Cost-Effectiveness of Empagliflozin in Adult Patients with Chronic Kidney Disease in the Netherlands

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Introduction

- Chronic kidney disease (CKD) is defined as a condition in which there is reduced renal function (estimated glomerular filtration rate (eGFR) <60 ml/min/1.73m2) and/or increased albuminuria (loss of albumin in the urine, determined by the albumin creatinine ratio (ACR)) or specific abnormalities in kidney structure/function, lasting more than 3 months, with health consequences [1].
- Medical treatment of CKD consists of the prevention of its progression through blood pressure control, renin-angiotensin blockade, dietary and glycemic control, prevention and management of cardiovascular and complications.
- Empagliflozin is a potent, selective, reversible inhibitor of sodium-glucose cotransporter 2 (SGLT2), which is currently available for the treatment of patients with type 2 diabetes mellitus and heart failure.
- In the recent EMPA-KIDNEY trial, empagliflozin showed a lower risk of progression of kidney disease or death from cardiovascular causes than placebo among a wide range of patients with CKD who were at risk for disease progression [2]. Based on the results of the EMPA-KIDNEY trial, empagliflozin was recently approved for the treatment in adult patients with CKD [3].
- It is unknown if empagliflozin is cost-effective for the treatment of CKD in the Netherlands. Therefore, we aimed to evaluate the cost-effectiveness of empagliflozin in adult patients with CKD in the Netherlands.

Methods

- A Markov state microsimulation model was developed in Microsoft Excel®. The cost-effectiveness of empagliflozin plus standard of care (SoC) and SoC alone was compared in Dutch patients with CKD.
- The model tracks CKD risk factors evolution and its impact on the disease outcomes. Microsimulation allows to simulate individual patients by randomly distributing the baseline characteristics within specific limits and to track individual disease histories over time, as well as to study the impact of the different factors. This is necessary for a heterogeneous population like patients with CKD.
- The analyses were performed from a healthcare system perspective with a lifetime horizon (maximum age 100).
- Health states were defined by the KDIGO classification, and in each health state acute events and long-term complications were defined and grouped per organ system (Figure 1).

