Bijlagen bij Conceptrichtlijn Hypofysechirurgie

INITIATIEF
Nederlandse Vereniging voor Neurologie

IN SAMENWERKING MET
Nederlandse Internisten Vereniging
Nederlands Oogheelkundig Gezelschap
Nederlandse Vereniging voor Keel-Neus-Oorheelkunde
Nederlandse Vereniging Radiotherapie en Oncologie
Nederlandse Vereniging voor Radiotherapie
Verpleegkundigen en Verzorgenden Nederland
Nederlandse Hypofyse Stichting

MET ONDERSTEUNING VAN
Het Kennisinstituut van de Federatie Medisch Specialisten.

FINANCIERING
De richtlijnontwikkeling werd gefinancierd uit de Stichting Kwaliteitsgelden Medisch Specialisten (SKMS).

Colofon
CONCEPTRICHTLIJN HYPOFYSECHIRURGIE

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Inhoudsopgave

Verantwoording

Voor meer details over de gebruikte richtlijnmethodologie verwijzen wij u naar de Werkwijze. Relevante informatie voor de ontwikkeling/herziening van deze richtlijnmodule is hieronder weergegeven.

Algemene gegevens

De ontwikkeling/herziening van deze richtlijnmodule werd ondersteund door het Kennisinstituut van de Federatie Medisch Specialisten (www.demedischspecialist.nl/kennisinstituut) en werd gefinancierd door de Stichting Kwaliteitsgelden Medisch Specialisten (SKMS).
De financier heeft geen enkele invloed gehad op de inhoud van de richtlijnmodule.

Samenstelling werkgroep

Voor het ontwikkelen van de richtlijnmodule is in 2024 een multidisciplinaire werkgroep ingesteld, bestaande uit vertegenwoordigers van alle relevante specialismen (zie hiervoor de Samenstelling van de werkgroep) die betrokken zijn bij de zorg voor patiënten die hypofyse chirurgie ondergaan.

Belangenverklaringen

Een overzicht van de belangen van werkgroepleden en het oordeel over het omgaan met eventuele belangen vindt u in onderstaande tabel. De ondertekende belangenverklaringen zijn op te vragen bij het secretariaat van het Kennisinstituut van de Federatie Medisch Specialisten via secretariaat@kennisinstituut.nl.

Tabel 1 Gemelde (neven)functies en belangen werkgroep

Naam	Hoofdfunctie	Nevenwerkzaamheden	Persoonlijke financiële belangen	Persoonlijke relaties	Extern gefinancierd onderzoek	Intellectuele belangen en reputatie	Overige belangen	Datum	Restrictie
Marco Verstegen (voorzitter)	Neurochirurg in LUMC	Neurochirurg in Alrijne ziekenhuis Leiderdorp; Voormalig trekker van thema hypofysechirurgie NVvN (onbetaald), voorzitter voormalige richtlijn (>3 jaar geleden), Organisatie CAPITAL hypofyse congress	geen	geen	geen	geen	Samenwerking met de Nederlandse Hypofysestichting (non-profit) in vorm van artikelen voor het tijdschrift, webinars etc.	25-03-2026	Geen restricties
Amir Zamanipoor Najafabadi	AIOS, LUMC	Bestuurdslid LVAO (Landelijke Vereniging van Arts-Assistenten Oogheelkunde)	Geen	Geen	Geen	Proefschrift op gebied van neurochirurgie en meningeomen (afgerond).	Geen	07-04-2026	Geen restricties
Annenienke van de Ven	internist-endocrinoloog, Radboudumc. Betaald.		geen	geen	Principal investigator in het Radboud van LINC-6 trial, gefinancieerd vanuit Recordati (studie naar langetermijn effecten van middel voor Cushing)	geen	Congres ECE stockholm (vergoeding reiskosten door Recordati)	26-03-2026	Geen restricties
Caroline van Rij	Radiotherapeut, ErasmusMC	Geen	Geen	Geen	Geen	Geen	Lid werkgroep zeldzame hersentumoren LWNO	09-04-2026	Geen restricties

Eline Leijtens	Verpleegkundig specialist hypofyse zorgpad LUMC	Bestuurslid landelijke werkgroep endocrinologie verpleegkundigen.	geen	geen	geen	geen	geen	31-03-2026	Geen restricties
Irene Notting	Oogarts LUMC fulltime	Geen	niet van toepassing	niet van toepassing	Geen	niet van toepassing	Geen	29-03-2026	Geen restricties
Jantien Hoogmoed	Neurochirurg in Amsterdam UMC	Neurochirurg in Zaans medisch Centrum en Anthonie van leeuwenziekenhuis	Ik heb geen persoonlijke financiële belangen	Er zijn geen mensen in mijn directe omgeving die baat kunnen hebben bij een bepaalde uitkomst.	Ipsen Farmaceutica BV Galant study: effect van lanreotide op groei van niet-functionerende hypofyse-adenomen Rol projectleider: nee	Ik ben voorzitter van de kwalteitsregistratie hypofysechirurgie (QRNS) van de Nederlandse Vereniging voor Neurochirurgie. In het Amsterdam UMC ben ik deel van de onderzoeksgroep hypofysetumoren waarin wij onder andere onderzoek doen naar het biologisch gedrag van hypofyse-adenomen.	Samenwerking met de Nederlandse Hypofysestichting in vorm van artikelen voor het tijdschrift, webinars etc.	25-03-2026	Geen restricties

Jeroen Vister	Radioloog UMCG	Geen	Geen	Nee	Geen	Geen	Geen	27-03-2026	Geen restricties
Johan de Graaf	Voorzitter Nederlandse Hypofyse Stichting (patientenorganisatie, onbetaald vrijwilligerswerk). Vanwege ziekte voortijdige beeïndiging arbeidscontract bij ING (sinds 2014, arbeidsongeschiktheidspensioen)	ePAG (European Patient Advocate Group) representative, verbonden aan Endo-ERN, het Europese Netwerk voor Zeldzame Endocriene Aandoeningen. Vrijwilligersfunctie, onbetaald, onkosten worden vergoed ePAG Steering Group Eurordis, vrijwilligersfunctie, onbetaald, onkostenvergoeding. Comité van de vertegenwoordigde ePAGs de 24 ERNs binnen Europa. (Meedenken over beleidsvraagstukken, onderling overleg en ideeënuitwisseling). Co-chair van de Patient Board van de European Society for Endocrinology (ESE), Vrijwilligersfunctie, onbetaald, onkosten worden gedeeltelijk vergoed Member of the Board of Directors van Eurordis, de Europese Koepelorganisatie voor zeldzame aandoeningen, Vrijwilligersfunctie, onbetaald, onkosten worden vergoed Lid van de Raad van Ervaringdeskundigen van de Hersenstichting, Vrijwilligersfunctie, onbetaald,	Geen	Geen	Hypofyse stichting voornamelijk gefinancieerd vanuit subsidie VWS en ledengelden. KIKA:Endo-Watch, ontwikkeling van een device voor het monitoren van kinderen met hypothalame schade, WKZ/PMC (geen projectleider) Pfizer:Towards an early diagnoses of growth hormone deficiency, WKZ/PMC (geen projectleider) KIKA:Hercules Study, onderzoek naar de lange termijn gevolgen van bestraling van het hypothalame/hypofysaire gebied bij kinderen, WKZ/PMC(geen projectleider) ZonMW:Prolact, onderzoek naar de verschillen tussen een medicamenteuze behandeling of neurochirurgische ingreep in het geval van een prolactnioom (geen projectleider).	Geen	lezingen met vergoeding bij pharmaceuten, niet specifiek over neurochirurgie. Deze gelden gaan naar de stichting.	26-03-2026	Geen restricties

		onkostenvergoeding (beoordelen voorstellen voor wetenschappelijk onderzoek op patientperspectief, meedenken over beleidsvraagstukken) Lid van de SEC (Scientific Evaluation Committee) van het EJP-RD-project (European Joint Program Rare Diseases, Vrijwilligersfunctie, onbetaald, onkostenvergoeding. (Beoordelen van Europees wetenschappelijk onderzoek op het patientpersectief) Lid van de HTA-Taskforce van Eurordis, vrijwilligersfunctie, onbetaald, onkostenvergoeding(meedenken over HTA-vraagstukken op Europees niveau) Co-chair Networking Evaluation Committee (NEC) van ERDERA's Networking Support Scheme. Beoordeling van voorstellen van Europese netwerkbijeenkomsten, vrijwilligersfunctie, onkostenvergoeding							
Maarten Kleijwegt	KNO arts bij LUMC	KNO arts in Alrijne ziekenhuis	geen	geen	geen	geen	Cursussen (over bijholte) gegeven aan KNO-artsen, honorarium betaald door Medtronic aan LUMC.	25-03-2026	Geen restricties

Melanie van der Klauw	Internist-endocrinoloog Universitair Medisch Centrum Groningen 1,0 fte	27-06-2023 Advisory board georganiseerd door Recordati Rare Diseases over de toekomst van gepersonaliseerde behandeling bij acromegalie patiënten: 1 bijeenkomst van 4,5 uur. De betaling hiervoor is ten gunste gekomen van het UMCG.	Geen	Geen	Diabetesfonds, Impaired awareness of hypoglycaemia in type 1 diabetes, projectleider (PI aanvankelijk niet, later wel)	Geen	11-14 mei 2024 Bezoek aan de European Congress of Endocrinologie 2024 gesponsord door Recordati Rare Diseases conform nationale wet- en regelgeving. Dit alles heeft mijn voorschrijfbeleid niet beïnvloed en zal dat ook niet doen. Noch heeft dit invloed op mijn mening over wat er beschreven gaat worden in de richtlijn hypofysechirurgie.	25-03-2026	Geen restricties
Nienke Biermasz	internist endocrinoloog LUMC	endoERN co chair hypofyse (EU referentie netwerk); Voorzitter Nationale hypofysenetwerk NVE; Organisatie CAPITAL hypofyse congress	geen	nee	Sharted PI van doelmatigheidsonderzoek ZonMW: Prolact, onderzoek naar de verschillen tussen een medicamenteuze behandeling of neurochirurgische ingreep in het geval van een prolactnioom	Geen	Samenwerking met de Nederlandse Hypofysestichting in vorm van artikelen voor het tijdschrift, webinars etc. Lezingen bij Recordati/ andere farmaceuten (incidenteel)	27-03-2026	Geen restricties
Rutger Balvers	Neurochirurg, Erasmus MC Rotterdam	Geen	Geen	Geen	Fase-1 studie ter onderzoek van de optimale dosering van FA-ICG als hulpmiddel bij de operatieve verwijdering van het maligne glioom, KWF GRANT 14121; gedeelde PI	Onderzoek PET-geleide chirurgie hypofysetumoren (geld beschikbaar vanuit Erasmus MC)	Geen	27-03-2026	Geen restricties

Inbreng patiëntenperspectief
De werkgroep besteedde aandacht aan het patiëntenperspectief door een afgevaardigde patiëntenorganisatie (Hypofyse Stichting) in de werkgroep. De conceptrichtlijn is tevens voor commentaar voorgelegd aan de Hypofyse Stichting en Patiëntenfederatie Nederland en de eventueel aangeleverde commentaren zijn bekeken en verwerkt.

Kwalitatieve raming van mogelijke financiële gevolgen in het kader van de Wkkgz
Bij de richtlijnmodule voerde de werkgroep conform de Wet kwaliteit, klachten en geschillen zorg (Wkkgz) een kwalitatieve raming uit om te beoordelen of de aanbevelingen mogelijk leiden tot substantiële financiële gevolgen. Bij het uitvoeren van deze beoordeling is de richtlijnmodule op verschillende domeinen getoetst (zie het stroomschema bij Werkwijze).

Module	Uitkomst raming	Toelichting
Module Preoperatieve workup	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling(en) niet breed toepasbaar zijn (<5.000 patiënten) en zal daarom naar verwachting geen substantiële financiële gevolgen hebben voor de collectieve uitgaven
Module Timing operatie bij chiasmasyndroom	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling(en) niet breed toepasbaar zijn (<5.000 patiënten) en zal daarom naar verwachting geen substantiële financiële gevolgen hebben voor de collectieve uitgaven
Module Timing operatie bij apoplexie	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling(en) niet breed toepasbaar zijn (<5.000 patiënten) en zal daarom naar verwachting geen substantiële financiële gevolgen hebben voor de collectieve uitgaven
Module Monitoring en behandeling van verstoringen waterhuishouding	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling(en) niet breed toepasbaar zijn (<5.000 patiënten) en zal daarom naar verwachting geen substantiële financiële gevolgen hebben voor de collectieve uitgaven
Module Postoperatieve surveillance	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling(en) niet breed toepasbaar zijn (<5.000 patiënten) en zal daarom naar verwachting geen substantiële financiële gevolgen hebben voor de collectieve uitgaven
Module Perioperatieve glucocorticoïdsubstitutie	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling(en) niet breed

		toepasbaar zijn (<5.000 patiënten) en zal daarom naar verwachting geen substantiële financiële gevolgen hebben voor de collectieve uitgaven
Module Rhinologische nazorg	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling(en) niet breed toepasbaar zijn (<5.000 patiënten) en zal daarom naar verwachting geen substantiële financiële gevolgen hebben voor de collectieve uitgaven
Module Uitval van functie als operatieindicatie	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling(en) niet breed toepasbaar zijn (<5.000 patiënten) en zal daarom naar verwachting geen substantiële financiële gevolgen hebben voor de collectieve uitgaven
Module Organisatie van zorg	Geen financiële gevolgen	Uit de toetsing volgt dat de aanbeveling(en) niet breed toepasbaar zijn (<5.000 patiënten) en zal daarom naar verwachting geen substantiële financiële gevolgen hebben voor de collectieve uitgaven

Module 1 – Preoperatieve workup

Uitgangsvraag

Hoe moet de preoperatieve work-up van patiënten met een hypofysetumor er uit zien?

Search and select

A systematic review of the literature was performed to answer the following question(s):
What is the predictive value of an OCT measurement on post-operative visual field outcomes and visual outcomes in people with a (suspected) pituitary tumor?

Table 1. PICOTS

Patients	Patients with pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst)
Instrument – 1	Prediction model of postoperative visual fields, based on numerical expression (continuous value of nerve damage) of OCT
Instrument – 2	Prediction model of postoperative best-corrected visual acuity (BCVA), based on numerical expression (continuous value of nerve damage) of OCT
Comparator instrument	None
Outcomes	Discrimination (Area Under the Curve (AUC) or C-statistic), calibration (slope of observed versus expected)
Timing	1 year postoperatively
Setting	Preoperative consultation with the ophthalmologist and multidisciplinary team meeting for treatment decision. (2nd/3rd line)
Other selection criteria	Study design: systematic reviews, randomized controlled trials and other comparative studies

Relevant outcome measures

The guideline panel considered discrimination and calibration as **critical** outcome measures for decision making.

The guideline panel considered definitions and thresholds for clinical relevance as defined in table 2.

Table 2. Definitions and thresholds

Outcome	Definition	Threshold
Critical outcome measures		
Discrimination	C-statistic/AUC: used definition in the used studies	C-statistic<0.6: poor discrimination 0.6≤C-statistic≤0.75: possibly helpful discrimination, C-statistic>0,75: useful discrimination AUC ≤0.5: no better than chance. 0.5<AUC <0.7: Poor. 0.7≤AUC <0.8: Generally considered acceptable. 0.8≤AUC <0.9: Considered excellent.

		AUC ≥ 0.9: Considered outstanding.
Calibration	Calibration slope; Observed/expected ratio, as defined in the used studies	Difference in calibration slope>0.1

Search and select (Methods)

A systematic literature search was performed by a medical information specialist using the following bibliographic databases: Embase.com and Ovid/Medline all. Both databases were searched from 2005 to March 4, 2025 for systematic reviews, RCTs and observational studies. Systematic searches were completed using a combination of controlled vocabulary and natural language keywords. The overall search strategy was derived from the following primary search concepts: (1) hypophysis tumor surgery; (2) optical coherence tomography. Duplicates were removed using EndNote software. After deduplication a total of 143 records were imported for title/abstract screening. Initially, 40 studies were selected based on title and abstract screening. After reading the full text, 37 studies were excluded (see the exclusion table under the tab 'Evidence tabellen'), and three studies were included.

Summary of literature

Description of studies

A total of three studies were included in the analysis of the literature. Important study characteristics and results are summarized in table 3. The assessment of the risk of bias is summarized in the risk of bias tables (under the tab 'Evidence tabellen').

Lee (2016) performed a retrospective cohort study to develop a nomogram that predicts postoperative recovery of visual field defects in patients with pituitary adenoma. Inclusion criteria were 1) histologically confirmed pituitary adenoma; (2) preoperative visual field impairment respecting the vertical meridian (bitemporal hemianopia or quadrantanopia on perimetry) caused by pituitary adenoma with external compression verified by MRI; (3) treatment via a trans-sphenoidal approach for decompression of the anterior visual pathway; and (4) comprehensive ophthalmological assessments performed at least once preoperatively (within 1 month before surgery) and at least twice postoperatively (at two or more of the following time points: within 1 week, 3 months, and 6 months after surgery). Exclusion criteria were: (1) a history of prior treatment (surgery or radiotherapy) and (2) the presence of any anterior segment, retinal, posterior segment, or optic nerve disease other than compressive optic neuropathy. In total, 111 eyes from 57 participants were included. Sequential changes in visual fields and retinal nerve fiber layer (RNFL) thickness were assessed. Restoration of visual field defect was considered achieved if the mean deviation (MD) was greater than –3 dB at the last follow-up. Multiple logistic regression analyses were used to construct nomograms. Model discrimination was evaluated with the area under the receiver operating characteristic curve (AUC), and calibration was assessed through graphical comparison of observed versus predicted outcomes. Internal validation was performed using the 200 bootstrapping method.

Meyer (2022) performed a single-center, 2 year, prospective, longitudinal cohort study to more definitively evaluate and compare the prognostic value of OCT macular ganglion cell layer (mGCL) and peripapillary retinal nerve fibre layers (pRNFL) measurements in predicting long-term visual outcomes following pituitary or parasellar surgical resection. Inclusion criteria were MRI evidence of pituitary or parasellar tumor compressing the optic chiasm, along with availability for two years of follow-up and written informed consent. Exclusion criteria were: (1) prior anterior segment, posterior segment, or optic nerve disease other than compressive optic neuropathy, including glaucoma; (2) cup-to-disc ratio asymmetry > 0.2; (3) focal notching or optic nerve hemorrhage; (4) unreliable visual field testing, defined

as > 25% false positives, false negatives, or fixation losses; or (5) spherical refractive error beyond >5 diopters (D) or astigmatism greater than 2D. In total, 216 eyes of 108 participants were included. Long-term visual field recovery and maintenance (defined as a mean deviation ≥– 3.5) and long-term visual acuity recovery and maintenance (defined as a logarithm of the minimum angle of resolution (LogMAR) of 0.3 (Snellen equivalent 20/40) or better at the 2 year postoperative follow-up visit) were outcomes of interest. One OCT parameter was fitted as a predictor at a time generating a total of 34 unique models. Multivariable logit risk prediction models were constructed and evaluated for the developmental and validation cohorts. Model discrimination was assessed in the validation cohort using the area under the receiver operating characteristic curve. The highest performing pRNFL and mGCL models were compared.

Wang (2020) performed a single-center, two-year prospective, longitudinal cohort study to evaluate the prognostic value of optical coherence tomography (OCT) parameters for long-term visual recovery and stability following pituitary tumor resection. Consecutive patients aged 16 years or older who underwent pituitary or parasellar tumor resection were included. Other inclusion criteria were MRI confirmation of optic chiasm compression due to the tumor and availability for a two-year postoperative follow-up. Exclusion criteria were: (1) previous anterior segment, posterior segment, or optic nerve disease (other than compressive optic neuropathy), including glaucoma; (2) cup-to-disc ratio asymmetry > 0.2, focal notching, or optic nerve hemorrhage; (3) spherical refractive error beyond >5D or astigmatism > 2D; and (4) unreliable preoperative visual field testing, defined as > 25% false positives, false negatives, or fixation losses. A total of 462 eyes of 239 patients were included. Outcomes of interest were long-term visual field recovery and maintenance (defined as a mean deviation greater than -3 at the 2-year post-operative follow-up visit) and long-term visual acuity recovery and maintenance (defined as a logMAR of 0 (Snellen visual acuity 20/20) or better at the 2-year post-operative follow-up visit). Developmental and validation samples for constructing and evaluating multivariable logit risk prediction models. Independent predictors (p<0.05) identified using multiple logistic regression analysis of the developmental sample were used to construct the multivariable logit risk prediction models.

Table 3. Characteristics of included studies

Study	Participants	Instrument	Follow-up	Outcome measures	Comments	Risk of bias (per outcome measure)*
Individual studies						
Lee, 2016	N at baseline N=57 Age (mean, SD) 48.1 ± 12.6 years Sex Not reported Event rate (%) Not reported Average preoperative MD: −10.1 ± 7.3 dB	<u>Index instrument:</u> Predictors: • MRI compression grade • Inferior RNFL thickness • Preoperative MD Outcome: Visual field recovery	6 months	Discrimination: AUC Calibration: observed outcome frequencies and predicted probabilities	Supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2013R1A1A2007865). No competing interests. Internal validation only.	High

	Average preoperative visual acuity (logMAR): 0.21 ± 0.32					
Meyer, 2022	N at baseline N=108 Age (mean, SD) 51.6 ± 17.04 Sex 55.6% male Event rate (%) Not reported Baseline best corrected visual acuity: 0.13 ± 0.27 Baseline visual field mean deviation: - 5.85 ± 6.77	Predictors: macular ganglion cell and retinal nerve fibre layer optical coherence tomographic parameters (see below) *RNFL thickness (per percent)* • Average • Superior nasal • Nasal • Inferior nasal • Superior temporal • Temporal • Inferior temporal *GCL thickness (per percent)* • Central • Nasal inner • Nasal Outer • Temporal Inner • Temporal Outer • Superior Inner • Superior Outer • Inferior Inner • Inferior Outer *GCL volume (per 0.1mm3)* Outcome: Visual field (mean deviation) recovery and maintenance & Visual acuity recovery and maintenance	2 years	Discrimination: AUC	Funded by Bayer Australia Limited, 875 Pacific Highway Pymble NSW 2073. No conflicts of interest. Internal validation only.	High
Wang, 2022	N at baseline N=239 Age (mean, SD) 52 ± 16 years Sex 54.0% male Event rate (%) 331 (78%) eyes exhibited a visual field mean deviation greater than -3dB, and 324 (76%) eyes exhibited a best-corrected logMAR visual acuity of 0 or better.	Predictors: Best-corrected visual acuity, visual fields, and OCT retinal nerve fibre layer (RNFL) thickness, macular thickness and volume *RNFL thickness (per 10μm)* • Average • Superior • Inferior • Temporal • Nasal *Macular thickness (per 10μm)* • Average • Foveal • Superior • Inferior	2 years	Discrimination: C-statistic	The research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. No conflicts of interest. Internal validation only.	High

		• Temporal • Nasal *Macular volume (per 0.1mm3)* • Total • Foveal • Superior • Inferior • Temporal • Nasal Outcome: Visual field (mean deviation) recovery and maintenance & Visual acuity recovery and maintenance				

*For further details, see risk of bias table in the appendix

Results

1. Discrimination (Area Under the Curve (AUC) or C-statistic)

Lee (2016) reported that the nomogram that predicts visual recovery had an AUC of 0.84. The confidence interval of AUC was not reported.

Meyer (2022) reported that the best performing RNFL model based on the inferior nasal RNFL sector thickness had an AUC of 0.58. Besides, the best performing GCL model based on superior inner GCL sector thickness had an AUC of 0.90. The confidence interval of AUC was not reported.

Wang (2020) reported multivariable risk prediction models incorporating independent predictors, including age, pre-operative visual function and RNFL thickness. For long-term visual field recovery and maintenance, a C-statics of 0.83 (95%CI 0.72 to 0.94) was found. For long-term acuity recovery and maintenance, a C-statistic of 0.69 (95%CI 0.55 to 0.84) was found.

2. Calibration (slope of observed versus expected)

Lee (2016) reported that the performance of the bootstrap-corrected nomogram was close to an ideal line, which represents good predictions. However, no value for the slope was presented.

Table 4. Summary of Findings table

Population: Patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst)
Instrument: Lee 2016

Outcome (performance measures)	**Study results and measurements**	**Certainty of the Evidence** (Quality of evidence)	**Conclusions**
Discrimination: AUC	AUC=0.84 based on data from 57 participants in one study.	**Very low**[1]	The evidence is very uncertain about the discrimination of the model used in the study of Lee 2016 predicting visual field recovery in patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst). *Lee (2016)*

Calibration: slope	Performance of the bootstrap-corrected nomogram was close to an ideal line, which represents good predictions based on data from 57 participants in one study.	**No GRADE**	No evidence was found regarding the calibration of the model used in the study of Lee 2016 predicting visual field recovery in patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst).

[1]Downgraded one level for Risk of Bias due to retrospective data-collection, one level for Indirectness because no external validation was performed and one level for Imprecision as no 95%CI is available and a small sample size was used.

Population: Patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst)
Instrument: Meyer 2022

Outcome (performance measures)	**Study results and measurements**	**Certainty of the Evidence** (Quality of evidence)	**Conclusions**
Discrimination: AUC	RNFL model (based on inferior nasal RNFL sector thickness): AUC=0.58 GCL model (based on superior inner GCL sector thickness): AUC=0.90 based on data from 108 participants in one study.	**Very low**[1]	The evidence is very uncertain about the discrimination of the model used in the study of Meyer 2022 predicting visual field recovery and visual acuity recovery and maintenance in patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst). *Meyer (2022)*
Calibration: slope	-	**No GRADE**	No evidence was found regarding the calibration of the model used in the study of Meyer 2022 predicting visual field recovery and visual acuity recovery and maintenance in patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst).

[1]Downgraded one level for Indirectness because no external validation was performed and two levels for Imprecision as no 95%CI is available and a small sample size was used.

Population: Patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst)
Instrument: Wang 2020

Outcome (performance measures)	**Study results and measurements**	**Certainty of the Evidence** (Quality of evidence)	**Conclusions**
Discrimination: C-statistic	Long-term visual field recovery and maintenance: 0.83 (95%CI 0.72 to 0.94) based on data from 239 participants in one study.	**Low**[1]	The model used in the study of Wang 2020 may result in useful discrimination predicting visual field recovery and maintenance in patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst). *Wang (2020)*
	Long-term acuity recovery and maintenance: 0.69 (95%CI 0.55 to 0.84) based on data from 239 participants in one study.	**Very low**[2]	The evidence is very uncertain about the discrimination of the model used in the study of Wang 2020 predicting visual acuity recovery and maintenance in patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst). *Wang (2020)*

Calibration: slope	-	**No GRADE**	No evidence was found regarding the calibration of the model used in the study of Wang 2020 predicting visual field recovery and visual acuity recovery and maintenance in patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst).

[1]Downgraded one level for Indirectness because no external validation was performed and one level for Imprecision as one border of the 95%CI crossed clinical relevance threshold.
[2]Downgraded one level for Indirectness because no external validation was performed and two levels for Imprecision as both borders of the 95%CI crossed clinical relevance threshold.

Overall comparison

Outcome (performance measures)	**Study results and measurements**	**Certainty of the Evidence** (Quality of evidence)	**Conclusions**
Discrimination and calibration	Three studies with 404 participants. Development of model only (and internal validation). No direct comparisons between models.	**Very low**	The evidence is very uncertain which model has the best predictive value for visual field recovery and visual acuity recovery in patients with (suspected) pituitary tumor (including craniopharyngiomas, Rathke's cleft cyst). *(Lee, 2016; Meyer, 2022; Wang, 2020)*

Kennisvragen

Tijdens de ontwikkeling van deze module is systematisch naar onderzoeken gezocht die de zoekvraag kunnen beantwoorden. Door gebruik te maken van een systematische literatuuranalyse met beoordeling van de bewijskracht is duidelijk geworden dat er binnen deze module nog kennisvragen bestaan. De werkgroep meent dat (vervolg)onderzoek wenselijk is om in de toekomst een duidelijker antwoord te kunnen geven op vragen uit de praktijk.

Kennisvraag:
Wat zijn de gunstige en ongunstige effecten van het toevoegen van een preoperatieve OCT aan de standaard oogheelkundige beoordeling voor het voorspellen van postoperatieve visus- en gezichtsvelduitkomsten één jaar na chirurgie bij patiënten met een hypofysetumor?

P: Patiënten met een hypofysetumor die een chirurgische behandeling ondergaan.
I: Standaard preoperatieve oogheelkundige beoordeling (visusmeting en gezichtsveldonderzoek) aangevuld met OCT van papil.
C: Standaard preoperatieve oogheelkundige beoordeling zonder OCT.
O: Postoperatief gezichtsveld na 1 jaar, postoperatieve visus na 1 jaar, nauwkeurigheid van de prognose van visueel herstel en verandering in behandelbeslissing.

Toelichting:
Bij patiënten met een hypofysetumor kan visusdaling en/of gezichtsvelduitval een belangrijke reden zijn voor chirurgische behandeling. De preoperatieve visus en het gezichtsveld zijn echter beperkt voorspellend voor het herstel van visuele functies na operatie. OCT kan structurele schade aan de retina en de visuele baan in kaart brengen, zoals de dikte van de retinale zenuwvezellaag en de ganglioncellaag. Vergelijkend onderzoek naar een diagnostische strategie met en zonder OCT kan helpen om vast te stellen of

toevoeging van OCT leidt tot een betere voorspelling van postoperatieve visus- en gezichtsvelduitkomsten.

Implementeren-tabel

De implementatietabel brengt in kaart welke factoren de uitvoering van een aanbeveling bevorderen of belemmeren, en welke aanvullende acties nodig zijn voor succesvolle invoering. De adviseur en (cluster)werkgroep vullen de tabel in op basis van gerichte vragen over het onderliggende probleem, relevante randvoorwaarden en mogelijke knelpunten. Op basis hiervan wordt geconcludeerd of een extra implementatie-impuls wenselijk is.

Implementatietabel

Vraag	***Antwoord:*** *Kruis aan en licht toe/ beschrijf*		***Toelichting keuze:***
I1. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?		Ongewenste praktijkvariatie	
	X	Nieuwe evidentie	Nieuwe studies waarin de toegevoegde waarde van preoperatieve OCT-scan voor het voorspellen van de postoperatieve gezichtsvelden wordt beschreven.
		Anders	
I2. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?	**X**	< 1000	
		< 5000	
		5000-40.000	
		> 40.000	
I3. Is de aanbeveling onderdeel van een bredere set interventies of verwant aan andere richtlijnen of modules? Zo ja, hoe verhoudt zij zich daartoe en moet hiermee rekening worden gehouden bij de implementatie, of kan de aanbeveling als losstaand worden beschouwd?	**X**	Ja	*De aanbevelingen maken onderdeel uit van de diagnostische en behandelketen rondom hypofysetumoren en hangen samen met andere modules binnen deze richtlijn, waaronder de modules over chiasmasyndroom en timing van operatie.*

		Nee	
I4. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:		**Belemmerende factoren**	**Bevorderende factoren/ kansen**
Richtlijn/ klinisch traject (innovatie)	**X**		Het OCT apparaat staat in elke oogheelkunde poli
Zorgverleners (artsen en verpleegkundigen)	**X**		Oogartsen gebruiken reeds de OCT voor andere aandoeningen
Patiënt/ cliënt (naasten)			
Sociale context			
Organisatorische context	**X**	Voor een deel van de aanbevelingen is samenwerking nodig tussen verschillende disciplines (bijvoorbeeld endocrinologie, oogheelkunde, radiologie en KNO).	Multidisciplinaire besluitvorming over hypofysechirurgie vindt plaats in een multidisciplinair overleg.
Financiële en juridische context			
I5. A) Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk? (kruis aan) **B) Wat is er nodig van deze personen/partijen**		**A**	**B**
	Patiënt/ cliënt (naaste)		
	Professional	Oogartsen	
	Beroepsvereniging, nl	Nederlands Oogheelkundig Genootschap	

om de aanbeveling in de praktijk te kunnen brengen? *Denk aan aanpassingen in gedrag, werkwijzen, beleid, samenwerking of andere randvoorwaarden.*	Ziekenhuis (raad van bestuur/UMCNL (voorheen NFU)/NVZ)		
	Zorgverzekeraars/ NZa		
	Zorginstituut [duiding nodig]		
	Anders		
I6. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?	**X**	< 1 jaar	<1 jaar
		binnen 2-3 jaar	
I7. Conclusie: is er extra actie en/of ondersteuning nodig voor implementatie van de aanbeveling? *De reguliere implementatieroutes (publicatie en disseminatie via officiele kanalen, opname in professionele standaarden, scholing en nascholing, gebruik van bestaande ICT systemen, audits en visitaties) van de richtlijnmodule alleen is onvoldoende.*		Ja	
	X	Nee	Nee
I8. Plaatsing op de Landelijke Implementatieagenda Medisch Specialistische zorg is gewenst. *Het gaat om zorg die (grotendeels) wordt uitgevoerd binnen de ziekenhuismuren. Succesvolle implementatie vraagt om actieve betrokkenheid en samenwerking van meerdere relevante partijen binnen de zorgpraktijk.*		Ja *	
	X	Nee	Nee

**Deze aanbeveling komt mogelijk in aanmerking voor plaatsing op de Landelijke Implementatieagenda van het programma Zorg Evaluatie & Gepast Gebruik (ZE&GG), waarin alle betrokken partijen in de medisch-specialistische zorg samenwerken aan de implementatie van*

bewezen beste zorg. De Federatie levert namens het veld goed onderbouwde aanbevelingen aan, die zijn getoetst op de behoefte aan een implementatie-impuls. De onderwerpen op de Implementatieagenda zijn onderdeel van landelijke zorginkoopafspraken tussen zorgverzekeraars en zorgaanbieders. Voor de beoordeling van aanbevelingen uit richtlijnen wordt gebruikgemaakt van de implementatietabel. Op basis hiervan kunnen we de andere partijen goed informeren en gezamenlijk besluiten of plaatsing op de Implementatieagenda passend is.

Literatuur

Lee J, Kim SW, Kim DW, Shin JY, Choi M, Oh MC, Kim SM, Kim EH, Kim SH, Byeon SH. Predictive model for recovery of visual field after surgery of pituitary adenoma. J Neurooncol. 2016 Oct;130(1):155-164. doi: 10.1007/s11060-016-2227-5. Epub 2016 Jul 30. PMID: 27476080.

Meyer J, Diouf I, King J, Drummond K, Stylli S, Kaye A, Kalincik T, Danesh-Meyer H, Symons RCA. A comparison of macular ganglion cell and retinal nerve fibre layer optical coherence tomographic parameters as predictors of visual outcomes of surgery for pituitary tumours. Pituitary. 2022 Aug;25(4):563-572. doi: 10.1007/s11102-022-01228-w. Epub 2022 May 13. PMID: 35552990.

Wang MTM, King J, Symons RCA, Stylli SS, Meyer J, Daniell MD, Savino PJ, Kaye AH, Danesh-Meyer HV. Prognostic Utility of Optical Coherence Tomography for Long-Term Visual Recovery Following Pituitary Tumor Surgery. Am J Ophthalmol. 2020 Oct;218:247-254. doi: 10.1016/j.ajo.2020.06.004. Epub 2020 Jun 10. PMID: 32533947.

Bijlagen bij module Preoperatieve work-up

Table of quality assessment – prediction modelling studies
(The criteria used in this checklist are based on PROBAST[A] version 15/05/2019)

5

Research question: What is the predictive value of an OCT papilla measurement on post-operative visual field outcomes and visual outcomes in people with a (suspected) pituitary tumor?

Study reference (first author, year of publication) Classification[1]	**Participant selection** 1) Appropriate data sources?[2] 2) Appropriate in- and exclusion?	**Predictors** 1) Assessed similar for all participants? 2) Assessed without knowledge of outcome? 3) Available at time the model is intended to be used?	**Outcome** 1) Pre-specified or standard outcome definition? 2) Predictors excluded from definition? 3) Assessed similar for all participants? 4) Assessed without knowledge of predictors? 5) Time interval between predictor and outcome measurement appropriate?	**Analysis** 1) Reasonable number of participants with event/outcome? 2) All enrolled participants included in analysis? 3) Missing data handled appropriately? 4) No selection of predictors based on univariate analysis? 5) Relevant model performance measures evaluated appropriately?[3] 6) Accounted for model overfitting[4] and optimism? 7) Predictors and weights correspond to results from multivariate analysis?	**Overall judgment** *High risk of bias: at least one domain judged to be at high risk of bias.* *Model development only: high risk of bias.*
Lee, 2016 Development of model only (Internal validation)	Conclusion: Probably yes; Reason: Cohort study. Appropriate in- and exclusion criteria.	Conclusion: Definitely no; Reason: Data was collected retrospectively. Assessed similar for all participants and available at the time the model is intended to be used.	Conclusion: Probably no; Reason: Data was collected retrospectively. Pre-specified outcomes. Predictors excluded from definition (is about pre-operative value). Assessed similar. Appropriate time interval.	Conclusion: Probably no; Reason: Unclear how many participants had the outcome. Enrolled participants included in analysis and no missing data. Selection of prognostic variables by multiple regression analysis. Calibration and discrimination were assessed. Not accounted for model overfitting and optimism. Predictors and weights probably correspond to results from multivariate analysis.	High
Meyer, 2022 Development of model only (Internal validation)	Conclusion: Probably yes; Reason: Cohort study. Appropriate in- and exclusion criteria.	Conclusion: Probably yes; Reason: Assessed similar for all participants without knowledge of outcome and available at time the model is intended to be used.	Conclusion: Probably yes; Reason: Pre-specified outcome definition, predictors excluded from definition (is about baseline value), assessed similar for all participants without knowledge of predictors, appropriate time interval between	Conclusion: Probably no; Reason: Unclear how many participants had the outcome. All enrolled participants included in the analysis. No missing data. General linear mixed models were used. Model performance was evaluated appropriately. Not accounted for	High

			predictor and outcome measurement.	model overfitting and optimism. Unclear whether predictors and weights correspond to results from multivariate analysis.	
Wang, 2020 Development of model only (Internal validation)	Conclusion: Probably yes; Reason: Cohort study. Appropriate in- and exclusion criteria.	Conclusion: Probably yes; Reason: Assessed similar for all participants without knowledge of outcome and available at time the model is intended to be used.	Conclusion: Probably yes; Reason: Pre-specified outcome definition, predictors excluded from definition (is about baseline value), assessed similar for all participants without knowledge of predictors, appropriate time interval between predictor and outcome measurement.	Conclusion: Probably no; Reason: Reasonable number of participants with outcome. All enrolled participants included in the analysis. No missing data. Multiple logistic regression analysis was used. Model performance was evaluated appropriately. Not accounted for model overfitting and optimism. Predictors and weights probably corresponded to results from multivariate analysis.	High

[A] Wolff RF, Moons KGM, Riley RD, Whiting PF, Westwood M, Collins GS, Reitsma JB, Kleijnen J, Mallett S; PROBAST Group. PROBAST: A Tool to Assess the Risk of Bias and Applicability of Prediction Model Studies. Ann Intern Med. 20191;170(1):51-58. doi: 10.7326/M18-1376. PubMed PMID: 30596875.

[1] Development of model only / Development and external validation of model / External validation of model

[2] Cohort, RCT or nested case-control study

[3] E.g. calibration (total O:E ratio; expected outcome probabilities versus observed outcome frequencies) and discrimination (range 0.5 (no discriminative ability) to 1.0 (perfect discriminative ability)

[4] Overfitting: for low ORs the predicted probability is too low, for high ORs the predicted probability is too high. Correcting is possible with shrinkage.

Table of excluded studies

Reference	Reason for exclusion
Agarwal R, Jain VK, Singh S, Charlotte A, Kanaujia V, Mishra P, Sharma K. Segmented retinal analysis in pituitary adenoma with chiasmal compression: A prospective comparative study. Indian J Ophthalmol. 2021 Sep;69(9):2378-2384. doi: 10.4103/ijo.IJO_2086_20. PMID: 34427226; PMCID: PMC8544063.	Diagnostic ability
Banc A, Stan C, Florian IS. Optical coherence tomography impacts the evaluation of visual pathway tumors. Neurosurg Rev. 2018 Apr;41(2):415-426. doi: 10.1007/s10143-016-0772-1. Epub 2016 Jul 28. PMID: 27465394.	No prognostic model
Chung YS, Na M, Yoo J, Kim W, Jung IH, Moon JH, Lee J, Kim SH, Kim EH. Optical Coherent Tomography Predicts Long-Term Visual Outcome of Pituitary Adenoma Surgery: New Perspectives From a 5-Year Follow-up Study. Neurosurgery. 2020 Dec 15;88(1):106-112. doi: 10.1093/neuros/nyaa318. PMID: 32735666.	No prognostic model
Danesh-Meyer HV, Wong A, Papchenko T, Matheos K, Stylli S, Nichols A, Frampton C, Daniell M, Savino PJ, Kaye AH. Optical coherence tomography predicts visual outcome for pituitary tumors. J Clin Neurosci. 2015 Jul;22(7):1098-104. doi: 10.1016/j.jocn.2015.02.001. Epub 2015 Apr 16. PMID: 25891894.	No prognostic model
Glebauskiene B, Liutkeviciene R, Zlatkute E, Kriauciuniene L, Zaliuniene D. Association of retinal nerve fibre layer thickness with quantitative magnetic resonance imaging data of the optic chiasm in pituitary adenoma patients. J Clin Neurosci. 2018 Apr;50:1-6. doi: 10.1016/j.jocn.2018.01.005. Epub 2018 Feb 3. PMID: 29398198.	No prognostic model
Hayat ŞÇ, Yılmaz YC, Erkan B, Erdim Ç, Önal İ, Ermiş S, Hatipoğlu E. Visual recovery following pituitary adenoma surgery: prognostic value of optical coherence tomography and suprasellar tumour volume. Can J Ophthalmol. 2025 Jun;60(3):163-169. doi: 10.1016/j.jcjo.2024.10.015. Epub 2024 Nov 9. PMID: 39532278.	No prognostic model
Iqbal M, Irfan S, Goyal JL, Singh D, Singh H, Dutta G. An Analysis of Retinal Nerve Fiber Layer Thickness before and after Pituitary Adenoma Surgery and its Correlation with Visual Acuity. Neurol India. 2020 Mar-Apr;68(2):346-351. doi: 10.4103/0028-3886.280634. PMID: 32189695.	No prognostic model
Jacob M, Raverot G, Jouanneau E, Borson-Chazot F, Perrin G, Rabilloud M, Tilikete C, Bernard M, Vighetto A. Predicting visual outcome after treatment of	No prognostic model

pituitary adenomas with optical coherence tomography. Am J Ophthalmol. 2009 Jan;147(1):64-70.e2. doi: 10.1016/j.ajo.2008.07.016. Epub 2008 Sep 6. PMID: 18774545.	
Jeon C, Park KA, Hong SD, Choi JW, Seol HJ, Nam DH, Lee JI, Shin HJ, Kong DS. Clinical Efficacy of Optical Coherence Tomography to Predict the Visual Outcome After Endoscopic Endonasal Surgery for Suprasellar Tumors. World Neurosurg. 2019 Dec;132:e722-e731. doi: 10.1016/j.wneu.2019.08.031. Epub 2019 Aug 14. PMID: 31421301.	No validated prognostic model
Jeong SS, Funari A, Agarwal V. Diagnostic and Prognostic Utility of Optical Coherence Tomography in Patients With Sellar/Suprasellar Lesions with Chiasm Impingement: A Systematic Review/ Meta-Analyses. World Neurosurg. 2022 Jun;162:163-176.e2. doi: 10.1016/j.wneu.2022.03.011. Epub 2022 Mar 9. PMID: 35276393.	No validated prognostic model
Johansson C, Lindblom B. The role of optical coherence tomography in the detection of pituitary adenoma. Acta Ophthalmol. 2009 Nov;87(7):776-9. doi: 10.1111/j.1755-3768.2008.01344.x. Epub 2008 Sep 3. PMID: 18771481.	No prognostic model
Kawaguchi T, Ogawa Y, Tominaga T. Retinal Nerve Fiber Layer Thickness Measurement for Predicting Visual Outcome after Transsphenoidal Surgery: Optic Disc Atrophy Is Not the Deciding Indicator. World Neurosurg. 2019 Jul;127:e427-e435. doi: 10.1016/j.wneu.2019.03.143. Epub 2019 Mar 22. PMID: 30910754.	No validated prognostic model
Kurian DE, V R, Horo S, Chacko AG, Prabhu K, Mahasampath G, Korah S. Predictive value of retinal nerve fibre layer thickness for postoperative visual improvement in patients with pituitary macroadenoma. BMJ Open Ophthalmol. 2022 Jul;7(1):e000964. doi: 10.1136/bmjophth-2021-000964. PMID: 36161840; PMCID: PMC9263901.	No validated prognostic model
Lee GI, Park KA, Lee D, Oh SY, Kong DS, Hong SD. Predicting visual outcomes after decompression of pituitary tumours based on stratified inner-retinal layer thickness and age. Acta Ophthalmol. 2023 May;101(3):301-309. doi: 10.1111/aos.15281. Epub 2022 Nov 18. PMID: 36398459.	No prognostic model
Lee GI, Park KA, Oh SY, Kong DS. Parafoveal and Peripapillary Perfusion Predict Visual Field Recovery in Chiasmal Compression due to Pituitary Tumors. J Clin Med. 2020 Mar 4;9(3):697. doi: 10.3390/jcm9030697. PMID: 32143464; PMCID: PMC7141271.	No prognostic model
Lee GI, Park KA, Oh SY, Kong DS. Changes in parafoveal and peripapillary perfusion after decompression surgery in chiasmal compression due to pituitary	No prognostic model

tumors. Sci Rep. 2021 Feb 10;11(1):3464. doi: 10.1038/s41598-021-82151-1. PMID: 33568736; PMCID: PMC7876027.	
Menon S, Nair S, Kodnani A, Hegde A, Nayak R, Menon G. Retinal nerve fiber layer thickness and its correlation with visual symptoms and radiological features in pituitary macroadenoma. J Neurosci Rural Pract. 2023 Jan-Mar;14(1):41-47. doi: 10.25259/JNRP_18_2022. Epub 2022 Dec 9. PMID: 36891116; PMCID: PMC9943945.	No prognostic model
Moon CH, Hwang SC, Kim BT, Ohn YH, Park TK. Visual prognostic value of optical coherence tomography and photopic negative response in chiasmal compression. Invest Ophthalmol Vis Sci. 2011 Oct 31;52(11):8527-33. doi: 10.1167/iovs.11-8034. PMID: 21960556.	No prognostic model
Moon JS, Shin SY. Segmented retinal layer analysis of chiasmal compressive optic neuropathy in pituitary adenoma patients. Graefes Arch Clin Exp Ophthalmol. 2020 Feb;258(2):419-425. doi: 10.1007/s00417-019-04560-3. Epub 2019 Dec 18. PMID: 31853626.	No prognostic model
Nair SS, Varsha AS, Hegde A, Raju B, Nayak R, Menon G, Menon S. Correlation of pre-operative and post-operative retinal nerve fibre layer thickness with visual outcome following decompression of pituitary macroadenoma. Clin Neurol Neurosurg. 2024 Sep;244:108446. doi: 10.1016/j.clineuro.2024.108446. Epub 2024 Jul 10. Erratum in: Clin Neurol Neurosurg. 2025 Mar;250:108765. doi: 10.1016/j.clineuro.2025.108765. PMID: 39018992.	No validated prognostic model
Ohkubo S, Higashide T, Takeda H, Murotani E, Hayashi Y, Sugiyama K. Relationship between macular ganglion cell complex parameters and visual field parameters after tumor resection in chiasmal compression. Jpn J Ophthalmol. 2012 Jan;56(1):68-75. doi: 10.1007/s10384-011-0093-4. PMID: 21975828.	No prognostic model
Pang Y, Tan Z, Chen X, Liao Z, Yang X, Zhong Q, Huang B, Zhong Q, Zhong J, Mo W. Evaluation of preoperative visual pathway impairment in patients with non-functioning pituitary adenoma using diffusion tensor imaging coupled with optical coherence tomography. Front Neurosci. 2023 Feb 9;17:1057781. doi: 10.3389/fnins.2023.1057781. PMID: 36845438; PMCID: PMC9947395.	Model for diagnostic ability
Pang Y, Zhao Q, Huang Z, Lu K, Zhou F, Mo W, Zhong Q, Tan Z. Visual Pathway Recovery Post Pituitary Adenoma Surgery: Insights from Retinal Structure, Vascular Density, and Neural Conduction Analysis. Ophthalmol Ther. 2024 Jul;13(7):1993-2008. doi: 10.1007/s40123-024-00966-3. Epub 2024 May 31. PMID: 38822193; PMCID: PMC11178691.	No prognostic model

