REAL-WORLD OUTCOMES ASSOCIATED WITH ANTI-OBESITY MEDICATION USE AND DISCONTINUATION

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INTRODUCTION

- Obesity is a condition characterized by excessive or abnormal body fat accumulation, typically defined as a body mass index (BMI) greater than 30 kg/m².[1]
- Over the past decade, anti-obesity pharmacotherapy has rapidly advanced, particularly with the introduction of incretin-based agents such as liraglutide, semaglutide, and tirzepatide, which have transformed the scope of obesity management.[2-4]
- Clinical trials have shown that these therapies produce substantial reductions in body weight and anthropometric measures while also lowering cardiometabolic risks, including blood pressure, glycemic control, and lipid profiles during treatment.[5-7]
- While clinical trials have demonstrated substantial benefits of the glucagon like peptide-1 receptor agonist (GLP-1RA) and glucose-dependent insulinotropic polypeptide(GIP)/GLP-1 dual agonists during active treatment, there remains limited real-world evidence regarding the sustainability of these effects following discontinuation.

OBJECTIVE

- This study aims to evaluate the effects of GLP-1 receptor agonists on cardiometabolic risk changes during active therapy and following treatment discontinuation.

METHODS

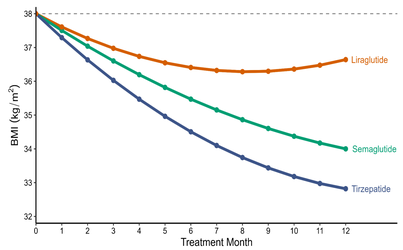
- This retrospective cohort study was conducted using electronic health record data obtained from a state sponsored healthcare institution in the U.S. Midwestern region.
- The study cohort included patients who had a record of filling a GLP-1RA or GIP/GLP-1 dual agonist with a labeled indication for obesity or overweight management, including Sexanda® (liraglutide), Wegovy® (semaglutide), or Zepbound® (tirzepatide) on or before August 30, 2025.
- Eligible subjects had records of BMI greater than or equal to 27.0 kg/m² within 180 days before the first date of dispensing an AOM (Index date) from an outpatient pharmacy.
- Study subjects were followed from treatment initiation for up to 12 months while on therapy and additionally observed for up to 12 months following treatment discontinuation. Treatment Discontinuation was defined by the end of the Index AOM supply with no additional records of AOM dispensing.
- Clinical characteristics over the 6-month period preceding the Index date or Discontinuation and demographics were summarized using descriptive statistics. Continuous variables were presented as means and standard deviations. Categorical variables were summarized as frequencies and percentages.
- Changes in the BMI (ΔBMI), systolic blood pressure (ΔSBP), and diastolic blood pressure (ΔDBP) were estimated a mixed effect modeling approach (MEM) and projected for the patients with average baseline value using the coefficient estimates.
    - Changes in outcomes were calculated relative to the point-of-care measures at the index date or discontinuation. When measurements at the index date or discontinuation were unavailable, the last observation carried forward method was applied.
    - The model included the fixed effect coefficients representing population-level trends for both linear trajectory (month) and quadratic time-term (month²) to capture the potential saturation effects. The interaction between the linear trajectory and baseline value was included to adjust for the regression toward mean.
    - Inter-individual variability was also modeled using random effects on the linear and quadratic terms.

RESULTS

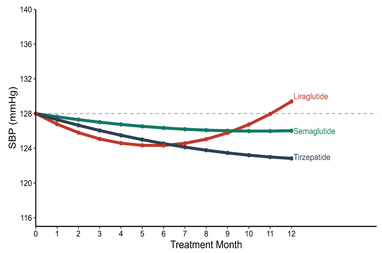
Characteristics	During AOM Treatment	After AOM Discontinuation
Total, n (%)	1310 (100%)	465 (100%)
Current AOM, n (%)		
Liraglutide	83 (6.3%)	47 (10.1%)
Semaglutide	809 (61.8%)	324 (79.8%)
Tirzepatide	418 (31.9%)	94 (20.2%)
Age, mean (SD)	46.3 (±10.6)	46.0 (±10.9)
Female, n (%)	1083 (82.7%)	383 (82.4%)
Race/Ethnicity, n (%)		
Hispanic white	259 (19.8%)	82 (17.6%)
Non-Hispanic white	226 (17.2%)	60 (12.9%)
Black	720 (55.0%)	283 (60.9%)
Asian	34 (2.6%)	14 (3.0%)
Other	71 (5.4%)	26 (5.6%)
Insurance, n (%)		
Commercial	1160 (88.6%)	384 (82.6%)
Medicare	71 (5.4%)	35 (7.5%)
Medicaid	47 (3.6%)	28 (6.0%)
Clinical characteristics		
BMI, mean (SD)	40.5 (±8.0)	39.3 (±8.5)
SBP, mean (SD)	129.0 (±16.2)	127.3 (±15.5)
DBP, mean (SD)	80.9 (±9.7)	79.8 (±8.9)
Diabetes, n (%)	181 (13.8%)	85 (18.3%)
Hypertension, n (%)	659 (50.3%)	262 (56.3%)
Heart Failure, n (%)	73 (5.6%)	30 (6.5%)
CCI ≥1, n (%)	390 (30.0%)	156 (33.9%)

AOM: Anti-obesity medication, N: number, SD: Standard deviation, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CCI: Charlson comorbidity index

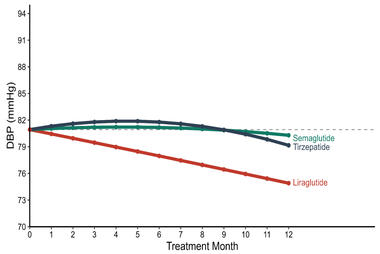
Projected Changes in Point-of-Care Measures During Active Treatment



