

April 6, 2011

Agency for Healthcare Research and Quality  
Effective Healthcare Program

RE: AHRQ Draft Comparative Effectiveness Review (CER) on Screening for and Management of Chronic Kidney Disease Stages 1-3

To Whom It May Concern:

On behalf of the American Society of Nephrology (ASN), a not-for-profit organization of 11,000 physicians and scientists dedicated to promoting excellence in the care of patients with kidney disease, thank you for the opportunity to provide comment on the Agency for Healthcare Research and Quality (AHRQ) Draft Comparative Effectiveness Review (CER) on Screening for and Management of Chronic Kidney Disease Stages 1-3. ASN members are committed to providing the best possible care and want to help ensure that physicians have the information necessary to make the most appropriate decisions concerning screening for, monitoring of, and treating, chronic kidney disease (CKD) for their patients, regardless of age, gender, or race/ethnicity.

CKD is a serious and growing public health threat. Most people with CKD are unaware they have the disease until the late stages, but when identified early, its progression can be slowed or halted. ASN supports AHRQ's efforts to address this issue through a draft CER, and appreciates that AHRQ took into account comments that ASN submitted in March 2010 as the agency was initiating work on the CER. ASN respectfully submits the following comments regarding the March 2011 draft CER on Screening for and Management of Chronic Kidney Disease Stages 1-3.

### **Lack of evidence on effectiveness of screening vs. Evidence that screening is ineffective**

The draft CER focuses on endpoints for end-stage renal disease (ESRD), cardiovascular disease (CVD), and all-cause mortality as the primary clinically meaningful outcomes, as these are the endpoints for most of the randomized clinical trials (RCTs) where screening benefit can be examined. A central theme of the draft CER is that insufficient evidence exists showing that screening for Stage 1-3 CKD would translate into effective interventions to improve outcomes.

ASN wishes to clarify, however, that a lack of evidence is not the same as evidence that screening, or subsequent intervention, are not effective. For instance, investigators have reported that CKD patients have traditionally been excluded from clinical trials of coronary artery disease (Charytan et al., *Kidney Int* 2006; 70: 2021-30). In particular on page 25, the draft CER suggests a rather negative viewpoint of screening benefits. ASN suggests that this be tempered to reflect the difference between a lack of available evidence and evidence that screening is not effective. ASN recommends that this subtle but important perspective should be added on page 25, and throughout the report, as AHRQ finalizes the draft CER.

## **High-risk patients: Minority populations**

ASN is concerned that the issue of patient race/ethnicity is relatively neglected in the CER. It is well-recognized that non-Caucasian groups, particularly African-Americans and Latinos, have an elevated risk for developing ESRD. The risk of developing CKD and ESRD in these groups is likely not explained entirely by the higher prevalence of diabetes and hypertension in these populations. African-Americans, for example, are at disproportionate risk for developing Focal Segmental Glomerulosclerosis (FSGS) and primary glomerulopathy. ASN strongly suggests that AHRQ reconsider whether non-caucasians might benefit from screening—especially among non-Caucasian patients who have a family history of kidney disease. ASN recognizes that insufficient data may exist regarding the benefits of screening in these subgroups, but recommends that more research be conducted in order to ensure the highest quality of care is available to patients of all races and ethnicities.

## **Relationship between early CKD and quality of life measures**

A recent and growing body of literature reports on the association between early CKD and quality of life (QOL) measures, such as cognitive and physical function. (Please refer to work by M. Kurella-Tamura, K. Yaffe, S. Jassal, and others in recent years for cognitive function, and to results from the Dynamics of Health, Aging and Body Composition study (M. Odden and M. Shlipak) and the Nurses' Health Study (J. Lin and G. Curhan) for physical function. These QOL outcomes represent an important public health issue in the aging U.S. population who are at risk for both CKD and QOL decline. While screening and intervention for early CKD on these QOL outcomes have yet to be demonstrated because awareness of this relationship has only recently been growing, ASN suggests that AHRQ should consider incorporating QOL outcomes besides those of ESRD, CVD, and all-cause mortality.

