

Comparing Out-of-Pocket Costs and Health-Related Quality of Life Between Sodium-Glucose Cotransporter 2 Inhibitors and Glucagon-Like Peptide-1 Receptor Agonists in Patients with Type 2 Diabetes

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Purpose: To compare the impact of sodium-glucose cotransporter 2 inhibitor (SGLT2 inhibitor), glucagon-like peptide-1 receptor agonist (GLP-1 RA), with or without metformin, on out of pocket and total prescription expenditure and health-related quality of life (HRQoL) for patients with type 2 diabetes mellitus (T2DM).

Patients and Methods: This observational study utilized 2017–2021 Medical Expenditure Panel Survey (MEPS) data from patients with T2DM (≥ 18 years) on SGLT2 inhibitor, GLP-1 RA, with or without metformin, from payer and self-perspective. HRQoL was assessed using physical (PCS) and mental component summary (MCS) scores based on Veterans Rand 12. This study estimated survey-weighted out-of-pocket (OOP) costs for prescription refills and total prescription expenditures. Propensity score matching was used to mitigate selection bias and health expenditures, and HRQoL were compared using the Mann–Whitney *U*-test. P-value thresholds were recalculated using Bonferroni adjustment (Total prescription expenditure or OOP, PCS, and MCS: $p=0.017$).

Results: Patients on GLP-1 RA alone had significantly higher OOP costs than those on SGLT2 inhibitor alone (median: \$166.50 vs \$81.00, $p<0.01$). No significant difference existed between the two treatments for total prescription expenditures (median: \$9831.53 vs. \$9458.80, $p=0.059$), MCS (median: 52.41 vs 53.48, $p=0.40$), or PCS (median: 45.22 vs 44.54, $p=0.19$). Patients on metformin with GLP-1 RA had higher OOP costs compared to those on SGLT2 inhibitor with metformin (median: \$140.40 vs \$107.33, $p<0.01$). There is a significant difference between the combination treatments for total prescription expenditure (median: \$9453.96 vs \$6711.47, $p<0.01$), MCS (median: 54.19 vs 54.30, $p=0.70$), or PCS (median: 45.69 vs 46.08, $p=0.55$).

Conclusion: Even though patients on GLP-1 RA have higher OOP costs, the difference in PCS or MCS scores between GLP-1 RA and SGLT2 inhibitor was not significant. Further investigation is needed to study the long-term impact on HRQoL and clinical outcomes.

Keywords: SGLT2 inhibitor, GLP-1 receptor agonist, medical expenditure panel survey, health care expenditure, health-related quality of life

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease that occurs when the pancreas fails to produce enough insulin to regulate glucose, or the body develops insulin resistance. In patients with T2DM excess glucose circulation in their blood for longterm, lead to complications affecting the circulatory, nervous, and immune systems. In 2022, 25.5 million Americans were diagnosed with diabetes, contributing to 107,000 deaths. The direct medical cost for diabetes in 2022 was \$306.6 billion. The cost for glucose-lowering medications was \$84.5 billion in 2022, an increase of

26% from 2017. The excess medical cost per person in 2022 was \$12,022. On average, patients with diabetes have a medical expenditure 2.6 times higher than those without the condition.¹ In addition to metformin, the 2024 American Diabetes Association (ADA) guideline recommends the use of sodium-glucose cotransporter 2 inhibitors (SGLT2 inhibitor) and/or glucagon-like peptide-1 receptor agonist (GLP-1 RA) for treating T2DM.² SGLT2 inhibitor and GLP-1 RA are relatively new classes of antidiabetic medications, expecting significant improvements in major adverse cardiovascular events (MACE) in patients with T2DM.^{3–6}

SGLT2 inhibitor decreases blood glucose by reducing glucose reabsorption at the proximal tubules in the kidney, which can lead to urine tract and genital infection.⁷ GLP-1 RA decreases blood glucose by enhancing insulin secretion from β -cells and decreasing glucagon release from α -cells in the pancreas. GLP-1 RA can cause gastrointestinal disorders, including nausea, vomiting, and diarrhea.^{7,8} However, these two medication classes are more expensive than traditional medications. SGLT2 inhibitor costs around \$600, and GLP-1 RA costs around \$1000 for one month's supply. In contrast, metformin and sulfonylureas cost less than \$100 for one month's supply. While showing significant benefits in clinical outcomes, the high cost of SGLT2 inhibitor and GLP-1 RA has become a significant burden for patients who require these medications but cannot afford them.

Studies have analyzed the cost-effectiveness of GLP-1 RA and SGLT2 inhibitor.^{9–11} Most of these studies used the Center for Outcomes Research (CORE) Diabetes Model and involved hypothetical patients. Several of the studies were funded by companies that manufactured one of these medications.^{12–16} The results of these cost-effective analyses were controversial. Furthermore, most of the studies compared a single medication to another instead of comparing between these two medication classes.

Luo et al conducted a study comparing the out-of-pocket (OOP) costs of SGLT2 inhibitor and GLP-1 RA using Medicare Advantage claims data. Their analysis found that GLP-1 RA were slightly more expensive than SGLT2 inhibitor, with an average OOP costs of \$118 vs \$91, respectively. However, the study only included patients with Medicare Advantage insurance, making the findings less generalizable to populations with other insurance types. The generalization of these findings to the wider type 2 diabetes population are limited as this study excluded patients not receiving metformin.¹⁷

To address these gaps in the literature, our study aimed to assess the expenditures and health-related quality of life (HRQoL) associated with SGLT2 inhibitor vs GLP-1 RA, either alone or in combination with metformin, for patients with T2DM from payer's and self-perspectives.¹⁸ By using the nationally representative Medical Expenditure Panel Survey - a real-world dataset, the aim of this study is to provide an assessment of the expenditure and -HRQoL for these two medication classes. This study hypothesized that SGLT2 inhibitor would have lower OOP costs and higher MCS or PCS scores than GLP-1 RA.

