Screening for chronic kidney disease in Canadian indigenous peoples is cost-effective

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Canadian indigenous (First Nations) have rates of kidney failure that are 2- to 4-fold higher than the non-indigenous general Canadian population. As such, a strategy of targeted screening and treatment for CKD may be cost-effective in this population. Our objective was to assess the cost utility of screening and subsequent treatment for CKD in rural Canadian indigenous adults by both estimated glomerular filtration rate and the urine albumin-to-creatinine ratio. A decision analytic Markov model was constructed comparing the screening and treatment strategy to usual care. Primary outcomes were presented as incremental cost-effectiveness ratios (ICERs) presented as a cost per quality-adjusted life-year (QALY). Screening for CKD was associated with an ICER of $23,700/QALY in comparison to usual care. Restricting the model to screening in communities accessed only by air travel (CKD prevalence 34.4%), this ratio fell to $7,790/QALY. In road accessible communities (CKD prevalence 17.6%) the ICER was $52,480/QALY. The model was robust to changes in influential variables when tested in univariate sensitivity analyses. Probabilistic sensitivity analysis found 72% of simulations to be cost-effective at a $50,000/QALY threshold and 93% of simulations to be cost-effective at a $100,000/QALY threshold. Thus, targeted screening and treatment for CKD using point-of-care testing equipment in rural Canadian indigenous populations is cost-effective, particularly in remote air access–only communities with the highest risk of CKD and kidney failure. Evaluation of targeted screening initiatives with cluster randomized controlled trials and integration of screening into routine clinical visits in communities with the highest risk is recommended.

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Chronic kidney disease (CKD) is a worldwide public health problem with an increasing prevalence.[1] CKD is a potent, independent risk factor for several adverse health outcomes, including kidney failure, hospitalization, cardiovascular events, and early death.[2,3] Early detection, appropriate risk stratification, and subsequent treatment of CKD may delay or prevent many of its associated complications, but at increased up-front cost.[4] With the availability of reliable point-of-care quantitative blood and urine tests, it is possible to screen for CKD and to present results quickly and accurately.[5]

Mass screening for CKD in the general population is not advised,[6,7] and it offers poor value for money in low-risk populations. In contrast, targeted screening in high-risk groups, such as those with diabetes and/or hypertension, has been shown to be cost-effective.[8] Furthermore, screening is also a cost-effective strategy in certain high-risk ethnic groups, such as African Americans, where there is an elevated risk of kidney failure and its associated complications.[9]

Canadian indigenous peoples (First Nations) have rates of kidney failure that are 2- to 4-fold higher than the nonindigenous general Canadian population.[10] These rates are largely attributable to elevated rates of diabetes,[11] with over 60% of kidney failure cases attributed to diabetic nephropathy in indigenous peoples compared with 35% in the general population.[12,13] Indigenous communities in rural locations often have reduced access to primary and specialist care and therefore have reduced access to opportunistic screening and treatment for chronic conditions. As a result, patients in these communities often travel long distances or else relocate entirely to receive complex care such as dialysis, adversely impacting their quality of life.[14–17]

To date, the cost-effectiveness of mass screening for CKD in Canadian First Nations or other high-risk indigenous populations has not been assessed. Therefore, the objective of this study was to assess the cost utility of one-off, point-of-care screening and treatment for CKD using both estimated glomerular filtration rate (eGFR) and urine

albumin-to-creatinine ratio (ACR), in a rural adult Canadian indigenous population. We hypothesized that, due to a higher prevalence of albuminuria, increased rates of progression to kidney failure,[18,19] and increased costs of providing renal replacement therapy in remote communities,[20] screening- and risk-based treatment for CKD in Canadian indigenous peoples would be cost-effective.

RESULTS

Model validity

The life expectancy remaining at age 45 years was 28.96 years in the usual care arm and 29.04 years in the screening arm; at age 65 years, life expectancy was 13.43 years in the screening arm and 13.42 years in the usual care arm (Supplementary Tables S1 and S2). This latter metric represents an approximately 8-year lower life expectancy in this indigenous population than in the general Manitoba population,[21] a finding consistent with the life expectancy gap previously described in Manitoba's indigenous population.[22]

Baseline findings

Screening for CKD in rural and remote Canadian indigenous peoples was associated with an incremental cost-effectiveness ratio (ICER) of $23,700 per quality-adjusted life-year (QALY). In the usual care scenario, total costs were $12,790 and effectiveness was 12.9869 QALYs, whereas screening was associated with a cost of $13,400 and effectiveness of 13.0124 QALYs (Table 1).

