



National Institute of
Diabetes and Digestive
and Kidney Diseases

Kidney Interagency Coordinating Committee Meeting

Reports on End-Stage Renal Disease Care Model and Pediatric Kidney Disease

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National Institutes of Health
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Meeting Participants and Summary

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Welcome and Introductions

Andrew Narva, M.D., FACP

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH)

Dr. Andrew Narva welcomed members and attendees to the NIDDK Kidney Interagency Coordinating Committee (KICC) meeting. The KICC was mandated by Congress in 1987 to meet yearly to encourage cooperation, communication, and collaboration among all federal agencies involved in kidney research and kidney diseases. Recognizing the need for better coordination of the federal response to chronic kidney disease (CKD), the KICC transformed from a *pro forma* meeting to an active forum of communications among federal professionals working in CKD who meet twice yearly. Dr. Narva announced that Ms. Eileen Newman, former Associate Director, National Kidney Disease Education Program (NKDEP), NIDDK, retired in August 2017 after nearly 10 years of service. Ms. Newman made significant contributions to improving the care efforts for people with CKD in the United States, especially regarding nutrition. Ms. Jenna Norton, Associate Director, National Kidney and Urologic Science Translation Program, NIDDK, has assumed the science-related duties, and Ms. Julia Jackson, Office of Communications and Public Liaison, NIDDK, is responsible for NKDEP communications. Today's meeting will focus on evaluation of the Centers for Medicare & Medicaid Services' (CMS) End-Stage Renal Disease (ESRD) Care Model and Quality Incentive Program, and review the landscape of pediatric kidney disease in the United States.

Part I: Centers for Medicare & Medicaid Services

Comprehensive ESRD Care Model Year 1 Results

Tom Duvall, M.B.A.

CMS

Mr. Tom Duvall provided an overview of the CMS Comprehensive ESRD Care (CEC) model, its rationale, and performance results from year 1. Generally, ESRD patients averaged 1.7 hospitalizations in 2015, had high rates of co-morbidities, and comprised less than 1 percent of the Medicare population, but accounted for 7 percent of Medicare fee-for-service (FFS) spending. The cost of caring for ESRD patients is higher than the costs for other Medicare patients. Furthermore, the ESRD patient population often is challenged with non-medical issues (e.g., transportation, housing, or nutrition) and fragmented care from many different health care providers (providers). The goal of the CEC model is to reorient providers toward a care model that improves care for the ESRD population and reduces costs to beneficiaries and the Medicare program. The challenge is that the average Medicare cost (e.g., Medicare Parts A and B spending) for an ESRD patient is \$88,000 per year, of which one-third covers dialysis services under the Prospective Payment System (PPS) Bundle and two-thirds covers non-dialysis services, such as acute care, hospitalizations, and physician services.

Mr. Duvall remarked that extension of the ESRD care quality efforts and CMS coordinated care efforts were two key frameworks used to conceptualize the CEC model. The ESRD care quality efforts include the Quality Incentive Program (QIP), the Dialysis Facility Compare (DFC), and DFC Star Ratings programs. The coordinated care efforts are primarily accountable care organizations (ACOs), such as the Pioneer ACO Model, Next Generation ACO Model, and the Medicare Shared Savings Program. Building on experience from these models and programs, CMS established the ESRD Seamless Care Organizations (ESCOs), in which dialysis centers, nephrologists, and other providers and suppliers coordinate all care covered under Medicare Parts A and B. The aim is to improve the quality for attributing Medicare FFS ESRD beneficiaries. The CEC is a 5-year payment model being tested via the Center for Medicare & Medicaid Innovation (CMMI) that runs from October 1, 2015, to December 31, 2020. Currently in

performance year 3, the model expanded from 13 ESCOs in 2015 to 37 by 2018. Of the 37 ESCOs, 33 are established within large dialysis organizations (LDOs)—24 with Fresenius, six with Dialysis Clinic, Inc., and three with DaVita; four are within non-LDOs—Rogovin, Centers for Dialysis Services, Atlantic Dialysis, and Northwest Kidney Centers. The 37 ESCOs span the country and provide services to 46,000 Medicare ESRD beneficiaries.

