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COST-EFFECTIVENESS OF SGLT2 INHIBITORS IN HEART FAILURE: A COMPARATIVE REVIEW OF ECONOMIC EVALUATIONS

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Purpose: The aim of this study was to review and compare published economic evaluations assessing the cost-effectiveness of sodium–glucose cotransporter-2 (SGLT2) inhibitors in patients with heart failure across different health care systems.
Methodology: A systematic literature review of economic evaluations was conducted using the Scopus database. Studies published within the last five years that assessed the cost-effectiveness of SGLT2 inhibitors in patients with heart failure or cardiovascular disease were identified. Due to heterogeneity among studies, a qualitative comparative analysis was performed.
Findings: The reviewed studies consistently demonstrated a favorable cost-effectiveness profile of SGLT2 inhibitor therapy in patients with heart failure. In most analyses, ICER values remained below commonly accepted willingness-to-pay thresholds. However, substantial regional differences in ICER estimates were observed, reflecting variations in drug pricing, health care system structures, and national economic conditions.
Practical implications: The results provide evidence supporting the economic value of SGLT2 inhibitor therapy in the management of heart failure. These findings may support health policy decisions, reimbursement strategies, and the broader implementation of these therapies in clinical practice.
Social implications: Improving access to cost-effective therapies for heart failure may reduce hospitalization rates, improve patients' quality of life, and decrease the overall burden of cardiovascular diseases on health care systems and society.
Value: This study provides a comparative synthesis of recent economic evaluations assessing SGLT2 inhibitors across different countries and health care systems. By highlighting regional differences in cost-effectiveness outcomes, the study contributes to a better understanding of the economic impact of these therapies and supports evidence-based decision-making in health care policy.
Keywords: cost-effectiveness, quality-adjusted life years (QALY), incremental costs and incremental (QALY), incremental cost-effectiveness ratio (ICER), sodium–glucose cotransporter-2 (SGLT2) inhibitors, heart failure.
Category of the paper: research paper.

1. Introduction

Cost-effectiveness analysis (CEA) is a widely used tool in health economics that evaluates the relationship between the costs of medical interventions and the health outcomes they generate. By comparing the resources required for a given therapy with the clinical benefits achieved, CEA supports evidence-based decision-making in health policy and resource allocation.

Health care systems worldwide are currently facing increasing financial pressure driven by population ageing, rising medical costs, and the growing prevalence of chronic diseases. Cardiovascular diseases constitute a major contributor to these expenditures. Among them, heart failure (HF) represents one of the most significant public health challenges due to its high morbidity, mortality, and frequent hospitalizations (Roger, 2021). Globally, heart failure affects more than 64 million people and its prevalence increases markedly with age, affecting approximately 1-2% of the adult population in developed countries and more than 10% of individuals over the age of 70 (Savarese, Lund, 2017; Ponikowski et al., 2016). As a result, HF generates a substantial burden on health care systems through both direct medical costs and indirect costs related to disability and loss of productivity.

In recent years, sodium–glucose cotransporter-2 (SGLT2) inhibitors have emerged as an important therapeutic option in the management of heart failure. Initially introduced for the treatment of type 2 diabetes, these agents have demonstrated significant cardiovascular and renal benefits in large randomized clinical trials. Current international guidelines recommend SGLT2 inhibitors as part of the standard pharmacological therapy for patients with heart failure across a broad spectrum of left ventricular ejection fraction (Heidenreich et al., 2022). The mechanisms underlying their clinical benefits include improved cardiac function, reductions in preload and afterload, enhanced renal protection, and favourable metabolic effects (Verma, McMurray et al., 2018).

Given their expanding role in clinical practice, it is important to evaluate not only the clinical effectiveness of SGLT2 inhibitors but also their economic value. Economic evaluations such as cost-effectiveness analyses allow assessment of whether the health benefits associated with a therapy justify the costs incurred by health care systems. Such analyses may be conducted from different perspectives, including those of the health care payer, the national health system, or society, each capturing different categories of direct and indirect costs.

