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Economic Evaluation

# Budget Impact Analysis of Empagliflozin in the Treatment of Patients With Type 2 Diabetes With Established Cardiovascular Disease in South Africa

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## ABSTRACT

*Objectives:* This study aimed to estimate the budget impact and affordability of empagliflozin added to usual care compared with usual care alone, in a diabetic population with established cardiovascular disease, from a private healthcare payer perspective in South Africa.

*Methods:* A budget impact model was adapted and localized. Epidemiological data were obtained from the South African Council for Medical Schemes. Clinical event rates were sourced from the EMPA-REG OUTCOME trial and drug costs from list prices. Clinical event costs were derived from a claims data analysis of the South African private healthcare sector and microcosting. Scenario analyses were performed on select inputs. The modeled outcomes included annual budget impact of empagliflozin, the incremental cost per life per month, cardiovascular deaths averted, and incremental cost per life saved, over 3 years.

*Results:* A total of 9 503 patients were eligible for empagliflozin (year 1), 12 670 (year 2), and 16 947 (year 3). The incremental cost was $1 272 297, $1 764 705, and $2 455 235, for years 1 to 3, respectively. The incremental cost per beneficiary per month was calculated as $0.012 (year 1), $0.016 (year 2), and $0.023 (year 3). The model estimated a 38.6% reduction in cardiovascular deaths, 305 lives saved, and an incremental cost per life saved of $17 999.

*Conclusions:* Adding empagliflozin to usual care has a marginal budget implication and is highly affordable for private healthcare payers, with an acceptable incremental cost based on clinical outcomes.

*Keywords:* budget impact, diabetes, empagliflozin, sodium-glucose cotransporter 2 inhibitor.

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## Introduction

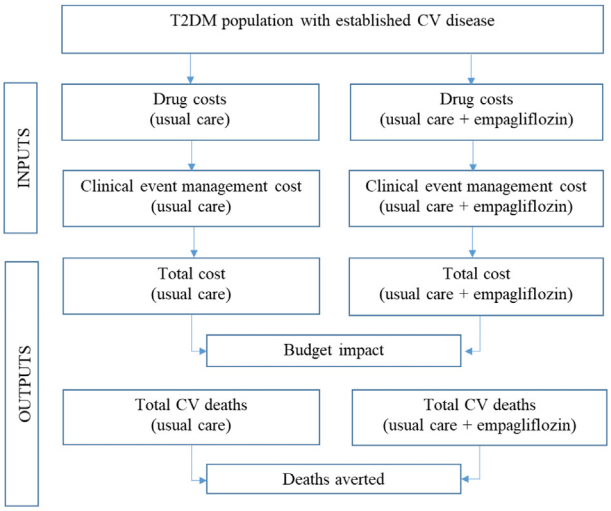
Patients with type 2 diabetes mellitus (T2DM) have a substantially increased cardiovascular (CV) risk[1,2] where myocardial infarction is the leading cause of death.[3] The clinical management of T2DM includes modifying risk factors for complications, in particular those associated with CV disease (CVD).[4,5] Sodium-glucose cotransporter 2 (SGLT2) inhibitors are a novel class of glucose-lowering drugs that act in the kidney by inhibiting SGLT2-mediated glucose reabsorption in the proximal tubule.[6,7] In addition, the drugs exhibit beneficial effects on CV risk factors. The SGLT2 inhibitor empagliflozin (Jardiance®, Boehringer Ingelheim) significantly reduces glycated hemoglobin[8-11] and has been shown to reduce major adverse CV events, CV death, and hospitalization for heart failure (HF) in patients with T2DM with established CVD, when administered as an add-on to usual care (EMPA-REG OUTCOME trial).[12] Results from the EMPRISE real-world study[13] in routine clinical care complement the outcomes data from the EMPA-REG OUTCOME trial.

