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Cost-effectiveness of treatment with finerenone in mild to advanced stage chronic kidney disease patients with type 2 diabetes from a societal perspective

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ABSTRACT

Introduction One in three patients with type 2 diabetes (T2D) suffers from any stage of chronic kidney disease (CKD), a chronic illness associated with a high global burden that impacts not only the healthcare system but also societal costs. Addition of finerenone to the standard of care (SoC) for patients with advanced CKD and T2D has been shown to be cost-effective by reducing healthcare and societal costs. This analysis explores the cost-effectiveness of finerenone in patients with CKD (stages 1–4 with albuminuria) associated with T2D from a societal perspective, as broader societal costs are a crucial consideration in managing chronic illnesses.

Research design and methods The validated FINE-CKD model was populated with data from the pooled FIDELITY analysis (ie, a patient population with early-to-late stage CKD associated with T2D) to investigate the cost-effectiveness of the addition of finerenone to SoC compared with SoC alone, from a Dutch societal perspective. Sensitivity analyses were conducted to evaluate the impact of parameter uncertainty on the robustness of the model.

Results Our analysis shows that by adding finerenone to SoC, patients with mild to severe stage CKD and T2D gain 0.14 quality-adjusted life years (QALYs) compared with SoC alone, mainly due to a reduction in renal and cardiovascular events. The societal costs of these events are considerable (ie, €8481 and €9799 per patient over a lifetime in the finerenone and SoC arm, respectively), showing the relevance of a societal perspective in chronic diseases. Overall, finerenone leads to savings of €2713 per patient over a lifetime. Therefore, the addition of finerenone to SoC emerges as the dominant treatment option when compared with SoC alone. The sensitivity analysis shows that finerenone has a 62.3% chance to be dominant and an 83.8% chance to be cost-effective, considering a willingness-to-pay threshold of €20 000/QALY.

Conclusions This study highlights the burden that chronic diseases impose on healthcare systems and society, emphasising the relevance of incorporating a societal perspective in cost-effectiveness analyses. The analysis estimates that adding finerenone to SoC treatment for patients with mild to advanced CKD associated with is cost-effective from a healthcare and societal perspective.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC

⇒ Chronic kidney disease (CKD) represents a global health challenge which highly increases the risk of cardiovascular events and end-stage renal disease, bringing considerable costs for healthcare and society.

⇒ The addition of finerenone to the standard of care (SoC) has already demonstrated a cost-effective, and even dominant, treatment option over SoC due to the inhibition of end-stage renal disease and cardiovascular events in patients with severe CKD and type 2 diabetes (T2D).

WHAT THIS STUDY ADDS

⇒ Current analysis shows that finerenone is also a cost-effective treatment option in patients with early-to-late-stage CKD (ie, stages 1–4 with albuminuria) associated with T2D.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study contributes to more insight into the cost and health impact of the use of finerenone in the total population of patients with CKD associated with T2D. Additionally, this study underscores the substantial burden chronic diseases such as T2D and CKD place on healthcare systems and society.

INTRODUCTION

The global prevalence of type 2 diabetes (T2D) and its complications—including chronic kidney disease (CKD)—is rising.[1] One in three T2D patients develops risk for CKD,[2] which affects 700 to 800 million people worldwide and represents a serious global health burden.[3] Progressed CKD leads to an elevated risk of renal and cardiovascular (CV) events, impacting morbidity and mortality. Besides the burden to the patients, CKD raises significant healthcare costs, with the annual expenditures for CKD projected to grow from $372.0 billion in 2022 to $406.7 billion in 2027 across 31 middle-income and high-income regions, including Europe, the USA, and large parts of Asia and South America.[4] The annual expenditures for dialyses and transplants are estimated to increase from $169.6 billion in 2022 to $186.6 billion in 2027 in this same region. These figures account for direct healthcare costs, but do not include societal costs.[5] Many patients experience reduced productivity, experience difficulty maintaining employment or require informal caregiving, further escalating the societal impact.

Since mild to moderate CKD often presents without symptoms and can go undetected, many countries recommend screening high-risk individuals.[6] Early detection and intervention can prevent progression to end-stage kidney disease and reduce the risk of renal and CV events. Therefore, screening can improve health outcomes, while being cost-effective.[7] These improved health outcomes of CKD go combined with early and appropriate treatment.

Finerenone has recently been introduced for the treatment of patients with CKD associated with T2D in addition to current standard of care (SoC) of those patients.[8] Finerenone is a selective non-steroidal mineralocorticoid receptor antagonist and is prescribed to reduce the risk for CKD progression and CV and renal events.[9] The reimbursement of finerenone is based on the FIDELIO-DKD and FIGARO-DKD trials. Data from these two trials were pooled in the prespecified 'FIDELITY'-analysis.[9–11] The FIDELIO-DKD and FIGARO-DKD trials assessed the effect of finerenone combined with SoC compared with SoC alone on time to CV events (ie, CV death, non-fatal MI, non-fatal stroke or hospitalisation due to heart failure (HF)) and renal outcomes (ie, renal death, ESKD, sustained estimated glomerular filtration rate (eGFR) less than 15 mL/min/1.73m^2 for at least 4 weeks, or sustained ≥40% decrease in eGFR from baseline for at least 4 weeks) in more than 13 000 patients.[10 11] The FIDELIO-DKD trial predominantly included patients with stage 3 or 4 CKD with moderately and severely elevated albuminuria and T2D.[10] The FIGARO-DKD trial included both patients with either stage 1 or 2 CKD and severely increased albuminuria and patients with stage 2 to 4 CKD and moderately increased albuminuria.[11] Both trials represent the eligible patient population for treatment with finerenone.

