Supplementary material

Additional analyses

The cumulative risks of post procedure de novo epilepsy were estimated in patients with ruptured or unruptured intracranial aneurysm who underwent endovascular treatment (NCSP: KAAL00) instead of a craniotomy, as endovascular procedure is unlikely to cause epilepsy. This was done for comparison with the risks among patients with similar diagnoses, but treated surgically, to get an impression of the impact of the craniotomy itself on the risk of epilepsy. Results are presented in Table 3.

The cumulative risks of de novo epilepsy were estimated according to the craniotomy being supra- or infratentorial. The following surgical procedure codes were used to define which ones of the craniotomies that were infratentorial: Retro sigmoid approach for intracranial pathology AAE55, Far lateral approach for intracranial pathology AAE70, Far lateral approach for vascular pathology AAE75, and Occipitocervical decompression ABE50. For tumours and haemorrhages of the brainstem or cerebellum, infratentorial surgeries were defined as a combination of craniotomy (AAB00, AAB10, AAB20, AAB30, AAB99) in combination with infratentorial brain cancer diagnosis (C715, C716, C717), or infratentorial intracranial haemorrhage (I613, I614). Cerebral abscesses are usually caused by bacterial spreading through the anterior circulation and are therefore located supratentorial. Traumatic hematomas are usually supratentorial as well and were therefore considered supratentorial. Results are presented in Table 4.

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The use of anti-epileptic drugs (ATC code N03A) was used as outcome measure in an additional analysis, instead of the ICD-diagnoses for epilepsy used in the main analyses. In this analysis specific diagnoses were used to exclude or censor due to the fact that anti-epileptic drugs might be used as treatment, thereby altering the risk of seizures. Patients were excluded if diagnosed before craniotomy and censored if diagnosed during follow-up. The diagnoses were ICD-10: DF31 (bipolar affective disorder), DG500 (trigeminal neuralgia), DG56, DG57, DG58, DG59 (neuropathies), DF411 (generalized anxiety disorder) and DG43 (migraine). Results are presented in supplementary table 6.

Furthermore, the cumulative risks of de novo epilepsy after craniotomy were estimated according to patient age at the time of surgery in intervals 0-9, 10-19, 20-44, 45-59, 60-69 and 70+ years of age). Results are presented in supplementary table 7. Finally, the cumulative risks of postoperative de novo epilepsy were estimated among the patients that were excluded due to 1) lack of diagnosis within the time limits, 2) ≥ 2 non-tumour indications, and 3) ≥ 2 diagnoses within the indication group. Results are presented in supplementary table 8, 9, and 10.

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Supplementary tables

Supplementary table 1. Procedure codes, Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures (NCSP), version 1.16.

Procedure	**NCSP**
Extirpation of intracranial lesion	AAB00
Partial excision of intracranial lesion	AAB10
Destruction of intracranial lesion	AAB20
Evacuation of spontaneous intracranial haematoma	AAB30
Other excision or destruction of intracranial lesion	AAB99
Ligature of intracranial aneurysm	AAC00
Ligature of feeding artery of intracranial aneurysm	AAC05
Intracranial occlusion of vascular fistula	AAC30
Extirpation of intracranial arterio-venous malformation	AAC40
Vascular malformations in the cavernous sinus	AAC45
Evacuation of epidural haematoma	AAD00
Evacuation of acute subdural haematoma	AAD05
Evacuation of traumatic intracerebral haematoma	AAD15
Sub frontal approach for intracranial pathology	AAE15
Trans labyrinthine total or partial excision of intracranial lesion	AAE30
Transtemporal total or partial excision of intracranial lesion	AAE40
Sub temporal approach for intracranial pathology	AAE45
Zygomaticotemporal total or partial excision of intracranial lesion	AAE50
Retro sigmoid approach for intracranial pathology	AAE55
Occipital approach for intracranial pathology	AAE65
Far lateral approach for intracranial pathology	AAE70
Far lateral approach for vascular pathology	AAE75
Other operation on skull or dura	AAK99
Puncture and evacuation of intracerebral abscess	AAM00
Excision of intracerebral abscess	AAM10
Evacuation of epidural or subdural empyema	AAM30
Other operation for intracranial infection	AAM99
Occipito-cervical decompression	ABE50

Supplementary table 2. Tumours, The Danish Cancer Register, International Classification of Diseases for Oncology, third edition (ICD-O-3).

