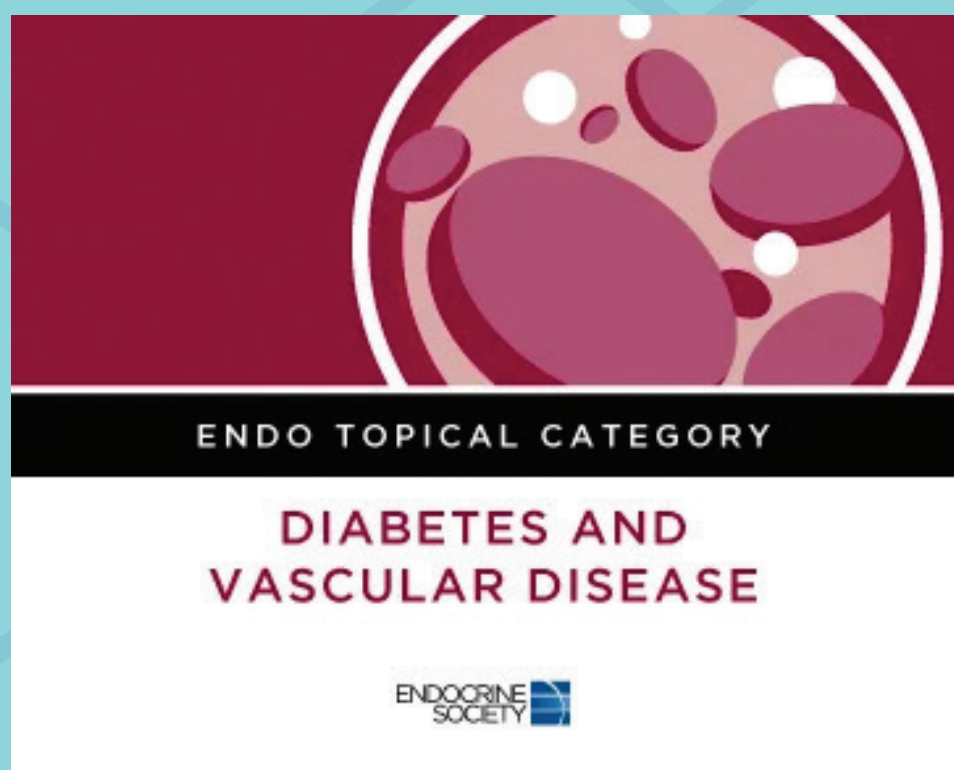




Characterization of Individuals With Difficult-to-Control Type 2 Diabetes and Post-Dexamethasone Suppression Test Cortisol Values <1.2, 1.2–1.8, and >1.8 µg/dL: Findings From the CATALYST Part 1 Study

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Poster MON-572



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SUMMARY AND CONCLUSIONS

- The findings from CATALYST Part 1 suggest that the glycemic and cardiovascular risk associated with endogenous hypercortisolism presents as a spectrum across post-dexamethasone suppression test (DST) cortisol levels
- Participant subgroups with DST cortisol 1.2–1.8 µg/dL and >1.8 µg/dL appeared to have many similarities in terms of glucose-lowering medication use, cardiac comorbidities, and renal comorbidities vs the subgroup with post-DST cortisol <1.2 µg/dL
 - Use of newer glucose-lowering medication classes, such as sodium-glucose cotransporter 2 inhibitors and glucagon-like peptide-1 receptor agonists, and combinations of these newer classes did not differ significantly between participants with post-DST cortisol 1.2–1.8 µg/dL vs >1.8 µg/dL
 - The prevalence of cardiac comorbidities (except for congestive heart failure) also did not differ significantly for participants with post-DST cortisol 1.2–1.8 µg/dL vs >1.8 µg/dL
 - Compared with participants with post-DST cortisol <1.2 µg/dL, the use of newer glucose-lowering medication classes and cardiac comorbidities were significantly more common in participants with post-DST cortisol of either 1.2–1.8 µg/dL or >1.8 µg/dL

