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

High Medication Burden in Individuals With Difficult-to-Control Type 2 Diabetes: Clinical Characteristics From the CATALYST Study

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Abstract 0098

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SUMMARY AND CONCLUSIONS

- At >1,000 participants, CATALYST Part 1 was the largest prospective study to investigate endogenous hypercortisolism in individuals with difficult-to-control type 2 diabetes, finding a prevalence of 23.8%
- The medication burden in CATALYST Part 1 participants was high overall, with participants reporting using a median of 10 medications
  - 43% of participants were taking ≥4 glucose-lowering medications, 27% were taking ≥3 antihypertensives, and 30% used psychiatric or analgesic medications
- CATALYST participants had persistently elevated hemoglobin A1c despite the use of multiple glucose-lowering medications, including newer classes of therapies (eg, glucagon-like peptide-1 receptor agonists, sodium-glucose cotransporter 2 inhibitors, tirzepatide)
- Many participants also had elevated systolic blood pressure despite extensive antihypertensive medication use
- Participants in CATALYST had a high cardiovascular disease burden, with a significantly higher prevalence of overall cardiovascular disease, coronary artery disease, atrial fibrillation, and heart failure in those with vs those without hypercortisolism

ABSTRACT

CATALYST (NCT05772169) was the largest prospective study to date to assess the prevalence of hypercortisolism in individuals with difficult-to-control type 2 diabetes (T2D), finding a prevalence of 23.8% (n=252/1,057). With a participant cohort of >1,000, the study was uniquely positioned to explore demographic and clinical characteristics associated with difficult-to-control T2D. Here we describe the characteristics of the CATALYST Part 1 population. Individuals with hemoglobin A1c (HbA1c) 7.5–11.5%, despite taking multiple antihyperglycemic medications, were screened for hypercortisolism using the 1-mg overnight dexamethasone suppression test (DST). Those with known causes of false-positive DSTs were excluded. The study population had a mean age of 60.7 years, 45% were female, 71% were White, 19% were African American, and 24% were Hispanic/Latino. Mean HbA1c was 8.8%, and mean systolic blood pressure (SBP) was 127.6 mm Hg. 31% had SBP ≥135 mm Hg. 43% were taking ≥4 glucose-lowering medications, including sodium-glucose cotransporter 2 inhibitors (52%), glucagon-like peptide-1 receptor agonists (48%), and tirzepatide (10%). Antihypertensive medications were used by 82% of participants, with 27% taking ≥3 antihypertensives. Lipid-modifying medications (primarily statins) were used by 83%, psychiatric medication by 30%, and analgesic medications by 30% of participants. Cardiac disorders were present in 33% and 21% of participants and hypertension was present in 89% and 79% of participants with and without hypercortisolism, respectively. In summary, CATALYST participants had a high medication and comorbid disease burden, with T2D that remained difficult to control despite multiple glucose-lowering medications. In addition, many participants had elevated SBP despite extensive use of antihypertensive medications.

BACKGROUND

- Despite advances in diabetes treatments and the use of multiple glucose-lowering medications, approximately 25% of individuals with type 2 diabetes (T2D) in the United States have inadequately controlled hyperglycemia (hemoglobin A1c [HbA1c] >8%)[1-3]
- Excess cortisol activity (hypercortisolism) can contribute to hyperglycemia and may lead to poor control of T2D, even with adherence to typically effective treatments[4]
  - Hypercortisolism can negatively impact glycemic control through various mechanisms (eg, insulin resistance, impaired beta-cell function, and increased hepatic glucose output) and is independently associated with hypertension in individuals with T2D[4-7]
  - Hypercortisolism is also independently associated with cardiovascular disease and the increased mortality seen in individuals with T2D[8,9]
- The CATALYST study (NCT05772169), the largest prospective study to date to evaluate the prevalence of hypercortisolism in individuals with difficult-to-control T2D, demonstrated a hypercortisolism prevalence of 23.8% (n=252/1,057) in this population[10]
- With its large participant cohort,[10] the study was uniquely positioned to explore demographic and clinical characteristics associated with difficult-to-control T2D

OBJECTIVES

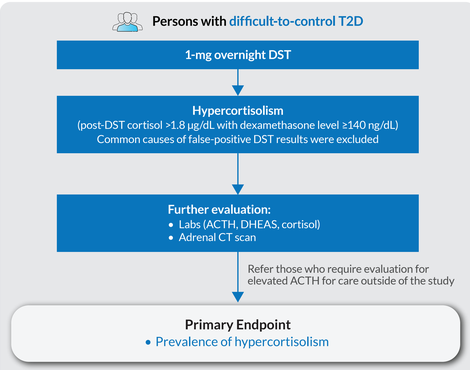
- To describe the demographics and clinical characteristics associated with difficult-to-control T2D in the CATALYST Part 1 population

