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Real-World Comparison of Adherence and Persistence Between Glucagon-like Peptide-1 (GLP-1) Receptor Agonist and Sodium-Glucose Cotransporter 2 (SGLT-2) Inhibitors in Patients With Type 2 Diabetes (T2D)

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Background

According to the Centers for Disease Control and Prevention (CDC), roughly 1 in 10 Americans have diabetes, and approximately 90.0% to 95.0% of them have type 2 diabetes (T2D). Americans over the age of 45 are most likely to have T2D.[1] Glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose cotransporter-2 (SGLT-2) inhibitors are recommended for patients with T2D at increased risk for cardiovascular complications.[2] It is well known, however, that the efficacy of medications observed in clinical trials often exceeds their real-world effectiveness due to patients' nonadherence and discontinuation of therapy.[3]

Objective

To address the gap in knowledge, the objective of this study is to assess the adherence and discontinuation of GLP-1 receptor agonists and SGLT-2 inhibitors among adult patients with T2D in the United States based on real-world claims and linked clinical data from ICON's Symphony Health Integrated Dataverse (IDV®).

Methods

Adults with T2D, with ≥1 year of follow-up, naïve to the drug class, and who initiated a newer GLP-1 receptor agonist or SGLT-2 inhibitor between 2017 and 2021 (the index date) were identified using ICON's Symphony Health Integrated Dataverse (IDV). Included drugs are listed in the results section. Individual drug information was tracked and aggregated into the 2 drug classes for the current analysis.

Data source:

The IDV is an open, multisource dataset representative of all 50 US states, as well as US territories. These claims data are captured through thousands of sources, including pharmacy direct feeds and lifecycle (Network Intelligence Bureaus) feeds. IDV encompasses medical, hospital, and prescription claims across all payment types (commercial, Medicare, Medicaid, Managed Medicaid, cash, and assistance programs). The dataset represents 17+ years of historical data for more than 307 million active deidentified patients, 1.9 million healthcare providers, and 18,000+ unique plans. IDV pharmacy and medical claims and lab data were integrated into a single enriched dataset using ICON's Symphony Health Synoma® tokenization.

Patient inclusion criteria:

- With ≥1 pharmacy claim for a newer GLP-1 receptor agonist or SGLT-2 inhibitor during the study period and naïve to the respective drug class
  - Study period: January 1, 2017 through October 31, 2021
  - Index therapy: first drug class (GLP-1 receptor agonist or SGLT-2 inhibitor) in the study period
  - Index date: first claim fill date in the study period for index therapy
- ≥1 diagnosis of T2D before the index date as captured from medical claims
- Age ≥18 years of age on index date
- ≥1 year of history and ≥1 year of follow-up as evidenced by at least 1 pharmacy claim for any drug before and after index date, respectively
- Hemoglobin A1c (HbA1c) ≥7% within 60 days of the index date

Patient exclusion criteria:

- Diagnosis of type 1 diabetes (TD1) or other diabetes before the index date captured from medical claims
- Pharmacy claim for the index therapy prior to index date

Study outcomes:

- Outcomes were measured from index date through last pharmacy fill date plus days supply or end of the study period in 2023.
  - Adherence to index therapy was measured by the proportion of days covered (PDC) ≥80%.
  - Persistence on index therapy was measured as time from index date to first discontinuation and as a proportion on treatment at 90, 180, 360, and 720 days post-index, where discontinuation was assigned if there was a gap of more than 90 days between one pharmacy fill date plus days supply and the subsequent fill date.

Analysis:

- Descriptive statistics such as counts, percentages, means, and standard deviations were used to characterize the patients.
- Chi-square tests or t-tests were used to compare treatment groups (GLP-1 receptor agonist vs SGLT-2 inhibitor) for categorical or continuous variables, respectively.

Results

In IDV, 1,789,151 and 1,953,547 patients who newly initiated a GLP-1 receptor agonist or SGLT- 2 inhibitor met the inclusion criteria with at least 1 year of follow-up and 165,758 and 233,222 patients, respectively, met the HbA1c criterion (**Figure 1**).

