

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

Kidney Interagency Coordinating Committee Meeting
June 18, 2010 – Natcher Conference Center

Meeting Participants and Summary

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I. Welcome and Introductions

Andrew Narva, MD

After participant introductions, Andrew Narva briefly explained the purpose of the Kidney Interagency Coordinating Committee (KICC) for the benefit of first-time participants. He also announced that the KICC Matrix will be updated and encouraged attendees to review their agencies' content and submit revisions.

While introducing the first speaker, Susan Crowley, Dr. Narva noted that the Department of Veterans Affairs (VA) and Department of Defense (DoD) serve populations at risk and have a track record for systematically altering how the healthcare system is structured to improve outcomes in chronic kidney disease (CKD).

Innovations in the Delivery of CKD Care in the VA and DoD Health Care Systems

II. Improving CKD Care for Veterans

Susan Crowley, MD

Dr. Crowley provided a brief history of dialysis care in the VA healthcare system, which has over eight million enrolled veterans and 200,000 professional support staff working in various hospitals and clinics. She compared past and current kidney disease statistics from VA, noting that the total number of veterans who require hemodialysis is projected to increase by approximately 6 percent by Fiscal Year 2015. She also discussed how VA has used a contracting group to help identify ways to provide cost-efficient care and reported on the four pillars of veteran care improvement as they relate to CKD:

1. Access to care,
2. Veteran-centered care,
3. Anticipate patient needs, and
4. Coordination of care.

To improve access to dialysis care, VA created an analysis tool to help predict the average cost of internal versus external treatment. It also proposed opening four free-standing dialysis units in regions chosen for their cost-saving abilities. Additionally, the program is exploring alternative financial models for providing dialysis, including the introduction of a national bundle rate and reinvigorating home dialysis to help improve rural healthcare. The program has tapped into the VA Innovation Initiative—a funding mechanism—to request solicitations for proposals that would address how to improve pre-ESRD care, as well as care for patients who need home dialysis.

To help improve access to pre-dialysis care for its CKD patients, VA is working to: open and expand its CKD clinics to non-traditional hours and days; recruit mobile vans to deliver specialty care within rural areas; provide specialist consultation via tele-health; train mid-level practitioners on the basics of CKD care in order to become a point-of-contact service for primary care clinics; and improve access to patient education materials through VA's "My HealtheVet" Program.

To help create veteran-centered care, the program will tap into existing VA registries to identify patients who are in need of targeted intervention and customized healthcare plans. **To anticipate veterans' needs**, the program plans to standardize CKD coding or workload identifiers throughout VA;

identify opportunities for additional professional education and/or patient education through a CKD metrics pilot; and improve drug safety by following patients on specific medications to mitigate the adverse effects.

To better coordinate care, VA is working towards reducing variability in care by providing clinical practice guidelines for the management of CKD within primary care. It currently offers training via webinars on how to use these guidelines. In addition, VA staff has created clinical practice guideline toolkits to serve as decision-support tools to help primary care physicians understand the guidelines and the basics of CKD. Lastly, the program established a dialysis steering committee that will provide programmatic analysis, oversight, and recommendations for how to change treatment of CKD and the delivery of ESRD services.

Dr. Crowley closed by saying that VA invites Federal collaboration and hopes to contribute to a historic change in the delivery of renal healthcare.

Participant Questions/Comments

- Dr. Narva suggested that VA may be able to learn from the Indian Health Service (IHS) in regards to contracting for ESRD care. As an example of inter-agency collaboration in the provision of care, he explained he provides tele-medicine from the National Institutes of Health to IHS patients in Zuni.
- Michael Flessner commented on his experience co-locating home dialysis units with CKD clinics in Mississippi. Dr. Flessner explained that co-location and training of practitioners, nurses, and associated staff in in-home peritoneal dialysis care help ensure that patients begin dialysis preparation and/or care at the time of referral. Dr. Crowley said that training is one of the goals of VA's home dialysis committee.

III. Measuring and Monitoring CKD Care through Data Collection and Analysis

Leonard Pogach, MD

Dr. Pogach reviewed the various types of data that VA collects, including prescription, diagnoses, procedures and self-report data. He pointed out the unique research applications within the Diabetes Epidemiology Cohorts (DEpiC), including quality assessment, quality improvement, cost of treatment, and evidence-based medicine. He discussed research methodologies and various findings across a broad range of issues, including incidence/prevalence of diabetes, CKD, and depression; intermediate outcomes in diabetes; longitudinal assessments of diabetes care; trends in HbA1c by subgroup; race and dialysis-free mortality among patients with diabetes and advanced CKD; facility-level variation in renin-angiotensin system (RAS) inhibitors and patient factors and RAS inhibitors; lower extremity complications; and diabetes clinical cohort elements, including lab values, glycemic medications, cardiovascular medications, comorbidities, and health care costs. He also presented aggregate data from the Veterans Health Administration Patient Care Services Diabetes Clinical Cohort, an operational database of patients with diabetes and multiple domains of demographic data, co-morbid conditions, laboratory and pharmacy data. Descriptive data presented demonstrates that a large number of veterans with presumptive CKD (serum creatinines >1.5 mg-2.5 mg/dl, and greater than 2.5 mg/dl on insulin had A1c values <7%.)

