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Navigating Therapeutic Choice Within a Class: SGLT2 Inhibitor Practice Patterns Across Cardiovascular Indications

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ABSTRACT

Background: Sodium–glucose cotransporter-2 inhibitors (SGLT2i) have evolved from glucose-lowering therapies to integral agents in cardiovascular and renal disease management. However, factors influencing physician selection within this therapeutic class remain incompletely understood. This study evaluated cardiologist prescribing preferences regarding SGLT2 inhibitor use across cardiovascular indications.
Methods: A cross-sectional survey was conducted among cardiologists attending the Cardiological Society of India conference. An 11-item structured questionnaire assessed prescribing patterns, decision drivers, and perceptions of comparative efficacy and safety across cardiovascular, renal, and heart failure scenarios. Participation was voluntary and anonymous. Responses from 100 cardiologists were analysed descriptively and reported as percentages.
Results: Empagliflozin was preferred in routine practice by 51% of respondents compared with 27% favouring dapagliflozin, while 17% reported equivalence, suggesting variability in therapeutic selection. Cardiovascular mortality reduction was the leading decision driver (42%), followed by major adverse cardiovascular event reduction and heart failure hospitalization reduction (31% each). In CKD without diabetes, 40% preferred empagliflozin, 24% dapagliflozin, and 28% reported equivalence; confidence in low eGFR settings favored empagliflozin in 53% of responses. In HFpEF, symptomatic benefit was attributed to empagliflozin by 39%, dapagliflozin by 18%, and 39% reported similar benefit, reflecting mixed perceptions of class effects. For ASCVD secondary prevention, empagliflozin was preferred by 45% versus 17%, and 67% favoured it when early post-MI initiation was considered. Safety perceptions were similar between agents.
Conclusion: Cardiologist prescribing preferences for SGLT2 inhibitors appear shaped by interpretation of outcome evidence and clinical context rather than uniform differentiation within the class. Continued comparative research and balanced dissemination of evidence may enhance consistency in therapeutic positioning and translation of trial findings into practice. These findings reflect perception-based preferences rather than comparative clinical efficacy

Keywords: SGLT2 inhibitors; Cardiovascular outcomes; Heart failure; chronic kidney disease; Prescribing patterns

INTRODUCTION

Sodium–glucose cotransporter-2 inhibitors (SGLT2i) have emerged as a pivotal therapeutic class in cardiometabolic medicine, demonstrating benefits that extend beyond glycemic control. Advances in medicinal chemistry led to selective synthetic SGLT2 inhibitors and their subsequent clinical translation, culminating in regulatory approvals and large-scale outcome trials establishing their therapeutic value [1,2].

Mechanistically, SGLT2 inhibition blocks renal proximal tubular glucose reabsorption, inducing glucosuria and natriuresis. These actions lead to hemodynamic and metabolic effects including plasma volume reduction, improved endothelial function, decreased ventricular preload and afterload, increased hematocrit through erythropoietin signaling, and favorable impacts on weight and glycemic control [3-5]. Such pleiotropic physiological effects are thought to underpin improvements in cardiac loading conditions and cardiometabolic outcomes.

Reflecting this evolving evidence base, contemporary European Society of Cardiology (ESC) guidelines recommend SGLT2 inhibitors, including empagliflozin or dapagliflozin, as Class I therapy in symptomatic heart failure across both reduced and preserved ejection fraction categories to reduce hospitalization and cardiovascular mortality risk [6]. These recommendations underscore their incorporation as foundational components of heart failure management independent of diabetes status.

Few comparative clinical data have evaluated differences within the drug class. A prospective observational study reported that both empagliflozin and dapagliflozin improved glycemic control and cardiometabolic parameters over 52 weeks in patients with inadequately controlled type 2 diabetes, with some analyses suggesting modestly greater metabolic improvement with empagliflozin [7]. Additional comparative analyses have similarly shown meaningful HbA1c reductions across SGLT2 inhibitors, reinforcing shared class effects on metabolic outcomes [8]. Notably, certain comparative evaluations have reported statistically greater HbA1c reductions with empagliflozin compared with dapagliflozin [9]. These differences were generally modest in magnitude. Overall findings across studies continue to support broadly comparable glycemic efficacy within the SGLT2 inhibitor class.

