

Real-World Clinical Characteristics and Factors Associated with Concurrent Glucagon-Like Peptide-1 Receptor Agonist (GLP-1 RA) Therapy Among Patients with Metabolic Dysfunction-Associated Steatohepatitis (MASH) Prescribed Resmetirom

HSD105

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INTRODUCTION

- Resmetirom, an oral thyroid hormone receptor (THR) β -selective agonist, was the first medication conditionally approved, as an adjunct to diet and exercise management, for treating fibrosis among adults with noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with moderate to advanced fibrosis in the United States^{1,2}
- Glucagon-like peptide-1 receptor agonists (GLP-1 RA), specifically semaglutide, have also been conditionally approved for the treatment of with noncirrhotic MASH with moderate to advanced fibrosis,³ and are also prescribed to patients with MASH given the frequent co-occurrence of obesity and type 2 diabetes in this population; however, real-world data on patients initiating resmetirom with or without concomitant GLP-1 RA therapy remain limited.
- Given their differing mechanism of action and that there are no contraindications to concomitant use specified in either drug's prescribing information, concurrent administration may occur in real-world clinical practice

OBJECTIVE

- To examine the real-world characteristics of US adults with MASH initiating resmetirom with or without concomitant GLP-1 RA therapy and predictors of concomitant therapy

METHODS

Data Source and Study Population

- Using the Veradigm Network EHR linked to Komodo Health claims, this study identified adult patients (18+ years) with ≥ 1 prescription record for resmetirom (earliest record=index date) between 03/14/2024-04/30/2025
 - Study inclusion/exclusion criteria are described in Figure 1
 - The index date was the date of the first resmetirom claim
- Patients were stratified by receipt of ≥ 1 GLP-1RA in the 6 months following and inclusive of the index date

Patient Characteristics

- Patient demographics were captured on the index date
- Fibrosis-4 (FIB-4) score, baseline GLP-1 RA use, and metabolic comorbidities were captured in the 1-year baseline period
 - Hyperlipidemia, hypertension, and prediabetes were identified by diagnosis codes
 - Type 2 diabetes was identified by diagnosis code or prescriptions (including GLP-1 RA prescription)
 - Obesity was identified by diagnosis code or body mass index ≥ 30

Study Measures

- Adherence to resmetirom was measured by proportion of days covered (PDC)

Modeling

- Factors associated with concomitant use of resmetirom and GLP-1 RAs were assessed using multivariable logistic regression
 - Covariates included age, sex, race, ethnicity, region, payer, baseline FIB-4 score (where available), baseline GLP-1 RA use, and baseline metabolic comorbidities
- Sensitivity analyses included models examining interactions between baseline GLP-1 RA use and comorbidities
 - baseline GLP-1 RA use * baseline type 2 diabetes
 - baseline GLP-1 RA use * baseline obesity
 - baseline GLP-1 RA use * baseline type 2 diabetes * baseline obesity