In Quist *et al*,[12] the cost-effectiveness of finerenone has been estimated in patients with severe CKD and T2D. Adding finerenone increases the quality-adjusted life years (QALYs) and provides cost savings, primarily due to its role in preventing renal and CV events. Moreover, earlier intervention could help prevent progression from mild CKD to more severe stages and improve health outcomes and save costs in the longer term. To further explore this, it is essential to understand the cost-effectiveness of finerenone in the treatment of mild to severe CKD. While many countries focus mainly on a healthcare perspective in their assessment of new treatments, chronic diseases can significantly impact productivity, informal care and society as a whole.[13 14] Therefore, it is relevant to evaluate the cost-effectiveness of finerenone by considering not only healthcare costs but also the broader societal costs.

This study evaluates the cost-effectiveness of adding finerenone to SoC for mild to severe CKD and T2D patients, focusing on its impact on patients' QALYs and the Dutch societal and healthcare costs of CKD.

METHODS

This analysis estimates the cost-effectiveness of finerenone from a Dutch societal perspective. The Netherlands was chosen as the reference country as they take society into account in their reimbursement decisions. The study uses the FINE-CKD Markov model that is described in detail in the previous publication.[12] The model was developed in Microsoft Excel 2016 (Redmond, WA, USA) and included all CKD progression stages (ie, CKD1 to CKD5 with and without renal replacement therapy (RRT)), acute and post-acute CV events (ie, non-fatal stroke, MI and hospitalisation for HF), and other health events (OHEs) (ie, subsequent CV event, hyperkalaemia and new onset of atrial fibrillation) (online supplemental appendix 1). OHEs were outcomes that showed significant differences in the FIDELIO-DKD and FIGARO-DKD trials, influencing QALYs and costs as identified through literature and expert input but did not affect the risk of subsequent renal events, CV events or survival. The rationale for the inclusion of OHEs can be found in the previous publication.[12] The validated FINE-CKD model is adapted to simulate the disease pathway of the FIDELITY population over a lifetime time horizon.[15] The model characteristics are presented in online supplemental appendix 2. The model inputs were derived from clinical trial data or literature and validated for their relevance to the Dutch context by local clinical experts. The transition probabilities are based on the individual patient-level data of the FIDELITY population and employ a 4-month cycle length, which resembles the measurement frequency of the endpoints of the clinical studies.[9] In the base case analysis, the incremental-cost-effectiveness ratio (ICER) for finerenone in addition to SoC compared with SoC was calculated for a willingness-to-pay (WTP) threshold of €20 000/QALY, which was based on the proportional disease shortfall method specified by the Dutch Healthcare Institute.[16]

Patient characteristics

Patient characteristics are based on the FIDELITY population (table 1).[8] Patients included those with CKD stage 1 and severely increased albuminuria, as well as CKD stages 2–4 with moderate or severely increased albuminuria. The distribution of CKD progression is presented in table 1, categorised by CKD stage alone, and in online supplemental appendix 3, categorised by both CKD stage and albuminuria level. Table 1 also shows the proportions of patients with CKD and albuminuria as observed in the Dutch population, which differ slightly from the

Table 1 Patient characteristics of the FIDELITY-ITT population

Parameter	FIDELITY population[9] (95% CI)	
Patient populations	FIDELITY population: base case population that consisted of the weighted average of FIDELIO* and FIGARO† population[14]	
Age	64.8 (46.2 to 83.4)	
Proportion male (%)	69.8% (69.0 to 70.6)	
	FIDELITY population[9]	**Dutch population**[2]
Proportion with CKD1 with severely increased albuminuria and CKD2 with moderate to severely increased albuminuria	39.9%	54.2%
Proportion with CKD3 with moderate to severely increased albuminuria	53.3%	38.5%
Proportion with CKD4 with moderate to severely increased albuminuria	6.8%	7.3%

*The FIDELIO population consisted of adults with stage 3 or 4 CKD and moderately and severely elevated albuminuria and T2D[11]
†The FIGARO population consisted of adult patients with stage 1 or 2 CKD and severely increased albuminuria or stage 2 to 4 and moderately elevated albuminuria[10]
CKD, chronic kidney disease; ESKD, end-stage kidney disease; RRT, renal replacement therapy.

percentages reported in the FIDELITY trial.[2] To assess the impact of the Dutch patient distribution, a scenario analysis was performed.

