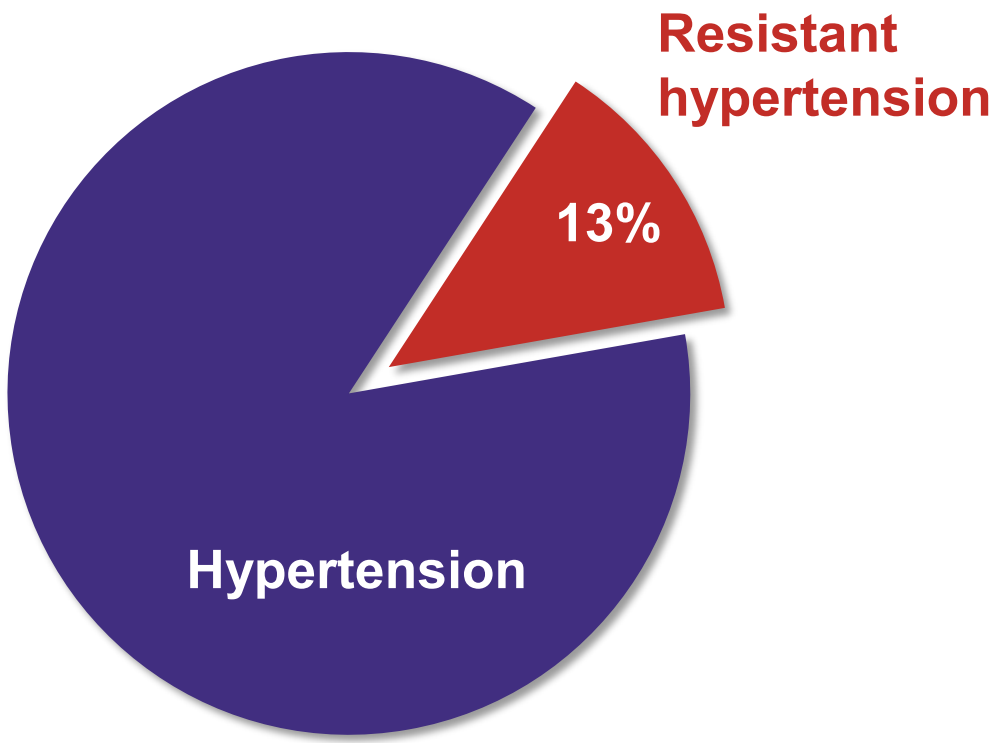
Co-secretion of Cortisol and Aldosterone in Individuals With Resistant Hypertension: Results From the MOMENTUM Trial

Lance A. Sloan,[1] Vanita R. Aroda, Deepak L. Bhatt, Robert S. Busch, Dianne S. Cheung, Ralph A. DeFronzo, Bradley Eilerman, Yehuda Handelsman, Mark Kipnes, John C. Parker, Pam R. Taub, Yuan Tian, Daniel Einhorn, Guillermo E. Umpierrez

[1]Texas Institute for Kidney and Endocrine Disorders, Lufkin, TX.