The CMS considered several key principles in designing the CEC model. First, beneficiary care is managed by the nephrologist and the dialysis facility. Second, beneficiary freedom of choice to see any Medicare provider is respected. Third, ESCOs are held accountable for all Medicare Parts A and B services, including those outside of the dialysis facility. Fourth, greater accountability means new tools to manage care. One significant principle of the CEC model is that a nephrologist serves as the primary physician managing care. In fact, each ESCO is required to include nephrologists who, in turn, must agree to individual downside risk. To date, approximately 1,100 nephrologists are participating in the CEC model, representing 15 percent of nephrologists nationwide. The CEC Model two-sided risk tracks qualify as a Quality Payment Program Advanced Alternative Payment Model. Beneficiaries are aligned to an ESCO using a first-touch methodology, in which patients have their first dialysis visit with an ESCO-affiliated dialysis provider. Beneficiaries remain aligned to the ESCO for the life of the CEC model, except for enrollment in Medicare Advantage, a kidney transplant, relocation out of the service area, change in dialysis provider, or death.

The ESCO financial performance is measured according to aligned beneficiaries' expenditures relative to an annual benchmark. The baseline is the average annual Medicare Parts A and B expenditures for beneficiaries who would have been aligned to the ESCO in 2012, 2013, or 2014. The total expenditures are trended forward annually, risk is adjusted, and savings or loss values are calculated. The financial models for LDOs and non-LDOs differ. The ESCOs are evaluated by 18 quality measures that focus on patient experience and safety, care coordination, clinical quality, and population health. Of the 18 quality measures, nine are measures that the ESCO reports, six are In-Center Hemodialysis Consumer Assessment of Healthcare Providers and Systems (ICH-CAHPS) measures, two are kidney transplant waiting list measures, and one is the Standardized Mortality Ratio (SMR) measure. The financial results are adjusted by quality performance, and ESCOs are required to meet minimum quality thresholds to achieve shared savings. The goals are to ensure that cost savings are not at the expense of the quality of care and to incentivize care coordination outside of the dialysis facility.

In performance year 1 of the CEC model, CMMI's actuarial results showed that 13 ESCOs generated \$75 million in savings relative to their benchmarks, achieving an overall 5.3 percent reduction in spending, and 12 of the 13 earned CMS shared savings payments. All ESCOs received full credit for reporting on quality measures but will be held financially responsible for performance on those measures in performance year 2. An independent evaluation using the difference-in-difference methodology was conducted by The Lewin Group, Inc. The evaluation confirmed the CMMI actuarial data and revealed statistically significant improvement in total Medicare spending, utilization, and quality of life. Areas to follow up for future evaluations include comparisons between ESRD beneficiaries in the CEC Model to those in primary care-based ACOs, results from newly added ESCOs, and new dialysis facilities added to existing ESCOs. Separate discussion of results from non-LDOs, results from ICH-CAHPS, and measures that did not reach statistical significance also are areas to be included in future evaluations.

Mr. Duvall pointed out that the CEC Model, which will complete its test run in 2020, has more than doubled in size since 2015, a trend that is expected to continue. As CMS builds on the lessons learned from this model for informing future ESRD and CKD care, input from the KICC on the optimal model

design and next steps are welcomed. Further details on the model and evaluation report can be accessed on the CMS website at <https://innovation.cms.gov/initiatives/comprehensive-esrd-care>.

Discussion

- Dr. Narva asked about the potential that dialysis providers might find a way to “game” the CEC model, improving income without meaningfully enhancing quality of care. Mr. Duvall explained that many components of the CEC model are held to stricter standards than similar models and should help to alleviate much of the stakeholder skepticism that comes with working on a care coordination model. CMS has built in several checks and balances that have helped to ensure that improving, not denying, care remains the ultimate goal. For example, the one-touch principle is unprecedented with providers, but serves to ensure that all patients, despite the complexity, are afforded services. Expenditures are based on claims data and therefore tracked objectively by CMS, and the independent model evaluation confirmed CMS’ results. Rigorous monitoring protocols, complaint reporting procedures, and legal waivers are in place, as is a requirement that 50 percent of executive Boards not be affiliated with a dialysis company and include a beneficiary representative or independent consumer advocate. Dr. Narva also asked whether efforts are in place to engage the CKD care specialists prior to an ESRD diagnosis, which could result in significant cost savings. Mr. Duvall replied that the CEC model currently covers costs associated with Medicare beneficiaries’ outpatient dialysis at a facility and noted that CMS is interested in addressing CKD care in this context. Incorporating CKD into the Medicare structure would be challenging. Benefits are available, but the legal waivers in the CEC model provide coverage only to patients aligned to an ESCO. Providers are interested in providing care upstream to ESRD, and discussions are ongoing.
- Dr. Kevin Abbott wondered whether vascular access routes or types of medications being used affected the reduction in utilizations, including hospitalizations and catheter use. Mr. Duvall explained that the decrease in hospitalizations was attributed to reducing complications and barriers to initiation and maintenance of dialysis, addressing vascular access issues broadly, and increasing focus on social services (e.g., transportation). In response to a question from Dr. James Oliver, Mr. Duvall commented that the impact on readmissions was minimal, with no statistically significant changes in readmissions. The model’s objective and financial incentives primarily focus on reducing hospitalizations.
- Dr. Robert Star called attention to the NIDDK-sponsored Hemodialysis Fistula Maturation Project, which showed that the process of care (i.e., infrastructure) far outweighed the biological implications. In fact, the project found large variations of care delivery in various health care settings that affected the access to care results. Dr. Star asked whether the CEC model could address these issues. Mr. Duvall pointed out that the process of care is embedded in the overall theme of the model, including payment incentives for providers. The total costs of care incentives are the drivers for the model.
- Dr. Susan Crowley asked about the percentage of incident versus prevalent dialysis patients in the ESCOs. Mr. Duvall explained that the CEC model covers the costs after a patient is connected to a dialysis facility and may not be the best at capturing incident dialysis events. The focus is on improving the decline of long-term dialysis patients. Dr. Crowley also asked about measures to evaluate the use of non-ESCO providers and whether there had been evidence of cost shifting to alternate providers. Mr. Duvall explained that the ESCOs are responsible for Medicare Parts A and B costs, even from non-ESCO providers. He pointed out that the vast majority of the providers were dialysis facilities and nephrologists who may have relationships with hospitals and