Figure 1. Patient Attrition for Study Inclusion

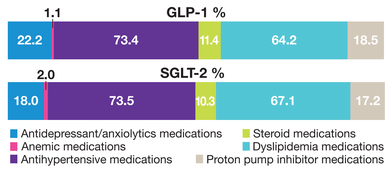
	GLP-1	SGLT-2
Patients treated with newer SGLT2 or GLP-1 between January 1, 2017 and October 31, 2021	N=3,915,024	N=3,985,391
Diagnosed with T2D any time prior to index date	2,476,857 (96.7%)	2,880,124 (72.3%)
Exclude patients diagnosed with T1D or other diabetes prior to index date	1,945,671 (78.6%)	2,815,303 (97.7%)
Exclude patients treated by index product prior to index date	1,943,086 (99.9%)	2,135,597 (75.9%)
Age 18+ on index date	2,561,074 (65.4%)	2,135,300 (100.0%)
12 months of baseline	1,874,159 (96.5%)	2,053,025 (96.1%)
12 months of follow-up	1,789,151 (95.5%)	1,953,547 (95.2%)
HbA1c ≥7% within 60 days prior to index date	165,758 (9.3%)	233,222 (11.9%)

Baseline Characteristics (Figure 2)

- Starting a GLP-1 receptor agonist, the main cohort was primarily female (51.4%) with a mean age of 59.0 years.
- Starting a SGLT-2 inhibitor, the main cohort was primarily male (56.4%) with a mean age of 59.7 years.
- Average HbA1c for patients taking the GLP-1 receptor agonist or SGLT-2 inhibitor at the index date (9.3% vs 9.1%, respectively) and years of follow-up (3.9 vs 4.1 years, respectively) were similar.

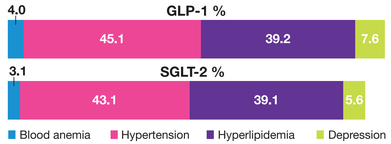
GLP-1 receptor agonist index therapy patients had a slightly higher proportion for patients on anti-depressants (22.2% vs 18.0%) while patients on SGLT-2 inhibitor index therapy had a slightly higher proportion of use for dyslipidemia medications (67.1% vs 64.2%) (**Figure 3**).

Figure 3. Concomitant Medications at Time of Index Therapy Initiation



The patient cohort indexed on GLP-1 receptor agonists had a higher proportion of patients with anemia, hypertension, and depression comorbidities (**Figure 4**).

Figure 4. Comorbid Conditions at Time of Index Therapy Initiation



- Proportion of days covered (PDC) was statistically higher for patients taking SGLT-2 inhibitors (mean of 0.78, with standard deviation of 0.26) compared to GLP-1 receptor agonists (mean of 0.74, with standard deviation of 0.27) as shown in **Table 1**.
- Based on the mean PDC, the claims data indicates that patients are missing on average 26.0% of GLP-1 receptor agonist doses and 22.0% of SGLT-2 inhibitor doses.

Table 1. Treatment Adherence for Patients Newly Initiating a GLP-1 Receptor Agonist or SGLT-2 Inhibitor

Treatment adherence (PDC)	GLP-1 (n=165,758)	SGLT-2 (n=233,222)
Mean (SD)	0.74 (0.27)	0.78 (0.26)
Patients with PDC ≥80% n (%)	90,613 (54.7%)	144,938 (62.2%)

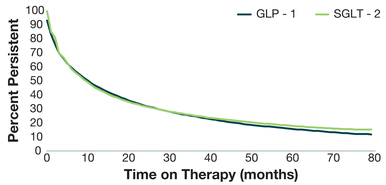
- GLP-1 receptor agonist and SGLT-2 inhibitor persistence at 360 days (48.1% vs 46.8%, respectively) and 720 days (33.1% vs 32.5%, respectively) were similar (**Table 2**).