Sensitivity and scenario analyses

The results of our one-way sensitivity analyses are illustrated in Figure 1 and Table 2. Primary model drivers were the baseline prevalence of any kidney damage, treatment effectiveness with respect to reduction of disease progression, the incremental costs of CKD management, treatment adherence, and the cost of dialysis. However, the model was found to be robust to univariate changes across plausible ranges of these variables. Probabilistic sensitivity analysis demonstrated that at a threshold of $50,000/QALY, approximately 72% of simulations found screening to be cost-effective (12% were dominant and <0.1% of simulations were inferior), and that at a threshold of $100,000/QALY, 93% of simulations found screening to be cost-effective (Figure 2).

In scenario analyses, extension of the benefits of treatment to those with moderately increased albuminuria (urine ACR ≥ 30 mg/g or 3 mg/mmol from baseline ≥ 300 mg/g or 30 mg/mmol) found screening to be the dominant treatment strategy when considering all communities together and those accessible only by air. When considering road access communities, screening was associated with an ICER of $9,800/QALY. Increase of home modality uptake by 25% produced an ICER of $4,240/QALY across all communities. Increasing uptake by 50% or 100% resulted in screening being the dominant treatment strategy. Results of scenario analyses are presented in Table 1.

Table 1 | Results of cost-effectiveness simulation and scenario analyses

Population	Incremental cost ($C)	Incremental QALYs	Cost/QALY (ICER)
Baseline model			
All FINISHED communities	605	0.0255	23,700
Air access communities	292	0.0375	7790
Road access communities	806	0.0154	52,480
Threshold for relative risk reduction afforded by treatment extended to patients with moderately increased albuminuria (urine ACR ≥ 3 mg/mmol)			
All FINISHED communities	−26	0.0643	Screening dominant
Air access	−620	0.0873	Screening dominant
Road access	430	0.0435	9800
Scenario analysis of increased home modality uptake			
Increase by 25%	108	0.0255	4240
Increase by 50%	−389	0.0255	Screening dominant
Increase by 100%	−1385	0.0255	Screening dominant

ACR, albumin-to-creatinine ratio; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

Comparison of road and air access communities

Due to higher assumed costs of satellite dialysis and treatment-related transportation, increased prevalence of progressive CKD, and higher levels of severely increased albuminuria, the incremental cost of screening in air access–only communities totaled $292 with an incremental effectiveness of 0.0375 QALYs (ICER $7790/QALY). Conversely, road accessible communities had lower assumed satellite dialysis costs, a lower prevalence of high-risk CKD, and lower levels of severely increased albuminuria, with a resulting incremental cost of $806 and incremental effectiveness of 0.0154 QALYs from the screening strategy (ICER $52,480/QALY) (Table 1).

DISCUSSION

In this study, we found that screening and treatment for CKD in comparison to usual care in Canadian rural indigenous is highly cost-effective (ICER $23,700/QALY). Moreover, in the most remote communities accessible only by air travel, screening was found to be even more cost-efficient (ICER $7,790/QALY). The primary model drivers of cost-effectiveness included treatment effectiveness, baseline CKD prevalence, adherence to prescribed treatment, and the incremental cost of managing CKD on case finding. Nonetheless, these drivers, when varied over a plausible range, consistently produced an ICER below or near $50,000/QALY. Together, these findings suggest that large-scale CKD screening initiatives in this high-risk population are economically justifiable.

To our knowledge, this is the first formal cost-effectiveness analysis examining the economic and health impact of a mass screening strategy for CKD in indigenous peoples. Several other studies have explored the question of mass versus opportunistic screening for CKD in a variety of different

