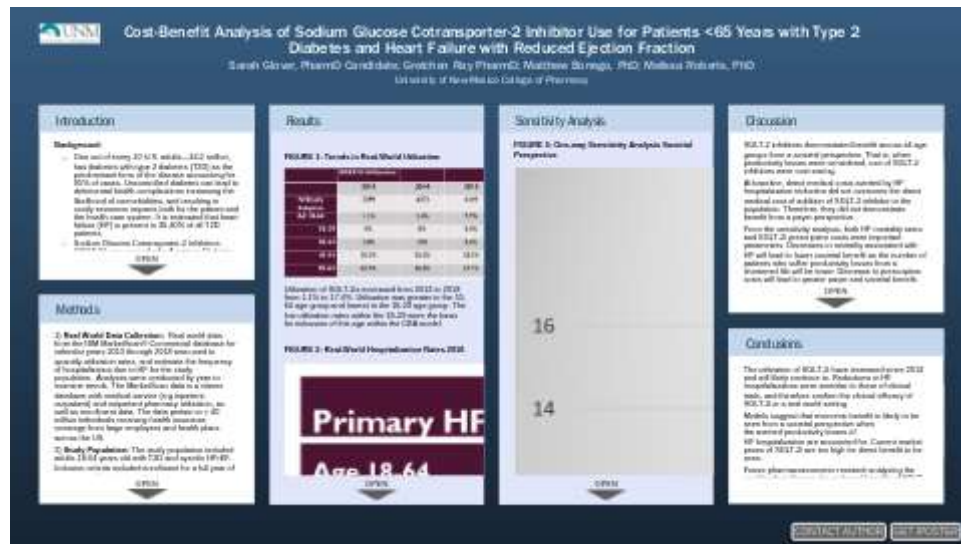# Cost-Benefit Analysis of Sodium Glucose Cotransporter-2 Inhibitor Use for Patients <65 Years with Type 2 Diabetes and Heart Failure with Reduced Ejection Fraction

Sarah Glover, PharmD Candidate; Gretchen Ray, PharmD; Matthew Borrego, PhD; Melissa Roberts, PhD

University of New Mexico College of Pharmacy

PRESENTED AT:

INTRODUCTION

Background:

- One out of every 10 U.S. adults—34.2 million, has diabetes with type 2 diabetes (T2D) as the predominant form of the disease accounting for 95% of cases. Uncontrolled diabetes can lead to detrimental health complications increasing the likelihood of comorbidities, and resulting in costly economic impacts both for the patient and the health care system. It is estimated that heart failure (HF) is present in 30-40% of all T2D patients.

- Sodium Glucose Cotransporter-2 Inhibitors (SGLT-2i) are currently the American Diabetes Association's recommended second line addition for patients with T2D and HF after metformin.

- This recommendation is based on the results of three pivtotal clinical trials: CANVAS, DECLARE-TIMI and EMPA-REG corresponding to the three SGLT-2i canagliflozin, dapagliflozin, and empagliflozin. In these trials SGLT-2i demonstrated significant reductions in HF hospitalizations.

- Despite their reported efficacy, the high prescription costs of SGLT-2i warrant further investigation of their overall economic benefit.

Our study objectives were to:

1) quantify actual and potential utilization rates of SGLT-2 inhibitors in patients with T2D and comorbid HFrEF within a real-world commercially insured population <65 years of age.

2) perform a cost-benefit analysis (CBA) of SGLT-2 inhibitor use in T2D and comorbid HF populations from a health care payer and societal perspective using potential real-world utilization

METHODS

1) **Real World Data Collection:** Real world data from the IBM MarketScan® Commercial database for calendar years 2013 through 2018 was used to quantify utilization rates, and estimate the frequency of hospitalization due to HF for the study population. Analyses were conducted by year to examine trends. The MarketScan data is a claims database with medical service (e.g inpatient, outpatient) and outpatient pharmacy utilization, as well as enrollment data. The data pertain to > 40 million individuals receiving health insurance coverage from large employers and health plans across the US.

2) **Study Population:** The study population included adults 18-64 years old with T2D and systolic HFrEF. Inclusion criteria included enrollment for a full year of coverage with at least one primary or secondary diagnosis of T2D and diagnosis of HFrEF, and at least one prescription fill for metformin during the year.

