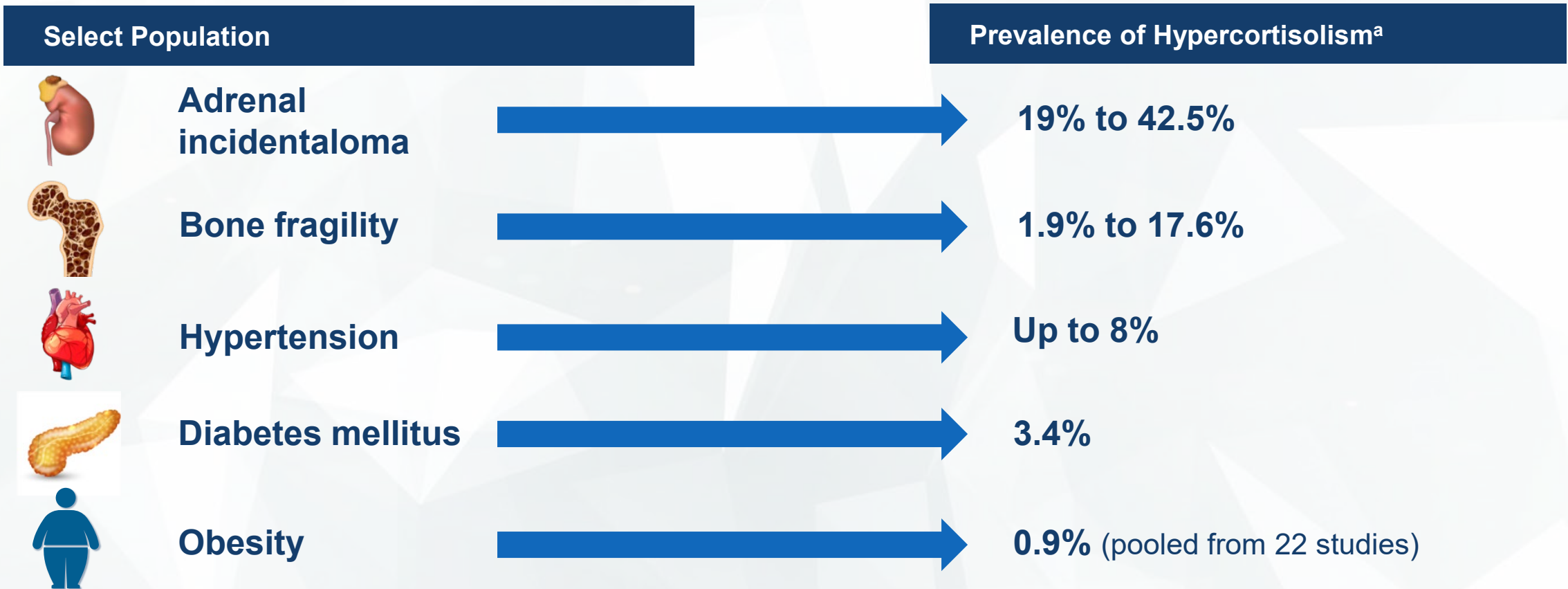


The Cortisol Reports

Episode 3 - Continuing the Search: New Data on Hypercortisolism Prevalence in Difficult-to-Control Metabolic Conditions



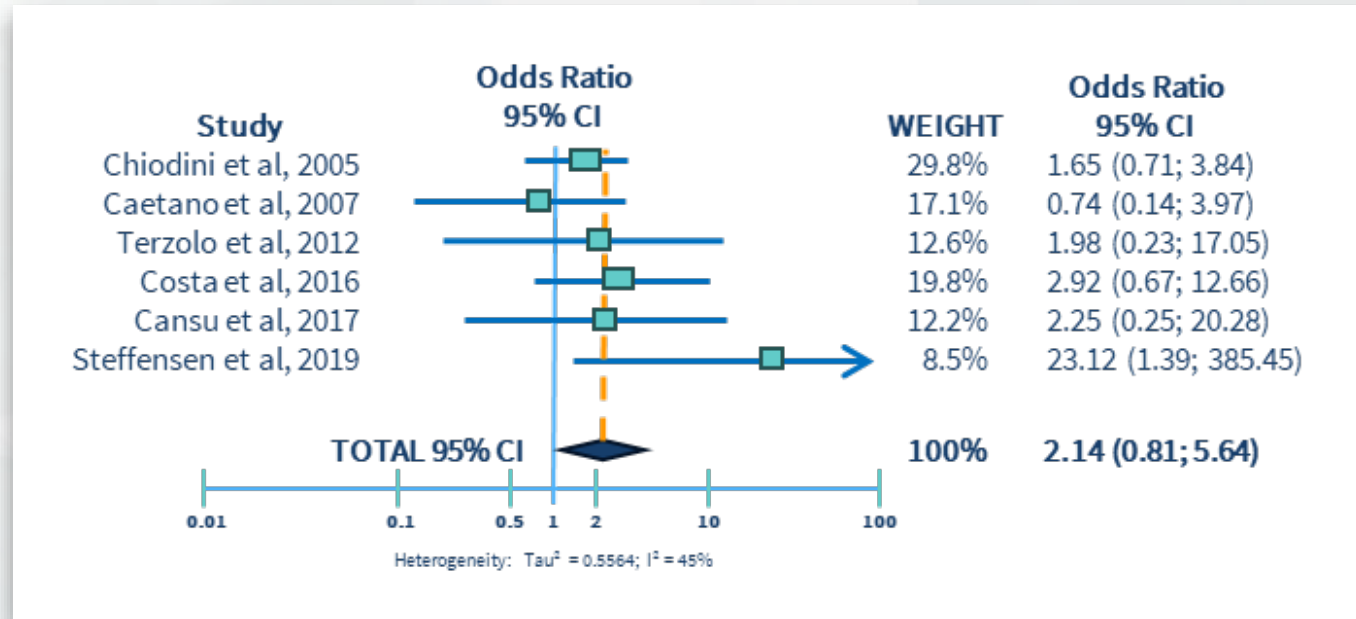
Excess Cortisol Linked to Cardiorenal Syndrome and More