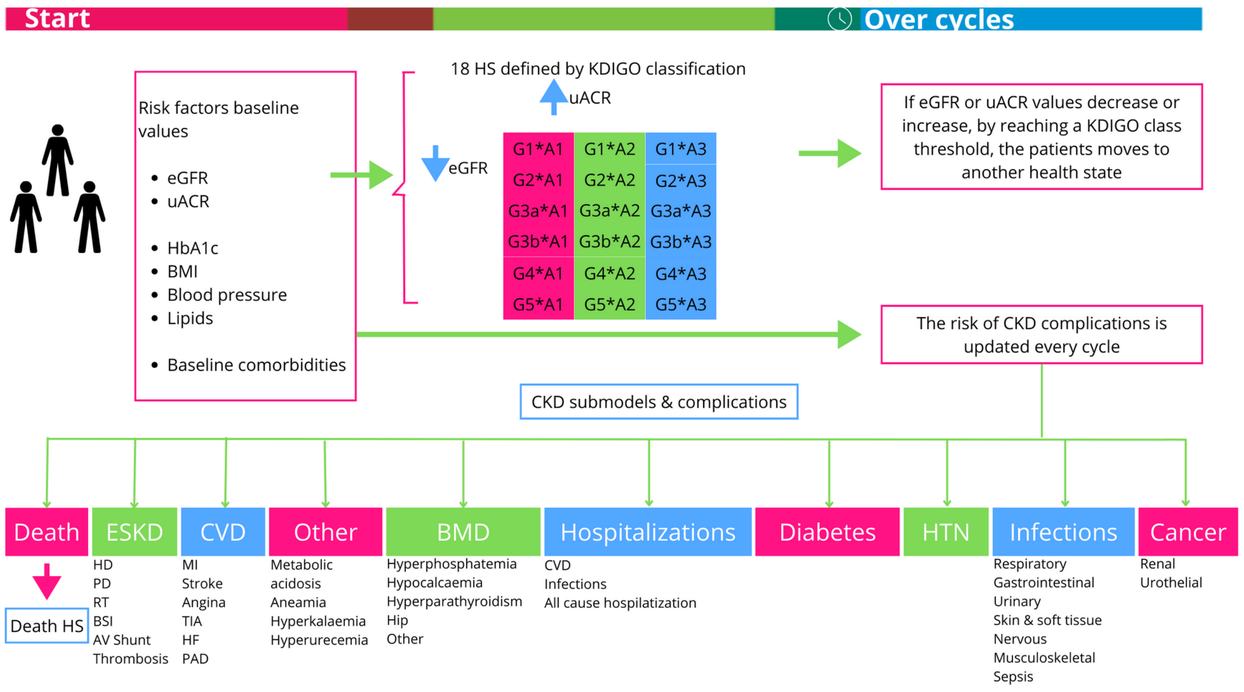

Figure 1. Complications and events stratified by disease type included in the CKD disease progression model.

Abbreviations: AV, arteriovenous; BMD, bone and mineral disease; BMI, body mass index; BSI, blood stream infection; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HD, haemodialysis; HF, heart failure; HTN, hypertension; HS, health state; KDIGO, Kidney Disease: Improving Global Outcomes; MI, myocardial infarction; PAD, Peripheral arterial disease; PD, peritoneal dialysis; RT, Renal transplantation; TIA, transient ischaemic attack; uACR, urine albumin-creatinine ratio.

- The input data were taken from the EMPA-KIDNEY trial (baseline characteristics and effectiveness), published data and national (Dutch) sources for mortality, treatment and event costs, and utilities.
- The analysis generates an incremental cost-effectiveness ratio (ICER) which allows identification of whether the intervention is cost-effective or not. The ICER is compared to the willingness-to-pay (WTP) of €50,000/QALY based on the disease severity (proportional hazard: 0.55) [4].
- A one-way sensitivity analysis was done by varying each single input sequentially while holding other parameters fixed and assessing the effect on the overall outcome. The most influential parameters of the model were plotted in a tornado diagram.
- A probabilistic sensitivity analysis (PSA), in which all parameters (i.e., ratios, probabilities, utilities, costs) are varied simultaneously, of 100 simulations was conducted to test the robustness of the model results. The results of the PSA were presented in a cost-effectiveness plane and a cost-effectiveness acceptability curve.

Results

- Using a lifetime horizon, the base case results showed a total discounted costs for empagliflozin plus SoC, and SoC alone of €180,301 and €214,174 respectively, with savings of €33,873 (Table 1).
- Empagliflozin plus SoC was associated with higher total discounted health benefits of 11.06 LYs and 9.01 QALYs, compared with 9.74 LYs and 7.79 QALYs for SoC alone, or an additional 1.31 LYs and additional 1.22 QALYs for empagliflozin plus SoC (Table 1).

Table 1. Cost-effectiveness results

	Empagliflozin + SoC	SoC	Incremental
Total discounted costs (€)	180,301	214,175	-33,873
Total discounted LYs	11.06	9.74	1.31
Total discounted QALYs	9.01	7.79	1.22
Incremental cost per LY	Dominant (less cost, more LY)		
Incremental cost per QALY	Dominant (less cost, more QALY)		
Net monetary benefit (NMB)	€94,676		

Abbreviations: LY, life year; QALY, quality-adjusted life year; SoC, standard of care.

- The univariate sensitivity analysis showed the most influential input parameters all concerned the incremental treatment effect for the G4A2 health state for empagliflozin plus SoC in terms of risk factor progression for uACR and eGFR (Figure 2).
- Other influential parameters included the acute event costs for haemodialysis for patients with ESRD, and the increment risk factor progression for uACR in the G3bA2 and G4A3 health states for the SoC arm.

