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Cost-utility analysis of add-on dapagliflozin in heart failure with reduced ejection fraction in the Philippines

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Abstract

Aim   We aim to determine the cost-effectiveness of dapagliflozin in addition to standard therapy versus standard therapy alone among patients with heart failure with reduced ejection fraction (HFrEF) using the public healthcare provider's perspective in the Philippines.

Methods and results   A thousand Filipino patients with HFrEF (with or without type 2 diabetes mellitus) were included in a simulation cohort using a lifetime Markov model. The model, which was developed based on the results of the Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure trial, was composed of three health states. These were 'alive without an event' (chronic heart failure state), 'alive but was hospitalized for heart failure' (worsening heart failure), and 'dead' (death from any cause). Data regarding costs and utilities were obtained from previous studies and local data. These were used to estimate the incremental cost per quality-adjusted life-year (ICER). A 3% annual discount rate was used for both costs and effects. One-way (deterministic) and probabilistic sensitivity analyses as well as scenario analyses were performed. The ICER for the addition of dapagliflozin to standard therapy among HFrEF patients was PHP177 868 (US$3434) and PHP160 983 (US$3108), respectively, if the present price (PHP44.00) and possible negotiated unit cost of dapagliflozin 10 mg tablet (PHP40.00) were used. These were deemed cost-effective because they were both below the threshold ICER which was equivalent to the gross domestic product per capita of the Philippines in 2019, PHP180 500 (US$3485). Using the unit costs of dapagliflozin previously mentioned, the ICERs among HFrEF patients with diabetes were PHP132 582 (US$2560) and PHP120 249 (US$2321), respectively. Doing PSA involving Monte Carlo simulation of 10 000 iterations and plotting the resulting ICERs against the threshold ICER in the cost-effectiveness acceptability curves, these ICERs for HFrEF among diabetics were determined to be 72% and 76% cost-effective.

Conclusion   Dapagliflozin added to standard therapy for HFrEF patients is likely to be cost-effective using the perspective of the Philippine public healthcare provider.

Introduction

In recent years, research on therapeutic options for type 2 diabetes mellitus (T2DM) has yielded a number of new information. One of these is on sodium-glucose cotransporter 2 inhibitor (SGLT2) class of molecules. Since 2008 and 2012, the United States Food and Drug Administration (USFDA) and the European Medicines Agency (EMA), respectively, have required cardiovascular (CV) safety trials for all antidiabetic medications. Beyond just showing proof of CV safety,

SGLT2 inhibitors have recently been shown to have cardio-vascular benefits. Currently, there are several SGLT2 inhibitors, and one of them is dapagliflozin.[1,2]

The Dapagliflozin Effect on Cardiovascular Events–Thrombolysis in Myocardial Infarction 58 (DECLARE-TIMI 58) trial evaluated dapagliflozin compared with placebo among patients with T2DM and high CV risk or established CV disease. It showed a lower rate of heart failure (HF) hospitalization and mortality.[3] A *post hoc* analysis among patients with HF with reduced ejection fraction (HFrEF) showed similar results.[4]

The Dapagliflozin Effects on Biomarkers, Symptoms and Functional Status in Patients with HF with Reduced Ejection Fraction (DEFINE-HF) trial included 263 patients with HFrEF and were randomized to dapagliflozin or placebo. It found that although NT-proBNP levels were not significantly reduced by dapagliflozin as compared with placebo, there was an improvement in symptoms and reduction in worsening heart failure and hospitalization in patients with HFrEF with or without diabetes.[5]

The Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA-HF) study is the first outcome trial to assess SGLT2 inhibitor on hard endpoints among patients with HFrEF with and without T2DM. It showed a significant reduction in worsening HF or cardiovascular death. There was also a significant reduction in the levels of NT-proBNP.[6] Its sub-analysis showed similar effects independent of diabetes status, background therapy, and age group.[7–9] It also improved the patients' quality of life.[10]

The Heart Failure Association of the European Society of Cardiology and the American College of Cardiology Expert Consensus Decision Pathway for Optimization of HF Treatment recommended dapagliflozin for HFrEF treatment in patients with and without diabetes.[11,12]

