Assessing factors associated with SGLT2i initiation in a contemporary cohort of newly-diagnosed heart failure patients from the United States

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BACKGROUND

- Since February 2022, sodium–glucose cotransporter 2 inhibitors (SGLT2i) have been approved for the treatment of heart failure (HF) across the full spectrum of left ventricular ejection fractions (LVEF).
- This follows earlier approvals of dapaglifozin (May 2020) and empaglifozin (Aug 2021) for the treatment of HFrEF, and for adults with type 2 diabetes (T2D) or chronic kidney disease (CKD) (**Fig. 1**).
- In the 2022 AHA/ACC/HFSA Guidelines for the Management of HF, dapaglifozin and empaglifozin have a class 1 recommendation in HFrEF, and class 2a recommendation in HFmrEF and HFpEF.
- This study identified factors associated with SGLT2i initiation in a contemporary cohort of US patients with newly-diagnosed HF.

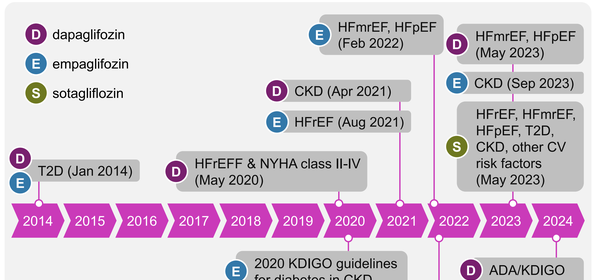

Fig. 1. FDA approvals (shown above timeline) and guideline recommendations (shown below timeline) for use of SGLT2i in adults.
ADA, American Diabetes Association; KDIGO, Kidney Disease Improving Global outcomes

METHODS

- We conducted a retrospective cohort study using Optum® de-identified Electronic Health Records (EHRs).
- We included adults with a first inpatient or outpatient HF diagnosis (ICD-10 codes) from Jan 2020 to Dec 2023 and ≥1 LVEF measurement within ±90 days of the first HF diagnosis. The index date was the date of the first HF code or index LVEF measurement, whichever came second.
- We excluded patients with <365 days' continuous baseline (pre-index) data, and those with a prior record of heart transplant or durable ventricular assist device (VAD) use (**Fig. 2**).
- Since we sought to evaluate factors associated with initiation of SGLT2i, we restricted our cohort to those who were naïve to SGLT2i, and had 6 months' available follow-up data.
- Patient characteristics were assessed at index or during the 365-day pre-index (baseline) period. Patients were observed from index to censorship (e.g. death, code for heart transplant, or durable VAD insertion, or end of the study period [31 Dec 2023]).
- Multivariable logistic regression was used to assess factors associated with SGLT2i initiation in treatment-naïve patients, including socio-demographics and comorbidities. Univariate analysis was used to select covariates for the final multivariate model. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) are reported.

RESULTS

Baseline characteristics

- A total of 161,376 newly-diagnosed HF patients, naïve to SGLT2i, were included in the study cohort. LVEF subtype distribution was: 25.9% HFrEF, 12.4% HFmrEF, 61.8% HFpEF.
- Median (Q1, Q3) age of patients at index was 71 (61, 80) years and 47% were female. Race distribution was: 79% White, 15% Black, 2% Asian, 5% unknown.
- Only 6% (n=9099) of the cohort initiated an SGLT2i within 6 months of HF diagnosis.

Factors associated with higher odds of SGLT2i initiation

- The most pronounced factors associated with higher odds of SGLT2i initiation were later index year (adj. OR 2.48 [95% CI: 2.42, 2.54] per calendar year later), living in the West (adj. OR 1.99 [95% 1.82, 2.18]), and T2D (adj. OR 2.82 [95% CI: 2.68, 2.97]) (**Fig. 3**).
- Other factors associated with higher odds of SGLT2i initiation were being obese, overweight, or Black/Asian, valvular heart disease, coronary artery disease, hypertension, and dyslipidemia (**Fig. 3**).

Factors associated with lower odds of SGLT2i initiation

- The strongest factors associated with lower odds of SGLT2i initiation were having HFmrEF or HFpEF (vs. HFrEF) (adj. OR 0.38 [95% CI: 0.34, 0.42] and 0.17 [95% CI: 0.16, 0.18] respectively), CKD stage 4 (adj. OR 0.54 [95% CI: 0.47, 0.61]), CKD stage 5 (adj. OR 0.05 [95% CI: 0.04, 0.08]), and dementia (adj. OR 0.54 [95% CI: 0.47, 0.61]) (**Fig. 3**).
- Other factors associated with lower odds of SGLT2i initiation were older age, being female or uninsured, being insured under Medicare (only), living in the South, and having anemia (**Fig. 3**).

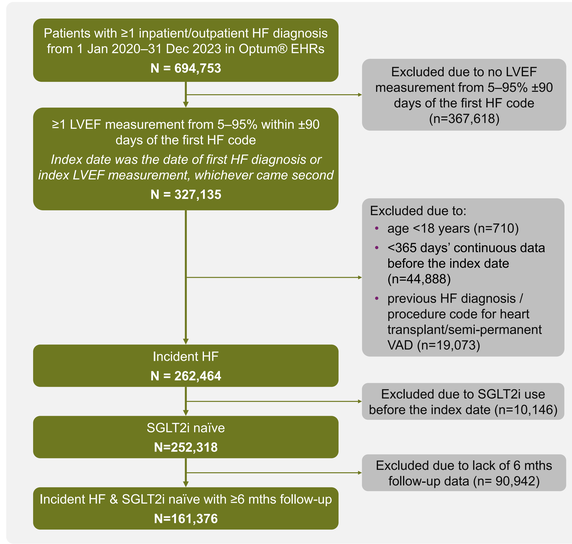

Fig. 2. Patient attrition chart for cohort of SGLT2i-naïve patients with newly-diagnosed HF.

