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ORIGINAL RESEARCH

Translating the efficacy of dapagliflozin in chronic kidney disease to lower healthcare resource utilization and costs: a medical care cost offset analysis

Phil McEwan[a], Marco Hafner[a], Vivekenand Jha[b], Ricardo Correa-Rotter[c], Gil Chernin[d], Luca De Nicola[e], Russell Villanueva[f], David C. Wheeler[g], Salvatore Barone[h], Stephen Nolan[i] and Juan Jose Garcia Sanchez[j]

[a]Health Economics and Outcomes Research Ltd, Cardiff, UK; [b]George Institute for Global Health India, New Delhi, India; [c]Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Ciudad de Mexico, Mexico; [d]Kaplan Medical Centre, Rehovet, Israel; [e]University L. Vanvitelli-Dept. Advanced Medical and Surgical Sciences, Naples, Italy; [f]Department of Adult Nephrology, National Kidney and Transplant Institute, Quezon City, Philippines; [g]Department of Renal Medicine, University College London, London, UK; [h]Global Medical Affairs, AstraZeneca, Gaithersburg, Maryland, United States; [i]Global Medical Affairs, AstraZeneca, Cambridge, UK; [j]Health Economic and Payer Evidence, AstraZeneca, Cambridge, UK

ABSTRACT

Aims: Dapagliflozin was approved for use in patients with chronic kidney disease (CKD) based on results of the DAPA-CKD trial, demonstrating attenuation of CKD progression and reduced risk of cardio-renal outcomes and all-cause mortality (ACM) versus placebo, in addition to standard therapy. The study objective was to assess the potential medical care cost offsets associated with reduced rates of cardio-renal outcomes across 31 countries and regions.

Materials and methods: A comparative cost-determination framework estimated outcome-related costs of dapagliflozin plus standard therapy versus standard therapy alone over a 3-year horizon based on the DAPA-CKD trial. Incidence rates of end-stage kidney disease (ESKD), hospitalizations for heart failure (HHF), acute kidney injury (AKI), and ACM were estimated for a treated population of 100,000 patients. Associated medical care costs for non-fatal events were calculated using sources from a review of publicly available data specific to each considered setting.

Results: Patients treated with dapagliflozin plus standard therapy experienced fewer incidents of ESKD (7,221 vs 10,767; number needed to treat, NNT: 28), HHF (2,370 vs 4,684; NNT: 43), AKI (4,110 vs. 5,819; NNT: 58), and ACM (6,383 vs 8,874; NNT: 40) per 100,000 treated patients versus those treated with standard therapy alone. Across 31 countries/regions, reductions in clinical events were associated with a 33% reduction in total costs, or a cumulative mean medical care cost offset of $264 million per 100,000 patients over 3 years.

Limitations and conclusions: This analysis is limited by the quality of country/region-specific data available for medical care event costs. Based on the DAPA-CKD trial, we show that treatment with dapagliflozin may prevent cardio-renal event incidence at the population level, which could have positive effects upon healthcare service delivery worldwide. The analysis was restricted to outcome-associated costs and did not consider the cost of drug treatments and disease management.

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acute kidney injury; chronic kidney disease; dapagliflozin; heart failure; kidney failure; sodium-glucose co-transporter 2 inhibitors

CONTACT Phil McEwan phil.mcewan@heor.co.uk Health Economics and Outcomes Research Ltd, Unit A, Copse Walk, Cardiff Gate Business Park, Pontprennau, Cardiff, CF23 8RB, UK

