Tumours of the Central Nervous System (CNS)

May 2021

European Commission

Content of the lesson

- Epidemiological information
  - Incidence & survival in Europe
- Symptoms & diagnostic procedures
- Topography
- Morphology
- Stage
- Treatment

Epidemiological information

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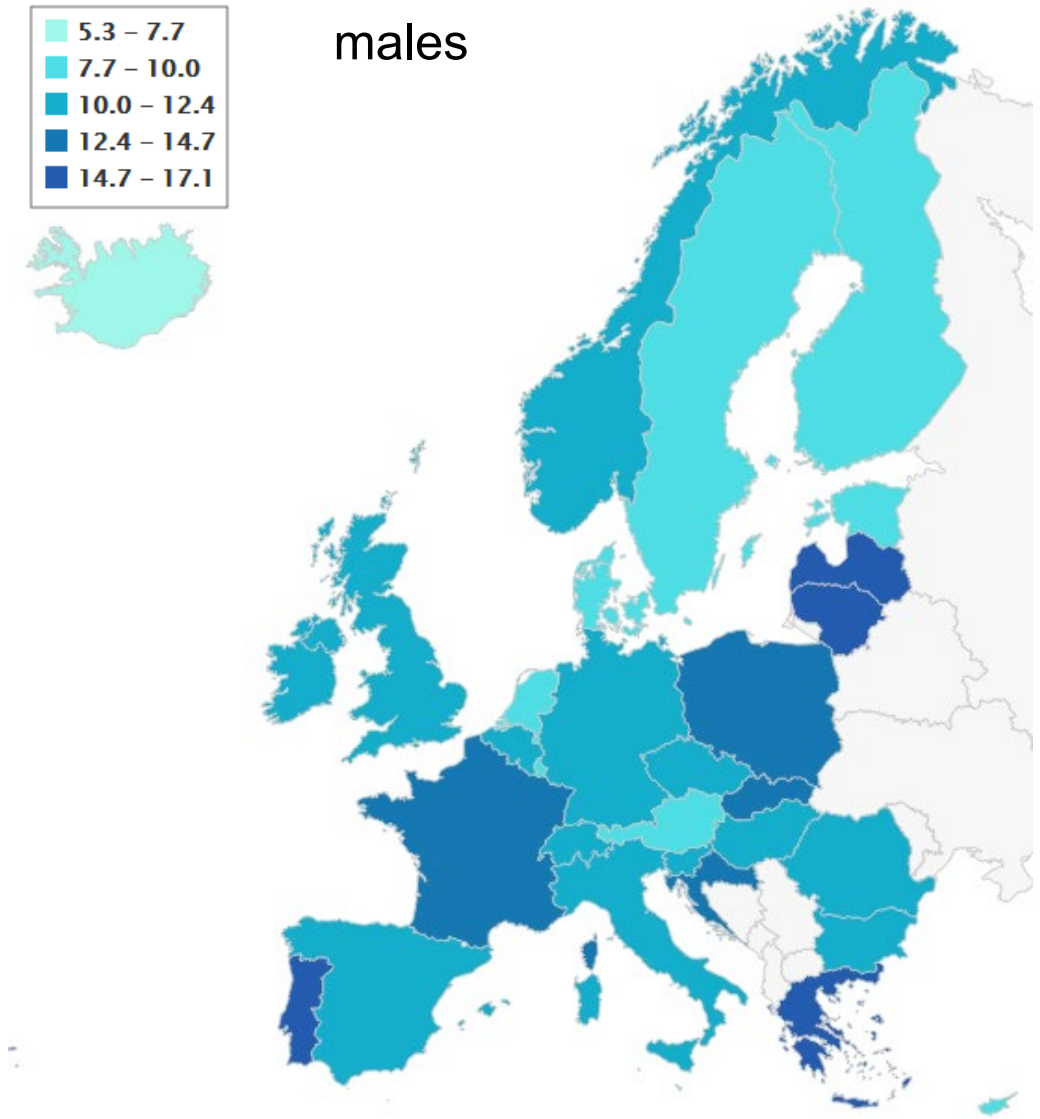
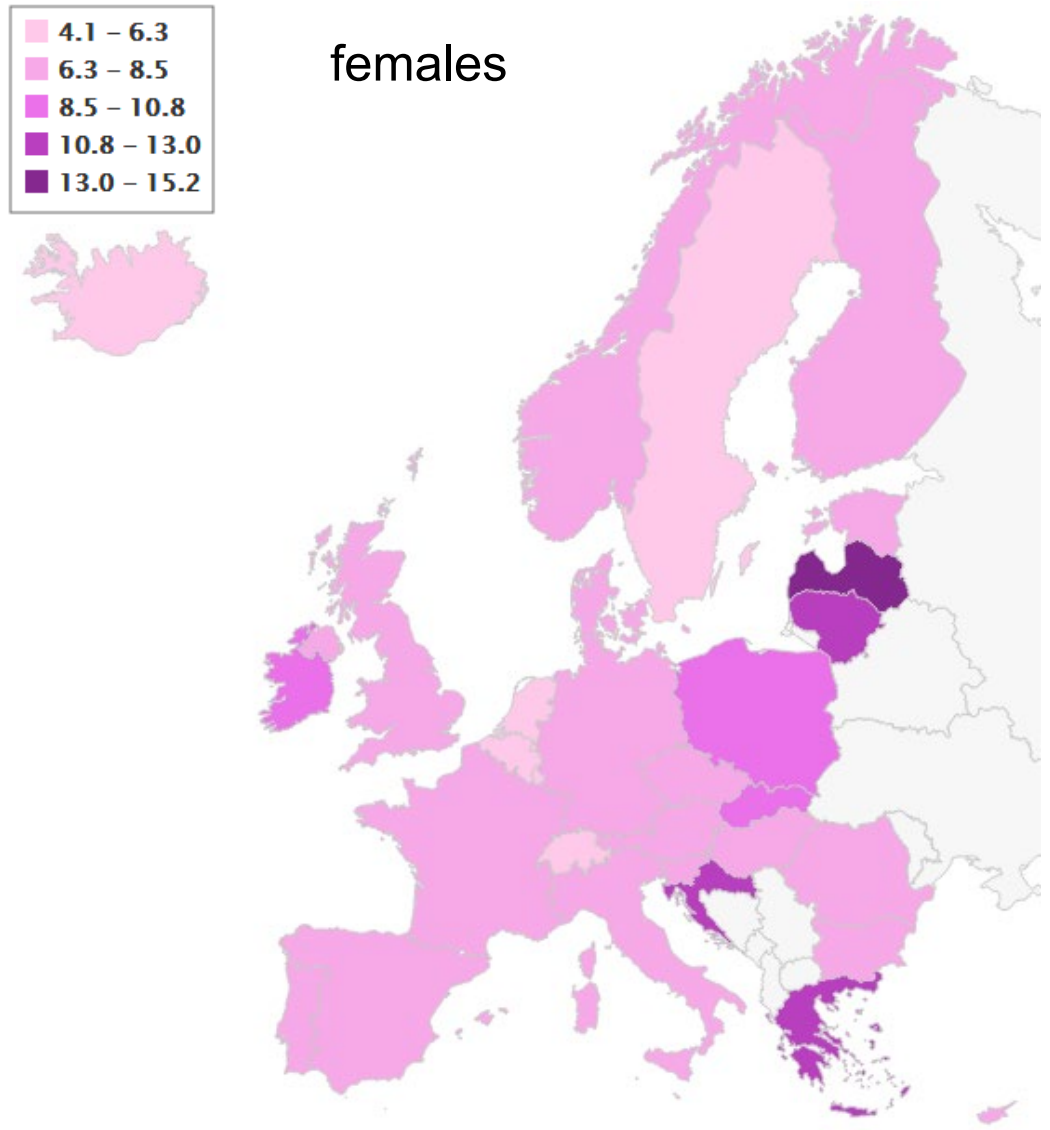
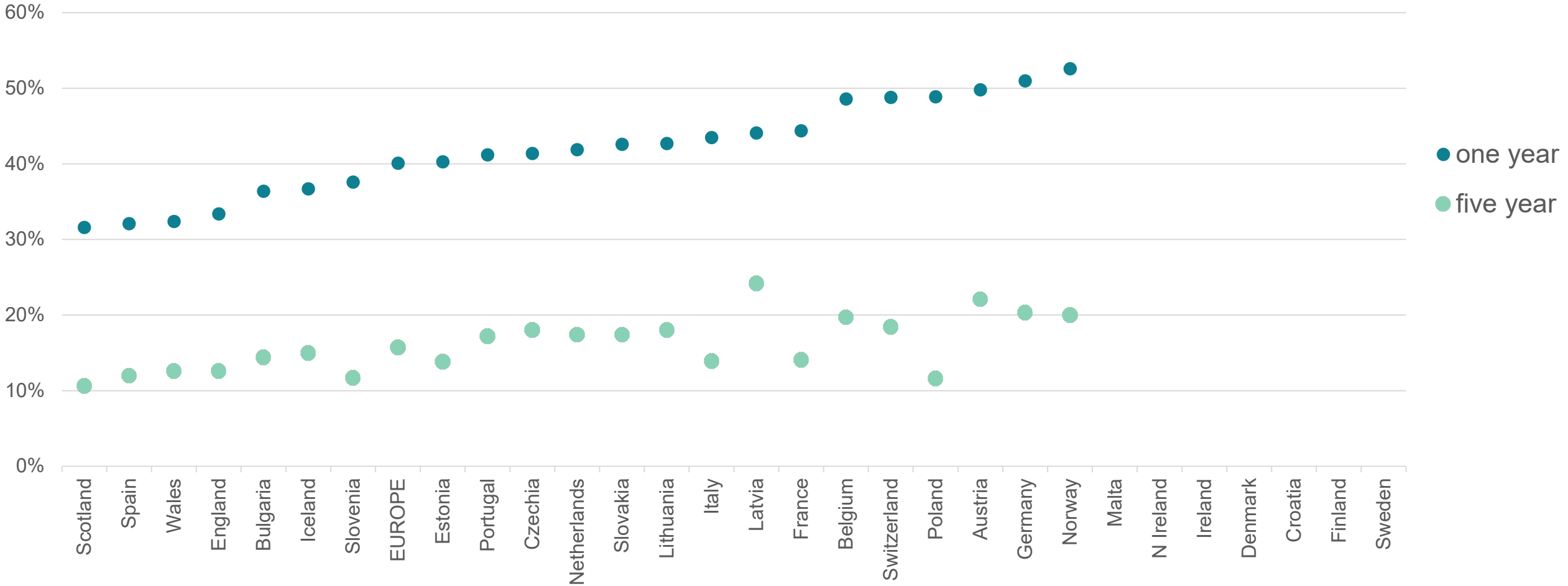
Incidence of CNS tumours in Europe – 2018 estimates (https://ecis.jrc.ec.europa.eu/)





Relative survival of brain tumours in 2000-2007
(EUROCARE-5)



Symptoms & diagnostic procedures

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Symptoms – brain tumours

- headaches
- seizures (convulsion or fits)
- nausea and vomiting
- changes to eyesight
- drowsiness/lethargy
- changes in personality
- language problems/slurring speech
- co-ordination problems
- dizziness
- difficulty swallowing
- problems with smell, hearing and sight
- inability to gaze upwards
- changes in facial expression

Symptoms – spinal cord tumours

- pain
- numbness
- weakness in either the arms or legs
- loss of bladder or bowel control

Diagnostic procedures

- History and physical examination
- Imaging
  - Magnetic resonance imaging (MRI)
  - Computed tomography (CT)
  - Sometimes: positron emission tomography (PET)
- Biopsy
  - Pathology for typing and grading
  - Immunohistochemistry and/or molecular/cytogenetic tests for mutational status and cytogenetic aberrations

