Characterisation of Patients With Difficult-to-Control Type 2 Diabetes and a Post-Dexamethasone Suppression Test Cortisol of 1.2–1.8 µg/dL: Findings From a Large Prospective Study

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CATALYST
Study of Hypercortisolism in Patients with Difficult-to-Control Type 2 Diabetes

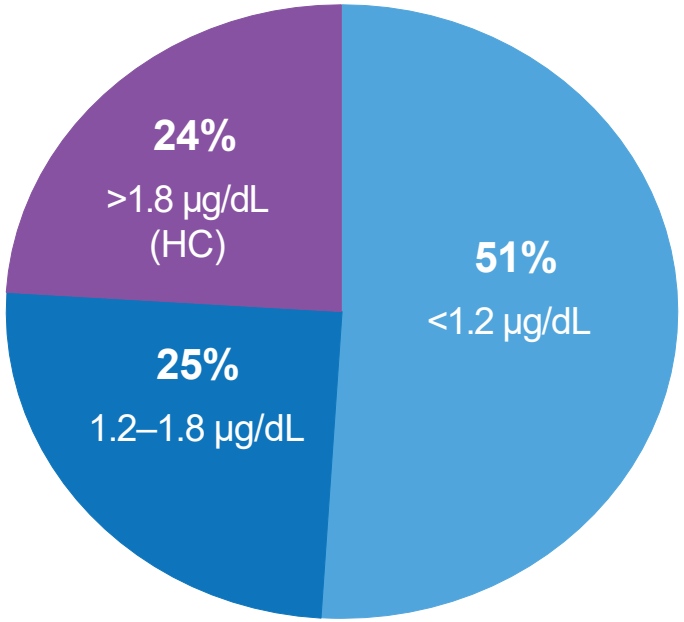
Conflict of Interest

John B. Buse reports: grants and contracts from Corcept Therapeutics Incorporated, Dexcom, Novo Nordisk; consulting fees from Altimmune, Amgen, Antag Therapeutics, APstem Therapeutics, Aqua Medical, AstraZeneca, Boehringer Ingelheim, CeQur, Corcept Therapeutics Incorporated, Dexcom, Eli Lilly, embecta, GentiBio, Glyscend, Insulet, Medtronic MiniMed, Mellitus Health, Metsera, Novo Nordisk, Pendulum Therapeutics, Praetego, Stability Health, Tandem, Terns Inc, Vertex, Zealand Pharma; stock options from Glyscend, Mellitus Health, Metsera, Pendulum Therapeutics, Praetego, Stability Health

CATALYST I Background

- Part 1 of the CATALYST study, the largest prospective study to date assessing the prevalence of endogenous hypercortisolism in US adults with difficult-to-control T2D, found a hypercortisolism prevalence of 23.8%[1]
- Any level of hypercortisolism is associated with increased cardiometabolic risk and morbidity[2]
- Although >1.8 µg/dL is the current cortisol threshold for diagnosing endogenous hypercortisolism with the DST,[3] 1.2 µg/dL is the 95th percentile value in normal control individuals[4]
- **Objective:** To compare the demographic and clinical characteristics of CATALYST participants across the post-DST cortisol levels of <1.2, 1.2–1.8, and >1.8 µg/dL

Post-DST cortisol levels in CATALYST participants[1]

