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ORIGINAL RESEARCH ARTICLE

# Economic Impact of PromarkerD In Vitro Diagnostic Testing on the Management of Chronic Kidney Disease in Type 2 Diabetes: A Budget Impact Analysis

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## Abstract

**Objectives** This study evaluated the clinical and economic impact of integrating Promarker®D, a validated biomarker-based blood test that predicts kidney function decline up to 4 years before clinical evidence of chronic kidney disease (CKD), into routine management of patients with type 2 diabetes (T2D) from a US healthcare payer perspective.

**Methods** A 10-year budget impact model simulated outcomes and costs of one million adults with T2D receiving standard of care (SoC) alone or SoC plus PromarkerD testing providing risk-stratified management. Model inputs were derived from published literature and included disease progression probabilities and healthcare costs associated with CKD, end-stage renal disease (ESRD), PromarkerD testing, and sodium-glucose cotransporter 2 inhibitor (SGLT2i) therapy. Costs were discounted at 3% annually. Scenario and one-way sensitivity analyses assessed parameter uncertainty. Results were translated to covered lives and national diagnosed T2D populations using epidemiologic prevalence estimates.

**Results** The model predicted that PromarkerD-guided early intervention delayed CKD progression, as reflected by reduced transition to advanced CKD stages over time, reduced ESRD incidence by ~6.4%, and reduced mortality by ~5.1% within 10 years. The PromarkerD-guided intervention generated net savings of US $1.2 billion (net present value) per million individuals over the study period. Annual savings began in year 4 (US $116 million), and cumulative savings became positive by year 6 (US $288 million). Results were most sensitive to assumptions regarding treatment benefit in moderate-risk individuals and baseline SGLT2i use but remained cost-offsetting across most scenarios.

**Conclusions** In this model-based analysis, PromarkerD-guided risk stratification enabled earlier intervention, was associated with delayed CKD progression, reduced ESRD incidence and mortality, and demonstrated long-term cost offsets from a US payer perspective. The magnitude of economic impact depends on the timely implementation of treatment in response to early risk identification in real-world practice.

## 1 Introduction

Chronic kidney disease (CKD) is the leading cause of end-stage renal disease (ESRD) and poses a substantial healthcare burden globally [1–3]. In the USA, approximately 40% of adults with type 2 diabetes (T2D) have CKD, with an overall population prevalence of 14% [3]. CKD progression is often asymptomatic until advanced stages [4], when irreversible kidney damage may necessitate renal replacement therapy (RRT), such as dialysis or transplantation [5]. The 2024 United States Renal Data System (USRDS) report shows that Medicare spent approximately US $30.8 billion in 2022 on end-stage renal disease (ESRD) alone, around 6% of the total Medicare fee-for-service expenditures [3].

The economic burden in the USA of CKD overall in T2D is substantial and escalates dramatically with disease progression. Recent data from commercially insured US adults aged 45–64 years demonstrate that individuals with both T2D and CKD incur annual healthcare costs exceeding US $35,000, of which nearly $16,000 are directly attributable to

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**Key Points for Decision Makers**

This study addresses the evidence gap in economic evaluation of biomarker-guided risk stratification for chronic kidney disease in type 2 diabetes, using a 10-year budget impact model aligned with ISPOR guidelines.

PromarkerD-guided management was associated with reduced progression to advanced CKD, lower end-stage renal disease incidence (~6.4%), and reduced mortality (~5.1%), while generating approximately US $1.2 billion in net savings over 10 years per one million US adults with type 2 diabetes.

Findings support the value of integrating biomarker-based diagnostics into diabetes care, providing evidence to inform payer coverage decisions, optimize allocation of renoprotective therapies, and advance precision medicine in health economics and outcomes research.

CKD, with costs increasing sharply as disease progresses to more advanced CKD stages [6]. Early risk identification and associated intervention are essential to delay CKD progression and reduce long-term expenditure [7].

Current CKD standard of care (SoC) monitoring, as defined by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) and Kidney Disease Improving Global Outcomes (KDIGO) guidelines [8, 9], relies on serial measurements of estimated glomerular filtration rate (eGFR) and urinary albumin:creatinine ratio (uACR), but these markers have limitations in detecting early disease and predicting progression [10, 11]. This current CKD SoC diagnostic shortcoming creates a clinical gap where patients may progress significantly before CKD diagnosis is identified and intervention is deemed necessary.

Promarker®D is a biomarker-based blood test that predicts kidney function decline in people with T2D up to 4 years before clinical evidence of CKD. PromarkerD also identifies risk of progression in individuals with established CKD [12]. Using two plasma protein biomarkers (apolipoprotein A4 (ApoA4) and CD5-antigen like (CD5L)) and two clinical parameters (age and eGFR), PromarkerD generates a risk score categorizing patients into low-, moderate-, and high-risk groups, supporting timely targeted intervention to reduce the risk of progression to CKD before symptoms appear or worsen.

Sodium-glucose cotransporter 2 inhibitors (SGLT2i), including empagliflozin, canagliflozin, dapagliflozin, and ertugliflozin, were initially developed for glycemic control but are now recognized for their cardio-renal benefits in T2D [13–17]. The American Diabetes Association (ADA) recommends SGLT2i use in patients with T2D and CKD with an eGFR $\geq$ 20 mL/min/1.73 $m^2$ and albuminuria [18]. Despite robust evidence and guideline recommendations, real-world uptake of SGLT2i remains suboptimal, with use reported in less than 20% of eligible US adults [19–21]. Low uptake is attributed to a combination of factors, including limited physician prescribing, therapeutic inertia, concerns about side effects, variable patient adherence, and cost. Earlier identification of patients at elevated risk, such as through PromarkerD-guided testing, could enable timelier initiation of these renoprotective therapies, potentially improving outcomes and reducing the high costs associated with dialysis and transplantation.

