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Health economic modelling of diabetic kidney disease in patients with type 2 diabetes treated with Canagliflozin in Belgium

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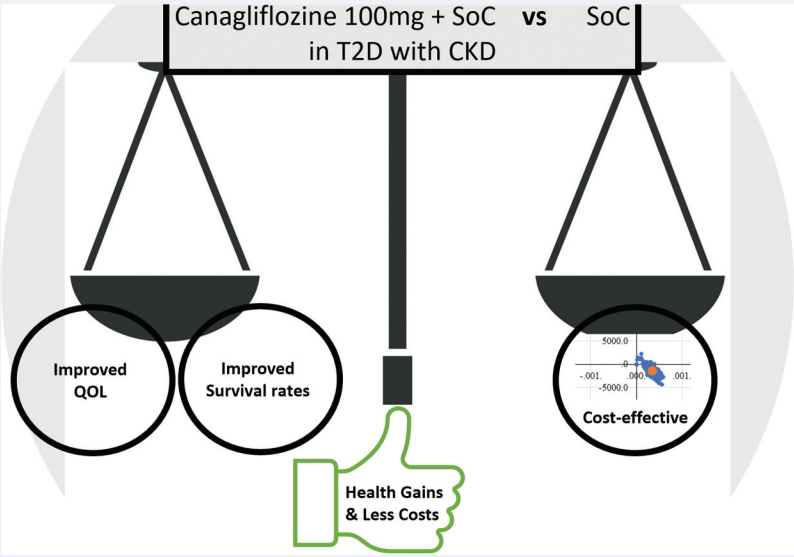
ABSTRACT

Objectives: The Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial showed reduced renal and cardiovascular (CV) events in patients with type 2 diabetes (T2D) and diabetic kidney disease (DKD) treated with canagliflozin 100 mg added to Standard of Care (SoC) versus SoC alone. This led to an extension of the canagliflozin 100 mg European marketing authorisation, making canagliflozin the first pharmacological therapy to receive authorisation for the treatment of DKD since the RENAAL and IDNT trials more than 20 years ago. Given the importance of cost-effectiveness analyses in health care, this study aimed to leverage the CREDENCE trial outcomes to estimate the cost-effectiveness of canagliflozin 100 mg from the perspective of the Belgian healthcare system.

Methods: A microsimulation model (CREDENCE Economic Model of DKD), developed using patient-level CREDENCE trial data, was leveraged to model the progression of DKD and CV outcomes, associated costs, and life quality. Unit costs and quality-adjusted life years (QALYs) were sourced from the literature. The time horizon was 10 years and sensitivity analyses were performed.

Results: Canagliflozin was associated with sizable gains in life-years and QALYs over 10 years, and the incremental cost-effectiveness ratio cost offsets associated with reductions in CV and renal complications resulted in overall net cost savings from the perspective of the Belgian healthcare system.

Conclusion: Model-based results suggest that adding canagliflozin 100 mg to SoC can improve outcomes for patients with DKD while reducing overall net costs for the Belgian healthcare system.



KEYWORDS

Cost-effectiveness; canagliflozin; diabetes; credence; diabetic kidney disease (DKD)

Introduction

Type 2 diabetes mellitus (T2DM) is a major public health problem with a prevalence of 6.3% of the Belgian population diagnosed [1] though the estimated true prevalence is expected to be much higher. Approximately 40% of patients with T2DM will develop diabetic kidney disease (DKD) [2], a debilitating, and life-threatening chronic and progressive condition in which systemic and intraglomerular hypertension results in proteinuria, leading to chronic tubular injury [3]. End-stage renal disease (ESRD) is associated with

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a substantial impact on health-related quality of life, mortality, and a significant cost burden [4,5]. DKD is also an independent risk factor for cardiovascular disease (CVD) and, consequently, T2DM patients are more likely to die from CVD than to survive up to the point of the development of end-stage kidney disease (ESKD) [6,7].

The Evaluation of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Participants With Diabetic Nephropathy (CREDENCE) trial was the first dedicated renal outcomes trial to report results for a sodium–glucose co-transporter 2 (SGLT2) inhibitor in T2DM patients with DKD [8], and the first trial to show improved renal and CV outcomes since the current standard of care (SoC) was established almost 20 years ago in the RENAAL and IDNT trials [9,10]. More specific, adding canagliflozin 100 mg to the current SoC, including a maximally tolerated dose of a renin–angiotensin–aldosterone system (RAAS) inhibitor, reduced the risk of the primary composite endpoint (doubling of serum creatinine, ESRD, or renal or CV death) by 30% ($p = 0.00001$) versus SoC alone [8]. Substantial risk reductions were also observed for secondary endpoints, including reductions of the composite of CV death or hospitalisation for heart failure (HHF) by 31% ($p < 0.001$), 3-point major adverse cardiovascular events (MACE: CV death, nonfatal myocardial infarction (MI), or nonfatal stroke) by 20% ($p = 0.01$), and HHF alone by 39% ($p < 0.001$) [8]. Based on the results of the CREDENCE trial, canagliflozin 100 mg received an indication extension for the treatment of DKD in patients with insufficiently controlled T2D in Europe in July 2020 [11].