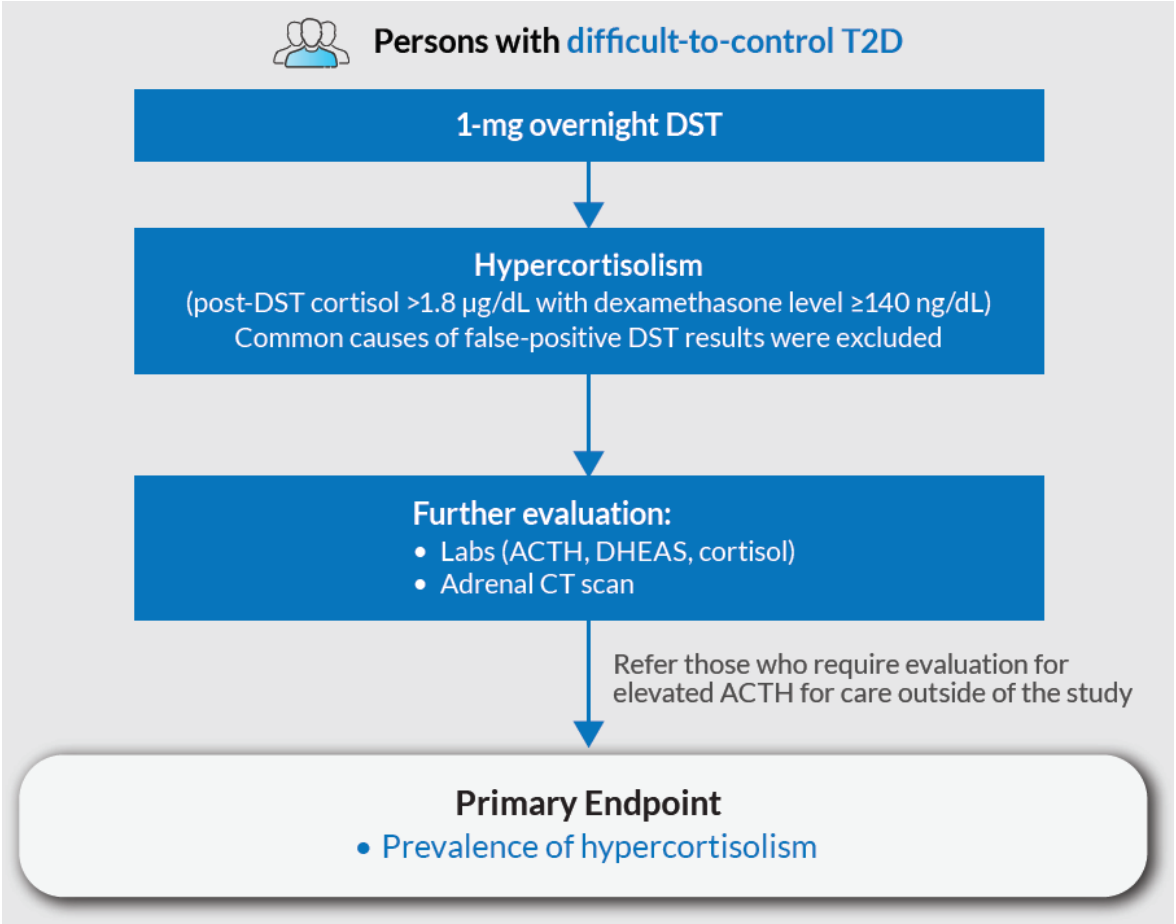


CATALYST is registered as NT05772169.
DST, dexamethasone suppression test; HC, hypercortisolism; T2D, type 2 diabetes; US, United States.
1. Buse JB, et al. *Diabetes Care.* 2025:dc242841. 2. Di Dalmazi G, et al. *Lancet Diabetes Endocrinol.* 2014;2(5):396–405. 3. Nieman LK. *Endocr Rev.* 2022;43(5):852–877. 4. Garg R, et al. *J Endocr Soc.* 2024;8(3):bvae002.

Methods

- 1057 participants aged 18–80 years with difficult-to-control T2D were screened with a 1-mg DST
- Baseline characteristics were assessed and summarized using descriptive statistics
- Univariate and multivariate logistic regression were performed

CATAYLST Study Design



ACTH, adrenocorticotropic hormone; CT, computed tomography; DHEAS, dehydroepiandrosterone sulfate; DST, dexamethasone suppression test; T2D, type 2 diabetes.

DeFronzo RA, et al. *BMJ Open* 2024;14:e08112.

