Cost-effectiveness of Primary Screening for CKD: A Systematic Review

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Background: Chronic kidney disease (CKD) is a major health problem with an increasing incidence worldwide. Data on the cost-effectiveness of CKD screening in the general population have been conflicting.

Study Design: Systematic review.

Setting & Population: General, hypertensive, and diabetic populations. No restriction on setting.

Selection Criteria for Studies: Studies that evaluated the cost-effectiveness of screening for CKD.

Intervention: Screening for CKD by proteinuria or estimated glomerular filtration rate (eGFR).

Outcomes: Incremental cost-effectiveness ratio of screening by proteinuria or eGFR compared with either no screening or usual care.

Results: 9 studies met criteria for inclusion. 8 studies evaluated the cost-effectiveness of proteinuria screening and 2 evaluated screening with eGFR. For proteinuria screening, incremental cost-effectiveness ratios ranged from $14,063-$160,018/quality-adjusted life-year (QALY) in the general population, $5,298-$54,943/QALY in the diabetic population, and $23,028-$73,939/QALY in the hypertensive population. For eGFR screening, one study reported a cost of $23,680/QALY in the diabetic population and the range across the 2 studies was $100,253-$109,912/QALY in the general population. The incidence of CKD, rate of progression, and effectiveness of drug therapy were major drivers of cost-effectiveness.

Limitations: Few studies evaluated screening by eGFR. Performance of a quantitative meta-analysis on influential assumptions was not conducted because of few available studies and heterogeneity in model designs.

Conclusions: Screening for CKD is suggested to be cost-effective in patients with diabetes and hypertension. CKD screening may be cost-effective in populations with higher incidences of CKD, rapid rates of progression, and more effective drug therapy.

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INDEX WORDS: Cost-effectiveness analysis; public health screening; chronic kidney disease (CKD); proteinuria; estimated glomerular filtration rate (eGFR); risk stratification; incremental cost-effectiveness ratio (ICER).

Chronic kidney disease (CKD) is a major public health problem with increasing incidence and prevalence worldwide.[1] It is a major risk factor for cardiovascular disease, early mortality, and kidney failure,[2] but early detection, appropriate risk stratification, and treatment may delay or prevent the complications of CKD. Screening and risk stratification can be performed easily using simple blood and urine tests, such as measurement of serum creatinine and urine albumin-creatinine ratio. Recent advances in point-of-care testing and reliable multivariable risk prediction algorithms can facilitate efficient screening further by allowing rapid reporting of results and instant stratification of risk.[3,4]

Despite the ready availability of screening tests for CKD, uncertainty remains regarding the appropriate target populations for the most cost-effective screening strategies. Although most studies have recommended screening in high-risk patients with diabetes and hypertension, data for the cost-effectiveness of CKD screening in the general population have been conflicting. Complicating this further is the fact that the costs of both screening and treating CKD have decreased during the past decade.

We hypothesize that assumptions regarding a higher incidence of CKD, more rapid rates of progression, and wide estimates of treatment effect of renin-angiotensin-aldosterone system (RAAS) inhibition would explain the variability in cost-effectiveness of CKD screening.

In order to examine differences in these influential assumptions, we conducted a systematic review of cost-effectiveness analyses examining screening strategies for CKD.

METHODS

Data Sources and Searches

We identified studies evaluating the cost-effectiveness of population-based screening for CKD in the general population and in patients with diabetes and hypertension. The studies included had to report an incremental cost-effectiveness ratio (ICER) of screening strategies based on estimated glomerular filtration rate (eGFR; serum creatinine) or proteinuria (proteinuria or micro-albuminuria) in comparison to no screening or usual care.

We retrieved information for the study from the following databases in collaboration with a medical librarian (K.M.): PubMed, Scopus, EMBASE, and Cochrane Database of Systematic Reviews. Our search of these databases ranged from their establishment until June 2012. The search strategy was tailored to each database and used a combination of key terms such as "cost effectiveness," "quality adjusted life years," "mass screening," "albuminuria," "proteinuria," "glomerular filtration rate," and "creatinine." Medical Subject Headings (MeSH) terms (Item S1, available as online supplementary material) also were applied in the search strategy. We downloaded all the received citations into RefWorks, version 2.0 (RefWorks-COS; 2011). Studies were limited to the English language.