Tumour type		ICD-O-3
Meningioma		
	Meningioma, Microcystic meningioma, Secretory meningioma, Lymphoplasmacyte-rich meningioma, Metaplastic meningioma	9530/0
	Meningothelial meningioma	9531/0
	Fibrous meningioma	9532/0
	Transitoria meningioma	9537/0
	Psammomatous meningioma	9533/0
	Angiomatous meningioma	9534/0
	Chordoid meningioma, Clear cell meningioma	9538/1
	Atypical meningioma	9539/1
	Papillary meningioma, Rhabdoid meningioma	9538/3
	Anaplastic meningioma	9530/3
Astrocytoma		
	Pilocytic astrocytoma	9421/1
	Pilomyxoid astrocytoma	9425/3
	Subependymal giant cell astrocytoma	9384/1
	Pleomorphic xanthoastrocytoma	9424/3
	Diffuse astrocytoma	9400/3
	Fibrillary astrocytoma	9420/3
	Gemistocytic astrocytoma	9411/3
	Protoplasmic astrocytoma	9410/3
	Anaplastic astrocytoma	9401/3
	Gliomatosis cerebri	9381/3
	Astroblastoma	9430/3
	Chordoid glioma of the third ventricle	9444/1
	Angiocentric glioma	9431/1
Glioblastoma		
	Glioblastoma	9440/3
	Giant cell glioblastoma	9441/3
	Gliosarcoma	9442/3
Oligodendroglioma		
	Oligodendroglioma	9450/3

	Anaplastic oligodendroglioma	9451/3
Oligoastrocytoma		
	Oligoastrocytoma, anaplastic oligoastrocytoma	9382/3
Ependymal		
	Subependymoma	9383/1
	Myxopapillary ependymoma	9394/1
	Ependymoma, cellular, clear cell, tanycytic	9391/3
	Papillary ependymoma	9393/3
	Anaplastic ependymoma	9392/3
Pineal region		
	Pineocytoma	9361/1
	Pineal parenchymal tumour of intermediate differentiation, pineoblastoma	9362/3
	Papillary tumour of pineal region	9395/3
Embryonal		
	Medulloblastoma	9470/3
	Desmoplastic/nodular medulloblastoma, medulloblastoma with extensive nodularity	9471/3
	Anaplastic medulloblastoma, large cell medulloblastoma	9474/3
	CNS primitive neuroectodermal tumour	9473/3
	CNS neuroblastoma	9500/3
	CNS ganglioneuroblastoma	9490/3
	Medulloepithelioma	9501/3
	Ependymoblastoma	9392/3
	Atypical teratoid/rhabdoid tumour	9508/3
Cranial nerves		
	Schwannoma, cellular, plexiform, melanotic	9560/0
Mesenchymal		
	Lipoma	8850/0
	Angiolipoma	8861/0
	Hibernoma	8880/0
	Liposarcoma	8850/3
	Solitary fibrous tumour	8815/0
	Fibrosarcoma	8810/3
	Malignant fibrous histiocytoma	8830/3
	Laiomyoma	8890/0

	Laiomyosarcoma	8890/3
	Rhabdomyoma	8900/0
	Rhabdomyosarcoma	8900/3
	Chondroma	9220/0
	Chondrosarcoma	9220/3
	Osteoma	9180/0
	Osteosarcoma	9180/3
	Haemangioma	9120/0
	Epithelioid haemangioendothelioma	9133/1
	Haemangiopericytoma	9150/1
	Anaplastic haemangiopericytoma	9150/3
	Angiosarcoma	9120/3
	Karposi sarcoma	9140/3
	Ewing sarcoma – PNET	9364/3
	Hemangioblastoma	9161/1
Germ cell		
	Germinoma	9064/3
	Embryonal carcinoma	9070/3
	Yolk sac tumour	9071/3
	Choriocarcinoma	9100/3
	Teratoma	9080/1
	Mature	9080/0
	Immature	9080/3
	Teratoma with malignant transformation	9084/3
	Mixed germ cell tumour	9085/3
Sellar region		
	Craniopharyngioma	9350/1
	Adamantinomatous	9351/1
	Papillary	9352/1
	Granular cell tumour	9582/0
	Pituicytoma	9432/1
	Spindle cell oncocytoma	8291/0
Metastasis		
	Carcinoma	8010/3
	Carcinoma, metastatic, NOS	8010/6
	Large cell carcinoma	8012/3

