ENDO TOPICAL CATEGORY
ADRENAL (EXCLUDING MINERALOCORTICOIDS)

Endogenous Hypercortisolism in Individuals With Resistant Hypertension and Difficult-to-Control Type 2 Diabetes: Results From Two Large, Prospective Studies

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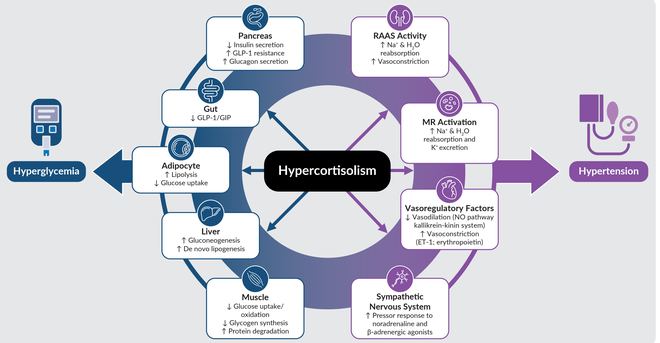
SUMMARY AND CONCLUSIONS

- The CATALYST and MOMENTUM studies, involving >1000 participants each, found a hypercortisolism (HC) prevalence of 23.8% in treatment-resistant type 2 diabetes (rT2D) and 27.3% in treatment-resistant hypertension (rHTN)
- Among CATALYST and MOMENTUM participants with the combination of both rT2D and rHTN, HC prevalence was 39.7% and 32.6%, respectively
- These results support a common pathophysiology for rT2D and rHTN in these individuals
  - In both studies, participants with the combination of rT2D and rHTN had a higher HC prevalence than the overall population and shared many characteristics, including higher frequency of cardiac disorders and use of more medications
- Clinical suspicion for HC should be high in individuals with both rT2D and rHTN, and HC screening should be performed accordingly

BACKGROUND AND OBJECTIVE

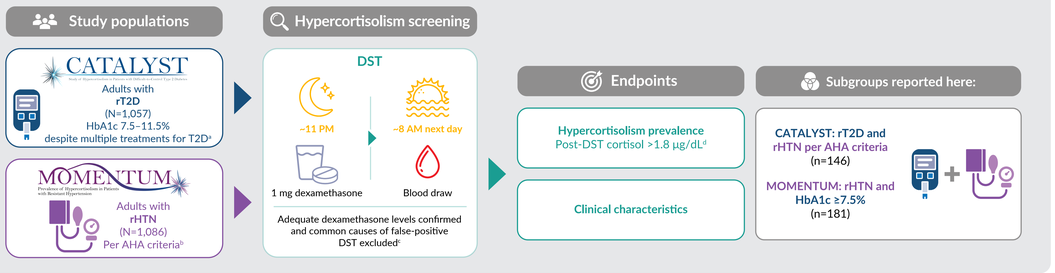
- Endogenous hypercortisolism (HC) is an important, underappreciated contributor to cardiometabolic diseases, such as type 2 diabetes (T2D) and hypertension (HTN), especially when they are resistant to standard-of-care treatment (**Figure 1**)[1-4]
- CATALYST (NCT05772169) and MOMENTUM (NCT06829537) were the first large (>1000 participants each), US-based studies to establish HC prevalence in adults with treatment-resistant T2D (rT2D) and treatment-resistant HTN (rHTN), respectively, using the 1-mg overnight dexamethasone suppression test[5,6]
  - CATALYST established a HC prevalence of 23.8% among individuals with rT2D[5]
    - The 2026 consensus algorithm from the American Association of Clinical Endocrinology recognizes that the CATALYST results support a high prevalence of HC in individuals with rT2D and recommends that these individuals be investigated for other types or causes of diabetes[7]
  - MOMENTUM found a HC prevalence of 27.3% in individuals with rHTN[6]
    - Current American Heart Association (AHA) guidelines for hypertension, including rHTN, recommend screening for secondary contributors, but consider HC to be uncommon[2,8]
- Here, we describe the prevalence of HC and characteristics of participants in these 2 studies who had both rT2D and rHTN

Figure 1. Role of HC in Hyperglycemia and Hypertension[1-3]



ET-1 endothelin-1; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; HC, hypercortisolism; MR, mineralocorticoid receptor; NO, nitric oxide; RAAS, renin-angiotensin-aldosterone system.

METHODS



[a]≥3 antihyperglycemics, insulin plus other antihyperglycemic(s), ≥2 antihyperglycemics with ≥1 microvascular or macrovascular complication(s), and/or ≥2 antihyperglycemics and ≥2 antihypertensives.
[b]Systolic blood pressure ≥130 mmHg despite taking medications from ≥3 antihypertensive classes (including a diuretic) or taking medications from ≥4 antihypertensive classes regardless of systolic blood pressure. Individuals with factors that could lead to an incorrect rHTN diagnosis (eg, investigator-determined white coat HTN, nonadherence to antihypertensive medication) were excluded.
[c]Including use of oral contraceptive pills; excessive alcohol consumption; severe untreated sleep apnea; severe psychiatric, medical, or surgical illness; night-shift work; hemodialysis/end-stage renal disease.
[d]With appropriate dexamethasone level (≥140 ng/dL).
AHA, American Heart Association; DST, dexamethasone suppression test; HbA1c, hemoglobin A1c; rHTN, treatment-resistant hypertension; rT2D, treatment-resistant type 2 diabetes.

