Nephrology Rapidly Transitioning to Race-Free Kidney Function Estimates Despite Hurdles

By Bridget M. Kuehn

Approximately 70% of laboratories using the Epic electronic health records system had implemented a recommendation to use race-free kidney function estimates as of late 2022, according to Paul Palevsky, MD, past president of the National Kidney Foundation (NKF) and professor at the University of Pittsburgh, PA.

The recommendation to use the race-free estimates was issued by the joint NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases in September 2021.

“That is a remarkable uptake in a year,” said Palevsky during a 2022 Kidney Week session titled “Implementing the Race-Free eGFR Equations in Clinical Practice: Where Are We Now?” He noted that two of the largest commercial laboratories, Labcorp and Quest Diagnostics, made the switch, as did the Veterans Affairs Health System.

The session highlighted rapid progress toward implementation of the NKF-ASN task force’s recommendations despite ongoing challenges (1). Task force Co-Chairs Neil Powe, MD, MPH, and Cynthia Delgado, MD, both professors at the University of California, San Francisco, moderated the session. As part of its 2021 report, the task force recommended immediate implementation of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation refit without a race adjustment, greater use of cystatin C to measure glomerular filtration rates (GFRs), and more research on GFR and health disparities.

“The underlying reason for the task force recommendation was the recognition that the use of race in clinical algorithms is problematic and inappropriate—race is a social and not a biological construct,” Palevsky explained. “When assessing race in clinical algorithms, we risk accepting health inequities as immutable facts rather than injustices driven by social factors.”

Value-Based Payment Models Aim to Boost Patient-Centered Care

By Bridget M. Kuehn

It takes a multidisciplinary team, including a nurse coordinator, psychologist, and pharmacist, to successfully run the Kidney Care First (KCF) program at The University of Alabama at Birmingham (UAB). The program’s lead nephrologist, Gaurav Jain, MD, a professor and associate division director of nephrology at UAB, described his experience during a Kidney Week 2022 session entitled, “Value-Based Payment Models Generating New Approaches to Kidney Disease Care.” Jain and his colleagues chose to join the Centers for Medicare & Medicaid Services’ (CMS) KCF value-based payment model (1) because they hoped it could decrease the cost of care and help boost patient transplant rates. Although assessing such outcomes will take more time, Jain said the program has already been rewarding and allowed him to access additional patient care resources. “It’s a small program, but it gives me a lot of joy,” he said. “It’ll definitely make patients’ lives better.”

The KCF program and the Comprehensive Kidney Care Contracting (CKCC) options are part of the latest evolution of value-based payment models for kidney care, along with the mandatory ESRD Treatment Choices (ETC) model. CMS designed the programs to incentivize nephrology practices to improve care for patients with late-stage chronic kidney disease (CKD) or kidney failure, also known as end stage kidney disease (ESKD). Panelists

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Most drugs approved over the past 40 to 50 years have dosing recommendations based on creatinine clearance, explained Thomas Nolin, PharmD, PhD, associate dean for research and associate professor of pharmacy and therapeutics in the Department of Medicine at the University of Pittsburgh.

“What do we do with the hundreds of drugs we use every day that have drug-dosing recommendations based on creatinine clearance?” he asked. Nolin said he is working on an NKF Pharmacy Engagement Work Group with Wendy St. Peter, PharmD, professor with the College of Pharmacy at the University of Minnesota in Minneapolis, to find ways to improve the dosing information available for clinicians.

Guidance from the US Food & Drug Administration for drug manufacturers on drug pharmacokinetics in patients with kidney impairment in 2020 called for dosing interface. Friedewald explained that a redefined GFR (eGFR) calculators (2), which could have a major impact on dosing recommendations going forward, Nolin said. Already, some pharmaceutical companies have incorporated eGFR recommendations on dosing labels for newer drugs, including canagliflozin, he noted.

Eliminating race from kidney function estimates also has implications for kidney transplants, said John Friedewald, MD, professor of medicine and surgery in the Divisions of Nephrology and Hypertension and Organ Transplantation, respectively, at Northwestern University. Chicago, IL. He explained that race-based equations could overestimate kidney function for Black adults leading to delayed referral for transplant.

“Exposure to dialysis is our patient’s greatest risk,” Friedewald said. “Continuing to use race as a modifier with the College of Medicine and other transplant centers means much more work, time, and resources.” Of concern, obtaining an accurate GFR is very important, he continued. He cited evidence that the new recommendations would help reduce racial disparities in wait list time (3).

“Timing is really important because you want to get patients [who] accumulated waiting time if they are preemptive (transplant candidates) so you can have time to find and evaluate appropriate living donors,” he said.

Living donor evaluations also rely on an accurate GFR, Friedewald said. He noted that ideally, living donors have a GFR greater than 90 mL/minute/body surface adjusted. However, transplant centers may consider people with GFRs between 60 and 90 mL/minute depending on several factors. Interindividual variability in the donor’s kidney function and recommendations for living donors with a better kidney, “GFR isn’t only the thing that goes into evaluating a donor for approval,” he said. “But GFR is one of the more important factors, and it is often a contraindication if someone does not have [an] adequate GFR. So, getting the right GFR is important.”