In this context, understanding the economic impact of SGLT2 inhibitor therapy in heart failure is particularly relevant for health policy and reimbursement decisions. Therefore, the aim of this study was to review and compare published economic evaluations of SGLT2 inhibitors in patients with heart failure, with particular emphasis on cost-effectiveness analyses conducted in different countries and health care systems.

2. Cost-effectiveness analysis as a tool for evaluating medical interventions

In pharmacoeconomic studies, health outcomes are most commonly expressed in quality-adjusted life years (QALYs). This measure integrates both life expectancy and health-related quality of life into a single metric, allowing the overall health benefit of a medical intervention to be quantified. One QALY represents one year of life in perfect health, whereas values below one reflect years lived with reduced health status due to illness or disability.

Economic evaluations typically estimate incremental costs and incremental QALYs, which represent the differences in costs and health outcomes between a new intervention and the comparator, often standard of care. Based on these values, results are commonly summarized using the incremental cost-effectiveness ratio (ICER). The ICER indicates the additional cost required to gain one additional unit of health benefit, most often expressed as cost per QALY gained (Schwarzer et al., 2015; Drummond et al.,2015).

To determine whether an intervention is considered economically justified, ICER values are compared with a willingness-to-pay (WTP) threshold, which represents the maximum amount a health care system is willing to pay for gaining one additional QALY. These thresholds vary between countries and health systems. In the United States, a commonly cited reference threshold is approximately 100,000 USD per QALY. This value is not formally established by a single regulatory institution but originates from cost-effectiveness analyses used in health technology assessment (HTA) and is widely applied in pharmacoeconomic literature as a benchmark for reimbursement and clinical decision-making (Grosse, 2008; Shiroiwa et al., 2010).

The interpretation of cost-effectiveness results may also depend on the analytical perspective adopted in the evaluation. Economic analyses may be conducted from the perspective of a health care payer, a national health care system, or society. Each perspective captures different categories of costs. While payer-based analyses focus primarily on direct medical expenditures, the societal perspective additionally incorporates indirect costs such as productivity losses, disability, and informal care.

In the case of heart failure, economic evaluations are particularly relevant due to the high costs associated with long-term disease management and frequent hospitalizations. The use of SGLT2 inhibitors may influence both direct and indirect costs by reducing the risk of hospitalization, improving patient prognosis, and enhancing quality of life. These potential clinical and economic benefits highlight the importance of assessing the cost-effectiveness of SGLT2 inhibitor therapy across different health care systems.

3. Methods

A systematic review of original studies evaluating the cost-effectiveness of SGLT2 inhibitors in patients with heart failure and cardiovascular diseases was conducted. A total of 82 articles were identified in the Scopus database on December 11, 2025. The search strategy included the following keywords: “costs”, “effectiveness”, “heart failure”, “SGLT-2”, “cost-effectiveness”, “cardiovascular disease”, “dapagliflozin”, “empagliflozin”, “sodium–glucose cotransporter-2 inhibitors”, and “risk of cardiovascular disease”.

A total of 54 articles were screened based on titles, abstracts, and conclusions, of which 22 reported outcomes related to QALY. Ultimately, eight texts assessing the cost-effectiveness of SGLT2 inhibitors (describing 9 studies) were included in the analysis.

The review focused on pharmacoeconomic evaluations reporting economic outcomes, particularly ICER.

Only the most recent studies published within the last five years were included. The majority of pharmacoeconomic analyses on SGLT2 inhibitors were conducted between 2021 and 2024.

The inclusion criteria required that the studies employed formal economic models, particularly Markov models or hybrid modeling approaches, used to assess the long-term clinical and economic outcomes of the interventions. The included analyses compared SGLT2 inhibitor therapy with standard of care or alternative pharmacological treatment strategies.

Exclusion criteria included studies involving patient populations treated with SGLT2 inhibitors solely for type 2 diabetes mellitus (T2DM), diabetic nephropathy, or chronic kidney disease without coexisting cardiovascular disease. Additionally, clinical guidelines, review articles, and methodological papers were excluded from the analysis.

During the analysis of the selected studies, the following data were extracted: country or health care system evaluated, patient population, intervention and comparator, economic model used, analytical perspective, time horizon, total costs, QALY, incremental costs, incremental QALY, and ICER.

