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

Kidney Interagency Coordinating Committee (KICC) Meeting
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Welcome and Introductions

Andrew Narva, M.D., FACP
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Dr. Andrew Narva welcomed the participants and provided an introduction to the KICC for those new to the Committee. Approximately 30 years ago, the Congress mandated the formation of the KICC, which was to meet annually to encourage cooperation, communication, and collaboration among all Federal agencies involved in kidney research and other activities. The mandate was a recognition of the need for better coordination of the Federal response to chronic kidney disease (CKD). The federal response to CKD is multifaceted, with overlaps among the missions of the agencies addressing the burden of CKD.

Veterans Health Administration Office of Research and Development: Renal Research Portfolio

Michael Burgio, Ph.D.
U.S. Department of Veterans Affairs

Dr. Michael Burgio provided an overview of the Veterans Health Administration (VHA) Office of Research and Development's (ORD) portfolio and the ways in which research is conducted by the ORD. The mission of the VHA ORD is "to discover knowledge and create innovations that advance the health and care of Veterans and the nation." The U.S. Department of Veterans Affairs (VA) research enterprise is an intramural research program embedded within a hospital system with $590 million in direct appropriations in fiscal year (FY) 2015 and more than 100 research stations; more than half of VA researchers are clinician scientists, a unique characteristic of the system. Under the direction of the Chief Research and Development Officer (CRADO), the system includes biomedical laboratory research and development (R&D), which does not involve intact humans; clinical science R&D, which includes epidemiology and clinical trials; health services R&D, which is research on such outcomes as quality, access, patient outcomes, and costs; and rehabilitation R&D. Biomedical laboratory and clinical science R&D comprise the major part of the VHA ORD portfolio.

Dr. Burgio described the eligibility, selection process, and types of awards in the ORD portfolio. Because the VHA ORD is an intramural program, all principal investigators (PIs) (clinician and medical center-nominated nonclinician scientists) must be employed by VA with at least 5/8 minimum salary support, but many VA researchers have strong academic affiliations and are encouraged to leverage non-VA resources to support research, including for salaries. Although an intramural program, the VHA ORD uses a selection process for projects that is similar to that of an extramural program, with a structured peer review process that historically resulted in the funding of 15 to 20 percent of applications, although budget constraints have reduced funding rates to as low as 12 percent in recent years. The most common type of award is the Merit Review Award, which is similar to NIH's R01 grant mechanism; other awards include the Merit Review Award for Clinical Trials, Career Development Award (similar to NIH's K08 grant mechanism), Pilot Project Award (similar to NIH's R21 grant mechanism), and Research Career Scientist Award (similar to NIH's K02 grant mechanism).

The VHA ORD currently is supporting renal disease-related projects. In FY 2014, these included biomedical laboratory R&D, clinical science R&D, multiple large clinical trials, and smaller projects in health services and rehabilitation R&D—for a total of $18 million dedicated to kidney-related disease research. The investment in renal disease-related research has remained fairly constant during the past 5 years, at $18 to $20 million annually.

Most VHA ORD research projects are driven by investigator initiative, determining the portfolio size in a given area and reflecting demand for medical specialties at VA medical centers. Dr. Burgio provided

examples of conditions with current requests for application (RFAs)—which are determined by the CRADO—including diseases prevalent among Veterans returning from Iraq and Afghanistan, traumatic brain injury, diseases connected with combat exposures, and Gulf War Veterans' Illness. The VHA ORD uses a variety of mechanisms to encourage applications in priority areas, including issuing subject-specific RFAs, having one criterion for eligibility of nonclinician scientists be alignment with current VA research topics, and giving preference to research projects on the margin for funding if they address priority research areas.

