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Population-Wide Screening for Chronic Kidney Disease: a Cost-Effectiveness Analysis

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Abstract

Background: Sodium glucose co-transporter 2 (SGLT2) inhibitors have the potential to meaningfully alter the natural history of chronic kidney disease (CKD). It is unknown whether population-wide screening for CKD is cost-effective in the modern era.

Objective: To determine the cost-effectiveness of population-wide screening for CKD in comparison to standard of care, i.e., status quo case detection and treatment.

Design: Markov model.

Data sources: Randomized clinical trials including the DAPA-CKD trial, National Health and Examination Survey, cohort studies, Centers for Medicare & Medicaid Services data.

Target population: 35- to-75-year-old U.S. adults.

Time horizon: Lifetime.

Perspective: U.S. healthcare sector.

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Registration: None

REPRODUCIBLE RESEARCH STATEMENT

Study protocol: N/A

Statistical code: https://github.com/marikamaecusick/CKDScreeningCEA

Data set: https://github.com/marikamaecusick/CKDScreeningCEA

IRB APPROVAL

IRB approval was not required for this study.

CONFLICTS OF INTEREST

There are no conflicts of interest to declare.

Intervention: Screening for albuminuria plus treatment with or without SGLT2 inhibitors added to standard care (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers).

Outcome measure: Quality-adjusted life-years (QALYs), costs, and incremental cost-effectiveness ratios, all discounted at 3% annually.

Results of base-case analysis: One-time CKD screening increased life expectancy (from 17.29 to 17.45 years) and QALYs (from 12.61 to 12.72); decreased incidence of kidney failure requiring dialysis or transplant by 0.29 percentage points; and increased costs from $249,800 to $259,000, translating to $86,300/QALY gained, for 55-year-olds. Screening 35- to 75-year-olds once prevents the need for dialysis or kidney transplant in 398,000 people. Periodic screening every ten years until age 75 cost less than $100,000/QALY gained for 35- to-75-year-olds.

Results of sensitivity analysis: If SGLT2 inhibitors were 30% less effective, periodic screening every ten years until age 75 cost between $145,400/QALY and $182,600/QALY gained across 35- to-75-year-olds; price reductions would be required for periodic screening to remain cost-effective.

Limitations: SGLT2 inhibitor efficacy was derived from a single randomized controlled trial.

Conclusions: Screening for CKD is cost-effective for the U.S. adult population.

INTRODUCTION

Chronic kidney disease (CKD) is a common, costly cause of morbidity and mortality in the United States. Approximately 15% of the U.S. adult population is affected by CKD, and 90% of these individuals are unaware of their CKD diagnosis (1) – perhaps because the disease is typically clinically silent until it progresses to advanced stages (2). Medicare spends $87 billion annually on care for CKD and an additional $37 billion for care of patients with kidney failure requiring kidney replacement therapy (1), demonstrating both the economic burden of CKD and the imperative to slow CKD progression to prevent or delay kidney failure.

Screening refers to the detection of previously unrecognized, or subclinical, disease among asymptomatic individuals in order to intervene early and thereby prevent morbidity and mortality (3). Despite the availability of several simple, inexpensive diagnostic tests for CKD, there is no consensus regarding the best approach for timely identification and intervention for CKD (4–7). The most recent United States Preventive Services Task Force review (6) of CKD screening in 2012 found insufficient evidence to assess the balance of benefits and harms of CKD screening, partially due to inadequate evidence that routine screening for CKD improves clinical outcomes for adults without diagnosed CKD (6). However, in the decade since this review, the introduction of sodium glucose co-transporter 2 (SGLT2) inhibitors has dramatically altered this landscape. Initially used to treat hyperglycemia in patients with type 2 diabetes, SGLT2 inhibitors subsequently demonstrated benefits out of proportion to those expected from improved glycemic control, including reductions in cardiovascular death and heart failure events, along with attenuated loss of kidney function (8–10) in large-scale cardiovascular outcome trials. These results prompted kidney disease-focused outcome trials (11–13), which confirmed SGLT2 inhibitors' disease-

modifying effects. These effects extend to patients with or without diabetes, albeit with slightly different effectiveness (13). As a result of these findings, specialty societies have begun to incorporate SGLT2 inhibitors into clinical practice guidelines for patients with CKD and albuminuria regardless of diabetes status (14,15). SGLT2 inhibitors have also been shown to be cost-effective for treating CKD in patients with or without diabetes (16–19).

The introduction of a practice-changing, cost-effective therapy can substantially alter the balance of benefits and harms associated with screening for a given disease. As such, a reevaluation of population-wide CKD screening is warranted. Indeed, the United States Preventive Services Task Force (20) is considering whether to review recommendations for CKD screening in adults. Herein, we assess the cost-effectiveness of population-wide CKD screening and treatment with or without SGLT2 inhibitors in U.S. adults from the healthcare sector perspective, using urine albumin-creatinine ratio (UACR) as the screening intervention and beginning screening at age 35.