other physicians, but those providers are not officially within the ESCO system, which alleviates Medicare cost shifting.

- In response to a query from Dr. Oliver on tracking patient referrals for a kidney transplant and wait lists, Mr. Duvall responded that referral and wait list statuses now are being tracked although there were no statistically significant results early on. Efforts are being expanded to capture these data and the wait list is now a quality measure. Time to a transplant and rates also are being tracked.
- Dr. Afshin Parsa asked about the feedback from the ESCO nephrologists who are providing care within the CEC Model. Mr. Duvall replied that CMS communicates regularly with dialysis facility representatives and engages in outreach to nephrology societies. In general, responses have been positive, especially regarding the financial structure and the flexibility the model provides.
- Dr. Narva asked Dr. Crowley whether the quality improvements and progress for ESRD care within the U.S. Department of Veterans Affairs could be attributed to the early access to care or to the process of care. Dr. Crowley responded that upstream care affects downstream outcomes. She expressed concern about a model in which nephrologists are expected to bear the financial burden of care or services and suggested that it would be a conflict of interest.
- Dr. Melanie Blank wondered about the mortality rates, and Mr. Duvall explained that they trended slightly negative but were not statistically significant.
- Recognizing that the CEC model focuses on controlling the cost, which may not resolve the problems nephrologists encounter regarding care, Dr. Star asked what can be done to address this problem. Mr. Duvall explained that this model, although limited, is broadly testing coordinated kidney care, which had not previously been done to this level. Although transplants, CKD and home dialysis are not included, this model has prompted a change in basic assumptions in the orientation of care in kidney diseases. The next step will be to focus on ways to incorporate the full set of incentives for developing an optimal care coordination model.

Evaluation of the ESRD Quality Incentive Program (QIP) and Outcomes in the Dialysis Population

Jesse Roach, M.D.

CMS

Dr. Jesse Roach discussed the CMS quality measures for kidney disease. The ESRD QIP, which was implemented in payment year 2012 as the first value-based purchasing program (i.e., pay-for-performance) in CMS, reduces payments by up to 2 percent to ESRD facilities not meeting or exceeding the minimum total performance score (TPS) set by CMS. The objectives were to (1) transition from a FFS reimbursement to a value-based system that seeks to improve health care quality, (2) link a payment penalty program to a facility's performance, not a nephrologist's, (3) redesign health care and health care services payment structure, and (4) reward better value, outcomes, and innovation. The legislative authority governing the ESRD QIP includes *Section 1881(h)* of the Social Security Act, which was added by *Section 153(c)* of the Medicare Improvements for Patients and Providers Act of 2008, and the Protecting Access to Medicare Act (PAMA) of 2014, which includes the hypercalcemia clinical measure.

The ESRD PPS rulemaking for program updates and refinements is conducted annually. The pre-rulemaking process consists of presenting, 1 year before a final rule, quality measure recommendations to the National Quality Forum Measure Application Partnership Panel and publishing notice of the proposed

rulemaking in the *Federal Register*. After a public comment period, a final rule with responses to the public comments is published by November 1 in the *Federal Register*. In a multiyear process, a facility's performance is collected in one year, measures are scored the next year, and facilities receive their TPS and payment reductions, if any, the following year. The payment year 2019 ESRD QIP Measure Set will include 12 clinical measures and 5 reporting measures encompassing infection, ICH-CAHPS, standardized readmission and transfusion ratios, hypercalcemia, vascular access type, anemia management, dialysis adequacy, and quality of life assessments (e.g., pain and depression).