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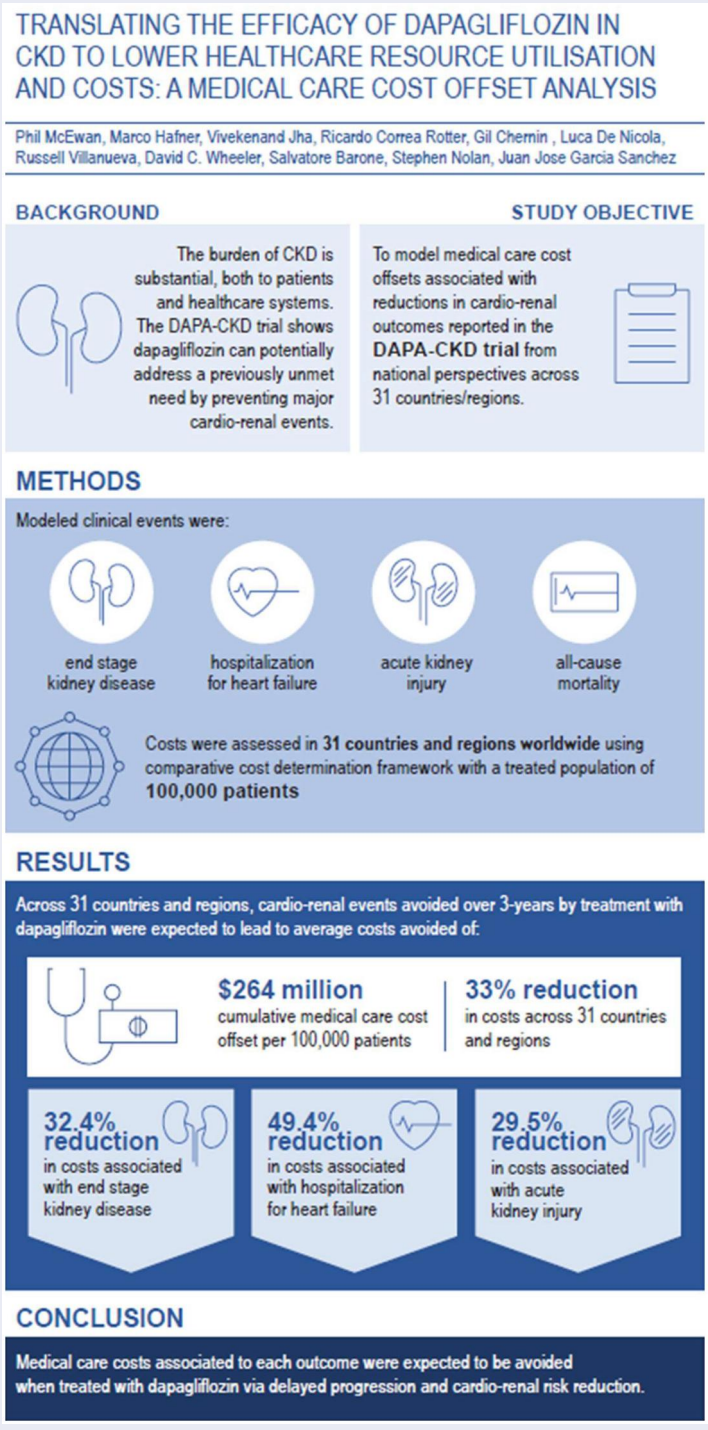
GRAPHICAL ABSTRACT



PLAIN LANGUAGE SUMMARY

Chronic kidney disease (CKD) has a high clinical, economic, and societal burden and it affects approximately 8-16% of the global population. The progressive nature of CKD may lead to complications, comorbidities, and mortality, costing healthcare systems millions and consuming a large proportion of healthcare resources. Dapagliflozin, a sodium-glucose co-transporter-2 inhibitor, has been demonstrated to slow CKD progression and reduce cardio-renal complications, as demonstrated in the DAPA-CKD trial. With the emergence of dapagliflozin as a treatment for CKD, it is important for clinicians and healthcare providers to understand how effective treatment can positively affect short-term healthcare service delivery and associated costs. This medical care cost offset modelling analysis considers a scalable population of 100,000 patients in 31 countries/regions worldwide. The analysis estimates treatment with dapagliflozin plus standard therapy to be offset by a 33% reduction in costs associated with key cardio-renal outcomes, translating to an average $264 million in cost offsets per

100,000 treated patients. This modelling analysis of pivotal trial data shows dapagliflozin could have considerable benefits to healthcare systems worldwide that are under strain from the rising burden of CKD.

Introduction

Chronic kidney disease (CKD) is a progressive condition that affects about 8–16% of the population,[1] with an estimated 700–840 million people affected worldwide.[2,3] Patients with CKD experience cardiovascular complications and hospitalizations at 2–4 times higher rates than the general population;[4] the risk worsens upon progression.[5]

CKD promotes inflammation of blood vessels, which can initiate and accelerate the development of heart failure (HF), stroke, peripheral vascular disease, and associated kidney complications including acute kidney injury (AKI).[6] AKI has a sudden onset, and affects approximately 13 million people worldwide every year.[2] The severe damage caused to the kidneys following AKI can lead to new incidence of CKD or exacerbate progression in existing CKD, which, in combination with other cardio-renal complications, can ultimately contribute towards all-cause mortality (ACM).

CKD imposes a remarkably high economic burden on society, healthcare systems and providers, absorbing a significant proportion of national healthcare system resources.[7–9] A review of patient-level costs across 31 higher and middle income countries/regions demonstrated that progression from CKD stage 3a to stage 5 (prior to initiating kidney replacement therapy) was associated with increased healthcare costs by an average factor of four.[8] Even in patients without end-stage kidney disease (ESKD), inpatient costs are considerable; a real-world multinational cohort study of medical costs in ten Western healthcare systems estimated substantially higher hospital costs for renal and HF events than for atherosclerotic events.[10]