For renal disease-related preclinical research, examples of currently funded biomedical laboratory R&D projects include assessing the nephrotoxicity of free light chains and using a mouse model to explore the role of AT1 angiotensin receptors in blood pressure regulation. In clinical science, two projects are exploring masked hypertension in CKD and investigating high-density lipoprotein (HDL) function and mortality in end-stage renal disease (ESRD). The Cooperative Studies Program is a national infrastructure comprised of data and statistical coordinating centers, a clinical research pharmacy coordinating center, and epidemiological resource centers. Cooperative Studies Program renal disease trials have included the Prevention of Serious Adverse Events Following Angiography (PRESERVE) trial, which is ongoing; VA NEPHRON-D, which was terminated early; and the Acute Renal Failure Trial Network (ATN) study, which found no difference in intensive versus conventional strategies of renal replacement therapy for acute kidney injury (AKI). The Million Veterans Program—a national, voluntary research program aimed at better understanding factors related to Veterans' health—is applicable to a wide range of diseases. Currently, biospecimen collection has produced more than 200,000 samples for genotyping, 24,000 samples for exome sequencing, and almost 2,000 samples for whole-genome sequencing. These data will be available to researchers behind the VA firewall, and two projects have been started to evaluate the computing infrastructure.

Discussion

- The participants discussed access to VHA data. Dr. Gregory Germino asked about alternative methods to access VHA data other than from behind the VA firewall. Dr. Burgio responded that per the preferences of the Veterans from whom data was obtained, data will be accessible only behind the firewall. Dr. Germino asked for clarification about how this restriction would affect the Precision Medicine Initiative. Dr. Burgio answered that this has not been decided, but acknowledged that some level of de-identified data may have to be released from behind the firewall. Dr. Paul Eggers stressed the importance of VA data for informing the decision making process regarding dialysis in late-stage CKD and ESRD. Only three data sets are large enough to follow patients who go onto dialysis and those that do not: VA, Kaiser, and Canadian data sets. Dr. Burgio answered that to have access to VA resources requires collaboration with VA researchers.
- Dr. Germino asked whether Dr. Burgio had communicated with researchers about what projects they would propose if there were opportunities to perform renal-specific research. Dr. Burgio replied that he had not yet gone out into the field to discuss a possible renal-focused RFA with researchers.
- Dr. Eggers queried Dr. Burgio about the extent of external funding being used by VA researchers. Dr. Burgio responded that obtaining external funding was fairly common, with approximately 30 percent of researchers being supported by funds from outside of VA (e.g., NIH). For example, there is joint project with the U.S. Department of Defense (DoD) on post-traumatic stress disorder (PTSD).
- Dr. Eggers commented that access to VA data has been restricted to certain approved applications without allowing a change to other possible uses. Dr. Burgio responded that developing new aims for an ongoing study would be considered a new study and would need to be approved by VA's peer review process.

Developing a Kidney Disease Research Agenda in the U.S. Department of Veterans Affairs
Michael Fischer, M.D., M.S.P.H.
Veterans Administration Center of Innovation for Complex Chronic Healthcare

Dr. Michael Fischer summarized and characterized the process of developing a kidney disease research agenda at VA. For background, Dr. Fischer noted that the VHA is the largest integrated health care system in the United States, with more than 50,000 practitioners who provide comprehensive care to more than 8.3 million Veterans each year. The mission of the VHA is to "honor America's Veterans by providing exceptional health care that improves their health and well-being." The vision statements of the VHA explicitly mention that VHA care will be delivered so as to support learning and discovery.

Regarding clinical research at the VHA, the VHA integrated national care network provides an unparalleled foundation for clinical research, with a variety of well-established clinical research centers and programs, including Centers of Innovation in Health Services Research and the Cooperative Studies Program. VHA clinical research is strong in the areas of health informatics and "big data," having the largest integrated medical record system, a variety of ongoing internal programs (e.g., Natural Language Processing, Million Veteran Project, Renal Operational Data Mart), and external partnerships showcasing VA data (e.g., the Centers for Disease Control and Prevention's [CDC] CKD Registry, United States Renal Data System's [USRDS] Special Study on Transitions of Care).