BACKGROUND AND OBJECTIVE

- Any level of hypercortisolism is associated with increased cardiometabolic morbidity, as well as cardiovascular and all-cause mortality¹
- Although >1.8 µg/dL is the current cortisol threshold for diagnosing endogenous hypercortisolism with the dexamethasone suppression test (DST),² data indicate that 1.2 µg/dL is the 95th percentile value in normal control individuals³
- CATALYST Part 1 (NCT05772169) was the largest prospective study to date to evaluate the prevalence of endogenous hypercortisolism in US adults with difficult-to-control type 2 diabetes (T2D)^{4,5}
- CATALYST also captured data on clinical characteristics associated with a wide range of post-DST cortisol values
- The objective of this analysis is to compare the demographic and clinical characteristics of CATALYST participants across the post-DST cortisol levels of <1.2 µg/dL, 1.2–1.8 µg/dL, and >1.8 µg/dL



METHODS

- CATALYST Part 1 was a multicenter, prospective, noninterventional study that enrolled adults aged 18 to 80 years
- Participants were defined as having difficult-to-control T2D if their hemoglobin A1c was 7.5% to 11.5% despite taking:
 - ≥3 glucose-lowering medications
 - Insulin plus other glucose-lowering medication(s)
 - ≥2 glucose-lowering medications and having 1 or more microvascular or macrovascular complication(s)
 - ≥2 glucose-lowering and ≥2 antihypertensive medicationsand/or
- Hypercortisolism was defined as 1-mg overnight DST cortisol >1.8 µg/dL with appropriate dexamethasone level (≥140 ng/dL)
- Participants were excluded if they had common causes for false-positive DST results, including use of oral contraceptive pills; excessive alcohol consumption; severe untreated sleep apnea; severe psychiatric, medical, or surgical illness; night-shift work; or hemodialysis/end-stage renal disease
- Baseline characteristics were summarized using descriptive statistics
- Univariate logistic regressions were performed

RESULTS

- Hypercortisolism prevalence in CATALYST Part 1 participants (defined as post-DST cortisol >1.8 µg/dL) was 24% (Figure 1); this subgroup was offered participation in CATALYST Part 2⁶
- Post-DST cortisol values appeared to follow a normal distribution (ie, similar within-group mean and median post-DST cortisol values) in the <1.2 µg/dL and 1.2–1.8 µg/dL groups (Table 1)
- Participants with post-DST cortisol <1.2 µg/dL were younger ($P<0.0001$) and more likely to be Hispanic/Latino ($P<0.001$) than participants in the other post-DST cortisol subgroups

