

## Background

- Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have emerged as key pharmacologic interventions approved by the United States (U.S.) Food and Drug Administration (FDA) for the management of type 2 diabetes (T2DM) and obesity<sup>1</sup>
- Tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA, has demonstrated significant efficacy in both glycemic control and weight reduction compared with semaglutide, a selective GLP-1 RA<sup>1,2</sup>
- However, real-world evidence (RWE) comparing treatment adherence, persistence, and dose escalation across agents and metabolic indications remains limited

## Objective

To evaluate real-world adherence, persistence, and dose escalation of GIP/GLP-1 RAs among U.S. commercially insured adults with T2DM, and overweight or obesity

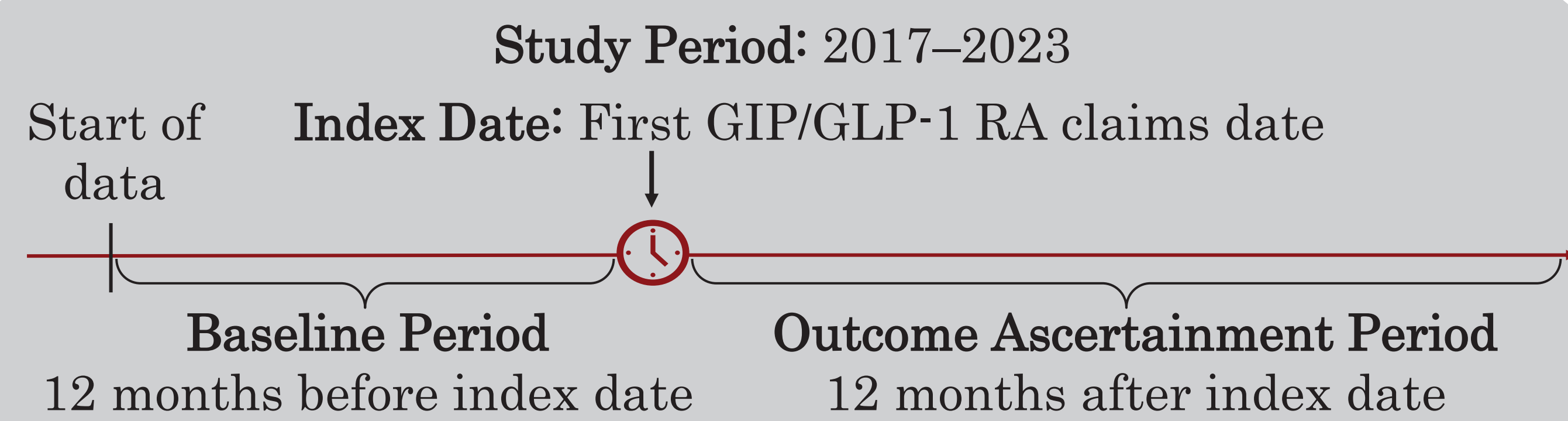
## Methods

Active comparator, new user retrospective cohort study using the MarketScan Database

**Study Cohorts**  
**T2DM**  
 Dulaglutide (Dula) vs. Semaglutide (Sema) vs. Tirzepatide (Tirz)  
**Obesity**  
 Liraglutide (Lira) vs. Sema vs. Tirz

- Inclusion Criteria**
- Aged 18-64 years
  - ≥12 months of continuous enrollment before index date
  - Newly initiated GLP-1RA between 2018-2023

- Exclusion Criteria**
- Evidence of T2DM (obesity cohort only), gestational diabetes, type 1 diabetes mellitus, pregnancy, end-stage renal disease, or bariatric surgery in baseline period



