Utilization of Type 2 Diabetes Mellitus Products in the Sentinel Distributed Database, 2008-2024

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Background

- Post-market safety studies of type 2 diabetes (T2D) products are routinely conducted using the United States (U.S.) Food and Drug Administration's Sentinel Distributed Database (SDD) of commercial and public insurance claims.
- Contemporary information on patterns of T2D product use in the SDD can inform the feasibility of complex exposure modeling for safety analyses.

OBJECTIVE: To characterize the population of T2D product initiators and duration of T2D product use from 2008-2024.

Methods

- **Study period:** Jan. 1, 2008 – latest available data (cut-off date: May 31, 2024)
- **Study population:** Initiators (identified at first observed dispensing in the database after a 365-day washout) of four classes of T2D products (including those with weight management indications):
  - dipeptidyl peptidase 4 inhibitors [DPP-4i]
  - sodium glucose co-transporter 2 inhibitors [SGLT-2i]
  - glucagon-like peptide-1 receptor agonists [GLP-1ra] and
  - glucose-dependent insulinotropic polypeptide [GIP]/GLP-1ra

  identified within four commercial and two public insurers that participate in the SDD.
- **Inclusion:** Continuous enrollment for 365 days prior to initiation. No other criteria implemented.
- **Characteristics:** We collected information on demographics and baseline health characteristics using procedure, diagnosis, and dispensing codes, as appropriate, in the 365 days prior to initiation.
- **Duration of exposure:** Assessed number of discontinuous exposure episodes per initiator and episode duration using days' supply; any overlapping days' supplies were shifted to be non-overlapping. We characterized cumulative exposure duration using all episodes after initiation.

Results

Table 1. Characteristics of Initiators by Drug Class at Initiation

	DPP-4i initiators (N=2,921,067) Mean/%[1]	SGLT-2i initiators (N=2,842,393) Mean/%[1]	GLP-1ra initiators (N=3,321,029) Mean/%[1]	GIP/GLP-1ra initiators (N=374,607) Mean/%[1]
Demographic Characteristics				
Mean age (years)	65.3	64.5	59.4	58.3
Age				
0-11 years	0.0%	0.0%	0.0%	***
12-17 years	0.0%	0.0%	0.3%	***
18-24 years	0.3%	0.3%	0.9%	0.8%
25-34 years	1.9%	1.9%	4.1%	4.0%
35-44 years	6.3%	6.5%	11.0%	12.1%
45-54 years	14.5%	14.9%	19.6%	22.6%
55-64 years	21.0%	22.2%	23.5%	25.1%
65-74 years	31.1%	32.5%	29.3%	26.2%
≥ 75 years	24.8%	21.6%	11.3%	9.1%
Sex				
Female	52.7%	46.5%	58.4%	62.0%
Male	47.3%	53.5%	41.6%	38.0%
Race[2]				
American Indian or Alaska Native	0.7%	0.7%	0.8%	0.3%
Asian	4.2%	3.9%	2.1%	1.3%
Black or African American	12.6%	11.4%	11.2%	8.6%
Multi-racial	0.3%	0.4%	0.7%	1.5%
Native Hawaiian or Other Pacific Islander	0.3%	0.3%	0.2%	0.1%
Unknown	26.5%	24.4%	27.7%	31.8%
White	55.4%	59.0%	57.3%	56.4%
Hispanic origin[2]				
Yes	7.0%	6.3%	5.6%	3.3%
No	70.2%	70.4%	66.1%	57.8%
Unknown	22.9%	23.3%	28.3%	38.9%
Health Characteristics				
aDCSI[3]	2.1	2.2	1.7	1.4
0	34.5%	30.5%	41.8%	48.2%
1	16.1%	15.9%	16.7%	16.2%
2	15.5%	17.8%	14.4%	13.5%
≥3	33.9%	35.8%	27.1%	22.1%
Frail[4]	11.6%	8.2%	6.7%	5.1%
Combined comorbidity score[5]	2.4	2.8	2.0	1.9
<1	34.2%	26.9%	33.4%	34.7%
1	17.2%	17.4%	20.7%	21.7%
2	12.2%	13.4%	14.1%	14.3%
≥3	36.5%	42.4%	31.8%	29.4%
Any T1DM code	8.7%	5.7%	6.9%	3.4%
T2DM (and no T1DM codes)	87.1%	83.7%	76.4%	72.1%
Obesity	29.2%	41.1%	53.3%	68.2%
Weight loss procedures	0.3%	0.2%	0.2%	0.2%
Body mass index (BMI, kg/m^2) 25-29	5.5%	8.5%	5.7%	6.6%
BMI 30-39	11.3%	20.0%	22.3%	32.4%
BMI 40-69	6.0%	10.3%	16.2%	24.5%
BMI 70+	0.1%	0.2%	0.4%	0.5%
Hypertension	83.5%	84.4%	77.1%	74.2%
Hyperlipidemia	77.8%	79.9%	73.3%	75.0%
Ischemic heart disease	28.3%	32.8%	22.1%	19.4%
Cerebrovascular disease	8.0%	6.6%	4.9%	3.5%
Peripheral vascular disease	17.9%	18.2%	13.6%	12.1%
Heart failure	15.7%	23.0%	11.7%	9.9%
Obstructive sleep apnea	12.0%	18.8%	21.4%	27.5%
Chronic kidney disease	44.9%	58.1%	49.5%	46.8%
Dialysis	2.1%	1.3%	1.3%	1.0%
Smoking	19.5%	24.7%	20.8%	19.0%
Other Diabetes Medication Use				
Prior use of metformin	67.7%	66.5%	63.0%	51.9%
Prior use of sulfonylurea	40.8%	32.3%	29.2%	16.0%
Prior use of thiazolidinedione	10.4%	7.3%	7.5%	5.3%
Prior use of LIA insulin	17.6%	24.8%	28.2%	21.4%
Prior use of short/rapid acting insulin	9.4%	13.3%	16.1%	12.8%
Prior use of combination insulin	2.8%	2.7%	3.1%	1.4%
Prior use of DPP-4 inhibitors	0.0%	21.8%	19.7%	6.8%
Prior use of SGLT-2 inhibitors	6.3%	0.0%	16.0%	23.9%
Health Service Utilization Intensity Metrics				
Mean number of ambulatory encounters	21.3	21.2	21.6	21.2
Mean number of ED encounters	0.7	0.7	0.7	0.5
Mean number of hospital admissions	0.4	0.3	0.2	0.1
Mean number of filled prescriptions	51.1	49.5	49.9	45.6
Mean number of generics dispensed	12.1	12.5	12.6	12.9
Mean number of unique drug classes	10.7	11.0	11.0	11.3