3) **CBA Model:** A CBA model was created to determine benefit in a hypothetical commercially insured population (n=1,000,000) that was nationally representative of the US within our specified age range of 18-64 and with comorbid T2D and HFrEF. Both direct medical and indirect productivity costs were included. Hospitalization rate reductions observed in real-world data and from the clinical trials were applied to the population under no SGLT-2i use and the SGLT-2i use scenarios. Under the SGLT-2i use scenario, prescription and adverse event costs were incorporated to account for impact of SGLT-2i use. The final CBA reporting metrics were calculated as net benefit and benefit-to-cost ratios

4) **Sensitivty Analysis:**One-way sensitivity analyses were performed to determine the impact of varying the mortality rate and SGLT-2i prescription cost. The estimate of mortality for HFrEF was derived from literature that focused on an older, primarily medicare, populations. Mortality rate was reduced by 50% to account for the possibility of a lower mortality rate in a younger population 30-64.

RESULTS

FIGURE 1: Trends in Real-World Utilization

SGLT-2i Utilization						
	2013	2014	2015	2016	2017	2018
N Study Subjects	3399	4073	4149	5502	5707	5924
All 18-64	1.1%	5.4%	9.9%	10.4%	14.6%	17.4%
18-29	0%	0%	0.5%	0%	0%	0.3%
30-44	2.8%	10%	8.6%	8.0%	8.3%	6.7%
45-54	33.3%	33.2%	33.3%	31.2%	32%	29.8%
55-64	63.9%	56.8%	57.7%	60.8%	59.7%	63.2%

Utilization of SGLT-2is increased from 2013 to 2018 from 1.1% to 17.4%. Utilization was greater in the 55-64 age group and lowest in the 18-29 age group. The low utilization rates within the 18-29 were the basis for exlcusion of this age within the CBA model.

FIGURE 2: Real-World Hospitalization Rates 2018

Primary HF Hospitalization Rate- NO SGLT-2	
Age 18-64	15.60%
Age 18-29	31.3%
Age 30-44	16.40%
Age 45-54	17.30%
Age 55-64	14.70%

Primary HF Hospitalization Rate- SGLT-2	
Age 18-64	10.9%
Age 18-29	0%
Age 30-44	13%%
Age 45-54	8.8%%
Age 55-64	11.8%

Patients recipient to an SGLT-2i inhibtior demonstrated reduced HF hospitalization rates across age groups. The greatest reductions were observed in the 45-54 age group at 8.5%. Reductions within the total population 18-64, 4.7%, were similar to those observed within the clinical trials (CANVAS 2.5%; DECLARE-TIMI 5.5%; EMPA-REG 1.4%).

FIGURE 3: Benefit to Cost Ratios

SGLT-2i Benefit to Cost Ratio in T2D patients with HFrEF

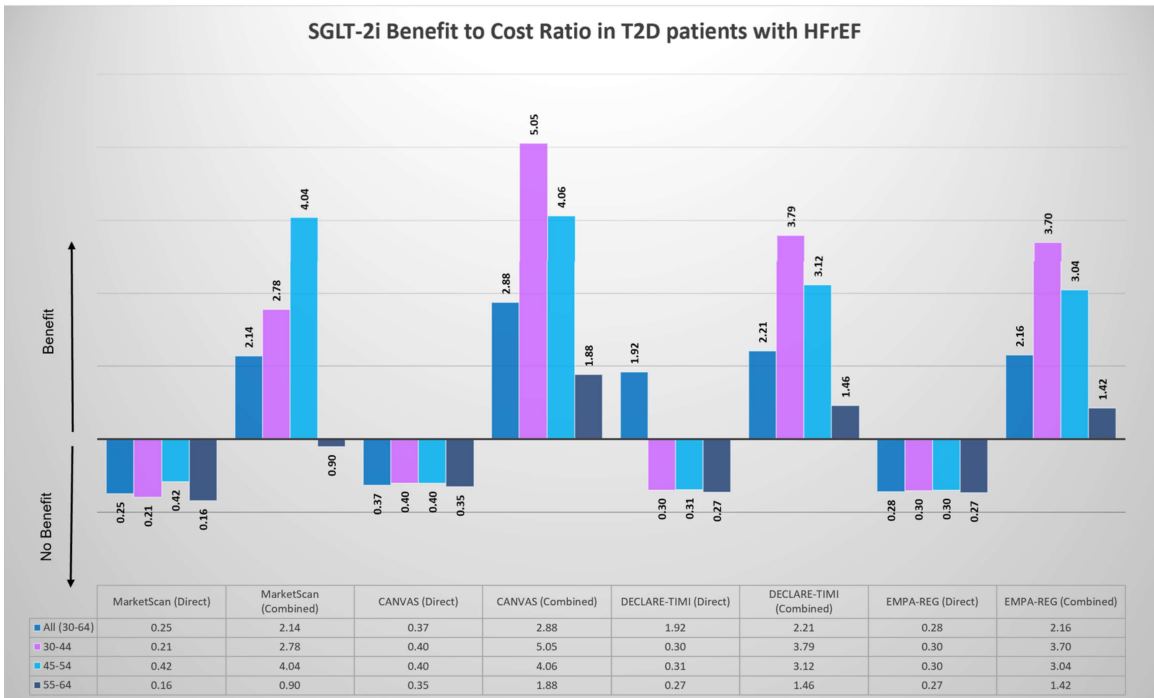|	MarketScan (Direct)	MarketScan (Combined)	CANVAS (Direct)	CANVAS (Combined)	DECLARE-TIMI (Direct)	DECLARE-TIMI (Combined)	EMPA-REG (Direct)	EMPA-REG (Combined)
All (30-64)	0.25	2.14	0.37	2.88	1.92	2.21	0.28	2.16
30-44	0.21	2.78	0.40	5.05	0.30	3.79	0.30	3.70
45-54	0.42	4.04	0.40	4.06	0.31	3.12	0.30	3.04
55-64	0.16	0.90	0.35	1.88	0.27	1.46	0.27	1.42