Sodium-glucose co-transporter 2 (SGLT2) inhibitors are an established therapy option for patients with type 2 diabetes (T2D). Recently, dapagliflozin was approved for the treatment of CKD in patients with and without T2D based on evidence from the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial.[11] The trial was terminated prematurely after a mean follow up of 2.4 years due to overwhelming efficacy with a 39% reduction in the risk of the primary composite endpoint (≥50% sustained decline in estimated glomerular filtration rate [eGFR], ESKD, and renal or cardiovascular death) and a 31% reduction in the risk of ACM.[11] A primary event occurred in 9.2% (197 of 2,152) of dapagliflozin-treated participants versus 14.5% (312 of 2,152) of those in the placebo group, and was consistent across prespecified subgroups including geographic region, eGFR, UACR, age, and systolic blood pressure.[11] A recent analysis of the generalizability of DAPA-CKD to the US population estimated more than 51,000 kidney or cardiovascular events could be prevented on the basis of the trial outcomes.[12]

The clinical efficacy demonstrated in the DAPA-CKD trial led to the approval of dapagliflozin in many countries and regions worldwide. Understanding how these effects can be scaled and translated to avoid costs for local and national healthcare systems globally would be of value to both clinicians and healthcare providers. Therefore, our objective of this original study was to develop a short-term economic model based on DAPA-CKD trial results to quantify potential healthcare costs avoided across high- and middle-income economies worldwide by treating eligible patients with CKD with dapagliflozin.

Methods

Analysis population

The analysis considered national populations that were reflective of the DAPA-CKD trial inclusion criteria: adult patients with CKD, with or without T2D, who had an eGFR 25-75 ml/min per 1.73 m^2 and urine albumin to creatinine ratio 200–5000 mg/g at baseline. The trial participants were randomized to receive 10 mg dapagliflozin or placebo treatment once daily, received in addition to a stable dose of ACE inhibitor or ARB for at least four weeks prior to trial initiation, defined as standard therapy. The DAPA-CKD study design, patients characteristics and outcomes have been published previously.[11,13,14]

Modelled endpoints

Four clinical endpoints for which dapagliflozin demonstrated statistically significant effects upon in the DAPA-CKD trial,[11,15] were considered:

1. The onset of ESKD, defined as maintenance dialysis for $\geq$ 28 days, kidney transplantation, or an estimated GFR of $<$ 15 ml/min/1.73 m^2 confirmed by a second measurement after $\geq$ 28 days.
2. Development of AKI, aligned to the adjudicated endpoint of abrupt decline in kidney function, defined as a doubling of serum creatinine between two visits.
3. Hospitalization for HF (HHF), with recurrent hospitalizations accounted for as separate events.
4. All-cause mortality (ACM).

These outcomes were selected from the DAPA-CKD trial endpoints given their importance to clinicians, patients, cost per event, and impact on healthcare services.[16]

Model structure

The cohort-level model translated trial outcomes based on patient-level data from the DAPA-CKD trial to a 3-year modeled period. Health state occupancy of the modeled cohort of 100,000 patients was estimated *via* an exponential survival distribution. Competing risks were not considered and mortality risks were assumed to apply equally to all patients.

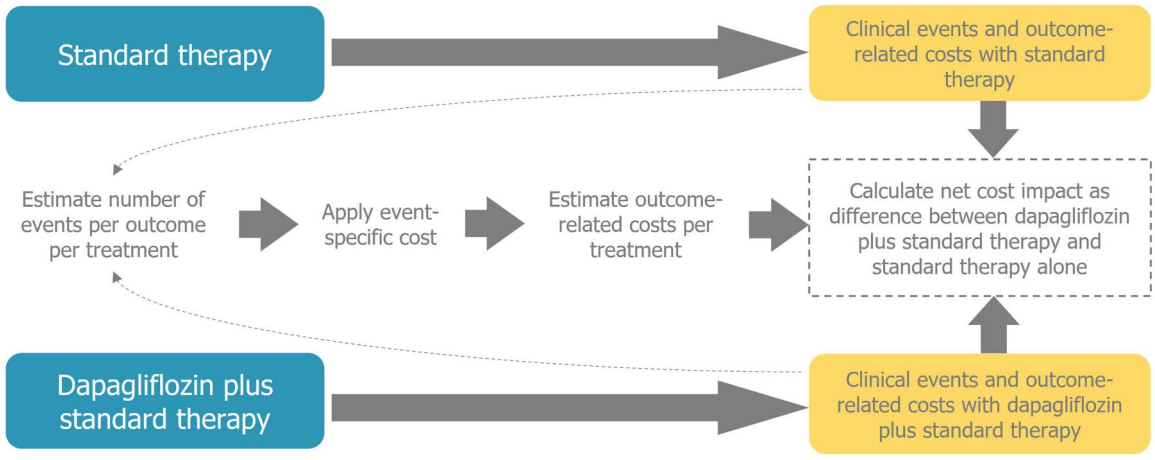


Figure 1. Model schematic.

Table 1. Medical care costs parameters associated with each clinical outcome per country/region across 31 countries/regions over three years, 2022 USD.

