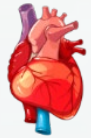
The Cortisol Reports

Episode 6 - From Prevalence to Practice: Practical Screening and Workup for Hypercortisolism in Resistant Hypertension

Previous Estimates of Hypercortisolism Prevalence

Select Population	Prevalence of Hypercortisolism
 Bone fragility	1.9% to 17.6%
 Hypertension	Up to 8%
 Diabetes mellitus	3.4%
 Obesity	**0.9%** (pooled from 22 studies)

[a]Includes a range of disease severity and etiology.

Paschou SA, et al. *Endocrine*. 2016; Chiodini I, et al. *Eur J Endocrinol*. 2016; Anderson GH Jr, et al. *J Hypertens*. 1994; Omura M, et al. *Hypertens Res*. 2004; Martins LC, et al. *J Hypertens*. 2012;. Steffensen C, et al. *Eur J Endocrinol*. 2016; van Hulsteijn LT, et al. *Eur J Endocrinol*. 2020; Steffensen C, et al. *Horm Metab Res*. 2019.

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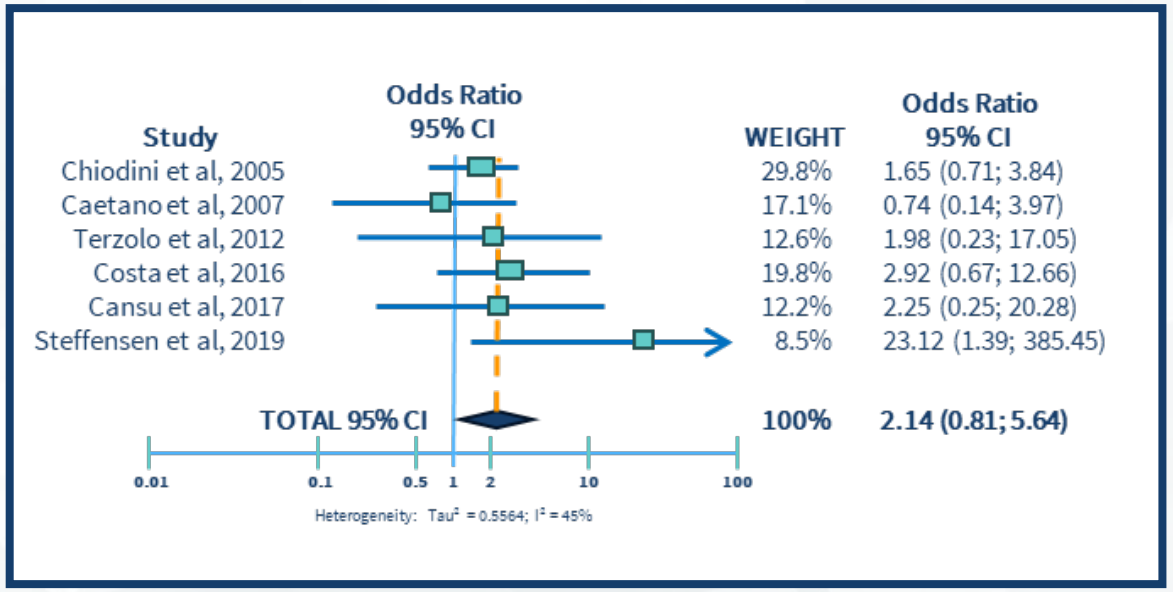
Association of Hypercortisolism and Consequences of Not Addressing Excess Cortisol

Association of cortisol excess and high blood pressure is well-known in patients with T2D



In hypertensive patients with hypercortisolism/Cushing Syndrome, **conventional antihypertensive therapy may not effective until normal cortisol levels are restored**, indicating a gap in care and significant need for new therapies

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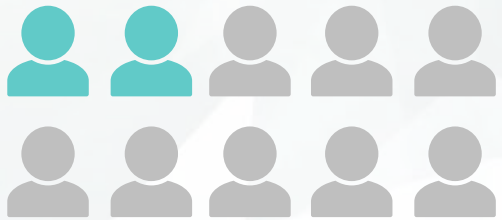
Aresta C, et al. *Endocr Pract*. 2021.