Assessment of treatment efficiency through an economic evaluation is important apart from evaluation of efficacy or effectiveness. Such studies, which showed that dapagliflozin as add-on therapy for HF is cost-effective, have been carried out in Australia, United Kingdom, Germany, Spain, and Thailand.[13–15] However, unlike randomized controlled trials, the results of which can be applied in other settings, and economic evaluation study results cannot be readily generalized to another country. Variability in the results of cost-effectiveness studies for drugs in Western Europe had been documented.[16] In addition, sacubitril-valsartan, an HF medication proven to be cost-effective in the United States and Europe, was determined to be not cost-effective in Thailand.[15] In this regard, this study was undertaken. The primary objective is to determine the cost-effectiveness of dapagliflozin in addition to standard therapy versus standard therapy alone among patients with HFrEF using the public healthcare provider's perspective in the Philippines. The secondary objectives are to determine the (i) cost-effectiveness of dapagliflozin in addition to standard therapy versus standard therapy alone among patients with HFrEF and diabetes; and (ii) cost-effectiveness of dapagliflozin in addition to standard therapy versus standard therapy alone among patients with HFrEF without diabetes.

Methods

Model composition and transition probabilities

The Markov model in this cost-utility analysis (CUA) used DAPA-HF[6] as the basis of dapagliflozin's efficacy. Recent economic evaluation studies using the perspective of the public healthcare payer from several countries also utilized DAPA-HF as the basis of their models.[13–15]

The following states in the model were identified: (i) chronic HFrEF patient, 'alive' without an event ('event-free'), (ii) chronic HFrEF patient, 'alive' but hospitalized due to HF (worsening HF), and (iii) 'dead' (death from any cause). Patients with worsening HF are at risk for recurrent HF hospitalization or death. The baseline state of all patients was 'alive' with chronic HFrEF and the patients go through the model in yearly cycles until death or lifetime horizon. *Figure 1* illustrates the Markov model with the three health states as mentioned and labelled as (i) event-free, (ii) post-hospitalization (due to HF), and (iii) dead.

The transition probabilities for the three Markov states were derived from the DAPA-HF outcomes. The annual probabilities were estimated for the overall population of the study and separately for those with and without diabetes. The transition probability for death incorporated the latest Philippine age-related mortality rate obtained from the global health data repository of the World Health Organization (WHO).[17]

Population

The population in the model simulated the patients included in the DAPA-HF study. These included HF patients with New York Heart Association class II, III, and IV whose ejection fraction was ≤40%. These patients either received standard treatment alone or dapagliflozin added to standard treatment for HF. Details of the patient characteristics in the DAPA-HF trial are published together with the study results.[6]

For this study, a cohort of 1000 Filipino patients with chronic HF with or without T2DM was included.

In the DAPA-HF trial, the patient's mean age was 66 years, and this was used as the starting age the patients entered the model in the CEA by Savira *et al*.[13] On the other hand, an HF registry showed a lower mean age of HFrEF patients from Asia as compared with Europeans.[18] Those from the Philippines had a mean age of 54.3 years.[18] This was similar to the mean age (55 years) of the Filipino patients who were

Figure 1 A Markov model for heart failure. This model illustrates the possible three health states for chronic heart failure patients with reduced ejection. This model is for both groups: the dapagliflozin plus standard of care and those given standard of care only.
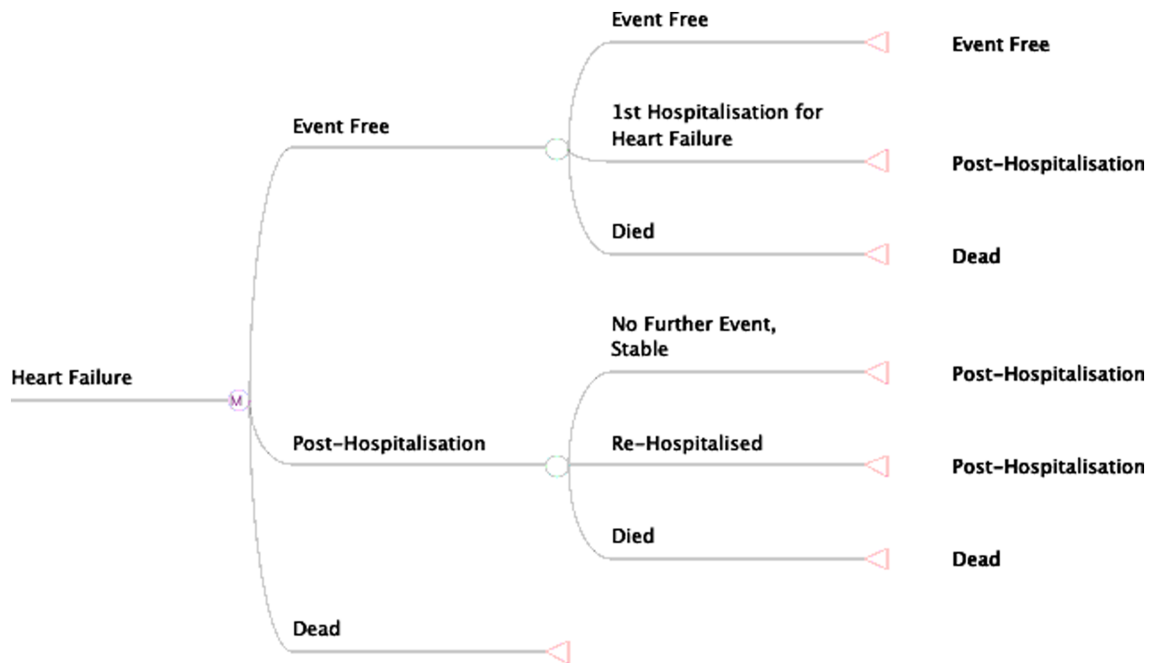
included in the pooled analysis of the two 'largest and globally representative' of HFrEF trials: PARADIGM-HF and ATMOSPHERE trials.[19] Therefore, this study's starting age for the model was set at 55 years.