Transition probabilities

The transition of patients between health states was based on the probabilities of CKD progression, CV events, death from renal and CV causes, and OHEs that were found in the independent patient data of the FIDELITY analysis (table 2).[9] The amount of missing data in this analysis was low, with further specifications in the FIDELIO-DKD and FIGARO-DKD publications.[10 11] The HRs of the FIDELITY population were used to account for the effect of finerenone on CKD progression, CV events and OHEs (table 2).[9] The effect of finerenone was assumed over the entire treatment period, taking into account a 2.8% risk of discontinuation per cycle, as observed in clinical trials, after which the therapeutic effect was assumed to cease immediately. Additionally, all patients who progressed to the dialysis or transplantation health state were assumed to discontinue treatment with finerenone. Since the median follow-up duration was 3 years, an HR to account for the longer-term hazard of a CV event was implemented after 4 years.[12 17–19] The mortality rate unrelated to renal and CV events was obtained from data provided by the Dutch Central Bureau of Statistics, and adjustments were applied to account for the proportion of deaths attributable to CV events and CKD.[20] All transition probabilities were adjusted to a 4-month duration, which is in line with the model's cycle length.

Utilities

Utility values, scaled from 0 (death) to 1 (perfect health), were retrieved from the FIDELITY population, using the Dutch value set for the 5-level EuroQol five-dimension questionnaire.[9 21] Utility values from the FIDELITY pooled analysis for CKD progression, CV events and OHEs were adjusted for age, using the population norms for the Netherlands.[21 22] Given the low number of patients who experienced dialysis, transplantation and hyperkalaemia in the FIDELITY population, utilities used during a former health technology analysis were used to estimate the disutility during dialysis, hyperkalaemia and transplantation.[23] Disutilities to account for CV events and OHE were employed for one cycle length. The resulting utilities are presented in online supplemental appendix 4. Utilities were discounted at a rate of 1.5% per year, following Dutch Pharmacoeconomics guidelines.[16]

Costs

The model accounted for healthcare resource utilisation (ie, medical costs), including medication, CKD management, dialyses, transplantations, treatment of CV events, treatment of hyperkalaemia and treatment of atrial fibrillation. Additionally, resource utilisation outside of the healthcare system (ie, indirect non-medical costs) for patients and caregivers was included, consisting of productivity losses and informal care due to CKD progression, dialysis, transplantations and CV events (online supplemental appendix 5). Separate travel costs (ie, direct non-medical costs) were excluded as these are included in the total cost of dialysis and to prevent double counting. All resource utilisation was predominantly sourced from Dutch literature, and related costs were inflated to 2023 prices with a discount rate of 4% per year according to Dutch Pharmacoeconomics guidelines[16 24]

Sensitivity analyses

To evaluate the impact of each input parameter on the ICER, we performed a deterministic sensitivity analysis (DSA) in which the input parameters were varied from lower to upper bound of their CIs (ie, 2.5%–97.5%). When the SE or 95% CI was not available, a SE corresponding to 25% of the deterministic value was assumed as an approximation. In addition, to assess the robustness of the model, a probabilistic sensitivity analysis (PSA) was performed. For 1000 simulations, input parameters were concurrently and randomly changed based on their CIs and appropriate distributions (ie, normal, beta, -beta, gamma and Dirichlet) (online supplemental appendix 6). All assumptions leading to uncertainty in the model are presented in online supplemental appendix 7. Additionally, to assess the impact of extrapolating data from

Table 2 Transition probabilities: CKD progression and first modelled CV event and OHE probabilities based on independent patient data of the FIDELITY analysis[9]

	CKD1/2	CKD3	CKD4	CKD5 w/o dialysis	Dialysis (acute)	Dialysis (post-acute)	Kidney transplant (acute)	Kidney transplant (post-acute)
Baseline transition probabilities for CKD progression in patients receiving SoC*†								
CKD1/2	0.8717	0.1272	0.001	0.0001				
CKD3	0.0619	0.8722	0.0647	0.0009	0.0002			
CKD4	0.0025	0.1597	0.7902	0.0388	0.0088			
CKD5 w/o dialysis		0.0183	0.1027	0.6872	0.1872		0.0046	
Dialysis (acute)						1		
Dialysis (post-acute)						0.9947	0.0053	
Kidney transplant (acute)								1
Baseline transition probabilities for CKD progression in patients receiving SoC and finerenone*†								
CKD1/2	0.8633	0.1356	0.001	0.0001				
CKD3	0.0576	0.8718	0.0696	0.0007	0.0002			
CKD4	0.0027	0.177	0.7817	0.0314	0.0072			
CKD5 w/o dialysis		0.0123	0.1409	0.6861	0.1561		0.0046	
Dialysis (acute)						1		
Dialysis (post-acute)						0.9947	0.0053	
Kidney transplant (acute)								1
Baseline transition probabilities for CV events per CKD stage†‡								
Any CV event probability§	0.0076	0.0119	0.0157	0.0332	0.0332	0.0332	0.0157	0.0157
CV death	0.0047	0.0058	0.0078	0.0155	0.0206	0.0206	0.0078	0.0078
Renal death	0	0	0	0.0001	0	0	0	0
Probabilities of OHEs¶	No CV events			CV event				
Subsequent CV event§	–			0.0668				
Hyperkalaemia leading to hospitalisation	0.0004			0.0025				
Hyperkalaemia not leading to hospitalisation	0.0149			0.0349				
New onset of atrial fibrillation	0.003			0.0194				
HRs used to reflect the effectiveness of finerenone				HR finerenone+SoC versus SoC (95% CI)				
The onset of eGFR decrease <15 mL/min/1.73 m^2 sustained over at least 4 weeks				0.81 (0.67–0.98)				
Progression to dialysis				0.82 (0.65–1.03)				
Progression to kidney transplant				1.00** (1.00–1.00)				
CV death				0.88 (0.76–1.02)				
Renal death, CKD5 w/o renal replacement therapy				0.53 (0.10–2.91)				
First modelled CV event†¶				0.88 (0.76–1.03)				
Subsequent CV event†¶				0.84 (0.68–1.05)				
Hyperkalemia leading to hospitalisation				2.93 (1.90–4.54)				
Hyperkalemia not leading to hospitalisation				1.91 (1.72–2.12)				
New onset of atrial fibrillation				0.87 (0.72–1.04)				

