AAVBC
AMERICAN ACADEMY OF VALUE BASED CARE

Cushing's Disease

Quick Reference Guide

2026

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1 CLINICAL SNAPSHOT

Definition: Cushing's disease (CD) is **pituitary-dependent** Cushing's syndrome — chronic endogenous hypercortisolism driven by an ACTH-secreting pituitary adenoma (corticotropinoma) that stimulates **bilateral adrenal cortisol overproduction**.[1] It is the most common cause of endogenous Cushing's syndrome, accounting for roughly **60–70%** of cases. The broader term **Cushing's syndrome** (CS) covers all causes of hypercortisolism — pituitary (CD), adrenal, ectopic ACTH, and exogenous glucocorticoid.[2] Once hypercortisolism is biochemically confirmed, **morning plasma ACTH** separates **ACTH-dependent disease** (≥10 pg/mL; pituitary or ectopic, **80–85%** of cases) from **ACTH-independent adrenal disease** (<10 pg/mL, **15–20%**).[3]

CLINICAL PEARL: CUSHING'S DISEASE VS CUSHING'S SYNDROME

Cushing's syndrome refers to any condition causing prolonged, excess cortisol exposure, whereas Cushing's disease is the ACTH-dependent subtype caused specifically by a pituitary adenoma. **All Cushing's disease is Cushing's syndrome, but not all Cushing's syndrome is Cushing's disease.**

The most common cause of **Cushing's Syndrome is exogenous corticosteroid use** (e.g., prednisone, dexamethasone), which typically suppresses ACTH, whereas **Cushing's disease instead produces high or high-normal ACTH due to continuous pituitary stimulation of the adrenal glands**. Both present with the classic phenotype of moon facies, buffalo hump, truncal obesity with thin limbs, proximal myopathy, purple striae, and easy bruising. Cushing's disease may additionally present with hyperpigmentation from elevated ACTH or visual field deficits if the adenoma compresses the optic chiasm.

Practically, the workup starts by confirming hypercortisolism (24-hour urinary free cortisol or late-night salivary cortisol), then checking plasma ACTH: a **low/suppressed level points to an adrenal source or exogenous steroids, while a high/normal level indicates an ACTH-dependent cause**, requiring further workup to distinguish a pituitary adenoma (Cushing's disease) from ectopic ACTH secretion (e.g., small cell lung cancer).

ICD-10 Codes:

Cushing's syndrome is reported in the **E24** category, and etiologic specificity is the central coding task. **E24.0** (pituitary-dependent Cushing's disease) is the primary code for CD and is the only **E24** subcode that maps to a risk-adjustment HCC. The remaining subcodes document distinct entities: **E24.1** (Nelson's syndrome), **E24.2** (drug-induced Cushing's syndrome), **E24.3** (ectopic ACTH syndrome), **E24.4** (alcohol-induced pseudo-Cushing's syndrome), and **E24.8** (other Cushing's syndrome). **E24.9** (Cushing's syndrome, unspecified) is acceptable only during active diagnostic workup and is the most frequently overused code in this category. Manifestations are coded separately with their causal relationship to hypercortisolism documented: **E08.-** (diabetes due to an underlying condition, not **E11.-**), **I15.2** (secondary hypertension from an endocrine disorder, not **I10**), **M80.-/M81.-** (osteoporosis with/without fracture), **F32.-/F33.-** (depressive disorder), **M62.81** (proximal muscle weakness), and **E27.40** (post-surgical adrenal insufficiency).[4]

Prevalence and Burden: Endogenous Cushing's syndrome is **rare**, with an estimated incidence of **2–8 per million per year**, of which Cushing's disease represents the **60–70%** majority.[2] Onset typically clusters between ages **30 and 49**, with an approximate **3:**[1] **female predominance** in pituitary-dependent disease.[1,2] Untreated or undertreated CS carries a standardized mortality ratio of **3.0** (95% CI 2.3–3.9), and **cardiovascular events** account for **43.4% of deaths**.[5] Crucially,

biochemical remission does not return risk to baseline: cardiovascular risk factors persist in **40–60%** of patients after successful treatment, neurocognitive and psychiatric burden improve only incompletely, and excess mortality remains elevated for years. These residual burdens make Cushing's disease a **lifelong-surveillance condition** rather than a one-time surgical cure.[6] **In adults ≥65**, the classic Cushingoid phenotype (moon facies, purple striae, centripetal obesity) is **frequently absent,** and 24-hour urinary free cortisol supports the diagnosis less reliably than in younger patients (P<.05).[7] Older adults instead present with **worsening treatment-resistant hypertension, difficult-to-control diabetes, unexplained proximal weakness, and new fragility fractures** — features that overlap almost completely with common primary-care conditions, producing an average diagnostic delay of **3–6 years**.[8]

HCC/RAF V28 Mapping

ICD-10 CODE(S)	HCC CATEGORY (V28)	RAF (CNA)	DOCUMENTATION REQUIREMENT
E24.0 (Pituitary-dependent Cushing's disease)	HCC 51 — Addison's and Cushing's Diseases/ Acromegaly/Other Specified Endocrine Disorders	**0.510**	**Pituitary-dependent Cushing's disease**. Document ACTH-dependent hypercortisolism, pituitary source (confirmed or suspected), and MRI findings
E24.1 (Nelson's syndrome)	HCC 51 — Addison's and Cushing's Diseases/ Acromegaly/Other Specified Endocrine Disorders	**0.510**	**Post-adrenalectomy syndrome** with pituitary tumor enlargement
E24.2 (Drug-induced Cushing's syndrome)	HCC 51 — Addison's and Cushing's Diseases/ Acromegaly/Other Specified Endocrine Disorders	**0.510**	**Must document the causative drug**; commonly long-term glucocorticoids (prednisone, etc.)
E24.3 (Ectopic ACTH syndrome)	HCC 51 — Addison's and Cushing's Diseases/ Acromegaly/Other Specified Endocrine Disorders	**0.510**	**ACTH from non-pituitary tumor** (lung, thymus, pancreas); document source tumor **separately**
E24.4 (Alcohol-induced pseudo-Cushing's syndrome)	HCC 51 — Addison's and Cushing's Diseases/ Acromegaly/Other Specified Endocrine Disorders	**0.510**	Elevated cortisol from **alcohol**; requires clinical distinction from true Cushing's
E24.8 (Other Cushing's syndrome)	HCC 51 — Addison's and Cushing's Diseases/ Acromegaly/Other Specified Endocrine Disorders	**0.510**	Use **only** when a **specific type is confirmed** but does not fit above categories

ICD-10 CODE(S)	HCC CATEGORY (V28)	RAF (CNA)	DOCUMENTATION REQUIREMENT
E24.9 (Cushing's syndrome, unspecified)	HCC 51 — Addison's and Cushing's Diseases/ Acromegaly/Other Specified Endocrine Disorders	**0.510**	**Only acceptable if etiology genuinely unknown after workup — never use as default**

ABBREVIATIONS: CD = Cushing's Disease; CS = Cushing's Syndrome; ACTH = Adrenocorticotropic Hormone; HCC = Hierarchical Condition Category; RAF = Risk Adjustment Factor; CNA = Community Non-Dual Eligible, Aged; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification. *RAF values represent the Community Non-Dual Eligible Aged (CNA) coefficient from the 2026 CMS-HCC model; values vary across patient populations based on eligibility and care setting