Phal PM, Steward C, Nichols AD, Kokkinos C, Desmond PM, Danesh-Meyer H, Sufaro YZ, Kaye AH, Moffat BA. Assessment of Optic Pathway Structure and Function in Patients With Compression of the Optic Chiasm: A Correlation With Optical Coherence Tomography. Invest Ophthalmol Vis Sci. 2016 Jul 1;57(8):3884-90. doi: 10.1167/iovs.15-18734. PMID: 27459665.	No prognostic model
Qiao N, Li C, Xu J, Ma G, Kang J, Jin L, Cao L, Liu C, Zhang Y, Gui S. Prognostic Utility of Optical Coherence Tomography for Visual Outcome After Extended Endoscopic Endonasal Surgery for Adult Craniopharyngiomas. Front Oncol. 2022 Jan 6;11:764582. doi: 10.3389/fonc.2021.764582. PMID: 35070970; PMCID: PMC8770264.	No validated prognostic model
Qiao N, Ma Y, Chen X, Ye Z, Ye H, Zhang Z, Wang Y, Lu Z, Wang Z, Xiao Y, Zhao Y. Machine Learning Prediction of Visual Outcome after Surgical Decompression of Sellar Region Tumors. J Pers Med. 2022 Jan 25;12(2):152. doi: 10.3390/jpm12020152. PMID: 35207641; PMCID: PMC8879436.	Not suitable for assessing the added value of OCT alone
Sasagawa Y, Nakahara M, Takemoto D, Nakada M. Optical coherence tomography detects early optic nerve damage before visual field defect in patients with pituitary tumors. Neurosurg Rev. 2023 Apr 14;46(1):85. doi: 10.1007/s10143-023-01990-w. PMID: 37058150.	No prognostic model
Singha S, Beniwal M, Mailankody P, Battu R, Saini J, Tyagi G, Srinivas D. Role of Optical Coherence Tomography in Predicting Visual Outcome after Surgery for Sellar and Supra-Sellar Tumors. Neurol India. 2024 Jan 1;72(1):50-57. doi: 10.4103/neurol-india.Neurol-India-D-23-00654. Epub 2024 Feb 29. PMID: 38443001.	No validated prognostic model
Solari D, Cennamo G, Amoroso F, Frio F, Donna P, Iodice D'Enza A, Melenzane A, Somma T, Tranfa F, Cavallo LM. Predicting the early visual outcomes in sellar-suprasellar lesions compressing the chiasm: the role of SD-OCT series of 20 patients operated via endoscopic endonasal approach. J Neurosurg Sci. 2022 Aug;66(4):362-370. doi: 10.23736/S0390-5616.19.04687-3. Epub 2019 Jul 23. PMID: 31339115.	No prognostic model
Tang Y, Jia W, Xue Z, Yuan L, Qu Y, Yang L, Wang L, Ma X, Wang M, Meng L, Lei K, Lu W, Peng X. Prognostic value of radial peripapillary capillary density for visual field outcomes in pituitary adenoma: A case-control study. J Clin Neurosci. 2022 Jun;100:113-119. doi: 10.1016/j.jocn.2022.04.012. Epub 2022 Apr 18. PMID: 35447509.	No prognostic model
Thammakumpee K, Buddawong J, Vanikieti K, Jindahra P, Padungkiatsagul T. Preoperative Peripapillary Retinal Nerve Fiber Layer Thickness as the Prognostic	No validated prognostic model

Factor of Postoperative Visual Functions After Endoscopic Transsphenoidal Surgery for Pituitary Adenoma. Clin Ophthalmol. 2022 Dec 15;16:4191-4198. doi: 10.2147/OPTH.S392987. PMID: 36544895; PMCID: PMC9762988.	
Toumi E, Almairac F, Mondot L, Themelin A, Decoux-Poullot AG, Paquis P, Chevalier N, Baillif S, Nahon-Esteve S, Martel A. Benefit of Optical Coherence Tomography-Angiography in Patients Undergoing Transsphenoidal Pituitary Adenoma Surgery: A Prospective Controlled Study. Diagnostics (Basel). 2024 Aug 12;14(16):1747. doi: 10.3390/diagnostics14161747. PMID: 39202235; PMCID: PMC11353360.	No validated prognostic model
Xia L, Wenhui J, Xiaowen Y, Wenfang X, Wei Z, Yanjun H, Xiaoyan P. Predictive value of macular ganglion cell-inner plexiform layer thickness in visual field defect of pituitary adenoma patients: a case-control study. Pituitary. 2022 Aug;25(4):667-672. doi: 10.1007/s11102-022-01248-6. Epub 2022 Jul 14. PMID: 35834154.	No validated prognostic model
Yoo YJ, Hwang JM, Yang HK, Joo JD, Kim YH, Kim CY. Prognostic value of macular ganglion cell layer thickness for visual outcome in parasellar tumors. J Neurol Sci. 2020 Jul 15;414:116823. doi: 10.1016/j.jns.2020.116823. Epub 2020 Apr 6. PMID: 32302803.	No validated prognostic model
Yu WJ, Xiao J, Wang GX, Jiang C, Zha W, Liao RF. Predictive visual field outcomes after optic chiasm decompressive surgery by retinal vessels parameters using optical coherence tomography angiography. Int J Ophthalmol. 2024 Feb 18;17(2):365-373. doi: 10.18240/ijo.2024.02.21. PMID: 38371253; PMCID: PMC10827611.	No validated prognostic model

Literature search strategy

Cluster/richtlijn: NVvN hypofysechirurgie	
Uitgangsvraag/modules: UV1 Hoe moet de preoperatieve work-up van hypofysetumoren er uit zien?	
Database(s): Embase.com, Ovid/Medline all	Datum: 4 maart 2025
Periode: vanaf 2005	Talen: geen restrictie
Literatuurspecialist: Alies Oost	Rayyan: https://new.rayyan.ai/reviews/1350540/screening
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/	
Toelichting: Voor deze vraag is gezocht op de elementen: - hypophysis tumor surgery - Optical Coherence Tomography (OCT)	
Te gebruiken voor richtlijntekst: A systematic literature search was performed by a medical information specialist using the following bibliographic databases: Embase.com and Ovid/Medline all. Both databases were searched from 2005 to March 4, 2025 for systematic reviews, RCTs and observational studies. Systematic searches were completed using a combination of controlled vocabulary and natural language keywords. The overall search strategy was derived from the following primary search concepts: (1) hypophysis tumor surgery; (2) optical coherence tomography. Duplicates were removed using EndNote software. After deduplication a total of 143 records were imported for title/abstract screening.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR	10	5	11
RCT	25	6	26
Observationele studies	90	70	106
Totaal	125	81	**143***

in Rayyan

Zoekstrategie

Embase.com

No.	Query	Results
#1	('hypophysis tumor'/exp OR 'acromegaly'/exp OR (((pituitar* OR hypophys* OR adenohypophys* OR neurohypophys* OR sellar OR parasellar) NEAR/4 (adenoma* OR microadenoma* OR macroadenoma* OR cancer* OR carcinoma* OR cyst* OR lesion* OR malignan* OR neoplasm* OR tumor* OR tumour*)):ti,ab,kw) OR ((cushing* NEAR/3 (syndrome* OR disease*)):ti,ab,kw) OR craniopharyngioma*:ti,ab,kw OR 'cranio pharyngioma*':ti,ab,kw OR craniopharyngeoma*:ti,ab,kw OR pharyngioma*:ti,ab,kw OR gonadotropinoma*:ti,ab,kw OR prolactinoma*:ti,ab,kw OR	46817

	microprolactinoma*:ti,ab,kw OR macroprolactinoma*:ti,ab,kw OR 'macro adenoma*':ti,ab,kw OR macroadenoma*:ti,ab,kw OR acromegal*:ti,ab,kw OR akromegal*:ti,ab,kw OR ((('non function*' OR nonfunction*) NEAR/3 adenoma*):ti,ab,kw) OR (((craniopharyngeal OR rathke*) NEAR/3 (tumor* OR tumour* OR cyst*)):ti,ab,kw)) AND ('surgery'/exp OR 'surgical patient'/exp OR 'surgical risk'/exp OR 'perioperative period'/exp OR 'surgery'/lnk OR surgic*:ti,ab,kw OR surger*:ti,ab,kw OR microsurg*:ti,ab,kw OR operation*:ti,ab,kw OR operative:ti,ab,kw OR presurg*:ti,ab,kw OR preoperati*:ti,ab,kw OR perisurg*:ti,ab,kw OR perioperati*:ti,ab,kw OR postsurg*:ti,ab,kw OR postoperati*:ti,ab,kw OR intraoperati*:ti,ab,kw OR resect*:ti,ab,kw OR laparoscop*:ti,ab,kw OR endoscop*:ti,ab,kw OR neuroendoscop*:ti,ab,kw OR neurosurg*:ti,ab,kw OR transsphenoid*:ti,ab,kw OR 'trans sphenoid*':ti,ab,kw OR transcranial*:ti,ab,kw OR 'trans cranial*':ti,ab,kw OR hypophysectom*:ti,ab,kw OR adenomectom*:ti,ab,kw OR craniotom*:ti,ab,kw OR craniostom*:ti,ab,kw)	
#2	'optical coherence tomography'/exp OR 'optical coherence tomography device'/exp OR 'retinal nerve fibre layer'/exp OR 'retinal nerve fibre layer thickness'/exp OR 'ganglion cell layer'/exp OR 'ganglion cell layer thickness'/exp OR 'ganglion cell complex'/exp OR 'ganglion cell complex thickness'/exp OR 'ganglion cell inner plexiform layer'/exp OR 'ganglion cell inner plexiform layer thickness'/exp OR (((optical OR ocular) NEAR/3 'coherence tomograph*'):ti,ab,kw) OR oct:ti,ab,kw OR octa:ti,ab,kw OR 'retinal nerve fibre layer':ti,ab,kw OR 'retinal nerve fiber layer':ti,ab,kw OR (('ganglion cell' NEAR/3 (layer OR complex)):ti,ab,kw) OR 'spectral domain':ti,ab,kw OR cirrus:ti,ab,kw OR spectralis:ti,ab,kw OR nidek:ti,ab,kw	163422
#3	#1 AND #2 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT (('adolescent'/exp OR 'child'/exp OR adolescent*:ti,ab,kw OR child*:ti,ab,kw OR schoolchild*:ti,ab,kw OR infant*:ti,ab,kw OR girl*:ti,ab,kw OR boy*:ti,ab,kw OR teen:ti,ab,kw OR teens:ti,ab,kw OR teenager*:ti,ab,kw OR youth*:ti,ab,kw OR pediatr*:ti,ab,kw OR paediatr*:ti,ab,kw OR puber*:ti,ab,kw) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab,kw OR man:ti,ab,kw OR men:ti,ab,kw OR woman:ti,ab,kw OR women:ti,ab,kw)) AND [2005-2025]/py	216
#4	'meta analysis'/exp OR 'systematic review'/exp OR 'scoping review'/exp OR 'rapid review'/exp OR 'umbrella review'/exp OR 'cochrane database of systematic reviews'/jt OR 'network meta-analysis'/exp OR 'networkmeta analy*':ti,ab,kw OR 'networkmetaanaly*':ti,ab,kw OR metaanaly*:ti,ab,kw OR 'meta analy*':ti,ab,kw OR metanaly*:ti,ab,kw OR prisma:ti,ab,kw OR prospero:ti,ab,kw OR metaanali*:ti,ab,kw OR 'meta anali*':ti,ab,kw OR metanali*:ti,ab,kw OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab,kw) OR (((structured OR systemic*) NEAR/3 (review* OR overview* OR	1085028

	synth*) NEAR/3 literature):ti,ab,kw) OR ((systemic* NEAR/1 review*):ti,ab,kw) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab,kw) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab,kw) OR (((literature NEAR/3 (review* OR overview*)):ti,ab,kw) AND (search*:ti,ab,kw OR database*:ti,ab,kw OR 'data base*':ti,ab,kw)) OR (('data extraction*':ti,ab,kw OR 'data source*':ti,ab,kw) AND ('study selection*':ti,ab,kw OR 'studies selection*':ti,ab,kw)) OR ('search strateg*':ti,ab,kw AND 'selection criteria*':ti,ab,kw) OR ('data source*':ti,ab,kw AND 'data synth*':ti,ab,kw) OR medline*:ti,ab,kw OR pubmed*:ti,ab,kw OR 'pub med*':ti,ab,kw OR embase:ti,ab,kw OR cochrane*:ti,ab,kw OR (((critical* OR rapid*) NEAR/2 (review* OR overview* OR synth*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synth*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynth*:ti,ab,kw OR 'meta synth*':ti,ab,kw OR 'review* of review*':ti,ab,kw	
#5	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	4218966
#6	'major clinical study'/de OR 'clinical study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'cohort analysis'/de OR 'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti) OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR	17846755

	participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#7	#3 AND #4	10
#8	#3 AND #5 NOT #7	25
#9	#3 AND #6 NOT (#7 OR #8)	90
#10	#7 OR #8 OR #9	125

Ovid/Medline

1	(exp Pituitary Neoplasms/ or exp Acromegaly/ or ((pituitar* or hypophys* or adenohypophys* or neurohypophys* or sellar or parasellar) adj4 (adenoma* or microadenoma* or macroadenoma* or cancer* or carcinoma* or cyst* or lesion* or malignan* or neoplasm* or tumor* or tumour*)).ti,ab,kf. or (cushing* adj3 (syndrome* or disease*)).ti,ab,kf. or craniopharyngioma*.ti,ab,kf. or 'cranio pharyngioma*'.ti,ab,kf. or craniopharyngeoma*.ti,ab,kf. or pharyngioma*.ti,ab,kf. or gonadotropinoma*.ti,ab,kf. or prolactinoma*.ti,ab,kf. or microprolactinoma*.ti,ab,kf. or macroprolactinoma*.ti,ab,kf. or 'macro adenoma*'.ti,ab,kf. or macroadenoma*.ti,ab,kf. or acromegal*.ti,ab,kf. or akromegal*.ti,ab,kf. or (('non function*' or nonfunction*) adj3 adenoma*).ti,ab,kf. or ((craniopharyngeal or rathke*) adj3 (tumor* or tumour* or cyst*)).ti,ab,kf.) and (exp Surgical Procedures, Operative/ or exp Specialties, Surgical/ or su.fs. or exp Perioperative Period/ or surgic*.ti,ab,kf. or surger*.ti,ab,kf. or microsurg*.ti,ab,kf. or operation*.ti,ab,kf. or operative.ti,ab,kf. or presurg*.ti,ab,kf. or preoperati*.ti,ab,kf. or perisurg*.ti,ab,kf. or perioperati*.ti,ab,kf. or postsurg*.ti,ab,kf. or postoperati*.ti,ab,kf. or intraoperati*.ti,ab,kf. or resect*.ti,ab,kf. or laparoscop*.ti,ab,kf. or endoscop*.ti,ab,kf. or neuroendoscop*.ti,ab,kf. or neurosurg*.ti,ab,kf. or transsphenoid*.ti,ab,kf. or 'trans sphenoid*'.ti,ab,kf. or transcranial*.ti,ab,kf. or 'trans cranial*'.ti,ab,kf. or hypophysectom*.ti,ab,kf. or adenomectom*.ti,ab,kf. or craniotom*.ti,ab,kf. or craniostom*.ti,ab,kf.)	29148
2	exp Tomography, Optical Coherence/ or ((optical or ocular) adj3 'coherence tomograph*').ti,ab,kf. or oct.ti,ab,kf. or octa.ti,ab,kf. or 'retinal nerve fibre layer'.ti,ab,kf. or 'retinal nerve fiber layer'.ti,ab,kf. or ('ganglion cell' adj3 (layer or complex)).ti,ab,kf. or	106473

	'spectral domain'.ti,ab,kf. or cirrus.ti,ab,kf. or spectralis.ti,ab,kf. or nidek.ti,ab,kf.	
3	(1 and 2) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/) not ((Adolescent/ or Child/ or Infant/ or adolescen*.ti,ab,kf. or child*.ti,ab,kf. or schoolchild*.ti,ab,kf. or infant*.ti,ab,kf. or girl*.ti,ab,kf. or boy*.ti,ab,kf. or teen.ti,ab,kf. or teens.ti,ab,kf. or teenager*.ti,ab,kf. or youth*.ti,ab,kf. or pediatr*.ti,ab,kf. or paediatr*.ti,ab,kf. or puber*.ti,ab,kf.) not (Adult/ or adult*.ti,ab,kf. or man.ti,ab,kf. or men.ti,ab,kf. or woman.ti,ab,kf. or women.ti,ab,kf.))	152
4	limit 3 to yr="2005 -Current"	136
5	exp Meta-Analysis/ or exp Network Meta-Analysis/ or exp Systematic Review/ or (networkmeta analy* or networkmetaanaly* or metaanaly* or meta analy* or metanaly* or prisma or prospero or metaanali* or meta anali* or metanali*).ti,ab,kf. or ((systemati* or scoping or umbrella or structured literature) adj3 (review* or overview*)).ti,ab,kf. or ((structured or systemic*) adj3 (review* or overview* or synth*) adj3 literature).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 (review* or overview*)) and (search* or database* or data base*)).ti,ab,kf. or ((data extraction* or data source*) and (study selection* or studies selection*)).ti,ab,kf. or (search strateg* and selection criteria*).ti,ab,kf. or (data source* and data synth*).ti,ab,kf. or (medline* or pubmed* or pub med* or embase or cochrane*).ti,ab,kf. or cochrane.jw. or ((critical* or rapid*) adj2 (review* or overview* or synth*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synth*)) and (search* or database* or data base*)).ab. or metasynth*.ti,ab,kf. or meta synth*.ti,ab,kf.	810523
6	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2851440
7	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or	7934983

	"parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or exp cohort studies/ or epidemiologic studies/ or ((multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.)) or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	
8	4 and 5	5
9	(4 and 6) not 8	6
10	(4 and 7) not (8 or 9)	70
11	8 or 9 or 10	81

Module 2 – Timing operatie bij chiasmasyndroom

Uitgangsvraag

Wat is de optimale timing van operatie bij patiënten met een chiasmasyndroom door een macroadenoom van de hypofyse?

Search and select

A systematic review of the literature was performed to answer the following question(s):
What is the optimal timing for surgery in patients with a chiasma syndrome caused by a pituitary macroadenoma?

Table 1. PICO

Patients	Patients with pituitary adenoma leading to chiasma syndrome, with minimal visual field loss and vision impairment.
Intervention	Early surgical intervention (≤ 3 weeks)
Control	Late surgical intervention (> 3 weeks)
Outcomes	Visual acuity (preservation and recovery), visual field, peri- and post-operative complications
Other selection criteria	Study design: systematic reviews and randomized controlled trials

Relevant outcome measures

The guideline panel considered visual acuity and visual field as **critical** outcome measures for decision making; and peri- and post-operative complications as an **important** outcome measure for decision making.

A priori, the guideline panel did not define the outcome measures listed above but used the definitions used in the studies.

The guideline panel defined the following thresholds as a minimal clinically (patient) important difference.

- For continuous outcomes a threshold of 10% for continuous outcomes
- For dichotomous outcomes a threshold of <0.80 and >1.25

Search and select (Methods)

A systematic literature search was performed by a medical information specialist using the following bibliographic databases: Embase.com and Ovid/Medline all. Both databases were searched from 1995 to March 17th 2025, for systematic reviews, RCTs and observational studies. Systematic searches were completed using a combination of controlled vocabulary and natural language keywords. The overall search strategy was derived from the following primary search concepts: (1) hypophysis tumor; (2) chiasmial compression; (3) timing of surgery. Duplicates were removed using EndNote software. After deduplication a total of 658 records were imported for title/abstract screening. Initially, 37 studies were selected based on title and abstract screening. After reading the full text, 37 studies were excluded (see the exclusion table under the tab 'Evidence tabellen'), and none of the studies were included.

Summary of literature

Description of studies

No literature was found that applied to the predefined PICO.

Results

No results are presented as there were no studies included in the analysis of the literature.

Outcome	Study results and measurements	Absolute effect estimates	Certainty of evidence (GRADE)	Conclusions
Visual field	No studies	-	**No GRADE**	No evidence was found regarding the effect of timing for surgery in patients with a chiasma syndrome caused by a pituitary macroadenoma on post-operative visual field recovery.
Visual acuity	No studies	-	**No GRADE**	No evidence was found regarding the effect of timing for surgery in patients with a chiasma syndrome caused by a pituitary macroadenoma on post-operative visual acuity recovery.
complications	No studies	-	**No GRADE**	No evidence was found regarding the effect of timing for surgery in patients with a chiasma syndrome caused by a pituitary macroadenoma on peri- and post-operative complications.

Kennisvragen

Tijdens de ontwikkeling van deze module is gebleken dat er binnen deze module nog te weinig bewijs is voor de onderbouwing van de aanbeveling en dus kennisvragen bestaan. De werkgroep meent dat (vervolg)onderzoek wenselijk is om in de toekomst een duidelijker antwoord te kunnen geven op vragen uit de praktijk.]

Kennisvraag

Wat is het effect van vroege versus uitgestelde chirurgische decompressie op visuele uitkomsten (visus en gezichtsveld) bij patiënten met een chiasmasyndroom veroorzaakt door een hypofyse-macroadenoom?

Toelichting

Voor deze module is geen vergelijkend wetenschappelijk bewijs gevonden dat de optimale timing van chirurgie bij chiasmacompressie onderbouwt. De huidige aanbevelingen zijn gebaseerd op consensus, pathofysiologische aannames en klinische ervaring, wat leidt tot praktijkvariatie. Prospectief observationeel onderzoek of multicentrische cohortstudies, waarin timing van chirurgie wordt gerelateerd aan visuele uitkomsten en patiëntkenmerken (zoals duur en progressie van klachten), kunnen bijdragen aan beter onderbouwde en meer gepersonaliseerde aanbevelingen. Indien randomisatie niet haalbaar is, kan gebruik worden gemaakt van zorgvuldig gecorrigeerde observationele designs (bijvoorbeeld met propensity score-analyse).

Implementatietabel

Tabel A: (De-)Implementatietabel met impuls analyse

Aanbeveling – 1	
1. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?	**X Ongewenste praktijkvariatie** **□ Nieuwe evidentie** **□ Anders** **Toelichting:** Binnen Nederland bestaat aanzienlijke variatie in de timing van chirurgie bij patiënten met chiasmacompressie door een hypofyse-adenoom, met name bij patiënten met milde of langzaam progressieve visuele klachten. Deze variatie wordt veroorzaakt door het ontbreken van eenduidig wetenschappelijk bewijs en uniforme triagecriteria, wat kan leiden tot zowel onnodige vertraging als onnodige spoedoperaties.
2. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?	*X* < **1000** □ < **5000** □ **5000-40.000** □ **> 40.000**
3. Maakt de aanbeveling deel uit van een set van interventies voor hetzelfde probleem?	**X Ja**: **Toelichting:** Deze aanbeveling maakt onderdeel uit van een samenhangende set van aanbevelingen binnen de richtlijn Hypofysechirurgie, waaronder modules over indicatiestelling, endocrinologische zorg, chirurgische techniek en postoperatieve follow-up. De timing van chirurgie moet in samenhang met deze andere aanbevelingen worden toegepast, maar kan inhoudelijk als een afzonderlijke triage-aanbeveling worden geïmplementeerd. □ Nee

4. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:	**Wat zijn mogelijke belemmerende factoren?**	**Wat zijn mogelijke bevorderende factoren?**
a) **Richtlijn/ klinisch traject (innovatie)**	Ontbreken van harde evidence kan leiden tot terughoudendheid bij implementatie.	Duidelijke, consensus-gedreven triagecriteria bieden houvast en uniformiteit.
b) **Zorgverleners (artsen en verpleegkundigen)**	Bestaande lokale routines en logistieke beperkingen in OK-planning.	Herkenning van klinische relevantie, multidisciplinaire consensus en aansluiting bij bestaande besluitvorming.
c) **Patiënt/ cliënt (naasten)**	Beperkte gezondheidsvaardigheden of late presentatie van visuele klachten.	Duidelijke uitleg over urgentie en verwachte opbrengst van tijdige chirurgie.
d) **Sociale context**	Verschillen in regionale verwijspatronen.	Samenwerking binnen regionale en landelijke netwerken voor hypofysezorg.
e) **Organisatorische context**	OK-capaciteit en prioritering ten opzichte van andere spoedzorg.	**Bestaande** concentratie van hypofysechirurgie in gespecialiseerde centra.

f) **Economische en politieke context**	Geen specifieke financiële prikkels gekoppeld aan timing.	Behandeling valt binnen bestaande DBC/DOT-structuren.
5. Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk?	XPatiënt/ cliënt (naaste) **X** Professional X Beroepsvereniging X Ziekenhuis(bestuurder) □ Zorgverzekeraars/ NZa □ Zorginstituut [duiding nodig]	
6. Wat zouden deze personen/ partijen moeten veranderen in hun gedrag of organisatie om de aanbeveling toe te passen?	Zorgverleners dienen bij de indicatiestelling expliciet gebruik te maken van de aanbevolen triagecriteria en de temporele evolutie van visuele klachten systematisch mee te wegen. Organisaties dienen multidisciplinaire afstemming en tijdige OK-planning te faciliteren voor patiënten met verhoogde urgentie.	
7. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?	□ < 1 jaar **X** < 2 jaar □ < 3 jaar **Toelichting:** De aanbeveling sluit grotendeels aan bij bestaande praktijk en vraagt vooral om uniformering en explicitering.	
8. Conclusie: is er extra aandacht nodig voor implementatie van de aanbeveling (anders dan publicatie van deze richtlijnmodule)?	□ **Ja*** **X Nee**	

**Deze aanbeveling komt in aanmerking voor plaatsing op de Implementatie Agenda van het programma Zorg Evaluatie & Gepast Gebruik (ZE&GG). In het programma ZE&GG werken patiënten, zorgverleners, zorgaanbieders, zorgverzekeraars en overheid samen aan de bewezen beste zorg voor de patiënt. Daarmee is ZE&GG een programma van alle betrokken partijen in de Medisch Specialistische Zorg. FMS is één van deze betrokken partijen.*

De implementatieagenda van ZE&GG bevat onderwerpen over wat de bewezen beste zorg is en die in de dagelijkse zorgpraktijk geïmplementeerd zouden moeten worden. Zorgverzekeraars Nederland (ZN) en de Nederlandse Vereniging voor Ziekenhuizen (NVZ) hebben landelijke afspraken gemaakt over de implementatie van de onderwerpen van de implementatieagenda. Deze afspraken zijn onderdeel van de zorginkoopafspraken tussen zorgverzekeraars en zorgaanbieders.

Vanuit FMS worden sterke, goed onderbouwde aanbevelingen, getoetst op de behoefte aan een implementatie impuls aangedragen. Voor de beoordeling van onderwerpen uit richtlijnen wordt gekeken naar bovenstaande tabel voor een inschatting van de implementatie impuls. Met de ingevulde implementatietabel kunnen we vanuit FMS de andere HLA-MSZ partijen goed informeren om zo samen te beslissen of de aanbeveling daadwerkelijk op de implementatie agenda zal worden geplaatst.

Literatuur

Dekkers OM, de Keizer RJ, Roelfsema F, van der Klaauw AA, Honkoop PJ, van Dulken H, Smit JW, Romijn JA, Pereira AM. Progressive improvement of impaired visual acuity during the first year after transsphenoidal surgery for nonfunctioning pituitary macroadenoma. Pituitary. 2007;10(1):61-65. doi:10.1007/s11102-007-0007-0.

Gnanalingham KK, Bhattacharjee S, Pennington R, Ng J, Mendoza N. The time course of visual field recovery following transphenoidal surgery for pituitary adenomas: predictive factors for a good outcome. J Neurol Neurosurg Psychiatry. 2005 Mar;76(3):415-419. doi:10.1136/jnnp.2004.035576.

Kerrison JB, Lynn MJ, Baer CA, Newman SA, Biousse V, Newman NJ. Stages of improvement in visual fields after pituitary tumor resection. Am J Ophthalmol. 2000 Dec;130(6):813-820. doi:10.1016/s0002-9394(00)00539-0.

Luomaranta T, Raappana A, Saarela V, Liinamaa MJ. Factors affecting the visual outcome of pituitary adenoma patients treated with endoscopic transsphenoidal surgery. World Neurosurg. 2017 Sep;105:422-431. doi:10.1016/j.wneu.2017.05.144.

Messerer M, Dubourg J, Raverot G, Bervini D, Berhouma M, George I, Chacko AG, Perrin G, Levivier M, Daniel RT, Trouillas J, Jouanneau E. Non-functioning pituitary macro-incidentalomas benefit from early surgery before becoming symptomatic. Clin Neurol Neurosurg. 2013 Dec;115(12):2514-2520. doi:10.1016/j.clineuro.2013.10.007.

Pelsma ICM, Verstegen MJT, de Vries F, Notting IC, Broekman MLD, van Furth WR, Biermasz NR, Pereira AM. Quality of care evaluation in non-functioning pituitary adenoma with chiasm compression: visual outcomes and timing of intervention clinical recommendations based on a systematic literature review and cohort study. Pituitary. 2020 Aug;23(4):417-429. doi:10.1007/s11102-020-01044-0.

Bijlagen bij module 02

Table of excluded studies

Reference	Reason for exclusion
Anik I, Anik Y, Koc K, Ceylan S, Genc H, Altintas O, Ozdamar D, Baykal Ceylan D. Evaluation of early visual recovery in pituitary macroadenomas after endoscopic endonasal transphenoidal surgery: Quantitative assessment with diffusion tensor imaging (DTI). Acta Neurochir (Wien). 2011 Apr;153(4):831-42. doi: 10.1007/s00701-011-0942-4. Epub 2011 Jan 26. PMID: 21267606.	No comparison of late and early surgery
Anik I, Anik Y, Cabuk B, Caklili M, Pirhan D, Ozturk O, Cirak M, Ceylan S. Visual Outcome of an Endoscopic Endonasal Transsphenoidal Approach in Pituitary Macroadenomas: Quantitative Assessment with Diffusion Tensor Imaging Early and Long-Term Results. World Neurosurg. 2018 Apr;112:e691-e701. doi:	No comparison of late and early surgery

10.1016/j.wneu.2018.01.134. Epub 2018 Feb 22. PMID: 29408649.	
Barzaghi LR, Medone M, Losa M, Bianchi S, Giovanelli M, Mortini P. Prognostic factors of visual field improvement after trans-sphenoidal approach for pituitary macroadenomas: review of the literature and analysis by quantitative method. Neurosurg Rev. 2012 Jul;35(3):369-78; discussion 378-9. doi: 10.1007/s10143-011-0365-y. Epub 2011 Nov 15. PMID: 22080165.	No comparison of late and early surgery
Cennamo G, Solari D, Montorio D, Scala MR, D'Andrea L, Tranfa F, Cavallo LM. The role of OCT- angiography in predicting anatomical and functional recovery after endoscopic endonasal pituitary surgery: A 1-year longitudinal study. PLoS One. 2021 Dec 2;16(12):e0260029. doi: 10.1371/journal.pone.0260029. PMID: 34855775; PMCID: PMC8638874.	No comparison of late and early surgery
Chen CY, Chen JS, Chen YS, Yin CH, Wang PC, Hsu SH, Yang YC, Liao WC. Morphometric Analysis of Radiological Features of Pituitary Tumors and Optic Pathway Distortion Associated with Visual Impairment in Pituitary Macroadenomas with Suprasellar Extension. World Neurosurg. 2025 Feb;194:123436. doi: 10.1016/j.wneu.2024.11.019. Epub 2024 Dec 6. PMID: 39561959.	No comparison of late and early surgery
Chen L, Wang L, Wu Y, Li N, Lin L, Li X, Gao Y, Zhao Y. Quantitative analysis of retinal and choroidal microvascular changes after endonasal endoscopic pituitary adenoma resection: An OCTA study. Photodiagnosis Photodyn Ther. 2025 Jun;53:104639. doi: 10.1016/j.pdpdt.2025.104639. Epub 2025 May 17. PMID: 40389085.	No comparison of late and early surgery
Chung SB, Park CW, Seo DW, Kong DS, Park SK. Intraoperative visual evoked potential has no association with postoperative visual outcomes in transsphenoidal surgery. Acta Neurochir (Wien). 2012 Aug;154(8):1505-10. doi: 10.1007/s00701-012-1426-x. Epub 2012 Jun 29. PMID: 22739773.	No comparison of late and early surgery
Dekkers OM, de Keizer RJ, Roelfsema F, Vd Klaauw AA, Honkoop PJ, van Dulken H, Smit JW, Romijn JA, Pereira AM. Progressive improvement of impaired visual acuity during the first year after transsphenoidal surgery for non-functioning pituitary macroadenoma. Pituitary. 2007;10(1):61-5. doi: 10.1007/s11102-007-0007-0. PMID: 17318437; PMCID: PMC1915635.	No comparison of late and early surgery
Dutta P, Gyurmey T, Bansal R, Pathak A, Dhandapani S, Rai A, Bhansali A, Mukherjee KK. Visual outcome in 2000 eyes following microscopic transsphenoidal surgery for pituitary adenomas: Protracted blindness should not be a deterrent. Neurol India. 2016 Nov-	No comparison of late and early surgery

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van Essen MJ, Muskens IS, Lamba N, Belunek SFJ, van der Boog ATJ, Amelink GJ, Gosselaar PH, van Doormaal TPC, Stades AME, Verhoeff JJC, van Genderen MM, Eenhorst CAE, Broekman MLD. Visual Outcomes after Endoscopic Endonasal Transsphenoidal Resection of Pituitary Adenomas: Our Institutional Experience. J Neurol Surg B Skull Base. 2021 Jul;82(Suppl 3):e79-e87. doi: 10.1055/s-0039-3402020. Epub 2020 Feb 3. PMID: 34306920; PMCID: PMC8289550.	No comparison of late and early surgery
Fernández-Balsells MM, Murad MH, Barwise A, Gallegos-Orozco JF, Paul A, Lane MA, Lampropulos JF, Natividad I, Perestelo-Pérez L, Ponce de León-Lovatón PG, Erwin PJ, Carey J, Montori VM. Natural history of nonfunctioning pituitary adenomas and incidentalomas: a systematic review and metaanalysis. J Clin Endocrinol Metab. 2011 Apr;96(4):905-12. doi: 10.1210/jc.2010-1054. PMID: 21474687.	No comparison of late and early surgery
Fredes F, Undurraga G, Rojas P, Constanzo F, Lazcano C, Pinto J, Schmidt T. Visual Outcomes after Endoscopic Pituitary Surgery in Patients Presenting with Preoperative Visual Deficits. J Neurol Surg B Skull Base. 2017 Dec;78(6):461-465. doi: 10.1055/s-0037-1604169. Epub 2017 Jul 19. PMID: 29134164; PMCID: PMC5680029.	No comparison of late and early surgery
Gnanalingham KK, Bhattacharjee S, Pennington R, Ng J, Mendoza N. The time course of visual field recovery following transphenoidal surgery for pituitary adenomas: predictive factors for a good outcome. J Neurol Neurosurg Psychiatry. 2005 Mar;76(3):415-9. doi: 10.1136/jnnp.2004.035576. PMID: 15716538; PMCID: PMC1739567.	No comparison of late and early surgery
Grigor'eva NN, Serova NK. [Visual functional changes in patients with pituitary adenoma: results of transnasal-transsphenoidal tumor removal]. Vestn Oftalmol. 2006 May-Jun;122(3):19-22. Russian. PMID: 16826780.	No comparison of late and early surgery
Han KE, Choi H, Kim SJ, Lee SM, Lee JE. Clinical efficacy of optical coherence tomography parameters to	No comparison of late and early surgery

predict the visual field outcome following pituitary adenoma surgery. PLoS One. 2024 Nov 12;19(11):e0313521. doi: 10.1371/journal.pone.0313521. PMID: 39531448; PMCID: PMC11556729.	
Hwang K, Kim YH, Kim JH, Lee JH, Yang HK, Hwang JM, Kim CY, Han JH. The outcomes of conservatively observed asymptomatic nonfunctioning pituitary adenomas with optic nerve compression. J Neurosurg. 2020 Jun 5;134(6):1808-1815. doi: 10.3171/2020.4.JNS192778. PMID: 32502994.	No comparison of late and early surgery
Iqbal M, Irfan S, Goyal JL, Singh D, Singh H, Dutta G. An Analysis of Retinal Nerve Fiber Layer Thickness before and after Pituitary Adenoma Surgery and its Correlation with Visual Acuity. Neurol India. 2020 Mar-Apr;68(2):346-351. doi: 10.4103/0028-3886.280634. PMID: 32189695.	No comparison of late and early surgery
Kerrison JB, Lynn MJ, Baer CA, Newman SA, Biousse V, Newman NJ. Stages of improvement in visual fields after pituitary tumor resection. Am J Ophthalmol. 2000 Dec;130(6):813-20. doi: 10.1016/s0002-9394(00)00539-0. PMID: 11124302.	No comparison of late and early surgery
Kim JH, Lee JH, Lee JH, Hong AR, Kim YJ, Kim YH. Endoscopic Transsphenoidal Surgery Outcomes in 331 Nonfunctioning Pituitary Adenoma Cases After a Single Surgeon Learning Curve. World Neurosurg. 2018 Jan;109:e409-e416. doi: 10.1016/j.wneu.2017.09.194. Epub 2017 Oct 7. PMID: 29017983.	No comparison of late and early surgery
Kristof RA, Kirchhofer D, Handzel D, Neuloh G, Schramm J, Mueller CA, Eter N. Pre-existing chiasma syndromes do not entirely remit following transsphenoidal surgery for pituitary adenomas. Acta Neurochir (Wien). 2011 Jan;153(1):26-32. doi: 10.1007/s00701-010-0792-5. Epub 2010 Sep 18. PMID: 20852901.	No comparison of late and early surgery
Luomaranta T, Raappana A, Saarela V, Liinamaa MJ. Factors Affecting the Visual Outcome of Pituitary Adenoma Patients Treated with Endoscopic Transsphenoidal Surgery. World Neurosurg. 2017 Sep;105:422-431. doi: 10.1016/j.wneu.2017.05.144. Epub 2017 Jun 2. PMID: 28583452.	No comparison of late and early surgery
Messerer M, Dubourg J, Raverot G, Bervini D, Berhouma M, George I, Chacko AG, Perrin G, Levivier M, Daniel RT, Trouillas J, Jouanneau E. Non-functioning pituitary macro-incidentalomas benefit from early surgery before becoming symptomatic. Clin Neurol Neurosurg. 2013 Dec;115(12):2514-20. doi: 10.1016/j.clineuro.2013.10.007. Epub 2013 Oct 22. PMID: 24262138.	No comparison of late and early surgery

Meyer J, Diouf I, King J, Drummond K, Stylli S, Kaye A, Kalincik T, Danesh-Meyer H, Symons RCA. A comparison of macular ganglion cell and retinal nerve fibre layer optical coherence tomographic parameters as predictors of visual outcomes of surgery for pituitary tumours. Pituitary. 2022 Aug;25(4):563-572. doi: 10.1007/s11102-022-01228-w. Epub 2022 May 13. PMID: 35552990.	No comparison of late and early surgery
Moon CH, Hwang SC, Ohn YH, Park TK. The time course of visual field recovery and changes of retinal ganglion cells after optic chiasmal decompression. Invest Ophthalmol Vis Sci. 2011 Oct 10;52(11):7966-73. doi: 10.1167/iovs.11-7450. PMID: 21896856.	No comparison of late and early surgery
Müslüman AM, Cansever T, Yılmaz A, Kanat A, Oba E, Çavuşoğlu H, Sirinoğlu D, Aydın Y. Surgical results of large and giant pituitary adenomas with special consideration of ophthalmologic outcomes. World Neurosurg. 2011 Jul-Aug;76(1-2):141-8; discussion 63-6. doi: 10.1016/j.wneu.2011.02.009. PMID: 21839965.	No comparison of late and early surgery
Parikh D, Robins JMW, Garretty T, Sheikh AJ, Tyagi AK, Nix PA, Phillips NI. Quantitative and functional visual field outcomes after endoscopic trans-sphenoidal pituitary adenectomy. Acta Neurochir (Wien). 2022 Jun;164(6):1605-1614. doi: 10.1007/s00701-022-05198-7. Epub 2022 Apr 15. PMID: 35426509.	No comparison of late and early surgery
Pelsma ICM, Verstegen MJT, de Vries F, Notting IC, Broekman MLD, van Furth WR, Biermasz NR, Pereira AM. Quality of care evaluation in non-functioning pituitary adenoma with chiasm compression: visual outcomes and timing of intervention clinical recommendations based on a systematic literature review and cohort study. Pituitary. 2020 Aug;23(4):417-429. doi: 10.1007/s11102-020-01044-0. Erratum in: Pituitary. 2020 Aug;23(4):430-431. doi: 10.1007/s11102-020-01061-z. PMID: 32419072; PMCID: PMC7316692.	Insufficient comparison of early and late surgery. Mentioned timelines regarding timing of surgery are based on expert opinion.
Pelsma ICM, Verstegen MJT, de Vries F, Notting IC, Broekman MLD, van Furth WR, Biermasz NR, Pereira AM. Quality of care evaluation in non-functioning pituitary adenoma with chiasm compression: visual outcomes and timing of intervention clinical recommendations based on a systematic literature review and cohort study. Pituitary. 2020 Aug;23(4):417-429. doi: 10.1007/s11102-020-01044-0. Erratum in: Pituitary. 2020 Aug;23(4):430-431. doi: 10.1007/s11102-020-01061-z. PMID: 32419072; PMCID: PMC7316692.	Insufficient comparison of early and late surgery. Mentioned timelines regarding timing of surgery are based on expert opinion.
Pereira AM, Biermasz NR. Treatment of nonfunctioning pituitary adenomas: what were the contributions of the last 10 years? A critical view. Ann Endocrinol (Paris). 2012 Apr;73(2):111-6. doi:	No comparison of late and early surgery

10.1016/j.ando.2012.04.002. Epub 2012 Apr 26. PMID: 22542000.	
Ryu WH, Tam S, Rotenberg B, Labib MA, Lee D, Nicolle DA, Van Uum S, Duggal N. Conservative management of pituitary macroadenoma contacting the optic apparatus. Can J Neurol Sci. 2010 Nov;37(6):837-42. doi: 10.1017/s0317167100051532. PMID: 21059548.	No comparison of late and early surgery
Sufaro Y, Shmueli M, Avraham E, Paran N, Blumkine T, Melamed I, Frenkel M, Azriel A. Early Surgical Intervention in Nonfunctioning Pituitary Macroadenomas in Adult Patients without Optic Apparatus Compression-Should We Consider It? A Matched Case-Control Study. World Neurosurg. 2024 Nov;191:e423-e428. doi: 10.1016/j.wneu.2024.08.151. Epub 2024 Sep 3. PMID: 39236806.	No comparison of late and early surgery
Tang Y, Jia W, Xue Z, Yuan L, Qu Y, Yang L, Wang L, Ma X, Wang M, Meng L, Lei K, Lu W, Peng X. Prognostic value of radial peripapillary capillary density for visual field outcomes in pituitary adenoma: A case-control study. J Clin Neurosci. 2022 Jun;100:113-119. doi: 10.1016/j.jocn.2022.04.012. Epub 2022 Apr 18. PMID: 35447509.	No comparison of late and early surgery
Uvelius E, Valdemarsson S, Bengzon J, Hammar B, Siesjö P. Visual acuity in patients with non-functioning pituitary adenoma: Prognostic factors and long-term outcome after surgery. Brain Spine. 2023 Aug 26;3:102667. doi: 10.1016/j.bas.2023.102667. PMID: 38020979; PMCID: PMC10668060.	No comparison of late and early surgery
Wang MTM, King J, Symons RCA, Stylli SS, Daniell MD, Savino PJ, Kaye AH, Danesh-Meyer HV. Temporal patterns of visual recovery following pituitary tumor resection: A prospective cohort study. J Clin Neurosci. 2021 Apr;86:252-259. doi: 10.1016/j.jocn.2021.01.007. Epub 2021 Feb 16. PMID: 33775337.	No comparison of late and early surgery
Xia L, Wenhui J, Xiaowen Y, Wenfang X, Wei Z, Yanjun H, Xiaoyan P. Predictive value of macular ganglion cell-inner plexiform layer thickness in visual field defect of pituitary adenoma patients: a case-control study. Pituitary. 2022 Aug;25(4):667-672. doi: 10.1007/s11102-022-01248-6. Epub 2022 Jul 14. PMID: 35834154.	No comparison of late and early surgery
Zheng Z, Wang H, Chen Q, Wang Z, Fu J, Fan W, Lin Y, Kang D, Jiang C, Lin Z, Yan X. A clinical practical model for preoperative prediction of visual outcome for pituitary adenoma patients in a retrospective and prospective study. Front Endocrinol (Lausanne). 2024 Dec 13;15:1479442. doi: 10.3389/fendo.2024.1479442. Erratum in: Front Endocrinol (Lausanne). 2025 Jan 28;15:1546763. doi:	No comparison of late and early surgery

10.3389/fendo.2024.1546763. PMID: 39735648; PMCID: PMC11671264.	

Literature search strategy

No.	Query	Results
#1	'hypophysis tumor'/exp OR 'acromegaly'/exp OR (((pituitar* OR hypophys* OR adenohypophys* OR neurohypophys* OR sellar OR parasellar) NEAR/4 (adenoma* OR microadenoma* OR macroadenoma* OR cancer* OR carcinoma* OR cyst* OR lesion* OR malignan* OR neoplasm* OR tumor* OR tumour*)):ti,ab,kw) OR ((cushing* NEAR/3 (syndrome* OR disease*)):ti,ab,kw) OR craniopharyngioma*:ti,ab,kw OR 'cranio pharyngioma*':ti,ab,kw OR craniopharyngeoma*:ti,ab,kw OR pharyngioma*:ti,ab,kw OR gonadotropinoma*:ti,ab,kw OR prolactinoma*:ti,ab,kw OR microprolactinoma*:ti,ab,kw OR macroprolactinoma*:ti,ab,kw OR 'macro adenoma*':ti,ab,kw OR macroadenoma*:ti,ab,kw OR acromegal*:ti,ab,kw OR akromegal*:ti,ab,kw OR ((('non function*' OR nonfunction*) NEAR/3 adenoma*):ti,ab,kw) OR (((craniopharyngeal OR rathke*) NEAR/3 (tumor* OR tumour* OR cyst*)):ti,ab,kw)	94759
#2	'chiasmal compression'/exp OR 'optic chiasm'/exp OR 'visual acuity'/exp OR 'visual impairment'/exp OR 'visual field defect'/exp OR 'vision'/exp OR ((chiasm* NEAR/4 (optic* OR compress* OR imping* OR displac* OR lesion* OR damag* OR involve*)):ti,ab,kw) OR ((compress* NEAR/3 (lesion* OR optic*)):ti,ab,kw) OR 'optic decussation':ti,ab,kw OR 'chiasm syndrom*':ti,ab,kw OR vision:ti,ab,kw OR visual:ti,ab,kw OR sight:ti,ab,kw	1077346
#3	'early intervention'/exp OR 'time to treatment'/exp OR 'time factor'/exp OR 'therapy delay'/exp OR 'conservative treatment'/de OR 'watchful waiting'/exp OR ('preoperative period'/exp AND ('pituitary surgery'/exp OR 'transsphenoidal surgery'/de OR 'hypophysectomy'/exp)) OR (((early OR timing OR 'as early as possible' OR timely OR 'wait time' OR late OR delay* OR postpon* OR conservative) NEAR/4 (surg* OR microsurg* OR neurosurg* OR operat* OR intervention* OR treat* OR decompress* OR hypophysectom*)):ti,ab,kw) OR (('time to' NEAR/2 surg*):ti,ab,kw) OR 'time to treat*':ti,ab,kw OR 'time to operat*':ti,ab,kw OR ((conservativ* NEAR/3 (manag* OR interven* OR treat* OR approach*)):ti,ab,kw) OR 'non surg*':ti,ab,kw OR nonsurg*:ti,ab,kw OR 'non operat*':ti,ab,kw OR nonoperat*:ti,ab,kw OR ((expect* NEAR/5 manag*):ti,ab,kw) OR ((natural NEAR/3 (course* OR history)):ti,ab,kw)	1006031
#4	#1 AND #2 AND #3 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) AND [1995-2025]/py	999
#5	'meta analysis'/exp OR 'systematic review'/exp OR 'scoping review'/exp OR 'rapid review'/exp OR 'umbrella review'/exp OR 'cochrane database of systematic reviews'/jt OR 'network meta-analysis'/exp OR 'networkmeta analy*':ti,ab,kw OR 'networkmetaanaly*':ti,ab,kw OR metaanaly*:ti,ab,kw OR 'meta	1089977

	analy*':ti,ab,kw OR metanaly*:ti,ab,kw OR prisma:ti,ab,kw OR prospero:ti,ab,kw OR metaanali*:ti,ab,kw OR 'meta anali*':ti,ab,kw OR metanali*:ti,ab,kw OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab,kw) OR (((structured OR systemic*) NEAR/3 (review* OR overview* OR synth*) NEAR/3 literature):ti,ab,kw) OR ((systemic* NEAR/1 review*):ti,ab,kw) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab,kw) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab,kw) OR (((literature NEAR/3 (review* OR overview*)):ti,ab,kw) AND (search*:ti,ab,kw OR database*:ti,ab,kw OR 'data base*':ti,ab,kw)) OR (('data extraction*':ti,ab,kw OR 'data source*':ti,ab,kw) AND ('study selection*':ti,ab,kw OR 'studies selection*':ti,ab,kw)) OR ('search strateg*':ti,ab,kw AND 'selection criteria*':ti,ab,kw) OR ('data source*':ti,ab,kw AND 'data synth*':ti,ab,kw) OR medline*:ti,ab,kw OR pubmed*:ti,ab,kw OR 'pub med*':ti,ab,kw OR embase:ti,ab,kw OR cochrane*:ti,ab,kw OR (((critical* OR rapid*) NEAR/2 (review* OR overview* OR synth*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synth*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynth*:ti,ab,kw OR 'meta synth*':ti,ab,kw OR 'review* of review*':ti,ab,kw	
#6	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	4229028
#7	'major clinical study'/de OR 'clinical study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'cohort analysis'/de OR 'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti) OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross	17895016

	over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#8	#4 AND #5	58
#9	#4 AND #6 NOT #8	84
#10	#4 AND #7 NOT (#8 OR #9)	414
#11	#4 NOT (#8 OR #9 OR #10)	443

Ovid/Medline

#	Searches	Results
1	exp Pituitary Neoplasms/ or exp Acromegaly/ or ((pituitar* or hypophys* or adenohypophys* or neurohypophys* or sellar or parasellar) adj4 (adenoma* or microadenoma* or macroadenoma* or cancer* or carcinoma* or cyst* or lesion* or malignan* or neoplasm* or tumor* or tumour*)).ti,ab,kf. or (cushing* adj3 (syndrome* or disease*)).ti,ab,kf. or craniopharyngioma*.ti,ab,kf. or 'cranio pharyngioma*'.ti,ab,kf. or craniopharyngeoma*.ti,ab,kf. or pharyngioma*.ti,ab,kf. or gonadotropinoma*.ti,ab,kf. or prolactinoma*.ti,ab,kf. or microprolactinoma*.ti,ab,kf. or macroprolactinoma*.ti,ab,kf. or 'macro adenoma*'.ti,ab,kf. or macroadenoma*.ti,ab,kf. or acromegal*.ti,ab,kf. or akromegal*.ti,ab,kf. or (('non function*' or nonfunction*) adj3 adenoma*).ti,ab,kf. or ((craniopharyngeal or rathke*) adj3 (tumor* or tumour* or cyst*)).ti,ab,kf.	65904
2	exp Optic Chiasm/ or exp Visual Acuity/ or exp Vision Disorders/ or exp Visual Fields/ or exp Vision, Ocular/ or (chiasm* adj4 (optic* or compress* or imping* or displac* or lesion* or damag* or involve*)).ti,ab,kf. or (compress* adj3 (lesion* or optic*)).ti,ab,kf. or 'optic decussation'.ti,ab,kf. or 'chiasm syndrom*'.ti,ab,kf. or vision.ti,ab,kf. or visual.ti,ab,kf. or sight.ti,ab,kf.	771735
3	exp Early Medical Intervention/ or exp Time-to-Treatment/ or exp Time Factors/ or exp Treatment Delay/ or exp Conservative Treatment/ or exp Watchful Waiting/ or (exp Preoperative Period/ and exp Hypophysectomy/) or ((early or timing or 'as early as possible' or timely or 'wait time' or late or delay* or postpon* or	1806954

	conservative) adj4 (surg* or microsurg* or neurosurg* or operat* or intervention* or treat* or decompress* or hypophysectom*)).ti,ab,kf. or (time adj1 to adj1 (surg* or treat* or operat*)).ti,ab,kf. or (conservativ* adj3 (manag* or interven* or treat* or approach*)).ti,ab,kf. or 'non surg*'.ti,ab,kf. or nonsurg*.ti,ab,kf. or 'non operat*'.ti,ab,kf. or nonoperat*.ti,ab,kf. or (expect* adj5 manag*).ti,ab,kf. or (natural adj3 (course* or history)).ti,ab,kf.	
4	(1 and 2 and 3) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/)	755
5	limit 4 to yr="1995 -Current"	631
6	exp Meta-Analysis/ or exp Network Meta-Analysis/ or exp Systematic Review/ or (networkmeta analy* or networkmetaanaly* or metaanaly* or meta analy* or metanaly* or prisma or prospero or metaanali* or meta anali* or metanali*).ti,ab,kf. or ((systemati* or scoping or umbrella or structured literature) adj3 (review* or overview*)).ti,ab,kf. or ((structured or systemic*) adj3 (review* or overview* or synth*) adj3 literature).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 (review* or overview*)) and (search* or database* or data base*)).ti,ab,kf. or ((data extraction* or data source*) and (study selection* or studies selection*)).ti,ab,kf. or (search strateg* and selection criteria*).ti,ab,kf. or (data source* and data synth*).ti,ab,kf. or (medline* or pubmed* or pub med* or embase or cochrane*).ti,ab,kf. or cochrane.jw. or ((critical* or rapid*) adj2 (review* or overview* or synth*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synth*)) and (search* or database* or data base*)).ab. or metasynth*.ti,ab,kf. or meta synth*.ti,ab,kf.	812948
7	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2855822
8	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase	7946678

	adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or exp cohort studies/ or epidemiologic studies/ or ((multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.)) or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	
9	5 and 6	30
10	(5 and 7) not 9	38
11	(5 and 8) not (9 or 10)	286
12	5 not (9 or 10 or 11)	277

Module 3 – Timing operatie bij apoplexie

Uitgangsvraag

Wat is de optimale timing van operatie bij apoplexie?