The cost of treating T2DM—particularly its complications—is expensive.[14] This further increases the financial burden of T2DM on healthcare payers.[15] Studies have related poor glycemic control to higher healthcare costs.[16-20] For example, Aargren et al[21] report that a 1-percentage-point increase in glycated hemoglobin will, on average, lead to a 4.4% increase in diabetes-related medical costs for T2DM.

Previous studies have investigated the budget impact of adding empagliflozin to usual care for the treatment of adult patients with T2DM and established CVD.[22-26] These studies found that adding empagliflozin to usual care was budget saving because of reduced CV-related management costs.

South Africa (SA) has a growing prevalence of T2DM fueled by increased urbanization and unhealthy lifestyle factors[27,28]; 12.8% of adults in SA have diabetes.[29] The high prevalence of this disease is compounded by the high cost of treating CV-related events. The Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) recommends the use of SGLT2 inhibitors as add-on to metformin (or other initial drug therapy) or a third glucose-lowering drug in selected diabetic patients not achieving or maintaining their glycemic targets. Furthermore, SEMDSA endorses the benefit of empagliflozin in patients with diabetes with CVD.[30] Consequently, there is a need for health economic assessment to investigate the financial impact of adding empagliflozin to usual care in patients with T2DM with established CVD.

**Figure 1.** Flow diagram of model structure.




CV indicates cardiovascular; T2DM, type 2 diabetes mellitus.

We conducted a budget impact analysis from an SA private healthcare payer perspective to quantify the budget impact of adding empagliflozin to usual care and to determine the affordability thereof (based on additional treatment costs being offset by clinical event reduction). In addition, we estimated the clinical impact of this new scenario in terms of reduced CV death. The evidence from this study could guide private healthcare payers in their reimbursement decisions to fund empagliflozin, while optimizing healthcare expenditure for the management of patients with T2DM.

## Methods

### Model Setup

An existing Microsoft Excel–based budget impact model[22,23,24,25,26] (based on the EMPA-REG OUTCOME trial[12]) was adapted and localized to the SA private healthcare setting. SA has a 2-tiered healthcare system. The public sector is state funded and caters to the majority—more than 80% of the population. The private sector is largely funded through individual contributions to medical aid schemes and out-of-pocket payments, accounting for < 20% of the population. In our analysis, the model population represents the number of patients in SA on medical aid.[31] The model considered patients with T2DM with established CVD and compared direct medical costs arising from treatment with empagliflozin as add-on to usual care compared with usual care alone, over a 3-year period (Fig. 1). Based on these costs, the budget impact of adopting the new scenario was analyzed. The base year for the analysis was 2019; the model encompassed the time period 2019 to 2021.

### Inputs and Assumptions

#### Epidemiology

Local epidemiological data were obtained from the Council for Medical Schemes Annexures for 2019/2020. The population size used in the model represents the number of patients on private healthcare (medical aid) in 2019 (8 953 076).[32] Growth of the private healthcare sector population was assumed to be 0.

The registered percentage of T2DM among the selected population is 5.49%.[32] This constitutes the proportion of beneficiaries registered on the medical schemes' chronic disease management programs for T2DM during 2019. The percentage was assumed to be the same over the model time horizon. The proportion of patients with T2DM with established CVD (32.2%) was obtained from Einarson et al.[33,34] The uptake of empagliflozin was assumed to increase by approximately 33% each year, from a baseline of 6%.

The number of patients eligible to receive empagliflozin in the new scenario was 9 503 (year 1), 12 670 (year 2), and 16 947 (year 3). These figures were calculated as follows:

$$\textit{Population receiving empagliflozin} = \textit{private health care sector population size} \times \textit{prevalence of T2DM} \times \textit{\% T2DM patients with established CVD} \times \textit{uptake of empagliflozin}$$