The Asian HF registry used the HFrEF definition of EF ≤ 40% similar to DAPA-HF, while the pooled analysis defined HPrEF as EF ≤ 35%.[6,18,19]

Utilities

The assessment of the quality of life among DAPA-HF patients used the Kansas City Cardiomyopathy Questionnaire (KCCQ). KCCQ scores were found to correlate with the New York Heart Association (NYHA) Functional Class, whether among patients with HFrEF or HF with preserved ejection fraction (HFpEF).[20] In turn, utility estimates had been derived for each of the NYHA class.[21]

In the pooled analysis of the two randomized trials, the left ventricular ejection fraction (LVEF) of Asians was lower than patients from Europe and the USA, but their KCCQ scores were higher. The mean KCCQ clinical summary score of patients from the Philippines was 80.2 with interquartile range of 69.4–96.4.[19] These might be related to the Asians' less severe functional limitation as per their NYHA functional classification (except for China and India). Using the utility inputs for the corresponding KCCQ total scores reported in the McEwan study, the aforementioned KCCQ scores of patients from the Philippines were equivalent to utility values of

0.705 to 0.833. The pooled analysis reported that majority of patients from the Philippines were mostly in NYHA Class I–II (94.6%) and none in Class IV.[19] Using the Gohler *et al.* study, the utilities would be 0.714–0.785 (for Class I–II) and 0.624 (for Class III).[21] In consideration of these previous publications, this study's base case analysis used the utility value 0.769, which corresponds to the mean KCCQ score of Filipinos with HF. In terms of dis-utilities for baseline comorbidities, for example, HF hospitalization or the presence of diabetes, the utility values reported by McEwan *et al.*[14] were used.

Costs

The study included HF hospitalization cost in the Philippines, cost of dapagliflozin, and cost of treating the adverse events —volume depletion and renal dysfunction.

The cost for HF hospitalization in both government and private hospitals in the country for 2014 was previously published.[22] The cost was converted to 2019 values, being the study's reference year. This was carried out through the use of the consumer price indices for 2014 and 2019.[23] The coverage provided by the Philippine Health Insurance Corporation (PhilHealth) for HF hospitalization (PHP15 700)[24] was used for HF hospitalization cost in the scenario analysis where adverse events were included in the model.

Regarding medication cost, the cost of standard care was not included because the options being compared were

standard therapy alone versus standard therapy plus dapagliflozin among patients with HFrEF. The incremental cost would be equivalent to the cost of dapagliflozin. Assuming 100% compliance, this corresponded to the annual cost of giving a daily dose of 10 mg dapagliflozin. In the Philippines, the unit cost of 10 mg dapagliflozin corresponded to its unit price in the local market in 2019 which was PHP46.50 (US $0.90). In mid-2020, the retail price in two drugstore chains decreased to PHP44.00 (US$0.85). This was because of the implementation of the maximum retail price (MRP) policy of the government. MRP represents the allowed maximum price of a drug in the retail market.[25] In connection with the study's perspective—that of the healthcare provider, the drug cost would be equivalent to the acquisition cost negotiated (without the mark-up or profit of the retailers) by the government with the manufacturer. However, for dapagliflozin, none exist at present. Given this, a possible negotiated unit cost, PHP40.00, was assumed in the sensitivity analysis.

PhilHealth's coverage for volume depletion and renal dysfunction are PHP4000 and PHP19 300,[24] respectively. These costs were used for these adverse events in the specific scenario analysis mentioned earlier.