Methods

Data Source

MEPS is one of the most complete and publicly available data sources on health expenditure, supported by the Agency for Healthcare Research and Quality (AHRQ).¹⁸ MEPS used large-scale surveys to collect health expenditure-related information from families, individuals, medical providers, and employers across the US. MEPS includes a household component and insurance component. The household component collects demographic characteristics, medical conditions, utilized medical services, and associated costs for families and individuals. The insurance component focused on private insurance plans, including premiums and benefits.¹⁸ With the information it collects, MEPS is a valuable resource for researchers to better understand healthcare usage and costs in the US. Current study extracted patient characteristics, physical (PCS) and mental component summary (MCS) scores, and total prescription expenditure from full-year consolidated files. Additionally, this study analyzed out-of-pocket (OOP) prescription payments from prescribed medicines files, specifically using the "amount paid, self or family (imputed)" variable. This study also used the CLINK file to link the full-year consolidated file, medical conditions file, and prescribed medicines files, consolidating all patient information into a single file. We utilized data from 2017 to 2021 to evaluate total prescription expenditure, OOP. Additionally, PCS, and MCS based on the Veterans Rand 12 (VR 12) were also assessed.

Population and Study Sample

Patients that were ≥ 18 years old with T2DM on SGLT2 inhibitor or GLP-1 RA, either alone or in combination with metformin were included in this study. Publicly available MEPS full-year consolidated, medical conditions, and prescribed medicines data files from 2017 to 2021 (N=146,994) were analyzed.¹⁸ Subsequently, patients' diagnoses with diabetes by professional healthcare providers using variable DSDIA53 from the full-year consolidated file (N=9083) were identified. Patients diagnosed with T2DM using variable ICD10CDX = E11 from medical conditions files (N=8222) (Figure 1) were separated. For OOP analysis, this study only includes patients with positive OOP costs.

Measures

Outcome Measures

Both types of expenditures utilized in this study were direct medical expenditures. This study identified OOP and total prescription expenditures from the full-year consolidated file and adjusted both expenditures to 2021-dollar value according to the Bureau of Labor Statistics.^{19–21} This study analyzed PCS using VPCS42, and MCS using VMCS42, as variables in MEPS from the full-year consolidated file.

Independent Variable and Covariates

Current study classified patients with T2DM into two groups: patients on SGLT2 inhibitor either alone or with metformin and patients on GLP-1 RA either alone or with metformin (Table 1). Medications were identified using the variable TC1S1_1. All groups' covariates according to patients' baseline characteristics from the full-year consolidated file were balanced. These characteristics included age, sex, race, region, education, marriage state, income level, employment, insurance type, perceived health status, whether had diabetes caused eye or kidney problems, and whether had MI or stroke. Additionally, total number of medical conditions a patient had from the medical conditions file using the variable ICD10CDX were also balanced. Then total conditions were divided into 1–2, 3–5, 6–10, 11–20, 21–30, and 31–40 categories. Meanwhile, this study used the Elixhauser comorbidity score, a commonly used measurement for comorbidity, healthcare utilization, and expenditures.²² Comorbidity score is calculated using Comorbidity package in R studio

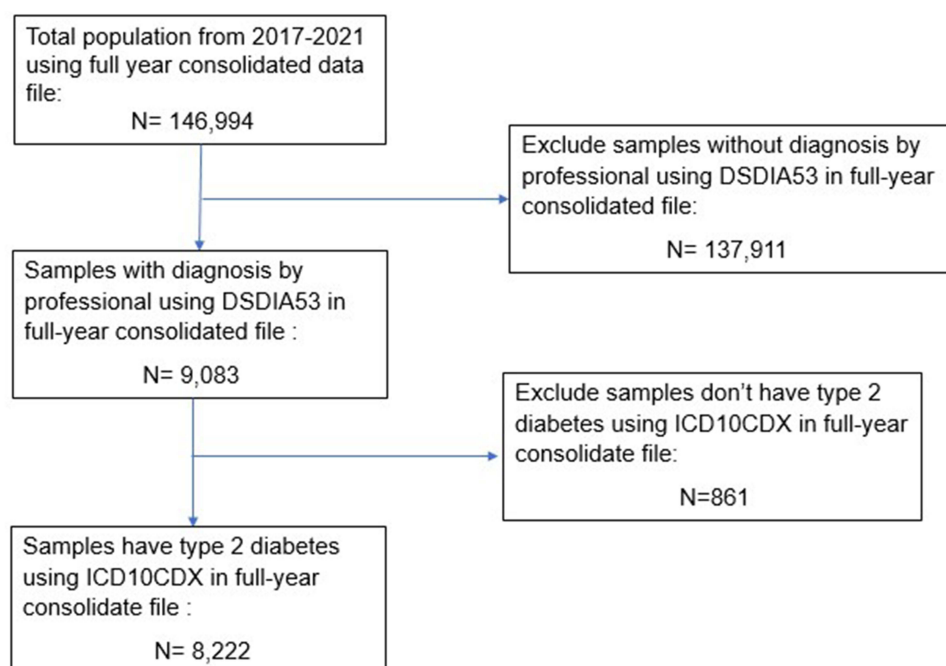


Figure 1 Flow diagram of adults with type 2 diabetes, medical expenditure panel survey, 2017–2021.

Abbreviation: DSDIA53, Diabetes diagnosis by health professional.