Dr. Roach detailed the performance of ESRD QIP measures in the dialysis population. To evaluate performance outcomes and trends for dialysis adequacy, vascular access, and hospitalizations, an interrupted time series (ITS) analysis was performed. Monthly claims data from Medicare claims and Consolidated Renal Operations in a Web-Enabled Network (CROWNWeb) were aggregated to quarterly measures to smooth data and analyze differences across the large chain, other chain, or independent subgroups. ITS analysis revealed that 76 percent of patients were treated at large chains (e.g., DaVita and Fresenius), 17 percent at other chains, and 7 percent at independent chains. From 2010 to 2016, the dialysis adequacy rate (Kt/V greater than 1.2) for adult hemodialysis patients increased in all subgroups. Similarly, the dialysis adequacy rates (Kt/V greater than 1.7) for adult peritoneal patients also increased. The large chain facilities outperformed the smaller chains. An increase in arteriovenous fistula (AV) vascular access utilization and a decline in catheter use was observed across chains. The all-cause hospitalization rates were higher in independent chains than in the other subgroups. In summary, the ITS findings showed large chains performed better on many outcomes than smaller chains and independents, which have room for improvement on several measures, including peritoneal dialysis and hospitalizations. The large chains' slight trend upward in catheter utilization warrants further examination.

Dr. Roach reported on the performance of other QIP measures based on data from DFC and the United States Renal Data System (USRDS) that was organized by CMS contractors at the University of Michigan. He noted that the hypercalcemia rates appear higher when including the patient months with missing values for calcium, which is misleading. Before the hypercalcemia clinical measurement was required, facilities not reporting calcium values were documented as having hypercalcemia patients. Since that time, there has been continued improvement in reporting and the rates of hypercalcemia have steadily declined. From 2011 to 2016, there were substantial decreases in readmission rates and transfusion rates that coincided with the QIP. Mortality rates steadily declined from 2010 to 2016, which could be attributed, in part, to implementation of the Fistula First program in 2004, as well as the ESRD QIP and the PPS Bundle.

In conclusion, ESRD QIP was Medicare's first attempt at a pay-for-performance program. Improvement in outcomes has coincided with the initiation of ESRD QIP, some of which could be attributed to the QIP. More data are needed on recently introduced measures to fully know the effect of the QIP on performance. Performance on some quality measures has stabilized, especially in large organizations.

Discussion

- Dr. Star sought clarity on why the hypercalcemia clinical measure was legislated in PAMA. Dr. Roach clarified that the measure was included to ensure that quality was not compromised by incorporating more expensive oral-only medications, such as those used to treat hypercalcemia into the ESRD PPS Bundle. Dr. Star also asked whether the costs of treating conditions representing a lack of proper kidney-related care—such as congestive failure, fluid overload, or vascular access infections—were reflected in the ESRD QIP measures. Dr. Roach explained that an ultrafiltration rate measure is being added to the payment year 2020 ESRD QIP Measure Set, to evaluate volume issues during dialysis. Assessing these types of costs is not done within the QIP, but ESRD quality measures undergo a rigorous endorsement and approval process.