Country/region	ESKD	HHF	AKI
Belgium	54,105	18,538	37,587
Australia	39,520	13,324	8,040
Brazil	9,699	2,933	970
Canada	42,955	10,448	10,038
China	15,897	8,152	6,261
Colombia	13,398	5,034	7,810
Denmark	32,977	5,387	5,044
France	69,810	11,543	24,434
Germany	56,637	5,430	2,767
Greece	37,526	8,633	2,139
Hungary	15,523	158	2,414
India	5,456	3,779	2,028
Israel	50,167	5,430	5,000
Italy	31,038	20,145	5,813
Japan	27,511	9,062	219
Mexico	14,334	10,036	1,116
Netherlands	64,977	8,916	7,393
Philippines	14,926	4,552	999
Poland	18,352	8,633	2,595
Romania	27,944	2,974	5,706
Saudi Arabia	26,480	11,710	6,289
Singapore	24,874	8,955	3,461
South Korea	29,162	384	3,461
Spain	43,593	12,341	7,322
Sweden	57,232	9,338	4,568
Taiwan	16,653	727	308
Thailand	15,488	3,779	1,506
Turkey	14,126	2,274	1,530
United Arab Emirates	9,019	20,145	6,289
United Kingdom	18,828	4,674	3,689
United States	58,279	24,930	8,684
Overall			
Mean	30,854	8,463	5,983
SD	18,047	6,007	7,275

All costs were inflated to 2022 prices using national consumer price indices and converted to USD based on exchange rates accounting for purchasing power parity.[8,38] ESKD calculated is based on CKD stage 5, one year of kidney transplantation, and hemodialysis costs (see Figure S1). HHF is based on costs taken for heart failure. AKI is defined as an abrupt decline in kidney function. US population is based on the commercial and Medicare population. Abbreviations. ESKD, end-stage kidney disease; HHF, hospitalization due to heart failure; AKI, acute kidney injury; CPI, Consumer Price Index; SD, standard deviation.

The model used a comparative cost determination framework to estimate the outcome-related costs of clinical outcomes from the DAPA-CKD trial (Figure 1). The model assigned country-specific costs associated with the outcomes recorded in the DAPA-CKD trial only (Table 1). As with similar published economic analyses of cardio-renal outcome trials,[17,18] this study only considered costs relating to the trial outcomes and not the wider treatment and disease management costs. The medical care cost offset analysis considered 31 higher and middle-income countries/regions across several geographical locations and healthcare contexts to provide a global overview of the potential clinical benefits and cost offset associated with the outcomes of the DAPA-CKD trial.

Cost inputs

Event-specific costs were applied to each outcome, and country/region-specific cost inputs were sourced from a published cost library derived from the Inside CKD global research program (Table 1).[8,19] Briefly, these estimations were sourced from peer-reviewed publications or reports generated from local databases by individual targeted literature reviews and local expert opinion.

The analysis considered the perspective of the healthcare system only, and therefore indirect costs were not considered in this analysis. Costs for ESKD were calculated as a weighted aggregate of annual disease management costs for patients with CKD stage 5, receiving hemodialysis, or in receipt of a kidney transplant, based on incidence in the DAPA-CKD trial, as detailed in Figure S1 of the supplementary materials.[11] Costs pertaining to HHF and AKI reflected medical event management costs, typically relating to inpatient care. Costs associated with ACM were not included due to poor data availability across modelled settings.

Costs taken from sources published in previous years were inflated to 2022 prices *via* country-specific inflation indices and converted to US dollars (USD) as defined in the Inside CKD cost library methodology.[8] Where cost data were unavailable, proxy estimates were selected following consultation with local experts as detailed in the Inside CKD cost library methodology.[8] A discount rate of 3% was applied to cost outcomes in all settings.

Model outputs

Clinical results were represented by cumulative event incidence with associated numbers needed to treat (NNT).

Clinical and economic outcomes were estimated for a treated population of 100,000 patients in each setting, for scalability. The cumulative complication costs for all countries and regions, the mean medical care cost offset per clinical outcome, the mean medical care cost offsets, and the median cumulative cost for each clinical outcome were represented graphically.

Results

Over a 3-year period, 2,491 fewer deaths from any cause were expected per 100,000 patients treated with dapagliflozin in addition to standard therapy (dapagliflozin: 6,383, standard therapy only: 8,874; NNT: 40; Table 2) - an estimated 28.1% reduction in ACM. Treatment with dapagliflozin was also associated with lower rates of non-fatal events, leading to substantial medical care cost offsets to treatment with dapagliflozin versus those treated with standard therapy alone in the considered countries/regions.