	Small cell carcinoma	8041/3
	Non-small cell carcinoma	8046/3
	Squamous cell carcinoma	8070/3
	Adenocarcinoma	8140/3
	Adenocarcinoma, metastatic	8140/6
	Renal cell carcinoma, unclassified	8312/3
	Malignant melanoma	8720/3
Miscellaneous		
	Choroid plexus papilloma	9390/0
	Atypical choroid plexus papilloma	9390/1
	Choroid plexus carcinoma	9390/3
	Dysplastic gangliocytoma of cerebrum	9493/0
	Desmoplastic infantile astrocytoma/ganglioglioma	9412/1
	Dysembryoplastic neuroepithelial tumour	9413/0
	Gangliocytoma	9492/0
	Ganglioglioma	9505/1
	Anaplastic ganglioglioma	9505/3
	Central neurocytoma, extra ventricular neurocytoma, cerebellar neurocytoma	9506/1
	Papillary glioneuronal tumour, rosette-forming glioneuronal tumour of fourth ventricle	9509/1
	Paraganglioma	8680/1
	Diffuse melanocytosis	8728/0
	Melanocytoma	8728/1
	Meningeal melanomatosis	8728/3

Supplementary table 3. Non-tumour pathology: Spontaneous intracranial haemorrhage, traumatic intracranial haemorrhage, abscess and congenital malformations, The National Patient Register,

Exclusion criteria	Data source	Codes	Number of excluded patients

International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10).

Disease	ICD-10
Spontaneous intracranial haemorrhage and other vascular conditions	
Ruptured aneurysm	DI601, DI602, DI603
Intracerebral haemorrhage and other non-traumatic intracranial haemorrhage	DI61, DI62
Cerebral aneurysm, non-ruptured	DI671
Arteriovenous malformation of cerebral vessels or Moya-Moya disease	DQ282, DI675
Traumatic intracranial haemorrhage	
Traumatic subdural haemorrhage	DS065, DS065A, DS065(B)
Epidural haemorrhage	DS064
Cerebral contusion or other intracranial injuries	DS068, DS063(C), DS062
Cerebral abscess	
Intracranial abscess or granuloma, extradural or subdural abscess, intracranial abscess or granuloma with other disease	DG060, DG062, DG079
Congenital malformations	
Chiari malformation or Dandy-Walker syndrome	DQ070, DQ031

Supplementary table 4. Definitions of the exclusion criteria used in the study, registers used and number of excluded patients.

Prior use of AED[1] or diagnosis of epilepsy	The National Prescription Register The National Patient Register	ATC[2]: N03A ICD-10[3]: DG40, DG41, DR252	3,752
Patients with no address in Denmark at the date of craniotomy	The Civil Registration System	-	15
Patients, in which none of the above-mentioned indications for craniotomy could be assessed, e.g., lack. of registered diagnosis within 30 days prior to the craniotomy for non-tumour indications, and before 90 days after the craniotomy for tumour indications.	The National Patient Register The Danish Cancer Register	Please, see supplementary table 2 and 3.	3,359
Patients with ≥2 non-tumour indications.	The National Patient Register The Danish Cancer Register	Please, see supplementary table 2 and 3.	367
Patients with ≥2 diagnoses within the indication group.	The National Patient Register The Danish Cancer Register	Please, see supplementary table 2 and 3.	89

1: Anti-epileptic drugs

2: Anatomic Therapeutical Codes

3: International Classification of Diseases

Supplementary table 5. The 6-months, 1-year and 5-years risks of postoperative de novo epilepsy and death after craniotomy in neurosurgical patients for all major neurosurgical diseases in Denmark, 2005-2016. Estimated state of occupancy probabilities of the four states: alive without epilepsy, alive with epilepsy, deceased without epilepsy and deceased with epilepsy.

