The complex landscape for drug development



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## ASN and ABIM Reach Out

Continued from page 1

appropriate specialty review committee—in this case the Internal Medicine Review Committee, which is made up of leading educators in the specialty, as well as a public member and resident—to review as we do with all recommendations. [The committee] will review the information provided and discuss the recommendations per our process. The ACGME will respond directly to the organizations that sent us the letter.”

### Some fellows lack procedural skills

Surveys have found that nationwide about 25% of graduating fellows have not achieved competence to perform dialysis catheter placement or kidney biopsies (or both) without supervision, despite being ACGME program requirements. “Some programs provide no hands-on training in one or both of these procedures or little to no experience with taking care of patients utilizing home dialysis (either home hemodialysis or peritoneal dialysis),” the letter states.

A recent survey of nephrology program directors published in *CJASN* found that “51% indicated that fellows should not be required to demonstrate minimal procedural competence in biopsy, although 97% agreed that fellows should demonstrate competence in knowing/managing indications, contraindications, and complications.”

A similar survey published in the *Journal of Vascular Access* found that only 55% of program directors believe that competence in non-tunneled temporary hemodialysis catheter insertion should be a requirement.

### Core competencies, says ASN

Despite these reservations by program directors, “the ASN Council just voted specifically to endorse the view that biopsies and lines are things that nephrology programs should provide training in because they are so essential to the practice of nephrology,” Ellison said.

He said he could envision a system in which fellows were offered different pathways, in which some fellows would receive hands-on training in performing biopsies and in another track the fellow would simply master the indications for and complications of biopsy, leading to two different certifications. But that idea would provide flexibility for the individual, but not the program. “ACGME should make sure that programs are only [accredited] if they can train people in all the things that are required to be certified. The programs should be able to demonstrate that they provide home dialysis training, biopsy training, and line training,” Ellison said.

Berns, chair of the ABIM nephrology board, said that when he interviews applicants for his fellowship program, they confirm that they have visited programs where they have been told they won't get any experience doing kidney

biopsies. Berns said this is a difficult situation for applicants, who can't know enough about the field to realize that by choosing the wrong program they could be limiting their future employment options.

“They can decide after the conclusion of training whether they ever want to do them again, but it is hard to expect somebody who is coming into fellowship training to make an intelligent decision about whether or not they want to develop these skills,” Berns said. An applicant should be able to go to every single training program in the country when they are applying for fellowships and know that they are going to get training across the entire breadth and scope of the field. That is not the case right now.”

how important it is to find what they may be looking for, perhaps making an extra pass when needed, Rope said.

### Data needed

The *CJASN* and *Journal of Vascular Access* studies surveyed the graduates of a single nephrology training program, and found that in their current practices, 58% place non-tunneled temporary hemodialysis catheters and 35% perform biopsies. But those numbers are from the Walter Reed National Military Medical Center so may not be generalizable.

In the surveys of training program directors, the most common barriers cited to fellows achieving competency in biopsies were time (45%), logistics (45%), a belief that

**Surveys have found that nationwide about 25% of graduating fellows have not achieved competence to perform dialysis catheter placement or kidney biopsies (or both) without supervision, despite being ACGME program requirements.**

### Distinction between lines and biopsies?

Rob Rope, MD, associate program director for the nephrology training program at Oregon Health and Science University, said he is “agnostic” about the need for training programs to cover all these procedures thoroughly. He sees a difference between the needs for competency in placing lines and performing biopsies.

When it comes to placing a temporary dialysis catheter, the primary decision a nephrologist makes is whether the patient needs dialysis. “If that decision is made, then a dialysis catheter has to be placed, and it doesn't matter to me who does it. It is whoever is qualified,” he said. “Given the way that nephrology practice has gone, a lot of people in private practice will never place a nephrology catheter again. And therefore, in some ways we are spending time training people for something that doesn't give them a lot of career benefit.

“My feeling is there is more variation with who does biopsies, so based on practice patterns, it makes more sense to [be trained in] that procedure than the dialysis catheter. Generally, kidney biopsies are done on patients who are going to be our long-term patients, and there is a risk/reward element,” he said. “It is helpful that the person doing the procedure knows how important the biopsy is [in terms of] how likely it is that the results will change the management of the patient.”

Clinicians may be more or less aggressive depending on

graduates were unlikely to perform biopsies (41%), and faculty unwillingness to supervise (30%). The most important barriers to achieving competence in installing catheters were “busyness of the service” (36%) and “disinterest” (21%).

Regarding that “unwillingness to supervise,” Rope noted that if nephrologists are no longer performing a procedure, it is not surprising they would experience difficulty teaching the next generation.

ASN and ABIM want to work with ACGME because it is “the only organization that can . . . make sure programs and program directors comply with the requirements and expectations of training . . . [and] close a training program, downsize a training program, [or] give citations to training programs,” Berns said.

The letter to ACGME notes “there are serious professionalism concerns stemming from false attestation of program directors to competencies that are not achieved, tacit acceptance of this inaccuracy by fellows knowing that their program directors are reporting dishonestly, and fellowship programs that continue to accept new fellows for training knowing that these fellows will not receive required training as well as procedural experiences and competencies.”

“We think this is a serious issue, and it is time to address it in a serious way,” Ellison said. The goal is not to shut programs down, but to have programs producing the kind of nephrologists we think should be in practice,” Ellison said. ■

## Pre-Eclampsia Linked to Increased Risk of Chronic Kidney Disease

Women who develop pre-eclampsia during pregnancy are at increased risk of developing kidney disease later in life, reports a study in the *British Medical Journal*.

Using national registry data, the researchers identified all women in Denmark who had at least one pregnancy lasting at least 20 weeks between 1978 and 2015. Hazard ratios for later diagnosis of kidney disease were compared for women with and without a history of pre-eclampsia, stratified by gestational age at delivery. The analysis included more than 1 million women, average follow-up of 18.6 years.

Kidney disease was diagnosed in 14,816 women, 7.2% of whom had a history of pre-eclampsia. Pre-eclampsia was associated with an increased risk of chronic

renal conditions, with hazard ratios (HRs) of 3.93 for early preterm pre-eclampsia (34 weeks), 5.33 for late preterm pre-eclampsia (34 to 36 weeks), and 2.27 for term pre-eclampsia (37 weeks or after). Associations were strongest for the diagnoses of chronic kidney disease, hypertensive kidney disease, and glomerular/proteinuric kidney disease. The associations were only somewhat weakened by adjustment for cardiovascular disease and hypertension.

The greatest pre-eclampsia-related increases in kidney disease risk were seen within 5 years of the last pregnancy: HR 6.11 for chronic kidney disease and 4.77 for glomerular/proteinuric disease. Though still significant, the associations were weaker at 5 years or longer after the

last pregnancy: HR 2.06 and 1.50, respectively. History of pre-eclampsia was not strongly related to acute renal conditions.

Although pre-eclampsia has been linked to end-stage renal disease, there are conflicting data on its association with chronic kidney disease and kidney dysfunction. In this nationwide cohort study, history of pre-eclampsia is strongly associated with increased risks of chronic but not acute kidney diseases. The association is strongest for chronic kidney disease and glomerular/proteinuric disease, particularly within 5 years of the latest pregnancy [Kristensen JH, et al. Pre-eclampsia and risk of later kidney disease: nationwide cohort study *BMJ* 2019; 365: 1516.] ■



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# Kidney Function and Albumin

Continued from page 1

“This paper is a nice addition to the research literature, because it monitors the effects of changes in both eGFR and UACR,” commented Kunihiro Matsushita, MD, PhD, of Johns Hopkins Bloomberg School of Public Health, Baltimore, and Director of the Chronic Kidney Disease Prognosis Consortium Data Coordinating Center.

“Although both markers have attracted attention in previous studies, this paper evaluates changes in both eGFR and UACR in the same patient population,” Matsushita added. “In terms of risk prediction, assessing changes in eGFR and UACR may provide additional information beyond the baseline values.”

Toshiaki Ohkuma, MD, PhD, of The George Institute, is lead author of the new report, on behalf of the ADVANCE Collaborative Group. Additional coauthors are Min Jun, Mark E. Cooper, Pavel Hamet, Stephen Harrap, Sophia Zoungas, Vlado Perkovic, and Mark Woodward (<https://doi.org/10.2215/CJN.13391118>).

## Predicting DKD outcomes: Can eGFR plus UACR improve accuracy?

The researchers analyzed long-term follow-up data on participants with type 2 diabetes enrolled in the ADVANCE-ON (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation Observational) study. In that study, increases in UACR from baseline to 2 years were independently associated with an increased risk of major macrovascular events, major kidney events, or death from any cause.

Specifically, for patients with a 30% or greater increase in UACR, the hazard ratio (HR) for the primary outcome was 1.26, compared to patients with a minor change in albuminuria at 2 years. There was no reduction in risk for patients who had a decrease in UACR.

However, on analysis accounting for expected regression to the mean, the effects of a decrease in UACR become significant for the composite outcome, major cardiovascular events, and all-cause mortality, although not for major renal events. “Our results suggest that change in UACR may have important prognostic utility as a surrogate for clinically important outcomes in type 2 diabetes,” the ADVANCE-ON authors concluded (1).

The new analysis sought to address important unanswered questions: What is the prognostic impact of changes in kidney function in type 2 diabetes, and how does it relate to the predictive value of UACR? As reported in a 2004 study in *JASN*, nephrology has fewer randomized controlled trials providing evidence for clinical decision-making than any other internal medicine subspecialty (2).

One factor may be the slowly progressive nature of kidney disease. “We need surrogate outcomes for kidney failure, because there is very little symptomatic evidence of disease for a long time,” Chalmers said. “Often you don’t get to know kidney disease is present until the patient develops kidney failure.”

As a result, clinical trials of kidney disease use surrogate endpoints to enable studies of interventions for patients at earlier stages of kidney disease. An eGFR reduction of 40% or even 30% is now a widely used surrogate in kidney disease studies, while many studies—ADVANCE-ON among them—have evaluated change in proteinuria or albuminuria.

“There has been less interest in UACR, but this could be an important predictor as well,” Chalmers said. “Surprisingly, no one has looked at UACR and eGFR in combination.” The new analysis focused on whether the combined use of UACR and eGFR can improve accuracy in predicting major clinical outcomes, compared to either variable alone.

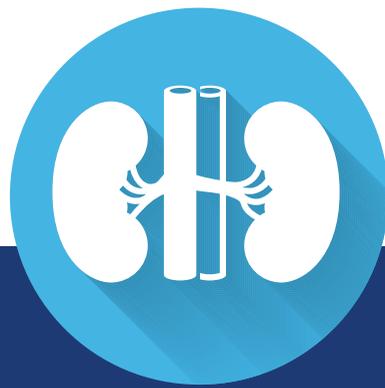
The study included 8766 (of 11,140) ADVANCE-ON participants with type 2 diabetes, enrolled from 215 centers in 20 countries, most in Asia or Europe. At enrollment,

all were 55 years or older and at high risk of cardiovascular events.

