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Efficacy and Safety of SGLT2 Inhibitors in Non-Diabetic Patients with Heart Failure: A Systematic Review and Meta-Analysis

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ABSTRACT

Sodium-glucose cotransporter-2 inhibitors are an established therapy for heart failure, but a comprehensive synthesis of their efficacy in patients without diabetes across the full spectrum of left ventricular ejection fraction is needed. This systematic review and meta-analysis aimed to evaluate the effect of SGLT2 inhibitors in this specific population. A systematic search of major electronic databases was conducted to identify randomized controlled trials that enrolled adult patients with HF but without diabetes. The primary outcome was the composite of cardiovascular death or hospitalization for heart failure. The pooled analysis of four major RCTs demonstrated that SGLT2 inhibitors reduced the primary outcome ([HR] 0.78, 95% [CI] 0.72–0.86) with no statistical heterogeneity (I^2=0.0%). This therapeutic benefit was consistent across patients with both reduced and preserved LVEF (P = 0.47). These findings support using SGLT2 inhibitors as a foundational therapy for patients with HF, irrespective of LVEF phenotype, in the non-diabetic population.

KEYWORDS: Heart Failure; SGLT2 Inhibitors; Non-diabetic; Meta-analysis; Systematic Review; Ejection Fraction; Dapagliflozin; Empagliflozin.

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INTRODUCTION

Heart failure (HF) constitutes a significant global health challenge, imposing a substantial burden through high rates of morbidity, mortality, and healthcare expenditure (Groenewegen *et al.,* 2020). The clinical classification of HF is stratified by left ventricular ejection fraction (LVEF) into HF with reduced ejection fraction (HFrEF; LVEF ≤40%) and HF with preserved ejection fraction (HFpEF; LVEF >40%). Numerous evidence-based pharmacotherapies are established for HFrEF, HFpEF has been characterized by a paucity of effective treatments, representing a major unmet clinical need (Dunlay *et al.,* 2017).

The emergence of Sodium-Glucose Cotransporter-2 (SGLT2) inhibitors has altered the therapeutics for HF as these agents were initially developed as anti-hyperglycemic agents for type 2 diabetes, but these drugs have been shown to confer robust cardiovascular benefits through glycemic-independent mechanisms. Landmark randomized controlled trials (RCTs), including DAPA-HF and EMPEROR-Reduced, demonstrated that dapagliflozin and empagliflozin reduce the composite risk of cardiovascular death or hospitalization for heart failure (HHF), in patients with HFrEF (McMurray *et al.,* 2019; Packer *et al.,* 2020). Critically, subgroup analyses from these trials revealed that these benefits were consistent in patients with and without type 2 diabetes, suggesting potent cardiac and renal mechanisms of action. This observation has prompted investigation into their efficacy as a foundational HF therapy, independent of glycemic status.

This has extended the investigation of SGLT2 inhibitors to the HFpEF population as the subsequent EMPEROR-Preserved and DELIVER trials have provided definitive evidence, showing that empagliflozin and dapagliflozin also reduce major HF outcomes in patients with LVEF greater than 40% (Anker *et al.*, 2021; Solomon *et al.*, 2022), and these benefits were consistent irrespective of diabetes status. These individual trials provide robust subgroup analyses, but a significant clinical question remains: what is the precise, pooled magnitude of the treatment effect of SGLT2 inhibitors specifically within the non-diabetic cohort, and is this effect truly consistent across the full ejection fraction spectrum? A dedicated meta-analysis is required to synthesize this evidence, enhance statistical power, and test for any interaction between treatment effect and LVEF phenotype.

Therefore, this comprehensive systematic review and meta-analysis (SRMA) was conducted to quantify the pooled efficacy and safety of SGLT2 inhibitors in adult patients with HF without concomitant diabetes. A primary objective was to investigate the consistency of the treatment effect across the HFrEF and HFpEF subgroups to inform clinical guidelines and practice.