Friedewald explained that a substantial number of potential donors could be misclassified based on eGFRs. One concern is that donors could be turned away during initial screening based on an inaccurate eGFR and never make it to the next step, he said. With the new equations, he noted, there may be more errors at the higher end of the GFR spectrum than at the lower end. Most transplant programs use a measured GFR to evaluate patients later in their candidacy. However, he expressed concerns that inaccurate estimates during early screening could dissuade candidates from completing a donor evaluation.

“The answer here is to cast a wide net and not rely on an estimation equation alone to evaluate a living donor,” he said. “For living-donor candidates, I stress [that] a measured GFR is preferred for accuracy and proper stratification.”

Laboratory hurdles

The NKF’s CKDintercept program (4) helped lay the ground for the rapid uptake of race-free kidney estimates, Palevsky said. Through the program, the NKF was already working with large commercial laboratories, pathology societies, and academic institutions to improve kidney disease diagnoses before the task force’s recommendations. However, he noted that hurdles to implementing the cystatin C recommendations remain.

Palevsky explained that the number of laboratories able to run cystatin C tests remains low, at approximately 200 across the country. However, an analysis of data from Labcorp suggests that the number of cystatin C tests increased between 2012 and 2019 (5), but cystatin C tests are still orders of magnitude less common than creatinine tests, he noted. For example, in 2018, laboratories conducted approximately 110,000 cystatin C tests compared with about 39 million creatinine tests, he said. “We don’t have clear-cut guidance on who should be tested with cystatin C,” he said.

The 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend using cystatin C to confirm testing when creatinine-based estimates may be less reliable (6), and Palevsky cited a review of the evidence and circumstances when cystatin C may be appropriate (7). Some examples included patients whose GFR is close to cutoff points or patients who are elderly, inactive, have cancer, are on chronic corticosteroids, or are living with HIV or cirrhosis for whom creatinine-based tests may overestimate kidney function. He noted that creatinine might underestimate kidney function in other patients, such as bodybuilders.

Cystatin C cost barriers

There are also barriers to broader cystatin C implementation, including a much higher cost than for creatinine, Palevsky said. For example, he noted that a cystatin C test costs $18.52 compared with $5.12 for a creatinine test based on Medicare pricing.

Amy Karger, MD, PhD, a clinical pathologist and associate professor in the Department of Laboratory Medicine and Pathology at the University of Minnesota, noted that they lack of standardized reagents and methods had stymied wider use of cystatin C. However, she cited data from the College of American Pathologists (CAP) that show standardized assays increased between 2014 and 2019 (8). She recommended that nephrologists make sure their labs are using a standardized assay. “There are still some old, outdated platforms being used in clinical laboratories that don’t use standardized reagents,” she said. “It’s an important question to ask as a nephrologist if you are looking at bringing in that assay.”

Traditionally, Karger noted, cystatin C was run primarily at reference labs or academic centers because it required specialized laboratory equipment. The 2019 CAP survey data show that only 7% of laboratories offered the test in-house, and 93% sent it to reference laboratories. More laboratory instrument manufacturers have made cystatin C tests available on equipment found in most clinical laboratories. However, it is still often considered a specialty test rather than a routine one because of low demand for the test, she explained. That may change as health systems push for greater access. She noted that the Veterans Affairs Health System standardizes at least one lab in each region network to offer cystatin C testing by September 1, 2022.

Karger explained that low use of cystatin C tests in a health system could create financial disincentives for bringing the testing in-house. She said there are one-time and continuous costs for adding and maintaining a new assay. Spreading these costs over a few tests drives up individual test costs. She explained that differences in costs among health care systems implementing different test volumes, she said. “They are not going to get those results in the same time frame,” she said.

Karger noted that working with manufacturers to make the tests more accessible and to lower reagent costs is a critical first step to overcoming these challenges. Greater use of the tests will help reduce the costs of reagents, she noted. She explained that updating clinical practice guidelines to include when it is appropriate to use cystatin C will help increase test volumes and justify reimbursement for the tests. “I encourage nephrologists to proactively engage their clinical laboratory directors about options for bringing testing in-house,” Karger said. “If nephrology can lead efforts to support evidence-based utilization and increase test volumes, this can make in-house testing financially sustainable for clinical laboratories.”

Palevsky agreed that nephrologists should be proactive about working with their colleagues in other specialties and laboratories regarding the use of the cystatin C test. He noted that the NKF published recommendations (9) to help laboratories implement race-free kidney function equations. However, he also cautioned that embracing the task force’s advice is the first step in what must be a larger effort for the field of nephrology.

While adopting race-free eGFR equations and increasing cystatin C use is important, these changes alone are inadequate for addressing the disparities in nephrology care,” Palevsky concluded. “We need not lose sight of the bigger picture we need to achieve.”

References