***Data are not presented in these cells due to counts <11 or to ensure a small cell cannot be recalculated.
aDCSI = adapted diabetes complications severity index; DPP-4 inhibitors=dipeptidyl peptidase-4 inhibitors; ED = emergency department; GIP=glucose-dependent insulinotropic polypeptide; GLP-1 agonists=glucagon-like peptide-1 receptor agonists; LIA = long- or intermediate-acting; SGLT-2 inhibitors=sodium-glucose cotransporter-2 inhibitors.

[1]Value represents mean where no % follows the value.
[2]Race and ethnicity data may not be completely populated at all Data Partners; therefore, these data may be incomplete.
[3]Chang H-Y, et al. Validating the adapted Diabetes Complications Severity Index in claims data. Am J Manag Care. 2012;18(11):721-726.
[4]Kim DH, et al. Measuring frailty in Medicare data: development and validation of a claims-based frailty index. J Gerontol A Biol Sci Med Sci. 2018;73(7)980-987.
[5]Gagne JJ, et al. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759. Sun JW, et al. Adaptation and validation of the combined comorbidity score for ICD-10-CM. Med Care. 2017;55(12):1046-1051.

Figure 1. Number of Initiators by Drug Class and Year*

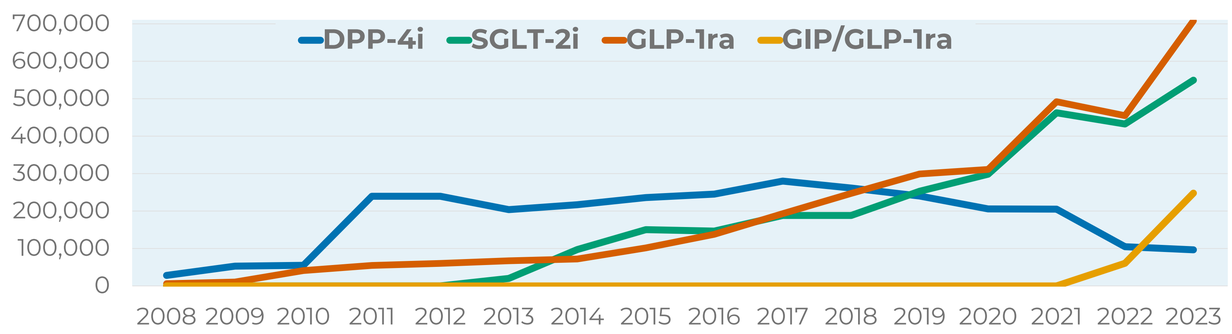


*Figure only includes years for which complete data was available

- **Uptake:** Initiations of SGLT-2i, GLP-1ra, and GIP/GLP-1ra increased annually in each year following marketing approval (through 2023), while DPP-4i initiations peaked in 2017 **(Figure 1)**
- **Demographics:** Mean age was between 58.3-65.3 years and 46.5%-62.0% of initiators were female **(Table 1)**. The majority of initiators in each drug class were White and non-Hispanic; race and ethnicity data was missing for >24% and >22% of initiators, respectively.