METHODS

Study Design and Procedures

- CATALYST was a prospective, 2-part, multicenter study conducted at 36 sites across the US in specialized diabetes centers
  - Part 1 was noninterventional and conducted between March 2023 and April 2024 (**Figure 1**)

Figure 1. CATALYST Part 1 Study Design



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

- Detailed study design and methods have been previously reported[8]
  - The study enrolled adults aged 18 to 80 years with difficult-to-control T2D and HbA1c 7.5% to 11.5% despite taking
    - ≥3 glucose-lowering medications
    - Insulin and any other glucose-lowering medication(s)
    - ≥2 glucose-lowering medications in those who had ≥1 microvascular or macrovascular complication(s), and/or
    - ≥2 glucose-lowering and ≥2 blood pressure-lowering medications
  - Participants were screened for hypercortisolism, defined as post–1-mg dexamethasone suppression test (DST) cortisol >1.8 µg/dL (50 nmol/L), with adequate dexamethasone levels (≥140 ng/dL)
  - Participants with common causes of false-positive DST results (eg, use of oral contraceptive pills; excessive alcohol consumption; severe untreated sleep apnea; severe psychiatric, medical, or surgical illness; night-shift work; or hemodialysis/end-stage renal disease) were excluded
- Baseline characteristics were assessed and summarized using descriptive statistics
- The prevalence of cardiovascular disease (CVD) in participants with vs without hypercortisolism was an exploratory endpoint in Part 1; differences between groups were tested using a chi-square test

RESULTS

Demographics and Baseline Characteristics

Table 1. Demographics and Baseline Characteristics

	Without hypercortisolism (n=805)	With hypercortisolism (n=252)	All participants (N=1,057)
Age, years, mean (SD)	59.8 (10.5)	63.8 (9.6)	60.7 (10.4)
Female, n (%)	370 (46.0)	109 (43.3)	479 (45.3)
BMI, kg/m^2, mean (SD)	33.7 (7.1)	33.1 (7.7)	33.5 (7.2)
Waist circumference, cm, mean (SD)	112.5 (16.8)	113.5 (17.7)	112.7 (17.0)
Weight, kg, mean (SD)	96.3 (23.6)	97.4 (23.6)	96.6 (23.6)
Race, n (%)			
White	561 (69.7)	187 (74.2)	748 (70.8)
Black or African American	146 (18.1)	55 (21.8)	201 (19.0)
Asian	42 (5.2)	5 (2.0)	47 (4.4)
Other[a]	56 (7.0)	5 (2.0)	61 (5.8)
Hispanic/Latino[b] ethnicity, n (%)	234 (29.1)	21 (8.3)	255 (24.1)

[a]Includes "American Indian or Alaska Native," "Native Hawaiian or Other Pacific Islander," "Multiple," "Other," and "Unknown."
[b]Missing participants include n=13 for the with hypercortisolism group; n=24 for the without hypercortisolism group; and n=37 for the all participants group.
BMI, body mass index; SD, standard deviation.

Table 2. Baseline Glycemic Control and Blood Pressure

	Without hypercortisolism (n=805)	With hypercortisolism (n=252)	All participants (N=1,057)
HbA1c, %, mean (SD)	8.8 (1.0)	8.8 (1.1)	8.8 (1.0)
SBP, mm Hg, mean (SD)	127.6 (16.1)	127.4 (16.4)	127.6 (16.1)
DBP, mm Hg, mean (SD)	75.5 (9.9)	74.8 (9.5)	75.3 (9.8)

DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; SBP, systolic blood pressure; SD, standard deviation.