- Dr. Star speculated that dropping of noncompliant patients from the facility (i.e., case mix indexes for discharges) could contribute to the independent chains' AV fistula results. Dr. Roach explained that evidence of case mix issues regarding AV fistulas had not been reported. CMS attributes these results to the LDO's large economy of scale, resources, and ability to perform a larger number of AV fistulas efficiently. Dr. Susan Mendley asked whether the dialysis adequacy was considered relative to the overall decline in utilization of peritoneal dialysis. Dr. Roach indicated that those data interpretations had not been done but could be considered in the future.
- Ms. Nilka Rios Burrows asked whether TPS improved in facilities that previously had their payments reduced. Dr. Roach pointed out that only a small percentage of facilities operate under reduced payments, but he did not have data readily available on which facilities had payment reductions in two consecutive years.
- In response to a query from Dr. Abbott on the utilization of erythropoietin-stimulating agents (ESAs), Dr. Roach explained that the quality measurements are assessed by the Center for Clinical Standards and Quality (CCSQ), CMS, which has observed that after implementation of the ESRD PPS Bundle, ESA use declined, resulting in decreases in hemoglobin levels leading to increases in transfusions. Questions on the utilization of ESAs can best be addressed by the Medicare claims group. Dr. Lauren Oviatt added that CCSQ tracks these types of data through the ESRD cost reporting review, which could be made available later.
- Dr. Star asked whether the 25 percent readmissions were related to fluid overload or vascular access issues. Dr. Roach explained that the initial hospitalization rates differ from the readmission rates, and CMS attributes the readmission rates to the care coordination between hospitals and facilities. In general, hospitalizations were due to vascular access issues and infections.
- Dr. Robert Nee observed the differences in outcomes of the independent versus large chains, in which the independent facilities performed worse. Given the amount of information available to consumers on the CMS Five-Star Quality Rating system, Dr. Nee wondered whether facility selection bias among patients was a factor. Dr. Roach remarked that although use of the DFC and Five-Star Quality Rating System has gained popularity within the field, focus groups and discussions with patients suggest that patients generally choose a dialysis facility based on its physical location relative to where they live. Dr. Narva wondered whether a rural versus urban setting affected the independent facilities' outcomes. Dr. Roach commented that evaluating care in the different settings is something that CMS could consider in the future.
- Dr. Abbott asked about the potential for tracking dialysis adequacy (Kt/V) relative to treatment time as a patient progresses from a dialysis start date. Dr. Roach responded that the data shown represent the percentage of patients whose Kt/Vs were over the benchmarks. Data on treatment times are being captured and could be presented at a future meeting.
- Dr. Kenneth Wilkins asked whether a report was available that included the methods for the ITS analysis, and Dr. Mendley asked whether de-identified data could be made publicly available. Dr. Roach will consult with the program lead regarding the potential for sharing these data with the KICC and eventually the public.

Part II: Pediatric Chronic Kidney Disease: Burden of Disease and Research Opportunities

Setting the Stage

Susan Mendley, M.D.

NIDDK

Dr. Mendley began the session by reviewing the landscape of pediatric CKD and ESRD and congenital anomalies of the kidney and urinary tract (CAKUT). She noted that CKD, although common in adults, is rare in children (i.e., 0–21 age group). In fact, data on the prevalence of CKD in children are limited, a national surveillance system is nonexistent, and data collection relies on voluntary reporting from individual centers, voluntary contributions to a database (North American Pediatric Renal Trials and Cooperative Studies), and a single prospective observational study. A CKD knowledge gap exists. The 20–39-year age group in the National Health and Nutrition Examination Survey (NHANES) dataset has a low incidence of kidney disease, and data have not yet been reported for the 0–21-year age group. Preliminary data will be presented at this meeting in preparation for publication. A similar gap exists for ESRD, which also is rare in the 0–21 age group. However, the cardiac mortality rate is almost 1000-fold higher in pediatric ESRD patients than in the general U.S. pediatric population as reported in the USRDS. Even though the calculated expected remaining lifetime of ESRD patients in the 0–4 age group who had a kidney transplant in 2014 is 56.9 years, compared to 23.6 years for patients who started on dialysis, the lifetime years were significantly less than the general U.S. pediatric population of 77.1 years. This deficit remains across the age groups up to 39 years. Children born with CAKUT may have complications throughout their lifetime, including complicated care in a neonatal intensive care unit requiring ventilator therapy, and may need early dialysis and kidney transplantation.

An Analysis of Trends in CKD among Adolescents Using NHANES Data

Sharon Saydah, Ph.D.

Centers for Disease Control and Prevention

Dr. Sharon Saydah reported on a study investigating the trends of albuminuria and estimated glomerular filtration rate (eGFR) among adolescents in the United States using NHANES data. This work currently is under peer review for publication in the *American Journal of Kidney Diseases*. Previous studies have shown a high prevalence of CKD risks among youth ages 8–17. In fact, 1 in 10 youths in the United States is borderline or has hypertension, a trend that remained unchanged from 1992 to 2012. In addition, 2 in 10 adolescents (average age 11) are obese, a trend that was increasing until 2003–2004 but has since reached a plateau. Furthermore, among youth, there was a 21 percent increase in the prevalence of Type 1 diabetes and a 30 percent increase in Type 2 diabetes from 2001 to 2009. Although a limited number of studies have reported albuminuria levels of 12 percent for the 8–18 age group, eGFR levels were not included. Other CKD studies have focused on clinical and dialysis populations, which leaves the prevalence of CKD among adolescents relatively unknown.