Figure 1. Post-DST Cortisol Levels in CATALYST Participants

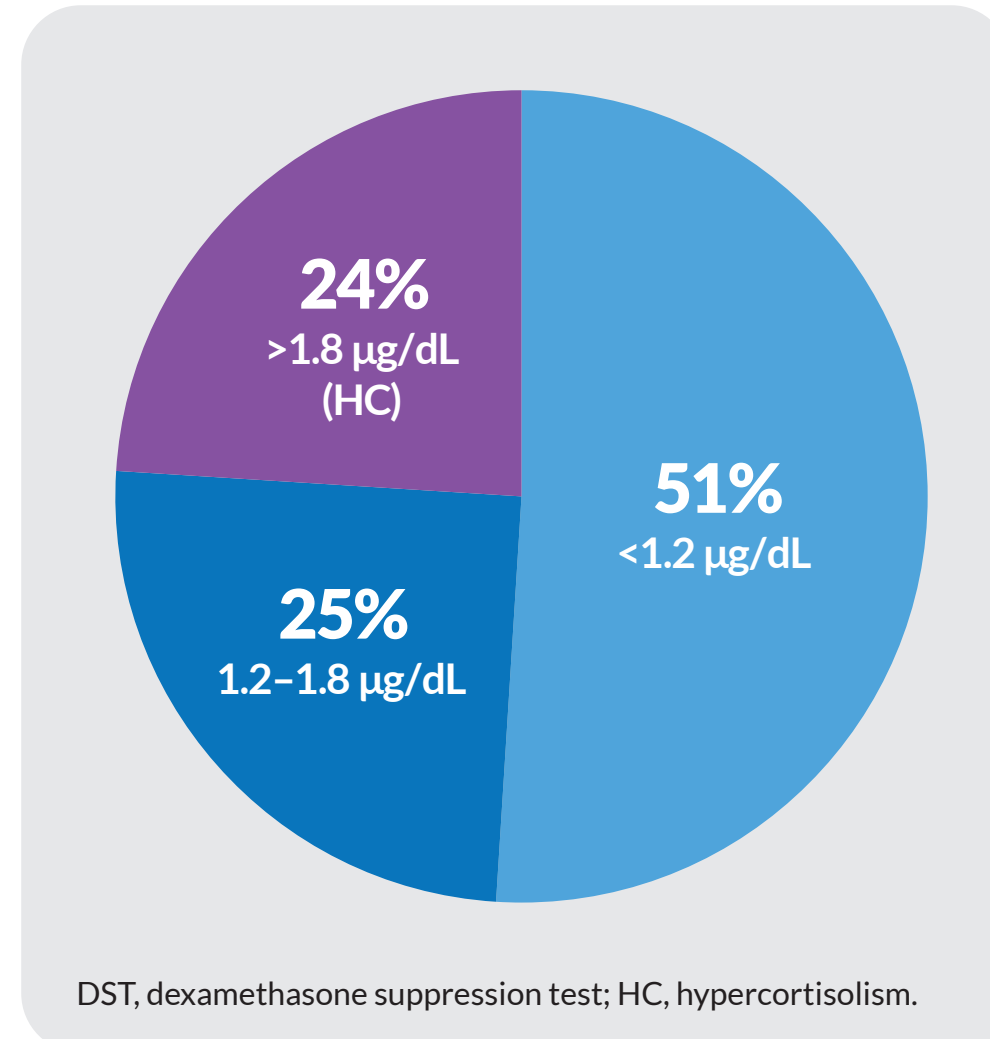


Table 1. Baseline Demographics and Characteristics Across Post-DST Cortisol Subgroups

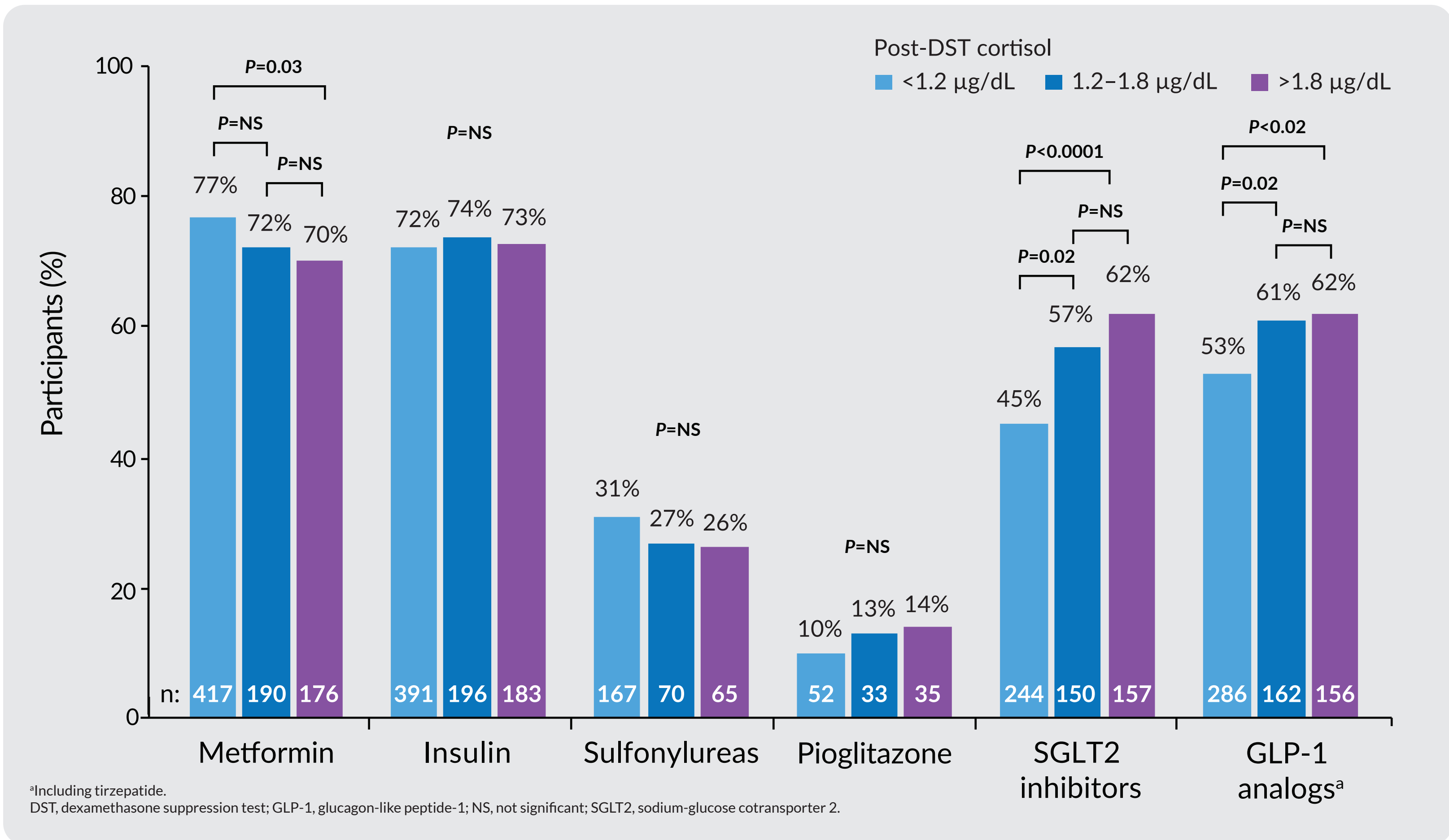
	Post-DST Cortisol Level		
	<1.2 µg/dL (n=541)	1.2–1.8 µg/dL (n=264)	>1.8 µg/dL (HC) (n=252)
Age, y, mean (SD)	58.3 (10.7)	62.8 (9.5)	63.8 (9.6)
Female, n (%)	250 (46.2)	120 (45.5)	109 (43.3)
Race, n (%)			
Asian	30 (5.5)	12 (4.5)	5 (2.0)
Black or African American	93 (17.2)	53 (20.1)	55 (21.8)
White	378 (69.9)	183 (69.3)	187 (74.2)
Other	40 (7.4)	16 (6.1)	5 (2.0)
Ethnicity not Hispanic/Latino, n (%)	347 (64.1)	200 (75.8)	218 (86.5)
BMI, kg/m ² , mean, (SD)	33.9 (7.1)	33.0 (7.0)	33.1 (7.7)
Waist circumference, cm, mean, (SD) [n]	113.1 (16.6) [534]	111.3 (17.1) [262]	113.5 (17.7) [249]
SBP, mmHg, mean (SD) [n]	127.6 (15.7) [541]	127.7 (16.9) [263]	127.4 (16.4) [252]
DBP, mmHg, mean (SD) [n]	75.5 (9.6) [541]	75.4 (10.6) [263]	74.8 (9.5) [252]
HbA1c, %, mean (SD)	8.8 (1.1)	8.7 (1.0)	8.8 (1.1)
Post-DST cortisol, µg/dL			
Mean (SD)	0.9 (0.2)	1.4 (0.2)	3.5 (2.8)
Median (range)	0.9 (0.1–1.2)	1.4 (1.2–1.8)	2.6 (1.8–24.8)

