# Benign and Malignant Primary Brain Tumours in the Swiss Population (2010-2014)

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**Key words**
Cancer registration, malignant brain cancer, non-malignant brain tumour, population-based, epidemiology, meningioma, glioblastoma, incidence

## Introduction

Brain tumours are rare diseases on a global scale, with about 1,570 incident cases, and 580 deaths in Switzerland each year [1, 2]. Brain tumour behaviours are grouped into benign, borderline, or malignant [3]. Benign and borderline (BB) tumours rarely invade adjacent tissue and do not metastasize to other parts of the body as the more aggressive malignant (M) tumours (i.e. «cancer») do. This is the reason why BB tumours are usually excluded from standard public health surveillance reports. However, in the brain, even BB tumours can apply pressure on sensitive tissue, thereby causing serious health problems, which may be equally life threatening as in the case of M cancers. Of the aforementioned 580 deaths due to brain tumours, about 70 (12%) occurred due to BB types [2]. Because brain tumours affect patients at younger ages than most other cancer types [1] and their poor prognosis [4], it has been estimated that M brain cancer alone causes as many potential years of life lost per annum in Switzerland (about 4,800) as the more common large bowel cancer (about 5,000 years) [1]. This is surpassed only by breast (7,200 years) and lung cancer (13,200 years) [1]. Brain tumours are thus of public health concern. This is particularly true for children, where, except in newborns, brain cancer is the most frequent cause of death, among all possible causes [2, 5]. The European Network of Cancer Registries (ENCR) has recommended in 1998 «that cancer registries include in their database all intracranial and intraspinal neoplasms irrespective of their behaviour» [6]. High quality and detailed population-based data is critical for providing a basis for aetiological clues. A plethora of intrinsic and extrinsic risk, and a few protective, factors have been proposed, with limited success for most, the exceptions being the established causative roles of ionizing radiation [7, 8] and certain rare genetic syndromes [9]. N-nitroso compounds are potent brain carcinogens in experimental animals, but the evidence in humans is inconclusive. Several lifestyle (e.g. tobacco smoking, alcohol drinking), environmental (e.g. occupational exposures) and medical (e.g. allergic conditions) factors have been suggested to play an aetiological role in brain cancer, but the evidence is not sufficient to draw any conclusion [10-12]. Very controversial are associations between heavy use of mobile phones and certain brain cancers, and causal interpretations are prone to error due to various biases [13]. The still limited knowledge about the aetiology of tumours of the central nervous system offers weak guidance for an effective preventive strategy.

In the present report, we will include the nationally available population-based data on primary BB brain tumours in Switzerland for the first time, alongside with providing more histological detail in the reporting of primary M cancers of brain/CNS.

## Methods

The Foundation National Institute of Cancer Epidemiology and Registration (NICER) manages the population-based national cancer dataset, with the purpose of providing comprehensive cancer surveillance for Switzerland, as well as supporting epidemiological cancer research [14]. Population-based cantonal cancer registries collect data directly from patients' medical records and transmit a defined and pseudonymized subset of the information to NICER. Diagnoses from 2010 to 2014, registered in eleven cantons (ZH, GR, GL, SG, AR, AI, VD, VS, GE, FR, and LU) with reportedly systematic collection of malignant and non-malignant primary brain tumours, are included in this report. The respective cancer registries cover close to 55% of the Swiss population. Case counts for whole Switzerland are extrapolations by sex, age, tumour group, and Swiss language region.