**Table 1.** Clinical event rates.

| Clinical event | Rate (per person-years) in usual care | Rate (per person-years) in usual care + empagliflozin | References |
|---|---|---|---|
| NFMI | 0.0185 | 0.0160 | EMPA-REG OUTCOME trial[12] |
| Nonfatal stroke | 0.0091 | 0.0112 | EMPA-REG OUTCOME trial[12] |
| Unstable angina hospitalization | 0.0100 | 0.0100 | EMPA-REG OUTCOME trial[12] |
| Heart failure hospitalization | **0.0145** | **0.0094** | EMPA-REG OUTCOME trial[12] |
| TIA | 0.0035 | 0.0029 | EMPA-REG OUTCOME trial[12] |
| Revascularization | 0.0291 | 0.0251 | EMPA-REG OUTCOME trial[12] |
| CV death | **0.0202** | **0.0124** | EMPA-REG OUTCOME trial[12] |
| Development of macroalbuminuria | **0.0649** | **0.0418** | Wanner et al[35] |
| Renal injury | **0.0097** | **0.0055** | Wanner et al[35] |
| Renal failure | **0.0021** | **0.0010** | Wanner et al[35] |

CV indicates cardiovascular; NFMI, nonfatal myocardial infarction; TIA, transient ischemic attack.

**Table 2.** Annual drug cost per class (year 1) and changes in drug usage from baseline.

| Drug class | Drug cost (USD) | Usage, % of patients initiated | | References |
|---|---|---|---|---|
| | | Usual care, % | Usual care + empagliflozin, % | |
| Empagliflozin | 410.56 | 0.0 | 100.0 | Cost: Database of Medicine Prices for November 2019[37]<br>Usage: Voorhaar et al[26] |
| Metformin | 60.77 | 4.2 | 2.8 | Cost: Database of Medicine Prices for November 2019[37]<br>Usage: Voorhaar et al[26] |
| Sulphonylurea | 50.31 | 6.3 | 3.0 | Cost: Database of Medicine Prices for November 2019[37]<br>Usage: Voorhaar et al[26] |
| Glitazone | 162.68 | 2.6 | 1.0 | Cost: Database of Medicine Prices for November 2019[37]<br>Usage: Voorhaar et al[26] |
| Glinide | 265.21 | 1.1 | 0.6 | Cost: Database of Medicine Prices for November 2019[37]<br>Usage: Voorhaar et al[26] |
| DPP-4 inhibitor | 263.48 | 6.5 | 4.2 | Cost: Database of Medicine Prices for November 2019[37]<br>Usage: Voorhaar et al[26] |
| GLP-1 agonist | 1429.38 | 2.2 | 1.1 | Cost: Database of Medicine Prices for November 2019[37]<br>Usage: Voorhaar et al[26] |
| Insulin (per unit) | 0.03 | 9.9 | 4.5 | Cost: Database of Medicine Prices for November 2019[37]<br>Usage: Voorhaar et al[26] |
| Insulin test strips, lancets, and needles | 457.38 | 9.9 | 4.5 | Cost: Discovery Medical Scheme formulary[40]<br>Usage: assume same as insulin |

DPP-4 indicates dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; USD, US dollars.

The population inputs are presented in Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2022.08.012.

### *Clinical event rates*

Clinical event rates for CV outcomes were sourced from the EMPA-REG OUTCOME trial[12] whereas those for renal outcomes were sourced from a post hoc analysis conducted by Wanner et al.[35] Renal injury was defined as doubling of serum creatinine level accompanied by estimated glomerular filtration rate of $\leq 45$ mL/min per 1.73 $m^2$. Renal failure was defined as initiation of renal-replacement therapy.

The clinical event rates are presented in Table 1.[12,35] Rates in bold indicate a statistically significant difference between the usual care and usual care plus empagliflozin treatment arms. The same rates were assumed across all 3 years.

