Impact of GLP-1 Receptor Agonist (GLP-1 RAs) Persistence versus Discontinuation on Cardiometabolic Measures in Polycystic Ovary Syndrome (PCOS) Over a Two-Year Follow-Up

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Introduction

- Polycystic ovary syndrome (PCOS) is one of the most common heterogenous endocrine disorders to affect females of reproductive age.
- Obesity is one of the most prominent features among PCOS phenotypes, affecting approximately 50% of patients with PCOS.[1]
- Weight loss greater than 5% is often recommended and may require multiple treatment strategies including pharmacotherapies, and even bariatric surgery for eligible patients.[1,2]
- Incretin memetics like GLP-1 RAs and dual GIP/GLP-1 RA are viable treatment options for PCOS, facilitating weight loss and improving metabolic markers.[3]

Objective

- To understand the impact of semaglutide and dual GIP/GLP-1 RA tirzepatide on cardiometabolic markers among females with PCOS in routine practice.

Methods

- This retrospective cohort study used data from the Veradigm Network EHR linked to Merative MarketScan claims to identify females with ≥1 of the following (**Figure 1**):
  - ≥1 claim/EHR record with an ICD-10-DX code for PCOS (E28.2)
  - ≥1 claim/EHR record for PCOS composite criteria of amenorrhea (N91.2), irregular menstruation, unspecified (N92.6), oligomenorrhea (N91.5), hirsutism (L68.0), and/or hyperandrogenism (E28.1).
- The index event was the earliest prescription claim for semaglutide or tirzepatide following the PCOS diagnosis, but at least after FDA indication for chronic weight management for semaglutide on 06/04/2021.
- Patient demographics were described at index and clinical characteristics were captured during the 12-month baseline and follow-up (over 12 and 24 month) periods.
- GLP-1 RA discontinuation during the follow-up period was defined as having a gap of >45 days in supply of semaglutide 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 value closest to the censoring event (± 60 days) 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 1: Patient Selection

Females with ≥1 claim/EHR record for the following criteria identifying PCOS between 01/01/2020 and 04/30/2025 (earliest event=PCOS diagnosis date)
N = 295,449

- PCOS diagnosis (ICD-10 DX: E28.2)
N = 92,186
- Composite criteria for PCOS diagnosis (≥1 ICD-10 DX): amenorrhea (N91.2), irregular menstruation, unspecified (N92.6), oligomenorrhea (N91.5) and/or hirsutism (L68.0) and/or hyperandrogenism (E28.1)
N = 229,311

↓

≥1 prescription for semaglutide or tirzepatide in claims data following PCOS diagnosis date (and at least after 06/04/2021) (first claim =index date)
N = 20,613

↓

≥12 months of continuous claims enrollment before (baseline period) AND ≥24 months of continuous claims enrollment after the index date
N = 1,743

↓

No GLP-1 RA use in 12M before index date OR pregnancy/delivery OR bariatric surgery in 12M baseline or 24M follow-up OR other GLP use in 24M follow-up
N = 867

↓

Age 12-50 at index
N = 710

Table 1: Baseline Demographic Characteristics

	All Patients
	N=710
Age, Mean (SD)	38.6 (8.5)
Race, N (%)	
Asian	13 (1.8%)
Black	81 (11.4%)
White	358 (50.4%)
Other	70 (9.9%)
Not Reported	188 (26.5%)
Ethnicity, N (%)	
Hispanic	19 (2.7%)
Non-Hispanic	420 (59.2%)
Not Reported	271 (38.2%)
Region of Residence, N (%)	
Northeast	17 (2.4%)
Midwest	95 (13.4%)
South	191 (26.9%)
West	57 (8.0%)
Other/Unknown	350 (49.3%)

Figure 2: Patient Selection Diagnoses, by Study Period

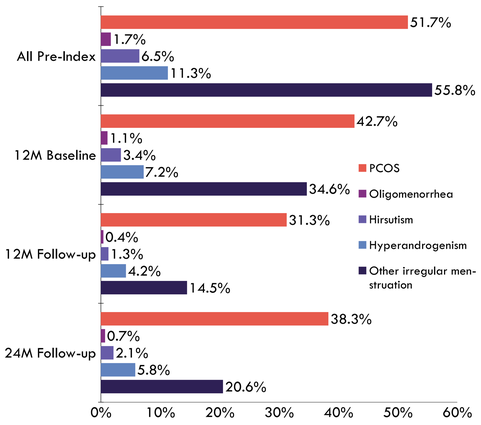


Figure 3: Select Clinical Characteristics, By Study Period

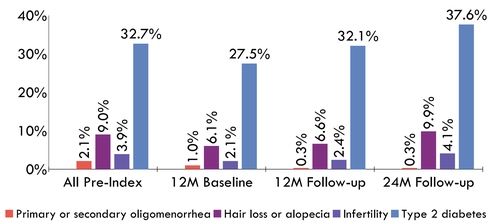


Figure 4: Select Treatments & Procedures, By Study Period

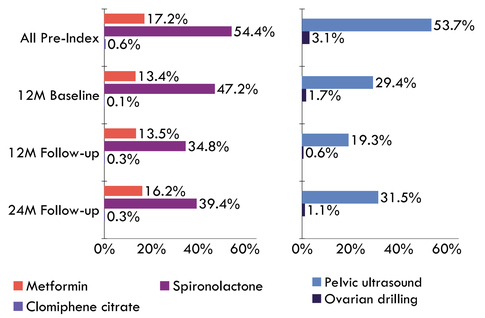


Table 2: Vitals and Select Lab Measures, 12-Month Baseline

	All Patients
	N=710
	Mean (SD)
Weight (lbs)	230.3 (48.7)
BMI (kg/m²)	36.1 (4.6)
Total Cholesterol (mg/dL)	189.0 (36.5)
LDL Cholesterol (mg/dL)	112.5 (31.9)
HDL Cholesterol (mg/dL)	51.1 (13.1)
Triglycerides (mg/dL)	142.5 (93.9)
Non-HDL Cholesterol (mg/dL)	134.9 (35.3)
ApoB (mg/dL)	96.1 (17.4)
Lp(a) (mg/dL)	70.9 (82.4)
HbA1c (%)	6.1 (1.4)

