Can SGLT-2 Inhibitors Treat Heart Failure with Preserved Ejection Fraction? A Systematic Review

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Introduction

- The NHS spends £5 billion a year on cardiovascular disease. Heart failure is the leading cause of hospitalisations worldwide and there is currently no cure for the disease
- However, emerging studies have shown that sodium-glucose co-transporter 2 inhibitors (SGLT-2is) may treat heart failure with preserved ejection fraction (HFpEF)
- This systematic review investigated the effectiveness of SGLT-2is as a potential treatment for HFpEF, regardless of a patient's diabetic status

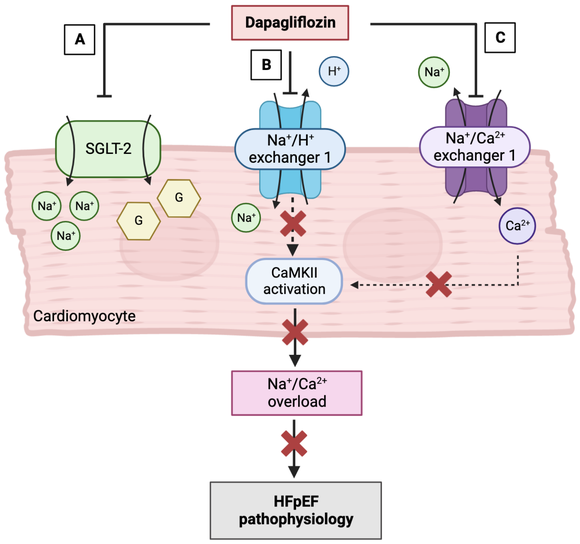

Figure 1. *Mechanism of action of Dapagliflozin.*

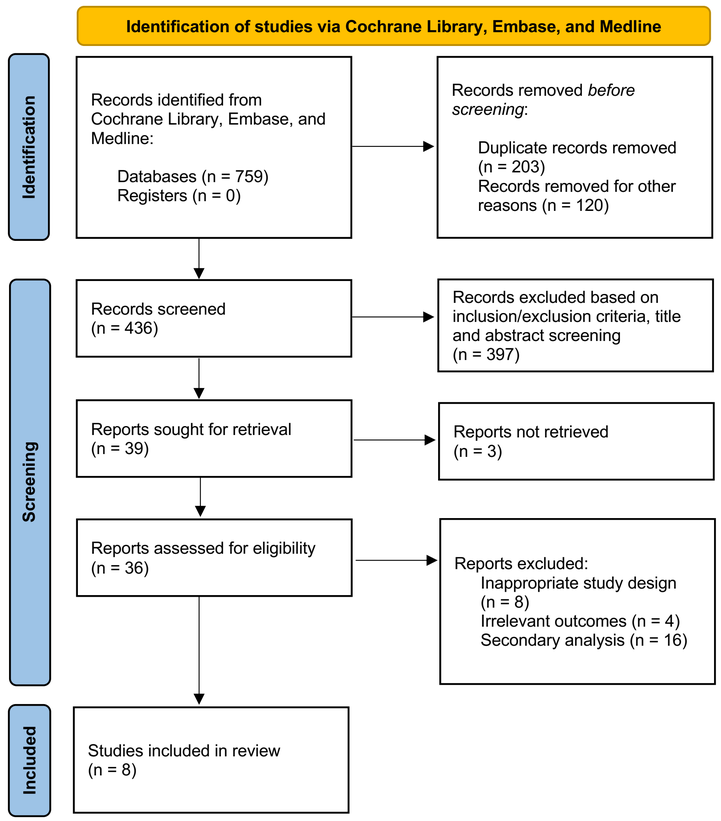

Figure 2. *PRISMA flow diagram of the screening process.*

Results

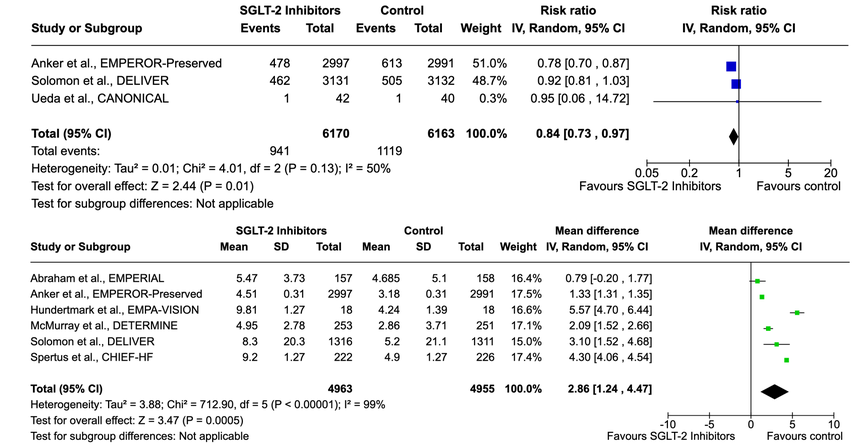

Figure 3. *Forest plots of trials that investigated CV death or HF hospitalisations (**A**) and KCCQ-TSS (**B**) in HFpEF patients treated with SGLT-2is or placebo.*

Author and Trial	Intervention	Intervention Mean Distance (m)	Placebo Mean Distance (m)	Mean Difference (m) (95% CI)
Abraham et al. (2021), EMPERIAL-Preserved	Empagliflozin	10.50±7.95 (n = 157)	5.75±10.0 (n = 158)	4.75(2.76-6.74)
McMurray et al. (2023), DETERMINE	Dapagliflozin	10.0±9.25 (n = 253)	9.50±8.90 (n = 251)	0.50(-1.08-2.08)
Nassif et al. (2021), PRESERVED-HF	Dapagliflozin	16.50±2.44 (n = 162)	2.25±2.24 (n = 162)	14.25(13.72-14.78)

Table 2. *Summary of 6MWTD. Mean distances reported as the mean change from baseline to the endpoints of each study ± SD, m: metres.*