Randomized cardiovascular outcome trials over the past decade have substantially broadened the clinical scope of SGLT2 inhibitors. Studies such as EMPA-REG OUTCOME, CANVAS, DECLARE-TIMI 58, and VERTIS-CV demonstrated cardiovascular safety and event reduction among patients with type 2 diabetes and elevated cardiovascular risk [10]. Dedicated heart failure and renal outcome trials further expanded their role, with DAPA-HF and EMPEROR-Reduced showing reductions in hospitalization for heart failure and cardiovascular death in reduced ejection fraction populations [11], and EMPEROR-Preserved and DELIVER confirming benefit across preserved ejection fraction phenotypes [12]. Collectively, these findings repositioned SGLT2 inhibitors as cardioprotective and reno protective therapies rather than purely glucose-lowering agents.

Despite the extensive clinical evidence and guideline integration, real-world physician preferences and perceptions regarding SGLT2 inhibitor selection across cardiovascular and renal contexts remain insufficiently characterized. The present survey was therefore undertaken to assess cardiologist preferences regarding SGLT2 inhibitor use across diverse clinical scenarios

MATERIALS & METHODS

This cross-sectional survey-based study was conducted to evaluate cardiologists' prescribing preferences and perceptions regarding SGLT2 inhibitors. The survey was administered among cardiologists attending the Cardiological Society of India

(CSI) conference. Participation was voluntary and anonymous, and responses were collected at a single time point. A total of 100 practicing cardiologists completed the questionnaire and were included in the analysis.

A structured questionnaire comprising 11 multiple-choice questions was developed to assess clinical decision-making across cardiovascular, renal, and metabolic scenarios relevant to SGLT2 inhibitor use. The questionnaire focused on routine prescribing patterns, factors influencing therapeutic choice, and perceptions of comparative efficacy and safety between empagliflozin and dapagliflozin.

Responses were collected and tabulated as absolute counts and percentages. Descriptive statistical analysis was performed to summarize cardiologist preferences across the different clinical domains. Ethical approval was not required because the survey did not involve any patient data.

RESULT

A total of 100 cardiologists participated in the survey evaluating clinical preferences and perceptions regarding SGLT2 inhibitors

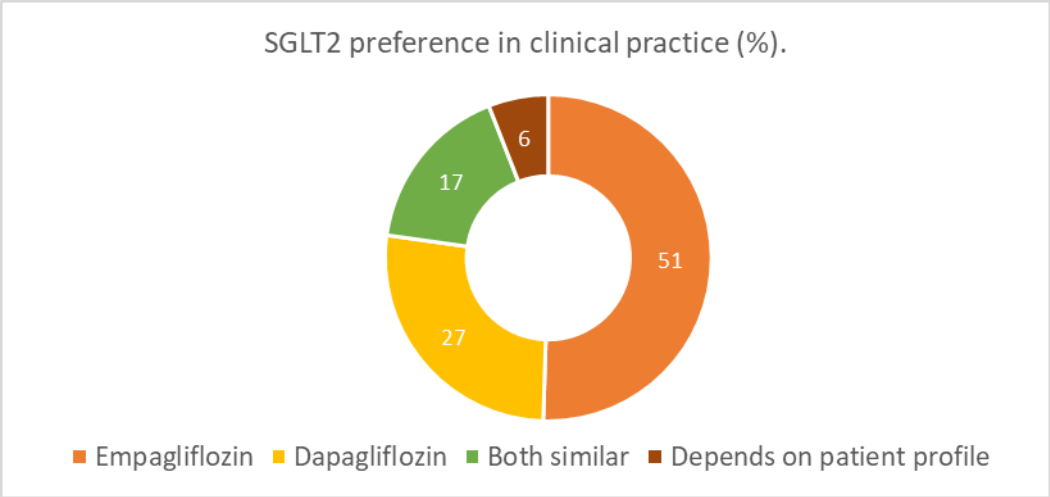
1. General prescribing patterns and perceptions

In routine clinical practice, empagliflozin was preferred by 51% of respondents compared with 27% preferring dapagliflozin, while 17% considered both similar and 6% based their choice on patient profile (Figure1). When selecting therapy based on cardiovascular outcomes, the most influential factor was evidence for reduction in cardiovascular death (42%), followed by major adverse cardiovascular event reduction (31%), reduction in heart failure hospitalization (31%), renal outcomes (20%), and cost considerations (8%). The results indicate that prescribing behavior is largely influenced by outcome-driven evidence, particularly cardiovascular mortality reduction, which may explain observed preference patterns. Furthermore, clinicians appear to prioritize clinically meaningful endpoints such as MACE and heart failure hospitalization over cost-related factors when choosing therapy.