DISCLOSURES AND ACKNOWLEDGEMENTS

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RESULTS

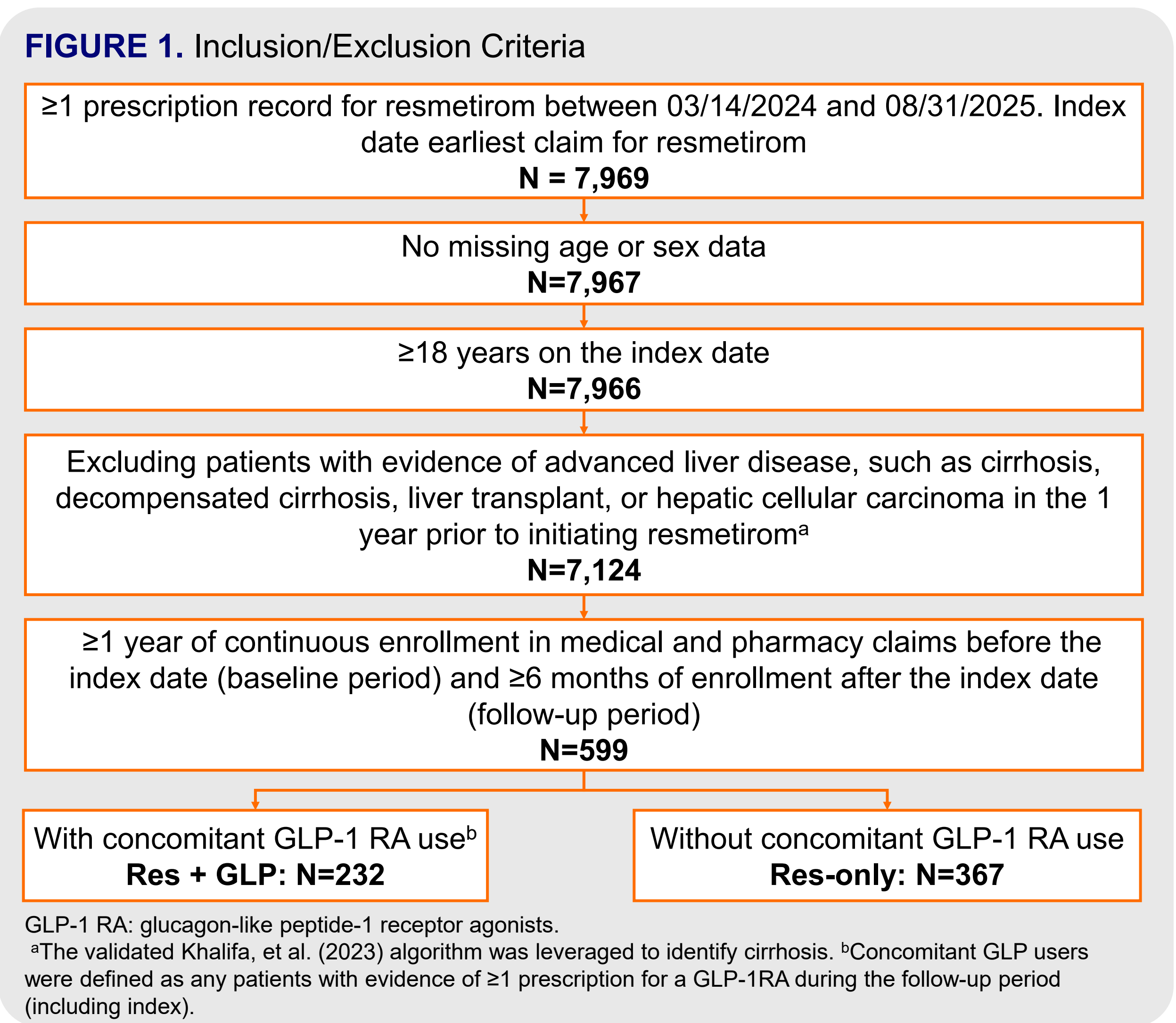


TABLE 1. Baseline Demographic Characteristics

	Res+GLP N=232	Res-Only N=367	P-value
Age, mean (SD)	58.7 (11.0)	59.6 (13.2)	0.397
Age, n (%)			0.020
18-44	24 (10.3)	52 (14.2)	
45-64	137 (59.1)	174 (47.4)	
65+	71 (30.6)	141 (38.4)	
Female, n (%)	135 (58.2)	198 (54.0)	0.309
Race, n (%)			0.554
Black	13 (5.6)	15 (4.1)	
White	143 (61.6)	212 (57.8)	
Other	32 (13.8)	67 (18.3)	
Unknown	44 (19.0)	73 (19.9)	
Hispanic, n (%)	22 (9.5)	33 (9.0)	0.839
Region, n (%)			0.246
Northeast	86 (37.1)	111 (30.2)	
Midwest	41 (17.7)	60 (16.3)	
South	68 (29.3)	123 (33.5)	
West	37 (15.9)	73 (19.9)	
Payer, n (%)			0.173
Commercial	126 (54.3)	172 (46.9)	
Medicare	81 (34.9)	156 (42.5)	
Medicaid	25 (10.8)	37 (10.1)	
Unknown	0 (0.0)	2 (0.5)	

