

BACKGROUND

- Prevalence of **obesity** is increasing among **people with HIV (PWH)**
- Antiretroviral therapy (ART)** particularly integrase strand transfer inhibitors (INSTIs) (e.g. dolutegravir and bictegravir) and tenofovir alafenamide (TAF) are associated with **weight gain**
- Glucagon-like peptide-1 receptor agonists (GLP-1RA) and sodium-glucose cotransporter-2 inhibitors (SGLT2i)** promote weight loss in the general population
- Limited data** exist on their effects on weight loss in **PWH**

OBJECTIVE

To compare the impact of GLP-1RA, SGLT2i, DPP-4 inhibitors (DPP-4i), and sulfonylureas (SU) on **weight change** among PWH

METHODS

Study Design & Data Source: Observational study using data from **9 sites** from the Centers for AIDS Research Network of Integrated Clinical Systems (**CNICS**) cohort

Inclusion Criteria:

- Adult PWH who initiated a GLP-1RA, SGLT2i, DPP-4i, or SU between 2013-2023
- ≥ 2 weight measurements:
 - Baseline weight measurement
 - Weight measurement after initiation of medication

Exposure:

GLP-1RA, SGLT2i, DPP-4i, or sulfonylureas

Outcomes:

(1) Trajectory of percent weight loss at 1 year

Overall and assessing effect modification by diabetes status

(2) Time to ≥5% weight loss

Statistical Analysis:

- Time-to-event: **Cox proportional hazards models**
- Weight change: **Linear mixed models**
- Models were adjusted** for age, sex, race/ethnicity, CNICS site, baseline weight, CD4 count, viral load, baseline diagnoses of hypertension, CKD, and diabetes, as well as use of ART, antipsychotics, statins, insulin, and metformin

RESULTS

Among PWH, GLP-1RAs led to the greatest bodyweight loss (-3.6%), while SGLT2 inhibitors had a modest effect (-1%). Both were significantly more effective than sulfonylureas in achieving ≥5% weight loss.

Table 1. Baseline Characteristics of PWH by Antidiabetic Medication Class

Characteristic	GLP-1RA (n=627)	SGLT2i (n=295)	DPP-4i (n=201)	SU (n=478)	Total (n=1,601)
Age (years), mean ± SD	52 ± 10	56 ± 10	56 ± 10	53 ± 10	53 ± 10
Female, n (%)	169 (27%)	59 (20%)	57 (28%)	112 (23%)	397 (25%)
Race, n (%)					
White	244 (39%)	104 (35%)	70 (35%)	149 (31%)	567 (35%)
Black	240 (38%)	150 (51%)	107 (53%)	245 (51%)	742 (46%)
Hispanic	113 (18%)	27 (9%)	17 (8%)	67 (14%)	224 (14%)
Other	30 (5%)	14 (5%)	7 (3%)	17 (4%)	68 (4%)
Weight (kg), mean ± SD	110 ± 25	93 ± 24	95 ± 26	95 ± 23	101 ± 25
BMI (kg/m ²), mean ± SD	36 ± 8	31 ± 8	32 ± 9	32 ± 8	33 ± 8
BMI Category, n (%)					
BMI < 30	120 (19%)	163 (55%)	99 (49%)	223 (47%)	605 (38%)
BMI 30-34.9	185 (30%)	56 (19%)	53 (26%)	131 (27%)	425 (27%)
BMI ≥ 35	322 (51%)	76 (26%)	49 (24%)	124 (26%)	571 (36%)
Diabetes, n (%)	376 (60%)	199 (68%)	201 (100%)	478 (100%)	1,254 (78%)
VL <200 copies/mL, n (%)	596 (95%)	265 (90%)	190 (95%)	427 (89%)	1,478 (92%)
CD4 Count (cells/mm ³), mean ± SD	790 ± 384	665 ± 376	705 ± 378	691 ± 387	727 ± 386

Abbreviations: GLP-1RA: Glucagon-like peptide-1 receptor agonist, SGLT2i: Sodium-glucose cotransporter-2 inhibitor, DPP-4i: Dipeptidyl peptidase-4 inhibitor, SU: Sulfonylurea, SD: Standard deviation, BMI: Body mass index, VL: Viral load

