

Epidemiology of tumor-related hypothalamic obesity in Germany – a representative claims data analysis

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Background

- Survivors of hypothalamic and sellar/suprasellar tumors face a risk for significant morbidity impacting health and quality of life.
- Hypothalamic obesity (HO), which presents with rapid weight gain, is often severe and associated with mechanical and metabolic consequences.
- Because HO is a rare disease, literature detailing HO underlying tumor entities and corresponding prevalence/incidence estimates is limited.

Objective

The purpose of this study was to develop a database algorithm for the standardized identification of HO-patients and related tumor diagnoses. Herein, we propose a transparent and reproducible methodological approach to refine the epidemiology of this rare disease. Based on this we calculate HO-incidence and prevalence.

Methods

Study Design

- Retrospective rolling-cohort design based on a representative German claims database (n=5.24 million) covering the years 2011-2019.

Inclusion Criteria

- Incident surgery or radiotherapy and HO-associated tumor diagnoses* (n=3,976).
- HO was identified by at least one incident obesity diagnosis and validated by incident diabetes insipidus diagnoses and desmopressin prescriptions within the quarter of surgery/radiotherapy or subsequent four quarters (Figure 1).**
- Definition of tumor diagnosis ICD-10 codes and other relevant patient identification criteria were made based on literature and after review of medical records of HO patients by the study team (JB, SB, HLM) treated at a large German pediatric clinic.

Exclusion Criteria

- To differentiate between acquired and congenital risk for HO, patients with a history of Prader-Willi syndrome (ICD-10-GM Q87.1) were excluded.

Statistical Analysis

- The primary outcome measure was the nine-year HO incidence rate using the midterm population at risk.
- Secondary outcome measures were the HO prevalence, and frequency of HO-related tumor entities.
- Sensitivity analyses: Alternating the algorithm on HO validation: #1 no mandatory diabetes insipidus diagnosis and/or desmopressin prescription, #2 including also patients with prevalent obesity before index hospitalization.

Results

HO incidence and prevalence

- Nine-year incidence of HO: 0.68 cases /100,000 persons (data: 2011-2019, Table 1). The estimated annual incidence of tumor-related HO in Germany was between 0.07 and 0.17 cases /100,000 persons.
- When extrapolated to the total German population, this would result in approx. 80 incident HO cases per year.
- The prevalence in 2019 was 1,262 cases in Germany (<20 years: 203 persons, 20-64 years: 784 persons, 65+ years: 274 persons).

HO patient characteristics

- Two HO incidence peaks are observed: children and young adults aged 10-24 years and adults aged 40-44 (Figure 2).
- Most frequent HO-validated tumor diagnoses: Benign cellular and sellar/suprasellar tumors, including tumors of the craniopharyngeal duct (0.31/100,000), neoplasms of the pituitary gland (0.41/100,000), and nonspecific brain tumors of endocrine glands (0.24/100,000, Table 2). Concerning calculated tumor-specific incidence rates, double patient counting might occur when multiple tumor entities are combined.

Uncertainty of HO diagnosis validation

- Removing the criterion of mandatory desmopressin prescription (sensitivity analysis #1) leads to substantially more patients with HO-related tumor diagnosis and subsequent incident obesity and diabetes insipidus diagnosis (Figure 3).
- Including also prevalent obesity patients (and not only obesity incident patients) does not significantly affect incidence estimations (sensitivity analysis #2).

Discussion

- This is the first claims database analysis of HCRU and costs after tumor-related HO incidence, contributing to a better understanding of the disease's relevance to healthcare systems.
- This analysis allows previously reported estimates of the economics of HO to be refined.
- A more comprehensive characterization of HO patients, along with a better understanding of its clinical and economic implications, will be crucial in developing optimal treatment strategies to improve patient outcomes.

Our model estimated the 2019 prevalence of HO in Germany to be 1,262 cases. Annual incidence of tumor-related HO in Germany range between 0.07 and 0.17 cases /100,000 persons.

Cohort Definitions

- Included tumor diagnoses based on ICD-10-GM 2011 to 2019-version: C96.6, D33.0, D33.2, D33.3, D33.7, D33.9, D35.2, D35.3, D43.2, D44.3, D44.4, D48.9, D76.3, Q04.8, Q85.0.
- Inclusion of obesity based on ICD-10-GM-codes: E66, E67, E68, R63.2, R63.5; diabetes insipidus: E23.0, E23.2, E23.3, E23.6, E23.7, P80, P81; Desmopressin prescription: ATC-code H01BA02.

