Real-world Impact of Semaglutide, Liraglutide, and Tirzepatide on Weight Loss and Cardiometabolic Lab Measures: A Look into Drug Persistence and Reasons for Discontinuation

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Introduction

- Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) semaglutide and liraglutide, along with the dual gastric inhibitory polypeptide/GLP-1RA tirzepatide are FDA-approved medications used for the treatment of type 2 diabetes and obesity.[1-3]
- Clinical trials have demonstrated the efficacy of these incretin mimetics in glycemic control and weight loss.[4-6]
- While many observational studies have evaluated the adherence to and persistence with these medications, currently, there are limited data assessing the impact of and any reasons for discontinuation (r/dc) in the real-world setting.[7,8]

Objective

- To assess the impact of 3 GLP-1 RAs on changes in weight and cardiometabolic measures by persistence and to uncover r/dc via a large language model (LLM) using real-world data.

Methods

- The Veradigm Network EHR linked to MarketScan claims data was used to identify adults newly initiating semaglutide, liraglutide, or tirzepatide between 06/04/2021-09/30/2023.
- Patient selection criteria for clinical outcomes are described in **Figure 1**.
- R/dc were extracted from unstructured clinical notes using an LLM and were evaluated by human review among a subset of patients from Figure 1 found in the Practice Fusion EHR database. The patient selection criteria used for examining r/dc are described in **Figure 2**.

Figure 1: Patient Selection for Clinical Outcomes

Evidence of ≥1 prescription for semaglutide, liraglutide, or tirzepatide in claims between 06/04/2021-09/30/2023 (earliest = index date)
N = 136,784

↓

Continuous medical and pharmacy benefit enrollment for ≥12 months before (baseline) AND ≥24 months after (follow-up) the index date
N = 15,560

↓

No GLP-1 RA use in the baseline period
N = 15,443

↓

No pregnancy/delivery OR bariatric surgery in baseline or follow-up
N = 14,503

↓

No non-index GLP-1 RA use in the follow-up period
N = 13,428

↓

Age ≥18 years at index
N =13,330

Study Variables

- Patient demographics were captured on the index date.
- GLP-1 RA discontinuation during the 24-month follow-up period was defined as: having a gap of >45 days in supply of semaglutide, liraglutide, or tirzepatide.
- Vitals and Lab Measures
  - The values closest to, but before the index date during the 12-month baseline period were used as baseline measures.
  - During the follow-up period, measures were captured monthly during the first period of persistence and monthly post-discontinuation. If multiple values were available during the month, the mean value was reported.
  - Patients were not required to have all measures available at every time period during follow-up; the N of patients contributing to each time point is displayed with the results.

Figure 2: Patient Selection for Extracting Reasons for GLP-1 Discontinuation

Patients with evidence of ≥1 GLP-1 RA prescription in their claims data between 06/04/2021-09/30/2023 found in the Practice Fusion EHR Database
N = 5,533

↓

≥1 clinical note in the Practice Fusion EHR AND ≥1 clinical note containing a GLP-1 related keyword/regex[a]
N = 1,254

↓

AND flagged in their claims data as having ≥1 discontinuation event
N = 840[b]

[a]keywords/regex included specific generic and brand GLP-1 RA medication names and non-specific grammatical variations in the spelling and spacing of "glp-1" and "glucagon-like peptide-1"; [b]no date restrictions were applied to the notes.

Methods (cont'd)

- Reasons for Discontinuation
  - The service date associated with the clinical transcript/note was used as a proxy for the discontinuation date.
  - Reported GLP-1 RA discontinuation categories are not mutually exclusive as there can be multiple reasons associated with medication discontinuation.
  - Definitions used for discontinuation in this study are as follows:
    - administration: reasons related to the patient's preference for how one medication is administered over another.
    - availability: reasons related to the patient's inability to obtain more medication due to availability issues.
    - efficacy: reasons related to the patient or provider's concern about the medication's efficacy.
    - financial: reasons related to the cost or issues with insurance that impedes the patient's ability to obtain the medication.
    - side effects: reasons related to the patient experiencing side effects.
    - other: other discontinuation reasons that do not fall into the above categories.
    - unknown: unknown reasons for medication discontinuation.