Table I OOP, Total Prescription Expenditure, PCS, MCS of SGLT2 Inhibitor and GLP-I RA Either Alone or with Metformin: Medical Expenditure Panel Survey 2017–2021

	SGLT2 Inhibitor (N = 117) Median (Range)	GLP-I RA (N = 117) Median (Range)	P value	SGLT2 Inhibitor (N = 160) Median (Range)	GLP-I RA (N = 160) Median (Range)	P value
OOP (\$)	81.00 (1.07–7218.80)	166.50 (4.17–10,119.57)	<0.001*			
MCS	53.48 (22.65–65.43)	52.32 (28.14–69.32)	0.15			
PCS	47.80 (16.59–58.10)	45.88 (17.33–65.84)	0.10			
Total prescription expenditure (\$)				9458.80 (415.76–90,040.81)	9831.53 (870.67–91,219.55)	0.059
MCS				53.48 (22.65–65.43)	52.41 (27.15–69.32)	0.40
PCS				44.54 (16.59–58.10)	45.22 (16.15–65.84)	0.19
	SGLT2 Inhibitor + Metformin (N = 271) Median (Range)	GLP-I RA + Metformin (N = 271) Median (Range)	P value	SGLT2 Inhibitor + Metformin (N = 313) Median (Range)	GLP-I RA + Metformin (N = 313) Median (Range)	P value
OOP (\$)	107.33 (3.85–4643.17)	140.40 (1.36–9126.79)	<0.001*			
MCS	54.37 (20.46–65.97)	54.24 (20.89–66.75)	0.59			
PCS	46.53 (17.20–60.88)	44.12 (14.75–64.92)	0.088			
Total prescription expenditure (\$)				6711.47 (393.87–80,660.56)	9453.96 (914.72–79,833.30)	<0.001*
MCS				54.30 (20.46–65.97)	54.19 (21.40–66.75)	0.69
PCS				46.08 (17.20–60.88)	45.69 (15.09–66.46)	0.55

Notes: *Statistical significance. P = 0.017 (after Bonferroni adjustment).

Abbreviations: OOP, out-of-pocket; PCS, physical component summary; MCS, mental component summary; SGLT2 inhibitor, SGLT2 inhibitor; GLP-I RA, GLP-I receptor agonist.

(version 2023.09.1. Build 494).²³ Based on the number of comorbidity scores identified, this study further categorized the comorbidity score into 0, 1, 2, and ≥ 3 .

Statistical Analysis

Since this was an observational study, it lacked the randomized allocations of patients between SGLT2 inhibitor and GLP-1 RA groups. To minimize selection bias and improve the likelihood that outcomes were only due to different treatments, this study used a 1:1 propensity score matching. This study matched and compared patients' baseline characteristics between groups using a chi-squared test. Before analyzing health expenditures, this study used the Kolmogorov–Smirnov test to confirm that the expenditures were not normally distributed. Consequently, this study used the Mann–Whitney *U*-test to compare health expenditures and HRQoL between treatments. This study also used Bonferroni adjustment for multiple comparisons to recalculate the p-value thresholds (Baseline characteristics: $p=0.0031$. Total prescription expenditure or OOP, PCS, and MCS: $p=0.017$). This study extracted and analyzed data using R studio (version 2023.09.1. Build 494).

Results

Patient Characteristics

For OOP, PCS, and MCS comparison, after propensity matching, both the SGLT2 inhibitor and GLP-1 RA groups have 117 patients each (Table 1). Additionally, 271 patients were included in both the SGLT2 inhibitor with metformin and GLP-1 RA with metformin group (Table 1). When comparing OOP, PCS, and MCS, before propensity score matching, the only statistical difference between the SGLT2 inhibitor and GLP-1 RA groups was whether patients had diabetes caused kidney problems (Table 2). However, after propensity matching, all baseline characteristics were well balanced (Table 2). Similarly, all baseline characteristics were well balanced for patients receiving SGLT2 inhibitor and GLP-1 RA in combination with metformin after propensity matching (Table 2). When comparing OOP, GLP-1 RA (GLP-1 RA alone, with metformin: \$166.50, \$140.40) was significantly higher than SGLT2 inhibitor (SGLT2 inhibitor alone, with metformin: \$81.00, \$107.33) either alone or with metformin ($P < 0.001$) (Table 1). The median prescription number for GLP-1 RA and SGLT2 inhibitor was 4 ($p=0.21$). The median prescription number for GLP-1 RA with metformin is 9 and for SGLT2 inhibitor with metformin is 8 ($p=0.18$). While there was no significant difference between PCS and MCS (Table 1).

After propensity matching, for total prescription expenditure, PCS, and MCS comparison, both SGLT2 inhibitor and GLP-1 RA groups have 160 patients each, and 313 patients were included for both SGLT2 inhibitor with metformin and GLP-1 RA with metformin groups (Table 1). Before propensity matching, the only statistical difference between SGLT2 inhibitor and GLP-1 RA, either alone or in combination with metformin, was race ($P < 0.001$, $P = 0.0016$, respectfully) (Table 3). All baseline characteristics were well balanced after propensity matching (Table 3). Although the median total prescription expenditure for GLP-1 RA (\$9453.96) was higher than for SGLT2 inhibitor (\$9458.80), there was no significant difference ($P=0.0059$) (Table 1). The PCS ($P=0.19$) and MCS ($P=0.40$) scores were similar for both groups (Table 1). The median total prescription expenditure for GLP-1 RA was statistically significantly higher than the one for SGLT2 inhibitor (\$ 9453.96 vs \$ 6711.47. $P < 0.001$). There was also no significant difference in PCS, and MCS for SGLT2 inhibitor and GLP-1 RA with metformin (Table 1).

Discussion

This study evaluated total prescription expenditure, OOP costs, MCS, and PCS among patients with T2DM who were on SGLT2 inhibitor or GLP-1 RA, either alone or in combination with metformin. The study found that the OOP for GLP-1 RA was higher than those for SGLT2 inhibitor, either alone or in combination with metformin.