- Figure 3A shows a significant reduction that was observed in CV death or HHF for patients administered with SGLT-2is
- HHF reduced significantly for patients treated with SGLT-2is (P=0.003)
- SGLT-2is improved KCCQ-TSS (Figure 3B) but did not improve 6MWT distances (P=0.19)

Methods

Database	Search Strategy	Search Results
Cochrane Library	(HFpEF **OR** Heart Failure with Preserved Ejection Fraction **OR** Diastolic Heart Failure) **AND** (SGLT-2 Inhibitors **OR** Empagliflozin **OR** Canagliflozin **OR** Dapagliflozin OR Ertugliflozin) **AND** (RCT **OR** RCTs **OR** Randomised **OR** Randomized **OR** Placebo **OR** Controlled Clinical Trial **OR** Randomised Control Trial **OR** Double Blinding **OR** Double Blind Trial)	160
Embase		467
PubMed/Medline		132

Table 1. *Summary of the databases, search strategies, and outcomes for data collection. Searches were conducted on Ovid Online.*

- PICOS formulated:
  - **Population**: HFpEF Patients
  - **Intervention**: SGLT-2is
  - **Comparator**: placebo / standard diabetic treatment
  - **Outcomes**: CV death, HF hospitalisations, all-cause mortality, KCCQ-TSS, 6MWTD
  - **Study Design**: any study excluding SRs
- Meta-analysis of 13,950 participants using random effects model was performed to calculate mean difference with inverse variance at 95% CI

Conclusions

Dapagliflozin, empagliflozin and canagliflozin reduced the rate of HF hospitalisations and improved the quality of life of patients with HFpEF, supporting the use of SGLT-2 inhibitors as the primary treatment for HFpEF. This discovery will aid the development of novel therapeutics that target the pathophysiology of HFpEF.