Difficult-to-Control Diabetes: Consider Hypercortisolism

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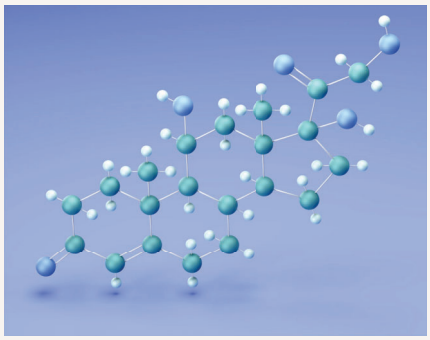

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Disclosures

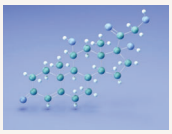
- **Stephen Brunton, MD, FAAFP, CDCES,** has disclosed that he is on the advisory board and/or speakers bureau for Abbott Diabetes, AstraZeneca, Bayer, Biolinq, Boehringer Ingelheim, Lifescan, Lilly, Novo Nordisk, Sanofi, and holds stock options for Paracrine.
- **Ashlyn Smith, PA-C,** has no disclosures to report.
- **Austin Ulrich, PharmD,** medical writer, and **Michael Hanak**, MD, CME Reviewer, have no disclosures to report.
- All relevant financial relationships have been mitigated.

Learning Objectives

Participants in this presentation should be able to ...
Screen patients presenting with multisystemic, heterogeneous manifestations of hypercortisolism for the disease.
Integrate evidence-based strategies for selecting appropriate patients and screening methods for identifying hypercortisolism into clinical practice.
Implement methods for working with the health care team, including initiating effective referrals to endocrinology, for patients with evidence of hypercortisolism.

Introduction

What primary care clinicians should know about hypercortisolism



What is Hypercortisolism?

Also referred to as Cushing's syndrome, hypercortisolism is:

"Prolonged, excessive cortisol activity that is not due to a normal physiological etiology."[1]

It consists of a family of disorders that elevate cortisol activity or disrupt the normal cortisol circadian cycle.[1,2]

1. Reincke M, et al. *JAMA.* 2023:330(2):170. 2. Nieman LK, et al. *J Clin Endocrinol Metab.* 2008:93(5):1526-1540.

Classification of Hypercortisolism

Hypercortisolism can be classified into two main categories[1]:

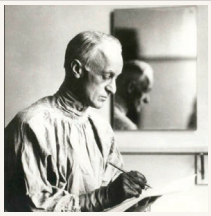
ACTH-Dependent Hypercortisolism	ACTH-Independent Hypercortisolism
Includes: • Excess adrenocorticotropic hormone (ACTH) secretion by pituitary tumors (Cushing's disease) • Non-pituitary tumors (ectopic ACTH secretion)	Includes autonomous cortisol secretion by one or both adrenal glands.

ACTH, adrenocorticotropic hormone

1. Reincke M, et al. *JAMA.* 2023:330(2):170.

Historical View of Hypercortisolism

- Historically, hypercortisolism was considered a very rare disease[1]
  - Disease with a pituitary source was traditionally viewed as the most common etiology
  - Estimated incidence in the United States of nearly 8 cases per million per year
  - Previously estimated to represent ~70% of Cushing's syndrome cases
- Originated from the "index case" of Cushing's syndrome described by Harvey Cushing in the early 1900s[2]



Dr. Harvey Cushing.
Photo credit: Medical Historical Library, Harvey Cushing/John Hay Whitney Medical Library, Yale University

1. Broder MS, et al. *Pituitary.* 2015:18(3):283-289. 2. Kelsall A, Newell-Price J. *Lancet Diabetes Endocrinol.* 2019:7(12):959-964.

Current View of Hypercortisolism

We now know that hypercortisolism is much more common than previously thought[1]:

With the introduction of computed tomography (CT) and magnetic resonance imaging (MRI)[2]:

- Incidental adrenal tumors were found in up to 50% of patients receiving routine abdominal imaging

Evidence of autonomous cortisol secretion **in the absence of clinical features of overt Cushing's syndrome** has been found in up to 30% of patients[3]

Studies historically assessing prevalence of hypercortisolism across the spectrum of severity have limitations, such as different definitions and methods – limiting their accuracy[4,5]

1. Mansmann G, et al. *Endocr Rev.* 2004:25(2):309–340. 2. Fassnacht M, et al. *Eur J Endocrinol.* 2023:189(1):G1–G42. 3. Mantero F, et al. *J Clin Endocrinol Metab.* 2000:85(2):637–644. 4. Chiodini I, et al. *Eur J Endocrinol.* 2005:153(6):837–844. 5. Steffensen C, et al. *Horm Metab Res.* 2019:51(1):62–68.