Contemporary Data on Prevalence of Hypercortisolism in People with Difficult-to-Control T2D +/- Resistant Hypertension

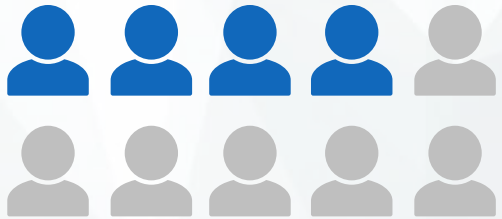
Hypercortisolism was defined as post-DST cortisol >1.8 µg/dL with Dex ≥140 ng/dL
(Those with known causes of false-positive test results were excluded from the study)



Patients with difficult-to-control T2D

23.8% of patients had **hypercortisolism**

(n=252/1057)



Patients with difficult-to-control T2D taking ≥3 BP medications

36.6% of patients had **hypercortisolism**

(n=86/235)

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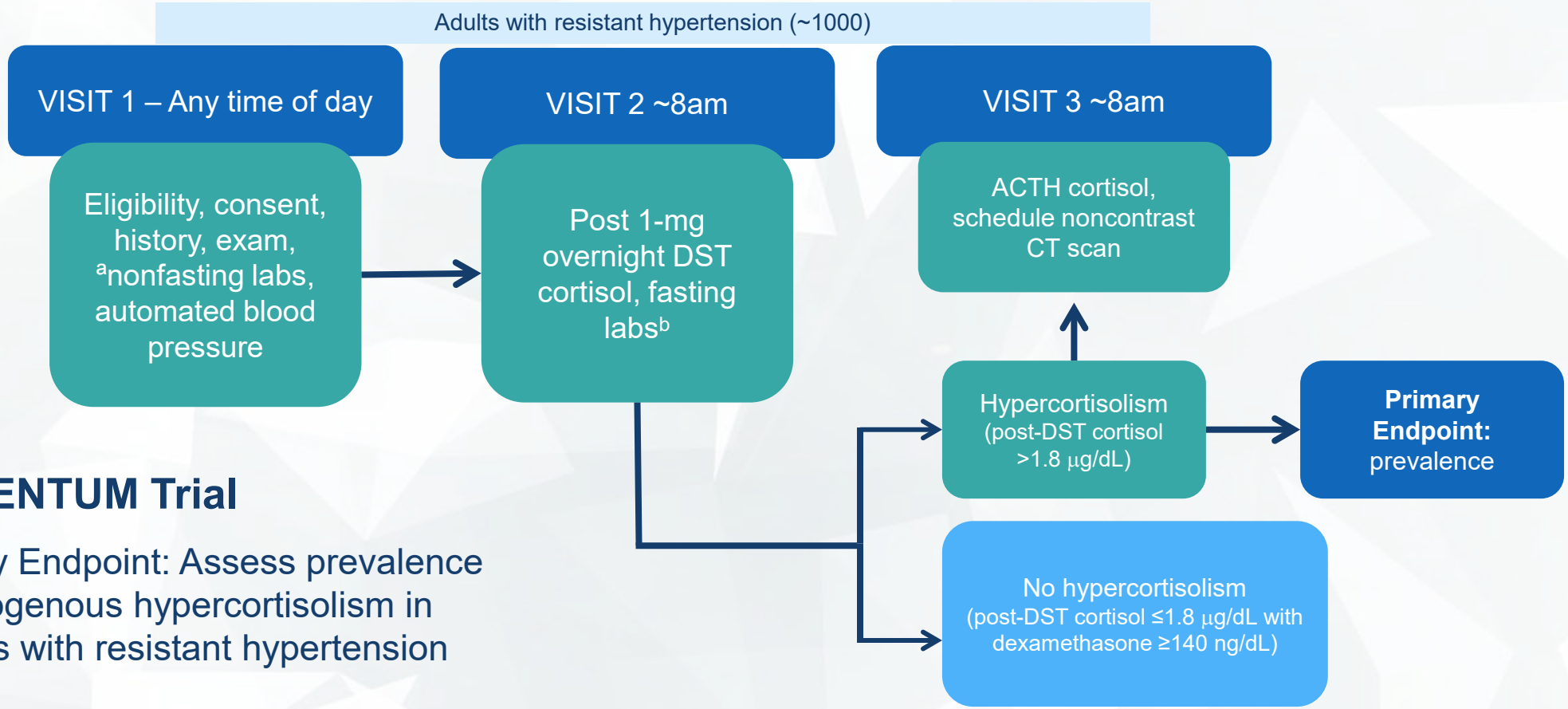
Buse JB, et al. *Diabetes Care*. 2025.