Selection criteria: all primary tumours of malignant, borderline, or benign behaviour with topography codes C70 (meninges), C71 (brain), and C72 (spinal cord, cranial nerves and other parts of the central nervous system) from the International Classification of Diseases for Oncology, third edition (ICD-O-3) [15]. Tumours were classified by ICD-O-3 morphology codes into broad subgroups (**Tab. 1**) based on the 2000 Consensus Conference on Brain Tumour

| Tumour group | | | ICD-O-3 Morhology* | N | | % of total N | | M/F Ratio | | Median Age | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | BB | M | BB | M | BB | M | BB | M |
| Tumours of Neuroepithelial Tissue | Glioma | Astrocytoma | Glioblastoma (9440, 9441, 9442/3) | 0 | 1750 | 0.0 | 22.3 | | 1.7 | | 65.5 |
| | | | Pilocytic A. (9421, 9425) | 138 | 9 | 1.8 | 0.1 | 1.4 | nd | 15.0 | 4.0 |
| | | | Diffuse A. (9400, 9410, 9411, 9420) | 0 | 151 | 0.0 | 1.9 | | 1.8 | | 44.6 |
| | | | Anaplastic A. (9401) | 0 | 195 | 0.0 | 2.5 | | 1.9 | | 50.9 |
| | | | Other A. (9381, 9384, 9424) | 7 | 25 | 0.1 | 0.3 | nd | 1.1 | 19.5 | 35.8 |
| | | Oligodendro-glioma | Oligodendroglioma (9450) | 0 | 96 | 0.0 | 1.2 | | 2.2 | | 48.7 |
| | | | Anaplastic oligodendroglioma (9451, 9460) | 0 | 89 | 0.0 | 1.2 | | 1.4 | | 56.4 |
| | | Mixed glioma | Oligoastrocytic tumours (9382) | 0 | 96 | 0.0 | 1.2 | | 1.3 | | 43.0 |
| | | Ependymal tumours | 9383, 9391, 9392, 9393, 9394 | 111 | 163 | 1.4 | 2.1 | 1.3 | 1.3 | 45.9 | 41.8 |
| | | Glioma malig., NOS | 9380, 9431, 9432 | 0 | 170 | 0.0 | 2.2 | | 1.2 | | 68.5 |
| | | | | 256 | 2744 | 3.3 | 35.0 | 1.3 | 1.6 | 26.8 | 61.1 |
| | Other neuroepithelial tumors | Neuronal and mixed neuronal-glial | Neuronal and mixed neuronal-glial (8680, 8681, 8690, 8693, 9412, 9413, 9442/1, 9492, 9493, 9505, 9506, 9522, 9523); Choroid plexus (9390); Other (9350, 9352, 9363, 9364, 9362, 9370, 9390, 9423, 9430, 9444, 9503, 9509) | 133 | 7 | 1.7 | 0.1 | 1.4 | nd | 35.2 | 40.6 |
| | | Embryonal | 8963, Medulloblastoma (9470, 9471, 9474), 9472, 9473, 9480, 9490, 9500, 9501, 9502, 9508 | 0 | 65 | 0.0 | 0.8 | | 1.1 | | 11.3 |
| | | | | 389 | 2816 | 5.0 | 35.9 | 1.3 | 1.6 | 31.1 | 60.6 |
| Tumours of Cranial and Spinal Nerves | | | Nerve sheath tumours (9540, 9541, 9550, 9560, 9561, 9570, 9571); Other (9562) | 620 | 8 | 7.9 | 0.1 | 0.8 | nd | 54.8 | 57.9 |
| Tumours of Meninges | | Meningioma | Meningioma (9530, 9531-9534, 9537-9539) | 2906 | 44 | 37.1 | 0.6 | 0.3 | 0.3 | 64.4 | 71.8 |
| | | Non-Meningioma | Mesenchymal (8324, 8800-8806, 8810, 8815, 8824, 8830, 8831, 8835, 8836, 8850-8854, 8857, 8861, 8870, 8880, 8890, 8897, 8900-8902, 8910, 8912, 8920, 8921, 8935, 8990, 9040, 9136, 9150, 9170, 9180, 9210, 9241, 9260, 9373, 9536); Primary melanocytic lesions (8720, 8728, 8770, 8771); Other (9161, 9220, 9231, 9240, 9243, 9370, 9371, 9372, 9535, 9536) | 98 | 18 | 1.2 | 0.2 | 1.3 | 2.1 | 50.6 | 60.4 |
| | | | | 3004 | 62 | 38.3 | 0.8 | 0.3 | 0.6 | 64.1 | 65.8 |
| Other specified unclassified tumours | | | Hemangioma (9120-9123, 9125, 9130, 9131, 9133, 9140); Germ cell (8440, 9060, 9064, 9070, 9080, 9081, 9084); Other (8140, 8260, 8711, 9580) | 25 | 8 | 0.3 | 0.1 | 1.2 | nd | 54.2 | 13.0 |
| Unspecified tumours | | | 8000-8005, 8010 | 658 | 251 | 8.4 | 3.2 | 0.6 | 0.8 | 74.1 | 81.3 |
| * Most frequent morphologies underlined. nd: not determined. | | | **Total (by behavior)** | 4696 | 3145 | 59.9 | 40.1 | 0.46 | 1.49 | 62.3 | 62.3 |
| | | | **Total** | 7841 | | 100.0 | | 0.75 | | 62.3 | |