METHODS

Natural history model

CKD is a spectrum of diseases associated with abnormal kidney function, typically with progressively declining estimated glomerular filtration rate (eGFR) (21). We developed a decision-analytic Markov cohort model of CKD progression among U.S. adults aged 35 years and older (Figure S16). The model simulates CKD progression over a patient's lifetime at 3-month intervals. Model stages are defined by eGFR, UACR, and CKD detection and treatment status.

We classified eGFR stages using the following cut-offs: eGFR stage G2 (60–75 mL/min/1.73m^2), G3a (45–59 mL/min/1.73m^2), G3b (30–44 mL/min/1.73m^2), G4 (15–29 mL/min/1.73m^2), kidney failure not necessarily requiring kidney replacement therapy (12–14 mL/min/1.73m^2), and kidney failure generally requiring kidney replacement therapy (<12 mL/min/1.73m^2). We refer to kidney failure not necessarily requiring kidney replacement therapy as "KF pre-KRT," and kidney failure requiring kidney replacement therapy as "KF on KRT." While there is no clear eGFR threshold at which patients initiate KRT, patients generally initiate KRT at eGFR between 5 and 15 mL/min/1.73m^2 (14,22). We classified albuminuria stages using the following cut-offs: UACR <30 mg/g, 30–300 mg/g, and >300 mg/g (albuminuria stages A1, A2 ("microalbuminuria"), and A3 ("macroalbuminuria")). We assumed that patients do not progress more than one eGFR or albuminuria stage within a 3-month interval, and patients do not experience improvements in eGFR such that they enter a less severe disease stage (23,24). Patients may discontinue treatment over time.

We used Bayesian calibration (Sample-Importance-Resampling) to fit our model to empirical data from the National Health and Nutrition Examination Survey (NHANES) (25). Further details on NHANES estimation, the calibration procedure, and calibration results are provided in the Methods S1–S2.

Screen-and-treat interventions

Screening—The UACR provides a quantitative assessment of albuminuria, thus detecting persons with albuminuria stages A2 or A3, which inform SGLT2 inhibitor treatment decisions. Patients who test positive on UACR (A2 or A3) are tested for serum creatinine, which along with age and sex, is used to calculate eGFR. We assumed that patients with an eGFR <60 mL/min/1.73m^2 undergo a retroperitoneal ultrasound to screen for structural abnormalities of the kidney(s).

Treatment—After detection of CKD, patients initiate treatment (see paragraph below for treatment types considered). Patients with false positive albuminuria test results who are treated for CKD do not derive benefits from treatment. All patients discontinue pharmacologic treatment once they enter KF on KRT.

We evaluated the effectiveness of screen-and-treat interventions that use conventional CKD therapy (ACE inhibitors/ARBs), which slow CKD progression without kidney-specific survival benefits (26–29). Patients are eligible for conventional CKD therapy if they have albuminuria or an eGFR <60 mL/min/1.73m^2. We also evaluated the effectiveness of screen-and-treat interventions that utilize SGLT2 inhibitors in addition to ACE inhibitors/ARBs (13). Patients initiate both treatments if they have both albuminuria and eGFR <60 mL/min/1.73m^2. If they have albuminuria and eGFR ≥60 mL/min/1.73m^2, they only initiate ACE inhibitors/ARBs (Table S12).

The DAPA-CKD trial demonstrated the efficacy of SGLT2 inhibitors in patients with CKD, with and without diabetes (23). Because our natural history model does not explicitly model incidence and prevalence of diabetes, we modeled age-specific SGLT2 inhibitor treatment effectiveness as a weighted average based on the age-specific diabetes prevalence from NHANES among persons eligible for SGLT2 inhibitor treatment (Methods S3).

Under both scenarios, patients may rarely experience severe adverse reactions to ACE/ARB and SGLT2 inhibitor treatment, specifically angioedema, euglycemic diabetic ketoacidosis, and genital infections (30,31). In the base case, we assumed patients discontinued all forms of treatment (ACE/ARB and SGLT2 inhibitor) at the discontinuation rate observed in the DAPA-CKD clinical trial.

Timing and frequency—We evaluated the effectiveness, costs, and cost-effectiveness of both one-time screening and periodic screening interventions for cohorts aged 35, 45, 55, 65, and 75 years. Periodic screening included screening every five and ten years at differential stopping ages. No persons were screened after the age of 75.

Mortality, costs, and quality of life

Mortality, costs, and health-related quality of life vary across CKD stages. We used CKD stage-specific mortality rates from published literature (32). We assumed that patients in KF pre-KRT had the same mortality rates as those in CKD Stage 4. All mortality rates account for sex-specific differences by usage of sex-specific U.S. life tables (33).