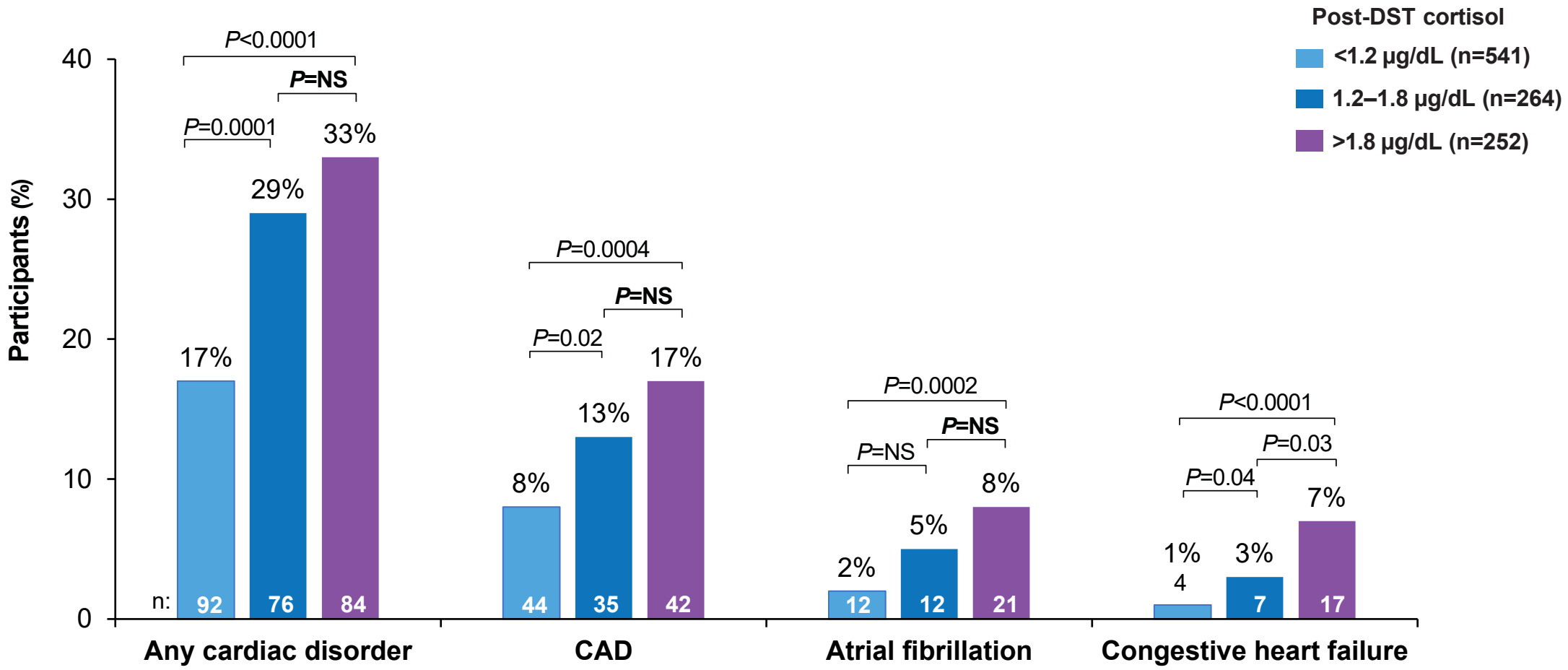
Patient Demographics & Baseline Characteristics

	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, years, 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,[a] 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)

[a]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.

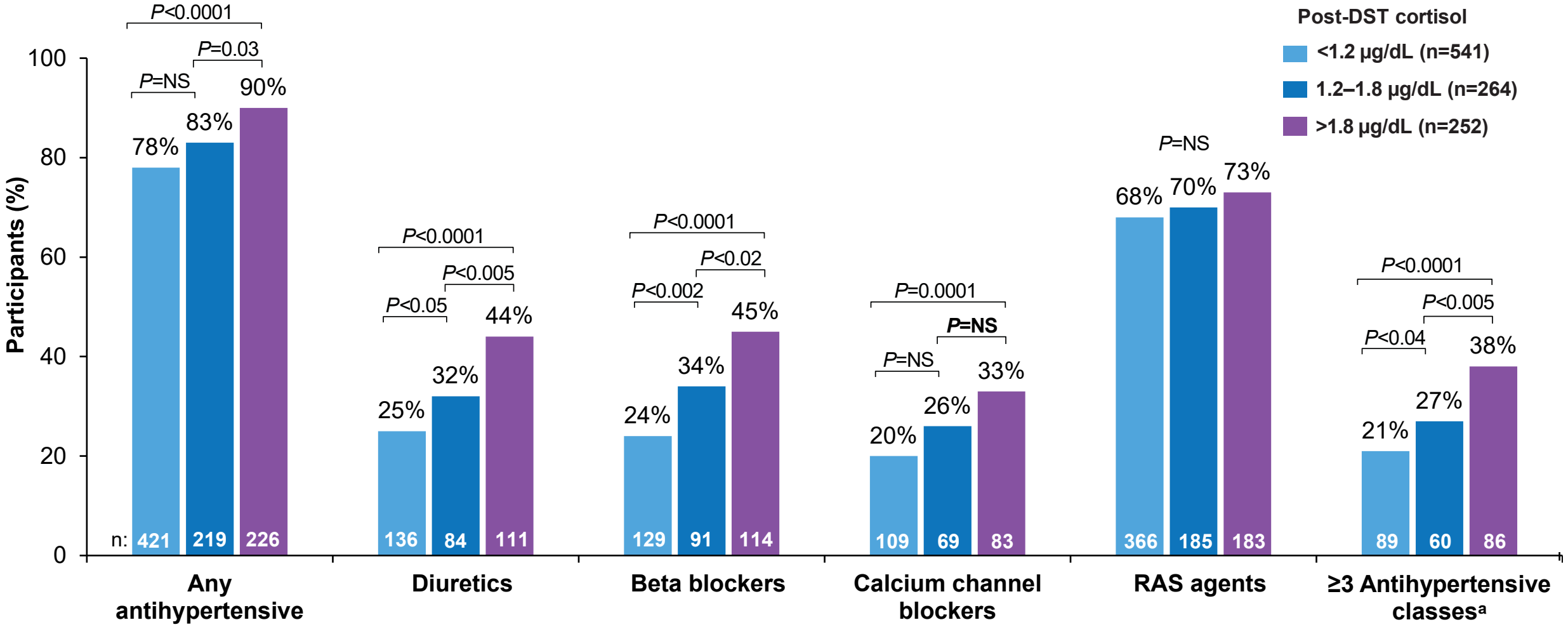
BMI, body mass index; DBP, diastolic blood pressure; DST, dexamethasone suppression test; HbA1c, hemoglobin A1c; HC, hypercortisolism; SBP, systolic blood pressure; SD, standard deviation.

