

Healthcare Utilization and Costs in Users of Once-Weekly GLP-1 Receptor Agonists vs Other Glucose-Lowering Therapies Among Medicare Beneficiaries With Type 2 Diabetes and Established Atherosclerotic Cardiovascular Disease

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Aim

To compare real-world healthcare resource utilization (HCRU) and costs among Medicare beneficiaries with type 2 diabetes (T2D) and atherosclerotic cardiovascular disease (ASCVD) who initiated once-weekly glucagon-like peptide-1 receptor agonists (OW GLP-1 RAs) such as semaglutide, dulaglutide, or extended-release (ER) exenatide, versus other non-insulin glucose-lowering therapies (ONIGLTs), including comparisons at both the drug class level and the individual drug level.

Introduction

- The cost of diabetes in the US in 2022 was estimated at \$413 billion, with \$307 billion of that being direct medical costs.¹
- CV disease is the leading cause of death among people with T2D.^{2, 3} A majority of those with T2D will develop ASCVD.⁴⁻⁶
- Usage of guideline-recommended sodium-glucose cotransporter-2 inhibitors (SGLT2is) or OW GLP-1 RAs in patients with T2D and ASCVD is associated with lower real-world healthcare costs including all-cause inpatient, outpatient, and total medical costs compared to those not treated with these therapies.^{7,8}
- Dipeptidyl peptidase-4 inhibitors (DPP-4is) are also commonly used in patients with T2D and ASCVD despite neutral CV effects.⁹
- A real-world comparison of OW GLP-1 RAs vs ONIGLTs, including DPP-4is and SGLT2is, on HCRU and costs is important to various stakeholders including payors, clinicians, healthcare systems, policy makers, and patients.

Methods

Study design and data source

- This was an observational cohort study of Medicare beneficiaries with T2D and ASCVD using propensity score matching (PSM) to compare beneficiaries initiating a new treatment with OW GLP-1 RAs or ONIGLTs.
- The study used Medicare fee-for-service (FFS) claims ranging from Jan. 1, 2006 – Dec. 31, 2022 (study period).

Treatment strategies

- Two major treatment strategies were compared: OW GLP-1 RA (semaglutide [Ozempic®], dulaglutide [Trulicity®], and ER exenatide [Bydureon®]) vs ONIGLTs (DPP-4is, SGLT2is, and other therapies [excluding biguanides]).
- Beneficiaries could be included twice (once per treatment arm). Those with claims for any GLP-1 RA or the index therapy during the drug-specific baseline period were excluded.

Study population

- The study included those 66+ years at index, with 12 months of continuous pre-index enrollment, and 2+ prescriptions for the index therapy, and excluded those with type 1 diabetes, and contraindications of GLP-1 RAs

Study outcomes

- HCRU outcomes included number of visits for the following categories: inpatient (IP), outpatient (OP) office, other OP visits/services, emergency department (ED), and total medical visits (IP + OP + ED).
- ASCVD-related HCRU was defined as visits/claims with ASCVD codes in a primary or secondary position. This included the number of coronary revascularization procedures (coronary artery bypass grafting or percutaneous coronary intervention).
- Costs of claims in each HCRU category were assessed and adjusted to 2022 US dollars.

Statistical methods

- Descriptive analyses were conducted for outcomes and covariate measures.
- For each comparison, PSM was utilized to balance baseline characteristics, estimated using logistic regression, with variable 3:1 (e.g., ONIGLT: OW GLP-1 RA) nearest neighbor matching to identify controls.
- Absolute standardized mean differences (SMDs) were used to assess covariate balance after PSM, and SMD < 0.1 was considered well-balanced for baseline characteristics.
- For HCRU outcomes, incidence rate ratios (IRRs) between the comparison groups were estimated using negative binomial regression models.
- Quasi-Poisson regression models were fit for cost outcomes to estimate mean cost ratios (MCRs).

Results

Patient attrition

- The study included 398,470 Medicare beneficiaries: 81,273 treated with OW GLP-1 RAs and 335,412 with ONIGLTs (Figure 1).

Baseline characteristics after PSM

- After matching, baseline characteristics were balanced between those treated with OW GLP-1 RAs (n=77,712) and ONIGLTs (n=174,620) (Table 1).
- Mean age was 73 years, most patients were White (80%), 40% were female, and average time from earliest ASCVD diagnosis to index was 6 years.