We estimated baseline health expenditures according to a patient's age and sex using AHRQ expenditure data (34). Patients with eGFR Stages G1 and G2 (eGFR >60 mL/min/1.73m^2) were assumed to incur the same costs as the general population. Detected patients in more advanced eGFR stages incur additional CKD stage-specific costs (Methods S4) (35). We took monthly costs for patients in KF on KRT from the United States Renal Data System estimate of per-person-per-year (PPY) spending (22).

CKD screening costs include costs of UACR screening, provider visit (primary care provider), and further diagnostics (eGFR and retroperitoneal ultrasound) if applicable. We estimated SGLT2 inhibitor costs based on the cost of dapagliflozin. We did not include treatment costs beyond drug costs, as other related expenditures are included in the annual cost of CKD care and baseline expenditures. Patients who experienced an adverse reaction to treatment incurred the costs specific to the type of reaction (e.g., inpatient hospitalization for angioedema) (36–38).

We used stage-specific quality-of-life adjustments (39,40). In the base case, we assumed no differences in quality-of-life weights according to albuminuria status, detection, or treatment status for a given stage. Patients with severe adverse reactions faced a cycle-length quality-of-life decrement (41–43).

Analyses

Base case model parameter estimates are provided in Table 1. We conducted our cost-effectiveness analysis in accordance with the Second Panel on Cost-Effectiveness in Health and Medicine (44). Our main outcomes are life years, QALYs, and healthcare sector costs over the lifetime horizon, all discounted at 3% annually (45). We represented costs in 2021 USD, and costs from other years are adjusted using the Personal Health Care Expenditure inflation adjustment (46,47). Our analysis is from the healthcare sector perspective, which includes all formal healthcare-related costs. In the main text, we present results primarily on the median age cohort of our study (55-year-old) with results on the other age cohorts in the Supplement (Figure S17–20, Table S29–S31).

Sensitivity analysis

We used probabilistic sensitivity analysis to evaluate how simultaneous uncertainties influenced outcomes and preferred strategies (60,61). To illustrate the uncertainty associated with our probabilistic sensitivity analysis results, we calculated 95% interquartile intervals, henceforth referred to as 95% uncertainty intervals (95% UIs). We ran univariate and bivariate sensitivity analyses for key model uncertainties using ranges identified in Table 1 (62). We quantified uncertainties in our policy decisions through cost-effectiveness acceptability curves (Tables S51–S52; Figures S54–S58) (63).

In scenario analyses, we tested the cost-effectiveness of screening for CKD stratified by self-reported diabetes status (Methods S5). We also considered alternative population-wide scenarios in which discontinuation of treatment was due to only adverse events and treatment usage at baseline was higher than as estimated in NHANES (Methods S6).

RESULTS

Outcomes from our calibrated model exhibited high concordance with empirical estimates from NHANES (25). Model-projected cumulative incidence of KF on KRT closely matched estimates from the literature. Full calibration results appear in the Supplement (Methods S2).

Effectiveness

Population-wide albuminuria screening followed by treatment with SGLT2 inhibitors in addition to conventional ACE inhibitor/ARB therapy for persons found to have albuminuria and a lower eGFR (Stage G3a or more severe) increased life expectancy and QALYs across all age groups compared to the standard of care, status quo case detection and treatment with ACE inhibitor/ARB therapy alone (Tables S33–S34). For a 55-year-old, adding one-time screening and SGLT2 inhibitor treatment to status quo increased discounted life years from 17.29 (95% UI: 17.09, 17.45) to 17.45 (95% UI: 17.24, 17.63). This strategy also increased discounted QALYs from 12.62 (95% UI: 11.10, 13.70) to 12.73 (95% UI: 11.19, 13.82) (Table 2). Incremental increases in life years and QALYs were therefore 0.16 (95% UI: 0.07, 0.26) and 0.11 (95% UI: 0.05, 0.18), respectively (Figure 1). Screening every 5 years for 55-year-olds increased life years by 0.24 (95% UI: 0.10, 0.39) and QALYs by 0.21 (95% UI: 0.08, 0.27) in comparison to status quo.