*The transition probabilities of CKD progression were based on patient-level data with a median follow-up of 3 years and were measured every 4 months of patients treated with finerenone and patients with SoC. The HR for the onset of eGFR decrease < 15 mL/min/1.73 m^2 sustained over at least 4 weeks was used to correct for the probability to transition to CKD5 in patients treated with finerenone. The probability to transition to dialysis and transplantation was adjusted with the HRs for progression to dialysis and transplantation.
†To account for longer-term increased risk for CV events after 4 years and renal and CV mortality due to CKD, additional HRs were applied to the baseline transition probabilities.[9 17–19]
‡For patients treated with finerenone, these event rates have been adjusted using the HRs for first modelled CV event, hyperkalemia leading to hospitalisation, hyperkalemia not leading to hospitalisation, and new onset of atrial fibrillation.
§First and subsequent CV events included non-fatal MI (ie, 22.8%), IS stroke (ie, 23.1%), ICH stroke (2.0%) or hospitalisation for heart failure (ie, 52.1%).
¶For patients treated with finerenone, these event rates have been adjusted using the HRs for subsequent CV event, CV death, renal death.
**No difference between treatments was assumed; validated with clinical expert input.
CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; OHE, other health events; SoC, standard of care; w/o, without.

clinical trials, an additional analysis was conducted in which the resulting cost savings were measured over a time horizon ranging from 1 to 35 years.

Scenario analyses

Scenario analyses were conducted to determine the effect of various input and model assumptions.

SGLT2 inhibitors incorporated in standard of care

A proportion of patients (ie, a weighted average of 10.2%) in the FIDELITY population was simultaneously treated with an SGLT2 inhibitor.[9] Recently, SGLT2 inhibitors have become SoC in the Netherlands in patients with CKD and a high risk for CV events.[25] A proportion of patients (ie, a weighted average of 10.2%) in the FIDELITY population was simultaneously treated with an SGLT2 inhibitor. To explore the cost-effectiveness of finerenone in treatment regimens that incorporate SGLT2-inhibitors, two scenario analyses were conducted.

In the first scenario, the intervention consisted of finerenone and SGLT2 inhibitors added to SoC versus previous SoC (without SGLT2 inhibitors). HRs from a recent meta-analysis were used that included trials studying SGLT2 inhibitors and the FIDELITY-ITT analysis.[26] These HRs were used to estimate the effect of finerenone with SGLT2 inhibitors on CV events, CV mortality and the kidney-related outcome described as kidney failure, doubling of serum creatinine and death due to kidney failure.[26] HRs for the other outcomes were not available from this pooled analysis, and for those, base case values were used. The medication cost in this scenario accounted for the combined expense of finerenone and SGLT2 inhibitors versus the previous SoC.

The second scenario focused on evaluating the cost-effectiveness of adding finerenone to the current SoC regimen that already includes SGLT2 inhibitors. In this analysis, the intervention consisted of finerenone added to the current SoC (including SGLT2 inhibitors) versus the current SoC (including SGLT2 inhibitors). The transition probabilities for the subpopulation concurrently treated with SGLT2 inhibitors and a subpopulation with increased use of SGLT2 inhibitors were adjusted to account for the effect of SGLT2 inhibitors on the baseline risk for CKD progression and CV events.[27] The baseline risk for CKD progression and CV events found in the FIDELITY population was adjusted with the HRs reported in the two pivotal SGLT2 inhibitor trials (ie, CREDENCE and DAPA-DKD) (Formula 1).[28 29]

$$P_{ALL} = \%\ SGLT2 * \left(1 - \left(1 - P_{nonSGLT2}\right)^{HR}\right) + \left(1 - \%\ SGLT2\right) * P_{nonSGLT2}$$

HR, hazard ratio; P, probability

Formula 1. The formula that was used to incorporate the effect of SGLT2 inhibitors on baseline risks

Patient resembling the clinical practice

The impact of the patient's characteristics was assessed. As age might impact treatment duration, we performed scenarios in which the age of patients at treatment initiation was either 59.8 or 69.8 years (ie, ±5 years of the trial population). Additionally, a scenario was performed in which the distribution of CKD severity fully reflected the label population in the Netherlands.