Table 2. GLP-1 Receptor Agonist and SGLT-2 Inhibitor Persistence Rates

Persistence time to treatment discontinuation (n, %)	GLP-1 165,758 n	GLP-1 165,758 %	SGLT-2 233,222 n	SGLT-2 233,222 %
At 90 days	126,401	76.3%	188,464	80.8%
At 180 days	103,328	62.3%	145,645	62.4%
At 360 days	79,668	48.1%	109,120	46.8%
At 720 days	52,857	33.1%	73,305	32.5%

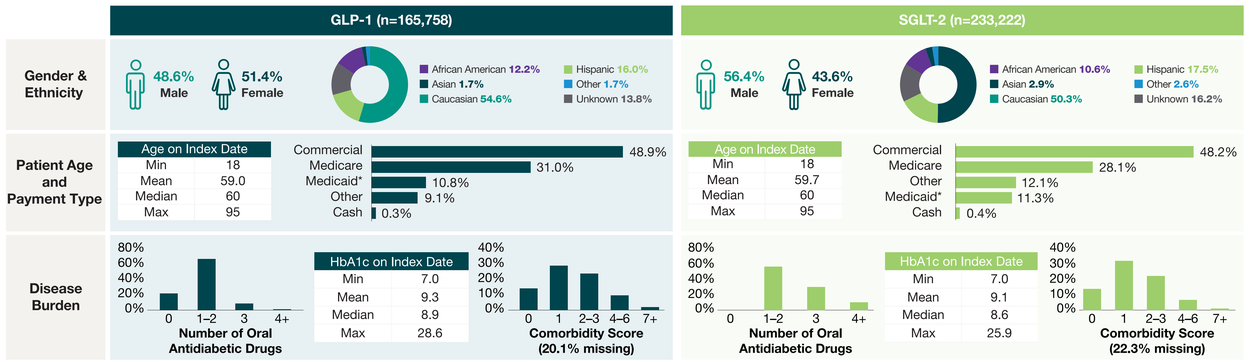
As seen in **Figure 5**, patients on SGLT-2 inhibitors are more persistent than patients on GLP-1 receptor agonists.

Figure 5. Patient Persistency for GLP-1 Receptor Agonists and SGLT-2 Inhibitors



Note: Time on therapy was censored at last pharmacy fill (end of follow-up) or end of study period.

Figure 2. Demographics and Baseline Characteristics for Analyses



* Medicaid FFS/Managed Medicaid.

Conclusions

The study population included in this real-world data analysis had poorly controlled HbA1c at the time of starting the index product (average HbA1c at the time of initiation, >9.0%) and justified significant treatment intensification according to diabetes treatment guidelines.[4, 5]

Of note, this study found only 55.0% of patients on GLP-1 receptor agonists and 62.0% of patients on SGLT-2 inhibitors with an adherence greater than 80.0%. This indicates potential ongoing challenges in this population with meeting target glycemic control. Further investigation into treatment intensification and associated clinical outcomes in this large RWE dataset is warranted.

Further, more research is needed to understand how to support adherence and improve patient outcomes in this patient population. This large dataset may be helpful in explaining some of the reasons for low persistence. The correlation with comorbid conditions in patients who dropped off the index therapy, HbA1c measures after drug initiation, other concomitant drugs, out-of-pocket costs for index treatments, and total cost of care are all areas worth further exploration. In addition, therapy switching once patients dropped off the index product may also be useful to examine.

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GLP-1 Products: Trulicity® (dulaglutide); Victoza® and Saxenda® (liraglutide); Ozempic®, Rybelsus® and Wegovy® (semaglutide); Mounjaro® (tirzepatide).
SGLT-2 Products: Invokana® (canagliflozin); Farxiga® (dapagliflozin propanediol); Jardiance® (empagliflozin); Steglatro® (ertugliflozin pidolate); Invokamet® (canagliflozin/metformin HCl); Xigduo® (dapagliflozin/metformin HCl); Synjardy® (empagliflozin/metformin HCl); Segluromet® (ertugliflozin/metformin); Qtern® (dapagliflozin/saxagliptin HCl); Glyxambi® (empagliflozin/linagliptin); Steglujan® (ertugliflozin/sitagliptin).