In addition, population-wide albuminuria screening with the addition of SGLT2 inhibitors to treatment decreased the number of individuals with kidney disease severe enough to require KRT. Without population-wide screening or SGLT2 inhibitor therapy, 2.33% (95% UI: 0.66%, 5.01%) of 55-year-olds received KRT over their lifetimes. Adding SGLT2 inhibitor therapy for persons with albuminuria detected through status quo case finding decreased the lifetime incidence of KF on KRT to 2.31% (95% UI: 0.61%, 5.00%) even without population-wide screening. Adding screening further reduced the incidence to 2.04% (95% UI: 0.51%, 4.52%) with one-time screening and 1.87% (95% UI: 0.45%, 4.22%) with screening every five years (Table 2). For 75-year-olds, for persons with albuminuria detected through status quo case finding increased lifetime incidence of KF on KRT from 2.0% (95% UI: 0.61%, 2.07%) to 2.07% (95% UI: 0.61%, 4.44%). This phenomenon is attributable to the effectiveness of SGLT2 inhibitors at decreasing all-cause mortality, paired with higher prevalence of advanced stages of CKD among 75-year-olds than in younger populations. As a result, 75-year-olds started on SGLT2 inhibitor therapy tend to then live long enough for CKD to advance farther into the range of requiring KRT (Figure 1, Table S29). However, like other age groups, adding population-wide CKD screening with SGLT2 inhibitors decreased lifetime incidence of KF on KRT (Figure 1, Table S29).

Extrapolating our results to the full U.S. population, implementing one-time screening and adding SGLT2 inhibitors to treatment for the 158 million 35- to 75-year-olds in the U.S. would prevent the need for KRT in approximately 398,000 people over their lifetimes, representing a 10% decrease in cases of KRT compared to status quo (64). Periodic screening every 10 or five years with SGLT2 inhibitors would prevent approximately 598,000 and 658,000 people from requiring KRT compared to status quo (Table S39).

Cost-effectiveness

Screening combined with SGLT2 inhibitors also increased healthcare expenses. Results for the median-age 55-year-old population are shown in Table 2 and summarized for the remaining age cohorts in Table S29. One-time screening and treatment including SGLT2 inhibitors increased discounted healthcare costs from $249,800 (95% CI: $189,000, $318,800) to $259,000 (95% CI: $197,700, $328,300) for 55-year-olds. The incremental cost-effectiveness ratio (ICER) for this strategy was $86,300/QALY gained for 55-year-olds (Figure 2) and ranged from $82,100 to $95,800/QALY gained for all age groups (Figure S17–S20, Table S31).

Increasing the frequency of screening to every ten years until age 75 further increased discounted healthcare costs to $262,500 (95% CI: $200,800, $331,900) for 55-year-olds, and cost $92,500/QALY gained for this group. This every-ten-year screening strategy cost $98,40/QALY gained for 35-year-olds, $93,100/QALY gained for 45-year-olds, and $89,800/QALY gained for 65-year-olds. Intensifying further to screening every five years cost $121,100/QALY gained for 55-year-olds and $183,700/QALY gained for 35-year-olds, $153,300/QALY gained for 45-year-olds, and $105,000/QALY gained for 65-year-olds.

Sensitivity analysis

In one-way sensitivity analysis, cost-effectiveness results were most influenced by the clinical effectiveness and costs of SGLT2 inhibitors. Decreasing the effectiveness of SGLT2 inhibitors in reducing all-cause mortality led to the largest changes in ICERs across all age groups. For example, for 55-year-olds, when effectiveness of SGLT2 inhibitors in reducing all-cause mortality decreased by 50%, ICER for screening every ten years until age 75 increased from $92,500/QALY gained to $173,000/QALY gained and screening every five years until 75 increased from $121,100/QALY gained to $184,300/QALY gained (Figure S24, Table S41). When effectiveness of SGLT2 inhibitors in slowing CKD progression decreased by 50%, the ICER for screening every ten and five years increased to $111,300/QALY and $138,130/QALY gained, respectively (Figure S23, Table S40). Finally, when costs of SGLT2 inhibitors rose by $109 (25% increase) to $474, the ICERs increased to $102,700/QALY and $132,600/QALY gained for screening every ten and five years until age 75, respectively (Tables S45–S46).

In two-way sensitivity analyses, as expected, simultaneous decreases in the effectiveness of SGLT2 inhibitors in reducing all-cause mortality and slowing CKD progression also increased costs per QALY of CKD screening more than decreases in either parameter alone: for example, a 30% decrease in overall SGLT2 inhibitor effectiveness increased the ICER for screening 55-year-olds every ten and five years until age 75 to $162,500/QALY and $177,200/QALY gained, respectively (Figure S25, Table S42). However, a decrease in the costs for SGLT2 inhibitors compensates for some of this change in ICERs: At this level of decreased SGLT2 inhibitor effectiveness, if monthly costs for SGLT2 inhibitors were lowered from $365 to $200, ICERs for screening every ten and five years until 75 were $119,100/QALY and $149,700/QALY gained, respectively (Figures S49–S50).