Risk-Adjusted Care Resources per Patient/Year[9,10]

Risk-adjusted care resource allocation — MA base rate (~$10,402.34) × RAF coefficient

Cushing's Disease

$5,305

HCC 51 · RAF 0.510

2 RECOGNITION AND DIAGNOSIS

Medicare Screenings and Diagnostic Workup (Adult and Geriatric)

TEST/SERVICE*	WHEN INDICATED	COVERAGE AND CADENCE	GERIATRIC NOTE
Late-night salivary cortisol (LNSC), ×2	**First-line screen** when CS suspected; preferred primary biochemical monitor in older adults	Diagnostic under Part B when medically indicated; **≥2 samples required**; no dedicated CPT — may bill HCPCS S3650/S3652 (verify with MA plan/MAC)	Sensitivity **95.8%**, specificity **93.4%**; preferred over UFC in elderly given lower UFC sensitivity (P<.05)[11]
24-hour urinary free cortisol (UFC), 2–3 collections	**First-line screen**; reflects integrated daily cortisol secretion	CPT 82530; covered under Part B when CS suspected; repeat for cyclical disease	Sensitivity **94%**, specificity **93%**;[3] supports the diagnosis less often in patients ≥65 (P<.05)[11]

TEST/SERVICE*	WHEN INDICATED	COVERAGE AND CADENCE	GERIATRIC NOTE
1-mg overnight dexamethasone suppression test (DST)	**First-line screen**; abnormal if morning cortisol ≥1.8 µg/dL	Component tests billed individually (cortisol 82533)	Sensitivity **98.6%**, specificity **90.6%**; abnormal at morning cortisol **≥1.8 µg/dL**; interpret alongside interacting medications[11]
Morning plasma ACTH	After hypercortisolism confirmed — **differentiates etiology**	CPT 82024; obtained once **two** screening tests are abnormal	ACTH **≥10 pg/mL** = ACTH-dependent (pituitary/ectopic); **<10 pg/mL = adrenal**[2]
Pituitary MRI (with/without contrast); IPSS if indicated	**Localization after biochemical + ACTH confirmation** — never a first-line screen	CPT 70553 (MRI); 75893 (inferior petrosal sinus sampling)	A sellar mass **>6 mm** with ACTH-dependent CS has near-**100%** specificity for CD; MRI misses many microadenomas, so a normal MRI does not exclude CD[12]

ABBREVIATIONS: LNSC = Late-Night Salivary Cortisol; UFC = Urinary Free Cortisol; DST = Dexamethasone Suppression Test; ACTH = Adrenocorticotropic Hormone; MRI = Magnetic Resonance Imaging; IPSS = Inferior Petrosal Sinus Sampling; CPT = Current Procedural Terminology; MA = Medicare Advantage; MAC = Medicare Administrative Contractor; CS = Cushing's Syndrome; CD = Cushing's Disease
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Subtle Early Signs in Older Adults (>65) — The 'Five P's'

THE 'FIVE P'S' SIGN	WHAT TO LOOK FOR (≥65)	WHY IT IS MISSED
Peripheral obesity	Central/visceral fat with thin extremities and dorsocervical/facial deposition; weight gain with **central redistribution** occurs in **70–95%** of CS patients[2]	**Attributed to age-related weight gain**; lower BMI in elderly CS blunts the classic habitus[7]

THE 'FIVE P'S' SIGN	WHAT TO LOOK FOR (≥65)	WHY IT IS MISSED
Purpura	Thin, **fragile skin** with easy bruising; spontaneous ecchymoses out of proportion to trauma[13]	**Mistaken for senile purpura or anticoagulant effect**; classic skin changes are less frequent in older adults
Proximal myopathy	Difficulty rising from a chair or climbing stairs; proximal weakness occurs in **60–82%** and drives falls and functional decline[3]	Attributed to **deconditioning, sarcopenia, or arthritis** rather than hypercortisolism
Psychiatric change	New or worsening depression (**50–80%**), anxiety, irritability, or cognitive shifts (memory, executive function)[2]	**Overlaps with age-related cognitive decline and primary mood disorder**; may be coded as dementia rather than CS
Polys (polyuria/ polydipsia)	Symptoms of new or difficult-to-control diabetes; glucose intolerance in **45–70%**, diabetes in **20–47%**[3]	Attributed to ordinary **type 2 diabetes**, delaying recognition of an endocrine driver

ABBREVIATIONS: CS = Cushing's Syndrome; BMI = Body Mass Index. The 'Five P's' frame the atypical older-adult presentation; classic moon facies and buffalo hump are late signs and are often absent in patients ≥65

Geriatric Risk Factors

RISK SIGNAL	ASSOCIATION	POPULATION/SOURCE
Difficult-to-control type 2 diabetes	Hypercortisolism prevalence **23.8%** in adults with difficult-to-control T2D, rising to **36.6%** on multiple antihypertensives[14]	CATALYST findings within the 2026 AACE T2D consensus[15]
Resistant/worsening hypertension	Hypertension occurs in **60–90%** of CS and is often resistant to standard agents **until cortisol is controlled**[2]	All CS; presents as worsening of pre-existing HTN in elderly
New fragility fractures	Pre-diagnosis fracture standardized incidence ratio **4.9**(95% CI 2.7–8.3);[16] osteoporosis/fractures in up to **80%**[2]	Swedish CD registry(n=502); higher fracture prevalence in elderly CS
Unexplained venous thromboembolism	>**10-fold** increased VTE risk[17]	Hypercoagulable state

RISK SIGNAL	ASSOCIATION	POPULATION/SOURCE
Combination of ≥3 atypical features	Co-occurrence of resistant HTN, difficult diabetes, proximal weakness, and/or fractures should trigger a structured CS screen in a Medicare patient[6]	**No guideline defines an age-specific screening threshold** — a recognized evidence gap

ABBREVIATIONS: T2D = Type 2 Diabetes; CS = Cushing's Syndrome; CD = Cushing's Disease; HTN = Hypertension; VTE = Venous Thromboembolism; AACE = American Association of Clinical Endocrinology; CI = Confidence Interval

Diagnostic Thresholds (Endocrine Society/Pituitary Society)

DIAGNOSTIC STEP	THRESHOLD/CRITERION	INTERPRETATION CAVEAT
Step 0 — exclude exogenous glucocorticoid	**Screen all routes** — oral, inhaled, topical, injectable, rectal — before ordering endogenous cortisol testing[6]	Topical/inhaled steroids can cause CS, especially when potentiated by **CYP3A4 inhibitors** (e.g., ritonavir, cobicistat)[8]
Step 1 — biochemical confirmation	At least **two** abnormal first-line tests (LNSC ×2, UFC ×2, or 1-mg DST); no single symptom is pathognomonic[2]	Up to **50%** of patients show variability between consecutive LNSC/UFC samples — a single test neither confirms nor excludes CS2
Step 2 — etiologic differentiation	**Morning** plasma ACTH: **≥10 pg/mL = ACTH-dependent** **<10 pg/mL = ACTH-independent (adrenal)**[2]	**Pseudo-Cushing states** (severe obesity, major depression, alcohol use) can elevate cortisol
Step 3 — localization	**Pituitary MRI**; sellar mass >6 mm with ACTH-dependent CS has near-**100%** specificity for CD[12]	A normal pituitary MRI does **NOT** exclude CD; IPSS is often required for definitive localization
Severity assessment	**No guideline-endorsed staging system exists**; severity is judged by degree of hypercortisolism (UFC), comorbidity count, and phenotype	Document number and severity of comorbidities to represent care intensity in the absence of a formal stage

