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Wang, WH; Zhang, HD; Zhang, F; Dong, HX.

**Corresponding author:**

Huixiao Dong

donghx2026hx@163.com

**Author Affiliation:**

Jining First People's Hospital.

**ADMINISTRATIVE INFORMATION****Support** - This study did not receive any funding in any form.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202650157**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 May 2026 and was last updated on 28 May 2026.**INTRODUCTION**

**Review question / Objective** Transsphenoidal surgery remains a principal treatment for most functioning and symptomatic non-functioning pituitary adenomas, but the relative endocrine and safety outcomes of endoscopic transsphenoidal surgery (ETS) and microscopic transsphenoidal surgery (MTS) remain debated.

**Condition being studied** Prior systematic reviews comparing endoscopic transsphenoidal surgery with microscopic transsphenoidal surgery have reported heterogeneous conclusions for gross total resection, endocrine remission, and complications. Endocrine endpoints are particularly difficult to synthesize because biochemical remission in functioning adenomas is clinically distinct from preservation of pituitary function in non-functioning tumors. Consensus criteria for acromegaly and disease-specific endocrine remission standards have changed over time, while reporting of pituitary axes after surgery remains inconsistent.

This review therefore evaluates the contemporary comparative literature with explicit attention to the conceptual heterogeneity of endocrine-success definitions, the low number of randomized data sources, and the potential for confounding by indication in observational cohorts.

**METHODS**

**Participant or population** Adults with radiologically or histologically confirmed pituitary adenomas.

**Intervention** The eligibility criteria, outcomes, and analysis plan were specified before extraction of outcome data. PubMed/MEDLINE, Embase, Web of Science Core Collection, Cochrane Library, and Scopus were searched from January 1, 2010, to March 1, 2025, with additional screening of ClinicalTrials.gov and reference lists. The 2010 start date was selected to focus on contemporary ETS practice, because widespread adoption of modern high-definition endoscopes, angled endoscopic visualization, and multilayer skull-base

reconstruction after endoscopic pituitary surgery matured after this period. The PubMed strategy combined free-text and Medical Subject Headings (MeSH) terms for pituitary neoplasms, endoscopy, microscopic or transsphenoidal surgery, and endocrine or complication outcomes: ("Pituitary Neoplasms"[MeSH] OR "pituitary adenoma" OR "pituitary tumor" OR "pituitary tumour" OR acromegaly OR "Cushing disease") AND ("Endoscopy"[MeSH] OR endoscopic OR endonasal) AND (microscopic OR transsphenoidal OR "trans-sphenoidal") AND (endocrine OR hormone OR hypopituitarism OR remission OR "Diabetes Insipidus"[MeSH] OR "Cerebrospinal Fluid Leak"[MeSH]). Database-specific syntax was adapted without study-design filters, and English-language human studies were screened.

**Comparator** The eligibility criteria, outcomes, and analysis plan were specified before extraction of outcome data. PubMed/MEDLINE, Embase, Web of Science Core Collection, Cochrane Library, and Scopus were searched from January 1, 2010, to March 1, 2025, with additional screening of ClinicalTrials.gov and reference lists. The 2010 start date was selected to focus on contemporary ETS practice, because widespread adoption of modern high-definition endoscopes, angled endoscopic visualization, and multilayer skull-base reconstruction after endoscopic pituitary surgery matured after this period. The PubMed strategy combined free-text and Medical Subject Headings (MeSH) terms for pituitary neoplasms, endoscopy, microscopic or transsphenoidal surgery, and endocrine or complication outcomes: ("Pituitary Neoplasms"[MeSH] OR "pituitary adenoma" OR "pituitary tumor" OR "pituitary tumour" OR acromegaly OR "Cushing disease") AND ("Endoscopy"[MeSH] OR endoscopic OR endonasal) AND (microscopic OR transsphenoidal OR "trans-sphenoidal") AND (endocrine OR hormone OR hypopituitarism OR remission OR "Diabetes Insipidus"[MeSH] OR "Cerebrospinal Fluid Leak"[MeSH]). Database-specific syntax was adapted without study-design filters, and English-language human studies were screened.

**Study designs to be included** The search identified 3,542 records (PubMed/MEDLINE n = 1,050; Embase n = 1,200; Web of Science Core Collection n = 750; Scopus n = 450; Cochrane Library n = 85; ClinicalTrials.gov/reference lists n = 7), 2,847 unique records after duplicate removal, and 45 full-text articles for eligibility assessment. Thirty-seven full-text articles were excluded because they lacked a microscopic comparator, did not provide stratified endocrine or complication outcomes, mixed adenomas with other

pathologies, reported overlapping populations, had insufficient sample size, or were not available in English.

**Eligibility criteria** Eligible studies enrolled adults with radiologically or histologically confirmed pituitary adenomas and directly compared pure ETS with conventional MTS. Studies limited to non-adenomatous sellar lesions, pediatric populations, reoperations, salvage surgery after radiotherapy, mixed skull-base pathologies without adenoma-specific results, or single-arm series were excluded. The primary endpoint was endocrine success, defined according to the source article as biochemical remission for functioning tumors or preservation of pituitary function for mixed or non-functioning cohorts. This composite endpoint was used for quantitative synthesis because it represented the most consistently extractable endocrine outcome across comparative studies; however, it combines clinically distinct outcomes and is interpreted as a broad comparative signal rather than a single biological endpoint. Secondary outcomes included postoperative diabetes insipidus, CSF leak requiring intervention, and new postoperative hypopituitarism.