HCRU and costs at drug class level

- OW GLP-1 RAs were associated with 25% and 23% lower all-cause and ASCVD-related IP visits, respectively, and 12% and 11% lower all-cause and ASCVD-related ED visits, respectively, compared with ONIGLTs. Results were similar when comparing OW GLP-1 RAs with DPP-4is (Figure 2).
- In comparison to SGLT2is, OW GLP-1 RAs were associated with 5% greater total all-cause HCRU and costs, but 3% and 6% less ASCVD-related total HCRU and costs, respectively.

HCRU and costs at individual drug level

- Semaglutide users had significantly lower all-cause and ASCVD-related IP visits (32% & 31% less, respectively), 21% lower all-cause and ASCVD-related ED visits, and 11% lower ASCVD-related total visits vs DPP-4i users (Figure 3).
- Semaglutide was associated with significantly lower all-cause and ASCVD-related IP visits (10% and 16% less, respectively), 10% lower ASCVD-related total visits and 14% less ASCVD-related total costs vs SGLT2is (Figure 4).
- HCRU and costs with dulaglutide were generally lower compared to DPP-4is, while the opposite was seen vs SGLT2is. A similar trend was observed for the comparisons of ER exenatide vs DPP-4is and SGLT2is (Figures 3 and 4).
- Semaglutide was associated with reduced coronary revascularization procedures: 9% less vs DPP-4is, and 11% less vs SGLT2is. Dulaglutide was associated with smaller reductions, 2% and 7% less vs DPP-4is and SGLT2is, respectively, while no reductions were seen with ER exenatide.