Previously thought prevalence of “hidden” hypercortisolism” was 0.2%-2% (up to 10% of the general population)

What we Know about Hypercortisolism and Hypertension

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

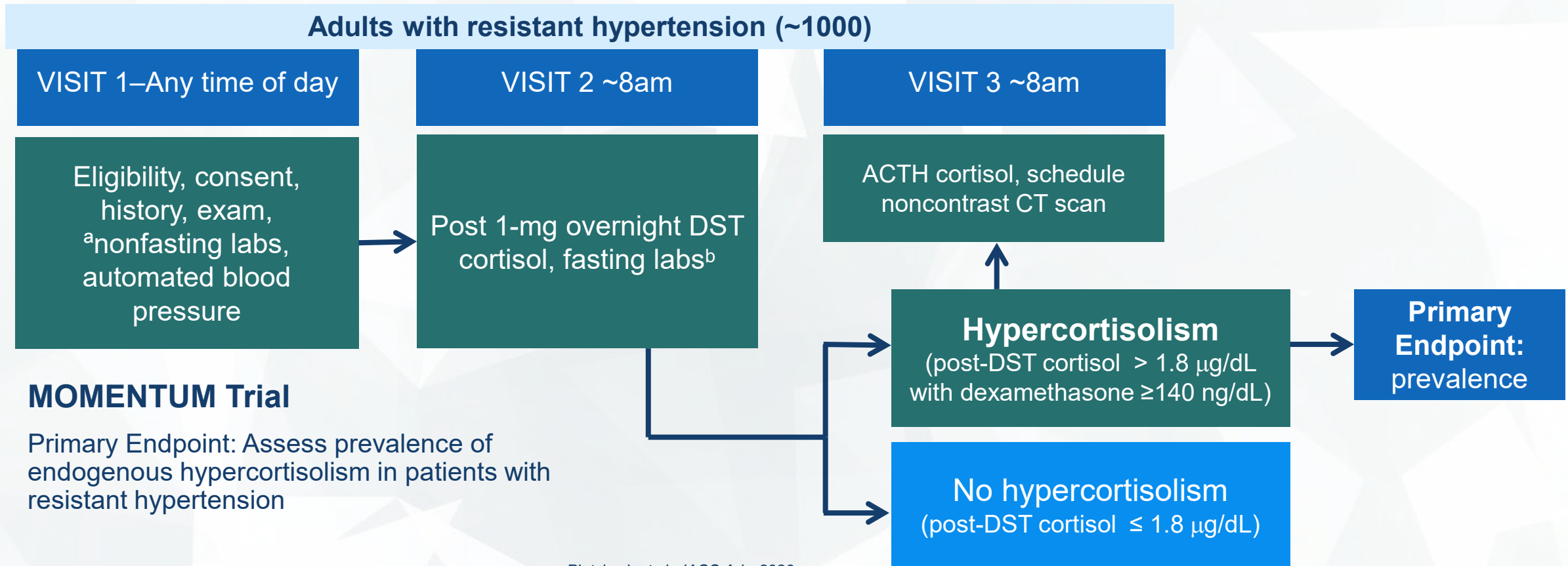


In hypertensive patients with hypercortisolism/Cushing Syndrome, **conventional antihypertensive therapy may not be effective until normal cortisol levels are restored**, indicating a gap in care and significant need for new therapies