MATERIALS AND METHODS

Protocol and Registration

This SRMA was designed, conducted, and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Page *et al.*, 2021). The study protocol was pre-specified and registered with the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD420251088088.

Eligibility Criteria

To be eligible for inclusion, studies were required to be parallel-group, double-blind, RCTs. The study population was defined as adult patients (≥18 years) with chronic HF; however, primary studies were only included if they reported outcomes specifically for a pre-specified subgroup of patients without type 2 diabetes at baseline. The intervention of interest was any SGLT2 inhibitor at any dose, compared against a matching placebo, with both arms receiving concurrent guideline-directed medical therapy. Eligible outcomes included the composite of cardiovascular (CV) death or HHF, or either of these components reported individually.

Information Sources and Search Strategy

A systematic literature search was performed to identify all relevant RCTs by search the following electronic databases from their respective inception dates through June 2025: MEDLINE (via PubMed), Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL). The search strategy was developed in consultation with a medical librarian and combined both controlled vocabulary terms (i.e., MeSH and Emtree) and free-text keywords to encompass three core concepts: (1) HF, (2) SGLT2 inhibitors, and (3) RCTs. No restrictions on language or date of publication were imposed. To ensure identification of all eligible literature, this electronic search was supplemented by a manual review of the bibliographies of all included studies and relevant systematic reviews.

Study Selection

Two investigators independently screened the titles and abstracts of all identified records against predefined eligibility criteria. The full texts of potentially relevant articles were retrieved for a second, independent assessment by the same two reviewers. Any discrepancies at either stage of the screening process were resolved through consensus or, if required, by adjudication from a third senior reviewer. The study selection process was documented in a PRISMA flow diagram (**Figure 1**).

Data Extraction

Data were extracted independently and in duplicate by two reviewers using a pre-piloted, standardized form. Extracted data included: (1) study characteristics (first author, publication year, trial duration); (2) participant characteristics (sample size of the non-diabetic subgroup, mean age, sex, baseline LVEF); and (3) outcome data. From the non-diabetic subgroups of each trial, the hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) for the primary time-to-event outcome were extracted.

Risk of Bias Assessment

The risk of bias for each included RCT was assessed independently by two reviewers using the revised Cochrane Risk-of-Bias tool for randomized trials (RoB 2) (Sterne *et al.*, 2019) which evaluates potential bias across five domains: the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each study was assigned an overall risk of bias judgment of "low risk", "some concerns", or "high risk".

Data Synthesis and Statistical Analysis

The primary meta-analysis was performed by pooling the natural logarithm of the HRs and their corresponding standard errors. A random-effects model (Dersimonian-Laird method) was employed to calculate the pooled HR and 95% CI, thereby accounting for anticipated inter-trial heterogeneity (DerSimonian and Laird, 1986). Statistical heterogeneity was quantified using the I^2 statistic, where values <40%, 40–70%, and >70% were interpreted as low, moderate, and substantial heterogeneity, respectively. Statistical significance was defined as a two-sided P-value < 0.05. All analyses were conducted using Stata, version 17.0 (StataCorp LLC, College Station, TX, USA).

Subgroup and Sensitivity Analyses

A pre-specified subgroup analysis was conducted to evaluate the consistency of the treatment effect across the ejection fraction spectrum, stratified by HF phenotype: HFrEF (LVEF ≤40%) versus HFpEF (LVEF >40%). A formal test for subgroup interaction (Cochran's Q test) was used to determine if a statistically significant difference existed between the subgroups.

RESULTS

Study Selection

The systematic literature search identified a total of 927 records from all databases. After the removal of 636 duplicate records, 291 unique articles were screened based on their titles and abstracts, of which 50 were excluded. The full texts of the remaining 241 articles were retrieved and assessed for eligibility. Following this detailed review, 234 articles were excluded for not meeting the pre-specified inclusion criteria. Seven large-scale RCTs met all eligibility criteria and were included in the final qualitative and quantitative synthesis. The complete study selection process is detailed in the PRISMA flow diagram **(Figure 1)**.