To ensure a high quality of study selection and evaluation, criteria derived from the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist and elements of the Drummond methodological framework for economic evaluation were applied (Husereau et al., 2022; Drummond et al., 2015).

The following parameters were assessed: clarity of the study objective, description of the study population, definition of the comparator, reporting of the economic model, stated analytical perspective, time horizon, reporting of costs, reporting of outcomes (QALY and/or ICER), and inclusion of sensitivity analysis.

Due to the heterogeneity of the included studies, resulting from differences in health care system structures across countries as well as variations in drug pricing in different geographical settings, a meta-analysis was not performed.

Instead, a qualitative synthesis was conducted, and the results were summarized in a comparative table including the main study characteristics, total costs, QALY, incremental costs, and ICER. A comparison of ICER values across different countries was also performed.

4. Results

A total of nine studies meeting the predefined inclusion criteria were included in the final analysis. These studies evaluated the cost-effectiveness of SGLT2 inhibitors in patients with heart failure or type 2 diabetes mellitus with increased cardiovascular risk.

The identified economic evaluations were conducted across health care systems, including the United States, China, Korea, India, Thailand, and countries from the Asia-Pacific region. Most studies evaluated the cost-effectiveness of adding an SGLT2 inhibitor, such as dapagliflozin or empagliflozin, to standard care in patients with heart failure with reduced ejection fraction.

The majority of analyses used Markov models to simulate disease progression and long-term outcomes. A lifetime time horizon was adopted in most studies to capture the long-term clinical and economic consequences of treatment. The perspective of the analyses varied between studies and included health care payer perspectives, national health system perspectives, and, in some cases, a societal perspective.

Clinical effectiveness inputs were typically derived from large randomized controlled trials, including DAPA-HF, EMPEROR-Reduced, and DECLARE–TIMI 58, or from meta-analyses of available trial data.

The main characteristics of the included studies are presented in Table 1.

Table 1.
Characteristics of included economic evaluations of SGLT2 inhibitors

Study	Name	Country	Population	Intervention	Comparator	Model	Perspective	Time horizon	Data source
S_1	Quadruple therapy analysis (Yan et al., 2023)	USA	HFrEF	SGLT2 inhibitor + GDMT	GDMT	Markov	healthcare system	lifetime	HF clinical trials
S_2	Dapagliflozin across EF (Bhatt et al., 2024)	USA	HF (all EF)	dapagliflozin + SOC	SOC	Markov	payer	lifetime	DAPA-HF, DELIVER
S_3	Dapagliflozin scenario analysis (Bhatt et al., 2024)	USA	HF	dapagliflozin + SOC	SOC	Markov	payer	lifetime	DAPA-HF

Cont. table 1.

S_4	Empagliflozin real-world study (Kim et al., 2024)	Korea	HF	empagliflozin + SOC	SOC	Markov	payer	-	real-world registry
S_5	Empagliflozin Asia-Pacific analysis (Liao et al., 2021)	Asia-Pacific	HFrEF	empagliflozin + SOC	SOC	Markov	payer	lifetime	EMPEROR-Reduced
S_6	Dapagliflozin vs empagliflozin (Nechi et al., 2023)	USA	HFrEF	dapagliflozin	empagliflozin	Markov	healthcare system	-	HF trials
S_7	Add-on SGLT2 therapy (Sasidharan et al., 2025)	India	HFrEF	SGLT2 inhibitor + SOC	SOC	Markov	healthcare system	lifetime	HF clinical studies
S_8	therapy HF (Huang et al., 2024)	China	HF	quadruple therapy including SGLT2	SOC	Markov	payer	20 years	meta-analysis of trials
S_9	Dapagliflozin add-on T2D (Deerochana wong et al., 2021)	Thailand	T2D + cardio-vascular risk	dapagliflozin + SOC	SOC	decision tree + Markov	societal	lifetime	DECLARE-TIMI 58

Note: - no data.

Source: own data summary.

