Utilization of Empagliflozin in Patients with Type 2 Diabetes Mellitus and Congestive Heart Failure

Carlos A. Alvarez, PharmD, MSc, MSCS, BCPS, Aaron Perkins. MS, Meredith A. Sigler, PharmD, BCPS, Hui Yang, MS, Harjeet Caberwal, PharmD, Ramin Ebrahimi, MD

Abstract

Introduction: Type 2 diabetes (T2DM) and heart failure (HF) are an epidemic. Randomized controlled trials demonstrated sodium glucose cotransporter 2 inhibitors (SGLT2i) are beneficial in these patients. Guidelines suggest SGLT2i, such as empagliflozin, as potential first line therapy. We sought to determine utilization patterns and compliance to empagliflozin.

Methods: We assessed utilization and compliance in patients with T2DM and HF from the Veterans Affairs national database from 2015-2022. Initiation was calculated as the number of new empagliflozin prescriptions per 1,000 eligible patients. Compliance was calculated using the proportion of days covered (PDC).Compliance to empagliflozin was defined as PDC > 80%.

Results: A total of 44,608 patients exposed to empagliflozin were included. The majority of patients are white (n=33,663; 75.5%) male (n=43,335; 97.1%). A total of 6.6% were Hispanic or Latino (n=2,955). Table 1 shows incident empagliflozin prescription by year. The average proportion of days covered (PDC) was 0.83(SD 0.21). The proportion of empagliflozin compliant patients was 66.2%.

Conclusions: Empagliflozin prescriptions have increased exponentially since 2015. Compliance to empagliflozin was moderate necessitating a potential intervention to increase compliance.

Introduction

- HF is four times more prevalent in patients with T2DM than in the general population.(1) This suggests a potential pathogenic role of T2DM in patients with HF. Moreover, >30% of patients with heart failure have concurrent diabetes.(2)
- SGLT2i enhance glucose control by increasing the urinary excretion of glucose.
- Empagliflozin showed a significant effect on cardiovascular (CV) protection in patients with T2DM and atherosclerotic cardiovascular disease (3)
- In HF patients, empagliflozin, when added to recommended therapy, has been shown to decrease CV death or hospitalization for HF(4)
- These favorable CV outcomes data have moved empagliflozin from non-formulary status in the Veterans Affairs Heath Care system to a formulary drug in patients with T2DM and HF.
- Guidelines suggest SGLT2is are a potential first line therapy(5)
- What is largely unknown, is what is the utilization of and adherence to empagliflozin

Scientific Aims

Aim 1: Determine empagliflozin initiation from 2015-2022 in patients with T2DM and HF.

Aim 2: Assess patient adherence to empagliflozin in patients with T2DM and HF.

Methods

- **Study Design**: Population-based, new-user cohort study
- **Data Source**: VA Corporate Data Warehouse (CDW) which holds data for Veterans receiving care throughout the US. CDW includes all data from Veterans Health Information Systems and Technology Architecture (VistA). Data included in the CDW includes inpatient and outpatient diagnosis/procedure codes, pharmacy, and laboratory data.
- **Patients**: Adult patients (≥18 years) with T2DM and HF treated at VA medical centers with a new prescription for any glucose lowering medication during FY 2015-22. T2DM was identified using a validated algorithm that uses both administrative claims and pharmacy data.(6) Patients with HF were identified using a validated algorithm that uses both inpatient and outpatient ICD-9-CM and ICD-10 codes.(7)
- **Initiation and Adherence Measures**:

Measure: Conceptual Definition	Operational Definition
Adherence: Taking the correct dosage at a prescribed frequency	Proportion of days covered (PDC): fills and refills divided by the number of days in the study period. Adherent is considered a PDC > 80%
Initiation: Filling first prescription of empagliflozin	First fill of empagliflozin after incident diagnosis of T2DM and HF. No exposure in the 2-years prior to diagnosis

Methods

- **Statistical Analysis:** Generally, dichotomous variables are described as counts and proportions of the total sample. Continuous variables are described as mean and standard deviation (SD).
  - **Aim 1:** Initiation was calculated as the number of new empagliflozin prescriptions per 1,000 eligible patients in each calendar year from 2015-2022.
  - **Aim 2:** Patient adherence was calculated as proportion of days covered (PDC). PDC is calculated by the days supply of fills/refills divided by the number of days of patient follow-up in the study period. The PDC is reported as mean and SD for the sample.