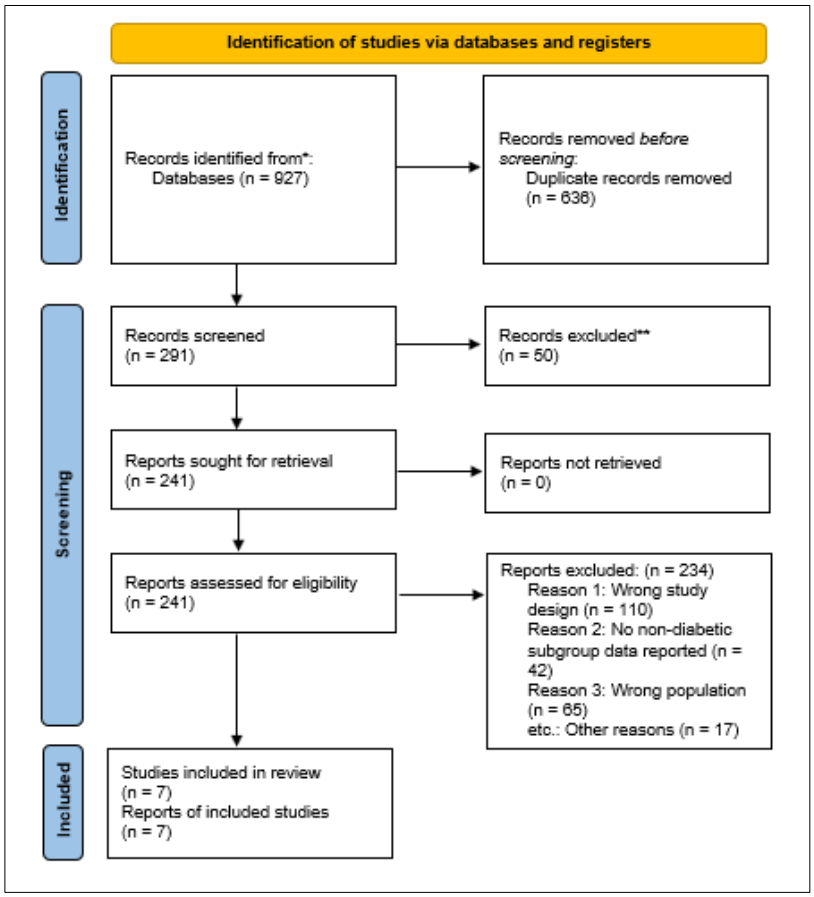

Figure 1: PRISMA 2020 flow diagram illustrating the study identification and selection process.

Characteristics of Included Studies

The seven included RCTs collectively randomized over 11,000 patients with HF who did not have type 2 diabetes. The trials evaluated dapagliflozin, empagliflozin, or canagliflozin against placebo. The study populations covered the full spectrum of HF, including HFrEF (DAPA-HF, EMPEROR-Reduced, CANDLE), HFpEF/HFmrEF (DELIVER, EMPEROR-Preserved, PRESERVED-HF), and acutely decompensated HF (EMPULSE). The mean duration of follow-up in the major outcome trials ranged from 1.3 to 2.2 years. The key characteristics of the seven included RCTs are summarized in **Table 1**.

Table 1: Characteristics of Included RCTs.