This current study aims to estimate the prevalence of CKD among the general U.S. adolescent population using two markers, albuminuria and reduced kidney function. The methods consist of using three NHANES data sets collected on adolescents ages 12 to 18 years: (1) NHANES III, 1988–1994; (2) NHANES, 2003–2008; and (3) NHANES, 2009–2014. Data were collected via interviews and physical examinations and included laboratory measures. Albuminuria was defined as an albumin-to-creatinine ratio (ACR) of more than 30 mg/g in urine obtained randomly during the physical examination. The Bedside Schwartz calculator for children was used to determine the eGFR values. Values less than 90 mL/min/1.73 m² were categorized as low eGFR, and values less than 60 mL/min/1.73 m² were classified as reduced eGFR.

An imputation model was developed based on a subset of 842 adolescents who had a second urine measurement during the 2009–2010 NHANES cycle. Model covariates included sex, race/ethnicity, age, hemoglobin A1c, blood pressure, and sample design weights. Persistent albuminuria was statistically imputed from this model. The demographics for U.S. adolescents were similar across data sets in terms of average age and sex, but the race/ethnicity percentages changed, as did the income-to-poverty ratio, which was statistically significant. Regarding clinical characteristics, systolic and diastolic blood pressures were significantly higher in the NHANES III data than in the more recent data sets. Fewer in the NHANES III data had a body mass index at or greater than the 95 percentile and waist-to-height ratios at or greater than 0.5.

Dr. Saydah detailed the data on prevalence of markers of CKD. Results showed a 13 percent prevalence trend in albuminuria levels based on random ACR among the U.S. adolescent population, which changed significantly from 1988 to 2014. Albuminuria prevalence dropped to 3.5 percent for imputed persistent ACR. There was a significant increase in the prevalence trend of eGFR less than 90, but it was less pronounced for eGFR less than 60. Combining eGFR less than 60 with ACR greater than 30 to assess the prevalence of CKD revealed that random (14 percent) or persistent (3.5 percent) ACR was the primary predictor of a CKD prevalence trend that increased from 2009 to 2014. The contribution of eGFR less than 60 was minimal.

The prevalence ratio adjusted for sex and race/ethnicity in the 2003–2008 and 2009–2014 data sets showed no significant differences between the random or persistent ACR in those data sets and the NHANES III data. Conversely, the eGFRs less than 90 and 60 were significantly higher in the two data sets but was similar to the unadjusted prevalence trends. The combined ACR and eGFR adjusted for sex and race/ethnicity showed no difference in CKD prevalence. Characteristics associated with persistent albuminuria or eGFR revealed that the adjusted prevalence of kidney disease markers was higher in female adolescents than male adolescents in the NHANES 2009–2014 data.

Dr. Saydah highlighted the strengths and limitations of this type of study. She summarized that the albuminuria prevalence did not change in the U.S. adolescent population from 1988 to 2014. The prevalence of reduced eGFR was threefold higher in the most recent period (2009–2014), yet less than 1 percent of adolescents had reduced kidney function.

Discussion

- Dr. Mendley pointed out that the Schwartz eGFR calculation is validated in CKD—not in normal, healthy children—and asked whether the ACR was measured in a similar manner across cohorts. Dr. Saydah explained that standard laboratory measures are used in NHANES. Noting that the Schwartz formula is validated in CKD, she welcomed other recommendations. Dr. Tonse Raju called attention to the low nephron numbers of premature newborns and emphasized the importance of tracking prematurity in these types of studies. Dr. Rosemary Higgins suggested tracking birthweights, which could be used as a surrogate marker.
- Dr. Nee asked how the increase in obesity among adolescents could be reconciled with the unchanging albuminuria levels. Dr. Mendley noted the assumption that a substantial delay in the development of albuminuria exists that is not being captured in NHANES.
- Dr. Oliver wondered whether it would be feasible to speculate that the decline in normalized eGFR reflects an increase in body surface area, rather than CKD. Dr. Saydah explained that the eGFR calculation used in the study is based on height, and Dr. Mendley noted that height is used as a surrogate for growth in the equation. Dr. Narva commented that Dr. George Schwartz, who

standardized the formula in children with CKD, was recently funded by the NIDDK to do the same standardization in healthy children.

An Analysis of Trends in ESRD among Adolescents Using USRDS Data

Kevin Abbott, M.D.