Increasing Post-DST Cortisol Correlated With a Greater Prevalence of Cardiac Comorbidities



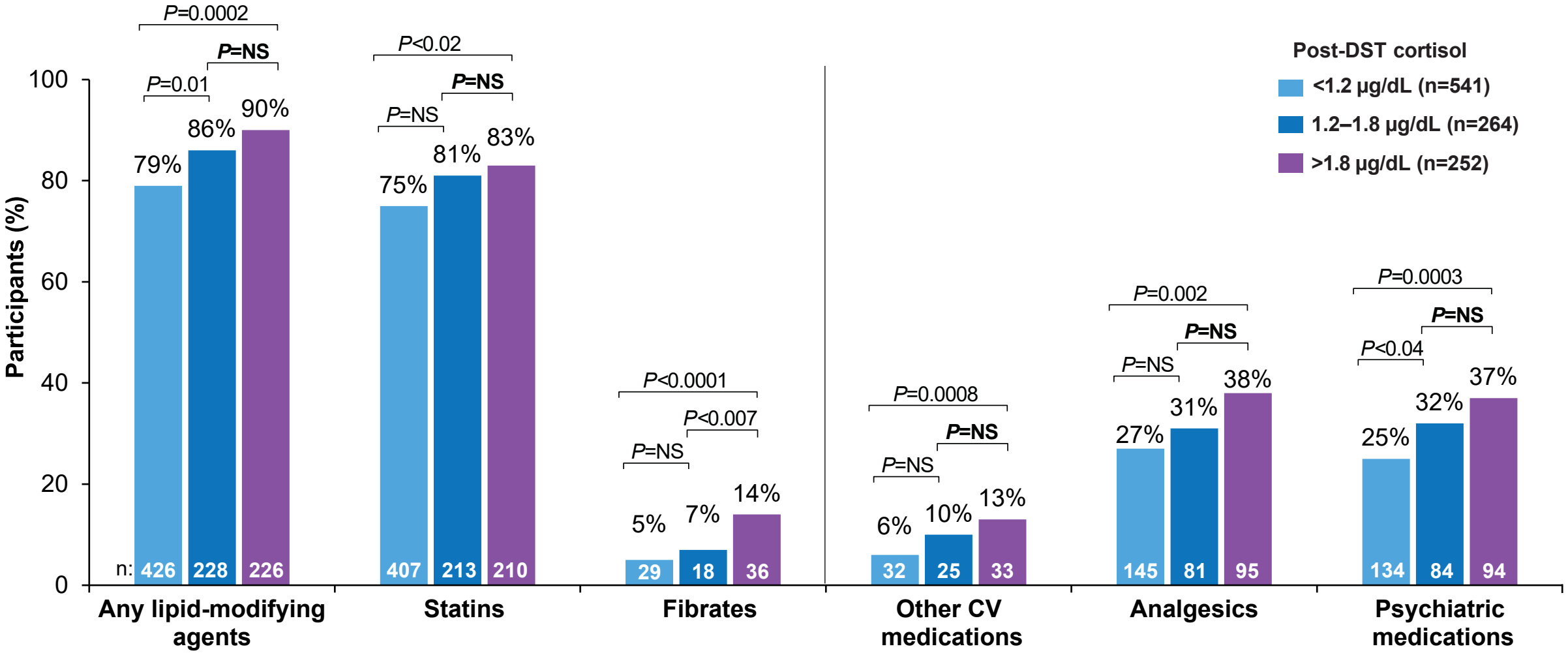
CAD, coronary artery disease; DST, dexamethasone suppression test; NS, not significant.