The Primary Care Clinician's (PCC's) Role in Managing Hypercortisolism

With an increasing focus on identifying and appropriately managing clinically inapparent hypercortisolism, **PCCs can play a key role[1]**:

- Many patients with hypercortisolism are missed or have a delayed diagnosis and may not have access to endocrinology care
- PCCs can identify patients at risk for hypercortisolism and use effective screening tools to identify the disease
- PCCs can initiate effective referrals to endocrinology as part of the health care team using specific approaches

1. Scoffings K, et al. *Br J Gen Pract.* 2022:72(721):399–401.

Patient Case Scenario

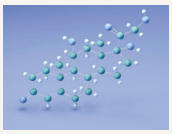
A 52-year-old man with T2D, hypertension, obesity, and hypothyroidism presents to his PCC for a routine visit.

During the visit, the PCC notes that his T2D is becoming increasingly difficult to control due to rising blood glucose despite appropriate treatment escalation.

What characteristics raise suspicion for the possibility of hypercortisolism in this patient?

T2D, type 2 diabetes

The Multisystemic, Heterogeneous Presentation of Hypercortisolism



How hypercortisolism presents clinically

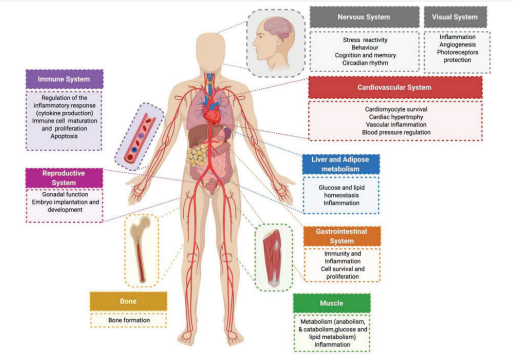
Hypercortisolism: Multisystemic, Heterogeneous Presentation

- Overt symptoms of hypercortisolism include those clearly identifiable in the "index case" of Cushing's syndrome described by Dr. Cushing in 1912[1,2]
- However, many patients with clinically significant hypercortisolism do not exhibit all of the classical overt symptoms and typically have a variety of nonspecific features[2,3]

Overt Symptoms of Hypercortisolism	Nonspecific Features of Hypercortisolism
Central obesity	Weight gain
Wasting of extremities	Diabetes
Easy bruising	Hypertension
Purple striae	Hypokalemia
Rounded "moon" face	Dyslipidemia
	Osteoporosis
	Kidney stones
	Reproductive and psychiatric disorders

1. Reincke M, et al. *JAMA.* 2023:330(2):170. 2. Scoffings K, et al. *Br J Gen Pract.* 2022:72(721):399–401. 3. Braun LT, et al. *J Clin Endocrinol Metab.* 2022:107(9):e3723–e3730.

Multisystemic, Heterogeneous Effects of Elevated Cortisol

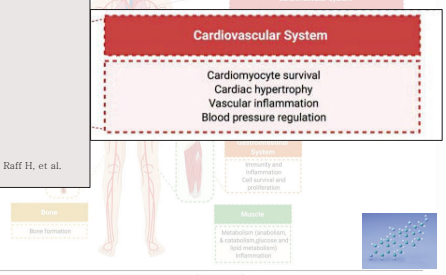


Multisystemic, Heterogeneous Effects of Glucocorticoid Excess

Cardiovascular clinical manifestations[1,2]:

- Hypertension
- Dyslipidemia
- Atherosclerosis
- Thromboembolic disease
- Myocardial infarction
- Stroke

1. Sharma ST, et al. *Pituitary*. 2015:18(2):188–194. 2. Raff H, et al. *Compr Physiol*. 2014:4(2):739–769.

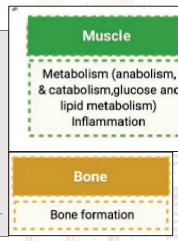


Multisystemic, Heterogeneous Effects of Glucocorticoid Excess

Musculoskeletal clinical manifestations[1,2]:

- Osteoporosis
- Increased fracture risk
- Myopathy and muscle weakness
- Skin atrophy
- Bruising
- Purple striae

1. Sharma ST, et al. *Pituitary*. 2015:18(2):188–194. 2. Raff H, et al. *Compr Physiol*. 2014:4(2):739–769.

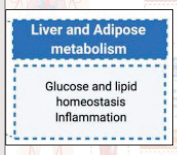


Multisystemic, Heterogeneous Effects of Glucocorticoid Excess

Metabolic clinical manifestations[1,2]:

- Obesity
- Insulin resistance
- Beta cell failure
- Glucose intolerance
- Diabetes mellitus
- Nonalcoholic steatohepatitis
- Kidney stones

1. Raff H, et al. *Compr Physiol*. 2014:4(2):739–769. 2. Tarantino G, Finelli C. *World J Gastroenterol*. 2013:19(40):6735–6743.

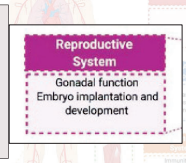


Multisystemic, Heterogeneous Effects of Glucocorticoid Excess

Reproductive clinical manifestations[1]:

- Menstrual cycle disturbances
- Polycystic ovary syndrome (PCOS)
- Hypogonadism
- Decreased libido
- Male and female infertility

1. Sharma ST, et al. *Pituitary*. 2015:18(2):188–194.

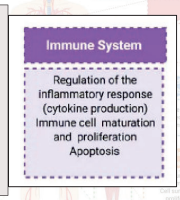


Multisystemic, Heterogeneous Effects of Glucocorticoid Excess

Immune system clinical manifestations[1,2]:

- Immunosuppression
- Dysregulation of the inflammatory response
- Infection
- Sepsis

1. Sharma ST, et al. *Pituitary*. 2015:18(2):188–194. 2. Hasenmajer V, et al. *Trends Endocrinol Metab*. 2020:31(9):655–669.

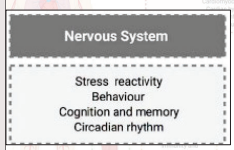


Multisystemic, Heterogeneous Effects of Glucocorticoid Excess

Psychiatric/nervous system clinical manifestations[1,2]:

- Impaired cognition
- Insomnia
- Depression
- Anxiety
- Emotional lability
- Personality changes
- Structural brain changes

1. Sharma ST, et al. *Pituitary*. 2015:18(2):188–194. 2. Miller BS, Auchus RJ. *JAMA Surg*. 2020:155(12):1152–1159.



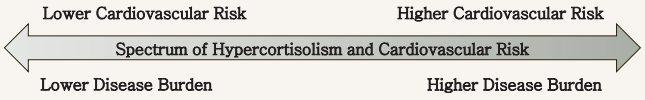
Detrimental Consequences of a Delayed Diagnosis

- Variable spectrum of clinical signs and symptoms can complicate diagnosis[1,2]
  - Diagnosis may be **delayed up to 10 years**
- The consequences of delayed diagnosis can be detrimental[3]
  - **Prolonged exposure to elevated cortisol** leads to an increased risk of cardiometabolic issues
- **Mortality 2–5 times higher** than the general population is reported in untreated hypercortisolism[4]
- Underscores the need for a **heightened awareness and timely intervention** in primary care settings[5]

1. Valassi E, et al. *Endocr Connect.* 2022:11(7):e220027. 2. Page-Wilson G, et al. *Pituitary.* 2023:26(4):364–374. 3. Braun LT, et al. *J Clin Endocrinol Metab.* 2022:107(9):e3723–e3730. 4. Dekkers OM, et al. *J Clin Endocr Metab.* 2013:98(6):2277–2284. 5. Yorke E, et al. *Int J Endocrinol.* 2017:2017:1–6.