Economic evaluations conducted in the United States demonstrated a favorable cost-effectiveness profile of SGLT2 inhibitor therapy. Yan et al. (2023) reported incremental costs of 39,386 USD and an incremental gain of 0.54 QALY, corresponding to an ICER of 73,000 USD/QALY. The analysis was based on a cohort of 8,399 adult patients from the United States. Similar findings were reported by Bhatt et al. (2024), who evaluated the cost-effectiveness of dapagliflozin in patients with heart failure across the full spectrum of ejection fraction. In this study, incremental costs amounted to 45,509 USD, with an incremental gain of 0.53 QALY, resulting in an ICER of 85,554 USD/QALY. In a scenario analysis incorporating a reduction in drug price, incremental costs decreased to 21,321 USD, while the incremental QALY remained unchanged (0.53), leading to a substantial reduction in ICER to approximately 40,081 USD/QALY. Nechi et al. (2023) compared the cost-effectiveness of dapagliflozin and empagliflozin in patients with heart failure with reduced ejection fraction, reporting incremental costs of 37,684 USD and an ICER of 44,763 USD/QALY.

Lower ICER values were observed in studies conducted in Asian countries. In a real-world analysis based on data from the Korean Acute Heart Failure (KorAHF) registry, including 3108 patients with HFrEF and 2070 patients with HFpEF, Kim et al. (2024) reported an ICER of 6764 USD/QALY. In the Asia-Pacific region, Liao et al. (2021) reported ICER values for empagliflozin ranging from 8846 to 53,791 USD/QALY. The lowest ICER was observed in a study conducted in China by Huang et al. (2024), where a minimal increase in costs of 353 USD and a substantial gain of 2.85 QALY resulted in an ICER of 124 USD/QALY. Deerochanawong et al. (2021) demonstrated that the addition of dapagliflozin to standard therapy in patients with type 2 diabetes and high cardiovascular risk in Thailand was associated

with incremental costs of 5,748 USD and an incremental gain of 0.30 QALY, corresponding to an ICER of 18,988 USD/QALY. In India, Sasidharan et al. (2025) reported incremental costs of 73,408 INR (approximately 842 USD) and an ICER of 612,406 INR/QALY (approximately 7,030 USD/QALY). The values reported in Indian rupees were converted to U.S. dollars using the average exchange rate for 2025 to enhance comparability.

The main economic outcomes are presented in Table 2.

Table 2.
Economic outcomes of included economic evaluations of SGLT2 inhibitors

Study	Total cost SOC	Total cost intervention	Incremental cost	QALY SOC	QALY intervention	Incremental QALY	ICER
S_1	124 001 USD	163 387 USD	39 386 USD	6.03	6.57	0.54	73 000 USD/QALY
S_2	109 003 USD	154 512 USD	45 509 USD	6.04	6.57	0.53	85 554 USD/QALY
S_3	-	-	21 321 USD	-	-	0.53	40 081 USD/QALY
S_4	-	-	-	-	-	-	6 764 USD/QALY
S_5	-	-	-	-	-	-	8 846–53 791 USD/QALY
S_6	-	-	37 684 USD	-	-	-	44 763 USD/QALY
S_7	299 793 ₹ (3440USD)	373 201 ₹ (4285USD)	73 408 ₹ (842 USD)	-	-	-	612 406 ₹ /QALY (7030 USD/QALY)
S_8	87 087 USD	87 441 USD	353 USD	18.60	21.44	2.85	124 USD/QALY
S_9	8 707 USD	14 455 USD	5 748 USD	9.28	9.58	0.30	18 988 USD/QALY

Note: - no data.

Source: own data summary.

Overall, the reporting quality of the included studies was high. Most economic evaluations clearly reported the study objective, population, comparator and economic model used, as well as key outcomes such as ICER. However, some studies did not provide complete information on incremental costs or QALY, which limited direct comparability between analyses. The detailed results of the quality assessment are presented in Table 3.