Dr. Fischer described the underlying motivation and rationale for the proposed development of a kidney disease research agenda in VA. Veterans are at high risk for kidney disease and poor outcomes, with approximately twice the CKD prevalence compared to non-Veterans because of risk factors and comorbidities, resulting in VA's being the largest provider of CKD care in the United States. Veterans on dialysis have a 6.5 to 7.4 times greater mortality rate than those who are not, with Veterans on chronic dialysis incurring an average of 35 hospital days per year. Kidney disease accounts for a substantial cost for care for Veterans, incurring the second highest total medical costs per person and second largest percentage of total VA medical annual costs. Chronic dialysis costs, in particular, are exceptionally high, including non-VA dialysis and VA dialysis facility care. VA research expenditures for kidney disease, however, remain low compared to that for other chronic conditions, staying flat at $20 million per year, a level that has funded approximately 95 projects per year. The majority of VA research expenditures for kidney disease are in preclinical research, with only approximated 35 percent of VA kidney research dollars devoted to clinical research.

Current Federal legislation has been introduced with bipartisan support "to improve the understanding of, and promote access to treatment for, chronic kidney disease, and for other purposes." The new VA Secretary's Strategic Plan affirms VA's commitment to research. The Strategic Plan highlights the particular role of clinical research at VA and stresses intramural opportunities with other agencies (e.g., U.S. Department of Health and Human Services [HHS], DoD, NIH). Dr. Susan Crowley directs the VHA Kidney Disease and Dialysis Program Office, which has implemented its detailed and robust 2012 Strategic Plan to promote evidence-based research to improve treatment and reduce disability from CKD and ESRD. The Office is partnering with VA clinical research centers and is leveraging interdisciplinary VA and non-VA expertise in its research teams and approaches to analyzing "big data."

The aims in developing a potential kidney disease research agenda are to establish an agenda that does the following:

- Engages a multidisciplinary stakeholder body.
- Identifies and targets evidence and performance gaps in kidney disease care.
- Represents prioritized evidence and performance gaps in kidney disease care.
- Is suitable to the VA research infrastructure.

- Is aligned with themes among VA services/departments.
- Is disseminated to and actionable by the VHA ORD and VA kidney research field.
- Increases kidney disease research opportunities and funding in VA and thereby improves kidney disease care in VA.

Dr. Fischer outlined the steps and processes involved in developing the agenda. These include engagement of stakeholders (e.g., VA kidney disease clinical and research communities, Veterans with kidney disease and their caregivers). Evidence and performance gaps in kidney disease care need to be identified through multiple approaches, including soliciting stakeholder input, reviewing clinical practice guidelines, reviewing the Evidence Synthesis Program, and conducting an environmental scan of non-peer reviewed literature. Prioritization of evidence and performance gaps in kidney disease care will involve collating and prioritizing research domains. A diverse stakeholder body will determine the suitability of priorities to VA research using criteria that include the following:

- Importance to VA, suitability for VA investigation.
- Actionability by VA, considering existing resources and infrastructure.
- Scalability by VA.

Alignment of themes among VA service lines and departments will be needed to ensure that prioritized research domains and themes are consistent across VA and give consideration to non-VA funded (e.g., DoD, NIH, Agency for Healthcare Research and Quality [AHRQ]) research studies with relevance for Veterans who have kidney disease. Communicating the kidney disease research portfolio of needs and priorities with VHA ORD and leadership (i.e., VA Kidney Disease and Dialysis National Program Director and the stakeholder body) will be critical. Dissemination of funding priorities to the VA nephrology research community will involve multiple approaches (e.g., RFAs, the Kidney Disease and Dialysis Program Office newsletter and Strategic Plan, nephrology society meetings). Some infrastructure for kidney disease research exists, but other infrastructure will need to be developed (e.g., VA Quality Enhancement Research Initiative for kidney disease research). The status, impact, and relevance of the kidney disease research agenda will need to be assessed and reported periodically regarding three issues:

- Have priorities named in the kidney disease research agenda received funding?
- Among those studies funded, how have they impacted clinical care for Veterans?
- Is the agenda updated in regard to important contemporary research domains and questions?