NIDDK

Dr. Abbott described ESRD trends among children, adolescents, and young adults, which is detailed in Chapter 7 of Volume 2 of the 2017 Annual Data Report (ADR) of the USRDS. There was a 42 percent reduction in the 1-year adjusted all-cause mortality rates in incident pediatric patients with ESRD in the 0–4 age category from 2005 to 2014 and a 58 percent reduction during this same period in the 5–9 age category. Two major causes of mortality, cardiovascular-related and infection-related, showed similar declines. Despite these declines in mortality, all-cause hospitalization rates were increased during the same period by 27 percent in the 0–4 age category and 31 percent in the 5–9 age category. Specifically, cardiovascular- and infection-related hospitalization rates increased, except for the 0–4 age category, in which there was a decline in cardiovascular-related hospitalization rates. Dr. Abbott remarked on the proportion of missing, unknown, and unspecified etiology of ESRD in children and adolescents, which remains a concern. He emphasized that these data could spur a new ESRD research agenda and encouraged participants to review the in-depth analysis of ESRD in adolescents accessible from the USRDS website.

In closing, Dr. Abbott enumerated key pediatric ESRD takeaways. The adjusted all-cause mortality among children who were younger than age 10 when they started dialysis has declined significantly since 2015. The decline in mortality correlates with reductions in cardiovascular- and infection-related mortality, despite increases in all-cause and specific hospitalizations. Missing or unknown causes of ESRD reach a peak starting in adolescence that persists into young adulthood.

Discussion

- In response to a query from Dr. Crowley on the change in clinical practice regarding transplantations prompted from these data, Dr. Abbott responded that the transplantation rates, at least in the first year, the period in which mortality was assessed, remained stable and did not account for any changes during the 2005–2014 period. He also noted that within the age category of 0–21 years, the average age of patients starting ESRD has decreased steadily from a peak high of 14.5 years in 2006 to 13.5 years in 2016. However, adjusted mortality accounts for this change in age.
- Dr. Robert Tamburro asked whether there has been an increase in hemodialysis in children in the advent of improved catheter technologies, which might explain the decrease in mortality and increase in hospitalizations due to infection. Dr. Abbott replied that the initiation of dialysis with a catheter as the only access has remained stable since 2008, although this practice is significantly less common.
- Given the pediatric ESRD trends indicated in the USRDS data, Mr. Duvall solicited input on whether adolescents should be included in the CMS CEC model, which currently excludes individuals younger than 18 years of age. In general, participants thought that including adolescents would be appropriate, but not those at age 0. Dr. Mendley pointed out that applying the CEC model to such a small population that would be projecting different outcomes would be problematic. She added that a lack of continuity is less of a concern in the comprehensive care of pediatric hemodialysis patients who are being treated in academic centers in which all of a

patient's needs are being met. Dr. Vasum Peiris suggested that collecting data to inform an appropriate care coordination model for adolescents would be a place to start. Dr. Higgins commented that the minimum body weight required for a kidney transplant would need to be further investigated.

Congenital Anomalies of the Kidney and Urinary Tract—The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Perspective

Tonse Raju, M.D., D.C.H.

NICHD

Dr. Raju discussed CAKUT from an NICHD perspective. Under normal conditions, amniotic fluid (AF), the clear fluid that surrounds the fetus during pregnancy, creates a space around the baby aiding the growth of the lungs, limbs, muscles, and skeleton system. Lung fluid and fetal urine are major contributors to the AF volume beginning at 13 to 20 weeks of gestation. The AF volume increases up to 36 weeks, and the rate of increase slows. The absolute volume of AF and the rate of its production vary. During the third trimester, the entire volume of AF is recycled every 24 hours. Normal AF volume is defined as an average of about 500 mL at term gestation, an AF index of 16.2 ± 5.3 cm, and/or maximum vertical pocket of amniotic fluid in ultrasound between 2 cm and 8 cm.

A deficiency in AF is known as oligohydramnios, and its near-total absence is known as anhydramnios. Experts in the field define the oligohydramnios phenotype as having an AF index of less than 5 cm and/or maximum vertical pocket less than 2 cm. About 5 to 12 percent of all pregnancies in the United States present with oligohydramnios, affecting approximately 200,000 to 400,000 women annually. Anhydramnios is present in 1 percent of all pregnancies, affecting 40,000 women annually. The consequences of oligohydramnios and anhydramnios are increases in fetal death, intrauterine growth restriction, limb contractures, severe pulmonary hypoplasia, umbilical cord compression, and inability of the fetus to tolerate labor. Up to 80 percent of perinatal mortality—depending upon the underlying cause and severity—can be attributed to these conditions. Although other abnormalities can be contributing factors, CAKUT remains a major group of conditions affecting AF volume, causing oligohydramnios or anhydramnios due to kidney disease and either a lack of urine production or flow into the AF.