A Continuum of Cardiovascular Risk

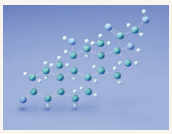
- Patients with hypercortisolism experience increased cardiometabolic comorbidities and mortality across the spectrum of disease[1]
- Even patients with less clinically apparent disease, lacking classically described overt features, have increased cardiometabolic comorbidities and mortality[1]
- Early detection and management are critical to mitigate these risks



1. Araujo-Castro M, et al. *Annales d'Endocrinologie.* 2023:84(2):272–284.

Screening for Hypercortisolism

Who to screen and how to screen



Certain Populations Have Higher Rates of Hypercortisolism

- While incidence of hypercortisolism in the general population is low, recent data suggest a higher prevalence in those with certain risk factors[1]
- Screening for hypercortisolism should occur in patients who have multiple risk factors[2]
  - Increased pre-test probability of hypercortisolism
  - Better positive predictive value of the screen
- If pre-test probability for hypercortisolism is high, further evaluation is recommended even with normal results[2]

1. Fonseca V. Results of the CATALYST Trial Part 1. Presented at the 84th American Diabetes Association (ADA) Scientific Sessions, June 21–24, 2024, Orlando FL. 2. Nieman LK, et al. *J Clin Endocrinol Metab.* 2008:93(5):1526–1540.

Enriched Population for Screening

According to the 2008 Endocrine Society Clinical Practice Guideline, screening should include (but not be limited to) the following[1]:

- Patients with unusual features for their age, such as osteoporosis/fragility fracture, T2D or hypertension in young individuals
- Patients with multiple and unexplained/progressive features, like worsening T2D outside of the normal progression or unexplained recent weight gain
- All patients with adrenal mass.

An observational study using a prospective hypercortisolism registry identified a prevalence of up to 50% using these screening criteria.[2]

1. Nieman LK, et al. *J Clin Endocrinol Metab.* 2008:93(5):1526–1540. 2. Braun LT, et al. *J Clin Endocrinol Metab.* 2022:107(9):e3723–e3730.

New Prevalence Data for Hypercortisolism: CATALYST Trial[1]

CATALYST

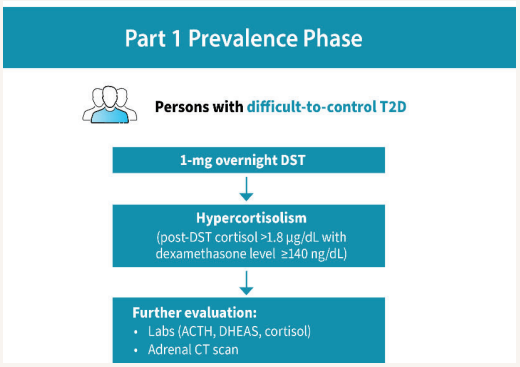
HyperCortisolism in PATients with Difficult-to-control Type 2 DiAbetes Despite Receiving Standard-of-care Therapies: PrevaLence and Treatment with KorlYm® (MifepriSTone)

- A 2-part, phase 4 study conducted in 36 sites in the United States to screen >1000 patients
- **Part 1 aim**: provide a robust estimate of the prevalence of hypercortisolism among patients with difficult-to-control T2D
  - Endogenous hypercortisolism is a potential underlying driver of T2D

Data from Part 2, Treatment Phase of CATALYST, are expected in 2025.

1. Philis-Tsimikas A. Presented at the 84th American Diabetes Association (ADA) Scientific Sessions, June 21–24, 2024, Orlando FL.

CATALYST: Study Design – Part 1[1]



DHEAS, dehydroepiandrosterone sulfate

1. Philis-Tsimikas A. Presented at the 84th American Diabetes Association (ADA) Scientific Sessions, June 21–24, 2024, Orlando FL.

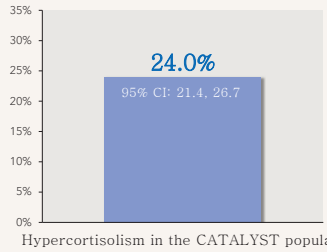
CATALYST: Patient Selection[1]

- Well-defined population with difficult-to-control T2D and high pre-test probability of hypercortisolism

Key Inclusion Criteria
18–80 years
HbA1c 7.5–11.5%
• Taking ≥3 anti-hyperglycemic drugs • Taking insulin and any other anti-hyperglycemic drugs • Taking ≥2 anti-hyperglycemic drugs and presence of ≥1 micro- or macro-vascular complications • Taking ≥2 anti-hyperglycemic and ≥2 anti-hypertensive drugs

1. Philis-Tsimikas A. Presented at the 84th American Diabetes Association (ADA) Scientific Sessions, June 21–24, 2024, Orlando FL.

