

## Real-World Data on the Use of SGLT2 Inhibitors in Heart Failure: Efficacy and Safety across Diverse Populations

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### Abstract

This article explores the real-world evidence on the utilization of sodium-glucose co-transporter 2 (SGLT2) inhibitors in the management of heart failure (HF), focusing on their efficacy and safety profiles across diverse patient populations. While randomized controlled trials have established the cardiovascular benefits of SGLT2 inhibitors, real-world data offer insights into their effectiveness and safety in routine clinical practice. Analysis of electronic health records, administrative claims databases, and other sources reveals consistent reductions in heart failure hospitalizations and cardiovascular mortality with SGLT2 inhibitor use. Importantly, these benefits extend across various subgroups, including elderly patients, individuals with comorbidities such as diabetes mellitus and chronic kidney disease, and diverse racial and ethnic backgrounds. Safety assessments underscore a favorable risk-benefit profile, with low incidences of serious adverse events. Overall, real-world evidence supports the integration of SGLT2 inhibitors into the treatment armamentarium for heart failure, emphasizing the need for personalized approaches to optimize patient outcomes.

**Keywords:** SGLT2 inhibitors; Heart failure; Real-world evidence; Efficacy; Safety; Diverse populations; Cardiovascular outcomes; Diabetes mellitus; Chronic kidney disease; Personalized medicine

### Introduction

Heart failure (HF) is a prevalent and debilitating condition that affects millions of people worldwide, imposing a substantial burden on both patients and healthcare systems. In recent years, the therapeutic landscape for heart failure has evolved significantly, with the emergence of sodium-glucose co-transporter 2 (SGLT2) inhibitors as a promising treatment option. Real-world evidence (RWE) plays a crucial role in complementing clinical trial data by providing insights into the effectiveness and safety of medications in diverse patient populations under routine clinical practice. This article delves into the real-world data on the use of SGLT2 inhibitors in heart failure, highlighting their efficacy and safety profiles across diverse populations [1].

### Understanding SGLT2 inhibitors

SGLT2 inhibitors, originally developed as antidiabetic agents, have garnered considerable attention for their cardiovascular benefits beyond glucose-lowering effects. These medications exert their therapeutic effects by inhibiting SGLT2 in the proximal renal tubules, thereby promoting glycosuria and natriuresis, leading to reductions in blood glucose levels, blood pressure, and body weight. Moreover, SGLT2 inhibitors have demonstrated remarkable cardiorenal protective effects, including a reduction in the risk of heart failure hospitalization and cardiovascular mortality, as evidenced by large-scale clinical trials such as EMPA-REG OUTCOME, DECLARE-TIMI 58, and DAPA-HF.

### Real-world evidence

While randomized controlled trials (RCTs) provide valuable insights into the efficacy and safety of medications under controlled settings, they often have strict eligibility criteria and may not fully represent real-world patient populations. Real-world evidence supplements these findings by evaluating the outcomes of treatments in broader and more diverse patient cohorts encountered in routine clinical practice. By analyzing data from electronic health records, administrative claims databases, and other sources, researchers can assess the effectiveness, safety, and healthcare utilization patterns

associated with SGLT2 inhibitors in real-world settings [2].

### Efficacy across diverse populations

Real-world data have consistently supported the efficacy of SGLT2 inhibitors in reducing the risk of heart failure events and improving clinical outcomes across diverse patient populations. Studies have demonstrated significant reductions in hospitalizations for heart failure, cardiovascular mortality, and all-cause mortality among patients with heart failure with reduced ejection fraction (HFrEF) treated with SGLT2 inhibitors. Importantly, these benefits have been observed across various subgroups, including elderly patients, those with comorbidities such as diabetes mellitus and chronic kidney disease, and individuals from different racial and ethnic backgrounds.

### Safety considerations

In addition to efficacy, real-world evidence provides valuable insights into the safety profile of SGLT2 inhibitors. While clinical trials have established a favorable safety profile for these medications, real-world data offer insights into the occurrence of rare or long-term adverse events that may not have been captured in RCTs. Common adverse events associated with SGLT2 inhibitors include genital mycotic infections, urinary tract infections, and volume depletion-related events such as hypotension and dehydration. However, the overall incidence of serious adverse events remains low, and the cardiorenal benefits of SGLT2 inhibitors outweigh the risks for most patients [3].

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## Implications for clinical practice

The real-world evidence supporting the use of SGLT2 inhibitors in heart failure has significant implications for clinical practice. Healthcare providers should consider incorporating these agents into the treatment regimens of patients with HFrEF, especially those with concomitant diabetes mellitus or chronic kidney disease, given their proven efficacy and favorable safety profile. Moreover, clinicians should be aware of the potential benefits of SGLT2 inhibitors across diverse patient populations and strive to optimize treatment strategies to improve outcomes in real-world settings [4].

## Materials and Methods

**Data Sources:** Utilization of real-world data necessitates access to diverse sources, including electronic health records (EHRs), administrative claims databases, and disease registries. These sources provide comprehensive information on patient demographics, clinical characteristics, medication use, healthcare utilization, and outcomes [5].

**Study Design:** Observational studies, including retrospective cohort studies and prospective observational analyses, are commonly employed to assess the effectiveness and safety of SGLT2 inhibitors in heart failure across diverse populations. Propensity score matching and inverse probability weighting techniques may be used to minimize selection bias and confounding in observational analyses.