Changes in eGFR and UACR were evaluated from baseline to 2 years. Both markers were categorized as a decrease of 40% or greater, an increase of 40% or greater, or a “minor change” of less than 40% in either direction. Ninety-three percent of patients had only a minor change in eGFR: 3% had a decrease while 4% had an increase.

Of the two predictors, changes in UACR were much more common: 29% of patients had a decrease, 34% had a minor change, and 37% had an increase. Only 108 patients—about 1%—had both a decrease in eGFR and an increase in UACR.

Over a median follow-up of 7.7 years, one or more primary outcome events occurred in 25% of patients. These included a major macrovascular event (fatal or nonfatal myocardial infarction or stroke or death from cardiovascular causes) in 16%, death from any cause in 16%, and major kidney event (renal replacement therapy or kidney death) in 1%.



**[W]e believe that there is value in considering combinations of changes in albuminuria and GFR as surrogate end points for CKD progression.**

**—Josef Coresh, MD, PhD, and Andrew S. Levey, MD**

On adjusted analysis, patients who had a 40% or greater decrease in eGFR from baseline to 2 years were at higher risk of the primary outcome: HR 1.58, compared to those with a minor change. For those with a 40% or greater increase in eGFR, the HR of 0.82 was not statistically significant.

Adjusted analysis also found a higher risk of the primary outcome among patients with a 40% or greater increase in UACR: HR 1.32. There was no significant reduction in risk for those with a 40% or greater decrease in UACR. “There was also a statistically significant trend for major macrovascular events alone, major kidney events alone, and all-cause mortality when considered alone,” the researchers write. Sensitivity analysis using a 30% cutoff for changes in eGFR and UACR showed a similar pattern.

The combination of decreased eGFR and increased UACR was associated with more than a twofold increase in risk of the primary outcome—HR 2.31—with evidence of an interaction between the two markers. The association was significant for all three components of the primary outcome, with HRs of 1.75 for major macrovascular events, 26.38 for major kidney events, and 3.70 for all-cause mortality.

The effects were similar on analysis using a 30% cutoff. The researchers add, “Furthermore, the addition of a combination of both change in eGFR and UACR, and their interaction term provided better prognostic information, when compared with adding any of the change individually.”

## Implications for clinical monitoring and CKD surrogate outcomes

The ADVANCE-ON collaborators believe their findings have important implications for making the critical assessment of risk of cardiovascular and kidney outcomes in people with type 2 diabetes. They note that the improvements in prediction statistics were small, although statistically significant. “However,” they write, “we believe that even a modest improvement could be beneficial to prevent adverse events in these high-risk populations.”

The potential advantages of monitoring both UACR and eGFR may be especially important in primary care, where most people with type 2 diabetes are treated. “These are simple blood and urine tests that are easily monitored, if you happen to think about it,” Chalmers said. “But busy GPs see patients with such a wide variety of complaints, it’s difficult for them to track and document everything.”

“That’s the sort of problem diabetes nurses and certified diabetes educators are so effective in managing. If patients have both rising UACR and falling eGFR, that’s a major signal of the need for increased attention to risk factors and therapy, or for referral to a nephrologist or diabetologist.”

Matsushita noted, “Current KDIGO guidelines recommend the use of both markers for monitoring individuals with chronic kidney disease. These findings should further encourage healthcare providers to follow guidelines for monitoring in patients with CKD, as well as other conditions including hypertension and diabetes.”

“While the idea of using these markers in combination is not necessarily new, this study further supports attention to changes in eGFR and UACR together. Because both markers are independently related to outcomes, it’s important for healthcare professionals to pay attention to them.”

The ADVANCE-ON authors note some important limitations of their study, including the relatively low end stage kidney disease event rate: 0.2% per year. Strengths include the separate and combined assessment of associations with change in two clinically relevant markers, in a large and diverse population with long-term follow-up.

“There is also interest in looking at changes in kidney measures as surrogate endpoints of hard kidney endpoints,” said Matsushita. “The combination of increased albuminuria and decreased eGFR may be able to capture individuals who would develop hard kidney outcomes in the future.”

“However, we need more data. The utility of the combined markers may be different for specific interventions—since, for example, we know the combination of ACEIs and ARBs can reduce albuminuria but may increase the risk of some adverse outcomes.”

In an accompanying editorial, Josef Coresh, MD, PhD, and Andrew S. Levey, MD, note that the findings “provide some support” for combined use of albuminuria and GFR, but raise several important questions that remain to be answered.

“[W]e believe that there is value in considering combinations of changes in albuminuria and GFR as surrogate end points for CKD progression,” Coresh and Levey conclude. “Subsequent studies should define when such risk prediction is clinically useful and how and when the combination of changes in ACR and eGFR can be used as an outcome for clinical trials.”

Chalmers agrees with the need for further research, especially in light of the relatively low number of ADVANCE-ON patients with major kidney events. “We need new studies with larger samples of patients with kidney disease and both rising UACR and falling eGFR.” ■

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# Anti-MOC Legislation Continues to Advance in Some States

## But Focus May Have Shifted to Reforms in Maintenance of Certification by Specialty Boards

By Eric Seaborg

In the past 12 months, three more states passed legislation backed by state medical associations limiting the use of maintenance-of-certification (MOC) tests. Washington and Michigan passed laws in 2018, and North Dakota passed a law earlier this year.

But considering legislative sessions and bills that have been introduced, no state other than North Dakota appears likely to act in 2019—and the momentum for reform may have passed to the efforts by the specialty boards themselves, including the changes proposed by the vision initiative of the American Board of Medical Specialties (ABMS).

The Washington legislation ensures that board certification cannot be a condition for state medical licensure or licensure renewal. This approach is considered “starter legislation” by anti-MOC advocates because few, if any, states require specialty certification for a medical license, so it has little real-world impact.

The Michigan legislation prohibits insurance companies from requiring MOC as a sole condition of reimbursement and pre-empts any future effort to make state medical licensure contingent upon completion of MOC.

The North Dakota legislation says that a physician may not be denied staff privileges or employment by a facility based solely on the physician’s decision to not participate in maintenance of certification and healthcare insurers may not deny reimbursement to or prevent a physician from being a preferred provider based solely on a physician’s decision to not participate in maintenance of certification.

The new legislation means that North Dakota and Michigan have joined Texas, Oklahoma, Georgia, Tennessee, and South Carolina in passing legislation beyond the “starter legislation” that limits the use of MOC in areas such as employment and insurance participation.

### Impact of new laws

Considering the time it takes to work through tasks like amending hospital bylaws, it may be too soon to gauge the impact of these laws, and so far, the picture is unclear.

“ABMS has detected no significant impact in the states where legislation has been adopted,” according to Tom Granatir, senior vice president of policy and external relations at ABMS. “Participation in continuing certification is growing, as we expect it to continue to do. Some boards have found the new approaches to assessment are inducing lifetime certificate holders to participate in continuing certification.”

Three years ago, Oklahoma became the first state to adopt legislation limiting the use of MOC, but it has not had the backers’ intended effects because hospitals in the state claimed that technicalities in the law’s wording meant it did not apply to them. Attempts to clarify the legislation have been blocked by the Oklahoma Hospital Association, Oklahoma Association of Health Plans, and ABMS, according to Jack Beller, MD, an orthopedic surgeon in Norman and former president of the Oklahoma State Medical Association.

Texas passed one of the most restrictive laws in the country about the use of maintenance of certification, according to Ori Hampel, MD, founder and managing partner of Adult and Pediatric Urology of Houston. The law has led some hospitals to change their bylaws to no longer require MOC by medical staff. However, two of the largest hos-

pital chains in the state “have been flaunting the law and not allowing the medical staff to vote on whether or not the medical staff wishes to have maintenance of certification as a requirement.” The Texas Medical Association, which supported the legislation restricting the use of MOC, has responded by passing a “straightforward” resolution saying it “opposes mandatory maintenance of certification,” Hampel said.

Donald J. Palmisano Jr., JD, executive director and CEO of the Medical Society of Georgia, which successfully pushed for MOC-limiting legislation in 2017, said he is seeing positive changes: “We have heard that the medical staffs at a number of hospitals are reviewing the bylaws to see what can be done to address this board certification issue. Medical staffs are saying, ‘We want our doctors to be initially board-certified, and when it comes to maintaining the certification, we may be willing to recognize other boards [in addition to ABMS].’ It has gotten doctors more engaged with their medical staffs, and that is a very positive thing, because they are realizing that these issues are very important.”

Palmisano added that the legislation is only a part of the picture in terms of MOC reform. He has been active on several fronts in the MOC reform movement, including serving on the ABMS Vision for the Future Commission. “I think the ABMS has taken the right approach by having the vision initiative,” Palmisano told *Kidney News*. “From the state medical society perspective, physicians were very pleased that they had a voice on the vision initiative. I think the doctors feeling like somebody is listening has really gone a long way.”

### Maryland sees lack of need

The legislative record in Maryland provides insight into why the effort for MOC-limiting legislation is stalling in some states. Maryland passed a law in 2017 prohibiting the use of certification or MOC in licensure, but that is as far as the legislature has ventured.

In 2018, a key Maryland legislator requested that the Maryland Health Care Commission (MHCC) study MOC requirements “with the goal of recommending legislation for consideration during the 2019 session.” The MHCC responded in a letter that its work group of key stakeholders was “not able to reach consensus on a legislative approach.” It noted that it could not reconcile the goals of hospitals and insurers set on defending their “independence in setting criteria for employment, privileges, and other credentialing-related decisions” with those of “physician members of the work group [who] expressed a preference to determining their own requirements for ongoing training and assessment.”

In addition, MHCC’s study of the issue undercut some arguments put forth by proponents of restricting MOC. For example, MHCC found no need to forbid health insurers from requiring board certification because the health insurers in the state do not require it to participate in their networks, with the one exception being Kaiser, which employs all its own physicians.



MHCC also discounted the charge by MOC critics that ABMS has a monopoly, noting that in 2014 some physicians created the National Board of Physicians and Surgeons (NBPAS) as an alternative entity for recertification “to provide an option for physicians looking for a less burdensome option. As of 2018,

104 hospitals in the United States had changed their bylaws to accept NBPAS as a board certifying entity. In Maryland, in September 2015, Frederick Memorial voted to accept NBPAS as a valid option for recertification (in addition to boards that had been previously recognized by the hospital).”

The MHCC concluded that “current law is not a barrier to some responses to physician concerns,” especially considering that “specialty boards are re-evaluating recertification requirements and processes.”

### Opposition and reform

ABMS continues to oppose legislative efforts to regulate recertification and “remains committed to our position of hospital, health system, and insurers’ right to self-determination,” said Granatir.

“I think [this legislation] is a slippery slope,” said Jeffrey Berns, MD, chair of the American Board of Internal Medicine’s nephrology board. “When states start saying to hospitals or health systems through legislation that we think we know better as a state legislature what value there is to board certification, continuing medical education, or what have you, and therefore we are going to tell you what you can and cannot utilize in making decisions, what is next?”