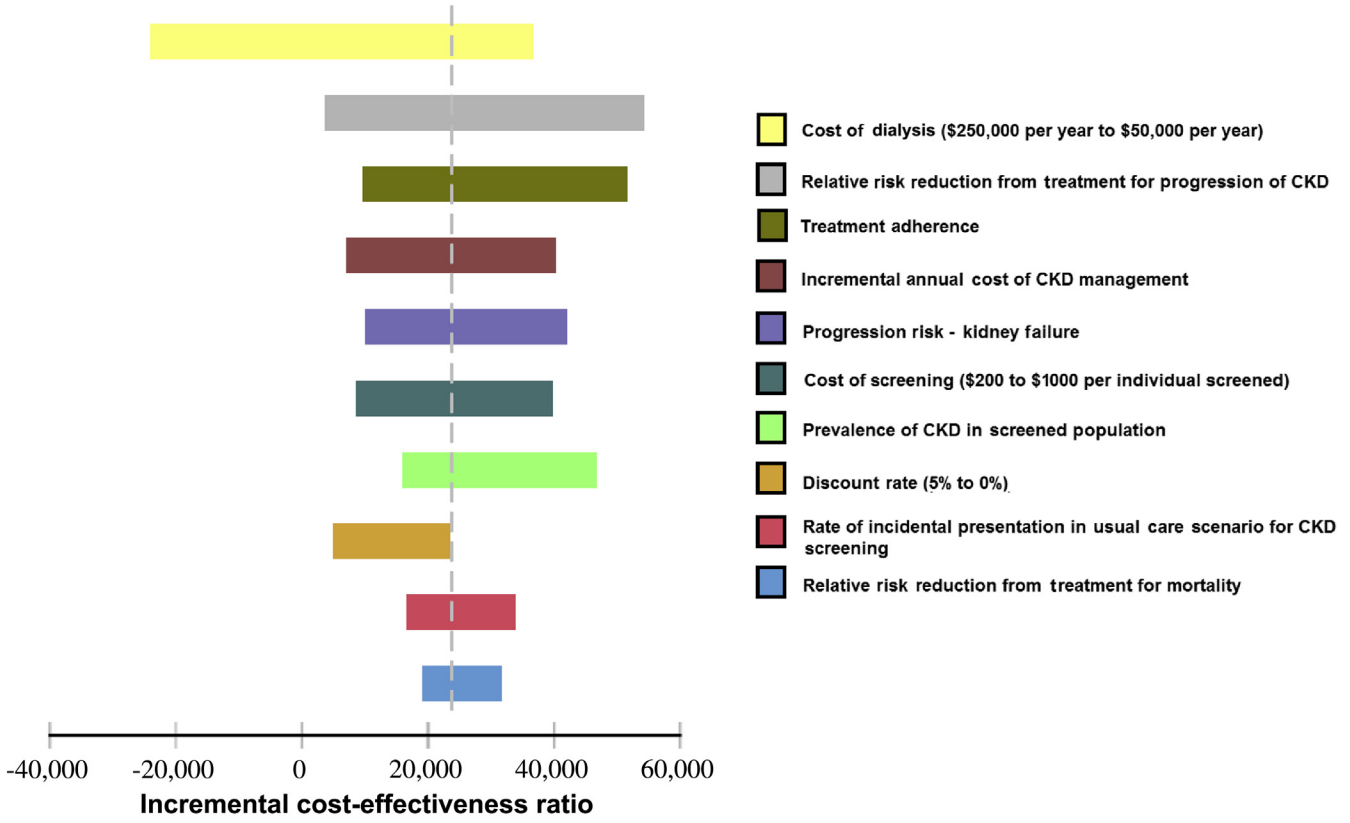

Figure 1 | One-way sensitivity analysis of influential model parameters. CKD, chronic kidney disease.

populations. In general, these studies have found that mass screening of an unselected community population is not cost-effective, whereas targeted screening in certain groups with high prevalence of CKD and high risk of progression to kidney failure (e.g., patients with diabetes and/or hypertension or African Americans[8,9]) would be cost-effective. Our study confirms these previous findings and extends them to a Canadian indigenous population.

Rates of progression to end-stage renal disease and prevalence of albuminuria were major drivers of cost-effectiveness across all studies.[8] Screening was thus most cost-effective in those populations with highest prevalence of albuminuria and propensity to kidney failure. Canadian indigenous groups appear to meet these criteria. The First Nations Community Based Screening to Improve Kidney Health and Prevent Dialysis (FINISHED) study[23] found that indigenous communities had a prevalence of kidney disease (defined as urine ACR $\geq$ 30 mg/g [3 mg/mmol] or GFR $<$ 60 ml/min per 1.73 m^2) that was twice as high as for the Canadian general population (25.5% vs. 12.5%).[24] Administrative data confirms a high incidence and young age of onset of kidney failure in these indigenous communities, consistent with rapid progression of kidney disease.[25]

The reasons for the high incidence of CKD and rate of progression to kidney failure in Canadian indigenous communities have been previously explored. The causes appear to be multifactorial. There is a consistently documented high prevalence of diabetes and hypertension among residents of rural indigenous communities.[26,27] Beyond this, nearly one-third of those screened in the FINISHED study were found to have kidney disease without evidence of concurrent diabetes or hypertension.[23] Thus a substantial portion of potentially treatable kidney disease could be missed if screening in these communities were limited to those with diabetes and hypertension.