Topography

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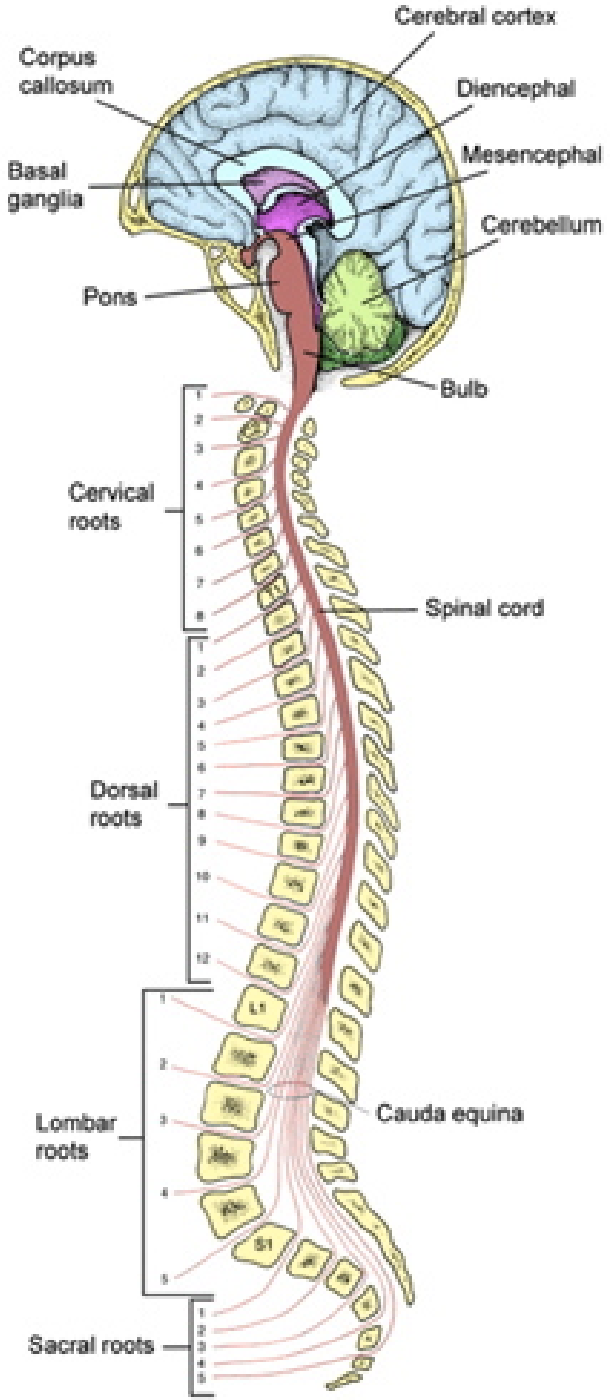
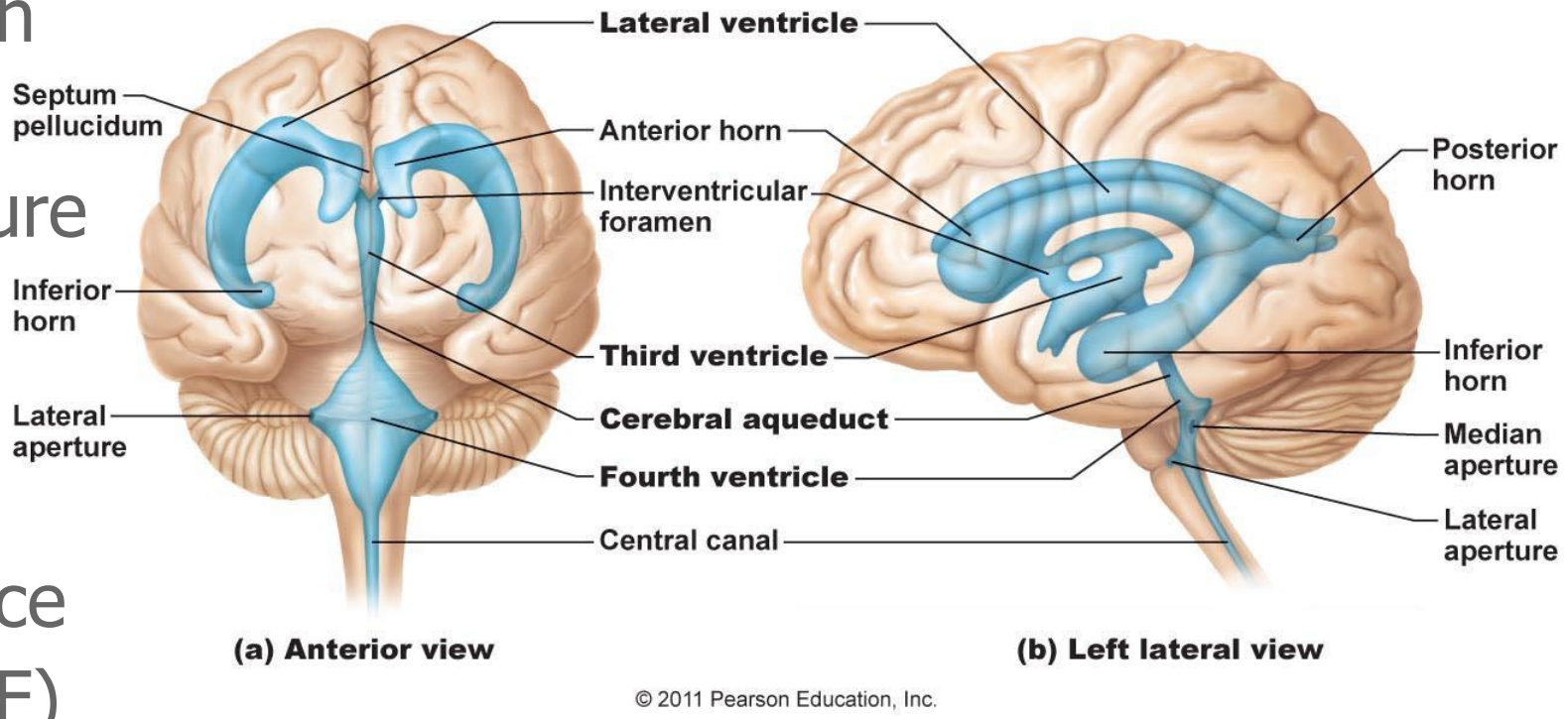
Brain and spinal cord

- Cortex
  - Frontal lobe (C71.1)
  - Temporal lobe (C71.2)
  - Parietal lobe (C71.3)
  - Occipital lobe (C71.4)
- Basal ganglia (C71.0)
- Cerebellum (C71.6)
- Brain stem (C71.7)
- Ventricles (C71.5)
- Spinal cord/cauda equina (C72.0/C72.1)



The ventricles of the brain

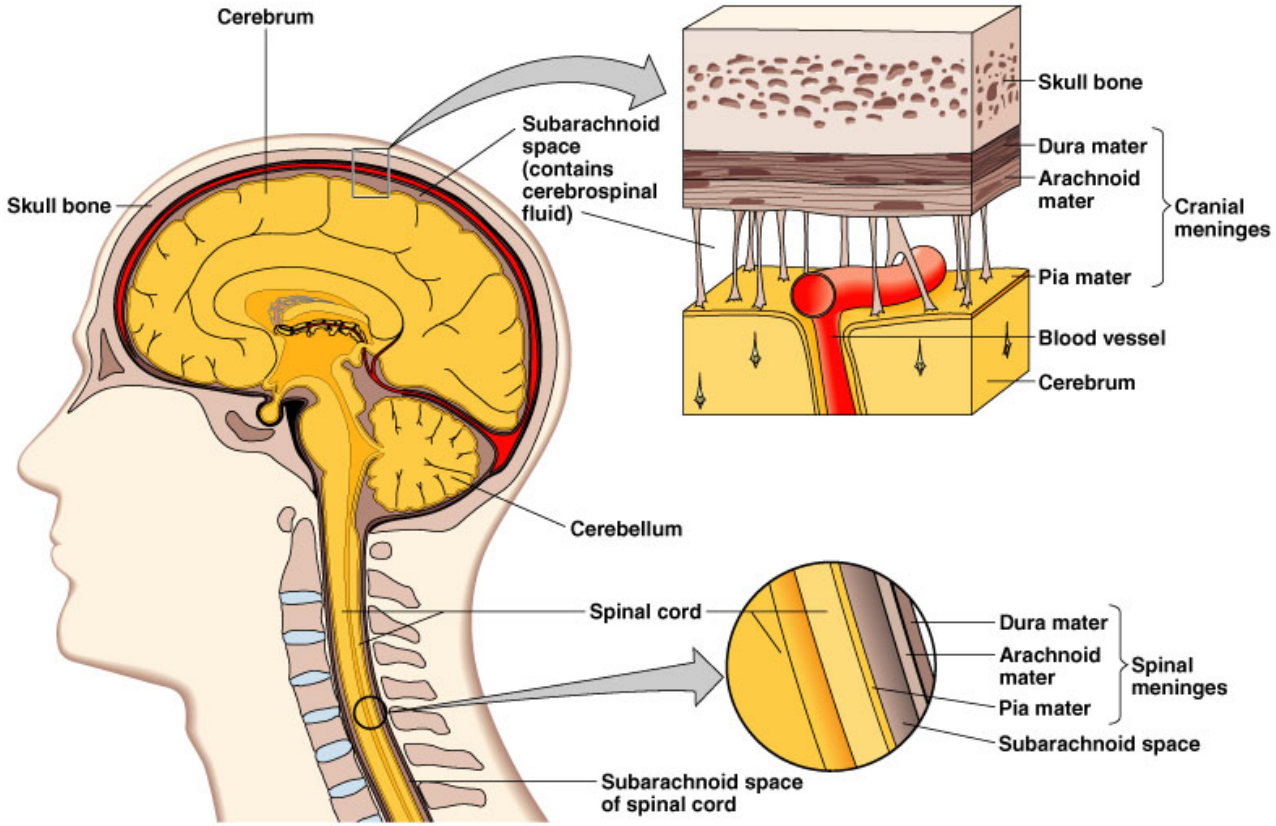
- the ventricles are lined with ependymal cells
- the only anatomical structure in the ventricles is the choroid plexus (also lined with ependymal cells)
- the ependymal cells produce the cerebrospinal fluid (CSF)



- the CSF circulates in the ventricles, the central canal and around the CNS

Meninges

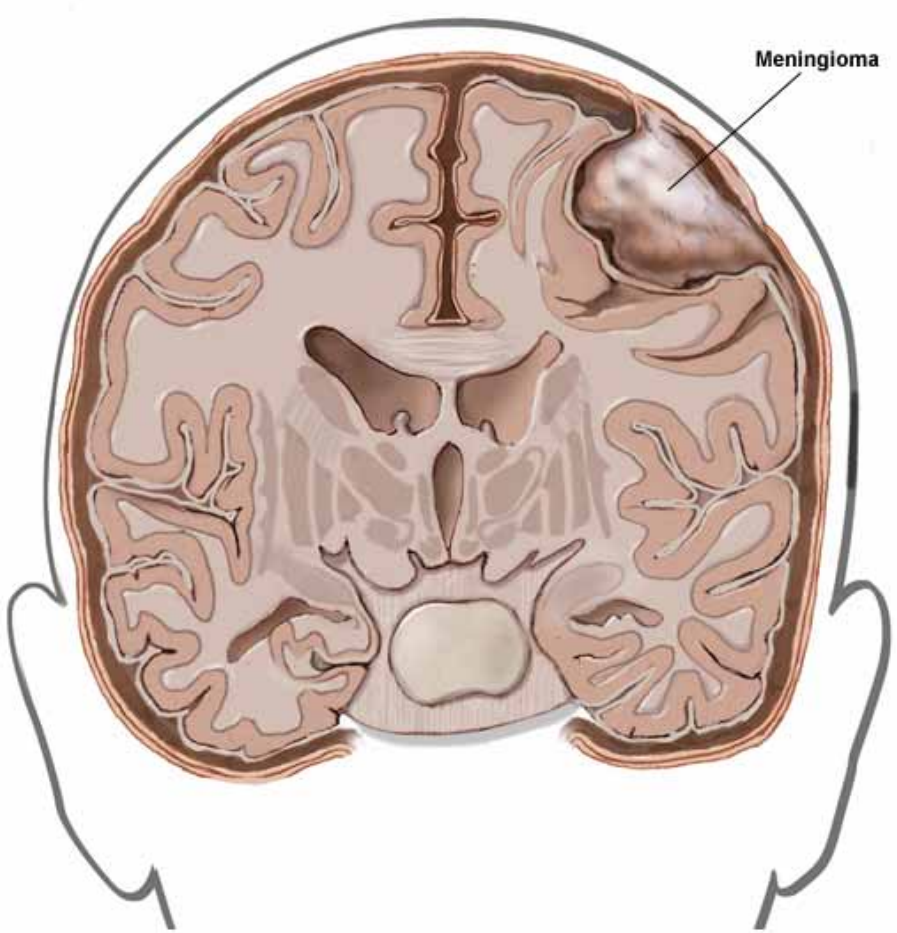
- Cerebral meninges C70.0
- Spinal meninges C70.1



Topography of the tumours of the meninges

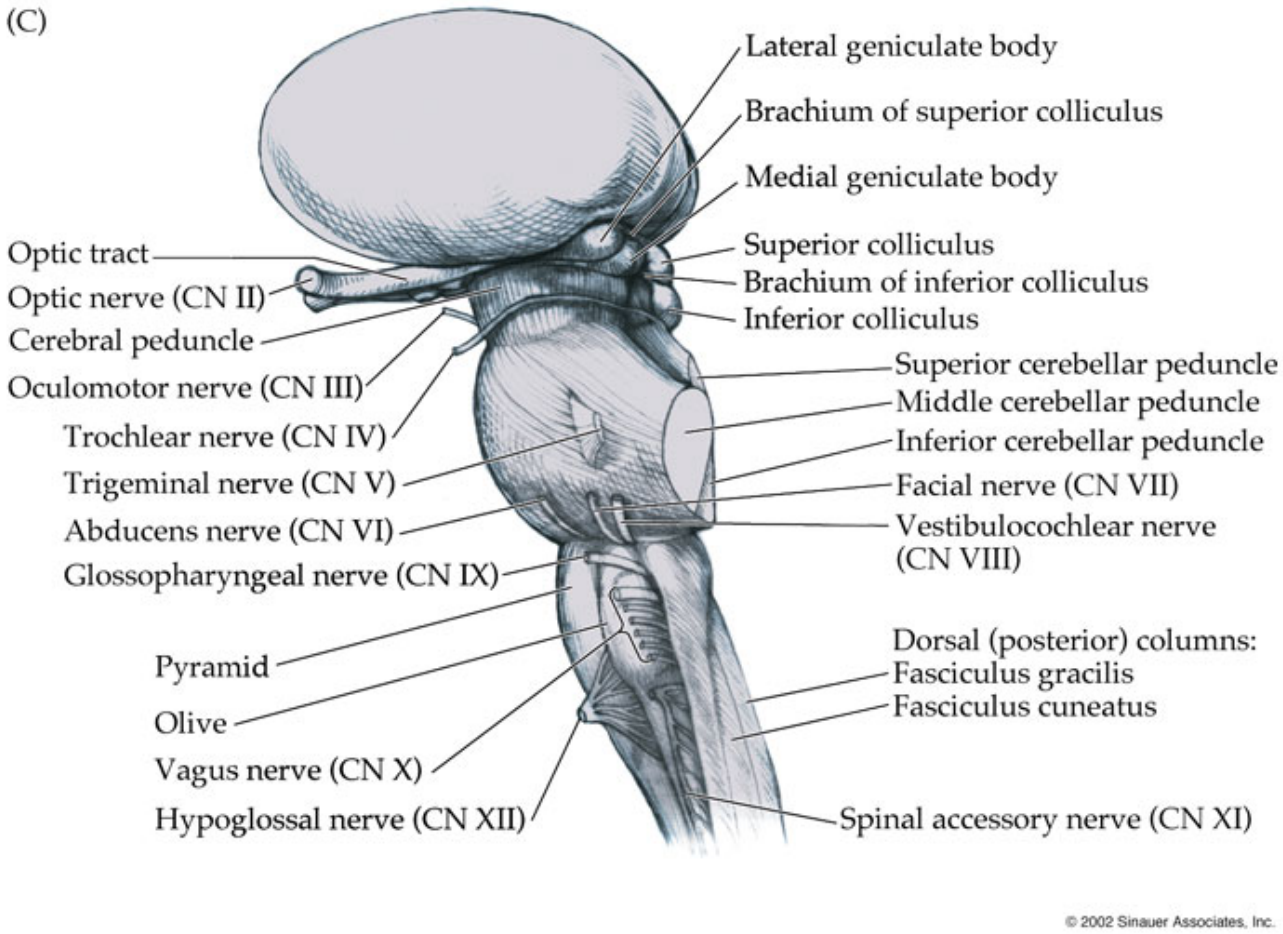
A meningioma of the CNS should always be coded on C70!