This study aims to quantify the potential clinical and economic value of incorporating PromarkerD testing into clinical practice through a comprehensive budget impact analysis. Healthcare costs and outcomes from the US payer perspective were modelled over a 10-year horizon for a cohort of one million US adults with T2D, comparing SoC alone versus SoC enhanced with early (pre-CKD) PromarkerD-guided risk stratification and targeted intervention.

## 2 Methods

### 2.1 Model Framework

A budget impact model was developed in Microsoft Excel following International Society for Pharmacoeconomics and Outcomes Research (ISPOR) guidelines [22]. The model employed a 10-year time horizon and simulated two parallel cohorts of one million US adults with T2D: one receiving standard of care (SoC) monitoring alone, and one receiving SoC plus PromarkerD testing with risk-stratified management. The model simulated a base-case cohort of 1 million US adults with T2D to enable transparent estimation of clinical and economic outcomes and facilitate proportional scaling to alternative populations. Results are presented both for this one-million-person T2D cohort and translated to a hypothetical health plan population with the estimated impact on national estimates also presented.

For contextualization within a health plan setting, national epidemiologic data from 2023 indicate that approximately 28.8 million US adults (10.8%) have diagnosed diabetes, of whom 90–95% are estimated to have T2D, corresponding to ~9.7–10.2% of the adult population [23]. A T2D prevalence of 10% was applied for translation purposes. Accordingly, in a hypothetical one-million-member health plan, ~100,000 individuals would be expected to have diagnosed T2D. Model outputs were proportionally scaled to this population. At the national level, approximately 26–28 million US adults are estimated to have diagnosed T2D [23]. Model results were similarly extrapolated to this population to provide contextual estimates of potential aggregate economic

impact. These extrapolations assume proportional scalability of costs and outcomes and are intended to illustrate magnitude rather than provide precise national forecasts.

The analysis adopted a US healthcare payer perspective, incorporating direct medical costs associated with CKD and ESRD management, PromarkerD testing, and SGLT2i treatment. All model inputs were derived from published literature and are summarized in Table 1 and the Electronic Supplementary Material (ESM) Fig. 1 and Tables 1, 2, 3. Model inputs were identified through targeted literature review of PubMed and guideline documents focusing on US CKD epidemiology, renal outcome trials, and healthcare cost studies relevant to T2D populations. Preference was given to large observational cohorts and RCTs reporting KDIGO stage-specific outcomes. Where multiple sources existed, the most recent US-representative dataset was selected with confidence intervals or alternative data sources explored in sensitivity analyses.

## 2.2 Study Population

The initial study population was stratified according to KDIGO-based CKD staging [8] using US national population estimates [24] (Supplementary Table 1A). The simulated cohort characteristics reflected real-world demographics: mean age 63.9 years, 52% male, with an average diabetes duration of 10.7 years. Prevalent comorbidities included hypertension (74%), retinopathy (22%), and coronary heart disease (12%). Ethnic distribution comprised 22% Mexican Americans, 38% non-Hispanic white Americans, and 27% non-Hispanic Black Americans [24]. CKD severity was categorized by eGFR (stages G1–G5) and albuminuria (categories A1–A3) according to KDIGO classification [8]. Owing to small numbers in advanced stages, G3b, G4, and G5 were not further stratified by albuminuria. To distinguish between patients with advanced kidney dysfunction (eGFR < 15 mL/min/1.73 $m^2$) and those receiving RRT, stage G5 (no RRT) and ESRD (with RRT) were modeled separately. The model assumed a closed cohort with no new patient entry and death as the only absorbing end-state.

## 2.3 Standard of Care Model

### 2.3.1 Annual CKD Progression Probabilities and SGLT2i Use

Annual CKD progression probabilities were derived from Nichols et al. [25] and represent the total 1-year probability of transitioning out of a given KDIGO category, including progression to more advanced CKD stages and all-cause mortality (Supplementary Table 1B; Supplementary Fig. 1). For example, the 7.5% annual progression probability for G1A1 reflects the sum of transitions from no CKD to moderate CKD (5.7%), advanced CKD (0.3%), ESRD (0.1%), and death (1.4%). Updated 1-year probabilities were obtained directly from the authors of Nichols et al. [25] owing to errors identified in the originally published supplementary figure and are presented in Supplementary Fig. 1. For advanced CKD stages (G3b–G5), transition probabilities were derived by aggregating published estimates across albuminuria strata, as the source data report outcomes separately by eGFR and albuminuria categories. Where direct transitions to ESRD were not available, ESRD risk was estimated using an incidence-based approach combined with hazard ratios from the CKD Prognosis Consortium [26]. Mortality was incorporated across all CKD stages. To account for competing risks, transitions to ESRD and death were modeled as mutually exclusive within each cycle.

A Markov process simulated annual transitions between KDIGO stages, with patient distributions updated annually on the basis of net transitions between categories. Transitions were modeled on the basis of eGFR decline; movement between albuminuria categories was not modeled owing to data limitations and the non-independence of eGFR and albuminuria changes. Death was modeled from all KDIGO stages. ESRD with initiation of RRT included 12% peritoneal dialysis, 85% hemodialysis, and 3% kidney transplantation [3]. The 5-year survival rate for ESRD was 25% [1]. Assuming exponential survival, this corresponds to an annual mortality rate of $1 - (0.25)^{1/5}$, or 24.2%, which was applied in the model.

Background SGLT2i use was based on 2020 US Centers for Disease Control and Prevention (CDC) prescription data: 18% for G1–G2 stages and 16% for stages G3a–G3b [27]. No additional pharmacologic or lifestyle interventions were assumed in the SoC model. The effectiveness of SGLT2i therapy was informed by hazard ratios from the EMPA-REG OUTCOME trial for the renal outcome of doubling of serum creatinine, initiation of RRT, or renal death, as this endpoint closely reflects clinically meaningful CKD progression [28]. For each KDIGO risk category, hazard ratios were applied to baseline progression probabilities (i.e., $1 - (1 - \text{baseline probability})^{\text{hazard ratio}}$) (Supplementary Table 1C). This transformation assumes proportional hazards and converts relative risk reductions into absolute transition probabilities under a constant hazard assumption.