Study Selection

Two reviewers (T.W.F. and C.K.) independently reviewed each citation by title and abstract and chose relevant articles for full-text review. The reviewers screened the reference lists in the articles selected for full-text review for studies missed by the search strategy. The reviewers then independently assessed the full-text articles that were finalized for their inclusion in the systematic review after consultation with the third and fourth reviewers (P.K. and N.T.). All disagreements were resolved by consensus.

Data Extraction, Synthesis, and Analysis

A data extraction form was created to capture relevant information from the included studies. Two reviewers (T.W.F. and C.K.) independently conducted the extraction, and inconsistencies in data were corrected and resolved by consensus and consultation with the third and fourth reviewers (P.K. and N.T.).

We extracted the following information from each study: (1) study characteristics, including year of publication, country of origin, the population considered, the comparator considered, the method of screening evaluated, perspective taken for the analysis, principal summary measure of outcome, and frequency of screening; (2) data pertaining to cost-effectiveness analysis, such as the currency and year of the reported costs and benefits, as well as the resulting ICERs; and (3) relevant study assumptions, such as cost-related assumptions: the applied discount rate, cost of a dipstick test (if applicable), overall cost of screening, the resulting cost of drug therapy, and annual cost of dialysis. Other factors included from the costing models included treatment and screening adherence, sensitivity and specificity of the screening method, relative risk reduction afforded by treatment, and prevalence assumptions relating to diabetes, CKD, microalbuminuria or proteinuria. We also determined whether the study concluded that the intervention was cost-effective based on established thresholds: the commonly used guideline of <$50,000/quality-adjusted life-year (QALY)[5] or a threshold of less than 1-3 times the ratio of per-capita gross domestic product (GDP) to QALY, based on World Health Organization (WHO) guidelines.[6]

The primary measure in our systematic review was the ICER of screening as compared with either a usual-care strategy, for which a rate of baseline screening was assumed to occur in the population, or a scenario in which no baseline screening occurred. The ICER was calculated as either cost per QALY or cost per life-year gained. All dollar amounts were inflated using the consumer price index of the country in which they reported to 2011 values and subsequently were exchanged to US dollars at that time.

Assessment of Quality of Reporting and Risk of Bias

Two reviewers (T.W.F. and C.K.) assessed all included studies for their quality of reporting and risk of bias using published guidelines.[7] These guidelines were adapted internally to select the most important determinants of bias in cost-effectiveness studies. In particular, we assessed potential risk of bias and quality of reporting by assessing: (1) how clear the alternatives being considered were described and the rationale behind these alternatives, (2) the sources of effectiveness estimates and the appropriateness of these sources, (3) estimates of quantities and unit care costs, (4) the underlying design of any models applied, (5) the approach to sensitivity analysis and the rationale behind the chosen variables, and (6) the chosen range behind the variables used in the sensitivity analysis.

RESULTS

Study Selection

A flow diagram outlining the selection strategy is shown in Fig 1. Our initial search strategy retrieved 1,462 citations for screening. Of these, 161 articles were selected for full-text review, and 9 studies[9-17] (1 of which was covered by 2 publications[10,11]) met criteria for inclusion in the review.

Characteristics of Selected Studies

Eight studies evaluated the cost-effectiveness of proteinuria-based screening. Four focused on microalbuminuria[9-13] and 4 focused on dipstick proteinuria.[14-17] Four studies originated in the United
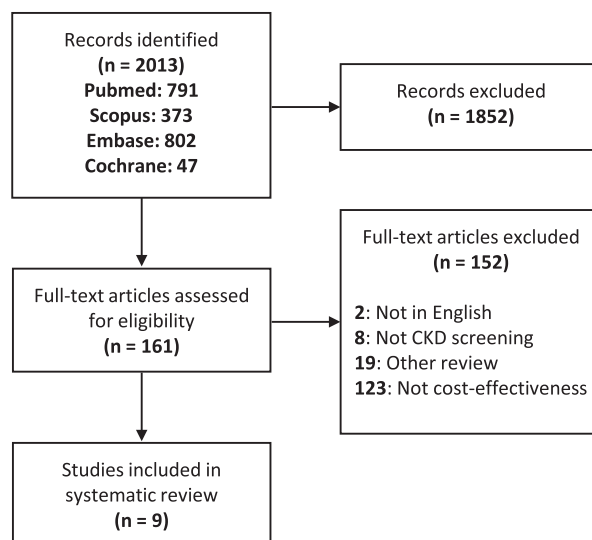

Figure 1. CONSORT[8] flow diagram. Abbreviation: CKD, chronic kidney disease.