ABBREVIATIONS:LNSC = Late-Night Salivary Cortisol; UFC = Urinary Free Cortisol; DST = Dexamethasone Suppression Test; ACTH = Adrenocorticotropic Hormone; MRI = Magnetic Resonance Imaging; IPSS = Inferior Petrosal Sinus Sampling; CS = Cushing's Syndrome; CD = Cushing's Disease

Clues to Dig Deeper

CLUE TO DIG DEEPER	WHAT IT MAY SIGNAL	NEXT STEP
Negative screen but persistent suspicion	**Cyclical Cushing's disease** — cortisol fluctuates, so a patient can be normal one day and elevated days later[2]	**Repeat testing at intervals**; document the cyclical pattern to justify continued monitoring
Adrenal incidentaloma on imaging	Possible autonomous **cortisol secretion** (subclinical/mild CS)[19]	**Order 1-mg DST**; expedited endocrinology referral if cortisol fails to suppress[20]
Hypokalemic metabolic alkalosis with rapid-onset severe weakness and weight loss	**Ectopic ACTH syndrome**, often from occult malignancy (bronchial carcinoid, SCLC)[21]	**Urgent endocrinology and oncology evaluation**; localize the ACTH source
Cushingoid features with documented alcohol use	Possible **alcohol-induced pseudo-Cushing's (E24.4)** versus true CS[22]	Use LNSC and confirm biochemically; **do not over-attribute to alcohol without adequate workup**

ABBREVIATIONS: CS = Cushing's Syndrome; CD = Cushing's Disease; ACTH = Adrenocorticotropic Hormone; DST = Dexamethasone Suppression Test; SCLC = Small-Cell Lung Cancer; LNSC = Late-Night Salivary Cortisol

Common Oversights

CLINICAL OVERSIGHT	CONSEQUENCE	BETTER PRACTICE
Waiting for the classic phenotype before screening	Diagnostic delay of **3–6 years**; in patients **≥65** the classic habitus is often absent[8]	**Screen on atypical features** — resistant HTN, difficult diabetes, proximal weakness, fractures — not on moon facies
Accepting a single negative test as exclusion	Cyclical disease produces **normal results during low-cortisol phases**, missing true CS[2]	Require **two concordant abnormal first-line tests**; repeat if suspicion persists
Treating a normal pituitary MRI as a rule-out	**Missed Cushing's disease**; MRI fails to show many microadenomas[6]	Pursue biochemical confirmation and IPSS for localization when ACTH-dependent CS is established
Assuming remission returns risk to baseline	Under-surveillance of persistent cardiovascular, psychiatric, and mortality risk	Cardiovascular risk persists in **40–60%** after remission and SMR stays **3.0**; maintain lifelong monitoring[2,6]

CLINICAL OVERSIGHT	CONSEQUENCE	BETTER PRACTICE
Overlooking VTE and infection risk during active disease	Preventable thromboembolism (HR **2.6**) and serious infection (HR **4.9**)[23]	**Assess VTE risk and provide perioperative prophylaxis**; keep a low threshold for febrile illness; offer vaccinations

ABBREVIATIONS: CS = Cushing's Syndrome; CD = Cushing's Disease; MRI = Magnetic Resonance Imaging; IPSS = Inferior Petrosal Sinus Sampling; HTN = Hypertension; VTE = Venous Thromboembolism; SMR = Standardized Mortality Ratio; HR = Hazard Ratio

CLINICAL PEARL

Waiting for classic Cushingoid features (moon facies, central obesity, purple striae) before screening drives a **3-6 year diagnostic delay**. This delay is worse in patients **≥65**, where the classic habitus is often absent altogether.

Clinicians often don't consider Cushing's until it's visually obvious, and older adults with hypercortisolism frequently present atypically. The classic fat redistribution pattern is blunted or absent with age, so the "look" clinicians are trained to wait for often never appears.

Better practice: Screen on atypical features instead of waiting for the classic phenotype: **resistant hypertension**, **difficult-to-control diabetes**, **proximal muscle weakness**, and **unexplained fractures**. These are the presentations most likely in older adults, and none require the patient to "look Cushingoid" first.

Key Differentials in Elderly

DIFFERENTIAL	OVERLAPPING FEATURES	DISTINGUISHING APPROACH
Metabolic syndrome/ simple obesity	Central obesity, hypertension, glucose intolerance[2]	**Look for discriminatory signs** (proximal myopathy, easy bruising, plethora); screen biochemically if multiple progressive features
Primary type 2 diabetes	Hyperglycemia, polyuria, polydipsia[14]	Escalating, difficult-to-control diabetes warrants targeted CS screening—hypercortisolism prevalence **23.8%** in this subgroup[15]
Major depressive disorder	Depressed mood, fatigue, cognitive slowing; depression can elevate cortisol **(pseudo-Cushing)**[24]	Use LNSC and clinical context; distinguish pseudo-Cushing before assigning **E24.0**
Age-related sarcopenia/frailty	Proximal weakness, falls, functional decline[13]	Weakness **disproportionate to age**, paired with other Five P's, should prompt screening

DIFFERENTIAL	OVERLAPPING FEATURES	DISTINGUISHING APPROACH
Primary (essential) hypertension	Elevated blood pressure[2]	**Resistant hypertension** despite appropriate polypharmacy, especially with hypokalemia, raises suspicion for CS

ABBREVIATIONS: CS = Cushing's Syndrome; CD = Cushing's Disease; LNSC = Late-Night Salivary Cortisol

Comorbidity Screening

COMORBIDITY DOMAIN	FREQUENCY/SIGNAL	PRIMARY-CARE SCREENING ACTION
Cardiovascular and hypertension	HTN in **60–90%**; cardiovascular deaths account for **43.4%** of CS mortality (rates from diagnosed CS cohorts)[2,5]	**Monitor BP to target**; aggressive risk-factor management; persists after remission in **40–60%**[24]
Diabetes/glucose metabolism	**Up to 50%** have altered glucose metabolism (Diabetes in **20-45%** of CD patients)[13]	**HbA1c surveillance**; recognize CS as a driver of difficult-to-control glycemia
Bone health	Osteopenia/osteoporosis and fractures up to **80%**; fragility fracture may be the presenting event[24,25]	**DEXA screening**; treat osteoporosis per standard guidelines
Venous thromboembolism	>**10-fold** VTE risk[6]	**Assess VTE risk**; perioperative prophylaxis during active hypercortisolism
Neuropsychiatric & cognitive	Depression prevalence; cognitive deficits persist after remission	**Screen for depression and cognitive change**; connect to mental-health resources
Infection/ immunosuppression	Infection HR **4.9** (95% CI 3.7–6.4); infection is the second leading cause of CS death (**12.7%**)[23]	Offer influenza, pneumococcal, and herpes zoster **vaccination**; low threshold to evaluate fever

ABBREVIATIONS: CS = Cushing's Syndrome; HTN = Hypertension; BP = Blood Pressure; HbA1c = Hemoglobin A1c; DEXA = Dual-Energy X-ray Absorptiometry; VTE = Venous Thromboembolism; HR = Hazard Ratio; CI = Confidence Interval