Figure 1. Study cohort definition

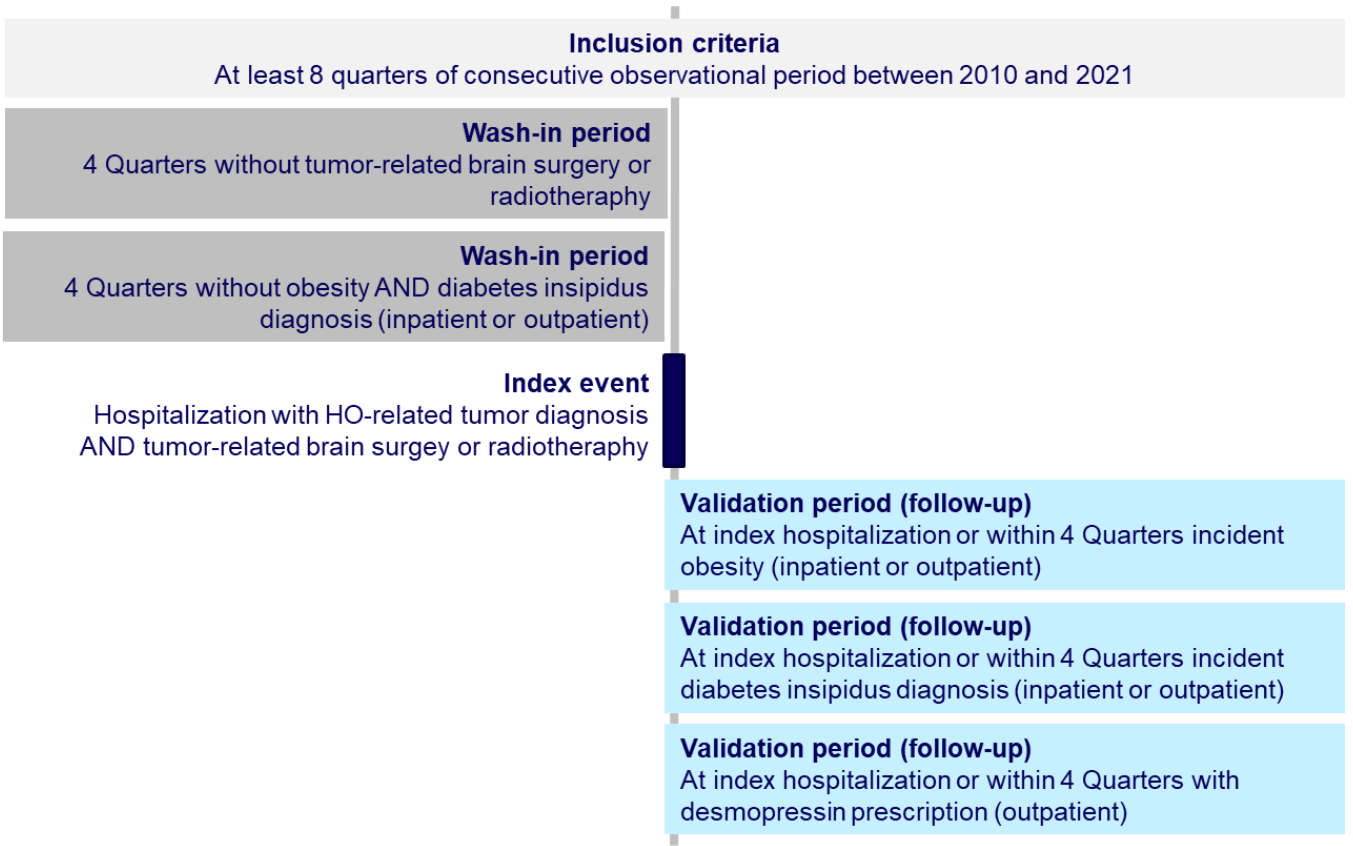


Table 1. Study population, validated HO population, estimated HO incidence rate and HO patient characteristics

	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Study population (N), (Million)	3.93	4.02	4.06	4.11	4.18	4.27	4.34	4.37	4.41	5.42
Patients with index hospitalization (n)	422	431	448	415	415	479	436	464	466	3,976
HO cases (n)	5	5	3	7	3	3	3	3	5	37
HO incidence rate (/100,000)	0.13	0.12	0.07	0.17	0.07	0.07	0.07	0.07	0.11	0.68
Mean age (SD)	40.0 (11.4)	44.0 (18.5)	44.3 (10.5)	38.4 (25.5)	26.3 (15.3)	47.3 (20.2)	31.7 (25.7)	22.7 (20.2)	40.0 (10.4)	38.0 (18.0)
Female (%)	40	60	33	86	100	33	33	67	60	59.5