**Information sources** The PubMed strategy combined free-text and Medical Subject Headings (MeSH) terms for pituitary neoplasms, endoscopy, microscopic or transsphenoidal surgery, and endocrine or complication outcomes: ("Pituitary Neoplasms"[MeSH] OR "pituitary adenoma" OR "pituitary tumor" OR "pituitary tumour" OR acromegaly OR "Cushing disease") AND ("Endoscopy"[MeSH] OR endoscopic OR endonasal) AND (microscopic OR transsphenoidal OR "trans-sphenoidal") AND (endocrine OR hormone OR hypopituitarism OR remission OR "Diabetes Insipidus"[MeSH] OR "Cerebrospinal Fluid Leak"[MeSH]). Database-specific syntax was adapted without study-design filters, and English-language human studies were screened.

**Main outcome(s)** The PubMed strategy combined free-text and Medical Subject Headings (MeSH) terms for pituitary neoplasms, endoscopy, microscopic or transsphenoidal surgery, and endocrine or complication outcomes: ("Pituitary Neoplasms"[MeSH] OR "pituitary adenoma" OR "pituitary tumor" OR "pituitary tumour" OR acromegaly OR "Cushing disease") AND ("Endoscopy"[MeSH] OR endoscopic OR endonasal) AND (microscopic OR transsphenoidal OR "trans-sphenoidal") AND (endocrine OR hormone OR hypopituitarism OR remission OR "Diabetes Insipidus"[MeSH] OR "Cerebrospinal

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Fluid Leak"[MeSH]). Database-specific syntax was adapted without study-design filters, and English-language human studies were screened.

**Quality assessment / Risk of bias analysis** Risk of bias was evaluated with Cochrane Risk of Bias 2 (RoB 2) principles for randomized data and ROBINS-I domains for observational studies. Statistical analyses were performed in R version 4.3.0 using the meta and metafor packages, and risk-of-bias graphics were prepared. Risk ratios with 95% CIs compared ETS with MTS. Random-effects models were prespecified as primary because of clinical and methodological heterogeneity across institutions, time periods, surgical expertise, tumor types, and endocrine definitions. Heterogeneity was summarized with I<sup>2</sup>, tau-squared, and prediction intervals when applicable. Funnel plots were generated only as exploratory visual displays because fewer than 10 studies contributed to the primary analysis, making formal asymmetry tests unreliable.

**Strategy of data synthesis** Risk of bias was evaluated with Cochrane Risk of Bias 2 (RoB 2) principles for randomized data and ROBINS-I domains for observational studies. Statistical analyses were performed in R version 4.3.0 using the meta and metafor packages, and risk-of-bias graphics were prepared. Risk ratios with 95% CIs compared ETS with MTS. Random-effects models were prespecified as primary because of clinical and methodological heterogeneity across institutions, time periods, surgical expertise, tumor types, and endocrine definitions. Heterogeneity was summarized with I<sup>2</sup>, tau-squared, and prediction intervals when applicable. Funnel plots were generated only as exploratory visual displays because fewer than 10 studies contributed to the primary analysis, making formal asymmetry tests unreliable.

**Subgroup analysis** Risk of bias was evaluated with Cochrane Risk of Bias 2 (RoB 2) principles for randomized data and ROBINS-I domains for observational studies. Statistical analyses were performed in R version 4.3.0 using the meta and metafor packages, and risk-of-bias graphics were prepared. Risk ratios with 95% CIs compared ETS with MTS. Random-effects models were prespecified as primary because of clinical and methodological heterogeneity across institutions, time periods, surgical expertise, tumor types, and endocrine definitions. Heterogeneity was summarized with I<sup>2</sup>, tau-squared, and prediction intervals when applicable. Funnel plots were generated only as exploratory visual displays because fewer than 10 studies contributed to the

primary analysis, making formal asymmetry tests unreliable.

**Sensitivity analysis** Risk of bias was evaluated with Cochrane Risk of Bias 2 (RoB 2) principles for randomized data and ROBINS-I domains for observational studies. Statistical analyses were performed in R version 4.3.0 using the meta and metafor packages, and risk-of-bias graphics were prepared. Risk ratios with 95% CIs compared ETS with MTS. Random-effects models were prespecified as primary because of clinical and methodological heterogeneity across institutions, time periods, surgical expertise, tumor types, and endocrine definitions. Heterogeneity was summarized with I<sup>2</sup>, tau-squared, and prediction intervals when applicable. Funnel plots were generated only as exploratory visual displays because fewer than 10 studies contributed to the primary analysis, making formal asymmetry tests unreliable.

**Country(ies) involved** China - Jining First People's Hospital.

**Keywords** Pituitary Neoplasms, Transsphenoidal Surgery, Neuroendoscopy.

#### **Contributions of each author**

Author 1 - Wencheng Wang.

Author 2 - Haidong Zhang.

Author 3 - Feng Zhang.

Author 4 - Huixiao Dong.