The incremental cost of treating DKD in patients with T2DM, also in Belgium, is significant, especially in case of late-stage disease requiring dialysis and transplantation [12]. For chronic and progressive diseases such as DKD, in which the decision-making time horizon is long, economic evidence, in the scope of an efficient allocation of healthcare resources, must often be generated using economic modelling, which permits extrapolation of finite trial data into the future [13,14]. An economic model was developed using patient-level data from the CREDENCE trial to support estimation of the cost-effectiveness of canagliflozin in the DKD indication [15]. The objective of this study was to estimate the cost-effectiveness of canagliflozin 100 mg added to SoC versus SoC alone for the treatment of T2D patients with DKD from the perspective of the Belgian healthcare system.

Methods

Model summary

The CREDENCE Economic Model of DKD (CREDEM-DKD model) uses a microsimulation approach to estimate the cost-effectiveness of treatment interventions from the perspective of the healthcare payer. The model is implemented with discrete event simulation (DES) methods [16], which are suited for situations in which there are competing clinical events with accelerating risks (e.g. of reaching ESKD) and where relatively long-term 'time-to-event' data are available to enable estimation of risk prediction equations, as are the case with DKD and the CREDENCE trial [8,17]. CREDEM-DKD is implemented in Microsoft® Excel (Microsoft Corporation, Redmond, Washington, USA) and Visual Basic for Applications. CREDEM-DKD was designed, constructed, and populated with patient-level data from CREDENCE. The model is described in detail elsewhere [15]. Briefly, though, hypothetical patients are defined by age, sex, smoking status, diabetes duration, estimated glomerular filtration rate (eGFR), urine albumin-to-creatinine ratio (UACR), MI history, stroke history, and heart failure history. Renal and cardiovascular health states are modelled independently. The mutually exclusive and exhaustive renal health states include traditional DKD Stages (1, 2, 3A, 3B, 4, or 5 predialysis), dialysis, and post-kidney transplant. The macrovascular health states (not mutually exclusive) include MI, stroke, and HF. The patients also face risks of all-cause mortality.

The CREDEM-DKD model has undergone internal validation (i.e. replicating the CREDENCE study results) and limited external validation based on replicating results of the sub-group of CANagliflozin cardioVascular Assessment Study (CANVAS) Program [18] subjects that met CREDENCE study recruitment criteria, which is summarised in an Assessment of the Validation Status of Health-Economic Decision Models evaluation (AdViSHE) [19] (see Electronic Supplementary Material (ESM) 2). More information and details about the model and model validation can be found in Willis et al 2020 [15].

Input data

Baseline patient characteristics were sourced from CREDENCE data [8,17] and are presented in ESM 1 Table 1. Treatment effects for the canagliflozin 100 mg + SoC arm were also obtained from CREDENCE [8,17] and the details are presented in ESM 1 Table 2. AEs were included only for the canagliflozin arm (loaded as the between-arm difference observed in CREDENCE) and consist of urinary tract infection (UTI), genital mycotic infection (GMI), diabetic ketoacidosis (DKA), and lower extremity amputation

Table 1. Unit costs and disutility weights.