Table 2. Nine-year HO-incidence per tumor entity and patient demographics

Tumor diagnosis (ICD-10-GM code)	HO incidence rate (/100,000)	Percentage of total cases (%)*	Mean age (SD)	Age groups, years (%)			Female (%)
				<20	20-64	65+	
Total	0.68	100	38.0 (18.0)	16.2	70.3	13.5	59.5
Benign neoplasm							
Brain, supratentorial (D33.0)	0.04	5.4	51.0 (12.7)	0	50	50	100
Brain, unspecified (D33.2)	0.02	2.7	25.0 (NA)	0	100	0	0
Cranial nerves (D33.3)	0.04	5.4	17.0 (9.9)	50	50	0	0
Pituitary gland (D35.2)	0.41	59.5	40.0 (16.2)	5	86	9	68
Craniopharyngeal duct (D35.3)	0.13	18.9	32.9 (22.7)	43	43	14	43
Neoplasm of uncertain or unknown behavior of endocrine glands							
Brain, unspecified (D43.2)	0.24	35.1	39.7 (20.9)	15	62	23	31
Pituitary gland (D44.3)	0.20	29.7	42.2 (15.3)	0	91	9	91
Craniopharyngeal duct (D44.4)	0.18	27.0	33.4 (20.7)	40	50	10	50
Unspecified (D48.9)	0.02	2.7	44.0 (NA)	0	100	0	0
Other histiocytosis syndromes (D76.3)	0.02	2.7	46.0 (NA)	0	100	0	0

* Diagnosis of two or more tumor entities per patient possible. "NA" Sample sizes are too small.

Figure 2. Estimated HO incidence rate per age and sex group based on a rolling nine-year cohort