Figure 3 visually depicts the benefit to cost ratios of SGLT-2i use from a societal perspective and a payer-only perspective for the model using real-world data, and those using clinical trial reduction rates. Benefit-to-cost ratios greater than 1 are considered beneficial from an economic standpoint, while those less than 1 are not. Throughout the models it can be seen that ratios were only above 1 when a societal perspective was taken. Mean benefit-to-cost ratio from a societal perspective for the population 30-64 was 2.35.

FIGURE 4: Net Benefit

SGLT-2i Net Benefit in T2D patients with HFrEF

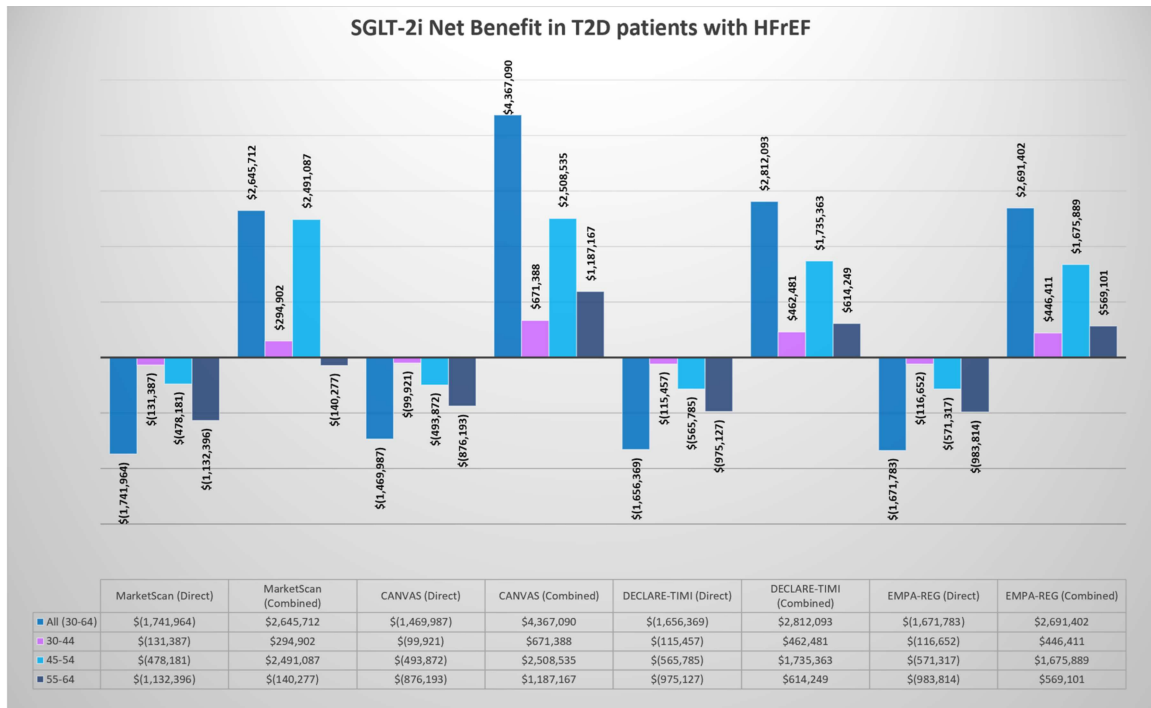|	MarketScan (Direct)	MarketScan (Combined)	CANVAS (Direct)	CANVAS (Combined)	DECLARE-TIMI (Direct)	DECLARE-TIMI (Combined)	EMPA-REG (Direct)	EMPA-REG (Combined)
All (30-64)	$(1,741,964)	$2,645,712	$(1,469,987)	$4,367,090	$(1,656,369)	$2,812,093	$(1,671,783)	$2,691,402
30-44	$(131,387)	$294,902	$(99,921)	$671,388	$(115,457)	$462,481	$(116,652)	$446,411
45-54	$(478,181)	$2,491,087	$(493,872)	$2,508,535	$(565,785)	$1,735,363	$(571,317)	$1,675,889
55-64	$(1,132,396)	$140,277	$(876,193)	$1,187,167	$(975,127)	$614,249	$(983,814)	$569,101