	Unit costs (€) inflated to 2021		Source	Utility (QALY) weights	Source
Canagliflozin (€ per year)	568.46		Belgian list price [20]	N/A	
SoC in canagliflozin arm (€ per year)	923.52		See ESM 1 Table 3	N/A	
SoC in placebo arm (€ per year)	918.85		See ESM 1 Table 3	N/A	
Test costs	15		Personal communications [28]	N/A	
Intercept	N/A			0.785	Clarke et al. 2002 [29]
Kidney	Event	Annual			
DKD stage 1	0	1725.84	Jommi et al. 2018 [30]	−0.15	Jesky et al. 2016 [31]
DKD stage 2	0	2223.37	Jommi et al. 2018 [30]	−0.15	Jesky et al. 2016 [31]
DKD stage 3a	0	2413.81	Jommi et al. 2018 [30]	−0.20	Jesky et al. 2016 [31]
DKD stage 3b	0	3772.04	Jommi et al. 2018 [30]	−0.20	Jesky et al. 2016 [31]
DKD stage 4	0	6122.39	Jommi et al. 2018 [30]	−0.26	Jesky et al. 2016 [31]
DKD stage 5	0	8050.48	Jommi et al. 2018 [30]	−0.27	Jesky et al. 2016 [31]
Dialysis	0	90,434.84	Dratwa et al. 2013 [12]	−0.53	Lee et al. 2005 [32]
Transplant	51,908.64*	8488.95**	Van Biesen et al. 2007 [33]	−0.29	Lee et al. 2005 [32]
Cardiovascular					
Nonfatal MI	12222.95	4106.93	Caekelbergh et al. 2016 [34]	−0.06	Clarke et al. 2002 [29]
Nonfatal Stroke	32225.99	8253.43	Caekelbergh et al. 2016 [34]	−0.16	Clarke et al. 2002 [29]
Nonfatal HHF	18918.7	7951.13	Caekelbergh et al. 2016 [34]	−0.11	Clarke et al. 2002 [29]
Adverse events					
GMI male	46.05		Van Haalen et al. 2013 [35]	−0.0046	Shingler et al. 2015 [36]
GMI female	46.05		Van Haalen et al. 2013 [35]	−0.0046	Shingler et al. 2015 [36]
UTI	46.05		Van Haalen et al. 2013 [35]	−0.0043	Shingler et al. 2015 [36]
DKA	4418.18		Roze et al. 2016 [37]	−0.0091	Peasgood et al. 2016 [38]
LEA	16455.67	679.74	Van Haalen et al. 2013 [35]	−0.169	Clarke et al. 2002 [29] Sullivan et al. 2016 [39]

**Transplant + 1st year after; ** all other years after the 1st year after*

CV cardiovascular, *DKA* diabetic ketoacidosis, *DKD* diabetic kidney disease, *GMI* genital mycotic infections, *HHF* hospitalization for heart failure, *LEA* lower extremity amputation, *MI* myocardial infarction, *SoC* standard of care, *UTI* urinary tract infection

Table 2. Health outcomes, life-year and QALY outcomes over 10 years.

	Canagliflozin + SoC	SoC	HR
Estimated Event Rates (per 100 Patient-Years)			
Mortality	3.96	5.40	0.73
Due to CVD	2.84	4.12	0.69
Due to other causes	1.10	1.27	0.87
Kidney			
Stage 4	4.67	14.92	0.31
Stage 5, pre-RRT	0.36	5.81	0.06
Dialysis	1.92	3.56	0.54
Transplant	0.14	0.96	0.14
CV			
HHF	1.81	2.71	0.67
Nonfatal MI	1.15	1.37	0.84
Nonfatal Stroke	0.97	1.16	0.83
Adverse Events (Incremental for Canagliflozin)			
UTI	0.30	–	–
GMI Males	0.43	–	–
GMI Females	0.22	–	–
DKA	0.19	–	–
LEA	0.10	–	–
			Difference
Life-years	7.87	7.5	0.37
Base QALYs*	6.18	5.89	0.29
Sources of disutility			
DKD	−1.71	−1.78	0.07
CV	−0.36	−0.36	0
Adverse events	−0.01	0	−0.01
Total QALYs	4.1	3.75	0.35
ICER per QALY gained			Canagliflozin dominates

**QALYs adjusted for survival but not other sources of disutility*

CV cardiovascular, *DKA* diabetic ketoacidosis, *DKD* diabetic kidney disease, *GMI* genital mycotic infections, *ICER* incremental cost-effectiveness ratio, HHF hospitalization for heart failure, HR hazard ratio, *LEA* lower extremity amputation, MI myocardial infarction, RRT renal replacement therapy, *SoC* standard of care, *QALY* quality-adjusted life-year

(LEA). AE rates are shown in ESM 1 Table 3. As per the label, canagliflozin was discontinued at the start of dialysis, when kidney transplant occurs, or when DKA or LEA was simulated to occur. Affected hypothetical patients were reverted to SoC alone treatment. The price of canagliflozin 100 mg was set at €47.54 for 30 days prescription (€568.46 annually), which corresponds to 100% patient compliance and 100% reimbursement coverage at Belgian list price [20]. The price of SoC was calculated based on the use of background therapy in CREDENCE, separately by arm (€923.52 annually for canagliflozin and €918.85 annually for the SoC alone arm) (See ESM 1 Table 4for description of SoC unit costs).