### 2.3.2 Annual Care Costs

Annual all-cause healthcare costs by KDIGO stage ranged from $29,993 (G1) to $119,944 (G5), covering inpatient, outpatient, emergency department, pharmacy, and skilled nursing services (Supplementary Table 4) [6]. ESRD-related costs included $172,788 annually for dialysis [29] and $9179 annually for transplant care [30], with an initial transplant procedure cost of $442,500 [31]. Death was assigned a one-time cost of $12,605 [5]. Monthly SGLT2i

**Table 1** Key model inputs

| Input | Base-case value | Source |
|---|---|---|
| Total test population | 1,000,000 | N/A |
| Distribution of target (initial) population by KDIGO stage | Supplementary Table 1A | [3, 24] |
| Annual probability of transitioning to another KDIGO stage* | Supplementary Table 1B | [1, 25] |
| CKD costs by KDIGO stage per year: | Supplementary Table 3 | [5, 6, 29–31] |
| PromarkerD cost per test | $390 | [42] |
| PromarkerD retesting rate for low/moderate/high-risk (months) | 48/24/0 | [43] & CAB |
| PromarkerD test sensitivity at moderate/high-risk cut-offs (%) | 85.1/50.5 | [12] |
| PromarkerD test specificity at moderate/high-risk cut-offs (%) | 71.7/94.5 | [12] |
| Adherence to PromarkerD results | 80% | N/A |
| Distribution of PromarkerD results by KDIGO stage | Supplementary Table 2 | [12] |
| SGLT2i treatment effect on CKD progression in PromarkerD high-risk | Supplementary Table 1C | [28] |
| Reduction in progression probabilities for PromarkerD moderate-risk | 20% | [41] |
| SGLT2i treatment costs (monthly/yearly) | $600, $7300 | [32] |
| Year SGLT2i treatment becomes generically available | 2026 | [33, 35] |
| SGLT2i treatment price discount post year of generic availability: | | |
| 1 year | 28% | [34] |
| 2 years | 38% | |
| 3 years | 53% | |
| 4 years | 60% | |
| 5 years | 67% | |
| 6 years | 72% | |
| 7 years | 77% | |
| 8 years | 82% | |
| SGLT2i usage in standard of care: | | |
| G1 | 18.2% | [27] |
| G2 | 18.4% | |
| G3 | 15.5% | |
| CPI (base-case value, % increase): | | |
| 2015 (Year 0) | 441.351 | [45] |
| Year 1 | 454.194, 2.91% | |
| Year 2 | 471.484, 6.83% | |
| Year 3 | 480.797, 8.94% | |
| Year 4 | 489.968, 11.02% | |
| Year 5 | 511.854, 15.97% | |
| Year 6 | 521.774, 18.22% | |
| Year 7 | 534.649, 21.14% | |
| Year 8 | 550.887, 24.82% | |
| Year 9 | 556.567, 26.11% | |
| Year 10 | 571.234, 29.43% | |
| Discount rate | 3% | [44] |

KDIGO, Kidney Disease Improving Global Outcomes; CKD, chronic kidney disease; SGLT2i, sodium-glucose cotransporter 2 inhibitor; CPI, consumer price index; ESM, electronic supplementary material; CAB, clinician expert opinion from Proteomics International's PromarkerD Clinical Advisory Board.

*Calculation as per Methods Sect. 2.3.

costs ranged from $450 to $800 [32], with a baseline modeled average of $600 per month ($7300 annually) (Table 1). The cost for generic SGLT2i was assumed from the start of the model given the recent FDA approval [33]. Following patent expiry, prices were reduced according to published post-patent erosion trends, with progressive annual reductions thereafter, reaching approximately $1314 annually by year 10 [34, 35] (Table 1).

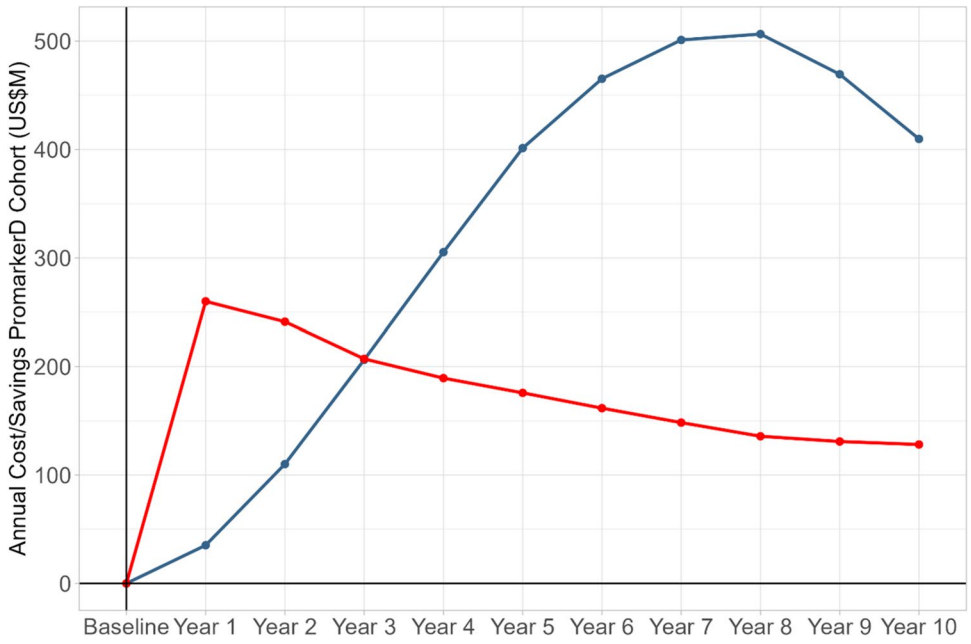


**Fig. 1** Annual intervention costs with PromarkerD (red line) versus annual savings from delayed CKD progression (blue line). US$M, million USD; CKD, chronic kidney disease