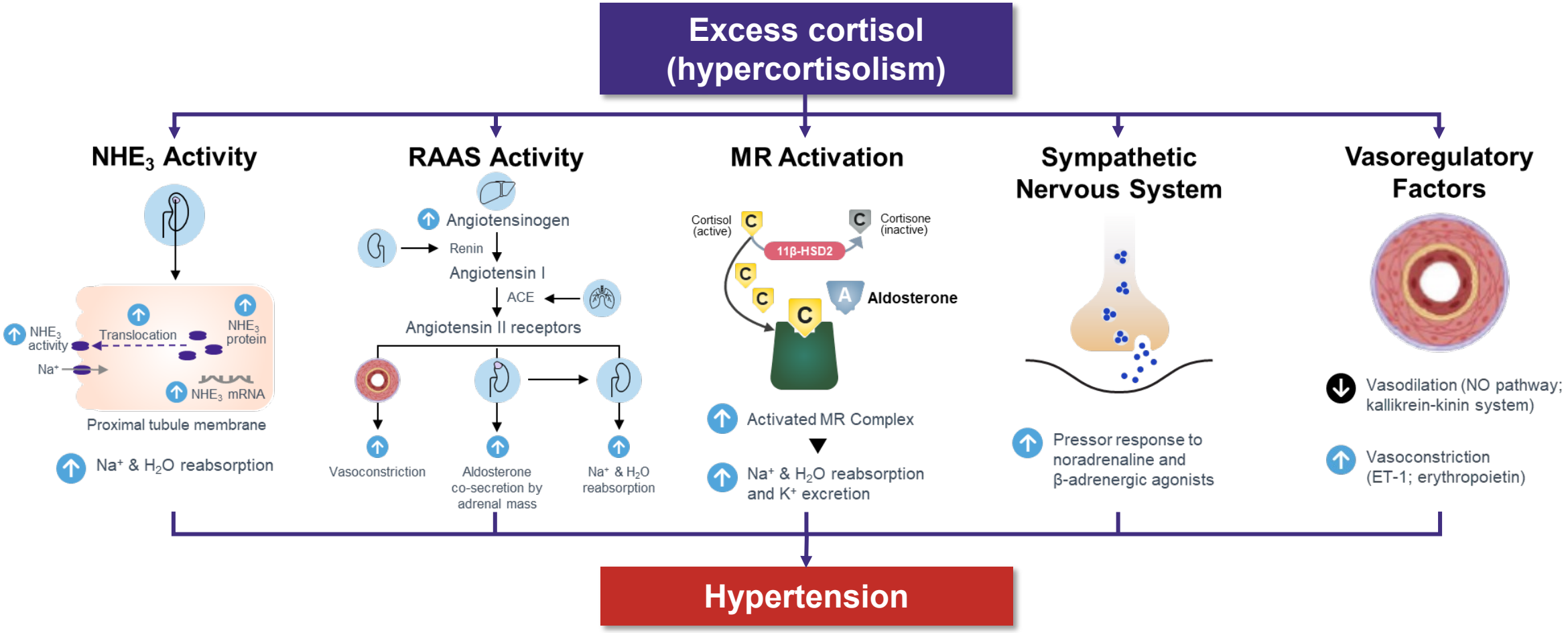
Why Study Hypercortisolism in Individuals With Resistant Hypertension?



- **A considerable number of individuals with hypertension have resistant hypertension**[1]
- **Secondary endocrine causes,** such as primary hyperaldosteronism or endogenous hypercortisolism, **may contribute to resistant hypertension**[2]
- Awareness for primary hyperaldosteronism is growing, but **hypercortisolism prevalence is still poorly understood**

1. Kumbhani et al. *Eur Heart J.* 2013. 2. Barbot et al. *Front Endocrinol (Lausanne).* 2019.

How Does Hypercortisolism Impact Blood Pressure?



11β-HSD2, 11β-hydroxysteroid dehydrogenase type 2; ACE, angiotensin-converting enzyme; ET-1, endothelin 1; MR, mineralocorticoid receptor; mRNA, messenger RNA; NHE_3, Na+/H+ exchanger 3; RAAS, renin-angiotensin-aldosterone system; rHTN, resistant hypertension. 1. Martino et al. *J Endocrinol Invest* 2025. 2. In rHTN specifically, up to 27% prevalence have been reported: Martins et al. *J Hypertens* 2012. 3. Loffing et al. *J Am Soc Nephrol* 1998. 4. Ambühl et al. *J Clin Invest* 1999. 5. Bobulescu et al. *Am J Physiol Renal Physiol* 2005.

Cardiovascular Consequences of Hypercortisolism

Physiological impacts of cortisol in the cardiovascular system[1]

↑ Renal sodium reabsorption
↑ Blood pressure
↑ Vascular inflammation
↑ Cardiac hypertrophy
↓ Cardiomyocyte survival

Consequences of excess cortisol

Up to 85%
Hypertension[1,2]

4.5x risk
Stroke[3]

2x risk
Myocardial infarction[3]

6x risk
Heart failure[3]

1. Braun et al. *Front Endocrinol (Lausanne)*. 2019. 2. Prete et al. *Ann Intern Med*. 2022. 3. Pivonello et al. *Lancet Diabetes Endocrinol*. 2016

Prior to MOMENTUM, a robust, US-based study in individuals with rHTN had not been conducted

rHTN, resistant hypertension.