⚠ RED FLAG — EMERGENCY/ACTIVATE CRISIS RESPONSE

- **Adrenal crisis** — **hypotension or shock resistant to fluids** accompanied by nausea, vomiting, severe fatigue, fever, or altered consciousness in any patient with known Cushing syndrome, particularly post-surgical patients or those on a **steroidogenesis inhibitor**. Give **hydrocortisone 100 mg IV/IM immediately**, followed by **200 mg/24-hour infusion** plus aggressive **0.9% saline resuscitation**. Do not delay treatment for laboratory confirmation
- **Critical exception — mifepristone patients:** the glucocorticoid receptor is blocked in patients taking mifepristone; hydrocortisone will not work. Adrenal crisis rescue in this population requires **high-dose dexamethasone 2–4 mg**, not hydrocortisone
- **Severe hypokalemia with arrhythmia** — particularly in ectopic ACTH syndrome or in patients on **osilodrostat** or **metyrapone**
- **Acute psychosis or suicidality** — psychiatric emergencies can be a direct manifestation of hypercortisolism; suicide is a recognized cause of death in Cushing syndrome
- **Severe sepsis** in the setting of **uncontrolled hypercortisolism** — immunosuppression from cortisol excess significantly elevates infection risk and severity

⚠ RED FLAG — URGENT (24-72 HOURS)

- **Suspected ectopic ACTH syndrome** — rapid-onset hypercortisolism with **hypokalemic alkalosis**, profound weakness, and weight loss warrants same-day specialist contact
- **QTc prolongation >480 ms** on **osilodrostat** — consider holding the drug and arrange urgent **cardiology and endocrinology review**
- **Symptomatic hypocortisolism** on a steroidogenesis inhibitor (nausea, vomiting, hypotension, fatigue) — **hold the drug**, initiate **glucocorticoid replacement**, and contact the prescribing endocrinologist the same day
- **New visual-field deficit or severe headache** in known Cushing disease — raises concern for **pituitary apoplexy** or **macroadenoma expansion**; requires urgent neurosurgical evaluation
- **Two abnormal first-line screening tests** confirming endogenous Cushing syndrome — arrange expedited endocrinology referral within days

AAVBC PERSPECTIVE

*AAVBC encourages providers to maintain the **clinical distinction between Cushing's Disease** and the broader category of **Cushing's Syndrome**, as etiology drives both the workup and the management.*

*AAVBC also supports moving from a passive recognition of Cushing's disease to an **active, targeted biochemical screening** when specific red flag features are present, without waiting for the hallmark Cushingoid appearance from patients. Weight gain, hypertension, depression and fatigue are common presentations in primary care that are often attributed to metabolic syndrome, PCOS, or mood disorders for years before the correct diagnosis is made. The clinical signature that separates CD from these mimics is the combination of symptoms rather than any single one.*

Recognizing this signature earlier shortens the diagnostic delay and reduces preventable cardiovascular, thromboembolic, and skeletal complications before they accumulate, aiming for the best outcomes for patients.

3 MEAT DOCUMENTATION ESSENTIALS

Cushing's disease documentation depends on establishing the **causal chain** between **pituitary-driven hypercortisolism** and each downstream manifestation into a record that supports **continuity**, **complication tracking**, and **accurate risk adjustment**. The most frequent pitfalls include defaulting to **E24.9** (unspecified Cushing's syndrome) when biochemical and imaging workup clearly confirms a pituitary source; conflating **Cushing's disease** (**E24.0**, pituitary-dependent) with adrenal (**E24.2**) or ectopic ACTH (**E24.3**) etiologies; failing to code hypercortisolism-driven comorbidities (diabetes, hypertension, osteoporosis, VTE) as linked manifestations; and charting active disease as resolved before biochemical remission and surveillance are fully established. The **MEAT** framework makes the causal linkage explicit and keeps the active diagnosis visible across a condition that requires **lifelong surveillance.**

*Case vignette: A female patient, 72, carries diagnoses of 'hypertension, type 2 diabetes, and Cushing's syndrome.' Her chart lists **I10**, **E11.9**, and **E24.9**. After her endocrinologist confirms a pituitary source, the record is reframed to pituitary-dependent Cushing's disease **(E24.0)** with secondary hypertension due to hypercortisolism **(I15.2)**, diabetes mellitus due to an underlying condition **(E08.-)**, and osteoporosis without current fracture due to Cushing's disease **(M81.0)**. The clinical reality is unchanged; the record now represents it accurately.*

Monitor: Late-night salivary cortisol (LNSC) x2 (date): **0.09 and 0.11 mcg/dL** (elevated, ref <0.09). 24-hr UFC (date): **145 mcg/24h** (elevated, ref <50). Low-dose DST (date): post-dexamethasone cortisol **4.2 mcg/dL** (fails to suppress). Plasma ACTH (date): **8 pg/mL** (suppressed, ACTH-independent pattern). Cyclicity noted: patient reports symptom waxing/waning over past **6 months**; one prior LNSC (3 months ago) was normal during presumed low-cortisol phase — does not exclude diagnosis, continued serial testing warranted. Comorbidity tracking: BP **148/92** (home log avg 145/88); HbA1c **7.1%**; DEXA lumbar spine **T-score -2.6; PHQ-9 = 13** (moderate depression); functional status — reports difficulty rising from chairs, no fall

Evaluate: Initial screening **(LNSC, UFC, DST)** all abnormal as above. Plasma ACTH suppressed at **8 pg/mL**, consistent with ACTH-independent hypercortisolism. Adrenal CT (date): **2.8 cm** left adrenal adenoma, 12 HU non-contrast, washout consistent with adenoma. Contralateral adrenal atrophic. No pituitary imaging indicated given suppressed ACTH. Etiology established: adrenal Cushing syndrome secondary to cortisol-producing adrenal adenoma — supports **E24.0** rather than unspecified **E24.9**

Assess: Cushing syndrome, adrenal origin (**E24.2** — code per adenoma etiology), due to left adrenal adenoma. Associated conditions attributed to hypercortisolism: secondary hypertension **(I15.2)**; diabetes due to underlying condition (**E08.65**, hyperglycemia); osteoporosis **(M81.0)**; depression, moderate **(F32.1)**; proximal myopathy **(M62.81)**. VTE risk elevated — no active clot, prophylaxis considered pre-operatively. Functional status: mild ADL limitation (transfers), no frailty index elevation, low fall risk at this time

Treat: **Plan discussed with patient — laparoscopic left adrenalectomy referral placed** (surgery, endocrinology co-management). **Ketoconazole held** pending surgical clearance; reserved as bridge therapy if surgery is delayed. **Anticipate post-op glucocorticoid replacement** (hydrocortisone taper) with HPA-axis recovery monitored via morning cortisol at **6 weeks** post-op. Comorbidity management continued: **lisinopril for BP, metformin for glucose, alendronate initiated for osteoporosis, sertraline continued for depression**. PT referral for proximal weakness. **Not currently frail** — surgical candidacy preferred over medical therapy alone.