The CREDENCE risk equations were used to model the risks of starting dialysis; experiencing MI, stroke, and HHF events; and death [15]. In the CREDENCE trial, event rates for starting up dialysis or for having renal replacement therapy (RRT) were relatively low due to the short follow-up period, with the majority of ESKD events being defined as a persistent eGFR below 15 mL/min/1.73 m^2 [8]. To enhance realism, hypothetical patients who reach the implausibly low eGFR of 6 mL/min/1.73 m^2 without having renal replacement therapy (RRT) were assigned to start dialysis. The threshold of 6 mL/min/1.73 m^2 is in line with clinical guidance on initiation of dialysis [21]. For patients simulated to reach stage 5 DKD or to start on dialysis, an 8%

Table 3. Health economic cost outcomes over 10 years for canagliflozin 100 mg + SoC versus SoC alone.

	Canagliflozin + SoC	SoC alone	Difference
Treatments			
Canagliflozin	3920	-	3920
SoC	6795	6459	336
DKD outcomes			
Stage 1	0	0	0
Stage 2	2931	2055	876
Stage 3a	5601	3768	1833
Stage 3b	9362	7725	1638
Stage 4	4840	8870	− 4030
Stage 5 pre-RRT	208	3494	− 3287
Dialysis	37006	46981	− 9976
Transplant	642	4244	− 3603
DKD subtotal	60589	77138	− 16548
CV outcomes			
MI	4497	4529	− 32
Stroke	8914	8928	− 14
HHF	13889	15245	− 1355
CV death	1668	2291	− 623
Adverse events (incremental for canagliflozin)			
UTI	2	-	2
GMI male	2	-	2
GMI female	1	-	1
DKA	29	-	29
LEA	63	-	63
Total costs	100471	114590	− 14119
Time on treatment (years)	6.85	0.00	6.85

CV cardiovascular, *DKA* diabetic ketoacidosis, *DKD* diabetic kidney disease, *GMI* genital mycotic infections, *HHF* hospitalization for heart failure, *LEA* lower extremity amputation, *MI* myocardial infarction, *SoC* standard of care, *RRT* renal replacement therapy, *UTI* urinary tract infection

annual probability of receiving a kidney transplant was assumed [22]. Unit costs were sourced from the literature (inflated to 2021 price levels and recalculated for gross domestic product when needed), see Table 1.

Health-related quality of life data were not collected in the CREDENCE trial. Disutility weights to enable the estimation of Quality Adjusted Life Years (QALYs) were sourced from the literature and have been used previously (Willis et al. [15]). While not Belgium-specific, the QALYs are sourced from UK sources for a similar UK health economic outcome analysis for canagliflozin [23], and thought to be reflective of Belgian patients as all QALY weights were with one exception (the AE QALY decrements) derived using EQ-5D methods for which Belgian and UK tariffs are relatively similar. Costs were discounted at 3% annually and health outcomes at 1.5% annually. All analyses consisted of simulating 500 cohorts of 500 hypothetical patients, which was shown to produce low root-mean-square error in convergence plots (ESM 1 Figure 1). The time horizon in the base case was 10 years, which captures much of the economic and health consequences of treatment for this patient population but avoids inducing undue uncertainty by extrapolating too far beyond the duration of the CREDENCE trial).

Sensitivity analysis

The robustness of model results to changes in key model parameters and assumptions was evaluated in sensitivity analysis. More specific,

- Longer decision-making horizons of 20 years and 40 years and a shorter horizon of 5 years.
- While there is no evidence suggesting that the treatment effects of canagliflozin decline over time, neither is there evidence that the benefits extend beyond the longest trial evidence thus far collected, about 6 years in CANVAS Program [18,24]. In the base case we assumed that there was no decline in treatment effect over time, but this assumption was tested in a sensitivity analysis, assuming HRs wane linearly from year 6 to year to end of time horizon.

Compliance with ethics guidelines

This article is based on previously conducted studies and does not contain any studies with human or animal subjects performed by any of the authors.

Results

The simulated health outcomes for the base case simulation of canagliflozin added to SoC vs SoC alone over 10 years are presented in Table 2. The clinical benefits observed for canagliflozin in CREDENCE, including preservation of eGFR, reduction in UACR, and substantial reductions in the risks of dialysis, CV events, and mortality resulted in 0.37 additional life-years for patients treated with canagliflozin 100 mg added to SoC compared with SoC alone over 10 years. This reduction in the rates of events is net of offsets due to increased survival and longer exposure to the risks. Progression through the different DKD stages for the base case simulation of 10 years is shown in Figure 1, and for a 30-year period is shown in ESM 1 Figure 2. The estimated evolution of the eGFR over 10 years and 30 years is shown in Figure 2. At 10 years, progression to worse DKD stages, dialysis and transplant was more frequent for patients who were receiving SoC alone, with 22% of the patients predicted to be in CKD stage 5 in the SoC group, compared to only 2% in the group which received canagliflozin added to SoC. Effects were even more pronounced after 30 years. Cumulative incidence curves for renal and CV events are shown in Figure 3. A 6%, 2%, 11%, 7%, and 10% reduction in favour of canagliflozin