Prevalence of Hypercortisolism in Resistant HTN – New Insights from MOMENTUM



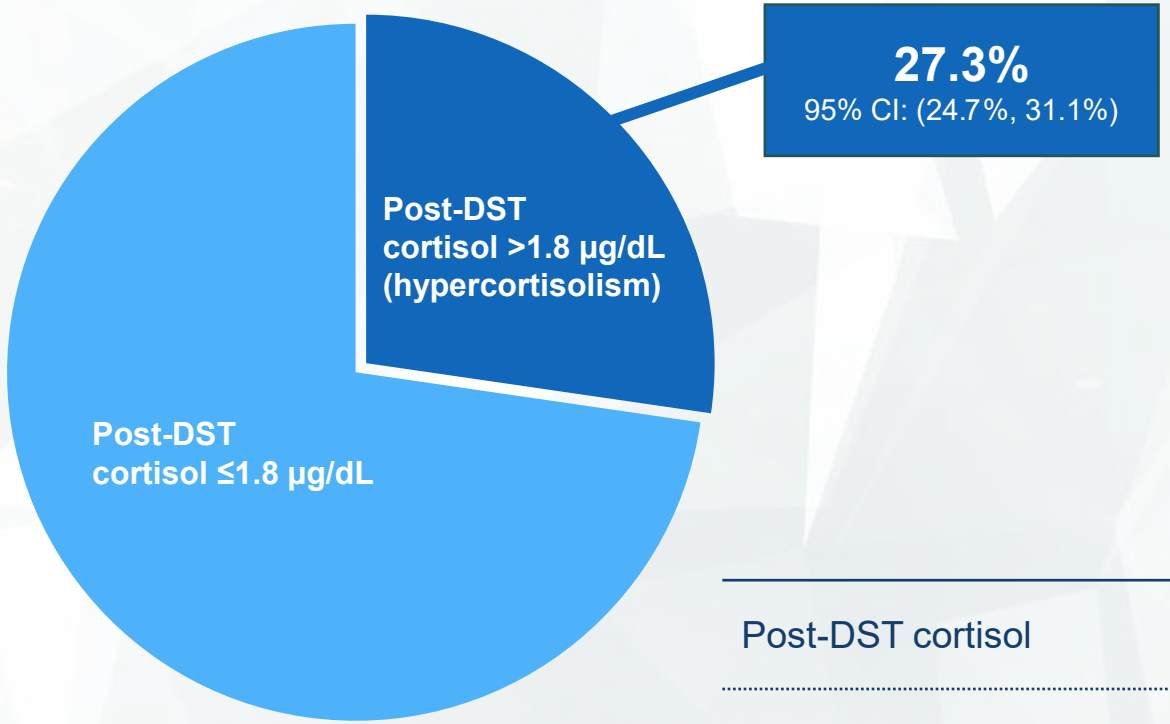
MOMENTUM Trial

Primary Endpoint: Assess prevalence of endogenous hypercortisolism in patients with resistant hypertension

[a]Plasma renin activity, aldosterone, dehydroepiandrosterone sulfate, N-terminal-pro-brain-natriuretic peptide, HbA1C, Fibrosis-4, aspartate aminotransferase-to-platelet-ratio index, uric acid, high-sensitivity C-reactive protein, complete blood count, comprehensive metabolic panel, eGFR and urine-albumin-to-creatine ratio.
[b]ACTH, fasting glucose, and fasting lipids.

Plutzky J, et al. *JACC Adv*. 2026.

New Data: Prevalence of Hypercortisolism in Resistant HTN



	Mean (SD)	Diagnostic Threshold for Hypercortisolism
Post-DST cortisol	4.2µg/dL (3.5 µg/dL)	≤1.8 µg/dL
Dexamethasone	484.2 ng/dL (336.8 ng/dL)	>140 ng/dL

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Bhatt DL, et al. *ACC*. 2026.

Increased Prevalence of Hypercortisolism in Resistant Hypertension: Are Other Factors to Blame?