Search and select

A systematic review of the literature was performed to answer the following question(s):

- What is the effect of surgery versus conservative management on outcomes and complications in patients with apoplexy?
- What is the effect of early versus late surgery on outcomes and complications in patients with apoplexy?

Table 1. PICO

	PICO 1	PICO 2
Patients	Adults with apoplexy	Adults with apoplexy
Intervention	Surgery	Early surgery
Control	Conservative treatment	Late surgery
Outcomes	Visual acuity, visual field, pituitary function (anterior and posterior lobe/AVP deficiency), headache, oculomotor function (N. oculomotorius, abducens, and/or trochlearis), quality of life, perioperative complications (*i.e*. cerebrospinal fluid leakage, postoperative bleeding, infection)	
Other selection criteria	Study design: systematic reviews and randomized controlled trials	

Relevant outcome measures

The guideline panel considered visual acuity, visual fields and pituitary function as **critical** outcome measures for decision making; and oculomotor function, quality of life and perioperative complications as **important** outcome measures for decision making.

The guideline panel defined the outcome measures as follows: for visual acuity, visual field, pituitary function, cranial nerve palsy and complications a difference in relative risk of 25% (RR<0,75 or >1,25) was set as threshold.
The threshold for headache and quality of life was set as a difference of 0,5 standard deviation.

Search and select (Methods)

A systematic literature search was performed by a medical information specialist using Embase.com and Ovid/Medline. Both databases were searched from 1995 to December 16, 2024 for systematic reviews, RCTs and observational studies. Systematic searches were completed using a combination of controlled vocabulary/subject headings (e.g., Emtree-terms, MeSH) wherever they were available and natural language keywords. The overall search strategy was derived from two primary search concepts: (1) Pituitary apoplexy and (2) Timing operation/ conservative. Duplicates were removed using EndNote software. After deduplication a total of 266 records were imported for title/abstract screening. Initially, 42 studies were selected based on title and abstract screening. After reading the full text, 31 studies were excluded (see the exclusion table under the tab 'Evidence tabellen'), and 11 studies were included.

Summary of literature

Description of studies

A total of 11 studies were included in the analysis of the literature. Important study characteristics and results are summarized in table 2. The assessment of the risk of bias is

summarized in the risk of bias tables (under the tab 'Evidence tabellen'). Of the 11 identified articles, 7 reported on the comparison of surgery versus conservative management, 2 on the comparison of early versus late surgery, and 2 on both.

PICO 1: Surgical versus conservative management
Nine articles reported on the comparison of surgery versus conservative management.

Marx (2021) compared the outcomes of patients with PA managed either by a conservative or surgical approach in a retrospective study. They included patients diagnosed between 2007 and 2018 with abrupt onset of severe headache and/or visual disturbances and brain imaging (MRI). Patients were excluded when the follow-up was shorter than 3 months or had a presentation of subclinical PA. Patients received surgical or conservative treatment based on clinical judgement. This decision was based on severity of symptoms, imaging findings, patient comorbidities and institutional practices and availability of neurosurgical expertise.

Ragate (2024) performed a retrospective record review of PA patients treated with a surgical or conservative approach. Patients were included when they were treated between 2000 and 2023 and had clinical and radiological confirmation. Subclinical PA patients were excluded. Conservative management included intravenous administration of dexamethasone (4.0mg) and mannitol (100 ml) every 8 hours for about five days. Cohorts were PAS-matched to compare surgical and conservative management.

Nakhleh (2021) assessed clinical characteristics of apoplexy between patients who received conservative or surgical treatment in a single center. Patients were included when they were hospitalized between January 2001 and October 2017 with pituitary apoplexy (confirmed by MRI or CT) and a minimal follow-up of one year. The decision to treat patients surgically or conservatively was based on clinical presentation such as altered level of consciousness, deteriorating visual acuity, persistent visual field defects, ocular palsy and functioning pituitary adenoma and physician judgement.

Mamelak (2024) compared presentation and outcomes in PA patients treated with surgical or medical management in a multicenter, international prospective registry. A comparison of conservative versus surgical treatment was performed as well as a comparison between early and late surgical interventions with two, three and four days as cutoff. Treatment decisions were made independently at each site and data was collected without influencing clinical management. Patients older than 18 years with a diagnosed PA based on established clinical and radiological graphic features were eligible. Patients with hemorrhage or infarction on imaging studies but with no clinical symptoms of PA were not eligible. Treatment decisions were based on the physicians' best judgement and treatment preferences at each site. Factors that influenced surgical decisions were visual field deficits, MRI findings, PAS and progressive deterioration of consciousness or worsening of visual fields despite of corticosteroids.

Budohoski (2022) analyzed patients from four neurosurgical centers in the UK that were treated between 2003 and 2020. PA was confirmed clinically and radiologically. Three groups of patients were analyzed: those who had surgery within 7 days, surgery between 7 days and 3 months after presentation and non-operative management. Treatment of the patients was based on physicians' judgement.

Pineda-Centeno (2024) included all patients with a diagnosis of pituitary apoplexy (PA) between April 2020 and September 2023 in a retrospective cohort study. PA diagnosis was

defined by clinical characteristics and an acute bleeding pituitary tumor on MRI. Patients with PA and a SARS-CoV-2 infection were conservatively treated, as well as patient with non-neurological deficits or only mild visual symptoms. Patients with severe visual symptoms (visual acuity 20/50 or worse) or neurological deterioration were considered for surgery.

Saktiwarawat (2024) compared neuroendocrine outcomes between surgical and conservative treatment in a single center. In a retrospective cohort study, consecutive patients with pituitary apoplexy who received surgery or conservative management between 2005 and 2022 were reviewed. A propensity score matching method was used to adjust bias from treatment selection (surgery or conservative treatment). Neurosurgeons determined treatment based on clinical presentation of visual function and radiological findings.

Almeida (2019) evaluated in a retrospective study (January 2007- June 2017) the results of conservative and surgical management. Patients with clinically and radiologically confirmed PA were included. When follow up was less than 3 months patients were excluded from the study. Patients who presented acute deterioration of visual status and/or level of consciousness were selected for surgery. Patients with no visual field deficit and those who had medical contraindications undergo a surgical procedure because of previous comorbidities were treated conservatively.

Shepard (2021) reviewed the radiological and clinical outcomes of patients with PA who were managed conservatively or surgically. Patients who were radiologically and clinically diagnosed with PA between January 1, 2007, and February 9, 2019 were included to the study. If patients did not have at least one radiological and clinical follow-up visit, they were excluded from the study. The institution initially managed patients with apoplexy in a conservative fashion. Only patients with worsening visual acuity, cranial neuropathies or progressive visual field deterioration were offered surgery within a week of presentation.

PICO 2: Early versus late surgery

Four articles reported on the comparison of early versus late surgery.

Zhu (2022) retrospectively analyzed if there is a difference in outcomes between late or early surgery in patients that were diagnosed with ischemic PA between January 2013 and December 2020. Confirmation of PA was done by CT or MRI. In addition, patients had to have complete clinical data and postoperative pathological confirmation. The timing of the surgical intervention was based on clinical judgement, the severity and progression of symptoms and the interval from initial onset to severe symptoms. Early intervention was defined as surgery within 7 days. The surgery was late after seven days.

Rutkowski (2018) investigated whether there was a significant difference in outcomes for patients with pituitary apoplexy, based on the time between symptom onset and surgical intervention. Surgical intervention within 72 hours after symptom onset was defined as early intervention. After 72 hours surgery was late intervention. A total of 32 patients with acute PA who underwent transsphenoidal resection between 2003 to 2014 were retrospectively analyzed. PA was demonstrated on MRI with evidence of apoplexy in the form of intratumoral hemorrhage, ischemia, and necrosis. Timing of surgical intervention for each patient was based on the severity of symptoms, delays in patient presentation to healthcare professionals, transfer delays form other hospitals and need for preoperative stabilization.

Mamelak (2024) and Budohoski (2022) also reported on the comparison of early versus late surgery, in addition to the comparison of surgical versus conservative management and are described above in more detail.

5

Table 2. Characteristics of included studies

<table>
<tr><th>Study</th><th>Participants</th><th>Comparison</th><th>Follow-up</th><th>Outcome measures</th><th>Comments</th><th>Risk of bias*</th></tr>
<tr><td colspan="7">Surgical versus conservative approach</td></tr>
<tr><td>Marx, 2021

Retrospective cohort study</td><td>N at baseline: 46
I: 19 | C: 27

Age: mean (range in years)
I: 51.1 (23.2 – 73.2) | C: 44.6 (22.3 – 76.4)

Sex (M:F):
I: 12:7 | C: 17:10

Characteristics:<table><tr><th></th><th>I (%)</th><th>C (%)</th></tr><tr><td>Decrease visual acuity</td><td>50</td><td>12.5</td></tr><tr><td>Visual field defects</td><td>73.7</td><td>24</td></tr><tr><td>Ocular palsy</td><td>63.2</td><td>50</td></tr><tr><td>Headache</td><td>73.7</td><td>88.9</td></tr></table></td><td>Intervention:
Surgery

Control:
Conservative management</td><td>3 months, 1 year and at final follow up.

The median follow-up was 28.3 months (106 days to 10.2 years)</td><td>Visual acuity

Visual field

Cranial nerve palsy</td><td></td><td>Some Concern</td></tr>
<tr><td>Ragate, 2024

Retrospective cohort study</td><td>N at baseline: 50
I: 25 | C: 25

Age: mean (range)
I: 38 (19-71) | C: 46 (23-80)

Sex (M:F)
I: 13:12 | C: 19:6

PAS: Cohorts were formed to have PAS-matched scores.

Characteristics:<table><tr><th></th><th>I (%)</th><th>C (%)</th></tr><tr><td>Decrease visual acuity</td><td>72.7</td><td>45.4</td></tr><tr><td>Visual field defects</td><td>36.3</td><td>22.7</td></tr><tr><td>Ocular palsy</td><td>68.1</td><td>68.1</td></tr><tr><td>Headache</td><td>80</td><td>84</td></tr></table></td><td>Intervention:
Surgery

Control:
Conservative management: intravenous administration of dexamethasone (4.0mg) and mannitol (100 ml) every 8 hours for about five days</td><td>3-6 monthly intervals for follow up.

Follow up duration in months (Median):
I: 23 | C: 12</td><td>Visual acuity

Visual field

Cranial nerve palsy

Neuroendocrine function</td><td>Cohorts were formed to have PAS-matched scores.</td><td>Low</td></tr>
</table>

<table>
<tr>
<td>Nakhleh, 2021

Retrospective cohort study</td>
<td>N at baseline: 27
I: 17 | C: 10

Age: Mean (SD)
I: 42.5 (11.3) | C: 37.7 (14.1)

Sex: (M:F)
I: 9:8 | C: 5:5

Characteristics:
<table>
<tr><th></th><th>I (%)</th><th>C (%)</th></tr>
<tr><td>Decrease visual acuity</td><td>0</td><td>10</td></tr>
<tr><td>Visual field defects</td><td>41</td><td>20</td></tr>
<tr><td>Ocular palsy</td><td>12</td><td>10</td></tr>
<tr><td>Headache</td><td>100</td><td>80</td></tr>
</table></td>
<td>Intervention:
Surgery

Control:
Conservative management</td>
<td>Intervention in years (median, [range]):
4[1-15]

Control in years (median [range]):
3[1-6]</td>
<td>Visual field

Cranial nerve palsy</td>
<td></td>
<td>Some concerns</td>
</tr>
<tr>
<td>Mamelak, 2024

Prospective observational cohort study</td>
<td>N at baseline: 107
I: 67 | C: 30

Age: Median (IQR)
I: 53 (40-62) | C: 50 (35-72)

Sex: (M:F)
I: 44:23 | C: 24:6

Characteristics:
<table>
<tr><th></th><th>I (%)</th><th>C (%)</th></tr>
<tr><td>Decrease visual acuity</td><td colspan="2">Not reported</td></tr>
<tr><td>Visual field defects</td><td>45</td><td>20</td></tr>
<tr><td>Ocular palsy</td><td>40</td><td>31</td></tr>
<tr><td>Headache</td><td>94</td><td>87</td></tr>
<tr><td>PAS score 0-3</td><td>86</td><td>100</td></tr>
</table></td>
<td>Intervention:
Surgery

Control:
Conservative management</td>
<td>3 months

Partial data at 6 months, so only qualitative conclusions are made from this data.</td>
<td>Visual field

Cranial nerve deficit

Neuroendocrine function

Headache

Quality of life</td>
<td></td>
<td>Low Risk</td>
</tr>
<tr>
<td>Budohoski, 2022

Retrospective cohort study</td>
<td>N at baseline: 160
I-1: 61 | I-2: 35 | C: 64

Age (mean, SD)
I-1 – 51 (14)| I-2 – 52 (16) | C: 55 (18)</td>
<td>Intervention:
group 1 –surgery within 7 days</td>
<td>Intervention months (Mean (SD)):
I-1: 66 (46)
I-2: 74 (39)</td>
<td>Visual Acuity

Visual fields

Cranial nerve deficit</td>
<td></td>
<td>Some concerns</td>
</tr>
</table>

<table>
<tr><td></td><td>Sex (M:F)
Total: 105:55
(not reported for I and C separately)

Characteristics:<table><tr><th></th><th>I-1 (%)</th><th>I-2 (%)</th><th>C (%)</th></tr><tr><td>Decrease visual acuity</td><td>61</td><td>46</td><td>23</td></tr><tr><td>Visual field defects</td><td>69</td><td>61</td><td>33</td></tr><tr><td>Ocular palsy</td><td>50</td><td>43</td><td>34</td></tr><tr><td>Headache</td><td>82</td><td>86</td><td>84</td></tr></table></td><td>Group 2 –surgery between 7 days and 3 months

Control: Conservative treatment.</td><td>Control months (Mean (SD)):
46 (39)

Outcomes measured at 6 months.</td><td></td><td></td><td></td></tr>
<tr><td>Pineda-Centeno, 2024

Retrospective cohort study</td><td>N at baseline: 27
I: 15 | C: 12

Age (mean, SD)
I: 38 ± 12 | C: 47 ± 13

Sex (M, %)
I: 67% | C: 58%

Characteristics:<table><tr><th></th><th>I (%)</th><th>C (%)</th></tr><tr><td>Decrease visual acuity</td><td>100</td><td>75</td></tr><tr><td>Visual field defects</td><td>73</td><td>67</td></tr><tr><td>3rd CN palsy</td><td>40</td><td>31</td></tr></table>Non-functioning adenoma (n, %)
I: 9 (60%) | C: 6 (50%)
PAS score (mean)
I: 2.93 | C: 2.67</td><td>Intervention: surgical intervention during first hospitalization plus initial 100mg hydrocortisone i.v. followed by 50mg every 8 hours

Control: i.v. dexamethasone 4mg every 8 hours plus 100mg of i.v. hydrocortisone initially, followed by 50mg every 8 hours</td><td>Up to 2 years</td><td>After 6 months, 1 year and 2 years:
Visual Acuity

Visual Field

Cranial nerve deficit

Neuroendocrine function</td><td>Selection for surgery based on severity of visual symptoms.</td><td>Some Concerns</td></tr>
<tr><td>Saktiwarawat, 2024

Retrospective cohort study</td><td>N at baseline: 127
I: 98 | C: 29
(both groups 28 after propensity score matching)

Age (mean, SD)</td><td>Intervention: surgical intervention, of which the timing was based on patient’s status,</td><td>Median follow-up (IQR):
Intervention: 42 months (19.5 - 76.5)</td><td>At last follow-up (at least 6 months)
Visual acuity

Visual field</td><td>Patients in the surgery group still [even after propensity score matching] had a significantly higher</td><td>Some Concerns</td></tr>
</table>

<table>
<tr>
<td></td>
<td>I: 51 ± 15 | C: 59 ± 17

<u>Sex (M, %)</u>
I: 46% | C: 46%

<u>Characteristics:</u>
<table><tr><th></th><th><u>I (%)</u></th><th><u>C (%)</u></th></tr><tr><td>Decrease visual acuity</td><td>75</td><td>86</td></tr><tr><td>Visual field defects</td><td>68</td><td>54</td></tr><tr><td>Ocular palsy</td><td>21</td><td>7</td></tr><tr><td>Headache</td><td>79</td><td>89</td></tr></table></td>
<td>visual function and radiographic findings. Microscopic technique until 2014; after 2014 transsphenoidal.

<u>Control:</u> no surgical treatment.</td>
<td><u>Control:</u> 28 months (14.5 - 51)</td>
<td>Cranial nerve deficit

Neuroendocrine function</td>
<td>incidence of preoperative hypothyroidism and hypogonadism, larger median tumor size, and higher suprasellar extension.</td>
<td></td>
</tr>
<tr>
<td>Almeida, 2019

Retrospective cohort study</td>
<td><u>N at baseline: 67</u>
I: 49 | C: 18

<u>Age (mean, SD)</u>
I: 58.8 ± 14.9 | C: 53.8 ± 19.4

<u>Sex (M, %)</u>
I: 65.3% | C: 50%

<u>Characteristics:</u>
<table><tr><th></th><th><u>I (%)</u></th><th><u>C (%)</u></th></tr><tr><td>Decrease visual acuity</td><td>55.1</td><td>38.8</td></tr><tr><td>Visual field defects</td><td>95.9</td><td>55.6</td></tr><tr><td>Ocular palsy</td><td>55.1</td><td>27.7</td></tr><tr><td>Headache</td><td>89.8</td><td>88.9</td></tr></table></td>
<td><u>Intervention:</u> surgical management

<u>Control:</u> conservative management.</td>
<td>Follow-up assessments were generally performed 6-8 weeks after surgery, at 3-month to 6-month intervals for the first year, and at 6-month to 12-month intervals thereafter.</td>
<td>Visual field

Cranial nerve deficit</td>
<td></td>
<td>Some concerns</td>
</tr>
<tr>
<td>Shepard, 2021

Retrospective cohort study</td>
<td><u>N at baseline: 64</u>
I: 17 | C: 47

<u>Age (mean, SD)</u>
Intervention: 52.5 ± 12.7
Control: 53.4 ± 17.9

<u>Sex (M, %)</u>
I: 52.9% | C: 55.3%</td>
<td><u>Intervention:</u> surgical management

<u>Control:</u> conservative management.</td>
<td>Conservative (months, IQR): 26.0 (12-53.0)

Intervention (months, IQR): 70 (40.5 – 98.5)</td>
<td>Visual acuity

Visual field

Cranial nerve deficit</td>
<td></td>
<td>Some concerns</td>
</tr>
</table>

<table>
<tr><td></td><td>Characteristics:<table><tr><td></td><td>I (%)</td><td>C (%)</td></tr><tr><td>Decrease visual acuity</td><td>52.9</td><td>12.8</td></tr><tr><td>Visual field defects</td><td>64.7</td><td>19.2</td></tr><tr><td>Ocular palsy</td><td>58.8</td><td>29.8</td></tr><tr><td>Headache</td><td>58.8</td><td>85.1</td></tr></table></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="7">Early versus late surgical intervention</td></tr>
<tr><td>Mamelak, 2024

Prospective observational cohort study</td><td>N at baseline 67
I: 12 | C: 55

Age (median, IQR)
I: 54 (42-64) | C: 53 (40-62)

Sex (M, %)
I: 58% | C: 67%

Characteristics:<table><tr><td></td><td>I (%)</td><td>C (%)</td></tr><tr><td>Decrease visual acuity</td><td>NR</td><td>NR</td></tr><tr><td>Visual field defects</td><td>NR</td><td>NR</td></tr><tr><td>Vision loss</td><td>42</td><td>49</td></tr><tr><td>Ocular palsy</td><td>42</td><td>35</td></tr><tr><td>Headache</td><td>83</td><td>96</td></tr><tr><td>PAS-score 0-3</td><td>100</td><td>83</td></tr></table></td><td>Intervention: Early surgery
3 day cutoff

Control: Late surgery
after 3 days</td><td>3 months</td><td>Cranial nerve deficit

Neuroendocrine function

Quality of life

Headache</td><td></td><td>Low Risk</td></tr>
<tr><td>Budohoski, 2022

Retrospective cohort study</td><td>See the section surgery vs. conservative management</td><td>Intervention:
Group 1 – surgery < 7 days

Group 2 –surgery between 7 days and 3 months

Control: Conservative treatment.</td><td></td><td>Visual Acuity

Visual fields

Cranial nerve deficit</td><td></td><td>Some concerns</td></tr>
</table>

<table>
<tr>
<td>Rutkowski, 2018

Retrospective cohort study</td>
<td><u>N at baseline: 31</u>
I: 13 | C: 19

<u>Age (mean, SD)</u>
Intervention: 45 ± NR
Control: 51 ± NR

<u>Sex (M, %)</u>
I: 54% | C: 74%

<u>Characteristics:</u>
Preoperative hypopituitarism (%):
I: 69% | C: 100%</td>
<td><u>Intervention:</u> Early surgical intervention (<72 hours of symptom onset)

<u>Control:</u> Delayed surgical intervention (>72 hours after onset)</td>
<td></td>
<td><u>Unclear follow-up:</u>
Headache</td>
<td>Unclear after what time outcomes were measured.</td>
<td>High Risk</td>
</tr>
<tr>
<td>Zhu, 2022

Retrospective cohort study</td>
<td><u>N at baseline: 46</u>
I: 12 | C: 33

<u>Age (mean, SD)</u>
Intervention: 46.58 ± 14.34
Control: 46.30 ± 11.65

<u>Sex (M/F)</u>
I: 11M/1F | C: 24M/9F

<u>Characteristics:</u>
<table>
<tr><th></th><th><u>I (%)</u></th><th><u>C (%)</u></th></tr>
<tr><td>Decrease visual acuity</td><td>91.7</td><td>90.9</td></tr>
<tr><td>Visual field defects</td><td>83.3</td><td>51.5</td></tr>
<tr><td>Ocular palsy</td><td>41.7</td><td>54.6</td></tr>
<tr><td>Headache</td><td>100</td><td>97</td></tr>
</table></td>
<td><u>Intervention:</u> Early surgical intervention (<7 days of symptom onset)

<u>Control:</u> Delayed surgical intervention (>7 days after onset)</td>
<td>Intervention (months): 72.11 ± 28.52

Control (months): 64.51 ± 34.90</td>
<td>Cranial nerve deficit

Neuroendocrine function</td>
<td>Unclear after what time outcomes were measured.

Study only included patients with ischemic PA.</td>
<td>Some concern</td>
</tr>
</table>

Abbreviations: F = Female; FPA = functioning pituitary adenoma, i.v. = intravenous; M = Male; MRI = Magnetic resonance imaging; NFPA = nonfunctioning pituitary adenoma; PAS = Pituitary Apoplexy Scoring

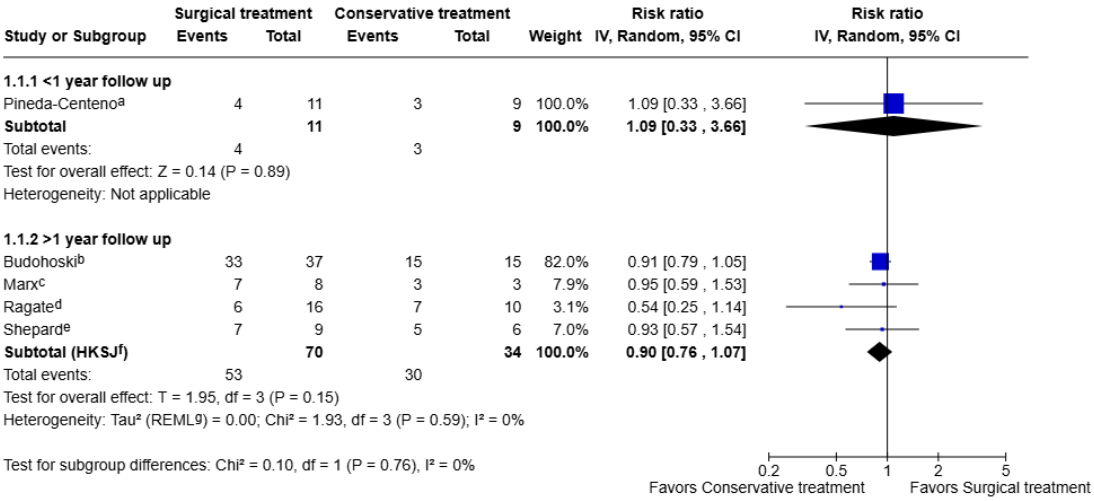
*For further details, see risk of bias table in the appendix

Results

PICO 1: Surgical versus conservative management

1. Visual acuity (crucial)

Visual acuity was described in six studies (Budohoski, 2022; Pineda-Centeno, 2024; Marx, 2021; Ragate, 2024; Shepard, 2021; Saktiwarawat, 2024). In each study visual acuity was determined by a physician. Figure 1 depicts the number of patients suffering from a visual acuity defect before the treatment (total) and the number of patients that recovered after the intervention (events). No clinically relevant results were reported between interventions.



Footnotes

[a]The follow up period was 6 months.
[b]The follow up period was between 66 and 74 months for the surgery group and 46 months for the conservative group.
[c]The follow up period was one year.
[d]The follow up period fot the surgery group was 23 months and 12 months for the conservative group.
[e]The follow up period was between two and five years.
[f]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[g]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 1. The pooled number of patients experiencing recovery of visual acuity, relative to those who had visual acuity deficits at inclusion. NB: the total number of patients in the intervention and control group were higher, yet only those with a visual defect at inclusion are shown in this figure.

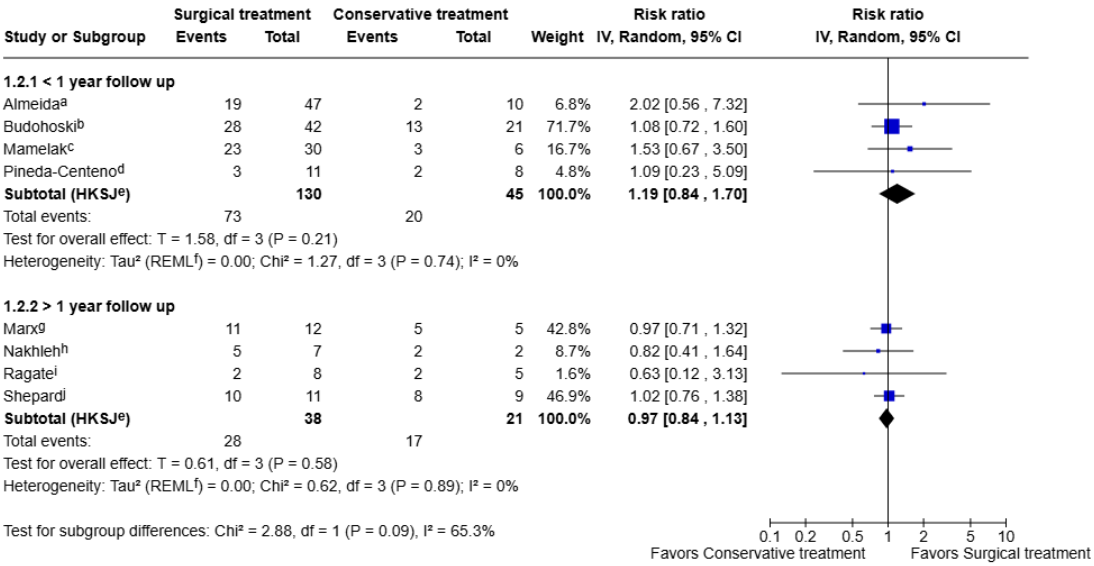
Saktiwarawat (2024) described the visual acuity per eye. Table 3 shows values regarding difference between groups. There was no clinically relevant difference between groups.

Table 3. Outcomes regarding visual outcomes (Saktiwarawat, 2024)

	Surgery, n (%) (total n in group = 28)	**Conservative, n (%) (total n in group = 28)**
Right VA recovery	16 (64)	15 (65)
Left VA recovery	18 (78)	15 (65)
Recovery of VA in at least one eye	22 (85)	16 (70)

2. Visual field (crucial)

Visual field was described in nine studies (Almeida, 2019; Budohoski, 2022; Mamelak, 2024; Pineda-Centeno, 2024; Marx, 2021; Nakhleh, 2021; Ragate, 2024; Shepard, 2021; Saktiwarawat, 2024). In each study, the visual field deficit was determined by a physician. Figure 2 depicts the number of patients suffering from a visual field deficit (total) before treatment and the number of patients with recovery of the defect after surgical or conservative management (events). The results were not clinically relevant.



Footnotes

[a]The follow up period was 6 weeks to 3 months.
[b]The follow up period was between 66 and 74 months for the surgery group and 46 months for the conservative group.
[c]The follow up period was 3 months.
[d]The follow up period was 6 months.
[e]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[f]Tau² calculated by Restricted Maximum-Likelihood method.
[g]The follow up period was one year.
[h]The follow up period was 3 to 4 years.
[i]The follow up period for the surgery group was 23 months and 12 months for the conservative group.
[j]The follow up period was 2 to 5 years.

Figure 2. The pooled number of patients experiencing recovery of visual fields, relative to those who had visual field deficits at inclusion. NB: the total number of patients in the intervention and control group were higher, yet only those with a visual defect at inclusion are shown in this figure.

Saktiwarawat (2024) described the visual field recovery per eye. Table 4 shows values regarding difference between groups. The difference was clinically relevant in favor of the surgical intervention.

Table 4. Outcomes regarding visual fields (Saktiwarawat, 2024)

	Surgery, n(%) (total n in group = 28)	**Conservative, n(%) (total n in group = 28)**
Right VF recovery	15 (83)	8 (50)
Left VF recovery	15 (79)	8 (50)
Recovery of VF in at least one eye	17 (85)	8 (50)

3. Pituitary function/ Neuroendocrine function

Pituitary function was analyzed by studies that described hypocortisolism, hypothyroidism and hypogonadism.

3.1 HPA-axis (Adrenal)

Hypocortisolism was described in six studies (Almeida, 2019; Pineda-Centeno, 2024; Mamelak, 2024; Marx, 2021; Ragate, 2024; Nakhleh, 2021). All studies reported pre- and post-intervention percentages of adrenal deficiency at the population level, however none provided patient-level data on hormonal recovery (table 5). The absence of individual recovery data prevents further analysis.

Table 5. Number of patient with adrenal deficiency before and after surgery or conservative treatment.

Study (year)	**Follow-up**	**Adrenal def before surgery**	**Adrenal def after surgery**	**Adrenal def before conservative**	**Adrenal def after conservative**
Almeida (2019)	unclear	12 (24.5%)	9 (18.7%)	0 (0%)	2 (11.7%)

Pineda-Centeno (2024)	1 month	3 (50%)	4 (100%)	2 (28.5%)	0 (0%)
Mamelak (2024)	3 months	44 (67%)	39 (89.4%)	19 (63%)	17 (89.5%)
Marx (2021)	1 year	7 (53.8%)	11 (64.7%)	12 (57.1%)	6 (28.6)
Ragate (2024)	12-23 months	12 (48%)	9 (36%)	10 (40%)	6 (24%)
Nakhleh (2021)	3-4 years	7 (46.6%)	9 (52.9%)	3 (37.5%)	4 (40%)

3.2 HPT-axis (Thyroid)

Hypothyroidism was described in seven studies (Almeida, 2019; Pineda-Centeno, 2024; Mamelak, 2024; Marx, 2021; Ragate, 2024; Saktiwarawat, 2024; Nakhleh, 2021). All studies reported pre- and post-intervention percentages of thyroid deficiency at the population level, however none provided patient-level data on hormonal recovery (table 6). The absence of individual recovery data prevents further analysis.

Table 6. Number of patients with thyroid deficiency before and after surgery or conservative treatment.

Study (year)	Follow-up	Thyroid def before surgery	Thyroid def after surgery	Thyroid def before conservative	Thyroid def after conservative
Almeida (2019)	unclear	1 (2.0%)	2 (4.1%)	0 (0%)	1 (5.8%)
Pineda-Centeno (2024)	1 month	9 (60%)	5 (100%)	5 (41.6%)	5 (83%)
Mamelak (2024)	3 months	34 (52%)	31 (91.1%)	13 (43%)	12 (91.7%)
Marx (2021)	1 year	8 (50%)	12 (70.6%)	13 (54.2%)	12 (54.5%)
Ragate (2024)	12-23 months	8 (32%)	4 (16%)	9 (36%)	4 (16%)
Saktiwarawat (2024)	28-42 months	16 (57%)	3 (19%)	7 (25%)	1 (14%)
Nakhleh (2021)	3-4 years	3 (20%)	7 (41.2%)	2 (22.2%)	1 (10%)

3.4 HPG-axis (sex hormones)

Hypogonadism was described in five studies (Pineda-Centeno, 2024; Mamelak, 2024; Marx, 2021; Ragate, 2024; Saktiwarawat). All studies reported pre- and post-intervention percentages of gonadal deficiency at the population level, however none provided patient-level data on hormonal recovery (table 7). The absence of individual recovery data prevents further analysis.

Table 7. Number of patient with gonadal deficiency before and after surgery or conservative treatment.

Study (year)	Follow-up	Gonadal def before surgery	Gonadal def after surgery	Gonadal def before conservative	Gonadal def after conservative
Pineda-Centeno (2024)	1 month	8 (53.3%)	4 (100%)	4 (33.3%)	1 (16%)
Mamelak (2024)	3 months	33 (52%)	31 (93.9%)	16 (53)	15 (93.7%)
Marx (2021)	1 year	8 (72.7%)	12 (80%)	16 (66.7%)	8 (44.4%)
Ragate (2024)	12-23 months	13 (52%)	10 (40%)	17 (68%)	12 (48%)
Saktiwarawat (2024)	28-42 months	15 (54%)	3 (21%)	8 (29%)	1 (13%)

4. Headache (crucial)

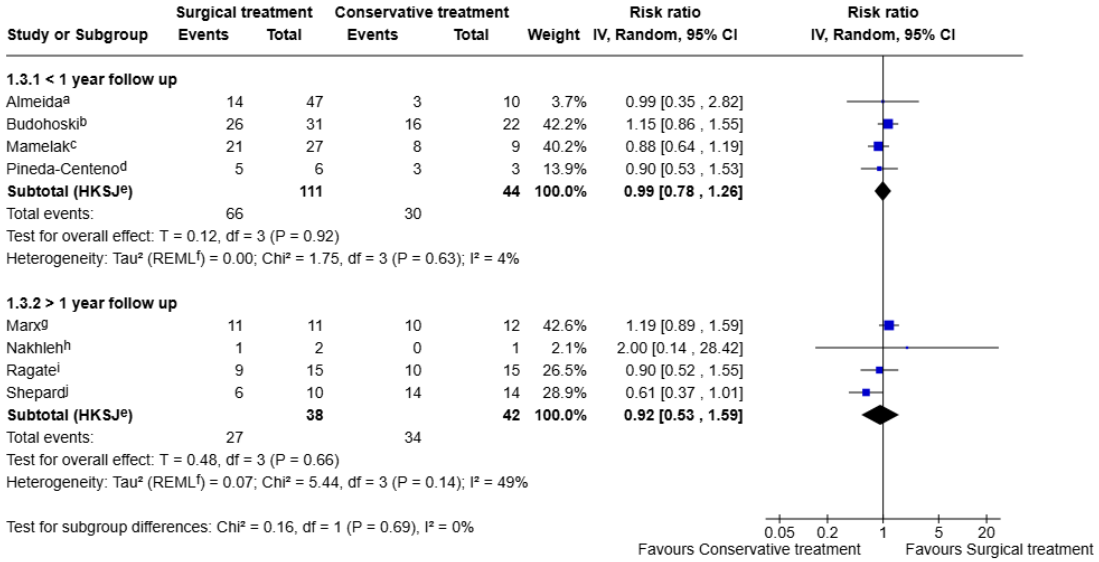
Mamelak (2024) reported on headache by using the headache impact test 6 (HIT-6) scale as an indicator. The scale goes from 36 (no headache) to 78 (always a headache). There was no clinically relevant difference between the groups (Table 8).

Table 8. Outcomes regarding headache.

	Surgical treatment (n=45)	Conservative treatment (n=14)	p-value
HIT-6 score, median (IQR)	44 (36-54)	40 (36-50)	0.6

5. Cranial nerve function

Cranial nerve function was described by nine studies (Almeida, 2019; Budohoski, 2022; Pineda-Centeno, 2024; Marx, 2021; Mamelak, 2024; Nakhleh, 2021; Ragate, 2024; Saktiwarawat, 2024; Shepard, 2021). In each study the cranial nerve deficit was determined by a physician. Results are shown in figure 3. The events include the number of patients that recovered from the deficit after the intervention. The total group notes the amount of patients that suffered from a decreased nerve function before the intervention. There was no clinically relevant difference between the groups of both <1 year follow up or >1 year follow up.



Footnotes

[a]The follow up period was 6 weeks to 3 months.
[b]The follow up period was between 66 and 74 months for the surgery group and 46 months for the conservative group.
[c]The follow up period was 3 months.
[d]The follow up period was 6 months.
[e]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[f]Tau² calculated by Restricted Maximum-Likelihood method.
[g]The follow up period was one year.
[h]The follow up period was 3 to 4 years.
[i]The follow up period for the surgery group was 23 months and 12 months for the conservative group.
[j]The follow up period was 2 to 5 years.

Figure 3. The pooled number of patients experiencing recovery of ocular palsy, relative to those who had ocular palsy at inclusion. NB: the total number of patients in the intervention and control group were higher, yet only those with ocular palsy at inclusion are shown in this figure.

Saktiwarawat (2024) described the cranial nerve function recovery per nerve. Table 9 shows values regarding differences between groups. There is no clinically relevant difference.

Table 9. Cranial nerve recovery in surgery versus conservative treatment.

	Surgery, n(%) (total n in group = 28)	Conservative, n(%) (total n in group = 28)
Recovery of CN III palsy	3 (75)	4 (100)
Recovery of CN IV palsy	2 (100)	-
Recovery of CN V palsy	1 (100)	1 (100)
Recovery of CN VI palsy	4 (80)	-

6. Quality of life (important)

Mamelak (2024) assessed the quality of life with the total score of the SF-36 form which indicates health in a scale from 0 (negative health) to 6400 (positive health). There was no clinically relevant difference between groups (Table 10).

Table 10. Outcomes regarding quality of life

	Surgical treatment (n=44)	Conservative treatment (n=13)	p-value
SF-36 score, median (IQR)	2605 (1280-3070)	2550 (1714-3168)	0.3

7. Peri-operative complications

Three studies described complications (Marx, 2021; Mamelak, 2024; Pineda-Centeno, 2024). Table 11 depicts an overview. Marx (2021) reports that three patients (15.8%) in the surgery group presented with cerebrospinal fluid fistule. In de medical group, two patients secondarily underwent operations due to an unfavorable clinical course with rapid progressive visual deterioration.

Mamelak (2024) reported on the following complications in the surgery group (n=67): cerebrospinal fluid leak (n=3), arginine vasopressin deficiency (n=3), delayed epistaxis (n=3), sinusitis (n=4), and hyponatremia (n=5). In de conservative group (n=30) patients demonstrated arginine vasopressin deficiency (n=2) and hyponatremia (n=1).

Pineda-Centeno (2024) reports the following complications in the surgical group (n=15): meningitis (n=1), Cerebrospinal fluid fistule (n=5) and arginine vasopressin deficiency (n=10). In the conservative group (n=12) there was one case of meningitis.

Table 11. Complications after surgical or conservative treatment.

		Surgical treatment % (n)	Conservative treatment % (n)
Marx (2021)	Cerebrospinal fluid fistule	15.8 (3)	0
	Surgery due to progressive deterioration	0	7.4% (2)
Mamelak (2024)	Cerebrospinal fluid leak	4.5 (3)	0
	Arginine vasopressin deficiency	4.5 (3)	6.6 (2)
	Delayed epistaxis	4.5 (3)	0
	Sinusitis	5.9 (4)	0
	Hyponatremia	7.5 (5)	16.6 (5)
Pineda-Centeno (2024)	Meningitis	6.6 (1)	8.3 (1)
	Cerebrospinal fluid	40 (5)	0
	Arginine vasopressin	66.6 (10)	0

PICO 2: Early versus late surgery

There is no clear consensus in the literature regarding the definition of early versus late surgery. The number of days between symptom onset and surgical intervention varies across studies. Therefore, two time points for surgical intervention are analyzed: a 3-day cutoff and a 7-day cutoff. Two studies analyzed a 3-day cutoff (Mamelak, 2024; Rutkowski, 2018) and two analyzed a 7-day cutoff (Budohoski, 2022; Zhu, 2022).

1. **Visual acuity (crucial)**

3-day cutoff

No studies comparing surgery <3 days to >3 days reported on visual acuity as an outcome.

7-day cutoff

Visual acuity comparing surgical intervention seven days before and after seven days was performed by Budohoski (2022). In the early surgery group (n = 37) 33 patients had a full visual acuity recovery (89%). In the late surgery group (n = 16) 11 recovered (69%). This results in a risk ratio of 1.30 (95% CI 0.92 to 1.84), indicating a clinically relevant difference between groups in favor of early surgery.

2. **Visual field (crucial)**

3 day cutoff

No studies comparing surgery <3 days to >3 days reported on visual field as an outcome.

7 day cutoff

Budohoski (2022) analyzed the visual field recovery with a 7-day cutoff. In the early surgery group 28 recovered (67%). In The late surgery group, 13 patients had recovery of their visual field (59%). This results in a risk ratio of 1.13 (95% CI 0.75 to 1.70) (not clinically relevant).

3. **Pituitary function/ Neuroendocrine function**

Pituitary function was analyzed by studies that described hypocortisolism, hypothyroidism and hypogonadism.

3.1 HPA-axis (Adrenal)

3 day cutoff

Mamelak (2024) assessed hypocortisolism between early and late surgery with a 3-day cutoff. 5 of the 7 patients (71%) recovered their hormonal function after early surgery. In the late surgery group 29 out of 42 (69%) patients recovered their function. The risk ratio is 1.03 (95% CI 0.62 to 1.72) indicating no clinically relevant result.

7 day cutoff

Zhu (2022) demonstrated hypocortisolism between early and late surgery. In the early surgery cohort, one of the five patients recovered from hypocortisolism (20%). 13% of the patients in the late surgery cohort recovered their function (n=15). This results in the risk ratio of 1.50 (95% CI 0.17 to 13.23), indicating a clinically relevant result in favor of early surgery.

3.2 HPT-axis (Thyroid hormone)

3 day cutoff

Mamelak, 2024 analyzed hypothyroidism in the 3-day cutoff. In the early surgery group, four of the seven patients demonstrated improvement (57%). In the late group, 23 of the 44

patients demonstrated improvement (52%). The risk ratio is 1.09 (95% CI 0.54 to 2.20) which indicates no clinically relevant result.

7 day cutoff

Zhu, 2022 assessed hypothyroidism for the 7-day cutoff. No patients showed improvement in the early surgery group (n=2). In the late surgery group, 5 (36%) of the patients showed improvement (n=14). This results in a risk ratio of 0.45 (95% CI 0.03 to 6.22) which is a clinically relevant result in favor of late surgery.

3.4 HPG-axis (sex hormones)

3 day cutoff

Mamelak, 2024 assessed hypogonadism for the 3-day cutoff. In the early surgery group four of the seven patients demonstrated improvement (57%). In the late surgery group 24 of the 45 patients showed improvement (53%). With a risk ratio of 1.07 (95% CI 0.53 to 2.15) this is not a clinically relevant result.

7 day cutoff

No studies comparing surgery <7 days to >7 days reported on hypogonadism as an outcome.

4. Headache (crucial)

3 day cutoff

Mamelak, 2024 reported on headache by using the HIT-6 scale as an indicator. The scale goes from 36 (no headache) to 78 (always a headache). There was no clinically relevant difference between the groups (table 12).

Table 12 HIT-6 score for patients in early and late surgery

	Surgery ≤3 days (n=12)	Surgery >3 days (n=55)	p-value
HIT-6 score, median (IQR)	36 (36-45)	39 (36-49)	0.3

Rutkowski, 2018 demonstrates that 85% of patients in the early surgery group had an improved headache. In the late surgery group 79% of patients reported headache improvement. No clinically relevant improvement was reported.

7 day cutoff

No studies comparing surgery <7 days to >7 days reported on headache as an outcome

5. Cranial nerve deficit

3 day cutoff

The cranial nerve deficits were analyzed by Mamelak (2024) for the three day cutoff. In the early surgery group all patients recovered from their defects (n=5). Thirteen of the patients (68%) in the late surgery group demonstrated recovery (n=19). The risk ratio is 1.36 (95% CI 0.92 to 2.00), indicating a clinically relevant result in favor of early surgery.

7 day cutoff

Two studies reported on cranial nerve deficits for the 7-day cutoff (Budohoski, 2022; Zhu, 2022). Results are pooled and presented in figure 10. The risk ratio is 1.02 (95% CI 0.76 to 1.37). This is not a clinically relevant result.

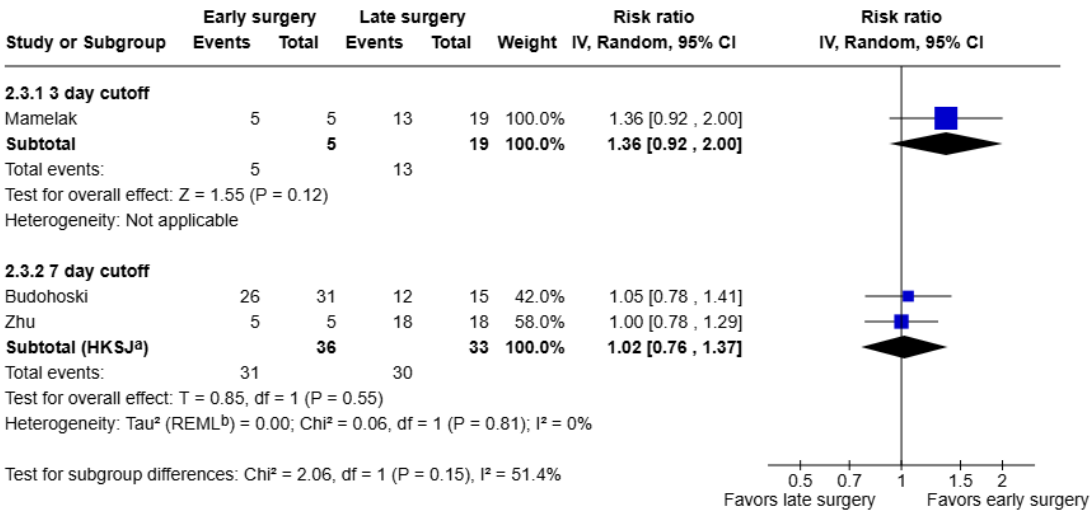


Figure 10. The pooled number of patients experiencing recovery of ocular palsy, relative to those who had ocular palsy at inclusion. NB: the total number of patients in the intervention and control group were higher, yet only those with ocular palsy at inclusion.

6. Quality of life

3 day cutoff

Mamelak, 2024 assessed the quality of life with the total score of the SF-36 form which indicates health in a scale from 0 (negative health) to 6400 (positive health). There was no relevant difference between groups (table 13)

Table 13 Outcomes regarding quality of life

	Early surgery (n=12)	Late surgery (n=55)	p-value
SF-36 score, median (IQR)	2850 (2770-2908)	2645 (2140-3100)	>.9

7 day cutoff

No studies comparing surgery <7 days to >7 days reported on quality of life as an outcome.

7. Peri-operative complications

No studies comparing late and early surgery reported on peri-operative complications as an outcome.