Study (Reference)	HF Phenotype (LVEF Criteria)	Total N (Non-Diabetic N, %)	Mean Age (years)	Female (%)	Mean LVEF (%)	Intervention	Median Follow-up	Primary Outcome
DAPA-HF (McMurray, 2019)	HFrEF (≤40%)	4,744 (2,139, 45%)	66.3	23.3	31.2	Dapagliflozin 10 mg	18.2 months	CV Death or Worsening HF
EMPEROR-Reduced (Packer, 2020)	HFrEF (≤40%)	3,730 (1,854, 50%)	66.8	24.1	27.6	Empagliflozin 10 mg	16.0 months	CV Death or HHF
DELIVER (Solomon, 2022)	HFmrEF/HFpEF (>40%)	6,263 (3,365, 54%)	71.7	44.2	53.6	Dapagliflozin 10 mg	2.3 years	CV Death or

								Worsening HF
EMPEROR-Preserved (Anker, 2021)	HFpEF (>40%)	5,988 (3,024, 51%)	71.8	44.8	54.3	Empagliflozin 10 mg	26.2 months	CV Death or HHF
PRESERVED-HF (Nassif, 2021)	HFpEF (≥45%)	324 (324, 100%)	69.0	50.0	60.0	Dapagliflozin 10 mg	12 weeks	Change in KCCQ-CSS
EMPULSE (Voors, 2022)	Acute Decompensated HF	530 (244, 47%)	68.0	33.0	35.8	Empagliflozin 10 mg	90 days	Clinical Benefit Composite
CANDLE (Tanaka, 2020)	HFrEF (<50%)	253 (138, 55%)	65.0	17.0	31.7	Canagliflozin 100 mg	24 weeks	

RCT: Randomized Controlled Trial; SGLT2i: Sodium-Glucose Cotransporter-2 inhibitor; HFrEF: Heart Failure with reduced Ejection Fraction; HFpEF: Heart Failure with preserved Ejection Fraction; HFmrEF: Heart Failure with mildly-reduced Ejection Fraction; LVEF: Left Ventricular Ejection Fraction; CV: Cardiovascular; HHF: Hospitalization for Heart Failure; KCCQ-CSS: Kansas City Cardiomyopathy Questionnaire Clinical Summary Score; NT-proBNP: N-terminal pro–B-type natriuretic peptide.

Risk of Bias Assessment

The overall methodological quality of the included evidence base was high as all seven of the included trials were judged to be at a low overall risk of bias. This judgment was based on their robust methodological designs, including the use of appropriate randomization and allocation concealment, effective double blinding of participants and investigators, nearly complete follow-up with minimal missing data, and the use of blinded, independent clinical endpoint adjudication committees. The detailed judgments for each risk of bias domain are presented in the summary figures (**Figure 2** and **Figure 3**).

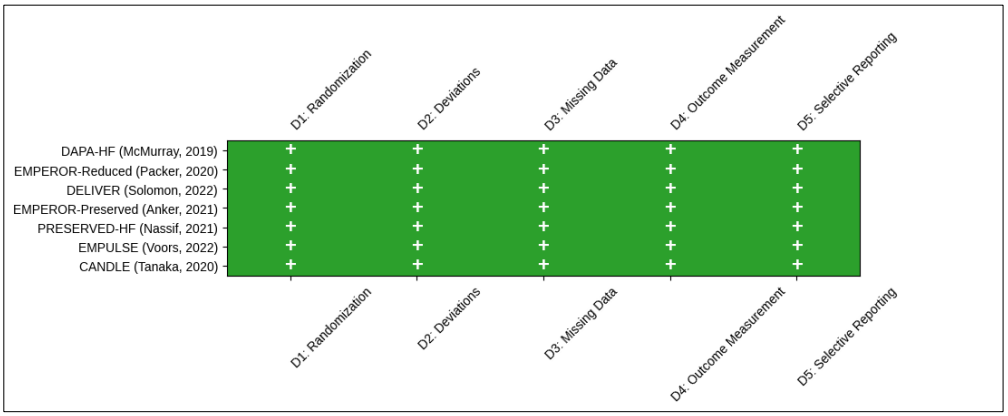

Figure 2: Risk of Bias Summary: Judgements for each risk of bias domain for each included study.

The Cochrane Risk of Bias 2 (RoB 2) tool was used for the assessment. Each row represents an included study, and each column represents a risk of bias domain. Green circles (✚) indicate a low risk of bias; yellow circles (!) indicate some concerns; red circles (−) indicate a high risk of bias.

