

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

Kidney Interagency Coordinating Committee (KICC) Meeting

September 14, 2012, Natcher Conference Center

Meeting Participants and Summary

Kevin Abbott, MD, MPH, COL, MC

Professor of Medicine, *Uniformed Services
University of the Health Sciences*
Nephrology Service, *Walter Reed Army Medical
Center*

Joel Andress, PhD

Medical Officer, Division of Quality Improvement
Centers for Medicare & Medicaid Services

Clarice Brown, MS

Division Director, Division of Health Care
Statistics National Center for Health Statistics
Centers for Disease Control and Prevention

Christine Chang, MD, MPH

Medical Officer, Center for Outcomes and
Evidence
Agency for Healthcare Research and Quality

Paul Eggers, PhD

Program Director, Kidney and Urology
Epidemiology
*National Institute of Diabetes and Digestive and
Kidney Diseases, NIH*

Dan Garver, PhD

Senior Writer
*National Kidney and Urologic Diseases
Information Clearinghouse, NIH*

Michael Flessner, MD, PhD

Senior Scientific Officer, Division of Kidney,
Urologic, and Hematologic Diseases
*National Institute of Diabetes and Digestive and
Kidney Diseases, NIH*

Gregory Germino, MD

Deputy Director
*National Institute of Diabetes and Digestive and
Kidney Diseases, NIH*

Mary Hand, RN, MSPH

Coordinator, Office of Prevention, Education,
and Control
National Heart, Lung, and Blood Institute

Frank Hurst, MD, FACP, FASN

LCDR, USPHS
Medical Officer, Gastroenterology and Renal
Devices Branch
Food and Drug Administration

Kevin McBryde, MD

Program Director, Office of Minority Health
Research Coordination
*National Institute of Diabetes and Digestive and
Kidney Diseases, NIH*

David Miller, MD, MPH

Health Science Policy Analyst
*National Institute of Diabetes and Digestive and
Kidney Diseases, NIH*

Andrew Narva, MD, FACP

Director, National Kidney Disease Education
Program
*National Institute of Diabetes and Digestive and
Kidney Diseases, NIH*

Eileen Newman, MS, RD

Associate Director, National Kidney Disease
Education Program
*National Institute of Diabetes and Digestive and
Kidney Diseases, NIH*

James Oliver III, MD, PhD

Colonel, Medical Corps, U.S. Army
Nephrology Service, *Walter Reed Army Medical
Center*
Nephrology Consultant to the Office of The
Surgeon General
Associate Professor and Director, Nephrology
Division, *Uniformed Services University of the
Health Sciences*

Eduardo Ortiz, MD, MPH

Senior Medical Officer, Division for the
Application of Research Discoveries
Senior Advisor, Center for Biomedical Informatics
National Heart, Lung, and Blood Institute, NIH

Uptal Patel, MD

Associate Professor of Medicine and Pediatrics
Duke University School of Medicine

Shona Pendse, MD, MMSc

Medical Officer
CDER, Division of Cardiovascular and Renal
Products
Food and Drug Administration

William Polglase, BA

Press Officer
Office Communications & Public Liaison
*National Institute of Diabetes and Digestive and
Kidney Diseases, NIH*

James Smith, MD, MS

Medical Officer, Division of Metabolism &
Endocrinology Products
Food and Drug Administration/CDER

Kimberly Smith, MD, MS

Medical Officer, Division of Quality Improvement
Policy for Chronic and Ambulatory Care
Quality Improvement Group, Office of Clinical
Standards and Quality
Centers for Medicare & Medicaid Services

Robert Star, MD

Director, Division of Kidney, Urologic, &
Hematologic Diseases
*National Institute of Diabetes and Digestive and
Kidney Diseases, NIH*

Aliza Thompson, MD

Medical Officer
Food and Drug Administration

Desmond Williams, MD, PhD

Team Lead, CKD Initiative, Division of Diabetes
Translation
National Center for Chronic Disease Prevention
and Health Promotion
Centers for Disease Control and Prevention

Tracy Wolff, MD, MPH (By Phone)

Medical Officer, USPSTF Program
Center for Primary Care, Prevention, and
Clinical Partnerships
Agency for Healthcare Research and Quality

I. Welcome and Introductions

Andrew Narva, MD, FACP

Dr. Narva welcomed committee members and thanked them for their participation.

The committee was created by Congress in 1987 and is mandated to meet yearly. The goal of the committee is to encourage cooperation, communication, and collaboration among all federal agencies involved in kidney research and other kidney-related activities. At the request of participants, the frequency of meetings was increased to two per year.