Regarding safety perceptions, 42% reported similar rates of urinary tract or genital infections between agents, whereas 36% perceived higher rates with dapagliflozin and 12% with empagliflozin; 8% had not observed differences clinically. Additionally, 42% believed empagliflozin had broader evidence across the ejection fraction spectrum compared with 30% favoring dapagliflozin and 21% considering both similar. When asked how important the reported all-cause mortality reduction with empagliflozin was in influencing choice between empagliflozin and dapagliflozin, the majority of cardiologists considered it very important (53%) or important (29%), whereas 13% were neutral and none regarded it as less or not important; 2% provided other responses. The results indicate that safety considerations are unlikely to be a major differentiating factor in drug selection, with most clinicians recognizing class-wide tolerability.

In contrast, perceived strength of evidence and mortality benefit appear to be dominant drivers of decision-making, underscoring the influence of outcome-focused data on prescribing behavior.

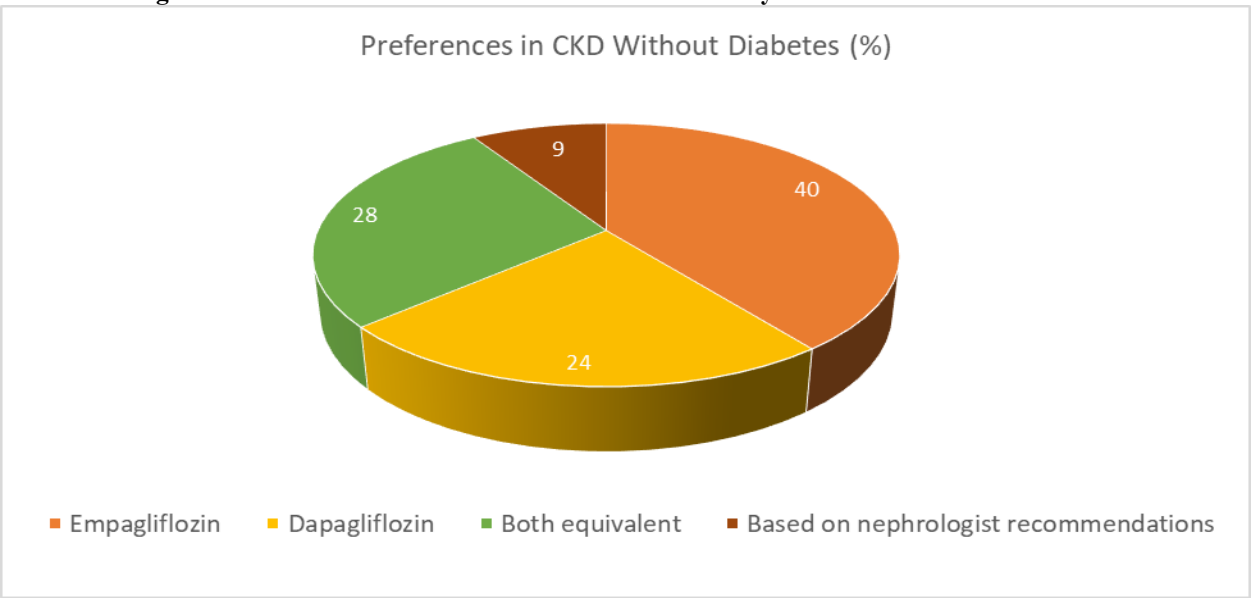
Figure 1: Cardiologist Preferences for SGLT2 Inhibitors in Routine Practice