Summary of Findings

PICO 1: Surgical versus conservative management

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Conservative treatment	Surgical treatment	**Certainty of the evidence** (Quality of evidence)	**Summary**
Visual Acuity	Risk ratio (<1 year FU): **1.09** (95% CI 0.33 to 3.66) Risk ratio (>1 year FU): **0.90** (95%CI 0.76 to 1.07) Based on data from 160 participants in 6 studies.			**Very low** Due to serious risk of bias, Due to serious imprecision[1]	We are uncertain whether surgery would be more beneficial than conservative treatment to improve visual acuity. *(Budohoski, 2022; Pineda-Centeno, 2024; Marx, 2021; Ragate, 2024; Shepard, 2021; Saktiwarawat, 2024)*
Visual Field	Risk ratio (<1 year FU): **1.19** (95% CI 0.84 to 1.70) Risk ratio (>1 year FU): **0.97** (95%CI 0.84 to 1.13) Based on data from 290 participants in 9 studies			**Very low** Due to serious risk of bias, Due to serious imprecision[2]	We are uncertain whether surgery improves or worsens visual field in comparison to conservative treatment. *(Almeida, 2019; Budohoski, 2022; Mamelak, 2024; Pineda-Centeno, 2024; Marx, 2021; Nakhleh, 2021; Ragate, 2024; Shepard, 2021; Saktiwarawat, 2024)*
Pituitary function	Based on data from participants in 7 studies			**Very low** Due to serious risk of bias, Due to serious inconsistency, Due to serious imprecision[3]	We are uncertain whether surgery would be more beneficial than conservative treatment to improve or worsen pituitary function. *(Mamelak, 2024; Pineda-Centeno, 2024; Ragate, 2024; Saktiwarawat, 2024)*

Headache	Measured by: HIT-6 Scale: 36 - 78 Lower better Based on data from 59 participants in 1 study Follow up 3 months	Difference: **4 points**	**Very low** Due to serious risk of bias, Due to serious inconsistency[4]	We are uncertain whether surgery would be more beneficial than conservative treatment to improve headache. *(Mamelak, 2024)*
Cranial Nerve Function	Risk ratio (<1 year FU): **0.99** (95% CI 0.78 to 1.26) Risk ratio (>1 year FU): **0.92** (95%CI 0.53 to 1.59) Based on data from 291 participants in 9 studies		**Very low** Due to serious risk of bias, serious imprecision and serious publication bias.[5]	We are uncertain whether surgery would be more beneficial than conservative treatment to improve or worsen ocular nerve function. *(Almeida, 2019; Budohoski, 2022; Pineda-Centeno, 2024; Marx, 2021; Mamelak, 2024; Nakhleh, 2021; Ragate, 2024; Saktiwarawat, 2024; Shepard, 2021)*
Quality of Life	Measured by: SF-36 Scale: 0 - 6400 High better Based on data from 57 participants in 1 studies Follow up 6 months	Difference: **55 points**	**Very low** Due to serious risk of bias, Due to serious inconsistency[6]	We are uncertain whether surgery would be more beneficial than conservative treatment to improve quality of life. *(Mamelak, 2024)*
Peri-operative complications			**No GRADE** (no evidence was found)	No conclusion can be drawn due to lack of GRADE.

1. **Risk of Bias: serious.** Due to lack of correction for confounding variables and risk of selection bias.; **Imprecision: serious.** Few patients and wide confidence intervals.
2. **Risk of Bias: serious.** Due to lack of correction for confounding variables, short follow up period and risk of selection bias. **Imprecision: serious.** Few patients.
3. **Risk of Bias: serious.** Due to lack of correction for confounding variables, short follow up period and risk of selection bias. **Inconsistency: serious. Imprecision: serious.** Few patients and wide confidence intervals.
4. **Risk of Bias: serious.** Due to lack of correction for confounding variables, short follow up period and risk of selection bias. **Imprecision: serious.** Few patients.
5. **Risk of Bias: serious.** Due to lack of correction for confounding variables, short follow up period and risk of selection bias. **Inconsistency: serious. Imprecision: serious.** Few patients and wide confidence intervals.
6. **Risk of Bias: serious.** Due to lack of correction for confounding variables, short follow up period and risk of selection bias. **Imprecision: serious.** Few patients

PICO 2: Early versus late surgery

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Late Surgery Early Surgery	**Certainty of the evidence** (Quality of evidence)	**Summary**
Visual Acuity	Risk ratio 7 day Cutoff: **1.30** (95% CI 0.92 to 1.84) Based on data from 64 participants in 1 study Follow up I: 66 months C: 74 months.		**Very low** Due to serious risk of bias, Due to serious imprecision[7]	We are uncertain whether early surgery improves or worsens visual acuity in comparison to late surgery. *(Budohoski, 2022)*
Visual Field	Risk ratio 7 day Cutoff: **1.13** (95% CI 0.75 to 1.70) Based on data from 64 participants in 1 study Follow up I: 66 months C: 74 months		**Very low** Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision[8]	We are uncertain whether early surgery improves or worsens visual field in comparison to late surgery. *(Budohoski, 2022)*
Pituitary function *Adrenal axis*	Risk ratio 3 day Cutoff: **1.03** (95% CI 0.62 to 1.72) Risk ratio 7 day Cutoff: **1.50** (95% CI 0.17 to 13.23) Based on data from 69 participants in 2 studies Follow up 3 to 72 months.		**Very low** Due to serious risk of bias, Due to serious imprecision[9]	We are uncertain whether early surgery improves or worsens pituitary function in comparison to late surgery. *(Mamelak, 2024; Zhu 2022)*
Pituitary function *Thyroid axis*	Risk ratio 3 day Cutoff: **1.09** (95% CI 0.54 to 2.20)		**Very low** Due to serious risk of bias, Due to serious imprecision[10]	We are uncertain whether early surgery improves or worsens pituitary function in comparison to late surgery.

	Risk ratio 7 day Cutoff: **0.45** (95% CI 0.03 to 6.22) Based on data from 67 participants in 2 studies Follow up 3 to 72 months.			*(Mamelak, 2024; Zhu 2022)*
Pituitary function *Gonadal axis*	Risk ratio 3 day Cutoff: **1.07** (95% CI 0.53 to 2.15) Based on data from 51 participants in 1 stud7 Follow up 3 to 72 months.		**Very low** Due to serious risk of bias, Due to serious imprecision[11]	We are uncertain whether early surgery improves or worsens pituitary function in comparison to late surgery. *(Mamelak, 2024)*
Headache	Based on data from 99 participants in 2 studies	Difference: **0 points**	**Very low** Due to very serious risk of bias., Due to serious imprecision[12]	We are uncertain whether early surgery improves or worsens headache in comparison to late surgery. *(Mamelak, 2024; Rutkowski, 2018)*
Cranial Nerve Function	Based on data from 93 participants in 3 studies Follow up 3 months to 74 months		**Very low** Due to serious risk of bias, Due to serious imprecision[13]	We are uncertain whether early surgery improves or worsens cranial nerve function in comparison to late surgery. (Budohoski, 2022; Mamelak, 2024; Zhu, 2022)
Quality of Life	Measured by: SF-36 Scale: 0 - 6400 High better Based on data from 25 participants in 1 study Follow up 3 months	Difference**: 205 points**	**Very low** Due to serious risk of bias, Due to serious imprecision[14]	We are uncertain whether early surgery improves or worsens quality of life in comparison to late surgery. *(Mamelak, 2024)*
Peri-operative complications			**No GRADE** (no evidence was found)	No conclusion can be drawn due to lack of GRADE.

7. **Risk of Bias: serious.** due to no correction for confounding factors and short follow up.; **Imprecision: serious.** Low number of patients;
8. **Risk of Bias: serious.** due to no correction for confounding factors. ; **Inconsistency: serious Imprecision: serious.** Wide confidence intervals, Low number of patients;
9. **Risk of Bias: serious.** due to no correction for confounding factors. ; **Imprecision: serious.** Wide confidence intervals, Low number of patients;
10. **Risk of Bias: serious.** due to no correction for confounding factors. ; **Imprecision: serious.** Wide confidence intervals, Low number of patients;

11. **Risk of Bias: serious.** due to no correction for confounding factors. ; **Imprecision: serious.** Wide confidence intervals, Low number of patients;
12. **Risk of Bias: serious.** due to no correction for confounding factors, short follow up and unclear timing of outcome measurements.; **Imprecision: serious.** Low number of patients, Wide confidence intervals;
13. **Risk of Bias: very serious.** due to no correction for confounding factors, short follow up and a unclear follow up period. ; **Imprecision: serious.** Low number of patients;
14. **Risk of Bias: serious.** due to no correction for confounding factors, short follow up and unclear timing of outcome measurements.; **Imprecision: serious.** Wide confidence intervals, Low number of patients.

Kennisvragen

Tijdens de ontwikkeling van deze module is gebleken dat er binnen deze module nog te weinig bewijs is voor de onderbouwing van de aanbeveling en dus kennisvragen bestaan. De werkgroep meent dat (vervolg)onderzoek wenselijk is om in de toekomst een duidelijker antwoord te kunnen geven op vragen uit de praktijk.

Kennisvraag:

Leidt vroege chirurgische decompressie (bijvoorbeeld binnen 24 uur, 3 dagen of 7 dagen na presentatie) vergeleken met latere chirurgische decompressie of initieel conservatief beleid tot betere visus-, gezichtsveld- en hypofyse-uitkomsten bij patiënten met hypofyse-apoplexie?

Toelichting:

Er bestaat momenteel grote onzekerheid over het optimale moment van chirurgisch ingrijpen bij hypofyse-apoplexie, mede door heterogene definities en beperkte bewijskracht van bestaande studies. Een prospectieve, bij voorkeur landelijke studie of kwaliteitsregistratie waarin timing van interventie systematisch wordt vastgelegd in relatie tot klinische uitkomsten, kan bijdragen aan het identificeren van optimale behandelstrategieën. Door gebruik te maken van gestandaardiseerde uitkomstmaten en stratificatie naar ernst van klachten kan de bewijskracht worden verhoogd en beter worden aangesloten bij de klinische besluitvorming in de Nederlandse praktijk.

Implementeren-tabel

De implementatietabel brengt in kaart welke factoren de uitvoering van een aanbeveling bevorderen of belemmeren, en welke aanvullende acties nodig zijn voor succesvolle invoering. De adviseur en (cluster)werkgroep vullen de tabel in op basis van gerichte vragen over het onderliggende probleem, relevante randvoorwaarden en mogelijke knelpunten. Op basis hiervan wordt geconcludeerd of een extra implementatie-impuls wenselijk is.

Implementatietabel

Vraag	***Antwoord:*** *Kruis aan en licht toe/ beschrijf*		***Toelichting keuze:***
I1. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?	**X**	**Ongewenste praktijkvariatie**	De indicatie voor vroege decompressie bij een apoplexie is tot op heden niet wetenschappelijk onderbouwd en houdt ruimte voor praktijkvariatie.
		Nieuwe evidentie	
		Anders	
I2. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?	**X**	**< 1000**	
		< 5000	
		5000-40.000	
		> 40.000	

I3. Is de aanbeveling onderdeel van een bredere set interventies of verwant aan andere richtlijnen of modules? Zo ja, hoe verhoudt zij zich daartoe en moet hiermee rekening worden gehouden bij de implementatie, of kan de aanbeveling als losstaand worden beschouwd?	**X**	**Ja**	**Apoplexie heeft een andere behandeloverweging dan een electieve operatie, al dan niet met visusverlies of gezichtsvelduitval. Dit uit zich voornamelijk in de urgentie van een eventuele operatie. Het is wel onderdeel van de richtlijn hypofysechirurgie.**
		Nee	
I4. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:		**Belemmerende factoren** -	**Bevorderende factoren/ kansen**
Richtlijn/ klinisch traject (innovatie)		**Nog steeds geen harde data over behandeltermijn**	**Mogelijkheid voor prospectief verzamelen gegevens apoplexie patiënten in landelijk verband**
Zorgverleners (artsen en verpleegkundigen)		**Lokale logistieke uitdagingen: beschikbaarheid operateurs, operatiekamers, opnamecapaciteit etc,**	**Ruimte voor samenwerking tussen de opererende centra om patiëntenstroom te coördineren.**
Patiënt/ cliënt (naasten)			
Sociale context		**nvt**	**Nvt**
Organisatorische context		**nvt**	**Nvt**
Financiële en juridische context		**nvt**	**Nvt**
I5. A) Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk? (kruis aan)		**A**	**B**
	X	Patiënt/ cliënt (naaste)	**Bewustwording via hypofysestichting**
	X	Professional	**Beoordeling oogheelkunde**

B) Wat is er nodig van deze personen/partijen om de aanbeveling in de praktijk te kunnen brengen? *Denk aan aanpassingen in gedrag, werkwijzen, beleid, samenwerking of andere randvoorwaarden.*	**X**	Beroepsvereniging, nl nvvn, nve	**Uitdragen richtlijn**
	X	Ziekenhuis (raad van bestuur/UMCNL (voorheen NFU)/NVZ)	**Ruimte op operatiekamers/afdeling**
		Zorgverzekeraars/ NZa	
		Zorginstituut [duiding nodig]	
		Anders	
I6. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?		< 1 jaar	**X**
		binnen 2-3 jaar	
I7. Conclusie: is er extra actie en/of ondersteuning nodig voor implementatie van de aanbeveling? *De reguliere implementatieroutes (publicatie en disseminatie via officiele kanalen, opname in professionele standaarden, scholing en nascholing, gebruik van bestaande ICT systemen, audits en visitaties) van de richtlijnmodule alleen is onvoldoende.*		Ja	
	X	Nee	
I8. Plaatsing op de Landelijke Implementatieagenda Medisch Specialistische zorg is gewenst. *Het gaat om zorg die (grotendeels) wordt uitgevoerd binnen de ziekenhuismuren. Succesvolle implementatie vraagt om actieve betrokkenheid en samenwerking van meerdere relevante partijen binnen de zorgpraktijk.*		Ja *	
	X	Nee	

**Deze aanbeveling komt mogelijk in aanmerking voor plaatsing op de Landelijke Implementatieagenda van het programma Zorg Evaluatie & Gepast Gebruik (ZE&GG), waarin alle betrokken partijen in de medisch-specialistische zorg samenwerken aan de implementatie van bewezen beste zorg. De Federatie levert namens het veld goed onderbouwde aanbevelingen aan, die zijn getoetst op de behoefte aan een implementatie-impuls. De onderwerpen op de Implementatieagenda zijn onderdeel van landelijke zorginkoopafspraken tussen zorgverzekeraars en zorgaanbieders. Voor de beoordeling van aanbevelingen uit richtlijnen wordt gebruikgemaakt van de implementatietabel. Op basis hiervan kunnen we de andere partijen goed informeren en gezamenlijk besluiten of plaatsing op de Implementatieagenda passend is.*

Literatuur

Almeida JP, Sanchez MM, Karekezi C, Warsi N, Fernández-Gajardo R, Panwar J, Mansouri A, Suppiah S, Nassiri F, Nejad R, Kucharczyk W, Ridout R, Joaquim AF, Gentili F, Zadeh G. Pituitary Apoplexy: Results of Surgical and Conservative Management Clinical Series and Review of the Literature. World Neurosurg. 2019 Oct;130:e988-e999. doi: 10.1016/j.wneu.2019.07.055. Epub 2019 Jul 11. PMID: 31302273.

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Nakhleh A, Assaliya Naffa M, Sviri G, Shehadeh N, Hochberg I. Outcomes of pituitary apoplexy: a comparison of microadenomas and macroadenomas. Pituitary. 2021 Aug;24(4):492-498. doi: 10.1007/s11102-020-01124-1. Epub 2021 Jan 19. PMID: 33462744.

Pineda-Centeno LM, Palacios-Rodríguez RA, Moncada-Habib T, Mondragon-Soto MG, Rodríguez-Hernández LA, Villalobos-Díaz R, Alcocer Barradas V, Portocarrero-Ortiz LA. Pituitary Apoplexy: Description of Medical and Surgical Treatment and Clinical, Visual, and Endocrinological Outcomes During the SARS-CoV-2 Pandemic and Over Three Years. Cureus. 2024 Jun 25;16(6):e63152. doi: 10.7759/cureus.63152. PMID: 39055441; PMCID: PMC11272388.

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Rutkowski MJ, Kunwar S, Blevins L, Aghi MK. Surgical intervention for pituitary apoplexy: an analysis of functional outcomes. J Neurosurg. 2018 Aug;129(2):417-424. doi: 10.3171/2017.2.JNS1784. Epub 2017 Sep 15. PMID: 28946177.

Saktiwarawat K, Tunthanathip T, Oearsakul T, Taweesomboonyat C. Comparing neuroendocrine recovery between surgical and conservative management in pituitary

apoplexy patients: a propensity score-matched analysis. Neurosurg Rev. 2024 May 28;47(1):236. doi: 10.1007/s10143-024-02461-6. PMID: 38802695.

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Zhu Q, Liang Y, Fan Z, Liu Y, Zhou C, Zhang H, Li T, Zhou Y, Yang J, Wang Y, Wang L. Ischemic Infarction of Pituitary Apoplexy: A Retrospective Study of 46 Cases From a Single Tertiary Center. Front Neurosci. 2022 Jan 24;15:808111. doi: 10.3389/fnins.2021.808111. PMID: 35140585; PMCID: PMC8818988.

Risk of Bias tables

Risk of bias table for interventions studies (cohort studies based on risk of bias tool by the CLARITY Group at McMaster University)

Author, year	Selection of participants	Exposure	Outcome of interest	Confounding-assessment	Confounding-analysis	Assessment of outcome	Follow up	Co-interventions	Overall Risk of bias
Pineda-Centeno, 2024	Definitely yes Reason: Participants were selected from hospital registry	Probably yes Reason: Extracted from the medical records.	Definitely no Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes Reason: extracted from medical records.	**Definitely no** Reason: Visual acuity although stated, not all variables were evenly matched. No multivariate analysis.	**Definitely yes** Reason: Extracted from the medical records.	**Definitely no** Reason: Follow up was 6 months (sufficient), but with large drop-out number afterwards.	Definitely yes Reason: Additional used medication was balanced between groups	**Some concerns** - No correction for confounding - Risk of selection bias
Rutkowski, 2018	Definitely yes Reason: Participants were selected from hospital registry	Probably yes Reason: MRI confirmation needed.	Definitely no Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes Reason: extracted from medical records.	**Definitely no** Reason: many confounding variables not stated.	**Definitely no** Reason: Unclear follow-up and therefore unclear how much data is missing.	**No information**	Problably yes Reason: Single center, however not noted.	**High** - No correction for confounding - Unclear follow-up
Saktiwarawat, 2024	Definitely yes Reason: Consecutive participants from hospital registry	Probably yes Reason: Only patients with symptomatic PA were included.	Definitely no Reason: visual acuity, visual fields and nerve function could be affected. Outcome of	Probably yes Reason: extracted from medical records.	Probably yes Reason: propensity score matching and multivariate adjustment.	Probably no Reason: Unclear	Probably yes Reason: sufficient amount of follow-up time, yet unclear how much missing data	Probably no Reason: more adjuvant treatments in surgery group	**Some concerns** - Risk of selection bias - Unclear after how much time outcome is presented

			interest was improvement.						
Zhu, 2022	Definitely yes Reason: Consecutive participants from hospital registry	Definitely yes, Assessment was extracted form medical record.	Definitely no Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes Reason: extracted from medical records	**Definitely no** Reason: many confounding variables not stated.	Probably yes Reason: extracted from medical records.	Probably yes, Reason: follow-up time not clear. Data complete??		**High risk,** - No correction for confounding - Unclear when outcome was measured.
Shepard , 2021	Definitely yes Reason: Consecutive participants from hospital registry	Probably yes Reason: MRI confirmation needed.	Definitely no Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes Reason: extracted from medical records	**Definitely no** Reason: many confounding variables not stated.	Probably yes Reason: extracted from medical records.	Probably yes, Follow up is sufficient and data was complete		**Some concerns,** - No correction for confounding
Nakhleh ,2021	Definitely yes, Participants were selected from a registry	Definitely yes, Assessment was extracted form medical record.	Definitely no Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes Reason: extracted from medical records.	**Definitely no,** Retrospecitve study with no adjustment of cofounding variables.	**Definitely yes** Reason: Extracted from the medical records..	Probably yes, Follow up was multiple years, but visual acuity (one of the outcomes) was missing. → they do mention it though, in all their tables: that the visual acuity was missing.	No information	**Some concerns,** - No correction for confounding - Risk of selection bias (visual acuity missing)

Mamelak, 2024	Definitely yes, It was a prospective study, enrollement was determined by the investigators at each site without central oversight.	Definitely yes, Assessment was extracted form medical record.	Definitely no, Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes, Reason: extracted from medical records.	**Definitely no,** Retrospecitve study with no adjustment of cofounding variables.	**Definitely yes** Reason: Extracted from the medical records..	**Probably no,** Follow up was 3 months. 'follow up was less complete at 6 months, so draw mostly qualitative conclusions for the 6-month data.	No information	**Some concerns,** - No correction for confounding - Short follow up.
Budohoski, 2022	Definitely yes, Participants were selected from a registry	Definitely yes, Assessment was extracted form medical record.	Definitely no, Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes, Reason: extracted from medical records.	**Definitely no,** Retrospective study with no adjustment of cofounding variables.	Definitely yes, Assessments were described in Materials and Methods	Probably yes, Follow up is sufficient and data was complete.	No information	**Some concerns** - No correction for confounding
Marx, 2021	Definitely yes Reason: Consecutive participants from hospital registry	Definitely yes, Assessment was extracted form medical record	Definitely no, Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes, Reason: extracted from medical records	**Definitely no,** Retrospective study with no adjustment of cofounding variables.	**Definitely yes** Reason: Extracted from the medical records.	Probably yes, Follow up is sufficient and data was complete.	No information	**Some Concerns** - No correction for confounding
Ragate, 2024	Definitely yes Reason: Consecutive participants	Definitely yes, Reason: Assessment was	Definitely no, Reason: visual acuity, visual fields and nerve	Probably yes, Reason: extracted from medical records	**Propbably yes,** Reason: cohorts adjusted for PAS score.	**Definitely yes** Reason: Extracted from the	Probably yes, Follow up is sufficient and	No information	**Low concern**

	from hospital registry.	extracted form medical record	function could be affected. Outcome of interest was improvement.			medical records.	data was complete.		
Almeida , 2019	Definitely yes Reason: Consecutive participants from hospital registry.	Definitely yes, Reason: Assessment was extracted form medical record	Definitely no, Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes, Reason: extracted from medical records	**Definitely no,** Retrospective study with no adjustment of cofounding variables.	**Definitely yes** Reason: Extracted from the medical records.	Probably no, Follow up is sufficient and data was incomplete.	No information	**Some Concerns** - No correction for confounding - Risk of selection bias
Shepard , 2021	Definitely yes Reason: Consecutive participants from hospital registry.	Definitely yes, Reason: Assessment was extracted form medical record	Definitely no, Reason: visual acuity, visual fields and nerve function could be affected. Outcome of interest was improvement.	Probably yes, Reason: extracted from medical records	**Definitely no,** Retrospective study with no adjustment of cofounding variables.	**Definitely yes** Reason: Extracted from the medical records.	Probably yes, Follow up is sufficient and data was complete.	No information	**Some Concerns** - No correction for confounding

Footnotes

Selection of participants Example of low risk of bias: Exposed and unexposed drawn for same administrative database of patients presenting at same points of care over the same time frame

Exposure Examples of low risk of bias: Secure record (e.g. surgical records, pharmacy records); Repeated interview or other ascertainment asking about current use/exposure

Confounding Examples of low risk of bias regarding assessment: Interview of all participants; Self-completed survey from all participants; Review of charts with reproducibility demonstrated; From database with documentation of accuracy of abstraction of prognostic data.

Example of low risk of bias regarding analysis: Comprehensive matching (e.g. with propensity score) or adjustment for all plausible confounding variables

Assessment of outcome Examples of low risk of bias: Independent blind assessment; Record linkage; For some outcomes (e.g. fractured hip), reference to the medical record is sufficient to satisfy the requirement for confirmation of the fracture

Follow up Examples of low risk of bias: No missing outcome data; Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring is unlikely to introduce bias); Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; Missing data have been imputed using appropriated methods

Co-interventions Example of low risk of bias: Most or all relevant co-interventions that might influence the outcome of interest are documented to be similar in the exposed and unexposed

Table of excluded studies

Reference	Reason for exclusion
Abbara A, Clarke S, Eng PC, Milburn J, Joshi D, Comninos AN, Ramli R, Mehta A, Jones B, Wernig F, Nair R, Mendoza N, Sam AH, Hatfield E, Meeran K, Dhillo WS, Martin NM. Clinical and biochemical characteristics of patients presenting with pituitary apoplexy. Endocr Connect. 2018 Oct;7(10):1058-1066. doi: 10.1530/EC-18-0255. PMID: 30139818; PMCID: PMC6198188.	Patients mostly treated with surgical technique from before 2000.
Arbunea-Ghenoiu S, Ciubotaru GV, Dumitrascu A, Alexandrescu D, Capatina C, Poiana C. Pituitary Apoplexy: A Retrospective Study of 36 Cases From a Single Center. Cureus. 2022 Sep 30;14(9):e29769. doi: 10.7759/cureus.29769. PMID: 36340531; PMCID: PMC9621731.	Outcomes not in line with PICO.
Ayuk J, McGregor EJ, Mitchell RD, Gittoes NJ. Acute management of pituitary apoplexy--surgery or conservative management? Clin Endocrinol (Oxf). 2004 Dec;61(6):747-52. doi: 10.1111/j.1365-2265.2004.02162.x. PMID: 15579190.	Patients mostly treated with surgical technique from before 2000.
Biagetti B, Cordero Asanza E, Pérez-López C, Araujo-Castro M, Camara R, Guerrero-Pérez F, Vicente A, Lamas C, Serra G, Echarri AI, Ollero MD, González Molero I, Villar-Taibo R, Moure Rodríguez MD, García-Feijoo P, Berrocal VR, Sánchez Ramirez MN, Gutiéerrez Hurtado A, Capristan-Díaz V, Simó-Servat A, Gallach M, Safont Perez E, González Rosa V, Civantos S, Asensio-Wandosell D, Martinez-Saez E, Menéndez Torre E, Aulinas A, Iglesias P, Diez JJ, Bernabéu I, Álvarez-Escolá C, Puig-Domingo M. Pituitary Apoplexy: Comorbidities, Management, and Outcomes-A Spanish Observational Multicenter Study. J Clin Endocrinol Metab. 2025 May 19;110(6):e1811-e1820. doi: 10.1210/clinem/dgae649. Erratum in: J Clin Endocrinol Metab. 2025 Jun 17;110(7):e2432. doi: 10.1210/clinem/dgaf222. PMID: 39298667.	Results insufficiently reported for analysis in the module.
Biagetti B, Sarria-Estrada S, Cordero Asanza E, Chaachou-Charradi A, Ng-Wong YK, Cicuendez M, Hernandez I, Rojano-Toimil A, Costa P, Martinez-Saez E, Casteràs A, Simò R. Risk Factors, Radiological and Clinical Outcomes in Subclinical and Clinical Pituitary Apoplexy. J Clin Med. 2022 Dec 8;11(24):7288. doi: 10.3390/jcm11247288. PMID: 36555904; PMCID: PMC9786023.	Results insufficiently reported for analysis in the module.
Biagetti B, Cordero Asanza E, García-Feijoo P, Araujo-Castro M, Rodríguez Berrocal V, Serra G, Guerrero-Pérez F, Cámara R, Lamas C, Ollero García MD, Vicente A, Irigaray Echarri A, Villar-Taibo R, Moure Rodríguez MD, Pérez-López C, González-Molero I, Sánchez Ramírez MN, Gutiérrez Hurtado A, Capristan-Díaz V, Simó-Servat A, Gallach M, Safont Pérez E, González Rosa V, Civantos S,	Outcomes not in line with PICO.

Martinez-Saez E, García-Arabehety J, Menéndez Torre E, Aulinas A, Iglesias P, Díez JJ, Bernabéu I, Álvarez-Escolá C, Puig-Domingo M; Neuroendocrinology Area of the Spanish Society of Endocrinology. Trends and Outcomes in Pituitary Apoplexy Management: A Spanish Observational Multicenter Study. Neurosurgery. 2024 Dec 5;97(1):82-90. doi: 10.1227/neu.0000000000003281. PMID: 39636106.	
Brown NJ, Patel S, Gendreau J, Abraham ME. The role of intervention timing and treatment modality in visual recovery following pituitary apoplexy: a systematic review and meta-analysis. J Neurooncol. 2024 Dec;170(3):469-482. doi: 10.1007/s11060-024-04717-z. Epub 2024 Nov 6. PMID: 39503840; PMCID: PMC11614942.	Included studies with patients treated with surgical technique form before 2000.
Bujawansa S, Thondam SK, Steele C, Cuthbertson DJ, Gilkes CE, Noonan C, Bleaney CW, Macfarlane IA, Javadpour M, Daousi C. Presentation, management and outcomes in acute pituitary apoplexy: a large single-centre experience from the United Kingdom. Clin Endocrinol (Oxf). 2014 Mar;80(3):419-24. doi: 10.1111/cen.12307. Epub 2013 Aug 26. PMID: 23909507.	Patients mostly treated with surgical technique from before 2000.
Cabuk B, Kaya NS, Polat C, Geyik AM, Icli D, Anik I, Ceylan S. Outcome in pituitary apoplexy patients, stratified by delay between symptom appearance and surgery: A single center retrospective analysis. Clin Neurol Neurosurg. 2021 Nov;210:106991. doi: 10.1016/j.clineuro.2021.106991. Epub 2021 Oct 14. PMID: 34700278.	Not in line with the PICO
Cavalli A, Martin A, Connolly DJ, Mirza S, Sinha S. Pituitary apoplexy: how to define safe boundaries of conservative management? Early and long-term outcomes from a single UK tertiary neurosurgical unit. Br J Neurosurg. 2021 Jun;35(3):334-340. doi: 10.1080/02688697.2020.1812523. Epub 2020 Sep 1. PMID: 32870049.	Too small sample size.
Chuang CC, Chang CN, Wei KC, Liao CC, Hsu PW, Huang YC, Chen YL, Lai LJ, Pai PC. Surgical treatment for severe visual compromised patients after pituitary apoplexy. J Neurooncol. 2006 Oct;80(1):39-47. doi: 10.1007/s11060-006-9148-7. Epub 2006 Apr 28. PMID: 16645717.	No comparison in line with PICO.
Cross KA, Desai R, Vellimana A, Liu Y, Rich K, Zipfel G, Dacey R, Chicoine M, Klatt-Cromwell C, McJunkin J, Pipkorn P, Schneider JS, Silverstein J, Kim AH. Surgery for Pituitary Tumor Apoplexy Is Associated with Rapid Headache and Cranial Nerve Improvement. Curr Oncol. 2022 Jul 12;29(7):4914-4922. doi: 10.3390/curroncol29070390. PMID: 35877250; PMCID: PMC9319222.	Too small sample size.

Giritharan S, Gnanalingham K, Kearney T. Pituitary apoplexy - bespoke patient management allows good clinical outcome. Clin Endocrinol (Oxf). 2016 Sep;85(3):415-22. doi: 10.1111/cen.13075. Epub 2016 May 4. PMID: 27038242.	Too small sample size.
Goshtasbi K, Abiri A, Sahyouni R, Mahboubi H, Raefsky S, Kuan EC, Hsu FPK, Cadena G. Visual and Endocrine Recovery Following Conservative and Surgical Treatment of Pituitary Apoplexy: A Meta-Analysis. World Neurosurg. 2019 Dec;132:33-40. doi: 10.1016/j.wneu.2019.08.115. Epub 2019 Aug 27. PMID: 31470146.	Outdated systematic review.
Gruber A, Clayton J, Kumar S, Robertson I, Howlett TA, Mansell P. Pituitary apoplexy: retrospective review of 30 patients--is surgical intervention always necessary? Br J Neurosurg. 2006 Dec;20(6):379-85. doi: 10.1080/02688690601046678. PMID: 17439089.	Patients mostly treated with surgical technique from before 2000.
Hadj Kacem F, Trimeche O, Gargouri I, Ben Salah D, Charfi N, Rekik N, Mnif F, Mnif M, Elleuch M, Abid M. Diagnosis and management of pituitary apoplexy: a Tunisian data. Chin Neurosurg J. 2023 Jul 1;9(1):17. doi: 10.1186/s41016-023-00331-6. PMID: 37391784; PMCID: PMC10314394.	Results insufficiently reported for analysis in the module.
Kelly PD, Fernando SJ, Malenke JA, Chandra RK, Turner JH, Chambless LB. The Effect of Timing of Surgery in Pituitary Apoplexy on Continuously Valued Visual Acuity. J Neurol Surg B Skull Base. 2021 Jul;82(Suppl 3):e70-e78. doi: 10.1055/s-0040-1701217. Epub 2020 Jan 24. PMID: 34306919; PMCID: PMC8289513.	No distinction between early and late surgery.
Kim SH, Lee KC, Kim SH. Cranial nerve palsies accompanying pituitary tumour. J Clin Neurosci. 2007 Dec;14(12):1158-62. doi: 10.1016/j.jocn.2006.07.016. Epub 2007 Oct 26. PMID: 17964787.	Too small sample size.
Kim YH, Cho YH, Hong SH, Kim JH, Kim MS, Khang SK, Lee EJ, Chong K, Kim CJ. Postoperative Neurologic Outcome in Patients with Pituitary Apoplexy After Transsphenoidal Surgery. World Neurosurg. 2018 Mar;111:e18-e23. doi: 10.1016/j.wneu.2017.11.124. Epub 2017 Nov 28. PMID: 29191540.	Patients treated with surgical technique from before 2000.
Lammert A, Walter MS, Giordano FA, Al Zhgloul M, Krämer BK, Nittka S, Schulte DM, Ratliff M, Hänggi D, Seiz-Rosenhagen M. Neuro-Endocrine Recovery After Pituitary Apoplexy: Prolactin as a Predictive Factor. Exp Clin Endocrinol Diabetes. 2020 May;128(5):283-289. doi: 10.1055/a-0640-2915. Epub 2018 Jul 2. PMID: 29966153.	Too small sample size.
Leyer C, Castinetti F, Morange I, Gueydan M, Oliver C, Conte-Devolx B, Dufour H, Brue T. A conservative management is preferable in milder forms of pituitary tumor apoplexy. J Endocrinol Invest. 2011 Jul-	Patients treated with surgical technique from before 2000.

Aug;34(7):502-9. doi: 10.3275/7241. Epub 2010 Aug 31. PMID: 20811169.	
Lubina A, Olchovsky D, Berezin M, Ram Z, Hadani M, Shimon I. Management of pituitary apoplexy: clinical experience with 40 patients. Acta Neurochir (Wien). 2005 Feb;147(2):151-7; discussion 157. doi: 10.1007/s00701-004-0413-2. PMID: 15570437.	Patients mostly treated with surgical technique from before 2000.
Maccagnan P, Macedo CL, Kayath MJ, Nogueira RG, Abucham J. Conservative management of pituitary apoplexy: a prospective study. J Clin Endocrinol Metab. 1995 Jul;80(7):2190-7. doi: 10.1210/jcem.80.7.7608278. PMID: 7608278.	Too small sample size.
Marin-Castañeda LA, Gorbachev J, Lopez-Zepeda PT, Choque-Ayala LC, Shubhangi F, De Nigris Vasconcellos F, Pichardo-Rojas PS. Pituitary Apoplexy and the Current Understanding of Its Management: A Meta-Analysis of 908 Patients. World Neurosurg. 2024 Oct;190:371-385.e1. doi: 10.1016/j.wneu.2024.07.103. Epub 2024 Jul 20. PMID: 39033812.	Outdated systematic review.
Paredes I, Rodríguez-Berrocal V, Pérez-López C, García-Feijoo P, Alvarez-Escola C, Acitores Cancela A, Araujo-Castro M, Calatayud M, Librizzi MS, Lagares A. Influence of surgical timing on the visual prognosis of patients suffering from a pituitary apoplexy with visual impairment. Neurosurg Rev. 2024 Nov 16;47(1):852. doi: 10.1007/s10143-024-03106-4. PMID: 39549159.	Not in line with the PICO.
Ricciuti R, Nocchi N, Arnaldi G, Polonara G, Luzi M. Pituitary Adenoma Apoplexy: Review of Personal Series. Asian J Neurosurg. 2018 Jul-Sep;13(3):560-564. doi: 10.4103/ajns.AJNS_344_16. PMID: 30283505; PMCID: PMC6159099.	Too small sample size.
Sahyouni R, Goshtasbi K, Choi E, Mahboubi H, Le R, Khahera AS, Hanna GK, Hatefi D, Hsu FP, Bhandarkar ND, Kuan EC, Cadena G. Vision Outcomes in Early versus Late Surgical Intervention of Pituitary Apoplexy: Meta-Analysis. World Neurosurg. 2019 Jul;127:52-57. doi: 10.1016/j.wneu.2019.03.133. Epub 2019 Mar 26. PMID: 30922898.	Outdated systematic review.
Salle H, Cane M, Rocher M, Auditeau E, Teissier MP, Raverot G, Salle L. Pituitary apoplexy score, toward standardized decision-making: a descriptive study. Pituitary. 2024 Feb;27(1):77-87. doi: 10.1007/s11102-023-01372-x. Epub 2023 Dec 27. PMID: 38150169.	Results insufficiently reported for analysis in this module.
Seaman SC, Dougherty MC, Zanaty M, Bruch LA, Graham SM, Greenlee JDW. Visual and Hormone Outcomes in Pituitary Apoplexy: Results of a Single Surgeon, Single Institution 15-Year Retrospective Review and Pooled Data Analysis. J Neurol Surg B Skull Base. 2020 Jun 19;82(4):392-400. doi: 10.1055/s-0040-1713104. PMID: 35573926; PMCID: PMC9100448.	Results insufficiently reported for analysis in the module.

Semple PL, Webb MK, de Villiers JC, Laws ER Jr. Pituitary apoplexy. Neurosurgery. 2005;56(1):65-72; discussion 72-3. doi: 10.1227/01.neu.0000144840.55247.38. PMID: 15617587.	Too small sample size.
Seuk JW, Kim CH, Yang MS, Cheong JH, Kim JM. Visual outcome after transsphenoidal surgery in patients with pituitary apoplexy. J Korean Neurosurg Soc. 2011 Jun;49(6):339-44. doi: 10.3340/jkns.2011.49.6.339. Epub 2011 Jun 30. PMID: 21887391; PMCID: PMC3158476.	Patients treated with surgical technique from before 2000.
Sibal L, Ball SG, Connolly V, James RA, Kane P, Kelly WF, Kendall-Taylor P, Mathias D, Perros P, Quinton R, Vaidya B. Pituitary apoplexy: a review of clinical presentation, management and outcome in 45 cases. Pituitary. 2004;7(3):157-163. doi: 10.1007/s11102-005-1050-3. PMID: 16010459.	Patients mostly treated with surgical technique from before 2000.
Simon S, Torpy D, Brophy B, Blumbergs P, Selva D, Crompton JL. Neuro-ophthalmic manifestations and outcomes of pituitary apoplexy--a life and sight-threatening emergency. N Z Med J. 2011 May 27;124(1335):52-9. PMID: 21946682.	Too small sample size.
Singh TD, Valizadeh N, Meyer FB, Atkinson JL, Erickson D, Rabinstein AA. Management and outcomes of pituitary apoplexy. J Neurosurg. 2015 Jun;122(6):1450-7. doi: 10.3171/2014.10.JNS141204. Epub 2015 Apr 10. PMID: 25859804.	Patients treated with surgical technique from before 2000.
Teixeira JC, Lavrador J, Simão D, Miguéns J. Pituitary Apoplexy: Should Endoscopic Surgery Be the Gold Standard? World Neurosurg. 2018 Mar;111:e495-e499. doi: 10.1016/j.wneu.2017.12.103. Epub 2017 Dec 26. PMID: 29288106.	Too small sample size.
Tu M, Lu Q, Zhu P, Zheng W. Surgical versus non-surgical treatment for pituitary apoplexy: A systematic review and meta-analysis. J Neurol Sci. 2016 Nov 15;370:258-262. doi: 10.1016/j.jns.2016.09.047. Epub 2016 Sep 23. PMID: 27772771.	Outdated systematic review.

Literature search strategy

Embase.com

No.	Query	Results
#1	'hypophysis apoplexy'/exp OR (((pituitar* OR hypophys* OR adenohypophys* OR neurohypophys* OR microadenoma* OR 'micro adenoma*' OR macroadenoma* OR 'macro adenoma*' OR prolactinoma*) NEAR/4 (apople* OR haemorrhag* OR hemorrhag* OR haematoma* OR hematoma* OR bleed* OR ischem* OR infarct* OR stroke)):ti,ab,kw) OR (('hypophysis tumor'/exp OR (((pituitar* OR hypophys*) NEAR/3 (adenoma* OR microadenoma* OR macroadenoma* OR cancer* OR carcinoma* OR lesion* OR malignan* OR neoplasm* OR tumor* OR tumour*)):ti,ab,kw) OR ((cushing* NEAR/3 (syndrome* OR disease*)):ti,ab,kw) OR craniopharyngioma*:ti,ab,kw OR 'cranio pharyngioma*':ti,ab,kw OR craniopharyngeoma*:ti,ab,kw OR pharyngioma*:ti,ab,kw OR gonadotropinoma*:ti,ab,kw OR prolactinoma*:ti,ab,kw OR microprolactinoma*:ti,ab,kw OR macroprolactinoma*:ti,ab,kw OR ((('non function*' OR nonfunction*) NEAR/3 adenoma*):ti,ab,kw) OR (((craniopharyngeal OR rathke*) NEAR/3 (tumor* OR tumour* OR cyst*)):ti,ab,kw)) AND ('tumor bleeding'/exp OR 'cerebrovascular accident'/exp OR 'brain hemorrhage'/exp OR 'brain infarction'/exp OR 'bleeding'/de OR 'hematoma'/de OR 'brain hematoma'/exp OR apople*:ti,ab,kw))	6583
#2	'time factor'/exp OR 'time to treatment'/exp OR (((surg* OR microsurg* OR neurosurg* OR operat* OR intervention* OR treat* OR decompress*) NEAR/3 (timing OR early OR late OR delay* OR conservative)):ti,ab,kw) OR 'time to treatment*':ti,ab,kw OR 'conservative treatment'/de OR 'watchful waiting'/exp OR ((conservativ* NEAR/3 (manag* OR interven* OR treat* OR approach*)):ti,ab,kw) OR 'non surg*':ti,ab,kw OR nonsurg*:ti,ab,kw OR 'non operat*':ti,ab,kw OR nonoperat*:ti,ab,kw OR ((expect* NEAR/5 manag*):ti,ab,kw) OR ((natural NEAR/3 (course* OR history)):ti,ab,kw)	844495
#3	#1 AND #2 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	475
#4	#3 AND [1995-2025]/py	452
#5	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR	1086572

	pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	
#6	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	4169425
#7	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	8554570
#8	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR	15644390

	cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#9	#4 AND #5	30
#10	#4 AND #6 NOT #9	33
#11	#4 AND (#7 OR #8) NOT (#9 OR #10)	162
#12	#9 OR #10 OR #11	225

Ovid/Medline

#	Searches	Results
1	exp Pituitary Apoplexy/ or ((pituitar* or hypophys* or adenohypophys* or neurohypophys* or microadenoma* or 'micro adenoma*' or macroadenoma* or 'macro adenoma*' or prolactinoma*) adj4 (apople* or haemorrhag* or hemorrhag* or haematoma* or hematoma* or bleed* or ischem* or infarct* or stroke)).ti,ab,kf. or ((exp Pituitary Neoplasms/ or ((pituitar* or hypophys*) adj3 (adenoma* or microadenoma* or macroadenoma* or cancer* or carcinoma* or lesion* or malignan* or neoplasm* or tumor* or tumour*)).ti,ab,kf. or (cushing* adj3 (syndrome* or disease*)).ti,ab,kf. or craniopharyngioma*.ti,ab,kf. or 'cranio pharyngioma*'.ti,ab,kf. or craniopharyngeoma*.ti,ab,kf. or pharyngioma*.ti,ab,kf. or gonadotropinoma*.ti,ab,kf. or prolactinoma*.ti,ab,kf. or microprolactinoma*.ti,ab,kf. or macroprolactinoma*.ti,ab,kf. or (('non function*' or nonfunction*) adj3 adenoma*).ti,ab,kf. or ((craniopharyngeal or rathke*) adj3 (tumor* or tumour* or cyst*)).ti,ab,kf.) and (exp Stroke/ or exp Intracranial Hemorrhages/ or Hemorrhage/ or Hematoma/ or Hematoma, Epidural, Cranial/ or apople*.ti,ab,kf.))	2733
2	exp Time Factors/ or exp Time-to-Treatment/ or ((surg* or microsurg* or neurosurg* or operat* or intervention* or treat* or decompress*) adj3 (timing or early or late or delay* or conservative)).ti,ab,kf. or 'time to treatment*'.ti,ab,kf. or exp Conservative Treatment/ or exp Watchful Waiting/ or (conservativ* adj3 (manag* or interven* or treat* or approach*)).ti,ab,kf. or 'non surg*'.ti,ab,kf. or nonsurg*.ti,ab,kf. or 'non operat*'.ti,ab,kf. or nonoperat*.ti,ab,kf. or (expect* adj5 manag*).ti,ab,kf. or (natural adj3 (course* or history)).ti,ab,kf.	1731359
3	(1 and 2) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/)	339
4	limit 3 to yr="1995 -Current"	310
5	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or	796322

	database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	
6	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2818611
7	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies]	4907614
8	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	5858843
9	4 and 5	28
10	(4 and 6) not 9	11

11	(4 and (7 or 8)) not (9 or 10)	118
12	9 or 10 or 11	157

Module 4 – Monitoring en behandeling van verstoringen waterhuishouding

Uitgangsvraag

Hoe kunnen verstoringen van de waterhuishouding na een hypofyseoperatie het best gemonitord, voorkomen en behandeld worden?

- Deelvraag 1: Voor AVP-deficiëntie?
- Deelvraag 2: Voor SIADH?

Search and select

Only the second subquestion regarding SIADH is addressed in the literature analysis.

A systematic review of the literature was performed to answer the following question(s):
What is the value of a fluid restriction on postoperative day 3-14 in preventing symptomatic hyponatremia and readmissions, compared to no fluid restriction in patients undergoing pituitary surgery?

Table 1. PICO

Patients	Adult patients undergoing pituitary surgery
Intervention	Fluid restriction between 3 days and 2 weeks postoperatively
Control	No fluid restriction postoperatively
Outcomes	Symptomatic hyponatremia, readmissions, complications (due to the fluid restriction: hypernatremia, renal insufficiency), intervention adherence
Other selection criteria	Study design: systematic reviews, randomized controlled trials, and observational comparative research Minimal follow-up: 3 weeks

Relevant outcome measures

The guideline panel considered symptomatic hyponatremia and readmissions as **critical** outcome measures for decision making; and complications and intervention adherence as **important** outcome measures for decision making.

The guideline panel defined the outcome measures as follows:

- Hyponatremia: sodium concentration of less than 135 or 136 mmol/L. The duration of hyponatremia and severity of symptoms are important factors to take into account when considering treatment.
- Readmissions: patients being readmitted to the hospital within 30 days after pituitary surgery for all causes, and specifically within 15 days for hyponatremia (if available in the literature).
- Complications: all adverse events can be considered, but of specific interest are hypernatremia, symptomatic dehydration and renal insufficiency/kidney failure.
- Intervention adherence: no definition was pre-specified, of interest was how well a fluid restriction is tolerated and followed.

The guideline panel defined 10-20% in (symptomatic) hyponatremia occurrence and readmission as a minimal clinically (patient) important difference (0.91 > Relative risk (RR) > 1.10)

Search and select (Methods)

A systematic literature search was performed by a medical information specialist using the following bibliographic databases: Embase.com and Ovid/Medline. Both databases were searched from 2000 to November 25, 2024, for systematic reviews, RCTs and observational studies. Systematic searches were completed using a combination of controlled

vocabulary/subject headings (e.g., Emtree-terms, MeSH) wherever they were available and natural language keywords. The overall search strategy was derived from two primary search concepts: (1) pituitary surgery; (2) fluid restriction. Duplicates were removed using EndNote software. After deduplication a total of 122 records were imported for title/abstract screening.

Initially, 12 studies were selected based on title and abstract screening. After reading the full text, 4 studies were excluded (see the exclusion table under the tab 'Evidence tabellen'), and 8 studies were included.

Summary of literature

Description of studies

Eight studies were included in the analysis of the literature: all observational studies. Important study characteristics and results are summarized in table 2. The assessment of the risk of bias is summarized in the risk of bias tables (under the tab 'Evidence tabellen').

All eight included studies had an observational design, with cohort groups divided over time: a control group that underwent standard of care before protocol change in the hospital, and an intervention group later in time, that had a postoperative fluid restriction imposed. All studies were performed in a single centre. Inclusion criteria varied between studies: some authors included all patients undergoing transsphenoidal surgery (TSS) for all sellar and parasellar lesions (including craniopharyngioma, Rathke's cleft cyst, meningioma; 5 studies) and some authors only included patients undergoing TSS for a pituitary adenoma (3 studies). See table 2 for the individual study characteristics.