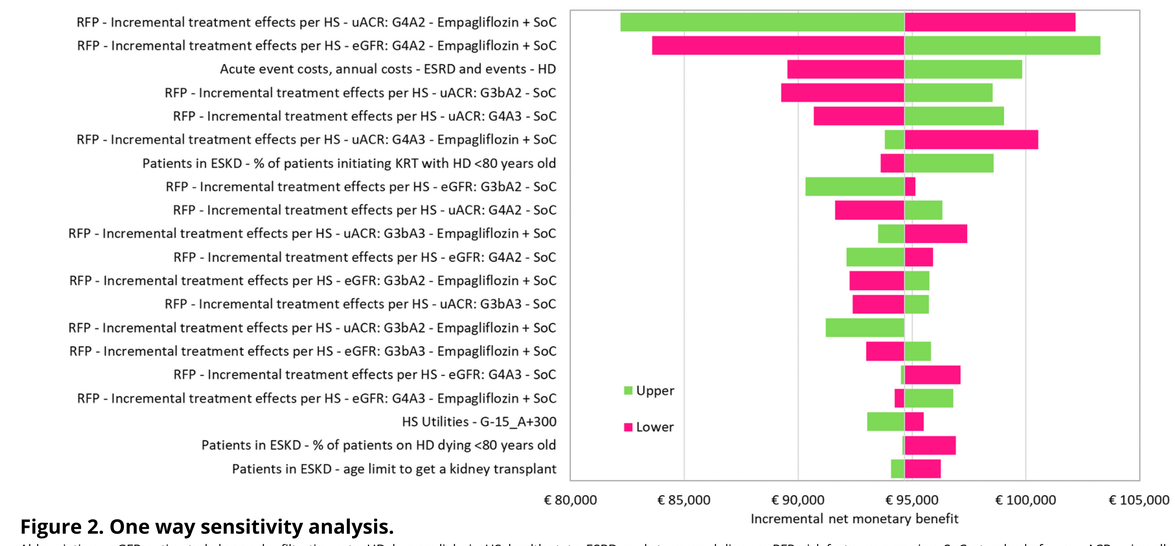

Figure 2. One way sensitivity analysis.

Abbreviations: eGFR, estimated glomerular filtration rate; HD, haemodialysis; HS, health state; ESRD, end stage renal disease; RFP, risk factor progression; SoC, standard of care; uACR, urine albumin-creatinine ratio.

- The PSA confirmed the robustness of the findings with all the results in the dominant quadrant of the cost-effectiveness plane (Figure 3).
- The cost-effectiveness acceptability curve showed that empagliflozin plus SoC has a probability of being cost-effective of 100% at a WTP of €50,000/QALY (Figure 4).

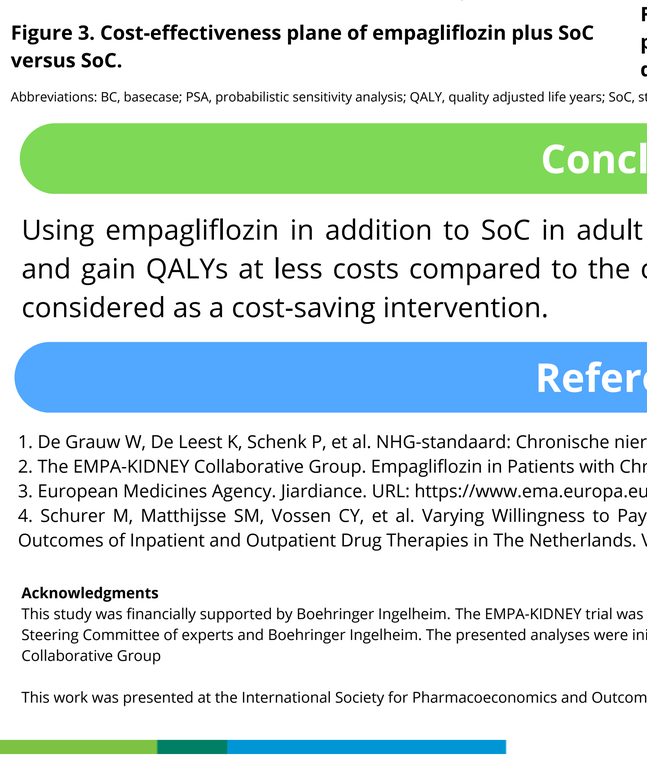

Figure 3. Cost-effectiveness plane of empagliflozin plus SoC versus SoC.

Figure 4. Cost-effectiveness acceptability curve depicting probability of empagliflozin + SoC being cost-effective at different willingness-to-pay thresholds versus SoC.

Abbreviations: BC, basecase; PSA, probabilistic sensitivity analysis; QALY, quality adjusted life years; SoC, standard of care

Conclusion

Using empagliflozin in addition to SoC in adult CKD patients is likely to extend life expectancy and gain QALYs at less costs compared to the current SoC in the Netherlands and thus can be considered as a cost-saving intervention.

References

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Acknowledgments

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