- **Baseline comorbidities:** >72% of each cohort had evidence of T2D at baseline **(Table 1)**. The most frequent comorbidities were hypertension (>74%), hyperlipidemia (>73%), and chronic kidney disease (>44%). Obesity prevalence ranged from 29.2% (DPP-4i) to 68.2% (GIP/GLP-1ra), and 19.0-24.7% of initiators had evidence of smoking at baseline.

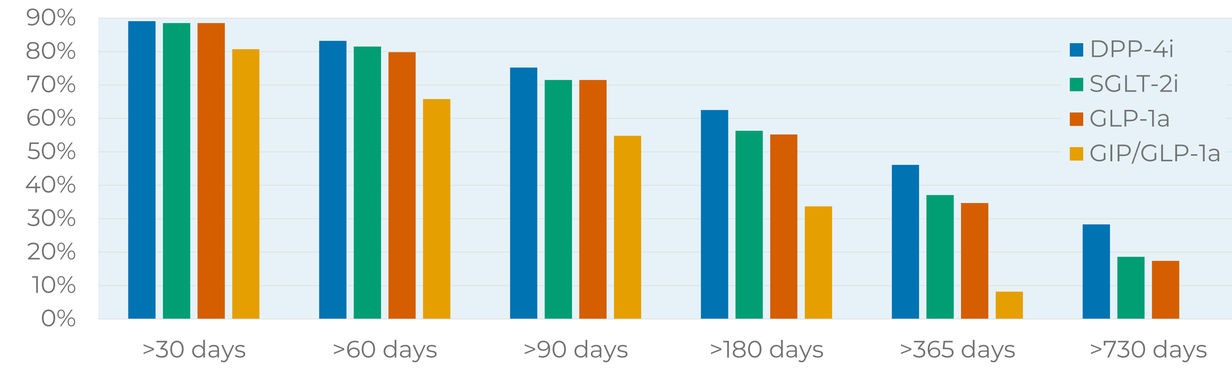
Table 2. Summary of Patients' Cumulative Treatment Episode Durations

Drug class	Initiators	Mean episodes per initiator	Distribution of Cumulative Treatment Duration, days						
			Min.	Q1	Q2	Q3	Max.	Mean	SD
DPP-4 inhibitors	2,921,067	5.60	1	94	328	838	5,884	611.7	739.5
SGLT-2 inhibitors	2,842,393	3.72	1	90	240	570	3,965	433.9	521.1
GLP-1 agonists	3,321,029	4.61	1	84	223	532	5,363	413.9	517.1
GIP/GLP-1 agonists	374,607	2.02	1	46	112	228	718	150.8	127.8

DPP-4 inhibitors=dipeptidyl peptidase-4 inhibitors; GIP=glucose-dependent insulinotropic polypeptide; GLP-1 agonists=glucagon-like peptide-1 receptor agonists; Max. = maximum; Min. = minimum; Q = quartile; SD = standard deviation; SGLT-2 inhibitors=sodium-glucose cotransporter-2 inhibitors

- **Exposure duration:** The mean number of exposure episodes was >3 for all drug classes except GIP/GLP-1ras **(Table 2)**, which were first approved in 2022 **(Figure 1)**. Median total exposure duration was between 112-328 days; means were notably higher than medians, suggesting some long-term users. <50% of initiators attained >365 days cumulative exposure **(Figure 2)**.

Figure 2. Proportion of Initiators by Cumulative Exposure Duration (Days)



Conclusions

Our data indicated that discontinuation or gaps in T2D product use were common, and our ability to study dose-response and conduct as-treated analyses may be limited by shorter exposure durations in the SDD.

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- The contents are those of the authors and do not necessarily represent the official views of, nor an endorsement by, FDA/HHS or the U.S. Government.
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