Figure 4 visually depicts the net benefit (2020 $US) of SGLT-2i use from both a societal and payer perspective. The interpretation of these trends is the same as when benefit-to-cost ratios were examined. Only a societal perspective results in a positive net benefit. Mean net benefit from a societal perspective for the population 30-64 was $3,129,074.

SENSITIVITY ANALYSIS

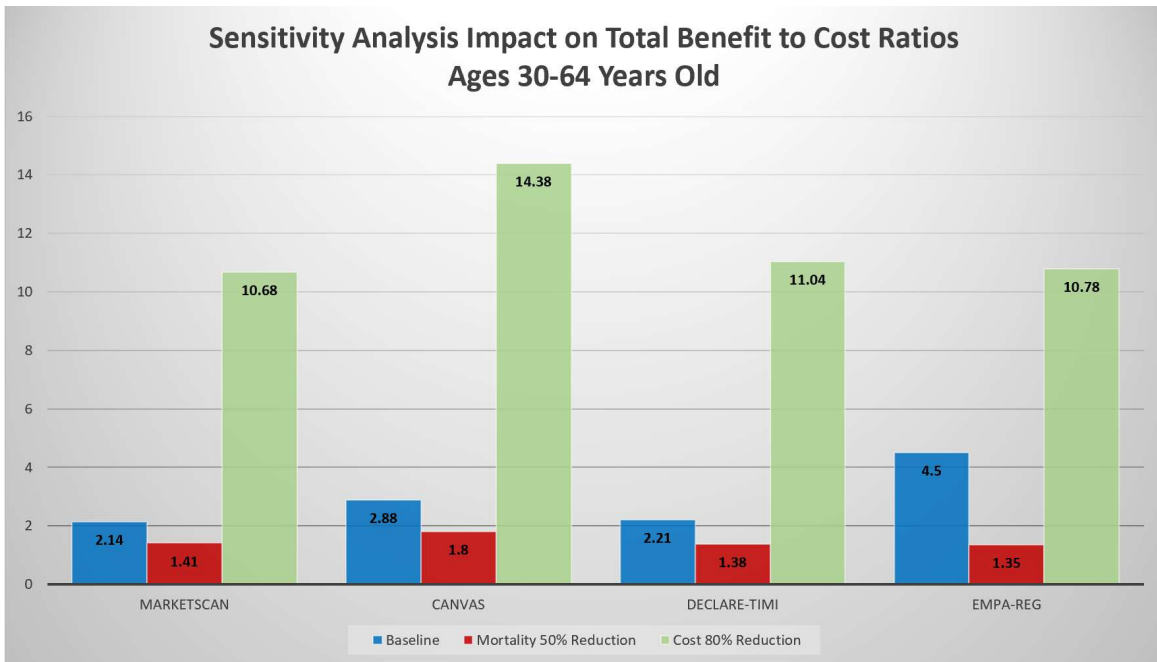**FIGURE 5: One-way Sensitivity Analysis Societal Perspective**

Figure 5 visually represents the impact of reducing mortality rates and SGLT-2i prescription costs on the benefit-to-cost ratios from a societal perspective. Ratios were reduced when mortality was reduced by 50%, whereas ratios were signficantly increased when cost of SGLT-2i were decreased by 80% -- the point at which direct medical benefits broke even or became positive.