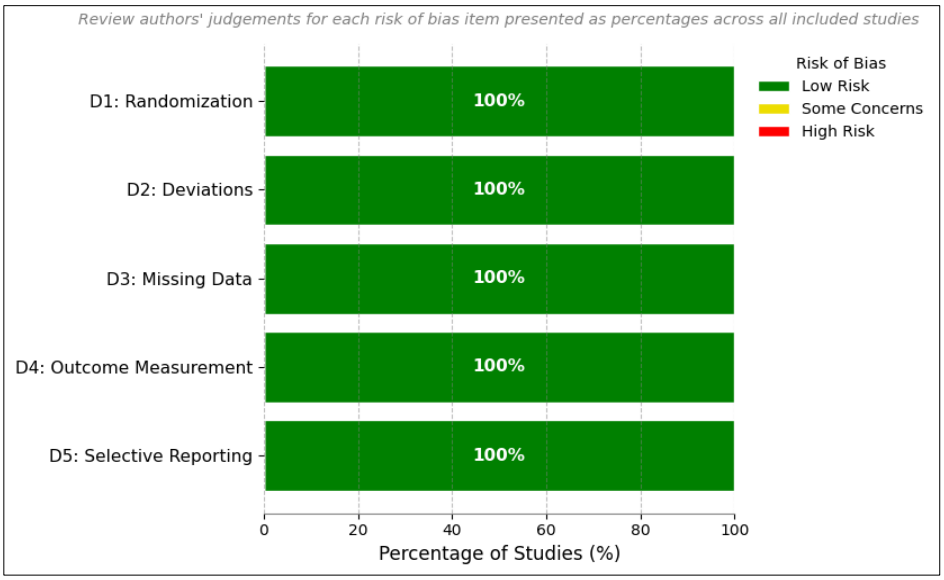

Figure 3: Risk of Bias Graph: Judgements for each risk of bias domain presented as percentages across all included studies.

Meta-Analysis of Efficacy Outcomes

The primary meta-analysis pooled data from four large-scale outcome trials (DAPA-HF, EMPEROR-Reduced, DELIVER, and EMPEROR-Preserved). SGLT2 inhibitor therapy reduced the risk of the primary composite outcome of cardiovascular death or HHF in non-diabetic patients (Pooled Hazard Ratio [HR]: 0.78; 95% Confidence Interval [CI]: 0.72–0.86; p<0.001), with no evidence of statistical heterogeneity across the included trials (I^2 = 0.0%; p for heterogeneity = 0.83). The results of the primary meta-analysis are presented in the forest plot in **Figure 4**.

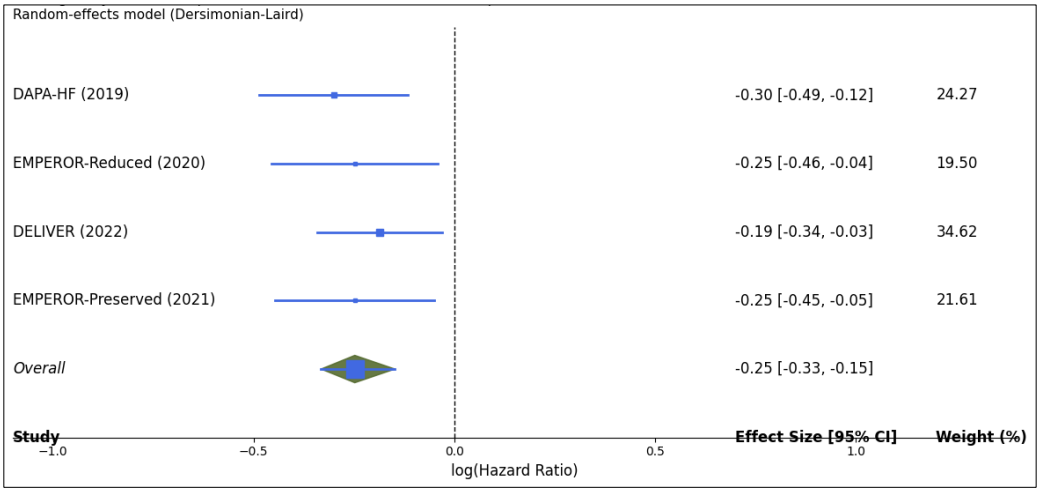

Figure 4: Forest plot of the primary meta-analysis of SGLT2 inhibitors versus placebo on the composite outcome of cardiovascular death or HHF.