**Table 2** Economic impact summary (10-year NPV, million USD per million population)

| Component | Standard of care | PromarkerD | Difference | Description |
|---|---|---|---|---|
| Cost of treatment of CKD | $438,329 | $435,605 | $2724 | Stage-specific CKD treatment costs |
| Cost of SGLT2i treatment | $3541 | $4186 | ($645) | SGLT2i treatment cost of $600 per month with progressive price reductions over time |
| Cost of PromarkerD tests | – | $858 | ($858) | Test cost of $390 per test |
| **Net savings (NPV)** | | | **$1221** | 3% discount rate, CPI based on trends from the previous 10 years |
| Equilibrium point | | | Year 3 to 4 | Annual PromarkerD costs lower than SoC |
| Breakeven point | | | Year 5 to 6 | Cumulative savings become positive |

NPV, net present value; USD, United States dollars; CKD, chronic kidney disease; SGLT2i, sodium-glucose cotransporter 2 inhibitor; CPI, consumer price index; SoC, standard of care.

## 2.4 PromarkerD Model

### 2.4.1 CKD Progression and SGLT2i Use

Individuals with eGFR ≥ 30 mL/min/1.73 $m^2$ (KDIGO G1-G3b) were eligible for PromarkerD testing. On the basis of data from the Fremantle Diabetes Study [12], patients were stratified as low-, moderate-, or high-risk for kidney function decline. Multiple randomized, placebo-controlled trials and prespecified or post hoc renal analyses demonstrate that SGLT2i therapy could slow CKD progression even in individuals with preserved renal function (eGFR ≥ 60 mL/min/1.73 $m^2$), including those classified as KDIGO low risk [17, 28, 36–40]. On the basis of the effectiveness of SGLT2i, the model assumed that PromarkerD implementation would reduce CKD progression through targeted interventions based on patient risk. Low-risk PromarkerD patients progressed as per the SoC model. High-risk patients initiated SGLT2i therapy, resulting in reductions in CKD progression probabilities, with greater absolute effects observed in higher-risk KDIGO categories (Supplementary Table 1C) [28]. The number of individuals receiving additional benefits from SGLT2i treatment was determined by the sensitivity of PromarkerD at the high-risk cutoff (50.5%), while unnecessary treatment costs were determined by the false positive rate (1 − specificity; specificity 94.5%) [12]. At the moderate-risk threshold, sensitivity (85.1%) determined the proportion of true moderate-risk individuals receiving the health management benefit, whereas the false positive rate (1 − specificity; specificity 71.7%) represented individuals incorrectly classified as moderate risk and therefore receiving management without corresponding risk reduction. Individuals incorrectly classified as low risk (false negatives) were assumed to follow SoC progression without additional intervention, while incurring testing costs. Treatment with SGLT2i was the only therapy considered in the present

**Table 3.** Sensitivity analysis results

| Scenario | Net savings ($ billions) | Equilibrium point | Breakeven point |
|---|---|---|---|
| Base model | $1.221 | Year 3 to 4 | Year 5 to 6 |
| CKD progression probability using the lower CI limit | $0.915 | Year 3 to 4 | Year 6 to 7 |
| CKD progression probability using the upper CI limit | $1.291 | Year 3 to 4 | Year 3 to 4 |
| No PromarkerD retesting | $2.079 | Year 2 to 3 | Year 3 to 4 |
| Double PromarkerD testing frequency | $0.363 | Year 3 to 4 | Year 7 to 8 |
| No SGLT2i use in the standard of care | $1.709 | Year 2 to 3 | Year 4 to 5 |
| 40% SGLT2i use in the standard of care | $0.529 | Year 3 to 4 | Year 6 to 7 |
| Health management benefits using the lower CI limit at 3% | −$0.859 | Year 10+ | Year 10+ |
| Health management benefits using the upper CI limit at 34% | $3.057 | Year 2 to 3 | Year 3 to 4 |
| PromarkerD Treatment adherence reduced to 60% | $0.693 | Year 3 to 4 | Year 5 to 6 |
| PromarkerD Treatment adherence increased to 100% | $1.758 | Year 2 to 3 | Year 4 to 5 |
| Decreased SGLT2i effectiveness to lower CI limit | $0.988 | Year 3 to 4 | Year 5 to 6 |
| Increased SGLT2i effectiveness to upper CI limit | $1.347 | Year 3 to 4 | Year 5 to 6 |
| SGLT2i drug cost lower limit ($450) | $1.382 | Year 2 to 3 | Year 4 to 5 |
| SGLT2i drug cost upper limit ($800) | $1.006 | Year 3 to 4 | Year 5 to 6 |
| SGLT2i used on moderate and high risk | $0.112 | Year 4 to 5 | Year 8 to 9 |
| Health management applying to moderate and high risk without SGLT2i | $1.697 | Year 2 to 3 | Year 2 to 3 |
| PromarkerD target only being high risk results | $1.256 | Year 2 to 3 | Year 5 to 6 |
| PromarkerD sensitivity/specificity from CANVAS | $0.234 | Year 3 to 4 | Year 7 to 8 |

CKD, chronic kidney disease; CI, confidence interval; SGLT2i, sodium-glucose cotransporter 2 inhibitor; CANVAS, Canagliflozin Cardiovascular Assessment Study

budget impact model, as robust stage-specific renal outcome data was not available for other renoprotective therapies (glucagon-like peptide-1 receptor agonists and nonsteroidal mineralocorticoid receptor antagonists) during model development. For moderate-risk patients, the model assumed a 20% reduction in CKD progression from enhanced clinical management. This estimate was informed by Lewis et al. [41], which demonstrated a similar risk reduction with irbesartan among patients with emerging nephropathy receiving targeted intervention. In the present model, the 20% reduction represents a management effect triggered by risk stratification rather than the effect of a specific pharmacologic effect. Because this parameter is uncertain, sensitivity analyses were performed across the reported 95% confidence interval (3–34%) to assess its influence on results. Adherence to treatment was assumed to be 80%, with sensitivity tested at 60% and 100%.