II. Collecting Creatinine Data on NCHS' National Ambulatory Medical Care Survey

Clarice Brown, MS

The National Center for Health Statistics (NCHS) will begin collecting serum creatinine data on the National Ambulatory Medical Care Survey (NAMCS) in 2013. The NAMCS is part of NCHS' National Health Care Surveys (NHCS), a family of nationally representative surveys of health care providers and encounters with the health care system.

NCHS's health care surveys differ from others conducted by NCHS in that they survey establishments, not households. Instead of providing estimates of the population, they provide estimates about encounters with health care providers. The surveys are:

- Nationally representative;
- Provider based;
- General purpose;
- Objective (record-based) clinical information;
- Multi-level data structure;
- Large sample sizes; and
- Flexible.

The surveys also collect a wide range of data on provider organizations, clinicians, patients, and encounters. For the surveys, patient-level data is largely abstracted from medical records (electronic or paper based) or administrative claims. Since 2010, NAMCS and NHAMCS have been collecting lab data associated with encounters (cholesterol, triglycerides, fasting blood glucose). In 2013, serum creatinine will be added.

National Health Care Surveys

- National Ambulatory Medical Care Survey (NAMCS) - collects data on physician offices/community health centers and the care provided in these settings.
- National Hospital Ambulatory Care Survey (NHAMCS) - collects data on hospital outpatient departments, emergency departments, ambulatory surgery centers, and free-standing ambulatory surgery centers.
- National Hospital Discharge Survey (NHDS) - collects data on inpatient discharges from hospitals (will be replaced with the National Hospital Care Survey in 2013).
- National Study of Long-Term Care Providers

NAMCS

The goals of the NAMCS are to: 1) produce national statistics on ambulatory care utilization; 2) provide data for health policy formulation; and 3) provide comparative data for medical practice management. The sample includes 3,000 non-federal, office-based physicians and 104 community health centers. Participation is voluntary.

In 2013, the sample size will be increased to nearly 20,000 physicians and the sample of community health centers will be increased to 2,000. To manage this increase, NCHS moved from a paper-based to an electronic data collection system. These changes will allow NCHS to increase the NAMCS sample for state-based estimates (for 34 states).

NCHS will also be implementing a "look back" module for both NAMCS and NHAMCS to evaluate the quality of care to prevent heart disease and stroke. Data will be abstracted from the previous 12 months. Serum creatinine data will be collected as part of the look back module.

III. AHRQ Evidence Review for Screening for and Management of CKD

Evidence Report on Management of Chronic Kidney Disease Stages 1-3

Christine Change, MD, MPH

The evidence report on management of CKD stages 1-3 was released in January 2012. The report was used by the U.S. Preventive Services Task Force (USPSTF) to develop recommendations and the American College of Physicians will be developing clinical guidelines based on the report. AHRQ is developing resources related to the evidence report for both clinicians and patients.

This evidence report on management of CKD addresses both screening and treatment.

Screening

Study Inclusion Criteria

- Age \geq 18 yrs with no known CKD

- Randomized ≥ 1000 subjects to screening vs. control
 - Approaches: eGFR, microalbuminuria, macroalbuminuria, combination, others
 - Distinct from assessments of renal function as part of regular clinical care
- Follow-up ≥ 1 yr

Studies

No studies were identified that linked screening to direct clinical outcomes. The authors did look for indirect evidence of screening in several areas including prevalence, association with adverse health consequences and/or costs, early identification of CKD, acceptability of testing, and effective treatment for health outcomes.

Conclusions

- Evidence is insufficient to determine if screening for or monitoring of early stage CKD improves clinical outcomes.
- Indirect evidence suggests that screening and monitoring may benefit specific subgroups of patients.