CATALYST: Results



Hypercortisolism in the CATALYST population

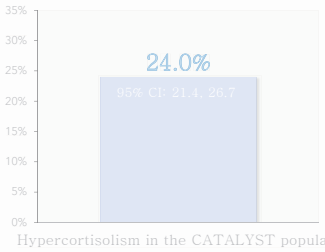
253 of 1055 CATALYST participants screened have hypercortisolism

24% of patients with difficult-to-control T2D in the US have hypercortisolism

Mean (SD) post-DST cortisol: 3.5 (2.8) µg/dL
Mean (SD) post-DST dexamethasone: 412.7 (220.5) ng/dL

1. Fonseca V. Presented at the 84th American Diabetes Association (ADA) Scientific Sessions, June 21–24, 2024, Orlando FL.

CATALYST: Results



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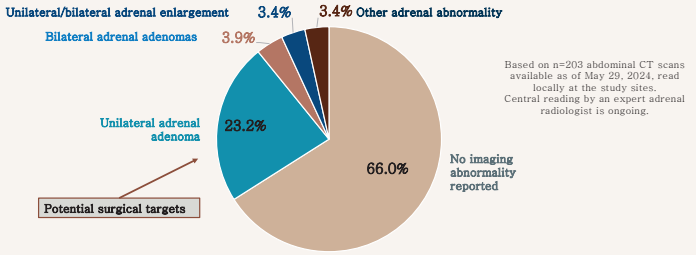
CATALYST: Adrenal CT Results[1]



Based on n=203 abdominal CT scans available as of May 29, 2024, read locally at the study sites. Central reading by an expert adrenal radiologist is ongoing.

1. Fonseca V. Presented at the 84th American Diabetes Association (ADA) Scientific Sessions, June 21–24, 2024, Orlando FL.

CATALYST: Strengths and Limitations[1]

Strengths	Limitations
• Large and rigorous study • First in US of its kind to date • Recruited patients with poor diabetes control despite current best therapies • Excluded those who may have false positive hypercortisolism testing • Recruited a diverse population in varied clinical practice settings	• Findings may not apply to all people with diabetes • CATALYST recruited a highly-selected, though common, phenotype • Imaging studies were "community standard" abdominal CTs, not dedicated adrenal CTs • Treatment of hypercortisolism in this population is not yet clear – currently being evaluated in Part 2

1. Buse J. Presented at the 84th American Diabetes Association (ADA) Scientific Sessions, June 21–24, 2024, Orlando FL.

Who to Screen for Hypercortisolism in Your Practice

At-risk patient populations and possible clinical presentations include:

Population	Prevalence of Hypercortisolism	Examples of Clinical Presentation
Patients with poorly controlled T2D	Up to 24%[1-5]	• Difficult-to-control T2D with HbA1c >7.5% despite multiple antihyperglycemic medications • T2D with poor glucose control despite insulin treatment, and other comorbidities including obesity, hypertension, hyperlipidemia, CVD, and PCOS • T2D, with high insulin dose requirements, especially prandial insulin • Patients with T2D onset before 40 years of age • Patients with both diabetes and hypertension, requiring 2 or more drugs to control blood pressure • Patients with both diabetes and hypertension, requiring insulin to control blood sugar • Patients with T2D and microvascular or macrovascular complications

HbA1c, glycated hemoglobin; CVD, cardiovascular disease

1. Fonseca V. Results of the CATALYST Trial Part 1. Presented at the 84th American Diabetes Association (ADA) Scientific Sessions, June 21–24, 2024, Orlando FL. 2. Costa DS, et al. *J Diabetes Complications.* 2016:30(6):1032–1038. 3. Chiodini I, et al. *Eur J Endocrinol.* 2005:153(6):837–844. 4. León-Justel A, et al. *J Clin Endocrinol Metab.* 2016:101(10):3747–3754. 5. Catargi B, et al. *J Clin Endocrinol Metab.* 2003:88(12):5808–5813.

Who to Screen for Hypercortisolism in Your Practice

At-risk patient populations and possible clinical presentations include:

Population	Prevalence of Hypercortisolism	Examples of Clinical Presentation
Patients with adrenal incidentaloma	Up to 50%[1]	Patients with unsuspected tumors discovered in one or both of their adrenal glands
Patients with osteoporosis/ fragility fractures	Up to 10.8%[2]	• Premenopausal women with fragility fracture • Eugonadal men with fragility fracture • Patients with very low or rapidly declining bone density, not responding to osteoporosis treatment • Patients with a history of vertebral fracture, especially obese patients with vertebral fracture
Patients with hypertension	Up to 8%[3,4]	• Treatment resistant hypertension (on 3 or more antihypertensive drugs including a diuretic) • Patients with hypertension onset before 30 years of age

1. Fassnacht M, et al. *Eur J Endocrinol.* 2023:189(1):G1–G42. 2. Chiodini I, et al. *Ann Intern Med.* 2007:147(8):541–548. 3. Trifanescu R, et al. *Maedica (Bucur).* 2013:8(2):108–115. 4. Martins LC, et al. *J Hypertens.* 2012:30(5):967–973.