Outcomes

After considering the endpoints (reduction in HF hospitalization, mortality, and change in KCCQ scores) reported in the DAPA-HF trial, incorporation of the Philippine age-related mortality, and local costs, the outcomes are expressed in incremental cost-effectiveness ratios (ICERs). The ICER represents the incremental cost for every additional quality-adjusted life-year gained from the addition of dapagliflozin to standard therapy among HFrEF patients. To determine whether these ICERs are cost-effective in the local setting, a comparison with the threshold or ceiling ICER as determined by the local policymakers was performed. The threshold ICER had been reported to be equivalent to the gross domestic product (GDP) per capita.[26] With 2019 as the reference year, the GDP per capita of the Philippines at that time was US $3485.10.[27] This was equivalent to PHP180 514 (rounded off to PHP180 500) using the average foreign exchange rate of 1US$ to Philippine peso in 2019 (1 US$ = PHP51.7958).[28]

Discount rates

Recommendations regarding discount rates in economic evaluation studies vary. One of them is to use 3% and 5% in the base-case analysis and 0%, 3% and 5% for the sensitivity analysis, both for costs and effects.[29] The World Health Organization Guide for CEA recommends a discount rate of 3% for the base-case analysis, both for costs and effects, while for

sensitivity analysis, its advice is to use 6% for costs and 0% for effects.[30] On the other hand, the guidelines for the use of a reference case in the presentation of the results of an economic evaluation include discounting at the real rate of 3% per annum for both costs and health outcomes (effects) and 5% for comparison with existing studies.[31] In consideration of these recommendations, a discount rate of 3% for cost and effects was used in this study.

Sensitivity analyses

Several sensitivity analyses were performed. These included one-way or univariate (deterministic) sensitivity analysis where the values of some parameters were changed one at a time. Using the lower and higher values of the parameters, the variations in the ICERs were estimated, and a tornado diagram was generated. In addition, scenario analyses, whereby the effect on the ICERs of changing the cost of dapagliflozin, HF hospitalization cost and the inclusion of the cost of adverse events were performed. Analyses for the scenarios involving different populations—'all' patients (whether with or without diabetes) or only those with or without diabetes were also performed. Lastly, a probabilistic sensitivity analysis (PSA) involving Monte Carlo simulation of 10 000 iterations was undertaken.

All analyses were performed using Excel 365.

Results

Table 1 shows the annual transition probabilities and the utilities. These values were estimated from the results of DAPA-HF trial. Data regarding costs derived from other studies are also shown in this table. These data were used in the determination of the corresponding ICERs depending on the analyses undertaken.

Base case, deterministic sensitivity, and scenario analyses

Using the 2019 price of dapagliflozin as the base case, the incremental cost for an additional quality-adjusted life year was computed to be PHP188 450 (US$3638). This amount is higher than the threshold ICER of PHP180 500 (US$3485); hence, dapagliflozin is deemed not cost-effective in this scenario. However, the present unit price has gone down to PHP44.00; thus, analyses based on this unit price and a possible negotiated unit cost of dapagliflozin were performed. The resulting ICERs based on the different scenarios are shown in *Table 2A*. Dapagliflozin is cost-effective among HFrEF patients if the unit cost is at least PHP44.00; however,

Table 1 Input parameters

Parameter	Allocation	Base case	Range	Distribution	References
Probabilities All Patients: All-cause death	Dapagliflozin[a]	0.0783	0.0658–0.0912	Beta	McMurray *et al.*
	Control[b]	0.0938	0.0803–0.1077	Beta	McMurray *et al.*
Hospitalization for HF	Dapagliflozin	0.0653	0.0537–0.0772	Beta	McMurray *et al.*
	Control	0.0906	0.0773–0.1043	Beta	McMurray *et al.*
Utilities					
Chronic HF (not hospitalized)		0.7690	0.7386–0.8004	Beta	McEwan *et al.* and Dewan *et al.*
Hospitalized for HF		0.7423	0.7119–0.7737	Beta	McEwan *et al.* and Dewan *et al.*
Probabilities patients with diabetes: All-cause death	Dapagliflozin	0.0898	0.0695–0.1101	Beta	Petrie *et al.*
	Control	0.1137	0.0913–0.1361	Beta	Petrie *et al.*
Hospitalization for HF	Dapagliflozin	0.0866	0.0666–0.1066	Beta	Petrie *et al.*
	Control	0.1098	0.0876–0.1319	Beta	Petrie *et al.*
Utilities					
Chronic HF (not hospitalized)		0.7520	0.7206–0.7834	Beta	McEwan *et al.* and Dewan *et al.*
Hospitalized for HF		0.7253	0.6939–0.7567	Beta	McEwan *et al.* and Dewan *et al.*
Probabilities patients without diabetes: All-cause death	Dapagliflozin	0.0688	0.0523–0.0853	Beta	Petrie *et al.*
	Control	0.0778	0.0604–0.0951	Beta	Petrie *et al.*
Hospitalization for HF	Dapagliflozin	0.0478	0.0338–0.0619	Beta	Petrie *et al.*
	Control	0.0751	0.0581–0.0922	Beta	Petrie *et al.*
Utilities					
Chronic HF (not hospitalized)		0.7690	0.7376–0.8004	Beta	McEwan *et al.* and Dewan *et al.*
Hospitalized for HF		0.7423	0.7109–0.7737	Beta	McEwan *et al.* and Dewan *et al.*
Cost of hospitalization for HF		PHP39 577	PHP31 901–47 253		Tumanan-Mendoza *et al.*
Cost of hospitalization for HF		PHP15 700			PhilHealth
Cost of adverse events: Volume Depletion		PHP4000			PhilHealth
Renal Dysfunction		PHP19 300			PhilHealth