Clinical Documentation Elements

- Name the **specific etiology** (**E24.0** for pituitary-dependent CD) and the supporting evidence — ACTH-dependent hypercortisolism, pituitary source, MRI/IPSS findings
- Document each manifestation with its **causal link** to hypercortisolism, listing **E24.0** as the underlying cause (**E08.-** for diabetes, **I15.2** for hypertension, **M80.-/M81.-** for osteoporosis)
- Record the **cyclical nature** of the disease when present, to justify negative tests and continued monitoring
- Document **functional status** — ADL limitations, fall risk, frailty markers — to support care intensity and specialist referral
- Note **post-surgical adrenal insufficiency (E27.40)** and the glucocorticoid-replacement and stress-dosing plan; remission does not end the documentation obligation
- Distinguish **Cushing's disease** from **Cushing's syndrome** in the narrative so the language supports **E24.0** rather than defaulting to **E24.9**

Reframing Common Documentation Shortcuts

COMMON SHORTCUT	WHY IT FALLS SHORT	ACCURATE REFRAME
'Cushing's syndrome' → E24.9	Defaults to unspecified even when a pituitary source is established; loses HCC 51 and medical-necessity support	'Pituitary-dependent Cushing's disease **(E24.0)**' with the documented ACTH/MRI basis
'Steroid-induced Cushing syndrome' → E24.9	Loses causal link to glucocorticoid therapy; obscures reversibility	Exogenous Cushing syndrome, drug-induced **(E24.2)**' with medication named

COMMON SHORTCUT	WHY IT FALLS SHORT	ACCURATE REFRAME
'Cortisol normalized after surgery'	Implies risk returned to baseline; under-represents persistent burden	Achieved biochemical remission; cardiovascular risk does not return to baseline — lifelong surveillance continues[7,24]
'On cortisol-blocking drug'	Vague class label obscures the agent-specific safety profile (e.g., mifepristone rescue)	**Name the agent and class** — steroidogenesis inhibitor or glucocorticoid receptor antagonist — and its monitoring plan. **Example:** "Ketoconazole (steroidogenesis inhibitor) — monitor LFTs monthly. Or mifepristone (receptor antagonist) — monitor K^+, clinical response, not cortisol"

ABBREVIATIONS: CD = Cushing's Disease; HCC = Hierarchical Condition Category; SMR = Standardized Mortality Ratio; ACTH = Adrenocorticotropic Hormone; MRI = Magnetic Resonance Imaging

DOCUMENTATION REMINDER IS COMPREHENSIVE CODING

Good documentation here is simply an accurate clinical record. When the note names the **specific etiology (E24.0, pituitary dependent Cushing's disease)** and links each manifestation to hypercortisolism with a causal code, it represents the true complexity of a multisystem disease. **Example:** "Pituitary-dependent Cushing's disease (**E24.0**), confirmed by MRI and elevated ACTH. Secondary hypertension due to hypercortisolism (**I15.2**). Steroid-induced diabetes mellitus due to underlying Cushing's disease (**E08.65**, hyperglycemia). Osteoporosis due to Cushing's disease (**M81.8**). Plan: continue postoperative surveillance for persistent cardiovascular and metabolic risk."

4 TREATMENT AND REFERRAL QUICK GUIDE

The primary goal in endogenous Cushing's disease is **complete resection of the causative tumor**. In value-based and geriatric care, the emphasis shifts toward functional independence, symptom-burden reduction, and avoidance of hospitalization, often favoring medical over surgical management in frail patients. Treatment is guided by the Pituitary Society 2021 consensus and the Endocrine Society 2015 treatment guideline.[24,26]

Therapy Escalation Criteria

ESCALATION TRIGGER	ACTION	NOTE
Newly confirmed CD, operable patient[26]	Refer for transsphenoidal selective adenomectomy (first-line)	**Remission ~80%** microadenoma, **Remission ~60%** macroadenoma at expert centers;[24] remission success is dependent on patient profile
Significant frailty or unacceptable operative risk[24]	**Assess with a frailty scale**; consider medical therapy or radiation as first-line and document the rationale	Older patients had **lower post-surgical remission** (P<.05) but lower recurrence after remission (**2.6%** vs **19.2%**, P=0.03)[27]
Surgical failure or recurrence	Escalate to medical therapy ± repeat surgery; recurrence occurs in **5–35%** within 5–10 years[24]	**Lifelong annual monitoring once HPA axis recovers**[24]
Persistent/recurrent disease after surgery	**Pituitary radiation** with steroidogenesis-inhibitor bridge therapy	Radiation effect is delayed (months–years); ~**30%** relapse[28]
Severe, refractory hypercortisolism[26]	Consider bilateral adrenalectomy (immediate control)	**Requires lifelong glucocorticoid + mineralocorticoid replacement**; Nelson's syndrome and adrenal-crisis risk

ABBREVIATIONS: CD = Cushing's Disease; HPA = Hypothalamic-Pituitary-Adrenal

Guideline-Aligned Treatment by Line and Patient Profile (Pituitary Society 2021/Endocrine Society 2015)

LINE/SETTING	GUIDELINE-ALIGNED APPROACH*	GERIATRIC/VBC CONSIDERATION
First-line — operable	Transsphenoidal selective adenomectomy; biochemical remission target = **morning cortisol <2 µg/dL**[24,26]	Frailty assessment precedes surgery; perioperative VTE prophylaxis
Second-line/surgery not feasible — steroidogenesis inhibitors	**Osilodrostat** , **levoketoconazole**, ketoconazole and metyrapone (off-label)[24]	Watch **QTc** and **hepatotoxicity**; correct K^+/Mg^{2+} first

LINE/SETTING	GUIDELINE-ALIGNED APPROACH*	GERIATRIC/VBC CONSIDERATION
Second-line — pituitary-directed	**Pasireotide**; **cabergoline** (off-label)	Pasireotide causes **hyperglycemia in ~70%** — hazardous in elderly diabetics; cabergoline efficacy ~**30% (not FDA-approved)**[24]
Adjunct for CS-related hyperglycemia	**Mifepristone** — glucocorticoid receptor antagonist (FDA-approved for hyperglycemia in CS with diabetes)	Cannot monitor cortisol (receptor blocked); adrenal crisis rescue = dexamethasone **2–4 mg, NOT hydrocortisone**[2]
Third-line[24]	**Pituitary radiation** (with medical bridge) or bilateral adrenalectomy for refractory disease	Weigh **lifelong-replacement burden** and **adrenal-crisis risk** carefully in geriatric patients

ABBREVIATIONS: CD = Cushing's Disease; CS = Cushing's Syndrome; ES = Endocrine Society; FDA = Food and Drug Administration; VTE = Venous Thromboembolism; VBC = Value-Based Care; QTc = Corrected QT Interval
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

CLINICAL PEARL

Frailty and function outweigh chronologic age in choosing therapy. Older patients more often received medical or radiation therapy first and had lower surgical remission rates. However, once remission was achieved, recurrence was lower than in younger patients (**2.6%** vs **19.2%**, P=0.03). Document the frailty rationale explicitly when medical management is chosen over surgery.[27]

Non-Pharmacologic Care and Supportive Interventions

INTERVENTION	PURPOSE	NOTE
Progressive exercise (flexibility → balance → resistance)[26]	Reverse sarcopenia and proximal myopathy; **reduce falls**	Essential for rehabilitation; Structured programs combining aerobic + resistance training, supervised by a physical therapist, improve muscle function and quality of life even after biochemical remission;no CS-specific geriatric exercise guideline exists;