### Outcomes

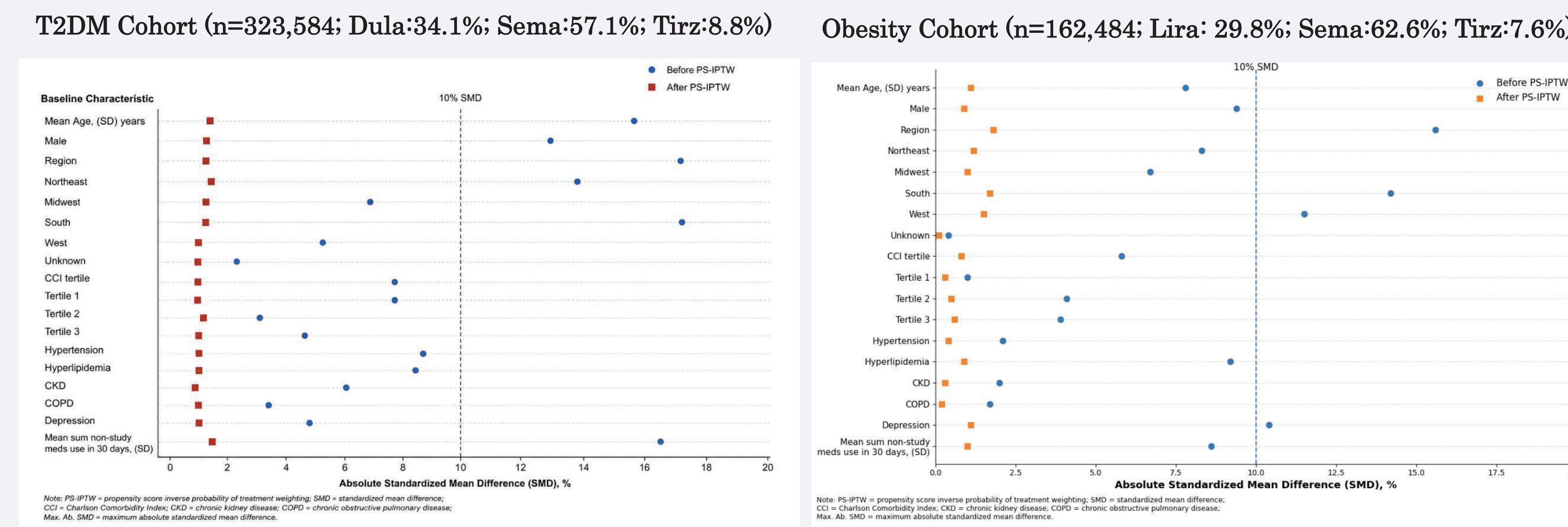
- Treatment adherence
- Treatment persistence
- Dose escalation

### Statistical Analysis

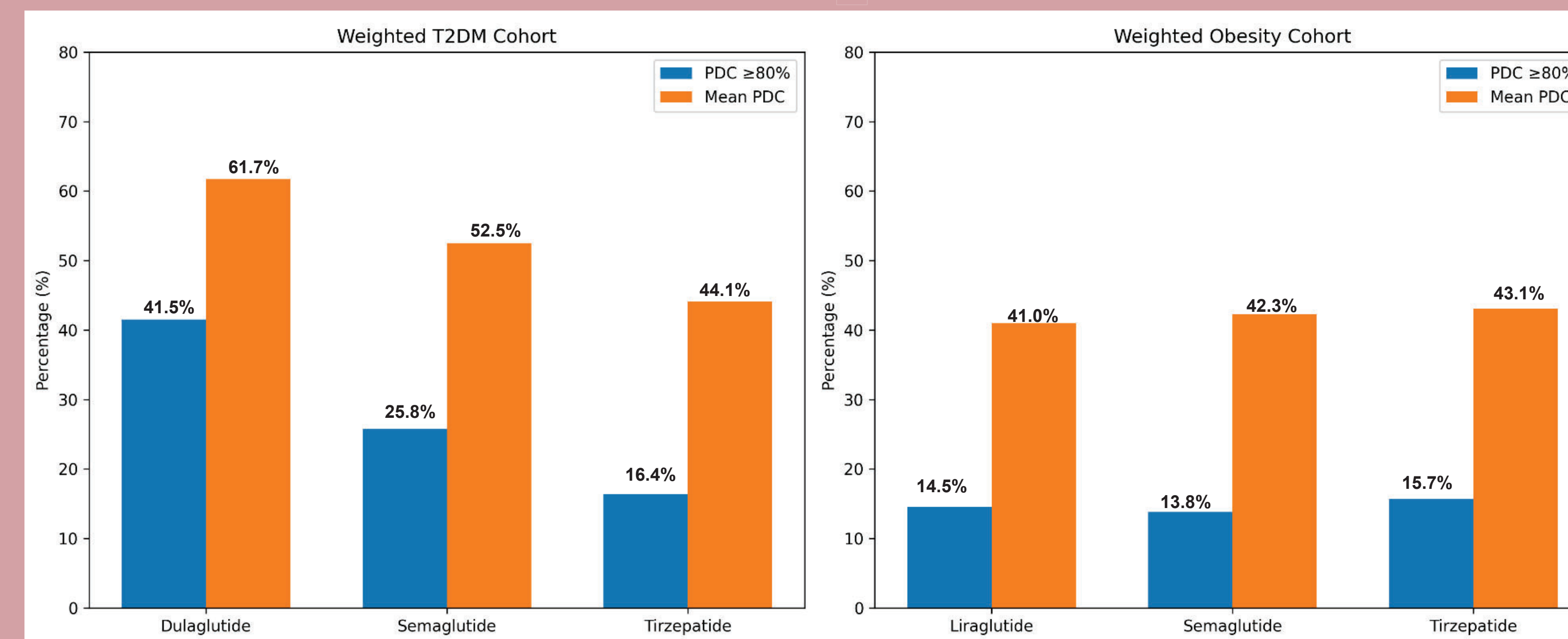
- Multinomial Propensity Score (PS)-based Inverse Probability of Treatment Weighting (IPTW) weighting to account for differences in baseline covariates (Figure 1)
- Adherence:** Evaluated at 12 months using proportion of days covered (PDC)
- Persistence:** Time to discontinuation assessed using IPTW-weighted Cox proportional hazards (PH) models
- Dose escalation:** Evaluated the 12-month dose-modification patterns