Resistant Hypertension According to 2017 AHA Guidelines

- 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

New Data: Prevalence of Hypercortisolism in Resistant HTN

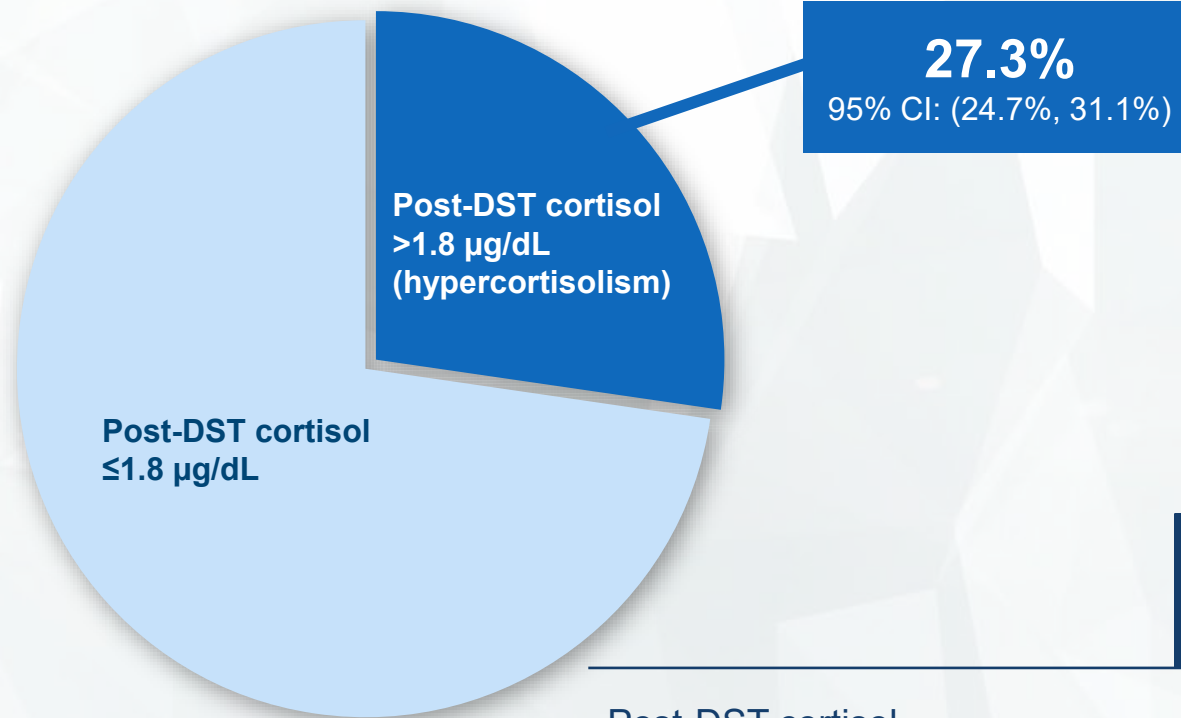


Plutzky J, et al. *JACC Adv.* 2026.

^aPlasma 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-creatinine ratio.