2. Chronic Kidney Disease (CKD)–related responses

Among patients with CKD without diabetes, empagliflozin was preferred by 40% of cardiologists, dapagliflozin by 24%, and 28% considered both equivalent, while 9% based decisions on nephrologist recommendations (Figure 2). In patients with low estimated glomerular filtration rate, 53% expressed greater trust in empagliflozin compared with 19% for dapagliflozin, with 19% reporting equal confidence and 9% indicating dependence on CKD stage. The results indicate heterogeneity in clinician confidence toward SGLT2 inhibitor selection in CKD, especially in advanced renal impairment, reflecting differing interpretations of available evidence as well as clinical experience. At the same time, reliance on individualized and multidisciplinary decision-making underscores the complexity of therapy selection in cardiorenal care.

Figure 2: Preferred SGLT2 Inhibitor in Chronic Kidney Disease Without Diabetes

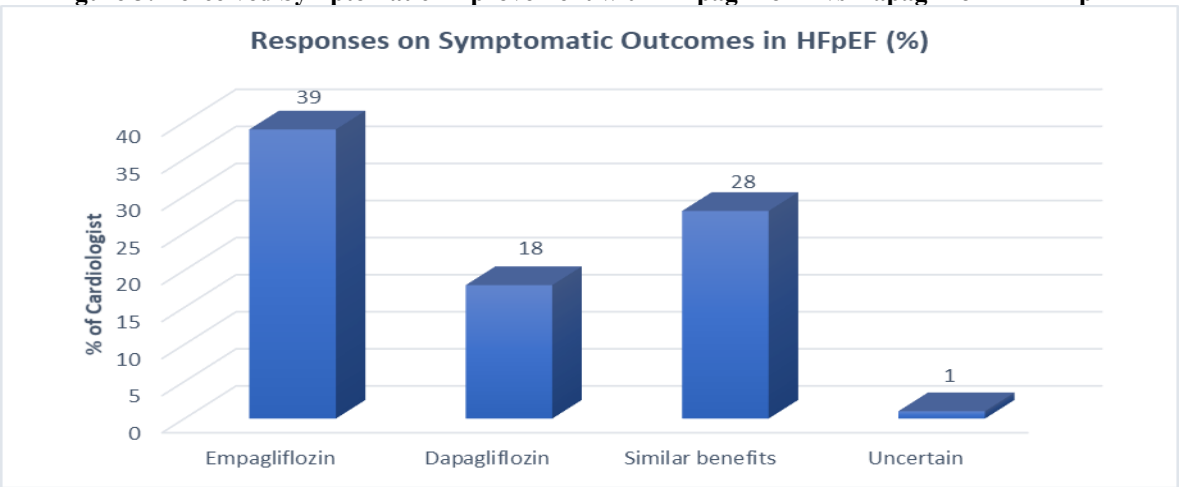


3. Heart Failure and LV remodeling- –related responses

In heart failure with preserved ejection fraction, symptomatic improvement was attributed to empagliflozin by 39% of respondents and dapagliflozin by 18%, whereas 39% reported similar benefits and 1% were uncertain. (Figure 3) Regarding

structural cardiac effects, 55% believed empagliflozin demonstrated superior left ventricular remodeling compared with 15% selecting dapagliflozin and 24% considering both equivalent. These findings suggest perceived variability in symptomatic and structural benefits among SGLT2 inhibitors in HFpEF, although many clinicians recognize comparable class effects. Responses indicate that clinical judgment and interpretation of evidence continue to shape decision-making in heart failure management.