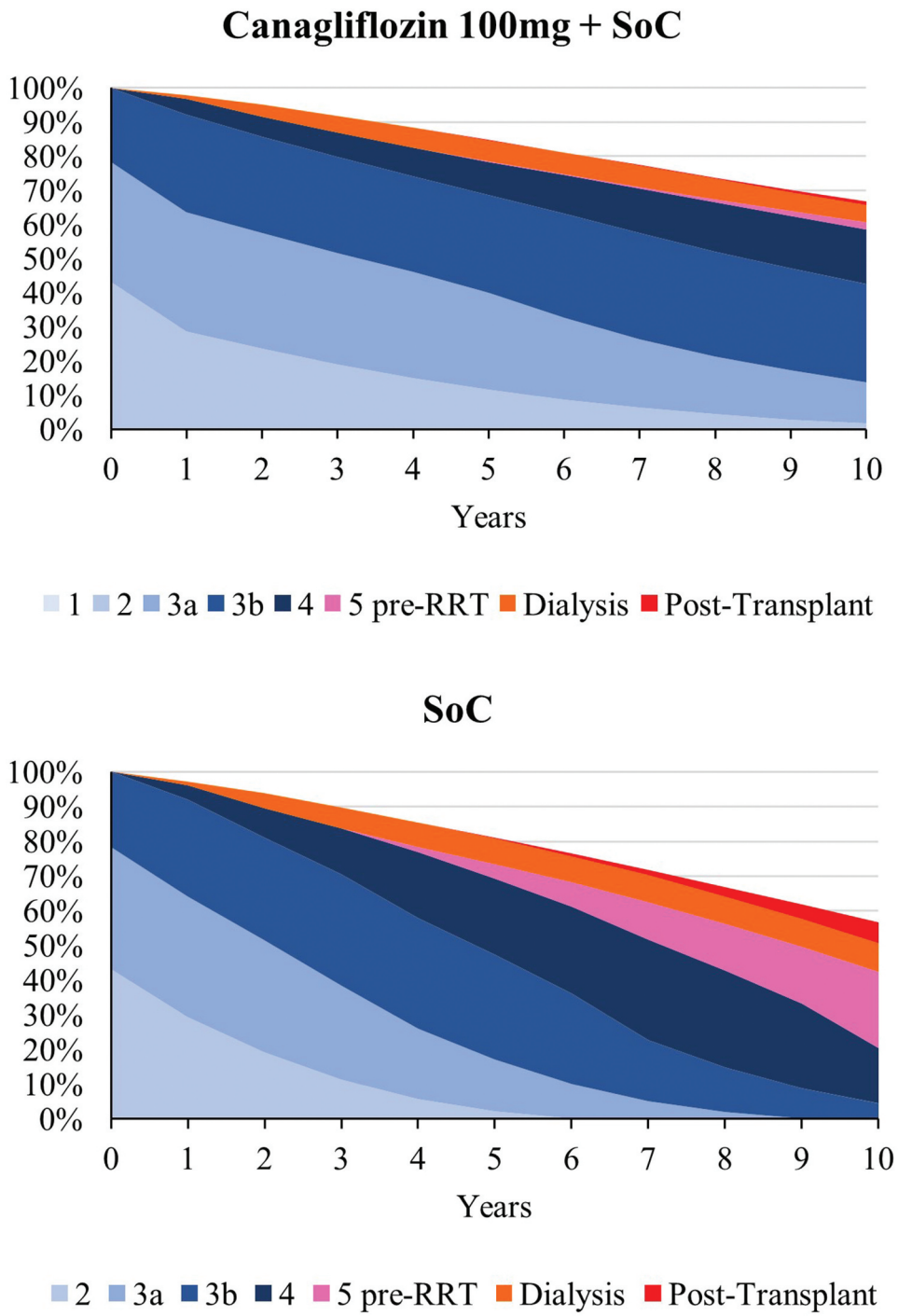

Figure 1. Progression of DKD stages over 10 years, by study arm.

was observed for, respectively, HHF, 3P MACE, dialysis, transplant, and overall survival (latter not shown).