As previous studies have indicated, patients with higher OOP costs might have lower adherence.²⁴ This could further worsen the clinical outcomes including A1C, blood glucose, and kidney function. Quach et al reported higher median annual OOP costs for SGLT2 inhibitor (\$430) and for GLP-1 RA (\$480) compared to those reported in this study.²⁵ This difference might be because their study used claims data from employer-sponsored pharmacy benefit plans, while this

Table 2 Baseline Characteristics of Adults with T2DM on SGLT2 Inhibitor and GLP-I RA Without and with Metformin for OOP, PCS, and MCS Before and After Matching Using MEPS Data 2017–2021. (N=234 vs N = 542*)

Baseline Characteristics		Before Matching			After Matching			Before Matching			After Matching		
		SGLT2 Inhibitor N = 117 n (%)	GLP-I RA N = 224 n (%)	P value	SGLT2 Inhibitor N = 117 n (%)	GLP-I RA N = 117 n (%)	P value	SGLT2 Inhibitor + Metformin N = 271 n (%)	GLP-I RA + Metformin N = 358 n (%)	P value	SGLT2 Inhibitor + Metformin N = 271 n (%)	GLP-I RA + Metformin N = 271 n (%)	P value
Age	18–44	14 (11.97)	17 (7.59)	0.57	14 (11.97)	11 (9.40)	0.88	20 (7.38)	26 (7.26)	0.75	20 (7.38)	18 (6.64)	0.97
	45–64	52 (44.44)	104 (46.43)		52 (44.44)	51 (43.59)		131 (48.34)	169 (47.21)		131 (48.34)	132 (48.71)	
	≥65	51 (43.59)	103 (45.98)		51 (43.59)	55 (47.01)		120 (44.28)	163 (45.53)		120 (44.28)	121 (44.65)	
Sex	Male	54 (46.15)	87 (38.84)	0.38	54 (46.15)	56 (47.86)	0.86	145 (53.51)	161 (44.97)	0.053	145 (53.51)	137 (50.55)	0.65
	Female	63 (53.85)	137 (61.16)		63 (53.85)	61 (52.14)		126 (46.49)	197 (55.03)		126 (46.49)	134 (49.45)	
Race	White	83 (70.94)	172 (76.79)	0.031	83 (70.94)	88 (75.21)	0.36	217 (80.07)	285 (79.61)	0.0094**	217 (80.07)	217 (80.07)	0.86
	Black	23 (19.66)	41 (18.30)		23 (19.66)	25 (21.37)		27 (9.96)	44 (12.29)		27 (9.96)	33 (12.18)	
	Multiple	1 (0.86)	7 (3.13)		1 (0.86)	0 (0)		9 (3.32)	15 (4.19)		9 (3.32)	7 (2.58)	
	Other	10 (8.55)	4 (1.79)		10 (8.55)	4 (3.42)		18 (6.64)	14 (3.91)		18 (6.64)	14 (5.17)	
Region	Northeast	13 (11.11)	29 (12.95)	0.81	13 (11.11)	9 (7.69)	0.88	41 (15.13)	56 (15.64)	0.95	41 (15.13)	38 (14.02)	0.99
	Midwest	20 (17.09)	40 (17.86)		20 (17.09)	24 (20.51)		72 (26.57)	90 (25.14)		72 (26.57)	72 (26.57)	
	South	70 (59.83)	123 (54.91)		70 (59.83)	70 (59.83)		105 (38.75)	150 (41.90)		105 (38.75)	109 (40.22)	
	West	14 (11.97)	32 (14.29)		14 (11.97)	14 (11.97)		53 (19.56)	62 (17.32)		53 (19.56)	52 (19.19)	
Education	No school	0 (0)	0 (0)	0.67	0 (0)	0 (0)	0.93	0 (0)	0 (0)	0.32	0 (0)	0 (0)	0.59
	Grade 1–8	3 (2.56)	3 (1.34)		3 (2.56)	3 (2.56)		26 (9.59)	18 (5.03)		26 (9.59)	17 (6.27)	
	Grade 9–12	62 (52.99)	101 (45.09)		62 (52.99)	59 (50.43)		98 (36.16)	132 (36.87)		98 (36.16)	101 (37.27)	
	Grade >12	52 (44.44)	120 (53.57)		52 (44.44)	55 (47.01)		147 (54.24)	208 (58.10)		147 (54.24)	153 (56.46)	
Marriage	Never married	14 (11.97)	23 (10.27)	0.62	14 (11.97)	11 (9.40)	0.86	29 (10.70)	49 (13.69)	0.31	29 (10.70)	30 (11.07)	0.81
	Widowed	39 (33.33)	77 (34.38)		39 (33.33)	38 (32.48)		99 (36.53)	104 (29.05)		99 (36.53)	89 (32.84)	
	Married	64 (54.70)	124 (55.36)		64 (54.70)	68 (58.12)		143 (52.77)	205 (57.26)		143 (52.77)	152 (56.09)	