“Slippery slope” is a term that even proponents of the legislation use. Frank McDonald Jr., MD, MBA, a neurologist who was president of the Medical Association of Georgia when the state passed its legislation, said he didn’t like the idea of involving the government in physician self-regulation, but his association turned to the legislature because physicians were so frustrated by specialty boards adding requirements to MOC without listening to their concerns.

ABMS’ Granatir said that physicians are starting to notice as various boards implement innovative knowledge assessment options to improve their recertification programs: “ABMS is on a path toward significant change in continuing certification programs. A recently convened commission has given the boards a roadmap. We hope our community will give the process a chance before looking for legislative solutions. Anecdotally, we have heard from a few state medical societies that our response to the commission’s recommendations has impacted their members’ desire to pursue legislation.”

But it is not a coincidence that the specialty boards’ efforts at reform came on the heels of the legislative efforts. Physicians went to their state medical societies—and then their state legislatures—as a last resort, Georgia’s Palmisano said: “These laws that started to pass across the country really got everybody’s attention on how dissatisfied the physicians were.” ■

FOR YOUR CKD PATIENTS

When you see risk factors of hyperkalemia...<sup>1,2</sup>



CKD=chronic kidney disease; K<sup>+</sup>=potassium; ARB=angiotensin II receptor blocker.

PATIENT PORTRAYAL

## Consider once-daily, sodium-free VELTASSA

### INDICATION AND USAGE

VELTASSA is indicated for the treatment of hyperkalemia.

Limitation of Use: VELTASSA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.

### IMPORTANT SAFETY INFORMATION

**Contraindications:** VELTASSA is contraindicated in patients with a history of a hypersensitivity reaction to VELTASSA or any of its components.

**Worsening of Gastrointestinal Motility:** Avoid use of VELTASSA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders, because VELTASSA may be ineffective and may worsen gastrointestinal conditions. Patients with a history of bowel obstruction or major gastrointestinal surgery, severe gastrointestinal disorders, or swallowing disorders were not included in clinical studies.

**Hypomagnesemia:** VELTASSA binds to magnesium in the colon, which can lead to hypomagnesemia. In clinical studies, hypomagnesemia was reported as an adverse reaction in 5.3% of patients treated with VELTASSA. Approximately 9% of patients in clinical trials developed hypomagnesemia with a serum magnesium value <1.4 mg/dL. Monitor serum magnesium. Consider magnesium supplementation in patients who develop low serum magnesium levels.

**Adverse Reactions:** The most common adverse reactions (incidence ≥2%) are constipation, hypomagnesemia, diarrhea, nausea, abdominal discomfort and flatulence. Mild to moderate hypersensitivity reactions were reported in 0.3% of patients treated with VELTASSA and included edema of the lips.

Please see Brief Summary of Prescribing Information on following page.



VELTASSA IS THE **#1 PRESCRIBED BRANDED K<sup>+</sup> BINDER**<sup>3,4</sup>

Join **thousands of physicians** helping their patients by treating hyperkalemia with VELTASSA.



ACCESS TO VELTASSA IS **BROAD AND IMPROVING**<sup>5</sup>

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**Veltassa**<sup>®</sup>  
(patiromer) for oral  
suspension  
8.4g | 16.8g | 25.2g

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## VELTASSA® (patiomer) for Oral Suspension

Brief Summary of Prescribing Information. Please see Full Prescribing Information for complete product information.

### INDICATION AND USAGE

VELTASSA is indicated for the treatment of hyperkalemia.

**Limitation of Use:** VELTASSA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.

### CONTRAINDICATIONS

VELTASSA is contraindicated in patients with a history of a hypersensitivity reaction to VELTASSA or any of its components [see *Adverse Reactions*].

### WARNINGS AND PRECAUTIONS

**Worsening of Gastrointestinal Motility** Avoid use of VELTASSA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders, because VELTASSA may be ineffective and may worsen gastrointestinal conditions. Patients with a history of bowel obstruction or major gastrointestinal surgery, severe gastrointestinal disorders, or swallowing disorders were not included in the clinical studies.

**Hypomagnesemia** VELTASSA binds to magnesium in the colon, which can lead to hypomagnesemia. In clinical studies, hypomagnesemia was reported as an adverse reaction in 5.3% of patients treated with VELTASSA [see *Adverse Reactions*]. Monitor serum magnesium. Consider magnesium supplementation in patients who develop low serum magnesium levels on VELTASSA.

### ADVERSE REACTIONS

The following adverse reaction is discussed in greater detail elsewhere in the label:

- Hypomagnesemia [see *Warnings and Precautions*]

**Clinical Trials Experience** Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of VELTASSA cannot be directly compared to rates in the clinical trials of other drugs and may not reflect the rates observed in practice. In the safety and efficacy clinical trials, 666 adult patients received at least one dose of VELTASSA, including 219 exposed for at least 6 months and 149 exposed for at least one year. Table 1 provides a summary of the most common adverse reactions (occurring in  $\geq 2\%$  of patients) in patients treated with VELTASSA in these clinical trials. Most adverse reactions were mild to moderate. Constipation generally resolved during the course of treatment.

**Table 1: Adverse Reactions Reported in  $\geq 2\%$  of Patients**

Adverse Reactions	Patients treated with VELTASSA (N=666)
Constipation	7.2%
Hypomagnesemia	5.3%
Diarrhea	4.8%
Nausea	2.3%
Abdominal discomfort	2.0%
Flatulence	2.0%

During the clinical studies, the most commonly reported adverse reactions leading to discontinuation of VELTASSA were gastrointestinal adverse reactions (2.7%), including vomiting (0.8%), diarrhea (0.6%), constipation (0.5%) and flatulence (0.5%). Mild to moderate hypersensitivity reactions were reported in 0.3% of patients treated with VELTASSA in clinical trials. Reactions have included edema of the lips.

**Laboratory Abnormalities** Approximately 4.7% of patients in clinical trials developed hypokalemia with a serum potassium value  $< 3.5\text{mEq/L}$ . Approximately 9% of patients in clinical trials developed hypomagnesemia with a serum magnesium value  $< 1.4\text{ mg/dL}$ .

### DRUG INTERACTIONS

In clinical studies, VELTASSA decreased systemic exposure of some coadministered oral medications. Binding of VELTASSA to other oral medications could cause decreased gastrointestinal absorption and loss of efficacy when taken close to the time VELTASSA is administered. Administer other oral medications at least 3 hours before or 3 hours after VELTASSA.

### USE IN SPECIFIC POPULATIONS

#### Pregnancy

##### Risk Summary

VELTASSA is not absorbed systemically following oral administration and maternal use is not expected to result in fetal risk.

#### Lactation

##### Risk Summary

VELTASSA is not absorbed systemically by the mother, so breastfeeding is not expected to result in risk to the infant.

**Pediatric Use** Safety and efficacy in pediatric patients have not been established.

**Geriatric Use** Of the 666 patients treated with VELTASSA in clinical studies, 59.8% were age 65 and over, and 19.8% were age 75 and over. No overall differences in effectiveness were observed between these patients and younger patients. Patients age 65 and older reported more gastrointestinal adverse reactions than younger patients.

**Renal Impairment** Of the 666 patients treated with VELTASSA in clinical studies, 93% had chronic kidney disease (CKD). No special dosing adjustments are needed for patients with renal impairment.

### OVERDOSAGE

Doses of VELTASSA in excess of 50.4 grams per day have not been tested. Excessive doses of VELTASSA may result in hypokalemia. Restore serum potassium if hypokalemia occurs.

### PATIENT COUNSELING INFORMATION

**Drug Interactions** Advise patients who are taking other oral medication to separate the dosing of VELTASSA by at least 3 hours (before or after) [see *Drug Interactions*].

**Dosing Recommendations** Inform patients to take VELTASSA as directed with or without food and adhere to their prescribed diets. Inform patients that VELTASSA should not be heated (e.g., microwaved) or added to heated foods or liquids and should not be taken in its dry form.

### Manufactured for:

Relypsa, Inc.  
Redwood City, CA 94063  
Version 05; May 2018

**References:** **1.** Weir MR, Bakris GL, Bushinsky DA, et al; for OPAL-HK Investigators. Patiomer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. *N Engl J Med*. 2015;372(3):211-221. doi:10.1056/NEJMoa1410853. **2.** Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Hypertension*. 2017. doi:10.1161/HYP.000000000000065. **3.** Data on file as of August 2018. Relypsa, Inc. **4.** Data on file as of December 2018. Relypsa, Inc. **5.** Data on file as of February 2019. Relypsa, Inc.

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## Kidney Recipients with Allograft Failure: An Important Opportunity for Collaborative Care and Improving Outcomes

Nephrologists from the American Society of Transplantation (AST) Kidney Pancreas Community of Practice (KPCOP) and the American Society of Nephrology (ASN) Quality Committee are partnering in consensus-building and educational efforts to improve the care of kidney patients after failed allograft—a vulnerable and growing group of kidney patients in need of more coordinated care. These efforts include formation of a cross-cutting “Kidney Recipients with Allograft Failure—Transition of Care (KRAFT)” workgroup.

Formed in 2018 by KPCOP Chair Darshana Dadhania, MD, the KRAFT workgroup seeks to address gaps in evidence and consensus for clinical care when kidney allograft function is declining and return to dialysis is inevitable. Under the leadership of Tarek Alhamad, MD, and Jim Rice, MD, the workgroup developed an AST-approved survey distributed to transplant nephrologists and surgeons across the country to assess opinions and practices for managing immunosuppressive therapy in patients with failing transplants. Now the hope is for general nephrologists to add their input to the research project.

According to Krista Lentine, MD, PhD, FASN, ASN Quality Committee and KRAFT workgroup member, “The time period when care is being transitioned from transplant nephrologist to general nephrologist requires a coordinated effort to balance the risk of sensitization against the risks of infectious complications associated with maintenance immunosuppressive therapies.”

Notes Dadhania, “Often it is not clear who takes the primary responsibility for immunosuppressive management during this transition period when a patient is returning to dialysis following a failed allograft—transplant nephrologist or general nephrologist?”

Surveying general nephrologists regarding their knowledge, approaches, and attitudes toward immunosuppressive therapy in a patient with a failed kidney allograft will support urgently needed initiatives to coordinate care and improve patient outcomes. The goal of this survey segment of the project is to identify areas of both consensus and controversy, ground discussions of best practices, and focus evidence gathering to address knowledge gaps. The results will eventually be submitted for publication and used to guide consensus-building efforts.

Clinicians may participate through the web-

based survey until September 1, 2019, at [https://redcap.ctsc.weill.cornell.edu/redcap\\_protocols/surveys/?s=NNYYY3A34N](https://redcap.ctsc.weill.cornell.edu/redcap_protocols/surveys/?s=NNYYY3A34N)

Among the nearly 100,000 patients currently awaiting a kidney transplant, 30% are sensitized with a panel reactive antibodies (PRA) value of >20%, and 12% of candidates have a previously

tions in practice protocols and the challenges associated with managing kidney recipients with allograft failure.