### *Drug costs*

The annual drug acquisition costs included those of empagliflozin, standard of care drugs, and insulin. Drug utilization per drug class was obtained from IQVIA Total Private Market Audit data for 2019, based on the relevant Anatomical Therapeutic Chemical classes for drugs used in diabetes.[36] The model excluded other SGLT2 inhibitors (eg, dapagliflozin) because these drugs were not included in the EMPA-REG OUTCOME trial.[12]

Drug unit costs consisting of the single exit price were obtained from the Database of Medicine Prices for November 2019.[37] Drug dosage (Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2022.08.012) was based on the World Health Organization defined daily dose[38] or relevant prescribing information for empagliflozin, where available. A weighted average annual cost per drug class was calculated using the unit costs, dosages, and drug utilization from IQVIA Total Private Market data.[36]

Drug costs were increased by 4.53% year-on-year, based on the single exit price adjustment for 2020.[39] The annual drug cost per class is presented in Table 2[26,37,40] for year 1. The changes in drug usage from baseline (expressed as the percentage of patients initiated on the particular drug) from usual care alone to usual care plus empagliflozin were obtained from Voorhaar et al[26] (constant annual rates) and are presented in Table 2.[26,37,40] This does not reflect the utilization at baseline, which was assumed to be the same in both arms. Fewer patients used usual care when empagliflozin was added to their glucose-lowering therapy. The number of insulin units per day was obtained from Voorhaar et al[26] (69.1 units in usual care alone compared with 60.0 units in usual care plus empagliflozin). The cost of lancets, needles, and test strips for patients using insulin was obtained from the Discovery Medical Scheme formulary using the monthly chronic drug amount (CDA).[40]

### *Clinical event costs*

For most clinical events, costs were derived from a claims data analysis of approximately 40% of the SA private healthcare sector and microcosting for the remainder. The data analysis was performed for the year 2019. Patients were classified as patients with T2DM where the data reflected claims with the International Classification of Diseases, Tenth Revision (ICD-10) code E11.x and Anatomical Therapeutic Chemical class A10 within the time horizon.

ICD-10 diagnostic and current procedural terminology (CPT)/reference price list (RPL) procedural coding was aligned with the EMPRISE study.[13]

To identify clinical events, patients were classified as having a nonfatal event if the data set showed that they had submitted at least one claim (related or unrelated to the specified ICD-10 codes) within 1 month after the relevant hospital admission. Codes used to identify clinical events are presented in Appendix Table 3 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2022.08.012. The cost of CV death was obtained from the claims data analysis. It is based on a weighted average of fatal HF, fatal myocardial infarction, and fatal stroke events, identified using the diagnostic and procedural codes as shown in Appendix Table 3 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2022.08.012. Fatal events were those where there were no claims 30 days or more after discharge.

**Table 3.** Cost of clinical events.

| Clinical event | Cost in 2019 (USD) | References |
|---|---|---|
| Nonfatal myocardial infarction | 7 132 | Claims data analysis |
| Nonfatal stroke | 5 547 | Claims data analysis |
| Unstable angina hospitalization | 3 852 | Claims data analysis |
| Heart failure hospitalization | 4 446 | Claims data analysis |
| Transient ischemic attack | 2 564 | Claims data analysis |
| Revascularization | 6 636 | Claims data analysis |
| CV death | 5 709 | Claims data analysis |
| Development of macroalbuminuria | 808 | Microcosting based on SEMDSA Guidelines 2017,[30] Gordois et al,[41] and Lopes et al,[42] South African Database of Medicine Prices,[37] RPL list for Medical Practitioners 2009,[43] Discovery Health Medical Scheme formulary[40] |
| Renal injury | 6 765 | Claims data analysis |
| Renal failure | 30 531 | Microcosting based on SA Renal Registry Annual Report for 2017,[44] SA Renal Society Guideline for the optimal care of patients on chronic dialysis in SA,[45] Spearman et al,[46] South African Database of Medicine Prices,[37] RPL lists for Medical Practitioners 2009,[43] and Clinical Technologists 2009[47] |

CV indicates cardiovascular; RPL, reference price list; SA, South Africa; SEMDSA, Society for Endocrinology, Metabolism and Diabetes of South Africa; USD, US dollars.

Given the challenges to accurately code the development of macroalbuminuria and renal failure, these events were microcosted.