Table 3.
Evaluation of the quality of economic analyses (CHEERS and Drummond)

Study	Objective clearly stated	Population described	Comparator defined	Economic model reported	Perspective stated	Time horizon reported	Costs reported	Outcomes (QALY / ICER)	Sensitivity analysis
S_1	✓	✓	✓	✓	✓	✓	✓	✓	✓
S_2	✓	✓	✓	✓	✓	✓	✓	✓	✓
S_3	✓	✓	✓	✓	✓	✓	△	✓	✓
S_4	✓	✓	✓	✓	✓	△	△	✓	✓
S_5	✓	✓	✓	✓	✓	✓	△	✓	✓
S_6	✓	✓	✓	✓	✓	△	△	✓	✓
S_7	✓	✓	✓	✓	✓	✓	✓	✓	✓
S_8	✓	✓	✓	✓	✓	✓	✓	✓	✓
S_9	✓	✓	✓	✓	✓	✓	✓	✓	✓

Note. ✓ criterion met; △ partially met; ✕ not reported.

Source: own data summary.

5. Discussion

5.1. ICER below the cost-effectiveness threshold

One of the key findings of this review is that, in the majority of the analyzed economic evaluations, the incremental cost-effectiveness ratios (ICERs) for SGLT2 inhibitor therapy remained below commonly accepted willingness-to-pay thresholds, suggesting that these interventions provide substantial health benefits relative to their costs.

These findings have important implications not only from a health economics perspective but also for clinical guideline development and reimbursement policies. In recent years, SGLT2 inhibitors have been incorporated into international guidelines for the management of heart failure as a key component of pharmacological therapy. The implementation of reimbursement policies for this class of drugs may significantly increase their real-world utilization, as treatment costs often represent a major barrier for patients. Fusco et al. (2023) and Gourzoulidis et al. (2017) have demonstrated that reduced out-of-pocket costs and drug reimbursement are associated with improved medication adherence, which in turn leads to better treatment effectiveness and clinical outcomes.

Importantly, the cost-effectiveness of SGLT2 inhibitors extends beyond the individual patient perspective and is also relevant at the level of public health care systems. The results of economic evaluations suggest that funding these therapies within reimbursement frameworks may be economically justified due to reductions in both direct and indirect costs. Clinical studies have shown that the use of SGLT2 inhibitors is associated with a lower risk of hospitalization for heart failure (Zannad et al., 2020) as well as shorter hospital stays (Singh et al., 2024), leading to a reduction in direct medical costs. At the same time, improvements in patient prognosis, increased survival (McMurray et al., 2019), and enhanced quality of life (Kosiborod et al., 2020) may contribute to lower indirect costs, such as productivity loss and disability-related expenditures.

It is also important to note that SGLT2 inhibitors represent a relatively recent class of therapeutic agents. As market competition increases and generic formulations become available, further reductions in drug prices can be expected. Lower pharmacotherapy costs are likely to improve cost-effectiveness outcomes even further, thereby enhancing the economic attractiveness of these therapies from a health system perspective.

This creates opportunities for price negotiations with manufacturers, the implementation of reimbursement agreements, and improved patient access to treatment. This is particularly relevant for patients with heart failure across the full spectrum of ejection fraction, as SGLT2 inhibitors are among the few therapies shown to be effective in both reduced and preserved ejection fraction, whereas many other pharmacological treatments are indicated primarily for HFrEF.

5.2. Regional differences in ICER values

A clear difference in ICER values between analyses conducted in the United States and Asian health care systems was observed in the reviewed studies. In general, economic evaluations from the United States reported substantially higher ICER values, whereas analyses conducted in Asian countries such as China, Korea, India, and Thailand tended to demonstrate considerably lower cost-effectiveness ratios. These differences are likely driven by several structural factors related to drug pricing, health system organization, and economic conditions across regions.

Differences in pharmaceutical pricing policies are therefore likely to be one of the key drivers of the variability in ICER values observed between countries. Higher drug prices increase the incremental costs associated with a given intervention, which directly influences the ICER calculated in economic evaluations. Consequently, even when clinical effectiveness remains comparable across settings, variations in drug pricing structures and reimbursement systems may substantially affect the estimated cost-effectiveness of the same therapy.

Drug prices in the United States are generally higher than in many other countries (Danzon, Chao, 2000), partly due to differences in pharmaceutical pricing policies. Unlike many health systems that implement centralized price negotiations or government price controls, the U.S. system allows manufacturers relatively greater flexibility in setting initial drug prices (Kang et al., 2020). As a result, pharmaceutical prices in the United States are often substantially higher than in other OECD countries, where pricing is frequently regulated through health technology assessment frameworks and national reimbursement negotiations.