HF, heart failure; PhilHealth, Philippine Health Insurance Corporation; PHP, Philippine peso.
[a]Dapagliflozin plus standard treatment.
[b]Control = standard treatment alone.

Table 2 Scenario analyses

A. Population and unit cost of dapagliflozin	ICERs (deterministic analysis)
All patients[a]	At 3% discount rate
Dapa @ PHP46.50	PHP188 450 (US$3638)
Dapa @ PHP44.00	PHP177 868 (US$3434)
Dapa @ PHP40.00	PHP160 983 (US$3108)
Diabetics	
Dapa @ PHP46.50	PHP140 290 (US$2708)
Dapa @ PHP44.00	PHP132 582 (US$2560)
Dapa @ PHP40.00	PHP120 249 (US$2321)
Non-diabetics	
Dapa @ PHP46.50	PHP295 131 (US$5698)
Dapa @ PHP44.00	PHP278 286 (US$5372)
Dapa @ PHP40.00	PHP251 333 (US$4852)
B. All patients[a] included in analyses	ICERs (deterministic analysis)
Dapagliflozin 10 mg @ PHP44.00	
cHosp = PhilHealth case rate	PHP182 912 (US$3531)
cHosp = lower limit	PHP179 490 (US$3465)
cHosp = higher limit	PHP176 247 (US$3402)
Dapagliflozin 10 mg @ PHP40.00	
cHosp = PhilHealth case rate	PHP165 982 (US$3204)
cHosp = lower limit	PHP162 560 (US$3138)
cHosp = higher limit	PHP159 317 (US$3076)

Dapa, dapagliflozin 10 mg tablet; PHP, Philippine peso.
[a]All patients in the DAPA-HF trial with or without diabetes.

it is more cost-effective if its unit cost is PHP40 and if given to HFrEF patients with diabetes.

Variations in the HF hospitalization cost apart from variations in the unit cost of dapagliflozin, also resulted in varying ICERs. This is demonstrated in the other scenario analyses (*Table 2B*). In these analyses, the population was set to 'all patients' (patients with and without diabetes mellitus). The ICERs become more cost-effective if the lower unit cost of dapagliflozin is combined with the higher hospitalization cost of HF.

The last scenario analysis involved the adverse events— volume depletion and renal dysfunction—as reported in the DAPA-HF study. Although there were no statistically significant difference between the rates (both less than 8%) in the dapagliflozin and control groups in either adverse event, the ICERs were determined. The population was again set at 'all patients'. Using the case rates provided by PhilHealth, the resulting ICERs were PHP188 500 and PHP169 910 for the PHP44.00 and PHP40.00 unit cost of dapagliflozin 10 mg tablet, respectively.

The tornado diagram (*Figure 2*) demonstrates the effect of changing one parameter at a time. It shows that the parameter–probabilities of dying (in both control and dapagliflozin arms) had the biggest effect on the ICERs. Changes in these probabilities resulted in a large variation in the ICERs. The diagram also shows the effect of variations in the cost of dapagliflozin on the ICERs. This effect is greater as compared with variations in utilities and probabilities in hospitalization.

