

# Screening for Chronic Kidney Disease: Time to Say No

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## Introduction

Chronic kidney disease (CKD) is common and often asymptomatic at the time of diagnosis. Yet CKD is associated with substantial increases in the risk for cardiovascular (CV) events and overall mortality. These facts suggest the potential value of population-based screening for CKD.

However, the US Preventive Services Task Force (USPSTF)<sup>[1]</sup> and American College of Physicians (ACP)<sup>[2]</sup> have not recommended broad screening for CKD, citing a lack of evidence that screening improves important outcomes. The American Society of Nephrologists (ASN)<sup>[3]</sup> retorts that all adults should undergo periodic screening for CKD.

Who is right? The current review examines the science behind these recommendations and offers a solution for the busy primary care clinician.

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## Background

Your next clinic patient is new to your practice. She is a 50-year-old woman who has been experiencing headaches and dizziness. She also told your medical assistant that she has chest pain on occasion during exercise. You complete a thorough evaluation with a history and physical examination for these problems but, thankfully, find no red flags.

You are about to discuss treatment options when she stops you. "Oh!" she says, "I'm so happy that you're taking the time to listen to me. I haven't been to the doctor in ages, but now that preventive care is covered by insurance, I wanted you to order 'the sampler.' Ha ha! No, but really, can you refer me for everything that I need? I promise to get it done!"

A well-performed study of over 46,000 outpatient primary care visits found that the average visit lasts approximately 20 minutes.<sup>[4]</sup> The research also demonstrated that the average number of clinical items addressed in these encounters was 7, with a temporal trend toward a reduced amount of time devoted to each issue between 1997 and 2005. The case described above

provides an example of the competing agendas that change and change again during an ordinary clinic visit.

What does it take to navigate these complexities? First, it requires a patient-centered approach. A systematic review and meta-analysis found that physicians trained in empathic care with an emphasis on communication were able to change their practice habits, even after a brief intervention.<sup>[5]</sup> However, only more complex programs were found to be reliably effective in improving patient health behaviors and satisfaction. The mixed results of this body of research reconfirm how challenging these outcomes are.

But good communication and people skills are not enough. Good primary care physicians know their science and are able to inform patients with understandable and pertinent data to practice shared decision-making. This includes an understanding of current guidelines for preventive care. If we as primary care physicians cannot provide evidence-based preventive care, who will?

So, let's summarize the arguments for and against screening everyone for CKD.

#### The Evidence for Screening

Medical conditions need to fulfill certain criteria in order to be recommended for screening.<sup>[6]</sup> They need to be detectable at an asymptomatic stage, and there must be an adequate screening test available. The screened condition must be amenable to an available intervention after screening that improves the chances of healthy outcomes, and the cost of this process should be acceptable to society.

There is no doubt that CKD fulfills at least some of these criteria. CKD is common and frequently undiagnosed, although the precise prevalence of undiagnosed CKD varies substantially with the population studied and the methods used to diagnose CKD. In a study of nearly 25,000 adults with at least 2 measurements of their estimated glomerular filtration rate (eGFR), the prevalence of CKD was 28.2%.<sup>[7]</sup> Only 26.5% of patients with evidence of CKD had an established clinical diagnosis of kidney disease. Studies conducted in India and Iceland found rates of CKD among community-dwelling adults that ranged between 4% and 13%, and the prevalence of proteinuria was 0.9%-2.4%.<sup>[8,9]</sup>

CKD is not only common, but it is also associated with profound health risks. A retrospective analysis of data from over 1 million adults found that compared with adults with an eGFR of 60 mL/min/1.72 m<sup>2</sup> of body surface area or more, the adjusted hazard ratios for both mortality and CV events increased linearly as eGFR declined (Table).

**Table. Mortality HR With Declining eGFR <sup>[10]</sup>**

eGFR (mL/min/1.72 m <sup>2</sup> )	Mortality HR	CV Event HR
45-59	1.2	1.4
30-44	1.8	2.0
15-29	3.2	2.8
< 15	5.9	3.4

*CV = cardiovascular; eGFR = estimated glomerular filtration rate; HR = hazard ratio*

A meta-analysis published in 2010 confirmed the positive association between eGFR and the risk for death, and also found a linear trend toward a higher risk for death as the degree of albuminuria increased. <sup>[11]</sup> Albuminuria and eGFR were independent variables associated with a higher risk for death in this study.

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### **The Evidence Against Screening**

Nonetheless, the USPSTF and ACP have failed to endorse routine screening for CKD among asymptomatic adults without substantial risk factors, such as diabetes or hypertension. <sup>[1,2]</sup> The principal argument against screening for CKD is the lack of randomized trials comparing outcomes in screened vs nonscreened adults. But both venerable organizations describe other specific problems with generalized screening for CKD.