Disease	**State**	**6 months, % (95% CI[a])**	**1 year, % (95% CI[a])**	**5 years, % (95% CI[a])**
All patients	Alive wo. epilepsy	72.3 (71.3 to 73.2)	62.2 (61.2 to 63.2)	44.2 (43.1 to 45.3)
N = 8,948	Alive w. epilepsy	8.4 (7.9 to 9.0)	10.7 (10.1 to 11.4)	10.6 (9.9 to 11.3)
	Deceased wo. epilepsy	18.0 (17.2 to 18.8)	23.9 (23.1 to 24.8)	35.4 (34.4 to 36.4)
	Deceased w. epilepsy	1.3 (1.1 to 1.5)	3.2 (2.8 to 3.6)	9.8 (9.1 to 10.4)
All intracranial tumours	Alive wo. epilepsy	72.4 (71.1 to 73.6)	58.4 (57.0 to 59.8)	35.6 (34.2 to 37.0)
N = 4,710	Alive w. epilepsy	9.2 (8.4 to 10.1)	10.4 (9.6 to 11.3)	6.9 (6.2 to 7.8)
	Deceased wo. epilepsy	16.6 (15.6 to 17.7)	26.2 (25.0 to 27.5)	42.6 (41.2 to 44.1)
	Deceased w. epilepsy	1.8 (1.4 to 2.2)	5.0 (4.4 to 5.6)	14.9 (13.8 to 16.0)
Astrocytoma	Alive wo. epilepsy	81.6 (76.9 to 86.6)	71.4 (66.0 to 77.3)	48.6 (42.5 to 55.7)
N = 245	Alive w. epilepsy	9.4 (6.4 to 13.9)	13.9 (10.2-19.0)	14.6 (10.4 to 20.5)
	Deceased wo. epilepsy	8.2 (5.4 to 12.4)	12.2 (8.8 to 17.1)	22.0 (17.3 to 28.0)
	Deceased w. epilepsy	0.8 (0.2 to 3.2)	2.4 (1.1 to 5.4)	14.8 (10.7 to 20.4)
Cranial nerves	Alive wo. epilepsy	97.2 (95.3 to 99.0)	96.8 (94.9 to 98.8)	95.7 (93.4 to 98.0)
N = 316	Alive w. epilepsy	0.6 (0.2 to 2.5)	0.9 (0.3 to 2.9)	1.4 (0.5 to 3.6)
	Deceased wo. epilepsy	1.9 (0.9 to 4.2)	1.9 (0.9 to 4.2)	2.6 (1.3 to 5.3)
	Deceased w. epilepsy	0.3 (0.0 to 2.2)	0.3 (0.0 to 2.2)	0.3 (0.0 to 2.2)
Embryonal	Alive wo. epilepsy	81.7 (74.6 to 89.5)	76.9 (69.2 to 85.5)	52.2 (43.0 to 63.4)
N = 104	Alive w. epilepsy	4.8 (2.0 to 11.3)	3.8 (1.5 to 10.1)	4.0 (1.3 to 11.9)
	Deceased wo. epilepsy	10.6 (6.0 to 18.5)	13.5 (8.3 to 21.9)	29.7 (21.8 to 40.5)
	Deceased w. epilepsy	2.9 (0.9 to 8.8)	5.8 (2.7 to 12.5)	14.1 (8.6 to 23.0)
Glioblastoma	Alive wo. epilepsy	60.9 (58.6 to 63.4)	37.1 (34.8 to 39.6)	2.1 (1.4 to 3.1)
N = 1,593	Alive w. epilepsy	12.9 (11.3 to 14.6)	13.1 (11.6 to 14.9)	1.6 (1.0 to 2.4)
	Deceased wo. epilepsy	22.6 (20.6 to 24.8)	39.3 (37.0 to 41.8)	67.1 (64.8 to 69.5)
	Deceased w. epilepsy	3.6 (2.8 to 4.6)	10.4 (9.0 to 12.0)	29.2 (27.0 to 31.6)
Meningioma	Alive wo. epilepsy	85.5 (83.6 to 87.5)	82.2 (80.2 to 84.4)	70.1 (67.5 to 72.9)
N = 1,245	Alive w. epilepsy	9.4 (7.9 to 11.2)	12.0 (10.3 to 13.9)	16.6 (14.5 to 18.9)
	Deceased wo. epilepsy	5.1 (4.0 to 6.4)	5.7 (4.6 to 7.1)	10.8 (9.1 to 12.8)