## Results

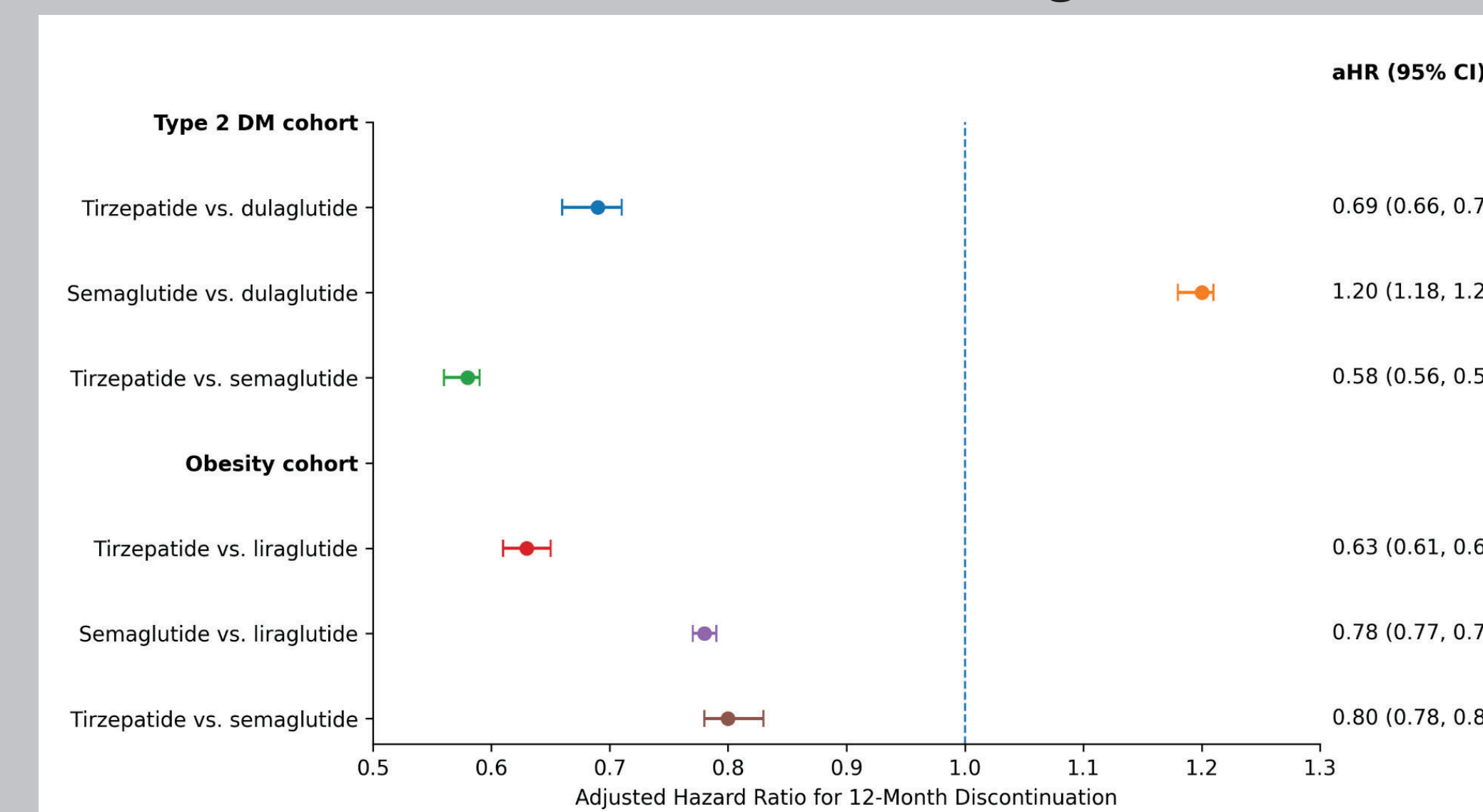
**Figure 1. Standardized Mean Differences (SMD) for Selected Baseline Characteristics of Dual GIP/GLP-1 RA Initiator with Newly Diagnosed T2DM and Obesity, 2017-2023**