- 'Meningioma of the brain' = C70.0
- 'Meningioma of the spinal cord' = C70.1

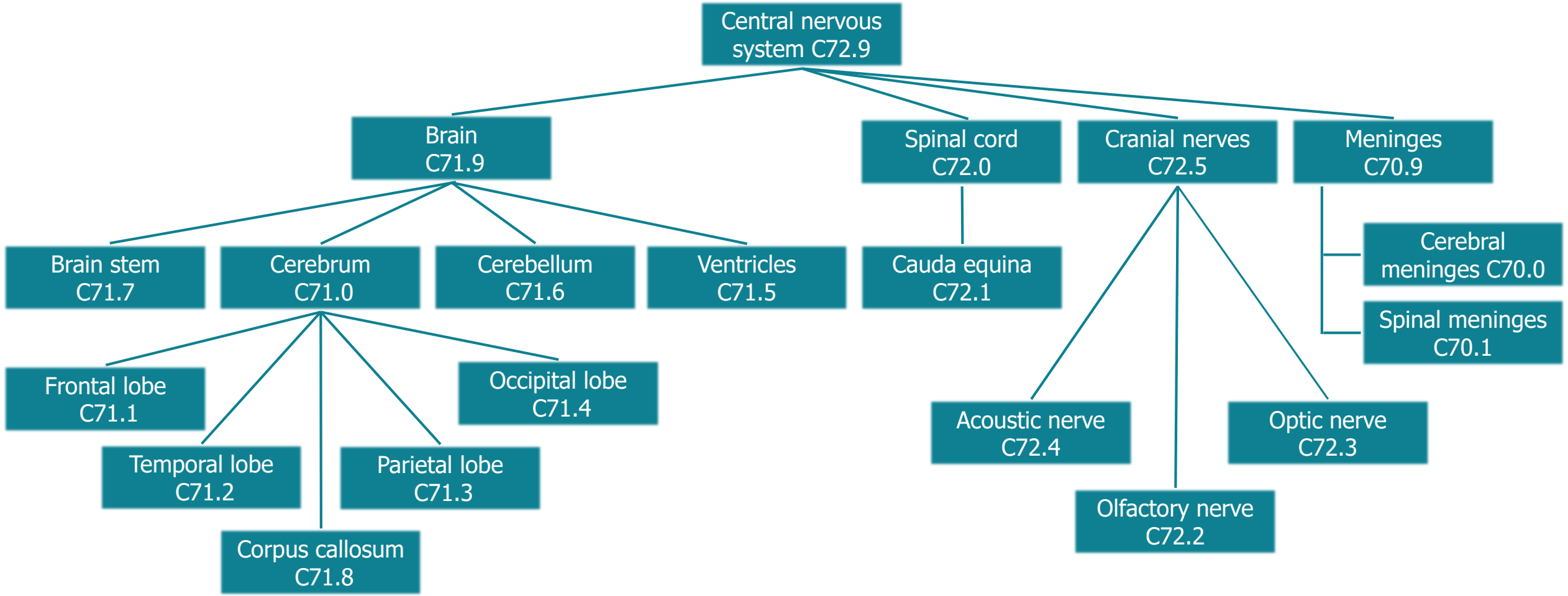


Cranial nerves

- Olfactory nerve (I) C72.2
- Optic nerve (II) C72.3
- Acoustic nerve (VIII) C72.4
- Other cranial nerves C72.5



The classification of anatomy of CNS is hierarchical – should use the most specific ICD-O code where possible



Morphology

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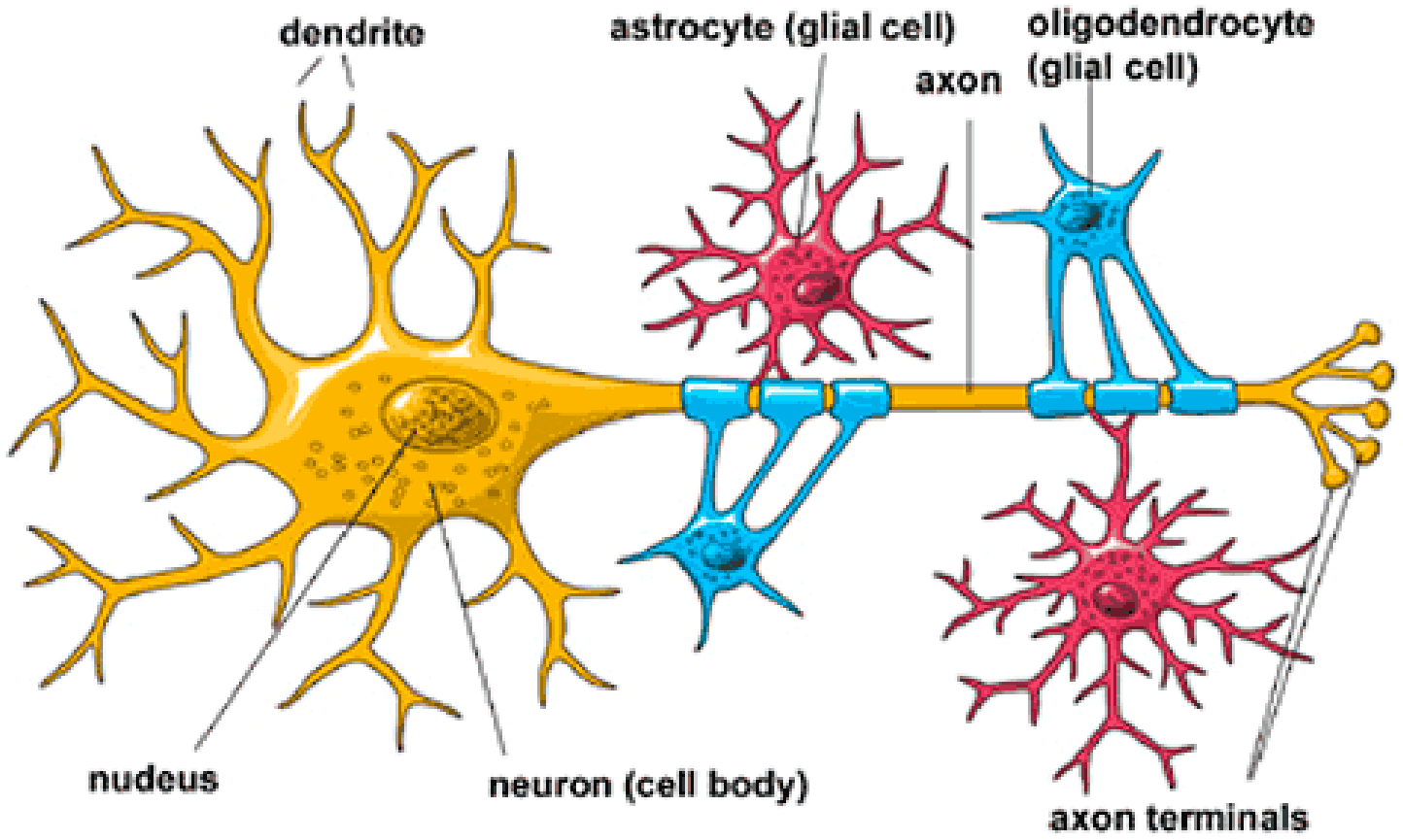
Brain cells


dendrite
astrocyte (glial cell)
axon
oligodendrocyte
(glial cell)
nucleus
neuron (cell body)
axon terminals

Site of the tumour

- Astrocytoma: 98% cerebral
- Oligodendroglioma: 99% cerebral
- Ependymoma: 50% cerebral (the wall of the ventricles [C71.5 or C71.7]), 50% spinal (the spinal canal [C72.0])
  - Subependymoma & anaplastic ependymoma mostly cerebral
  - Myxopapillary ependymoma mostly spinal (cauda equina/filum terminale [C72.1])
- Choroid plexus tumour: always cerebral (ventricle [C71.5 or C71.7])

WHO grade

The grade aims to predict the biological behaviour of the tumour

- Grade I: tumour with low proliferation and potential cure after resection
- Grade II: infiltrative tumour with low proliferation but with risk of recurrence after resection
- Grade III: histological malignant tumour (nuclear atypia & many mitoses) which requires (adjuvant) Rt and/or Ct after resection
- Grade IV: histological malignant tumour with necrosis and fast progression with fatal outcome

Transformation from a lower to a higher grade can occur.

Grading in CNS tumours differs from other cancers

If no specific WHO grade is mentioned in the pathology report and the grade cannot be found in table 27 of ICD-O-3, code as follows:

- low grade* = WHO grade 2
- high grade** = WHO grade 3
- 'anaplastic' = WHO grade 3

Examples:

- Low grade astrocytoma=9400/32
- High grade glioma=9380/33
- High grade glioma, grade IV=9380/34
- High grade glioma, glioblastoma=9440/34

Table 27. **WHO grading system (malignancy scale) for central nervous system tumors (*10*)**

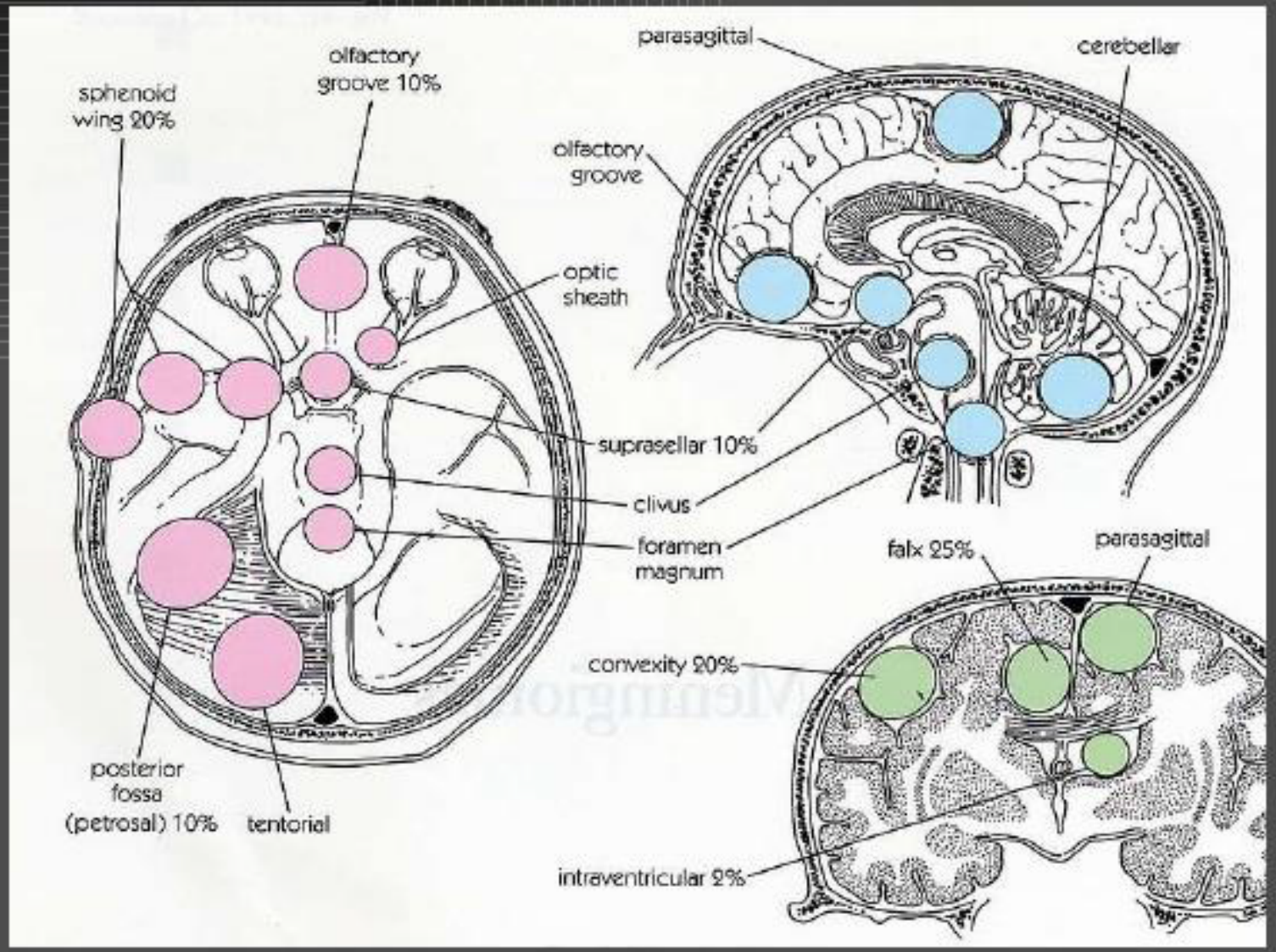
Tumor type to be coded	WHO grade	ICD-O code	ICD-O behavior code (5th digit)
Astrocytic tumors			
Subependymal giant cell astrocytoma	I	9384	1
Pilocytic astrocytoma	I	9421	1
Pilomyxoid astrocytoma	II	9425	3
Diffuse astrocytoma	II	9400	3
Pleomorphic xanthoastrocytoma	II	9424	3
Anaplastic astrocytoma	III	9401	3
Glioblastoma	IV	9440	3
Giant cell glioblastoma	IV	9441	3
Gliosarcoma	IV	9442	3