Tab. 1. All brain/CNS diagnoses in Switzerland during 2010-2014 with benign/borderline (BB) and malignant (M) behaviour. Values are extrapolations based on registered cases in eleven Swiss cantons. M/F: male/female ratio.

Definition for Registration [16]. Excluded are all systemic tumours (M9582 and higher). Diagnoses were either confirmed microscopically or non-microscopically (i.e. based on neuroradiological methods).
Incidence rates are expressed as N cases per 100,000 person-years, and age-adjustment of rates for all ages combined, as well as within age groups, was based on the EU standard population [17]. The study is observational, thus confidence intervals should only be interpreted as rough descriptors of uncertainty [18].

## Results

**Tables** 1 and 2 summarize the present brain/CNS tumour situation in Switzerland, based on 4,159 observed diagnoses from 2010 until the most recent available year 2014. The national extrapolated five-year grand total of 7,841 primary brain/CNS cases in **Table** 1 dispersed into 59.9% with benign/borderline (BB) behaviour, and 40.1% with malignant (M) behaviour.

*Distribution by morphology*
The major morphologic entities were BB meningioma (N=2,906; 37.1% of total cases), M glioblastoma (N=1,750; 22.3%), unspecified tumours (BB: N=658; 8.4%, and M: N=251; 3.2%), and BB tumours of cranial and spinal nerves (N=620; 7.9%) (**Table** 1).

*Distribution by sex*
Overall, more women were diagnosed with brain/CNS tumours than men: M/F ratio 0.75, or 4,473 female and 3,368 male cases, respectively. More than twice as many women than men were diagnosed with BB tumours: M/F ratio 0.46 (3,212 women, 1,487 men). On the other hand, men were more often diagnosed with M tumours: M/F ratio 1.49 (1,881 men, 1,261 women) (**Tab.** 1). Irrespective of tumour behaviour, men were more often diagnosed with glioma, and women with meningioma and unspecified tumours.