The microcosting of the development of macroalbuminuria was based on the SEMDSA Guidelines 2017,[30] Gordois et al,[41] and Lopes et al.[42] These include treatment with statins (at the average cost per day for all simvastatins and atorvastatins according to the Discovery Health Medical Scheme formulary[40]) and angiotensin-converting enzyme inhibitors (at the average cost per day for all angiotensin-converting enzyme inhibitors according to the Discovery Health Medical Scheme formulary[40]), 1 low-density lipoprotein-cholesterol test, 3 albumin/creatinine ratio tests, 2 serum creatinine tests, 1 urine dipstick and microscopy, and 2 potassium tests. In addition, the costs of 4 outpatient visits, phosphate binders (calcium carbonate as per the Discovery Health Medical Scheme formulary CDA amount),[40] erythropoietin (in 7% of patients), oral iron/folic acid combination (in 10.5% of patients), and intravenous iron (in 4.5% of patients) were included. The percentage of patients requiring each anemia treatment was calculated based on Lopes et al.[42] This is a conservative estimate, and based on expert input, most patients initiating erythropoietin would also use intravenous iron in the SA private sector. Unit costs were obtained from the South African Medicine Price Registry,[37] the RPL list for Medical Practitioners 2009,[43] and the Discovery Health Medical Scheme formulary CDA amount.[40]

The microcosting of renal failure was based on the weighted average cost of dialysis (excluding arteriovenous fistula surgery) and maintenance drug costs for renal transplant. Weighting was performed based on the number of patients undergoing hemodialysis and peritoneal dialysis compared with those undergoing a transplant, as per the SA Renal Registry Annual Report for 2017.[44] Microcosting for dialysis was performed according to the SA Renal Society Guideline for the optimal care of patients on chronic dialysis in SA.[45] This included the laboratory tests required for patient monitoring, as well as the dialysis sessions and physician time. The microcosting for maintenance therapy after renal transplant was performed based on the results of a study conducted by Spearman et al[46] and consisted of the average drug costs for the following 2 regimens: ciclosporin (10 mg/kg/day) plus azathioprine (2 mg/kg/day) plus prednisone (5 mg/day) and tacrolimus (0.1 mg/kg/day) plus mycophenolate mofetil (2 g/day) plus prednisone (5 mg/day). Patients were assumed to have an average body weight of 80 kg. Unit costs were obtained from the South African Medicine Price Registry[37] and the RPL lists for Medical Practitioners 2009[43] and Clinical Technologists 2009.[47]

Clinical event costs were inflated from 2019 to subsequent years using medical services inflation from Statistics SA, for 2019 to 2020 (4.9%).[48] The same inflation was assumed from 2020 to 2021. The inflation reflects the pre-COVID-19 period (year-on-year inflation from January 2019 to January 2020). Other costs used in the microcosting were similarly inflated from the relevant years to the baseline of 2019. The cost of clinical events is presented in Table 3.[30,37,40-47] Costs were converted from South African Rand to US dollars using the average exchange rate for 2019.[49]