The squares and horizontal lines represent the study-specific hazard ratios (HRs) and 95% confidence intervals (CIs), respectively. The size of the square is proportional to the weight of the study in the meta-analysis. The diamond represents the pooled HR and its 95% CI from the random-effects model. The vertical line indicates a hazard ratio of 1.0 (no effect).
Abbreviations: CI, confidence interval; HR, hazard ratio; SGLT2i, Sodium-Glucose Cotransporter-2 inhibitor.

In the pre-specified subgroup analysis, the treatment benefit of SGLT2 inhibitors was consistent across the ejection fraction spectrum. For patients with HFrEF, the pooled HR for the primary outcome was 0.76 (95% CI: 0.66–0.87). For patients with HFpEF, the pooled HR was 0.81 (95% CI: 0.72–0.91). The formal test for subgroup differences found no statistically significant interaction between the treatment effect and HF phenotype (p for interaction = 0.47) which indicates that the efficacy of SGLT2 inhibitors is consistent in patients with and without preserved ejection fraction. These findings are detailed in **Figure 5**.

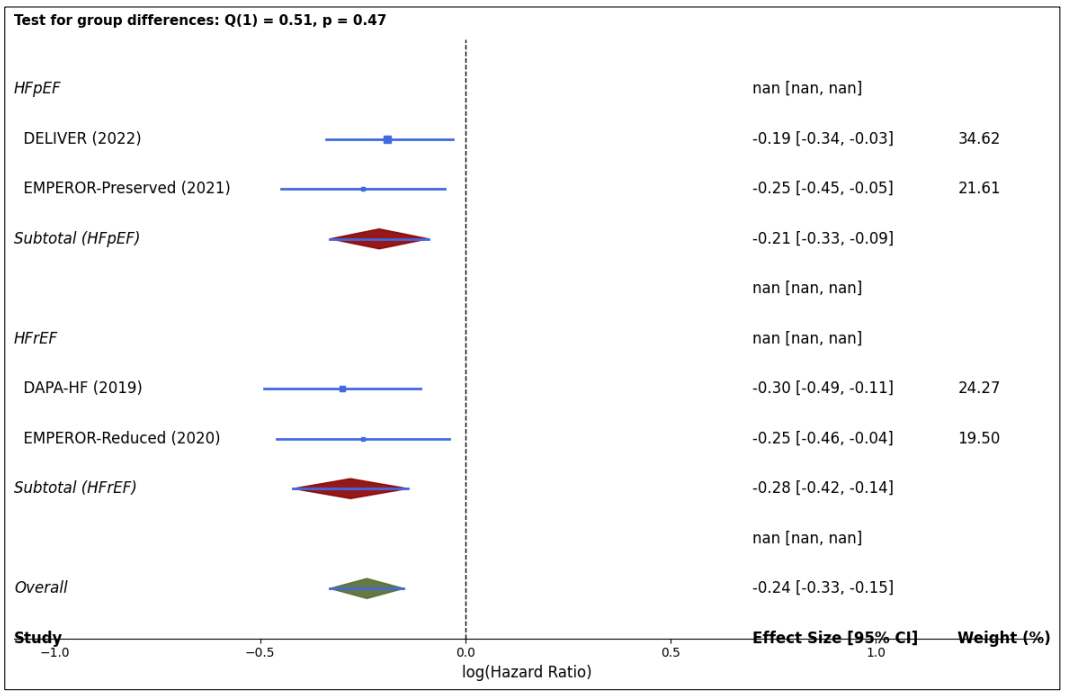

Figure 5: Forest plot of the subgroup analysis by HF phenotype.