#### 2.4.2 PromarkerD Test and Treatment Costs

PromarkerD testing cost was set at US $390 per test, reflecting the 2026 US CMS Clinical Lab Fee Schedule published rate [42]. Retesting frequencies were every 48 months for low-risk, 24 months for moderate-risk, and no retesting for high-risk individuals (remained on continuous SGLT2i therapy), on the basis of recommendations from the ADA diabetes-related CKD Consensus report [43] and the PromarkerD Clinical Advisory Board, being intended for guidance only. CKD stage-specific healthcare costs and SGLT2i treatment expenses were as per the SoC model.

### 2.5 Economic Analysis

Annual costs and savings were calculated over 10 years in USD. All costs are reported in 2026 USD. A 3% annual discount rate was applied to future costs and savings to reflect their present value [44]. The consumer price index (CPI) inflation adjustment was based on US inflation rate trends from the last 10 years and extrapolated out to the next 10 years [45]. Net savings were defined as:

$$\text{Net savings} = (\text{CKD\_Cost\_SoC} - \text{CKD\_Cost\_PromarkerD}) - (\text{Test\_Cost\_PromarkerD} + \text{Retesting}) - (\text{SGLT2i\_Cost\_PromarkerD} - \text{SGLT2i\_Cost\_SoC})$$

Net present value (NPV) represents the sum of discounted annual net savings over the 10-year period, providing a time-adjusted measure of the total economic benefit. Since progression of chronic kidney disease to ESRD is very slow, a time horizon of 10 years was considered appropriate to capture the potential benefits of early detection of the disease.

### 2.6 Sensitivity Analysis

One-way sensitivity analyses tested model robustness by varying key assumptions. CKD progression probabilities, the assumed benefit of enhanced health management in moderate-risk individuals, SGLT2i costs, and the effectiveness of SGLT2i therapy were each varied across the extremes of their reported 95% confidence intervals [25, 28, 32, 41]. Scenario analyses also examined the impact of doubling the frequency of PromarkerD retesting or removing retesting entirely, as well as applying treatment effects to both moderate- and high-risk, or only high-risk, individuals. Additional scenarios explored alternative levels of SGLT2i use under SoC, including no background use and increased background use to 40% [27]. Finally, treatment adherence varied by assuming either 60% adherence or perfect adherence to SGLT2i therapy.

## 3 Results

### 3.1 Clinical Outcomes

The PromarkerD cohort demonstrated improved clinical outcomes compared with SoC with a corresponding shift in the distribution of patients toward earlier CKD stages over time (Supplementary Table 4). By year 10, ESRD incidence was reduced by approximately 6.4%, while mortality decreased by 5.1% (Supplementary Table 4). These clinical benefits reflect earlier identification of at-risk individuals and timely initiation of renoprotective therapy.

### 3.2 Economic Impact

Table 2 summarizes the total economic impact after 10 years, with detailed annual breakdown provided in Supplementary Table 5. In the SoC cohort, total CKD treatment costs increased from $37.5 billion at baseline to $55.9 billion by year 10, with a total NPV of $438 billion. The PromarkerD cohort achieved CKD treatment costs of $55.5 billion by year 10 (total NPV: $436 billion), generating $2.7 billion in savings from delayed CKD progression. This equates with a 0.6% reduction in CKD treatment costs over 10 years with PromarkerD. Although initial costs were higher owing to PromarkerD testing and earlier, additional SGLT2i therapy, net annual savings began in year 4 ($116 million), marking the equilibrium point (Supplementary Table 5; Fig. 1). The breakeven point, when cumulative net savings became positive, was reached in year 6 ($288 million) (Supplementary Table 5; Fig. 2). By year 10, cumulative net savings totaled over $1.6 billion (Supplementary Table 5; Fig. 2). Thus, the overall net savings (all costs included) had an NPV of approximately $1.2 billion by year 10 (Table 2), corresponding to a 0.3% reduction in overall costs.

The model projected savings with an NPV of ~$1200 per person with T2D over 10 years. Applying a 10% diagnosed T2D prevalence to a hypothetical one-million-member health plan corresponds to ~100,000 members with diagnosed T2D. Under this scenario, projected total savings through the incorporation of PromarkerD testing for CKD risk stratification have an NPV of ~$120 million over 10 years, corresponding to ~$12 per covered member per year. When proportionally scaled to the estimated 26–28 million US adults with diagnosed T2D, the model corresponds to an NPV of ~$31–33 billion in savings over 10 years.

### 3.3 Sensitivity Analysis

Table 3 presents the one-way sensitivity analyses and demonstrates that the model was generally robust across a range of assumptions. Increasing baseline SGLT2i use in SoC to 40% reduced savings to $0.53 billion and delayed breakeven timing by 1 year. Changes in PromarkerD testing frequency had a smaller effect; doubling testing reduced savings to $0.36 billion owing to higher testing costs, whereas eliminating retesting increased savings to $2.08 billion. The most significant impact came from the assumed health management benefit in moderate-risk patients. Reducing this benefit to 3% resulted in a net cost of $859 million and no breakeven within the 10-year model time horizon, while increasing it to 34% produced $3.06 billion in savings and accelerated breakeven to years 3–4. Variations in CKD progression probabilities, SGLT2i effectiveness, adherence, and SGLT2i costs affected the magnitude and timing of savings but did not alter the overall direction of results. Collectively, the analyses indicate that economic outcomes are primarily driven by assumptions regarding moderate-risk management benefit and baseline SGLT2i uptake, with testing frequency and SGLT2i pricing exerting secondary effects.