How to Screen for Hypercortisolism

Three tests commonly used to screen for hypercortisolism[1,2]:

1. 1-mg overnight dexamethasone suppression test (DST)
2. Late-night salivary cortisol (LNSC)
3. 24-hour urine-free cortisol (UFC)

- While each has strengths and limitations, the **DST is recommended as the most sensitive** first line screening test—up to 95% sensitivity[1]
- 24-hour UFC and LNSC tests are less sensitive in patients with less prominent symptoms[3]
  - Abnormally high results with these tests strongly indicates hypercortisolism
- When interpreting test results, accounting for clinical index of suspicion and the patient's history and comorbidities is essential

1. Nieman LK, et al. *J Clin Endocrinol Metab.* 2008:93(5):1526–1540. 2. Galm BP, et al. *J Clin Endocrinol Metab.* 2020:105(6):dgaa105. 3. Scoffings K, et al. *Br J Gen Pract.* 2022:72(721):399–401.

Overnight Dexamethasone Suppression Test (DST)

Performing the test	Interpreting results
1 mg oral dexamethasone at 11 pm  Blood sample at 8 am (~9 hours after dose) for serum cortisol and dexamethasone levels 	 <1.8 mcg/dL serum cortisol with >140 mg/dL dexamethasone level: hypercortisolism not likely  ≥1.8 mcg/dL serum cortisol with >140 mg/dL dexamethasone level: consult endocrinologist

1. Scoffings K, et al. *Br J Gen Pract.* 2022:72(721):399–401.

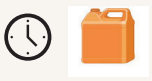
Overnight Dexamethasone Suppression Test (DST)

Testing considerations	
Potential Factors for False Positive	*Potential Factors for False Negative*
• Estrogen-containing medications • Pregnancy • Genetic causes of rapid dexamethasone metabolism • Dexamethasone malabsorption, failure to take dexamethasone • Undisclosed use of exogenous glucocorticoids • Secondary hypercortisolism due to non-adrenal disease • Chronic renal disease	• Chronic renal disease • Chronic liver disease • Concomitant medications that inhibit CYP3A4 leading to very high dexamethasone levels • Cyclic hypercortisolism

CYP3A4, cytochrome P450 isoform 3A4

1. Scoffings K, et al. *Br J Gen Pract.* 2022:72(721):399–401.

24-Hour Urine Free Cortisol (UFC)

Performing the test	Interpreting results
Collect all urine for 24 hours  Due to intrapatient variability, may require >2 collections	 Within reference range: hypercortisolism cannot be dismissed if high index of suspicion  Above reference range: consult endocrinologist

1. Scoffings K, et al. *Br J Gen Pract.* 2022:72(721):399–401.

24-Hour Urine Free Cortisol (UFC)

Testing considerations

- UFC is insensitive because free cortisol does not become detectable in the urine until serum cortisol levels are high enough to saturate serum CBG.
- UFC is often normal in cases less clinically apparent hypercortisolism typical of primary adrenal disease.

Potential Factors for False Positive	*Potential Factors for False Negative*
• High level of fluid intake • Secondary hypercortisolism due to non-adrenal disease	• Incomplete urine collection • eGFR <60 mL/min/1.73 m^2 • Cyclic hypercortisolism

CBG, cortisol-binding globulin; eGFR, estimated glomerular filtration rate

1. Scoffings K, et al. *Br J Gen Pract.* 2022;72(721):399-401.

Late Night Salivary Cortisol (LNSC)

Performing the test	**Interpreting results**
Collect sample at bedtime  Saliva collection Conduct test at least 2 or 3 times	 Within reference range: hypercortisolism cannot be dismissed if high index of suspicion  Above reference range: consult endocrinologist

1. Scoffings K, et al. *Br J Gen Pract.* 2022;72(721):399-401.

Late Night Salivary Cortisol (LNSC)

Testing considerations

- LNSC levels are often normal in less clinically apparent hypercortisolism typical of primary adrenal disease.
- LNSC is useful to detect early signs of recurrent Cushing's syndrome.