Table 2. Characteristics of included studies

Study	Participants	Comparison	Outcomes + follow-up	Comments	Risk of bias*
Burke, 2018 Retrospective cohort Single centre, UK	N at baseline: 785 I: 203 | C: 582 Age (mean, SD) I: 48.8 (16.7) | C: 47.3 (15.9) Sex (% male) I: 38% | C: 47% Preoperative symptoms (n, %) Apoplexy: I: 1% | C: 4.4% Visual deficits: I: 39% | C: 36%	Intervention: fluid restriction of 1000 mL/day on postoperative days 1-8 (patients undergoing TSS between 2015-2017) Control: drink to thirst (patient undergoing TSS between 2008-2014)	*1 week postoperatively:* Readmission	Funding: non-commercial grant. Conflict of interest: authors report no conflict of interest Population: patients undergoing TSS (for all types of clinical diagnoses)	Some concerns (hyponatremia) High (readmission)
Deaver, 2018 Retrospective cohort Single centre, USA	N at baseline: 287 I: 169 | C: 118 Age (mean, SD) I: 53.8 (14.8) | C: 52.0 (15.5) Sex (% male) I: 47% | C: 55% Preoperative symptoms (%) Apoplexy: I: 6.5% | C: 6.8% Macroadenoma: I: 82% | C: 92% Stress-dose glucocorticoids: I: 20.8% | C: 14.4%	Intervention: fluid restriction of 1500 mL/day on postoperative days 1-7 (and encouragement of liberal intake of salt >2g/day) (patients undergoing TSS between March 2014-Sept 2015) Control: not reported (patients undergoing TSS between Oct 2015-March 2017)	*30 days:* Readmission (including readmission for hypernatremia)	Funding: non-commercial grant. Conflict of interest: authors report no conflict of interest Population: patients undergoing TSS for pathologically confirmed pituitary adenomas (other pathologies such as craniopharyngeomas and Rathke's cleft cysts were excluded)	Some concerns
Matsuyama, 2014 Retrospective cohort Single centre, Japan	N at baseline: 207 I: 64 | C: 143 Age (mean, SD): 44.6 (18.1) Not reported for I and C Sex (% male): 38% overall *No other information reported.*	Intervention: if 2 out of 3 were present: serum sodium <140 mmol/L, daily urine volume <1000mL, body weight gain *Then:* fluid restriction of 200 ml/day fluids (+ 1600 mL/day in food) from postoperative day 6-12 (in-hospital) Control: not reported	*At least 11 days:* Hyponatremia (<135 mmol/L)	Funding: no funding received Conflict of interest: authors report no conflict of interest Population: all underlying pathologies for transsphenoidal surgery were included: Rathke's cleft cyst (112), adenomas and prolactinomas.	High

Snyder, 2021 Retrospective cohort Single centre, USA	N at baseline: 217 I: 135 | C: 82 <u>Age (mean, SD)</u> I: 50 (16) | C: 53 (16) <u>Sex (% male):</u> I: 50% | C: 51% <u>Preoperative symptoms (%)</u> SSRI medication: I: 13% | C: 7% Diuretic medication: I: 21% | C: 20%	<u>Intervention:</u> fluid restriction of 1000 mL/day for 7 days after discharge (patients undergoing TSS after March 2018) <u>Control:</u> fluid-unrestricted cohort (patients undergoing TSS between March 2016 - March 2018)	*Within 10 days postoperatively:* Hyponatremia (≤136 mmol/L) *Within 30 days:* Readmission Adherence	Funding: no funding information available. Conflicts of interest: authors report no conflict of interest <u>Population:</u> Involved patients undergoing transsphenoidal resection of pituitary adenoma (Patients with Rathke's cleft cyst, craniopharyngioma, and other lesions were excluded)	Some concerns
Takeuchi, 2014 Retrospective cohort Single centre, Japan	N at baseline: 185 I: 93 | C: 92 <u>Age (mean, SD)</u> I: 49 (14) | C: 52 (16) <u>Sex (% male):</u> I: 44% | C: 52% <u>Preoperative symptoms (%)</u> Non-functioning adenoma: I: 53% | C: 60%	<u>Intervention:</u> restriction of water intake of 2500 mL/day for postoperative days 1-10 (patients undergoing TSS between Sept 2009 – June 2012) <u>Control</u>: drink freely after surgery (patients undergoing TSS between September 2005 – August 2009)	*Within 11 days postoperatively:* Hyponatremia (<135 mmol/L) Hypernatremia	Funding: no funding received Conflict of interest: authors report no conflict of interest <u>Population:</u> patients who had sellar and parasellar lesions and underwent purely endoscopic endonasal TSS.	Some concerns
Winograd, 2020 Retrospective cohort Single centre, USA	N at baseline: 122 I: 65 | C: 57 <u>Age (mean, SD)</u> I: 48.9 (16.2) | C: 50.9 (14.9) <u>Sex (% male):</u> I: 32% | C: 37% <u>Preoperative symptoms (%)</u> Macroadenoma: I: 62% | C: 88% Non-functioning adenoma: I: 47% | C: 47%	<u>Intervention:</u> 1000-1250 mL/day for postoperative days 4-8 (patients undergoing TSS between March 2018 – Jan 2019) <u>Control:</u> not reported (patients undergoing TSS between July 2016 – Feb 2018)	*Within 8 days postoperatively:* Hyponatremia (≤133 mmol/L) Readmission (only reported if due to hyponatremia) Hypernatremia Adherence	Funding: no funding information available. Conflict of interest: authors report no conflict of interest <u>Population:</u> patients who underwent TSS or biopsy of sellar lesions (including Rathke's cyst).	Some concerns

	Intraoperative glucocorticoids: I: 35% | C: 56% Repeat surgery: I: 12% | C: 11%				
Cooper, 2023 Retrospective cohort Single centre, USA	N at baseline: 722 I-1: 110 | I-2: 316| C: 296 <u>Age (mean, SD)</u> I-1: 55 (15.8) I-2: 53 (16.7) | C: 52 (15.7) <u>Sex (% male)</u> I-1: 55% | I-2: 46% | C: 52% <u>Preoperative symptoms (%)</u> Pituitary adenomas I-1: 71% | I-2: 83% | C: 82% Non-functioning adenoma: I-1: 50% | I-2: 37% | C: 63% Macroadenoma: I-1: NR | I-2: 86% | C: 85% Optic chiasm compression: I-1: NR | I-2: 59% | C: 50%	<u>Intervention-1:</u> fluid restriction of 1000 mL/day for postoperative days 2-7, and if sodium 135-145 on day 7, restriction to 1500 mL/day for 3 more days. (patients undergoing TSS between 2019 and 2021) <u>Intervention-2:</u> drink to thirst, but with sodium testing on day 7 and written information about signs and symptoms of hyponatremia (patients undergoing TSS between 2012 and 2018) <u>Control:</u> not reported (patients undergoing TSS between 2006 and 2011)	*(unclear follow-up; more than 7 days):* Hyponatremia (<135 mmol/L) Readmission Adherence	Funding: no funding received Conflict of interest: authors report no conflict of interest <u>Population</u>: patients with pituitary adenoma, Rathke's cleft cyst, and other sellar or parasellar pathologies	Some concerns
Ghiam, 2022 Retrospective cohort Single centre, USA	N at baseline: 542 I: 133 | C: 409 <u>Age (mean, SD):</u> I: 55 (16.2) | C: 54 (16.5) <u>Sex (% male):</u> I: 44% | C: 47% <u>Preoperative symptoms (%)</u> Non-functioning adenoma: I: 66% | C: 61%	<u>Intervention:</u> fluid restriction 1000-1500 mL/day from discharge for 10 days and education pamphlet on signs of sodium abnormalities (patients undergoing TSS from July 2020 to May 2021) <u>Control:</u> not reported (patients undergoing TSS from Dec 2010 to 2018)	*30 days:* Readmission (including readmission for hypernatremia)	Funding: no funding information available. Conflict of interest: authors report no conflict of interest <u>Population</u>: patients with pituitary adenomas (i.e. craniopharyngioma, Rathke's cleft cyst, meningioma, malignancy, etc. were excluded).	High

*For further details, see risk of bias table in the appendix

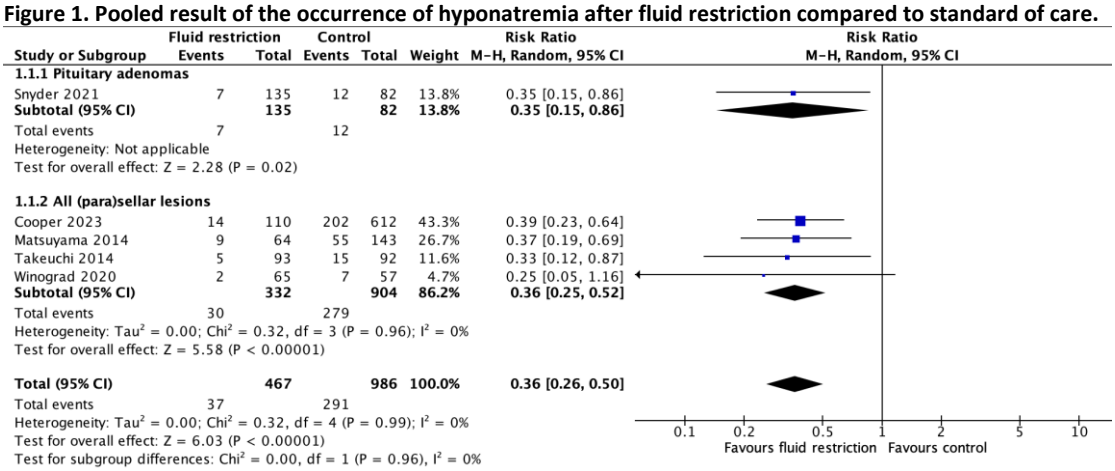
Results

The results of the included studies are summarized per outcome measure.

1. Hyponatremia

Five studies reported on the occurrence of hyponatremia within 7 to 11 days after surgery. See figure 1 for the pooled effect of a fluid restriction of 1000-2500 mL/day compared to no fluid restriction.

Figure 1. Pooled result of the occurrence of hyponatremia after fluid restriction compared to standard of care.



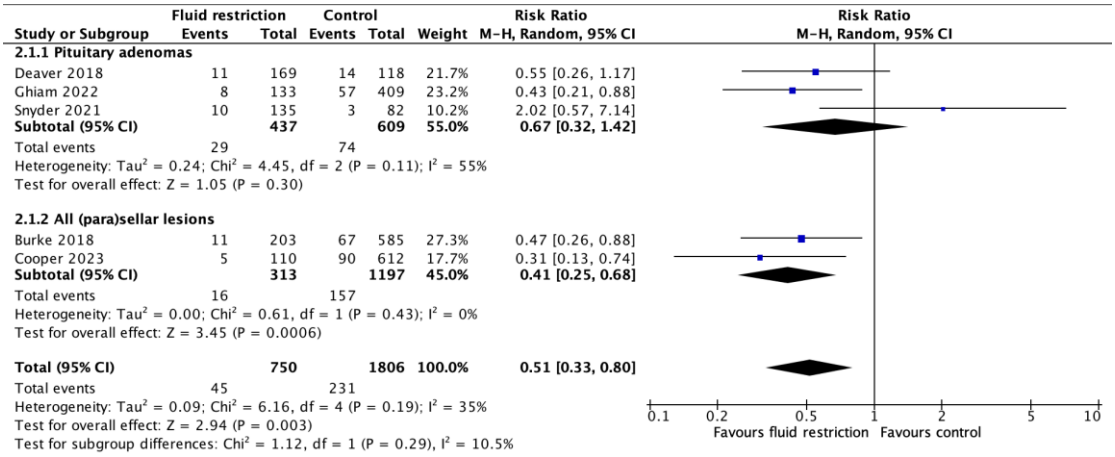
Some authors reported how many patients presented with symptomatic hyponatremia:

	Symptomatic hyponatremia		Comments
Author	**In fluid restriction group**	**In control group**	
Cooper, 2023	Of those with hyponatremia: 64% mild 29% moderate 7% severe	Of those with hyponatremia*: 50% mild 20% moderate 30% severe Of these, 41% was symptomatic*	*Applies only to those with delayed hyponatremia (≥4 days postoperatively); no information for patients with early hyponatremia Mild: 130-134 mmol/L Moderate: 125-129 Severe: <125 mmol/L
Matsuyama, 2014	Only one patient (of 64 with hyponatremia) showed symptoms of SIADH		
Takeuchi, 2014	Of those with hyponatremia 1 symptomatic (20%)	Of those with hyponatremia: 6 symptomatic (40%)	1.1% of fluid restriction group as a total had symptomatic hyponatremia, compared to 6.5% of control group.
Winograd, 2020	Of those with hyponatremia: 2 symptomatic (all) *Sodium:* 116 and 127 mEq/L	Of those with hyponatremia: 5 symptomatic (71%) *Sodium:* 103-129 mEq/L	Complaints in fluid restriction group: headache and nausea/vomiting. Complaints in control group: 3x headache, 4x nausea/vomiting, 1x fatigue and weakness. Sodium of asymptomatic patients was 129 and 132 mEq/L

2. Readmission

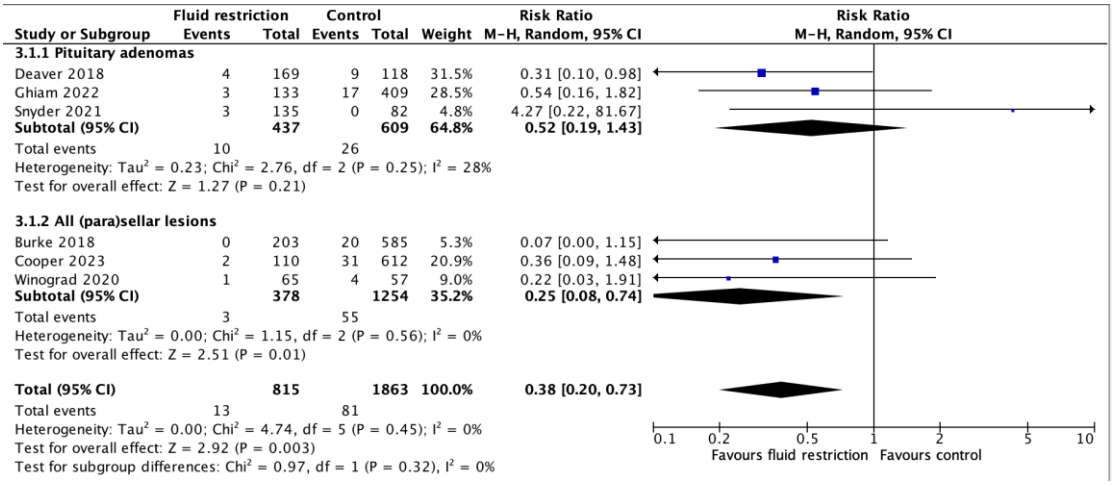
Five studies reported on 30-day readmission (except Burke 2018, in whose study the follow-up for readmissions is unclear), for any reason. The pooled results can be found in figure 2.

Figure 2. Pooled result of 30-day all cause readmission after fluid restriction compared to standard of care.



Six studies reported on readmission due to hyponatremia. The pooled results can be found in figure 3.

Figure 3. Pooled result of readmission due to hyponatremia after fluid restriction compared to standard of care.



With regard to readmissions due to hypernatremia, Deaver (2018) reported that “the fluid restriction did not result in any admissions for hypernatremia”. Ghiam (2022) reported that 5 patients in the control group (out of 409, 1.2%) and 1 patient in the fluid-restriction group (out of 133, 0.5%) were readmitted for hypernatremia (difference not clinically relevant).

3. Complications (hypernatremia)

Readmissions due to hypernatremia are reported under “Readmission”. The occurrence of hypernatremia was low; Takeuchi (2014) reported 3 patients in each group having hypernatremia (6 total), and Winograd (2020) a total of 4 (unclear in which group).

4. Adherence

Three studies reported on compliance of the fluid restriction:

- Snyder (2021) reported a compliance rate of 90%
- Winograd (2020) reported a compliance rate of 98% (with 1 non-complier, a patient stating that he was unable to restrict intake to 1000 mL on the first day of protocol because of a dry mouth)
- Cooper (2023) reported a compliance rate of 95% (with 5 non-compliers)

Summary of Findings

Outcome [Timeframe]	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the evidence** (Quality of evidence)	**Summary**
		Control	**Fluid restriction**		
Hyponatremia [7 to 11 days]	**Relative risk: 0.36 (CI 95% 0.26 - 0.50)** Based on data from 1453 participants in 5 studies	**295** per 1000	**106** per 1000	**Low** Due to serious risk of bias[1]	A fluid restriction may reduce the occurrence of hyponatremia in patients after pituitary surgery, compared to standard of care. *(Cooper 2023, Matsuyama 2014, Takeuchi 2014, Winograd 2020, Snyder 2021)*
		Difference: 189 fewer per 1000 (CI 95% 218 fewer - 148 fewer)			
30-day Readmission [30 days]	**Relative risk: 0.51 (CI 95% 0.33 - 0.80)** Based on data from 2556 participants in 5 studies	**128** per 1000	**65** per 1000	**Low** Due to very serious risk of bias[1]	A fluid restriction may reduce the number of 30-day readmissions in patients after pituitary surgery, compared to standard of care. (*Burke 2018, Cooper 2023, Deaver 2018, Ghiam 2022, Snyder 2021)*
		Difference: 63 fewer per 1000 (CI 95% 86 fewer - 26 fewer)			
Readmission due to hyponatremia	**Relative risk: 0.38 (CI 95% 0.20 - 0.73)** Based on data from 2678 participants in 6 studies	**43** per 1000	**16** per 1000	**Low** Due to serious risk of bias[1]	A fluid restriction may reduce the readmissions due to hyponatremia in patients after pituitary surgery, compared to standard of care. *(Burke 2018, Cooper 2023, Deaver 2018, Ghiam 2022, Snyder 2021, Winograd 2020)*
		Difference: 27 fewer per 1000 (CI 95% 34 fewer - 12 fewer)			
Hypernatremia	Narrative information in 2 studies	See information in result section.		**No GRADE**	-
Adherence	Is a non-comparative outcome, information in 3 studies.	See information in result section.		**No GRADE**	-

[1]**Risk of bias:** Risk of patient selection due to different time frames of cohorts, possible confounding in most studies.

Kennisvragen

Tijdens de ontwikkeling van deze module is gebleken dat er binnen deze module nog te weinig bewijs is voor de onderbouwing van de aanbeveling en dus kennisvragen bestaan. De werkgroep meent dat (vervolg)onderzoek wenselijk is om in de toekomst een duidelijker antwoord te kunnen geven op vragen uit de praktijk.

<u>Kennisvraag – AVP-deficiëntie</u>

Wat is het effect van een gestandaardiseerde strategie voor monitoring en behandeling van postoperatieve AVP-deficiëntie (met vaste criteria voor vochtbalans, natriummonitoring en inzet van desmopressine) vergeleken met gebruikelijke zorg, op het optreden van hypernatriëmie, dehydratie, verstoringen in de vochtbalans en heropnames bij volwassen patiënten na hypofysechirurgie?

Toelichting:

De huidige aanbevelingen laten ruimte voor variatie in monitoring en behandeling van AVP-deficiëntie. Vergelijkend onderzoek tussen een gestandaardiseerd zorgpad en gebruikelijke zorg is nodig om het effect op patiëntuitkomsten vast te stellen. Dit kan in de Nederlandse context worden uitgevoerd via een prospectieve (multicenter) studie of binnen bestaande kwaliteitsregistraties, zodat resultaten geschikt zijn voor toekomstige aanscherping van aanbevelingen.

<u>Kennisvraag – SIADH</u>

Wat is het effect van postoperatieve vochtbeperking (bijvoorbeeld start dag 3–5, maximale intake 1500 ml/dag) vergeleken met geen of minder strikte vochtbeperking, op het optreden van symptomatische hyponatriëmie, heropnames en complicaties bij volwassen patiënten na hypofysechirurgie?

Toelichting

De huidige aanbevelingen voor vochtbeperking laten ruimte voor variatie in timing, duur en uitvoering. Vergelijkend onderzoek tussen verschillende strategieën (bijvoorbeeld gestandaardiseerde vochtbeperking versus gebruikelijke zorg) is nodig om te bepalen welke aanpak leidt tot betere patiëntuitkomsten. Dit kan in Nederland worden uitgevoerd in een multicenter opzet, bijvoorbeeld via een prospectieve cohortstudie of gerandomiseerde studie, zodat de resultaten bruikbaar zijn voor verdere uniformering van zorg.

(De-)Implementatietabel met impuls analyse – <u>AVP-deficiëntie</u>

Aanbeveling	• Wees alert op dorst bij patiënten en vraag naar dorstgevoel
	  • Houd een vochtbalans bij (elke 4-6 uur, en sluit deze elke 24 uur af)
	  • Prik minimaal dagelijks natrium gedurende de opname
	  • Wees alert op een mogelijke AVP-deficiëntie bij verschillende klachten/symptomen/factoren
	  • Streef bij een vastgestelde AVP-deficiëntie naar een neutrale vochtbalans door voldoende te laten drinken en eenmalig desmopressine te geven	

9. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?	**X Ongewenste praktijkvariatie** ☐ Nieuwe evidentie ☐ Anders **Toelichting:** Verschillende centra hebben eigen protocollen voor monitoring en behandeling.	
10. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?	**X < 1000** ☐ < 5000 ☐ 5000-40.000 ☐ > 40.000	
11. Maakt de aanbeveling deel uit van een set van interventies voor hetzelfde probleem?	**X Ja** ☐ Nee **Toelichting:** Zie de aanbevelingen in deze module voor AVP-deficiëntie, kunnen gebundeld gelezen worden.	
12. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:	**Wat zijn mogelijke belemmerende factoren?**	**Wat zijn mogelijke bevorderende factoren?**
Richtlijn/ klinisch traject (innovatie)		
Zorgverleners (artsen en verpleegkundigen)		Sluit aan bij huidige praktijk
Patiënt/ cliënt (naasten)		
Sociale context		
Organisatorische context	In ziekenhuizen waar weinig hypofyse operaties worden verricht, is er mogelijk minder ervaring/minder routine met deze controles.	
Economische en politieke context		Goedkope interventies.
13. Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk?	**X Professional** ☐ Beroepsvereniging ☐ Ziekenhuis(bestuurder) ☐ Zorgverzekeraars/ NZa ☐ Zorginstituut [duiding nodig]	
14. Wat zouden deze personen/ partijen moeten veranderen in hun gedrag of organisatie om de aanbeveling toe te passen?	Elk ziekenhuis met hypofysechirurgie zou een protocol moeten hebben over de monitoring van het ontstaan van een AVP-deficiëntie na hypofyse operaties.	
15. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?	**X < 1 jaar** ☐ < 2 jaar ☐ < 3 jaar	
16. Conclusie: is er extra aandacht nodig voor implementatie van de aanbeveling (anders dan publicatie van deze richtlijnmodule)?	☐ **Ja*** **X Nee** **Toelichting:** Actie ligt bij professional, zorgaanbieders of verzekeraars kunnen hier niet (gemakkelijk) in ondersteunen.	

(De-)Implementatietabel met impuls analyse – SIADH

Aanbeveling	• Wees alert op het ontwikkelen van een SIADH in de eerste 3-14 dagen na de operatie. Monitoren kan op verschillende manieren. • Geef een preventieve vochtbeperking om SIADH postoperatief te voorkomen (tenzij er sprake is van een AVP-deficiëntie). • Behandel een SIADH conform het acute boekje hyponatriëmie.	
1. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?	☐ Ongewenste praktijkvariatie **X Nieuwe evidentie** ☐ Anders **Toelichting:** nieuwe studies gepubliceerd over preventieve vochtbeperking na hypofysechirurgie.	
2. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?	**X < 1000** ☐ < 5000 ☐ 5000-40.000 ☐ > 40.000	
3. Maakt de aanbeveling deel uit van een set van interventies voor hetzelfde probleem?	**X Ja** ☐ Nee **Toelichting:** Zie de aanbevelingen in deze module voor SIADH, kunnen gebundeld gelezen worden.	
4. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:	**Wat zijn mogelijke belemmerende factoren?**	**Wat zijn mogelijke bevorderende factoren?**
Richtlijn/ klinisch traject (innovatie)		Geloofwaardig, grote studies die voor en na implementatie van protocol uitkomsten laten zien.
Zorgverleners (artsen en verpleegkundigen)	Routine: Het toepassen van vochtbeperking is nog geen standaard protocol	Motivatie: Gemakkelijk toe te passen met goede patiëntuitkomsten.
Patiënt/ cliënt (naasten)	Beperkte compliance	
Sociale context		
Organisatorische context		Makkelijk te implementeren, vereist geen extra capaciteit, personeel of scholing
Economische en politieke context		Goedkoop en kan heropnames voorkomen.
5. **Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk?**	**X Patiënt/ cliënt (naaste)** **X Professional** ☐ Beroepsvereniging ☐ Ziekenhuis(bestuurder) ☐ Zorgverzekeraars/ NZa ☐ Zorginstituut [duiding nodig]	
6. Wat zouden deze personen/ partijen moeten veranderen in hun gedrag of organisatie om de aanbeveling toe te passen?	**Professional:** vochtbeperking invoeren en actief adviseren aan patiënten **Patiënt:** compliance aan vochtbeperking	
7. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?	**X < 1 jaar** ☐ < 2 jaar ☐ < 3 jaar	
8. Conclusie: is er extra aandacht nodig voor implementatie van de aanbeveling (anders dan publicatie van deze richtlijnmodule)?	☐ **Ja*** **X Nee** **Toelichting:** Er zijn maar enkele hypofysecentra in Nederland, en de meesten nemen deel aan de ontwikkeling van deze richtlijn. Andere centra zullen via het netwerk op de hoogte worden gebracht. Meer acties dan disseminatie van de richtlijn lijkt niet nodig voor implementatie van de aanbevelingen van deze module.	

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Risk of Bias tables

Risk of bias table for interventions studies (cohort studies based on risk of bias tool by the CLARITY Group at McMaster University)

Author, year	Selection of participants Was selection of exposed and non-exposed cohorts drawn from the same population?	Exposure Can we be confident in the assessment of exposure?	Outcome of interest Can we be confident that the outcome of interest was not present at start of study?	Confounding-assessment Can we be confident in the assessment of confounding factors?	Confounding-analysis Did the study match exposed and unexposed for all variables that are associated with the outcome of interest or did the statistical analysis adjust for these confounding variables?	Assessment of outcome Can we be confident in the assessment of outcome?	Follow up Was the follow up of cohorts adequate? In particular, was outcome data complete or imputed?	Co-interventions Were co-interventions similar between groups?	Overall Risk of bias Low, Some concerns, High
Burke, 2018	Definitely no *Reason:* Participants were not from same time frame (control cohort older than intervention)	Probably yes *Reason:* postoperative advice was given and one week follow up visit for control.	Probably no *Reason:* readmission cannot happen at start of study. Hyponatremia can be present at study start	Probably yes *Reason:* review of charts.	Probably no *Reason:* more women in the intervention group	Definitely yes *Reason*: need for readmission from health record; sodium testing standard protocol in both cohorts.	Definitely no *Reason:* Follow up was too short for the outcome readmission. No information on missing outcome data.	Probably yes *Reason:* No co-interventions given.	**High (readmission)** - patient selection - high risk of confounding - follow up too short **Some concerns (hyponatremia)** - patient selection - high risk of confounding
Deaver, 2018	Definitely no *Reason:* Participants were not from same time frame (control cohort older than intervention)	Definitely yes *Reason*: nursing records an labs were reviewed to determine the fluid intake/output and sodium levels	Definitely no Reason:	Probably yes *Reason:* review of medical health records	Probably no *Reason*: more microadenoma in intervention group	Definitely yes *Reason*: need for readmission standardized, from health record.	Definitely no *Reason*: Those patients without at least 1 month of follow-up in the electronic medical record were excluded	Probably yes Reason: similar frequency of stress-dose glucocorticoids administered	**Some concerns** - patient selection - risk of confounding - unclear attrition
Matsuyama , 2014	Definitely no *Reason:* Participants were not from same time frame (control cohort	Probably yes *Reason:* postoperative advice was given based on presence of criteria.	Definitely no Reason:	Unclear *Reason:* no information reported on how preoperative information was gathered.	Definitely no *Reason:* subgroup information not provided, unclear if groups were equal at baseline	Definitely yes *Reason*: postoperative serum sodium levels were measured as protocol.	Unclear *Reason:* unclear how long follow-up took place (at least 11 days)	Unclear *Reason:* no information on co-interventions provided	**High** - patient selection - unclear influence of confounders - unclear follow-up

	older than intervention)								
Snyder, 2021	Definitely no *Reason:* Participants were not from same time frame (control cohort older than intervention)	Probably yes *Reason:* postoperative advice was given and follow up visit 7-10 days after for control.	Definitely yes *Reason:* Patients who received desmopressin or had SIADH during hospitalization were excluded from analysis.	Probably yes *Reason:* review of charts.	Unclear *Reason:* more confounding factors of interest not assessed.	Definitely yes *Reason:* postoperative serum sodium levels were measured as protocol. Unclear how readmission was assessed.	Probably no *Reason:* unclear how much drop-out or missing information.	Probably yes *Reason:* seemingly yes from table 1.	**Some concerns** - patient selection - possible confounding - unclear attrition rate
Takeuchi, 2014	Definitely no *Reason:* Participants were not from same time frame (control cohort older than intervention)	Definitely yes *Reason*: urine output was monitored to determine the fluid intake/output	Definitely yes *Reason:* patients with a medical history op hyponatremia were excluded from the study	Probably yes *Reason:* review of charts.	Unclear *Reason:* more confounding factors of interest not assessed.	Definitely yes *Reason:* blood tests for serum levels of electrolytes were performed on postoperative days 1, 7, and 10	Probably yes *Reason:* few patients excluded. Unclear how long follow-up took place (at least 10 days, which is sufficient for outcome)	Unclear *Reason:* no information on co-interventions provided	**Some concerns** - patient selection - possible confounding - unclear information on co-interventions
Winograd, 2020	Definitely no *Reason:* Participants were not from same time frame (control cohort older than intervention)	Probably yes *Reason:* monitor over phone for symptoms of hyponatremia after 2 and 4 days	Probably yes *Reason:* Our final source of data was the patient population in which hyponatremia could not be easily predicted.	Probably yes *Reason:* retrospective chart review.	Probably yes *Reason:* differences in lesion size and intraoperative glucocorticoid use. However, correction in multivariable model.	Definitely yes *Reason:* patients were assessed in clinic on POD 8 as routine care with sodium assessment.	Probably yes Reason: information of 8 prior patients with 1250 mL protocol reported. Follow-up too short for readmission.	Probabaly yes *Reason:* See table 1 patient characteristics	**Some concerns** - patient selection - change of protocol during study - follow-up too short for readmission
Cooper, 2023	Definitely no *Reason:* Participants were not from same time frame (control cohort older than intervention)	Probably yes *Reason:* patients had sheet to chart all fluid intake and had follow up visit at day 7	Definitely yes *Reason:* preoperative median sodium measured and reported.	Probably yes *Reason:* retrospective chart review.	Probably no *Reason:* no multivariable analyses performed. Baseline differences between groups.	Probably no *Reason:* patients in control group did not receive standard postoperative sodium testing. For 2 other	Unclear *Reason:* period of follow-up not reported (at least 7 days).	Probabaly yes *Reason:* See tables with patient characteristics	**Some concerns** - patient selection - possible confounding - unclear follow-up

						groups: probably yes.			
Ghiam, 2022	Definitely no *Reason:* Participants were not from same time frame (control cohort older than intervention)	Probably yes *Reason:* fluid restriction as part of hospital-wide postoperative care pathway.	Definitely no Reason:	Probably yes *Reason:* retrospective chart review.	Unclear *Reason:* more confounding factors of interest not assessed.	Definitely yes *Reason:* retrospective review of electronic health record for readmissions	Unclear *Reason:* amount of missing data not reported.	Unclear *Reason:* intraoperative medications and pre-operative characteristics unclear	**High** - patient selection - possible confounding - unclear missing data/attrition rate - unclear information on co-interventions

Table of excluded studies

Reference	Reason for exclusion
Perez-Vega C, Tripathi S, Domingo RA, Ramos-Fresnedo A, Lee SJ, Chaichana KL, Quinones-Hinojosa A, Samson SL. Fluid Restriction After Transsphenoidal Surgery for the Prevention of Delayed Hyponatremia: A Systematic Review and Meta-Analysis. Endocr Pract. 2021 Sep;27(9):966-972. doi: 10.1016/j.eprac.2021.07.003. Epub 2021 Jul 13. PMID: 34265453.	Is an SR; relevant individual studies included
Yu S, Taghvaei M, Reyes M, Piper K, Collopy S, Gaughan JP, Prashant GN, Karsy M, Evans JJ. Delayed symptomatic hyponatremia in transsphenoidal surgery: Systematic review and meta-analysis of its incidence and prevention with water restriction. Clin Neurol Neurosurg. 2022 Mar;214:107166. doi: 10.1016/j.clineuro.2022.107166. Epub 2022 Feb 10. PMID: 35158166.	Is an SR; relevant individual studies included
Castle-Kirszbaum M, Goldschlager T, Shi MDY, Kam J, Fuller PJ. Postoperative fluid restriction to prevent hyponatremia after transsphenoidal pituitary surgery: An updated meta-analysis and critique. J Clin Neurosci. 2022 Dec;106:180-184. doi: 10.1016/j.jocn.2022.10.032. Epub 2022 Nov 9. PMID: 36369079.	Is an SR; relevant individual studies included
Kazempour M , Simani L, Sadeghi M, Maghsoudi Nejad F, Saber A, et al. Prevention of Hyponatremia After Transsphenoidal Surgery: A Systematic Review. Nephro-Urol Mon. 2022;14(4):e128929. https://doi.org/10.5812/numonthly-128929.	Is an SR; relevant individual studies included. Two studies included in Kazempour were not according to PICO.

Literature search strategy

Algemene informatie

Cluster/richtlijn: NVvN Hypofysechirurgie	
Uitgangsvraag/modules: UV4 Hoe kunnen verstoringen van de waterhuishouding na een hypofyseoperatie het best gemonitord, voorkomen en behandeld worden?	
Database(s): Embase.com, Ovid/Medline	Datum: november 2024
Periode: vanaf 2000	Talen: geen restrictie
Literatuurspecialist: Alies Oost	Rayyan: https://new.rayyan.ai/reviews/1240930/screening
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/	
Toelichting: Voor deze vraag is gezocht op de elementen: Hypofysechirurgie Vochtrestrictie De sleutelartikelen worden gevonden met deze search.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR	22	6	23
RCT	28	3	28
Observationele studies	66	36	71
Totaal	116	45	**122***

***in Rayyan**

Zoekstrategie

Embase.com

No.	Query	Results
#1	'pituitary surgery'/exp OR 'hypophysectomy'/exp OR 'transsphenoidal surgery'/de OR hypophysectom*:ti,ab,kw OR cryohypophysectom*:ti,ab,kw OR pituitectom*:ti,ab,kw OR (((pituitar* OR hypophys* OR adenohypophys* OR neurohypophys* OR prolactinoma*) NEAR/4 (surg* OR microsurg* OR operation* OR operative OR excis* OR resect* OR remov* OR laparoscop* OR endoscop* OR neuroendoscop* OR craniotom* OR craniostom* OR endonasal OR intranasal OR transnasal* OR transcran* OR transsphenoid* OR 'trans sphenoid*')):ti,ab,kw) OR (('hypophysis disease'/exp OR 'hypophysis'/exp OR hypophysis:ti,ab,kw OR ((pituitar* NEAR/3 (gland* OR lobe*)):ti,ab,kw) OR (((pituitar* OR hypophys* OR adenohypophys* OR neurohypophys*) NEAR/5 (adenoma* OR cancer* OR carcinoma* OR lesion* OR malignan* OR neoplasm* OR tumor* OR tumour*)):ti,ab,kw) OR prolactinoma*:ti,ab,kw) AND ('surgery'/exp OR 'surgical patient'/exp OR 'surgical risk'/exp OR 'perioperative period'/exp OR 'surgery'/lnk OR surgic*:ti,ab,kw OR surger*:ti,ab,kw OR microsurg*:ti,ab,kw OR operation*:ti,ab,kw OR operative:ti,ab,kw OR presurg*:ti,ab,kw OR preoperati*:ti,ab,kw OR perisurg*:ti,ab,kw OR perioperati*:ti,ab,kw OR postsurg*:ti,ab,kw OR postoperati*:ti,ab,kw OR intraoperati*:ti,ab,kw OR laparoscop*:ti,ab,kw OR endoscop*:ti,ab,kw OR neuroendoscop*:ti,ab,kw OR transsphenoid*:ti,ab,kw OR 'trans sphenoid*':ti,ab,kw OR craniotom*:ti,ab,kw OR craniostom*:ti,ab,kw))	74588
#2	'water deprivation'/exp OR 'fluid intake'/exp OR (((water OR fluid*) NEAR/3 (restrict* OR deprivat* OR drink* OR intake OR consump*)):ti,ab,kw)	146497

#3	#1 AND #2 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	486
#4	#3 AND [2000-2025]/py	418
#5	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	1079860
#6	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	4148612
#7	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	8506313
#8	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR	15559155

	'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#9	#4 AND #5	22
#10	#4 AND #6 NOT #9	28
#11	#4 AND (#7 OR #8) NOT (#9 OR #10)	66
#12	#9 OR #10 OR #11	116

Ovid/Medline

1	exp Pituitary Gland/su or exp Pituitary Diseases/su or exp Hypophysectomy/ or hypophysectom*.ti,ab,kf. or cryohypophysectom*.ti,ab,kf. or pituitectom*.ti,ab,kf. or ((pituitar* or hypophys* or adenohypophys* or neurohypophys* or prolactinoma*) adj4 (surg* or microsurg* or operation* or operative or excis* or resect* or remov* or laparoscop* or endoscop* or neuroendoscop* or craniotom* or craniostom* or endonasal or intranasal or transnasal* or transcran* or transsphenoid* or 'trans sphenoid*')).ti,ab,kf. or ((exp Pituitary Diseases/ or exp Pituitary Gland/ or hypophysis.ti,ab,kf. or (pituitar* adj3 (gland* or lobe*)).ti,ab,kf. or ((pituitar* or hypophys* or adenohypophys* or neurohypophys*) adj5 (adenoma* or cancer* or carcinoma* or lesion* or malignan* or neoplasm* or tumor* or tumour*)).ti,ab,kf. or prolactinoma*.ti,ab,kf.) and (exp Surgical Procedures, Operative/ or exp Specialties, Surgical/ or su.fs. or exp Perioperative Period/ or surgic*.ti,ab,kf. or surger*.ti,ab,kf. or microsurg*.ti,ab,kf. or operation*.ti,ab,kf. or operative.ti,ab,kf. or presurg*.ti,ab,kf. or preoperati*.ti,ab,kf. or perisurg*.ti,ab,kf. or perioperati*.ti,ab,kf. or postsurg*.ti,ab,kf. or postoperati*.ti,ab,kf. or intraoperati*.ti,ab,kf. or laparoscop*.ti,ab,kf. or endoscop*.ti,ab,kf. or neuroendoscop*.ti,ab,kf. or transsphenoid*.ti,ab,kf. or 'trans sphenoid*'.ti,ab,kf. or craniotom*.ti,ab,kf. or craniostom*.ti,ab,kf.))	45960
2	exp Water Deprivation/ or exp Drinking/ or ((water or fluid*) adj3 (restrict* or deprivat* or drink* or intake or consump*)).ti,ab,kf.	106170
3	(1 and 2) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/)	220
4	limit 3 to yr="2000 -Current"	148
5	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	791726
6	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2809456

7	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies]	4889671
8	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	5842298
9	4 and 5	6
10	(4 and 6) not 9	3
11	(4 and (7 or 8)) not (9 or 10)	36
12	9 or 10 or 11	45

Module 5 – Postoperatieve surveillance

Uitgangsvraag

Wat is de beste follow-up strategie na hypofyse chirurgie?

De uitgangsvraag omvat de volgende deelvragen:

1. Wat is de beste timing voor postoperatieve MRI in de eerste 6 maanden?
2. Welke factoren kunnen aanleiding geven tot vervroegde postoperatieve MRI?
3. Welke aanvullende postoperatieve follow-up is aangewezen na hypofysechirurgie?

Search and select

A systematic review of the literature was performed to answer the following question(s): What is the optimal timing for first MRI after pituitary resection for treatment outcomes of residual adenoma?

Table 1. PICO

Patients	Patients who have undergone pituitary surgery
Intervention	early post operative MRI (<3 months)
Control	late post operative MRI (>3 months)
Outcomes	Return to the operating room (reoperation), timing of reoperation for residual adenoma, visual field, visual acuity, post-operative complications
Other selection criteria	Study design: systematic reviews and randomized controlled trials

Relevant outcome measures

The guideline panel considered return to the operating room (reoperation), as a **critical** outcome measure for decision making; and timing of reoperation for residual adenoma, visual field, visual acuity, post-operative complications as an **important** outcome measure for decision making.

A priori, the guideline panel did not define the outcome measures listed above but used the definitions used in the studies.

The guideline panel defined a relative difference of 10% as the minimal clinically important difference for all postoperative outcomes—including return to the operating room, worsened visual acuity, worsened visual fields and postoperative complications—which corresponds to an effect size of **1.10 ≥ RR ≤ 0.90**, as thresholds for clinical relevance.

Search and select (Methods)

A systematic literature search was performed by a medical information specialist using the following bibliographic databases: Embase.com and Ovid/Medline all. Both databases were searched from 2005 to May 19th, 2025 for systematic reviews, RCTs and observational studies. Systematic searches were completed using a combination of controlled vocabulary and natural language keywords. The overall search strategy was derived from the following primary search concepts: (1) pituitary tumor; (2) surgery; (3) postoperative MRI. Duplicates were removed using EndNote software. After deduplication a total of 769 records were imported for title/abstract screening. Initially, six studies were selected based on title and

abstract screening. After reading the full text, five studies were excluded (see the exclusion table under the tab 'Evidence tabellen'), and one study was included.

Summary of literature

Description of studies

One study (Kunigelis, 2020) was included in the analysis of the literature. Important study characteristics and results are summarized in table 2. The assessment of the risk of bias is summarized in the risk of bias tables (under the tab 'Evidence tabellen').

The study by Kunigelis (2020) was conducted as a retrospective observational cohort study at a single tertiary academic medical centre. All data were obtained from institutional clinical and imaging records covering the period 2012–2017. The investigators identified all patients who underwent surgery for pituitary adenoma during this time frame and subsequently screened these cases for the availability of postoperative MRI.

The inclusion criteria consisted of:

1. patients who underwent transsphenoidal surgery for a pituitary adenoma at the study institution, and
2. availability of at least one postoperative MRI scan in the hospital imaging system.

From 519 surgically treated patients identified, 443 patients were included in the final analysis based on the presence of postoperative imaging data.

Table 2. Characteristics of included studies

Study	Participants	Comparison	Follow-up	Outcome measures	Comments	Risk of bias (per outcome measure)*
Kunigelis, 2020	N at baseline Early MRI group: n = 71; Late MRI group: n = 372. Age (mean, SD) Early MRI group:49 (range 16-83); Late MRI group: 52 (range 13-92) Sex (% female) Early MRI group: 30/71 women (42.3%) Late MRI group: 190/372 women (51.1%) Tumour volume cm^3) mean: Early: 12.33 (range 0.16–90.59), Late: 4.64 (range 0.008–124.75).	Intervention: early postoperative MRI obtained <90 days after pituitary surgery (n = 71). Comparator: late postoperative MRI obtained ≥90 days after surgery (n = 372). Early MRI practice reflected an older institutional protocol with immediate and 3-month MRI; later protocol generally omitted early routine MRI and used delayed (≥3-month) MRI.	Early MRI: mean 470 days (range 2–1819) late MRI: and 459 days (range 2–2302)	Return to the operating room (any indication). Return to the operating room for residual or recurrent tumour. Visual acuity (improved, stable or worsened from preoperative baseline). Visual fields (improved, stable or worsened).	the early MRI group had larger and more invasive tumours and more endoscopic approaches than the late group. Follow-up duration and clinical data were incomplete for some patients; visual outcomes were only available in subsets of the cohort.	HIGH

*For further details, see risk of bias table in the appendix

Results

Return to the operating room (any indication)
For this outcome, data were available for 71 patients in the early MRI group and 372 patients in the late MRI group. A total of 12/71 (16.9%) early MRI patients returned to the operating room compared with 18/372 (4.8%) in the late MRI group. The corresponding effect estimate was RR 0.28 (95% CI 0.14 to 0.57), in favour of the late MRI group. The absolute difference was 12.1%, which exceeds the predefined threshold of 10% and can therefore be considered clinically relevant.

Reoperation for residual or recurrent tumour
Data were available for all patients in both groups (71 early, 372 late). The early group experienced 6/71 (8.5%) tumour-related reoperations, whereas the late group experienced 10/372 (2.7%). The effect estimate was RR 0.32 (95% CI 0.12 to 0.85), in favour of the late MRI group. The absolute difference was 5.8%, which does not exceed the 10% threshold for clinical relevance.

Worsened visual acuity
Postoperative visual acuity data were available for 45 early MRI patients and 191 late MRI patients. Worsening occurred in 3/45 (6.7%) in the early group and 28/191 (14.7%) in the late group. The effect estimate was RR 2.19 (95% CI 0.70 to 6.94), in favour of the early MRI group. The absolute difference of 8.0% does not exceed the 10% threshold for clinical relevance.

Worsened visual fields
Visual field data were available for 62 early MRI patients and 302 late MRI patients. Worsening occurred in 2/62 (3.2%) early MRI patients and 2/302 (0.7%) late MRI patients. The effect estimate was RR 0.22 (95% CI 0.03 to 1.43), in favour of the late MRI group. The absolute difference of 2.5% does not exceed the 10% threshold for clinical relevance.

Postoperative complications
No information reported on this outcome.

Summary of Findings

Population: Patients who have undergone pituitary surgery
Intervention: early post-operative MRI (<3 months)
Comparator: late post-operative MRI (>3 months)

Outcome	Study results and measurements	Absolute effect estimates		Certainty of the Evidence (Quality of evidence)	Conclusions
		Early MRI	Late MRI		
Return to the operating room (any indication)	Relative risk: 0.28 (95% CI 0.14–0.57) Based on data from 443 participants in 1 study	**169 per 1000**	**48 per 1000**	Very Low GRADE[1]	The evidence is very uncertain about the effect of early MRI on return to the operating room when compared with late MRI in patients undergoing pituitary surgery.
		Difference: 121 fewer per 1000 *(95% CI 192 fewer – 51 fewer)*			
Reoperation for residual/recurrent tumour	Relative risk: 0.32 (95% CI 0.12–0.85) Based on data from 443 participants in 1 study	**85 per 1000**	**27 per 1000**	Very Low GRADE[2]	The evidence is very uncertain about the effect of early MRI on reoperation for residual or recurrent tumour when compared with late MRI in patients undergoing pituitary surgery.
		Difference: 58 fewer per 1000 *(95% CI 115 fewer– 1 fewer)*			
Worsened visual acuity	Relative risk: 2.19 (95% CI 0.70–6.94) Based on data from 236 participants in 1 study	**67 per 1000**	**147 per 1000**	Very Low GRADE[2]	The evidence is very uncertain about the effect of early MRI on worsened visual acuity when compared with late MRI in patients undergoing pituitary surgery.
		Difference: 80 more per 1000 *(95% CI 6 fewer – 167 more)*			
Worsened visual fields	Relative risk: 0.22 (95% CI 0.03–1.43) Based on data from 364 participants in 1 study	**32 per 1000**	**7 per 1000**	Very Low GRADE[2]	The evidence is very uncertain about the effect of early MRI on worsened visual fields when compared with late MRI in patients undergoing pituitary surgery.
		Difference: 25 fewer per 1000 *(95% CI 80 fewer – 30 more)*			
Postoperative complications	Not reported	—		NO GRADE	No evidence was found regarding the effect of early MRI on postoperative complications when compared with late MRI in patients undergoing pituitary surgery.

[1]Due to very serious risk of bias (confounding).
[2]Due to very serious risk of bias (confounding) and imprecision (wide confidence intervals, only one study

Kennisvragen

Tijdens de ontwikkeling van deze module is gebleken dat er binnen deze module nog te weinig bewijs is voor de onderbouwing van de aanbeveling en dus kennisvragen bestaan. De werkgroep meent dat (vervolg)onderzoek wenselijk is om in de toekomst een duidelijker antwoord te kunnen geven op vragen uit de praktijk.

Kennisvraag:

Welke patiënt-, tumor- of behandeling gerelateerde factoren kunnen helpen om het optimale moment voor de eerste postoperatieve MRI na hypofysechirurgie te bepalen? In het bijzonder: kunnen preoperatieve of perioperatieve parameters worden geïdentificeerd die patiënten selecteren bij wie vroege beeldvorming (<3 maanden) leidt tot relevante beleidsverandering (bijvoorbeeld vroege heroperatie of radiotherapie), en daarmee een doelmatige en kosteneffectieve strategie vormt? Eveneens is het van belang te onderzoeken bij welke patiënten het veilig is de eerste controle-MRI uit te stellen tot na 6 maanden.

Toelichting:

Het beter beantwoorden van deze kennisvraag is benodigd om stratificatie van risicogroepen te verbeteren en het postoperatieve traject beter af te stemmen op de individuele patiënt. Hierdoor kan in de toekomst mogelijk ook de frequentie van follow-up interval afnemen, hetgeen leidt tot een duurzamer en kostenefficiënter scanbeleid.

Implementeren-tabel

De implementatietabel brengt in kaart welke factoren de uitvoering van een aanbeveling bevorderen of belemmeren, en welke aanvullende acties nodig zijn voor succesvolle invoering. De adviseur en (cluster)werkgroep vullen de tabel in op basis van gerichte vragen over het onderliggende probleem, relevante randvoorwaarden en mogelijke knelpunten. Op basis hiervan wordt geconcludeerd of een extra implementatie-impuls wenselijk is.

