AAVBC
AMERICAN ACADEMY OF VALUE BASED CARE

Cushing's Disease

Quick Reference Guide

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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,

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