*Ethnicity group missing for 14 participants for the <1.2 µg/dL group, 10 participants for the 1.2–1.8 µg/dL group, and 13 participants for the >1.8 µg/dL group. BMI, body mass index; DBP, diastolic blood pressure; DST, dexamethasone suppression test; HbA1c, hemoglobin A1c; HC, hypercortisolism; SBP, systolic blood pressure; SD, standard deviation.

RESULTS

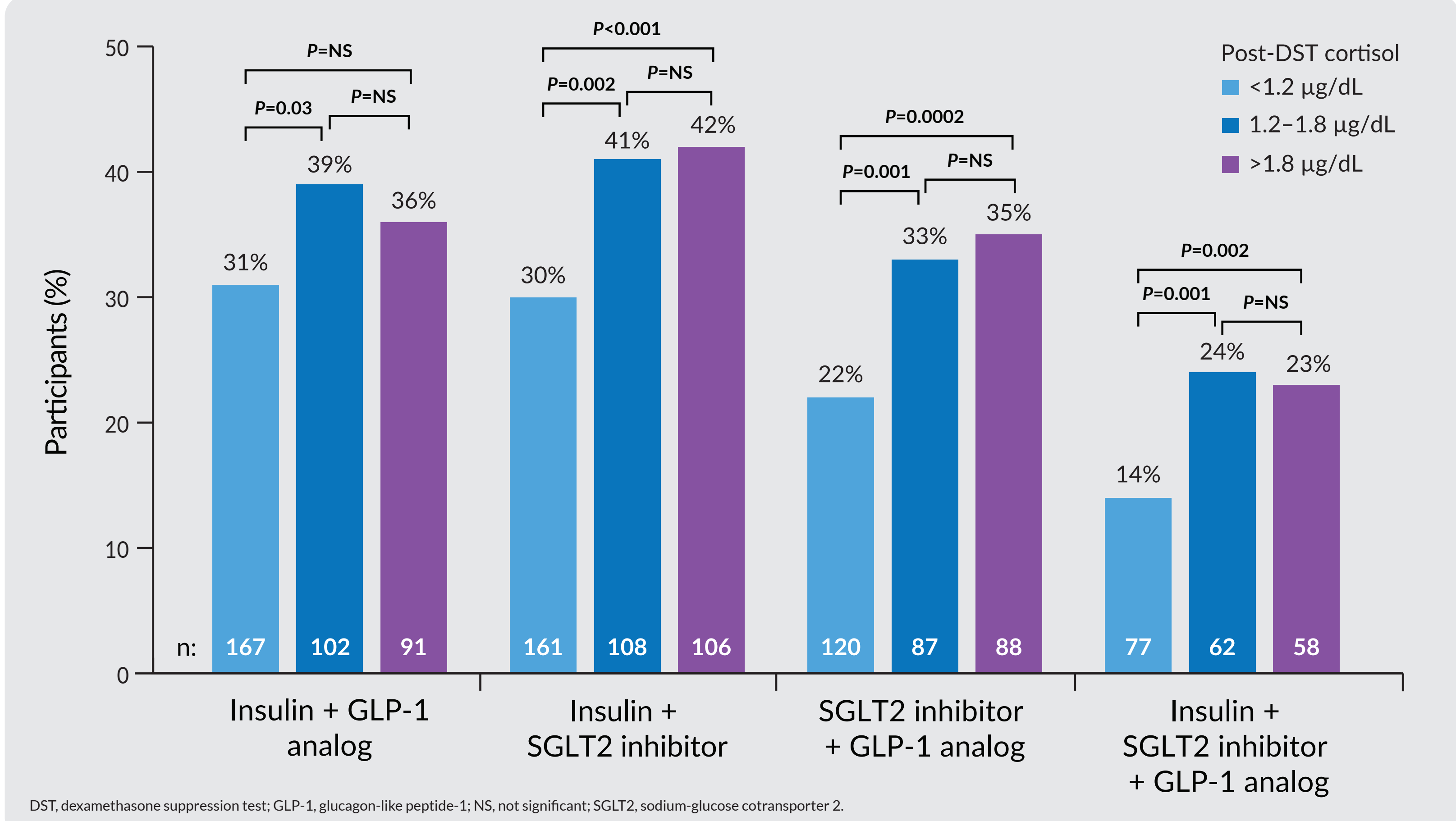
- Compared with post-DST cortisol <1.2 µg/dL, post-DST cortisol 1.2–1.8 µg/dL and >1.8 µg/dL was associated with significantly increased use of the newer glucose-lowering medications, sodium-glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) analogs (including tirzepatide; $P<0.05$; Figure 2)
- Use of metformin, insulin, sulfonylureas, and pioglitazone did not differ between the <1.2 µg/dL and 1.2–1.8 µg/dL post-DST cortisol groups