Discussion

- Dr. Christine Chang asked about the prioritization criteria for VA research, particularly in regard to actionability and how the criteria would apply to research gaps. She commented that typically, she considered actionability as applying to implementing an intervention. She is part of a prioritization group at AHRQ and is interested in the ways other groups are operationalizing criteria. Dr. Fischer responded that prioritization would involve consideration of how actionable an item would be, as well as scalability within current resources. Dr. Robert Star indicated that the Kidney Research National Dialog recently underwent a similar prioritization process. Drs. Chang, Fischer, and Star agreed to discuss the prioritization process in greater detail following the meeting.

NIH Health Care Systems Research Collaboratory: Pragmatic Trial Demonstration Projects

Catherine Meyers, M.D.
National Center for Complementary and Integrative Health (NCCIH), NIH

Dr. Catherine Meyers described Pragmatic Trial Demonstration Projects within the NIH Health Care Systems Research Collaboratory. The Collaboratory is funded by the NIH Common Fund, which was established by Congress through the 2006 NIH Reform Act, supporting cross-cutting, trans-NIH programs and requiring encouragement of collaboration across the NIH Institutes and Centers (ICs). Common Fund Programs are unique by definition, transformative (i.e., lead to new methods and treatments), catalytic (i.e., short-term), synergistic, and cross-cutting. A 2010 Commentary in the *Journal of the American Medical Association* raised several important issues that present challenges for clinical research that need to be addressed to improve the U.S. health care system, including stakeholder interactions, new approaches for clinical trials, methods for optimizing use of observational data, dissemination and implementation, and leveraging multidisciplinary expertise. Dr. Meyers indicated that the need to increase the value of clinical research in clinical decision making and health policy through "practical" or pragmatic clinical trials also had been recognized prior to the 2010 Commentary.

To help trial designers identify what is pragmatic research, the pragmatic-explanatory continuum indicator summary (PRECIS) tool was developed to allow consideration of variables that are important to the design of pragmatic research trials. Pragmatic trials can be distinguished from explanatory trials by characteristics that include the following:

- Broad eligibility.
- Flexible interventions.
- Typical practitioners.
- No followup visits.
- Objective clinical outcome.
- Usual compliance.
- Intent to treat.

The NIH Health Care Systems Research Collaboratory was established with two goals: (1) strengthening the national capacity to implement cost-effective, large-scale research studies that engage health care delivery organizations as research partners; and (2) developing methods and best practices to enable the participation of many health care systems in clinical research. Opportunities for the Collaboratory focused on trials that inform practice, integration of research into the routine health care environment, and engagement of integrated health care systems with electronic infrastructure. The NIH issued three Collaboratory RFAs: one to develop a Coordinating Center to make data, tools, and resources available to pragmatic trials; and two for pragmatic clinical trials demonstration projects, the second of which focuses on patients with multiple chronic conditions. The Collaboratory Coordinating Center (CCC) is located at Duke University. The CCC has work groups/cores that focus on critical areas for the successful implementation of pragmatic research: regulatory/ethics, which has presented a challenge for identifying the appropriate regulatory agency; design/biostatistics; electronic health records and phenotype/standards, which are important to encourage partnerships among health care systems with different record systems; patient-reported outcomes; health system interactions; and stakeholder engagement.

Ten Pragmatic Trial Demonstration Projects were supported by the two RFAs, and all projects had a milestone-driven, 1-year planning phase before transitioning from a UH2 planning phase to a UH3 implementation phase. The Demonstration Projects are being implemented at sites across the United States, and the project on reducing mortality in ESRD will have locations in all 50 states. The first set of trials includes the Time to Reduce Mortality in (Incident) ESRD Trial (TiME Trial), which began in

January 2014, as well as trials on health care-associated infections, back pain, colon cancer screening, managing chronic pain, and suicide prevention. The TiME Trial is led by Dr. Laura Dember, with DaVita and Fresenius Medical Care North as health care system partners. It is a cluster randomized trial of more than 400 units, with a recruiting goal of more than 6,400 patients, an intervention of 4.25 hours hemodialysis (HD) versus the usual care HD prescription, and the primary outcome of all-cause mortality with secondary outcomes of hospitalizations and health-related quality of life. A second set of pragmatic trials demonstration projects on improving chronic disease management (ICD) with Parkland Intelligent e-Coordination Evaluation System (Pieces™, an electronic health record-linked decision support tool), video education on end-of-life planning in nursing homes, and care for PTSD and co-morbidities is in the UH2 planning phase. The ICD trial will focus on CKD, diabetes, and hypertension. It is a cluster randomized trial with a recruitment goal of 25,000 patients, partners that include VA North Texas, an intervention that uses Pieces™ versus standard medical care, and a primary outcome of hospitalizations at 1 year with secondary outcomes of readmissions, cardiovascular events, and mortality.