Results

Table 1: Patient Demographics, Baseline

	New GLP-1 RA Users	
	N = 13,330	
Age Group, N (%)		
18-24	47	0.4%
25-34	251	1.9%
35-44	1,415	10.6%
45-54	4,230	31.8%
55-64	5,347	40.2%
65-80	1,834	13.8%
81+	188	1.4%
Sex, N (%)		
Male	5,476	41.1%
Female	7,829	58.8%
Unknown/Not Reported	7	0.1%
Race, N (%)		
White	5,710	42.9%
Black	1,556	11.7%
Asian	396	3.0%
Other	1,489	11.2%
Unknown/Not Reported	4,161	31.3%

GLP-1 RA, glucagon-like peptide-1 receptor agonist.

Disclosures

All authors are employees of Veradigm which funded and provided the data used in the execution of this study.

Table 2: Vitals and Lab Measures, Baseline

	New GLP-1 RA Users	
	N	Mean (SD)
Weight (lbs)	4,515	227.1 (52.2)
BMI (kg/m²)	4,561	34.3 (5.2)
HbA1c (%)	4,196	7.3 (1.7)
Total Cholesterol (mg/dL)	3,720	166.8 (43.7)
LDL Cholesterol (mg/dL)	3,721	90.8 (35.1)
HDL Cholesterol (mg/dL)	3,728	46.8 (13.4)
Non-HDL Cholesterol (mg/dL)	1,504	118.3 (40.2)
Triglycerides (mg/dL)	3,693	167.6 (131.8)
ApoB (mg/dL)	23	84.5 (23.7)
Lp(a) (mg/dL)	24	47.5 (63.2)

ApoB, apolipoprotein B; BMI, body mass index; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Lp(a), lipoprotein (a).

Table 3: Reasons for GLP-1 RA Discontinuation[a]

	Liraglutide	Semaglutide	Tirzepatide
	n = 146	n = 265	n = 46
Administration, N (%)	17 (11.6%)	5 (1.9%)	0 (0.0%)
Availability, N (%)	3 (2.1%)	34 (12.8%)	18 (39.1%)
Efficacy, N (%)	17 (11.6%)	41 (15.5%)	3 (6.5%)
Financial, N (%)	18 (12.3%)	38 (14.3%)	10 (21.7%)
Side Effects, N (%)	20 (13.7%)	55 (20.8%)	7 (15.2%)
Other, N (%)	10 (6.9%)	16 (6.0%)	1 (2.2%)
Unknown, N (%)	61 (41.8%)	80 (30.2%)	8 (17.4%)

[a]The most common r/dc of a medication type is highlighted in pink and the second most common is highlighted in blue. The n's represent the number of discontinuation events associated with each medication, not patient counts.

Results

- Of the 13,330 patients included, most were 55-64 years of age (40%), female (59%), and White (43%) **(Table 1)**.
- The mean (years) duration of persisting with an index GLP-1 RA medication over the 2-year follow up was 1.1 years. 33% of patients persisted with their index therapy over follow-up; of those non-persistent, 27% discontinued use without restarting.
- Overall mean baseline BMI and HbA1c were 34 kg/m² and 7%, respectively; total cholesterol was 167 mg/dL, LDL-C was 91 mg/dL, HDL-C was 47 mg/dL, triglycerides was 168 mg/dL, apoB was 85 mg/dL, and lp(a) was 48 mg/dL **(Table 2)**.
- During persistence with GLP-1 RAs, weight, BMI, total cholesterol, and LDL-C values trended downwards; post-discontinuation, these same measures trended back upwards **(Figure 3)**.
- Of the 840 patients with a discontinuation flag in their claims data found in the Practice Fusion EHR, 5,814 clinical notes were extracted. 281 patients had ≥1 discontinuation event extracted from their clinical notes with a total of 534 events identified.
- Overall, the most common r/dc among patients were unknown and side effects.
- By medication, these same r/dc were also seen for semaglutide and liraglutide; for tirzepatide, availability and financial issues were most common **(Table 3)**.