Income	Negative/poor/ near poor	25 (21.37)	56 (25.00)	0.93	25 (21.37)	26 (22.22)	0.91	57 (21.03)	54 (15.08)	0.084	57 (21.03)	49 (18.08)	0.84
	Low	16 (13.68)	26 (11.61)		16 (13.68)	12 (10.26)		29 (10.70)	57 (15.92)		29 (10.70)	36 (13.28)	
	Middle	33 (28.21)	65 (29.02)		33 (28.21)	37 (31.62)		72 (26.57)	105 (29.33)		72 (26.57)	71 (26.20)	
	High	43 (36.75)	77 (34.38)		43 (36.75)	42 (35.90)		113 (41.70)	142 (39.66)		113 (41.70)	115 (42.44)	
Employment	Not employed	63 (53.85)	141 (62.95)	0.48	63 (53.85)	67 (57.26)	0.71	147 (54.24)	210 (58.66)	0.34	147 (54.24)	150 (55.35)	0.87
	Employed	54 (46.15)	83 (37.05)		54 (46.15)	50 (42.74)		124 (45.76%)	148 (41.34%)		124 (45.76%)	121 (44.65%)	
Insurance	Uninsured	3 (2.56)	5 (2.23)	0.45	3 (2.56)	3 (2.56)	0.94	8 (2.95)	3 (0.84)	0.30	8 (2.95)	3 (1.11)	0.38
	Private	69 (58.97)	132 (58.93)		69 (58.97)	66 (56.41)		165 (60.89)	232 (64.80)		165 (60.89)	174 (64.21)	
	Public	45 (38.46)	87 (38.84)		45 (38.46)	48 (41.03)		98 (36.16%)	123 (34.36%)		98 (36.16%)	94 (34.69%)	
Perceived health status	Poor	2 (1.71)	26 (11.61)	0.17	2 (1.71)	1 (0.85)	0.92	15 (5.54)	26 (7.26)	0.11	15 (5.54)	15 (5.54)	0.94
	Fair	36 (30.77)	69 (30.80)		36 (30.77)	35 (29.91)		56 (20.66)	78 (21.79)		56 (20.66)	55 (20.30)	
	Good	49 (41.88)	86 (38.39)		49 (41.88)	54 (46.15)		112 (41.33)	157 (43.85)		112 (41.33)	121 (44.65)	
	Very good	22 (18.80)	37 (16.52)		22 (18.80)	21 (17.95)		80 (29.52)	84 (23.46)		80 (29.52)	71 (26.20)	
	Excellent	8 (6.84)	6 (2.68)		8 (6.84)	6 (5.13)		8 (2.95)	13 (3.63)		8 (2.95)	9 (3.32)	
Comorbidity score	0	24 (20.51)	40 (17.86)	0.93	24 (20.51)	26 (22.22)	0.99	40 (14.76)	45 (12.57)	0.96	40 (14.76)	38 (14.02)	0.99
	1	55 (47.01)	78 (34.82)		55 (47.01)	53 (45.30)		135 (49.82)	165 (46.09)		135 (49.82)	135 (49.82)	
	2	25 (21.37)	57 (25.45)		25 (21.37)	25 (21.37)		70 (25.83)	108 (30.17)		70 (25.83)	70 (25.83)	
	≥3	13 (11.11)	49 (21.88)		13 (11.11)	13 (11.11)		26 (9.59)	40 (11.17)		26 (9.59)	28 (10.33)	
Total condition	1–2	12 (10.26)	18 (8.04)	0.14	12 (10.26)	11 (9.40)	0.99	16 (5.90)	20 (5.59)	0.73	16 (5.90)	15 (5.54)	0.98
	3–5	29 (24.79)	48 (21.43)		29 (24.79)	32 (27.35)		84 (31.00)	96 (26.82)		84 (31.00)	85 (31.37)	
	6–10	56 (47.86)	75 (33.48)		56 (47.86)	55 (47.01)		127 (46.86)	149 (41.62)		127 (46.86)	120 (44.28)	
	11–20	19 (16.24)	68 (30.36)		19 (16.24)	18 (15.38)		41 (15.13)	83 (23.18)		41 (15.13)	48 (17.71)	
	21–30	1 (0.86)	14 (6.25)		1 (0.86)	1 (0.85)		2 (0.74)	9 (2.51)		2 (0.74)	2 (0.74)	
	31–40	0 (0)	1 (0.45)		0 (0)	0 (0)		1 (0.37)	1 (0.28)		1 (0.37)	1 (0.37)	
Eye	No	91 (77.78)	162 (72.32)	0.12	91 (77.78)	93 (79.49)	0.81	221 (81.55)	285 (79.61)	0.75	221 (81.55)	218 (80.44)	0.81
	Yes	26 (22.22)	62 (27.68)		26 (22.22)	24 (20.51)		50 (18.45)	73 (20.39)		50 (18.45)	53 (19.56)	

(Continued)

Table 2 (Continued).

Baseline Characteristics		Before Matching			After Matching			Before Matching			After Matching		
		SGLT2 Inhibitor N = 117 n (%)	GLP-I RA N = 224 n (%)	P value	SGLT2 Inhibitor N = 117 n (%)	GLP-I RA N = 117 n (%)	P value	SGLT2 Inhibitor + Metformin N = 271 n (%)	GLP-I RA + Metformin N = 358 n (%)	P value	SGLT2 Inhibitor + Metformin N = 271 n (%)	GLP-I RA + Metformin N = 271 n (%)	P value
Kidney	No	105 (89.74)	163 (72.77)	0.0028**	105 (89.74)	98 (83.76)	0.28	249 (91.88)	319 (89.11)	0.40	249 (91.88)	245 (90.41)	0.66
	Yes	12 (10.26)	61 (27.23)		12 (10.26)	19 (16.24)		22 (8.12%)	39 (10.89)		22 (8.12)	26 (9.59)	
MI	No	104 (88.89)	196 (87.50)	0.40	104 (88.89)	102 (87.18)	0.79	235 (86.72)	315 (87.99)	0.42	235 (86.72)	236 (87.08)	0.92
	Yes	13 (11.11)	28 (12.50)		13 (11.11)	15 (12.82)		36 (13.28)	43 (12.01)		36 (13.28)	35 (12.92)	
Stroke	No	106 (90.60)	196 (87.50)	0.98	106 (90.60)	107 (91.45)	0.85	250 (92.25)	317 (88.55)	0.26	250 (92.25)	250 (92.25)	1
	Yes	11 (9.40)	28 (12.50)		11 (9.40)	10 (8.55)		21 (7.75)	41 (11.45)		21 (7.75)	21 (7.75)	

Notes: *N=sample size after propensity score matching. **Statistical significance. P = 0.0031 (after Bonferroni adjustment).