Figure 1. Patient attrition

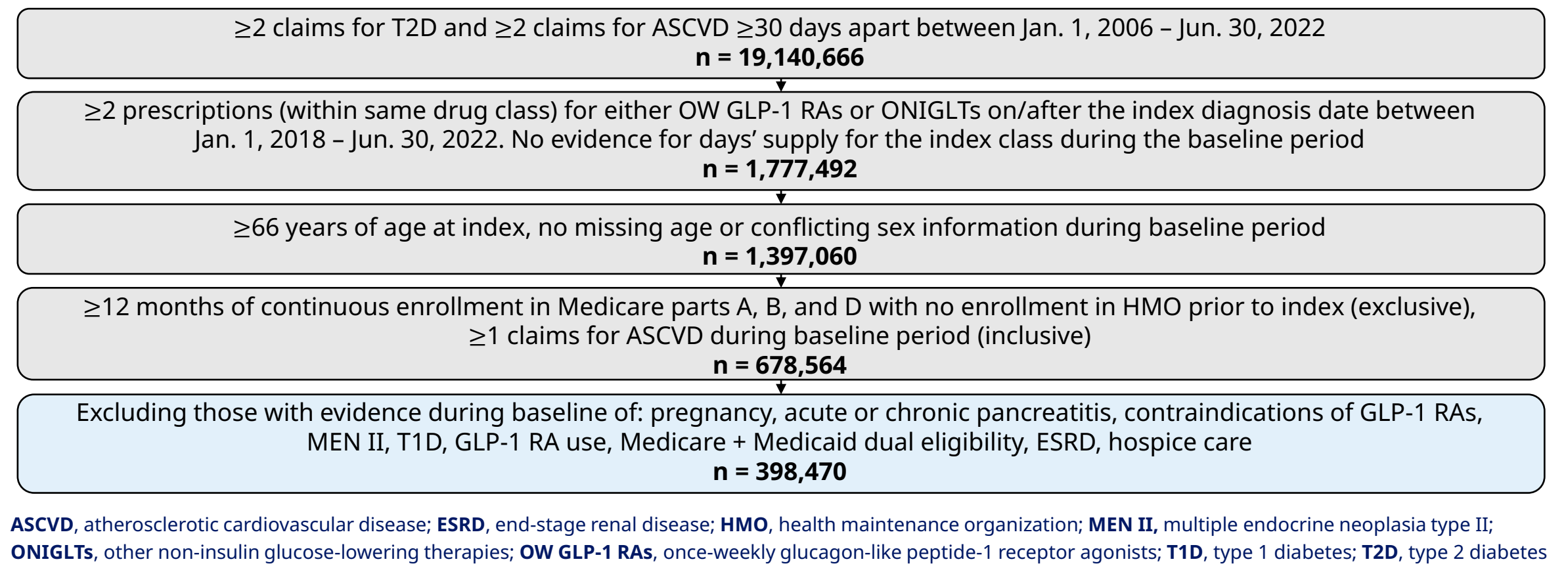


Table 1. Selected baseline characteristics after PSM

	OW GLP-1 RAs (n = 77,712)	ONIGLTs (n = 174,620)	SMD after PSM
Age at index date, n (%)			0.016
66-69	20,661 (26.6)	46,807 (26.8)	
70-74	27,204 (35.0)	61,706 (35.3)	
75-79	18,141 (23.3)	40,800 (23.4)	
≥80	11,706 (15.1)	25,306 (14.5)	
Sex, n (%)			0.004
Male	46,743 (60.1)	104,702 (60.0)	
Female	30,969 (39.9)	69,918 (40.0)	
Years from earliest ASCVD diagnosis to index, mean (SD)	6.36 (4.33)	6.33 (4.37)	0.008
CCI (excluding diabetes), mean (SD)	2.50 (1.88)	2.48 (1.90)	0.008
Index ASCVD Type, n (%)			0.002
IS	3,220 (4.1)	7,283 (4.2)	
MI	3,441 (4.4)	7,695 (4.4)	
Other	71,051 (91.4)	159,643 (91.4)	
Selected comorbidities, n (%)			
AF and flutter	18,637 (24.0)	41,428 (23.7)	0.006
Heart failure	19,715 (25.4)	43,995 (25.2)	0.004
Severe CKD (stage 3-4)	12,135 (15.6)	26,215 (15.0)	0.017
Cancer	10,957 (14.1)	24,477 (14.0)	0.002
Obesity	41,839 (53.8)	94,495 (54.1)	0.006