## Model Outputs

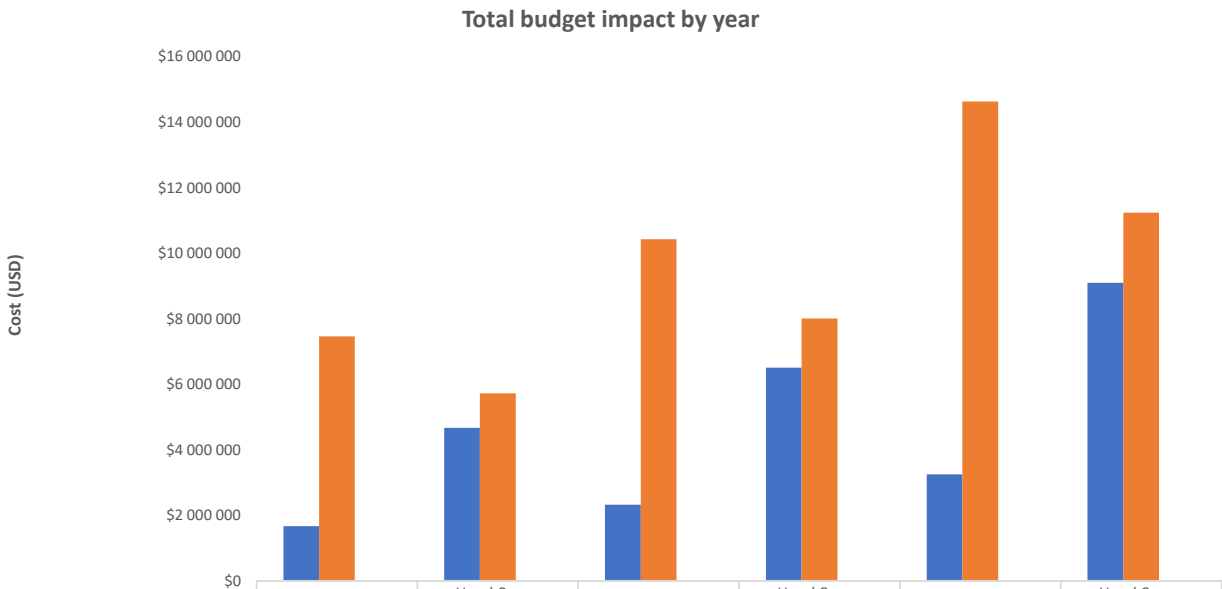
The primary model output was the budget impact of empagliflozin. The incremental budget impact was estimated as the difference in total costs between the scenarios with and without empagliflozin for the population of patients with T2DM with established CVD, year-on-year. The total costs in both scenarios were estimated as the sum of total drug acquisition and clinical event management costs incurred, for each year.

In addition to total budget impact, the incremental cost per beneficiary per month (ICPBPM) was estimated.

The secondary model outputs (clinical benefits) were the total number of CV deaths averted because of the introduction of empagliflozin, which were estimated as the difference in the total number of CV deaths between the scenarios with and without empagliflozin, for the total study population on an annual basis.

Based on the total number of CV deaths averted (lives saved), an additional model output was considered: incremental cost per life saved.

**Figure 2.** Total budget impact based on the year.




| | Year 1 | | Year 2 | | Year 3 | |
|---|---|---|---|---|---|---|
| | Usual Care | Usual Care + Empagliflozin | Usual Care | Usual Care + Empagliflozin | Usual Care | Usual Care + Empagliflozin |
| Drug acquisition costs | $1 667 788 | $4 670 731 | $2 324 451 | $6 509 754 | $3 249 789 | $9 101 213 |
| Clinical event management costs | $7 459 390 | $5 728 744 | $10 433 201 | $8 012 603 | $14 638 172 | $11 241 982 |
| Total budget | $9 127 178 | $10 399 475 | $12 757 652 | $14 522 357 | $17 887 961 | $20 343 196 |

USD indicates US dollars.

## Results

### Base Case Scenario

The results focused on total cost per year for both scenarios, stratified by clinical event management and drug acquisition costs (the additional costs attributed to changes in drug usage from baseline). These costs and the budget impact over 3 years are shown in Figure 2.

The 3-year cumulative net budget impact was $5 492 237 in the usual care plus empagliflozin arm compared with the usual care alone arm, corresponding to a net increase of 13.8% in total costs over 3 years (ie, an incremental $1 272 297, $1 764 705, and $2 455 235 for years 1, 2, and 3, respectively). This was calculated as the difference in total direct medical costs over 3 years between the usual care plus empagliflozin arm and the usual care alone arm, divided by the total direct medical costs over 3 years in the usual care alone arm. Drug acquisition costs increased by 180% compared with usual care alone. This increase was partially offset by a 23% reduction in clinical event management costs, because of a reduction in event rates (based on the incidence of events) as per the EMPA-REG OUTCOME trial.[12]

The budget impact associated with the introduction of empagliflozin as add-on therapy to usual care is presented in Appendix Table 4 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2022.08.012. The budget impact analysis results indicate that the ICPBPM increased over the 3-year period. The ICPBPM for year 1 to year 3 is shown in Figure 3.