FIGURE 6: One way Sensitivty Analysis Payer Perspcetive
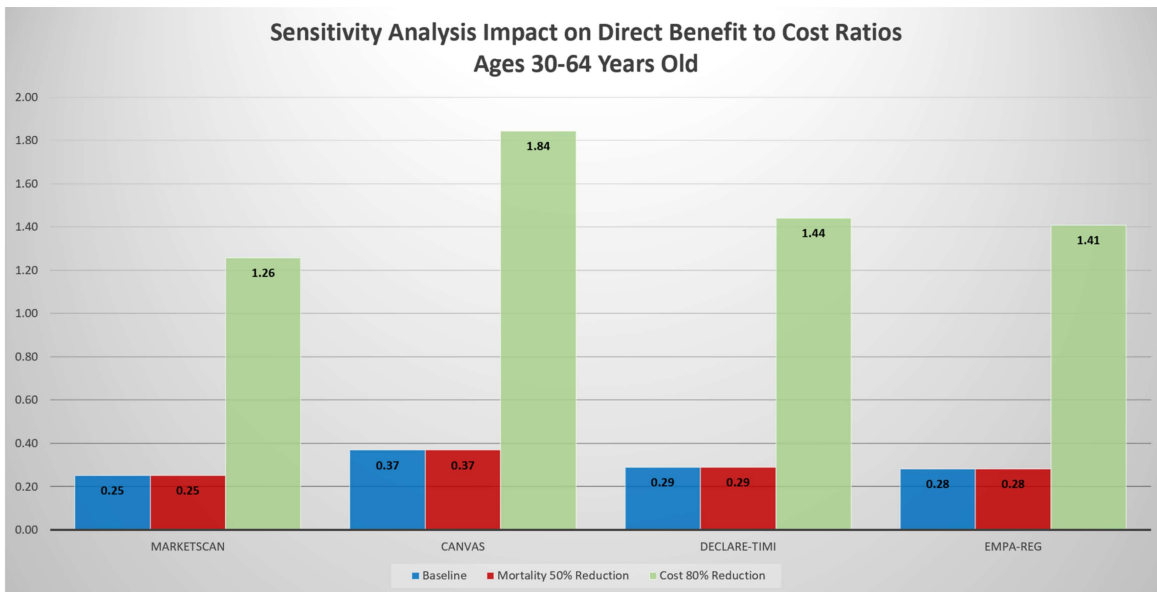

Figure 6 depicts the results of the sensitivity analysis on benefit-to-cost ratios from a payer-only perspective. There is no impact seen by reduction of mortality rates at the payer level. However, ratios are significantly increased by an 80% reduction of SGLT-2i costs.

DISCUSSION

SGLT-2 inhibitors demonstrated benefit across all age groups from a societal perspective. That is, when productivity losses were considered, use of SGLT-2 inhibitors were cost saving.

At baseline, direct medical costs averted by HF hospitalization reduction did not overcome the direct medical cost of addition of SGLT-2 inhibitor to the population. Therefore, they did not demonstrate benefit from a payer perspective.

From the sensitivity analysis, both HF mortality rates and SGLT-2i prescription costs were important parameters. Decreases in mortality associated with HF will lead to lower societal benefit as the number of patients who suffer productivity losses from a shortened life will be lower. Decrease in prescription costs will lead to greater payer and societal benefit.

Possible limitations:

- Time Horizon: the model only captured hospitalizations in a one-year time frame. Extension of the time horizon may demonstrate an additive effect and thus contribute to greater benefit.

- Population: Working age adults 18-64 were analyzed due to availability of claims data. It would be interesting to see impact in older populations when HF rates are expected to increase

- Outcome: this study only evaluated effects on HF hospitalizations. However clinical trials have demonstrated the benefit of SGLT-2i on renal function and composite cardiovascular function. The effect of the combined outcomes would be interesting to analyze.

CONCLUSIONS

The utilization of SGLT-2i have increased since 2013 and will likely continue to. Reductions in HF hospitlalizations were simmilar to those of clinical trials, and therefore confirm the clinical efficacy of SGLT-2i in a real world setting.

Models suggest that economic benefit is likely to be seen from a societal perspective when the averted producitvity losses of HF hospitalization are accounted for. Current market prices of SGLT-2i are too high for direct benefit to be seen.

Future pharmacoeconomic research analyzing the combined cardiovascular and renal benefits of SGLT-2i is warranted.