At commonly-used willingness-to-pay thresholds of $100,000 per QALY gained and $150,000 per QALY gained, probabilistic sensitivity analysis showed that screening was preferred in ≥74% and ≥96% of probabilistic sensitivity analysis samples across all age groups (Table S51). At these thresholds, screening interventions that added SGLT2 inhibitors were preferred in ≥42% and ≥89% of probabilistic sensitivity analysis samples across all age groups, respectively. When screening interventions were not preferred, this was most often a result of the worst-case scenario combination of simultaneously higher SGLT2 monthly costs and lower effectiveness of SGLT2 inhibitors on both CKD progression and all-cause mortality.

In scenario analyses, cost-effectiveness of population-wide screening was robust to lower discontinuation rates and higher rates of treatment for CKD in the absence of screening (Table S57, S59). For those with self-reported diabetes, at least one-time screening with SGLT2 inhibitors cost between $90,300/QALY to $97,400/QALY gained for all age groups (Figures S59–S63, Table S53). For those without self-reported diabetes, the ICERs were between $76,000/QALY to $99,500/QALY gained (Figures S64–S68, Table S55). For 55-year-olds, intensifying screening to five years until age 75 cost $114,900/QALY and $136,1000/QALY gained for those with and without self-reported diabetes, respectively (Tables S53, S55)

DISCUSSION

We analyzed the cost-effectiveness of several population-wide UACR-based CKD screening strategies, including those that add SGLT2 inhibitors to treatment, from a U.S. healthcare sector perspective. In comparison to status quo, we find that screening and early diagnosis increases life expectancy, adding at least 0.07 life years for 35- to 75-year-olds. Screening also improves morbidity in terms of increased QALYs and decreased incidence of KF on KRT; screening would prevent KF requiring KRT in 398,000 to 658,000 individuals over their lifetimes, depending on the frequency of screening. Screening for CKD also increases costs by identifying individuals with clinically silent CKD who undergo treatment and thus incur these treatment costs. Nevertheless, and in contrast to studies performed prior to the introduction of SGLT2 inhibitors (66), we find that both one-time and periodic screening for CKD represent good value in every age group when SGLT2 inhibitors are included in treatment.

The optimal frequency of periodic screening varies by age, reflecting the epidemiology of CKD over the life course. For 35- to 45-year-olds, screening every 10 years provides good value, whereas in 55- to 65-year-olds the prevalence of CKD rises such that screening every five years is reasonable.

The value of these screening strategies varies with the costs of SGLT2 inhibitors and their effectiveness in reducing progression of CKD and all-cause mortality. In worst-case scenarios where SGLT2 inhibitors are much more expensive and much less effective than in clinical trials, screening is less cost-effective. However, the more likely set of scenarios involves some decrease in SGLT2 inhibitor prices as patent protections sunset (67), paired with modest decreases in effectiveness compared to those demonstrated under ideal clinical

trial conditions. When we tested this scenario (30% decreases in CKD progression reduction and all-cause mortality reduction with a 30% decrease in the monthly cost of SGLT2 inhibitors), screening every ten years and adding SGLT2 inhibitors to treatment cost at most $140,500 per QALY gained across all age groups. While willingness-to-pay thresholds vary by individual (68), screening at least once is less than commonly-used thresholds in the United States of $100,000 per QALY gained and $150,000 per QALY gained (68–71). Cost-effectiveness of screening was robust across tested scenarios, including a subpopulation analysis for those with and without self-reported diabetes.

Our study has limitations. The literature capturing the natural history of CKD treated with SGLT2 inhibitors is in an early phase; without a wealth of randomized controlled trials or observational studies, longer-term outcomes for patients with CKD on SGLT2 inhibitor treatment derive from modeling studies and a single, time-limited randomized controlled trial (13). To accommodate these limitations and to improve the generalizability of our model findings, we conducted sensitivity analyses reducing the anticipated effectiveness of SGLT2 inhibitors. Nonetheless, the transportability of our evidence is limited by our underlying data sources. We included a cost for retroperitoneal ultrasound – a risk-free test that could detect structural abnormalities of the kidney(s) – for screened patients found to have CKD, but ignored associated downstream healthcare costs (e.g., subspecialty referral) and potential benefits (e.g., early detection of an asymptomatic kidney cancer). We ignored costs of repeated laboratory testing associated with conventional therapy (ACE inhibitors/ARBs), owing to controversy surrounding the frequency of testing and at what levels (e.g., of serum potassium or creatinine) therapy should be modified. While modeling incidental findings is beyond the scope of the model, our sensitivity analysis explored variation in costs of screening and diagnostic testing. Because our model does not explicitly simulate the incidence of key comorbidities including diabetes, hypertension, obesity, or a family history of kidney disease, we are limited in producing subpopulation-specific policy recommendations. However, prior work has already demonstrated cost-effectiveness of screening for CKD in some of these selected populations (72,73), and we did analyze the cost-effectiveness of screening in individuals with and without self-reported diabetes in sensitivity analysis. We did not include the anticipated benefits of SGLT2 inhibitors on non-fatal cardiovascular events, including heart failure hospitalization, in our model; ICERs for screening would be more favorable with these benefits included. Due to data limitations, we did not conduct our analysis from the societal perspective. However, had we included changes in productivity or care-giving time, cost-effectiveness of population-wide CKD screening may have been more favorable than we estimated. Numerous barriers are likely to arise in the real-world implementation of a large population-wide screening program due to differential healthcare access, health-seeking behaviors, and treatment adherence. Our analysis does not consider all implementation scenarios.