Probabilistic sensitivity analysis (PSA)

Adding dapagliflozin to the standard regimen was 58% and 64% cost-effective for 'all' HFrEF patients if the unit cost was PHP44.00 and PHP40.00, respectively. Among diabetics with HFrEF, it was 72% and 76% cost-effective using the same unit costs. These per cent cost-effectiveness were obtained by performing probabilistic sensitivity analysis (PSA). Using the population of HFrEF patients with diabetes and dapagliflozin's unit cost of PHP40.00, the scatterplot and corresponding cost-effectiveness acceptability curve (CEAC) were obtained and are shown in *Figures 3 and 4*. *Figure 4* demonstrates the CEAC for the addition of dapagliflozin to standard therapy among HFrEF patients with diabetes. It shows that the ICERs below the threshold ICER of PHP180 500 constitute 76% of all the ICERs generated in the scatterplot in *Figure 3*.

On the other hand, even though deterministic analyses have shown that dapagliflozin was not cost-effective in some scenarios, PSA has shown that dapagliflozin among HFrEF patients who have no diabetes mellitus was cost-effective 57%, 59%, and 63% of the time if the unit cost was PHP46.50,

Figure 2 Tornado diagram (deterministic sensitivity analyses). Tornado diagram showing the resulting ICERs across the values of the parameters (one-way sensitivity analysis). Red corresponds to the lower limit while blue corresponds to the upper limit of the parameter. Dapa, dapagliflozin; HF, heart failure.
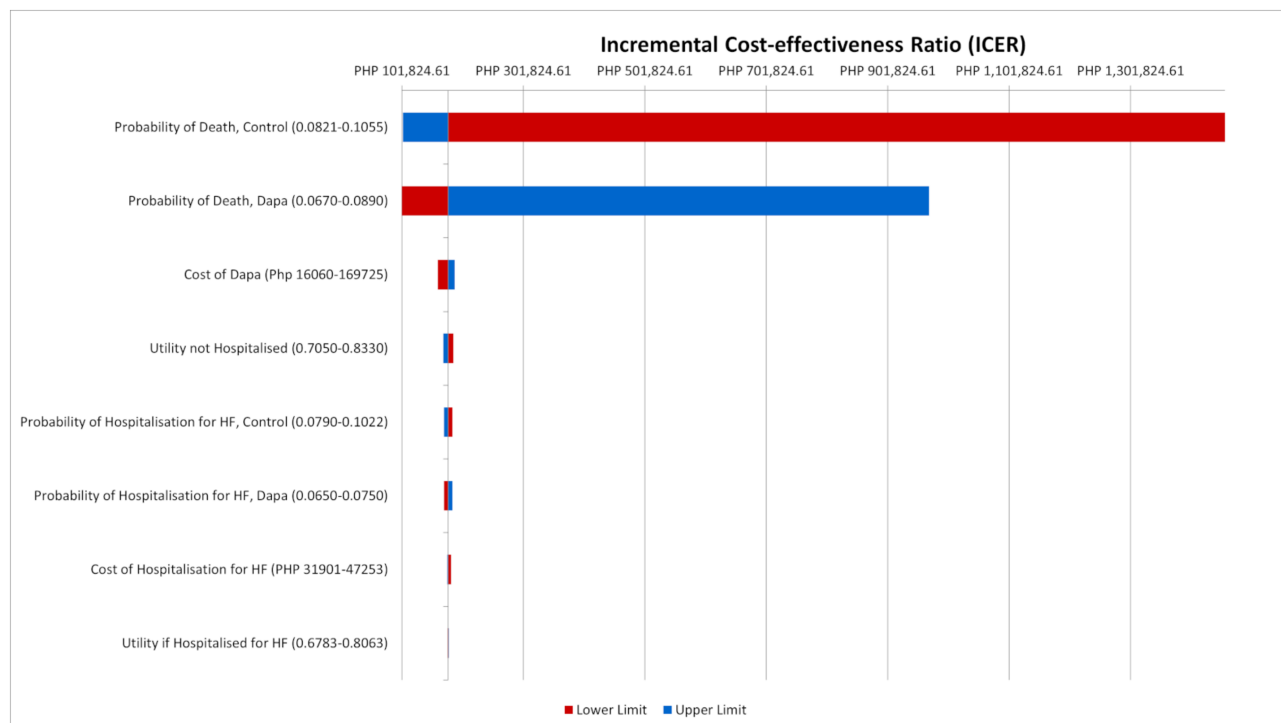
Figure 3 Scatterplot showing the incremental cost per quality-adjusted life-year for 10 000 simulations. Jagged line represents the threshold ICER or willingness to pay threshold (PHP180 500). Circles below the dashed line represent the ICERs below the threshold ICER. PHP, Philippine peso.
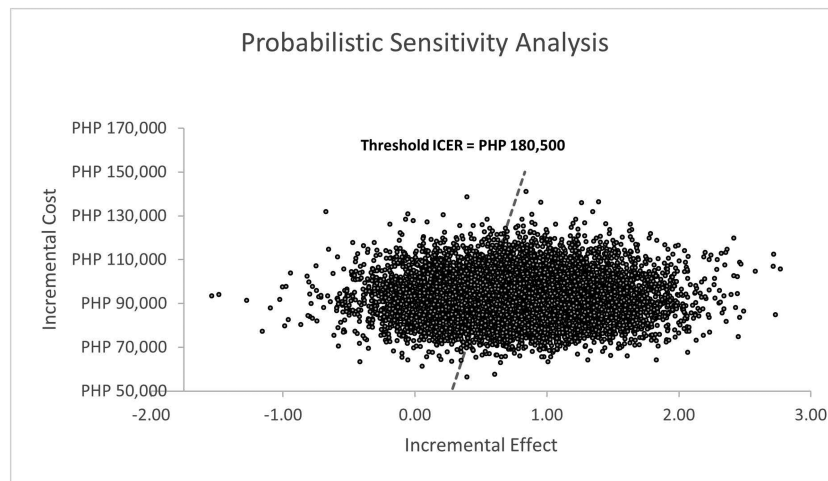
Figure 4 Cost-effectiveness acceptability curve showing that 76% ICERs are below the threshold ICER of PHP180 500.
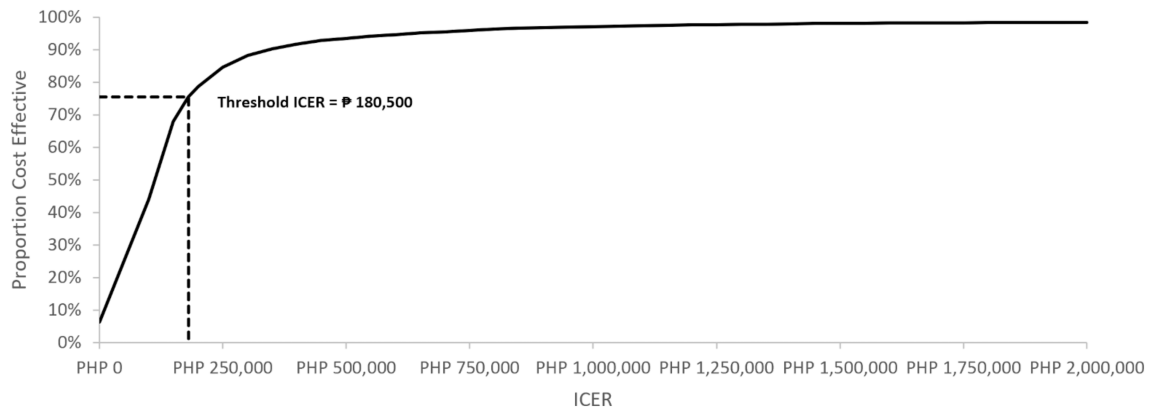
PHP44.00, and PHP40.00, respectively. If the unit price was PHP46.50, dapagliflozin was cost-effective 54% of the time if given to 'all' patients, that is, irrespective of the presence or absence of diabetes.