Utilities

Given the small number of patients with more severe CKD and RRT in the population,[9] the utility values of patients who underwent dialysis or a transplant were estimated using a combination of data from the trial and the literature. Therefore, two further analyses were carried out which addressed the potential ambiguity arising from the utility data. The first scenario disregarded trial utility data and used utility data gathered in a literature review[23 30–33] and the second employed utility data based on literature that was validated by the Dutch health technology assessment (HTA) agency.[33–36]

Costs

The base case incorporated all costs relevant to a societal perspective. Additionally, a scenario explored the costs relevant from a healthcare payer setting. Moreover, as the indirect costs for transplantation and dialysis were substantial, we performed a scenario in which indirect dialysis costs were excluded. In addition, a scenario was performed using alternative sources for productivity losses to acknowledge the potential uncertainty arising from the use of a mix of literature in the base case.

Time horizon and discount rates

Finally, we assessed technical model settings with several scenarios, including a 10-year time horizon, and fluctuation of the discount rates (ie, 0% and 5% for both costs and effects).

RESULTS

Base case analysis

Our base case analysis showed that patients treated with finerenone in addition to SoC gained 0.15 life years and 0.14 QALYs over a lifetime horizon compared with patients treated with SoC alone (table 3). Finerenone brought a gain in life years without RRT and CV events of 0.21 and 0.26, respectively, which means that treatment of 100 patients would save 6.6 CV events over their lifetime. Furthermore, treatment with finerenone and SoC incurred a total lifetime cost of €67 491 per patient versus €70 204 per patient for treatment with SoC alone, with the costs for society amounting to €8481 and €9799. Thus, the addition of finerenone to SoC saved €2713 per patient over a lifetime horizon. This was mainly due to lower dialysis costs (−€5103), lower transplantation costs (−€117), lower first (modelled) CV event costs (−€343) and lower costs for patient and caregivers (−€1298).

Deterministic sensitivity analyses

The deterministic sensitivity analysis identified the parameters for which the incremental QALYs and costs were most sensitive (online supplemental appendix 8). The model outcomes were most sensitive to the average

Table 3 Results of the base case analysis: disaggregated costs, incremental costs, incremental life years, incremental QALYs, over a lifetime horizon and the resulting ICER per patient

	Finerenone+SoC	SoC	Difference*
Effects on life years (per patient**)**			
Life years without CV	8.79	8.52	0.26
Life years without RRT	10.75	10.54	0.21
Total life years	11.16	11.01	0.15
Total QALY	8.58	8.44	0.14
Costs within the healthcare system (per patient**)**			
Medication costs finerenone	€4014	€0	€4014
Medication costs SoC	€7901	€7792	€109
CKD treatment	€4047	€3926	€121
Dialysis	€32 926	€38 065	−€5103
Transplant	€930	€1046	−€117
Total first CV event costs	€7063	€7406	−€343
Non-fatal stroke	€1282	€1345	−€62
MI	€3909	€4098	−€190
Hospitalisation for HF	€1871	€1962	−€91
Subsequent CV event	€1631	€1821	−€190
Non-fatal stroke	€251	€281	−€29
MI	€1169	1305	−€136
Hospitalisation for HF	€211	€235	−€25
Hyperkalaemia leading to hospitalisation	€120	€63	€57
Hyperkalaemia not leading to hospitalisation	€158	€105	€53
New onset of atrial fibrillation	€185	€202	−€17
Costs for patient and caregiver (per patient**)**			
Productivity losses and informal care	€8481	€9799	−€1298
Total costs (per patient)	€67 491	€70 204	−€2713
Costs/QALY (per patient**)**	Finerenone+SoC is a dominant treatment option		

*Incremental outcomes can deviate slightly due to rounding.
CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HF, heart failure; ICER, incremental cost-effectiveness ratio; MI, myocardial infarction; QALY, quality-adjusted life year; RRT, renal replacement therapy; SoC, standard of care.

age of patients at the start of the model. A reduction in age to 46.2 years led to an increase in incremental QALYs of 0.15 and an increase in cost savings of €17 302. Besides age, parameters that specifically affected incremental QALYs include baseline patient distribution over CKD stages (ie, 0.10–0.33), HR for CV death (ie, 0.04–0.22), utility for health states (ie, 0.04–0.16) and HR for the onset of an eGFR decrease (ie, 0.09–0.17). Other parameters that affected incremental costs include baseline patient distribution (−€15 385 to −€385), HR for the progression to dialysis (ie, −€5786 to −€784), HR for the onset of eGFR decrease (ie, −€4656 to −€422) and HR for increased mortality risk due to dialysis (ie, −€4494 to −€2009).