In sum, UACR-based screening for CKD followed by treatment with ACE inhibitors/ARB therapy and SGLT2 inhibitors is cost-effective for the general U.S. population aged 35 and above.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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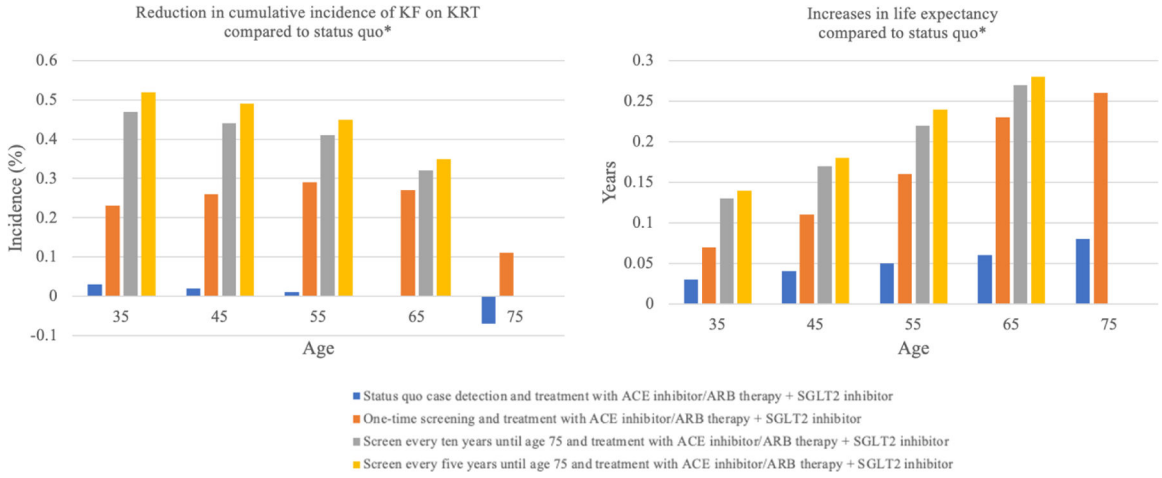

Figure 1.

Changes in incidence of KF on KRT (a) and average life expectancy (b) from population-wide CKD screening in comparison to status quo detection and treatment with ACE inhibitors/ARB therapy