INTERVENTION	PURPOSE	NOTE
Nutrition and weight optimization[26]	**Support recovery of muscle strength and weight** normalization	**Protein-forward, whole-food diet** to rebuild muscle mass lost to catabolic myopathy; refer to a **registered dietitian** for individualized protein targets given renal/metabolic comorbidities; avoid processed foods and excess refined carbohydrates given elevated diabetes risk
Age-appropriate vaccination[26]	**Reduce infection risk** from immunosuppression	Influenza, pneumococcal, and herpes zoster recommended
Mental-health support[26]	Address depression, anxiety, and cognitive impairment that persist **after remission**	Baseline depression predicts **worse** long-term QoL
VTE risk reduction[26]	**Prevent thromboembolism** during active hypercortisolism	Perioperative prophylaxis; evaluate all CS patients for VTE risk

ABBREVIATIONS: CS = Cushing's Syndrome; QoL = Quality of Life; VTE = Venous Thromboembolism

Medication Safety and Key Interactions

AGENT (STATUS)*	KEY SAFETY CONCERN	MONITORING/GERIATRIC CAUTION
Osilodrostat — Isturisa (approved)[29]	**QTc prolongation**; adrenal insufficiency (~**28%**); nausea (**42%**)[13]	**Baseline ECG required**; correct K^+/Mg^{2+} first; UFC q1–2wk during titration; only 10/167 trial patients ≥65, **none >75**
Levoketoconazole (approved)[30]	**Hepatotoxicity**; QTc prolongation; CYP3A4 interactions	LFT monitoring; major polypharmacy concern with statins/warfarin/cardiac drugs in elderly
Ketoconazole ([OFF-LABEL])[24]	**Hepatotoxicity (boxed warning)**; QTc prolongation; CYP3A4 interactions	LFTs q1–2wk initially; normalizes UFC in ~**50%**; preferred in female patients[28]
Metyrapone ([OFF-LABEL])[3]	**Hypokalemia;** hypertension worsening; hirsutism (**36%**)	**Rapid onset** (hours); monitor electrolytes and BP closely; preferred in male patients

AGENT (STATUS)*	KEY SAFETY CONCERN	MONITORING/GERIATRIC CAUTION
Pasireotide — Signifor (approved for CD)[31]	**Hyperglycemia** — near-universal; gallstones; QTc prolongation[2,6]	**Hazardous in elderly diabetics**; close glucose monitoring, often insulin initiation
Cabergoline ([OFF-LABEL])[24]	**Orthostatic hypotension**; impulse-control disorders; valve fibrosis at high dose (rare)	**Lower efficacy** (~**30%** normalization); orthostatic risk in elderly
Mifepristone — Korlym (approved for hyperglycemia in CS)[32]	**Cannot monitor cortisol** (blocks receptor); hypokalemia (**44%**); CYP3A4 inhibition	**Adrenal-crisis rescue = dexamethasone 2–4 mg, NOT hydrocortisone**; hypokalemia compounded by diuretics[2]

ABBREVIATIONS:CD = Cushing's Disease; CS = Cushing's Syndrome; ECG = Electrocardiogram; QTc = Corrected QT Interval; UFC = Urinary Free Cortisol; LFT = Liver Function Test; BP = Blood Pressure. [OFF-LABEL] = used off-label in the US for Cushing's syndrome
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

When to Refer

WHO REFERS	TO WHOM	TRIGGER
Primary care	Endocrinology	Two abnormal first-line tests confirming endogenous CS — **refer within days**, do not attempt etiologic workup in primary care[26]
Primary care/ endocrinology	Neurosurgery (high-volume pituitary center)	Confirmed Cushing's disease for transsphenoidal surgery; new visual-field deficit or severe headache **(urgent)**[24]
Endocrinology	Oncology	Suspected ectopic ACTH syndrome from occult malignancy[2]
Primary care	Cardiology/diabetology	QTc concern on osilodrostat; **worsening hyperglycemia on pasireotide**[29]

ABBREVIATIONS: CS = Cushing's Syndrome; ACTH = Adrenocorticotropic Hormone; QTc = Corrected QT Interval

Follow-Up Timing

PHASE	CADENCE	FOCUS
Active medical therapy	UFC q1–2wk during titration, then q1–2mo[29]	**Cortisol control;** adrenal insufficiency; agent-specific labs (LFTs, K^+, glucose, ECG)
Early post-surgery	Morning cortisol checked **every 3 months** until HPA-axis recovery (typically **6-18 months**); confirmatory ACTH stimulation test once levels approach the recovery threshold[26]	**Glucocorticoid replacement and stress-dosing education**; all remission patients develop central adrenal insufficiency
Long-term surveillance	Annual, indefinitely, once HPA axis recovers[24]	**Biochemical recurrence monitoring** (UFC, LNSC, DST) — recurrence up to **35%** in CD; USP8 genotype and tumor size may help predict recurrence risk; cardiovascular focus[24]
Comorbidity review	Per comorbidity schedule (e.g., HbA1c, BP, DEXA)	**Cardiovascular risk** persists in **40–60%** after remission — sustained management required[7]

ABBREVIATIONS: UFC = Urinary Free Cortisol; LNSC = Late-Night Salivary Cortisol; DST = Dexamethasone Suppression Test; HPA = Hypothalamic-Pituitary-Adrenal; LFT = Liver Function Test; ECG = Electrocardiogram; CD = Cushing's Disease; BP = Blood Pressure; DEXA = Dual-Energy X-ray Absorptiometry; HbA1c = Hemoglobin A1c

Comorbidity Management — Primary Care Role

COMORBIDITY	APPROACH	CAUTION
Secondary hypertension (I15.2, with E24.0 as underlying cause)[33]	**First-line antihypertensives (ACE inhibitors/ARBs**, calcium channel blockers); add mineralocorticoid receptor antagonist if resistant; reassess as cortisol normalizes	Expect resistance until cortisol is controlled
CS-related diabetes (E08.-, with E24.0 as underlying cause — not E11.-)[34]	**Metformin first-line**; insulin often required due to steroid-induced insulin resistance; monitor HbA1c closely	Anticipate worsening on pasireotide

COMORBIDITY	APPROACH	CAUTION
Osteoporosis (M80.-/M81.-, with E24.0 as underlying cause)[26]	**DEXA screening**; calcium/vitamin D **supplementation**; weight-bearing/resistance exercise; consider biologics (e.g., denosumab) for high fracture risk	Fragility fracture may be the presenting event
Depression/cognition (F32.-/F33.-, coded as separate manifestation)[26]	**Standardized screening** (e.g., PHQ-9); refer to psychiatry/psychology; consider SSRIs if indicated; cognitive rehabilitation as needed	Persists after remission
Post-surgical adrenal insufficiency (E27.40)[26]	**Glucocorticoid replacement**; stress-dosing plan; patient education on sick-day rules; provide emergency injectable hydrocortisone kit	Document emergency-kit and medical-alert education

ABBREVIATIONS: CS = Cushing's Syndrome; DEXA = Dual-Energy X-ray Absorptiometry

Cost-Smart Options

BRAND (EST. COST)*	COST-SMART OPTION*	EST. SAVINGS	NOTE
Recorlev (levoketoconazole), brand (~$20,040/50 tablets, ~28–30-day course)[35]	Generic **ketoconazole**, off-label (**~$23–$84/30-day supply** at standard dose)[36]	**~$19,950+/month**	Reserve levoketoconazole for patients who fail or cannot tolerate generic ketoconazole; **both carry boxed warnings for hepatotoxicity and QT prolongation** requiring monitoring
Isturisa (osilodrostat), brand (~$11,550–$16,187/month)[37,38]	**Metyrapone** (Metopirone), brand-only — no generic exists (**~$501/supply**)[39]	**~$11,000–$16,000/month**	Metyrapone is used off-label in the US; may serve as a **lower-cost second-line option** pending response and tolerability
Korlym (mifepristone), brand (~$19,777–$49,046/28 tablets)[40,41]	Generic **mifepristone** (**~$10,325** with discount coupon)[41]	**~$9,000–$38,000/month**	Confirm specialty-pharmacy benefit allows generic substitution before prescribing brand