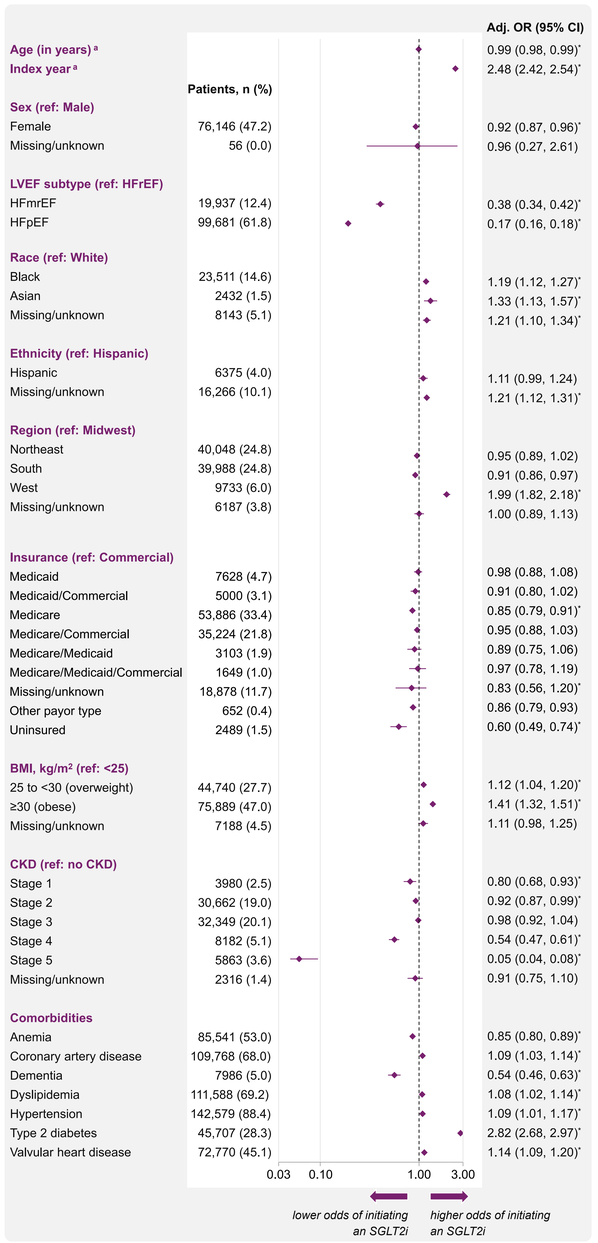

Fig. 3. Factors associated with initiation of an SGLT2i in the first 6 months after HF diagnosis. [a]Modelled as a continuous variable. *p-value <0.05

Time to treatment initiation

- Among patients who initiated an SGLT2i during follow-up, the median (Q1, Q3) time to treatment initiation was 23 (3, 82) days.
- Patients with HFrEF initiated treatment earlier than those with HFmrEF or HFpEF. Median (Q1, Q3) time to treatment initiation was: HFrEF 20 (3, 74) days, HFmrEF 23 (3, 85) days, and HFpEF 30 (3, 92) days (**Fig. 4**).

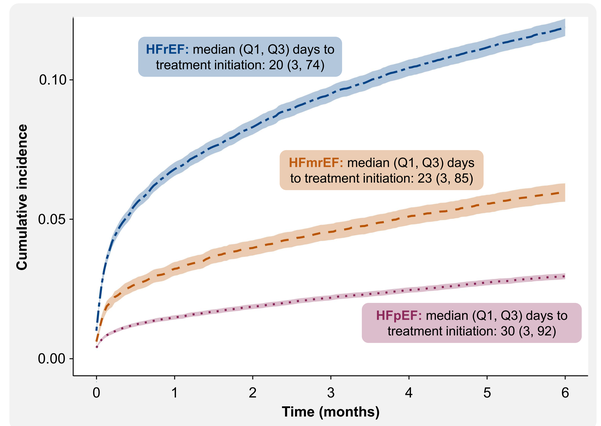

Fig. 4. Cumulative incidence of SGLT2i treatment initiation among treatment-naïve patients with newly-diagnosed HFrEF, HFmrEF, or HFpEF.

CONCLUSIONS

- These findings from real-world clinical practice in the US suggest that initiation of SGLT2i in patients with newly-diagnosed HF is suboptimal, and is lower and slower in those with HFmrEF/HFpEF than HFrEF.
- The increased odds of SGLT2i initiation with calendar year was in line with expectations given rolling approvals in HF from 2020 onwards and inclusion in the US treatment guidelines from 2022.
- Lower odds of SGLT2i initiation in patients with stage 4/5 CKD, dementia, or anemia could reflect difficulties in the management of these patients in the real-world.
- Being uninsured in the US could correspond with a lower likelihood of receiving non-generic treatments, resulting from inability to pay/access barriers.
- Further research is needed to understand the most effective means of ensuring timely and optimal use of therapeutics targeting newly-diagnosed patients with HF across the full LVEF spectrum.

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