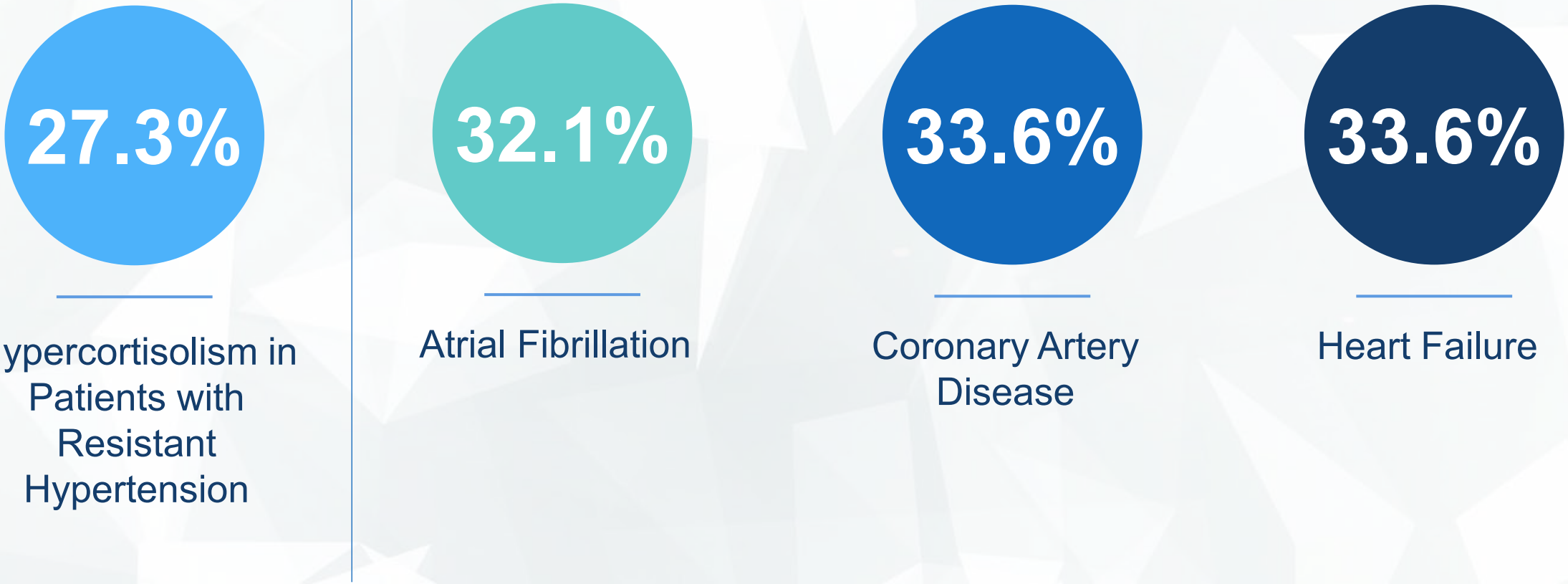
	Post-DST cortisol		
	≤1.8 µg/dL (n=789)	>1.8 µg/dL (hypercortisolism) (n=297)	*P*-value
Age, years, mean (SD)	65.0 (10.9)	66.2 (10.2)	NS
Female, %	53.9%	43.8%	0.003
Body mass index, kg/m^2, mean (SD)	33.5 (7.1)	32.0 (6.9)	0.002
Waist circumference, cm, mean (SD)	109.3 (17.0)	106.9 (18.0)	0.048
Race, %			
White	57.0%	57.2%	NS
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

Patients with hypercortisolism "look no different" than those without, except for *lower* body mass index and waist circumference

DBP, diastolic blood pressure; DST, dexamethasone suppression test; HbA1c, hemoglobin A1c; NS, not significant (*P*>0.05); SBP, systolic blood pressure; SD, standard deviation.

Bhatt DL, et al. *ACC*. 2026.