* Low grade is also applicable to grade 1 tumours
** High grade is also applicable to grade 4 tumours

Tumours of the meninges

- Meningioma
  - Mostly benign (9530/0 – 9537/0) = WHO grade I
  - Atypical (9538/1) = WHO grade II
  - Rarely malignant/anaplastic = WHO grade III (9530/3 or 9539/3)
  - Invasion of the skull (bone) or dura does not influence the classification of a meningioma (/0, /1 or /3)
  - Invasion of the brain means that the meningioma is at least atypical (/1 or /3)
- Hemangiopericytoma - Now referred to as solitary fibrous tumour. Different codes according to grade - 8815/0, 8815/1 or 8815/3
- Melanocytic lesions, including melanoma
  - Solitary (8720/3) or diffuse (8728/0, 8728/1, 8728/3)

Location


parasagittal
cerebellar
olfactory groove 10%
sphenoid wing 20%
olfactory groove
optic sheath
suprasellar 10%
clivus
foramen magnum
falx 25%
parasagittal
convexity 20%
intraventricular 2%
posterior fossa (petrosal) 10%
tentorial

Note

- Malignant meningitis - not a tumour type and it would be unusual to see this written on its own. It is a clinical term used to describe a patient having clinical symptoms of meningitis when it is thought to be caused by the presence of malignant cells in the cerebral spinal fluid.

Tumours of the cranial nerves

- Pilocytic astrocytoma (optic nerve)
  - in children
  - may be bilateral or in the chiasma
  - Some times called "optic nerve glioma"
- Schwannoma (mostly acoustic nerve, but also in other cranial nerves)
  - vestibular schwannoma, acoustic neurinoma, acoustic neuroma
  - benign in the vast majority of cases (M9560/0)
  - malignancy extremely rare (MPNST=M9540/3; epitheliod MPNST=9542/3; MPNST with rhabdomyoblastic differentiation=9561/3)
  - often the diagnosis is made on imaging only
  - may be bilateral

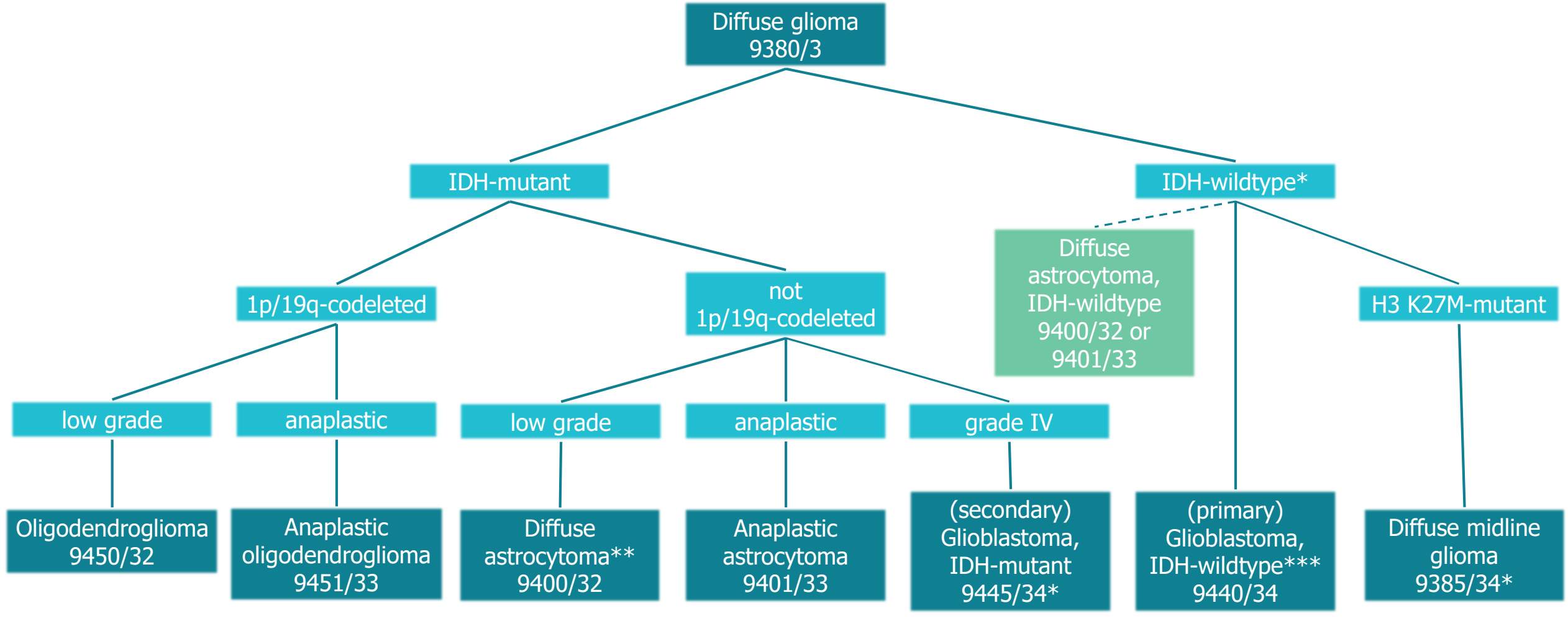
Neuro-epithelial tumours of the brain and spinal cord

- Gliomas (glioma='tumour of glial cell', not a specific diagnosis)
  - Diffuse astrocytic & oligodendroglial tumours
  - Other astrocytic tumours
  - Ependymal tumours
  - Other gliomas
- Embryonal tumours
- Neuronal and mixed neuronal-glial tumours
- Choroid plexus tumours
- Tumours of the pineal region

Notes

- Chordoma is coded to bone rather than spinal cord (common error).
- 'Nasal glioma' is not a brain tumour, but a non-neoplastic congenital lesion.

Classification of diffuse astrocytic and oligodendroglial tumours with molecular testing



European Network of Cancer Registries

* new codes in ICD-O-3 2nd revision
** subtype: gemistocytic astrocytoma 9411/32
*** subtypes: giant cell glioblastoma 9441/34, gliosarcoma 9442/34

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Terminology

- IDH-mutant: there is a mutation in the IDH1 or (sometimes) IDH2 gene
- wildtype: there is no mutation
- 1p deletion: loss* of the short arm (p) of chromosome 1
- 19q deletion: loss* of the long arm (q) of chromosome 19
- 1p/19q-codeleted: both 1p and 19q are lost
- K3 K27M-mutant: there is a K27M-mutation in the K3 gene

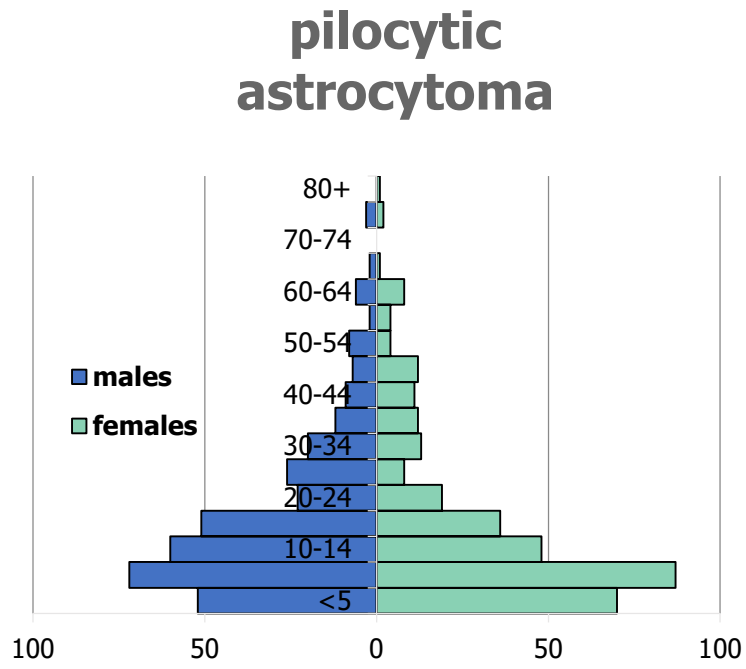
* the loss may be partial or complete

Classification of diffuse astrocytic and oligodendroglial tumours

- If molecular testing is available the results should be used for the classification
- Oligoastrocytoma (9382/32 or [anaplastic] 9382/33) is no longer recognized and should only be coded in the absence of molecular testing or if the results are inconclusive

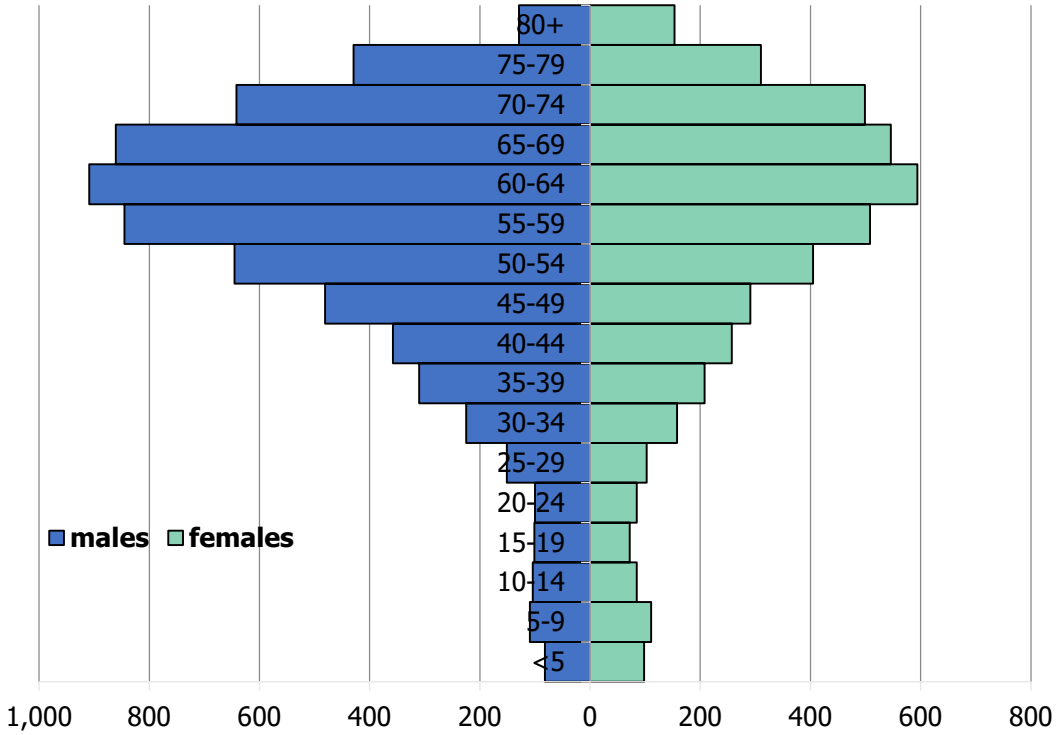
Other astrocytic tumours: classification and age distribution

type	morphology	WHO grade
Pilocytic astrocytoma subtype: pilomyxoid astrocytoma (9425/3, grade II)	9421/1	I
Subependymal giant cell astrocytoma (SEGA)	9384/1	I
Pleomorphic xanthoastrocytoma	9424/3	II
Anaplastic pleomorphic xanthoastrocytoma	9424/3	III