ACE inhibitor: angiotensin-converting enzyme inhibitors

ARB therapy: angiotensin receptor blocker therapy

SGTL2 inhibitor: Sodium glucose co-transporter 2 inhibitor

KF on KRT: kidney failure on kidney replacement therapy

Status quo*: case detection and treatment with ACE inhibitor/ARB therapy

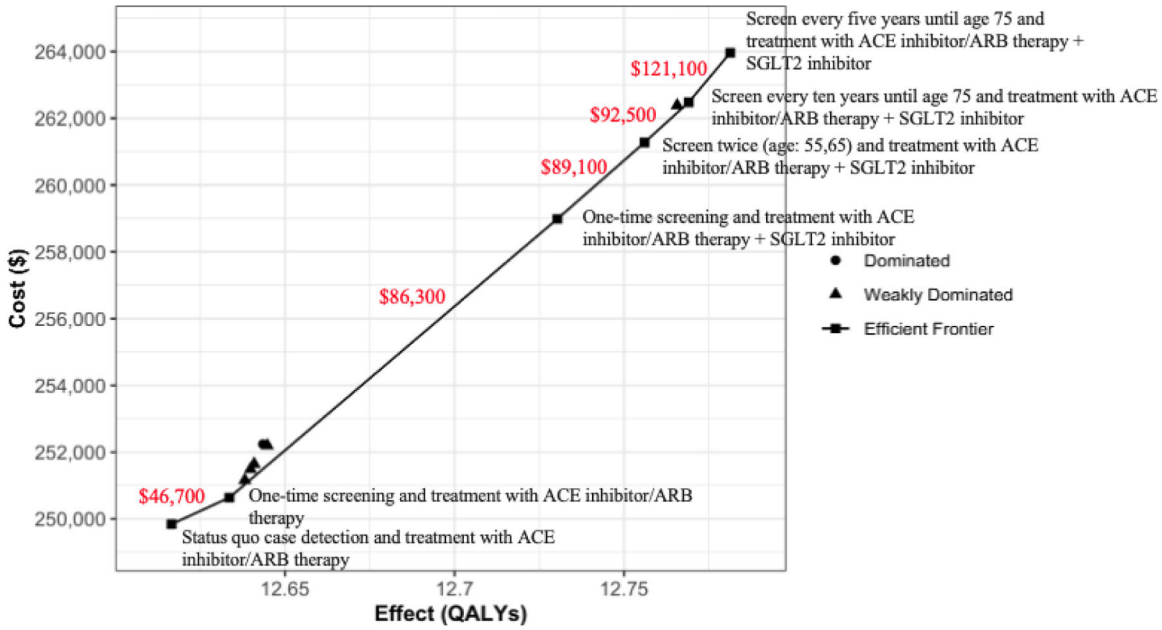

Figure 2.

Cost-effectiveness plane (55-year-olds) (65)*

*Red numbers indicate incremental cost-effectiveness ratios represented in costs ($) per QALY gained

ACE inhibitor: angiotensin-converting enzyme inhibitors

ARB therapy: angiotensin receptor blocker therapy

SGTL2 inhibitor: Sodium glucose co-transporter 2 inhibitor

QALYs: quality-adjusted life years

Table 1.

Base case model inputs with uncertainty ranges

Parameters	Value	Range (95% UI)
Screening parameters		
UACR screening sensitivity (48)	0.87	(0.81, 0.91)
UACR screening specificity (48)	0.88	(0.84. 0.91)
Cost of UACR screening (49,50)	$49	($36, $64)
Probability of treatment initialization after diagnosis (51,52)	0.75	(0.5,1)
Cost of screening visit with primary care provider (53)	$200	($147, $259)
Diagnosis parameters		
Cost of estimated GFR (49,54)	$23	($17, $30)
Cost of retroperitoneal ultrasound (49,55)	$420	($312, $544)
Treatment parameters		
ACE inhibitor/ARB therapy – CKD progression reduction – hazards ratio (26–29)	0.81	(0.52, 1)
Monthly cost of ACE inhibitor/ARB therapy (36,49,56)	$14	($10, $18)
SGLT2 inhibitors – CKD progression reduction – hazards ratio (persons without diabetes) (13)	0.51	(0.34, 0.75)
SGLT2 inhibitors – all-cause mortality reduction – hazards ratio (persons without diabetes) (13)	0.52	(0.29, 0.93)
SGLT2 inhibitors – CKD progression reduction – hazards ratio (persons with diabetes) (13)	0.57	(0.45, 0.73)
SGLT2 inhibitors – all-cause mortality reduction – hazards ratio (persons with diabetes) (13)	0.74	(0.56, 0.98)
Monthly cost of SGLT2 inhibitors (dapagliflozin) (49,57)	$365	($273, $474)
Disutility associated with medication related angioedema adverse event (42)	0.01	(0.0025, 0.03)
Cost increase from angioedema medication-related adverse event (49,58)	$3879	($2897, $4993)
Proportion of diagnosed persons who experience an angioedema medication-related serious adverse event (36)	0.1%	(0.1%, 0.9%)
Disutility associated with genital infection adverse event (43)	0.001	(0.0002, 0.006)
Cost increase from genital infection adverse event (37)	$153	($111, $193)
Annual rate of genital infection adverse event (31)	0.037	(0.027, 0.051)
Disutility associated with euglycemic diabetic ketoacidosis adverse event (41)	0.0091	(0.004, 0.016)
Cost increase from diabetic euglycemic ketoacidosis adverse event (38)	$31,304	($22,655, $39,789)
Annual rate of diabetic euglycemic ketoacidosis adverse event (59)	0.002	(0.0002, 0.006)
Age-specific diabetes prevalence (among those eligible for SGLT2 inhibitor treatment) (25)		
Diabetes prevalence (30–39-year-olds)	9.6%	(4.17%, 20.8%)
Diabetes prevalence (40–49-year-olds)	29.2%	(17.6%, 38.2%)
Diabetes prevalence (50–59-year-olds)	57.2%	(47.9%, 63.0%)
Diabetes prevalence (60–69-year-olds)	39.8%	(35.6%, 46.3%)
Diabetes prevalence (70–79-year-olds)	43.5%	(39.8%, 48.0%)
CKD mortality parameters		
Age and sex specific mortality rate (33)	U.S. life tables	(+/−10%)
Mortality risk - CKD stage G2 - hazard ratio (32)	1.0	(1.0, 1.0)
Mortality risk - CKD stage G3a - hazard ratio (32)	1.2	(1.1, 1.2)