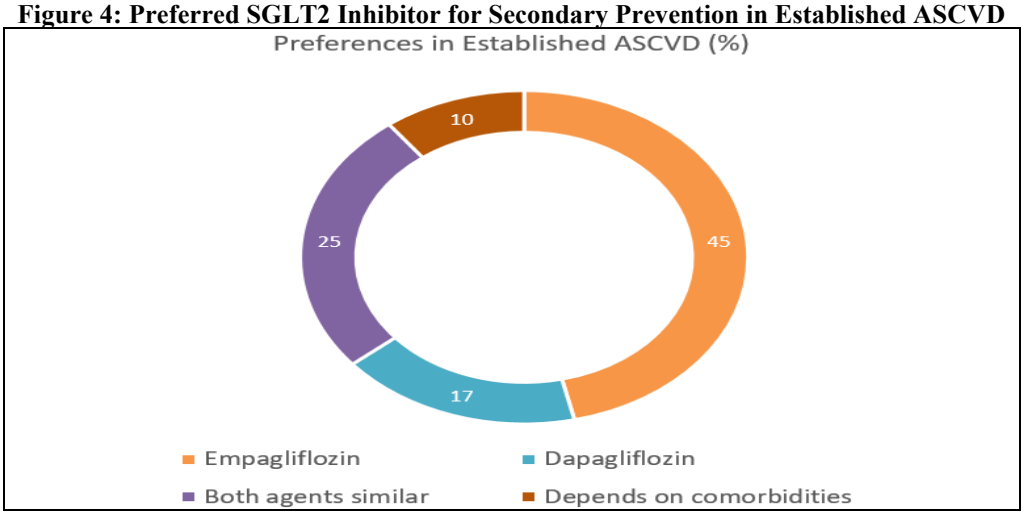
Figure 3: Perceived Symptomatic Improvement with Empagliflozin vs Dapagliflozin in HFpEF



4. Coronary Artery Disease (CAD) – related responses

For secondary prevention in established ASCVD, empagliflozin was preferred by 45% of respondents compared with 17% favoring dapagliflozin, while 25% considered both agents similar and 10% based their choice on comorbidities (Figure 4). Furthermore, awareness that empagliflozin could be initiated early after myocardial infarction influenced prescribing preference, with 67% favoring empagliflozin compared with 15% favoring dapagliflozin and 15% reporting no difference. These findings suggest that therapeutic selection in secondary prevention is influenced by perceptions of early initiation feasibility and clinical context. The variability in responses further highlights the role of patient comorbidity profiles and clinician interpretation of evidence in guiding SGLT2 inhibitor choice.

Figure 4: Preferred SGLT2 Inhibitor for Secondary Prevention in Established ASCVD



DISCUSSION

This survey provides insights from cardiologist prescribing perspectives regarding SGLT2 inhibitors, revealing preference patterns that appear aligned with evolving clinical evidence across cardiovascular, renal, and heart failure domains. Respondents favored empagliflozin in several clinical scenarios, particularly in secondary prevention, low estimated glomerular filtration rate settings, and heart failure contexts, while also acknowledging class equivalence in selected outcomes. These findings reflect the interplay between landmark trial familiarity, guideline integration, and real-world interpretation of comparative effectiveness data. no randomized head-to-head cardiovascular outcome trial has demonstrated superiority of one SGLT2 inhibitor over another. Observed differences across trials largely reflect variation in study populations and design rather than intrinsic pharmacologic divergence. Notably, no randomized head-to-head cardiovascular outcome trial has demonstrated superiority of one SGLT2 inhibitor over another.

Large cardiovascular outcome trials established the cardioprotective profile of SGLT2 inhibitors and significantly shaped clinician confidence. The EMPA-REG OUTCOME trial demonstrated that empagliflozin reduced cardiovascular death, hospitalization for heart failure, and major adverse cardiovascular events (MACE) in patients with type 2 diabetes and established cardiovascular disease [1]. Conversely, the DECLARE-TIMI 58 trial showed dapagliflozin reduced heart failure hospitalization and renal composite outcomes, although effects on MACE were comparatively modest in a broader and lower-risk population [10].

Heart failure outcome trials further reinforced the therapeutic importance of SGLT2 inhibition. In patients with reduced ejection fraction, dapagliflozin and empagliflozin demonstrated nearly identical reductions in cardiovascular death or first hospitalization for heart failure, with hazard ratios approximating 0.75 in both the DAPA-HF and EMPEROR-Reduced trials, supporting class-wide efficacy [13,14]. Evidence subsequently expanded to preserved ejection fraction populations, where DELIVER and EMPEROR-Preserved showed consistent reductions in composite cardiovascular endpoints and pooled analyses confirmed approximately 20–25% relative reductions in heart failure hospitalization across left ventricular ejection fraction strata [15,16]. These robust findings underpin contemporary guideline recommendations positioning SGLT2 inhibitors as foundational therapy across the ejection fraction spectrum irrespective of diabetes status, and they likely contributed to the high confidence reported by respondents regarding their use in heart failure management.