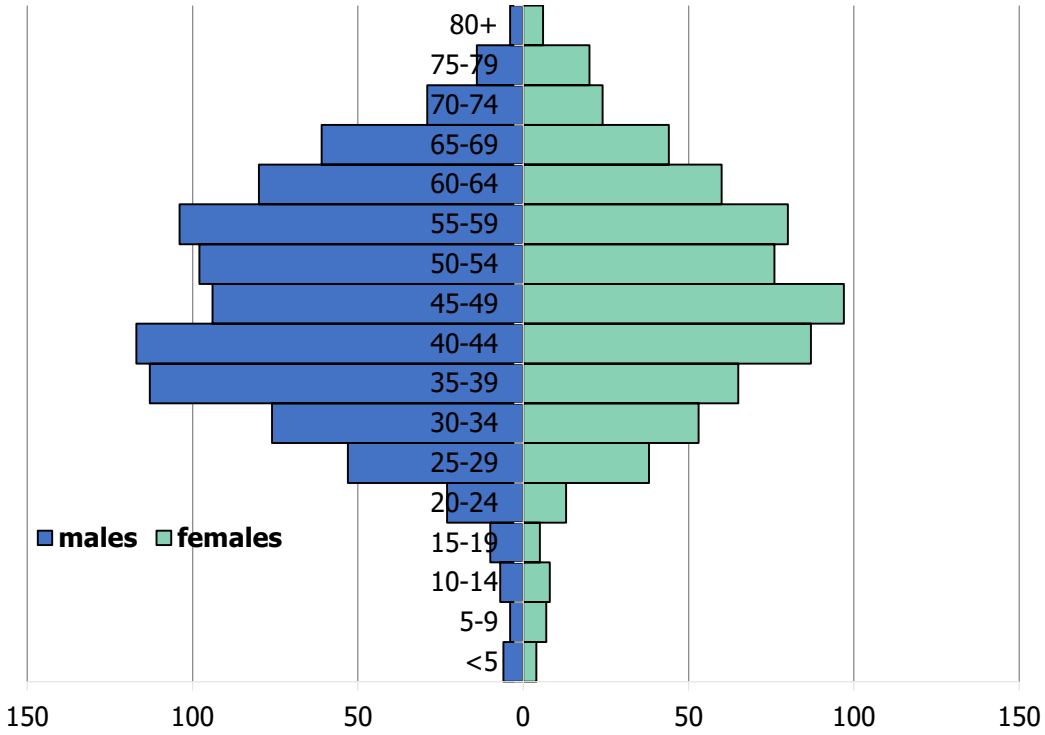


Source: IKNL

Astrocytoma & oligodendroglioma: age distribution

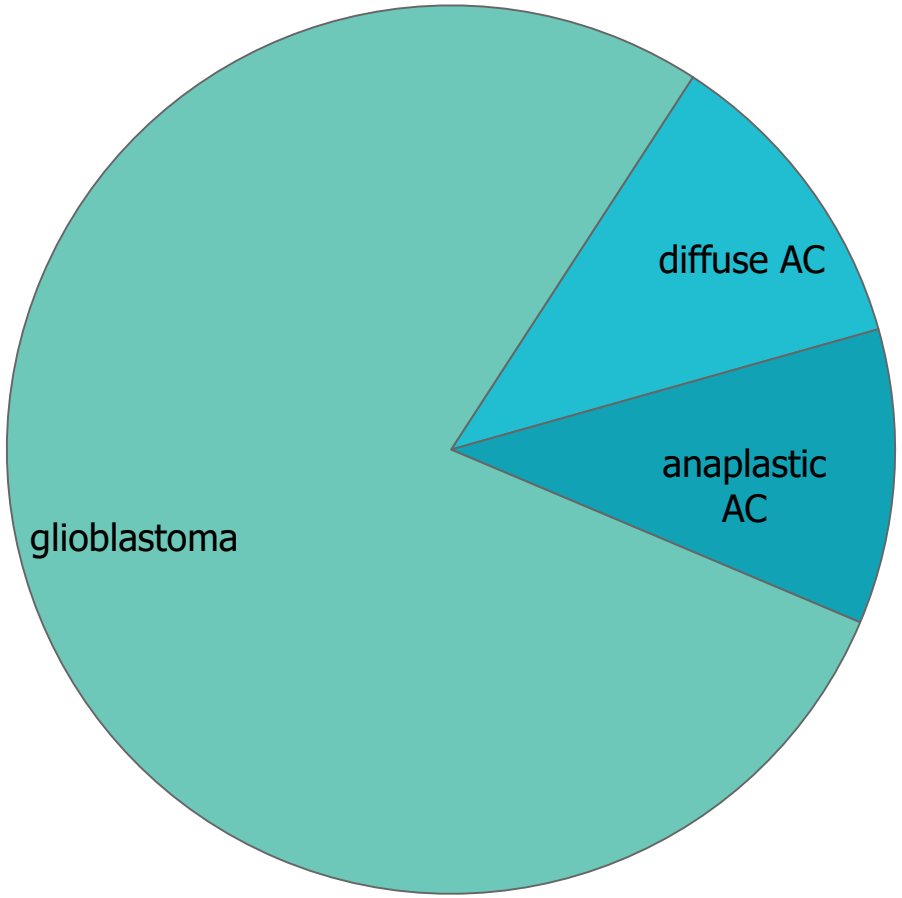


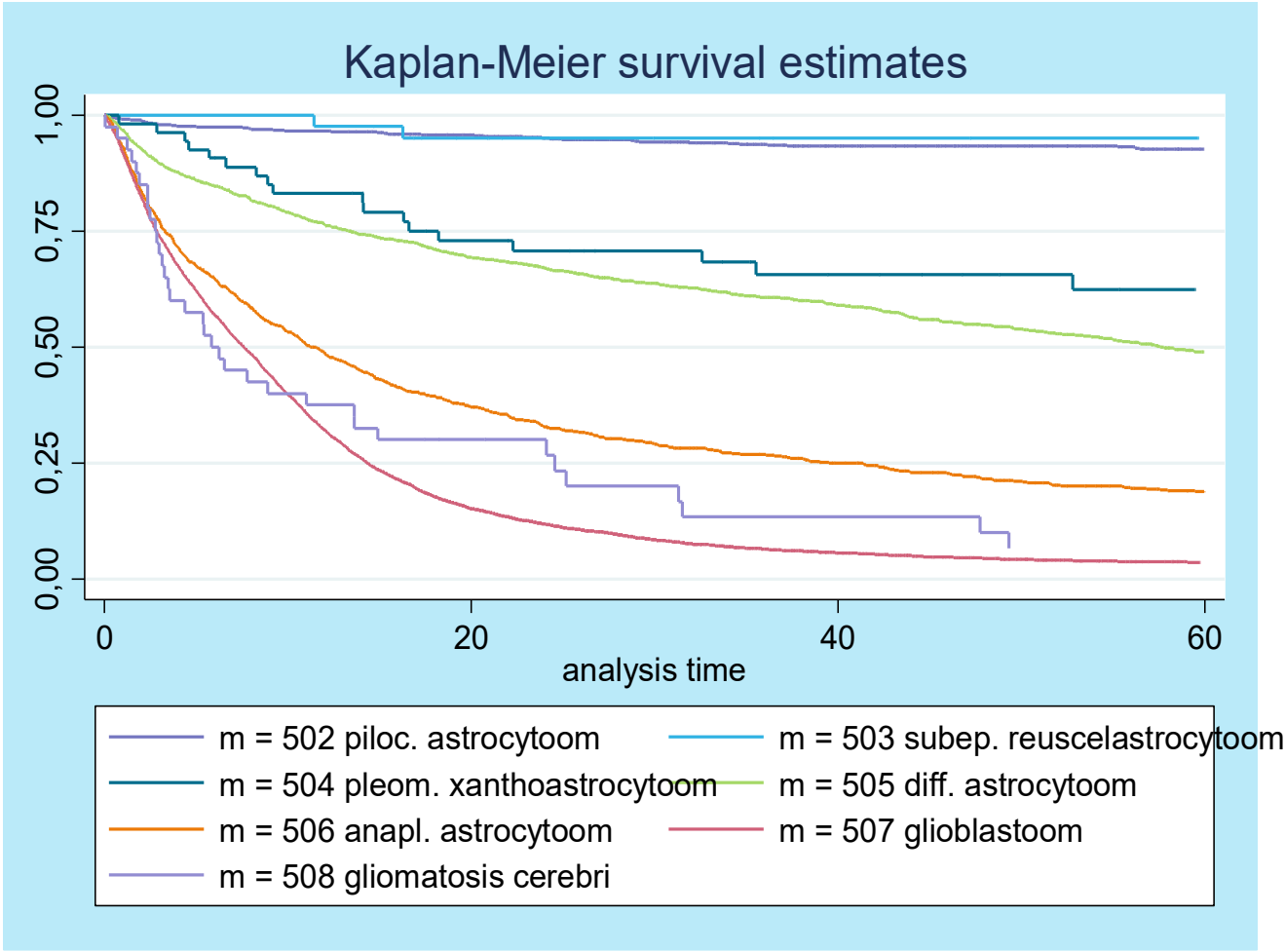
astrocytoma



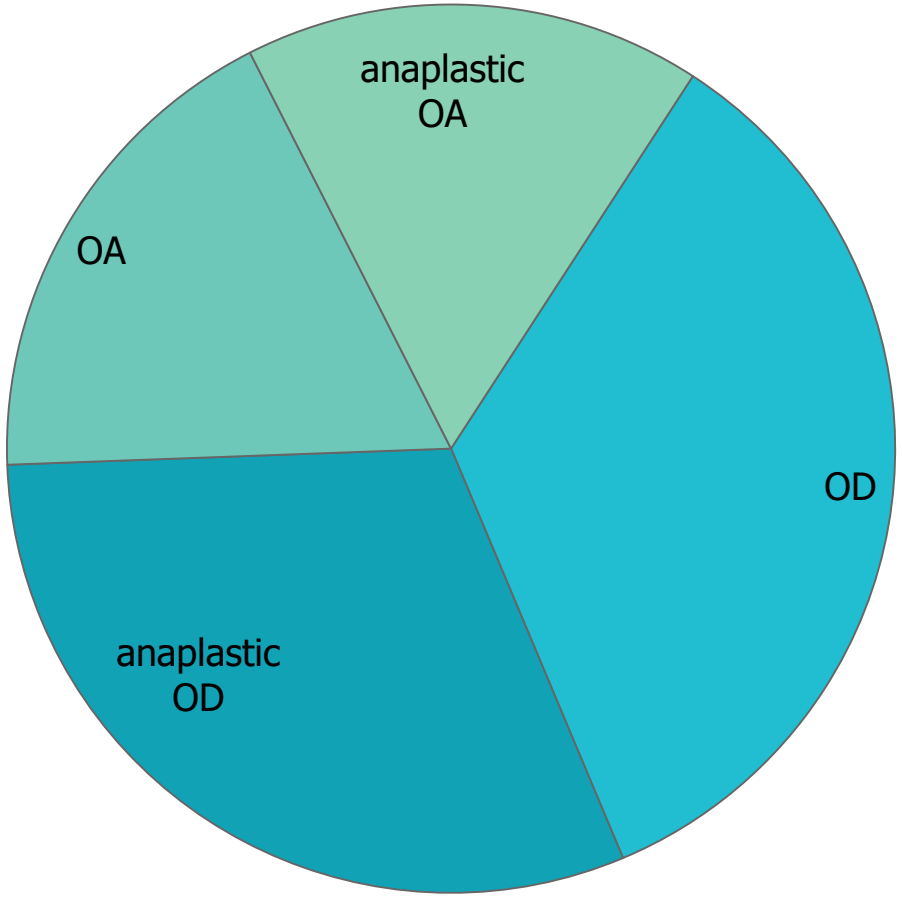
oligodendroglioma

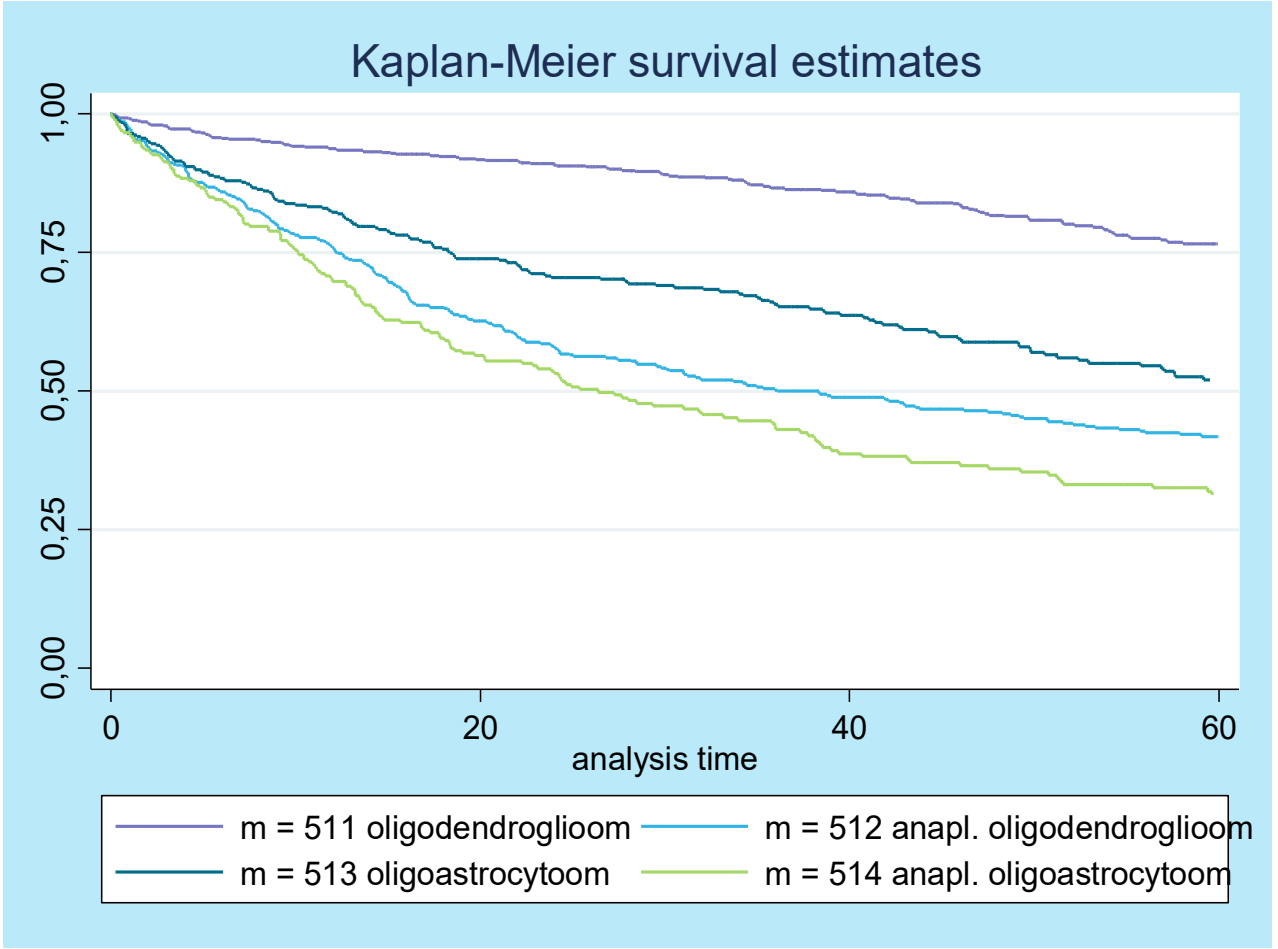
Astrocytoma





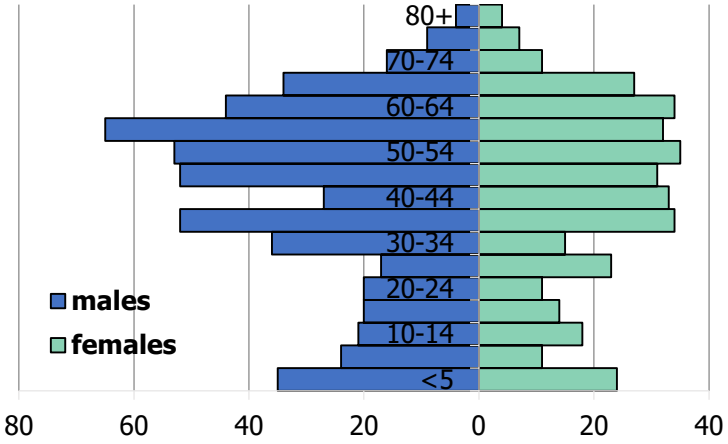
Oligodendroglioma





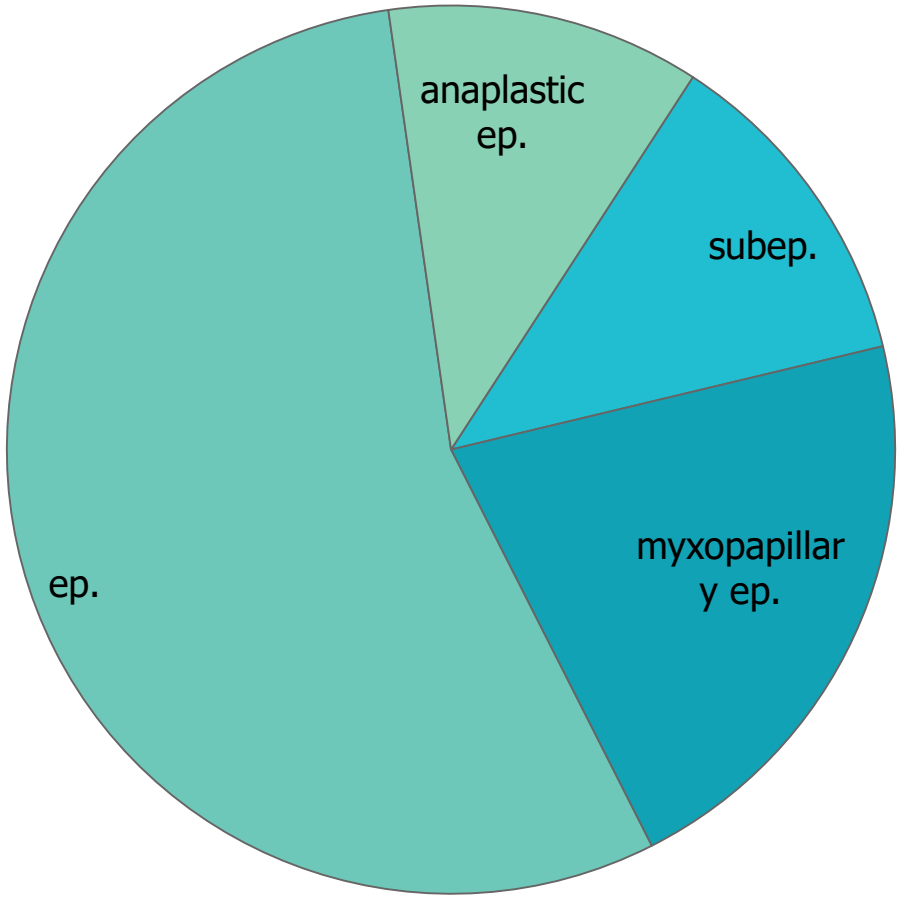
Ependymoma: classification and age distribution

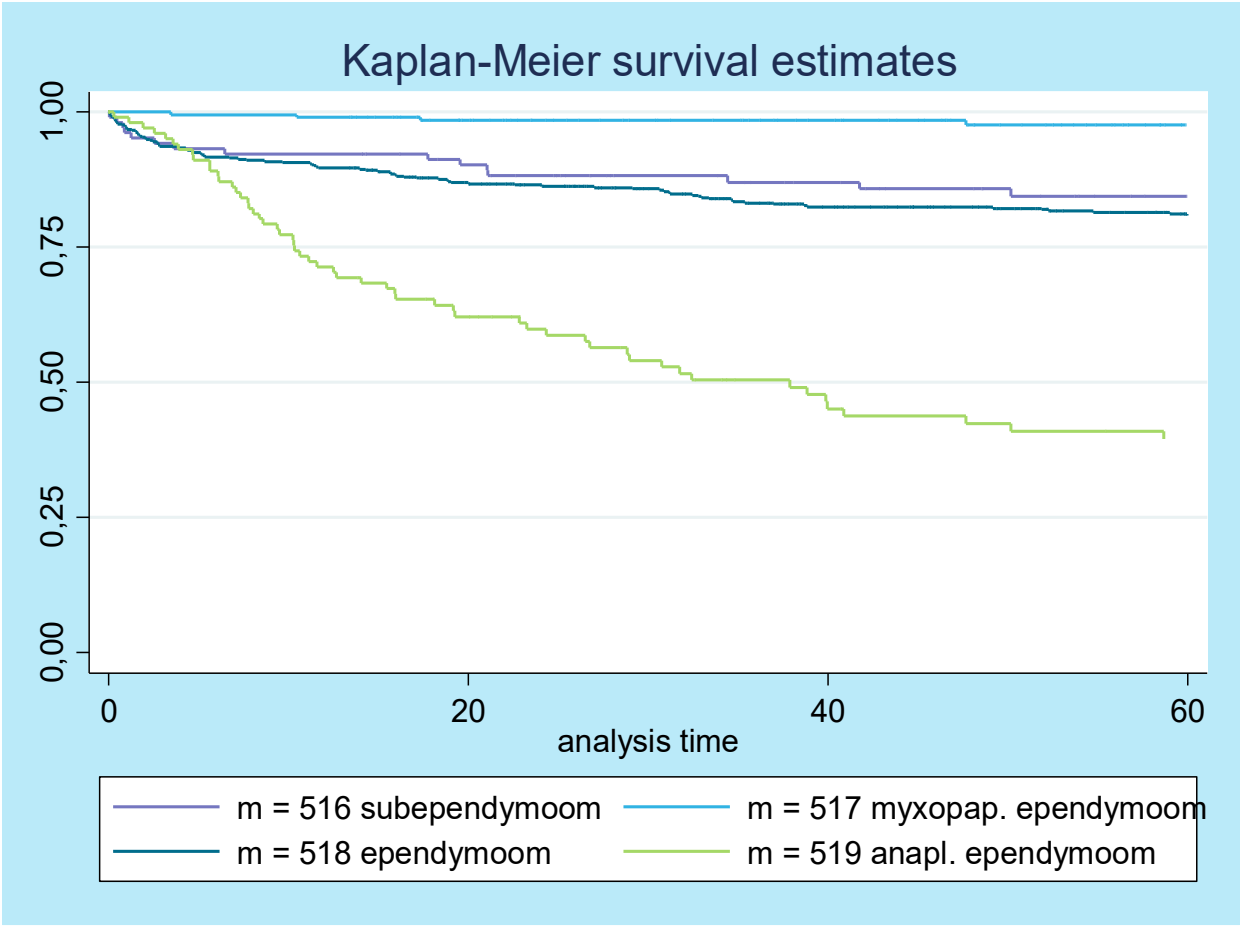
type	morphology	WHO grade
Subependymoma	9383/1	I
Myxopapillary ependymoma	9394/1	I
Ependymoma • papillary [9393/3] • clear cell • tanycytic	9391/3	II