BRAND (EST. COST)*	COST-SMART OPTION*	EST. SAVINGS	NOTE
Xarelto (rivaroxaban) for VTE prophylaxis, brand (~$600/30-day supply)[42]	Generic **enoxaparin** (**~$30–$150/30-day supply**)[43]	~$350–$600/ month	**VTE prophylaxis is low-cost relative to a single thromboembolism hospitalization**; proactive prescribing protects against the highest-cost complication of hypercortisolism

ABBREVIATIONS: CD = Cushing's Disease; LNSC = Late-Night Salivary Cortisol; UFC = Urinary Free Cortisol; VTE = Venous Thromboembolism; HR = Hazard Ratio ***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

CLINICAL PEARL

Successful treatment often results in lifelong glucocorticoid (and sometimes mineralocorticoid) dependence, as the adrenal glands no longer respond to physiologic stress independently. Patients require education on **sick-day dosing**(doubling or tripling oral doses during illness or physical stress), an **emergency injection kit**, and **medical-alert identification**. A missed dose or unrecognized stressor can precipitate adrenal crisis. These behaviors require reinforcement at every visit, as adherence often declines during extended periods without acute illness.

Patient Education and Adherence

- Explain that Cushing's syndrome reflects **too much cortisol** (usually from a small tumor) and that **symptoms are caused by the disease, not personal failings**
- **Set expectations honestly:** after successful treatment, patients may **feel unwell for 6–9 months**. Mood improves gradually, and recovery may continue beyond a year. A prospective study found clinically meaningful quality-of-life improvement in only **64.6%** of treated patients, and a meta-analysis confirmed that QoL and cognition improve but do not normalize versus controls[44,45]
- **Teach adrenal-insufficiency awareness**: stress dosing for illness, an emergency injectable-steroid kit, a medical-alert bracelet, and the signs of adrenal crisis. Emphasize that recurrence can occur years later, so annual follow-up is lifelong

DOCUMENTATION REMINDER — PATIENT EDUCATION AND SAFETY

Record the **patient-education encounter** itself: adrenal-insufficiency and stress-dosing counseling, the emergency-steroid plan, vaccination offers, and the lifelong-monitoring discussion. For any patient on **mifepristone**, document in the medication list and to ED providers that adrenal-crisis rescue requires **dexamethasone**, not hydrocortisone.

CLINICAL PEARL: CUSHING'S SICK DAY MANAGEMENT

Cushing's sick-day management depends on the treatment phase. In **active, untreated Cushing's disease**, minor illness generally does not require medication changes, but acute stress can transiently worsen hyperglycemia, hypertension, and psychiatric symptoms. Therefore PCPs should monitor glucose and blood pressure more closely and adjust concurrent medications with endocrinology guidance.

In **post-surgical or post-radiation adrenal insufficiency**, patients on daily glucocorticoid replacement must follow steroid sick-day rules: no dose change for mild illness without fever, **double the hydrocortisone dose** for fever >38.5°C or infection, and repeat the dose if vomited within 30 minutes; if oral dosing cannot be tolerated, an **emergency hydrocortisone injection** is required to prevent adrenal crisis.

Quality Metrics Tie-In

There are no HEDIS, Star, or MIPS measures that specifically target Cushing's disease. Quality performance is documented indirectly through standard comorbidity measures for the conditions Cushing's disease drives, such as **hypertension, diabetes, and osteoporosis.**

MEASURE[46,47,48]	STANDARD	APPLICABILITY TO CUSHING'S DISEASE
Controlling High Blood Pressure (HEDIS CBP/NQF 0018; MIPS #236)	**Denominator:** patients 18-85 with hypertension (≥2 outpatient visits with HTN diagnosis in MP or year prior) **Numerator:** most recent BP <140/90 mmHg during MP **Exclusions:** ESRD, hospice, palliative care, pregnancy[50]	Hypertension in CS has a multifactorial pathogenesis and is a major driver of cardiovascular mortality, the **leading cause of death** in this disease
Comprehensive Diabetes Care: Glycemic Status (HEDIS GSD; MIPS #001)	**Denominator:** patients 18-75 with diabetes (≥2 diagnoses on different service dates in MP or prior year, or diagnosis + dispensed diabetes medication) **Numerator (inverse):** most recent HbA1c >9.0% or missing **Exclusions:** hospice, palliative care, frailty + advanced illness (≥66)[51]	**Unrecognized CS undermines glycemic control** independent of standard diabetes management

MEASURE[46,47,48]	STANDARD	APPLICABILITY TO CUSHING'S DISEASE
Comprehensive Diabetes Care: Eye Exam (HEDIS EED; MIPS #117)	**Denominator:** patients 18-75 with diabetes **Numerator:** retinal or dilated eye exam by an eye care professional during MP, or in the prior 12 months if no diagnosed retinopathy **Exclusions:** hospice, palliative care[52]	Complete annual retinal exam **alongside HbA1c** and nephropathy screening as part of the full diabetes surveillance bundle for CS-related secondary diabetes
Osteoporosis Management in Women After Fracture (HEDIS OMW; MIPS #418)	**Denominator:** women 50-85 with a fracture during MP or year prior **Numerator:** BMD test or pharmacotherapy for osteoporosis prescribed within 180 days of fracture **Exclusions:** fractures of finger, toe, face, skull; hospice; frailty + advanced illness (≥66)[53]	CS-associated osteoporotic fractures in women **≥67** trigger this measure; ensure pharmacologic treatment is initiated within 6 months of fracture, not just within the measure's 180-day window
Statin Therapy for CVD/ Diabetes (HEDIS SPC; MIPS #438)	**Denominator:** patients with ASCVD diagnosis; OR age ≥20 with LDL-C ≥190 mg/dL or familial hypercholesterolemia; OR age 40-75 with diabetes; OR age 40-75 with 10-year ASCVD risk ≥20% **Numerator:** statin therapy prescribed or active during performance period **Exclusions:** active liver disease, ESRD, hospice, palliative care[54]	CS patients with cardiovascular disease or diabetes are documented under standard SPC criteria; **ensure all CS-related comorbidities** (hypertension, diabetes, dyslipidemia) **are accurately coded so the denominator correctly identifies these patients**

ABBREVIATIONS: ASCVD = atherosclerotic cardiovascular disease; BMD = bone mineral density; BP = blood pressure; CBP = Controlling High Blood Pressure; CS = Cushing's syndrome; CVD = cardiovascular disease; EED = Eye Exam for Patients with Diabetes; ESRD = end-stage renal disease; GSD = Glycemic Status Assessment; HbA1c = hemoglobin A1c; HEDIS = Healthcare Effectiveness Data and Information Set; LDL-C = low-density lipoprotein cholesterol; MIPS = Merit-based Incentive Payment System; MP = measurement period; NQF = National Quality Forum; OMW = Osteoporosis Management in Women Who Had a Fracture; SPC = Statin Therapy for Patients with Cardiovascular Disease. No HEDIS, Star, or MIPS measure is specific to Cushing's syndrome; relevance is via comorbidity measures

QUALITY OUTCOME

Early recognition of Cushing's disease in the at-risk patient is essential. The current **3-6 year** diagnostic delay allows preventable cardiovascular, thromboembolic, and skeletal complications to accumulate before treatment begins. Good practices that align with quality metrics will reduce preventable cardiovascular, thromboembolic, and fracture events.
This means the concerns in a patient with resistant hypertension, difficult diabetes, proximal weakness, or new fractures are addressed early. Accurate coding follows naturally from a record that represents this complexity, and better outcomes follow from earlier, coordinated care: reduced cardiovascular events given that risk persists in patients even after remission, lower fracture incidence through earlier DEXA screening and osteoporosis treatment, and reduced VTE-related hospitalization through proactive prophylaxis during active hypercortisolism.