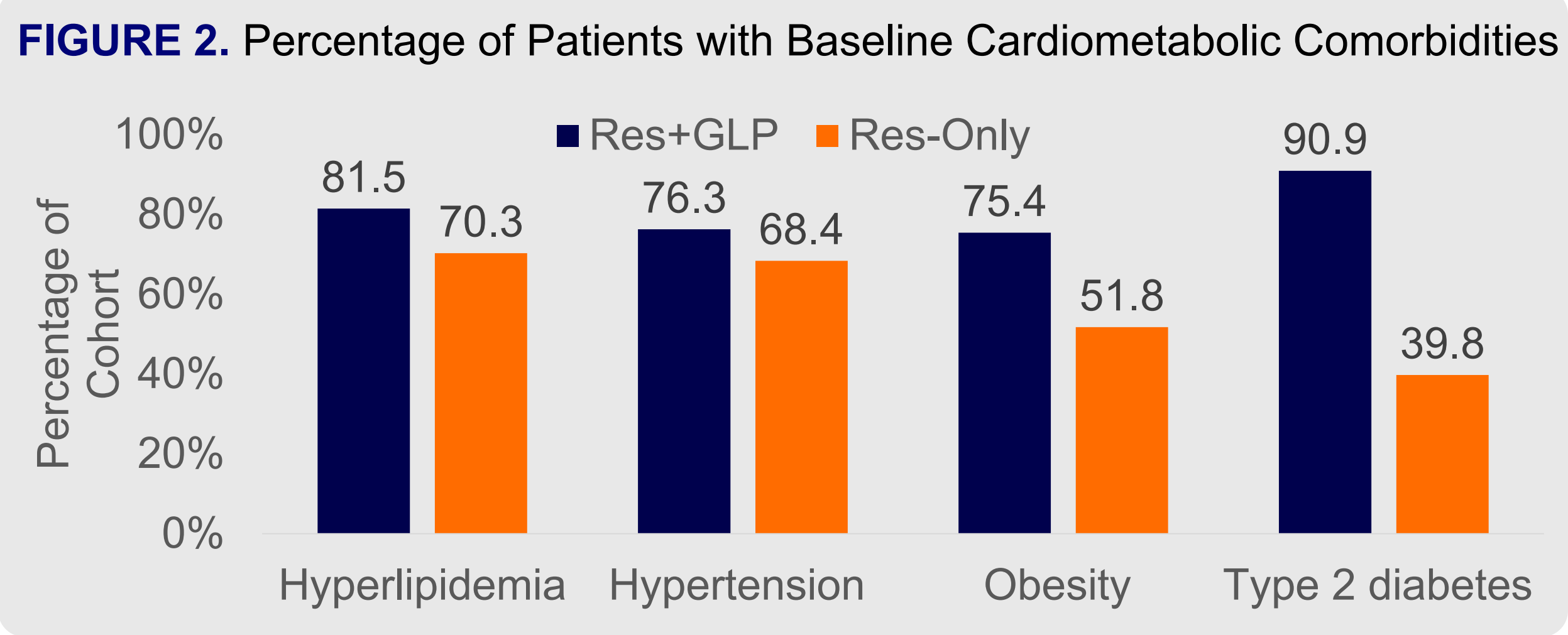


TABLE 2 Baseline Clinical Characteristics

	Res+GLP N=232	Res-Only N=367	P-value
Had ≥ 1 record of weight in baseline or index, n (%)	73 (31.5)	117 (31.9)	0.915
Weight, kg, mean (SD)	101.1 (24.8)	95.0 (21.3)	0.001
Weight Category, n (%)			0.051
< 100 kg	37 (50.7)	76 (65.0)	
≥ 100 kg	36 (49.3)	41 (35.0)	
Baseline cardiometabolic comorbidities, n (%)			
0	1 (0.4)	32 (8.7)	<0.001
1 or more	231 (99.6)	335 (91.3)	<0.001
2 or more	220 (94.8)	284 (77.4)	<0.001
3 or more	193 (83.2)	193 (52.6)	<0.001
≥ 1 GLP-1 RA Prescription	191 (82.3%)	33 (9.0%)	<0.001

GLP-1 RA: glucagon-like peptide-1 receptor agonists.