AF, atrial fibrillation; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; PSM, propensity score matching; SMD, absolute standardized mean difference. Covariates included in the PSM and outcome models were: sex, age category at index, T2DM diagnosis year, ASCVD diagnosis year, time from ASCVD diagnosis to index, CCI (excl. diabetes), Diabetes Complications Severity Index (DCSI), type of index ASCVD, presence of the following comorbidities during baseline (atrial fibrillation, heart failure, CKD, cancer, depression, obesity), presence of the following medications during baseline (biguanides, sulfonylureas, thiazolidinediones, alpha glucosidase inhibitors, meglitinides, DPP-4i, SGLT2i, combination NRTI, basal insulin, non-basal insulin, anti-angina, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), statins, anticoagulants, antiplatelets), number of IP visits in 60 days prior to index, number of ER visits in 60 days prior to index, and specialty for the prescriber of the index medication.

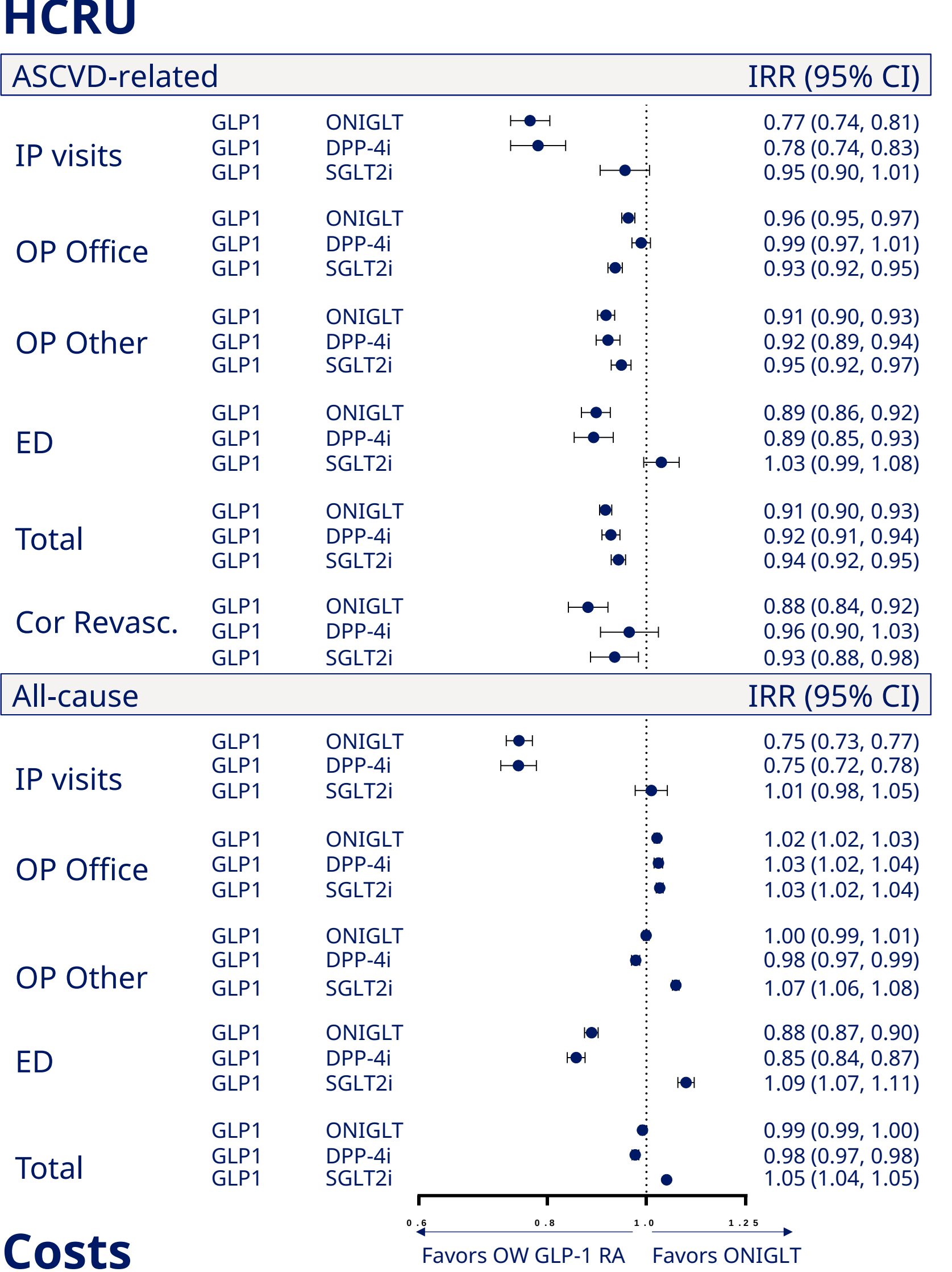
Disclosures:

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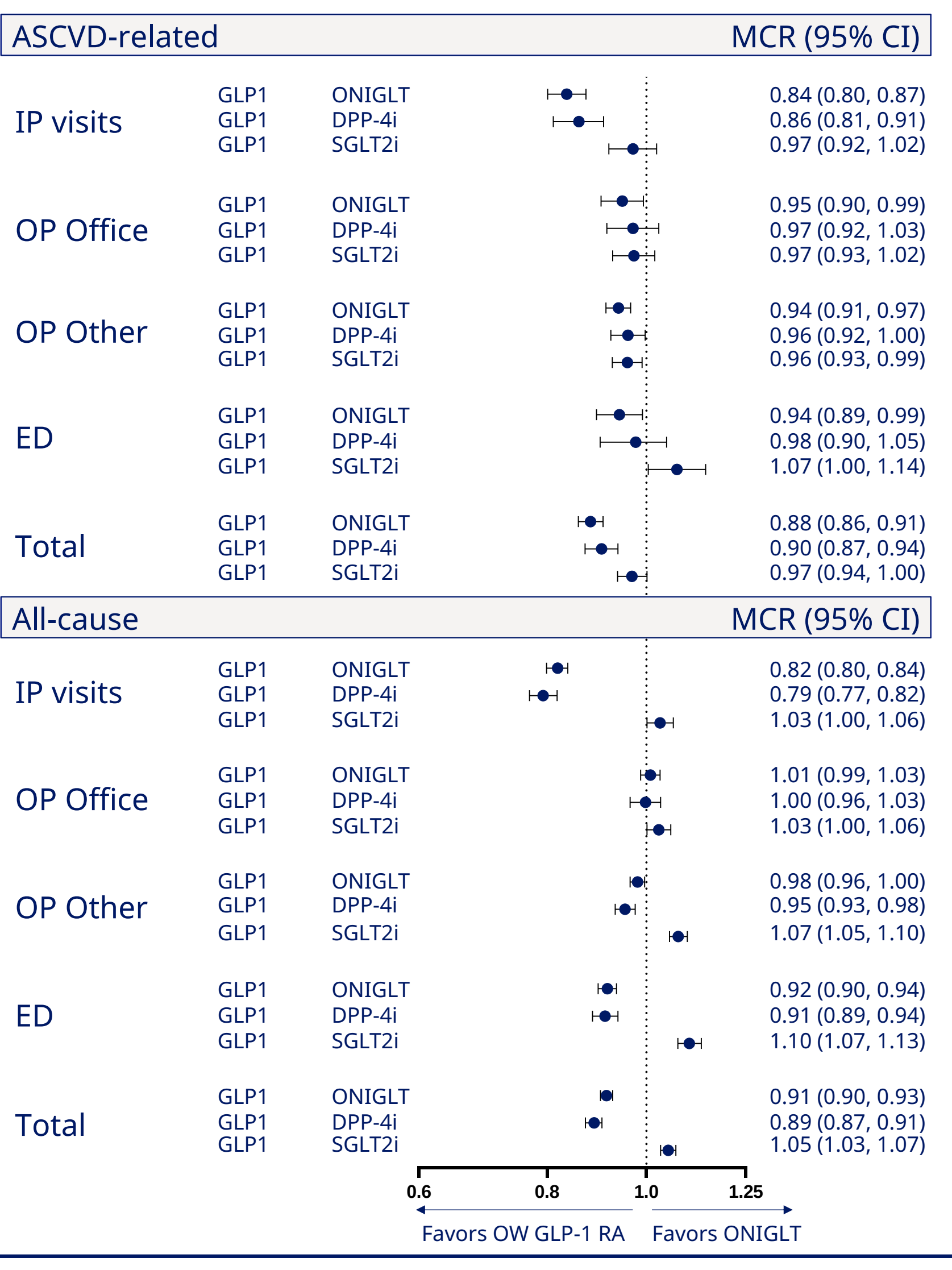
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Figure 2. HCRU and cost comparisons at the drug class level