Results

- Over a third had type 2 diabetes (**Figure 3**); 17.2% were treated with metformin and 54.4% with spironolactone at baseline (**Figure 4**).
- Mean (SD) starting weight was 230.3 (48.7) lbs and Hba1c was 6.1(1.4) % overall (**Table 2**); mean (SD) starting total cholesterol and triglycerides were 189.0 (36.5) mg/dL and 142.5 (93.9) mg/dL, respectively.
- A total of 124 patients (18%) remained persistent over two years of follow-up; average time of persistence on index was 10 months.
- During follow-up, mean (SD) weight and A1c were 218.5 (51.5) lbs and 5.7 (1.0) % among persistent patients versus 223.4 (48.0) lbs and 6.0 (1.4) % among discontinuers.
- Total mean (SD) cholesterol decreased for both cohorts, while triglycerides decreased to 128.1 (81.4) mg/dL among persistent patients and returned to baseline for discontinuers 142.3 (94.7) mg/dL.

Conclusions

- While only 18% of patients remained on therapy for a full two years, those who did experienced sustained improvements in weight, BMI, HbA1c, and triglycerides compared to those who discontinued.
- In contrast, those who discontinue, even if they eventually restart, tend to lose these gains, particularly with respect to triglycerides returning to baseline levels.

Figure 5: Vitals and Lab Measures During GLP-1 RA Persistence and Post-GLP-1 RA Discontinuation

Figure 5A: Weight

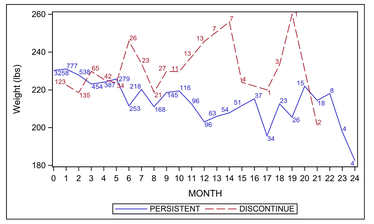


Figure 5B: BMI

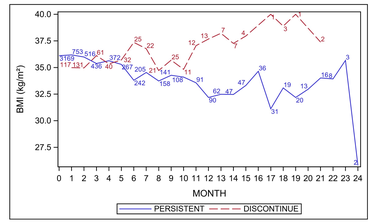


Figure 5C: Total Cholesterol

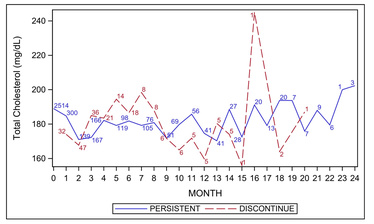


Figure 5D: LDL Cholesterol

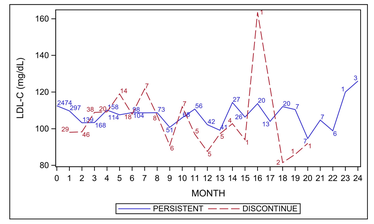


Figure 5G: HDL Cholesterol

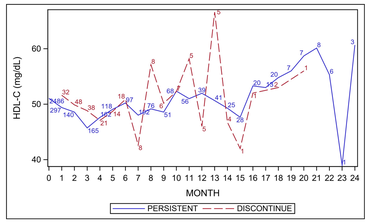


Figure 5H: Triglycerides

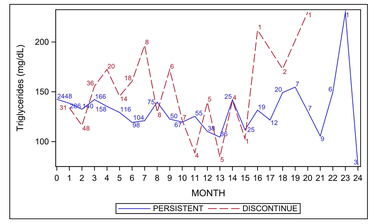


Figure 5E: Non-HDL Cholesterol

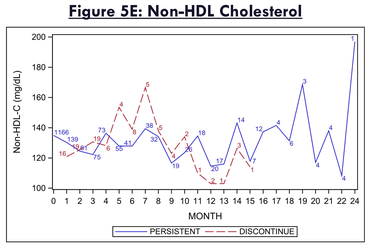


Figure 5F: ApoB

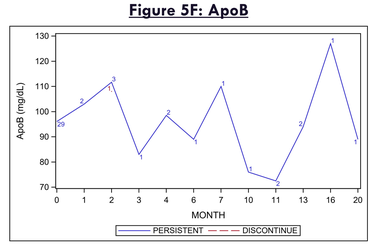


Figure 5G: Lp(a)

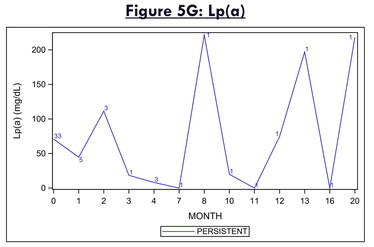
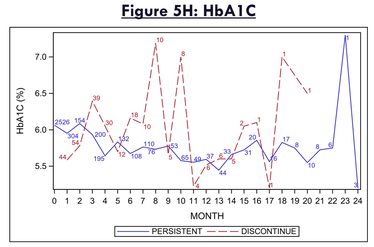


Figure 5H: HbA1C



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.

Abbreviations

GIP RA, glucose-dependent insulinotropic polypeptide receptor antagonist; GLP-1 RA, glucagon-like peptide-1 receptor antagonist; PCOS, polycystic ovary syndrome; SD, standard deviation.

References

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2. Kim CH, Lee SH. *Life (Basel)*. 2022;12(2).
3. Teede HJ, et al. *J Clin Endocrinol Metab*. 2023;120(4):767-793.

Disclosures

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