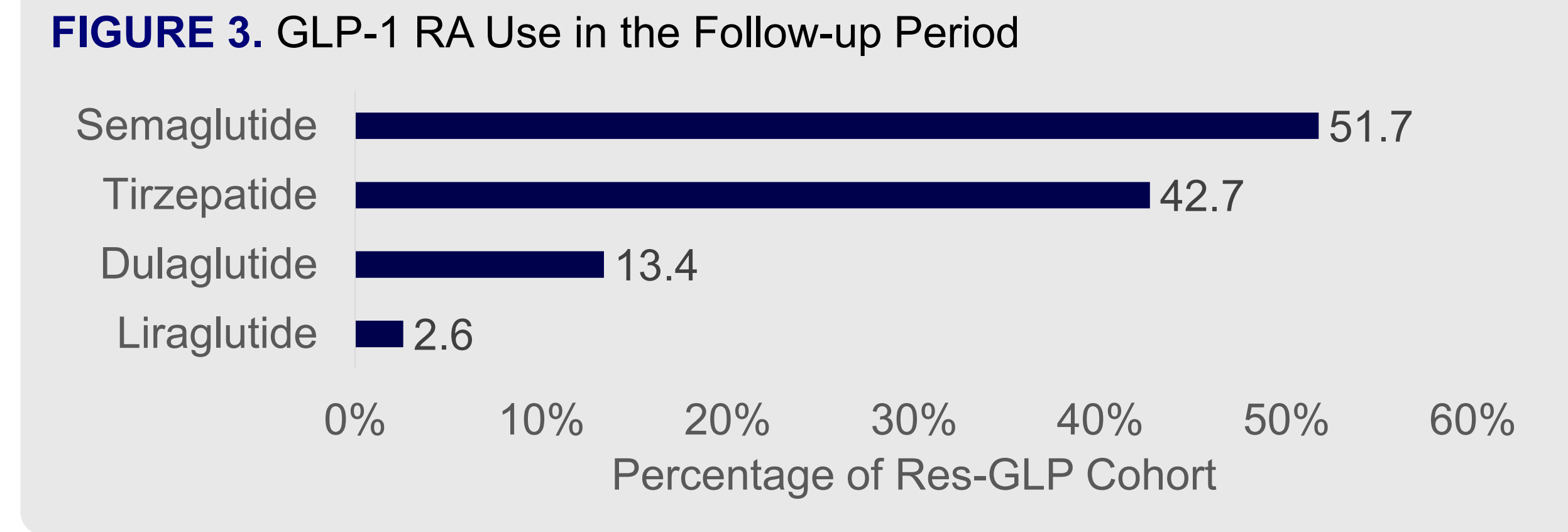


TABLE 3. 6 Month Resmetirom Adherence

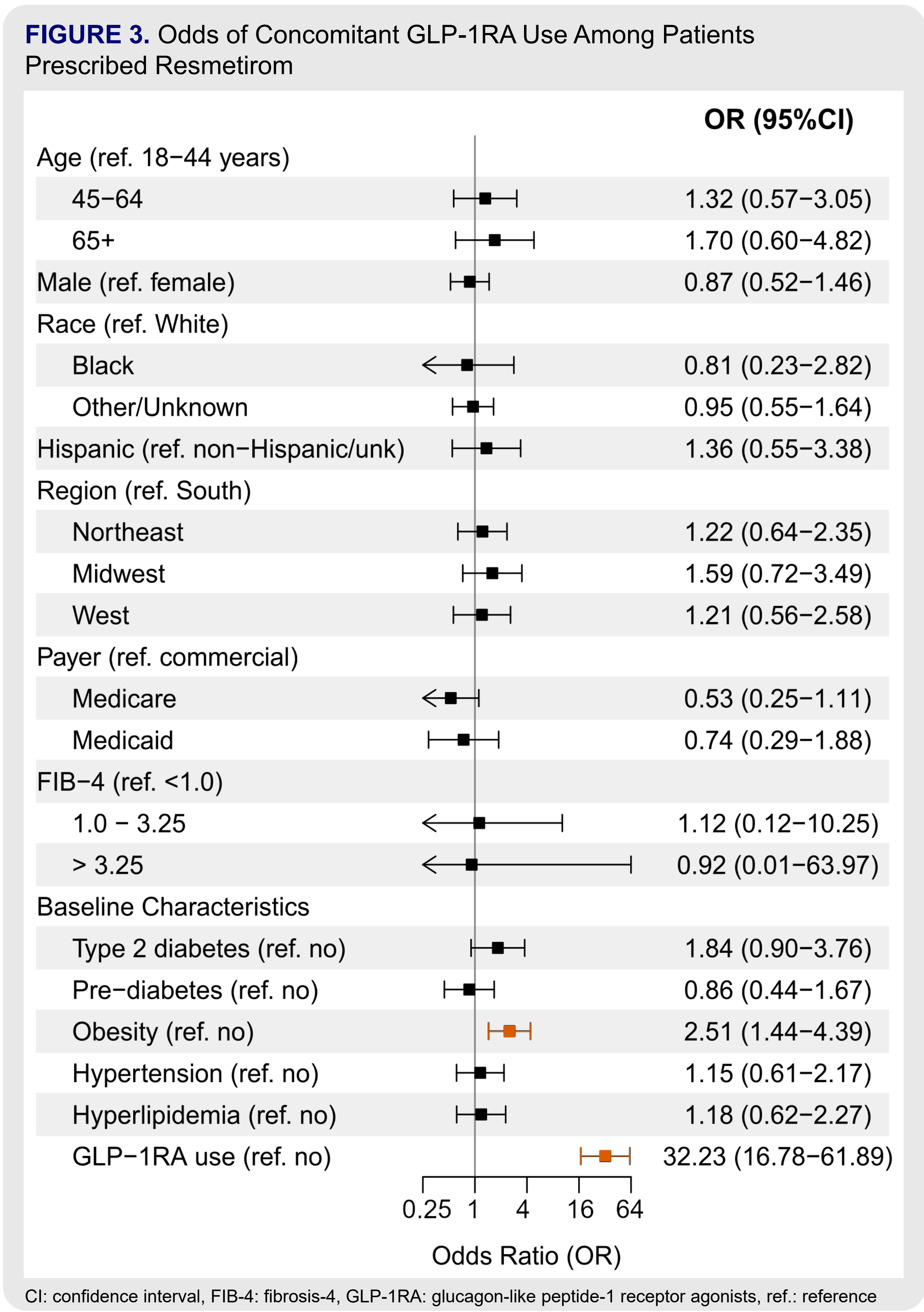
	Res+GLP N=232	Res-Only N=367	P-value
PDC, mean (SD)	0.728 (0.303)	0.729 (0.301)	0.965