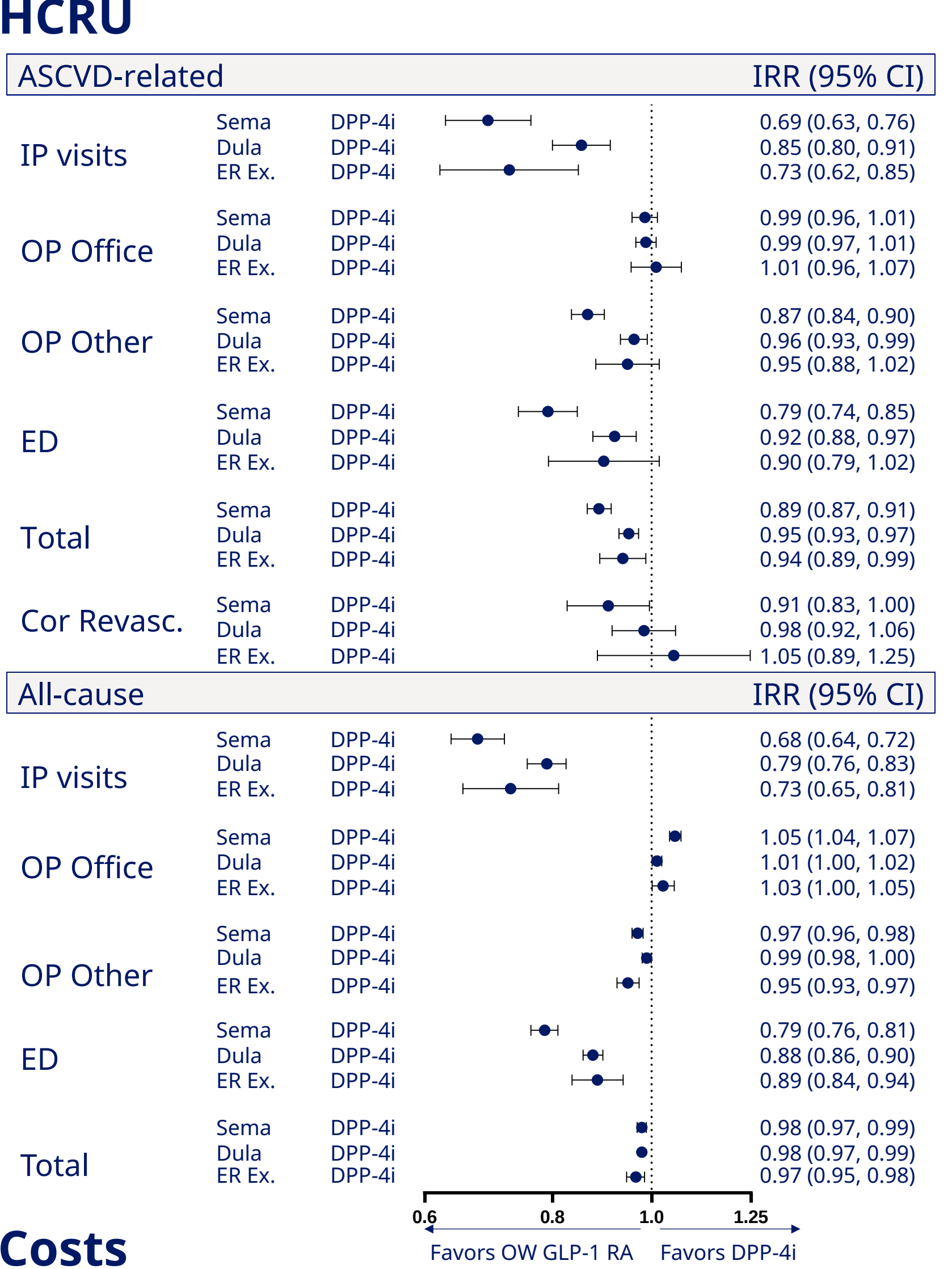
Costs



Limitations

- Standard limitations for observational cohort studies apply; no causal inferences should be made.
- This study only includes FFS Medicare beneficiaries, therefore caution is needed when generalizing the conclusions to other populations.
- Data availability and limitations may further limit the interpretation or applicability of these findings, including but not limited to potential measurement errors (e.g., misclassified billing codes), missing data, and lack of detailed clinical granularity in Medicare claims data.