In a population of 100,000 patients, 3,546 fewer patients were expected to progress to ESKD (dapagliflozin: 7,221, standard therapy: 10,767; NNT: 28; Table 2) over the 3-year period if treated with dapagliflozin plus standard therapy versus standard therapy alone - a 32.4% lower rate of progression. The reduced risk of progression through dapagliflozin treatment was associated with a mean medical care cost offset of $235 million (dapagliflozin: $491 million, standard therapy only: $727 million; Table 3) across the 31 considered countries/regions; Median cumulative costs were typically lower than the mean cost offset (dapagliflozin: $430 million [IQR: $231-685 million]; standard therapy: $637 million [IQR: $342-1,013 million], Figure 2 and Table 4). Management costs for ESKD were largest in France and Netherlands ($1.69 billion and $1.67 billion associated to 100,000 patients treated with standard therapy only, respectively) with dapagliflozin treatment leading to cost offsets of $546 million and $542 million in France and the Netherlands respectively (see Table S2 in the supplementary materials).

Treatment with dapagliflozin is also associated with protective cardiovascular effects in patients with CKD. Therefore, 2,314 fewer incidents of HHF were predicted to occur in 100,000 patients treated with dapagliflozin plus standard therapy versus standard therapy only (dapagliflozin: 2,370, standard therapy only: 4,684; NNT: 43; Table 2) - a reduced

Table 2. Clinical outcomes per 100,000 patients over a 3-year time horizon, stratified by treatment received in the DAPA-CKD trial.[11]

	Event incidence			
Outcome	Dapagliflozin plus standard therapy	Standard therapy	Incremental	Number needed to treat
ESKD	7,221	10,767	−3,546	28
HHF	2,370	2,684	−2,314	43
AKI	4,110	5,821	−1,709	58
All-cause mortality	6,383	8,875	−2,492	40

Abbreviations. AKI, Acute kidney injury; ESKD, End-stage kidney disease; HHF, Hospitalization for heart failure.

Table 3. Total mean cumulative clinical event costs across 31 countries/regions over three years, 2022 USD.

	Average costs per 100,000 patients		
Outcome	Dapagliflozin plus standard therapy (SD)	Standard therapy (SD)	Medical care cost offset per 100,000 patients
ESKD	491,155,352 (294,764,194)	726,530,877 (435,947,895)	235,375,525 (141,183,958)
HHF	19,480,945 (13,827,762)	38,506,289 (27,332,134)	19,025,344 (13,504,372)
AKI	23,889,901 (29,045,933)	33,829,440 (41,130,669)	9,939,538 (12,084,736)
Overall	534,526,199	798,866,606	264,340,407

All costs were inflated to 2022 prices using national consumer price indices and converted to USD based on exchange rates accounting for purchasing power parity.[8,38] ESKD calculated is based on CKD stage 5, kidney transplantation, and dialysis costs (see Figure S1 in the supplementary materials). AKI is defined as an abrupt decline in kidney function. Abbreviations. ESKD, end-stage kidney disease; HHF, hospitalization due to heart failure; AKI, acute kidney injury; CPI, Consumer Price Index; SD, standard deviation.

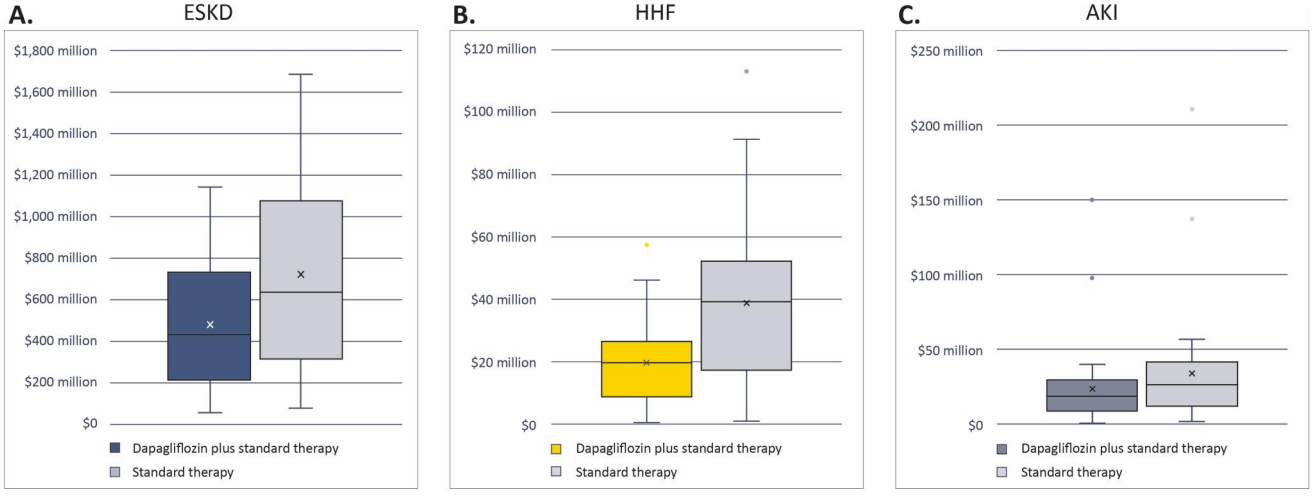


Figure 2. Median cumulative costs per clinical outcome for (A) ESKD (B) HHF and (C) AKI. Upper and lower bars indicate maximum and minimum values and the line within the boxes indicates the median. The x indicates the mean. Abbreviations. ESKD, end-stage kidney disease; HHF, hospitalizations due to heart failure; AKI, acute kidney injury.