Probabilistic sensitivity analyses

The outcomes of the PSA are presented in a cost-effectiveness plane and cost-effectiveness acceptability curve (figure 1A, B, respectively). Figure 1A shows a mean of 0.14 incremental QALYs and −€3574 incremental costs. Figure 1B shows that at a WTP threshold of €20 000, finerenone had an 83.8% probability of being cost-effective when added to SoC. Additionally, finerenone has a 62.3% probability of being dominant when added to SoC.

Incremental costs over time

The figure in online supplemental appendix 9 estimates the incremental costs over an increasing time horizon. The results suggest that treatment with finerenone becomes cost-saving after 1 year, with the majority of benefits occurring during the period from 4 to 14 years of treatment.

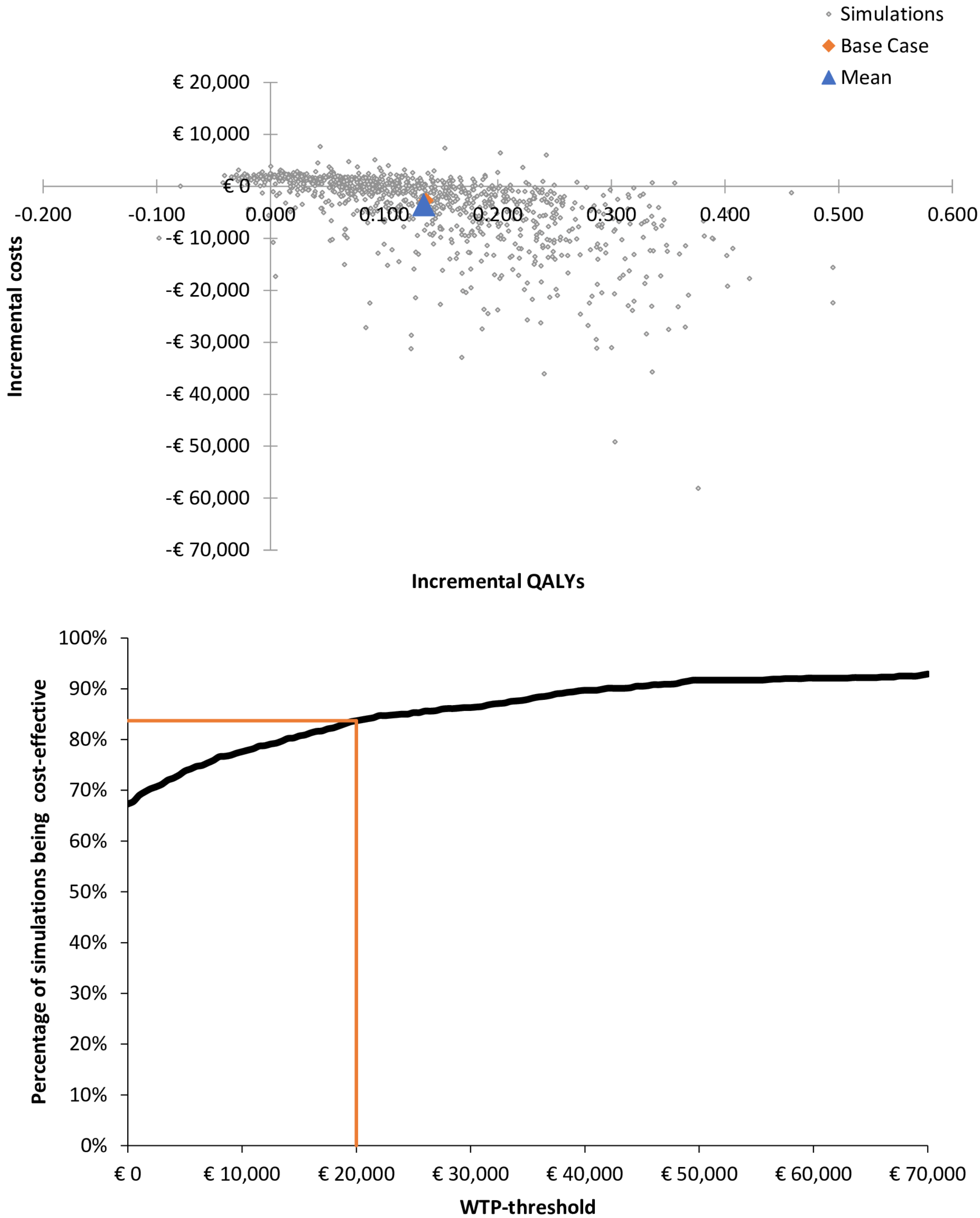

Figure 1 (A) Cost-effectiveness plane and (B) cost-effectiveness acceptability curve. QALYs, quality-adjusted life years; WTP, willingness-to-pay.