References

1. DeFronzo RA, Auchus RJ. *Diabetes*. 2025;74(12):2168–2178. **2.** Carey RM, et al. *Hypertension*. 2018;72(5):e53–e90. **3.** Fallo F, et al. *J Hypertens*. 2022;40(11):2085–2101. **4.** DeFronzo RA, et al. *Diabetes Care*. 2025;48(12):2036–2044. **5.** Buse JB, et al. *Diabetes Care*. 2025;48(12):2012–2020. **6.** Bhatt DL, et al. Presented at: American College of Cardiology Annual Meeting; March 28–30, 2026; New Orleans, LA. **7.** Samson SL, et al. *Endocr Pract*. 2026;32(4):473–518. **8.** Jones DW, et al. *Hypertension*. 2025;82(10):e212–e316.

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Presenter Disclosure

Dr. Ralph DeFronzo reports: advisory board with AstraZeneca, Novo Nordisk, Boehringer Ingelheim, Intarcia, Renalytix, Corcept Therapeutics; research support from Boehringer Ingelheim, AstraZeneca; speaker's bureau with AstraZeneca

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RESULTS

- Baseline demographics for individuals with both rT2D and rHTN were generally similar between studies (**Table 1**) and between groups within each study
  - This finding supports that individuals with cardiometabolic disease who have HC "look no different" than those who do not have HC
  - In both studies, individuals with HC were slightly older than those who did not have HC

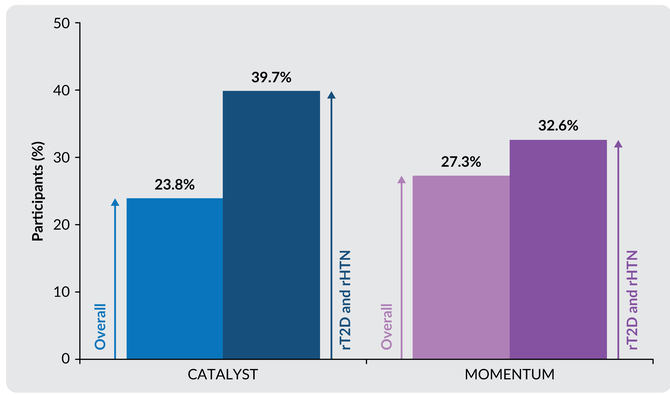
Table 1. Baseline Demographics and Characteristics of Individuals With Both rT2D and rHTN in CATALYST and MOMENTUM

	CATALYST rT2D and rHTN			MOMENTUM rT2D and rHTN		
	Overall (N=146)	With HC (n=58)	Without HC (n=88)	Overall (N=181)	With HC (n=59)	Without HC (n=122)
Age, y, mean (SD)	62.9 (9.8)	**65.3 (9.7)**	61.3 (9.6)	63.1 (10.3)	**65.1 (9.6)**	62.1 (10.6)
Female, n (%)	63 (43.2)	**29 (50.0)**	34 (38.6)	87 (48.1)	**21 (35.6)**	66 (54.1)
Race, n (%)						
White	101 (69.2)	**45 (77.6)**	56 (63.6)	92 (50.8)	**32 (54.2)**	60 (49.2)
Black or African American	36 (24.7)	**13 (22.4)**	23 (26.1)	74 (40.9)	**22 (37.3)**	52 (42.6)
Asian	6 (4.1)	**0**	6 (6.8)	6 (3.3)	**3 (5.1)**	3 (2.5)
Other[a]	3 (2.1)	**0**	3 (3.4)	9 (5.0)	**2 (3.4)**	7 (5.7)
Ethnicity not Hispanic/Latino,[b] n (%)	109 (74.7)	**49 (84.5)**	60 (68.2)	126 (69.6)	**45 (76.3)**	81 (66.4)
BMI, kg/m^2, mean, (SD)	35.8 (7.6)	**35.3 (7.7)**	36.1 (7.5)	34.4 (7.0)	**34.1 (7.6)**	34.5 (6.7)
Weight, kg, mean (SD)	103.4 (24.3)	**101.8 (24.5)**	104. 4 (24.3)	99.1 (25.2)	**102.2 (28.2)**	97.6 (23.5)
Waist circumference, cm, mean, (SD) [n]	118.5 (16.4) [144]	**118.5 (16.7) [57]**	118.6 (16.3) [87]	112.2 (20.9) [178]	**112.5 (22.6) [57]**	112.0 (20.1) [121]
SBP, mmHg, mean (SD)	135.5 (17.8)	**134.9 (19.2)**	135.8 (16.9)	141.3 (18.5)	**138.6 (17.6)**	142.6 (18.8)
DBP, mmHg, mean (SD)	76.0 (9.8)	**75.1 (10.4)**	76.6 (9.4)	84.2 (12.8)	**82.3 (12.0)**	85.1 (13.1)

[a]American Indian or Alaska native, native Hawaiian or other Pacific islander, multiple, other, and unknown.
[b]Ethnicity group missing for 12 participants for CATALYST.
BMI, body mass index; DBP, diastolic blood pressure; HC, hypercortisolism; rHTN, treatment-resistant hypertension; rT2D, treatment-resistant type 2 diabetes; SBP, systolic blood pressure; SD, standard deviation.