Improvements in clinical outcomes for canagliflozin correspond to improvements in quality of life of 0.35 additional QALYs. The QALY gains were driven mainly by the longer survival rate for canagliflozin with some benefits originating from reduced DKD progression. Moreover, the improved clinical outcomes translated into important economic benefits as well (Table 3). Each patient treated with canagliflozin 100 mg added to SoC had cost savings of €14,119 over a 10-year period. The cost offsets associated with the reductions in progression to DKD stages 4 and 5 (€4,030 and €3,287, respectively), as well as the reduction in the need for dialysis (€9,976) were main driven of the total cost saving. Canagliflozin was also associated with modest cost savings for MI (€32), stroke (€14), and HF

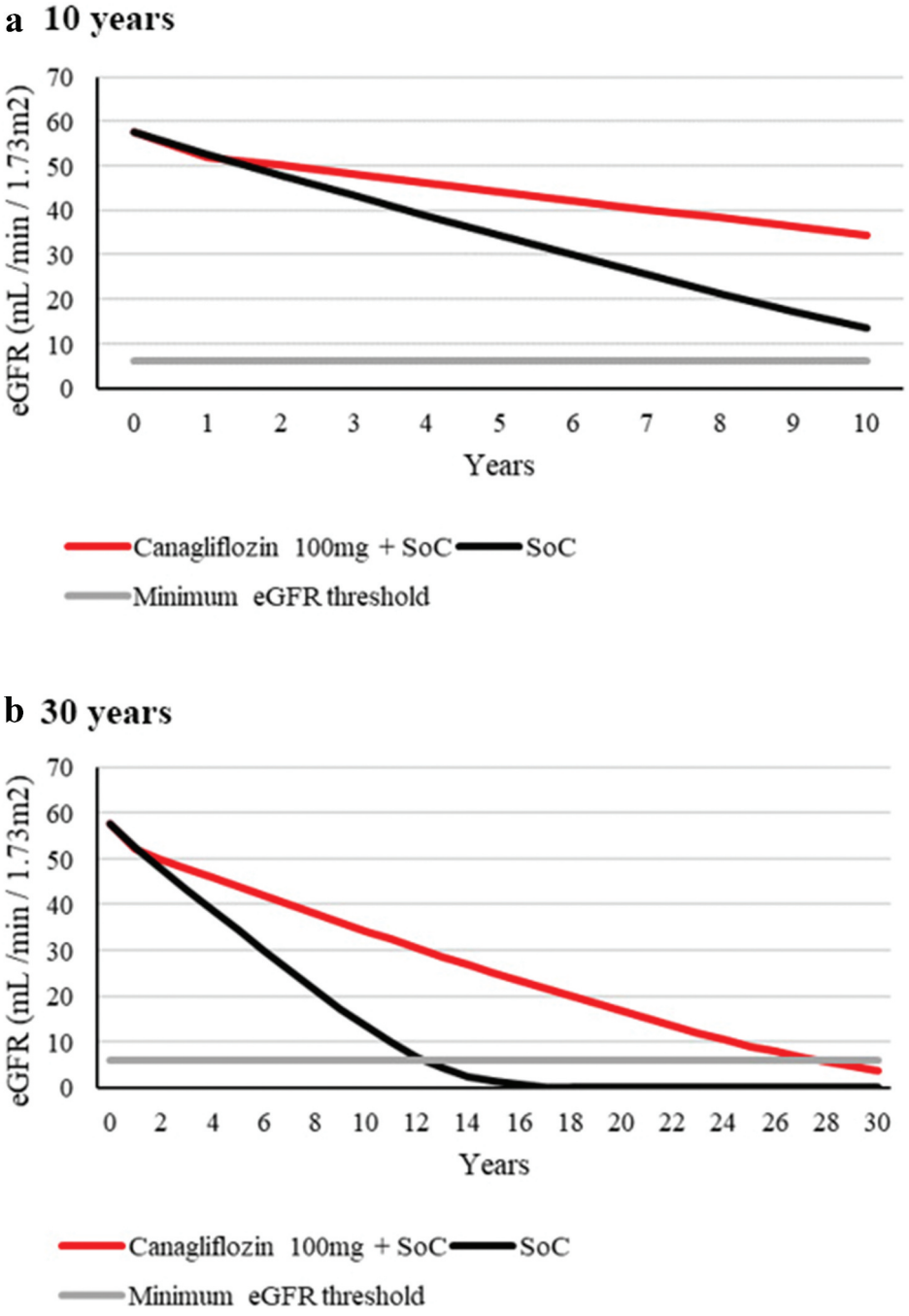

Figure 2. Estimated evolution of eGFR over 10 years and 30 years.

(€1,355) but the magnitude was constrained by the longer exposure to CV risks in this treatment arm. Net AE costs were low due to low AE event rates in the CREDENCE trial and relative balance between the two study arms.