Abbreviations: T2DM, type 2 diabetes mellitus; SGLT2 inhibitor, SGLT2 inhibitor; GLP-I RA, GLP-I receptor agonist; OOP, out-of-pocket; PCS, physical component summary; MCS, mental component summary; MEPS, Medical Expenditure Panel Survey.

Table 3 Baseline Characteristics of Adults with T2DM on SGLT2 Inhibitor and GLP-I RA Without and with Metformin for Total Prescription Expenditure, PCS, and MCS Before and After Matching Using MEPS Data 2017–2021 (N=320 vs N = 626*)

Baseline Characteristics		Before Matching			After Matching			Before Matching			After Matching		
		SGLT2 Inhibitor N=160 n (%)	GLP-I RA N = 285 n (%)	P value	SGLT2 Inhibitor N = 160 n (%)	GLP-I RA N = 160 n (%)	P value	SGLT2 Inhibitor + Metformin N=313 n (%)	GLP-I RA + Metformin N = 404 n (%)	P value	SGLT2 Inhibitor + Metformin N = 313 n (%)	GLP-I RA + Metformin N = 313 n (%)	P value
Age	18–44	17 (10.63)	25 (8.77)	0.43	17 (10.63)	15 (9.38)	0.93	24 (7.67)	31 (7.67)	0.91	24 (7.67)	21 (6.71)	0.89
	45–64	82 (51.25)	128 (44.91)		82 (51.25)	80 (50.00)		154 (49.20)	198 (49.01)		154 (49.20)	162 (51.76)	
	≥65	61 (38.13)	132 (46.32)		61 (38.13)	65 (40.63)		135 (43.13)	175 (43.32)		135 (43.13)	130 (41.53)	
Sex	Male	76 (47.50)	106 (37.19)	0.08	76 (47.50)	68 (42.50)	0.56	166 (53.04)	178 (44.06)	0.054	166 (53.04)	159 (50.80)	0.72
	Female	84 (52.50)	179 (62.81)		84 (52.50)	92 (57.50)		147 (46.96)	226 (55.94)		147 (46.96)	154 (49.20)	
Race	White	110 (68.75)	212 (74.39)	<0.001**	110 (68.75)	117 (73.13)	0.20	250 (79.87)	312 (77.23)	0.0016**	250 (79.87)	245 (78.27)	0.58
	Black	28 (17.50)	56 (19.65)		28 (17.50)	33 (20.63)		32 (10.22)	60 (14.85)		32 (10.22)	45 (14.38)	
	Multiple	4 (2.50)	11 (3.86)		4 (2.50)	4 (2.50)		10 (3.19)	18 (4.46)		10 (3.19)	9 (2.88)	
	Other	18 (11.25)	6 (2.11)		18 (11.25)	6 (3.75)		21 (6.71)	14 (3.47)		21 (6.71)	14 (4.47)	
Region	Northeast	19 (11.88)	39 (13.68)	0.80	19 (11.88)	20 (12.50)	0.94	50 (15.97)	61 (15.10)	0.87	50 (15.97)	47 (15.02)	0.96
	Midwest	33 (20.63)	51 (17.89)		33 (20.63)	32 (20.00)		82 (26.20)	101 (25.00)		82 (26.20)	81 (25.88)	
	South	86 (53.75)	149 (52.28)		86 (53.75)	91 (56.88)		116 (37.06)	168 (41.58)		116 (37.06)	125 (39.94)	
	West	22 (13.75)	46 (16.14)		22 (13.75)	17 (10.63)		65 (20.77)	74 (18.32)		65 (20.77)	60 (19.17)	
Education	No school	0 (0)	0 (0)	0.83	0 (0)	0 (0)	0.76	0 (0)	0 (0)	0.15	0 (0)	0 (0)	0.41
	Grade 1–8	6 (3.75)	11 (3.83)		6 (3.75)	9 (5.63)		34 (10.86)	22 (5.45)		34 (10.86)	21 (6.71)	
	Grade 9–12	84 (52.50)	131 (45.96)		84 (52.50)	82 (51.25)		111 (35.46)	157 (38.86)		111 (35.46)	120 (38.34)	
	Grade >12	70 (43.75)	143 (50.18)		70 (43.75)	69 (43.13)		168 (53.67)	225 (55.69)		168 (53.67)	172 (54.95)	
Marriage	Never married	21 (13.13)	38 (13.33)	0.81	21 (13.13)	19 (11.88)	0.87	35 (11.18)	58 (14.36)	0.31	35 (11.18)	38 (12.14)	0.74
	Widowed	53 (33.13)	107 (37.54)		53 (33.13)	58 (36.25)		118 (37.70)	123 (30.45)		118 (37.70)	104 (33.23)	
	Married	86 (53.75)	140 (49.12)		86 (53.75)	83 (51.88)		160 (51.12)	223 (55.20)		160 (51.12)	171 (54.63)	

(Continued)

Table 3 (Continued).