The management of patients after allograft failure will be discussed at an upcoming ASN Kidney Week symposium in November 2019. ■

**Often it is not clear who takes the primary responsibility for immunosuppressive management during this transition period when a patient is returning to dialysis following a failed allograft—transplant nephrologist or general nephrologist?**

failed allograft (1). The risk of high-level sensitization (PRA >80%) increases substantially over time after allograft failure, mainly attributable to weaning off immunosuppressive therapies (2). Indeed, prolonged treatment with immunosuppressive therapies following kidney graft failure can decrease the rate of sensitization by half (3).

In a survey of US transplant programs, however, the majority of responding centers stated that greater than 80% of patients are off all immunosuppressive therapies by one year post graft failure (4), driven by concerns for immunosuppression-related side effects such as infections. As sensitization status greatly affects the patient’s opportunity for re-transplantation and long-term survival (5), clarifying appropriate management after allograft failure to minimize complications while supporting opportunities for re-transplantation is a critical concern. In current practice, the period of allograft failure is associated with higher mortality than any other phase of kidney care (6). Many of these issues were highlighted in a presentation by Martha Pavlakis, MD, entitled “Managing the Failing Kidney Allograft” as a Timely Topics in Transplantation series sponsored by AST.

At the present time, the only published guidelines on the topic of immunosuppressive management during this transition period were based on “very low” quality of evidence by the British Transplantation Society (7). To understand and help resolve these deficits, the community must work together to develop additional knowledge about current varia-

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## Pneumococcal Vaccine Is Cost-Effective for Younger CKD Patients

Pneumococcal vaccination is a cost-effective intervention for adults with chronic kidney disease (CKD) under age 65, in the absence of other clinical indications, reports a study in the *American Journal of Kidney Diseases*.

Using data from the National Health and Nutrition Examination Survey 1999 to 2004, the researchers estimated the prevalence of pneumococcal vaccination among patients with CKD, based on age and clinical indications. For patients aged 65 to 79—for whom the vaccine is indicated by age

—vaccination prevalence was 56.6%. For CKD patients aged 50 to 64, prevalence was 28.5% for those with clinical indications (such as diabetes, lung or heart disease, kidney failure, and nephrotic syndrome) and 9.7% for those without indications.

Forty-one percent of the younger CKD patients had clinical indications, most commonly lung disease. The prevalence of vaccination did not differ significantly by CKD risk status.

The cost of pneumococcal vaccination

was higher and effectiveness was lower in older adults and in patients with higher CKD risk status. Based on a willingness-to-pay threshold of \$100,000 per quality-adjusted cost year (QALY), vaccination was cost-effective in CKD patients aged 50 to 64 (\$38,000/QALY) and in those aged 65 to 79 (\$15,000/QALY).

In the younger group, incremental cost-effectiveness ratio increased from \$1000/QALY for patients with kidney failure or nephrotic-range albuminuria, to \$17,000/

QALY for CKD with high risk, to \$25,000/QALY for CKD with moderate risk, to \$43,000/QALY for those without CKD. Sensitivity analysis suggested that vaccination for younger patients was cost-effective even at lower vaccine efficacy or 50% higher cost.

Cost-effectiveness of pneumococcal vaccination among patients with CKD in the United States. *Am J Kidney Dis* 2019; DOI: 10.1053/j.ajkd.2019.01.025. ■

# Findings

## Why Don't Trainees Want to Become Nephrologists?



Lack of interest in the subject is the most common reason why medical students and residents say they wouldn't want to pursue a career in nephrology, reports a survey study in the open-access journal *BMC Nephrology*.

The researchers distributed an anonymous survey regarding specialty choice to 4199 US upper-level medical students and internal medicine residents. The survey targeted respondents at institutions with an associated nephrology fellowship program. Perceptions of nephrology and factors affecting specialty choice were evaluated.

Response rate was 15.3%, including 315 medical students and 308 residents from 30 institutions. Ninety-two percent of trainees cited personal interest in a subject as the most important factor affecting their choice of a specialty. Other factors included work-life balance, access to mentors, and exposure to the subject.

Lack of interest was the most common reason for not choosing nephrology as a specialty, cited by 79% of respondents overall. Other factors included concerns about remuneration, 43%; work-life balance, 39%; and lack of exposure to nephrology, 32%. For residents, financial compensation was the most common reason.

Responses to open-ended questions raised other issues such as frustrations in dealing with hemodialysis patients, including perceived nonadherence. Several trainees expressed interest in a combined nephrology-critical care program. Respondents who said they would consider nephrology cited an interest in renal physiology and interactions with a respected mentor.

Despite the rising prevalence of advanced kidney disease, 40% of nephrology positions went unfilled in the 2018 fellowship match. This survey explores some of the reasons why trainees may not choose nephrology as a specialty. The authors discuss approaches to help "sustain a passionate and dynamic nephrology workforce" [Nair D, et al. Perceptions of nephrology among medical students and internal medicine residents: a national survey among institutions with nephrology exposure. *BMC Nephrol* 2019; 20:146]. ■

## Metformin Linked to Better Long-term Weight Loss

Among patients who successfully lost weight in the Diabetes Prevention Program (DPP) study, long-term maintenance of weight loss is better for those initially assigned to metformin compared to a lifestyle intervention, reports a study in *Annals of Internal Medicine*.

In the original DPP, 3234 overweight or obese patients with elevated glucose levels were randomly assigned to met-

formin, an intensive lifestyle intervention, or placebo. At an average follow-up of 2.8 years, diabetes risk was reduced by 31% with metformin and 58% with the lifestyle intervention, compared to placebo. Weight loss averaged 2.1 and 5.6 kg, respectively, and was the main factor responsible for diabetes prevention. At 1 year, 28.5% of patients in the metformin group, 62.6% in the lifestyle intervention

group, and 13.4% in the placebo group had lost at least 5% of body weight.

In the DPP Outcomes Study (DP-POS), 1066 patients with at least 5% weight loss were followed up for 15 years, after the end of masked treatment. Long-term weight loss management was compared among patients in the three DPP intervention groups. Baseline and post-baseline factors associated with mainte-



nance of weight loss were assessed as well.

From year 6 to 15, mean weight loss relative to baseline was 6.2% in patients originally assigned to metformin, compared to 3.7% in those assigned to the lifestyle intervention and 2.8% in the placebo group. Mean percentages of patients with long-term weight loss throughout follow-up were 56.5%, 48.9%, and 41.7%, respectively.

Across groups, greater weight loss in year 1 was significantly related to long-

term weight loss. Other independent predictors included continued metformin use in the metformin group, absence of diabetes or family history of diabetes in the lifestyle intervention group, and higher fasting plasma glucose in the placebo group.

Among patients who initially lost at least 5% of body weight in the DPP, long-term maintenance of weight loss in the DPPOS is greatest for those originally assigned to metformin. Older age

and initial weight loss are key predictors of maintenance of weight loss over 15 years. The researchers call for further studies of metformin to promote weight loss maintenance, whether initial weight loss is achieved with lifestyle interventions, anti-obesity drugs or devices, or bariatric surgery [Apolzan JW, et al. Long-term weight loss with metformin or lifestyle intervention in the Diabetes Prevention Program Outcomes Study. *Ann Intern Med* 2019; DOI: 10.7326/M18-1605]. ■

## No ‘Clinically Relevant Benefit’ of Early Dialysis in Children

In children with end stage kidney disease (ESKD), there is no specific level of renal function at which dialysis initiation leads to improved patient outcomes, concludes a registry study in *Nephrology Dialysis Transplantation*.

The researchers analyzed data on 2963 children enrolled in the European Society for Pediatric Nephrology/European Renal Association–European Dialysis and Transplant Association (ESPN/ERA-EDTA) Registry between 2000 and 2014. Drawn from 21 countries, all patients were less than 18 years old when they initiated renal replacement therapy. Patient survival and access to transplantation were compared for 1411 children with early initiation, estimated glomerular filtration rate (eGFR) 8 mL/min/1.73 m<sup>2</sup> or greater, versus 1552 with late initiation, eGFR less than 8 mL/min/1.73 m<sup>2</sup>.

Median eGFR at the start of dialysis was 10.5 mL/min/1.73 m<sup>2</sup> in the early-initiation group and 6.1 mL/min/1.73 m<sup>2</sup> in the late-initiation group. Children with early initiation were older: median age 11.0 versus 9.4 years. Early starters were more likely to have glomerulonephritis or hereditary nephropathies, while late starters were more likely to have congenital anomalies of the kidney and urinary tract or unknown diagnosis.



Overall median survival on dialysis was 98.2% at 1 year, 96.3% at 2 years, and 91.1% at 5 years. There was no difference in mortality for the early versus late starters, including after adjustment for patient and clinical characteristics. Access to kidney transplantation was similar as well: 82.0% of early starters and 81.4% of late starters received their first transplant within 5 years.

Most secondary outcomes were also similar between groups, including growth and cardiovascular risk factors. Late starters were more likely to develop hypertension.

There is no consensus as to the timing of dialysis initiation in children with ESKD. This large population-based analysis finds “no evidence for a clinically relevant benefit of early start of dialysis.” The researchers conclude: “[O]ur data suggest that the decision to start dialysis in paediatric ESKD should not be merely based on eGFR, but should be a personalized decision in which benefits, burden, complexity and potential risks of dialysis are carefully balanced” [Preka E, et al. Association between timing of dialysis initiation and clinical outcomes in the paediatric population: an ESPN/ERA-EDTA registry study. *Nephrol Dial Transpl* 2019; DOI: 10.1093/ndt/gfz069]. ■

## He has her eyes. And maybe her Alport syndrome.

When you see patients with abnormal kidney function, think Alport syndrome. It can filter through the family.<sup>1</sup>

- Alport syndrome is a rare disease and is the second leading cause of inherited chronic kidney disease after polycystic kidney disease<sup>2</sup>
- Alport syndrome is a progressive, genetic kidney disease that can lead to dialysis, transplant, and/or death<sup>3</sup>
- Women are just as likely to have Alport syndrome as men<sup>1</sup>
- Investigating a patient’s family history could be a determining factor toward improving outcomes for other relatives<sup>1</sup>

Reata is focused on targeting novel molecular pathways to treat life-threatening diseases that have few or no FDA-approved therapies, including Alport syndrome.

Abnormal kidney function could be Alport syndrome.  
It’s time to start making the family connection.



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# The Complex Landscape of Drug Development for Children with Chronic Kidney Disease

By Debbie S. Gipson and Howard Trachtman

**C**hronic kidney disease (CKD) in children involves a host of rare diseases affecting children of all ages. The therapeutic needs of these children are largely unmet because of limited disease- and age-specific drug development. The absence of pediatric testing to document appropriate pediatric dosing, safety, and efficacy has many consequences:

- Few drugs are labeled for use in children with CKD.
- Off-label prescribing is often extrapolated from product labels written for adult patients with kidney disease or other non-kidney-related conditions.
- Little progress has been made to fill the information gaps required to guide the pharmacologic treatment of children with kidney diseases.