Table 4. Median cumulative costs per clinical outcome, 2022 USD.

	Dapagliflozin plus standard therapy			Standard therapy		
Measure	ESKD	HHF	AKI	ESKD	HHF	AKI
Min	55,972,530	363,213	874,000	82,938,238	717,932	1,237,633
INQ1	231,103,664	9,587,290	8,320,097	341,983,783	18,950,361	11,781,724
Median	430,487,367	19,871,180	18,238,037	636,823,316	39,277,632	25,826,083
INQ3	685,189,486	25,309,371	27,172,500	1,013,369,729	50,026,831	38,477,783
Max	1,140,207,947	57,383,737	150,079,458	1,686,494,656	113,425,440	212,520,927

Abbreviations. ESKD, End-stage kidney disease; HHF, Hospitalizations due to heart failure; AKI, Acute kidney injury; min: Minimum value; INQ1, Lower quartile; INQ3, Upper quartile; max, Maximum value.

incidence rate of 49.4% over three years. Treatment with dapagliflozin led to a mean medical care cost offset of $19.0 million through avoided HHF (dapagliflozin: $19.5 million, standard therapy only: $38.5 million; Table 3). Median estimates across settings were similar (Figure 2 and Table 4). Patients experiencing HHF in the US incurred the highest medical care costs for HHF, $113 million per 100,000 patients treated with standard therapy only over three years, with $56.0 million potentially avoided through treatment with dapagliflozin (see Table S2 in the supplementary materials).

Patients receiving dapagliflozin in addition to standard therapy were predicted to experience 1,709 fewer incidents of AKI per 100,000 treated patients compared to standard therapy alone (dapagliflozin: 4,110, standard therapy: 5,819; NNT: 58; Table 2) – a 29.4% lower incidence rate of 3 years. The economic burden associated with AKI in the DAPA-CKD-like population was smaller than for the onset of ESKD, nevertheless the reduced risk of AKI with dapagliflozin treatment associated with an average medical care cost offset of $9.94 million per 100,000 treated patients across setting (dapagliflozin: $23.9 million, standard therapy only: $33.8 million; Table 3). Median estimates across settings were lower than mean estimates (Figure 2 and Table 4). Belgium and France were estimated to experience the greatest economic burden associated with AKI per 100,000 patients treated with standard therapy only (Belgium: $213 million, France: $138 million), and treatment with dapagliflozin expected to lead to medical care cost offsets of $62.4 and $40.6 million per 100,000 treated patients over 3-years, respectively (see Table S2 in the supplementary materials).

Across 31 countries over the 3-year period, the cumulative medical costs associated with the collective incidence of ESKD, AKI, and HHF amounted to a mean $534 million (min: $72.7 million; max: $1,264 million) in those treated with dapagliflozin versus $799 million (min: $112 million; max: $1,877 million) for standard therapy alone (Figure 3). Therefore, the mean medical care cost offsets through dapagliflozin treatment were $264 million per 100,000 patients in the presented analysis (Table 3) – a mean 33% reduction in medical care costs associated with these adverse clinical events. Costs associated with each outcome stratified by treatment received for each country/region are available in the supplementary materials (Table S2 in the supplementary materials); the setting with the greatest cost offset to treatment with dapagliflozin was France, totaling $613 million per 100,000 treated patients over three years. India had the lowest medical care cost offset to treatment with dapagliflozin, though this was still considerable, at $38.8 million over a 3-year period.

Discussion

An unmet need has existed for new therapies that reduce the rate of CKD progression and protect against cardio-renal complications in this population, owing to a lack of innovation in the management of CKD over recent decades. Using cost data derived from the global Inside CKD research program, this study was able to project the cost offsets associated with the introduction of dapagliflozin on a multinational scale from the perspectives of national healthcare systems. Substantial healthcare expenditure, particularly for the treatment of ESKD, could be avoided worldwide through the enrollment of these patients on dapagliflozin in addition to standard therapy within a relatively short period of time. Similar short-term effects have been demonstrated in recent retrospective cohort studies,[20] and modeled analyses of SGLT2 inhibitors.[21,22]

Interventions such as improved screening rates, promotion of healthy lifestyles, and classical pharmacological management, namely by renin-angiotensin-aldosterone inhibitors, should be augmented by treatment with newly emerging therapies with demonstrated benefit in relevant populations that delay or prevent kidney failure.[23] Prevention of ESKD can be cost effective, given the context of the relatively low NNT demonstrated in this analysis and the quality of life decrement and cost burden associated with kidney replacement therapy.[7] Cost offset analyses provide an alternative method to demonstrate scalable value independent of drug pricing, focusing on healthcare burden and service delivery, which are important factors for healthcare budget holders when considering methods to alleviate the disease-associated burden.