Comparative effectiveness data provide additional nuance to clinician perception. Meta-analytic evidence comparing empagliflozin and dapagliflozin across large populations has demonstrated no statistically significant differences in major adverse cardiovascular events (MACE), myocardial infarction, stroke, or all-cause mortality. These findings support the presence of a class effect of SGLT2 inhibitors for atherosclerotic cardiovascular protection. This evidence is reported in Dhana R, et al [17]. However, observational registry and subgroup analyses have reported signals suggesting lower hospitalization or event rates with empagliflozin in selected patient groups, including individuals with heart failure, potentially influencing prescribing behavior despite inherent limitations of nonrandomized data interpretation [18]. Such signals emphasize how emerging real-world evidence may shape perception even when randomized comparisons demonstrate equivalence.

Timing of therapy initiation also appears to influence prescribing preference. Recent investigations evaluating early post-myocardial infarction initiation have demonstrated feasibility of empagliflozin

initiation within 24-72 days following acute coronary events, with early signals toward reduced heart failure–related outcomes, whereas dapagliflozin evidence has generally involved later initiation windows in 7-10 days [19-21]. These differences reflect variation in evidence generation timelines rather than mechanistic divergence, yet may contribute to clinician perception favoring certain agents in acute cardiovascular contexts, as reflected in survey responses.

Renal outcome considerations also play an important role in therapeutic selection. SGLT2 inhibitors have demonstrated consistent nephroprotective effects across cardiovascular outcome trials and dedicated kidney studies through mechanisms including restoration of tubuloglomerular feedback and reduction in intraglomerular pressure. [3][22-24] Although class benefits appear consistent, heterogeneity in trial populations and inclusion thresholds across studies may influence physician interpretation and confidence in specific clinical scenarios. These contextual factors align with survey findings indicating differential preference patterns despite broadly comparable evidence supporting renal protection.

Safety perceptions reported by respondents were largely concordant with established clinical evidence demonstrating favorable tolerability profiles across the class. Both empagliflozin and dapagliflozin exhibit low rates of serious adverse events, and genitourinary infections remain manageable and predictable class effects related to glucosuria. [24-27] Comparative analyses suggest broadly similar safety profiles, with some observational data reporting slightly lower infection incidence with empagliflozin in specific cohorts [8]. These findings correspond with the survey observation that most clinicians perceived minimal safety differentiation between agents.

Collectively, the present findings illustrate how prescribing patterns among cardiologists reflect a combination of guideline-supported class benefits and exposure to influential landmark trials. While the totality of evidence consistently demonstrates comparable efficacy between agents across cardiovascular and heart failure outcomes, differential familiarity with trial data, subgroup signals, and early initiation studies appears to shape clinical perception and therapeutic preference. Understanding these behavioral drivers is important for contextualizing real-world prescribing patterns and ensuring alignment between clinical practice and comprehensive interpretation of evidence.

Continued dissemination of comparative randomized and real-world research will be essential to refine therapeutic positioning within the class. Future head-to-head trials and harmonized outcome analyses may further clarify whether perceived differences represent meaningful pharmacologic divergence or cognitive bias driven by historical exposure to specific datasets. Ultimately, integrating evolving evidence with clinician education may enhance consistency in treatment selection and optimize cardiometabolic outcomes across diverse patient populations.

CONCLUSION

This survey highlights contemporary cardiologist perspectives on SGLT2 inhibitor use across cardiovascular, renal, and metabolic indications. Prescribing trends appear to be shaped by interpretation of outcome data, guideline alignment, and individual clinical experience. Although many respondents recognized class-wide efficacy and safety, empagliflozin was more commonly preferred in specific clinical contexts, likely reflecting perceived strength of supporting evidence. These findings emphasize the influence of clinical familiarity and real-world decision-making in therapeutic selection. Importantly, adequately powered head-to-head randomized controlled trials are necessary to further clarify comparative effectiveness and validate whether observed preference

patterns translate into meaningful differences in patient outcomes.

Declaration by Authors:

Ethical Approval: Not applicable

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