The NIH Collaboratory website (https://www.nihcollaboratory.org/) is a resource that includes archived weekly Grand Rounds presentations, explanations about Pragmatic Trial Demonstration Projects, and a Living Textbook. The Living Textbook is updated constantly and provides resources for investigators and interested individuals from authors across the Collaboratory Program. The website's Knowledge Repository is a joint project of NIH and the Patient-Centered Outcomes Research Institute (PCORI) that archives the Collaboratory's presentations, documents, and other resources.

Dr. Meyers offered final thoughts:

- Rapid implementation of informative trials that engage decision makers (i.e., patients, health care systems, practitioners) as partners is possible. The Collaboratory was able to take advantage of investigators who were already working in the research space. The challenge for the future is to train more researchers who will be comfortable working in the pragmatic research space.
- Shared knowledge and learning with work groups and study teams is an effective strategy for planning trials across many disciplines. A number of different disease communities have been engaged in the Collaboratory.
- A Planning Phase is critical prior to implementation. Not all of the UH2 planning phase projects were successful. An administrative review process is needed for the end of the UH2 phase.
- Trials that integrate clinical research methods into routine health care delivery are feasible and essential to continue to address real-world applications.

Challenges for performing pragmatic trials include using real patients, settings, conditions, and outcomes; leveraging infrastructure to maximize efficiencies; and aligning incentives, research culture (including the regulatory climate), expertise, and finances. Implementing the pragmatic trials provided lessons on leveraging resources and finances.

Discussion

- The participants discussed data sharing. Dr. Narva commented on the potential difficulty in accessing even de-identified VA data from outside the VA firewall, which would be necessary for the Pieces™ collaboration with the VA North Texas. He observed that DoD also has a large health care system and asked whether there are plans to engage DoD in any of the Pragmatic Trials. Dr. Meyers replied that for the first round of pragmatic trials, one of the review criteria was that investigators had experience with pragmatic research, and the second RFA expanded the population of health care systems involved, but it is unclear what the Collaboratory should do next (e.g., issue another RFA, seek additional data partners such as DoD). Data sharing has been an ongoing discussion among investigators and their partners. The Collaboratory developed a

data sharing policy, which committed the investigators to share the research data sets on which their primary publications were based, but new data partners, not just VA, have raised issues about data sharing. Dr. James Oliver noted the difficulties of multicenter collaborations with DoD because, with some exceptions, there is a lack of infrastructure for data sharing. This is one of the issues that the restructuring of the VA health care system plans to address with the formation of centralized internal review boards (IRBs) for disease-specific research.

New Opportunities from and for the United States Renal Data System

Kevin Abbott, M.D., M.P.H.
NIDDK, NIH

Dr. Kevin Abbott discussed new opportunities from and for the USRDS. The 2014 Data Report has been released, although a few aspects of data analysis are still underway. Data on the ESRD incidence rate show that it has declined in recent years, beginning approximately in the early 2000s; the cause of the decline is multifactorial, resulting from advances in many areas. The overall death rate for patients with ESRD also has declined and the survival of transplant patients has improved somewhat. Dr. Abbott characterized these improvements as "low-hanging fruit," but he speculated that some fruit might still remain to be picked.