Discussion

The DAPA-HF trial established the efficacy of dapagliflozin on top of standard treatment for HFrEF patients, whether with or without diabetes.[6,7] In this CUA, the Philippines age-adjusted mortality rate and local costs were incorporated to come up with the cost per quality-adjusted life-year if dapagliflozin will be added to standard therapy for Filipino patients with HFrEF. The results showed that the incremental cost per quality-adjusted life-year using the

present unit price of dapagliflozin and possible negotiated unit cost are PHP177 868 (US$3434) and PHP169 983 (US $3108), respectively. These are deemed cost-effective because they are below the ceiling ICER set by the local policy-makers.

On the other hand, it was shown that the ICER was lower among HFrEF patients with T2DM; thus, dapagliflozin is more cost-effective in this population. This can be traced to the higher efficacy rate of add-on dapagliflozin among those with diabetes (particularly in all-cause death). This higher efficacy rate translated to higher incremental effectiveness which then led to lower ICER among diabetics. This result of lower ICER among diabetics was also seen in the CUA that was carried out in Thailand.[15]

This better efficacy and cost-effectiveness among diabetics is relevant due to the increasing prevalence of diabetes in the Philippines. The Food and Nutrition Research Institute (FNRI)

reported a prevalence of 5.6% in 2013 and 7.9% in 2018 of high fasting blood sugar (FBS $\geq$ 126) among Filipino aged $\geq$20 years old.[32]

The WHO Choosing Interventions that are Cost-effective project (WHO-CHOICE) considers an intervention to be cost-effective if the cost of preventing one 'disability-adjusted-life-year (DALY)' is less than three times its annual GDP per capita, while it is very cost-effective if it prevents one DALY at a cost of less than one GDP per capita.[33] This recommendation is followed in several countries especially those that do not have a specific ceiling or threshold ICER. In the Philippines, the local policy-makers have chosen the cut-off one GDP per capita per QALY as the country's willingness to pay or threshold ICER.[26] This may reflect a more stringent policy in terms of supporting a recommendation regarding the use of a new intervention which in turn may result in the provision of coverage by PhilHealth. On the other hand, some authors recommend the use of other approaches in addition to a threshold ICER in coming up with a decision to adopt or provide coverage for a new intervention.[34,35]

The year 2019 was chosen as the reference year for the study because this was the time that the study protocol was developed. It was noted that the GDP for this year was higher as compared with the earlier years. This in turn resulted in a higher threshold ICER.

Several sensitivity analyses were performed in the study. These were performed to handle uncertainties in parameters that one encounters in doing an economic evaluation.[31] One such analysis is PSA. As shown in the results, ICERs obtained through deterministic analyses may be deemed outright cost-effective or not cost-effective when compared with the threshold ICER. Performing PSA showed the distribution of ICERs that were below the threshold ICER. Through a cost-effectiveness acceptability curve, the percentage of ICERs below the threshold ICER was determined.

In keeping with the study's public healthcare provider perspective, the drug cost should not correspond to its retail price in the market or drugstore; instead, this should refer to the acquisition cost from the manufacturer by the healthcare provider (which may acquire the drug in bulk). This cost excludes mark-ups or profits by drugstores in the sale of drugs. However, the study was constrained by the lack of this cost at present. In view of this, the study used the prevailing market price and estimated a possible acquisition cost. The lower possible acquisition cost resulted to lower ICERs, thus making the use of dapagliflozin for HFrEF patients more cost-effective.

Cost-utility analyses of the add-on dapagliflozin had also been undertaken for several countries like Australia, United Kingdom, Germany, Spain, and Thailand.[13–15] Although these studies found that the add-on dapagliflozin was cost-effective, there is a need to undertake individual CUA in different countries. This is due to problems in applicability or generalizability of results of economic evaluation studies. Reasons for variability in the results include differences in the following: (i) resources used and their costs, (ii) unit cost of the drug, (iii) healthcare delivery system, (iv) treatment compliance, (v) health state valuations, (vi) perspective of the analysis, and (vii) threshold ICERs. In addition, variations in discount rates may also occur. This was demonstrated in the previous studies—5% was used for the CUA for Australia, 3% for Germany and Spain, 3.5% for UK, and 0–6% per annum for Thailand.[16,36–39] Lastly, it should be noted that ICERs reported in other studies cannot be simply converted to a specific country's currency through the use of foreign exchange rates.

In the Philippines, more than 50% of healthcare delivery is obtained through out-of-pocket expenses. PhilHealth provides hospitalization coverage; however, this does not cover the entire hospitalization cost as demonstrated in the study on hospitalization for HF.[22] In addition, for most diseases, provision for maintenance medications is through out-of-pocket expenses. This must be considered for chronic conditions like heart failure. The addition of dapagliflozin to the HF regimen in this study was shown to be cost-effective using the perspective of the public healthcare provider. This has important implications in terms of healthcare policies because one of the requirements of a new drug to be listed in the national formulary is for it to be cost-effective. Being listed in the formulary on the other hand is a requirement by PhilHealth. Cost-effectiveness, however, does not translate to affordability. This problem is especially relevant and demonstrated in the individual patient setting. Patients need to shoulder the cost of medications not only for HF but also for other concomitant conditions. For the average Filipino, the daily cost of medications may be prohibitive leading to problems in compliance.

The study has several limitations. As mentioned in the earlier sections, the unit cost of dapagliflozin was based on the prevailing market price and an assumed acquisition cost between the government and the manufacturer. This assumption may be an over or under-estimation of the cost that the two parties may agree on in the near future. Moreover, the utilities used were derived from the KCCQ scores and NYHA classification of HF patients obtained from the DAPA-HF trial and other studies where some patients from the Philippines (although a relatively small percentage of the study population) were included.

Conflict of Interest

Funding

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