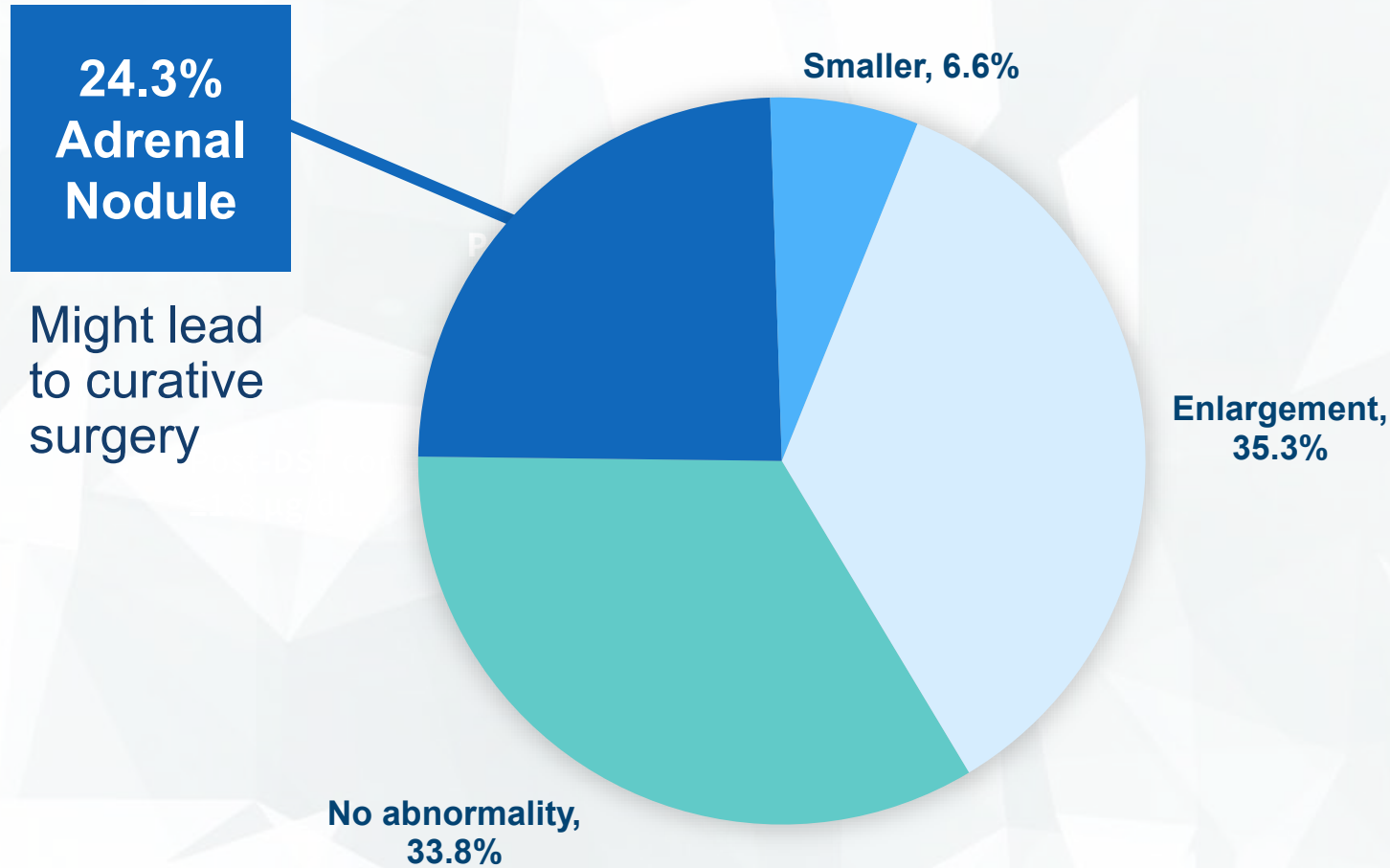
^bACTH, fasting glucose, and fasting lipids.

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

New Data: Prevalence of Adrenal Nodules (via CT Scan) in Patients with Hypercortisolism



Few differences in baseline characteristics

	Post-DST cortisol		P-value
	≤1.8 µg/dL (n=789)	>1.8 µg/dL (hypercortisolism) (n=297)	
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**

Limitations of MOMENTUM

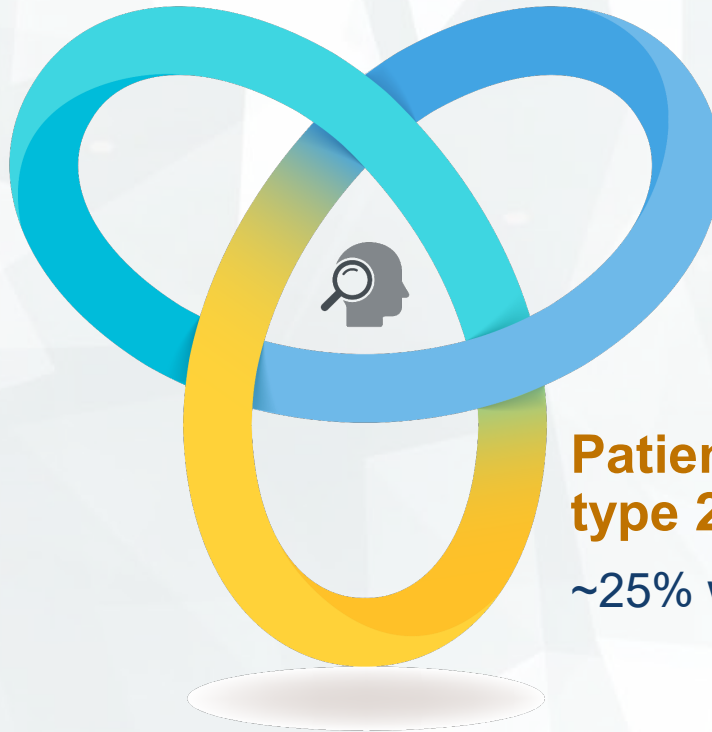
- US only
 - Of note: MOMENTUM prevalence (27.3%)¹ aligns with a prior, smaller Brazilian study (26.5%)² that used the same enrollment criteria
- Diversity: low proportion of Asian patients; but substantial representation of women, Black, and Hispanic patients
- Study did not differentiate between heart 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

Recognizing the Need for Increased Screening

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