Results

- 44,608 patients were included in the study.
- Most were white (75.5%), non-Hispanic (90.4%), males (97.1%).
- The mean age was 68.0.
- Most were either married or divorced.
- Veterans prescribed empagliflozin were dispersed throughout the five national districts.
- Empagliflozin initiation rates are shown in Figure in panel 3.
- Demographic and social factors are shown on Table in panel 2.
- Mean PDC was 0.83 (0.21) in each patient.
- The proportion of patients considered to be adherent to therapy was 66.2%.

Characteristics	Overall, N(%)
n	44,608
Male Gender	43,335 (97.1)
Age at cohort entry	68.0 (8.5)
Race	
White	33,663 (75.5)
Black/African American	7,456 (16.6)
Asian	380 (0.9)
Other/Missing/Unknown	3,109 (7)
Ethnicity	
Not Hispanic or Latino	40,307 (90.4)
Hispanic or Latino	2,955 (6.6)
Declined to answer/Unknown/Missing	1,346 (3)
Marital Status	
Married	26,120 (58.6)
Divorced	10,827 (24.3)
Single	3,651 (8.2)
Separated	1,485 (3.3)
Widowed	2,405 (5.4)
Missing/Unknown	120 (0.2)
District of Care	
Continental	7,900 (17.7)
Midwest	10,346 (23.2)
North Atlantic	9,009 (20.2)
Pacific	7,084 (15.9)
Southeast	10,269 (23.0)
Proportion of days covered (mean (SD))	**0.83 (0.21)**
Adherent to empagliflozin (%)	**18,933 (66.2)**

Empagliflozin Incidence in Patients with T2DM and CHF
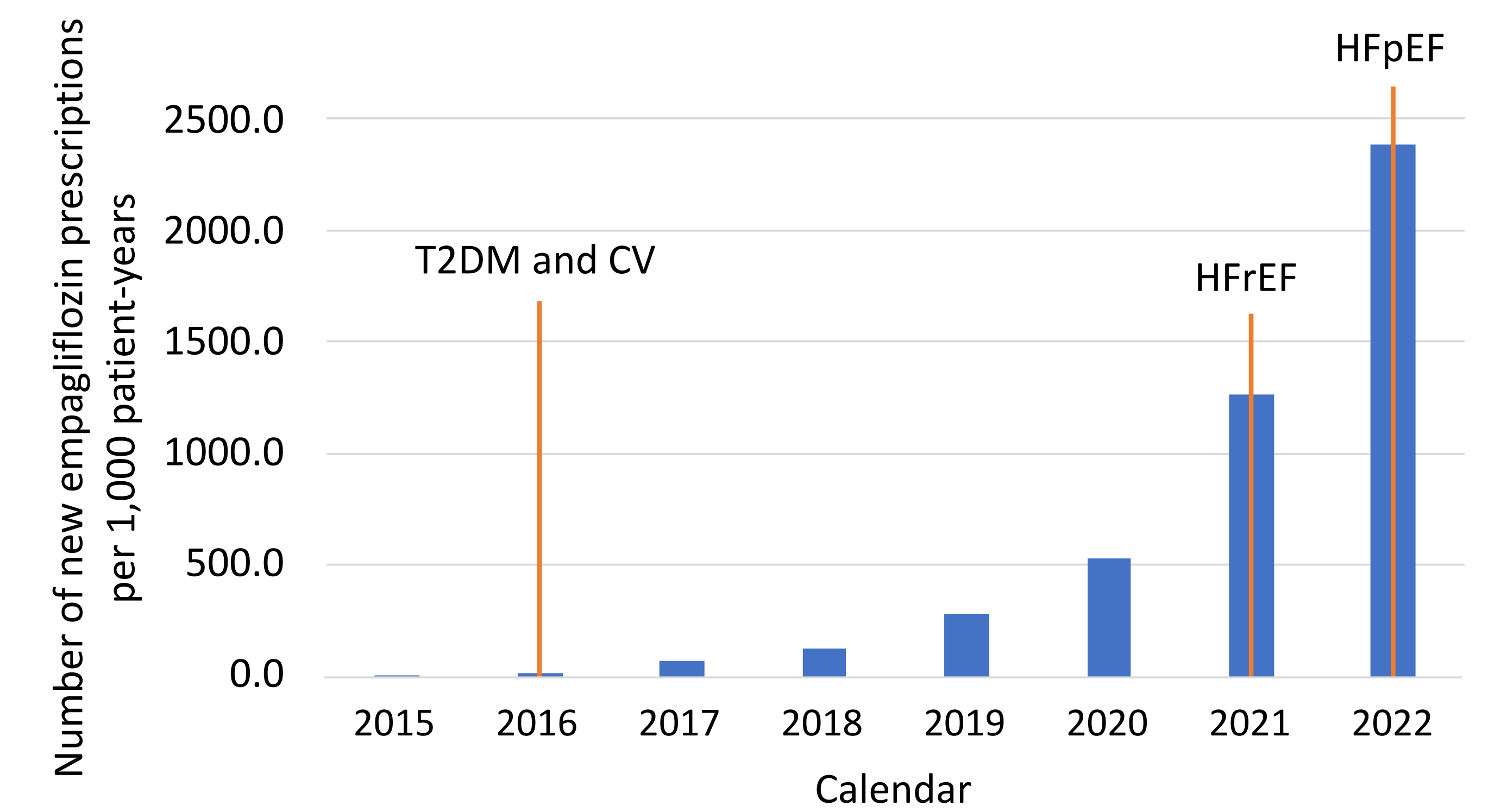
T2DM and CV = Type 2 diabetes mellitus and cardiovascular outcome indication; HFrEF = Heart failure with reduced ejection fraction indication; HFpEF = Heart failure with preserved ejection fraction indication.