MOMENTUM Eligibility Criteria[1]

Key inclusion criteria

18–80 years

rHTN based on 2017 AHA criteria:

- SBP ≥130 mmHg despite use of ≥3 BP medications from different classes at maximally tolerated doses, including a diuretic
- SBP at any level with use of ≥4 BP medications from different classes

Note on BP measurement:

- BP assessed using the same in-office, automated device at each site
- Measured 3× automatically (1-min between measurements), without the investigator present
- Mean BP used for eligibility

Key exclusion criteria

- White-coat hypertension
- Non-adherence to BP medications
- Systemic glucocorticoid exposure (excluding inhalers or topical)
- eGFR <30 mL/min/1.73 m^2
- Severe psychiatric, medical, or surgical illness
- Excessive alcohol consumption
- Pregnant or lactating
- Use of oral contraceptive pills
- Severe untreated sleep apnea
- Diagnosed with endogenous hypercortisolism

AHA, American Heart Association; BP, blood pressure; eGFR, estimated glomerular filtration rate; rHTN, resistant hypertension; SBP, systolic blood pressure.

1. Plutzky et al. *JACC Advances.* 2026.

Endogenous Hypercortisolism Definition in Individuals With rHTN

Post-DST cortisol >1.8 µg/dL and dexamethasone ≥140 ng/dL
in a population with common causes of false-positive DSTs excluded

Why use the 1-mg DST?

- The 1-mg DST is convenient and the most sensitive screening test in patients with adrenal autonomous cortisol secretion[1-4]
- If cortisol is >1.8 µg/dL:
  - Labs (ACTH, DHEAS, cortisol)
  - Adrenal CT scan

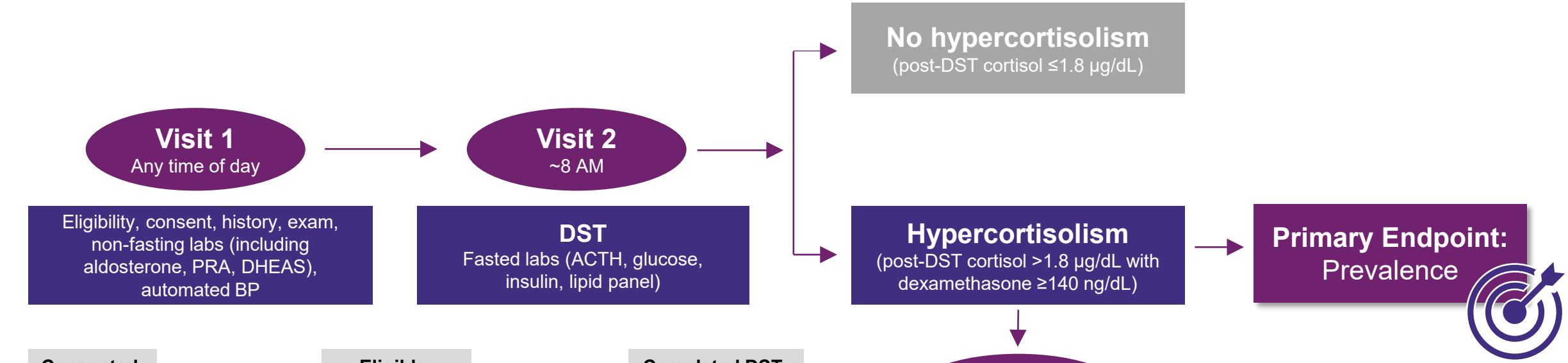
Limitations of other tests

- UFC test results are frequently normal in patients with adrenal autonomous cortisol secretion[5]
- LNSC tests may have low sensitivity for screening patients with adrenal autonomous cortisol secretion[4]

ACTH, adrenocorticotropic hormone; CT, computed tomography; DHEAS, dehydroepiandrosterone sulfate; DST, dexamethasone suppression test; LNSC, late-night salivary cortiscol; rHTN, resistant hypertension; UFC, urinary free cortisol.