Implementatietabel

Vraag	***Antwoord:*** ***Kruis aan en licht toe/ beschrijf***		***Toelichting keuze:***
I1. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?	**X**	**Ongewenste praktijkvariatie**	
		Nieuwe evidentie	
		Anders	
I2. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?		**< 1000**	
	X	**< 5000**	
		5000-40.000	
		> 40.000	
I3. Is de aanbeveling onderdeel van een bredere set interventies of verwant aan andere richtlijnen of modules? Zo ja, hoe verhoudt zij zich daartoe en moet hiermee		**Ja**	
	X	**Nee**	

rekening worden gehouden bij de implementatie, of kan de aanbeveling als losstaand worden beschouwd?			
I4. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:		**Belemmerende factoren**	**Bevorderende factoren/ kansen**
Richtlijn/ klinisch traject (innovatie)			
Zorgverleners (artsen en verpleegkundigen)			
Patiënt/ cliënt (naasten)			
Sociale context			
Organisatorische context	**x**	Beperkte MRI-capaciteit en druk op radiologen vormt grootste knelpunt	Aanbeveling leidt waarschijnlijk tot een afname in uit te voeren MRIs
Financiële en juridische context			
I5. A) Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk? (kruis aan) **B) Wat is er nodig van deze personen/partijen om de aanbeveling in de praktijk te kunnen brengen? *Denk aan aanpassingen in gedrag, werkwijzen, beleid, samenwerking of andere randvoorwaarden*.**		**A**	**B**
		Patiënt/ cliënt (naaste)	
	x	**Professional**	Terughoudend zijn met vroege postoperatieve MRI bij ontbreken van klinische aanwijzingen
		Beroepsvereniging, nl	
		Ziekenhuis (raad van bestuur/UMCNL (voorheen NFU)/NVZ)	
		Zorgverzekeraars/ NZa	
		Zorginstituut [duiding nodig]	

		Anders	
I6. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?	**x**	**< 1 jaar**	
		binnen 2-3 jaar	
I7. Conclusie: is er extra actie en/of ondersteuning nodig voor implementatie van de aanbeveling? ***De reguliere implementatieroutes (publicatie en disseminatie via officiële kanalen, opname in professionele standaarden, scholing en nascholing, gebruik van bestaande ICT systemen, audits en visitaties) van de richtlijnmodule alleen is onvoldoende.***		**Ja**	
	X	**Nee**	
I8. Plaatsing op de Landelijke Implementatieagenda Medisch Specialistische zorg is gewenst. ***Het gaat om zorg die (grotendeels) wordt uitgevoerd binnen de ziekenhuismuren. Succesvolle implementatie vraagt om actieve betrokkenheid en samenwerking van meerdere relevante partijen binnen de zorgpraktijk.***		**Ja ***	
		Nee	

**Deze aanbeveling komt mogelijk in aanmerking voor plaatsing op de Landelijke Implementatieagenda van het programma Zorg Evaluatie & Gepast Gebruik (ZE&GG), waarin alle betrokken partijen in de medisch-specialistische zorg samenwerken aan de implementatie van bewezen beste zorg. De Federatie levert namens het veld goed onderbouwde aanbevelingen aan, die zijn getoetst op de behoefte aan een implementatie-impuls. De onderwerpen op de Implementatieagenda zijn onderdeel van landelijke zorginkoopafspraken tussen zorgverzekeraars en zorgaanbieders. Voor de beoordeling van aanbevelingen uit richtlijnen wordt gebruikgemaakt van de implementatietabel. Op basis hiervan kunnen we de andere partijen goed informeren en gezamenlijk besluiten of plaatsing op de Implementatieagenda passend is.*

Literatuur

Kunigelis KE, Arnone G, Chatain G, Hoffman J, Chatain O, Coulter I, et al.Defining the timing and role of acute postoperative imaging in pituitary adenoma surgery: clinical study. Acta Neurochir (Wien). 2020;162(10):2493–2503. doi:10.1007/s00701-020-04515-2.

Modak N, Patel SK, Moorthy R, Rajaratnam V, Trivedi J.Early versus delayed postoperative magnetic resonance imaging following transsphenoidal pituitary surgery: a systematic review. World Neurosurg. 2025;185:322–334. doi:10.1016/j.wneu.2025.01.011.

Bijlagen bij module UV05

Table of excluded studies

Reference	Reason for exclusion
Alhilali LM, Little AS, Yuen KCJ, Lee J, Ho TK, Fakhran S, White WL. Early postoperative MRI and detection of residual adenoma after transsphenoidal pituitary surgery. J Neurosurg. 2020;134(3):761-770. doi:10.3171/2019.11.JNS191845.	Not aligned with PICO / descriptive diagnostic study
Caulley L, Dijk SW, Krijkamp E, Dong SX, Alkherayf F, Amrani L, Doyle MA, Eid A, Johnson-Obaseki S, Khoury M, Malcolm J, Mavedatnia D, Sahlollbey N, Schramm D, Whelan J, Thavorn K, Kilty S, Hunink MGM. Cost-effectiveness of postoperative imaging surveillance strategies for nonfunctional pituitary adenomas after resection with curative intent. J Neurosurg. 2023;139(5):1207-1215. doi:10.3171/2023.2.JNS221903.	Economic study (cost-effectiveness) not relevant to the research question (focus on long-term surveillance strategies rather than timing of first postoperative MRI).
Ghorbani M, Keykhosravi E, Hasanpour M, Abbasian Ardakani A, Mohammad Hosseini E. The optimal time for postoperative magnetic resonance imaging of the sella in patients with pituitary adenoma. Basic Clin Neurosci. 2024;15(5):649-658. doi:10.32598/bcn.2023.5005.1.	Within-patient comparison only (no comparator group)
Hassan HA, Bessar MA, Herzallah IR, Laury AM, Arnaout MM, Basha MAA. Diagnostic value of early postoperative MRI and diffusion-weighted imaging following trans-sphenoidal resection of non-functioning pituitary macroadenomas. Clin Radiol. 2018;73(6):535-541. doi:10.1016/j.crad.2017.12.007.	Background study (no relevant comparison)
Kim HY, Kim ST, Kim HJ, Jeon P, Byun HS, Kim YK, Cha J, Park GM, Nam DH, Kong DS. Differentiation of postoperative changes and residual tumors in dynamic contrast-enhanced sella MRI after transsphenoidal resection of pituitary adenoma. Medicine (Baltimore). 2019;98(27):e16089. doi:10.1097/MD.0000000000016089.	Background/diagnostic study (no relevant comparator)
Mansouri A, Symons S, Schwartz M, Chen J, Pirouzmand F. Quantitative volumetric analysis post	Background/technical study (no clinical comparison)

transsphenoidal pituitary adenoma surgery. Can J Neurol Sci. 2012;39(5):600-604. doi:10.1017/s0317167100015328.	
Modak A, Gross E, Yang A, Mullick M, Jani RN, Williams BJ. Early postoperative magnetic resonance imaging for transsphenoidal pituitary surgery: A systematic literature review and the proposed imaging algorithm. Cureus. 2025;17(1):e77597. doi:10.7759/cureus.77597.	Review / background article
Nachtigall LB, Karavitaki N, Kiseljak-Vassiliades K, Ghalib L, Fukuoka H, Syro LV, Kelly D, Fleseriu M. Physicians' awareness of gadolinium retention and MRI timing practices in the longitudinal management of pituitary tumors: a Pituitary Society survey. Pituitary. 2019;22(1):37-45. doi:10.1007/s11102-018-0924-0.	Not aligned with PICO (survey study)
Patel KS, Dhawan S, Wang R, Carter BS, Chen JY, Chen CC. Post-operative imaging assessment of non-functioning pituitary adenomas. Acta Neurochir (Wien). 2018;160(5):1029-1039. doi:10.1007/s00701-018-3491-2.	Not aligned with PICO (background/follow-up imaging)
Patel KS, Kazam J, Tsiouris AJ, Anand VK, Schwartz TH. Utility of early postoperative high-resolution volumetric magnetic resonance imaging after transsphenoidal pituitary tumor surgery. World Neurosurg. 2014;82(5):777-780. doi:10.1016/j.wneu.2014.07.014.	No between-group comparison
Stofko DL, Nickles T, Sun H, Dehdashti AR. The value of immediate postoperative MR imaging following endoscopic endonasal pituitary surgery. Acta Neurochir (Wien). 2014;156(1):133-140. doi:10.1007/s00701-013-1834-6.	No between-group comparison
Yuen KCJ, Ghalib L, Buchfelder M, Hughes J, Langlois F, Molitch ME. Surveillance imaging strategies for pituitary adenomas: When, how frequent, and when to stop. Endocr Pract. 2024;30(3):282-291. doi:10.1016/j.eprac.2023.12.014.	Review (no primary data)

Literature search strategy

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR	14	15	17
RCT	53	24	68
Observationele studies	353	365	436
Overig	218	227	248
Totaal	638	631	**769***

****in Rayyan***

Zoekstrategie

Embase.com

No.	Query	Results
#1	'hypophysis tumor'/exp OR 'acromegaly'/exp OR (((pituitar* OR hypophys* OR adenohypophys* OR neurohypophys* OR sellar OR parasellar) NEAR/4 (adenoma* OR microadenoma* OR macroadenoma* OR cancer* OR carcinoma* OR cyst* OR lesion* OR malignan* OR neoplasm* OR tumor* OR tumour* OR mass*)):ti,ab,kw) OR ((cushing* NEAR/3 (syndrome* OR disease*)):ti,ab,kw) OR craniopharyngioma*:ti,ab,kw OR 'cranio pharyngioma*':ti,ab,kw OR craniopharyngeoma*:ti,ab,kw OR pharyngioma*:ti,ab,kw OR gonadotropinoma*:ti,ab,kw OR prolactinoma*:ti,ab,kw OR microprolactinoma*:ti,ab,kw OR macroprolactinoma*:ti,ab,kw OR 'macro adenoma*':ti,ab,kw OR macroadenoma*:ti,ab,kw OR 'micro adenoma*':ti,ab,kw OR microadenoma*:ti,ab,kw OR acromegal*:ti,ab,kw OR akromegal*:ti,ab,kw OR ((('non function*' OR nonfunction*) NEAR/3 adenoma*):ti,ab,kw) OR (((craniopharyngeal OR rathke*) NEAR/3 (tumor* OR tumour* OR cyst*)):ti,ab,kw)	96829
#2	'surgery'/exp OR 'surgical patient'/exp OR 'surgical risk'/exp OR 'perioperative period'/exp OR 'surgery'/lnk OR surgic*:ti,ab,kw OR surger*:ti,ab,kw OR microsurg*:ti,ab,kw OR operation*:ti,ab,kw OR operative:ti,ab,kw OR presurg*:ti,ab,kw OR preoperati*:ti,ab,kw OR perisurg*:ti,ab,kw OR perioperati*:ti,ab,kw OR postsurg*:ti,ab,kw OR postoperati*:ti,ab,kw OR intraoperati*:ti,ab,kw OR resect*:ti,ab,kw OR laparoscop*:ti,ab,kw OR endoscop*:ti,ab,kw OR neuroendoscop*:ti,ab,kw OR neurosurg*:ti,ab,kw OR transsphenoid*:ti,ab,kw OR 'trans sphenoid*':ti,ab,kw OR hypophysectom*:ti,ab,kw OR adenomectom*:ti,ab,kw	8713215
#3	(((postoperative OR 'post operative' OR postsurg* OR 'post surg*' OR followup OR 'follow up' OR surveillanc*) NEAR/7 ('magnetic resonance imag*' OR mri OR mris OR nmr OR mra OR mras OR zeugmatograph* OR 'mr tomography' OR 'mr tomographies' OR 'mr tomographic' OR 'mr imag*' OR 'proton spin' OR fmri OR fmris OR rsfmri)):ti,ab,kw) OR (('nuclear magnetic resonance imaging'/exp/mj OR 'magnetic resonance imag*':ti OR mri:ti OR mris:ti OR nmr:ti OR mra:ti OR mras:ti OR zeugmatograph*:ti OR 'mr tomography':ti OR 'mr tomographies':ti OR 'mr tomographic':ti OR 'mr imag*':ti OR 'proton spin':ti OR fmri:ti OR fmris:ti OR rsfmri:ti) AND ('postoperative period'/exp OR 'postoperative care'/exp OR postoperative:ti OR 'post operative':ti OR postsurg*:ti OR 'post surg*':ti OR followup:ti OR 'follow up':ti OR surveillanc*:ti))	46564
#4	#1 AND #2 AND #3 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'clinical trial':dtype) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT (('adolescent'/exp OR 'child'/exp OR adolescent*:ti,ab,kw OR child*:ti,ab,kw OR	777

	schoolchild*:ti,ab,kw OR infant*:ti,ab,kw OR girl*:ti,ab,kw OR boy*:ti,ab,kw OR teen:ti,ab,kw OR teens:ti,ab,kw OR teenager*:ti,ab,kw OR youth*:ti,ab,kw OR pediatr*:ti,ab,kw OR paediatr*:ti,ab,kw OR puber*:ti,ab,kw) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab,kw OR man:ti,ab,kw OR men:ti,ab,kw OR woman:ti,ab,kw OR women:ti,ab,kw))	
#5	#4 AND [2005-2025]/py	638
#6	'meta analysis'/exp OR 'systematic review'/exp OR 'scoping review'/exp OR 'rapid review'/exp OR 'umbrella review'/exp OR 'cochrane database of systematic reviews'/jt OR 'network meta-analysis'/exp OR 'networkmeta analy*':ti,ab,kw OR 'networkmetaanaly*':ti,ab,kw OR metaanaly*:ti,ab,kw OR 'meta analy*':ti,ab,kw OR metanaly*:ti,ab,kw OR prisma:ti,ab,kw OR prospero:ti,ab,kw OR metaanali*:ti,ab,kw OR 'meta anali*':ti,ab,kw OR metanali*:ti,ab,kw OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab,kw) OR (((structured OR systemic*) NEAR/3 (review* OR overview* OR synth*) NEAR/3 literature):ti,ab,kw) OR ((systemic* NEAR/1 review*):ti,ab,kw) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab,kw) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab,kw) OR (((literature NEAR/3 (review* OR overview*)):ti,ab,kw) AND (search*:ti,ab,kw OR database*:ti,ab,kw OR 'data base*':ti,ab,kw)) OR (('data extraction*':ti,ab,kw OR 'data source*':ti,ab,kw) AND ('study selection*':ti,ab,kw OR 'studies selection*':ti,ab,kw)) OR ('search strateg*':ti,ab,kw AND 'selection criteria*':ti,ab,kw) OR ('data source*':ti,ab,kw AND 'data synth*':ti,ab,kw) OR medline*:ti,ab,kw OR pubmed*:ti,ab,kw OR 'pub med*':ti,ab,kw OR embase:ti,ab,kw OR cochrane*:ti,ab,kw OR (((critical* OR rapid*) NEAR/2 (review* OR overview* OR synth*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synth*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynth*:ti,ab,kw OR 'meta synth*':ti,ab,kw OR 'review* of review*':ti,ab,kw	1114396
#7	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	4476451
#8	'major clinical study'/de OR 'clinical study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'cohort analysis'/de OR 'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind	18294613

	procedure'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti) OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#9	#5 AND #6	14
#10	#5 AND #7 NOT #9	53
#11	#5 AND #8 NOT (#9 OR #10)	353
#12	#5 NOT (#9 OR #10 OR #11)	218

Ovid/Medline

#	Searches	Results
1	exp Pituitary Neoplasms/ or exp Acromegaly/ or ((pituitar* or hypophys* or adenohypophys* or neurohypophys* or sellar or parasellar) adj4 (adenoma* or microadenoma* or macroadenoma* or cancer* or carcinoma* or cyst* or lesion* or malignan* or neoplasm* or tumor* or tumour* or mass*)).ti,ab,kf. or (cushing* adj3 (syndrome* or disease*)).ti,ab,kf. or craniopharyngioma*.ti,ab,kf. or 'cranio pharyngioma*'.ti,ab,kf. or craniopharyngeoma*.ti,ab,kf. or pharyngioma*.ti,ab,kf. or gonadotropinoma*.ti,ab,kf. or prolactinoma*.ti,ab,kf. or microprolactinoma*.ti,ab,kf. or	67212

	macroprolactinoma*.ti,ab,kf. or 'macro adenoma*'.ti,ab,kf. or macroadenoma*.ti,ab,kf. or 'micro adenoma*'.ti,ab,kf. or microadenoma*.ti,ab,kf. or acromegal*.ti,ab,kf. or akromegal*.ti,ab,kf. or (('non function*' or nonfunction*) adj3 adenoma*).ti,ab,kf. or ((craniopharyngeal or rathke*) adj3 (tumor* or tumour* or cyst*)).ti,ab,kf.	
2	exp Surgical Procedures, Operative/ or exp Specialties, Surgical/ or su.fs. or exp Perioperative Period/ or surgic*.ti,ab,kf. or surger*.ti,ab,kf. or microsurg*.ti,ab,kf. or operation*.ti,ab,kf. or operative.ti,ab,kf. or presurg*.ti,ab,kf. or preoperati*.ti,ab,kf. or perisurg*.ti,ab,kf. or perioperati*.ti,ab,kf. or postsurg*.ti,ab,kf. or postoperati*.ti,ab,kf. or intraoperati*.ti,ab,kf. or resect*.ti,ab,kf. or laparoscop*.ti,ab,kf. or endoscop*.ti,ab,kf. or neuroendoscop*.ti,ab,kf. or neurosurg*.ti,ab,kf. or transsphenoid*.ti,ab,kf. or 'trans sphenoid*'.ti,ab,kf. or hypophysectom*.ti,ab,kf. or adenomectom*.ti,ab,kf.	6114108
3	((postoperative or 'post operative' or postsurg* or 'post surg*' or followup or 'follow up' or surveillanc*) adj7 ('magnetic resonance imag*' or mri or mris or nmr or mra or mras or zeugmatograph* or 'mr tomography' or 'mr tomographies' or 'mr tomographic' or 'mr imag*' or 'proton spin' or fmri or fmris or rsfmri)).ti,ab,kf. or ((exp magnetic resonance imaging/ or 'magnetic resonance imag*'.ti. or mri.ti. or mris.ti. or nmr.ti. or mra.ti. or mras.ti. or zeugmatograph*.ti. or 'mr tomography'.ti. or 'mr tomographies'.ti. or 'mr tomographic'.ti. or 'mr imag*'.ti. or 'proton spin'.ti. or fmri.ti. or fmris.ti. or rsfmri.ti.) and (Postoperative Care/ or exp Postoperative Period/ or postoperative.ti. or 'post operative'.ti. or postsurg*.ti. or 'post surg*'.ti. or followup.ti. or 'follow up'.ti. or surveillanc*.ti.))	30976
4	(1 and 2 and 3) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/) not ((Adolescent/ or Child/ or Infant/ or adolescen*.ti,ab,kf. or child*.ti,ab,kf. or schoolchild*.ti,ab,kf. or infant*.ti,ab,kf. or girl*.ti,ab,kf. or boy*.ti,ab,kf. or teen.ti,ab,kf. or teens.ti,ab,kf. or teenager*.ti,ab,kf. or youth*.ti,ab,kf. or pediatr*.ti,ab,kf. or paediatr*.ti,ab,kf. or puber*.ti,ab,kf.) not (Adult/ or adult*.ti,ab,kf. or man.ti,ab,kf. or men.ti,ab,kf. or woman.ti,ab,kf. or women.ti,ab,kf.))	798
5	limit 4 to yr="2005 -Current"	631
6	exp Meta-Analysis/ or exp Network Meta-Analysis/ or exp Systematic Review/ or (networkmeta analy* or networkmetaanaly* or metaanaly* or meta analy* or metanaly* or prisma or prospero or metaanali* or meta anali* or metanali*).ti,ab,kf. or ((systemati* or scoping or umbrella or structured literature) adj3 (review* or overview*)).ti,ab,kf. or ((structured or systemic*) adj3 (review* or overview* or synth*) adj3 literature).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 (review* or overview*)) and (search* or database* or data base*)).ti,ab,kf. or ((data	833048

	extraction* or data source*) and (study selection* or studies selection*)).ti,ab,kf. or (search strateg* and selection criteria*).ti,ab,kf. or (data source* and data synth*).ti,ab,kf. or (medline* or pubmed* or pub med* or embase or cochrane*).ti,ab,kf. or cochrane.jw. or ((critical* or rapid*) adj2 (review* or overview* or synth*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synth*)) and (search* or database* or data base*)).ab. or metasynth*.ti,ab,kf. or meta synth*.ti,ab,kf.	
7	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2895061
8	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or exp cohort studies/ or epidemiologic studies/ or ((multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.)) or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	8042669
9	5 and 6	15
10	(5 and 7) not 9	24
11	(5 and 8) not (9 or 10)	365

12	5 not (9 or 10 or 11)	227

Module 6 – Perioperatieve glucocorticoïdsubstitutie

Uitgangsvraag

Wat is de aanbevolen strategie voor het indiceren en toepassen van glucocorticoïdsubstitutie bij patiënten die transsfenoïdale hypofysechirurgie ondergaan?

Search and select

A systematic review of the literature was performed to answer the following question(s):
What are the benefits and risks of peri- and early postoperative high dose glucocorticoid replacement compared with no- or low dose glucocorticoid replacement for patients undergoing transsphenoidal surgery for pituitary adenomas?

Table 1. PICO

Patients	Patients who are undergoing transsphenoidal surgery for pituitary adenomas
Intervention	peri- and postoperative glucocorticoid replacement therapy (cumulative high dosage scheme)
Control	peri- and postoperative glucocorticoid replacement therapy (cumulative low dosage scheme), or no glucocorticoid replacement therapy
Outcomes	Occurrence of adrenal insufficiency, occurrence of hyponatremia, quality of life, complications, mortality, duration of stay, hospital readmission, hormonal recovery (result of early basal cortisol, result of early function test, number of patients with steroid replacement after 6 wk / 6 m), number of patients with Addisonian crisis
Other selection criteria	Study design: systematic reviews and randomized controlled trials

<u>Relevant outcome measures</u>

The guideline panel considered occurrence of adrenal insufficiency, morning basal cortisol, duration of stay and hyponatremia as a **critical** outcome measure for decision making; and quality of life, complications, mortality, hospital readmission as an **important** outcome measure for decision making.

A priori, the guideline panel did not define the outcome measures listed above but used the definitions used in the studies.

For early basal cortisol, the guideline panel defined a difference of 140 nmol/L as a minimal clinically (patient) important difference. For adrenal insufficiency, hyponatremia, complications and other outcomes, the guideline panel defined a difference of 10% as a minimal clinically (patient) important difference(0.91 > Relative risk (RR) > 1.10).

<u>Search and select (Methods)</u>

A systematic literature search was performed by a medical information specialist using the following bibliographic databases: Embase.com and Ovid/Medline. Both databases were searched from 1995 to 6th of January 2025 for systematic reviews and RCT. Systematic searches were completed using a combination of controlled vocabulary/subject headings (e.g., Emtree-terms, MeSH) wherever they were available and natural language keywords.

The overall search strategy was derived from two primary search concepts: (1) surgery for pituitary adenoma; (2) glucocorticoid replacement therapy. Duplicates were removed using EndNote software. After deduplication a total of 262 records were imported for title/abstract screening. Initially, ten studies were selected based on title and abstract screening. After reading the full text, six studies were excluded (see the exclusion table under the tab 'Evidence tabellen'), and four studies were included.

Summary of literature

Description of studies

A total of four studies were included in the analysis of the literature. Important study characteristics and results are summarized in table 2. The assessment of the risk of bias is summarized in the risk of bias tables (under the tab 'Evidence tabellen').

All four included studies were RCTs. Three studies (Guo 2022; Lee, 2021; Sterl, 2019) compared a glucocorticoid group with no glucocorticoid treatment. Guo (2022) and Lee (2021) were double-blinded and used a placebo with intravenous saline, whereas in Sterl (2019) was an open label trial. Guo (2022) and Lee (2021) treated patients in the intervention group with hydrocortisone, whereas Sterl (2019) treated patients with hydrocortisone at induction, followed by dexamethasone every six hours.
Inclusion criteria varied slightly between these studies: Guo (2022) and Lee (2021) included adult patients with pituitary adenomas with without preoperative adrenal insufficiency who would undergo either gross total or subtotal resection via transsphenoidal surgery. Sterl (2019) included adult patients undergoing transsphenoidal surgery for either pituitary adenomas or cysts.
In this study, all patients with early postoperative adrenal insufficiency were treated with prednisone from moment of discharge.

The fourth study (Rajaratnam, 2003) did not compare hydrocortisone to no hydrocortisone, but compared three different dosing protocols. Only patients with pituitary macroadenoma undergoing transsphenoidal pituitary surgery leading to radical resection were included in the final analysis. The study only assessed the risk of AVP deficiency (complication).

Table 2. Characteristics of included studies

Study	Participants	Comparison	Follow-up	Outcome measures	Comments	Risk of bias*
Guo, 2022 Non-inferiority RCT single centre, China	N at baseline Intervention: 218 Control: 218 Age (mean, SD): Intervention: 45.4 ± 13.0 Control: 44.5 ± 13.8 Sex (% F): Intervention: 62.4% Control: 58.7% Maximal diameter tumor (mean, SD): Intervention: 20.6, 7.9 Control: 20.5, 8.6 Tumor type (% non-functioning: Intervention: 58.3% Control: 61.5% Baseline ACTH (mean, SD): Intervention: 28.7 (18.1) Control: 31.2 (21.5) Preoperative hypopituitarism (%): Intervention: 58.7% Control: 48.6% Degree of tumor resection (% total resection):	Intervention: Intravenous hydrocortisone (100 mg) every 12 hours for 3 days (2 post-op). Subsequently a taper program with 20 mg oral hydrocortisone tablets, twice a day (1 wk) to once a day (1 wk) to withdrawal. Control: no hydrocortisone, 100 ml intravenous saline (sham) followed by placebo tablets simulating the intervention program.	3 months	- Incidence early postoperative adrenal insufficiency (AI) - Incidence permanent AI at 12 weeks - Incidence hyponatremia - Complications (bone mineral density loss, deep vein thrombosis, severe infections, diabetes mellitus, and electrolyte disturbance)	Morning serum cortisol measured on postoperative day 1, day 2, and at 12 weeks. Cortisol values <5 µg/dL (~138 nmol/L) were considered adrenal insufficiency (AI) Authors declared no conflicts of interest	LOW

	Intervention:67.0 Control: 62.4					
Lee, 2021 RCT single centre, South-Korea	N at baseline Intervention: 20 Control: 20 Age (mean, SD): Intervention: 48 ± 16 Control: 50 ± 14 Sex (% female): Intervention: 55% Control: 60% Maximal diameter tumor (mean, SD): Intervention: 19.5 ± 6.8 mm Control: 24.3 ± 8.1 mm Tumor type (% non-functioning): 100% in both groups Baseline ACTH (mean, SD): Intervention: 10.1 ± 54.4 pmol/L Control: 10.6 ± 44.0 pmol/L Preoperative hypopituitarism (%): ACTH: 0% GH: 90% (I), 85% (C) Gonadotropin: 75% in both groups TSH: 0% (I), 5% (C)	Intervention: 100 mg IV hydrocortisone 30 min before anesthesia, diluted in 100 ml saline. Control: 100 ml IV saline placebo. Blinded protocol; other treatments identical.	3 months	- Incidence early postoperative adrenal insufficiency (AI) - Incidence hyponatremia - Incidence complications - hormone deficiency at 3 months.	Morning serum cortisol measured on post-op days 1, 2, and 3. Early AI was defined by the attending endocrinologist based on clinical signs and cortisol levels, but no fixed cutoff was explicitly stated for diagnosis. At 3 months post-op, hormone panels were reviewed to assess ACTH deficiency and panhypopituitarism Authors declared no conflicts of interest	LOW

	Degree of tumor resection (% total resection): Intervention: 90% Control: 70%					
Sterl, 2019 RCT single centre, USA	N at baseline: Intervention (STER): 19 Control (NOSTER): 17 Age (mean, SD): STER: 55 ± 15, NOSTER: 47 ± 15 Sex (% female): STER: 63%, NOSTER: 41% Tumor size (% macroadenoma) STER: 76%, NOSTER: 68% Tumor type (% non-functioning): STER: 68%, NOSTER: 53% Baseline ACTH (mean, SD): NA Preoperative hypopituitarism (%): STER: 50%, NOSTER: 56% Degree of tumor resection (% total resection): STER: 70%, NOSTER: 90%	STER: 100 mg IV hydrocortisone at induction + dexamethasone 0.5 mg IV every 6 hours for 4 doses NOSTER: No corticosteroids (open label, no placebo)	6 weeks	- Incidence early postoperative adrenal insufficiency (AI) - Incidence of headache (HIT-6) - Incidence hyponatremia - Duration hospital stay	Morning serum cortisol on postoperative day 1 and 2, using <300 nmol/L (~10.9 µg/dL) as threshold for possible AI. Patients whose 08.00 h cortisol was <414 nmol/L were treated and discharged on prednisone 5 mg daily. Patients with low levels cortisol were retested at 6 weeks using Synacthen or ITT to confirm permanent AI	Some concerns (open label)
Rajaratnam, 2003	N at baseline: High dose: 23, Intermediate: 28, Low dose: 41	High dose: 100 mg hydrocortisone IV every six hours for 72 hours, starting from	6 weeks	- complications (AVP deficiency)	Dose-dependent effect on AVP deficiency observed. No reports of AI or cortisol data.	HIGH

RCT, single centre, India	Age (mean, SD): Approx. 39–41 years Sex (% female): NA Maximal diameter tumor (mean, SD): NA Tumor type (% non-functioning): High dose: 39% Intermediate dose: 46% Low dose: 51% Baseline ACTH (mean, SD): NA Preoperative hypopituitarism (%): NA Degree of tumor resection (% total resection): 100% (inclusion in analysis based on total resection)	the night prior to surgery. Intermediate dose: hydrocortisone for 72 hours starting from the time of induction of anaesthesia. They received 100 mg intravenously every 6 hours on day 1, every 8 hours on day 2 and every 12 hours on day 3 following surgery. Low dose: 25 mg hydrocortisone intravenously every 6 hours on day one, every 8 hours on day 2 and every 12 hours on day 3 following surgery.				

*For further details, see risk of bias table in the appendix

Results

High versus low cumulative glucocorticoid replacement therapy dosage

One RCT (Rajaratnam, 2003) compared three different dosing protocols. For this analysis, these are dichotomised into two groups:

- High/ intermediate cumulative dose: either 100 mg hydrocortisone IV every six hours for 72 hours (starting from the night prior to surgery), or 100 mg intravenously every 6 hours on day 1, every 8 hours on day 2 and every 12 hours on day 3 following surgery.
- Low dose: 25 mg hydrocortisone intravenously every 6 hours on day one, every 8 hours on day 2 and every 12 hours on day 3 following surgery

This study did not report on any of the critical outcome measures, but only reported on AVP deficiency as a complication, as described below

1. Complications

1.1. AVP deficiency

Rajaratnam (2003) assessed the difference in risk of both transient and permanent AVP deficiency among patients undergoing transsphenoidal pituitary surgery. When comparing high/intermediate dosage glucocorticoid replacement therapy with low glucocorticoid replacement therapy dosage, 24/51 patients in the high to intermediate dosage group and 10/41 patients in the low dosage group experienced AVP deficiency, resulting in a Risk Ratio (RR) of 1.77 (95% CI 0.95 to 3.30) and a risk difference of 0.19 (95% CI 0.00 to 0.38), with a higher risk for the high/intermediate dose group. This is a clinically relevant difference.

Glucocorticoid replacement therapy versus no glucocorticoid replacement therapy

1. Adrenal insufficiency (AI)

All three studies comparing perioperative glucocorticoid replacement therapy vs. no glucocorticoid replacement therapy (Guo 2022; Lee, 2021; Sterl, 2019) assessed early adrenal insufficiency (AI) in the first days post-operation. Guo (2022) also compared peri- and postoperative glucocorticoid replacement therapy vs. no glucocorticoid replacement therapy after discharge until 12 weeks.

Guo (2022) defined early postoperative AI as a serum morning cortisol level lower than 138 nmol/L (5 µg/dL) with at least 1 adrenal insufficiency–related symptom within two postoperative days. Lee (2021) defined early postoperative AI as a serum morning cortisol level lower than 138 nmol/L within 3 postoperative days. Sterl (2019) used a different definition of postoperative AI within 3 postoperative days, with cut-off of <414 nmol/L serum morning cortisol for AI.

Results for difference in early adrenal insufficiency between glucocorticoid replacement therapy (n= 257) and no glucocorticoid replacement therapy (n= 255) are pooled and presented in figure 1. Early post-operation the pooled risk-ratio for AI was 0.96 (95% CI 0.33 to 2.81). As can be seen in figure 1, the risk difference was 0.03 (-95% CI -0.18 to 0.25). This is not a clinically relevant risk difference. For a 12-week follow-up comparison, Guo (2022) reported 7/218 in de glucocorticoid replacement therapy group and 8/218 of the no-glucocorticoid replacement therapy group experiencing permanent AI. This results in a risk ratio of 0.88 (95% CI 0.32 to 2.37) and risk difference of 0.00 (95% CI -0.04 to 0.03). This is also not a clinically relevant difference.

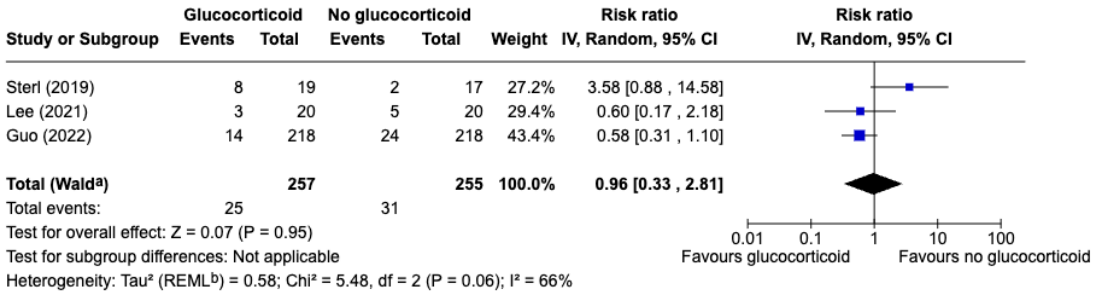

Figure 1. Pooled result of the risk ratio for adrenal insufficiency (AI) events when comparing glucocorticoid replacement therapy treatment to no glucocorticoid replacement therapy treatment.

2. Hormonal recovery - Result of early basal cortisol

Two studies (Guo 2022; Lee, 2021) assessed cortisol levels directly post-surgery, and at one-and two days post-surgery. Results are pooled and presented in figure 2.

This shows that directly post-surgery, the serum cortisol levels in de glucocorticoid replacement therapy group (n = 238) were higher when compared to the no glucocorticoid replacement therapy group (n = 238), as can be expected, with a mean difference (MD) of 36.8 (95% CI 29.4 to 44.3) µg/dL in favour of the glucocorticoid replacement therapy group. This corresponds to approximately 1015 nmol/L (95% CI 811 to 1222 nmol/L). This is a clinically relevant difference. However, the figure shows that at postoperative day 2 and 3 the difference between groups is smaller, with a pooled MD of -0.24 (95% CI -11.73 to 11.25) µg/dL at day 2 and -4.04 (95% CI -5.71 to -2.38) at day 3 respectively. These correspond to approximately -6.6 nmol/L (95% CI -323 to 310 nmol/L) and -111 nmol/L (95% CI -158 to -66 nmol/L).

These differences are not clinically relevant.

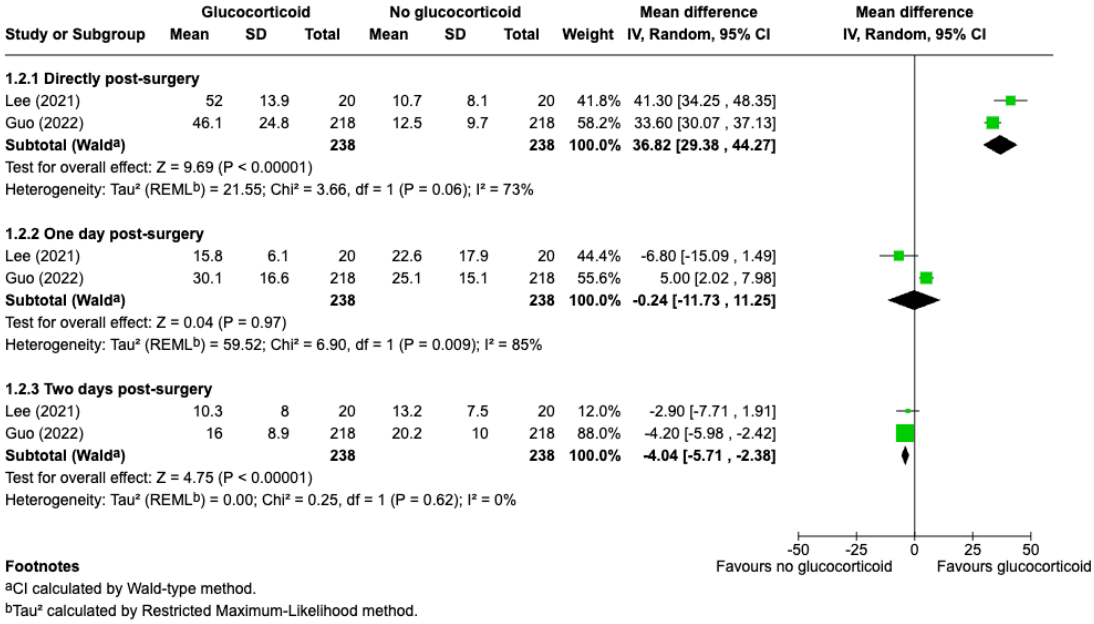

Figure 2. Pooled results of the serum cortisol level (in µg/dL) at different times post-surgery when comparing peri- and postoperative glucocorticoid replacement therapy treatment to no glucocorticoid replacement therapy treatment.

Sterl (2019) only reported a mean morning serum cortisol over the first 3 days post operation. This results in a mean difference of -13.00 (95% CI -19.93 to -6.07) µg/dL in favour of no glucocorticoid replacement therapy, corresponding to approximately -359 nmol/L (95% CI -550 to -167 nmol/L).

3. Hyponatremia

All three studies (Guo 2022; Lee, 2021; Sterl, 2019) assessed the difference in postoperative hyponatremia events between glucocorticoid replacement therapy (n= 257) and no glucocorticoid replacement therapy (n= 255). Lee (2021) and Sterl (2019) assessed plasma sodium levels at two days post-operation, whereas Guo (2022) assessed levels of serum sodium during the first 3 postoperative months. Guo (2022) and Sterl (2019) defined hyponatremia as plasma sodium <135 mEq/L. The results are pooled in figure 3, which results in a pooled risk ratio of 0.58 (95% CI 0.27 to 1.24) and a risk difference of -0.06 (95% CI -0.11 to -0.02), with a lower risk in favour of glucocorticoid replacement therapy. This is a clinically relevant difference.

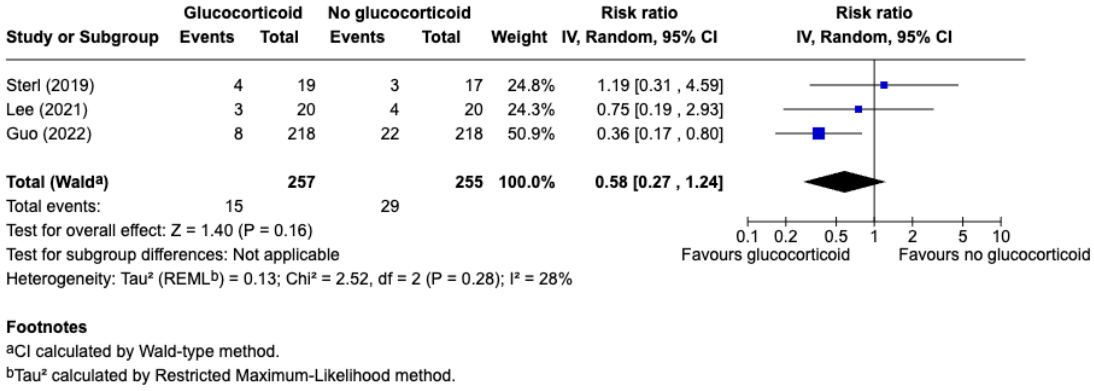

Figure 3. Pooled results of post-operative hyponatremia events when comparing glucocorticoid replacement therapy treatment to no glucocorticoid replacement therapy treatment.

4. Complications

All three RCTs assessed difference in complications. Each RCT assessed a different set of complications, with only severe CNS infection and new onset AVP deficiency being monitored in all three studies. Pooled results of adverse events are shown in figure 4. As can be noted, overall, relatively few complications occurred in both the glucocorticoid replacement therapy group and the No glucocorticoid replacement therapy group. There were only clinically relevant differences seen for two complications: new-onset AVP deficiency and headache.

All three RCTs (Guo 2022; Lee, 2021; Sterl, 2019) assessed the difference in postoperative AVP deficiency between glucocorticoid replacement therapy (n= 257) and no glucocorticoid replacement therapy (n= 255). This resulted in a pooled risk ratio of 0.53 (95% CI 0.32 to 0.89) and a risk difference of -0.10 (95% CI -0.23 to 0.03) in favour of the glucocorticoid replacement therapy group, who appeared to have a lower risk. As stated above, this is a clinically relevant difference.

Sterl (2019) assessed adverse impact of headaches on social functioning, role functioning, vitality, cognitive functioning, and psychological distress using the Headache Impact Test (HIT-6). A score ≥50 indicates headache that has moderate to severe impact on a person's life. When comparing glucocorticoid replacement therapy (n = 19) with no glucocorticoid replacement therapy (n=17), this resulted in a risk ratio of 0.33 (95% CI 0.13 to 0.83) and a risk difference of -0.44 (95% CI -0.73 to -0.14) in favour of glucocorticoid replacement therapy, as 11/17 patients in the no glucocorticoid

replacement therapy group experienced moderate/severe headache as opposed to 4/19 in the glucocorticoid replacement therapy group. As stated above, this is a clinically relevant difference.

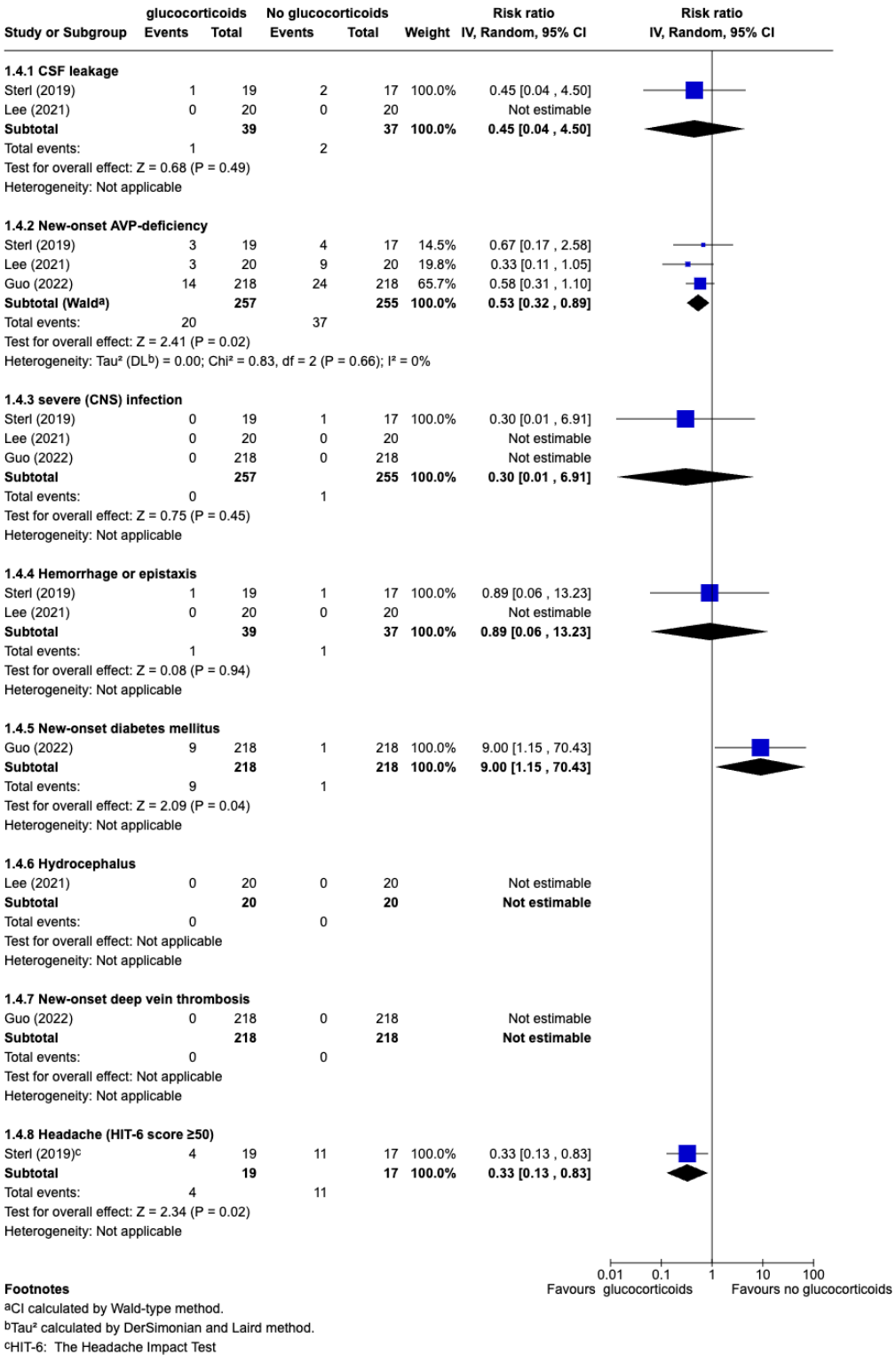

Figure 4. Pooled results of post-operative complications when comparing glucocorticoid replacement therapy treatment to no glucocorticoid replacement therapy treatment.

5. Duration of hospital stay

Only Sterl (2019) reported on difference in duration of hospital stay between patients receiving glucocorticoid replacement therapy (n= 19) and no glucocorticoid replacement therapy (n = 17). With a mean (SD) length of 5.2 (1.5) days in the glucocorticoid replacement therapy group and 5.4 (1.1) days in the no glucocorticoid replacement therapy group, this results in a mean difference of -0.20 (95% CI -1.05 to 0.65) days. This is not a clinically relevant difference.

6. Mortality

None of the included studies assessed mortality as an outcome.

7. Quality of life

None of the included studies assessed quality of life as an outcome.

8. Hospital readmission

None of the included studies assessed hospital readmission as an outcome.

9. Addisonian crise events

None of the included studies reported on Addisonian crise events as an outcome.

Summary of Findings

High versus low cumulative glucocorticoid replacement therapy dosage

Outcome	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the evidence** (Quality of evidence)	**Summary**
		Low dosage hydrocortison	High dosage hydrocortison		
Adrenal insufficiency				**No GRADE**	No studies were found that looked at adrenal insufficiency
Hyponatremia				**No GRADE**	No studies were found that looked at hyponatremia
Hormone recovery				**No GRADE**	No studies were found that looked at hormone recovery
Complications- AVP deficiency	**Relative risk: of 1.77 (95% CI 0.95 to 3.30)** Based on data from 92 participants in 1 study, Follow up 6 weeks	**243** per 1000	**430** per 1000 Difference: **187 more per 1000** (CI 95% 912 fewer - 559 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether low dose glucocorticoid replacement therapy increases or decreases the risk of AVP deficiency
Other complications				**No GRADE**	No studies were found that looked at other complications
Duration of hospital stay				**No GRADE**	No studies were found that looked at duration of hospital stay.
Quality of life				**No GRADE**	No studies were found that looked at quality of life.
Hospital readmission				**No GRADE**	No studies were found that looked at hospital readmission
Addisonian Crise				**No GRADE**	No studies were found that looked at Addisonian crise

1. Risk of Bias: very serious. Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Missing intention-to-treat analysis; Imprecision: very serious. Wide confidence intervals, Low number of patients, only data from one study;

Glucocorticoid replacement therapy versus no glucocorticoid replacement therapy

Outcome		**Absolute effect estimates**	**Certainty of the evidence**	**Summary**

	Study results and measurements	No hydrocortisone	Hydrocortisone	(Quality of evidence)	
Adrenal insufficiency 2 days post-surgery	Relative risk: 0.96 (CI 95% 0.33 - 2.81) Based on data from 512 participants in 3 studies Follow up 2 post-operative days	**150** per 1000	**144** per 1000	**Low** Due to serious inconsistency, Due to serious imprecision[1]	Glucocorticoid replacement therapy may have little or no difference on perioperative adrenal insufficiency when compared to no glucocorticoid replacement therapy.
		Difference: **6 fewer per 1000** (CI 95% 100 fewer - 272 more)			
Adrenal insufficiency 12 weeks postop	Relative risk: 0.88 (CI 95% 0.32 - 2.37) Based on data from 436 participants in 1 studies Follow up 12 weeks	**37** per 1000	**33** per 1000	**Low** Due to very serious imprecision[3]	Glucocorticoid replacement therapy may reduce the risk of adrenal insufficiency at 12 weeks slightly when compared to no glucocorticoid replacement therapy
		Difference: **4 fewer per 1000** (CI 95% 25 fewer - 51 more)			
Early basal cortisol	Measured by: serum morning cortisol Scale: - High better Based on data from 476 participants in 2 studies Follow up 12 weeks	**13.2** µg/dL (≈ 364 nmol/L) Mean	**16** µg/dL (≈ 441 nmol/L) Mean	**Moderate** Due to serious imprecision[7]	Peri-operative glucocorticoids probably have little or no effect on early basal cortisol when compared to no peri-operative glucocorticoids
		Difference: **MD 4.04 lower (≈ 111 nmol/L lower)** (CI 95% 5.71 lower - 2.38 lower; ≈ 158 to 66 nmol/L lower))			
Hyponatremia	Relative risk: 0.58 (CI 95% 0.27 - 1.24) Based on data from 512 participants in 3 studies Follow up 6 weeks	**150** per 1000	**87** per 1000	**Low** Due to serious inconsistency, Due to serious imprecision[4]	Glucocorticoid treatment may reduce the risk of hyponatremia when compared with no glucocorticoid treatment
		Difference: **63 fewer per 1000** (CI 95% 109 fewer - 36 more)			
AVP deficiency	Relative risk: 0.53 (CI 95% 0.32 - 0.89) Based on data from 3 participants in 512 studies Follow up 6 weeks	**145** per 1000	**77** per 1000	**Moderate** Due to serious inconsistency[5]	Glucocorticoid treatment probably decreases the risk of AVP deficiency when compared to no glucocorticoid treatment.
		Difference: **68 fewer per 1000** (CI 95% 99 fewer - 16 fewer)			
Headache with moderate/severe impact	Relative risk: 0.33 (CI 95% 0.13 - 0.83) Based on data from 36 participants in 1 studies Follow up 6 weeks	**647** per 1000	**214** per 1000	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Glucocorticoids may have little or no difference on severe/moderate headache
		Difference: **433 fewer per 1000** (CI 95% 563 fewer - 110 fewer)			
Duration of hospital stay	Measured by: Scale: - Lower better	**5.4** daysMean	**5.2** daysMean	**Low** Due to very serious imprecision[8]	

	Based on data from 36 participants in 1 studies Follow up 6 weeks	Difference: **MD 0.20 lower** (CI 95% 1.05 lower - 0.65 higher)		glucocorticoid treatment may have little or no difference on duration of hospital stay
Other complications	Based on data from 512 participants in 3 studies Follow up 6 weeks		**Low** Due to very serious imprecision[8]	We are uncertain whether glucocorticoid treatment increases or decreases the risk of other complications
Mortality			**No GRADE**	No studies were found that looked at mortality
Quality of life			**No GRADE**	No studies were found that looked at quality of life.
Hospital readmission			**No GRADE**	No studies were found that looked at hospital readmission
Addisonian Crise			**No GRADE**	No studies were found that looked at addisonian crise

15. **Inconsistency: serious.** Point estimates vary widely, the direction of the effect is not consistent between the included studies; **Imprecision: serious.** Wide confidence intervals;
16. **Imprecision: very serious.** Wide confidence intervals, only data from one study;
17. **Inconsistency: serious.** The direction of the effect is not consistent between the included studies; **Imprecision: serious.** Wide confidence intervals;
18. **Inconsistency: serious.** Point estimates vary widely;
19. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: serious.** Low number of patients;
20. **Imprecision: serious.** Wide confidence intervals;
21. **Imprecision: very serious.** Wide confidence intervals, Low number of patients;

22.