Our findings have implications for clinical care and research. Our study confirms that mass screening of high-prevalence, high-progression risk communities is likely to be cost-effective. This finding is generalizable to other at-risk indigenous populations. For example, a high prevalence of CKD and kidney failure has been observed in the United States among the Navajo, Zuni, and Pima Indians,[28–31] and in Australia and New Zealand among the Pacific Islanders, Maori, and Aboriginal and Torres Strait Islanders.[32–34] Ideally, the cost-effectiveness of such an intervention would be confirmed in a cluster randomized controlled trial. Such a trial appears well justified by our findings. However, as a trial of this magnitude will take years to perform and would be costly, and as the human cost of inaction appears substantial, consideration could be given to implementing mass screening in communities with the highest risk.

Integrating additional potential benefits of screening and treatment in the existing model framework may improve the cost-effectiveness of a screening intervention. Previous studies

Table 2 | One-way sensitivity analysis of influential model parameters

Variable	Incremental cost ($C)	Incremental QALYs	Cost/QALY
Baseline	605	0.0255	23,700
Initial CKD risk strata prevalence (baseline low = 19.5%, intermediate = 4.5%, high = 1.5%)			
Initial CKD risk strata prevalence increased 50%	613	0.0383	16,000
Initial CKD risk strata prevalence decreased 50%	597	0.0128	46,770
Discount rate (baseline = 5%)			
Discount rate decreased to 0%	346	0.0691	5000
Discount rate decreased to 3%	534	0.0370	14,450
Treatment adherence (baseline = 75%)			
Treatment adherence increased to 100%	330	0.0340	9700
Treatment adherence decreased to 50%	880	0.0170	51,690
Annual risk of CKD progression			
Risk of progression increased 50%	217	0.0313	6940
Risk of progression decreased 50%	962	0.0188	51,150
ACE-I/ARB treatment effectiveness—progression reduction (baseline = 33% progression reduction)			
Relative risk reduction increased 50%	116	0.0314	3700
Relative risk reduction decreased 50%	1081	0.0199	54,300
ACE-I/ARB treatment effectiveness—mortality reduction (baseline = 23% mortality reduction)			
Relative risk reduction increased 50%	654	0.0340	19,230
Relative risk reduction decreased 50%	558	0.0176	31,780
Utility value associated with CKD (baseline = 0.85)			
Utility value increased to 0.90	605	0.0273	22,200
Utility value decreased to 0.75	605	0.0221	27,400
Utility value associated with dialysis (baseline = 0.72)			
Utility value increased to 0.85	605	0.0245	24,670
Utility value decreased to 0.60	605	0.0265	22,860
Expected cost of dialysis (baseline = $92,900)			
Cost of dialysis increased 50%	244	0.0255	9560
Cost of dialysis decreased 50%	966	0.0255	37,830
Cost of screening (baseline = $589)			
Cost of screening increased to $1000 per person	1016	0.0255	39,790
Cost of screening decreased to $200 per person	215	0.0255	8450
Average incremental CKD treatment costs (baseline for high risk = $2,083, intermediate risk = $399, low risk = $210)			
Incremental CKD treatment costs increased 50%	1032	0.0255	40,440
Incremental CKD treatment costs decreased 50%	177	0.0255	6950
Annual incidental screening rate (baseline = 5%)			
Incidental screening rate increased to 10%/yr	563	0.0165	34,100
Incidental screening rate decreased to 2.5%/yr	654	0.0331	19,770
Rate of ACE-I/ARB usage in those screened (baseline = 0%)			
Increased usage to 20% of all those screened	766	0.0201	38,190
Increased usage to 40% of all those screened	929	0.0145	64,112

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; CKD, chronic kidney disease; QALY, quality-adjusted life-year.

have considered the impact of albuminuria screening on the reduction of cardiovascular events and found screening to be cost-effective even in the general population.[35,36] Some potential benefits include the reduction of cardiovascular events in patients with diabetes using blood pressure–lowering pharmacotherapy,[37] and the potential for increased uptake of statin prescriptions in newly identified CKD cases.[38,39] In addition, prescription of new therapies such as sodium-glucose cotransporter 2 inhibitors can provide benefit in patients with type 2 diabetes and high cardiovascular risk.[40] Multiple factors would influence the efficacy of these treatments in a decision analysis model, including prevailing rates of usage of each pharmacotherapy, the underlying prevalence of untreated diabetes in screened communities, and ancillary effects of a screening program such as community education, increased awareness, and lifestyle interventions. Overall effectiveness of a screen and treat initiative could therefore be better measured with a cluster randomized trial that can better capture multiple concurrent effects and their influence on patient outcomes. Nonetheless, the model framework incorporating only the effects of angiotensin-converting enzyme inhibitor (ACE-I) and angiotensin-receptor blocker (ARB) prescriptions in patients with severely increased albuminuria demonstrates a high likelihood that screening for CKD in this population would be cost-effective.