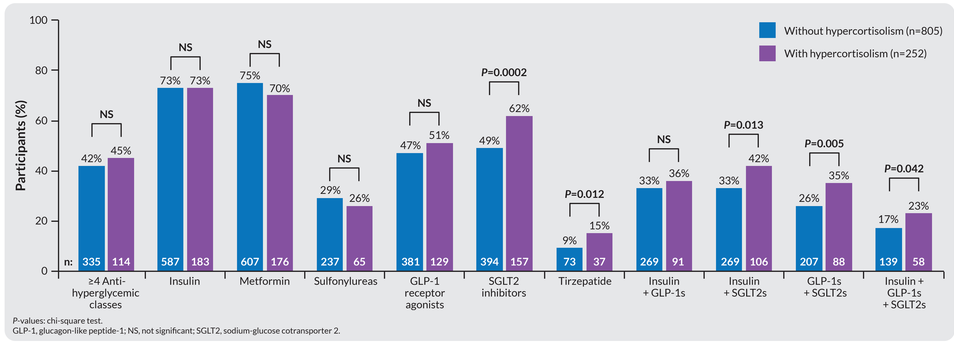
Medication Usage

- The median number (range) of medications participants reported using was 10 (2–39) in the overall population, 12 (3–34) in participants with hypercortisolism, and 9 (2–39) in participants without hypercortisolism
- A total of 568 (54%) participants in the overall population, 182 (72%) participants with hypercortisolism, and 386 (48%) participants without hypercortisolism took ≥10 medications

Antihyperglycemic Medications

- There was no difference in the median number of antihyperglycemic medication classes used in the overall population vs participants with and without hypercortisolism (3, range, 2–6). However, a higher proportion of participants with vs without hypercortisolism were taking antihyperglycemic medications from ≥4 classes (**Figure 3**)
  - A higher proportion of participants with vs those without hypercortisolism were using glucose-lowering medications from the newer classes (eg, glucagon-like peptide-1 [GLP-1] receptor agonists, sodium-glucose cotransporter 2 inhibitors, tirzepatide)
  - 23% of participants with vs 17% of participants without hypercortisolism received the maximum dose of any GLP-1 receptor agonist

Figure 3. Antihyperglycemic Medication Use in CATALYST Part 1 Study Participants



P-values: chi-square test.
GLP-1, glucagon-like peptide-1; NS, not significant; SGLT2, sodium-glucose cotransporter 2.

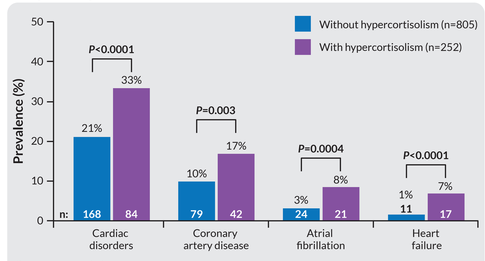
Antihypertensive Medications

- Antihypertensive medications were used by 82% of CATALYST participants
- Similar to antiglycemic medications, the number of antihypertensive medication classes used was the same for the overall population and among participants with and without hypercortisolism (median, 2.0; range, 1–5). However, use of ≥3 antihypertensive medication classes was higher in participants with hypercortisolism (38%) compared with those without hypercortisolism (23%)
  - Antihypertensive medications were taken by 90% of participants with hypercortisolism and 80% of participants without hypercortisolism
  - With the exception of angiotensin-converting enzyme inhibitors, use of all classes of antihypertensive agents was higher in participants with vs without hypercortisolism (**Figure 4**)

Cardiovascular Disease

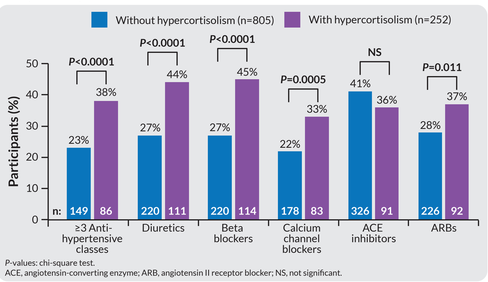
- CATALYST participants with hypercortisolism had a significantly higher prevalence of CVD compared with participants without hypercortisolism (**Figure 2**)

Figure 2. Cardiovascular Disease Prevalence in CATALYST Part 1 Study Participants



P-values: chi-square test.

Figure 4. Antihypertensive Medication Use in CATALYST Part 1 Study Participants

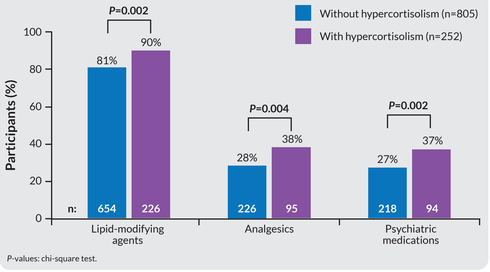


P-values: chi-square test.
ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; NS, not significant.

Other Medications

- Most participants (83%) were taking lipid-modifying medications (primarily statins), and approximately one-third of participants used psychiatric and analgesic medications
  - Usage of these 3 medication classes was higher in those with vs without hypercortisolism (**Figure 5**)

Figure 5. Use of Select Other Medications Among CATALYST Part 1 Study Participants



P-values: chi-square test.

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