Increasing Post-DST Cortisol Correlated With Higher Use of Antihypertensive Medications



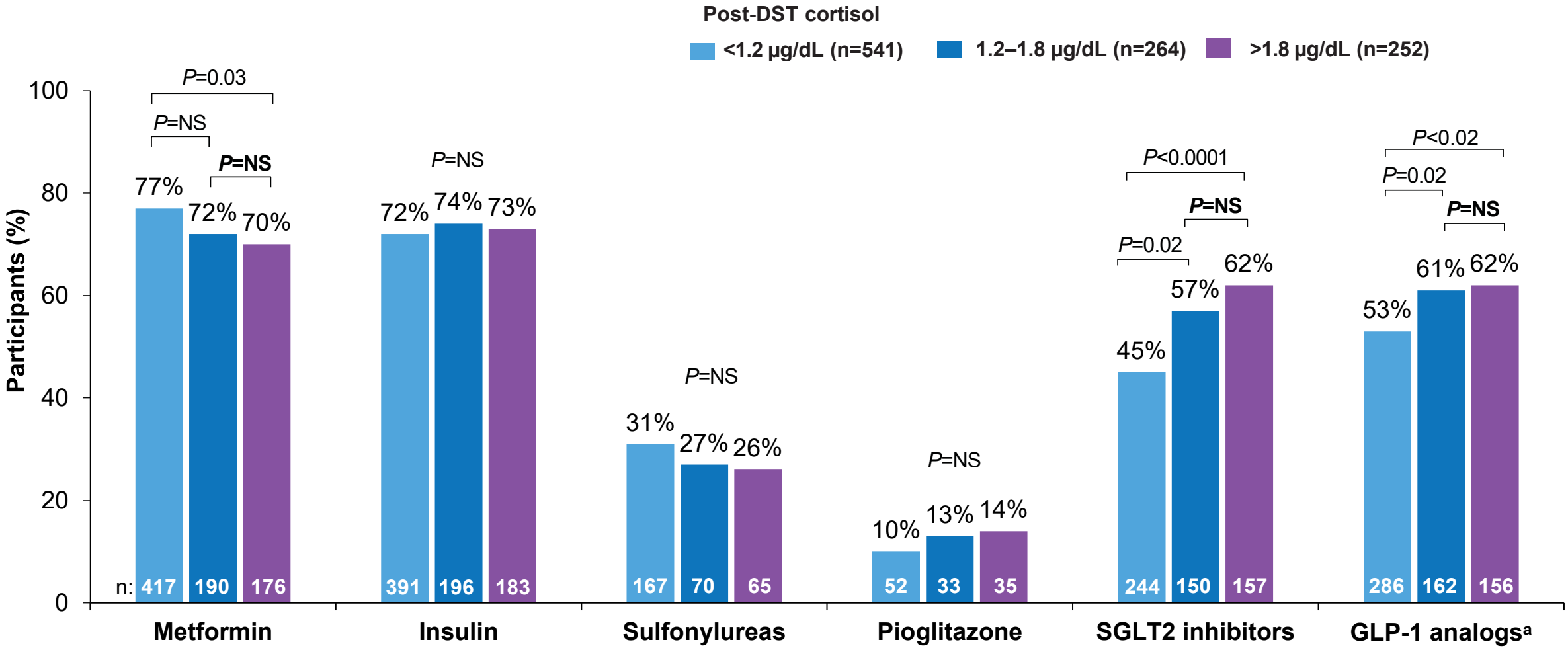
[a]Total population numbers by post-DST cortisol level: <1.2 µg/dL, n=421; 1.2–1.8 µg/dL, n=219; >1.8 µg/dL, n=226.
DST, dexamethasone suppression test; NS, not significant; RAS, renin-angiotensin system.