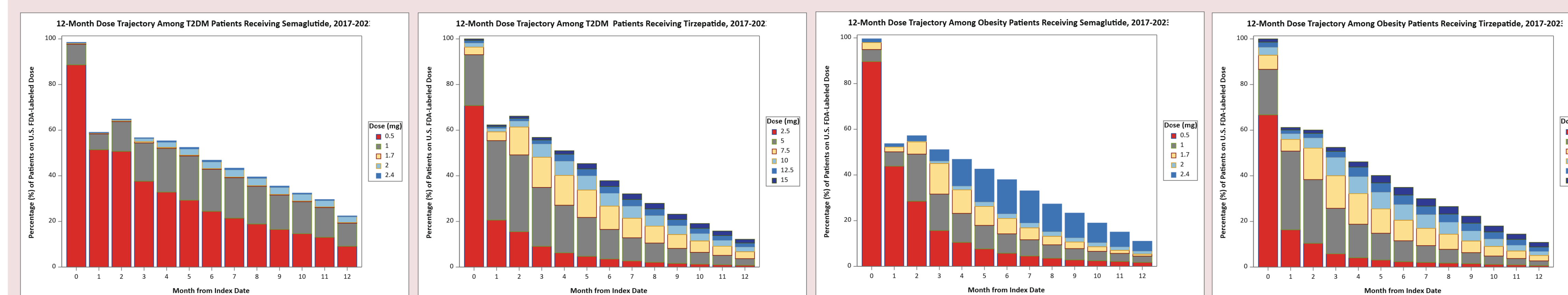
**Figure 2. 12-Month Proportion of Days Covered Following Dual GIP/GLP-1 RA Initiation Among Patients with Newly Diagnosed T2DM and Obesity, 2017-2023**



**Figure 3. 12-Month Discontinuation Hazard Ratios Among Dual GIP/GLP-1 RA Initiators in T2DM and Obesity, 2017-2023**



**Figure 4. 12-Month Dose Trajectory Among Dual GIP/GLP-1 RA Initiators in T2DM and Obesity, 2017-2023**



## Key Takeaways & Conclusions

### Key Takeaways

- Among commercially insured adults, real-world adherence to GLP-1RA or dual GIP/GLP-1RAs was low overall and particularly lower among patients treated for obesity
- Persistence varied by agent, with tirzepatide demonstrating lower discontinuation in both indications
- Across T2DM and obesity cohorts, semaglutide and tirzepatide initiators demonstrated progressive dose escalation over 12 months, with higher maintenance doses more common in obesity

### Adherence

- T2DM cohort: Dulaglutide demonstrated the highest 12-month adherence, with the greatest proportion achieving ≥80% PDC and highest mean PDC, followed by semaglutide, while tirzepatide showed the lowest adherence (Figure 2)
- Obesity cohort: Tirzepatide demonstrated the highest 12-month adherence, while liraglutide and semaglutide have comparable adherence. Liraglutide had a higher proportion of adherent patients, whereas semaglutide had better overall medication coverage (Figure 2)

### Discontinuation

- T2DM cohort: Tirzepatide was associated with a significantly lower risk of discontinuation versus both dulaglutide and semaglutide, while semaglutide showed the highest discontinuation risk (Figure 3)
- Obesity cohort: Tirzepatide was associated with a significantly lower risk of discontinuation versus both liraglutide and semaglutide, while liraglutide showed the highest discontinuation risk (Figure 3)

### Dose Escalation Patterns

- T2DM cohort: Tirzepatide initiators demonstrated progressive dose escalation, while semaglutide initiators mainly received start dose, with gradual dose escalation over time (Figure 4)
- Obesity cohort: Tirzepatide and semaglutide users demonstrated stepwise, and progressive dose escalation, respectively (Figure 4)

### Conclusion

- Overall, adherence to GLP-1RA or dual GIP/GLP-1RAs was low, particularly among obesity cohort. Persistence varied by agents with tirzepatide showing lower risk of discontinuation across indications
- Across T2DM and obesity cohorts, semaglutide and tirzepatide initiators demonstrated progressive dose escalation
- Understanding these patterns is valuable to optimize clinical management, identify key attrition points across therapeutic indications, and inform payer decisions
- Findings are limited by unmeasured drug shortages and formulary restrictions

## References

- The Lancet Diabetes & Endocrinology. The era of GLP-1 receptor agonists: Costs versus benefits. *The Lancet Diabetes & Endocrinology*. 2025;13(1):1. [https://doi.org/10.1016/S2213-8587\(24\)00376-0](https://doi.org/10.1016/S2213-8587(24)00376-0). doi: 10.1016/S2213-8587(24)00376-0.
- Frias Juan P., Davies Melanie J., Julio R, et al. Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. *N Engl J Med*. 2021;385(6):503-515. <https://doi.org/10.1056/NEJMoa2107519>. doi: 10.1056/NEJMoa2107519.

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