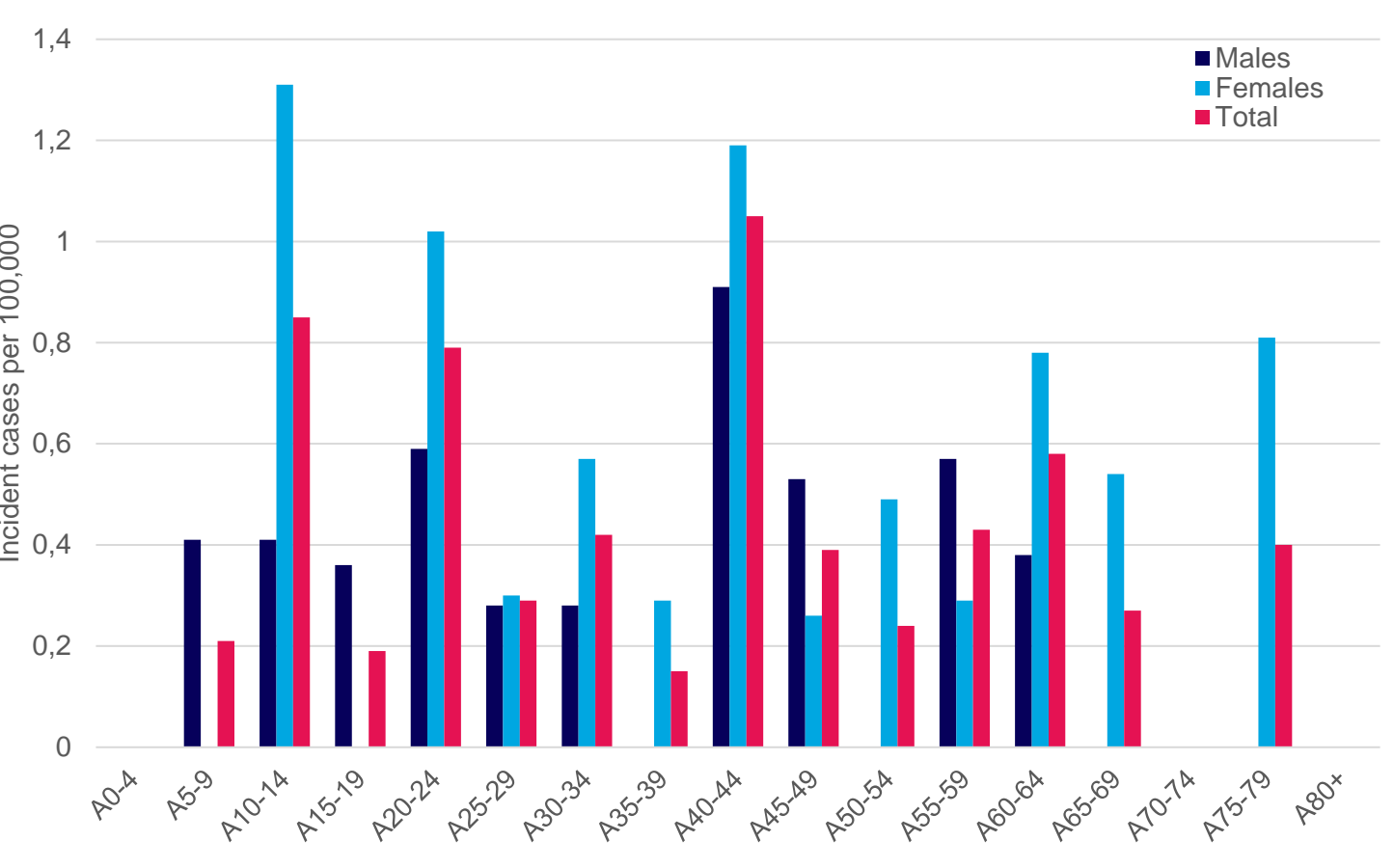
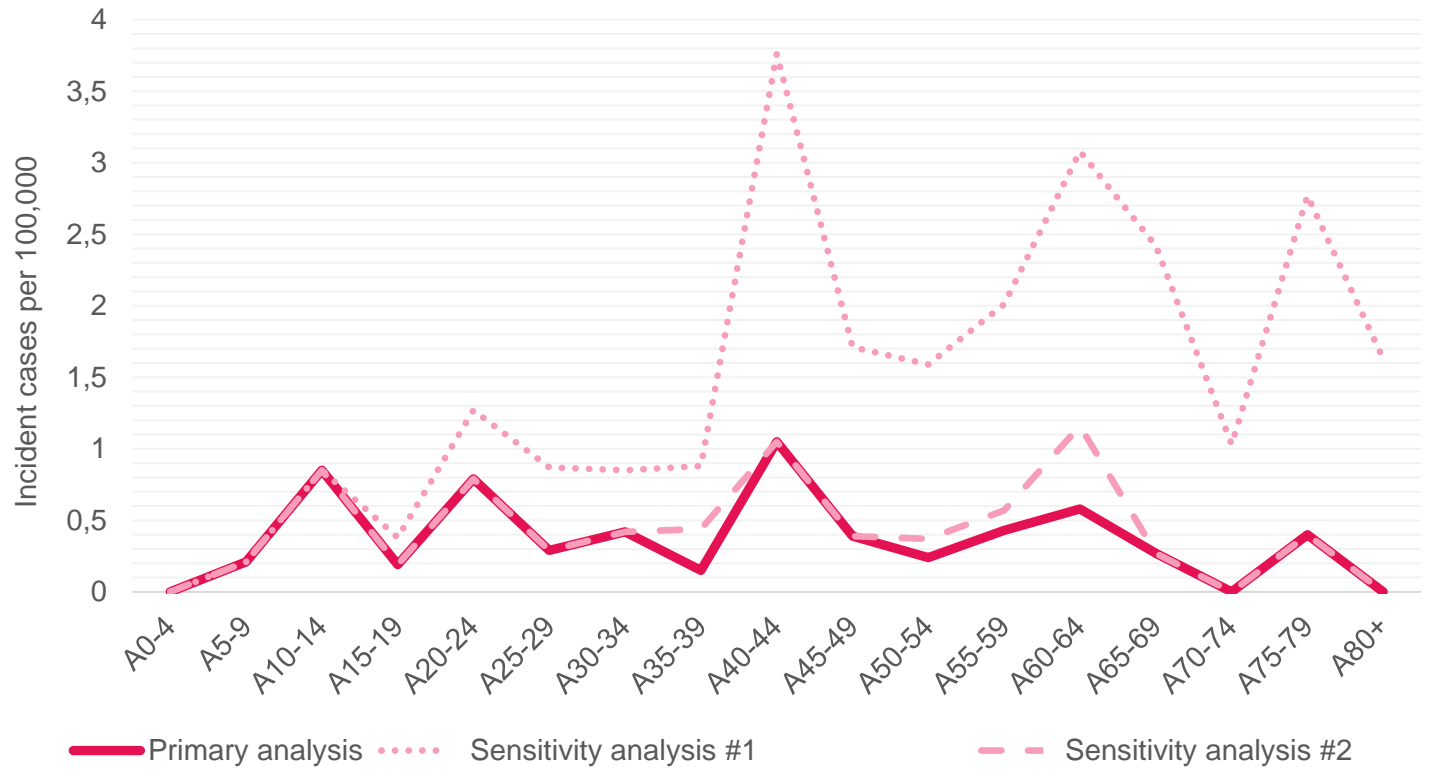


Figure 3. Sensitivity analysis on HO incidence rate per age group, total population based on a rolling 9-year cohort



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Data availability: Project-specific access to an anonymized, selected study data set for the analyses was provided by the GWQ ServicePlus AG. The data analyzed in this study are not publicly available due to data protection regulations and national legislation. All data-related processes of Vandage are under the data protection supervision of an external data protection officer.