	Deceased w. epilepsy	0 (NA)	0.1 (0.0 to 0.6)	2.5 (1.7 to 3.7)
Mesenchymal	Alive wo. epilepsy	90.5 (85.0 to 96.3)	88.6 (82.7 to 94.9)	83.9 (76.8 to 91.5)
N = 105	Alive w. epilepsy	5.7 (2.6 to 12.4)	6.7 (3.3 to 13.6)	5.8 (2.7 to 12.7)
	Deceased wo. epilepsy	2.9 (0.9 to 8.7)	3.8 (1.5 to 10.0)	7.4 (3.6 to 15.4)
	Deceased w. epilepsy	1.0 (0.1 to 6.7)	1.0 (0.1 to 6.7)	2.9 (0.9 to 8.8)
Metastasis	Alive wo. epilepsy	53.4 (49.9 to 57.1)	32.3 (29.1 to 35.8)	5.8 (4.3 to 8.0)
N = 746	Alive w. epilepsy	4.6 (3.3 to 6.3)	4.4 (3.2 to 6.2)	0.7 (0.1 to 3.2)
	Deceased wo. epilepsy	39.5 (36.2 to 43.2)	57.8 (54.3 to 61.4)	82.2 (79.4 to 85.0)
	Deceased w. epilepsy	2.5 (1.6 to 4.0)	5.5 (4.1 to 7.4)	11.3 (9.1 to 14.0)
Oligodendroglioma	Alive wo. epilepsy	74.1 (68.2 to 80.5)	52.3 (45.7 to 59.9)	14.6 (10.1 to 21.2)
N = 193	Alive w. epilepsy	16.6 (12.1 to 22.8)	19.7 (14.8 to 26.2)	15.3 (10.7 to 22.0)
	Deceased wo. epilepsy	9.3 (6.0 to 14.5)	22.3 (17.1 to 29.0)	41.8 (35.2 to 49.6)
	Deceased w. epilepsy	0 (NA)	5.7 (3.2 to 10.1)	28.3 (22.2 to 36.0)
All spontaneous intracranial	Alive wo. epilepsy	74.5 (72.8 to 76.2)	68.6 (66.8 to 70.5)	57.0 (55.1 to 59.1)
haemorrhages	Alive w. epilepsy	6.5 (5.6 to 7.5)	10.5 (9.4 to 11.8)	15.1 (13.7 to 16.6)
N = 2,519	Deceased wo. epilepsy	18.7 (17.2 to 20.2)	20.1 (18.6 to 21.7)	24.7 (23.0 to 26.4)
	Deceased w. epilepsy	0.4 (0.2 to 0.7)	0.8 (0.5 to 1.2)	3.2 (2.6 to 4.1)
Ruptured aneurysm	Alive wo. epilepsy	77.2 (74.2 to 80.2)	71.9 (68.7 to 75.2)	63.3 (59.8 to 67.0)
N = 740	Alive w. epilepsy	5.3 (3.9 to 7.2)	9.6 (7.7 to 12.0)	13.9 (11.5 to 16.7)
	Deceased wo. epilepsy	17.6 (15.0 to 20.5)	18.4 (15.8 to 21.4)	21.4 (18.6 to 24.6)
	Deceased w. epilepsy	0 (NA)	0.1 (0.0 to 1.0)	1.5 (0.8 to 2.8)
AVM or	Alive wo. epilepsy	83.6 (78.2 to 89.5)	82.4 (76.8 to 88.4)	67.9 (60.8 to 75.7)
Moya-Moya disease	Alive w. epilepsy	12.7 (8.5 to 19.0)	13.3 (9.0 to 19.7)	22.0 (16.4 to 29.6)
N = 165	Deceased wo. epilepsy	3.6 (1.7 to 8.0)	3.6 (1.7 to 8.0)	7.3 (4.1 to 13.0)
	Deceased w. epilepsy	0 (NA)	0.6 (0.1 to 4.3)	2.8 (1.1 to 7.6)
Non-ruptured	Alive wo. epilepsy	94.2 (92.1 to 96.5)	91.9 (89.4 to 94.5)	84.8 (81.4 to 88.4)
aneurysm	Alive w. epilepsy	3.5 (2.1 to 5.7)	5.1 (3.4 to 7.6)	6.5 (4.4 to 9.4)
N = 434	Deceased wo. epilepsy	2.1 (1.1 to 4.0)	2.8 (1.6 to 4.8)	6.9 (4.8 to 9.9)
	Deceased w. epilepsy	0.2 (0.0 to 1.6)	0.2 (0.0 to 1.6)	1.8 (0.9 to 3.8)
Intracerebral	Alive wo. epilepsy	64.2 (61.5 to 67.0)	56.1 (53.3 to 59.0)	41.4 (38.5 to 44.4)
haemorrhage	Alive w. epilepsy	7.5 (6.1 to 9.1)	12.7 (11.0 to 14.8)	18.0 (15.8 to 20.5)
	Deceased wo. epilepsy	27.5 (25.1 to 30.2)	29.8 (27.3 to 32.6)	35.7 (33.0 to 38.6)
N = 1,180	Deceased w. epilepsy	0.8 (0.4 to 1.5)	1.4 (0.8 to 2.2)	4.9 (3.7 to 6.5)
All traumatic intracranial	Alive wo. epilepsy			
haemorrhages		66.2 (63.7 to 68.7)	60.6 (58.1 to 63.2)	46.3 (43.6- to 49.1)
N = 1,366	Alive w. epilepsy	7.1 (5.9 to 8.6)	9.3 (7.9 to 11.0)	11.6 (9.9 to 13.6)