Kennisvragen

Tijdens de ontwikkeling van deze module is gebleken dat er binnen deze module nog te weinig bewijs is voor de onderbouwing van de aanbeveling en dus kennisvragen bestaan. De werkgroep meent dat (vervolg)onderzoek wenselijk is om in de toekomst een duidelijker antwoord te kunnen geven op vragen uit de praktijk.

Kennisvraag:

Wat is bij volwassen patiënten die transsfenoïdale hypofysechirurgie ondergaan de optimale perioperatieve glucocorticoïdstrategie, vergeleken tussen een cumulatief hoge dosering (≥200 mg hydrocortison op dag 1) en een cumulatief lage dosering (≤50 mg hydrocortison op dag 1), al dan niet gevolgd door continuering op basis van postoperatieve ochtendcortisolwaarden, ten aanzien van de duur van glucocorticoïdsuppletie en het moment waarop behandeling veilig kan worden gestaakt?

Patients	Volwassen patiënten die transsfenoïdale hypofysechirurgie ondergaan in de Nederlandse setting, met of zonder pre-existente bijnierinsufficiëntie
Intervention	Cumulatief hoge dosering hydrocortison (≥200 mg op dag 1), met continuering of staken op basis van postoperatieve ochtendcortisolwaarden
Control	Cumulatief lage dosering hydrocortison (≤50 mg op dag 1), met continuering of staken op basis van postoperatieve ochtendcortisolwaarden
Outcomes	Duur van glucocorticoïdsuppletie; moment waarop glucocorticoïden veilig kunnen worden gestaakt; postoperatieve bijnierinsufficiëntie; hyponatriëmie; AVP-deficiëntie; lengte van ziekenhuisopname; tijd tot veilig ontslag
Other selection criteria	Interpretatie van postoperatieve ochtendcortisolwaarden (bijv. afkappunten 240–300 nmol/L, rekening houdend met inter-observer variatie), met uitzondering van patiënten met AVP-deficiëntie

Toelichting:

Deze kennisvraag richt zich op optimalisatie van de perioperatieve glucocorticoïdstrategie in de Nederlandse praktijk, waarbij zowel de initiële cumulatieve dosering als het beleid op basis van postoperatieve ochtendcortisolwaarden wordt vergeleken. Doel is te bepalen welk schema leidt tot veilige en tijdige beëindiging van substitutie, zonder toename van complicaties, en daarmee mogelijk tot verkorting van de ziekenhuisopname.

Implementatietabel

Tabel A: (De-)Implementatietabel met impuls analyse

Aanbevelingen		
17. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?	□ **Ongewenste praktijkvariatie** **Toelichting:** Start minimaal één uur vóór hypofysechirurgie bij alle patiënten met glucocorticoïdsubstitutie (hydrocortison). Hanteer hierbij een dosering binnen de gebruikelijke range van 50–200 mg hydrocortison op dag 1 gevolgd door een afbouwschema volgens het lokale protocol. Personaliseer het schema afhankelijk van bijzondere omstandigheden	
18. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?	□ **< 5000**	
19. Maakt de aanbeveling deel uit van een set van interventies voor hetzelfde probleem?	□ **Nee**	
20. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:	**Wat zijn mogelijke belemmerende factoren?**	**Wat zijn mogelijke bevorderende factoren?**
g) **Richtlijn/ klinisch traject (innovatie)**	Er bestaat variatie tussen centra in de toegepaste dosering van glucocorticoïdsubstitutie, in het startmoment en in de interpretatie van postoperatieve ochtendcortisolwaarden bij besluitvorming over continueren of staken.	Glucocorticoïdsubstitutie rond hypofysechirurgie is in Nederland standaard geïndiceerd; de aanbevolen doseringsrange (50–200 mg hydrocortison op dag 1) sluit aan bij de gangbare Nederlandse praktijk en afbouw volgens lokaal protocol is reeds gebruikelijk.

	aanpassing van bestaande protocollen (met name bij hogere doseringen en langere afbouw) kan tijd en terughoudendheid met zich meebrengen.	
h) **Zorgverleners (artsen en verpleegkundigen)**	In sommige centra bestaat mogelijk gewoontevorming rond hogere stressdoseringen en kan onzekerheid bestaan over het veilig toepassen van een lagere hydrocortisondosering bij patiënten perioperatief.	Het beleid past binnen de bestaande perioperatieve werkprocessen rond hypofysechirurgie. Een standaard protocol voorkomt het missen van adequate steroidsubstitutie bij patiënten die dit nodig hebben.
i) **Patiënt/ cliënt (naasten)**	Bij patiënten zonder pre-existente bijnierinsufficiëntie kan onbegrip bestaan over de noodzaak van tijdelijke glucocorticoïdsubstitutie, juist omdat de hypofysefunctie preoperatief intact kan zijn en het risico op uitval laag wordt ingeschat. Bij patiënten zonder pre-existente bijnierinsufficiëntie kan onbegrip bestaan over de noodzaak van tijdelijke glucocorticoïdsubstitutie, juist omdat de hypofysefunctie preoperatief intact kan zijn en het risico op uitval laag wordt ingeschat. Gerichte patiënteducatie is daarom belangrijk. Vroege postoperatieve herbeoordeling, waarbij glucocorticoïden zo nodig snel kunnen worden gestaakt, kan onnodig langdurig gebruik en bijbehorende zorgen over bijnierfunctie beperken.	
j) **Sociale context**	Het risico op het missen van (acute) bijnierinsufficiëntie wordt als klinisch te groot gepercipieerd, wat terughoudendheid geeft ten aanzien van het achterwege laten of verminderen van glucocorticoïdsubstitutie.	Er is breed draagvlak voor routinematige glucocorticoïdsubstitutie rond hypofysechirurgie, wat de implementatie van aanbevelingen die uitgaan van standaard substitutie voor alle patiënten vergemakkelijkt.
k) **Organisatorische context**	In sommige centra moeten lokale protocollen worden aangepast om het aanbevolen startmoment, de	De middelen vergen geen extra infrastructuur en geen extra personele inzet. Bij voortzetting van glucocorticoïdsubstitutie in de thuissituatie kan wel

	doseringsrange en de werkwijze rond vervolgbeleid expliciet vast te leggen	beperkte poliklinische begeleiding nodig zijn, wat aansluit bij de gebruikelijke zorgpaden.
l) **Economische en politieke context**		

21. Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk?	■ Professional □ Beroepsvereniging □ Ziekenhuis(bestuurder)
22. Wat zouden deze personen/ partijen moeten veranderen in hun gedrag of organisatie om de aanbeveling toe te passen?	Waar nodig harmoniseren van lokale hydrocortison-protocollen naar een dosering binnen de aanbevolen range, inclusief expliciete afspraken over startmoment en interpretatie van postoperatieve cortisolwaarden
23. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?	□ < 1 jaar Het betreft grotendeels standaardzorg; implementatie vraagt primair protocolharmonisatie binnen bestaande structuren
24. Conclusie: is er extra aandacht nodig voor implementatie van de aanbeveling (anders dan publicatie van deze richtlijnmodule)?	□ **Nee** **Toelichting:** Perioperatieve hydrocortison-substitutie is reeds gangbaar in alle centra; publicatie en reguliere disseminatie volstaan

**Deze aanbeveling komt in aanmerking voor plaatsing op de Implementatie Agenda van het programma Zorg Evaluatie & Gepast Gebruik (ZE&GG). In het programma ZE&GG werken patiënten, zorgverleners, zorgaanbieders, zorgverzekeraars en overheid samen aan de bewezen beste zorg voor de patiënt. Daarmee is ZE&GG een programma van alle betrokken partijen in de Medisch Specialistische Zorg. FMS is één van deze betrokken partijen.*

De implementatieagenda van ZE&GG bevat onderwerpen over wat de bewezen beste zorg is en die in de dagelijkse zorgpraktijk geïmplementeerd zouden moeten worden. Zorgverzekeraars Nederland (ZN) en de Nederlandse Vereniging voor Ziekenhuizen (NVZ) hebben landelijke afspraken gemaakt over de implementatie van de onderwerpen van de implementatieagenda. Deze afspraken zijn onderdeel van de zorginkoopafspraken tussen zorgverzekeraars en zorgaanbieders.

Vanuit FMS worden sterke, goed onderbouwde aanbevelingen, getoetst op de behoefte aan een implementatie impuls aangedragen. Voor de beoordeling van onderwerpen uit richtlijnen wordt gekeken naar bovenstaande tabel voor een inschatting van de implementatie impuls. Met de ingevulde implementatietabel kunnen we vanuit FMS de andere HLA-MSZ partijen goed informeren om zo samen te beslissen of de aanbeveling daadwerkelijk op de implementatie agenda zal worden geplaatst.

Literatuur

Guo X, Zhang D, Pang H, Wang Z, Gao L, Wang Y, Ma W, Lian W, Xing B; ZS-2608 Trial Team. Safety of withholding perioperative hydrocortisone for patients with pituitary adenomas with an intact hypothalamus-pituitary-adrenal axis: a randomized clinical trial. JAMA Netw Open. 2022;5(11):e2242221. doi:10.1001/jamanetworkopen.2022.42221.

Lee HC, Yoon HK, Kim JH, Kim YH, Park HP. Comparison of intraoperative cortisol levels after preoperative hydrocortisone administration versus placebo in patients without adrenal insufficiency undergoing endoscopic transsphenoidal removal of nonfunctioning pituitary adenomas: a double-blind randomized trial. J Neurosurg. 2021;134(2):526-534. doi:10.3171/2019.11.JNS192381.

Rajaratnam S, Seshadri MS, Chandy MJ, Rajshekhar V. Hydrocortisone dose and postoperative diabetes insipidus in patients undergoing transsphenoidal pituitary surgery: a prospective randomized controlled study. Br J Neurosurg. 2003;17(5):437-442. doi:10.1080/02688690310001611233.

Sterl K, Thompson B, Goss CW, Dacey RG, Rich KM, Zipfel GJ, Chicoine MR, Kim AH, Silverstein JM. Withholding perioperative steroids in patients undergoing transsphenoidal resection for pituitary disease: randomized prospective clinical trial to assess safety. Neurosurgery. 2019;85(4):E706-E714. doi:10.1093/neuros/nyy479.

Bijlagen bij module UV06

Risk of Bias tables

Research question:

Study reference (first author, publication year)	**Was the allocation sequence adequately generated?**	**Was the allocation adequately concealed?**	**Blinding: Was knowledge of the allocated interventions adequately prevented?**	**Was loss to follow-up (missing outcome data) infrequent?**	**Are reports of the study free of selective outcome reporting?**	**Was the study apparently free of other problems that could put it at a risk of bias?**	**Overall risk of bias** **If applicable/necessary, per outcome measure**
Guo, 2022	Definitely yes Reason: A statistician generated the randomization sequence before patient recruitment	Definitely yes Reason: The executive nurses and neurosurgical residents of the Trial Team who allocated drugs or placebos knew the treatment assignment, but were not involved in other medical care and data interpretation.	Definitely yes, Reason: the principal investigators who provided medical care and study participants and their families were all blinded to group assignment.	Definitely yes Reason: No participants had been lost to follow-up, and intention-to-treat analysis was used for all end points.	Definitely yes Reason: All outcomes of study protocol reported	Definitely yes Reason: No other potential risk for bias noted, no reported conflicts of interest.	**LOW**
Lee, 2021	Definitely yes Reason: Patients were randomly assigned to the steroid group or the placebo group using a computer-generated 1-to-1 random allocation table with a	Definitely yes Reason: The allocation order was concealed in an opaque envelope and was disclosed one hour before anaesthesia induction by a neurosurgical	Definitely yes, **Reason:** All neurosurgeons, anaesthesiologists, intensivists, and patients were blinded to the groups.	Definitely yes Reason: No intention to treat analysis, but only loss to follow up of one (<5%) patient in both groups due to withdrawal of informed consent and change in the operating schedule	Definitely yes Reason: All outcomes reported	Definitely yes Reason: No other potential risk for bias noted, no reported conflicts of interest.	**LOW**

	block size of 4 and 6 generated by a research assistant who did not otherwise participate in the study.	nurse who did not participate in the overall care of patients					
Sterl, 2019	Definitely yes Reason: Computer-generated randomization sequence was created by a nonmedical member of the study team with sole access.	Definitely yes Reason: Participants were assigned with a 1:1 allocation to study groups using randomized blocks of 6 and 4.	Definitely no, No blinding of participants and personnel, no blinding of outcome assessment	probably no Reason: No intention to treat analysis, in the intervention group 3 patients were excluded due to violation of study protocol	Definitely yes Reason: All outcomes reported	Definitely yes Reason: No other potential risk for bias noted, no reported conflicts of interest.	**Some concerns**
Rajaratnam, 2003	Not reported	Not reported	Definitely no, No blinding of personnel, no blinding of outcome assessment	Definitely no, Inclusion in analysis based on radical excision, which was not equal between groups (23/32 in Group 1, 28/30 in Group 2 and 41/52 in Group 3)	Definitely yes Reason: All outcomes reported	Probably no, No reporting on potential conflicts of interest	**HIGH**

Table of excluded studies

Reference	Reason for exclusion
Zarzour F, Hage M, Sanson MR, Baussart B, Chakhtoura M. A suggested protocol for the endocrine postoperative management of patients undergoing pituitary surgery. Ann Endocrinol (Paris). 2023 Aug;84(4):413-423. doi: 10.1016/j.ando.2023.03.026. Epub 2023 Apr 4. PMID: 37019429.	Wrong study design, no systematic review
Jia X, Pendharkar AV, Loftus P, Dodd RL, Chu O, Fraenkel M, Katznelson L. Utility of a glucocorticoid sparing strategy in the management of patients following transsphenoidal surgery. Endocr Pract. 2016 Sep;22(9):1033-9. doi: 10.4158/EP161256.OR. Epub 2016 Apr 28. PMID: 27124693.	Wrong study design, no comparator
Kristof RA, Wichers M, Haun D, Redel L, Klingmüller D, Schramm J. Peri-operative glucocorticoid replacement therapy in transsphenoidal pituitary adenoma surgery: a prospective controlled study. Acta Neurochir (Wien). 2008 Apr;150(4):329-35; discussion 335. doi: 10.1007/s00701-008-1517-x. Epub 2008 Mar 6. PMID: 18309452.	No RCT, but treatment allocation based on impaired vs. preserved HPA
Batista S, Almeida JA, Koester S, Gasparri LG, Santana LS, Gallo BHD, Palavani LB, Bertani R, Landeiro JA. Safety of withholding perioperative steroids for patients with pituitary resection with an intact hypothalamus-pituitary-adrenal axis: A meta-analysis of randomized clinical trials. Clin Neurol Neurosurg. 2023 Nov;234:107974. doi: 10.1016/j.clineuro.2023.107974. Epub 2023 Sep 20. PMID: 37797363.	Systematic review with unknown study included, possibly retracted.
Lin F, Su Y, Zhang X, Liang B, Qin M. The safety of withholding hydrocortisone during preoperative periods in pituitary adenomas patients with an intact HPA axis: A meta-analysis of randomized controlled trials. Neuro Endocrinol Lett. 2023 Jun 14;44(3):131-139. PMID: 37392440.	Insufficient search strategy
Tohti M, Li J, Zhou Y, Hu Y, Yu Z, Ma C. Is peri-operative steroid replacement therapy necessary for the pituitary adenomas treated with surgery? A systematic review and meta analysis. PLoS One. 2015 Mar 16;10(3):e0119621. doi: 10.1371/journal.pone.0119621. PMID: 25775019; PMCID: PMC4361329.	no risk of bias assessment

5 **Literature search strategy**

Cluster/richtlijn: NVvN Hypofyse chirurgie	
Uitgangsvraag/modules: UV6 Wat is de aanbevolen strategie voor het indiceren en toepassen van glucocorticoidsubstitutie bij patiënten die transsfenoïdale hypofysechirurgie ondergaan?	
Database(s): Embase.com, Ovid/Medline	Datum: 6 januari 2025
Periode: vanaf 1995	Talen: geen restrictie

Literatuurspecialist: Alies Oost	Rayyan: https://new.rayyan.ai/reviews/1279060/screening
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/	
Toelichting: Voor deze vraag is gezocht op de elementen: - surgery for pituitary adenoma - glucocorticoid replacement therapy De sleutelartikelen worden gevonden met deze search.	
Te gebruiken voor richtlijntekst: A systematic literature search was performed by a medical information specialist using the following bibliographic databases: Embase.com and Ovid/Medline. Both databases were searched from 1995 to January 6, 2025 for systematic reviews, RCTs and observational studies. Systematic searches were completed using a combination of controlled vocabulary/subject headings (e.g., Emtree-terms, MeSH) wherever they were available and natural language keywords. The overall search strategy was derived from two primary search concepts: (1) surgery for pituitary adenoma; (2) glucocorticoid replacement therapy. Duplicates were removed using EndNote software. After deduplication a total of 1082 records were imported for title/abstract screening.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR	78	39	81
RCT	154	71	181
Observationele studies	726	601	820
Totaal	958	711	**1082***

****in Rayyan***

5 ***Zoekstrategie***

Embase.com

No.	Query	Results
#1	('hypophysis tumor'/exp OR 'acromegaly'/exp OR (((pituitar* OR hypophys* OR adenohypophys* OR neurohypophys*) NEAR/4 (adenoma* OR microadenoma* OR macroadenoma* OR cancer* OR carcinoma* OR cyst* OR lesion* OR malignan* OR neoplasm* OR tumor* OR tumour*)):ti,ab,kw) OR ((cushing* NEAR/3 (syndrome* OR disease*)):ti,ab,kw) OR craniopharyngioma*:ti,ab,kw OR 'cranio pharyngioma*':ti,ab,kw OR craniopharyngeoma*:ti,ab,kw OR pharyngioma*:ti,ab,kw OR gonadotropinoma*:ti,ab,kw OR prolactinoma*:ti,ab,kw OR microprolactinoma*:ti,ab,kw OR macroprolactinoma*:ti,ab,kw OR 'macro adenoma*':ti,ab,kw OR macroadenoma*:ti,ab,kw OR acromegal*:ti,ab,kw OR akromegal*:ti,ab,kw OR ((('non function*' OR nonfunction*) NEAR/3 adenoma*):ti,ab,kw) OR	45865

	(((craniopharyngeal OR rathke*) NEAR/3 (tumor* OR tumour* OR cyst*)):ti,ab,kw)) AND ('surgery'/exp OR 'surgical patient'/exp OR 'surgical risk'/exp OR 'perioperative period'/exp OR 'surgery'/lnk OR surgic*:ti,ab,kw OR surger*:ti,ab,kw OR microsurg*:ti,ab,kw OR operation*:ti,ab,kw OR operative:ti,ab,kw OR presurg*:ti,ab,kw OR preoperati*:ti,ab,kw OR perisurg*:ti,ab,kw OR perioperati*:ti,ab,kw OR postsurg*:ti,ab,kw OR postoperati*:ti,ab,kw OR intraoperati*:ti,ab,kw OR resect*:ti,ab,kw OR laparoscop*:ti,ab,kw OR endoscop*:ti,ab,kw OR neuroendoscop*:ti,ab,kw OR neurosurg*:ti,ab,kw OR transsphenoid*:ti,ab,kw OR 'trans sphenoid*':ti,ab,kw OR hypophysectom*:ti,ab,kw OR adenomectom*:ti,ab,kw OR craniotom*:ti,ab,kw OR craniostom*:ti,ab,kw)	
#2	'corticosteroid therapy'/exp OR corticotherap*:ti,ab,kw OR 'cortico* therap*':ti,ab,kw OR 'steroid therapy'/de OR 'steroid therap*':ti,ab,kw OR (((presurg* OR preoperati* OR perisurg* OR perioperati* OR postsurg* OR postoperati* OR intraoperati* OR withhold* OR withdraw* OR cessat* OR abstinenc* OR infusion* OR replac* OR substitut* OR dose* OR dosage* OR dosing) NEAR/4 (steroid* OR corticostero* OR glucocortico* OR gc OR adrenocortic* OR corticoid* OR cyclosteroid* OR hormon* OR hydrocortison* OR dexamethason*)):ti,ab,kw)	242162
#3	#1 AND #2 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT (('adolescent'/exp OR 'child'/exp OR adolescent*:ti,ab,kw OR child*:ti,ab,kw OR schoolchild*:ti,ab,kw OR infant*:ti,ab,kw OR girl*:ti,ab,kw OR boy*:ti,ab,kw OR teen:ti,ab,kw OR teens:ti,ab,kw OR teenager*:ti,ab,kw OR youth*:ti,ab,kw OR pediatr*:ti,ab,kw OR paediatr*:ti,ab,kw OR puber*:ti,ab,kw) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab,kw OR man:ti,ab,kw OR men:ti,ab,kw OR woman:ti,ab,kw OR women:ti,ab,kw))	2304
#4	#3 AND [1995-2025]/py	1951
#5	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR	1092936

	overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	
#6	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	4179959
#7	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	8580754
#8	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR	15689553

	observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#9	#4 AND #5	78
#10	#4 AND #6 NOT #9	154
#11	#4 AND (#7 OR #8) NOT (#9 OR #10)	726
#12	#9 OR #10 OR #11	958

Ovid/Medline

#	Searches	Results
1	(exp Pituitary Neoplasms/ or exp Acromegaly/ or ((pituitar* or hypophys*) adj3 (adenoma* or microadenoma* or macroadenoma* or cancer* or carcinoma* or lesion* or malignan* or neoplasm* or tumor* or tumour*)).ti,ab,kf. or (cushing* adj3 (syndrome* or disease*)).ti,ab,kf. or craniopharyngioma*.ti,ab,kf. or 'cranio pharyngioma*'.ti,ab,kf. or craniopharyngeoma*.ti,ab,kf. or pharyngioma*.ti,ab,kf. or gonadotropinoma*.ti,ab,kf. or prolactinoma*.ti,ab,kf. or microprolactinoma*.ti,ab,kf. or macroprolactinoma*.ti,ab,kf. or 'macro adenoma*'.ti,ab,kf. or macroadenoma*.ti,ab,kf. or acromegal*.ti,ab,kf. or akromegal*.ti,ab,kf. or (('non function*' or nonfunction*) adj3 adenoma*).ti,ab,kf. or ((craniopharyngeal or rathke*) adj3 (tumor* or tumour* or cyst*)).ti,ab,kf.) and (exp Surgical Procedures, Operative/ or exp Specialties, Surgical/ or su.fs. or exp Perioperative Period/ or surgic*.ti,ab,kf. or surger*.ti,ab,kf. or microsurg*.ti,ab,kf. or operation*.ti,ab,kf. or operative.ti,ab,kf. or presurg*.ti,ab,kf. or preoperati*.ti,ab,kf. or perisurg*.ti,ab,kf. or perioperati*.ti,ab,kf. or postsurg*.ti,ab,kf. or postoperati*.ti,ab,kf. or intraoperati*.ti,ab,kf. or resect*.ti,ab,kf. or laparoscop*.ti,ab,kf. or endoscop*.ti,ab,kf. or neuroendoscop*.ti,ab,kf. or neurosurg*.ti,ab,kf. or transsphenoid*.ti,ab,kf. or 'trans sphenoid*'.ti,ab,kf. or hypophysectom*.ti,ab,kf. or adenomectom*.ti,ab,kf. or craniotom*.ti,ab,kf. or craniostom*.ti,ab,kf.)	28152
2	(corticotherap* or 'cortico* therap*' or 'steroid therap*' or ((presurg* or preoperati* or perisurg* or perioperati* or postsurg* or postoperati* or intraoperati* or withhold* or withdraw* or cessat* or abstinenc* or infusion* or replac* or substitut* or dose* or dosage* or dosing) adj4 (steroid* or corticostero* or glucocortico* or gc or adrenocortic* or corticoid* or cyclosteroid* or hormon* or hydrocortison* or dexamethason*))).ti,ab,kf.	108702
3	(1 and 2) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/) not ((Adolescent/ or Child/ or Infant/ or adolescen*.ti,ab,kf. or child*.ti,ab,kf. or	1753

	schoolchild*.ti,ab,kf. or infant*.ti,ab,kf. or girl*.ti,ab,kf. or boy*.ti,ab,kf. or teen.ti,ab,kf. or teens.ti,ab,kf. or teenager*.ti,ab,kf. or youth*.ti,ab,kf. or pediatr*.ti,ab,kf. or paediatr*.ti,ab,kf. or puber*.ti,ab,kf.) not (Adult/ or adult*.ti,ab,kf. or man.ti,ab,kf. or men.ti,ab,kf. or woman.ti,ab,kf. or women.ti,ab,kf.))	
4	limit 3 to yr="1995 -Current"	1458
5	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	798757
6	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2826383
7	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies]	4923335
8	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or	5873318

	trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	
9	4 and 5	39
10	(4 and 6) not 9	71
11	(4 and (7 or 8)) not (9 or 10)	601
12	9 or 10 or 11	711

Module 7 – Rhinologische nazorg

Uitgangsvraag

Wat is de rol van rhinologische nazorg rondom hypofyse chirurgie?

Search and select

A systematic review of the literature was performed to answer the following question(s):
What is the effectiveness and safety of postoperative sinonasal care after pituitary surgery?

Table 1. PICO

Patients	Patients who underwent endoscopic Transsphenoidal Resection of Pituitary Adenoma
Intervention	Nasal rinsing alone and/or nasal debridement
Control	No sinonasal care
Outcomes	Postoperative nasal complications: Rhinorrhea, nasal discharge, nasal blockage (NOSE scale), loss or change of sense of smell (anosmia/hyposmia), epistaxis, nasal synechiae, sinusitis, pain (crucial), quality of life (ASK-12, SNOT-22) (crucial)
Other selection criteria	Study design: systematic reviews and randomized controlled trials

Relevant outcome measures

The guideline panel considered pain, quality of life and postoperative nasal complications as **critical** outcome measures for decision making.

A priori, the guideline panel did not define the outcome measures listed above but used the definitions used in the studies.

Search and select (Methods)

A systematic literature search was performed by a medical information specialist using the following bibliographic databases: Embase.com and Ovid/Medline all. Both databases were searched from 2005 to May13th, 2025 for systematic reviews, RCTs and observational studies. Systematic searches were completed using a combination of controlled vocabulary and natural language keywords. The overall search strategy was derived from the following primary search concepts: (1) pituitary adenoma; (2) endoscopic transsphenoidal resection; (3) nasal rinsing or nasal debridement. Duplicates were removed using EndNote software. After deduplication a total of 82 records were imported for title/abstract screening. Initially, 12 studies were selected based on title and abstract screening. After reading the full text, 9 studies were excluded (see the exclusion table under the Evidence tabellen'), and 3 studies were included.

Summary of literature

Description of studies

A total of 3 studies were included in the analysis of the literature. Important study characteristics and results are summarized in table 2. The assessment of the risk of bias is summarized in the risk of bias tables (under the tab 'Evidence tabellen').

Gu (2024) investigated the effectiveness of nasal irrigation in relieving postoperative headache after endoscopic endonasal surgery in a single centre retrospective cohort study. Patients that had pituitary adenoma surgery during July 2018 and November 2021 were included when their follow-up data was complete and of which pathology was confirmed. Exclusion criteria were patients who underwent craniotomy resection or incomplete follow-up data. Patients in the cohort with nasal rinsing used a nasal irrigator filled with saline and rinse every two days for 2 months.

Xu (2021) examined the effects of nasal irrigation after endoscopic transsphenoidal pituitary adenoma resection was performed. Patients were included in the RCT during April 2019 and December 2019. Inclusion criteria were 18 to 70 years of age and a confirmed pituitary adenoma. The control group was given 20 mL of normal saline as an inhalation twice daily. The intervention received the same but also received 50 mL of 2% saline through bilateral nasal irrigation the first week after the gauze was removed. In the second week it changed to 50 mL 0.9% normal saline.

Mu (2021) evaluated the effects of nasal irrigation on the nasal related quality of life in patients undergoing transsphenoidal pituitary adenoma resection. Patients who underwent surgery from September 2019 to September 2020 were included in the study. The control group did not irrigate after the surgery. The intervention group irrigated with isotonic saline solution for 5-6 times a day in the first month. The second month the irrigation was performed 3-4 times a day and in the third month it was reduced to 1-2 times a day.

Table 2. Characteristics of included studies

Study	Participants	Comparison	Follow-up	Outcome measures	Comments	Risk of bias (per outcome measure)*
Individual studies						
Xu, 2021 RCT	N at baseline I: 30 | C: 30 Age (mean, SD) I: 55.2 ± 13.52 C: 53.97 ± 13.09 Sex (M:F) I: 12:18 | C: 13:17	Intervention: given the same nursing therapy as the control group. However, these patients received 50mL of 2% saline at 37°C to 38°C through bilateral nasal irrigation the first week after the gauze removed. This was followed by a bilateral nasal flush BID for another 1week consisting of 50mL 0.9% normal saline at 37°C to 38°C. Control: given 20mL of normal saline as an inhalation therapy twice daily (BID) after the surgical resections as directed by a neurologist. The gauze was removed 7 days after surgery, and the nasal cavity was cleaned. The nasal cavity crust was cleaned using nasal endoscopy until the nasal cavity wound was completely epithelialized.	3 months	Postoperative nasal complications	Authors' conclusion: Nasal irrigation helps reduce the incidence of complications such as epistaxis and nasal adhesions in the early postoperative period. It can also promote the elimination or reduction of olfactory disturbances.	Some concerns
Mu, 2024 RCT	N at baseline I: 42 | C: 40 Age (mean, SD) I: 43.14 ± 12.98 C: 40.17 ± 11.60	Intervention: nasal irrigation with isotonic saline solution after gauze was removed 5-6 times a day for the first month after surgery. 3-4 times a day for the second month and 1-2 times a day for the third month. Control: no irrigation.	3 months	Quality of life (SNOT-22)	Authors' conclusion: Nasal irrigation is associated with improved quality of life in patients undergoing transsphenoidal pituitary adenoma resection compared with the control group.	Some concerns

	Sex (M:F) I: 23:19 | C: 17:23 SNOT-22 score I: 14.29 ± 2.87 C: 15.02 ± 3.26					
Gu, 2024 Retrospective cohort study.	N at baseline I: 72 | C: 101 Age (mean, SD) I: 48,28 ± 13.04 C: 45.71 ± 11.90 Sex (M:F) I: 39:33 | C: 49:52 Headache (n): I: 20 | C: 26 Sinusitis (n): I: 30 | C: 32	Intervention: Nasal irrigation every two days for 2 months by using a nasal irrigator filled with saline. Control: No nasal irrigation	3 months	Pain (headache?) Complications (sinusitis)	Authors' conclusion: Prophylactic nasal irrigation helps relieve postoperative headache, possibly by preventing the occurrence of sinusitis.	Low concerns

*For further details, see risk of bias table in the appendix

Results

1. Postoperative nasal complications

The postoperative nasal complications sinusitis, olfactory disturbance, epistaxis or nasal synechiae were reported across the three studies (Gu, 2024; Mu, 2024; Xu, 2021), although not all complications were described in each individual study. Each complication will be presented separately.

1.1 Sinusitis

Sinusitis was described by Gu (2024) and Xu (2021). The results are presented in figure 1 . The pooled risk ratio is 0.51 (95% CI 0.45 to 0.58) which is a clinically relevant result in favor of nasal irrigation.

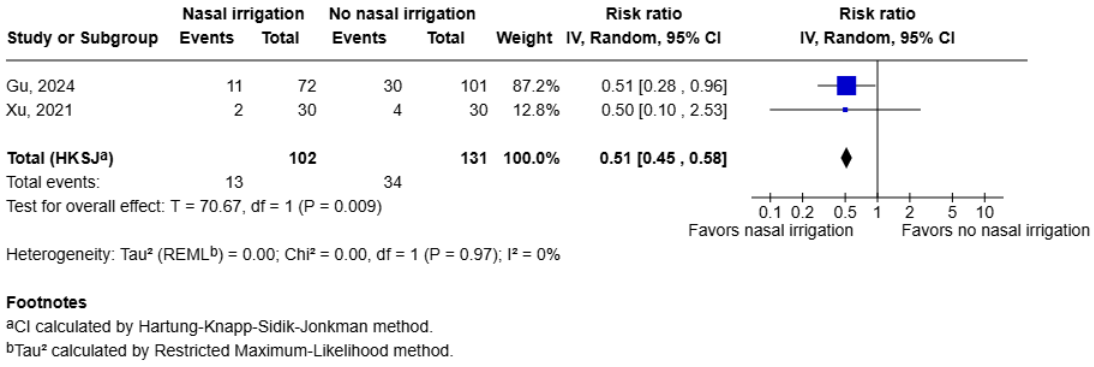

Figure 1. The pooled number of patients experiencing sinusitis in either the nasal irrigation group or no nasal irrigation group after surgery.

1.2 Olfactory disturbance

Olfactory disturbance was described by Mu (2024) and Xu (2021); however, the outcome was reported differently in each study, which prevented the pooling of results. Xu (2021) showed 1 (3,3%) and 3 (10%) with olfactory disturbances in the intervention and control group, respectively. This results in a risk ratio of 0.33 (95% CI 0.04 to 3.03), indicating a clinically relevant result in favor of nasal irrigation.

Mu (2024) reported on hyposmia grading it in 5 levels. Level 1 indicating a normal sense of smell and level 5 indicating a complete loss of sense of smell. Table 3 depicts the results.

Table 3. The number of patients with olfactory disturbance after surgery in the nasal irrigation group and the control group from Mu 2024.

Olfactory function	Nasal irrigation group (n=42)	Control group (n=40)
Level I	14 (33.33%)	10 (25%)
Level II	16 (38.10%)	13 (32.50%)
Level III	10 (23.81%)	11 (27.50%)
Level IV	2 (4.76%)	5 (12.50%)
Level V	0	1 (2.50%)

1.3 Epistaxis

Xu (2021) reported on epistaxis with only one case in the control group (3,33%) and no cases in the nasal irrigation group. The risk ratio resulted in 0.33 (95% CI 0.01 to 7.87). This indicates a clinically relevant result in favor of the nasal irrigation group.

1.4 Nasal synechiae

Only Xu (2021) reported on nasal synechiae. Only one patient (3,33%) in the control group reported nasal synechiae and no cases in the nasal irrigation group. This resulted in a risk ratio of 0.33 (95% CI 0.01 to 7.87). This indicates a clinical relevant result in favor of the nasal irrigation group.

2. Pain

Gu (2024) depicted pain as patients experiencing headaches. Only in the control group patients reported on experiencing a headache; 6 of the 101 (5.94%) patients reported on experiencing headache; 6 of the 101 (5,94%) patients. This resulted in a risk ratio of 0.11 (95% CI 0.01 to 1.88). This indicates a clinically relevant result in favor of the nasal irrigation group.

3. Quality of life

Only Mu (2024) reported on quality of life. Quality of life measured with the 22-item sino-nasal outcome test (SNOT-22). It is a scale for quality of life for nasal diseases that ranges from 0 to 110 with higher scores indicating a greater impact of the disease on the quality of life. The nasal irrigation group (15.82 ± 2.86) had a lower SNOT-22 score than the control group (21.82 ± 3.36). The mean difference is -5.99 (95% CI -7.34 to -4.64), indicating a clinically relevant difference in favor of nasal irrigation.

Summary of Findings

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** No sinonasal care	 Nasal rinsing alone and/or nasal debridement	**Certainty of the evidence** (Quality of evidence)	**Summary**
Postoperative nasal complications ***(Sinusitis)***	Relative risk: 0.51 (CI 95% 0.45 - 0.58) Based on data from 233 participants in 2 studies Follow up 3 months	**26** per 100	**13** per 100 Difference: **13 fewer per 100** (CI 95% 14 fewer - 11 fewer)	**Very low** Due to serious risk of bias, Due to serious imprecision[1]	We are uncertain whether nasal rinsing alone and/or nasal debridement improves or worsens postoperative nasal complications (sinusitis) *(Gu, 2024; Xu, 2021)*
Postoperative nasal complications ***(Olfactory Disturbance)***	Relative risk: 0.33 (CI 95% 0.04 – 3.03) Based on data from 142 participants in 2 studies Follow up 3 months	per 1000	per 1000 Difference: **fewer per 1000**	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Nasal rinsing alone and/or nasal debridement may decrease postoperative nasal complications (olfactory disturbance) *(Mu, 2024; Xu, 2021)*
Postoperative nasal complications ***(Epistaxis)***	Relative risk: 0.33 (CI 95% 0.04 - 3.03) Based on data from 60 participants in 1 studies Follow up 3 months	**2** per 100	**1** per 100 Difference: **1 fewer per 100** (CI 95% 2 fewer - 4 more)	**Low** Due to serious risk of bias, Due to serious imprecision[3]	Nasal rinsing alone and/or nasal debridement may decrease postoperative nasal complications (epistaxis) *(Xu, 2021)*
Postoperative nasal complications ***(Nasal synechiae)***	Relative risk: 0.33 (CI 95% 0.01 - 7.87) Based on data from 60 participants in 1 studies Follow up 3 months	**2** per 100	**1** per 100 Difference: **1 fewer per 100** (CI 95% 2 fewer - 14 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Nasal rinsing alone and/or nasal debridement may decrease postoperative nasal complications (nasal synechiae) *(Xu, 2021)*
Pain (headache)	Relative risk: 0.11 (CI 95% 0.01 - 1.88) Based on data from 173 participants in 1 studies Follow up 3 months	**6** per 100	**1** per 100 Difference: **5 fewer per 100** (CI 95% 6 fewer - 5 more)	**Very low** Due to serious imprecision[5]	We are uncertain whether nasal rinsing alone and/or nasal debridement improves or worsen pain (headache) *(Gu, 2024)*

Quality of life	Measured by: SNOT-22 Scale: 0 - 110 Lower better Based on data from 82 participants in 1 studies Follow up 3 months	**21.82** Mean **15.82** Mean Difference: **MD 5.99 lower** (CI 95% 7.34 lower - 4.64 lower)	**Moderate** Due to serious imprecision[6]	Nasal rinsing alone and/or nasal debridement probably improves quality of life *(Mu, 2024)*

1. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: serious.** Low number of patients;
2. **Risk of Bias: serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: serious.** Low number of patients;
3. **Risk of Bias: serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious.** Low number of patients, Only data from one study, Wide confidence intervals;
4. **Risk of Bias: serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious.** Wide confidence intervals, Low number of patients, Only data from one study;
5. **Imprecision: serious.** Wide confidence intervals, Low number of patients, Only data from one study;
6. **Risk of Bias: no serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious.** Low number of patients, Only data from one study;

Kennisvragen

Tijdens de ontwikkeling van deze module is gebleken dat er binnen deze module nog te weinig bewijs is voor de onderbouwing van de aanbeveling en dus kennisvragen bestaan. De werkgroep meent dat (vervolg)onderzoek wenselijk is om in de toekomst een duidelijker antwoord te kunnen geven op vragen uit de praktijk.

Kennisvraag:

Is KNO-consultatie na hypofysechirugie van meerwaarde of is neusspoelen alleen afdoende? Waar zit de meerwaarde in? Wat is het effect van hypofysechirurgie op reuk?

Toelichting:

Goede nazorg is relevant voor de kwaliteit van zorg. Het is dus relevant of we hier nog een bijdrage in kunnen leveren. Echter is het de vraag of je met neusspoelen alleen niet voldoende nazorg levert en de zorg zo efficiënt maakt. Bepaalde aanbevelingen zijn lastig hard te krijgen omdat bijvoorbeeld reukonderzoek niet standaard is na hypofyse chirurgie en uitkomsten hiervan dus ook lastig te genereren zijn.

Implementatietabel

Tabel A: (De-)Implementatietabel met impuls analyse

Aanbeveling	postoperatief neusspoelen na endoscopische transsfenoïdale hypofysechirurgie	
25. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?	**x Ongewenste praktijkvariatie** ☐ **Nieuwe evidentie** ☐ **Anders**	
26. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?	*X* < **1000** ☐ < **5000** ☐ **5000-40.000** ☐ **> 40.000**	
27. Maakt de aanbeveling deel uit van een set van interventies voor hetzelfde probleem?	☐ **Ja**: hoe verhoudt deze aanbeveling zich tot de andere aanbevelingen uit deze module/ richtlijn of uit andere richtlijnen(modules)? Dient hier rekening mee gehouden te worden bij de implementatie of kan dit worden gezien als een losstaande aanbeveling? **Toelichting:** [toelichting] **x Nee**	
28. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:	**Wat zijn mogelijke belemmerende factoren?**	**Wat zijn mogelijke bevorderende factoren?**
m) **Richtlijn/ klinisch traject (innovatie)**	*lage bewijskracht kan leiden tot terughoudendheid bij centra die deze zorg nog niet standaard toepassen.*	*Interventie sluit aan bij bestaande rhinologische praktijk en is in veel centra al onderdeel van nazorg.*

n) **Zorgverleners (artsen en verpleegkundigen)**	*Onbekendheid bij zorgverleners.*	*Eenvoudig toepasbaar, goed inpasbaar in bestaande protocollen en voorlichting*
o) **Patiënt/ cliënt (naasten)**	*Neusspoelen kan als vervelend worden ervaren, wat therapietrouw kan beïnvloeden.*	*Zorg dat iemand vrij door zijn neus kan ademen en daardoor juist motiverend werken*
p) **Sociale context**	-	-
q) **Organisatorische context**	*opname in zorgpaden en structurele patiëntinstructie vereist afstemming binnen het team.*	*eenvoudig te borgen via standaard postoperatieve protocollen en ontslaginformatie.*
r) **Economische en politieke context**	*hulpmiddelen (zoals spoelkannetje) worden meestal niet vergoed en komen voor rekening van de patiënt.*	*lage kosten en mogelijke reductie van complicaties en daarmee zorggebruik.*

29. Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk?	**x**Patiënt/ cliënt (naaste) **x**Professional ☐ Beroepsvereniging ☐ Ziekenhuis(bestuurder) ☐ Zorgverzekeraars/ NZa ☐ Zorginstituut [duiding nodig] ☐ ..... *(graag aanvullen met alle relevante partijen, e.g., industrie)*
30. Wat zouden deze personen/ partijen moeten veranderen in hun gedrag of organisatie om de aanbeveling toe te passen?	*Zorgverleners dienen neusspoelen structureel op te nemen in de postoperatieve zorg, onder andere door dit standaard te verwerken in protocollen, ontslaginformatie en patiëntvoorlichting. Daarnaast is het nodig dat zorgverleners patiënten actief instrueren over het gebruik en het doel van neusspoelen.* *Patiënten dienen neusspoelen daadwerkelijk uit te voeren volgens instructie en gedurende de aanbevolen periode voort te zetten, waarbij goede uitleg en praktische ondersteuning de therapietrouw kunnen bevorderen.*
31. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?	**x** < 1 jaar ☐ < 2 jaar ☐ < 3 jaar *De aanbeveling betreft een eenvoudige en laagdrempelige interventie die in veel centra al (deels) wordt toegepast. Implementatie kan snel plaatsvinden door opname in bestaande postoperatieve protocollen en patiëntvoorlichting, zonder dat aanvullende scholing of structurele aanpassingen nodig zijn*
32. Conclusie: is er extra aandacht nodig voor implementatie van de aanbeveling (anders dan publicatie van deze richtlijnmodule)?	☐ **Ja* x Nee** **Toelichting:** Er is geen aanvullende implementatie-impuls nodig, omdat de interventie eenvoudig uitvoerbaar is, weinig middelen vereist en goed aansluit bij de huidige klinische praktijk. Implementatie kan plaatsvinden via reguliere verspreiding van de richtlijn en aanpassing van bestaande protocollen en voorlichtingsmaterialen.

**Deze aanbeveling komt in aanmerking voor plaatsing op de Implementatie Agenda van het programma Zorg Evaluatie & Gepast Gebruik (ZE&GG). In het programma ZE&GG werken patiënten, zorgverleners, zorgaanbieders, zorgverzekeraars en overheid samen aan de bewezen beste zorg voor de patiënt. Daarmee is ZE&GG een programma van alle betrokken partijen in de Medisch Specialistische Zorg. FMS is één van deze betrokken partijen.*

De implementatieagenda van ZE&GG bevat onderwerpen over wat de bewezen beste zorg is en die in de dagelijkse zorgpraktijk geïmplementeerd zouden moeten worden. Zorgverzekeraars Nederland (ZN) en de Nederlandse Vereniging voor Ziekenhuizen (NVZ) hebben landelijke afspraken gemaakt over de implementatie van de onderwerpen van de implementatieagenda. Deze afspraken zijn onderdeel van de zorginkoopafspraken tussen zorgverzekeraars en zorgaanbieders.

5 *Vanuit FMS worden sterke, goed onderbouwde aanbevelingen, getoetst op de behoefte aan een implementatie impuls aangedragen. Voor de beoordeling van onderwerpen uit richtlijnen wordt gekeken naar bovenstaande tabel voor een inschatting van de implementatie impuls. Met de ingevulde implementatietabel kunnen we vanuit FMS de andere HLA-MSZ partijen goed informeren om zo samen te beslissen of de aanbeveling daadwerkelijk op de implementatie agenda zal worden geplaatst.*

Literatuur

- Gu J, Chen X, Cheng X, Zou Y, Deng Z, Li D, Zhou Z, Jiang X. Headache alleviation with nasal irrigation following endoscopic endonasal surgery for pituitary adenomas. BMC Endocr Disord. 2024 Apr 15;24(1):45. doi: 10.1186/s12902-024-01573-w. PMID: 38622616; PMCID: PMC11017480.
- Mu A, Ni Z, Ma C. Nasal Irrigation Improves the Nasal Related Quality of Life in Patients Undergoing Transsphenoidal Resection of Pituitary Adenoma. Biol Res Nurs. 2024 Apr;26(2):293-302. doi: 10.1177/10998004231221548. Epub 2023 Dec 11. PMID: 38079151.
- Xu P, Liu S, Dong Y, Liang W, Li Z, Liu F. Effects of nasal irrigation after endoscopic transsphenoidal resection in patients with pituitary adenomas: A randomized controlled trial. Medicine (Baltimore). 2021 Dec 23;100(51):e28317. doi: 10.1097/MD.0000000000028317. PMID: 34941128; PMCID: PMC8702231.

Bijlagen bij module [7]
Risk of Bias tables

Study reference (first author, publication year)	**Was the allocation sequence adequately generated?** Definitely yes Probably yes Probably no Definitely no	**Was the allocation adequately concealed?** Definitely yes Probably yes Probably no Definitely no	**Blinding: Was knowledge of the allocated interventions adequately prevented?** **Were patients blinded?** **Were healthcare providers blinded?** **Were data collectors blinded?** **Were outcome assessors blinded?** **Were data analysts blinded?** Definitely yes Probably yes Probably no Definitely no	**Was loss to follow-up (missing outcome data) infrequent?** Definitely yes Probably yes Probably no Definitely no	**Are reports of the study free of selective outcome reporting?** Definitely yes Probably yes Probably no Definitely no	**Was the study apparently free of other problems that could put it at a risk of bias?** Definitely yes Probably yes Probably no Definitely no	**Overall risk of bias** **If applicable/necessary, per outcome measure** **LOW** **Some concerns** **HIGH**
Xu, 2021	No information Reason: paper mentions it was a randomized trial, but how the	No information Reason:	**Definitely no** Reason: Patients and healthcare professionals were aware of which	Definitely yes Reason: all 60 patients were reported on in each follow up.	Probably yes Reason: All relevant outcomes were reported;	Definitely yes; Reason: No other problems noted	Some Concerns Reason: Due to an unclear randomisation process and no

	allocation was performed is not mentioned.		treatment each patient was receiving. No information is available about the concealment of the assessors or data analysts.				blinding of patients and healthcare professionals possible. **Postoperative complications: Some concerns.**
Mu, 2024	Definitely yes, Reason: patients were divided into a both groups according to a random sequence generated by SPSS22.0 software.	No information	**Definitely no** Reason: Patients and healthcare professionals were aware of which treatment each patient was receiving. No information is available about the concealment of the assessors or data analysts.	Definitely yes Reason: all 82 patients were reported on in each follow up.	Probably yes Reason: All relevant outcomes were reported;	Definitely yes; Reason: No other problems noted	Some Concerns Reason: no blinding of patients and healthcare professionals possible Quality of life: Some concerns.