## 4 Discussion

This budget impact analysis evaluated the clinical and economic impact of incorporating PromarkerD-guided CKD risk identification into routine T2D care. Earlier identification of individuals at elevated risk of CKD may shift treatment toward earlier intervention, increasing short-term costs while reducing downstream expenditure associated

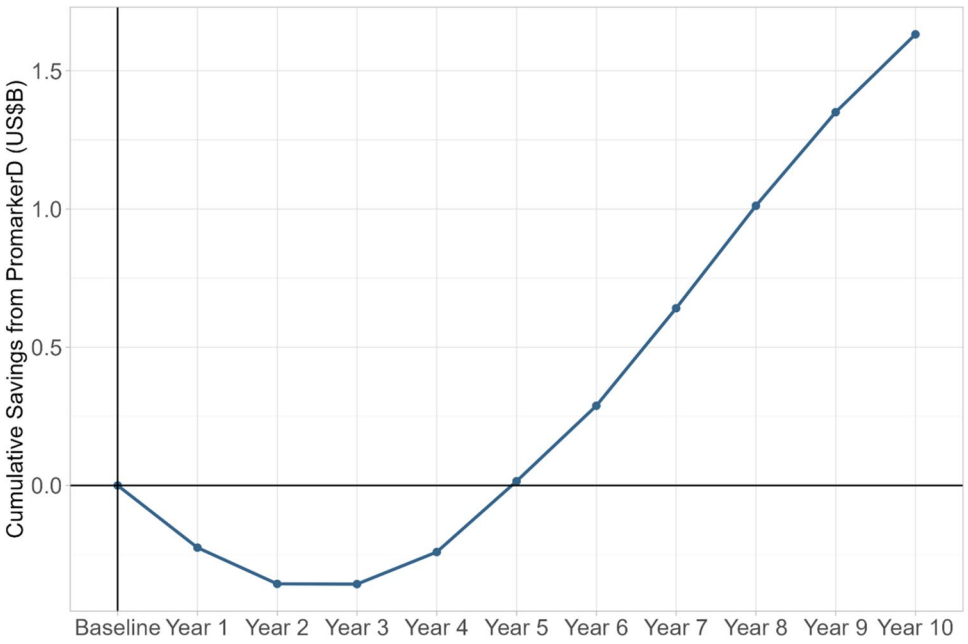


**Fig. 2** Cumulative net savings with PromarkerD implementation. US$B, billion USD

with advanced CKD. This effect is mediated through earlier initiation of renoprotective therapy in high-risk individuals and enhanced management in moderate-risk individuals. As expected for prevention-focused strategies, economic benefits emerged gradually over time.

The projected savings primarily reflect the cost differential between advanced CKD/ESRD management and earlier pharmacologic intervention. The Inflation Reduction Act of 2022 caps out-of-pocket costs for Medicare beneficiaries at $2100 per year, which may shift a greater proportion of costs to CMS. In this context, optimizing treatment allocation through identification of individuals at highest risk who are most likely to benefit from renoprotective therapy becomes increasingly important. Despite initial investment in PromarkerD testing and increased SGLT2i utilization, the model achieved positive net returns by year 6, with approximately $1.2 billion in discounted savings per one million individuals over 10 years. These findings are consistent with prior economic evaluations supporting early CKD intervention [46, 47]. The modeled 6.4% reduction in ESRD incidence indicates delayed progression to kidney failure within the simulated population. However, real-world impact will depend on treatment uptake. SGLT2i use remains suboptimal despite guideline recommendations [19–21], but risk-stratified information may facilitate earlier initiation of renoprotective therapies, consistent with evidence that SGLT2i slow CKD progression [17, 28, 36–40], and may also improve prescribing behavior [48] and patient adherence. Whether this translates into sustained changes in clinical practice warrants further evaluation.

The strengths of this study include adherence to established health economic guidelines, use of robust clinical data sources, comprehensive sensitivity analysis, and a realistic 10-year time horizon. The model incorporates real-world treatment patterns and cost structures, enhancing external validity. However, several limitations should be acknowledged. The closed cohort design excludes incident cases and may underestimate long-term benefits as diabetes and CKD prevalence continues to rise. The Markov model applies annual progression probabilities at the start of each cycle rather than continuously throughout the year. In practice, CKD progression is time-varying and occurs continuously. Patients do not transition across ACR categories (in addition to eGFR categories) as there were limited longitudinal data to support the progression assumptions. This may underestimate progression in patients whose albuminuria worsens prior to eGFR decline. The model assumes 80% treatment adherence, which may not reflect real-world effectiveness. The assumed 20% reduction in progression among moderate-risk individuals significantly influenced model outcomes and represents a key driver of model uncertainty. This parameter reflects extrapolated management effects rather than direct evidence specific to PromarkerD-guided care. Future research should better characterize the real-world benefits achievable in moderate-risk populations. Additionally, the model does not incorporate cardiovascular complications associated with CKD, which may underestimate the full economic burden and potential benefits of earlier intervention.

When scaled to the estimated 26–28 million US adults with diagnosed T2D, the model suggests a potentially substantial aggregate economic impact. However, this extrapolation assumes similar risk distribution, treatment uptake, and payer cost structures across settings and should be

interpreted with caution. Further research should evaluate real-world test utilization, treatment uptake, and outcomes, as well as assess budget impact across different payer types and dynamic populations.

## 5 Conclusions

In this model-based budget impact analysis, PromarkerD-guided risk stratification was associated with delayed CKD progression, lower mortality, and modest cost offsets from a payer perspective. Economic outcomes were sensitive to assumptions regarding moderate-risk management benefit and baseline SGLT2i use. Prospective real-world evaluation is warranted to confirm both clinical and economic effects. As the cost of SGLT2i declines over time, the economic value of targeted treatment strategies such as PromarkerD-guided risk stratification may increase, as therapy can be more efficiently directed toward individuals at highest risk who derive the greatest clinical benefit.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s41669-026-00669-4.