Figure 1. Percent Weight Loss at 1 year by Antidiabetic Class

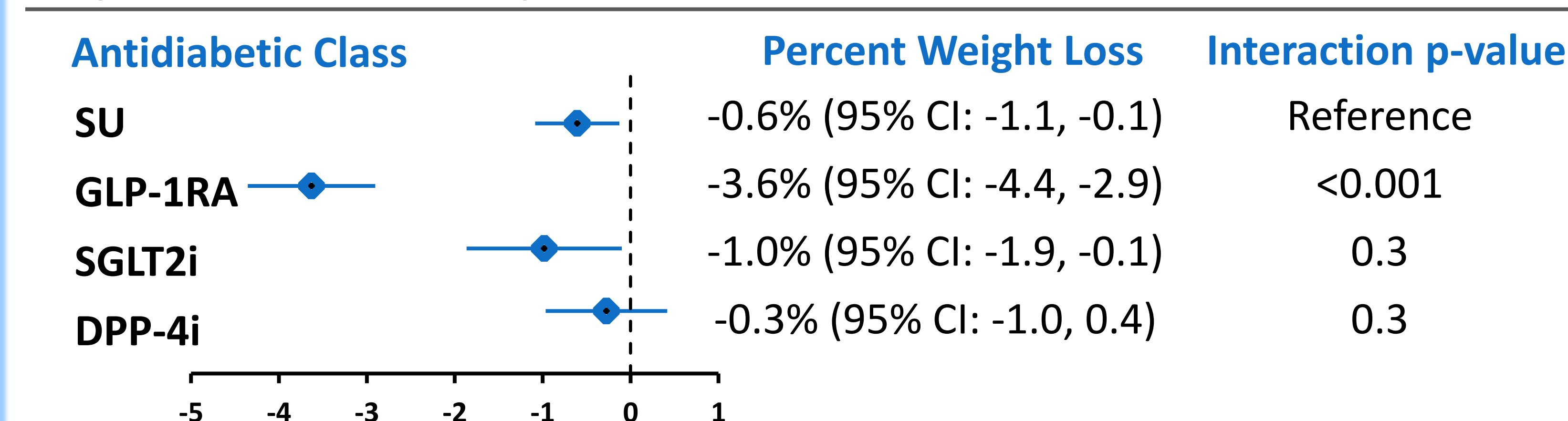


Figure 2. Percent Weight Loss by Diabetes Status

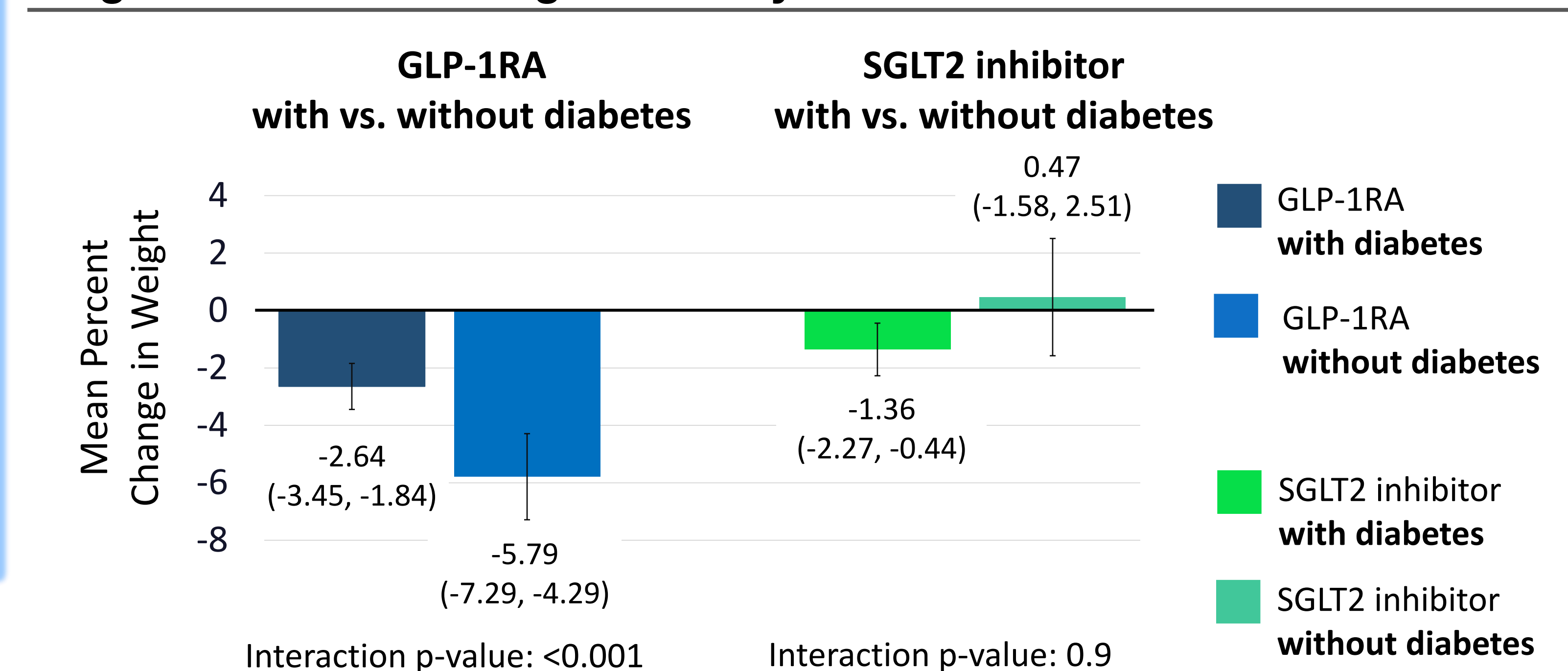


Figure 3. Proportion Achieving ≥5% Weight Loss at 1 Year

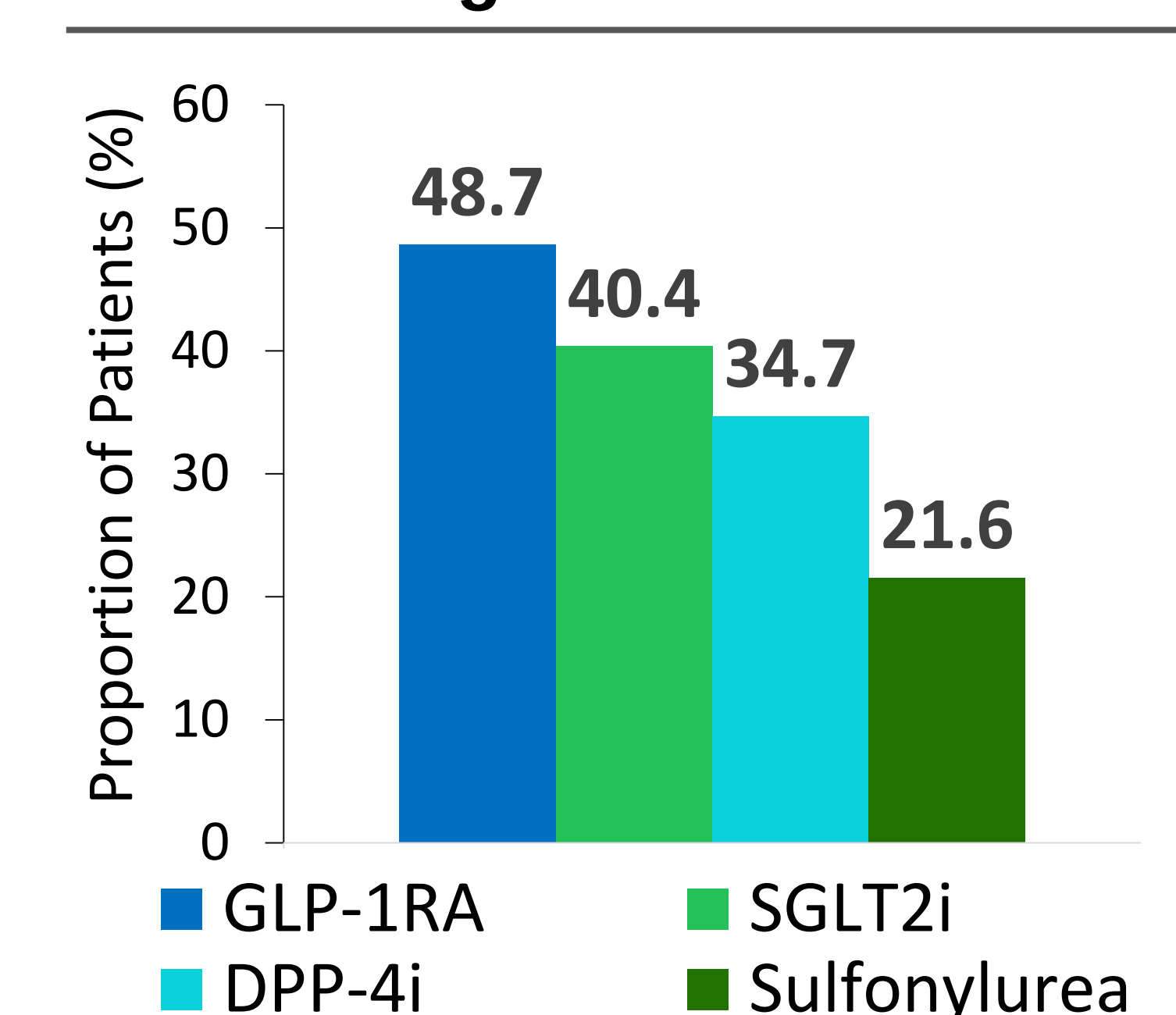