CROWNWeb (http://mycrownweb.org/) is an online database that all Medicare-approved, non-VA dialysis facilities are required to use for electronic submission of administrative and clinical data. Facilities submit patient information via form CMS-2728 Medical Evidence, but CROWNWeb also has a clinical module that records patient data (e.g., anemia, adequacy of dialysis), as well as such data as hospitalizations and vascular access. CROWNWeb has strengths and weaknesses, providing details of dialysis treatment, including Kt/V, as well as pre- and post-dialysis weight, but not dialyzer used or dialysis flow rate. It includes data on the type of access used on the dialysis date reported, whereas previously, information was available only on initial access. The availability of information on non-Medicare patients with ESRD, other than mortality and ESRD incidence, is a crucial step forward for researchers and others interested in the data. The fraction of incident patients using hemodialysis who are on Medicare has changed from 90 percent in 1978 to the current rate of approximately 50 percent. A similar trend is seen among prevalence patients using hemodialysis. Previous to CROWNWeb, data on vascular access only was available at initiation, but CROWNWeb records data on access at intervals subsequent to initial access.

Dr. Abbott raised the potential problem of new kidney diseases being masked by diabetes- or hypertension-related disease. Dr. Abbott described a new disease, MesoAmerican Nephropathy (MeN), which has been characterized in Central America. There is evidence that MeN, which is not diabetes-related, might be a global phenomenon with the potential for a very large impact on the health care systems where it occurs (e.g., Sri Lanka). The question arises whether an epidemic of interstitial kidney disease in the United States would be recognized, given the high background of diabetes- and hypertension-related disease. Diagnosis is important because it affects therapy, prognosis, and research funding priorities; generally, the first time patients see a nephrologist is when they are beginning dialysis, without having the underlying cause identified in the early stages of CKD. The best data on the etiology of ESRD are reported in national registries, such as USRDS, but they are not verified histologically. From recent USRDS data, 44 percent of patients with ESRD had diabetes, and 28 percent had hypertension. A study of participants in the National Health and Nutrition Examination Survey (NHANES) found that approximately 30 percent of adults with type 2 diabetes and renal insufficiency did not have retinopathy or albuminuria, suggesting that their CKD was not due to diabetic glomerulosclerosis. Another study found that 53 percent of patients with type 2 diabetes had nondiabetic renal disease (NDRD). Among the combination of diseases that were the causes of the NDRD, the leading etiology was focal segmental

glomerulosclerosis. In a cohort of Korean patients with type 2 diabetes, 53.6 percent had NDRD. A 2013 study found 63 percent of a cohort of patients with type 2 diabetes had NDRD; 27 percent had both NDRD and acute tubular necrosis.

VA is not alone in recognizing that renal disease imposes a heavy health cost burden and is relatively underfunded in research. Identifying whether the cause of ESRD is diabetes would have a high payoff. The USRDS has the following research priorities:

- Vascular access (a key NIDDK priority as well).
- Change in estimated glomerular filtration rate (eGFR) at dialysis start.
- Peritoneal dialysis (PD) versus HD for initiation.
- Treatment time and ultrafiltration rate.

Dr. Abbott identified diagnostic validation at ESRD as being on his "wish list" for research priorities.

Discussion

- The participants discussed diagnosis of the etiology of ESRD. Dr. Narva commented that the ethnic groups of the participants often determines the diagnosis in underserved populations, with African Americans most often diagnosed with hypertensive CKD and Native Americans with diabetic nephropathy. Many patients have albuminuria for years, however, before developing diabetes.
- Given that the causes of kidney disease often are misdiagnosed, Dr. Sharrilyn Evered asked about the barriers to biopsies. Dr. Abbott responded that the procedure involves a certain degree of risk and is an invasive procedure. The criterion for performing a biopsy should be whether its results might change management. He noted that the studies he showed were from academic medical centers with strict criteria for biopsies (e.g., atypical presentation); there are studies that show that even among patients with diabetes and retinopathy, 20 to 30 percent have NDRD. A current indication for a biopsy is having diabetes but no retinopathy or an atypical presentation.
- Dr. Evered asked whether meeting participants were interested in joining an interagency work group that will determine the data fields to be included in CROWNWeb. There was a general indication of interest among members of the group. She will send an invitation to the group via email.
- Dr. Narva mentioned that the National Kidney Disease Education Program (NKDEP) Health Information Technology Work Group is sponsoring a meeting in October 2015 on health information technology and population management in kidney disease. The Steering Committee is seeking to engage more Federal partners. He will send a draft description of the meeting with the minutes to solicit volunteers to participate in the meeting or the Steering Committee.