Treatment

Study Inclusion Criteria

- Aged ≥ 18 yrs with CKD stages 1-3
- Randomized ≥ 50 subjects to treatment vs. control
- Follow-up ≥ 6 mos.
- Reported clinical outcomes or harms

Studies

The authors looked at treatment studies in the following areas:

- ACEI vs. placebo
- ARB vs. placebo
- Beta-blocker vs. placebo
- Calcium channel blocker vs. placebo
- Calcium channel blocker vs. beta-blocker
- Statin vs. a control
- Strict vs. standard blood pressure control
- Low-protein diet vs. usual diet
- Carbohydrate-restricted, low-iron-available, polyphenol-enriched diet vs. low-protein diet

Included Treatment
• Angiotensin-converting enzyme inhibitor
• Angiotensin II receptor blocker
• Calcium channel blocker
• Beta-blocker
• Diuretic
• Various diets
• Multi-component interventions

Conclusions

- In patients with CKD stages 1–3 who have overt proteinuria (macroalbuminuria) with concomitant diabetes and hypertension, an ACEI or an ARB will reduce the risk of end-stage renal disease (ESRD).
- In patients with CKD stages 1–3 with only microalbuminuria or impaired eGFR, ACEIs did not reduce the risk for ESRD when compared with a placebo, but these trials were not powered to detect a difference.
- There was no increased benefit for reducing the risk of ESRD if an ACEI and an ARB were taken as combination therapy when compared with taking either an ACEI or an ARB alone.
- Taking an ACEI or an ARB did not reduce the risk of mortality, except when an ACEI was used for patients with microalbuminuria and cardiovascular disease or diabetes and other cardiovascular risk factors.
- Statins reduced the risk for mortality, myocardial infarction, and stroke in patients with hyperlipidemia and impaired eGFR.
- Beta-blockers may reduce mortality in patients with congestive heart failure and impaired eGFR.

- Many patients who experienced improved outcomes had a pre-existing clinical indication for the treatment studied regardless of CKD status.
- Adverse events were reported in but a few clinical trials. Those reported generally were consistent with known potential adverse effects of these treatments.

USPSTF Recommendation on Screening for CKD

Tracy Wolff, MD, MPH

The USPSTF released its final recommendation on screening for CKD in adults in August 2012. It concluded that the evidence is insufficient to assess the balance of benefits and harms of routine screening for CKD in asymptomatic adults. The USPSTF also reviewed indirect evidence concerning the harms and benefits of screening. Indirect evidence was found related to:

- Accuracy of screening for CKD;
- Yield of CKD screening;
- Treatment improving outcomes in CKD patients who might be identified by screening; and
- Limited harms resulting from CKD screening.

While there are no data related to the possible harms of CKD screening there is indirect evidence. The chain of indirect evidence related to the benefits and harms of CKD screening indicate:

- Unrecognized CKD prevalent, especially with albuminuria;
- Sensitivity/specificity of CKD screening uncertain;
- Treatment benefits limited to specific CKD subtypes (e.g. eGFR) and co-morbidity subgroups;
- Many patients already with treatment indication or on treatment regardless of whether they have CKD; and
- Harms of CKD screening are uncertain.

Per expert opinion, potential harms may include:

- Adverse effects of screening and follow-up tests;
- Adverse effects of treatment;
- Misclassification/false positive diagnosis/labeling;
- Unneeded tests to follow up false positive screens;
- Increased clinic visits, including to kidney specialists; and
- Difficulty with health insurance coverage.

Indirect evidence suggests CKD screening benefit, if it exists, is most likely limited to specific subgroups, comprising a minority of patients. These subgroups include patients with co-morbid conditions, such as diabetes and/or hypertension, who are not already on treatment or with indication, and people with certain subtypes of CKD (e.g., impaired eGFR, macroalbuminuria).

Based on the review of evidence, the USPSTF made the following suggestions for practice. These suggestions are intended to help clinicians and patients make treatment decisions.

- CKD is very prevalent. Most people affected have risk factors for CKD, particularly older age, diabetes, and hypertension.
- CKD is usually asymptomatic until its advanced stages. Although there is no evidence on the benefits and harms of screening in the general population of asymptomatic adults, evidence shows that specific treatments for patients with diabetes reduce risk for advanced CKD.
- The American Diabetes Association recommends screening for CKD in all patients with diabetes. The USPSTF found very limited evidence about whether knowledge of CKD status in patients with isolated hypertension helps in making treatment decisions. However, several organizations

recommend screening patients who are being treated for hypertension, including the Joint National Committee (JNC).

- There are no studies on the benefits of early treatment in persons without diabetes or hypertension.
- Persons who have positive results on a screening test for CKD but do not have CKD may experience the harms associated with interventions and treatments without the potential for benefit.
- Many patients with CKD stages 1 to 3 seem to have at least some testing in usual clinical care, probably for other conditions or in response to guidelines from other organizations

The recommendations are available on the USPSTF website at <http://www.uspreventiveservicestaskforce.org>. A fact sheet that explains the recommendation statement in plain language is also available.