Liraglutide: ΔBMI = - 0.322(M) – 0.003(M×Baseline_BMI) + 0.025(M²)*
Semaglutide: ΔBMI = - 0.155(M) – 0.009(M×Baseline_BMI)*+ 0.015(M²)*
Tirzepatide: ΔBMI = - 0.094(M) – 0.017(M×Baseline_BMI)* + 0.025(M²)*
M: month
*p<0.001

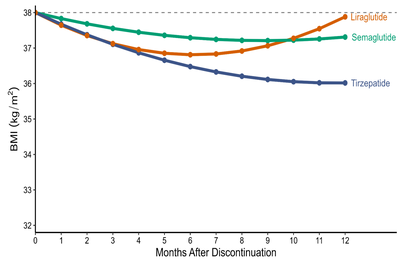


Liraglutide: ΔSBP = 7.43(M)* – 0.069(M×Baseline_BMI)* + 0.121(M²)*
Semaglutide: ΔSBP = 10.65(M)* – 0.086(M×Baseline_BMI)* + 0.019(M²)*
Tirzepatide: ΔSBP = 9.28(M)* – 0.078(M×Baseline_BMI)* + 0.025(M²)
M: month
*p<0.001

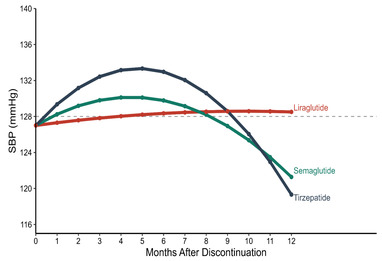


Liraglutide: ΔDBP = 20.48(M)* – 0.26(M×Baseline_BMI)* - 0.0014(M²)*
Semaglutide: ΔDBP = 20.03(M)* – 0.246(M×Baseline_BMI)*- 0.016(M²)*
Tirzepatide: ΔDBP = 17.92(M)* – 0.216(M×Baseline_BMI)* - 0.048(M²)*
M: month
*p<0.001

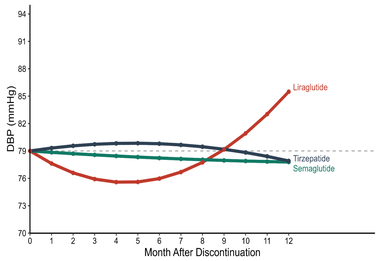
Projected Changes in Point-of-Care Measures After Discontinuation



Liraglutide: ΔBMI = 0.90(M) – 0.034(M×Baseline_BMI) + 0.031(M²)
Semaglutide: ΔBMI = 0.33(M) – 0.013(M×Baseline_BMI)*+ 0.01(M²)*
Tirzepatide: ΔBMI = 0.15(M) – 0.005(M×Baseline_BMI) + 0.014(M²)
M: month
*p<0.001



Liraglutide: ΔSBP = 10.96(M)* – 0.084(M×Baseline_BMI)* - 0.016(M²)*
Semaglutide: ΔSBP = 12.76(M)* – 0.08(M×Baseline_BMI)*- 0.157(M²)*
Tirzepatide: ΔSBP = 38.28(M)* – 0.281(M×Baseline_BMI)* - 0.27(M²)
M: month
*p<0.001



Liraglutide: ΔDBP = 6.91(M)* – 0.11(M×Baseline_BMI)* + 0.17(M²)*
Semaglutide: ΔDBP = 8.98(M)* – 0.116(M×Baseline_BMI)*+ 0.0047(M²)
Tirzepatide: ΔDBP = 17.12(M)* – 0.21(M×Baseline_BMI)* - 0.037(M²)
M: month
*p<0.001

DISCUSSION

- A significant decrease in the BMI was observed from the population-level estimates during the first 12-month of the active supply period, which was consistently observed across the three incretin-mimetic AOMs.
- The magnitude of BMI reduction is a subject of the baseline measure as estimated by the negative and significant MONTH × baseline BMI interaction effect across the three AOMs.
- During active treatment, tirzepatide demonstrated greater BMI reduction compared with semaglutide and liraglutide, which are consistent with the SURMOUNT, STEP, and SCALE clinical trial programs, demonstrating greater weight reduction improvement with semaglutide and tirzepatide compared with liraglutide, including mean weight reductions of approximately 14.9% with semaglutide and up to 22.5% with tirzepatide in clinical trials.[7-10]
- During active treatment, tirzepatide and semaglutide demonstrated greater sustained reductions in SBP compared with liraglutide, suggesting stronger and more durable cardiometabolic benefit during and after treatment discontinuation.
- Semaglutide and tirzepatide demonstrated more stable decline in DBP trajectories compared with liraglutide.
- Rebound effect of the discontinuation on BMI, SBP and DBP was not observed from the fixed-effect estimate.
- Following treatment discontinuation, semaglutide and tirzepatide generally maintained more sustained BMI reductions compared with liraglutide.
- Findings from the analysis of post-discontinuation data should be interpreted cautiously because of limited follow-up observations and smaller sample sizes during this phase.
- Sustained BMI and blood pressure after the discontinuation could be explained by compounding drug use, which would not be monitored by the traditional healthcare delivery systems nor be analyzed using current electronic healthcare records.
- The number of data points decrease over the observation period, that would influence on the precision of the estimates.
- A significant heterogeneity in the trajectories of the point-of-care measures was calculated from the random-effect estimates. Heterogeneity across the patients in the benefits of the continuous utilization of AOMs and discontinuation effects should be further addressed in a larger databases

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