Figure 3. HCRU and cost comparisons individual OW GLP-1 RAs vs DPP-4i



Costs

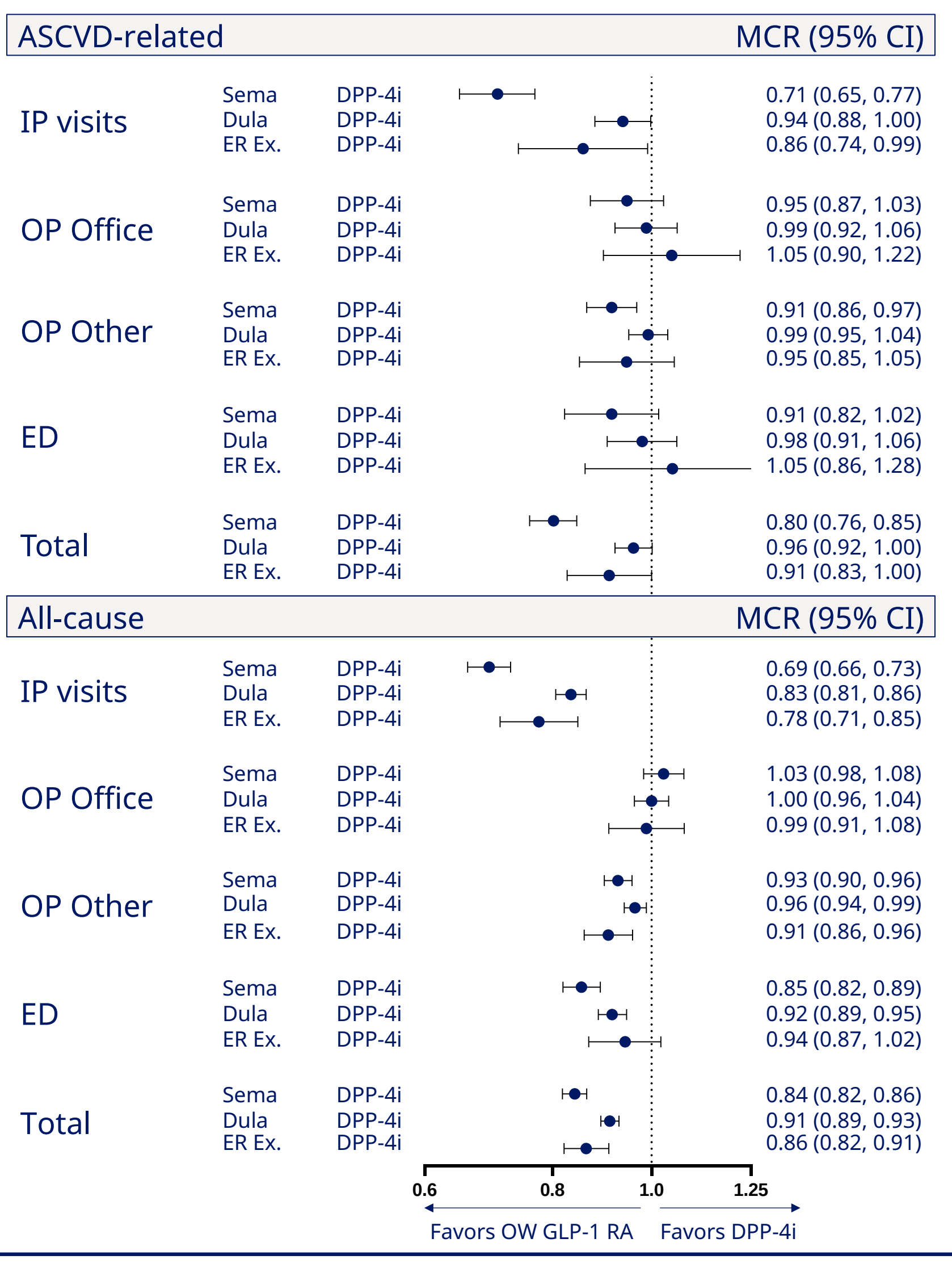
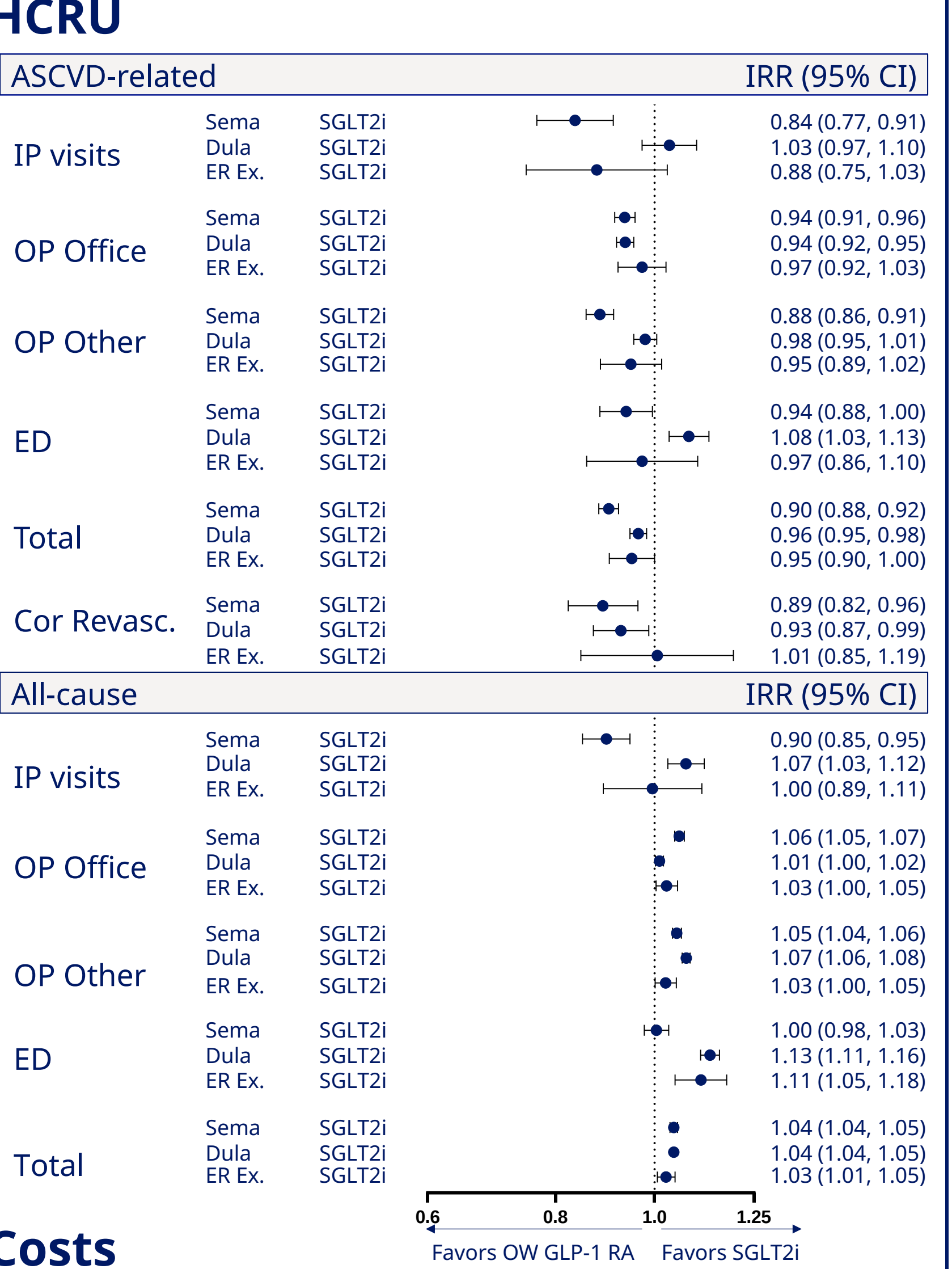
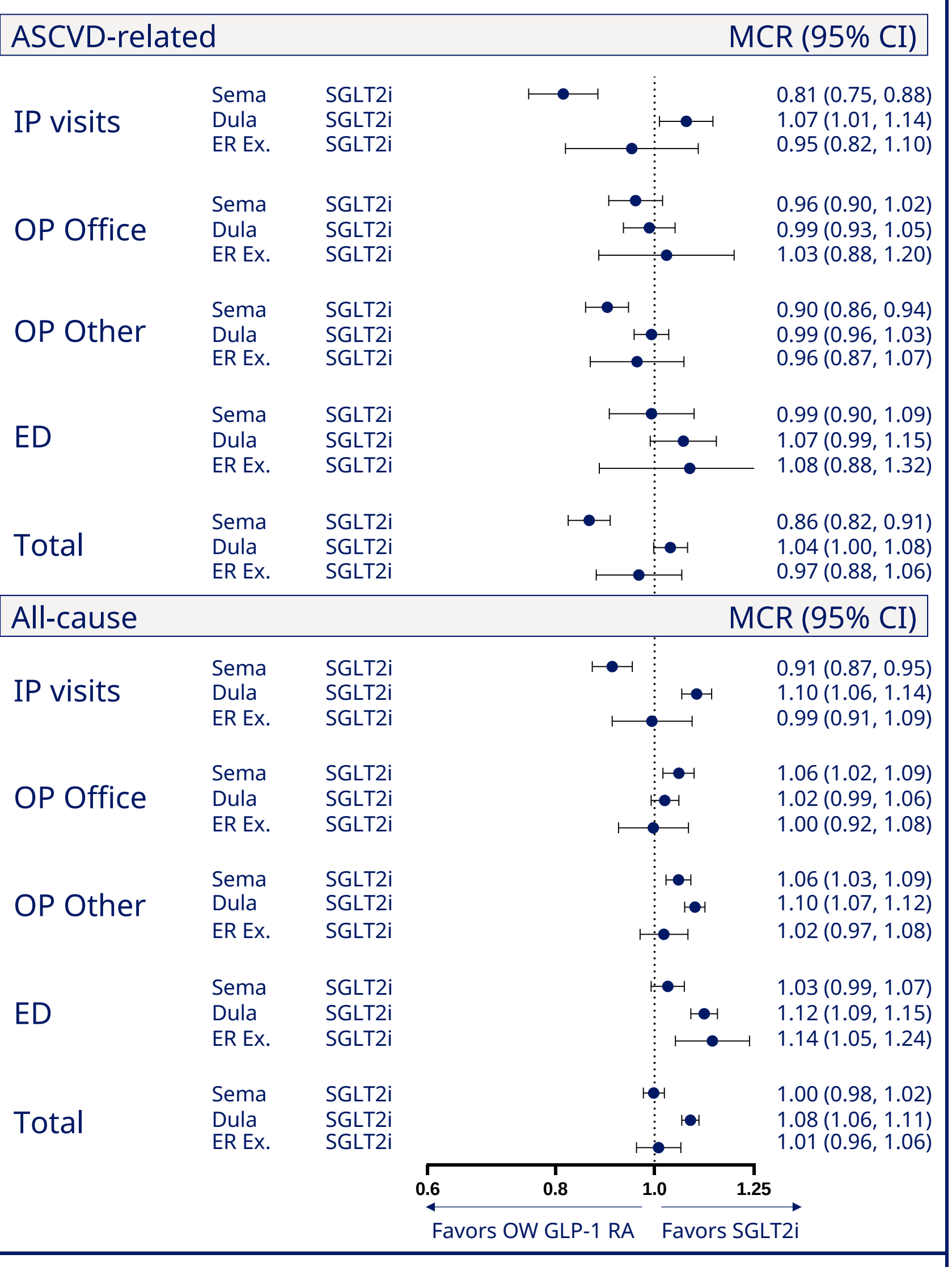


Figure 4. HCRU and cost comparisons individual OW GLP-1 RAs vs SGLT2i



Costs



Conclusion

- High-cost, avoidable HCRU and costs such as IP and ED visits were significantly lower among those initiating OW GLP-1 RAs compared to ONIGLTs.
- These findings suggest the CV benefits associated with OW GLP-1 RAs may reduce the clinical and economic burden of comorbid T2D and ASCVD.

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