Drug development for children with kidney diseases must consider issues unique to this vulnerable population. Legislation by the United States and the European Union mandates plans for pediatric development as part of an overall product development strategy. This highlights the need to prioritize those programs that may be deemed most necessary and impactful and to optimize designs to facilitate their successful completion.

The Kidney Health Initiative (KHI) is engaging with relevant stakeholders, including patients, healthcare providers, researchers, professional organizations, industry partners, and regulators, to address these issues by developing recommendations to foster drug development for children with kidney diseases.

## Ethics of pediatric drug development

The ethics of clinical research inclusive of children has evolved “from a culture of protecting children from research to protecting children through research” (1). This perspective incorporates the understanding that access to safe and effective therapies requires testing of these same therapies in children. Failure to control pediatric kidney diseases has a documented adverse impact on the incidence and prevalence of pediatric kidney failure, the reduction in life expectancy after the onset of kidney failure, and the everyday lives of affected children (2).

Studies inclusive of children must pay particular attention to considerations for direct benefit, risk minimization, and study designs that are well suited for the adolescent, child, or infant age groups, or a combination of these, depending on the intended treatment population. The ethical inclusion of children in well-designed clinical trials is a key consideration.

Depending on the specific condition under investigation, pediatric inclusion in kidney disease clinical trials may include 1) adults and children simultaneously when there is a potential for direct benefit in the background of limited or unfeasible options for children, 2) children after demonstration of preliminary or robust evidence suggesting efficacy in adults, or 3) children alone when the disease under study does not occur in adults. Early consultation with experts in the pediatric nephrology community, with patients and family caregivers, and with members of the regulatory agencies such as the US Food and Drug Administration (FDA) can help to guide the clinical development plan.

## Improving opportunities for pediatric drug development: legislation and regulation

The limited drug development for children has been acknowledged by the United States government and the FDA. A series of legislative initiatives have provided incentives to include children in drug development activities by adding a 6-month extension on marketing exclusivity (3) and by establishing a framework for the FDA to request testing of prioritized therapies in children (4). Proposals are requested by the National Institute of Child Health and Human Development for priority (off-patent) drugs and therapeutic areas for testing. The Best Pharmaceuticals Act for Children program pro-

**In 1963, Dr. Harry C. Shirkey observed that “By an odd twist of fate, infants and children are becoming therapeutic or pharmaceutical orphans.”**

vides an opportunity for the pediatric nephrology community to advocate for therapeutics testing for children with kidney disease (5).

In 2007, the Pediatric Research Equity Act included the option for the FDA to require a pediatric investigation plan for new drug applications. However, orphan diseases (defined by the FDA as rare diseases and disorders that affect fewer than 200,000 people in the United States, or that affect more than 200,000 persons but for which drug development is not expected to recover the costs of developing and marketing a treatment drug) are excluded from these pediatric testing requirements. Despite the implementation of a series of legislative initiatives, rare and orphan diseases remain a neglected area of drug development.

The RACE for Children Act was enacted as a part of Title V of the FDA Reauthorization Act (FDARA) in 2017. This act requires the evaluation of new molecularly targeted drugs and biologics for oncology indications to be tested for use in children. Importantly, this act eliminates the orphan exemption for pediatric studies for new molecularly targeted cancer drugs. This legislation and the resulting program provide an example that may be replicated for children with kidney diseases in which precision medicine trials are emerging.

## Building a new reality of drug development for children with chronic kidney diseases

In partnership with experts from American Society of Nephrology’s (ASN) KHI, NephCure Kidney International’s (NKI) Gateway Initiative, and the American Society of Pediatric Nephrology (ASPN) Therapeutics Development Committee, complementary programs are

being launched to facilitate pediatric drug development for children with kidney diseases. All three entities are identifying ways to collaborate to improve the national capacity to conduct clinical trials in children.

KHI launched the Kidney-PATCH (Pediatric Accelerator Trial Clearing House) program in 2018. The program implementation committee is being led by H. William Schnaper, MD, of Northwestern University, who summarized the objective of Kidney-PATCH: “We’d like to serve as an honest broker for sponsors to conduct trials in children with CKD.” The goals of Kidney-PATCH are as follows:

- To enable feasibility assessment in terms of the available patient populations through data sharing and access to CKD pediatric registries.
- To facilitate assessment of the capacity of various pediatric kidney clinical trial organizations.
- To assist with the identification of expertise that can provide consultation on study planning.

Subject matter expertise has been identified from the United States and Europe to participate in the pilot phase of this program. Additional information about Kidney-PATCH and the request form can be accessed through the KHI website: [www.kidneyhealthinitiative.org](http://www.kidneyhealthinitiative.org).

NKI’s Gateway Initiative is bringing patients and family caregivers, clinicians, industry partners, and regulatory authorities together with professional society and foundation leadership to improve the clinical trial development and participation by individuals affected by glomerular disease. This initiative includes a Pediatric Working Group specifically charged to assist with strategies for the inclusion of children in clinical trials and for expanding the participation of patients and pediatric nephrology practices in glomerular disease clinical trials (KidneyHealthGateway.com).

“The success of the Gateway Initiative Pediatric Work Group is essential to drug development for glomerular disease,” said Joshua Tarnoff, chief executive officer, NephCure Kidney International. “With the wonderful evolution of regulatory pathways, there are currently 20 clinical nephrotic syndrome trials under way, up from only two a few years ago. Clinical trials simply must include adults and children in order to enroll the necessary population to bring trials to completion and drugs to market for the rare glomerular diseases.”

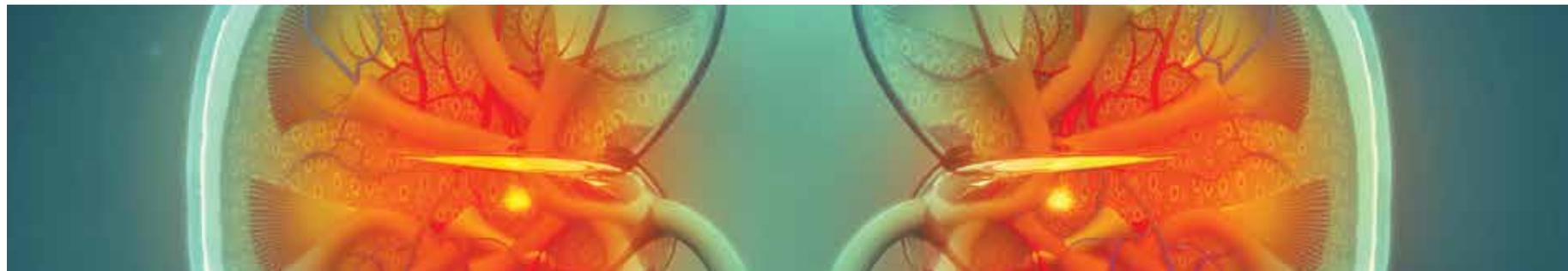
The opportunities for new pathways for drug development for children with kidney diseases are tremendous. We are observing an alignment of interest in drug development from the full spectrum of stakeholders, and we fully intend that children with kidney diseases will be the beneficiaries of this collective effort. ■

*Debbie S. Gipson, MS, MD, is professor of pediatrics, division of nephrology, University of Michigan. Howard Trachtman, MD, is professor of pediatrics and chief, division of nephrology, New York University Langone Health.*

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## Policy Update



# Administration Addresses Transplantation through Two Upcoming Rules

By Ryan Murray

**O**n May 22, 2019, the White House released its Unified Spring Agenda outlining the issues the administration will address through a proposed rule process in the coming months. The agenda highlighted administration priorities of improving the data used to evaluate Organ Procurement Organizations (OPOs) and removing financial barriers to living donation. Both policy priorities were discussed when ASN met with Department of Health and Human Services (HHS) Secretary Alex Azar and other senior administration officials in February to urge the department to address these issues.

The administration will address transplantation through two upcoming rules by:

- 1) changing standards used to evaluate Organ Procurement Organizations (OPOs) and ensure proper data on available organs and transplants is collected; and
- 2) removing financial barriers to living organ donation by expanding allowable costs that can be reimbursed.

### Organ procurement organization metrics

One of the upcoming rules deals with changes to the “standards used to evaluate OPOs and ensure proper data on available organs and transplants is collected” so that the metrics used to evaluate OPOs are objective and verifiable.

ASN President Mark E. Rosenberg, MD, FASN, wrote to CMS Administrator Seema Verma in May recommending an alternative quality metric for OPOs to increase transplantation. Rosenberg wrote about how reforming OPO metrics can improve outcomes for patients and their families by driving “meaningful increases in our deceased donation system by improving our understanding of OPO performance through the use of objective data and a consistent standard for the denominator.”

Rosenberg wrote to CMS after the ASN Council endorsed changing “the metrics by which OPOs are evaluated to actual deceased donors as a percentage of in-hospital deaths among patients 75 years of age or younger with a cause of death consistent with organ donation. The data for this metric are already available from the Detailed Mortality File of the Centers for Disease Control and Prevention (CDC). This measure was one of several that were thoroughly examined in the article “Changing Metrics of Organ Procurement Organization Performance in Order to Increase Organ Donation Rates in the United States” in the July 2017 *American Journal of Transplantation* (1), and was found to be a significant improvement over the current eligible death metric and can be easily implemented without requirements for the collection of new data.

### Living organ donation

The administration also intends to issue a proposed rule to

amend the Organ Procurement and Transplantation Network final rule to “further remove financial barriers to living organ donation by expanding allowable costs that can be reimbursed.”

This proposed change has long been supported by ASN, which backed a Rep. Jaime Herrera Beutler (R-WA-3)–led letter requesting that the Health Resources and Services Administration (HRSA) change its policy to allow the National Living Donor Assistance Center (NLDAC) to reimburse lost wages and other non-travel expenses of living donors as currently permitted under the National Organ Transplant Act of 1984 (NOTA).

Furthermore, the NLDAC received \$10 million in funding from the House Appropriations Committee (a \$6.5 million increase over prior levels). The NLDAC was encouraged through report language to use the funds to reimburse lost wages and other non-travel expenses.

Once finalized, the increased funding coupled with the upcoming proposed rule will allow HRSA to reimburse living organ donors for lost wages and other non-travel expenses.

### Extending immunosuppressant coverage past three years

Currently, all individuals living with kidney failure are Medicare eligible. Patients fortunate enough to receive a kidney transplant retain their Medicare coverage for 36 months post-transplant, unless the patient is otherwise eligible for Medicare in which their coverage would continue.

When a patient loses their Medicare coverage after 36 months and does not have another form of healthcare coverage, they may lose their immunosuppressive drug coverage and the medications may prove too costly for the patient to continue using them. The patient in turn could lose their transplant if they discontinue the use of immunosuppressants and revert to developing kidney failure. By redeveloping kidney failure, the patient regains their eligibility for Medicare and the process begins again.

There has been a groundswell of support for extending coverage of immunosuppressive drugs under Medicare. HHS is now recognizing the costs to Medicare associated with patients losing their transplant and requiring dialysis and/or another subsequent kidney transplantation. The Office of the Assistant Secretary for Planning and Evaluation released a report on May 10 that estimates that extending Medicare coverage of immunosuppressants beyond 36 months would result in 10-year accumulated savings of approximately \$73 million. In addition, the Centers for Medicare & Medicaid Services Office of the Actuary released a memo on May 22 that further showed how the Medicare program would see net savings if coverage for immunosuppressive drugs was extended beyond three years.