States[10,11,13,14,17] and the rest were from the Netherlands,[9] Australia,[15] Switzerland,[12] and Japan.[16] Two studies took a societal perspective,[14,16] whereas the others held a health care payor perspective. The applied screening frequency typically was annual; however, one study analyzed a one-off scenario, in which screening is not repeated,[9] and one study considered a biannual scenario.[17] Two studies also considered screening at 2-, 5-, and 10-year intervals.[10-12]

Two studies evaluated the cost-effectiveness of eGFR-based screening. One study was published in Canada and considered screening in a one-off scenario in comparison to usual care,[18] whereas the other was published in Japan and considered screening on an annual basis in comparison to no screening.[16] The characteristics of the included studies are summarized in Table 1.

Results of Cost-Effectiveness Analysis

Proteinuria-Based Screening

Comparable ICERs were determined in the following cohorts: the general population and those with/without diabetes and hypertension. The reported cost ratios for proteinuria screening in the general population ranged from $14,063-$160,018/QALY across 3 studies.[10-12,16] One study reported a cost of $31,707/life-year gained in the general population.[9] In 4 studies evaluating those with diabetes, the reported cost ranged from $5,298-$54,943/QALY.[10-12,15,16] One study reported a cost of $26,943/life-year gained in a diabetic population.[17] In a hypertensive population, the reported cost ratios ranged from $23,028-$73,939/QALY across 3 studies.[10-12,14] In the population without diabetes and

Table 1. Characteristics of Included Studies

Study	Study Population	Screening Method	Summary Measure	Comparator	Perspective	Screening Frequency
Proteinuria-Based Screening						
Boersma et al[9] (2010)	General Dutch population aged 28-75 y	Microalbuminuria (UAE 30-300 mg/d)	Cost/LYG	No screening	Health care payor	One-off
Boulware et al[14] (2003)	US adults aged 50-75 y	Proteinuria (dipstick)	Cost/QALY	Usual care	Societal	Annual
Hoerger et al[10,11] (2010)	US adults aged 50-90 y	Microalbuminuria (ACR 30-299 mg/g)	Cost/QALY	No screening and usual care	Health care payor	1-, 2-, 5-, 10- y intervals
Howard et al[15] (2010)	Hypertensive and diabetic Australian adults aged 50-69 y	Proteinuria (dipstick followed by spot UPCR > 0.20 mg/mg confirmatory test)	Cost/QALY	Usual care	Health care payor	Annual
Kessler et al[12] (2012)	Swiss adults aged 50-90 y	Microalbuminuria (ACR 30-299 mg/g)	Cost/QALY	No screening and usual care	Health care payor	1-, 2-, 5-, 10- y intervals
Kondo et al[16] (2012)	Japanese adults aged 40-74 y	Proteinuria (dipstick)	Cost/QALY	No screening	Societal	Annual
Palmer et al[13] (2008)	US hypertensive type 2 diabetics	Microalbuminuria (UAE 20-199 μg/min)	Cost/QALY	No screening	Health care payor	Annual
Siegel et al[17] (1992)	US insulin-dependent diabetics (aged 15 y at diagnosis)	Proteinuria (dipstick; >300 μg/min)	Cost/LYG	Usual care	Health care payor	Biannual
eGFR-Based Screening						
Kondo et al[16] (2012)	Japanese adults aged 40-74 y	eGFR (<50 mL/min/ 1.73 m² and hypertension, diabetes, or hyperlipidemia)	Cost/QALY	No screening	Societal	Annual
Manns et al[18] (2010)	Canadian health care system	eGFR (<60 mL/min/ 1.73 m²)	Cost/QALY	Usual care	Health care payor	One-off

Abbreviations: ACR, albumin-creatinine ratio; eGFR, estimated glomerular filtration rate; LYG, life-year gained; QALY, quality-adjusted life-year; UAE, urinary albumin excretion; UPCR, urinary protein-creatinine ratio.

hypertension, cost ratios ranged from $98,673-$349,758/QALY across 3 studies (Fig 2).[10-12,14]

eGFR-Based Screening

A study published in Canada reported cost ratios of $109,912/QALY, $23,680/QALY, and $1,478,515/QALY in the general population, a population with diabetes, and a population without diabetes and hypertension, respectively.[18] A study published in Japan reported a cost ratio of $100,253/QALY in the general population.[16] An overview of these ratios is shown in Table 2 and Fig 2.