		Deceased wo. epilepsy	25.4 (23.2 to 27.8)	28.3 (26.0 to 30.8)	36.7 (34.2 to 39.4)
		Deceased w. epilepsy	1.3 (0.8 to 2.1)	1.8 (1.2 to 2.7)	5.4 (4.3 to 6.9)
	Cerebral	Alive wo. epilepsy			
	contusion		61.7 (55.5 to 68.5)	55.1 (48.8 to 62.2)	40.3 (34.1 to 47.7)
	N = 214	Alive w. epilepsy	6.1 (3.6 to 10.3)	11.7 (8.1 to 17.0)	19.5 (14.6 to 26.0)
		Deceased wo. epilepsy	30.4 (24.8 to 37.2)	31.3 (25.7 to 38.2)	34.5 (28.7 to 41.6)
		Deceased w. epilepsy	1.9 (0.7 to 4.9)	1.9 (0.7 to 4.9)	5.7 (3.2 to 10.0)
	Epidural	Alive wo. epilepsy			
	haematoma		84.8 (80.7 to 89.2)	83.4 (79.1 to 87.9)	77.1 (72.2 to 82.3)
	N = 277	Alive w. epilepsy	6.1 (3.9 to 9.7)	7.2 (4.7 to 11.0)	9.5 (6.6 to 13.8)
		Deceased wo. epilepsy	9.0 (6.2 to 13.1)	9.0 (6.2 to 13.1)	11.0 (7.9 to 15.5)
		Deceased w. epilepsy	0 (NA)	0.4 (0.1 to 2.6)	2.3 (1.1 to 5.2)
	Traumatic	Alive wo. epilepsy			
	subdural		61.4 (58.2 to 64.7)	54.7 (51.5 to 58.1)	37.7 (34.5 to 41.3)
	haematoma	Alive w. epilepsy	7.7 (6.1 to 9.6)	9.4 (7.6 to 11.5)	10.2 (8.3 to 12.7)
	N = 875	Deceased wo. epilepsy	29.4 (26.5 to 32.5)	33.6 (30.6 to 36.9)	45.6 (42.3 to 49.2)
		Deceased w. epilepsy	1.6 (1.0 to 2.7)	2.3 (1.5 to 3.5)	6.4 (4.9 to 8.5)
Intracranial abscess		Alive wo. epilepsy	74.2 (69.2 to 79.5)	66.5 (61.2 to 72.4)	53.3 (47.4 to 59.9)
N = 275		Alive w. epilepsy	20.4 (16.1 to 25.7)	25.8 (21.1 to 31.5)	29.7 (24.6 to 36.0)
		Deceased wo. epilepsy	4.4 (2.5 to 7.6)	5.8 (3.6 to 9.4)	10.9 (7.6 to 15.7)
		Deceased w. epilepsy	1.1 (0.4 to 3.4)	1.8 (0.8 to 4.3)	6.0 (3.6 to 10.1)
Congenital malformations		Alive wo. epilepsy	96.2 (92.0 to 100.0)	96.2 (92.0 to 100.0)	89.8 (82.8 to 97.4)
N = 78		Alive w. epilepsy	3.8 (1.3 to 11.7)	3.8 (1.3 to 11.7)	5.6 (2.1 to 14.7)
		Deceased wo. epilepsy	0 (NA)	0 (NA)	4.6 (1.5 to 14.2)
		Deceased w. epilepsy	0 (NA)	0 (NA)	0 (NA)