Updated Data: Prevalence of Cardiovascular Disease in Patients with Hypercortisolism



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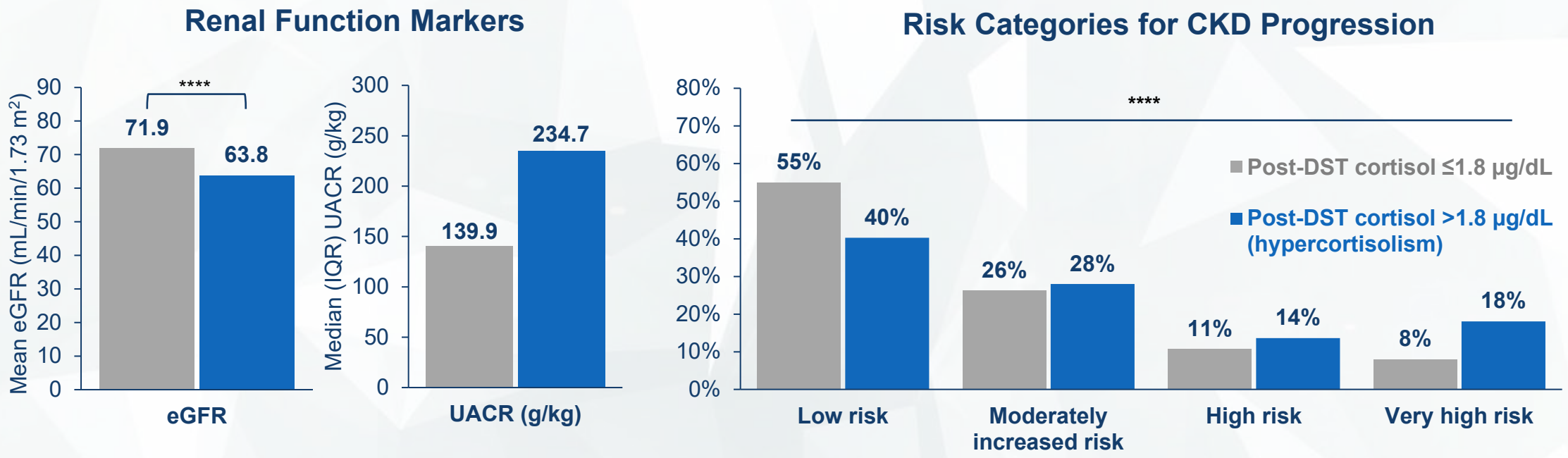
Bhatt DL, et al. *ACC*. 2026.

Relationship Between Hypercortisolism and Renal Function + CKD Progression Risk



Hypercortisolism prevalence in participants with eGFR <45 mL/min/1.73 m²: 43.6%

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Only *P*-values <0.05 shown. **** = *P*<0.0001.
CKD progression risk categories defined based on KDIGO 2012 guidelines

Bhatt DL, et al. *ACC*. 2026.

Limitations of MOMENTUM

- US only
  - MOMENTUM prevalence (27.3%)[1] aligns with a prior, smaller Brazilian study (26.5%)[2] that used the same enrollment criteria
- Diversity
  - Low proportion of Asian patients
  - Substantial representation of women, Black, and Hispanic patients
- Study did not differentiate between heart failure with or without reduced ejection fraction
- No longitudinal follow-up to assess cardiovascular event rates
  - But other studies have shown higher rates of cardiovascular events in patients with hypercortisolism[3,4]
- Causation cannot be established in this study

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1. Bhatt DL, et al. *ACC*. 2026; 2. Martins LC, et al. *J Hypertens*. 2012; 3. Di Dalmazi G, et al. *J Clin Endocrinol Metab*. 2020; 4. Petramala L, et al. *Endocrine*. 2020.

Recognizing the Need for Increased Screening for Hypercortisolism

Consistent with the Endocrine Society Guidelines and now AACE Diabetes Guidelines, hypercortisolism screening is recommended as a secondary cause of (uncontrolled) cardiometabolic/endocrine disorders.