Baseline Characteristics		Before Matching			After Matching			Before Matching			After Matching		
		SGLT2 Inhibitor N=160 n (%)	GLP-1 RA N = 285 n (%)	P value	SGLT2 Inhibitor N = 160	GLP-1 RA N = 160 n (%)	P value	SGLT2 Inhibitor + Metformin N=313 n (%)	GLP-1 RA + Metformin N = 404 n (%)	P value	SGLT2 Inhibitor + Metformin N = 313 n (%)	GLP-1 RA + Metformin N = 313 n (%)	P value
Income	Negative/poor/ near poor	39 (24.38)	87 (30.53)	0.63	39 (24.38)	42 (26.25)	0.94	76 (24.28)	77 (19.06)	0.15	76 (24.28)	65 (20.77)	0.81
	Low	20 (12.50)	36 (12.63)		20 (12.50)	17 (10.63)		36 (11.50)	63 (15.59)		36 (11.50)	42 (13.42)	
	Middle	45 (28.13)	74 (25.96)		45 (28.13)	49 (30.63)		78 (24.92)	115 (28.47)		78 (24.92)	83 (26.52)	
	High	56 (35.00)	88 (30.88)		56 (35.00)	52 (32.50)		122 (38.98)	149 (36.88)		122 (38.98)	123 (39.30)	
Employment	Not employed	85 (53.13)	189 (65.61)	0.20	85 (53.13)	88 (55.00)	0.81	179 (57.19)	241 (59.65)	0.70	179 (57.19)	179 (57.19)	1
	Employed	75 (46.88)	98 (34.39)		75 (46.88)	72 (45.00)		134 (42.81)	163 (40.35)		134 (42.81)	134 (42.81)	
Insurance	Uninsured	3 (1.88)	8 (2.81)	0.82	3 (1.88)	3 (1.88)	0.95	8 (2.56)	3 (0.74)	0.32	8 (2.56)	3 (0.96)	0.41
	Private	90 (56.25)	147 (51.58)		90 (56.25)	87 (54.38)		176 (56.23)	246 (60.89)		176 (56.23)	187 (59.74)	
	Public	67 (41.88)	130 (45.61)		67 (41.88)	70 (43.75)		129 (41.21)	155 (38.37)		129 (41.21)	123 (39.30)	
Perceived health status	Poor	6 (3.75)	36 (12.63)	0.17	6 (3.75)	4 (2.50)	0.74	23 (7.35)	31 (7.67)	0.17	23 (7.35)	20 (6.39)	0.95
	Fair	52 (32.50)	89 (31.23)		52 (32.50)	51 (31.88)		66 (21.09)	89 (22.03)		66 (21.09)	64 (20.45)	
	Good	62 (38.75)	109 (38.25)		62 (38.75)	72 (45.00)		126 (40.26)	176 (43.56)		126 (40.26)	137 (43.77)	
	Very good	31 (19.38)	45 (15.79)		31 (19.38)	28 (17.50)		89 (28.43)	94 (23.27)		89 (28.43)	84 (26.84)	
	Excellent	9 (5.63)	6 (2.11)		9 (5.63)	5 (3.13)		9 (2.88)	14 (3.47)		9 (2.88)	8 (2.56)	
Comorbidity score	0	33 (20.63)	50 (17.54)	0.93	33 (20.63)	32 (20.00)	0.99	48 (15.34)	51 (12.62)	0.90	48 (15.34)	46 (14.70)	0.98
	1	70 (43.75)	97 (34.04)		70 (43.75)	69 (43.13)		157 (50.16)	180 (44.55)		157 (50.16)	154 (49.20)	
	2	35 (21.88)	74 (25.96)		35 (21.88)	34 (21.25)		75 (23.96)	119 (29.46)		75 (23.96)	81 (25.88)	
	≥3	22 (13.75)	64 (22.46)		22 (13.75)	25 (15.63)		33 (10.54)	54 (13.37)		33 (10.54)	32 (10.22)	

Total condition	1–2	16 (10.00)	21 (7.37)	0.27	16 (10.00)	17 (10.63)	0.89	18 (5.75)	23 (5.69)	0.58	18 (5.75)	17 (5.43)	0.80
	3–5	39 (24.38)	59 (20.70)		39 (24.38)	37 (23.13)		97 (30.99)	103 (25.50)		97 (30.99)	93 (29.71)	
	6–10	71 (44.38)	98 (34.39)		71 (44.38)	70 (43.75)		143 (45.69)	167 (41.34)		143 (45.69)	144 (46.01)	
	11–20	32 (20.00)	83 (29.12)		32 (20.00)	31 (19.38)		51 (16.29)	99 (24.50)		51 (16.29)	58 (18.53)	
	21–30	2 (1.25)	22 (7.72)		2 (1.25)	5 (3.13)		3 (0.96)	11 (2.72)		3 (0.96)	0 (0)	
	31–40	0 (0)	2 (0.70)		0 (0)	0 (0)		1 (0.32)	1 (0.25)		1 (0.32)	1 (0.32)	
Eye	No	117 (73.13)	208 (72.98)	0.84	117 (73.13)	119 (74.38)	0.86	250 (79.87)	319 (78.96)	0.39	250 (79.87)	250 (79.87)	1
	Yes	43 (26.88)	77 (27.02)		43 (26.88)	41 (25.63)		63 (20.13)	85 (21.04)		63 (20.13)	63 (20.13)	
Kidney	No	138 (86.25)	207 (72.63)	0.0056***	138 (86.25)	134 (83.75)	0.63	285 (91.05)	359 (88.86)	0.48	285 (91.05)	281 (89.78)	0.69
	Yes	22 (13.75)	78 (27.37)		22 (13.75)	26 (16.25)		28 (8.95)	45 (11.14)		28 (8.95)	32 (10.22)	
MI	No	143 (90.38)	246 (86.32)	0.86	143 (90.38)	145 (90.63)	0.79	271 (86.58)	358 (88.61)	0.43	271 (86.58)	276 (88.18)	0.62
	Yes	17 (10.63)	39 (13.68)		17 (10.63)	15 (9.38)		42 (13.42)	46 (11.39)		42 (13.42)	37 (11.82)	
Stroke	No	147 (91.88)	246 (86.32)	0.42	147 (91.88)	140 (87.50)	0.26	287 (91.69)	359 (88.86)	0.28	287 (91.69)	285 (91.05)	0.82
	Yes	13 (8.13)	39 (13.68)		13 (8.13)	20 (12.50)		26 (8.31)	45 (11.14)		26 (8.31)	28 (8.95)	

