

Changes in Glucose-Lowering Treatments Among Glucagon-like Peptide-1 Receptor Agonists (GLP-1 RAs) Users by Medication Adherence Trajectory

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Background

- Adherence to glucagon-like peptide-1 receptor agonists (GLP-1 RAs) is often dynamic in real-world practice.
- In one study, 64.7% of patients discontinued treatment (≥90-day prescription gap) within 24 months,¹ and many subsequently restarted therapy.²
- Discontinuation and reinitiation by a patient may reflect adverse events, treatment response, socioeconomic factors, or medication access.³
- These patterns are not fully captured by traditional static adherence measures.
- Examining changes in other glucose-lowering therapies across distinct GLP-1 RA adherence trajectories may improve understanding of patient behavior with regard to the use of GLP-1 RAs in real-world diabetes management.

Objective

To characterize GLP-1 RA adherence trajectories for patients enrolled in Medicare Advantage with Part D (MAPD) and evaluate if adherence trajectories were associated with differences in use of other glucose-lowering medications.

Methods

Data source: Humana Research Database

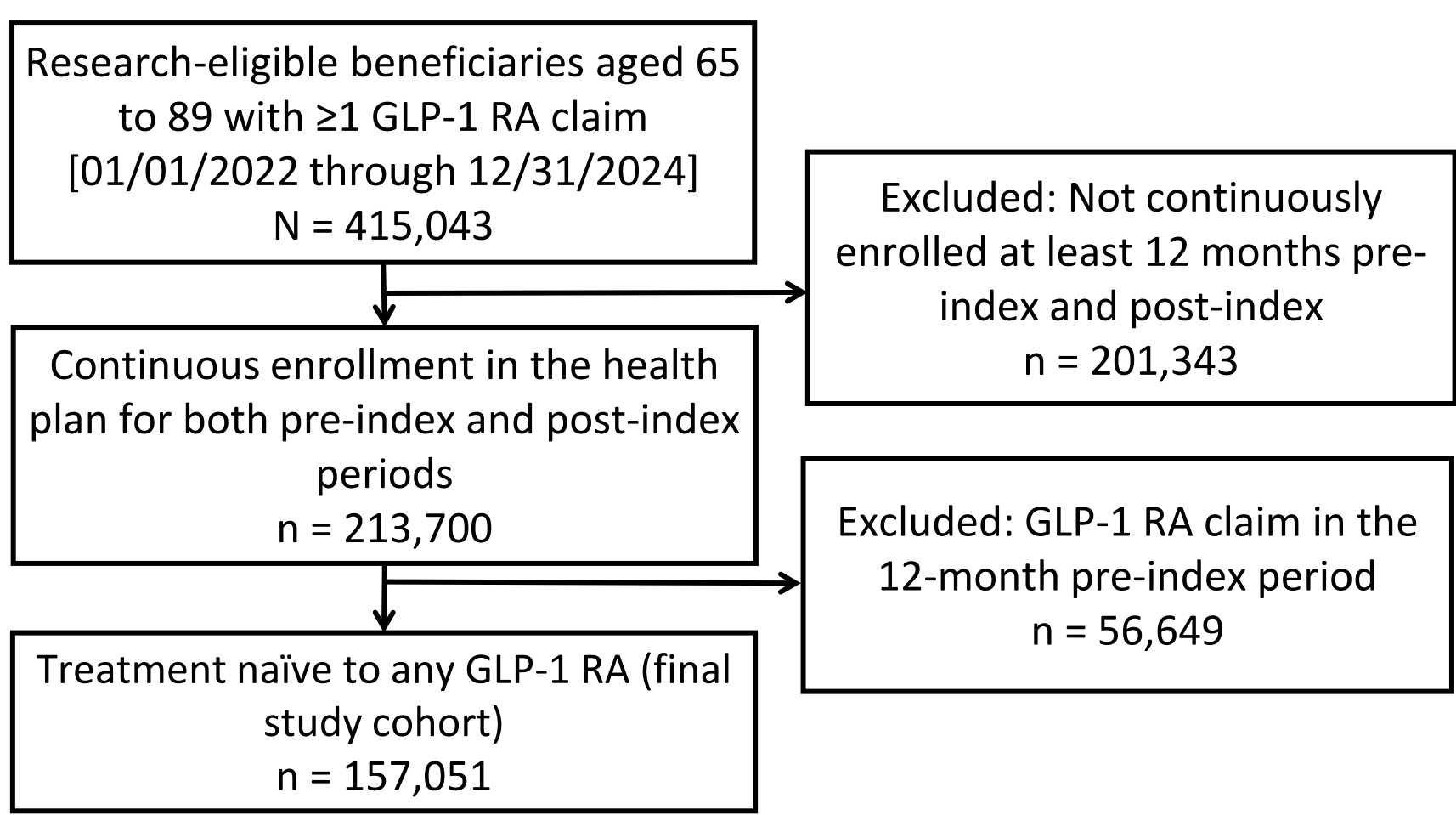
Study design: Retrospective claims analysis