Our analysis has many strengths. We stratified risk of progression using both eGFR and quantitative urine ACR, whereas many previous analyses have evaluated the cost utility

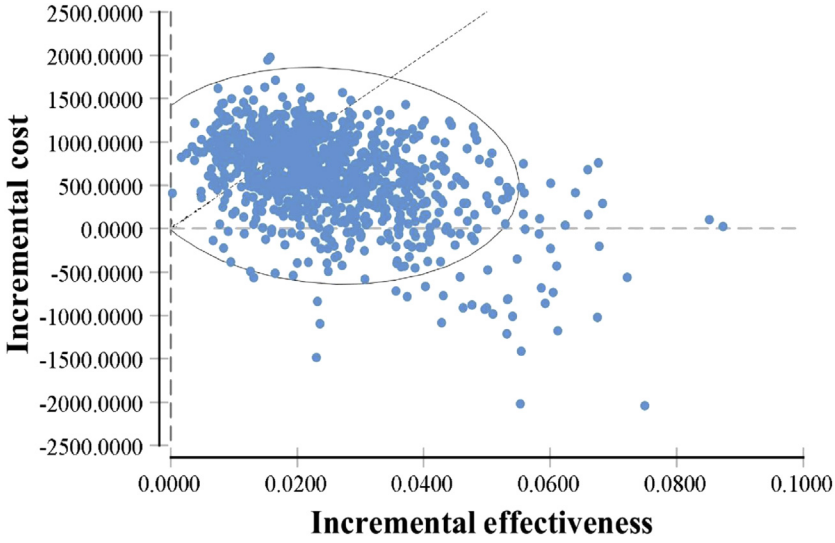

Figure 2 | Probabilistic sensitivity analysis comparing screening strategy versus usual care. The diagonal dashed line represents a $50,000 per quality-adjusted life-year threshold. Points falling below this line represent simulations that were cost-effective (cost at most $50,000 for each additional quality-adjusted life-year). Points situated below the *x*-axis (<0 incremental costs) and to the right of the *y*-axis (>0 incremental effectiveness) represent simulations in which the screening strategy was found to be dominant (both less costly and more effective).

of screening for CKD based on urine ACR or eGFR screening alone.[8] This classification of progression risk aligns with current CKD evaluation and management guidelines, and there has been a demonstrated relationship between the dual staging system by both eGFR and urine ACR and adverse outcomes, including kidney failure, progressive CKD, cardiovascular events, and increased mortality.[41] Additionally, we used demographic, progression, and cost data derived directly from a real-world screening program in indigenous communities. Our study has conservatively assumed that early detection of CKD and treatment with ACE-Is or ARBs would only benefit patients with severely increased albuminuria.

There were also some limitations to our analysis. The source data from FINISHED used a single measurement of urine ACR to classify persistent albuminuria, whereas an ideal classification of CKD would be made with elevated urine ACR sustained over a 3-month period.[41] In addition, the self-selected nature of the FINISHED cohort may underestimate the prevalence of CKD if the healthiest individuals self-select for presentation or overestimate the prevalence if those with risk factors, such as hypertension or diabetes, self-select for presentation.

Conclusions

Our findings suggest that targeted screening and treatment for CKD using point-of-care testing equipment in rural Canadian indigenous populations is cost-effective, particularly in remote air access–only communities that had the highest risk of CKD and kidney failure. These findings are relevant to other high-risk indigenous groups with a similar burden of

Table 3 | Demographic characteristics of the FINISHED screening cohort[23]

Variable	All communities *n* = 1346	Road access *n* = 716	Air access only *n* = 630	*p*
Age (yr)	44.9 ± 14.5	45.2 ± 14.4	44.6 ± 14.6	0.48
Sex (female)	61 (816)	59 (424)	62 (392)	0.27
$HgbA_{1c}$	5.8 (5.4–7.4)	5.6 (5.3–7.0)	6.0 (5.4–8.0)	<0.01
$HgbA_{1c}$ (≥6.5%)	35	29	42	<0.01
eGFR (ml/min per 1.73 m^2)				
≥60	96	96	95	0.89
45–59	2.5	2.1	2.9	
30–44	1.3	1.1	1.4	
15–29	0.3	0.3	0.3	
<15	0.2	0.1	0.2	
Urine ACR (mg/mmol)	1.4 (0.6–3.2)	1.0 (0.5–1.9)	1.9 (0.8–5.1)	<0.01
Elevated blood pressure (≥140 mm Hg SBP or ≥90 mm Hg DBP)	15	16	14	0.32

ACR, albumin-to-creatinine ratio; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FINISHED, First Nations Community Based Screening to Improve Kidney Health and Prevent Dialysis; HbA_{1c}, hemoglobin A_{1c}; SBP, systolic blood pressure.
Continuous variables expressed as mean ± SD or median (interquartile range). Categorical variables expressed as percentages or percentage (*n*). Continuous variables compared using the *t* test for normally distributed variables and the Wilcoxon rank-sum test otherwise. Categorical variables compared used the chi-squared test.