## Declarations

**Conflicts of Interest** Proteomics International is a beneficiary of patent PCT/AU2011/001212 that relates to biomarkers used in the PromarkerD in vitro test described in this manuscript. KEP and RJL are named inventors of this patent. GCF, IAJ, KEP, LKC, JSG, PLT, and RJL are past or present employees and shareholders of Proteomics International. MS is a member of the Clinical Advisory Board for Proteomics International. The authors acknowledge that commercial adoption of PromarkerD could provide financial benefit to Proteomics International and affiliated individuals.

**Authorship Contributions** All authors certify that they meet the ICMJE criteria for authorship. Conceptualization of study: GCF, KEP, LKC, JSG, PLT, RJL; input data curation: IAJ, KEP, LKC, PLT; model development and programming: GCF, IAJ, LKC, JSG; formal analysis and interpretation: GCF, IAJ, KEP, LKC, JSG, PLT, MS; validation: IAJ, KEP, LKC, JSG, PLT; manuscript preparation (original draft): GCF, IAJ; manuscript preparation (review and editing): GCF, KEP, LKC, JSG, MS; supervision: KEP, JSG, PLT, RJL.

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**Availability of Data and Materials** The data that support the findings of this study were generated by and are the property of Proteomics International. These data contain proprietary information that is not publicly available owing to commercial restrictions. Summary data and model assumptions derived from publicly available sources are included in the article and its Supplementary Material. Further details of the budget impact model may be made available from the corresponding author upon reasonable request.

**Ethics Approval** Not applicable. This study used published literature and modelling data and did not involve human participants or identifiable patient data.

**Consent to Participate** Not applicable.

**Consent for Publication (from Patients/Participants)** Not applicable.

**Code Availability** The budget impact model was developed in Microsoft Excel and contains proprietary components. Additional details may be available from the corresponding author upon reasonable request.



## References

1. Rout P, Aslam A. End-stage renal disease. StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
2. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. Kidney Int Suppl (2011). 2022;12(1):7–11.
3. National Institute of Diabetes and Digestive and Kidney Diseases NIoH. United States renal data system 2024 Annual Data Report. 2024; Available from: https://usrds-adr.niddk.nih.gov/2024
4. Vaidya SR, Aeddula NR. Chronic kidney disease. StatPearls. Treasure Island (FL): StatPearls Publishing; 2024.
5. Betts KA, Song J, Faust E, Yang K, Du Y, Kong SX, et al. Medical costs for managing chronic kidney disease and related complications in patients with chronic kidney disease and type 2 diabetes. Am J Manag Care. 2021;27(20 Suppl):S369–74.
6. Chung H, Crowe CL, Kong SX, Singh R, Farej R, Elliott J, et al. Descriptive study of the economic burden among patients with type 2 diabetes mellitus, chronic kidney disease, and chronic kidney disease and type 2 diabetes mellitus in a large US commercially insured population. J Manag Care Spec Pharm. 2023;29(1):80–9.
7. Francis A, Harhay MN, Ong ACM, Tummalapalli SL, Ortiz A, Fogo AB, et al. Chronic kidney disease and the global public health agenda: an international consensus. Nat Rev Nephrol. 2024;20(7):473–85.
8. Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024;105(4s):S117–s314.
9. Navaneethan SD, Bansal N, Cavanaugh KL, Chang A, Crowley S, Delgado C, et al. KDOQI US Commentary on the KDIGO 2024 clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2025;85(2):135–76.
10. Dunkler D, Gao P, Lee SF, Heinze G, Clase CM, Tobe S, et al. Risk prediction for early CKD in Type 2 diabetes. Clin J Am Soc Nephrol. 2015;10(8):1371–9.