1. Fassnacht et al. *Eur J Endocrinol.* 2023. 2. Nieman et al. *J Clin Endocrinol Metab*. 2008. 3. Zeiger et al. *Endocr Pract*. 2009. 4. Chiodini et al. *J Endocr Soc*. 2019. 5. Vaidya et al. *Endocr Pract*. 2019.

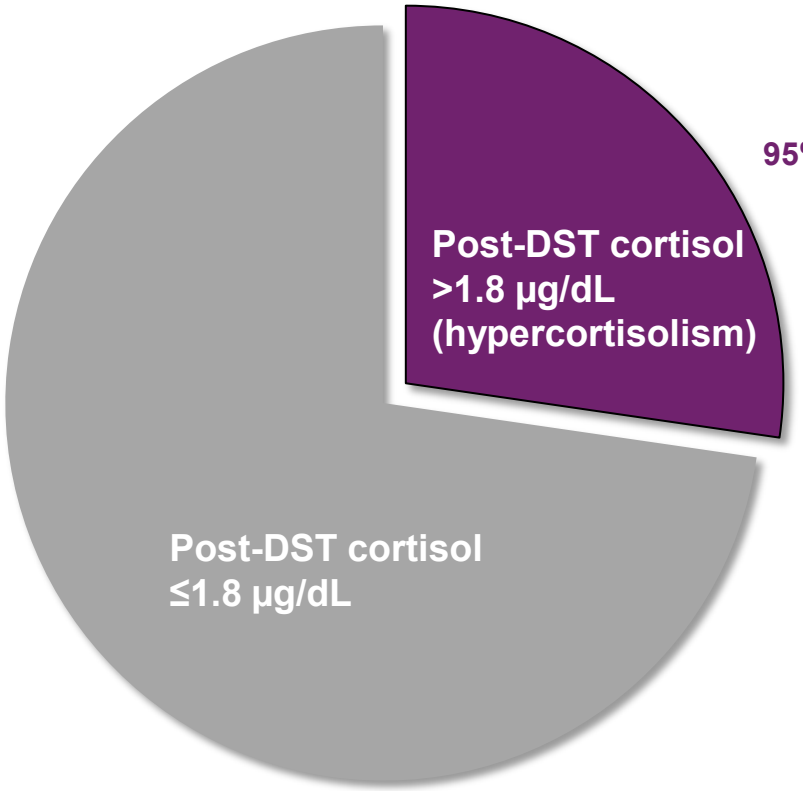
The MOMENTUM Study[1]



Conducted at 50 sites across the US
First participant enrolled: Mar 2025
Last participant enrolled: Dec 2025

ACTH, adrenocorticotropic hormone; BP, blood pressure; CT, computed tomography; DHEAS, dehydroepiandrosterone sulfate; DST, dexamethasone suppression test; PRA, plasma renin activity; rHTN, resistant hyertension. 1. Plutzky et al. *JACC Advances.* 2026.

Primary Endpoint: Hypercortisolism Prevalence



27.3%

95% CI: (24.7%, 31.1%)

297/1086

	Mean (SD)	Normal
Post-DST cortisol[a], µg/dL	4.2 (3.5)	≤1.8
Dexamethasone[a], ng/dL	484.2 (336.8)	>140

Adrenal nodules were reported in 24.3% of participants with post-DST cortisol >1.8 µg/dL

CI, confidence interval; DST, dexamethasone suppression test; SD, standard deviation.
[a]In individuals with hypercortisolism.