Figure 2. Antihyperglycemic Medication Use Across Post-DST Cortisol Subgroups



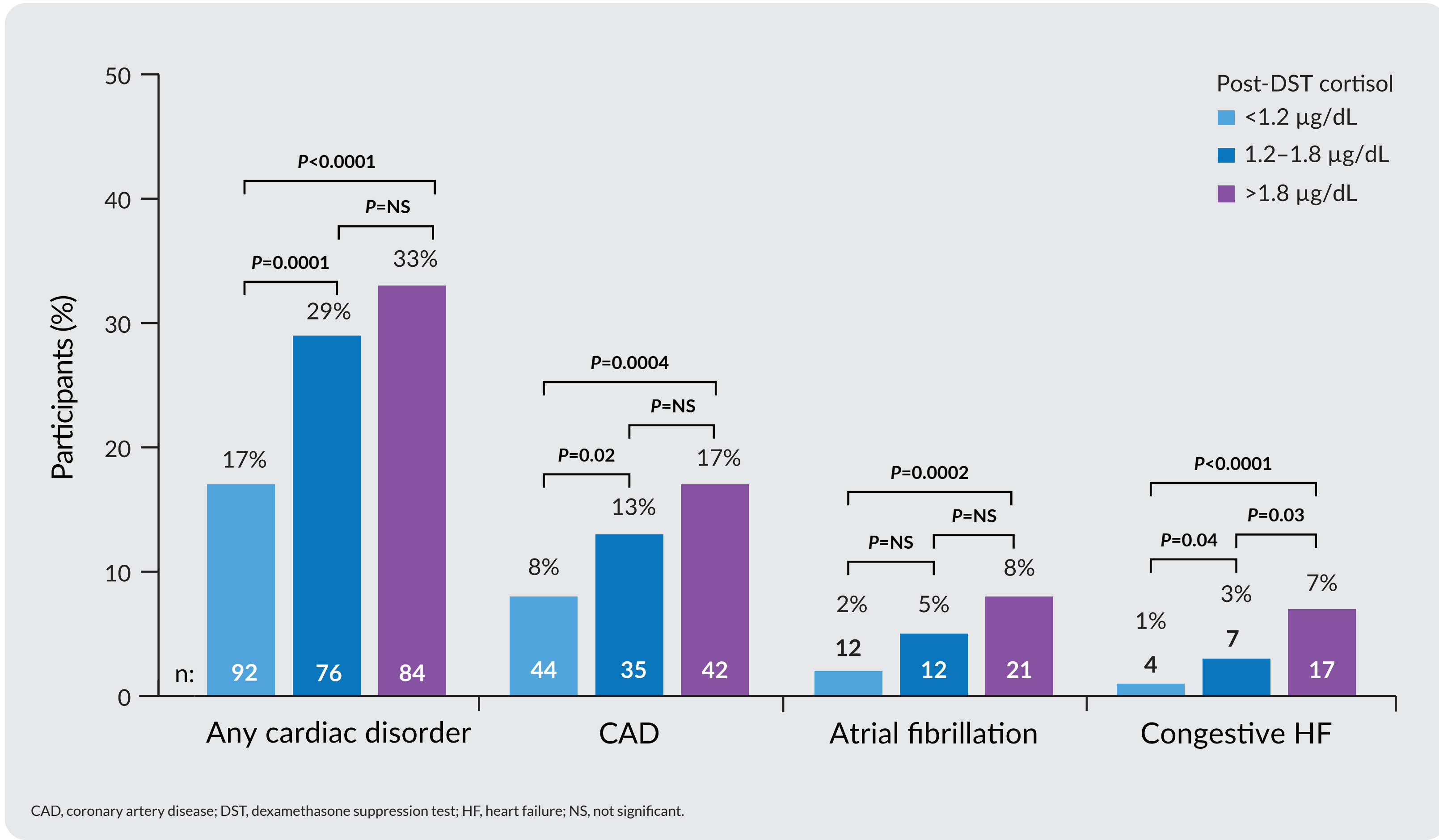
- Combination glucose-lowering therapy with an SGLT2 inhibitor plus insulin, a GLP-1 analog, or both was significantly more common in participants with post-DST cortisol 1.2–1.8 µg/dL and >1.8 µg/dL compared with participants with post-DST cortisol <1.2 µg/dL ($P<0.05$; Figure 3)
- Taking ≥4 antihyperglycemic classes of medications was independently associated with post-DST cortisol 1.2–1.8 µg/dL vs <1.2 µg/dL (50% vs 38%, respectively; $P<0.001$ on multivariate analysis)

Figure 3. Combination Antihyperglycemic Medication Use Across Post-DST Cortisol Subgroups