Previous Congresses have tried to pass legislation that would extend coverage of immunosuppressants under Medi-

care but were unsuccessful due to some members’ concern about the estimated cost increase to the program. These new reports from the administration provide renewed hope to the kidney community that passing such legislation at an expedited pace is possible. ASN will continue to advocate for this policy by leading and tracking any legislative movement in Congress on the issue.

### KHAD advocacy secures congressional support for KidneyX

The American Society of Nephrology (ASN) and the American Association of Kidney Patients (AAKP) partnered together for the 7th Annual Kidney Health Advocacy Day on March 20. Advocates from both organizations met with representatives, senators, and their respective staffs to urge Congress to support KidneyX.

Due to their advocacy and the efforts from other ASN and AAKP members, a bipartisan group of nearly 60 members of Congress wrote to the House Appropriations Labor, Health and Human Services, and Education Subcommittee asking them to include \$25 million in funding for KidneyX in Fiscal Year (FY) 2020.

Leading the letter were Congressional Kidney Caucus Co-Chair Reps. Suzan DelBene (D-WA-01) and Larry Bucshon (R-IN-08), as well as two champions of patient-centered innovation, Reps. Terri Sewell (D-AL-07) and Brian Babin (R-TX-36). A similar letter supporting the \$25 million request was spearheaded by Sen. Todd Young (R-IN) to the Senate Labor, Health and Human Services (LHHS) and Education Appropriations Subcommittee.

Sen. Young, Rep. DelBene, Rep. Bucshon, and Rep. Babin participated in the KidneyX Summit on April 29–30, 2019, which highlighted promising future innovation in kidney care. Winners of KidneyX’s inaugural prize competition, Redesign Dialysis Phase I, provided feature presentations on their winning submissions. Their winning solutions can be viewed on KidneyX.org.

The congressional champions of KidneyX announced at the summit that the House LHHS Subcommittee included \$10 million in new funding for KidneyX, which will allow KidneyX to run more and larger prize competitions to accelerate innovation in the prevention, diagnosis, and treatment of kidney diseases.

While the House took a historic step in the fight against kidney diseases, ASN will continue to advocate for KidneyX as the Senate advances its own LHHS bill this summer. ■

1. Goldberg D, et al. Changing metrics of organ procurement organization performance in order to increase organ donation rates in the United States. *Am J Transplant* 2017; 17:3183–3192.
2. [https://www.asn-online.org/policy/webdocs/OPO\\_Metrics\\_Letter\\_to\\_CMS\\_Final.pdf](https://www.asn-online.org/policy/webdocs/OPO_Metrics_Letter_to_CMS_Final.pdf)

## Fellows Corner

# Global Health, Nephrology, and International Rotations

By Aditya S. Pawar and Sarvie Esmaeilzadeh



**Aditya S. Pawar**

The past two decades have seen a surge in kidney disease with a significant impact on morbidity and mortality worldwide. An estimated 5 million to 10 million deaths are attributable to kidney disease annually (1–3). This has economic repercussions worldwide, with a larger estimated impact on low- and middle-income countries.

Multiple organizations have developed campaigns to increase awareness among both physicians and the public. For example, the International Society of Nephrology's (ISN) "0 by 25" program aims to prevent avoidable death from acute kidney injury by 2025 in low- and middle-income countries (4,5).

In the United States, we are privileged to have access to the most advanced techniques and resources to care for our patients' conditions. Moreover, nephrology training is well structured, and access to resources helps further patient care and research. Increasingly, a growing body of literature in nephrology is shedding light on global disparities in the effective prevention and treatment of kidney diseases (5). The density per population of nephrologists varies, with more prominent deficits noted in lower- and middle-income countries, particularly in Africa and South Asia (Figure 1) (6).

The combination of public health and nephrology is an interesting field, and with existing disparities, this combination is the need of the hour. A particular focus on training and education programs is required to help build a workforce with a capacity for sustainable growth. Exposure to international health training during nephrology training may strengthen the nephrology community worldwide by creating and recruiting a workforce.

Rotations during residency are cited as one of the most important experiences influencing career decisions (7). A career in international health can include research, clinical medicine, medical education, and population and global health. Skill sets such as point-of-care ultrasound, basic laboratory techniques (gram stain, acid-fast stain), x-ray interpretation, cultural competency, advocacy and policy, quality improvement, and patient safety are useful. Early



**Sarvie Esmaeilzadeh**

identification in either primarily clinical activity or global health and systems policy may help in deciding which skills to focus on during training.

Increased trainee participation requires effort on the part of trainees and organizations such as the American Society of Nephrology and the ISN, specifically aimed at involving trainees in field-based hands-on experience and in strategic systems planning. At present, few nephrology programs offer international rotations, and expanding such experiences to all trainees may increase participation.

International rotations have helped us immensely to

grow both professionally and as individuals. Such rotations offer unmatched experience in global health delivery, and the principles learned can be applied to providing high-value care in the United States (i.e., judicious use of resources and exposure to different pathologic conditions) (8). On the other hand, short-term rotations can easily be mistaken as "medical tourism" and therefore require preparation, an understanding of pros and cons, and a healthy awareness of how to maximize collaborative learning for the partner organization and for oneself. Understanding the complexities of global health delivery before visiting another country can make a significant difference, and adequate preparation for such a rotation is highly recommended. The Global Health Practice Certificate by Unite for Sight is a good start ([www.uniteforsight.org/global-health-university/global-health-practice-certificate/](http://www.uniteforsight.org/global-health-university/global-health-practice-certificate/)) (Table 1).

Practically, international rotations often benefit visiting trainees, especially resident trainees, more than the partner institution. It is important to build long-term relationships and collaborations focusing on the needs of the partnering organization, establishing a longitudinal presence. For example, the development of teaching curricula and longitudinal visits from trainees and staff can help build the capacity of local participants and encourage sustainability. Among such programs are the Botswana/Harvard partnership and the Yale Global Health Scholars Program.

To understand context-specific hurdles and successfully plan and implement programs can be challenging. It is crucial to involve and align goals with local priorities. Local residents have a thorough understanding of barriers to care delivery within their environmental context. Even in clinical settings, the involvement of local doctors

**Table 1. Websites for prospective global health applicants**

Program	Access	Type
Saving Young Lives	<a href="https://www.theisn.org/programs/saving-young-lives-project">https://www.theisn.org/programs/saving-young-lives-project</a>	Clinical
ISN Sister Renal Center	<a href="http://src.theisn.org/">http://src.theisn.org/</a>	Clinical
Renal Disaster Relief Task Force	<a href="https://www.theisn.org/programs/renal-disaster-relief-task-force-rdrtf">https://www.theisn.org/programs/renal-disaster-relief-task-force-rdrtf</a>	Clinical/Policy/Research
KCMC	<a href="https://www.kcmc.ac.tz/?q=collaboration">https://www.kcmc.ac.tz/?q=collaboration</a>	Clinical/Research
Heal Initiative	<a href="https://healinitiative.org/?utm_medium=referral&amp;utm_source=r360">https://healinitiative.org/?utm_medium=referral&amp;utm_source=r360</a>	Clinical/Policy
Global Health Program for Fellows and Scholars	<a href="https://www.fic.nih.gov/Programs/pages/scholars-fellows-global-health.aspx?utm_medium=referral&amp;utm_source=r360">https://www.fic.nih.gov/Programs/pages/scholars-fellows-global-health.aspx?utm_medium=referral&amp;utm_source=r360</a>	Clinical/Research/Policy
Seed Global Health	<a href="http://seedglobalhealth.org/about/?utm_medium=referral&amp;utm_source=r360#.XEjxk9i-WxaR">http://seedglobalhealth.org/about/?utm_medium=referral&amp;utm_source=r360#.XEjxk9i-WxaR</a>	Clinical/Research/Policy
WHO Internship Program	<a href="https://www.who.int/careers/internships/en/">https://www.who.int/careers/internships/en/</a>	Research/Policy
CDC	<a href="https://www.cdc.gov/fellowships/">https://www.cdc.gov/fellowships/</a>	Clinical
Partners in Health	<a href="https://www.pih.org/programs">https://www.pih.org/programs</a>	Clinical/Research

WHO, World Health Organization. KCMC, Kilimanjaro Christian Medical Center. CDC, Centers for Disease Control and Prevention.

is essential because they understand the needs and situation of the local community better, including etiologic factors and disease distribution patterns. This has an impact on sustainability and therefore on long-term population health outcomes, given the importance of physician-patient continuity. Medical treatments without adequate follow-up and support can have deleterious effects, and a visiting physician must maintain a primary focus on skills transfer to those providing care to the local population on an ongoing basis. Such an approach is important for implementing a successful international exchange program.

Noncommunicable diseases, including chronic kidney disease, are major contributors to mortality in low- and middle-income countries. The improvement of nephrology care worldwide can be a cost-effective intervention to curtail said mortality and morbidity (9). When addressing strategies for improving care in such settings, there are challenges and hurdles at every corner that may be overcome with the right preparation and approach. As trainees, we can contribute to nephrology education with a focus on improving the local workforce in resource-limited settings. Individual initiative and adequate support from

capable organizations can improve the recognition and care of patients with kidney diseases worldwide.