Comparison of Influential Assumptions

Proteinuria-Based Screening

A comparison of influential modeling assumptions is shown in Table 3. The prevalence and incidence of CKD and diabetes were similar in most studies, other than a Japanese study assuming a CKD prevalence > 40%. Four studies used data from NHANES III (Third National Health and Nutrition Examination Survey)[19] and others used data from population-based cohort studies.[16,20-23] In at least 3 studies, the incidence of microalbuminuria was a major driver of the ICER, and doubling of the incidence would have changed the conclusions considerably.[10-12,14]

Progression to macroalbuminuria or kidney failure also was identified as an influential assumption in 2 studies.[10,11,16] In these studies, an increase of 50%-100% in the CKD progression rate was a major influence on the ICER. Furthermore, the reported relative risk reduction in progression to kidney failure from RAAS inhibition, as well as the effect of RAAS inhibitors on mortality, also was influential.

Estimates for the relative risk reduction afforded by treatment with RAAS inhibitors ranged from 30%-44% for kidney failure[13,14] and 23%-40% for all-cause mortality. Only 2 studies assumed an effect of RAAS inhibition on cardiovascular risk (40%-70% risk reduction in cardiovascular morbidity and mortality), and both found screening to be highly cost-effective in the general population[9,16] (Table 4). The baseline rate of RAAS inhibitor use in those screened

also was considered. One study showed through sensitivity analysis that if the baseline rate of RAAS use in the hypertensive population was 60% instead of 20%, the reported base-case ICER would be ~$40,000/QALY[14] as opposed to $18,621/QALY (2002 US dollars).

Screening adherence, discount rates, and cost of medical treatment were influential in some studies. Treatment and screening adherence ranged from 40%-100%, and the cost of the screening ranged from $85 per visit[17] to $158 per visit.[10,11] The cost of drug therapy varied across studies, with reported costs ranging from $114 per annum[9] to $740 per annum,[13] and discount rates varied from 3%-5%. The cost of dialysis ranged from $57,233 per annum[15] to $104,430 per annum[9] and was not a major driver of the reported ICERs (Table 4).

eGFR-Based Screening

Assumptions for CKD prevalence varied greatly between the 2 studies evaluating eGFR-based screening. The Japanese study[16] reported a CKD prevalence of 43.9% in the population older than 40 years, whereas the study published in Canada[18] assumed an overall CKD prevalence of 11%. Although the effect of RAAS inhibition on progression to kidney failure in patients with proteinuric CKD was similar in both studies (40% and 42%, respectively), the Canadian study assumed no effect of RAAS inhibition on nonproteinuric CKD. In contrast, the Japanese study also assumed a 70% cardiovascular risk reduction from treatment of CKD with RAAS inhibitors,[16] whereas the Canadian study assumed a null effect of RAAS inhibition on all-cause mortality in patients without diabetes (base-case ICER, $572,000/QALY; $40,800/QALY assuming 16% mortality reduction afforded by treatment).[18] The Canadian study also assumed no baseline rate of RAAS inhibitor use because those screened would have had no previous measurement of eGFR. When baseline use increased to 20%, the reported ICER increased to $31,100/QALY (base-case ICER, $22,600/QALY) in the diabetic population.[18]

Figure 2. Tornado plot compares reported incremental cost-effectiveness ratios (ICERs) in selected populations; $80,000 ICER selected based on 1-3 times gross domestic product per capita threshold for most G8 ("The Group of 8") countries.

