Cushing's disease etiology

- Postoperative Initiation of Thromboprophylaxis in patients with Cushing's Disease (PIT-CD): a randomized controlled trial
- Predictors of cancer in patients with endogenous Cushing's syndrome
- Survival probabilities in patients with ectopic Cushing's syndrome-a systematic review and a single-arm meta-analysis
- From hyperplasia to carcinoma: a molecular driven adrenal disease
- Symptomatic venous thromboembolism after transsphenoidal surgery in Cushing's disease: incidence and risk factors
- Prevalence and clinical associations of USP8 variants in corticotroph tumours: a systematic review and aggregate data meta-analysis of 2171 cases
- Utility of intraoperative ultrasound in identifying pituitary adenoma hidden behind a cystic lesion in Cushing's disease
- Non-recurrent mutations and copy number changes predominate pituitary adenoma genomes

The etiology of Cushing's disease involves the development of an adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma, leading to excessive production of cortisol by the adrenal glands. Below are the main components of its etiology:

1. Pituitary Adenomas (Corticotroph Adenomas): Cushing's disease is caused by benign tumors of the pituitary gland (corticotroph adenomas) that secrete excess ACTH. These adenomas stimulate the adrenal cortex to overproduce cortisol, leading to hypercortisolemia. The adenomas are usually microadenomas (<10 mm in size), though macroadenomas (>10 mm) can also occur. 2. Genetic Factors: While most cases of Cushing's disease are sporadic, there are rare familial cases associated with genetic syndromes such as: Multiple Endocrine Neoplasia type 1 (MEN1): A genetic syndrome that predisposes individuals to multiple endocrine tumors, including pituitary adenomas. Carney Complex: A genetic disorder that involves the development of various tumors, including pituitary adenomas. Familial Isolated Pituitary Adenomas (FIPA): A hereditary condition that leads to the formation of pituitary tumors, including ACTH-secreting adenomas. Mutations in genes such as USP8 (ubiquitin-specific protease 8) have been identified in a subset of patients with Cushing’s disease, affecting tumor growth and ACTH secretion. 3. Hormonal Dysregulation: The pituitary corticotroph adenoma is thought to arise from dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. Normally, cortisol secretion is regulated by negative feedback: cortisol inhibits ACTH secretion. In Cushing's disease, this feedback loop is disrupted, leading to unchecked ACTH and cortisol production. 4. Possible Triggers: Although the exact cause of the development of the pituitary adenoma is often unknown, certain risk factors may contribute to the formation of adenomas: Somatic mutations (e.g., in USP8) are believed to play a role in altering cell signaling pathways and promoting tumor development. Growth factors and altered signaling pathways in pituitary cells could contribute to adenoma formation. 5. Secondary Causes: Rarely, external factors such as irradiation or previous pituitary surgery for other conditions may be implicated in the development of secondary pituitary adenomas, though this is uncommon. In summary, the primary etiology of Cushing's disease is the formation of a pituitary corticotroph adenoma that secretes excessive ACTH, leading to increased cortisol production. While most cases are sporadic, a subset may be associated with genetic mutations or syndromes.