It is important to note that this analysis encapsulates perspectives of countries from a wide range of economic backgrounds, where healthcare resource allocation - notably costly kidney replacement therapies - may differ or be limited. The global scale of this study, including countries of middle income and healthcare resources, is important in demonstrating the relevant cost offsets that dapagliflozin may elicit in these countries and regions. Nevertheless, it should be noted that, with poorer medical cost data availability in lower income countries, the scope of our analysis was not extended to lower income countries. CKD disproportionally affects populations in lower income countries, comprising an estimated 80% the global CKD population.[24,25] Limited access to kidney replacement therapies upon

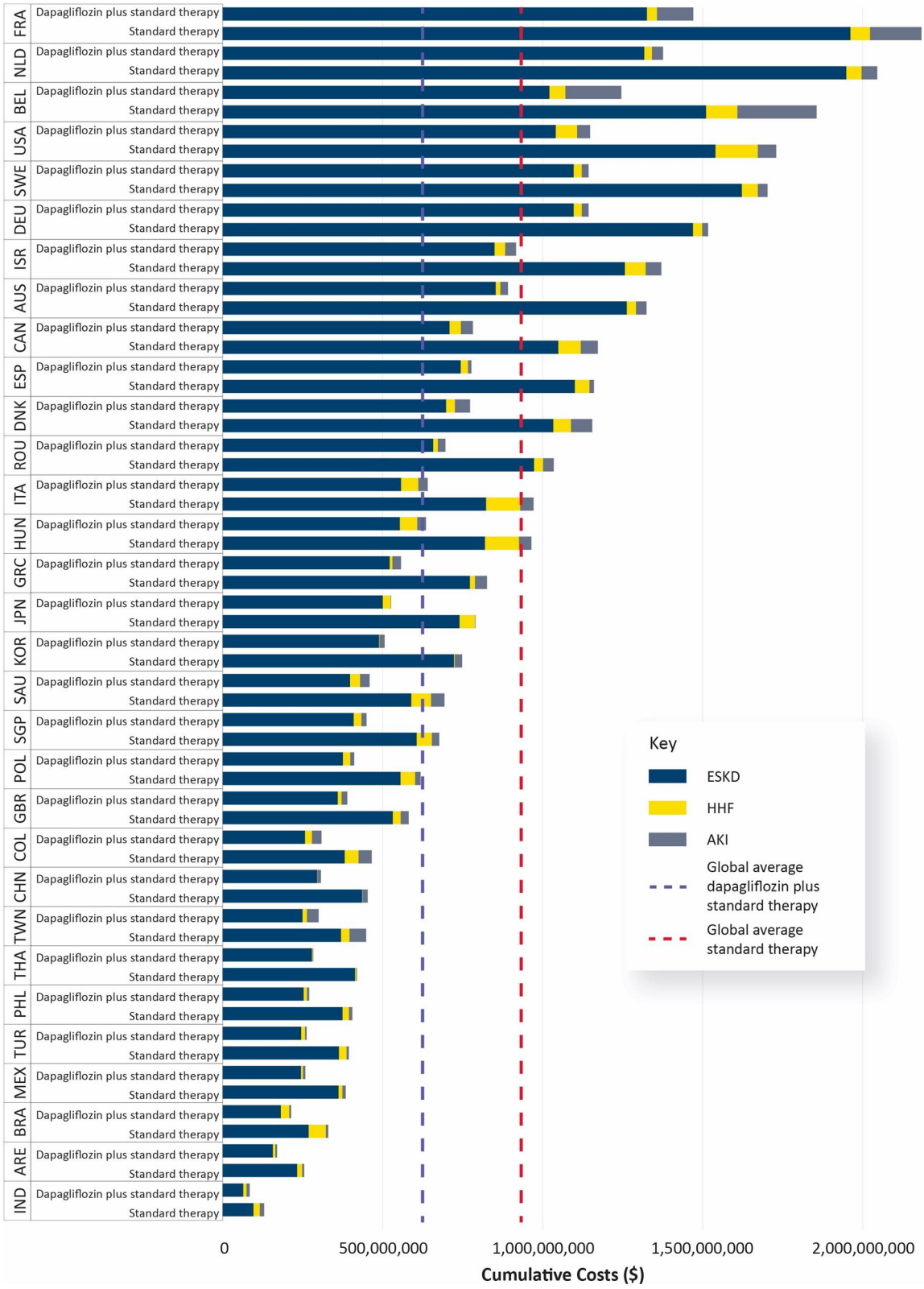


Figure 3. Cumulative clinical event costs per 100,000 patients over 3 years. Abbreviations. ESKD, End-stage kidney disease; HHF, Hospitalization due to heart failure; AKI, Acute kidney injury. A full list of countries/regions are provided in Table S1 in the supplementary materials. For a detailed list of costs associated to each treatment group, please see Table S2 in the supplementary materials.