The model predicted a 38.6% reduction in CV deaths (305 lives saved) over 3 years in the usual care plus empagliflozin arm compared with the usual care alone arm. This resulted in an incremental cost per life saved of $17 999.

### Sensitivity Analysis

One-way sensitivity analysis was performed by subjecting various model inputs to relative changes in value. Appendix Figure 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2022.08.012 illustrates the impact of increasing and decreasing the values. Base case values were changed by 25%, except for the upper bound proportion of patients with T2DM with increased CV risk, which was increased to 100%.

### Scenario Analysis

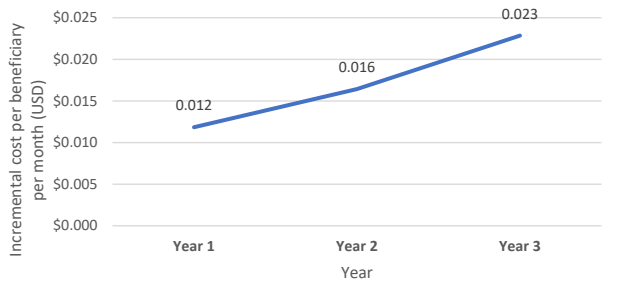
#### Empagliflozin-metformin combination

A scenario was investigated that considered a combination medication containing 2 active ingredients: empagliflozin and metformin (an empagliflozin-metformin combination). This combination is available in the SA market at the same price as empagliflozin. In this scenario, metformin utilization was set to 0% in the empagliflozin-treated arm (treated with the single or combination product). Notably, 79.7% of patients with established CVD would receive the combination product plus usual care, excluding metformin (assuming a 20.3% rate of early non-persistence to metformin),[50] and the remainder would use empagliflozin plus usual care (excluding metformin). In this scenario, the net budget impact decreased slightly to $5 422 023, with an incremental cost per life saved (death averted) of $17 769.

#### Statistically significant clinical event costs

When considering only clinical events with a statistically significant difference between usual care and usual care plus empagliflozin (HF, CV death, development of macroalbuminuria, renal injury, and renal failure), the budget impact increased to

**Figure 3.** Incremental cost per beneficiary per month.




USD indicates US dollars.

$6 912 243, with an incremental cost per life saved (death averted) of $22 653.

## Discussion

CVD has a substantial impact on direct medical costs of T2DM; this is mainly because of an increase in clinical event rates and hospital admission costs and additional chronic medication. According to studies evaluating the population-level impact of treating CVD and T2DM, the cost of treating CVD comprised 20% to 49% of the total costs of T2DM treatment.[34]

The EMPA-REG OUTCOME trial[12] demonstrated that empagliflozin reduces major CV events in patients with T2DM with established CVD, when administered as an add-on to usual care. Given the disease burden of T2DM in SA and the clinical benefit of empagliflozin on a patient level, it is important for private healthcare payers to understand the financial implications of adopting the usual care plus empagliflozin scenario before making decisions on how to allocate health resources.[51]

In this study, a budget impact model was used to analyze the potential impact on costs and clinical outcomes of adding empagliflozin to usual care compared with usual care alone, in a diabetic population with established CVD, to guide private healthcare payers in their reimbursement decisions.

The results delineate the following key findings based on the adoption of an empagliflozin plus usual care scenario:

- The 3-year cumulative net budget impact was $5.5 million.
- Drug acquisition costs increased by 180%.
- Clinical event management costs decreased by 23%.
- ICPBPM was $0.012 (year 1), $0.016 (year 2), and $0.023 (year 3).
- The number of lives saved was 305.
- Incremental cost per life saved was estimated at $17 999.