The cost-effectiveness scatter plot is shown in ESM 1 Figure 3. The scatter plot suggest that model uncertainty was low, and nearly all cohort replications nearly all fell in quadrant IV (when both costs are lower and a higher amount of QALYs for patients treated with canagliflozin added to SoC versus SoC alone). The likelihood that the canagliflozin plus SoC arm has lower total costs than the SoC alone arm over the 10-year time period was 95%. This percentage is indicated by the height of the cost-effectiveness acceptability curve at a willingness-to-pay threshold of €0 for a QALY in ESM 1 Figure 4.

Sensitivity analysis

Results of the sensitivity analysis are summarized in ESM 1 Table 5. Canagliflozin added to SoC dominated SoC alone at all simulation time horizons, even the shorter 5-year period, and when the treatment effects were assumed to diminish starting at year 6. Increasing

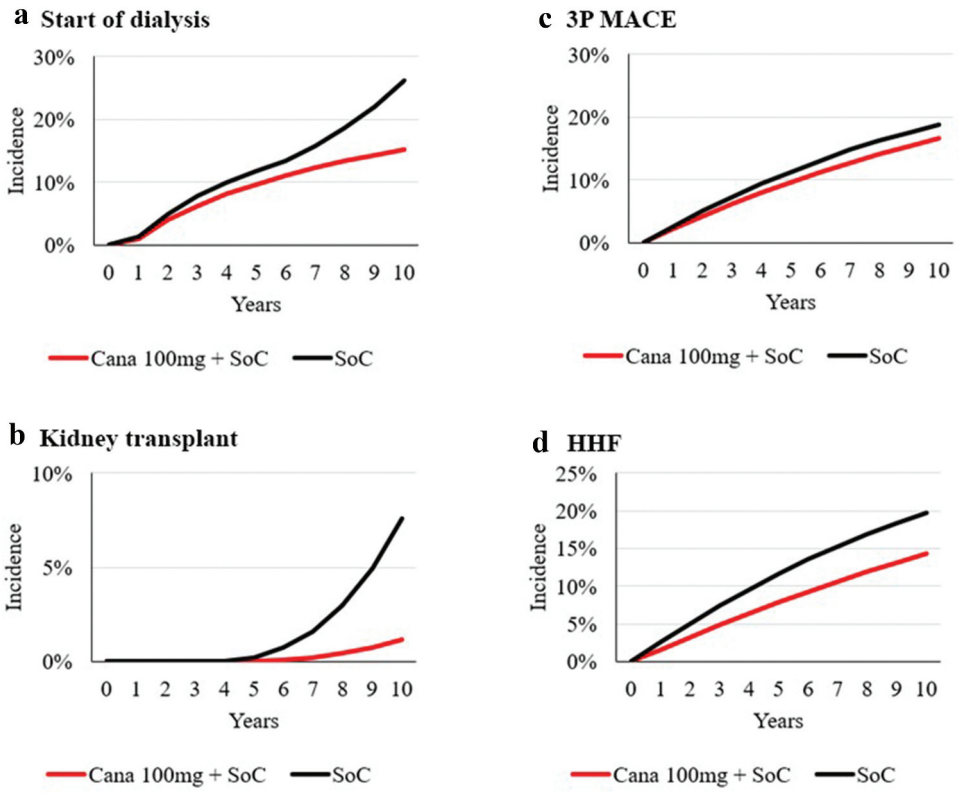

Figure 3. Cumulative incidence curves for renal and CV outcomes over 10 years, by study arm.

the time horizons for the simulation, increased both the magnitude of clinical benefit as well as the cost savings, although substantial mortality in this patient population sets a natural limit.

Discussion

There is compelling evidence that SGLT2 inhibitors are associated with cardiorenal protective effects that exceed the effects that would be expected from glucose-lowering effects alone [8,25], which addresses a fundamental unmet medical need in T2D patients with DKD. Because the impact of having T2D (and DKD) on the healthcare budget in Belgium is substantial [12], we performed health-economic simulations from the perspective of the Belgian healthcare system, based on the results from the CREDENCE [8,17] trial. In this Belgian-specific study, treating T2D patients with DKD with the combination of canagliflozin 100 mg and SoC resulted in improved survival rates and QALY gains (0.35) at a substantially lower total cost (−14,119€ per patient) for the Belgian payer perspective, over a relatively short 10-year time horizon. Even over 5-years, combination therapy of canagliflozin with SoC was associated with improved health outcomes at lower costs (-€3,000). Moreover, increasing the time horizon in the sensitivity analysis further increased the health gains and cost savings for patients treated with canagliflozin. Over a 30-year timeframe, adding canagliflozin to SoC showed to delay the onset of dialysis by 15 years compared to SoC alone. Linear diminishing canagliflozin treatment effects (HRs) on renal, CV, and mortality outcomes as applied following year 6 in line with the longest observed trial data for canagliflozin (CANVAS trial [18,24]) had only a modest effect on the results, with canagliflozin remaining dominant but with slightly reduced cost-offsets. Taken together, the addition of canagliflozin to SoC was found to be cost saving, and sensitivity analyses indicate that the results from this study are robust. While this is not a budget impact analysis, scaling the long-term net cost savings from the modelled closed cohort by the size of the Belgian DKD population matching the CREDENCE indication resulted in more than €270 million and €1,300 million in saved costs for the Belgian healthcare system over 5 and 10 years, respectively.