Parameters	Value	Range (95% UI)
Mortality risk - CKD stage G3b - hazard ratio (32)	1.8	(1.7, 1.9)
Mortality risk - CKD stage G4 - hazard ratio (32)	3.2	(3.1, 3.4)
Mortality risk - kidney failure not requiring KRT - hazard ratio (32)	3.2	(3.1, 3.4)
Mortality risk - kidney failure not requiring KRT - hazard ratio (32)	5.9	(5.4, 6.5)
CKD Quality-of-Life adjustments for health states parameters		
Quality of life adjustment - CKD Stage G2 (39)	0.85	(0.7, 1.0)
Quality of life adjustment - CKD Stage G3a (39)	0.80	(0.69, 1.0)
Quality of life adjustment - CKD Stage G3b (39)	0.80	(0.68, 1.0)
Quality of life adjustment - CKD Stage G4 (39)	0.74	(0.62, 0.85)
Quality of life adjustment - kidney failure not requiring KRT (39)	0.74	(0.62, 0.85)
Quality of life adjustment – kidney failure requiring KRT (39)	0.60	(0.55, 0.64)
CKD stage-specific cost parameters		
Monthly added cost of CKD Stage G3a (35,46)	$136	($102, $176)
Monthly added cost of CKD Stage G3b (35,46)	$369	($275, $479)
Monthly added cost of CKD Stage G4 (35,46)	$1069	($787, $1369)
Monthly added cost of kidney failure not requiring KRT (35,46)	$1069	($787, $1369)
Monthly added cost of kidney failure requiring KRT (22,46)	$7,018	($5,210, $9,059)
Monthly added cost of diabetes (undetected CKD Stage G3a)	$103	($78, $135)
Monthly added cost of diabetes (undetected CKD Stage G3b)	$260	($192, $338)
Monthly added cost of diabetes (undetected CKD Stage G4)	$601	($447, $778)
Monthly added cost of diabetes (undetected kidney failure not requiring KRT)	$601	($447, $778)
Baseline costs (34,49)	AHRQ * US expenditure table (2013 converted to 2021)	(75%, 125%)
Calibration parameters (25) (Table S11)		

* Costs are reported in 2021 USD

UACR: urine albumin-creatinine ratio

GFR: glomerular filtration rate

CKD: chronic kidney disease

ACE inhibitor: angiotensin-converting enzyme inhibitors

ARB therapy: angiotensin receptor blocker therapy

SGTL2 inhibitor: sodium glucose co-transporter 2 inhibitor

Table 2.

Results: main health outcomes and costs (mean value and 95% uncertainty interval) of screening interventions (55-year-olds)

Screening intervention	Cumulative incidence of KF on KRT (%)	QALYs	LYs	Healthcare costs ($)	SGLT2 inhibitor costs ($)
Status quo case detection and treatment with ACE inhibitor/ARB therapy	2.33% [0.66%, 5.01%]	12.62 [11.1, 13.7]	17.29 [17.09, 17.45]	249,800 [189,000, 318,800]	N/A
One-time screening and treatment with ACE inhibitor/ARB therapy	2.16% [0.59%, 4.7%]	12.63 [11.11, 13.71]	17.3 [17.11, 17.46]	250,600 [189,800, 319,500]	N/A
Status quo case detection and treatment with ACE inhibitor/ARB therapy + SGLT2 inhibitor	2.31% [0.61%, 5.0%]	12.64 [11.11, 13.73]	17.33 [17.14, 17.49]	252,200 [191,200, 321,300]	1,100 [700, 1,800]
One-time screening and treatment with ACE inhibitor/ARB therapy + SGLT2 inhibitor	2.04% [0.51%, 4.52%]	12.73 [11.19, 13.82]	17.45 [17.24, 17.63]	259,000 [197,700, 328,300]	5,200 [3,300, 7,500]
Screen twice (age: 55,65) and treatment with ACE inhibitor/ARB therapy + SGLT2 inhibitor	1.95% [0.48%, 4.36%]	12.76 [11.22, 13.85]	17.49 [17.27, 17.68]	261,300 [199,800, 330,700]	6,200 [3,900, 9,000]
Screen every ten years until age 75 and treatment with ACE inhibitor/ARB therapy + SGLT2 inhibitor	1.92% [0.47%, 4.3%]	12.77 [11.23, 13.86]	17.51 [17.29, 17.71]	262,500 [200,800, 331,900]	6,700 [4,200, 9,700]
Screen every five years until age 75 and treatment with ACE inhibitor/ARB therapy + SGLT2 inhibitor	1.87% [0.45%, 4.22%]	12.78 [11.23, 13.88]	17.52 [17.3, 17.73]	264,000 [202,400, 333,600]	7,100 [4,500, 10,400]

ACE inhibitor: angiotensin-converting enzyme inhibitors

ARB therapy: angiotensin receptor blocker therapy

SGTL2 inhibitor: sodium glucose co-transporter 2 inhibitor

KF on KRT: kidney failure on kidney replacement therapy

LY: life years

QALYs: quality-adjusted life years