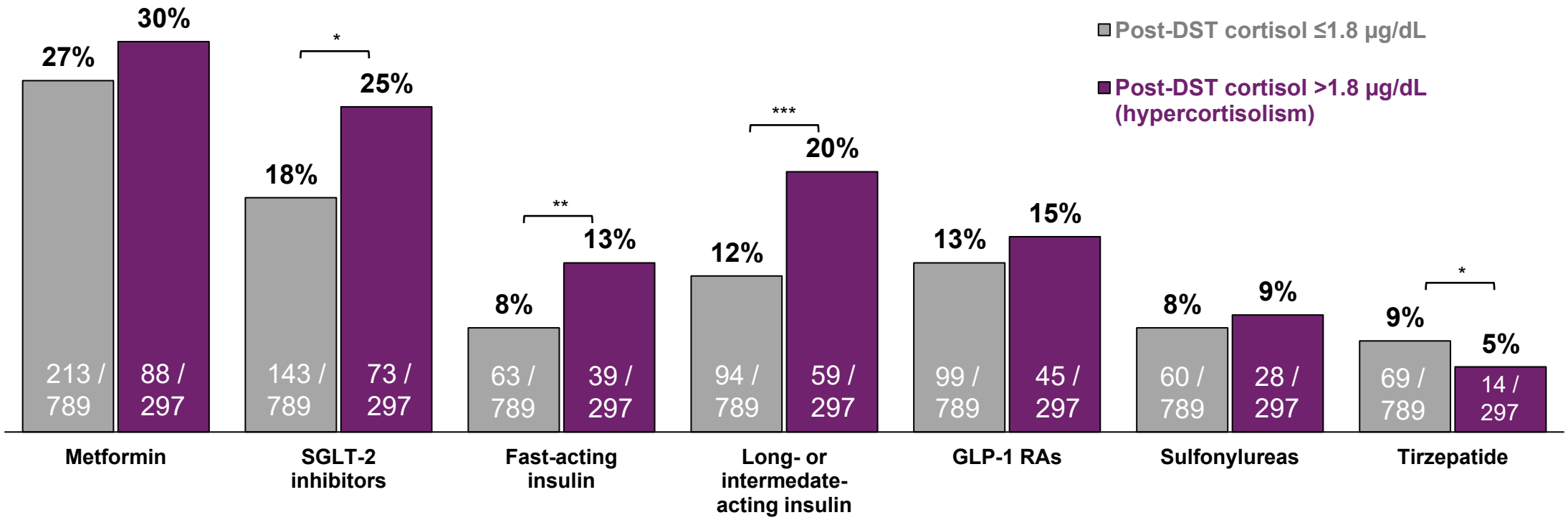
Few Differences in Baseline Characteristics

	Post-DST cortisol		
	≤1.8 µg/dL (n=789)	>1.8 µg/dL (hypercortisolism) (n=297)	*P*-value[a]
Age, years, mean (SD)	65.0 (10.9)	66.2 (10.2)	NS
Female, %	53.9%	43.8%	0.003
Body mass index, kg/m^2, mean (SD)	33.5 (7.1)	32.0 (6.9)	0.002
Waist circumference, cm, mean (SD)	109.3 (17.0)	106.9 (18.0)	0.048
Race, %			
White	57.0%	57.2%	NS[b]
Black or African American	36.4%	36.7%	
Asian	2.9%	4.0%	
Other	3.7%	2.0%	
Ethnicity, %			
Hispanic/Latino	26.6%	25.3%	NS
Non-Hispanic/Latino	73.4%	74.7%	
SBP, mmHg, mean (SD)	140.2 (17.5)	141.3 (18.3)	NS
DBP, mmHg, mean (SD)	83.9 (12.3)	84.4 (13.1)	NS
HbA1c, %, mean (SD)	6.4 (1.4)	6.6 (1.6)	NS

- **Individuals with hypercortisolism "look no different" than those without, except for *lower* body mass index and waist circumference, and more likely to be male**
- **No difference in BP medications**