He closed his presentation by describing patient safety concerns, including generalization to individuals with multiple complex conditions who would have been excluded from clinical studies, such as Action to

Control Cardiovascular Risk in Diabetes, VA Diabetes Trial, Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation, and United Kingdom Prospective Diabetes Study . He expressed a concern that although public health systems emphasize intermediate outcomes such as A1c of <7% (e.g., Healthy People 2010, 2020) there are no monitoring system for harms such as hypoglycemia, and A1C measuring/reporting is not presented for cohorts with less benefit and greater harms (such as later-stage CKD).

Participant Questions/Comments

- Dr. Narva echoed Dr. Pogach’s messages about using high-level evidence and the importance of looking at patients individually.
- Dr. Williams acknowledged the importance of finding middle ground between public health and individual patient care, and asked for clarification regarding loss to follow-up and death in race data. Dr. Pogach responded that race data from his research took into account the issue of death, and noted that in prior publications (Thompson et al, HSR 2005) the findings were consistent when loss to follow-up analyses were performed.
- Ann Bullock noted that VA and IHS populations are similar and that IHS would be open to collaborating with VA. She also asked if VA has data on other markers, like poverty status. Dr. Pogach said that most VA patients are either of lower economic status and/or have disabilities. However, VA health outcomes (e.g. HEDIS measure comparison) are better than outcomes for the general US population.

IV. Improving Care for VA/DoD Beneficiaries with a CKD Toolkit

Angela Klar, RN, MSN, ANP-CS

Angela Klar began by reviewing her presentation’s objectives: describe the development process of the VA/DoD Evidence-Based Clinical Practice Guidelines (CPG), discuss the current VA/DoD CPG implementation approach, and identify tools available to support CKD CPG implementation.

The development process for VA/DoD Evidence-Based CPGs includes:

- A decision from the Evidence-Based Practice Working Group on what should be updated/developed;
- The selection of working group members to update/revise the guidelines; and
- A systematic review of the literature.

Once the review has been completed, working group members will select studies that meet inclusion criteria, analyze data, and formulate recommendations. The draft guidelines will be sent for public review and comment and, upon finalization, will be posted on the VA website which is linked to the DoD website. Last year, a group of multidisciplinary providers from VA, Army, Navy, and Air Force met to discuss CKD and the development of a toolkit to support CKD care and education. The group recommended NKDEP’s materials as a supplement to the toolkit and the agency is now working to print these and other new materials before the end of the fiscal year.

Ms. Klar showed participants the features of the web-based toolkit, which includes tools for provider support, patient self-management, and system support—some of which will be available online or on CD-Rom, while others will be available for all VA and DoD medical treatment facilities by ordering at no

charge through the DoD CPG shopping cart website. In addition to the website, VA/DoD plans to also develop a continuing medical education in-service to help providers understand CKD basics, the guidelines, and toolkit. VA/DoD has guideline implementation manuals for providers, facility champions, and VA/DoD guideline champions, as well as implementation worksheets and a champion brief to help facilities implement and monitor change. Lastly, DoD is working with AHLTA, its electronic medical records vendor, to add a button that leads to VA/DoD CPGs for reference.

In closing, Ms. Klar explained that DoD plans to evaluate these efforts by tracking web hits and performing a needs-assessment with providers regarding the extent to which the efforts support implementation of evidence-based strategies.

V. Progress Report on USPSTF Screening Guidelines for CKD

Therese Miller, DrPH and Christine Chang, MD, MPH

Therese Miller began by defining the United States Preventative Services Task Force (USPSTF) as a 16-member, independent, non-governmental panel which provides non-regulatory recommendations. AHRQ supports USPSTF by providing scientific, technical, and administrative support. USPSTF uses up-to-date evidence on benefits and harms and synthesizes it to create new and updated recommendations—for use by primary care clinicians—on screening, counseling, and medications to prevent illness.

In 2008, CKD screening was nominated for review by USPSTF by two outside groups, the National Kidney Foundation (NKF) and LabCorp. NKF was interested in screening high-risk populations; LabCorp was interested in screening for high risk for ESRD using estimated GFR. The topic was given a high priority for review by USPSTF and nominated through the effective healthcare program.

Christine Chang explained that the topic, Screening for Management of Chronic Kidney Disease Stages 1 to 3, reflects the combination of two topic nominations, the first by USPSTF (described above) and the second, by the American College of Physicians. The topic was assigned to an Evidence-based Practice Center (EPC) to proceed with further topic refinement (completed) and a comparative effectiveness review (underway). The review process entails getting input from multiple stakeholders, including key informants, technical experts, and the public. Dr. Chang listed the six questions that the research review will attempt to answer and briefly outlined the analytic framework. As a part of the research review and report, the EPC will identify research gaps and unanswered questions. In the future, the EPC will develop a formal document that outlines research needs and unanswered questions.