Table 2. Comparison of ICERs

Study	Currency	General Population		Diabetic Population		Hypertensive Population		Nondiabetic and Nonhypertensive Population	
		Reported ICER	$US 2011 ICER	Reported ICER	$US 2011 ICER	Reported ICER	$US 2011 ICER	Reported ICER	$US 2011 ICER
Proteinuria-Based Screening: Cost/LYG									
Boersma et al[9] (2010)	Euros, 2008	22,000	31,707	—	—	—	—	—	—
Siegel et al[17] (1992)	US $, 1991	—	—	16,494	26,943	—	—	—	—
Proteinuria-Based Screening: Cost/QALY									
Boulware et al[14] (2003)	US $, 2002	—	—	—	—	18,621	23,028	282,818	349,758
Hoerger et al[10,11] (2010)	US $, 2006	NS: 73,000, UC: 145,000	NS: 80,561, UC: 160,018	NS: 21,000, UC: 40,000	NS: 23,175, UC: 44,143	NS: 55,000, UC: 67,000	NS: 60,696, UC: 73,939	NS: 155,000, UC: 253,000	NS: 171,054, UC: 279,204
Howard et al[15] (2010)	Australian $, 2008	—	—	4,793	5,298	—	—	—	—
Kessler et al[12] (2012)	Swiss francs, 2010	NS: 66,000, UC: 83,000	NS: 74,005, UC: 93,067	NS: 29,000, UC: 49,000	NS: 32,517, UC: 54,943	NS: 40,000, UC: 47,000	US: 44,852, UC: 52,701	NS: 88,000, UC: 100,000	NS: 98,673, UC: 112,129
Kondo et al[16] (2012)	Japanese yen, 2009	1,139,399	14,063	—	—	—	—	—	—
Palmer et al[13] (2008)	US $, 2000	—	—	20,011	25,854	—	—	—	—
eGFR-Based Screening: Cost/QALY									
Kondo et al[16] (2012)	Japanese yen, 2009	8,122,492	100,253	—	—	—	—	—	—
Manns et al[18] (2010)	Canadian $, 2009	104,900	109,912	22,600	23,680	—	—	1,411,100	1,478,515

Abbreviations: eGFR, estimated glomerular filtration rate; ICER, incremental cost-effectiveness ratio; LYG, life-year gained; NS, no screening; QALY, quality-adjusted life year; UC, usual care comparator; US, United States.

Table 3. Comparison of Influential Modeling Assumptions

	Proteinuria-Based Screening								eGFR-Based Screening	
	Boersma et al[9] (2010)	Boulware et al[14] (2003)	Hoerger et al[10,11] (2010)	Howard et al[15] (2010)	Kessler et al[12] (2012)	Kondo et al[16] (2012)	Palmer et al[13] (2008)	Siegel et al[17] (1992)	Kondo et al[16] (2012)	Manns et al[18] (2010)
Population data	PREVEND Study	NHANES	NHANES	AusDiab Study	CoLaus cohort	Japan Tokutei-Kenshin CKD cohort 2008	NHANES	Literature review	Japan Tokutei-Kenshin CKD cohort 2008	NHANES
Screening adherence	Implicit	75%	75%	75%	75%	40%	—	—	40%	50%
Treatment adherence	Implicit	75%	75%	75%	75%	100%	—	—	100%	75%
RR reduction in ESRD progression	—	30%	33%	34%	33%	42%	44%	—	42%	36% (DM with proteinuria); 41% (non-DM with proteinuria)
RR reduction in all-cause mortality	40%	23%	23%	—	23%	—	—	—	—	21% (DM with proteinuria); 0% (non-DM with proteinuria)

Abbreviations: AusDiab, Australian Diabetes, Obesity, and Lifestyle; CoLaus, Cohorte Lausannoise; CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; NHANES, National Health and Nutrition Examination Survey; PREVEND, Prevention of Renal and Vascular Endstage Disease; RR, relative risk.

Quality of Reporting and Risk of Bias Within Studies

Most studies were found to be of reasonable reporting quality and moderate risk of bias. One criterion that was found to have potential for a higher risk of bias was the source of effectiveness estimates. The studies were inconsistent in their estimates of treatment effectiveness and many did not use high-quality meta-analyses. The chosen variables for sensitivity analysis also presented a potential risk for elevated bias. The quality of reporting in the considered studies is shown in Fig 3.

DISCUSSION

Our systematic review found that screening for CKD by eGFR and/or albuminuria in high-risk populations (those with diabetes or hypertension) was suggested to be cost-effective (<$50,000/QALY).[10-15,17] In contrast, screening was not cost-effective in the general population, except in situations in which screening could be added to mandatory health checkups[16] or rates of CKD progression were rapid and RAAS inhibitors could be considered highly effective for renal and cardiovascular risk reduction.[9,16,18] Additionally, the reported ICERs improved in the general population when screening was performed in older patients[14] or when considering longer intervals between screening events.[10,11] Together, these findings suggest that screening for CKD in the general population without risk stratification and targeted treatment is unlikely to be cost-effective.