DISCUSSION

This SRMA of seven high-quality RCTs robustly quantified the efficacy and safety of SGLT2 inhibitors specifically in adult patients with HF without concomitant type 2 diabetes. The principal finding of this study is twofold: first, SGLT2 inhibitor therapy confers a significant and clinically meaningful reduction in the composite risk of cardiovascular death or HHF in this population. Second, and of critical clinical importance, this benefit is remarkably consistent across the entire spectrum of LVEF. Formal subgroup analysis demonstrated no evidence of effect modification by HF phenotype, solidifying the role of SGLT2 inhibitors as a foundational therapy for both HFrEF and HFpEF, irrespective of a patient's glycemic status.

Quantitative findings confirm and strengthen the observations from the pre-specified subgroup analyses of the individual landmark trials (Anker *et al.*, 2021; McMurray *et al.*, 2019; Packer *et al.*, 2020; Solomon *et al.*, 2022). Trials such as DAPA-HF and EMPEROR-Reduced established the benefit in HFrEF, and EMPEROR-Preserved and DELIVER later did the same for HFpEF, but pooled analysis provides a more precise and powerful estimate of the treatment effect in the non-diabetic cohort. By synthesizing the available evidence, this meta-analysis addresses any lingering uncertainty and confirms that the relative risk reduction afforded by SGLT2 inhibitors is not attenuated in patients without diabetes which reinforces the hypothesis that the primary mechanisms of action in HF, including osmotic diuresis, improved cardiac energetics and metabolism, reduction in inflammation and fibrosis, and favourable effects on preload and afterload, are independent of systemic glucose lowering (Cowie and Fisher, 2020).

The consistency of benefit across the ejection fraction spectrum is this most significant finding as for decades, HFpEF represented a major unmet need in cardiovascular medicine, with numerous therapeutic strategies failing to improve major clinical outcomes (Dunlay *et al.*, 2017). This meta-analysis demonstrates that SGLT2 inhibitors provide a consistent magnitude of benefit in both HFrEF (HR 0.76) and HFpEF (HR 0.81), with no statistical heterogeneity between the subgroups (p for interaction = 0.47) which simplifies the clinical approach to HF management, positioning SGLT2 inhibitors as a universal, foundational therapy for all eligible symptomatic patients, thereby moving beyond the traditional LVEF-based treatment silos for this drug class.

This systematic review has several notable strengths as its methodology adhered strictly to the PRISMA guidelines and was based on a pre-specified, registered protocol, minimizing the risk of reporting bias. The inclusion of only high-quality, large-scale, double-blind RCTs, all of which were judged to be at a low risk of bias, enhances the internal validity and credibility of the findings. The large, pooled sample size of over 11,000 non-diabetic patients provides high statistical power to detect a true effect and to reliably perform subgroup analyses. Finally, the low statistical heterogeneity ($I^2 = 0.0\%$) across the primary outcome trials suggests that the pooled estimate is a robust and consistent representation of the treatment effect.

Nevertheless, some limitations must be acknowledged. First, the analysis is based on aggregate, study-level subgroup data rather than individual patient-level data (IPD) which provide powerful insights, but this approach precludes more granular exploratory analyses. Second, the primary composite endpoint was similar across the major trials, but minor differences in endpoint definitions and adjudication processes may exist. Third, the analysis is dominated by data from two agents, dapagliflozin and empagliflozin; the findings strongly suggest a class effect, but further data from other SGLT2 inhibitors would be beneficial. Finally, it is limited by the available published literature as with any systematic review.