a: CI: Confidence interval

b: No analyses done for the six small cancer groups (oligoastrocytoma, ependymal, pineal region, germ cell, sellar region and miscellaneous)

Supplementary table 6. The 6-months, 1-year and 5-years cumulative risks of postoperative de novo epilepsy and death after craniotomy in neurosurgical patients for all major neurosurgical diseases in Denmark, 2005-2016 measured by use of anti-epileptic drugs (AED).

Disease	**Total no. of patients**	**Patients with AED treatment**	**CR[a] 6 months, % (95% CI[b])**	**CR[a] 1 year, % (95% CI[b])**	**CR[a] 5 years, % (95% CI[b])**
All patients	8,550	2,412	13.2 (12.5-13.9)	19.0 (18.2-19.9)	27.9 (27.0-28.9)
All intracranial tumours	4,515[c]	1,388	16.1 (15.0-17.2)	21.8 (20.6-23.0)	30.8 (29.5-32.3)
Astrocytoma	236	80	16.9 (12.8-22.5)	21.2 (16.6-27.1)	33.1 (27.5-40.0)
Cranial nerves	300	29	2.3 (1.1-4.9)	4.0 (2.3-7.0)	10.2 (7.1-14.7)
Embryonal	101	17	2.0 (0.5-7.8)	4.0 (1.5-10.3)	15.4 (9.5-25.1)
Glioblastoma	1,539	615	22.3 (20.3-24.5)	31.2 (29.0-33.6)	40.8 (38.3-43.3)
Meningioma	1,187	325	13.4 (11.6-15.5)	17.2 (15.2-19.5)	26.5 (24.0-29.3)
Mesenchymal	103	19	7.8 (4.0-15.2)	9.8 (5.4-17.6)	15.4 (9.6-24.7)
Metastasis	713	178	14.7 (12.4-17.6)	19.8 (17.1-23.0)	25.2 (22.1-28.6)
Oligodendroglioma	179	93	26.8 (21.1-34.2)	36.9 (30.4-44.7)	54.5 (47.4-62.8)
All spontaneous intracranial haemorrhages	2,386	598	8.5 (7.5-9.7)	15.3 (13.9-16.8)	24.3 (22.5-26.1)
Ruptured aneurysm	711	161	7.0 (5.4-9.2)	13.0 (10.7-15.7)	21.4 (18.5-24.7)
AVM or Moya Moya disease	150	41	12.7 (8.3-19.3)	16.0 (11.1-23.1)	25.9 (19.6-34.3)
Cerebral aneurysm, non-ruptured	390	70	5.9 (4.0-8.8)	9.0 (6.6-12.4)	17.9 (14.3-22.5)
Intracerebral haemorrhage	1,135	326	9.8 (8.2-11.7)	18.8 (16.6-21.2)	28.1 (25.5-30.9)
All traumatic intracranial haemorrhages	1,311	295	9.5 (8.0-11.2)	13.9 (12.1-15.9)	21.7 (19.5-24.1)
Cerebral contusion	207	63	8.2 (5.2-13.0)	15.6 (11.3-21.4)	29.3 (23.5-36.4)
Epidural haematoma	271	38	4.1 (2.3-7.3)	6.3 (4.0-10.0)	13.8 (10.1-18.8)
Traumatic subdural haematoma	833	194	11.5 (9.6-13.9)	15.9 (13.6-18.6)	22.4 (19.6-25.5)
Intracranial abscess	266	117	26.7 (21.9-32.6)	33.8 (28.6-40.0)	43.8 (38.0-50.4)
Congenital malformations	72	14	7.0 (3.0-16.2)	9.8 (4.9-19.8)	21.1 (12.8-34.8)