To our knowledge, our systematic review is the first to examine the cost-effectiveness of screening for CKD in diabetic, hypertensive, and general populations. A previously published study considered the effectiveness of CKD screening in improving clinical outcomes on the basis of several randomized controlled trials (RCTs).[24] The study concluded an uncertainty in improving clinical outcomes through CKD screening, but found the strongest evidence was seen for use of RAAS inhibition in patients found to have albuminuria combined with diabetes or cardiovascular disease. The information provided by RCTs may not always be ideal for the purpose of informing health policy decisions because even clear findings of efficacy in a trial setting often are difficult to replicate in a real-world setting.[25] Although RCTs are recognized gold standards for assessment of efficacy, an RCT of screening would be costlier[26] and take years to perform. We would encourage such an RCT, but in the interim, policy needs to be informed and there is not enough current RCT evidence.

Several factors were influential in determining the outcome of the considered cost-effectiveness analyses. In particular, the incidence of microalbuminuria and rate of transition to macroalbuminuria or kidney

Table 4. Comparison of Influential Cost Assumptions

	Proteinuria-Based Screening								eGFR-Based Screening	
	Boersma et al[9] (2010)	Boulware et al[14] (2003)	Hoerger et al[10,11] (2010)	Howard et al[15] (2010)	Kessler et al[12] (2012)	Kondo et al[16] (2012)	Palmer et al[13] (2008)	Siegel et al[17] (1992)	Kondo et al[16] (2012)	Manns et al[18] (2010)
Discount rate	4%	3%	3%	5%	3%	3%	3%	5%	3%	5%
Dipstick cost	—	4	—	1	—	3	—	3	NA	NA
Initial screening visit cost	—	55	89	—	49	—	—	41	—	—
Follow-up visit cost	—	41	69	—	60	—	—	41	—	—
Total screening cost	97	100	158	—	109	—	—	85	—	—
Annual cost of drug therapy	114 (ACEi)	481 (ACEi); 632 (ARB)	210 (ACEi); 523 (ARB)	156 (ACEI); 144 (ARB)	639 (DM); 275 (non-DM)	—	740 (ARB)	423 (ACEi)	—	396 (ACEi)
Annual cost of dialysis	104,430	89,012	79,841 (1st year); 59,963 (following)	103,963 (hospital); 57,233 (home); 62,330 (satellite)	87,515	74,056	77,648	59,513	74,056	67,286

Note: All costs reported in 2011 US dollars.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; NA, not applicable.
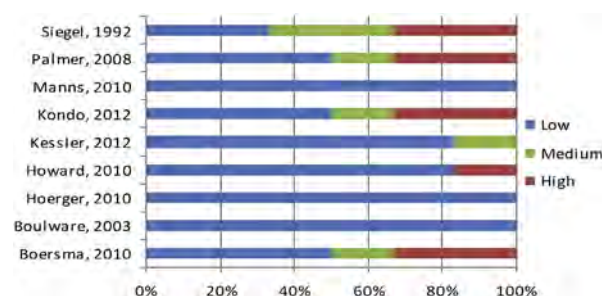

Figure 3. Risk of bias within studies. Items evaluated included: (1) the alternatives being compared are clearly described and the rationale for choosing these alternatives is stated, (2) the source(s) of effectiveness estimates used are stated and these estimates are clearly described, (3) methods for the estimation of quantities and unit care costs are described, (4) details of any model used are given and justified, (5) the approach to sensitivity analysis is given and the choice of variables for the sensitivity analysis is justified, and (6) the ranges over which the variables are varied are stated. Based on guidelines from Drummond and Drummond.[7]

failure were influential. Increasing the transition rate was shown to be the most influential factor in several sensitivity analyses, and therefore we believe that in a population with even moderately higher rates of progression, it may be worthwhile considering general population screening.[10,11,16] Prevalence estimates were relatively similar across most studies with the exception of one study focusing on only those with type 1 diabetes[17] and the Japanese study that assumed an extremely aggressive estimate of >40% in a population older than 40 years.[16] Many studies used prevalence and incidence estimates from NHANES III[19] and as such, may not be applicable to higher risk ethnic groups.[27-29] In these groups, for which prevalence and incidence of CKD are higher and rates of progression to overt nephropathy or kidney failure are greater, CKD screening may be cost-effective even using existing models.