Renal Research and Policy

David Miller, Ph.D.
NIDDK, NIH

Dr. David Miller discussed the ways in which the Office of Scientific Program and Policy Analysis (OSPPA) interacts with the NIDDK Divisions and the Director. OSPPA has a staff of approximately a dozen people, most of whom hold Ph.D. degrees. The Office acts as liaison between Congress, which funds NIDDK and directs its spending; researchers; and patients, including patient advocates. OSPPA performs coordinating activities and reports on NIDDK undertakings, including producing an annual report to Congress, *Recent Advances and Emerging Opportunities*. The report is developed with the help of NIDDK Divisions, which review their research portfolios for relevant projects, and is written for an

interested lay audience. The report highlights NIDDK-funded research advances in the previous fiscal year. The report also includes stories of patients who have been affected by the diseases studied by NIDDK, as well as "stories of discovery," which profile research over a longer timescale of 5, 10, 15, and 20 years.

In addition, OSPPA is involved with strategic planning, program analysis, and program evaluation. NIDDK has a very broad research mission and so does not have one single strategic plan, but rather several disease-specific plans. For program analysis, OSPPA produces topic-specific reports as required by Congress, as well as draft *ad hoc* responses to Congressional inquiries. As necessary, OSPPA performs program evaluations, including a regular report to Congress evaluating NIDDK's program on type 1 diabetes. OSPPA also supports the NIDDK leadership, including drafting testimony and the justification for NIDDK's budget. Dr. Miller expressed interest in learning more about the ways in which non-NIH organizations inform research with policy.

Discussion

- Dr. Narva stated that the KICC provides an opportunity not only for researchers at different agencies to interact, but also for interagency interactions among individuals involved in research policy.
- Dr. Burgio stated that as a small organization, VHA ORD does not have a group dedicated to research policy. Requests from Congress are responded to by the individuals with expertise that matches most closely the request. To distinguish VHA ORD's research from that of NIH, research must be translational or the justification for preclinical research must be made that it will translate to clinical applications.
- Dr. Oliver stated that the DoD has core funding (approximately $10 to 20 million) and funding through the Congressionally Directed Medical Research Programs (CDMRP; $100 to $200 million). Unlike NIH funding, CDMRP funding comes to DoD through riders to bills and reflects the type of research that the electorate is calling for. Core funding is almost always directed toward combat casualty care. DoD does not control the type of research funded through CDMRP.
- Dr. Chang stated that AHRQ is a small office and so has an approach similar to that of the VHA ORD for responding to inquiries from Congress. Like DoD, AHRQ faces the challenge of ensuring that its research is distinct from other entities, including NIH and PCORI. Under new leadership, AHRQ is focusing more on dissemination and implementation.
- Dr. Miller stated that there is interest in the community and in Congress to improve research and care for individuals with CKD, as well as improve coordination across the U.S. government.
- Dr. Narva suggested that OSPPA might be able to help other agencies without research policy offices in information gathering.

Centers for Medicare & Medicaid Services End-Stage Renal Disease Program: Research Topics

Indira Jevaji, M.D., M.S.L.
Centers for Medicare & Medicaid Services

Dr. Indira Jevaji indicated that in presenting research topics of the Centers for Medicare & Medicaid Services (CMS) ESRD Program, she is seeking guidance from the group on prioritizing research topics. As background, Dr. Jevaji stated that the statutory authority for Medicare to extend coverage to individuals with ESRD originated with the 1972 Social Security Amendments, and a 1978 amendment created ESRD Network Organizations, with ESRD Network areas established by the 1986 Omnibus Budget Reconciliation Act. In 2008, Congress required implementation of an ESRD quality incentive program (QIP) that would result in payment reductions to providers of dialysis services and dialysis

facilities that do not meet performance standards. CMS ESRD Programs include the ESRD QIP and the ESRD Network Program, which includes provisions to ensure access to care, patient safety, and quality incentive initiatives.