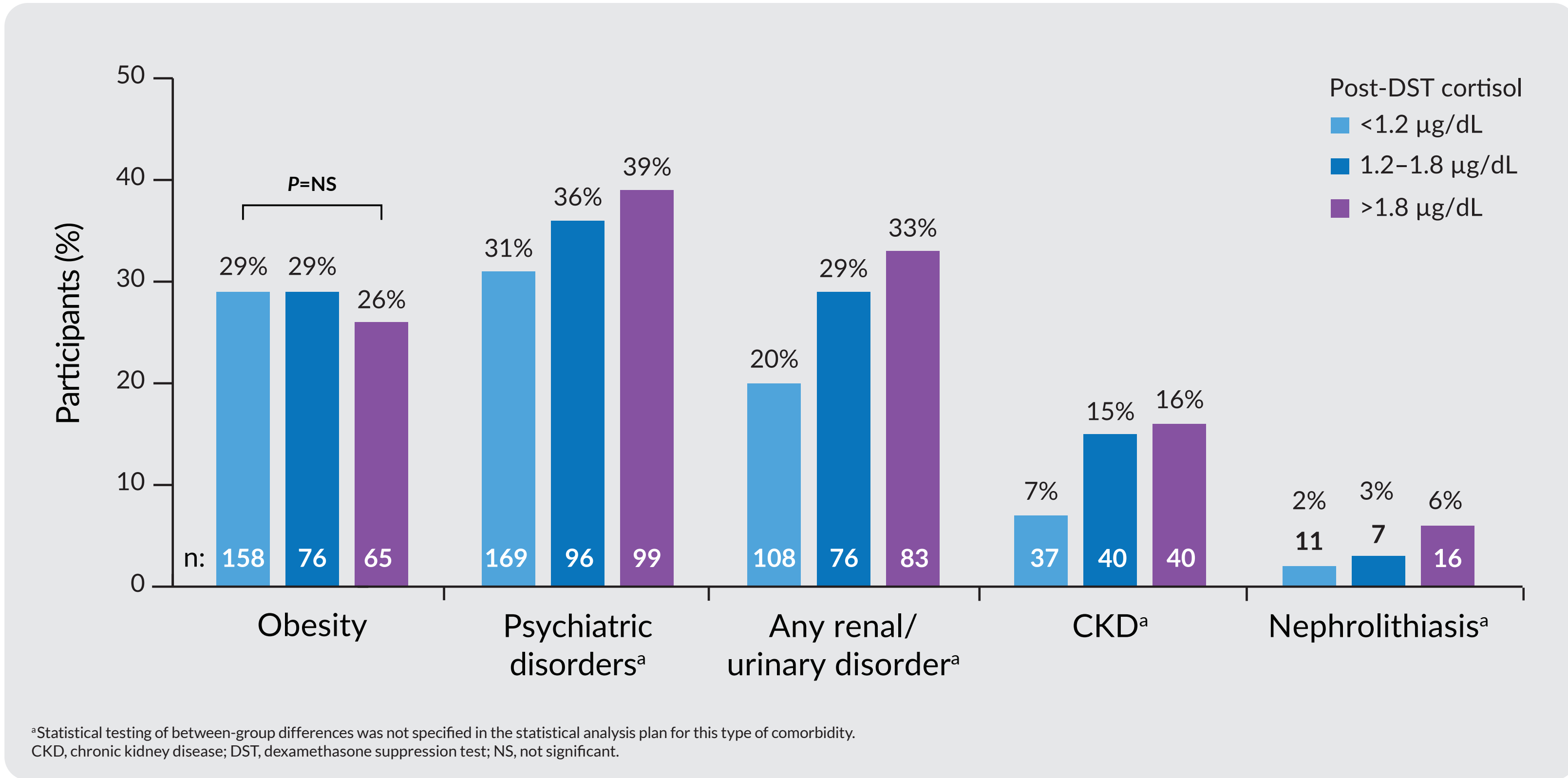
- Post-DST cortisol subgroups 1.2–1.8 µg/dL and >1.8 µg/dL had a significantly higher prevalence of any cardiac disorder vs the <1.2 µg/dL post-DST cortisol subgroup ($P<0.0001$; Figure 4)

Figure 4. Prevalence of Cardiac Comorbidities Across Post-DST Cortisol Subgroups



- The prevalence of psychiatric disorders and renal/urinary disorders, including chronic kidney disease and nephrolithiasis, increased across groups with higher post-DST cortisol (Figure 5)
- Consistent with previously presented results,^{7–9} the prevalence of obesity was similar across post-DST cortisol subgroups

Figure 5. Prevalence of Select Comorbidities Across Post-DST Cortisol Subgroups



*Statistical testing of between-group differences was not specified in the statistical analysis plan for this type of comorbidity. CKD, chronic kidney disease; DST, dexamethasone suppression test; NS, not significant.

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Acknowledgments

The authors want to thank all those who participated in this study: The study participants and their families, the Investigators, and the Sponsor team. This study is sponsored by Corcept Therapeutics Incorporated. Medical writing assistance was provided by Valerie Hilliard, PhD, CMPP of Corcept, and R&R Healthcare Communications.

Author Disclosures

Potential conflicts of interest may exist. Refer to the Meeting App.