AAVBC PERSPECTIVE

*AAVBC supports the **initiation of biochemical screening once the 5 P's are present in patients**. Preferred first-line screening includes late-night salivary cortisol or the one milligram overnight dexamethasone suppression test. The 24-hour urinary free cortisol result is **insufficient** to exclude the diagnosis when cyclical disease is suspected, as cortisol elevation in CD can be intermittent and a single normal result does not rule out the condition.**This ensures the right patients get the right evaluation and the right treatment at the right time.***

5 CODING REMINDERS AND CASE EXAMPLES

Coding Specificity

CODE	SPECIFICITY REQUIREMENT	COMMON ERROR
E24.0 (Pituitary-dependent Cushing's disease)	**Document ACTH-dependent hypercortisolism + pituitary source** (confirmed or suspected) + MRI findings; maps to HCC 51	Defaulting to **E24.9** when the pituitary source is known

CODE	SPECIFICITY REQUIREMENT	COMMON ERROR
E24.1 (Nelson's) **E24.2 (drug-induced)** **E24.3 (ectopic ACTH)** **E24.4 (alcohol-induced pseudo)** **E24.8 (other CS)**	**Document the specific etiology**	Confusing **E24.2** with **E24.0**; using **E24.8** as a catch-all
E24.9 (Cushing's syndrome, unspecified)	Replace with a specific subcode once etiology is determined	Most overused code in the category; retained after etiology is known
E08.- (list E24.0 first;CS-related diabetes)	**Diabetes due to an underlying condition**; preserves the causal chain and separate HCC	Using **E11.-** (type 2 diabetes), which severs the causal link
I15.2 (list E24.0 first;Secondary hypertension from an endocrine disorder)	**Hypertension secondary to hypercortisolism**	Using **I10** (essential hypertension)
M80.-/M81.- (Osteoporosis with/without current pathological fracture)	Document DEXA and **E24.0** as the underlying cause	Omitting the causal link to Cushing's disease[23]
Z87.39 (Personal history of endocrine disorder — after confirmed remission)	**Does not carry risk-adjustment weight**; use only post-remission	Applying it while disease is still clinically active

ABBREVIATIONS: CD = Cushing's Disease; CS = Cushing's Syndrome; ACTH = Adrenocorticotropic Hormone; MRI = Magnetic Resonance Imaging; HCC = Hierarchical Condition Category; DEXA = Dual-Energy X-ray Absorptiometry; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification

Annual Clinical Review and Confirmation

- **Annual clinical review and confirmation:** Cushing's disease requires lifelong surveillance, so the active diagnosis must be confirmed and re-documented at least annually for as long as it remains clinically active. Each year, restate the specific etiology **(E24.0)** and the evidence that supports it rather than allowing the record to drift back to **E24.9**
- **Re-document each manifestation and its causal link to hypercortisolism:** secondary hypertension **(I15.2)**, diabetes due to an underlying condition **(E08.-)**, osteoporosis **(M80.-/M81.-)**, depression **(F32.-/F33.-)**, and proximal myopathy **(M62.81)**. Manifestations do not carry forward automatically; they must be addressed in the note each year to be documented
- **After confirmed remission, transition the active E24.0 code to Z87.39** (personal history) only once the disease is truly inactive — recognizing that **Z87.39** does not carry risk-

adjustment weight and that recurrence requires ongoing monitoring. If surveillance detects recurrence, the active diagnosis returns to the record

- **Where cyclical disease has been demonstrated, document the pattern so that intermittently normal biochemical results are interpreted in context and continued monitoring is supported.** The annual review is the moment to reconcile imaging, biochemistry, and functional status into a single accurate clinical picture

Good Documentation — EHR Tips

EHR TIP	HOW IT HELPS
Problem-list entry: 'Pituitary-dependent Cushing's disease (E24.0)' — not 'Cushing's syndrome'	Anchors the specific code and prevents drift to **E24.9**
Causal-chain SmartPhrase linking each comorbidity to E24.0	Generates **I15.2, E08.-, M80.-/M81.-** with the underlying cause in one structured note
Cyclical-disease flag in the chart	Explains intermittently normal results and supports continued testing
Medication-list alert for mifepristone: 'adrenal-crisis rescue = dexamethasone, NOT hydrocortisone'	Communicates the non-intuitive rescue protocol to any ED provider
Annual recurrence-surveillance reminder	Prompts UFC/LNSC/DST monitoring given recurrence in CD

ABBREVIATIONS: EHR = Electronic Health Record; CD = Cushing's Disease; UFC = Urinary Free Cortisol; LNSC = Late-Night Salivary Cortisol; DST = Dexamethasone Suppression Test; ED = Emergency Department

Brief Case Examples

SUCCESS: Pattern Recognized, Etiology Specified, Complexity Represented

Patient: Female patient, 71, with 3 years of worsening 'resistant hypertension,' new difficult-to-control diabetes, and a recent low-trauma vertebral fracture.

Documentation: 71 y/o F with 3-year history of resistant HTN on 3 agents, new-onset T2DM poorly controlled despite metformin and insulin, and a low-trauma T12 compression fracture last month. Exam notable for central weight gain, facial plethora, dorsocervical fat pad, and violaceous striae. Given ≥3 atypical features, hypercortisolism suspected; exogenous glucocorticoid use excluded on review of medication history. Ordered LNSC x2 and 1-mg overnight DST — both abnormal. Referred to endocrinology for further workup.

Coding: Record reframed to **E24.0** (pituitary-dependent Cushing's disease) with **I15.2**, **E08.-**, and **M80.-** each linked causally to hypercortisolism; **E24.0** maps to **HCC 51.**

Outcome: Transsphenoidal surgery achieved biochemical remission; glucocorticoid replacement and stress-dosing education documented; lifelong annual surveillance initiated with cardiovascular focus.

PITFALL: Unspecified Coding and a Severed Causal Chain

Documentation as written: 71 y/o F with history of hypertension, type 2 diabetes, obesity, and Cushing's syndrome. Continue current antihypertensives and diabetes medications. Follow up in 6 months. **Coded as: I10**, **E11.9**, and **E24.9**, despite a prior confirmed pituitary source on record.

Consequence: The unspecified code (**E24.9**) and the severed causal chain under-represent a multisystem disease; the record loses **HCC 51** and the separate manifestation complexity.

Risk-Representation Impact: E24.0 + E08.- + I15.2 + M80.- represents the true complexity; **E24.9 + E11.9 + I10** does not.

Fix: Reframe to **E24.0** with each comorbidity (**I15.2**, **E08.-**, **M80.-**) linked causally to hypercortisolism; confirm and re-document the active diagnosis annually until remission.

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