A substantial proportion of early-stage biomedical research is conducted in the United States and is frequently supported by federal research funding programs, particularly through the National Institutes of Health (NIH) (Galkina Cleary et al., 2018). Previous analyses have shown that publicly funded research contributed to the scientific foundations of many newly approved drugs, highlighting the important role of government-funded biomedical research in pharmaceutical innovation. The high costs associated with drug discovery, development, and clinical testing may therefore be partly reflected in the final prices of innovative therapies.

Another important factor contributing to regional differences in ICER values is the overall cost of health care services. International comparisons indicate that the United States has substantially higher health care expenditures than most other countries, partly driven by higher prices of medical services and significantly higher salaries of health care professionals (Papanicolas et al., 2018). In contrast, several Asian health care systems operate with lower labor costs, different reimbursement models, and more centralized health insurance structures, which may reduce the overall cost of treatment (Gauld et al., 2006).

Finally, differences in ICER values may also be influenced by variation in willingness-to-pay (WTP) thresholds across countries. WTP thresholds used in health technology assessment are often linked to macroeconomic indicators such as gross domestic product (GDP) per capita,

national health care expenditure, the financial capacity of health systems (Woods et al., 2016) and individual patients. Countries with higher GDP and greater health care spending, such as the United States, typically adopt higher willingness-to-pay thresholds for cost-effectiveness. For example, the United States allocates approximately 17–18% of its GDP to health care, which is the highest among OECD countries and nearly twice the OECD average (OECD, 2023). Consequently, higher ICER thresholds are often considered acceptable in economic evaluations conducted within high-income health systems.

Together, these factors illustrate how regional economic conditions and health system structures play a critical role in determining the observed variability in ICER estimates, highlighting the importance of interpreting pharmacoeconomic results within the context of the specific health care system in which the analysis was conducted.

6. Conclusions

The present review summarized economic evaluations assessing the cost-effectiveness of SGLT2 inhibitors in patients with heart failure and in individuals with type 2 diabetes with increased cardiovascular risk. Overall, the analyzed studies demonstrated a favorable cost-effectiveness profile of SGLT2 inhibitor therapy, with most reported incremental cost-effectiveness ratios (ICER) remaining below commonly accepted willingness-to-pay thresholds, particularly the reference threshold of 100,000 USD per quality-adjusted life year (QALY).

The results also revealed substantial regional differences in ICER estimates. Economic evaluations conducted in the United States generally reported higher ICER values compared with analyses from Asian health care systems. These variations appear to be influenced by differences in pharmaceutical pricing policies, health care system structures, overall treatment costs, and national willingness-to-pay thresholds.

Despite these differences, the available evidence consistently indicates that SGLT2 inhibitors provide clinically meaningful benefits and represent a cost-effective therapeutic strategy in the management of heart failure across multiple health care systems. The findings support the inclusion of these agents in contemporary clinical guidelines and suggest that improving access to SGLT2 inhibitor therapy may be justified not only from a clinical perspective but also from a health-economic standpoint.

Further economic evaluations conducted in diverse health care settings are warranted to better understand the long-term economic impact of these therapies, particularly as drug prices evolve and generic formulations become available, which may further improve the cost-effectiveness of SGLT2 inhibitor treatment. Resources management must take into account employees' perceptions of distributive. procedural. interpersonal and informational justice.

which refer to decisions taken by companies towards employees and results that come from these decisions. because this perception influences the behaviour and attitudes in a workplace. and these behaviours and attitudes directly affect companies' performance. In the economic practice. a better understanding of human behaviour in the context of professional work is very important.

Several limitations should be acknowledged. First, the number of included studies was relatively small and limited to a few health care systems, primarily the United States and selected Asian countries. Second, the studies differed in modeling approaches, analytical perspectives, time horizons, and input parameters, which may limit the direct comparability of ICER estimates. Additionally, some analyses did not report complete economic outcomes, particularly incremental costs or QALY values. Finally, the literature search was conducted in a single database, which may introduce potential publication bias.

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