Conclusions

- Persistent patients initiating GLP-1 RAs showed sustained improvements in weight loss and cardiometabolic lab levels.
- Reasons unknown and side effects were most common r/dc overall and among semaglutide or liraglutide; drug availability and financial issues were most prevalent in tirzepatide users.
- LLMs can enhance structured data fields to gain a deeper understanding of the patient clinical experience.

Figure 3: Vitals and Lab Measures During GLP-1 RA Persistence and Post-GLP-1 RA Discontinuation

Figure 3A: Weight

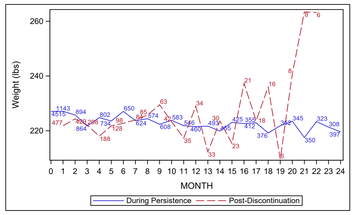


Figure 3B: BMI

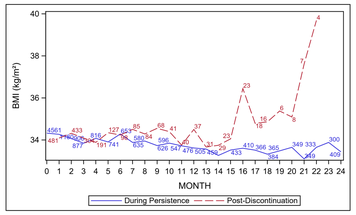


Figure 3C: HbA1c

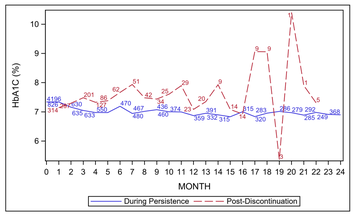


Figure 3D: Total Cholesterol

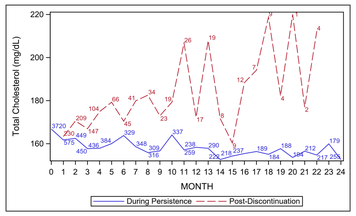


Figure 3E: LDL Cholesterol

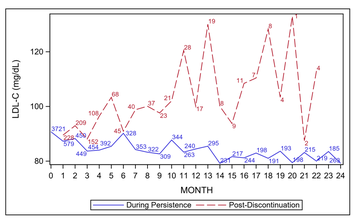


Figure 3F: HDL Cholesterol

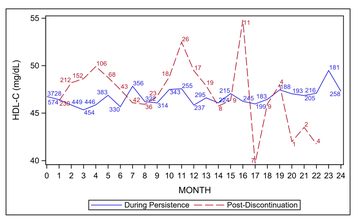


Figure 3G: Non-HDL Cholesterol

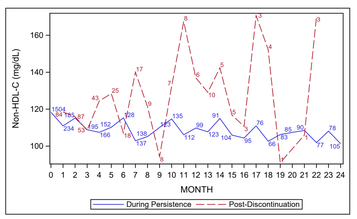


Figure 3H: Triglycerides

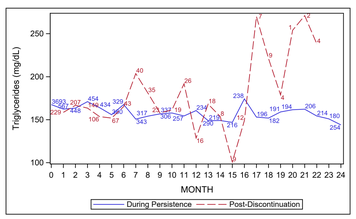


Figure 3I: ApoB

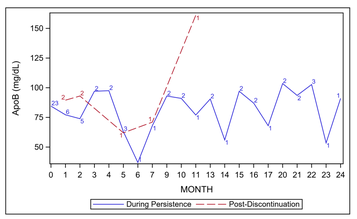
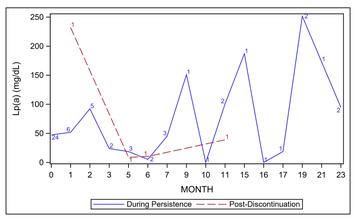


Figure 3J: Lp(a)



N's represent the number of patients persistent, or non-persistent, with a lab measurement available during that time point during follow-up.

ApoB, apolipoprotein B; BMI, body mass index; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Lp(a), lipoprotein (a); non-HDL, non-high-density lipoprotein.

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