Patients with resistant hypertension

>1/4 of people with SBP above goal on 3 antihypertensives (including a diuretic) or people on at least 4 antihypertensives will have hypercortisolism

Patients with uncontrolled hypertension and difficult-to-control type 2 diabetes

~1/3 will have hypercortisolism

Patients with difficult-to-control type 2 diabetes

~25% will have hypercortisolism

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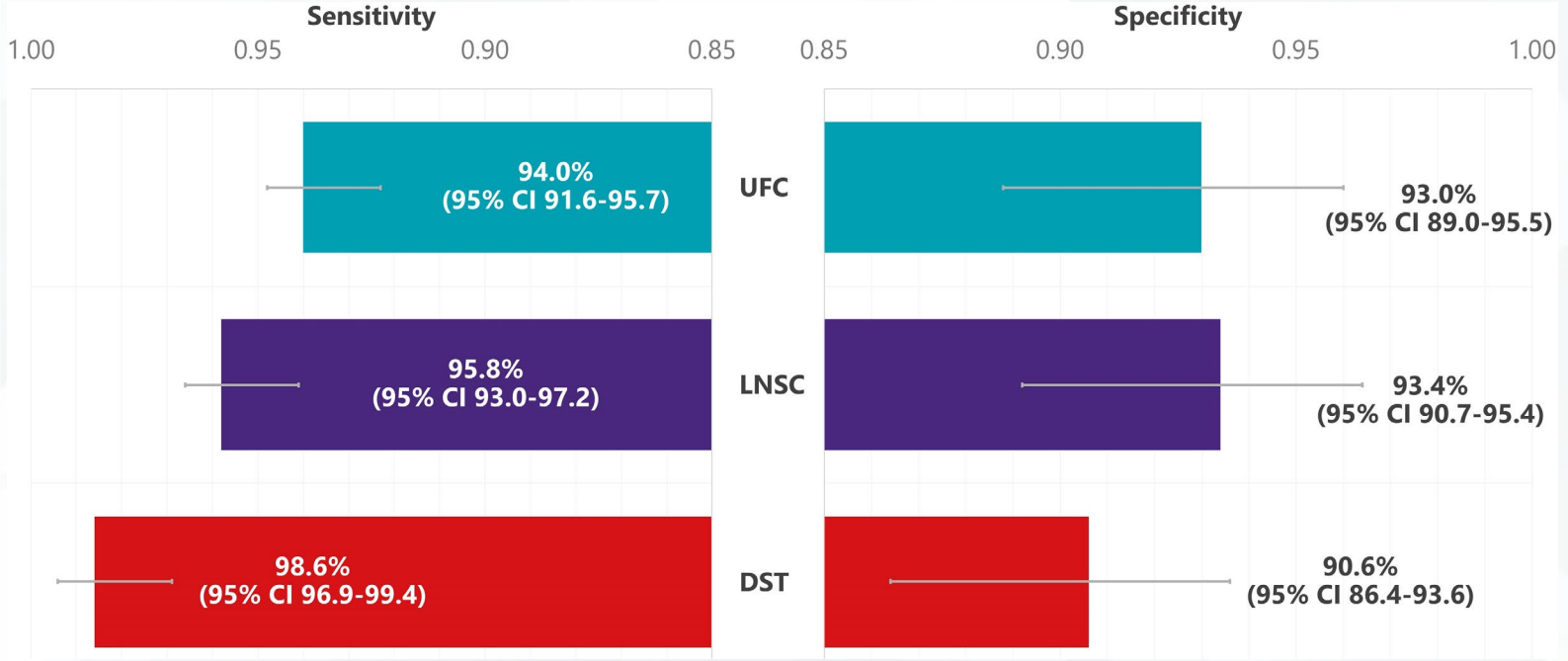
Fleseriu M, et al. *Lancet Diabetes Endocrinol*. 2021; DeFronzo RA, et al. *Diabetes Care*. 2025; Buse JB, et al. *Diabetes Care*. 2025; Bhatt DL, et al. *ACC*. 2026; Samson SL. *Endocr Pract*. 2026.

Screening Tests for Hypercortisolism

Test	Sensitivity	Specificity	Caveat
UFC	94.0% (95% CI 91.6-95.7)	93.0% (95% CI 89.0-95.5)	Improper collection, high fluid intake (>5 liters), CKD
LNSC	95.8% (95% CI 93.0-97.2)	93.4% (95% CI 90.7-95.4)	Improper collection, shift workers
1 mg DST (≤1.8 µg/dL)	98.6% (95% CI 96.9-99.4)	90.6% (95% CI 86.4-93.6)	CBG effect, Dex clearance



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Sharma ST, et al. *Clin Epidemiol*. 2015; Hamidi O, et al. *J Clin Endocrinol Metab*. 2026; Fassnacht M, et al. *Eur J Endocrinol*. 2023.