Ependymoma, RELA fusion positive	9396/3*	II or III
Anaplastic ependymoma (ependymoblastoma)	9392/3	III



*new code in ICD-O-3 2nd revision

Ependymoma


anaplastic ep.
subep.
myxopapillary ep.
ep.


Kaplan-Meier survival estimates
1,00
0,75
0,50
0,25
0,00
0
20
40
60
analysis time
m = 516 subependymoom
m = 517 myxopap. ependymoom
m = 518 ependymoom
m = 519 anapl. ependymoom

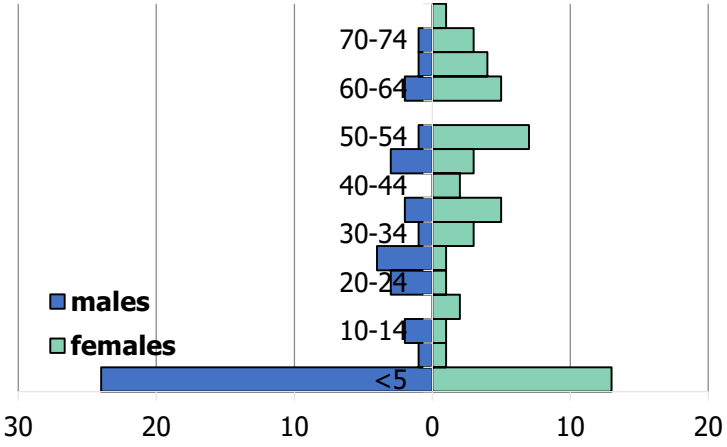
Other gliomas: classification

type	morphology	WHO grade
Chordoid glioma of the third ventricle	9441/1	II
Angiocentric glioma	9431/1	I
Astroblastoma	9430/3	-
Gliomatosis cerebri	9381/3	-