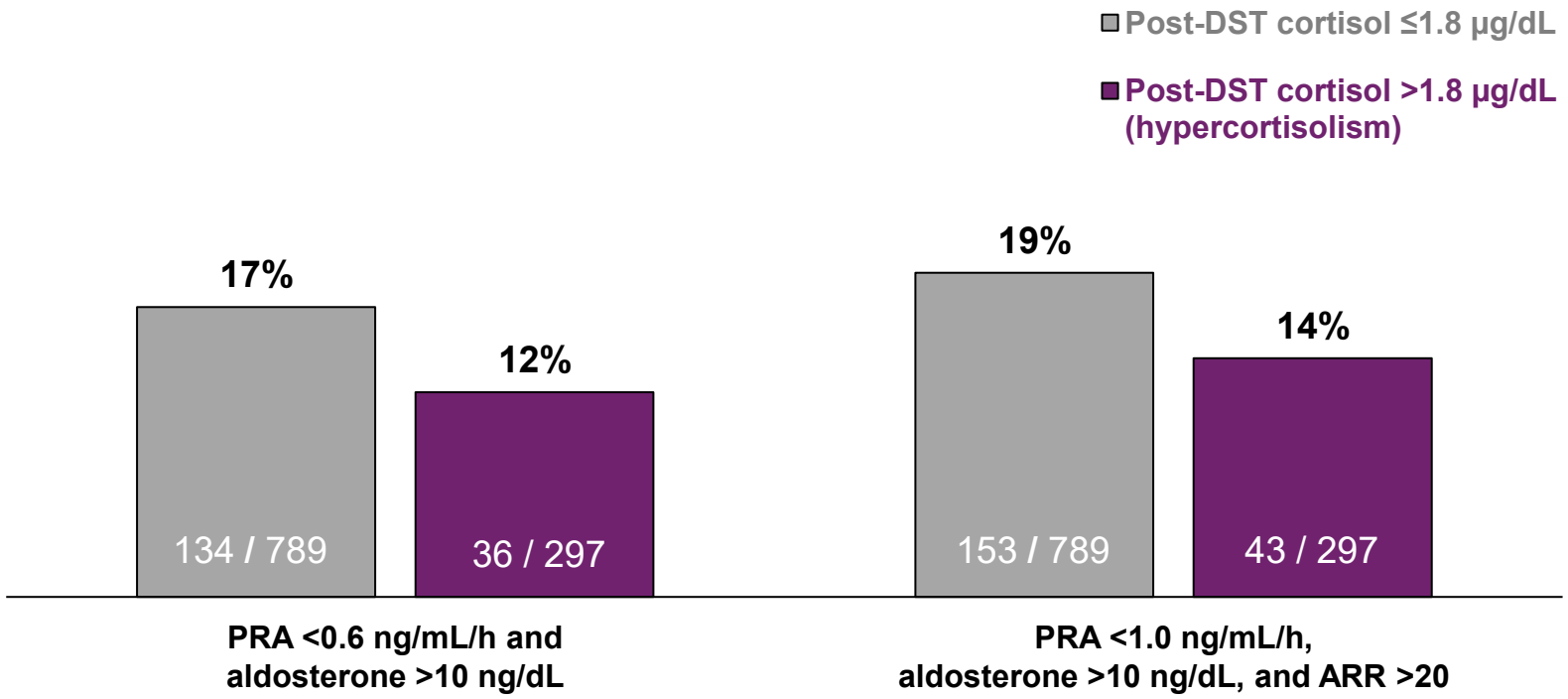
BP, blood pressure; DBP, diastolic blood pressure; DST, dexamethasone suppression test; HbA1c, hemoglobin A1c; NS, not significant (*P*>0.05); SBP, systolic blood pressure; SD, standard deviation. [a]*P*-value for binary variables from a χ^2 test (expected counts ≥5) or Fisher's exact test (expected counts <5). *P*-value for continuous variables from two-sample t-test (n≥5 per group) or Wilcoxon rank-sum test (n<5 per group). [b]White vs non-White.