Sensitivity analysis showed that the model is most sensitive to changes in the drug acquisition costs of empagliflozin, the proportion of patients with T2DM with increased CV risk, the prevalence of T2DM, the cost of CV death, and the mean insulin dose in the usual care arm.

Scenario analysis showed that the budget impact would be lower in the case of an empagliflozin-metformin combination. In the base case, statistically significant and statistically nonsignificant events were included. In the scenario analysis, the budget impact would increase if only statistically significant clinical event costs were included.

In this analysis, adding empagliflozin to usual care substantially improved clinical outcomes: 38.6% reduction in CV deaths resulting in 305 lives saved.

The ICPBPM is considered low and affordable from a private healthcare payer perspective. The cost per life saved should be viewed as an input into a discussion about resource allocation. Although a budget impact model does not have a threshold for affordability, it is reasonable to compare the incremental cost per life saved of adding empagliflozin to usual care with interventions that are currently funded by private healthcare payers. In SA, an incremental cost per life saved of $17 999 is considered low compared with interventions (funded by healthcare payers) such as renal dialysis, which comes at a far higher cost per life saved of $30 531 (Table 3[30,37,40-47]). Notwithstanding the higher cost of empagliflozin compared with most of the comparators (with the exception of glucagon-like peptide-1 agonists and insulin), a proportion of this increased medicine cost is offset by a reduction in other healthcare costs. The affordability of empagliflozin is driven by the substantial clinical benefits that patients would derive and the implicit clinical event management costs these benefits offset, particularly when contextualized within the current "willingness to fund" environment in the SA private healthcare sector.

Studies in other countries such as Italy, the United Kingdom, South Korea, and The Netherlands[23-26] have found budget savings driven by the reduction in CV events. Internationally, substantially higher clinical event costs were reported for most events. Furthermore, because of the balance of costs varying worldwide, some countries have a balance shifted more heavily toward hospital costs (favorable to savings) whereas others, like SA, are more skewed toward relative drug acquisition costs. The latter is likely influenced by under-reporting and the exclusion of complicated cases in the data sets used.

Clinical event costs reported in literature vary substantially and are dependent on the definition of the events (in-hospital costs only vs total annual cost), as well as the methods used to calculate the costs, and the setting. The cost for revascularization from the claims data was lower than reported in the local literature. This could in part be because of patients with nonfatal myocardial infarction being excluded from revascularization claims in the claims data analysis. Nevertheless, costs for HF, transient ischemic attack, and nonfatal myocardial infarction were higher in the claims data than in the local literature.[52-54]

The evidence from this study could assist private healthcare payers in making informed reimbursement decisions where adding empagliflozin to usual care has a marginal budget implication and is highly affordable, with an acceptable incremental cost based on clinical outcomes. The strengths of the study include using a budget impact model, which has been used extensively in a global setting; the results from these analyses have been published; and using medical schemes claims data that are representative of the SA private healthcare sector (medical aid schemes) to estimate the cost of CV events.

This analysis has limitations, which should be considered when interpreting the results. The inflation rate from January 2019 to January 2020 was used to inflate costs from 2019 to 2020, as well as from 2020 to 2021. This might be an underestimation given the effect of the COVID-19 pandemic on the SA economy. In addition, only direct medical costs were considered. Direct nonmedical costs and indirect costs were not included because of the healthcare payer perspective that was used for this model, for which these costs are not relevant. For renal failure and macroalbuminuria, 1-year costs were considered, whereas for the other events, only hospitalization event costs were included.

## Conclusions

The substantial clinical benefits of empagliflozin (cardioprotection resulting in lives saved), as add-on to usual care for patients with T2DM with established CVD, come at a reasonable and highly affordable cost with a marginal budget impact for private healthcare payers in SA and should be considered a worthy addition to usual care in these patients. It is recommended that a cost-effectiveness analysis is performed to further strengthen the body of economic evidence regarding empagliflozin in the SA private healthcare sector.

## Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.vhri.2022.08.012.

## Article and Author Information

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*Critical revision of the paper for important intellectual content:* Snyman, Ker, Stander

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