Use of Other Cardiovascular, Analgesic, and Psychiatric Medications Was More Prevalent With Increasing Post-DST Cortisol



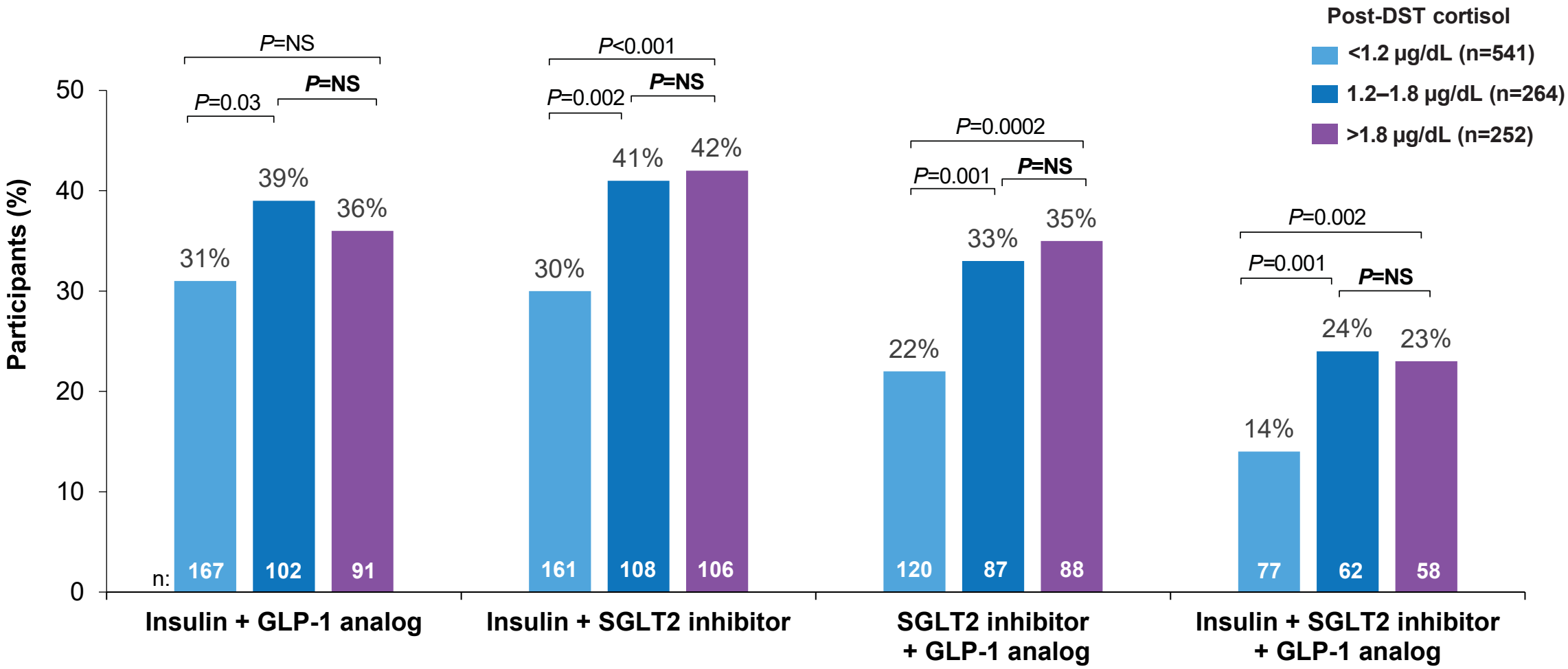
CV, cardiovascular; DST, dexamethasone suppression test; NS, not significant.

Use of Newer Antihyperglycemic Medications Was Significantly Higher With Increasing Post-DST Cortisol



[a]Including tirzepatide.
DST, dexamethasone suppression test; GLP-1, glucagon-like peptide-1; NS, not significant; SGLT2, sodium-glucose cotransporter 2.

Combination Antihyperglycemic Medication Use Was More Common With Increasing Post-DST Cortisol



DST, dexamethasone suppression test; GLP-1, glucagon-like peptide-1; NS, not significant; SGLT2, sodium-glucose cotransporter 2.

Conclusions

- While current guidelines recommend a post–1-mg DST cortisol cutoff of >1.8 µg/dL for hypercortisolism screening, a continuum of cardiometabolic risk appears to exist as a function of non-suppressible cortisol
- Cardiac comorbidities and the use of glucose-lowering and antihypertensive medications among the participants with post-DST cortisol 1.2–1.8 µg/dL more closely resembled the subgroup with post-DST cortisol >1.8 µg/dL than the subgroup with post-DST cortisol <1.2 µg/dL
- Further investigation of individuals with post-DST cortisol below 1.8 µg/dL is warranted, as they show similarities to those above the current hypercortisolism diagnostic cutoff

DST, dexamethasone suppression test.

Acknowledgments

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The investigators and their teams

The study patients and their families

The sponsor team