Trend Toward More Antihyperglycemic Medications Observed in Those With Hypercortisolism



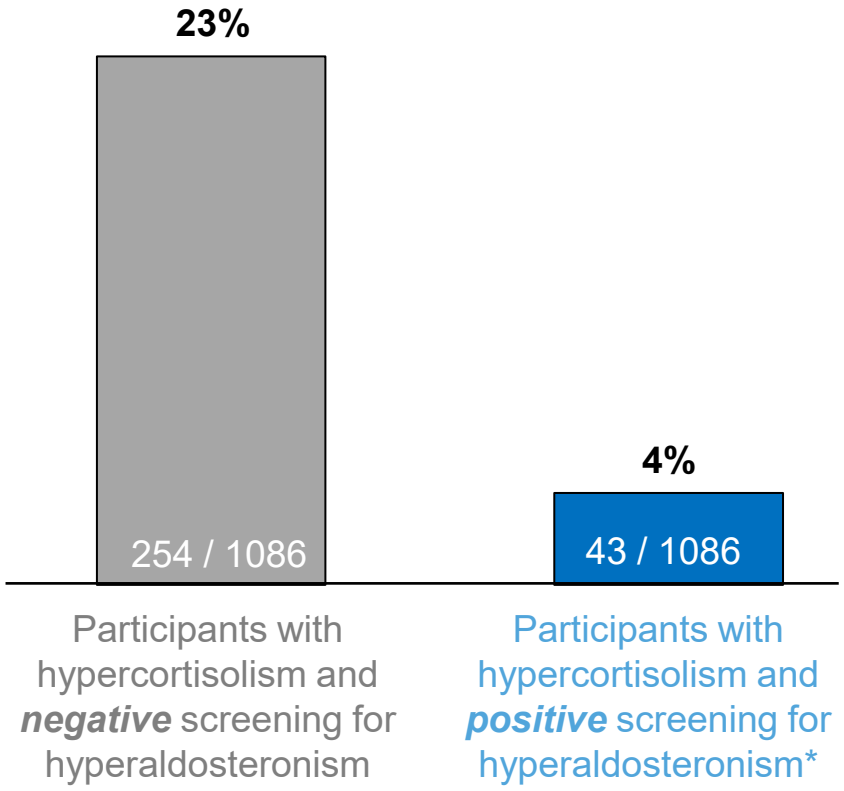
DST, dexamethasone suppression test; GLP-1 RAs, glucagon-like peptide-1 receptor agonists; SGLT-2, sodium-glucose co-transporter. *P*-value for binary variables from a χ^2 test (expected counts ≥5) or Fisher's exact test (expected counts <5). Only *P*-values <0.05 shown. *, *P*<0.05; **, P<0.01; ***, P<0.001.

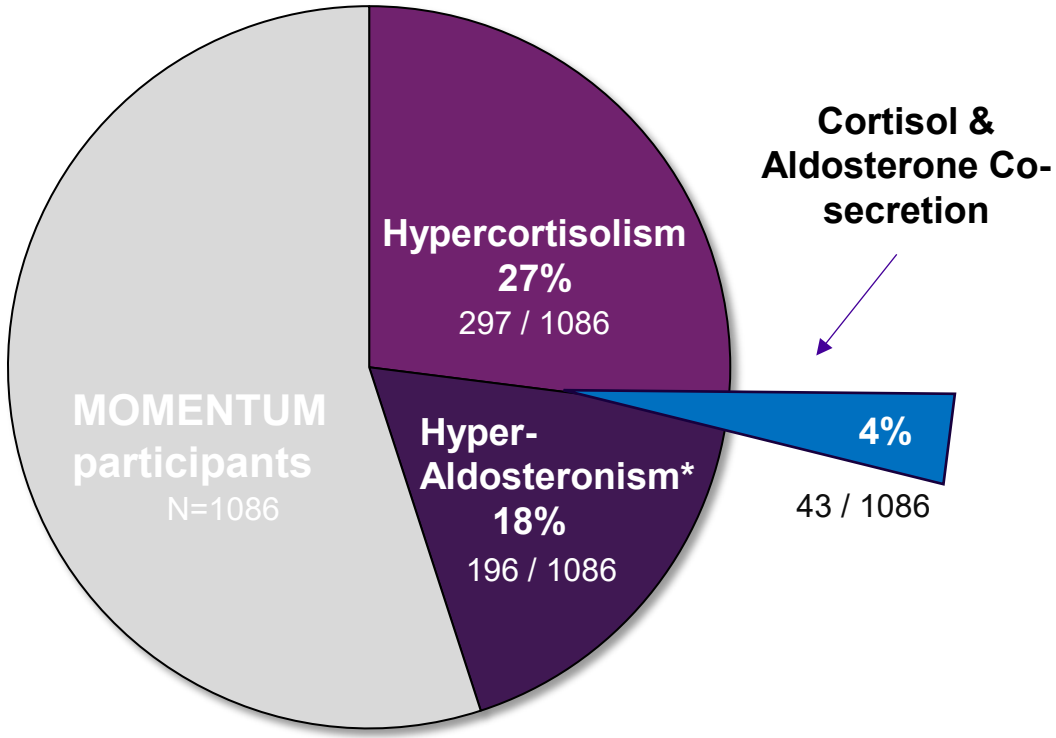
Similar Prevalence of Primary Hyperaldosteronism in Individuals With or Without Hypercortisolism