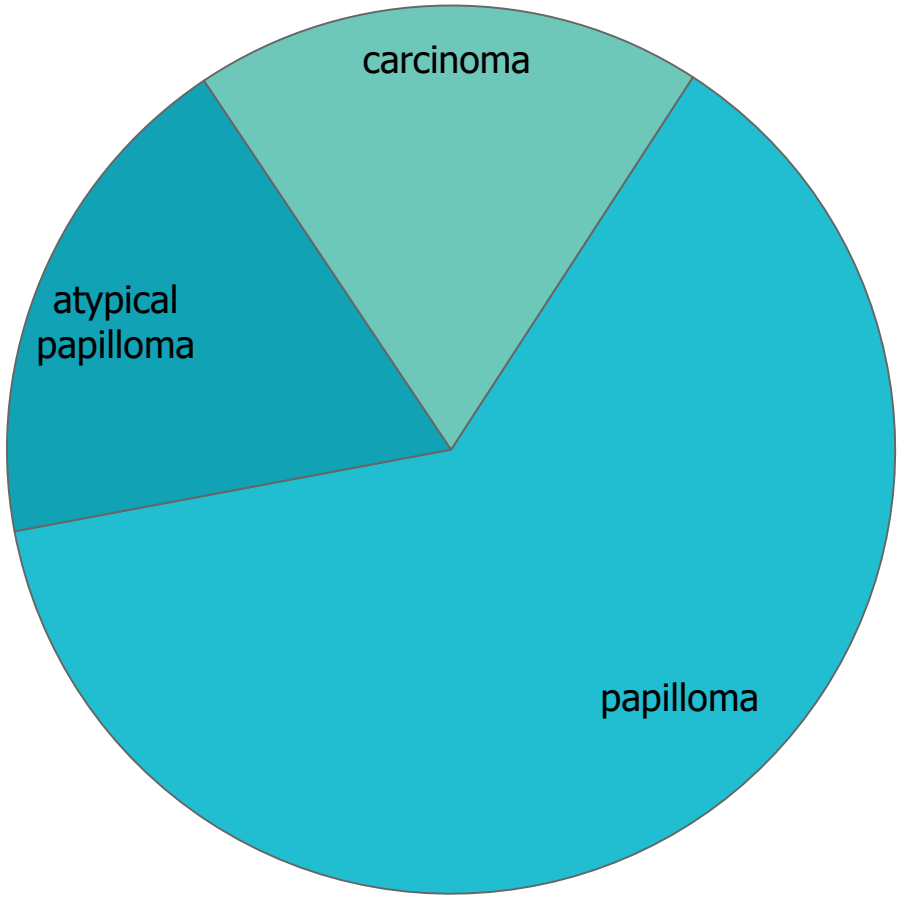
Source: IKNL

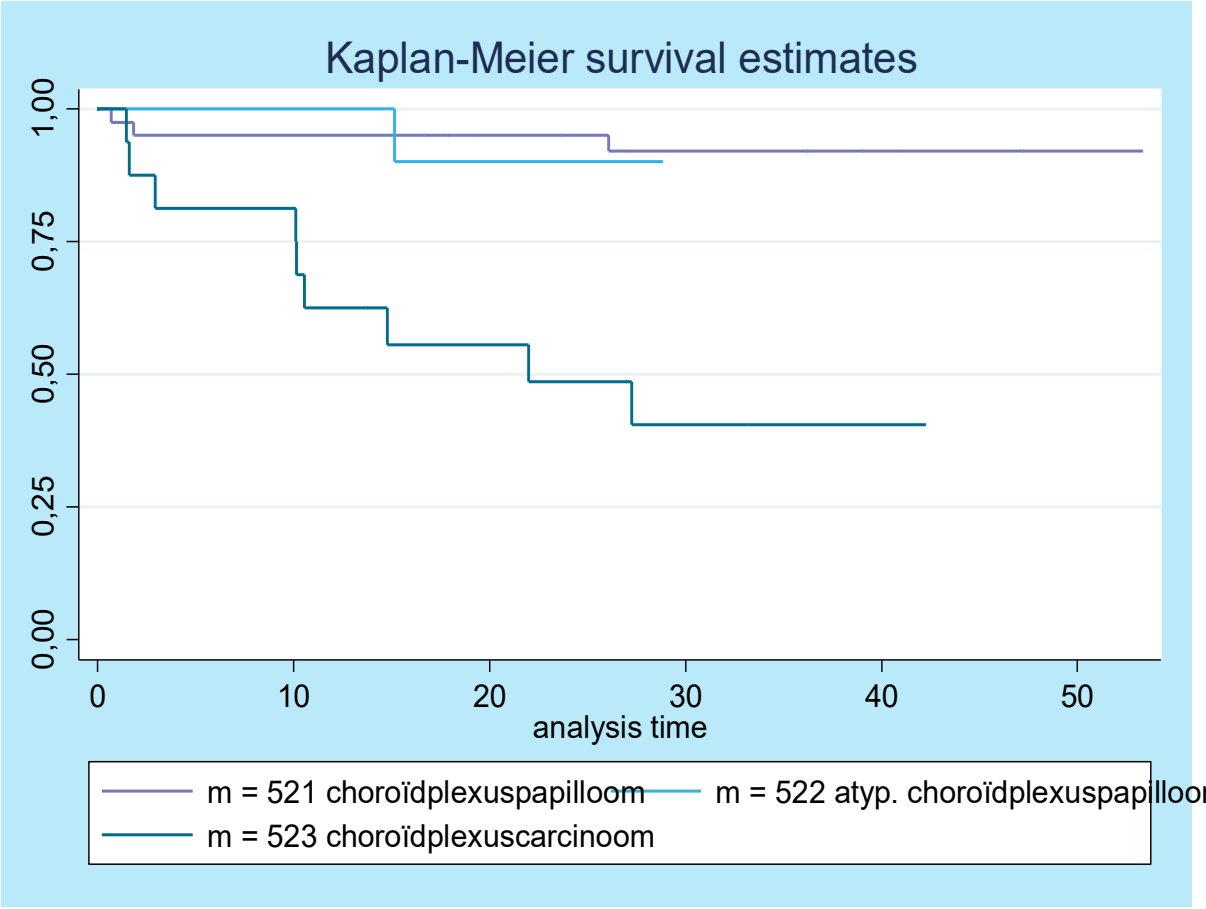
Choroid plexus tumours: classification and age distribution

type	morphology	WHO grade
Choroid plexus papilloma	9390/0	I
Choroid plexus papilloma, atypical	9390/1	II
Choroid plexus carcinoma	9390/3	III



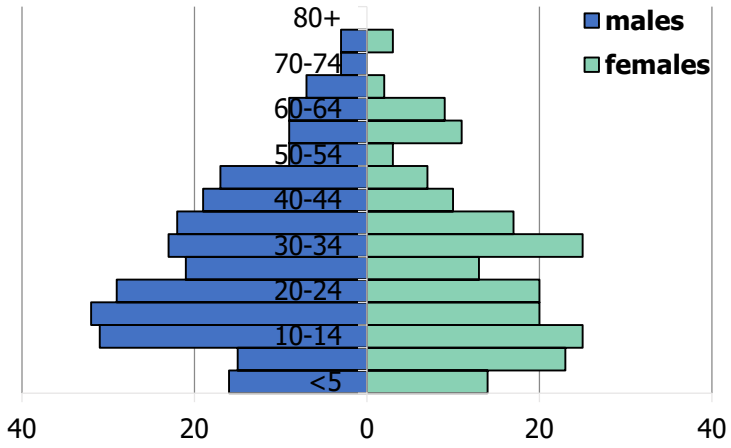
Choroid plexus tumours





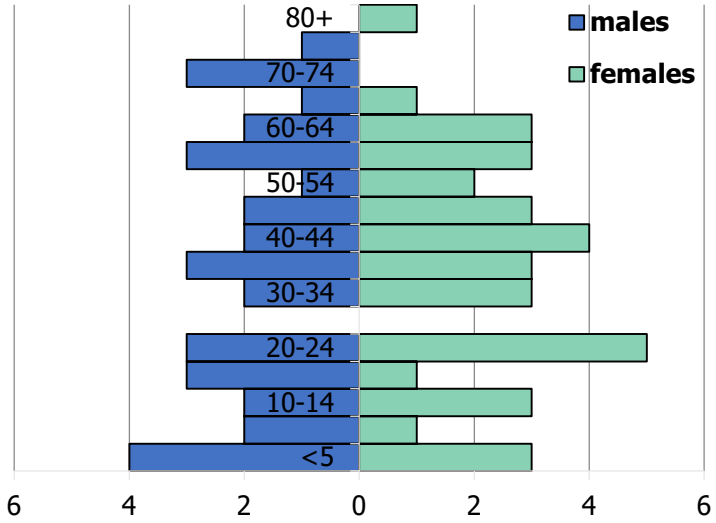
Neuronal & mixed neuronal-glial tumours: classification and age distribution

type	morphology	WHO grade
Dysplastic cerebellar gangliocytoma	9493/0	I
Desmoplastic infantile astrocytoma/ganglioglioma	9412/1	I
Dysembryoplastic neuroepithelial tumour	9413/0	I
Gangliocytoma	9492/0	I
Ganglioglioma	9505/1	I (or II)
Anaplastic ganglioglioma	9505/3	III
Neurocytoma (central, extraventicular, cerebellar)	9506/1	I or II
Papillary glioneural tumour Rosette-forming glioneural tumour Diffuse leptomengial glioneural tumour	9509/1	I
Spinal paraganglioma	8680/1	I

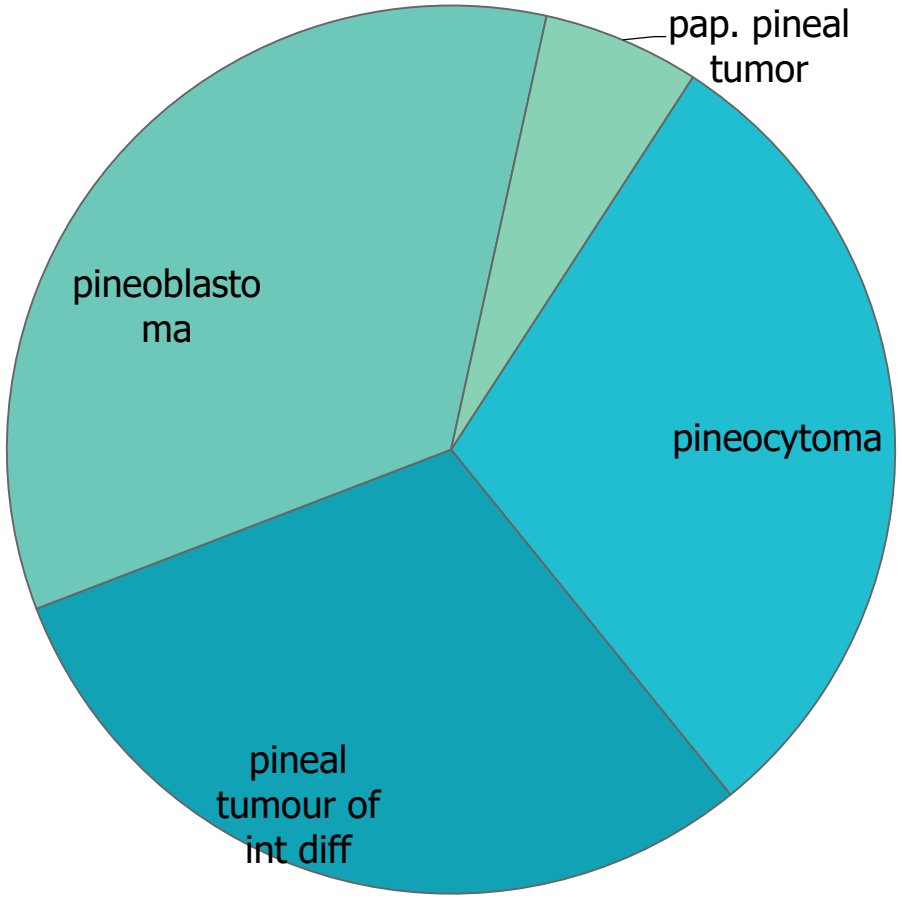


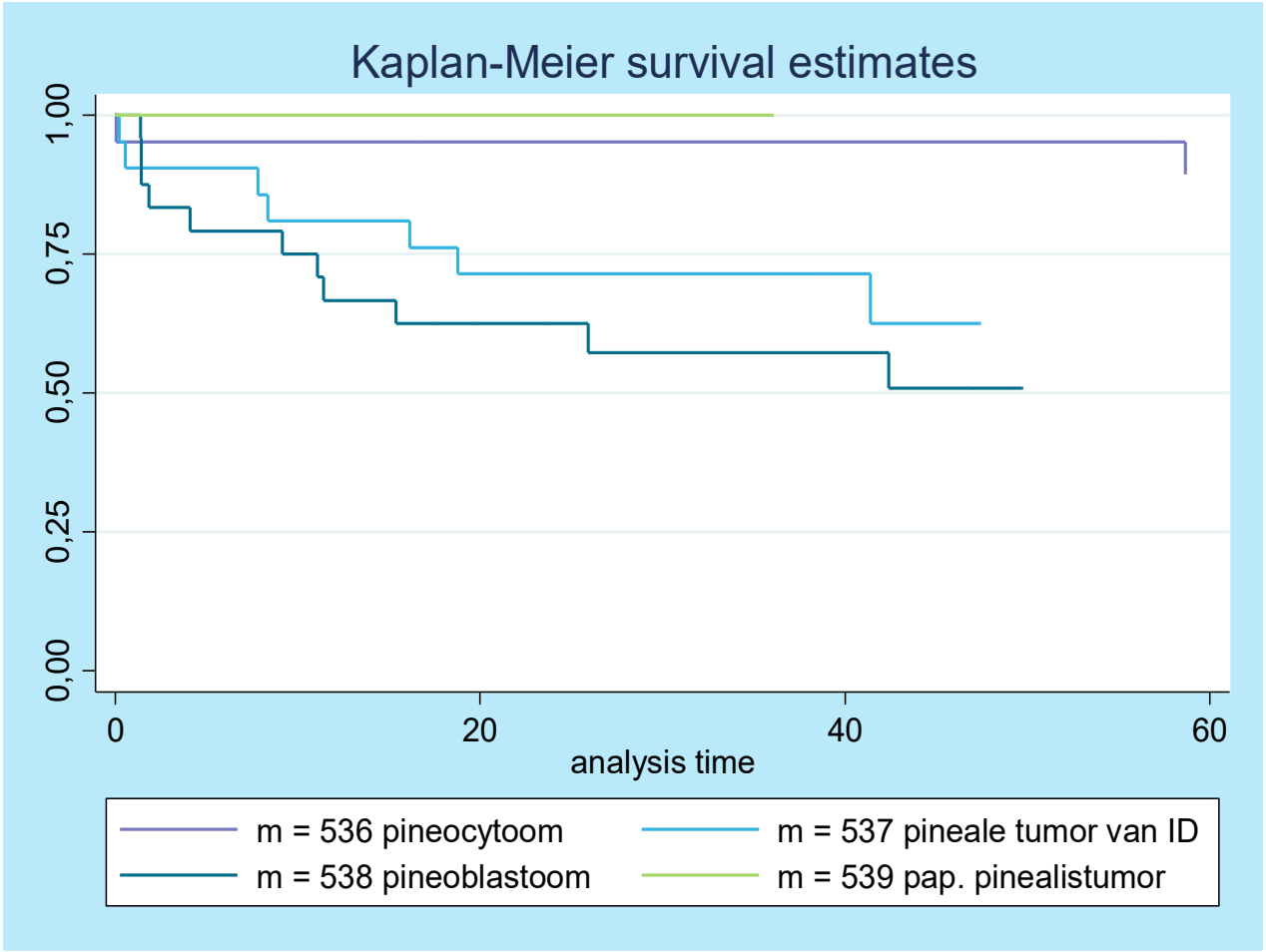
Tumours of the pineal region: classification and age distribution

type	morphology	WHO grade
Pineocytoma	9361/1	I (was II)
Pineal parenchymal tumour of intermediate differentiation	9362/3	II of III (was III of IV)
Pineoblastoma	9362/3	IV
Papillary tumour of the pineal region	9395/3	II of III