Potential Factors for False Positive	*Potential Factors for False Negative*
• Any blood contamination of the sample (e.g., associated with brushing teeth, flossing, toothpicks, etc.) • Smoking, use of chewing tobacco • Eating licorice • Use of a steroid inhaler, steroid eye drops, or steroid lip balm • Abnormal sleep-wake cycle (e.g., night shift worker or sleep-wake cycle disorder) • Hypercortisolism due to non-adrenal disease	• Insufficient specimen volume • Incorrect specimen collection technique • Improper specimen storing and handling

1. Scoffings K, et al. *Br J Gen Pract.* 2022;72(721):399-401.

Effective Screening for Hypercortisolism – Summary

- **Appropriate Patient Selection**
  - Signs and symptoms suggestive of hypercortisolism
  - High pre-test probability of hypercortisolism
- **Sensitive Screening Tests**
  - Use a sensitive screening test (1-mg overnight DST)
- **Clinical Context**
  - Interpret test results in the context of the patient's medical history and presentation
  - Avoid false positives and negatives

1. Nieman LK, et al. *J Clin Endocrinol Metab.* 2008;93(5):1526-1540. 2. Scoffings K, et al. *Br J Gen Pract.* 2022;72(721):399-401.

Patient Case Scenario (continued)

A 52-year-old man with T2D, hypertension, obesity, and hypothyroidism presents to his PCC for a routine visit.

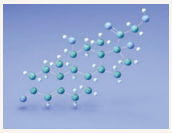
During the visit, the PCC notes that his T2D is becoming increasingly difficult to control due to rising blood glucose despite appropriate treatment escalation.

What is the likelihood this patient has hypercortisolism based on his comorbidities and noted clinical presentation?

What test would you use to screen for hypercortisolism in this patient?

Referral to Endocrinology

How to successfully send a referral for further evaluation and management of hypercortisolism



Components of a Successful Referral

- A successful referral is highly dependent on clear communication within the healthcare team, specifically the endocrinologist

Components of a successful referral include the following:

- Relevant clinical findings and the patient's medical history
- Reasons for suspecting hypercortisolism
  - Key factors contributing to high clinical suspicion
- Description of testing procedures and results of initial screening tests
  - Including dexamethasone serum level for patients with 1-mg overnight DST

Example Flowchart for Hypercortisolism Referral

Step 1: Clinical Suspicion
High index of clinical suspicion should trigger screening for hypercortisolism

Step 2: Patient History
Review medications, physical exam, comorbidities, lab results

Step 3: Biochemical Testing
Start with overnight 1 mg DST as the most sensitive first-line test

Step 4: Interpret Results
If test results suggest hypercortisolism, proceed with referral to endocrinology.

Step 5: Refer to Endocrinology
Include all necessary information for a successful referral

Patient Case Scenario (continued)

A 52-year-old man with T2D, hypertension, obesity, and hypothyroidism presents to his PCC for a routine visit.

During the visit, the PCC notes that his T2D is becoming increasingly difficult to control due to rising blood glucose despite appropriate treatment escalation.

He is screened for hypercortisolism with 1-mg overnight DST and results are consistent with hypercortisolism. The patient is to be referred to endocrinology for further evaluation and management.

What should be communicated in the referral to the endocrinologist to help ensure a successful referral?

Working With the Multidisciplinary Health Care Team[1,2]

Many patients with hypercortisolism can be identified in primary care.

However, the complex diagnosis and nuanced treatment necessitates long-term follow up and management involving the health care team:

- Primary care clinic staff, including medical assistants, nurses, physician associates (PAs), nurse practitioners (NPs), physicians, social workers, and mental health clinicians
- Specialists, primarily endocrinologists, endocrinology NPs/PAs

1. Scoffings K, et al. *Br J Gen Pract.* 2022;72(721):399-401. 2. Uwaifo GI, Hura DE. Hypercortisolism. *StatPearls [Internet].* Updated July 4, 2023. Accessed January 8, 2025. https://www.ncbi.nlm.nih.gov/books/NBK551526/

Role of the Health Care Team in Diagnosis and Treatment[1]

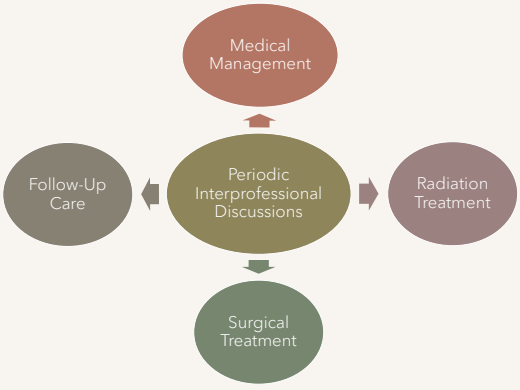
- PCCs may be the first to recognize the possibility of a hypercortisolism diagnosis.