Scenario analyses

Finerenone remained dominant in all scenarios. Finerenone and SGLT2 inhibitors with SoC compared with SoC without SGLT2 inhibitors led to an increased gain in incremental QALYs and cost savings than stand-alone finerenone. Finerenone with SoC that includes SGLT2 inhibitors compared with SoC that includes SGLT2 inhibitors induced a slight reduction in the additional cost savings and incremental QALYs provided by finerenone. The age at treatment initiation had a large impact on the cost savings and incremental QALYs, with a higher age at baseline reducing cost savings to −€23. The inclusion of solely direct dialysis costs reduced the cost savings to −€1512 and had no impact on incremental QALYs. Implementation of different sources of utility data had minimal impact on the outcomes, leading to incremental QALYs almost equal to the base case outcomes. Finerenone continued to be cost-effective and cost-saving with other technical model settings, including a healthcare payer's perspective, a shorter time horizon and a varying discount rate. The outcomes of the scenario analyses are presented in table 4.

Table 4 Outcomes from the scenario analysis

Description	Incremental costs (discounted)	Incremental QALYs (discounted)	ICER (discounted)
Base case	–€2713	0.14	Dominant
Finerenone and SGLT2i added to SoC compared with SoC without SGLT2i (comparison: finerenone+SGLT2i+SoC vs SoC)*	–€7226	0.34	Dominant
100% of patients use canagliflozin in SoC and effectiveness is considered (comparison: finerenone+SoC (with SGLT2i) vs SoC (with SGLT2i))†	–€953	0.11	Dominant
100% of patients use dapagliflozin in SoC and effectiveness is considered (comparison: finerenone+SoC (with SGLT2i) vs SoC (with SGLT2i))†	–€909	0.11	Dominant
50% of patients use canagliflozin in SoC and effectiveness is considered (comparison: finerenone+SoC (with SGLT2i) vs SoC (with SGLT2i))†	–€1980	0.13	Dominant
50% of patients use dapagliflozin in SoC and effectiveness is considered (comparison: finerenone+SoC (with SGLT2i) vs SoC (with SGLT2i))†	–€1956	0.13	Dominant
Patients are 59.8 years old at treatment initiation	–€7029	0.18	Dominant
Patients are 69.8 years old at treatment initiation	–€23	0.09	Dominant
CKD distribution of patients with CKD and albuminuria is equal to the distribution seen in the Netherlands	–€2226	0.13	Dominant
Solely direct dialysis and transplantation costs are incorporated	–€1512	0.14	Dominant
Utility data are based on literature retrieved from the literature that was validated by Dutch National Healthcare Institute	–€2713	0.14	Dominant
Utility data are based on literature retrieved in a systematic literature review	–€2713	0.14	Dominant
Healthcare payer's perspective	–€1415	0.14	Dominant
Time horizon 10 years	–€2134	0.07	Dominant
Discount rate is 5% for effects and costs	–€2522	0.10	Dominant
Discount rate is 0% for effects and costs	–€3670	0.16	Dominant

*The effectiveness of SGLT2i and finerenone added to SoC versus SoC without SGLT2i is based on the study of Neuen *et al.*
†Effectiveness of the SGLT2 inhibitors is calculated with the HRs of the CREDENCE and DAPA-CKD trials with the following formula: $P_{ALL} = \%\ SGLT2 \times \left(1 - \left(1 - P_{nonSGLT2}\right)^{HR}\right) + \left(1 - \%\ SGLT2\right) \times P_{nonSGLT2}$
HR, hazard ratio; ICER, incremental cost-effectiveness ratio; P, probability; QALYs, quality-adjusted life year; SGLT2i, sodium glucose cotransporter 2 inhibitor; SoC, standard of care.

DISCUSSION

This analysis demonstrates that adding finerenone to the SoC for mild to advanced CKD related to T2D is cost-effective and dominant from both a societal and healthcare payer's perspective. Finerenone improves QALYs and reduces healthcare and societal costs by lowering the incidence of renal and cardiovascular events in CKD patients with T2D. The use of the FIDELITY pooled dataset allowed for a comprehensive evaluation of a diverse CKD population, and both probabilistic and deterministic sensitivity analyses confirmed the robustness of the results, with minimal impact from individual variables. These findings highlight the potential of finerenone to prevent CKD progression, reduce CV and renal events and generate cost savings. This also emphasises the importance of early CKD detection and treatment, including at-home screening for high-risk patients, which has been shown to be cost-effective in the Netherlands.

The analysis shows that the portion of CKD costs attributed to productivity losses and informal caregiving are considerable (ie, €8481 and €9799 per patient over a lifetime in the finerenone and SoC arm, respectively). By assessing these societal costs, our study underscores the impact that chronic diseases like CKD and T2D may have on society through extended periods of productivity loss and informal care, and the importance of considering those costs in the assessment of the economic value of treatment. The Netherlands is a country in which the societal perspective is recommended,[16] and therefore, can help generate insight into the impact of a societal perspective for other HTA-focused countries, such as Canada and the UK, which often focus on healthcare perspective solely in their HTA.[13 14]

The health benefits of finerenone are observed in a heterogeneous population that included mild to severe CKD patients from 48 countries and are not country specific.[9] However, the outcomes of this cost-effectiveness analysis provide an estimate of the impact to healthcare and society for the Netherlands specifically, as (healthcare) resource utilisation and their related costs differ per country. For example, in the Netherlands, dialysis costs are relatively high as they take into account transport of the patient to the dialysis centre and other resource use. Therefore, to fully understand the cost-effectiveness of adding finerenone to the SoC in other countries, local adaptations of this model are needed.