**Population Selection:** The study population comprises patients with heart failure, including those with reduced ejection fraction (HFrEF) or preserved ejection fraction (HFpEF), who have been prescribed SGLT2 inhibitors. Patients with comorbidities such as diabetes mellitus, chronic kidney disease, and cardiovascular diseases are included to reflect real-world clinical practice [6].

**Exposure and Outcome Definition:** Exposure to SGLT2 inhibitors is defined based on medication dispensing records or prescription data, utilizing drug codes and dispensing dates. The primary outcomes of interest include heart failure hospitalizations, cardiovascular mortality, all-cause mortality, and adverse events associated with SGLT2 inhibitor use [7].

**Statistical Analysis:** Descriptive statistics are employed to characterize the study population, including demographics, clinical characteristics, and baseline comorbidities. Comparative analyses, such as incidence rates and hazard ratios, are used to assess outcomes between SGLT2 inhibitor users and non-users. Subgroup analyses based on age, sex, race/ethnicity, and comorbid conditions are conducted to evaluate treatment effects across diverse populations [8].

**Sensitivity Analyses:** Sensitivity analyses are performed to assess the robustness of study findings, including alternate exposure definitions, adjustment for additional confounders, and assessment of residual confounding.

**Ethical Considerations:** Institutional review board approval and adherence to data privacy regulations are essential to ensure the ethical conduct of real-world studies. Measures to protect patient confidentiality and data security are implemented throughout the study process [9].

**Limitations:** Recognizing the inherent limitations of observational studies, including potential confounding and bias, is crucial. Efforts to address these limitations through rigorous study design, sensitivity analyses, and cautious interpretation of findings are integral to ensuring

the validity and reliability of study results.

By employing rigorous methodological approaches, real-world studies provide valuable insights into the effectiveness and safety of SGLT2 inhibitors in heart failure management across diverse patient populations encountered in routine clinical practice [10].

## Discussion:

Real-world data on the use of sodium-glucose co-transporter 2 (SGLT2) inhibitors in heart failure (HF) provide valuable insights into their effectiveness and safety profiles across diverse patient populations encountered in routine clinical practice. The discussion of these findings encompasses several key points:

**Consistency with Clinical Trial Evidence:** The observed reductions in heart failure hospitalizations and cardiovascular mortality among SGLT2 inhibitor users in real-world studies are consistent with findings from landmark clinical trials such as EMPA-REG OUTCOME, DECLARE-TIMI 58, and DAPA-HF. This consistency underscores the robustness of SGLT2 inhibitor benefits across different study settings and patient populations.

**Generalizability to Diverse Populations:** Real-world evidence demonstrates the effectiveness of SGLT2 inhibitors across diverse patient populations, including elderly patients, individuals with comorbidities such as diabetes mellitus and chronic kidney disease, and various racial and ethnic backgrounds. These findings highlight the generalizability of SGLT2 inhibitor benefits beyond select patient groups included in clinical trials.

**Potential Mechanisms of Benefit:** While the precise mechanisms underlying the cardiorenal protective effects of SGLT2 inhibitors remain under investigation, real-world data offer insights into potential mechanisms of benefit. Beyond their glucose-lowering effects, SGLT2 inhibitors may exert favorable effects on cardiac remodeling, myocardial energetics, and renal function, contributing to their observed reductions in heart failure events and mortality.

**Safety Considerations:** Real-world studies provide reassurance regarding the safety profile of SGLT2 inhibitors in routine clinical practice. While concerns have been raised regarding potential adverse events such as genital mycotic infections and volume depletion-related events, the overall incidence of serious adverse events remains low, with the cardiorenal benefits of SGLT2 inhibitors outweighing the risks for most patients.

**Implications for Clinical Practice:** The robust efficacy and safety profile of SGLT2 inhibitors demonstrated in real-world studies have significant implications for clinical practice. Healthcare providers should consider incorporating these agents into the treatment regimens of patients with heart failure, especially those with concomitant diabetes mellitus or chronic kidney disease, to optimize outcomes and reduce the burden of heart failure-related hospitalizations and mortality.

**Need for Personalized Medicine:** While SGLT2 inhibitors offer substantial benefits across diverse patient populations, individualized treatment approaches are essential to account for patient-specific factors such as age, comorbidities, medication tolerability, and preferences. Clinicians should engage in shared decision-making with patients to tailor treatment strategies and optimize outcomes in real-world settings.

**Future Directions:** Ongoing research efforts are needed to further elucidate the long-term effects of SGLT2 inhibitors in diverse patient

populations and explore potential predictors of treatment response. Additionally, comparative effectiveness studies and real-world analyses of combination therapies may provide insights into optimal treatment strategies for patients with heart failure.

### Conclusion:

Real-world data on the use of SGLT2 inhibitors in heart failure provide compelling evidence of their efficacy and safety across diverse patient populations encountered in routine clinical practice. By supplementing findings from clinical trials, real-world evidence enhances our understanding of the real-world effectiveness and safety of these medications, thereby informing clinical decision-making and optimizing patient care. As the therapeutic landscape continues to evolve, ongoing research and surveillance efforts are essential to further elucidate the role of SGLT2 inhibitors in the management of heart failure and improve outcomes for patients worldwide.

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