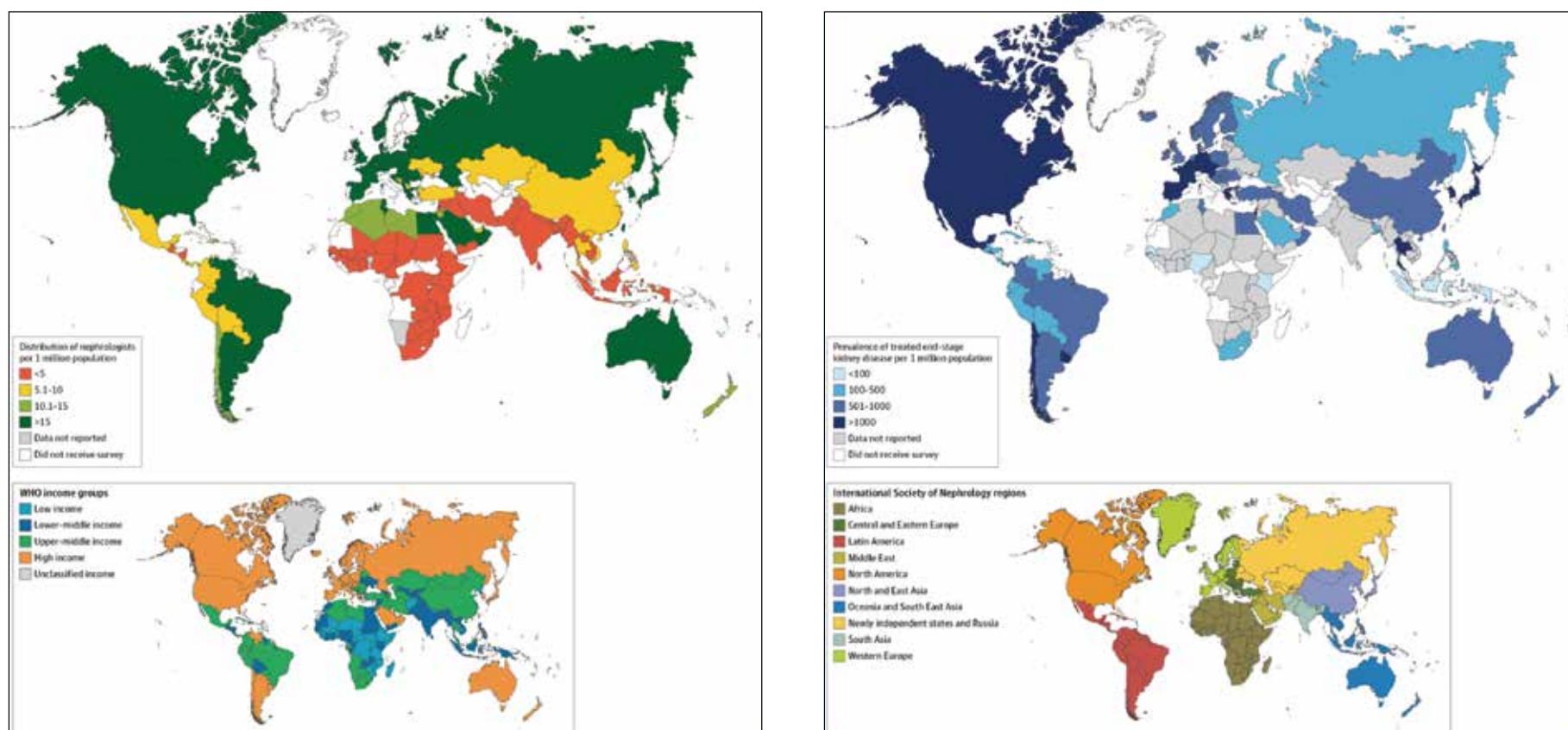
We thank Drs. Fredric O. Finkelstein, Yale University, New Haven, CT, and Robert Rope, Oregon Health Science University, Portland, OR, for guidance in writing this article. Aditya S. Pawar would like to thank and acknowledge support from Mayo International Health Program and ISN in making his travel possible. ■

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**Figure 1. Global distribution of nephrologists, treated ESRD**



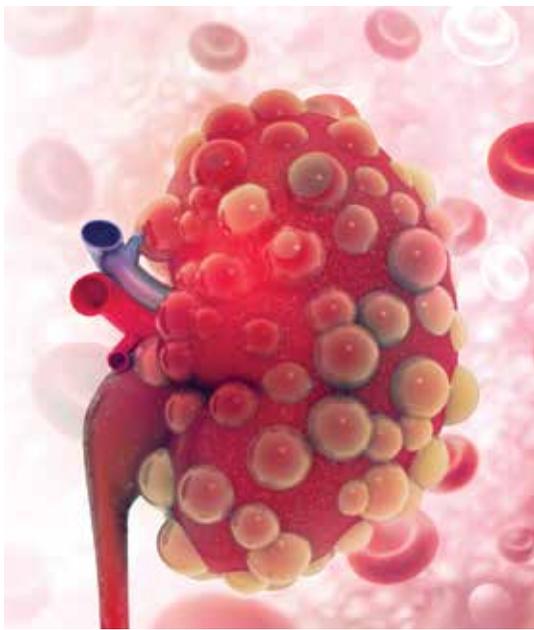
**A. Global Distribution of Nephrologists Per 1 Million.**

**B. Global Prevalence of Treated ESRD Per 1 Million Population.**

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

Send your idea to the Kidney News Fellows Corner column at [kidneynews@asn-online.org](mailto:kidneynews@asn-online.org)



## ADPKD Drug News

Although its drug for use in patients with autosomal dominant polycystic kidney disease (ADPKD) is still pending FDA approval, Reata (Irving, TX) recently won orphan drug designation for the candidate drug, bardoxolone methyl, according to Zacks Equity Research.

In early June, the company started its phase 3 clinical trial, called the FALCON study, for patients with ADPKD, which is caused by mutations in the PKD1 and PKD2 genes, and often leads to end stage kidney disease.

This is the second orphan drug designation for treating patients with rare forms of kidney disease with bardoxolone. It is the third designation for using bardoxolone to treat a kidney disease characterized by cellular mitochondrial dysfunction.

According to the FDA, orphan drug status is based on factors including the pathogenesis of the disease or condition, course of the disease or condition, prognosis of the disease or condition, and resistance to treatment.

According to Zack's Equity Research, the designation also entitles Reata to certain tax credits related to clinical trial expense exemption from the FDA user fee, and eligibility for seven years of exclusive marketing rights in the United States.

Recently a set of findings relevant to ADPKD patients using a different medication was published in *Gastroenterology*. In a phase 3 trial over 120 weeks (about 2.5 years) treatment with Somatuline Depot (lanreotide [Ipsen, Paris]) was effective at reducing organ volume. The drug lowered the growth of liver and combined liver and kidney volume in patients with polycystic liver disease. According to the official website for the drug, lanreotide is “the first and only FDA-approved treatment for adults both to slow the growth of gastrointestinal and pancreatic neuroendocrine tumors (GEP NETs) that have spread or cannot be removed by surgery . . . and to treat carcinoid syndrome to reduce the need for the use of short-acting somatostatin medicine.”

The study was launched to follow patients over a longer time period because previous studies with somatostatin analogues were “underpowered and of too short duration to reach a definitive conclusion about renal and hepatic protective efficacy for the drug candidate,” according to Clinicaltrials.gov.

van Aerts RMM. Lanreotide reduces liver growth in patients with autosomal dominant polycystic liver and kidney disease. *Gastroenterol* 2019; DOI: 10.1053j.gastro.2019.04.018. ■

## Diabetes and Kidney Clinical Trials

Several clinical trials presented at the American Diabetes Association meeting in June 2019 show promise in terms of improved renal function in type 2 diabetes patients.

Ertugliflozin, a type 2 diabetes drug manufactured as Steglatro by Merck (White House Station, NJ) and in partnership with Pfizer (New York, NY) appeared to protect renal function among this patient population, according to data pooled from two randomized trials, reported EndocrinologyAdvisor.com. Participants were divided into groups taking ertugliflozin 5 mg, ertugliflozin 15 mg, glimepiride, or placebo. The drug is a sodium-glucose co-transporter 2 (SGLT2) inhibitor.

At baseline, mean estimated glomerular filtration rate (eGFR) was 88.2 mL/min/1.73 m<sup>2</sup>. After 6 weeks, patients receiving ertugliflozin 5 or 15 mg showed greater reductions in eGFR compared with patients not receiving ertugliflozin (-2.3 and -2.7 vs -0.7 mL/min/1.73 m<sup>2</sup>, respectively). However, over 104 weeks, the eGFR values increased with the ertugliflozin group compared with controls, which suggested renal function preservation.

Dulaglutide (brand name Trulicity [Eli Lilly, Indianapolis, IN]) results were also shared during the meeting. The GLP-1 receptor agonist slowed renal function decline in some type 2 diabetes patients with poor kidney function. The researchers also announced they found a biomarker that predicted which patients exhibit decline in kidney function.

In the AWARD-7 study, among patients with macroalbuminuria at enrollment, only 7.1% of those patients on a weekly injection of 1.5 mg dulaglutide had 40% or greater eGFR decline, progression to ESKD, or kidney-related death, compared with 22.2% of patients on insulin glargine.

“The benefits of dulaglutide were driven by results in this group of participants [excreting large amounts of albumin], who’s a group at very high risk for CKD

progression,” said researcher Katherine Tuttle, MD, of the University of Washington, Seattle, during a press conference about the findings.

In the CREDENCE trial, which enrolled 4401 patients with type 2 diabetes and CKD, canagliflozin (Invokana [Janssen, Beerse, Belgium]), a SGLT2 inhibitor, lowered the risk for progression to ESKD and other primary outcome factors by 30% compared with the placebo arm. The primary outcome was a composite of ESKD (dialysis, transplantation, or a sustained eGFR of less than 15 mL/min/1.73 m<sup>2</sup>), a doubling of the serum creatinine level, or death from renal or cardiovascular causes. The risk of the renal-specific composite outcome of ESKD, doubling of serum creatinine, and death from renal causes was lowered by 34% in the canagliflozin group compared with placebo. According to the American Diabetes Association, the CREDENCE trial is the first study in 18 years to show a drug can reduce cardiovascular and renal outcomes in people with type 2 diabetes and CKD, regardless of their previous history of cardiovascular disease.

Cherney D, et al. Two-year effects of ertugliflozin on renal function. Presented at: American Diabetes Association 79th Scientific Sessions, June 7–11, 2019; San Francisco, CA. Poster 1197-P. *Diabetes* 2019; 68(Supplement 1); <https://doi.org/10.2337/db19-1197-P>.

Tuttle KR, et al. Chronic Kidney Disease (CKD) outcomes with dulaglutide (DU) vs. insulin glargine (IG) in type 2 diabetes (T2D) and moderate-to-severe CKD by albuminuria status: AWARD-7. American Diabetes Association 79th Scientific Sessions. *Diabetes* 2019; 68 (Supplement 1); <https://doi.org/10.2337/db19-233-OR>

Perkovic V, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med* 2019; DOI: 10.1056/NEJMoa1811744. ■



## Dialyzer Recall

Certain lots of a Baxter International dialyzer have been voluntarily recalled. The Deerfield, IL-based company reported one “serious injury” possibly associated with the issue.

The Revaclear Dialyzer 300 and 400 model lots were being recalled due to blood leaks. One product line at the manufacturing facility was traced as the problem area and corrections were implemented, according to a two-page letter from Merle Goddard, senior director of quality at Baxter HealthCare.

For more information, contact Baxter at 888-229-0001. Baxter Healthcare Center for Service is providing a credit for returned dialyzers.

Any adverse reactions or quality problems experienced with the dialyzers may be reported to Baxter

Product Surveillance at 800-437-5176 or by emailing Baxter at [corporate\\_product\\_complaints\\_round\\_lake@baxter.com](mailto:corporate_product_complaints_round_lake@baxter.com).

Problems with the dialyzers may also be reported through the FDA MedWatch Adverse Event Reporting Program at [www.fda.gov/medwatch/report](http://www.fda.gov/medwatch/report).

As of early June, the Optiflux F160NR Capillary High Flux hemodialyzer from Fresenius was listed as being under an open recall status for lot numbers 18HU06016, 18HU06017, 18HU06018 and 18HU06019. The problem was reported to the FDA as “potential for external blood leaks from the dialyzer header.” Customers with questions may contact Medical Information and Communications at 855-616-2309 or at [www.fresenius-medinfo.com](http://www.fresenius-medinfo.com). ■

ASN has a new look and feel. Ten years ago, we were a society on the peak of incredible growth. Today, we represent more than 20,000 kidney health professionals working to help people with kidney diseases and their families. This new ASN logo allows to continue our growth and work toward a goal of a world without kidney diseases.