A prespecified subgroup and post hoc analysis of the FIDELITY analysis showed no significant difference in results between patients who received SGLT2 inhibitors at baseline and patients who did not receive SGLT2 inhibitors at baseline.[37] Although indicative of the stand-alone effect of finerenone, this post hoc analysis was not fully powered for this comparison. Recent trial-based meta-analyses explored the effect of finerenone combined with SGLT2 inhibitors further.[26 38] These analyses showed that a combination of finerenone and SGLT2 inhibitors leads to a relevant larger effect compared with SGLT2 inhibitors alone. As SGLT2 inhibitors have become SoC in the Netherlands after the initiation of the FIDELIO and FIGARO trials,[10 11] scenario analyses were performed that assessed the cost-effectiveness of finerenone with SGLT2 inhibitors compared with SoC without SGLT2 inhibitors and the cost-effectiveness of finerenone when it is being added to a SoC that includes SGLT2 inhibitors. These exploratory scenario analyses suggested that combining finerenone with SGLT2 inhibitors, compared with SoC without SGLT2 inhibitors, may be more cost-effective than adding finerenone alone. However, even when finerenone is added to SoC that includes SGLT2 inhibitors—and a reduced baseline risk for renal and CV events was considered—finerenone remained dominant.

The transition probabilities were based on a combination of patient-level data from the FIDELITY analysis.[9] HRs were employed to consider the impact of finerenone on the reduced progression to CKD5 with and without RRT. However, for transitions between other CKD levels, independent patient-level data were used with a small number of events over the trial period for some of the transitions. Consequently, some of the progression rates exhibited inconsistencies, leading to a slightly higher probability of progression from CKD1 to CKD3 for patients treated with finerenone and SoC, compared with patients treated with SoC alone. Given that finerenone has demonstrated a significant reduction in CKD progression, we do not anticipate these discrepancies to be representative of real-world scenarios, and the scenario shows that it leads to conservative estimates of finerenone's cost-effectiveness.

Besides the transition probabilities, our analysis has some limitations caused by the lack of data. First, the follow-up duration of the FIDELIO-DKD trial was 2.6 years and the FIGARO-DKD trial was 3.4 years,[10 11] but in cost-effectiveness analyses of chronic diseases, a lifetime horizon should be considered.[16] The FINE-REAL study demonstrated the safety of finerenone in the real world, but long-term efficacy data are not yet available.[39] To estimate the long-term transition probabilities, HRs were retrieved from multiple sources.[17–19] For future studies, it would be valuable to assess the cost-effectiveness of finerenone while using more long-term data. In this study, to also understand the cost-effectiveness of finerenone for a shorter time period, a sensitivity analysis studied the incremental costs over time. This analysis showed that most cost savings were made in the first years of the treatment and not during the end of the lifetime horizon, reducing the uncertainty around our conclusions. Finally, the HR obtained for renal death in the FIDELITY pooled analysis was not statistically significant due to the low incidence of renal death in populations that were assessed in the FIDELITY pooled analysis (ie, 0.53 (0.10–2.91)). Nevertheless, due to the low incidence of renal death, the HR for renal death did not come forward as a parameter with a major impact on model outcomes in the DSA.

This study highlights the significant burden that chronic diseases like T2D and CKD impose on healthcare systems and society, emphasising the difference between a healthcare and society perspective, and the importance of incorporating a societal perspective to understand the burden of a disease on a society.

From a societal and healthcare perspective, finerenone is a cost-saving intervention that improves QALYs for patients with CKD associated with T2D across a wide spectrum of disease severity, offering both cost savings and an increase in QALYs.

Contributors SWQ adapted the FINE-CKD model to a Dutch societal perspective, analysed and interpreted outcomes, and was a major contributor in writing the manuscript. SB validated model inputs and structure for Dutch healthcare setting and was a contributor in writing the manuscript. MP developed the original FINE-CKD model. MJP analysed and interpreted data and was a contributor in writing the manuscript. JvL contributed to the model adaptation, analysed and interpreted outcomes, and was a contributor in writing the manuscript. JP contributed to the model adaptation, analysed and interpreted outcomes, and was a contributor in writing the manuscript. SWQ accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Competing interests MJP reports grants and honoraria from various pharmaceutical companies, all unrelated to this specific work but some originating from companies developing, producing and marketing drugs in the field of CKD and T2D. SWQ, JvL and MP all were employed by consultancy firms that received payment from Bayer pharmaceuticals. JP was an employee of Asc Academics at the time the research was conducted. He is currently employed by Daiichi Sankyo Nederland B.V. SB has no competing interests to declare.

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