IV. Urine Albumin Standardization

Andrew Narva, MD, FACP

Educating clinicians about the uncertainty in the laboratory assessment of CKD is an ongoing challenge. While the estimated equations perform fairly well for populations, at the patient level, the best assessments available can give a wide range of results, which can impact the clinician's ability to diagnose the condition. Urine albumin measurements are key to public health, measuring response to clinical treatment, and are important biomarkers in research.

Since the urine albumin test is not standardized, the results do not provide the necessary precision for diagnosis of CKD. Yet, approximately half of the people with CKD are diagnosed as a result of albuminuria.

Standardizing the measurement and reporting of urine albumin will be a challenge technically, in implementation, and in educating clinicians. It has implications for drug review, for performance measures, and for public health assessment. Challenges related to standardization include:

- Pre-analytic factors (e.g., time of collection, type of collection container);
- Lack of reference system for urine albumin or urine creatinine; and
- Interpretive criteria (e.g., minimal evidence base for current cut off).

NIDDK's Laboratory Working Group (LWG) is supporting research in this area.

Evaluation of Harmonization of Urine Albumin Measurement

Project Objectives

- Assess the current state of harmonization among routine urine albumin methods vs. an ID-LCMS cRMP using native patient samples
- Evaluate analytical performance characteristics among methods
- Evaluate commutability characteristics of JSCC and diluted ERM-DA470k/IFCC reference materials
- Assess utility of candidate reference materials for use in standardization of routine methods

Observations

- Difference range in agreement among medians: ~40%
- Bias of routine methods vs. cRMP as slope: 0.82 – 1.34
- Freeze-thaw effects were not significant (<1% difference in medians)

Study Design

- 333 native samples collected for routine urine albumin measurement
- Non-frozen aliquots measured by 16 routine methods
- Frozen aliquots measured by LCMS
- Fresh-frozen paired samples for assessment of freeze/thaw effects
- Study QC materials used to estimate imprecision
- JSCC and diluted IRMM cRMs included

- Dilution caused changes in bias for some methods
- Imprecision as CV (total):
 - 9 methods \leq 5%
 - 2 methods 6-10% (plus LCMS)
 - 5 methods $>$ 10%
- Sample specific effects: 4-8% CV

The study indicates the lack of precision in the measurements, which has significant clinical implications. Providers do not understand the meaning of albuminuria and are unable to use quantitative albumin effectively. The reporting methods are confusing (e.g., use of the terms microalbuminuria and macroalbuminuria) and variable (e.g., different cut off rates, differences across race and gender). The existing recommendations related to urine albumin also vary.

To further support standardization, the LWG convened a conference in 2007 and formed a joint working group with the International Federation in Clinical Chemists (IFCC). An article describing the challenges was published in *Clinical Chemistry* in 2008. Also in 2008, NIDDK provided funding to develop:

- Reference measurement procedure;
- Reference material for urine albumin;
- Reference material for urine creatinine; and
- Reference ranges for ACR and AER.

Work is progressing on the funded projects. As they develop findings, the evidence will be provided to stakeholders for more discussion and to develop consensus.

V. NKDEP's New Health Information Technology Working Group

Uptal Patel, MD

NIDDK's focus on health information technology (HIT) grew out of a pilot project that funded six community health centers. The goal of the project was to improve patient outcomes through the use of simple performance measures. During the course of the study, all the community health centers began using electronic health records (EHR), with each center in the study adopting a different EHR. Because the EHRs were not compatible, it was impossible to collect and compare the data in a systematic way. This failure emphasized the many factors involved in the adoption of HIT.

NIDDK has convened a HIT Working Group to support researchers, clinicians, and patients. The goal of the Work Group is to enable and support the widespread interoperability of data related to kidney health to optimize CKD detection and management among software applications. This effort will help to support the free flow of information through EHRs, personal health records, decision support systems, disease registries, surveillance systems, and other sources of health information. In addition, the activities of the Work Group will also support efforts to achieve meaningful use requirements, promote CKD surveillance and registries, provide data for research, and improve management of CKD through integration with emerging technologies. The major challenges will continue to be the interoperability of systems and the incorporation of patient information.

NIDDK has identified members for the Working Group and will be adding more members over time. The Working Group also welcomes input from KICC participants. During the course of the work, the Working Group will be engaging the essential stakeholders from decision-makers, key influences, advocacy groups, providers, payers, and patients.

Adjournment

Dr. Narva announced that the next KICC meeting is scheduled for March 15, 2013.