The CMS undertook a literature review of dialysis adequacy measures to evaluate whether evidence was being used to implement the best methodology. It was determined that nephrologists caring for patients receiving dialysis typically have used clearance of urea from the body as a measure of dialysis "adequacy"; in a 1985 analysis, a connection was established between K_t/V and clinical outcomes, leading to the use of single pool K_t/V (spK_t/V) as the standard for measuring dialysis adequacy. It was also learned from observational studies that a higher K_t/V was associated with improved clinical outcomes, but the HEMO trial—a large, randomized, controlled study—found no improvement in clinical outcomes when patients received higher K_t/V, leading to a definition of a spK_t/V of 1.2 as adequate hemodialysis.

Regarding clinical guidelines, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative recommended a spK_t/V of 1.2, with two options for determining K_t/V: urea kinetic models (UKM) or a multivariable equation, such as Daugirdas II. Comparing the effectiveness of different methods to determine dialysis treatment adequacy, UKM attempts to estimate explicitly all mechanisms of urea removal and generation and is used by some providers to guide dialysis prescription. Evidence exists that Daugirdas II is as good as UKM for estimating dialysis; several studies suggest that the urea reduction ratio (URR) does not always correlate with K_t/V as determined by UKM, so it is not used as the a primary measure of adequacy. There is no evidence that the use of UKM versus Daugirdas II leads to improved clinical outcomes.

Several research topics related to dialysis adequacy measures are recommended: comparative effectiveness research (CER) for K_t/V methodologies, identification of other uremic toxins for inclusion in determination of dialysis adequacy, and identification of other methods to improve the determination of adequate dialysis. Regarding volume control, stakeholders recommended topping off K_t/V, establishing the clinical relevance of volume control because it is linked to the patient's feeling of well-being, and conducting pragmatic trials on this topic. For patient selection for PD, research showed that patients prefer PD to HD, reporting better quality of life and satisfaction, and in the absence of evidence to support a difference in outcomes, the European Renal Best Practice Advisory Board recommends that the choice be made by the well-informed patient; research on patient selection for PD may lead to clinical guidelines for the United States. For dialysis treatment frequency, early research has produced varying conclusions, suggesting the need for CER or meta-analysis on existing research to evaluate the established norm of three times per week. Another research topic, which should include both Medicaid and private insurance patients, is high mortality at dialysis initiation, the causes of which might be investigated to promote better outcomes. There exists a knowledge gap about how to preserve renal function, including better management of water and electrolyte metabolism, anemia, and metabolism, which would lead to better outcomes in terms of less frequent use of dialysis and decreased use of erythropoietin (EPO) therapy. Implementation of new methodologies requires evidence-based research.

Discussion

- Dr. Narva commented that Dr. Jevaji had raised some of the most important clinical issues related to ESRD. The topics described might lead to interagency research efforts. He suggested that opportunities for collaborative research efforts with CMS be the focus of the next KICC meeting.
- Dr. Evered stated that she and CMS colleagues had started an ESRD affinity group in CMS that now has approximately 150 members. The group was planning to hold its first meeting, which Dr. Eggers and Dr. Abbott were to attend to talk about the history of ESRD and the birth of the

USRDS, but the meeting had to be rescheduled due to weather. She plans to compile a searchable list of members, including topics in which each member has expertise (i.e., "Ask me about…").

Adjournment

Dr. Narva thanked the attendees for their participation, apologized for the sound quality for those participating via telephone, and noted that the next meeting of the KICC is scheduled for September 25, 2015. He adjourned the meeting at 12:00 p.m. EDT.

Action Items

- Dr. Evered will invite the participants to join an interagency work group that will determine which data fields will be included in CROWNWeb.
- Dr. Narva will send a description of the October 2015 meeting of the NKDEP Health Information Technology Work Group to solicit volunteers from other Federal agencies to participate in the meeting or the Steering Committee.