Conclusion and Discussion

- **Prescriptions for empagliflozin have seen a sharp increase from 2015 to 2022.**

- **The increase in SGLT2i prescriptions is consistent with changes in clinical practice guidelines and the findings of high-quality studies that have shown benefits.**

- **The level of empagliflozin adherence was similar to what has been observed in studies of metformin.(8)**

- **Compliance to empagliflozin was moderate with a mean PDC of 0.83 necessitating interventions to increase adherence.**

- **Additional studies are needed to identify patient, provider, and system level factors that are associated with poor adherence.**

References

1. Metra M, Zaca V, Parati G, Agostoni P, Bonadies M, Ciccone M, et al. Cardiovascular and noncardiovascular comorbidities in patients with chronic heart failure. J Cardiovasc Med (Hagerstown). 2011;12(2):76-84
2. From AM, Leibson CL, Bursi F, Redfield MM, Weston SA, Jacobsen SJ, et al. Diabetes in heart failure: prevalence and impact on outcome in the population. Am J Med. 2006;119(7):591-9.
3. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015;373(22):2117-28
4. Packer M, Anker SD, Butler J, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. N Engl J Med. 2020;383(15):1413-1424. doi:10.1056/NEJMoa2022190
5. ElSayed NA, Aleppo G, Aroda VR, et al. 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2023 [published correction appears in Diabetes Care. 2023 Jan 26;:]. Diabetes Care. 2023;46(Suppl 1):S158-S190. doi:10.2337/dc23-S010
6. Miller DR, Safford MM, Pogach LM. Who has diabetes? Best estimates of diabetes prevalence in the Department of Veterans Affairs based on computerized patient data. Diabetes Care. 2004;27 Suppl 2:B10-21
7. Saczynski JS, Andrade SE, Harrold LR, Tjia J, Cutrona SL, Dodd KS, et al. A systematic review of validated methods for identifying heart failure using administrative data. Pharmacoepidemiol Drug Saf. 2012;21 Suppl 1:129-40
8. McGovern A, Tippu Z, Hinton W, Munro N, Whyte M, de Lusignan S. Comparison of medication adherence and persistence in type 2 diabetes: A systematic review and meta-analysis. Diabetes Obes Metab. 2018;20(4):1040-1043. doi:10.1111/dom.13160

Acknowledgements

SC-US-76206

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER™

Jerry H. Hodge School of Pharmacy