Abbreviation: aSAH: Aneurysmal subarachnoid haemorrhage, AVM: Arteriovenous malformation of cerebral vessels, ICH: Intracerebral haemorrhage

a: Cumulative risks are the summation of patients alive with epilepsy and deceased with epilepsy

b: CI: Confidence interval

c: No analyses done for the six small cancer groups (oligoastrocytoma, ependymal, pineal region, germ cell, sellar region and miscellaneous)

Supplementary table 7. The 6-months, 1-year and 5-years cumulative risks of postoperative de novo epilepsy in neurosurgical patients according to age of patient at the time of surgery.

Age-groups	**Total patients** **N = 8,948**	**Patients with epilepsy** **N = 1,833**	**CR[a] 6 months, %** **(95% CI[b])**	**CR[a] 1 year, %** **(95% CI[b])**	**CR[a] 5 years, %** **(95% CI[b])**
0 – 9	255	42	8.6 (5.8-12.9)	9.8 (6.8-14.2)	14.2 (10.4-19.3)
10 – 19	300	49	7.7 (5.2-11.4)	10.0 (7.1-14.0)	14.8 (11.2-19.6)
20 – 44	1,384	316	9.5 (8.1-11.2)	13.9 (12.2-15.8)	22.5 (20.3-24.9)
45 – 59	2,648	639	10.6 (9.5-11.9)	16.0 (14.7-17.5)	24.3 (22.6-26.0)
60 – 69	2,417	492	9.9 (8.8-11.2)	14.1 (12.8-15.6)	20.5 (18.9-22.2)
70+	1,944	295	8.7 (7.6-10.1)	11.7 (10.3-13.2)	15.0 (13.5-16.7)

a: Cumulative risks are the summation of patients alive with epilepsy and deceased with epilepsy

b: CI: Confidence interval

Supplementary table 8. The 6-months, 1-year and 5-years cumulative risks of postoperative de novo epilepsy in patients excluded from the main analyses due to lack of diagnosis within the time limits.

Total no. of patients	**Patients with epilepsy**	**CR[a] 6 months, % (95% CI[b])**	**CR[a] 1 year, % (95% CI[b])**	**CR[a] 5 years, % (95% CI[b])**
3,359	399	5.7 (5.0-6.5)	7.7 (6.8-8.6)	11.9 (10.8-13.0)

a: Cumulative risks are the summation of patients alive with epilepsy and deceased with epilepsy

b: CI: Confidence interval

Supplementary table 9. The 6-months, 1-year and 5-years cumulative risks of postoperative de novo epilepsy in patients with ≥2 non-tumour indications.

	Total no. of patients	**Patients with epilepsy**	**CR[a] 6 months, % (95% CI[b])**	**CR[a] 1 year, % (95% CI[b])**	**CR[a] 5 years, % (95% CI[b])**
Patients with ≥2 non-tumour indications.	367	76	12.5 (9.6-16.4)	15.3 (12.0-19.4)	21.3 (17.4-26.0)

a: Cumulative risks are the summation of patients alive with epilepsy and deceased with epilepsy

b: CI: Confidence interval

Supplementary table 10. The 6-months, 1-year and 5-years cumulative risks of postoperative de novo epilepsy among patients with more than two diagnoses within the indication group. .

	Total no. of patients	**Patients with epilepsy**	**CR[a] 6 months, % (95% CI[b])**	**CR[a] 1 year, % (95% CI[b])**	**CR[a] 5 years, % (95% CI[b])**
Patients with ≥2 diagnoses within the indication group	89	14	3.4 (1.1-10.3)	6.7(3.1-14.6)	16.4(10.1-26.5)

a: Cumulative risks are the summation of patients alive with epilepsy and deceased with epilepsy

b: CI: Confidence interval

Supplementary figure 1. Representation of the multistate model with states i) alive without epilepsy, ii) alive with epilepsy, iii) deceased without epilepsy and iv) deceased with epilepsy.