## **Effect of Screening on Treatment**

With regard to whether evidence exists that systematic screening or routine care that identifies CKD stages 1-3 amongst adults leads to treatment that affects clinical outcomes, the authors state that there is no evidence that treating patients with greater doses of angiotensin converting enzyme inhibitors or angiotensin receptor blockers (ACE/ARB) or beta blockers (BB) improve clinical outcomes. They therefore conclude that the evidence for screening affecting treatment would be low.

ASN suggests that AHRQ consider whether patients in the trials studied were treated to pre-specified treatment goals (such as a specific blood pressure goal range). If patients in the studies were treated to goals, then screening might be useful in some cases—such as, for instance, for patients who are already under care for a given condition (e.g. high blood pressure).

## **Plasma creatinine measurement vs. Direct glomerular filtration rate measurement**

The abstract of the draft CER states that "GFR testing is already common in usual care". ASN wishes to clarify that, it is plasma creatinine measurements, which in turn yield an estimated GFR (eGFR), that are common in usual care. Importantly, the eGFR is not a direct measurement of GFR, which the sentence as currently worded might imply. Furthermore, some primary care providers are strongly encouraged to not obtain "unnecessary" tests on otherwise healthy patients. Based on anecdotal feedback from members of ASN's CKD Advisory Group, relatively few patients receive plasma creatinine measurements or, perhaps more importantly,

screening for microalbumin if there are no existing risk factors. As such, ASN suggests that AHRQ may wish to modify this sentence in the abstract to clarify the difference between plasma creatinine and eGFR measurements and to consider rephrasing the prevalence of such testing amongst patients with no existing risk factors.

## **Future Research**

ASN concurs with principle outlined in the “Future Research” section that more investigation is necessary to fully understand the benefits and harms of screening for CKD. The “Future Research” section appropriately notes that the “most direct [research direction] would be to conduct a large-scale RCT of CKD screening plus treatment for confirmed diagnoses versus usual care... However, such an RCT likely would require tens of thousands of participants followed for a dozen or more years to have adequate power to evaluate final clinical outcomes. Such a study is not likely to be feasible.” It also appropriately reviews cost-effective alternatives, such as prospective evaluations of the impact of Kidney Early Evaluation Program (KEEP) and other existing screening programs, which could provide some useful information without requiring a trial. In the future, these data could be used with simulation models to help inform policy decisions and future patient care recommendations.

ASN suggests that the draft CER specify the potential harms that leaders of large cohort screening studies, such as KEEP, should be aware of. For instance, a final CER could include explicit mention of the potential for over-diagnosis leading to unnecessary workups, as well as issues related to labeling.

An additional consideration for future research that was not mentioned in the draft CER is the possibility of targeting suitable funded cohort studies or clinical trials (either on-going or starting) for additional resources to collect biosamples and data on renal parameters for eGFR and albuminuria. This may represent a cost-efficient and scientifically strong approach to addressing the relevant issues raised in the document.

AHRQ also may wish to consider recommending that, as future studies are conducted, investigators could weigh screening for eGFR and macroalbuminuria. If one were to screen for macroalbuminuria, which clearly identifies increased risk of progression to ESRD, then screening interventions might be proven useful and could possibly be studied in a trial since the outcomes would be more proximal.

Finally, given the significance of the growing CKD burden and the importance of building consensus for support of the final CER within the kidney community, ASN recommends that AHRQ convene a meeting of kidney community stakeholders—including ASN, the National Kidney Foundation, and the National Institutes of Diabetic, Digestive, and Kidney Disease—to discuss the draft CER.

On behalf of ASN, thank you for your willingness to consider these comments regarding the draft CER on Screening for and Management of CKD Stages 1-3. ASN would be pleased to discuss these comments with the Effective Healthcare Program if it would be helpful at any time. Please feel free to contact ASN director of Policy and Public Affairs, Paul C. Smedberg, at (703) 625-3366 or at [psmedberg@asn-online.org](mailto:psmedberg@asn-online.org).

Sincerely,

A handwritten signature in black ink that reads "Joseph V. Bonventre". The signature is written in a cursive style with a long horizontal flourish extending to the right.

Joseph V. Bonventre, MD, PhD, FASN  
President, American Society of Nephrology