CKD and progression risk to kidney failure. Evaluation of targeted screening initiatives with cluster randomized controlled trials, as well as integration of screening into routine clinical visits in high-risk communities is recommended.

MATERIALS AND METHODS

Overview

We performed an incremental cost-utility analysis of one-off screening and risk-based treatment for CKD versus usual care in Manitoba's rural indigenous peoples (age ≥18 years). We examined a screening strategy employing both eGFR and urine ACR in comparison to usual care. Our analysis took the perspective of the universal Canadian public health payer. All costs and benefits were discounted at 5% annually.[42] All historic cost estimates were inflated using the Canadian health and personal care consumer price index and are presented in 2013 Canadian dollars.[43] All benefits were presented using QALYs. Final results were presented as ICERs. This study received ethical approval from the University of Manitoba Health Research Ethics Board (file number HS16070).

Simulation model

We constructed a computer-simulated Markov model using decision-analysis software (TreeAge Pro 2015, Williamstown, MA). Risk of progression to kidney failure was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) heat map classification diagram.[41] Model states were divided into normal kidney function; low, intermediate and high risk of progression to kidney failure; being on dialysis; surviving with a kidney transplant; and death. The model was executed using 1-year cycles and followed those screened for 45 years or until death. We assessed model validity by comparing life tables in Manitoba's indigenous population with the life expectancy determined in the Markov simulation.

Data inputs

Initial risk classification of patients was completed using results of the FINISHED screening study ($n = 1346$).[23] An overview of the demographics of this population is provided in Table 3. Estimated GFR was calculated using the Chronic Kidney Disease Epidemiology (CKD-EPI) study equation.[44] The FINISHED population had a mean age of 45 years, and the initial proportions of patients at low, intermediate, and high kidney failure progression risk were 19.5% (yellow cells on the KDIGO heat map), 4.5% (orange cells), and 1.5% (red cells), respectively[23] (Supplementary Figure S1). Longitudinal data on CKD progression and regression rates were adapted from the Canadian indigenous cohort within the Alberta Kidney Disease Network.[45] Transition probabilities for CKD progression and regression are presented in Supplementary Table S3.

Mortality rates were adapted from a baseline population using life tables from Statistics Canada and modified using relative risk ratios from previously published meta-analyses that applied a 2-axis staging system of eGFR and urine ACR to predict all-cause mortality risk in each respective kidney failure risk stratum.[46,47] Mortality rates for those surviving with a transplant or who were on dialysis, as well as the chance of graft failure, were taken from the Canadian Organ Replacement Register (CORR),[13] and a previously published Canadian screening cost-effectiveness study.[48] Transition probabilities for both preemptive transplant and transplant for those on dialysis were also taken from the CORR. In addition, the effect of transplantation chance from indigenous status was adjusted using a hazard ratio of 0.43.[49] Annual mortality and transplant probabilities are summarized in Table 4.

Adherence to treatment was assumed to be 75% in accordance with most existing CKD screening models.[48,50–52] We assumed in the model that those screened and determined to be at risk of kidney failure would be referred to a nephrologist if (1) eGFR ≤ 30 ml/min per 1.73 m^2, or if (2) urine ACR ≥ 300 mg/g or 30 mg/mmol and eGFR between 30 and 45 ml/min per 1.73 m^2.[6,53]

Treatment effectiveness estimates for reduction in both progression and mortality were taken from previous CKD screening cost-effectiveness models.[50–52] ACE-Is and ARBs were assumed to offer benefit only in individuals with severely increased albuminuria. We assumed treatment offers a 23% relative risk reduction to mortality rates and 33% relative risk reduction in rates of progression to