progression to ESKD leads to millions of premature deaths globally every year.[26–28]

As with any modeling analysis, this study is subject to certain assumptions and limitations. Firstly, it is assumed that the event rates are applied to a patient population with the same characteristics as the DAPA-CKD trial population, thereby restricting the effect of treatment that may be indicated across the considered healthcare systems. Mortality

risks are assumed to apply equally to all patients. It was assumed that the socioeconomic background of the participants of the DAPA-CKD trial, a global multinational study including a diversity of countries with different health systems, was adequately representative of the considered settings. It should be noted that dapagliflozin demonstrated similar clinical benefits in patients of different races[29] and across Asia, Europe, Latin America, and North America across all trial outcomes.[30]

The cost inputs of this analyses were country/region specific where possible, reflecting the particular economic circumstances prevailing in the countries/regions. Differences between healthcare systems and reimbursement structures were accounted for by setting the patient population to 100,000 treated patients per country. Nevertheless, there may be inconsistent definitions and reporting of costs in the available data as identified by the Inside CKD published cost library that was used to inform our economic analysis.[8] In addition, while ACM was incorporated as an outcome in this analysis, given the statistically significant effect demonstrated in the DAPA-CKD trial, medical costs could not be incorporated owing to poorer data availability for ACM across the considered settings.

The cost offset analysis presented here does not consider the total costs attributed to the considered population, including any drug acquisition or disease management costs not pertaining to the clinical outcomes considered, in line with other similar published analysis.[17,18] Nevertheless, dapagliflozin has already been shown as cost effective for the treatment of CKD in several settings,[31–36] and our analysis does not account for protective effect of dapagliflozin in those who do not progress to ESKD in the modelled period. Costs pertaining to treatment-related adverse events were also not included in the analyses. However, the overall safety profile of dapagliflozin is well known,[37] and the drug was well tolerated in patients in the DAPA-CKD trial, with no statistically significant increases in treatment-related adverse events observed.[11] Therefore, we would not expect any substantive impact on the results by the inclusion of treatment-related adverse events. Lastly, a significant limitation to the interpretation of the data is the use of average cumulative costs across 31 countries and regions, as there is considerable variance between the 31 healthcare settings, hence, we presented median and interquartile range values to characterize this variance.

Conclusion

The DAPA-CKD trial demonstrated that dapagliflozin is associated with beneficial effects on CKD progression, cardio-renal events and ACM in patients with CKD. This modelling study translated those outcomes to a scalable population level and provided the associated effects on healthcare spending through diminished rates of adverse cardio-renal events across 31 high- and middle-income countries/regions worldwide. Overall, we estimate dapagliflozin to lower outcome-associated spending by 33%, therefore demonstrating treatment of CKD patients on dapagliflozin may potentially lead to substantial short-term positive benefits from the healthcare payer perspective.

Transparency

Declaration of funding

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Declaration of financial/other interests

P.M. and M.H. are employees of Health Economics and Outcomes Research Ltd., who received fees from AstraZeneca in relation to this study. V.J is an employee of the George Institute for Global Health and has received grant funding from GSK, Baxter Healthcare and Biocon and honoraria from Bayer, AstraZeneca, Boehringer Ingelheim, NephroPlus and Zydus Cadilla, under the policy of all honoraria being paid to the organization. R.C.R has received honoraria as a consultant for AstraZeneca, Boehringer Ingelheim, Janssen, Bayer, Chinook, Novo Nordisk and research support from AstraZeneca, Boehringer Ingelheim, GSK, and Novo Nordisk. G.C. has received grant funding from Teva Pharmaceutical Industries Ltd. And honoraria from Astellas, Bayer, AstraZeneca, Boehringer Ingelheim, Novo Nordisk and Sanofi. L.D.N has received honoraria for lectures and scientific consultation from Astellas, AstraZeneca, Bayer, and Novo Nordisk. R.V. is a member of the AstraZeneca speakers bureau. D.C.W has an ongoing consultancy contract with AstraZeneca and in the last two years has received payments from Astellas, Bayer, Boehringer Ingelheim, Eledon, Galderma, Gilead, GlaxoSmithKline, Janssen, ProKidney, Tricida and Vifor for clinical trials activities and educational events. J.G.S, S.B. and S.N. are employees and shareholders of AstraZeneca.

Author contributions

All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of this article, take responsibility for the integrity of the work, and have approved the article for publication.

P.M. and J.G.S. conceptualized and designed the study. M.H. was responsible for data analysis. All authors contributed to interpretation of the results, preparation, and review of the manuscript, and approval of the final manuscript for publication.

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Data availability statement

Data underlying the findings described in this manuscript may be obtained in accordance with AstraZeneca's data sharing policy described at: https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure.

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ORCID

Juan Jose Garcia Sanchez http://orcid.org/0000-0001-6546-7769

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