By providing comprehensive and detailed referrals, PCCs can facilitate timely and effective specialist care, ultimately improving patient outcomes.

- Endocrinology is typically the first specialty sought for full evaluation and management of a patient with hypercortisolism.
- Other specialists may be involved in diagnosing and treating hypercortisolism, such as radiologists, nuclear medicine clinicians, general surgeons, and neurosurgeons.
- Patients with hypercortisolism who receive care in a structured interprofessional setting have improved outcomes.

1. Uwaifo GI, Hura DE. Hypercortisolism. *StatPearls [Internet].* Updated July 4, 2023. Accessed January 8, 2025. https://www.ncbi.nlm.nih.gov/books/NBK551526/

Involving the Health Care Team Across Treatment Settings



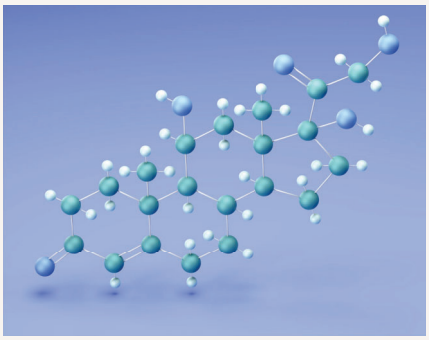
1. Uwaifo GI, Hura DE. Hypercortisolism. *StatPearls [Internet].* Updated July 4, 2023. Accessed January 8, 2025. https://www.ncbi.nlm.nih.gov/books/NBK551526/

Selected Health Care Team Roles by Treatment Setting

Medical Management	• Pharmacists work with the care team to select treatment and discuss details of drugs for treatment of hypercortisolism, including optimal dosing, potential drug interactions, and other considerations. • Nurses participate in patient consultations with other members of the health care team to facilitate drug administration and monitor for treatment response and adverse reactions.
Radiation Treatment	These definitive therapies often require hospital admission. • Hospital care teams evaluate patients and administer these therapies. • Hospital care teams often include anesthesiology, nursing staff, clinical nutrition, social workers, physical rehabilitation, and mental health specialists.
Surgical Treatment	
Follow-Up Care	• PCCs, endocrinologists, and surgeons typically drive the structured long-term follow up plan. • Plans should include periodic evaluation to assess for recurrent or persistent hypercortisolism.

1. Uwaifo GI, Hura DE. Hypercortisolism. *StatPearls [Internet]*. Updated July 4, 2023. Accessed January 8, 2025. https://www.ncbi.nlm.nih.gov/books/NBK551526/

Visit our hypercortisolism toolkit to download slides, read more about the CATALYST trial and much, much more.



HTTPS://WWW.PCMG-US.ORG/TOOLKIT/HYPERCORTISOLISM

Summary and Key Takeaways

- Hypercortisolism as a diagnosis is often delayed or missed, leading to adverse consequences for patients, including mortality and unnecessary morbidity.
- Current data, including from the recent CATALYST trial, suggest the prevalence of hypercortisolism is higher than previously estimated.
- Hypercortisolism is a heterogeneous, multisystemic disease with variable presentation along a spectrum of signs and symptoms from classically overt to clinically inapparent.
- Hypercortisolism occurs along a continuum of cardiometabolic risks that increase with disease severity and duration.

Summary and Key Takeaways

- Screening for hypercortisolism in primary care requires:
  - Appropriately selecting patients with suspected hypercortisolism
  - Using a sensitive screening test
  - Interpreting results within the patient's clinical context
- A successful referral to endocrinology requires communicating:
  - The patient's relevant clinical findings and medical history
  - Reasons for suspecting hypercortisolism
  - Screening test results
- Working with the multidisciplinary health care team is essential for optimal outcomes in hypercortisolism diagnosis and management.

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