PDC: proportion of days covered, SD: standard deviation

- The study included 599 adults initiating resmetirom, 232 (38.7%) of whom had ≥ 1 GLP-1 RA prescription during the 6-month follow-up (Figure 1)
- Patients were, on average, 59 years old in both cohorts; however, the shape of the distribution differed with the Res-Only cohort having fewer patients 45-64 years old compared to the Res+GLP cohort (Table 1)
- Metabolic comorbidities were more common among patients in the Res-GLP cohort (hyperlipidemia: $\Delta 11.2$ percentage points, $p=0.002$; hypertension: $\Delta 7.9$ percentage points, $p=0.037$; obesity: $\Delta 23.7$ percentage points, $p<0.001$; and type 2 diabetes: $\Delta 51.2$ percentage points, $p<0.001$) (Figure 2)
- 17.7% of the Res-GLP cohort newly initiated a GLP-1RA in the follow-up period, while the remainder were continuing baseline therapy (Figure 3)
- Semaglutide (51.7%) and tirzepatide (42.7%) were the most common
- Index resmetirom dose was higher among the Res-GLP cohort reflecting the higher percentage of patients with a baseline weight ≥ 100 kg (Table 2)
- Both cohorts had a mean resmetirom PDC of 0.7 during the fixed 6-month follow-up period
- In the model, the two factors significantly associated with higher odds of receipt of a concomitant GLP-1 RA were baseline GLP-1 RA use and baseline obesity (Table 3)
 - By definition, baseline GLP-1 RA use was strongly correlated with baseline T2D, but sensitivity analyses confirmed baseline GLP-1 RA use, not T2D, was the significant predictor.

REFERENCES

1. Rezdiffra [package insert]. West Conshohocken, PA: Madrigal Pharmaceuticals, Inc. 2. Liss KH, Finck BN. *Biochimie*. 2017;136:65-74. 3. Sanyal AJ et al. *New Engl J Med*. 2025;392:2089-2099



CONCLUSION

- Resmetirom adherence was similar irrespective of concomitant GLP-1 RA use
- Prior GLP-1 RA use and baseline obesity were significantly associated with concomitant GLP-1 RA use in the follow-up period

LIMITATIONS

- In this study, MASH diagnosis was inferred from receipt of resmetirom
- Due to recency of resmetirom approval, follow-up was capped at 6 months
 - Longer follow-up is needed to evaluate treatment adherence
- Concomitant use was assumed from receipt of GLP-1 RA during follow-up, but patients may have discontinued resmetirom before initiating GLP-1 RA



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