A draft report will be available for public comment in November on the Effective Health Care Program site and will undergo peer review. The final report will be released in February 2011 and posted on the site. In March 2011, USPSTF will meet to discuss screening recommendations based on the final report. The report and recommendations will be translated into patient guides, clinician guides, and other translational documents. Dr. Chang encouraged all participants to sign up for the Effective Health Care Program and Task Force email alerts.

Participant Questions/Comments

- Dr. Narva asked about the use of unpublished data during the review process. Dr. Chang responded that part of the systematic evidence search is looking for unpublished data.

VI. New Study Design and Dosing Adjustment Issues in Renal Impairment

Nancy Xu, MD

Nancy Xu began by acknowledging Dr. Shiew-Mei Huang, the Deputy Director in the Office of Clinical Pharmacology, for spearheading this effort. The current draft renal guidance was published for public comment in March of this year. This document is intended to provide guidance on both when to conduct renal impairment studies and the design and conduct of such studies to efficiently and effectively assess the impact of renal impairment on the pharmacokinetics (PK) of investigational drugs. Three new recommendations appear in the current draft, which was last revised in 1998.

1. **Renal impairment studies for drugs that are eliminated predominately via non-renal route.** Studies have shown increases in drug concentrations with renal impairment even for drugs that are eliminated predominately by non-renal route.
2. **GFR staging by MDRD, in addition to estimated creatinine clearance (eCrCl) (Cockcroft-Gault [CG]), as reference measures of renal function to enroll subjects into renal impairment studies.** A classification of renal function is used to ensure adequate enrollment/representation of subjects with various degrees of renal impairment (e.g., CKD stages one through five) and “normal” control in a dedicated renal PK study. By this parallel approach, the utility of any new and improved measure of renal function could be prospectively studied for drug dosing purposes.
3. **Studies in patients under both dialysis and non-dialysis (between dialysis) conditions.** This will help determine the extent to which dialysis contributes to the elimination of the drug and potentially active metabolites.

The draft guidance also includes an updated decision tree to determine when a renal impairment study is recommended and how to conduct such a study. The flow chart recognizes that in many cases the effects of impaired renal function can be evaluated initially with a reduced PK study design that studies the “worst case” in terms of the effect of renal impairment on PK.

FDA received approximately 20 comments from pharmaceutical/biopharmaceutical companies, organizations, and academic centers. They are revising the guidance as a result of the comments and planning training workshops.

Dr. Xu also briefed the participants on ongoing research at the Agency that compares the ability of equations to predict dose-related safety and efficacy.

Participant Questions/Comments

- Dr. Flessner commented that it is not difficult to find stage-five patients who are not on dialysis.
- Dr. Narva applauded FDA’s efforts to study different body types, age, and races and noted that dialysis is changing considerably so the clearances will be different. He added that patients with CKD and congestive heart failure should also be evaluated.
- Dr. Crowley asked if members of the European Union have a unified approach to drug dosing. Dr. Xu recalled that they recommend a measured CrCl (or its estimate by CG) or measured GFR with the 80/50/30 cutoffs as the ways to classify renal impairment and enroll subjects. Dr. Star confirmed this.

- Dr. Star asked about the possibility of replacing classification systems with continuous variables to eliminate the problems with the “edges.” Dr. Xu acknowledged that it is a good point, and that other thought leaders also have advocated for this approach. Dose adjustment with renal function as a continuous variable would require multiple dosage forms, not usually the case for oral formulations. It is more feasible with IV formulation.
- Dr. Pogach asked if there is a possibility of FDA revisiting current label recommendations for older medications that could be effective and safe in lower doses. Dr. Xu responded that it might be difficult to find the needed data sets for such medications to perform meaningful analyses.

VII. Agency Updates

- Dr. Williams announced that the CDC’s CKD fact sheet is complete and will be available on CDC’s website soon. He provided a printed version of the fact sheet for KICC members.
- Dr. Narva announced that NKDEP is developing a comprehensive resource for educating people with CKD, which can be used to support the new Medicare-covered Kidney Disease Education services. The tool will incorporate patient and provider materials and content developed by NKDEP, National Kidney and Urologic Diseases Information Clearinghouse, and other agencies/programs. NIDDK is also planning a meeting to discuss type II translation research for CKD. Dr. Star added that NIDDK has hosted similar initiatives in the area of diabetes and believes this initiative will be a good way for researchers to obtain funding to test creative ways of communicating messages.
- Shona Pendse updated participants on two FDA projects. The first, which focuses on polycystic kidney disease, is reviewing data standards to help make regulatory decisions. The program has collaborated with academia and industry, specifically NIH, to gather prospective and retrospective data into a common database to eventually facilitate drug development. The second program, in collaboration with NKF, has started to review patient-reported outcomes in CKD and will host a workshop at FDA in September.

VIII. Closing Remarks

Dr. Narva

Dr. Narva closed the meeting with an announcement about the next meeting in January 2011 and suggested the meeting’s agenda include an update on USPSTF Screening Guidelines for CKD, Healthy People 2020, the revised Quality Improvement Organization scope of work on CKD, and the Chronic Renal Insufficiency Cohort Study. He also encouraged participants to submit ideas for additional topics for the next meeting.