Author, year	**Selection of participants** **Was selection of exposed and non-exposed cohorts drawn from the same population?**	**Exposure** **Can we be confident in the assessment of exposure?**	**Outcome of interest** **Can we be confident that the outcome of interest was not present at start of study?**	**Confounding-assessment** **Can we be confident in the assessment of confounding factors?**	**Confounding-analysis** **Did the study match exposed and unexposed for all variables that are associated with the outcome of interest or did the statistical analysis adjust for these confounding variables?**	**Assessment of outcome** **Can we be confident in the assessment of outcome?**	**Follow up** **Was the follow up of cohorts adequate? In particular, was outcome data complete or imputed?**	**Co-interventions** **Were co-interventions similar between groups?**	**Overall Risk of bias**

	Definitely yes, probably yes, probably no, definitely no	Definitely yes, probably yes, probably no, definitely no	Definitely yes, probably yes, probably no, definitely no	Definitely yes, probably yes, probably no, definitely no	Definitely yes, probably yes, probably no, definitely no	Definitely yes, probably yes, probably no, definitely no	Definitely yes, probably yes, probably no, definitely no	Definitely yes, probably yes, probably no, definitely no	Low, Some concerns, High
Gu, 2024	Definitely yes, All patients were from the hospital registry	Definitely yes, Extracted from the medical record.	**Definitely no,** Headache was already present before nasal irrigation was administered. Outcome of interest was improvement.	Definitely yes, Extracted from medical records and questionnaires.	Probably no, Multivariate analysis for variables associated with postoperative headache was performed.	Definitely yes, Follow up data was complete and extracted from medical record.	Probably yes, Follow up was sufficient (3 months)	No information	**Low concerns for all outcomes**

Table of excluded studies

Reference	Reason for exclusion
Cheng Y, Xue F, Wang TY, Ji JF, Chen W, Wang ZY, Xu L, Hang CH, Liu XF. Analyses and treatments of postoperative nasal complications after endonasal transsphenoidal resection of pituitary neoplasms. Medicine (Baltimore). 2017 Apr;96(15):e6614. doi: 10.1097/MD.0000000000006614. PMID: 28403108; PMCID: PMC5403105.	No comparison
Curran K, Adepoju A, Pinheiro-Neto C, Peris-Celda M, Kenning T. Nasal Crust-Related Morbidity and Debridement After Endoscopic Skull Base Surgery. Int Arch Otorhinolaryngol. 2023 Apr 28;27(2):e336-e341. doi: 10.1055/s-0042-1745853. PMID: 37125356; PMCID: PMC10147474.	Incorrect comparison
Dağli E, Ocak E, Mirici E, Kaya M, Acar A. Effects of early postoperative nasal decongestant on symptom relief after septoplasty. Int Forum Allergy Rhinol. 2018 Dec;8(12):1476-1480. doi: 10.1002/alr.22183. Epub 2018 Jul 12. PMID: 29999597.	Incorrect comparison
Kim DH, Kim Y, Lim IG, Cho JH, Park YJ, Kim SW, Kim SW. Effect of Postoperative Xylitol Nasal Irrigation on Patients with Sinonasal Diseases. Otolaryngol Head Neck Surg. 2019 Mar;160(3):550-555. doi: 10.1177/0194599818802815. Epub 2018 Oct 2. PMID: 30274540.	Incorrect patients
Kurtaran H, Ugur KS, Yilmaz CS, Kaya M, Yuksel A, Ark N, Gunduz M. The effect of different nasal irrigation solutions following septoplasty and concha radiofrequency: a prospective randomized study. Braz J Otorhinolaryngol. 2018 Mar-Apr;84(2):185-190. doi: 10.1016/j.bjorl.2017.01.005. Epub 2017 Feb 22. PMID: 28325622; PMCID: PMC9449243.	Incorrect patients
Ng BHK, Tang IP, Narayanan P, Raman R, Carrau RL. Effects of nasal lavage with and without mupirocin after endoscopic endonasal skull base surgery: a randomised, controlled study. J Laryngol Otol. 2019 Dec;133(12):1059-1063. doi: 10.1017/S0022215119002329. Epub 2019 Nov 27. PMID: 31774052.	Incorrect comparison
Prabhu V, Pandey A, Ingrams D. Comparing the efficacy of alkaline nasal douches versus decongestant nasal drops in postoperative care after septal surgery: a randomised single blinded clinical pilot study. Indian J Otolaryngol Head Neck Surg. 2011 Apr;63(2):159-64. doi: 10.1007/s12070-011-0231-9. Epub 2011 Apr 6. PMID: 22468254; PMCID: PMC3102164.	Incorrect patients
Süslü N, Bajin MD, Süslü AE, Oğretmenoğlu O. Effects of buffered 2.3%, buffered 0.9%, and non-buffered 0.9% irrigation solutions on nasal mucosa after septoplasty. Eur Arch Otorhinolaryngol. 2009 May;266(5):685-9. doi: 10.1007/s00405-008-0807-5. Epub 2008 Sep 18. PMID: 18802718.	Incorrect patients

Tugrul S, Dogan R, Senturk E, Eren SB, Meric A, Ozturan O. A prospective randomized blinded clinical trial: large-volume nasal irrigation with fluticasone propionate in the early postoperative period following septoplasty. Int Forum Allergy Rhinol. 2015 Jul;5(7):610-5. doi: 10.1002/alr.21527. Epub 2015 Apr 6. PMID: 25845978.	Incorrect patients

Literature search strategy

Embase.com

No.	Query	Results
#1	'hypophysis tumor'/exp OR 'acromegaly'/exp OR (((pituitar* OR hypophys* OR adenohypophys* OR neurohypophys* OR sellar OR parasellar) NEAR/4 (adenoma* OR microadenoma* OR macroadenoma* OR cancer* OR carcinoma* OR cyst* OR lesion* OR malignan* OR neoplasm* OR tumor* OR tumour*)):ti,ab,kw) OR ((cushing* NEAR/3 (syndrome* OR disease*)):ti,ab,kw) OR craniopharyngioma*:ti,ab,kw OR 'cranio pharyngioma*':ti,ab,kw OR craniopharyngeoma*:ti,ab,kw OR pharyngioma*:ti,ab,kw OR gonadotropinoma*:ti,ab,kw OR prolactinoma*:ti,ab,kw OR microprolactinoma*:ti,ab,kw OR macroprolactinoma*:ti,ab,kw OR 'macro adenoma*':ti,ab,kw OR macroadenoma*:ti,ab,kw OR acromegal*:ti,ab,kw OR akromegal*:ti,ab,kw OR ((('non function*' OR nonfunction*) NEAR/3 adenoma*):ti,ab,kw) OR (((craniopharyngeal OR rathke*) NEAR/3 (tumor* OR tumour* OR cyst*)):ti,ab,kw)	95527
#2	'transsphenoidal surgery'/exp OR 'endoscopic endonasal surgery'/exp OR 'endoscopic surgery'/de OR transsphenoid*:ti,ab,kw OR 'trans sphenoid*':ti,ab,kw OR endoscop*:ti,ab,kw OR neuroendoscop*:ti,ab,kw	487412
#3	'nasal lavage'/exp OR 'debridement'/exp OR (((nasal OR sinonasal OR sinus OR sinal OR endonasal OR intranasal OR rhinologic* OR mucosal*) NEAR/3 (rins* OR irrigat* OR lavage* OR douch* OR debridement* OR 'wound care' OR toilet OR cleaning OR wash*)):ti,ab,kw) OR ((('post operative' OR postoperative OR posthypophysectom* OR 'post hypophysectom*') NEAR/3 (nasal OR sinonasal OR sinus OR sinal OR endonasal OR intranasal OR rhinologic* OR mucosal*) NEAR/3 (care OR healing OR consult*)):ti,ab,kw) OR ((('ear nose throat' OR ent) NEAR/3 consult*):ti,ab,kw)	68774
#4	#1 AND #2 AND #3 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT (('adolescent'/exp OR 'child'/exp OR adolescent*:ti,ab,kw OR child*:ti,ab,kw OR schoolchild*:ti,ab,kw OR infant*:ti,ab,kw OR girl*:ti,ab,kw OR boy*:ti,ab,kw OR teen:ti,ab,kw OR teens:ti,ab,kw OR teenager*:ti,ab,kw OR youth*:ti,ab,kw OR pediatr*:ti,ab,kw OR paediatr*:ti,ab,kw OR puber*:ti,ab,kw) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab,kw OR man:ti,ab,kw OR men:ti,ab,kw OR woman:ti,ab,kw OR women:ti,ab,kw)) AND [2005-2025]/py	54

#5	'meta analysis'/exp OR 'systematic review'/exp OR 'scoping review'/exp OR 'rapid review'/exp OR 'umbrella review'/exp OR 'cochrane database of systematic reviews'/jt OR 'network meta-analysis'/exp OR 'networkmeta analy*':ti,ab,kw OR 'networkmetaanaly*':ti,ab,kw OR metaanaly*:ti,ab,kw OR 'meta analy*':ti,ab,kw OR metanaly*:ti,ab,kw OR prisma:ti,ab,kw OR prospero:ti,ab,kw OR metaanali*:ti,ab,kw OR 'meta anali*':ti,ab,kw OR metanali*:ti,ab,kw OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab,kw) OR (((structured OR systemic*) NEAR/3 (review* OR overview* OR synth*) NEAR/3 literature):ti,ab,kw) OR ((systemic* NEAR/1 review*):ti,ab,kw) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab,kw) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab,kw) OR (((literature NEAR/3 (review* OR overview*)):ti,ab,kw) AND (search*:ti,ab,kw OR database*:ti,ab,kw OR 'data base*':ti,ab,kw)) OR (('data extraction*':ti,ab,kw OR 'data source*':ti,ab,kw) AND ('study selection*':ti,ab,kw OR 'studies selection*':ti,ab,kw)) OR ('search strateg*':ti,ab,kw AND 'selection criteria*':ti,ab,kw) OR ('data source*':ti,ab,kw AND 'data synth*':ti,ab,kw) OR medline*:ti,ab,kw OR pubmed*:ti,ab,kw OR 'pub med*':ti,ab,kw OR embase:ti,ab,kw OR cochrane*:ti,ab,kw OR (((critical* OR rapid*) NEAR/2 (review* OR overview* OR synth*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synth*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynth*:ti,ab,kw OR 'meta synth*':ti,ab,kw OR 'review* of review*':ti,ab,kw	1111306
#6	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	4392629
#7	'major clinical study'/de OR 'clinical study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'cohort analysis'/de OR 'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti) OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR	18206352

	((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR (('or' OR 'rr') NEAR/6 ci):ab)))	
#8	#4 AND #5	2
#9	#4 AND #6 NOT #8	9
#10	#4 AND #7 NOT (#8 OR #9)	27
#11	#8 OR #9 OR #10	38
#12	34941128:ui OR 38079151:ui	2
#13	#11 AND #12	2
#14	'septoplasty'/de OR 'nose septum'/exp OR septoplast*:ti,ab,kw OR rhinoseptoplast*:ti,ab,kw OR septorhinoplast*:ti,ab,kw OR (((septum OR septal) NEAR/3 (surg* OR operat* OR correct* OR reconstruct* OR repair* OR hemitransfi*)):ti,ab,kw)	20109
#15	#14 AND #3 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT (('adolescent'/exp OR 'child'/exp OR adolescent*:ti,ab,kw OR child*:ti,ab,kw OR schoolchild*:ti,ab,kw OR infant*:ti,ab,kw OR girl*:ti,ab,kw OR boy*:ti,ab,kw OR teen:ti,ab,kw OR teens:ti,ab,kw OR teenager*:ti,ab,kw OR youth*:ti,ab,kw OR pediatr*:ti,ab,kw OR paediatr*:ti,ab,kw OR puber*:ti,ab,kw) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab,kw OR man:ti,ab,kw OR men:ti,ab,kw OR woman:ti,ab,kw OR women:ti,ab,kw)) AND [2005-2025]/py	202
#16	#5 AND #15 NOT #11	5
#17	#6 AND #15 NOT (#11 OR #16)	36
#18	#8 OR #16	7
#19	#9 OR #17	45

Ovid/Medline

#	Searches	Results
1	exp Pituitary Neoplasms/ or exp Acromegaly/ or ((pituitar* or hypophys* or adenohypophys* or neurohypophys* or sellar or parasellar) adj4 (adenoma* or microadenoma* or macroadenoma* or cancer* or carcinoma* or cyst* or lesion* or malignan* or neoplasm* or tumor* or tumour*)).ti,ab,kf. or (cushing* adj3 (syndrome* or disease*)).ti,ab,kf. or craniopharyngioma*.ti,ab,kf. or 'cranio pharyngioma*'.ti,ab,kf. or craniopharyngeoma*.ti,ab,kf. or pharyngioma*.ti,ab,kf. or gonadotropinoma*.ti,ab,kf. or prolactinoma*.ti,ab,kf. or microprolactinoma*.ti,ab,kf. or macroprolactinoma*.ti,ab,kf. or 'macro adenoma*'.ti,ab,kf. or macroadenoma*.ti,ab,kf. or acromegal*.ti,ab,kf. or akromegal*.ti,ab,kf. or (('non function*' or nonfunction*) adj3 adenoma*).ti,ab,kf. or ((craniopharyngeal or rathke*) adj3 (tumor* or tumour* or cyst*)).ti,ab,kf.	66401
2	Endoscopy/ or Neuroendoscopy/ or transsphenoid*.ti,ab,kf. or 'trans sphenoid*'.ti,ab,kf. or endoscop*.ti,ab,kf. or neuroendoscop*.ti,ab,kf.	302748
3	exp Nasal Lavage/ or exp Debridement/ or ((nasal or sinonasal or sinus or sinal or endonasal or intranasal or rhinologic* or mucosal*) adj3 (rins* or irrigat* or lavage* or douch* or debridement* or 'wound care' or toilet or cleaning or wash*)).ti,ab,kf. or (('post operative' or postoperative or posthypophysectom* or 'post hypophysectom*') adj3 (nasal or sinonasal or sinus or sinal or endonasal or intranasal or rhinologic* or mucosal*) adj3 (care or healing or consult*)).ti,ab,kf. or (('ear nose throat' or ENT) adj3 consult*).ti,ab,kf.	24550
4	(1 and 2 and 3) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/) not ((Adolescent/ or Child/ or Infant/ or adolescen*.ti,ab,kf. or child*.ti,ab,kf. or schoolchild*.ti,ab,kf. or infant*.ti,ab,kf. or girl*.ti,ab,kf. or boy*.ti,ab,kf. or teen.ti,ab,kf. or teens.ti,ab,kf. or teenager*.ti,ab,kf. or youth*.ti,ab,kf. or pediatr*.ti,ab,kf. or paediatr*.ti,ab,kf. or puber*.ti,ab,kf.) not (Adult/ or adult*.ti,ab,kf. or man.ti,ab,kf. or men.ti,ab,kf. or woman.ti,ab,kf. or women.ti,ab,kf.))	19
5	limit 4 to yr="2005 -Current"	19
6	exp Meta-Analysis/ or exp Network Meta-Analysis/ or exp Systematic Review/ or (networkmeta analy* or networkmetaanaly* or metaanaly* or meta analy* or metanaly* or prisma or prospero or metaanali* or meta anali* or metanali*).ti,ab,kf. or ((systemati* or scoping or umbrella or structured literature) adj3 (review* or overview*)).ti,ab,kf. or ((structured or systemic*) adj3 (review* or overview* or synth*) adj3 literature).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 (review* or overview*)) and (search* or database* or data base*)).ti,ab,kf. or ((data extraction* or data source*) and (study selection* or studies selection*)).ti,ab,kf. or (search strateg* and selection	833098

	criteria*).ti,ab,kf. or (data source* and data synth*).ti,ab,kf. or (medline* or pubmed* or pub med* or embase or cochrane*).ti,ab,kf. or cochrane.jw. or ((critical* or rapid*) adj2 (review* or overview* or synth*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synth*)) and (search* or database* or data base*)).ab. or metasynth*.ti,ab,kf. or meta synth*.ti,ab,kf.	
7	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2895488
8	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or exp cohort studies/ or epidemiologic studies/ or ((multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.)) or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	8044172
9	5 and 6	0
10	(5 and 7) not 9	4
11	(5 and 8) not (9 or 10)	7
12	9 or 10 or 11	11
13	exp Nasal Septum/ or septoplast*.ti,ab,kf. or rhinoseptoplast*.ti,ab,kf. or septorhinoplast*.ti,ab,kf. or ((septum	15326

	or septal) adj3 (surg* or operat* or correct* or reconstruct* or repair* or hemitransfi*)).ti,ab,kf.	
14	(13 and 3) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/) not ((Adolescent/ or Child/ or Infant/ or adolescen*.ti,ab,kf. or child*.ti,ab,kf. or schoolchild*.ti,ab,kf. or infant*.ti,ab,kf. or girl*.ti,ab,kf. or boy*.ti,ab,kf. or teen.ti,ab,kf. or teens.ti,ab,kf. or teenager*.ti,ab,kf. or youth*.ti,ab,kf. or pediatr*.ti,ab,kf. or paediatr*.ti,ab,kf. or puber*.ti,ab,kf.) not (Adult/ or adult*.ti,ab,kf. or man.ti,ab,kf. or men.ti,ab,kf. or woman.ti,ab,kf. or women.ti,ab,kf.))	77
15	limit 14 to yr="2005 -Current"	61
16	(6 and 15) not 12	2
17	(7 and 15) not (12 or 16)	15
18	9 or 16	2
19	10 or 17	19

Module 8 – Uitval van functie als operatieindicatie

Uitgangsvraag

Wat is het beste (klinische) beleid bij patiënten met een hypofyseadenoom en recent ontstane (partiele) hypofyse uitval (zonder andere tekenen van compressie)?

Search and select

A systematic review of the literature was performed to answer the following question(s):
What is the clinical benefit of surgical intervention in patients with (new-onset) pituitary insufficiency due to a pituitary macroadenoma?

Table 1. PICO

Patients	Patients with pituitary insufficiency due to a non-functioning adenoma (without visual field defects).
Intervention	Surgery (via transsphenoidal endoscopic surgery)
Control	Conservative approach/ no surgery
Outcomes	Pituitary function (per axis) / pituitary recovery, quality of life, and surgical complications.
Other selection criteria	Study design: systematic reviews, randomized controlled trials and observational studies. Minimal follow-up: Outcomes measured between 6 weeks and 1-2 years after the operation.

Relevant outcome measures

The guideline panel considered pituitary function as a **critical** outcome measure for decision making; and quality of life and complications as an **important** outcome measure for decision making.

The guideline panel defined the following thresholds as a minimal clinically (patient) important difference.

- For continuous outcomes a threshold of 10% for continuous outcomes
- For dichotomous outcomes a threshold of <0.8 and >1.25

Search and select (Methods)

A systematic literature search was performed by a medical information specialist using the following bibliographic databases: Embase.com and Ovid/Medline all. Both databases were searched from 2000 to May 20th, 2025 for systematic reviews, RCTs and observational and other studies. Systematic searches were completed using a combination of controlled vocabulary and natural language keywords. The overall search strategy was derived from the following primary search concepts: (1) nonfunctioning pituitary adenoma; (2) hypopituitarism; (3) surgery. Duplicates were removed using EndNote software. After deduplication a total of 929 records were imported for title/abstract screening.

Initially, 5 studies were selected based on title and abstract screening. After reading the full text, 5 studies were excluded (see the exclusion table under the tab 'Evidence tabellen'), and no studies were included.

Summary of literature

Description of studies

No literature was found that applied to the predefined PICO.

Implementeren-tabel

De implementatietabel brengt in kaart welke factoren de uitvoering van een aanbeveling bevorderen of belemmeren, en welke aanvullende acties nodig zijn voor succesvolle invoering. De adviseur en (cluster)werkgroep vullen de tabel in op basis van gerichte vragen over het onderliggende probleem, relevante randvoorwaarden en mogelijke knelpunten. Op basis hiervan wordt geconcludeerd of een extra implementatie-impuls wenselijk is.

Implementatietabel

Vraag	***Antwoord:*** *Kruis aan en licht toe/ beschrijf*		***Toelichting keuze:***
I1. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?		**Ongewenste praktijkvariatie**	
	x	**Nieuwe evidentie**	**X**
		Anders	
I2. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?	**x**	**< 1000**	
		< 5000	
		5000-40.000	
		> 40.000	
I3. Is de aanbeveling onderdeel van een bredere set interventies of verwant aan andere richtlijnen of modules? Zo ja, hoe verhoudt zij zich daartoe en moet hiermee rekening worden gehouden bij de implementatie, of kan de aanbeveling als losstaand worden beschouwd?	**x**	**Ja**	**Zie overige modules**
		Nee	
I4. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:		**Belemmerende factoren**	**Bevorderende factoren/ kansen**
Richtlijn/ klinisch traject (innovatie)	**x**	Volume normen zijn gekoppeld aan chirurgische uitkomsten. Lager volume centra hebben mogelijk een andere balans tussen kansen en risico's	Er is nu verschil in beleid tussen centra. Deze aanbeveling kan dit verbeteren.
Zorgverleners (artsen en verpleegkundigen)		Onzekerheid over de balans tussen kans op herstel van hypofysefunctie en risico op nieuwe uitval kan leiden tot terughoudendheid bij indicatiestelling.	Besluitvorming vindt doorgaans plaats binnen multidisciplinaire teams, wat gezamenlijke afweging van risico's en baten ondersteunt.

Patiënt/ cliënt (naasten)		De keuze tussen chirurgische interventie en afwachtend beleid kan voor patiënten complex zijn door onzekerheid over het te verwachten effect op hypofysefunctie.	Mogelijkheid tot herstel van hypofysefunctie kan voor sommige patiënten een belangrijke motivatie zijn om chirurgie te overwegen.
Sociale context			
Organisatorische context		Indicatie voor operatie dient vaker afgewogen te worden in het MDT / expertise centrum waardoor wellicht meer patienten in een hoogvolume expertisecentrum gevolgd dienen te worden.	Bestaande multidisciplinaire structuren voor hypofysezorg ondersteunen gezamenlijke besluitvorming.
Financiële en juridische context			
I5. A) Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk? (kruis aan) **B) Wat is er nodig van deze personen/partijen om de aanbeveling in de praktijk te kunnen brengen?** *Denk aan aanpassingen in gedrag, werkwijzen, beleid, samenwerking of andere randvoorwaarden.*		**A**	**B**
		Patiënt/ cliënt (naaste)	
		Professional	
		Beroepsvereniging, nl NVvN, NVE	Relevante wetenschappelijke verenigingen ondersteunen implementatie van de aanbeveling en stimuleren registratie en evaluatie van uitkomsten via de QRNS.
		Ziekenhuis (raad van bestuur/UMCNL (voorheen NFU)/NVZ)	
		Zorgverzekeraars/ NZa	
		Zorginstituut [duiding nodig]	
		Anders	
I6. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?	**X**	< 1 jaar	De aanbeveling betreft een aanpassing in de klinische afweging bij patiënten met recent ontstane (partiele) hypofyseuitval . De

			benodigde diagnostiek, multidisciplinaire besluitvorming en chirurgische expertise zijn reeds onderdeel van de huidige zorg. Implementatie kan daarom plaatsvinden via reguliere verspreiding van de richtlijn en bespreking binnen bestaande multidisciplinaire teams.
		Binnen 2-3 jaar	
I7. Conclusie: is er extra actie en/of ondersteuning nodig voor implementatie van de aanbeveling? *De reguliere implementatieroutes (publicatie en disseminatie via officiele kanalen, opname in professionele standaarden, scholing en nascholing, gebruik van bestaande ICT systemen, audits en visitaties) van de richtlijnmodule alleen is onvoldoende.*		Ja	
	X	Nee	De aanbeveling sluit aan bij bestaande diagnostiek en behandelstructuren binnen de hypofysezorg. Implementatie kan plaatsvinden via de gebruikelijke kanalen van richtlijnpublicatie, nascholing en multidisciplinaire besluitvorming. De werkgroep ziet daarom geen noodzaak voor aanvullende implementatieactiviteiten
I8. Plaatsing op de Landelijke Implementatieagenda Medisch Specialistische zorg is gewenst. *Het gaat om zorg die (grotendeels) wordt uitgevoerd binnen de ziekenhuismuren. Succesvolle implementatie vraagt om actieve betrokkenheid en samenwerking van meerdere relevante partijen binnen de zorgpraktijk.*		Ja *	
	X	Nee	De aanbeveling betreft een conditionele aanbeveling met zeer lage bewijskracht en een beperkte populatie. Implementatie vraagt voornamelijk om klinische afweging binnen bestaande zorgstructuren en niet om een landelijke implementatie-impuls.

**Deze aanbeveling komt mogelijk in aanmerking voor plaatsing op de Landelijke Implementatieagenda van het programma Zorg Evaluatie & Gepast Gebruik (ZE&GG), waarin alle betrokken partijen in de medisch-specialistische zorg samenwerken aan de implementatie van bewezen beste zorg. De Federatie levert namens het veld goed onderbouwde aanbevelingen aan, die zijn getoetst op de behoefte aan een implementatie-impuls. De onderwerpen op de Implementatieagenda zijn onderdeel van landelijke zorginkoopafspraken tussen zorgverzekeraars en zorgaanbieders. Voor de beoordeling van aanbevelingen uit richtlijnen wordt gebruikgemaakt van de implementatietabel. Op basis hiervan kunnen we de andere partijen goed informeren en gezamenlijk besluiten of plaatsing op de Implementatieagenda passend is.*

Agenderen-tabel

Kennisvragen zijn vragen over bestaande zorg, die nog onvoldoende zijn onderbouwd met wetenschappelijke literatuur. Het richtlijncluster heeft een belangrijke rol bij het identificeren van kennisvragen bij het ontwikkelen van een richtlijnmodule. De input uit deze Agenderen-tabel wordt gebruikt bij het opstellen van een kennisagenda. Alle geïnventariseerde kennisvragen (vanuit achterban, patiënten en richtlijnen) op het gebied van zorgevaluatie worden beoordeeld door de kennisagenda werkgroep en daarna geprioriteerd door alle relevante partijen tijdens een prioriteringsbijeenkomst. Het is belangrijk om de kennisvraag scherp te formuleren, zodat resultaten van een zorgevaluatie onderzoek daadwerkelijk opgenomen kunnen worden in een richtlijnmodule.

Vraag	***Antwoord*** *Kruis aan*	*Vul in*
A1. Is onderzoek wenselijk om de <u>uitgangsvraag of zoekvraag</u> (met meer/voldoende zekerheid) te kunnen beantwoorden?		Nee. *Tijdens de ontwikkeling van deze module is gebleken dat er volgens het cluster sprake is van passend bewijs voor de uitgangsvraag en zoekvraag.*
	X	Ja
A2. Wat is de kennisvraag?	Kennis-vraag	Wat is het effect van chirurgische interventie ten opzichte van afwachtend beleid op herstel van hypofysefunctie bij patiënten met hypofyse-uitval veroorzaakt door een niet-functionerend hypofyseadenoom zonder andere operatie-indicatie?
	P	Patiënten met hypofyse-uitval door een niet-functionerend hypofyseadenoom zonder visusstoornissen of andere duidelijke operatie-indicatie
	I	Transsfenoïdale chirurgische resectie van het hypofyseadenoom.
	C	Afwachtend beleid/conservatieve behandeling.
	O	erstel of stabilisatie van hypofysefunctie per hormoonas, kwaliteit van leven, en chirurgische complicaties (waaronder nieuwe hypofyse-uitval).
A3. Waarom is dit een belangrijke kennisvraag?	Toelichting	Er is momenteel geen vergelijkend wetenschappelijk bewijs beschikbaar dat het effect van vroege chirurgische interventie op herstel van hypofysefunctie onderzoekt bij patiënten met hypofyse-

		uitval zonder andere operatie-indicatie. In de klinische praktijk bestaat onzekerheid over de balans tussen mogelijke voordelen van decompressie van de hypofyse en het risico op nieuwe hypofyse-uitval door chirurgie. Betere evidence kan helpen bij het onderbouwen van de indicatiestelling en de gezamenlijke besluitvorming met patiënten.
A4. Welk onderzoeksdesign is passend om deze kennisvraag te beantwoorden?		RCT
	X	Observationeel onderzoek
	X	Kwaliteitsregistratie
		Anders, namelijk
	Toelichting	Gezien de zeldzaamheid van de patiëntengroep en de klinische context waarin de indicatiestelling voor chirurgie individueel wordt bepaald, lijkt een gerandomiseerde studie moeilijk uitvoerbaar. Analyse van prospectief verzamelde gegevens uit een nationale kwaliteitsregistratie, zoals de QRNS, kan inzicht geven in het herstel van hypofysefunctie, het optreden van nieuwe hypofyse-uitval en andere relevante uitkomsten na chirurgie. Registratie van uitkomsten op zowel nationaal als centrumgebonden niveau kan daarnaast bijdragen aan betere onderbouwing van de indicatiestelling en gezamenlijke besluitvorming met patiënten.
A5. Zijn er een andere kennisvragen naar voren gekomen die passen bij het <u>onderwerp van de module</u>, maar niet hetzelfde zijn als de uitgangs- of zoekvraag en waar *geen* passend bewijs voor is?	X	Nee
		Ja

Bijlagen bij module [8]

Table of excluded studies

Reference	Reason for exclusion
Dekkers OM, Pereira AM, Romijn JA. Treatment and follow-up of clinically nonfunctioning pituitary macroadenomas. J Clin Endocrinol Metab. 2008 Oct;93(10):3717-26. doi: 10.1210/jc.2008-0643. Epub 2008 Aug 5. PMID: 18682516.	Does not include the outcomes included in the PICO
Detomas M, Altieri B, Nasi-Kordhishti I, Ryba A, Haberbosch L, Chierigo F, Deutschbein T, Fassnacht M, Mortini P, Flitsch J, Honegger J, Losa M. Recovery of hypopituitarism in macroprolactinomas: a comparison of medical vs. surgical treatment. Results from a European multicenter study. J Endocrinol Invest. 2025 Jun;48(6):1363-1370. doi: 10.1007/s40618-025-02559-8. Epub 2025 Mar 4. PMID: 40035956; PMCID: PMC12226669.	Analyses a functional adenoma. This is not part of the PICO.
Iglesias P, Arcano K, Triviño V, García-Sancho P, Díez JJ, Villabona C, Cordido F. Prevalence, Clinical Features, and Natural History of Incidental Clinically Non-Functioning Pituitary Adenomas. Horm Metab Res. 2017 Sep;49(9):654-659. doi: 10.1055/s-0043-115645. Epub 2017 Jul 31. PMID: 28759937.	Does not include the outcomes included in the PICO
Lucas JW, Bodach ME, Tumialan LM, Oyesiku NM, Patil CG, Litvack Z, Aghi MK, Zada G. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guideline on Primary Management of Patients With Nonfunctioning Pituitary Adenomas. Neurosurgery. 2016 Oct;79(4):E533-5. doi: 10.1227/NEU.0000000000001389. PMID: 27635961.	Does not compare surgery versus conservative treatment.
Pedersen MB, Dukanovic S, Springborg JB, Andreassen M, Krogh J. Endocrine Function after Transsphenoidal Surgery in Patients with Non-Functioning Pituitary Adenomas: A Systematic Review and Meta-Analysis. Neuroendocrinology. 2022;112(9):823-834. doi: 10.1159/000522090. Epub 2022 Jan 21. PMID: 35172314.	Does not compare surgery versus conservative treatment.

5 Literature search strategy

Embase.com

No.	Query	Results
#1	'nonfunctioning pituitary adenoma'/exp OR ((('non function*' OR nonfunction* OR chromafob* OR chromophob* OR functionless OR 'non secret*' OR nonsecret* OR silent) NEAR/3 (adenoma* OR microadenoma* OR macroadenoma* OR tumor* OR tumour*)):ti,ab,kw) OR nfpa*:ti,ab,kw OR macroprolactinoma*:ti,ab,kw	13088
#2	'hypopituitarism'/exp OR 'adenohypophysis hypofunction'/de OR 'corticotropin deficiency'/exp OR 'gonadotropin deficiency'/exp OR 'growth hormone deficiency'/exp OR 'hypogonadotropic hypogonadism'/exp OR 'luteinizing hormone deficiency'/exp OR 'follicle stimulating hormone deficiency'/exp OR 'follitropin deficiency'/exp OR 'cortisol deficiency'/exp OR 'secondary hypothyroidism'/exp OR hypopituitarism:ti,ab,kw OR 'hypo pituitarism':ti,ab,kw OR panhypopituitarism:ti,ab,kw OR (((pituitar* OR hypophys* OR adenohypophys* OR neurohypophys* OR sellar OR parasellar) NEAR/3 (hypofunction* OR 'hypo function*' OR deficien* OR insufficien* OR fail* OR 'loss of function*')):ti,ab,kw) OR (((corticotrop* OR adrenocorticotrop* OR acth OR gonadotropin* OR somatotrop* OR hyposomatotrop* OR 'growth hormone*' OR gh OR 'luteinising hormon*' OR 'luteinizing	78601

	hormon*' OR lh OR isch OR 'interstitial cell stimulating hormone*' OR 'interstitial stimulating hormone*' OR lutotropin OR lutropin OR 'follicle stimulating hormone*' OR 'folliculostimulating hormone*' OR fsh OR follitropin* OR folltropin* OR fertiline OR follicotropin* OR follitrophin* OR cortisol OR thyrotropin OR 'thyroid stimulating hormone*' OR tsh) NEAR/3 (deficien* OR insufficien*)):ti,ab,kw) OR (((pituitary OR secondary OR tsh) NEAR/3 hypothyroidism):ti,ab,kw) OR hypogonadotrop*:ti,ab,kw OR 'hypo gonadotrop*':ti,ab,kw OR hypogonadism:ti,ab,kw OR 'hypo gonadism':ti,ab,kw OR hypocortisolism:ti,ab,kw OR 'hypo cortisolism':ti,ab,kw	
#3	'surgery'/exp OR 'surgical patient'/exp OR 'surgical risk'/exp OR 'perioperative period'/exp OR 'surgery'/lnk OR surgic*:ti,ab,kw OR surger*:ti,ab,kw OR microsurg*:ti,ab,kw OR operation*:ti,ab,kw OR operative:ti,ab,kw OR presurg*:ti,ab,kw OR preoperati*:ti,ab,kw OR perisurg*:ti,ab,kw OR perioperati*:ti,ab,kw OR postsurg*:ti,ab,kw OR postoperati*:ti,ab,kw OR intraoperati*:ti,ab,kw OR resect*:ti,ab,kw OR laparoscop*:ti,ab,kw OR endoscop*:ti,ab,kw OR neuroendoscop*:ti,ab,kw OR neurosurg*:ti,ab,kw OR transsphenoid*:ti,ab,kw OR 'trans sphenoid*':ti,ab,kw OR hypophysectom*:ti,ab,kw OR adenomectom*:ti,ab,kw	8720342
#4	#1 AND #2 AND #3 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT (('adolescent'/exp OR 'child'/exp OR adolescent*:ti,ab,kw OR child*:ti,ab,kw OR schoolchild*:ti,ab,kw OR infant*:ti,ab,kw OR girl*:ti,ab,kw OR boy*:ti,ab,kw OR teen:ti,ab,kw OR teens:ti,ab,kw OR teenager*:ti,ab,kw OR youth*:ti,ab,kw OR pediatr*:ti,ab,kw OR paediatr*:ti,ab,kw OR puber*:ti,ab,kw) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab,kw OR man:ti,ab,kw OR men:ti,ab,kw OR woman:ti,ab,kw OR women:ti,ab,kw))	1048
#5	#4 AND [2000-2025]/py	878
#6	'meta analysis'/exp OR 'systematic review'/exp OR 'scoping review'/exp OR 'rapid review'/exp OR 'umbrella review'/exp OR 'cochrane database of systematic reviews'/jt OR 'network meta-analysis'/exp OR 'networkmeta analy*':ti,ab,kw OR 'networkmetaanaly*':ti,ab,kw OR metaanaly*:ti,ab,kw OR 'meta analy*':ti,ab,kw OR metanaly*:ti,ab,kw OR prisma:ti,ab,kw OR prospero:ti,ab,kw OR metaanali*:ti,ab,kw OR 'meta anali*':ti,ab,kw OR metanali*:ti,ab,kw OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab,kw) OR (((structured OR systemic*) NEAR/3 (review* OR overview* OR synth*) NEAR/3 literature):ti,ab,kw) OR ((systemic* NEAR/1 review*):ti,ab,kw) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab,kw) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab,kw) OR (((literature NEAR/3 (review* OR overview*)):ti,ab,kw) AND (search*:ti,ab,kw OR database*:ti,ab,kw OR 'data base*':ti,ab,kw)) OR (('data extraction*':ti,ab,kw OR 'data source*':ti,ab,kw) AND	1115102

	('study selection*':ti,ab,kw OR 'studies selection*':ti,ab,kw)) OR ('search strateg*':ti,ab,kw AND 'selection criteria*':ti,ab,kw) OR ('data source*':ti,ab,kw AND 'data synth*':ti,ab,kw) OR medline*:ti,ab,kw OR pubmed*:ti,ab,kw OR 'pub med*':ti,ab,kw OR embase:ti,ab,kw OR cochrane*:ti,ab,kw OR (((critical* OR rapid*) NEAR/2 (review* OR overview* OR synth*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synth*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynth*:ti,ab,kw OR 'meta synth*':ti,ab,kw OR 'review* of review*':ti,ab,kw	
#7	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	4497112
#8	'major clinical study'/de OR 'clinical study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'cohort analysis'/de OR 'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti) OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR	18315944

	observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR (('or' OR 'rr') NEAR/6 ci):ab)))	
#9	#5 AND #6	45
#10	#5 AND #7 NOT #9	63
#11	#5 AND #8 NOT (#9 OR #10)	445
#12	#5 NOT (#9 OR #10 OR #11)	325

Ovid/Medline

#	Searches	Results
1	((('non function*' or nonfunction* or chromafob* or chromophob* or functionless or 'non secret*' or nonsecret* or silent) adj3 (adenoma* or microadenoma* or macroadenoma* or tumor* or tumour*)) or nfpa* or macroprolactinoma*).ti,ab,kf.	8132
2	exp Hypopituitarism/ or hypopituitarism.ti,ab,kf. or 'hypo pituitarism'.ti,ab,kf. or panhypopituitarism.ti,ab,kf. or ((pituitar* or hypophys* or adenohypophys* or neurohypophys* or sellar or parasellar) adj3 (hypofunction* or 'hypo function*' or hyposecret* or deficien* or insufficien* or fail* or 'loss of function*')).ti,ab,kf. or ((corticotrop* or adrenocorticotrop* or acth or gonadotropin* or somatotrop* or hyposomatotrop* or 'growth hormone*' or gh or 'luteinising hormon*' or 'luteinizing hormon*' or lh or isch or 'interstitial cell stimulating hormone*' or 'interstitial stimulating hormone*' or lutotropin or lutropin or 'follicle stimulating hormone*' or 'folliculostimulating hormone*' or fsh or follitropin* or folltropin* or fertiline or follicotropin* or follitrophin* or cortisol or thyrotropin or 'thyroid stimulating hormone*' or tsh) adj3 (deficien* or insufficien*)).ti,ab,kf. or ((pituitary or secondary or tsh) adj3 hypothyroidism).ti,ab,kf. or hypogonadotrop*.ti,ab,kf. or 'hypo gonadotrop*'.ti,ab,kf. or hypogonadism.ti,ab,kf. or 'hypo gonadism'.ti,ab,kf. or hypocortisolism.ti,ab,kf. or 'hypo cortisolism'.ti,ab,kf.	41486
3	exp Surgical Procedures, Operative/ or exp Specialties, Surgical/ or su.fs. or exp Perioperative Period/ or surgic*.ti,ab,kf. or surger*.ti,ab,kf. or microsurg*.ti,ab,kf. or operation*.ti,ab,kf. or operative.ti,ab,kf. or presurg*.ti,ab,kf. or preoperati*.ti,ab,kf. or perisurg*.ti,ab,kf. or perioperati*.ti,ab,kf. or postsurg*.ti,ab,kf. or postoperati*.ti,ab,kf. or intraoperati*.ti,ab,kf. or resect*.ti,ab,kf. or laparoscop*.ti,ab,kf. or endoscop*.ti,ab,kf. or neuroendoscop*.ti,ab,kf. or neurosurg*.ti,ab,kf. or transsphenoid*.ti,ab,kf. or 'trans sphenoid*'.ti,ab,kf. or hypophysectom*.ti,ab,kf. or adenomectom*.ti,ab,kf.	6116145
4	(1 and 2 and 3) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/) not ((Adolescent/ or Child/ or Infant/ or adolescen*.ti,ab,kf. or child*.ti,ab,kf. or schoolchild*.ti,ab,kf. or infant*.ti,ab,kf. or girl*.ti,ab,kf. or boy*.ti,ab,kf. or teen.ti,ab,kf. or teens.ti,ab,kf. or	669

	teenager*.ti,ab,kf. or youth*.ti,ab,kf. or pediatr*.ti,ab,kf. or paediatr*.ti,ab,kf. or puber*.ti,ab,kf.) not (Adult/ or adult*.ti,ab,kf. or man.ti,ab,kf. or men.ti,ab,kf. or woman.ti,ab,kf. or women.ti,ab,kf.))	
5	limit 4 to yr="2000 -Current"	533
6	exp Meta-Analysis/ or exp Network Meta-Analysis/ or exp Systematic Review/ or (networkmeta analy* or networkmetaanaly* or metaanaly* or meta analy* or metanaly* or prisma or prospero or metaanali* or meta anali* or metanali*).ti,ab,kf. or ((systemati* or scoping or umbrella or structured literature) adj3 (review* or overview*)).ti,ab,kf. or ((structured or systemic*) adj3 (review* or overview* or synth*) adj3 literature).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 (review* or overview*)) and (search* or database* or data base*)).ti,ab,kf. or ((data extraction* or data source*) and (study selection* or studies selection*)).ti,ab,kf. or (search strateg* and selection criteria*).ti,ab,kf. or (data source* and data synth*).ti,ab,kf. or (medline* or pubmed* or pub med* or embase or cochrane*).ti,ab,kf. or cochrane.jw. or ((critical* or rapid*) adj2 (review* or overview* or synth*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synth*)) and (search* or database* or data base*)).ab. or metasynth*.ti,ab,kf. or meta synth*.ti,ab,kf.	833764
7	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2896739
8	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or exp cohort studies/ or epidemiologic studies/ or ((multicenter	8046303

	study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.)) or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	
9	5 and 6	30
10	(5 and 7) not 9	32
11	(5 and 8) not (9 or 10)	288
12	5 not (9 or 10 or 11)	183

Module 9 – Organisatie van zorg

Uitgangsvraag

Wat is de optimale organisatie van zorg en follow-up voor patiënten die hypofysechirurgie ondergaan?

De uitgangsvraag omvat de volgende deelvragen:

1. Hoe moet het multidisciplinair overleg (MDO) voor hypofyseaandoeningen worden ingericht en uitgevoerd?
2. Hoe moet de organisatie van postoperatieve follow-up en overdracht tussen chirurgisch centrum en perifere centra worden vormgegeven?
3. Onder welke voorwaarden kan follow-up van hypofysepatiënten plaatsvinden in een perifeer ziekenhuis?
4. Hoe moet informatieoverdracht en patiëntcommunicatie binnen het zorgtraject worden ingericht?

Search and select

No systematic review of the literature has been performed, as the organizational questions addressed in this module cannot be answered using study designs suitable for a PICO-based approach.

Implementeren-tabel

De implementatietabel brengt in kaart welke factoren de uitvoering van een aanbeveling bevorderen of belemmeren, en welke aanvullende acties nodig zijn voor succesvolle invoering. De adviseur en (cluster)werkgroep vullen de tabel in op basis van gerichte vragen over het onderliggende probleem, relevante randvoorwaarden en mogelijke knelpunten. Op basis hiervan wordt geconcludeerd of een extra implementatie-impuls wenselijk is.

Implementatietabel

Vraag	***Antwoord:*** *Kruis aan en licht toe/ beschrijf*		***Toelichting keuze:***
I1. Wat was het onderliggende probleem om deze uitgangsvraag uit te werken?	**X**	**Ongewenste praktijkvariatie**	Zorgprocessen zijn in de verschillende ziekenhuizen anders ingericht.
		Nieuwe evidentie	
		Anders	
I2. Maak een inschatting over hoeveel patiënten het ongeveer gaat waar de aanbeveling betrekking op heeft?		**< 1000**	
	X	**< 5000**	
		5000-40.000	
		> 40.000	
I3. Is de aanbeveling onderdeel van een bredere set interventies of verwant aan andere richtlijnen of modules? Zo ja, hoe verhoudt zij zich daartoe en moet hiermee rekening worden gehouden bij de implementatie, of kan de	**X**	**Ja**	Sluit aan bij bestaande kwaliteitskaders en organisatorische documenten (o.a. NVvN, PTCOE, EndoERN).

aanbeveling als losstaand worden beschouwd?		**Nee**	
I4. Belemmeringen en kansen op verschillende niveaus voor landelijke toepassing van de aanbeveling:		**Belemmerende factoren**	**Bevorderende factoren/ kansen**
Richtlijn/ klinisch traject (innovatie)			Sluit aan bij bestaande zorgstructuren en kwaliteitskaders.
Zorgverleners (artsen en verpleegkundigen)		Onvoldoende beschikbaarheid van verpleegkundig specialisten en betrokken disciplines (zoals oogheelkunde) kan de implementatie en coördinatie van zorg bemoeilijken. Variatie in ziekenhuisinformatiesystemen kan adequate informatieoverdracht tussen centra bemoeilijken.	Actieve betrokkenheid van diverse specialismen bij de het MDO.
Patiënt/ cliënt (naasten)		geen	Goede patiëntvoorlichting en duidelijke communicatie over het zorgpad, verantwoordelijkheden en overdracht tussen zorgverleners.
Sociale context		nvt	nvt
Organisatorische context		Variatie in EPD-systemen, beperkte MDO-capaciteit en verschillen in radiologieprotocollen kunnen de uniforme toepassing van de aanbeveling bemoeilijken.	Bestaande regionale samenwerking en zorgpaden kunnen benut worden
Financiële en juridische context		nvt	nvt
I5. A) Welke personen/partijen zijn van belang bij het toepassen van de aanbeveling in de praktijk? (kruis aan) **B) Wat is er nodig van deze personen/partijen om de**		A	B
	X	Patiënt/ cliënt (naaste)	
	X	Professional	Implementeren richtlijn in dagelijks praktijk

aanbeveling in de praktijk te kunnen brengen? *Denk aan aanpassingen in gedrag, werkwijzen, beleid, samenwerking of andere randvoorwaarden.*	**X**	Beroepsvereniging, nl NVE, NVvN, NOG, NVRO	Uitdragen richtlijn
	X	Ziekenhuis (raad van bestuur/UMCNL (voorheen NFU)/NVZ)	Digitale structuur voor informatieoverdracht met omliggende ziekenhuizen. ICT-structuur voor deelname aan MDO's. Waarborgen van personele capaciteit voor deelname aan MDO.
		Zorgverzekeraars/ NZa	
		Zorginstituut [duiding nodig]	
		Anders	
I6. Binnen welk tijdsbestek moet de aanbeveling zijn geïmplementeerd?	**X**	< 1 jaar	Betreft vastleggen en expliciteren van bestaande werkwijzen.
		binnen 2-3 jaar	
I7. Conclusie: is er extra actie en/of ondersteuning nodig voor implementatie van de aanbeveling? *De reguliere implementatieroutes (publicatie en disseminatie via officiële kanalen, opname in professionele standaarden, scholing en nascholing, gebruik van bestaande ICT systemen, audits en visitaties) van de richtlijnmodule alleen is onvoldoende.*		Ja	
	X	Nee	Implementatie kan via reguliere kanalen plaatsvinden.
I8. Plaatsing op de Landelijke Implementatieagenda Medisch Specialistische zorg is gewenst. *Het gaat om zorg die (grotendeels) wordt uitgevoerd binnen de ziekenhuismuren. Succesvolle implementatie vraagt om actieve betrokkenheid en samenwerking van meerdere relevante partijen binnen de zorgpraktijk.*		Ja *	
	X	Nee	Implementatie is binnen bestaande structuren uitvoerbaar.

**Deze aanbeveling komt mogelijk in aanmerking voor plaatsing op de Landelijke Implementatieagenda van het programma Zorg Evaluatie & Gepast Gebruik (ZE&GG), waarin alle betrokken partijen in de medisch-specialistische zorg samenwerken aan de implementatie van bewezen beste zorg. De Federatie levert namens het veld goed onderbouwde aanbevelingen aan, die zijn getoetst op de behoefte aan een implementatie-impuls. De onderwerpen op de Implementatieagenda zijn onderdeel van landelijke zorginkoopafspraken tussen*

zorgverzekeraars en zorgaanbieders. Voor de beoordeling van aanbevelingen uit richtlijnen wordt gebruikgemaakt van de implementatietabel. Op basis hiervan kunnen we de andere partijen goed informeren en gezamenlijk besluiten of plaatsing op de Implementatieagenda passend is.

Agenderen-tabel

Kennisvragen zijn vragen over bestaande zorg, die nog onvoldoende zijn onderbouwd met wetenschappelijke literatuur. Het richtlijncluster heeft een belangrijke rol bij het identificeren van kennisvragen bij het ontwikkelen van een richtlijnmodule. De input uit deze Agenderen-tabel wordt gebruikt bij het opstellen van een kennisagenda. Alle geïnventariseerde kennisvragen (vanuit achterban, patiënten en richtlijnen) op het gebied van zorgevaluatie worden beoordeeld door de kennisagenda werkgroep en daarna geprioriteerd door alle relevante partijen tijdens een prioriteringsbijeenkomst. Het is belangrijk om de kennisvraag scherp te formuleren, zodat resultaten van een zorgevaluatie onderzoek daadwerkelijk opgenomen kunnen worden in een richtlijnmodule.

Vraag	***Antwoord*** *Kruis aan*	*Vul in*
A1. Is onderzoek wenselijk om de <u>uitgangsvraag of zoekvraag</u> (met meer/voldoende zekerheid) te kunnen beantwoorden?	X	Nee. *Tijdens de ontwikkeling van deze module is gebleken dat er volgens het cluster sprake is van passend bewijs voor de uitgangsvraag en zoekvraag.* [Geef toelichting indien gewenst] *Ga verder bij vraag A5.*
		Ja
A2. Wat is de kennisvraag?	Kennis-vraag	Wat is het effect van een gestandaardiseerd protocol voor informatieoverdracht en postoperatieve follow-up vergeleken met gebruikelijke zorg op klinische uitkomsten en zorggebruik bij patiënten na hypofysechirurgie?
	P	Patiënten die hypofysechirurgie ondergaan
	I	informatieoverdracht volgens standaard protocol
	C	Huidige (variabele) praktijk
	O	Heropnames, complicaties (bv. bijnierinsufficiëntie), zorggebruik, patiënttevredenheid
A3. Waarom is dit een belangrijke kennisvraag?	Toelichting	[tekst] [b)]
A4. Welk onderzoeksdesign is passend om deze kennisvraag te beantwoorden?		RCT
	X	Observationeel onderzoek
		Kwaliteitsregistratie
		Anders, namelijk
	Toelichting	[tekst]
A5. Zijn er een andere kennisvragen naar voren gekomen die passen bij het <u>onderwerp van de module</u>,	X	Nee
		Ja

maar niet hetzelfde zijn als de uitgangs- of zoekvraag en waar *geen* passend bewijs voor is? *Bijvoorbeeld:* het onderwerp van de module is 'Behandeling van aandoening X', waarin behandeling A en behandeling B met elkaar worden vergeleken. De voor- en nadelen van behandeling C ten opzichte van A en/of B is dan nog een openstaande kennisvraag als hier geen passend bewijs voor is. Het past wel bij het onderwerp van deze module en de resultaten van zorgevaluatie onderzoek zouden wel in deze module geduid kunnen worden.		

[a)] Formuleer hier de kennisvraag als een onderzoekvraag. Dit kan de zoekvraag zijn, maar kan ook afwijken. Om het juiste onderzoek te doen is het van groot belang dat de kennisvragen scherp geformuleerd worden, in de vorm van een PICO. Uitgangspunt is dat een kennisvraag met één zorgevaluatie onderzoek opgelost kan worden.

5 [b)] Beschrijf in 2 à 3 zinnen waarom dit een relevante kennisvraag is.