Patient selection: Beneficiaries aged 65-89 years who initiated any GLP-1 RA between January 1, 2022 and March 31, 2025 (date of initiation = index), and had continuous enrollment for at least 12 months pre-index (baseline) and post-index (follow-up).

Statistical Analyses:

- Longitudinal k-means trajectory modeling clustered beneficiaries into adherence trajectory groups.
- Percent changes in concomitant biguanide, insulin, and sodium-glucose cotransporter-2 inhibitor (SGLT2i) use were assessed between baseline and follow-up. Conditional multivariable logistic regression examined pre-post index pairwise differences in glucose lowering drugs for each adherence trajectory compared to steady maintainers.

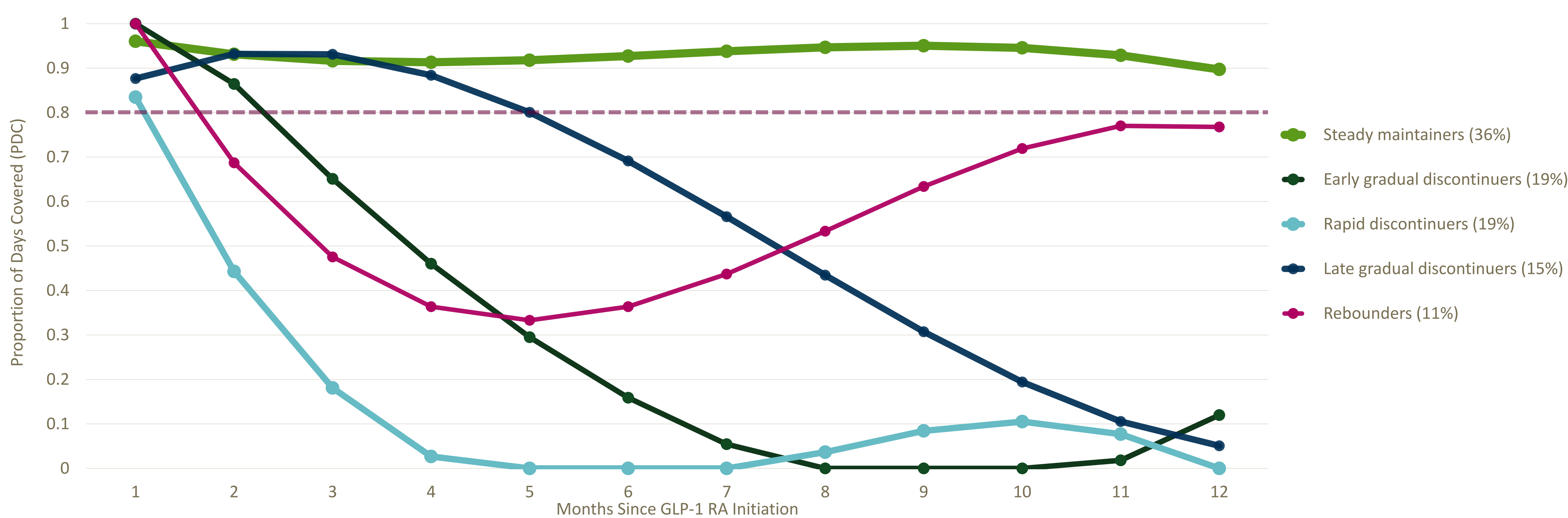
Figure 1. Attrition Diagram



Steady maintainers were more likely female (62.9%), more likely low-income subsidy (LIS) and dual-eligible (DE) (38.2%), more likely to have age in as reason for original Medicare eligibility (42.5%), higher use of tirzepatide at index (22.8%) and had the highest comorbidity burden than the other trajectory groups.