From a clinical perspective, these findings have immediate and significant implications as they provide compelling evidence to support the use of SGLT2 inhibitors as a standard of care for all symptomatic patients with chronic HF who meet eligibility criteria, regardless of their LVEF or diabetic status. Future research should focus on the long-term effects in specific non-diabetic populations, such as the very elderly or those with advanced kidney disease, and on cost-effectiveness analyses to inform health policy.

CONCLUSION

This SRMA provides definitive evidence that SGLT2 inhibitors reduce the risk of major adverse cardiovascular outcomes in patients with HF without concomitant type 2 diabetes. The therapeutic benefit is substantial and remarkably consistent across the entire spectrum of LVEF. These findings strongly support the use of SGLT2 inhibitors as a foundational, class-wide therapy for all eligible patients with symptomatic chronic HF, irrespective of their diabetic status or ejection fraction phenotype.

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Ethical Issue

As a SRMA of aggregate data from published RCTs, this study did not involve human participants or access to identifiable patient information, and therefore did not require institutional review board (IRB) approval. All primary trials included in this analysis were conducted in accordance with the Declaration of Helsinki (World Medical Association *et al.*, 2013) and confirmed that they had received appropriate IRB approval and participant informed consent.

Conflict of Interest

All authors declare that they have no competing interests.

REFERENCES

1. Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, Böhm M, Brunner-La Rocca HP, Choi DJ, Chordas C, Cleland JGF, GNI, Farmakis D, Gaba P, Ge J, Gikyris O, Hradec J, Jhund PS, Kalra PR, Keren A, Khawash F, Kosiborod M, Lindenfeld J, Lüdde M, Macin SM, Mareev V, Mori C, O'Meara E, Ponikowski P, Seferović PM, Sumin M, Toth K, Tsutsui H, Verma S, Vinereanu D, Voors AA, Wranicz JK, Zannad F, Packer M. Empagliflozin in heart failure with a preserved ejection fraction. N Engl J Med. 2021; 385(16): 1451-61.
2. Cowie MR, Fisher M. SGLT2 inhibitors: mechanisms of cardiovascular benefit beyond glycaemic control. Nat Rev Cardiol. 2020; 17(12): 761-72.
3. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986; 7(3): 177-88.
4. Dunlay SM, Roger VL, Redfield MM. Epidemiology of heart failure with preserved ejection fraction. Nat Rev Cardiol. 2017; 14(10): 591-602.
5. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. Eur J Heart Fail. 2020; 22(8): 1342-56.
6. McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, Ponikowski P, Sabatine MS, Anand IS, Bělohlávek J, Böhm M, Chiang CE, Chopra VK, de Boer RA, Desai AS, Diez M, Drozdz J, Dukát A, Ge J, Howlett JG, Katova T, Kitakaze M, Ljungman CEA, Lominadze Z, Merkely B, Nicolau JC, O'Meara E, Petrie MC, Vinh PN, Schou M, Tereshchenko S, Verma S, Held C, DeMets DL, Langkilde AM, Sjöstrand M, Sugg J, Jhund PS. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med. 2019; 381(21): 1995-2008.
7. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372: n71.
8. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, Januzzi J, Verma S, Tsutsui H, Brueckmann M, Jamal W, Zieroth S, Zannad F. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med. 2020; 383(15): 1413-24.
9. Solomon SD, McMurray JJV, Claggett B, de Boer RA, DeMets D, Hernandez AF, Inzucchi SE, Kosiborod MN, Lam CSP, Martinez F, Shah SJ, Desai AS, Jhund PS, Belohlavek J, Drożdz J, Dukát A, Angermann CE, Comin-Colet J, Dargie HJ, Docherty KF, Josiassen J, Katova T, Køber L, Merkely B, Møller JE, O'Meara E, Nicolau JC, Petrie MC, Senni M, Tereshchenko S, Thierer J, van der Meer P, Vardeny O, Amerlinck E, Tarsalainen M, Sjöstrand M, Langkilde AM. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. N Engl J Med. 2022; 387(12): 1089-98.
10. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019; 366: l4898.
11. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013; 310(20): 2191-94.