11. Lin CH, Chang YC, Chuang LM. Early detection of diabetic kidney disease: present limitations and future perspectives. World J Diabetes. 2016;7(14):290–301.
12. Lui JKC, Peters KE, Fernandez G, Joubert IA, Lumbantobing TSC, Davis TME, et al. Analytical and clinical performance of a novel immunoassay-based test system to predict diabetic kidney disease. J Appl Lab Med. 2025;10(5):1140–53.
13. Ghosh RK, Ghosh SM, Chawla S, Jasdanwala SA. SGLT2 inhibitors: a new emerging therapeutic class in the treatment of type 2 diabetes mellitus. J Clin Pharmacol. 2012;52(4):457–63.
14. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med. 2015;373(22):2117–28.
15. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondu N, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med. 2017;377(7):644–57.
16. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2019;380(4):347–57.
17. Wanner C, Inzucchi SE, Lachin JM, Fitchett D, von Eynatten M, Mattheus M, et al. Empagliflozin and progression of kidney disease in type 2 diabetes. N Engl J Med. 2016;375(4):323–34.
18. American Diabetes Association Professional Practice Committee. 11. Chronic kidney disease and risk management: standards of care in diabetes—2024. Diabetes Care. 2023;47(Supplement_1):S219–S30.
19. Scheen AJ. Real-life underuse of SGLT2 inhibitors for patients with type 2 diabetes at high cardiorenal risk. Diabetes Epidemiol Manage. 2024;13:100184.
20. Eberly LA, Yang L, Eneanya ND, Essien U, Julien H, Nathan AS, et al. Association of race/ethnicity, gender, and socioeconomic status with sodium-glucose cotransporter 2 inhibitor use among patients with diabetes in the US. JAMA Netw Open. 2021;4(4):e216139.
21. Centers for Disease Control and Prevention. Kidney Disease Surveillance System: Percentage of adults aged ≥18 years with CKD stages 1–4 aware of their condition, by stage, United States. 2025; Available from: https://nccd.cdc.gov/CKD/detail.aspx?Qnum=Q719
22. Sullivan SD, Mauskopf JA, Augustovski F, Jaime Caro J, Lee KM, Minchin M, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. Value Health. 2014;17(1):5–14.
23. Centers for Disease Control and Prevention. National diabetes statistics report. 2026; Available from: https://www.cdc.gov/diabetes/php/data-research/index.html
24. Bailey RA, Wang Y, Zhu V, Rupnow MF. Chronic kidney disease in US adults with type 2 diabetes: an updated national estimate of prevalence based on Kidney Disease: Improving Global Outcomes (KDIGO) staging. BMC Res Notes. 2014;7:415.
25. Nichols GA, Déruaz-Luyet A, Brodovicz KG, Kimes TM, Rosales AG, Hauske SJ. Kidney disease progression and all-cause mortality across estimated glomerular filtration rate and albuminuria categories among patients with vs without type 2 diabetes. BMC Nephrol. 2020;21(1):167.
26. Writing Group for the CKD Prognosis Consortium. Estimated glomerular filtration rate, albuminuria, and adverse outcomes: an individual-participant data meta-analysis. JAMA. 2023;330(13):1266–77.
27. Centers for Disease Control and Prevention. CDC Surveillance System: SGLT2i use among Patients with CKD and Diabetes. 2020 2024/09/11; Available from: https://nccd.cdc.gov/CKD/detail.aspx?Qnum=Q719
28. Levin A, Perkovic V, Wheeler DC, Hantel S, George JT, von Eynatten M, et al. Empagliflozin and cardiovascular and kidney outcomes across KDIGO risk categories: post hoc analysis of a randomized, double-blind, placebo-controlled, multinational trial. Clin J Am Soc Nephrol. 2020;15(10):1433–44.
29. GoodRx. How much does dialysis cost? 2025; Available from: https://www.goodrx.com/health-topic/kidneys/dialysis-cost
30. Łabuś A, Niemczyk M, Czyżewski Ł, Fliszkiewicz M, Kulesza A, Mucha K, et al. Costs of long-term post-transplantation care in kidney transplant recipients. Ann Transplant. 2019;24:252–9.
31. Bentley T, Ortner N. 2020 U.S. organ and tissue transplants: cost estimates, discussion, and emerging issues. https://www.milliman.com/en/Insight/2020-us-organ-and-tissue-transplants2020.
32. Cost Digest. Cost of SGLT2 inhibitors: price ranges and budget guide 2026. 2026; Available from: https://costdigest.org/cost-sglt2-inhibitors-price-ranges-budget/
33. Bharadwaj S. Aurobindo Pharma receives USFDA nod for two dapagliflozin tablets. 2026; Available from: https://timesofindia.indiatimes.com/business/india-business/aurobindo-pharma-receives-usfda-nod-for-two-dapagliflozin-tablets/articleshow/130093345.cms
34. Serra-Burriel M, Martin-Bassols N, Perényi G, Vokinger KN. Drug prices after patent expirations in high-income countries and implications for cost-effectiveness analyses. JAMA Health Forum. 2024;5(8):e242530.
35. Drugs.com. Generic Drugs - Availability and Patent Status. 2026; Available from: https://www.drugs.com/availability/
36. Perkovic V, de Zeeuw D, Mahaffey KW, Fulcher G, Erondu N, Shaw W, et al. Canagliflozin and renal outcomes in type 2 diabetes: results from the CANVAS Program randomised clinical trials. Lancet Diabetes Endocrinol. 2018;6(9):691–704.
37. Mosenzon O, Wiviott SD, Cahn A, Rozenberg A, Yanuv I, Goodrich EL, et al. Effects of dapagliflozin on development and progression of kidney disease in patients with type 2 diabetes: an analysis from the DECLARE-TIMI 58 randomised trial. Lancet Diabetes Endocrinol. 2019;7(8):606–17.
38. Heerspink HJL, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, Hou FF, et al. Dapagliflozin in patients with chronic kidney disease. N Engl J Med. 2020;383(15):1436–46.
39. Cherney DZI, Charbonnel B, Cosentino F, Dagogo-Jack S, McGuire DK, Pratley R, et al. Effects of ertugliflozin on kidney composite outcomes, renal function and albuminuria in patients with type 2 diabetes mellitus: an analysis from the randomised VERTIS CV trial. Diabetologia. 2021;64(6):1256–67.
40. Neuen BL, Ohkuma T, Neal B, Matthews DR, de Zeeuw D, Mahaffey KW, et al. Relative and absolute risk reductions in cardiovascular and kidney outcomes with canagliflozin across KDIGO risk categories: findings from the CANVAS program. Am J Kidney Dis. 2021;77(1):23–34 (**e1**).
41. Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med. 2001;345(12):851–60.
42. Centers for Medicare & Medicaid Services (CMS). Clinical Laboratory Fee Schedule: 2026 Annual Update. 2026; Available from: https://www.cms.gov/files/document/mm14312-clinical-laboratory-fee-schedule-2026-annual-update.pdf
43. Tuttle KR, Bakris GL, Bilous RW, Chiang JL, de Boer IH, Goldstein-Fuchs J, et al. Diabetic kidney disease: a report from an ADA Consensus Conference. Diabetes Care. 2014;37(10):2864–83.
44. Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second

panel on cost-effectiveness in health and medicine. JAMA. 2016;316(10):1093–103.
45. U.S. Bureau of Labor Statistics. Consumer price index for all urban consumers: medical care in U.S. City average [CPIMEDSL]. 2026. Available from: https://fred.stlouisfed.org/series/CPIMEDSL
46. Thornton Snider J, Sullivan J, van Eijndhoven E, Hansen MK, Bellosillo N, Neslusan C, et al. Lifetime benefits of early detection and treatment of diabetic kidney disease. PLoS ONE. 2019;14(5):e0217487.
47. Datar M, Burchenal W, Donovan MJ, Coca SG, Wang E, Goss TF. Payer budget impact of an artificial intelligence in vitro diagnostic to modify diabetic kidney disease progression. J Med Econ. 2021;24(1):972–82.
48. Fusfeld L, Murphy JT, Yoon Y, Kam LY, Peters KE, Lin Tan P, et al. Evaluation of the clinical utility of the PromarkerD in-vitro test in predicting diabetic kidney disease and rapid renal decline through a conjoint analysis. PLoS ONE. 2022;17(8):e0271740.