- HC prevalence in the subgroups with the combination of rT2D and rHTN was higher than for the overall populations (**Figure 2**)

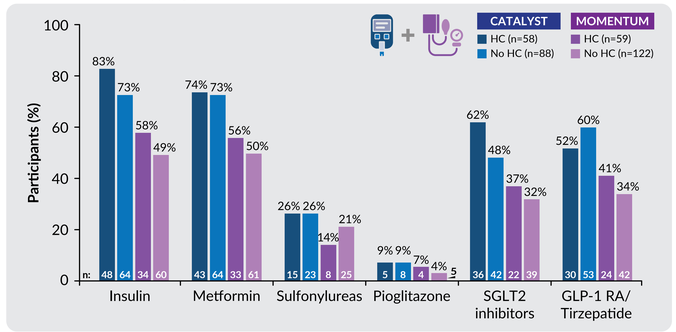
Figure 2. HC Prevalence in Individuals With Both rT2D and rHTN in CATALYST and MOMENTUM



HC, hypercortisolism; rHTN, treatment-resistance hypertension; rT2D, treatment-resistant type 2 diabetes.

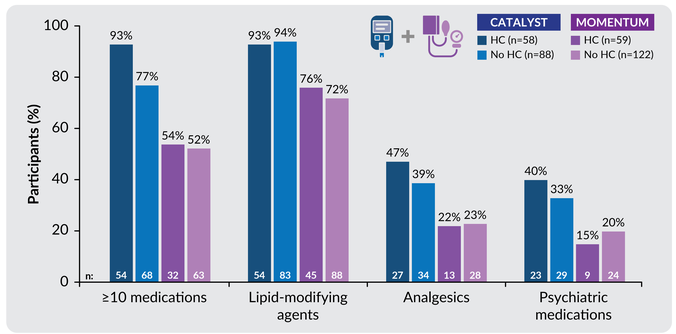
- Medication burden trended higher in individuals with HC vs without HC in the subgroups with both rT2D and rHTN (**Figures 3 and 4**)
  - Antihypertensive use was similar in both subgroups (data not shown), reflecting the American Heart Association criteria used to define rHTN
  - Antihyperglycemic use was more frequent in CATALYST, likely due to the study eligibility criteria requiring at least 2 antihyperglycemic medications
  - rT2D in the MOMENTUM subgroup was defined based on hemoglobin A1c (HbA1c) ≥7.5% only, which may explain the lower frequency of antihyperglycemic medication use in the MOMENTUM subgroup with both rT2D and rHTN. In fact, 7% of individuals in the MOMENTUM subgroup did not receive any antihyperglycemic medications

Figure 3. Medication Use in Individuals Who Had Both rT2D and rHTN in CATALYST and MOMENTUM: Antihyperglycemics[a]



[a]7% of individuals in the MOMENTUM subgroup did not receive any antihyperglycemic medications.
GLP-1 RA, glucagon-like peptide-1 receptor agonist; HC, hypercortisolism; rHTN, treatment-resistant hypertension; rT2D, treatment-resistant type 2 diabetes; SGLT2, sodium-glucose cotransporter 2.

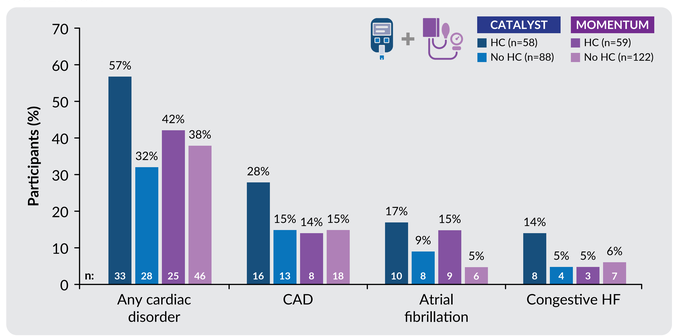
Figure 4. Medication Use in Individuals Who Had Both rT2D and rHTN in CATALYST and MOMENTUM: Other Medications[a]



[a]7% of individuals in the MOMENTUM subgroup did not receive any antihyperglycemic medications.
HC, hypercortisolism; rHTN, treatment-resistant hypertension; rT2D, treatment-resistant type 2 diabetes.

- In the subgroups with the combination of rT2D and rHTN, there were more individuals with cardiac disorders, especially atrial fibrillation, among those with HC vs without HC (**Figure 5**)

Figure 5. Cardiac Comorbidities in Individuals Who Had Both rT2D and rHTN in CATALYST and MOMENTUM



CAD, coronary artery disease; HC, hypercortisolism; HF, heart failure; rHTN, treatment-resistant hypertension; rT2D, treatment-resistant type 2 diabetes.

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