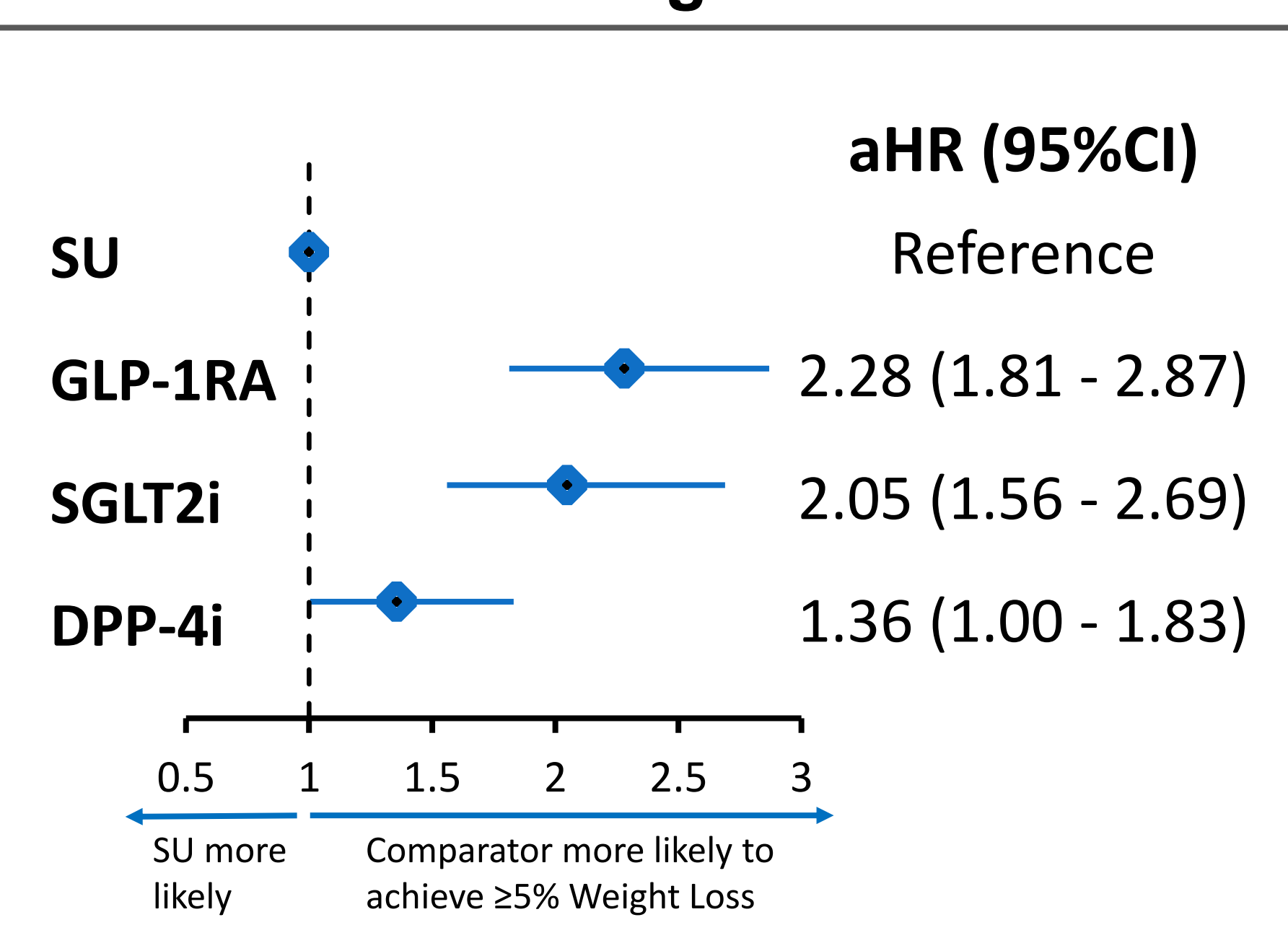


Figure 4. Adjusted Hazard Ratios for ≥5% Weight Loss



CONCLUSIONS

- GLP-1RAs led to the greatest weight loss**, especially in PWH without diabetes, while **SGLT2 inhibitors had more modest weight loss effects**
- DPP-4 inhibitors and sulfonylureas showed no/minimal weight loss
- Newer antidiabetic medications may help address the growing obesity epidemic among PWH**, but further research is needed to evaluate their long-term sustainability and cardiometabolic effects

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