In addition, assumptions about the treatment effect of RAAS inhibitors on kidney failure, all-cause mortality, and cardiovascular disease were major drivers of cost across most studies.[9-11,14,18] Most studies assumed that RAAS inhibition reduced the risk of kidney failure by 30%-40% for all causes of CKD; however, a more recent study countered this assumption and suggested that RAAS inhibition may be ineffective in preventing kidney failure in patients with CKD without proteinuria.[18] The same study also assumed no effect of RAAS inhibition on all-cause mortality, except in patients with diabetes. These findings are in direct contrast to all other models, which uniformly assumed a 20%-30% reduction in all-cause mortality from RAAS inhibition.[10-12,14] The accuracy of this assumption of no treatment effect of RAAS inhibition in nondiabetic CKD remains debatable.[14,18] Finally, the effect of RAAS inhibition on cardiovascular events was assumed in only 2 studies,

both of which found general population screening to be highly cost-effective.[9,16] We believe that these treatment estimates may be optimistic because more recent studies have not shown an advantage of RAAS inhibitors over antihypertensive agents.[30] Although there may be cardiovascular benefits of using RAAS inhibition in the CKD population, the studies from Japan and the Netherlands used effectiveness estimates from single RCTs.[31,32] A consensus could be achieved on the efficiency of RAAS inhibition with an updated meta-analysis of the effects on kidney disease and cardiovascular outcomes.

Whether CKD screening can be deemed cost-effective is contingent on a conservative historical $50,000/QALY threshold.[5] According to the WHO, an appropriate ICER threshold for health interventions should be standardized to 1-3 times GDP per capita.[6] This would place an appropriate range for the threshold at about $40,000-$120,000/QALY for most G8 ("The Group of 8") countries according to the World Bank estimates of GDP per capita for 2011.[33] If we aggressively assume the top level of the threshold range, all the reviewed studies would be cost-effective in screening the diabetic, hypertensive, and general populations on an annual or one-off basis with the exception of one American study evaluating screening in the general population comparing to a usual-care scenario[10,11] (Table 2). Thus, the deemed suitability of cost-effectiveness for CKD screening should be tailored to local regions and health care environments.

The potential unintended consequences of screening also must be considered. There is a chance that screening may have unexpected implied harm when patients are labeled with a disease. This labeling may be a concern, with the possibility of patients reverting to non-CKD status in the future.[34] However, advances in filtration markers combined with more conservative thresholds applied in screening for proteinuria may mitigate some of this concern. For example, use of the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation for estimating GFR or use of cystatin C as a confirmatory test for CKD may identify a lower prevalence of CKD, but select higher risk individuals for intervention.[35,36] The effect of these strategies on the cost-effectiveness of screening in the general population requires further study.

Our review has several strengths. We included numerous electronic databases in the search strategy to try to be certain that all published literature examining the cost-effectiveness of albuminuria or eGFR screening for CKD was captured. Furthermore, we manually searched the bibliographies of included articles to ensure our search strategy's sensitivity. We considered the quality of the included studies applying validated criteria[7] and ensured that bias was not a principal determinant of the presented results. The studies selected for review covered several countries and are representative of various health care systems.

There also are limitations present in the study. Our review focused solely on the published literature and thus publication bias might have had a role. Only 2 studies evaluated eGFR-based screening, and it is difficult to draw definitive conclusions from a small sample of representative studies. We included only studies that focused on no screening or usual-care comparators and did not include those that compared other strategies. All the studies drew conclusions based on the development of a model and there is a degree of uncertainty with simulated results. Performance of a quantitative meta-analysis on influential assumptions was not conducted because there are few available studies of CKD screening by either proteinuria or eGFR and because of the presence of heterogeneity in model designs.

In conclusion, our systematic review found that a screening strategy targeting high-risk individuals in diabetic or hypertensive populations was suggested to be a cost-effective intervention under all assumptions. Screening for CKD in the general population may be cost-effective if a higher incidence of CKD is present, rapid progressors can be identified, and aggressive treatment with RAAS inhibitors reduces the risk of nonrenal events.

SUPPLEMENTARY MATERIAL

Item S1: Search strategy MeSH terms.

Note: The supplementary material accompanying this article (http://dx.doi.org/10.1053/j.ajkd.2013.12.012) is available at www.ajkd.org

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