The results from this analysis are consistent with a previously reported cost-effectiveness analyses in T2D patients with DKD in the UK [23]. Compared to the UK analysis [23], cost savings in Belgium were even greater, which is mainly due to higher events costs in Belgium. Total QALY gains over the 10-year period were also slightly higher for the Belgian population

(0.35) in comparison to the UK population (0.28). A similar analysis also found substantial cost-offsets for the health sector in the US, primarily by lowering the need for dialysis, associated with canagliflozin added to standard of care [26].

Strengths of our analysis include the use of the best available data to date [15], the preservation of the evidence generated in the CREDENCE trial, and the use of a parsimonious and internally validated model designed for this purpose with avoidance of overfitting [15]. Unlike other DKD models, the whole spectrum of the disease (using granular NKF/KDOQI stages), dialysis, kidney transplant, and key CV events are modelled [27]. An external validation of the model predictions against a subgroup of 567 patients from the CANVAS Program which met CREDENCE eligibility criteria, matched closely for nonfatal MI and HHF, and were reasonably close for the less stable nonfatal stroke and all-cause mortality outcomes [15]. These validation results provide additional confidence that the predictive accuracy of the model will be acceptable. Nevertheless, unlike patients in the CREDENCE trial, Belgian patients are not always treated with an 'optimal' SoC, so model results may be conservative.

As is the case in most modelling studies, a potential weakness of this study is the extrapolation of short-term clinical trial results to longer time horizons. To reduce the uncertainty over longer time horizons, we limited the base-case analysis to 10 years. Given the high rate of mortality in this patient population, however, the effects are self-limiting and the conclusion is unchanged for time horizons ranging from 5 to 40 years. The risk equations in this model (except for kidney transplant) were derived from the CREDENCE trial. Because the CREDENCE trial was stopped early, based on the achievement of prespecified efficacy criteria, it was not possible to develop risk equations for kidney transplant or for 2nd CV events. Such risk equations would have further reduced decision making uncertainty, and their inclusion would have presumably increased between-arm separation (given that 2nd events are conditioned on 1st events). Accordingly, differences between improvements in renal outcomes predicted by the model and those observed in clinical practice may exist. Another potential limitation of this study is the use of UK specific QALY weights rather than Belgian specific QALY weights, however, we expect the impact to the results to be limited.

For future model exercises, studies analysing the health-related quality of life for patients with DKD in Belgium would be useful for more precise estimations. Furthermore, it would be of interest to assess the impact of the cost-effectiveness results in patients treated with sub-optimal SoC, which might be more reflective of real-world practice. In addition, it would also be interesting to assess cost-effectiveness compared with an alternative active comparator. However, there are currently no clinical evidence to support these types of model exercises. Finally, given the results of this analysis, suggesting that canagliflozin 100 mg added to SoC is cost saving compared to SoC alone, future research should assess the potential budget impact in real-world practice in Belgium.

Taken together, a model-based extrapolation of the results observed in the CREDENCE trial over 10-years indicates that canagliflozin 100 mg added to SoC with maximal tolerated doses of a RAAS inhibitor can substantially reduce rates of CV and renal outcomes. Furthermore, adding canagliflozin to the SoC increase longevity and QALYs versus SoC alone in this high unmet need T2D population in Belgium, with a significant impact on the costs for the Belgian healthcare system. The findings from this trial justify the recent decisions of rijksinstituut voor ziekte en invaliditeitsverzekering (RIZIV) to reimburse canagliflozin for patients with T2D and CKD.

Authorship

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

Compliance with ethics guidelines

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Disclosure statement

Michael Willis, and Andreas Nilsson are employees of the Swedish Institute for Health Economics, which provides consulting services for governmental bodies, academic institutions, and commercial life science enterprises (including Mundipharma). Michael Willis is also a minority owner and board member of the Swedish Institute for Health Economics.

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Data availability

All model inputs used in this study are described or included in this article and the Electronic Supplementary Material (ESM). The economic model used in this study is proprietary intellectual property. For access, please contact Michael Willis (mw@ihe.se).

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