ARR, aldosterone-to-renin ratio; DST, dexamethasone suppression test; PRA, plasma renin activity (measured by radioimmunoassay).

Cortisol & Aldosterone Secretion: A Common Occurrence





Prevalence of hyperaldosteronism was consistent with the literature for individuals with rHTN[1]

rHTN, resistant hypertension. *Hyperaldosteronism defined as PRA <1.0 ng/mL/h, aldosterone >10 ng/dL, and ARR >20. Using a hyperaldosteronism definition of aldosterone >20 ng/dL or aldosterone >15 ng/dL and aldosterone-to-renin ratio >20, the prevalence of hyperaldosteronism was 6%. 1. Adler et al. J Clin Endocrinol Metab. 2025.

Conclusions

- MOMENTUM is the largest study to date assessing the prevalence of hypercortisolism in participants with rHTN.
  - Demonstrated that the **prevalence of hypercortisolism was 27.3%.**
- MOMENTUM also collected data on markers of primary aldosteronism, another potential secondary cause of rHTN.
- Based on various primary aldosteronism markers collected, **primary aldosteronism** may be present in **18% of the MOMENTUM cohort**, consistent with the literature for individuals with rHTN.
- In >40% of participants in MOMENTUM, hypercortisolism, primary aldosteronism, or both contributed to the rHTN.
- Primary aldosteronism markers were similar in MOMENTUM participants with and without hypercortisolism.
- **Approximately 4% of MOMENTUM participants** had markers of **both hypercortisolism and primary aldosteronism.**
- **Concomitant screening for both should be considered in patients with rHTN.**

rHTN, resistant hypertension.

Thanks to All Who Contributed to MOMENTUM

The study participants and their families

The MOMENTUM investigators and their teams

- Al Dhaybi, Omar
- Ali, Abdallah
- Ali, Hassan
- Alvi, Saad
- Aroda, Vanita
- Basile, Jan
- Bloch, Michael
- Budoff, Matthew
- Busch, Robert
- Buse, John
- Chang, Margaret
- Cheung, Dianne
- Christofides, Elena
- Cromwell, William
- Delgado, Irina
- Desai, Anant
- Eilerman, Bradley
- Galindo, Rodolfo
- Ghazi, Adline
- Gupta, Shaveta
- Handelsman, Yehuda
- Harbison, Rosio
- Harrison, Alex
- Hsia, Stanley
- Khetan, Shishir
- Kipnes, Mark
- Laffin, Luke
- Lender, Dan
- Lewy-Alterbaum, Lorena
- Luna, Eduardo
- Miller, Harold
- Mills, Richard
- Moscoso, Barbara
- Nakhle, Samer
- Nijmeh, George
- Olivera, Esteban
- Park, Jean
- Parker, John
- Philis-Tsimikas, Athena
- Rader, Florian
- Rajper, Naveed
- Ravid, Joseph
- Sandberg, Jay
- Shah, Nishant
- Sloan, Lance
- Taub, Pam
- Tsang, Dennis
- Umpierrez, Guillermo
- Wenker, Matthew
- Zimmerman, Michael

This study was funded by Corcept Therapeutics