Table 4 | Annual mortality and transplant probabilities

	Annual mortality—CKD			
Cycle	Healthy risk	Low risk	Intermediate risk	High risk
1–5	0.0033	0.0051	0.0096	0.0130
6–10	0.0050	0.0078	0.0146	0.0197
11–15	0.0071	0.0110	0.0206	0.0279
16–20	0.0114	0.0177	0.0331	0.0448
21–25	0.0193	0.0301	0.0562	0.0761
26–30	0.0314	0.0489	0.0914	0.1237
30–35	0.0481	0.0748	0.1398	0.1892
36–40	0.0750	0.1167	0.2181	0.2952
41–45	0.1288	0.2004	0.3747	0.5070
46+	0.2508	0.3904	0.7192	0.8800
Cycle	**Annual mortality—dialysis (first year)**			
1–10	0.0780			
11–20	0.1280			
21–30	0.1800			
31+	0.2500			
Cycle	**Annual mortality—dialysis (yr 2+)**			
1–2	0.0680			
3–10	0.0860			
11–12	0.1040			
13–20	0.1190			
21–22	0.1330			
23–30	0.1520			
31–32	0.1800			
33+	0.1940			
Cycle	**Transplant—failure**			
All	0.0400			
Cycle	**Transplant—mortality**			
1-20	0.0120			
21+	0.0710			
Cycle	**Transplant chance–preemptive**			
1–20	0.0194			
21–30	0.0039			
31+	0.0000			
Cycle	**Transplant chance—patient on dialysis**			
1–20	0.0046			
21+	0.0003			

CKD, chronic kidney disease.

kidney failure[50–52] and assumed equivalent outcomes for both ACE-Is and ARBs.[54] Model probability parameters are summarized in Table 5.

Costs

The per-patient cost of screening was taken directly from the financials for the FINISHED screening project. This included all expenses relative to provision of screening services, including transportation of equipment and personnel to remote locations, advertisement, human resources, laboratory, testing device–related costs, and dissemination of results to community stakeholders, totaling $589 per individual screened. The cost of an incidental presentation to care was calculated relative to the location in the KDIGO heat map, with all patients incidentally screened being assessed the cost of general practitioner visit (complete history and physical examination) at $76.25,[55] and the costs of a CKD screening test and associated laboratory fees (electrolytes, urea, creatinine, urinalysis, and urine ACR) at a total cost of $30.43 based on a provider quote. For the highest risk patients who require referral to nephrology, an additional cost of $175.25 was applied in the first year.[55]

The cost of dialysis was determined as a weighted average of the cost of facility-based hemodialysis (HD), peritoneal dialysis (PD), home HD, and satellite HD based on the prevalence of each modality's utilization (Supplementary Table S4). The cost of HD, PD, and home HD were adjusted for additional costs of shipping consumables and travel expenses to remote locations. The annual cost of facility-based HD totaled $74,590, PD totaled $43,500 ($29,603 + $13,897 shipping and travel), and home HD totaled $61,305 ($47,408 + $13,897 shipping and travel).[20,56] The cost of satellite HD was estimated to be $130,711 per patient, per year and was based on a previous study describing the costs of satellite dialysis in Manitoba's rural communities[20] (Supplementary Table S5). The cost of receiving a transplant was estimated as $94,987 in the first year and $39,942 in subsequent years.[57]

The annual incremental cost of managing detected CKD through routine clinic care was taken from a previously published Canadian costing study.[48] Costs were applied as a weighted average to each cell on the KDIGO heat map risk classification system. Patients at low risk of kidney failure (yellow) were assumed to have an annual incremental cost $210, those with intermediate risk (orange) had an annual incremental cost of $399, and those with high risk (red) had an annual incremental cost of $2083.

Valuation of health benefits

The annual utility values of living with normal kidney function, CKD, or being on dialysis were estimated to be 0.90, 0.85, and 0.72, respectively.[58] For patients surviving with a transplant, the annual utility value was estimated to be 0.816.[48,57] We assumed similar utility for diagnosed and undiagnosed CKD.[48] Model cost and utility parameters are summarized in Table 6.

Sensitivity and scenario analyses

One-way sensitivity analyses were performed on model variables using a range of ±50% from baseline. We varied cost of screening from $200 to $1000 per patient (baseline $589). The annual chance of incidental presentation to a provider for screening varied from 2.5% to 10% per year. Discount rates were evaluated at values of 0% and 3%.[42] We also considered increasing the rate of baseline ACE-I and ARB prescriptions to 20% and 40% (baseline 0%). In addition, a probabilistic sensitivity analysis was performed in which model inputs were simultaneously varied over plausible distributions (Supplementary Table S6).