ASN launched its foundation in 2012, the Kidney Health Initiative (KHI) in 2012, Nephrologists Transforming Dialysis Safety (NTDS) in 2016, and KidneyX in 2018. ASN's vision is simple, singular, and meaningful. At the forefront, at every level, ASN, the ASN Foundation for Kidney Research, KHI, NTDS, and KidneyX are leading the fight against kidney diseases.

As part of this vision, these groups each refreshed their individual brands to create a unified look and feel. This transformation resulted in a new focus for the ASN Foundation, which is now called KidneyCure. We will operate in unison as the ASN Alliance for Kidney Health, working toward — and most of all, looking forward to — a world without kidney diseases.



A world without kidney diseases





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## Second Annual

# IDEAS CONFERENCE

## Brings Together Innovators of Dialysis Technologies to Drive Innovations for Kidney Patients

The University of Washington Center for Dialysis Innovation (CDI), a collaboration between the Northwest Kidney Centers and UW Medicine, is hosting the 2nd Annual IDEAS Conference: Innovations in Dialysis—Expediting Advances Symposium. The meeting will take place August 18–20, 2019, in Seattle, WA, on the University of Washington campus.

Nearly 500,000 Americans have kidney failure treated with dialysis and 50,000 die each year from kidney disease. There has been little significant innovation advancing dialysis technology since chronic hemodialysis was launched 59 years ago in Seattle.

IDEAS brings together innovators of wearable, portable, and implantable dialysis technologies, including researchers, entrepreneurs, physicians, patients, industry representatives, and government officials committed to improving outcomes and reducing costs for people with end stage kidney disease to discuss one goal: transform dialysis.

Keynote talks and panel discussions will cover the landscape of dialysis today, how governments and foundations look at dialysis, vascular access challenges and advances, bio- and cell-based approaches, portable dialysis, and membranes and toxin separation.

IDEAS 2019 plenary speakers include:

- **Robert Califf**, MD, MACC, the Vice Chancellor for Health Data Science, Director of Duke Forge, the Center for Actionable Health Data Science at Duke Health, Donald F. Fortin, MD, Professor of Cardiology in the Duke University School of Medicine, Chair of the Board of the

People Centered Research Foundation, and an advisor for Verily Life Sciences, a member of the Alphabet family of companies formed by Google. Califf served in the administration of President Barack Obama as Deputy Commissioner for Medical Products and Tobacco in the U.S. Food and Drug Administration from 2015 to 2016, and as Commissioner of Food and Drugs from 2016 to 2017.

- **Dean Kamen**, serial entrepreneur and inventor, who invented the first wearable infusion pump, founded AutoSyringe to manufacture and market the pumps, and later founded DEKA Research & Development Corporation, which developed the HomeChoice™ peritoneal dialysis system along with many other innovative medical devices. He also founded *FIRST*® (For Inspiration and Recognition of Science and Technology), an organization dedicated to moving the next generation to understand, use, and enjoy science and technology. He also has many other notable inventions including the iBOT™ mobility device and the Segway® Human Transporter.
- **John Rogers**, PhD, Louis Simpson and Kimberly Querrey Professor of Materials Science and Engineering, Biomedical Engineering, Mechanical Engineering, Electrical Engineering and Computer Science, Chemistry and Neurological Surgery, and Founding Director of the Center on Bio-Integrated Electronics at Northwestern

MD, CVS Health; **Karin Hehenberger**, MD, PhD, Lyfebulb; **Kazuhiko Ishihara**, PhD, University of Tokyo; **Michael Sefton**, PhD, University of Toronto; **Sandeep Patel**, PhD, U.S. Department of Health and Human Services and the KidneyX Innovation Accelerator; **John Sedor**, MD, FASN, Cleveland Clinic, Lerner College of Medicine, Case Western Reserve University, and the KidneyX Innovation Accelerator; **Buddy Ratner**, PhD, University of Washington; and **Jonathan Himmelfarb**, MD, University of Washington.

In addition to these speakers, the agenda will include 2 interactive panel sessions with dialysis patients and caregivers to explore their perspectives on what is needed to improve the paradigm of care, lightning talks from dialysis innovators, and a poster session showcasing new dialysis technologies in development. Attendees are also invited to the Night at the Museum Tour and Reception on August 18, sponsored by the Northwest Kidney Centers, which will showcase iconic photos, artifacts, and dialysis machines and equipment used throughout the U.S. over the past 50 years.

We invite you to help make life better for people on dialysis—join us at IDEAS 2019 on August 18–20, 2019, in Seattle, WA.

Registration information may be found at [cdi.washington.edu/ideas](http://cdi.washington.edu/ideas). AAKP members receive a 50% discount on registration with the code **IDEAS19\_AAKP**. The first 20 dialysis patients to register are eligible for free registration with the code **IDEAS19\_patient**. Register today! ■



University. His research focuses on fundamental and applied aspects of nano and molecular scale fabrication as well as materials and patterning techniques for unusual electronic and photonic devices, with an emphasis on bio-integrated and bio-inspired systems.

IDEAS 2019 will also showcase a diverse lineup of speakers from many sectors of the dialysis and kidney communities, including **Bruce Culleton**,



Northwest Kidney Centers | UW Medicine



# SEXUAL HEALTH

## An Important Concern for Kidney Disease Patients

By Bridget M. Kuehn

**S**exual dysfunction and fertility are major concerns for patients with kidney disease that are important for clinicians to discuss, according to Silvi Shah, MD, FASN, assistant professor of nephrology at the University of Cincinnati.

More than half of both male and female patients with kidney disease experience some form of sexual dysfunction, which can be linked to their disease or its treatment, noted Shah. Many also face concerns about fertility, and women may require counseling about pregnancy or contraception. Yet, many nephrologists feel ill-prepared to discuss women's health and often neglect these conversations, according to the results of a survey presented recently by Monica Reynolds, MD, a clinical instructor in the division of nephrology at the University of North Carolina Chapel Hill. *Kidney News* interviewed both Shah and Reynolds, who also spoke at Kidney Week 2018.

### Low libido and infertility

Reductions in progesterone, estrogen, and testosterone may cause women with kidney disease to stop ovulating, Shah said. This contributes to declining fertility as kidney disease progresses. Shah noted that women with kidney disease also frequently experience sexual dysfunction. They may experience a low libido or conditions like vaginal dryness or vaginitis that may lead to sexual aversion.

"About 40% of women on dialysis do not engage in sexual intercourse," she said.

Three-quarters experience menstrual disorders, including missing or irregular periods, heavy bleeding, or premature menopause, Shah said. In fact, studies have found that 50% to 100% of women with stage 5 chronic kidney disease (CKD) do not have menstrual cycles, she said.

"All these changes also lead to infertility," she said.

Shah recommended that clinicians evaluate why women are experiencing these symptoms, starting with a review of medications that may contribute. Their hormone levels should also be considered. For example, if a woman experiences low libido and has low estrogen levels, a trial of estrogen may be considered, she said.

Men with kidney disease also frequently experience sexual dysfunction, with 50% to 80% reporting erectile dysfunction, Shah said. This may be caused by vascular changes owing to arterial or venous diseases, neurologic problems related to uremia, or medications. These men may also experience low libido, which can be exacerbated by low testosterone, and infertility, she said.

A medication review is also recommended for men with erectile dysfunction, Shah said. She noted that two drugs have been shown to improve erectile dysfunction in men with CKD: phosphodiesterase type 5 inhibitors and oral zinc supplements for those with zinc deficiency. Both work by boosting testosterone levels, she said.

### Pregnancy counseling concerns

Counseling women with kidney disease about pregnancy and contraception is also critical, Shah noted.

"Nephrologists are uniquely positioned to provide disease-specific [pregnancy] counseling," Reynolds said. Yet, many nephrologists feel unprepared to offer such counseling. Reynolds and her colleagues found in a recent survey. The survey of 154 nephrologists in the United States and

Canada by investigators from the women's health working group of the Cure Glomerulonephritis (CureGR) study found that fewer than 10% of nephrologists are confident about managing menstrual disorders or diagnosing or managing menopause. Fewer than half reported being comfortable talking about contraception, pregnancy outcomes by disease stage, and fertility treatment referrals. Most nephrologists reported counseling fewer than one woman per month about contraception (64%) and before conception (68%), according to the survey.

"The most common reasons cited for not providing counseling were lack of training, and little knowledge or confidence in the subject area," Reynolds said. Education seminars or case-based materials would boost their knowledge, 67% of responding nephrologists said. Routinely discussing these topics can also help physicians become more comfortable, Reynolds said.

"While we may not be as comfortable discussing these topics, it's important that our patients understand the possible connections to their kidney disease as well as what is normal/abnormal," she said.

Such counseling can be essential to optimizing patients' and their children's outcomes. For example, Shah noted that women who have had a kidney transplant may regain fertility within 6 months after transplantation.

"Pregnancy can happen in all CKD stages, and kidney transplant restores fertility," Shah said. "Birth control is therefore very important to prevent unplanned pregnancies, as they can be [taking medications that may cause birth defects in the fetus]."

Women with CKD may struggle with decisions about pregnancy. They must weigh the perceived and real risks to their own health and the health of their baby, Shah explained. These pregnancies are high risk and are associated with preterm birth, fetal growth restriction, and high perinatal mortality, she said. Women with CKD who become pregnant may experience rapid progression of their disease, which may cause them to require dialysis or a transplant, she said. They also have higher rates of preeclampsia and severe infections. Reynolds noted that many women with kidney disease feel traumatized by being advised against becoming pregnant.

"What I want you to remember here is that having a child is integral in a woman's life, and this does not change for women with CKD," Shah said. "Pregnancy is further very challenging for these women because they face emotional decisions."

But physicians can counsel them on ways to optimize their pregnancy outcomes, for example by planning pregnancies during earlier stages of disease when the risks are lower, Shah said. For women who are in the later stages of disease, a transplant may be advised, she said.

The most important thing, Shah emphasized, is for nephrologists to be supportive about women's reproductive choices and to help them by providing family planning options to those who would like to avoid pregnancy and working to optimize outcomes for those who wish to conceive.

"Remember, the choice is theirs to make," Shah said. "Whatever decision they make, we should be supportive." ■

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Confidence in women's health: An international survey of nephrologists (abstract FR-OR078).

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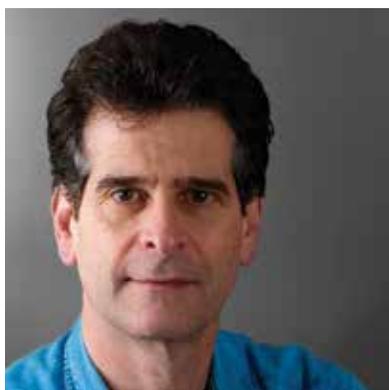
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Reata .....Pages 8-9  
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