Notes: *N=sample size after propensity score matching. **Statistical significance. P = 0.0031 (after Bonferroni adjustment). ***Not statistical significance. P = 0.0031 (after Bonferroni adjustment).
Abbreviations: T2DM, type 2 diabetes mellitus; SGLT2 inhibitor, SGLT2 inhibitor; GLP-I RA, GLP-I receptor agonist; PCS, physical component summary; MCS, mental component summary; MEPS, Medical Expenditure Panel Survey.

study used nationally representative survey data. Around 40% of this study's population had public insurance with a lower co-pay. Another reason was that their study did not exclude patients receiving SGLT2 inhibitor or GLP-1 RA for weight loss purposes. However, this study focused on patients using these two medication classes for T2DM treatment. Currently, majority of the employer pharmacy plans exclude coverage for weight loss drugs. While most previous studies focused on the economic perspective between these two medication classes, this study also focused on the HRQoL. Dadwani et al conducted a study using the National Health and Nutrition Examination Survey (NHANES) 2013–2018 database and the United Kingdom Prospective Diabetes Study model to measure HRQoL between SGLT2 inhibitor and GLP-1 RA.²⁶ Their study had similar results as this study. However, the difference was that their study focused on older patients with an average age of 73 years and used life year (LY) and quality-adjusted life year (QALY) to measure HRQoL. Their study indicated that GLP-1 RA (+0.29) has a similar LY compared to SGLT2 inhibitor (+0.26). The QALY also showed similar results (GLP-1 RA vs SGLT2 inhibitor: +0.15 vs 0.13). Torre et al used EQ-5D to compare HRQoL between 2014 and 2015 on patients with T2DM on either SGLT2 inhibitor or GLP-1 RA.²⁷ The baseline scores between SGLT2 inhibitor (0.71) and GLP-1 RA (0.69) groups were similar. After 26 weeks of treatment, there were similar improvements in EQ-5D scores between these two medication classes (SGLT2 inhibitor vs GLP1 RA: 0.76 vs 0.71). Both previous studies and this study demonstrate that patients on SGLT2 inhibitor and GLP-1 RA had similar HRQoL.^{26,27}

When comparing total prescription expenditure between SGLT2 inhibitor and GLP-1 RA, Insiya et al found that patients on GLP-1 RA had significantly higher total prescription expenditure than those on SGLT2 inhibitor.²⁸ This discrepancy was likely because they used Medicare Advantage claim data, resulting in an older population (mean age: 65.1 years (GLP-1 RA), 65.3 years (SGLT2 inhibitor)) than this study (mean age: 59.9 years (GLP-1 RA), 59.2 years (SGLT2 inhibitor)). Another reason for the discrepancy was that the study population in their study was followed for the first 12 months after the patient was started on SGLT2 inhibitor or GLP-1 RA, and the patient needed to have at least two prescription claims.²⁸ In the current study, total prescription expenditure was evaluated disregarding their diagnosis year and the year they were first prescribed the medication.

This study analyzed health expenditure and HRQoL using MEPS data from 2017 to 2021, which included the COVID-19 pandemic period, during which patients with T2DM reduced their health utilization.²⁹ Parker et al conducted a study using the Cost of Diabetes Economic Model to estimate the difference with and without the COVID-19 pandemic's impact. Their study found that the direct medical cost of patients with T2DM showed a change of < 5%.¹ Because the study by Parker et al used a model to estimate the cost, further real-world study on the COVID pandemic's impact is needed to be assessed. Additionally, the MEPS data were self-reported survey based. This study cannot rule out recall bias in survey data. MEPS data does not contain any clinical data, therefore SGLT2 inhibitor or GLP-1 RA's effect on efficacy or side effects in the real world cannot be determined.

Current study has a few limitations. In this study recall bias given MEPS is a self-reported survey database was not omitted.¹⁸ Another limitation is, this study cannot compare efficacy or safety outcomes between SGLT2 inhibitor or GLP-1 RA. Thus, further investigation using claims data and electronic medication records to compare health expenditure, efficacy or safety outcomes, and HRQoL between SGLT2 inhibitor and GLP-1 RA with a larger sample size is needed.

Conclusion

This study revealed that GLP-1 RA had significantly higher OOP costs than SGLT2 inhibitor. However, the study results need to be validated with larger patient data sets, since there was no significant difference in PCS or MCS. The findings nevertheless have implications for guiding healthcare providers when they prescribe SGLT2 inhibitor or GLP-1 RA for patients with T2DM. Further investigation using claims data and electronic medical records is needed to compare the economic outcome, clinical outcome, and HRQoL between SGLT2 inhibitor and GLP-1 RA.

Abbreviations

T2DM, type 2 diabetes; ADA, American Diabetes Association; SGLT2 inhibitor, sodium-glucose cotransporter 2 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; MACE, major adverse cardiovascular events; GI, gastrointestinal disorders; CORE, Center for Outcomes Research Diabetes Model; MEPS, Medical Expenditure Panel

Survey; HRQoL, health-related quality of life; AHRQ, Agency for Healthcare Research and Quality; PCS, physical component summary; MCS, mental component summary; OOP, out-of-pocket; VR 12, veterans rand 12.

Data Sharing Statement

Used data from publicly available files (MEPS). The first author takes responsibility for integrating data, subdata has not been published anywhere. The first author considers sharing with those who are interested.

Ethics Approval and Informed Consent

Under HHS CFR 46.104, this non-interventional study does not require IRB approval, as data obtained in the study, the patients whose information is not identified even to researchers received marketed drugs during routine medical practice and are not assigned to an intervention based on a protocol.

Consent for Publication

No images were copied or used.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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