Due to statistically significant differences in the risk profile of road accessible and air access–only communities, including higher median urine ACR and hemoglobin A_{1c} (Table 3), we performed scenario analyses on the baseline estimates by running the model for both air access–only and road accessible community subsets. In addition, we tested the threshold for treatment effectiveness using ACE-Is and ARBs, reducing the cut-off in our model from severely increased albuminuria to moderately increased albuminuria, based on research suggesting that angiotensin-receptor antagonists may provide benefit in those with type 2 diabetes and moderately increased albuminuria.[59] Lastly, we tested the model for the impact

Table 5 | Model probability parameters

Parameter	Estimate	Road access—sensitivity analysis	Air access—sensitivity analysis	Reference
Proportion of individuals screened as healthy risk	0.7451	0.8240	0.6556	Komenda *et al.*[23]
Proportion of individuals screened as low risk	0.1954	0.1397	0.2587	Komenda *et al.*[23]
Proportion of individuals screened as intermediate risk	0.0446	0.0223	0.0698	Komenda *et al.*[23]
Proportion of individuals screened as high risk	0.0149	0.0140	0.0159	Komenda *et al.*[23]
Proportion of patients with severely increased albuminuria (healthy)	0	0	0	Komenda *et al.*[23]
Proportion of patients with severely increased albuminuria (low risk)	0	0	0	Komenda *et al.*[23]
Proportion of patients with severely increased albuminuria (intermediate risk)	0.87	0.88	0.86	Komenda *et al.*[23]
Proportion of patients with severely increased albuminuria (high risk)	0.75	0.6	0.90	Komenda *et al.*[23]
Annual incidental screening rate	0.05	0.05	0.05	Manns *et al.*[48]
Treatment adherence	0.75	0.75	0.75	Boulware *et al.*[50]
Relative risk of receiving a transplant in Canadian indigenous patients	0.43	0.43	0.43	Tonelli *et al.*[49]
Relative risk, mortality reduction from ACE-I or ARB in patients with severely increased albuminuria	0.77	0.77	0.77	Hoerger *et al.*[51,52] Boulware *et al.*[50]
Relative risk, progression reduction from ACE-I or ARB in patients with severely increased albuminuria	0.67	0.67	0.67	Hoerger *et al.*[51,52] Boulware *et al.*[50]

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker.

Table 6 | Model cost and utility parameters

Parameter	Estimate	Reference
Screening (per person)	$589	Komenda *et al.*[23]
In-center dialysis (annual)	$74,590	Klarenbach *et al.*[56]
Peritoneal dialysis (annual)	$43,500	Klarenbach *et al.*[56]
Home hemodialysis (annual)	$61,300	Klarenbach *et al.*[56]
Transplant (first year)	$94,987	Laupacis *et al.*[57]
Transplant (year 2+)	$39,942	Laupacis *et al.*[57]
Annual incremental CKD treatment (high risk)	$2083	Manns *et al.*[48]
Annual incremental CKD treatment (intermediate risk)	$399	Manns *et al.*[48]
Annual incremental CKD treatment (low risk)	$210	Manns *et al.*[48]
Incidental screening (high risk)	$801	Manitoba Health[55] and provider quote
Incidental screening (intermediate risk)	$177	Manitoba Health[55] and provider quote
Incidental screening (low risk)	$141	Manitoba Health[55] and provider quote
Incidental screening (healthy)	$107	Manitoba Health[55] and provider quote
Utilities (0–1)		
Healthy	0.9	Gorodetskaya *et al.*[58]
CKD	0.85	Gorodetskaya *et al.*[58]
Dialysis	0.72	Gorodetskaya *et al.*[58]
Transplant	0.816	Manns et al.[48] and Laupacis *et al.*[57]
Discount rate		
Costs	0.05	Canadian Agency for Drugs and Technologies in Health[42]
Utilities	0.05	Canadian Agency for Drugs and Technologies in Health[42]

CKD, chronic kidney disease.
Provider quotes for laboratory tests were obtained from a personal communication (March 3, 2015) with Diagnostic Services Manitoba, the not-for-profit corporation responsible for all of Manitoba, Canada's public laboratory services and for rural diagnostic imaging services.

of changing the dialysis modality mix, as home dialysis modalities cost less than in-center dialysis does[60] and earlier nephrology intervention may increase home modality uptake.[61] In the screening arm, we considered the impact of increasing the prevalence of home modalities (PD and home HD) by 25%, 50%, and 100%.

DISCLOSURE

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SUPPLEMENTARY MATERIAL

Figure S1. Classification of FINISHED Participants in the KDIGO Heat Map[23] Entire Screened Population.
Table S1. Life expectancy—usual care arm.
Table S2. Life expectancy—screening arm.
Table S3. Chronic kidney disease risk stratum transition probabilities for Canadian indigenous from the AKDN cohort. AKDN, Alberta Kidney Disease Network.
Table S4. Prevalence of dialysis modality utilization in Manitoba.
Table S5. Distribution of satellite dialysis costs and calculation of weighted cost of dialysis.[20]
Table S6. Distributions used in probabilistic sensitivity analysis.
Supplementary material is linked to the online version of the paper at www.kidney-international.org.

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