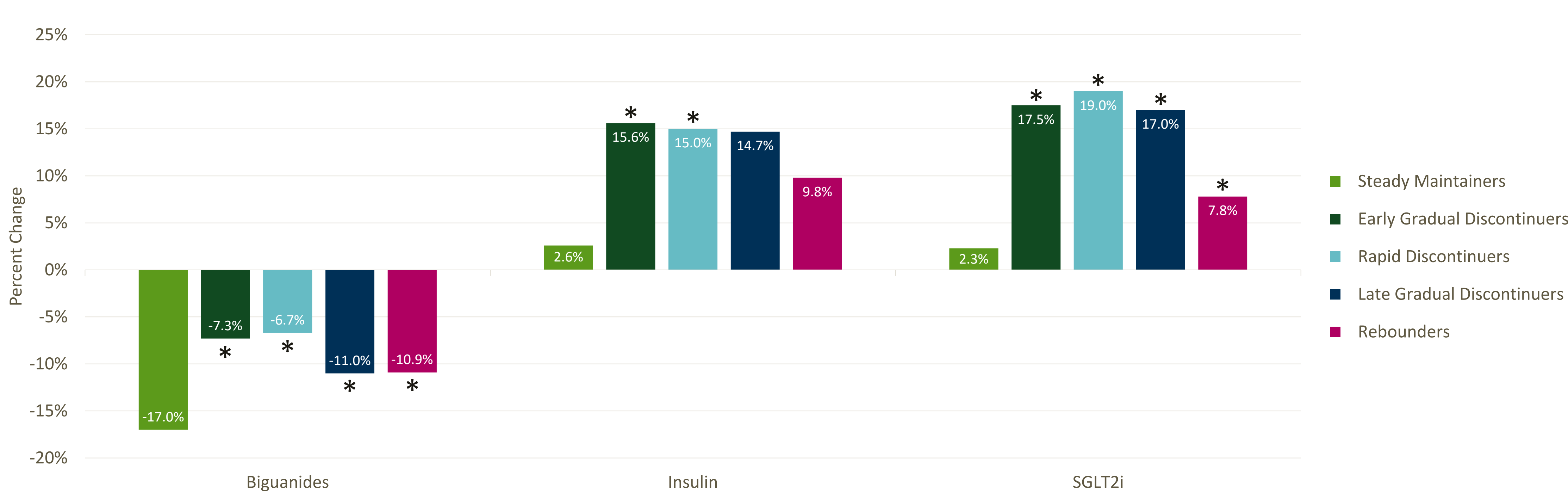
Results

Figure 2. GLP-1 RA Adherence Trajectories



Note: Dashed line denotes 80% adherence threshold; thickness of lines corresponds to percent population in each group

Figure 3. Percent Change in Glucose-Lowering Medication Use by GLP-1 RA Adherence Trajectory



* indicates significance at the alpha = 0.05 level; Reference group was the steady maintainers

Conclusions

- Steady maintainers experienced the greatest reduction in biguanide utilization (–17%), potentially reflecting greater opportunity for regimen simplification following sustained GLP-1 RA therapy.
- Less optimal adherence patterns had greater increases in insulin use. These shifts could increase the need for glucose monitoring, provider follow-up, and hypoglycemia risk, potentially raising healthcare resource utilization.
- The SGLT2i increase could reflect comorbidity-driven treatment, particularly HF, rather than replacement of GLP-1 RA therapy because of poor glycemic control.

Limitations

- Claims data is unable to capture self pay or compounded GLP-1 RA use and only indicates that the drug was dispensed so there is no guarantee of actual drug use.
- Descriptive analysis only so cannot conclude causation.
- Unable to account for all factors that may affect glucose lowering medication changes such as comorbidities.
- Using data from patients only enrolled in MAPD limits generalizability to other populations.

Acknowledgements

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References

- Tichy EM, Rim MH, Tadrous M, et al. National trends in prescription drug expenditures and projections for 2026. Am J Health Syst Pharm. 2026;83(14):728-744. doi:10.1093/ajhp/zxag115.
- Rodriguez PJ, Zhang V, Gratzl S, et al. Discontinuation and reinitiation of dual-labeled GLP-1 receptor agonists among US adults with overweight or obesity. JAMA Netw Open. 2025;8(1):e2457349. doi:10.1001/jamanetworkopen.2024.57349.
- Sikirica MV, Martin AA, Wood R, et al. Reasons for discontinuation of GLP1 receptor agonists: data from a real-world cross-sectional survey of physicians and their patients with type 2 diabetes. Diabetes Metab Syndr Obes. 2017;10:403-412. doi:10.2147/DMSO.S141235.