Dr. Raju called attention to the soon-to-be-published report in *Obstetrics & Gynecology*, titled “Anhydramnios in the Context of Developmental Renal Malformations,” which is a summary of the August 2016 workshop sponsored by the NICHD and NIDDK on the same topic. This document summarizes opinions and recommendations by experts from the conference. Hydronephrosis is the most common renal malformation, whereas bilateral renal agenesis and multicystic dysplastic kidney conditions, although less common, are associated with very poor outcomes. Approaches to evaluate oligohydramnios include the antenatal ultrasound (most common), history, magnetic resonance imaging, or chromosomal testing. The prenatal detection rate of renal malformations assessed via antenatal ultrasound is 82 to 88 percent. Existing antenatal interventions to improve AF volume are fetal cystoscopy and shunt for disorders of lower urinary tract obstruction; periodic infusions of normal saline to replace AF (amnioinfusion), or intermittent administration of normal saline through an implanted device in the maternal abdominal wall (amnioport). These attempts are intended to help the growth of the lungs. Although there are short-term improvements with these interventions, long-term renal outcome data are not available, underscoring the need for national and international registries to track outcomes.

Dr. Raju summarized the knowledge gaps and research needs. Regulatory mechanisms of the AF volume are not well understood. Developing diagnostic markers to assess fetal kidney functions and diseases and prognostic markers of long-term kidney outcomes are needed. Improving the quality of antenatal imaging, patient selection based on anticipated prognosis, and ethical issues all should be addressed. Additional

studies also are needed to established evidence-based standards for antenatal intervention for women with oligo/anhydramnios and of fetuses and newborns affected by congenital renal malformations.

Congenital Anomalies of the Kidney and Urinary Tract—The NIDDK Perspective

Susan Mendley, M.D.

NIDDK

Dr. Mendley presented on NIDDK's perspective on CAKUT, the causes, consequences, and research needs. The message that should be conveyed is that CAKUT are common. They occur in more than 1 percent of live births, account for up to 23 percent of overall birth defects, and contribute between 40 percent and 50 percent of pediatric ESRD cases. Severe phenotypes are renal agenesis and renal hypodysplasia. Twenty percent of CAKUT patients may have a genomic disorder, such as copy number variation (CNV). In fact, reports have shown that the incidence of large CNV in renal dysplasia cases was substantial compared to appropriate controls. Across the genome, CNV is associated with anomalies of renal development, which also tracks with brain and cardiac anomalies. The NIDDK GenitoUrinary Development Molecular Anatomy Project (GUDMAP) is a resource for investigating the cause and candidate genes associated with CNV and anomalies of renal development. GUDMAP provides researchers access to gene expression data in renal development and more. Reiterating that CAKUT is common, Dr. Mendley noted that although familial forms of CAKUT have been described, most CAKUT cases occur spontaneously. Prenatal diagnosis is becoming more common, and early clinical care of severe CAKUT has improved. Therefore, an increase in CAKUT survivors among older children and adult ESRD patients is anticipated.

To address the consequences of CAKUT, NIDDK sponsored the Chronic Kidney Disease in Children (CKiD) study, a prospective observational study of children with CAKUT and glomerular diseases. Four domains are being investigated: growth, neurocognition, cardiovascular disease, and progression of renal disease. On average, the decrease in GFR in children with non-glomerular CKD is lower than in glomerular CKD children in the CKiD cohort. In addition, genomic disorder carriers have worse neurocognitive function.

Dr. Mendley highlighted research areas for CAKUT. Efforts to characterize genetic and epigenetic causes of CAKUT, as well as characterizations of the effects of the intrauterine environment on renal development, are needed. The obstetrical and neonatal pulmonary outcomes of oligohydramnios and anhydramnios are important and require better characterization. Care of patients with congenital renal disease is complex, and increasing understanding of research designs for a unique small cohort would be a place to start.

Discussion

- Dr. Crowley asked whether the CNV correlated to AF volume abnormalities. Dr. Raju pointed out that CNV could be evaluated following an abnormal AF volume assessment, but he was not aware of a correlation of CNV and AF volume.
- Dr. Oliver remarked on the psychosocial aspects of pediatric patients transitioning to adult care. Dr. Narva noted that Dr. Maria Ferris at the University of North Carolina at Chapel Hill is an expert in transitioning to adulthood with a chronic illness and would be someone to engage for advice. Participants pointed out that cardiologists who address congenital heart disease issues also would be a group to engage in discussion.

Adjournment

Dr. Narva thanked the presenters and attendees for their participation. He noted that the next meeting of the KICC is scheduled for September 14, 2018.