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Characteristics, diagnosis and management of Cushing's disease - A systematic review and meta-analysis

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Introduction: The clinical practice and research in the diagnosis and management of Cushing's disease remains heterogeneous and challenging to this day. We sought to establish the characteristics of Cushing's disease, and the trends in diagnosis, management and reporting in this field.

Methods: Searches of PubMed and Embase were conducted. Study protocol was registered a-priori. Random-effects analyses were conducted to establish numerical estimates.

Results: Our screening returned 159 papers.

The average age of adult patients with Cushing's disease was 39.3, and 13.6 for children. The male:female ratio was 1:3. 8% of patients had undergone previous transsphenoidal resection. The ratio of macroadenomas: microadenomas:imaging-undetectable adenomas was 18:53:29. The most commonly reported preoperative biochemical investigations were serum cortisol (average 26.4µg/dL) and ACTH (77.5pg/dL). Postoperative cortisol was most frequently used to define remission (74.8%), most commonly with threshold of 5µg/dL (44.8%). Average remission rates were 77.8% with recurrence rate of 13.9%. Median follow-up was 38 months.

Majority of papers reported age (81.9%) and sex (79.4%). Only 56.6% reported whether their patients had previous pituitary surgery. 45.3% reported whether their adenomas were macroadenoma, microadenoma or undetectable. Only 24.1% reported preoperative cortisol, and this did not improve over time. 60.4% reported numerical thresholds for cortisol in defining remission, and this improved significantly over time ($p=0.004$). Visual inspection of bubbleplots showed increasing preference for threshold of 5µg/dL. 70.4% reported the length of follow up.

Conclusion: We quantified the characteristics of Cushing's disease, and analysed the trends in investigation and reporting. This review may help to inform future efforts in forming guidelines for research and clinical practice.