The USPSTF acknowledges the lack of a unified definition of CKD and the variability of testing results. For example, intraindividual variability for urinary albumin testing may be as high as 50%. Moreover, the USPSTF casts doubt on whether the discovery and treatment of CKD among asymptomatic adults improves clinical outcomes. Specifically, they cite a lack of studies regarding early treatment of CKD among persons without diabetes or hypertension. The USPSTF could not find a precise estimation of harms associated with CKD screening, although they imply that some patients would suffer false-positive diagnoses and adverse events associated with treatment.

The ACP argument follows these same lines, but provides more of a focus on the treatment of CKD. Angiotensin-converting enzyme inhibitors (ACEIs) can retard the progression of CKD to end-stage renal disease (ESRD). However, there is no evidence that ACEIs afford this same

benefit to patients with isolated impaired GFR or albuminuria, and ACEIs have a weak, if any, effect on the risk for mortality among patients with CKD.

Angiotensin II receptor blockers (ARBs) similarly can reduce the risk for ESRD among patients with CKD. However, they are unproven among CKD patients without hypertension or diabetes, and ARBs are not associated with a CV or mortality benefit among patients with CKD alone. In contrast, statins also do not have an effect on the risk for ESRD among patients with CKD and dyslipidemia, but they are associated with improved CV and overall mortality outcomes.

The ACP also goes beyond a recommendation against the universal screening of adults for CKD. They recommend against testing for urinary protein among patients treated with an ACEI or an ARB, even among patients with diabetes. In their rationale for this recommendation, they cite a lack of evidence of the benefits of monitoring proteinuria.

#### The ASN Response

The USPSTF recommendations finding insufficient evidence to support universal screening for CKD were released in 2012. The more robust ACP recommendations specifically advocating against routine screening were published in December 2013. In between the release of these documents, the ASN released the contrarian viewpoint that all patients should be screened for kidney disease.<sup>[3]</sup>

The ASN acknowledges the ACP's position, but argues that the identification of patients with CKD can help to prevent episodes of acute kidney injury mediated by nephrotoxic drugs or radiographic contrast agents. The ASN also underscores the critical role for hypertension and diabetes in promoting CKD, but they provide nowhere near the degree of evidence delivered by the USPSTF and ACP.

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#### **The Bottom Line for Primary Care**

The ASN has a good point regarding the possibility of iatrogenic kidney injury among adults with unrecognized CKD. However, given the ubiquity of screening laboratory work for patients in the hospital and clinics, the risk for these injuries should be minimized with routine conscientious practice.<sup>[12]</sup>

In trying to reconcile these disparate recommendations, it is helpful to remember that all 3 guidelines discuss the relationship among hypertension, diabetes, and CKD. The vast majority of cases of CKD are related to diabetes and hypertension. However, between 1988 and 1994, the prevalence of undiagnosed diabetes among US adults was estimated to be 2.7%.<sup>[13]</sup> This level

remained stable through 2002 but was twice as high among non-Hispanic black adults and Mexican-American adults compared with non-Hispanic white adults. <sup>[14]</sup> It is not only adults who might have unrecognized diabetes. Among adolescents, the rate of undiagnosed diabetes has been found to be 0.12%. <sup>[15]</sup>

Hypertension may similarly be underdiagnosed. Data from the National Health and Nutrition Examination Survey found that the overall prevalence of hypertension among US adults between 1999 to 2004 was 28.9%, and disease was undiagnosed in 28.2% of these patients. <sup>[16]</sup> Another study demonstrated that the prevalence of CKD among individuals with undiagnosed hypertension was 22.0%, which was nearly twice the rate of adults with normal blood pressure. <sup>[17]</sup>

It is clear that we must do a better job in identifying individuals with chronic high blood pressure and diabetes. Rather than using precious time to chase the unproven practice of generalized screening for CKD, doesn't it make more sense to focus on screening for the disease states that promote CKD, as well as other critical outcomes, such as CV disease and mortality? Discover the hypertension or diabetes, and the CKD will often reveal itself. Moreover, physicians can feel confident that renoprotective therapy in the context of hypertension and diabetes is effective, whereas this is a matter of debate among patients with CKD discovered on screening alone.

We cannot minimize the danger of CKD. But we also need to use the evidence to guide us in our best practice. We should focus on the risk factors for CKD and leave generalized screening possibly to another day in the future.

#### Clinical Pearls

- CKD may have a prevalence rate as high as 28% among US adults. Most of these individuals have no symptoms and have no formal diagnosis of CKD.
- CKD is independently associated with higher risks for CV disease and mortality.
- There are no adequate randomized trials on which to judge the value of universal screening of adults for CKD.
- The ACP and USPSTF cite this lack of evidence in their failure to endorse screening for CKD.
- The ASN disagrees with these recommendations and instead advocates routine periodic screening for CKD among adults.

- Given the close association between hypertension and diabetes and the risk for CKD, as well as the paucity of evidence that treatment of CKD in the absence of these comorbid conditions improves outcomes substantially, it makes sense for clinicians to focus on the identification and treatment of hypertension and diabetes instead of CKD.