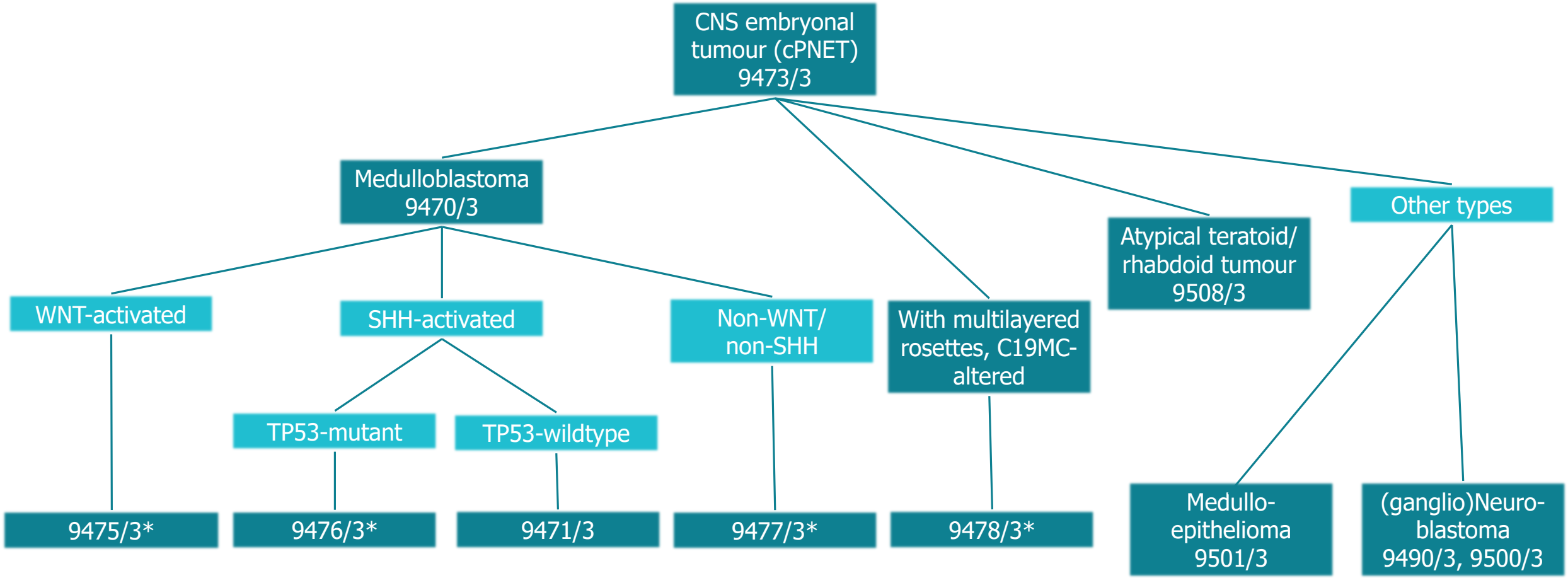


Tumours of the pineal region





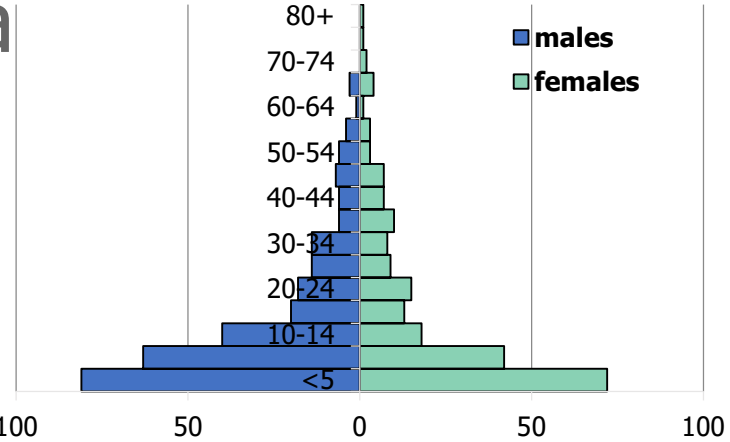
Classification of embryonal tumours of the CNS



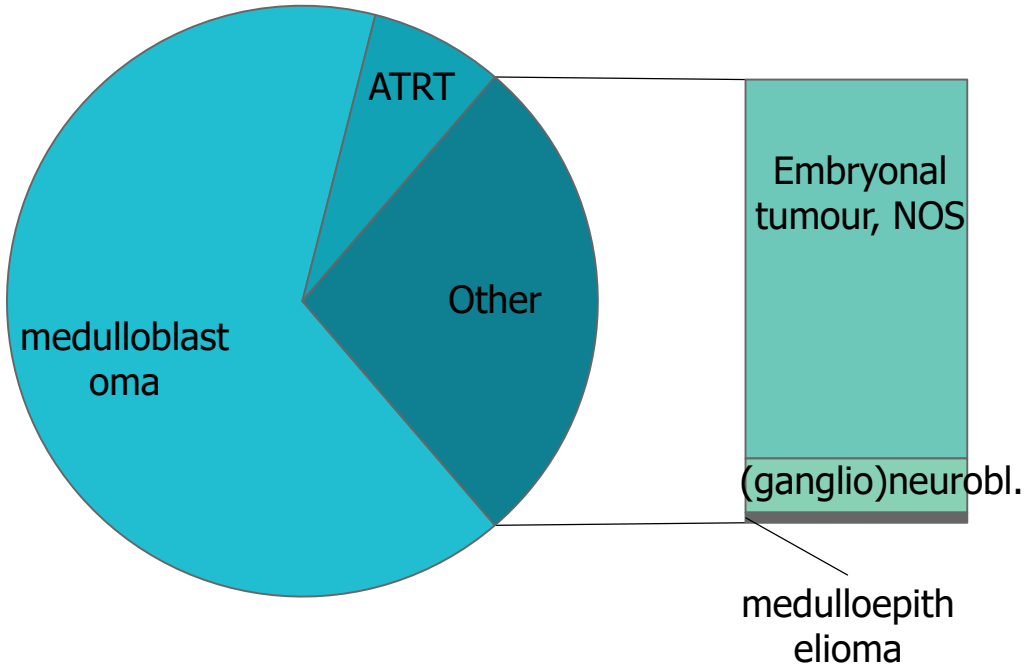
*new codes in ICD-O-3 2nd revision

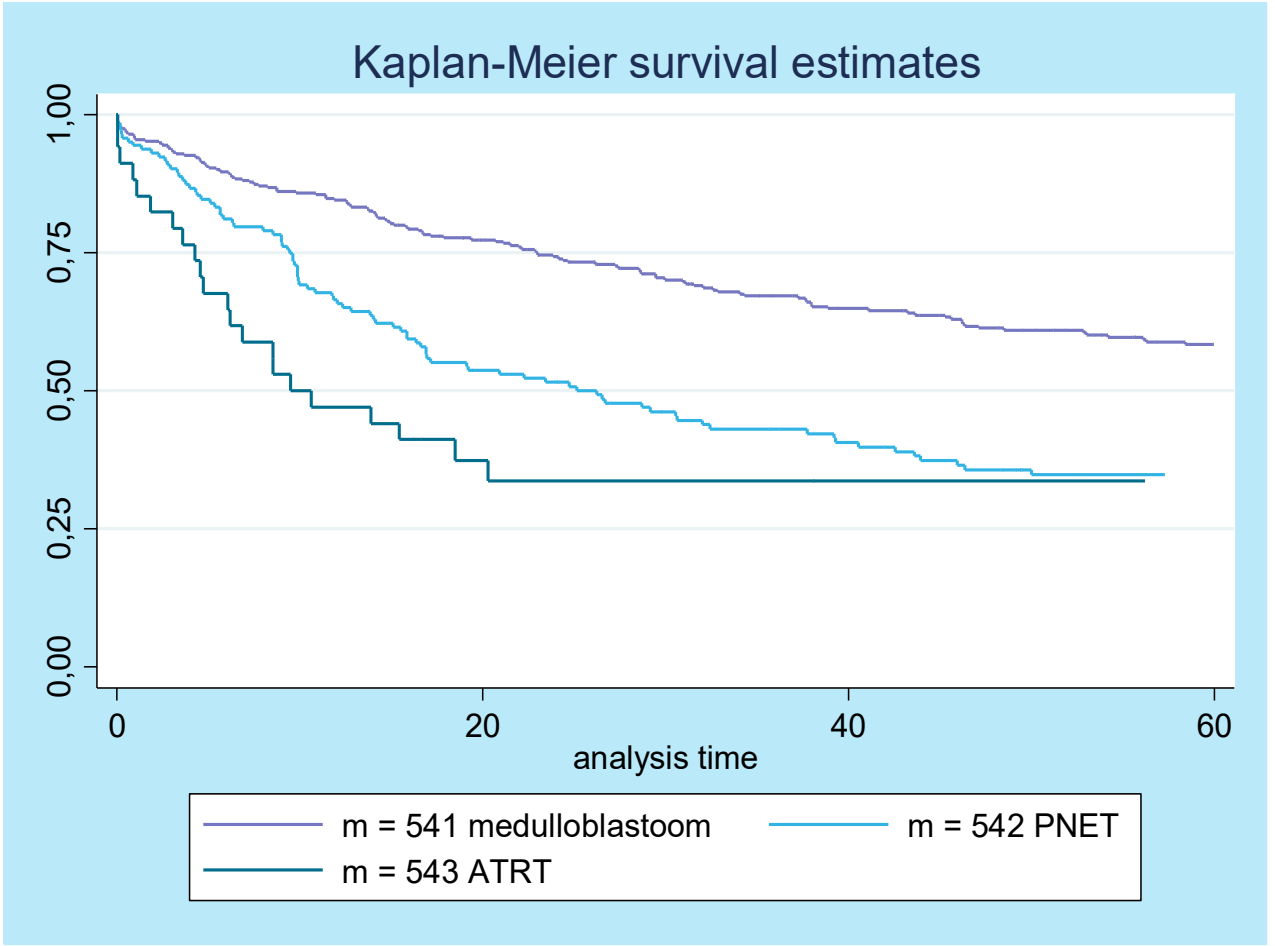
Classification of embryonal tumours

- If molecular testing is available the results should be used for the classification
- For medulloblastoma without molecular testing the following subtypes are recognized:
  - Desmoplastic nodular medulloblastoma (9471/3)
  - Large cell/anaplastic medulloblastoma (9474/3)
- Embryonal tumours are all grade IV



Embryonal tumours





Tumours of the sellar region: classification

type	morphology	WHO grade
Craniopharyngioma subtypes: adamantinomatous craniopharyngioma (9451/1) papillary craniopharyngioma (9452/1)	9350/1	I
Granular cell tumour of the sellar region	9582/0	I
Pituicytoma	9432/1	I
Spindle cell oncocytoma	8290/0	I

Stage

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Stage

- Local extension of the tumour appeared not to be a prognostic factor
- There is no lymphatic drainage and no lymph nodes in the central nervous system
- Most tumours of the central nervous system rarely metastasize
- Because of the above reasons there is no stage-classification for most tumours of the central nervous system

Stage

- In rare cases of metastatic disease (mostly medulloblastoma) it is relevant to register the site of the metastases
- For medulloblastoma and ependymoma in childhood the distinction between localized and metastatic disease is obligatory according to the Toronto consensus, while the M staging system is recommended:
  - M0 – no visible disease on imaging beyond primary site; no tumour cells in CSF
  - M1 – tumour cells in the CSF
  - M2 – visible metastasis in the brain
  - M3 – visible metastasis in the spine or cervicomedullary junction
  - M4 – metastasis outside the CNS (e.g. bone)

Treatment

European Commission

Treatment

- Wait & scan (watchful waiting) policy
- Surgery
- Radiosurgery
- Radiotherapy (conventional or proton therapy)
- Chemotherapy

Surgery versus 'wait & scan'

- In low grade CNS tumours a wait & scan policy may have the preference, depending on (among others):
  - the site of the tumour
  - the potential (negative) effect of a resection on the quality of life
  - the certainty of the diagnosis (benign versus low grade)
- If surgery has the preference (which is the case in most high grade tumours) a resection should be performed in which as much tumour is resected as possible, taking into account the consequences for the quality of life

Adjuvant treatment after surgery

- Radiotherapy
- Chemotherapy
  - Temozolomide for astrocytoma and glioblastoma
  - PCV (Procarbazine, CCNU [lomustine], Vincristine) for oligodendroglioma
  - Other schemes for other tumours, mostly containing lomustine (CCNU), carmustine (BCNU), procarbazine, methotrexate and/or vincristine

Primary radiotherapy or chemotherapy

- If a resection is not possible, is risky or will have too many negative effects on quality of life
- Radiosurgery (stereotactic radiotherapy) for smaller localized tumours
  - High precision localised irradiation
  - A high dose to a small area in one session
  - Often used in vestibular schwannoma, meningioma at the base of the skull, pituitary gland tumour (or distant metastasis to the brain)
- Chemotherapy for larger irresectable tumours, such as for butterfly glioma (= a high grade glioma with bilateral cerebral hemisphere involvement that crosses the corpus callosum)

EXERCISES

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