*Distribution by age at diagnosis*
The overall age distribution for BB tumours and M tumours was very similar: median age 62 years for both, with interquartile ranges IQR 48-75 years (BB) and 48-74 years (M). However, within many individual morphological groups, BB tumour diagnoses occurred at younger ages than M tumour diagnoses (**Tab.** 1). We estimated that annually about 31 BB tumours were diagnosed in Switzerland in age group 0-19 years, and about 34 M tumours (not shown). Corresponding annual estimates for age group 20-39 were: 87 BB and 66 M tumours, respectively (not shown). For age group 40-59: 305 BB and 175 M cases, respectively (not shown). For age 60-79: 392 BB and 272 M annual cases, respectively (not shown). Finally, for age 80 and more: 130 BB and 79 M cases, respectively (not shown). Major brain/CNS tumours in children and adolescents (below 20 years of age) were M embryonal tumours (median age 11 years), and BB pilocytic astrocytoma (median age 15 years) (**Tab.** 1). A range of different types of glioma affected persons in their 40s and 50s. At increasing median age, these consisted of ependymal tumours (median 42 years; IQR 26-56 years), mixed glioma (median 43; IQR 32-51 years), diffuse astrocytoma (median 45; IQR 30-61 years), oligodendroglioma (median 49; IQR 37-63 years), and anaplastic astrocytoma (median 51; IQR 38-62 years). Ependymal tumours were special because BB and M behaviour types were similar common (**Tab.** 1). BB tumours of cranial and spinal nerves are also associated with the 5$^{th}$ decade in life (median 55; IQR 46-67 years). The most frequent types of brain/CNS tumour affect mainly persons in their 6$^{th}$ decade: BB meningioma and M glioblastoma, at median ages 64 (IQR 52-75 years) and 66 (IQR 56-74 years), respectively. At the high end of the age spectrum appeared M glioma NOS (median 69; IQR 41-81 years), and unspecified tumour types of either BB or M behaviour: median ages 74 years (IQR 57-82 years) and 81 years (IQR 73-86 years), respectively (**Tab.** 1).

*Incidence rates by sex and age group*
We calculated incidence rates for diagnoses during 2010 to 2014. **Table 2** and **Figure** 1 present age-specific incidence rates for major brain/CNS tumour groups, selected by expressing rates of N > 1.0 case per 100,000 person-years in any age group for both sexes combined. The age-adjusted incidence rate for total BB brain/CNS tumour types was 9.69 (both sexes combined), 12.63 in women, and only 6.59 in men (**Tab.** 2). The age-adjusted incidence rate of total M tumours was lower: 6.64 (both sexes combined), 8.37 in males, and only 5.05 in females, respectively (**Tab.** 2). These sex differences were less apparent in children and adolescents (age 0-19), but the age-specific incidence rates were small (BB, in both sexes combined: 2.02; M, in both sexes combined: 2.20) (**Tab.** 2). Sex differences became obvious in the second (20-39) up to the fifth age group (80+), concomitant with a dramatic increase in the incidence rates, up to 38.9 in females (total BB diagnoses), and 29.8 in males (total M diagnoses) (**Tab.** 2). The strong age-dependence of BB meningioma incidence rates is also depicted in **Figure** 1. The influence of age on incidence was special for unspecified tumour types (BB or M), with high rates only at age 80+ (**Fig.** 1 and **Tab.** 2). In contrast, the age group with peak incidence rate was the second oldest group (60-79) for BB tumours of cranial and spinal nerves (3.39 in both sexes combined), as well as for M tumours of neuroepithelial tissue, e.g. glioblastoma (13.9 in both sexes combined) (Fig. 1 and Table 2). Children and adolescents expressed the highest incidence rates for BB tumours of neuroepithelial tissue (1.50 in both sexes combined), predominantly pilocytic astrocytoma (0.99 in both sexes combined) (**Fig.** 1 and **Tab.** 2).

| Tumour group | | | | Beh. | Sex | All ages* | | | Age 0-19 | | | Age 20-39 | | | Age 40-59 | | | Age 60-79 | | | Age 80+ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | IR$ | LB# | UB# | IR$ | LB# | UB# | IR$ | LB# | UB# | IR$ | LB# | UB# | IR$ | LB# | UB# | IR$ | LB# | UB# |
| Tumours of Neuroepithelial Tissue | Glioma | Astrocytoma | Glio-blastoma | M | M | 4.72 | 4.33 | 5.13 | 0.15 | 0.05 | 0.48 | 1.04 | 0.73 | 1.49 | 5.80 | 5.02 | 6.69 | 18.2 | 16.3 | 20.3 | 14.4 | 10.9 | 18.9 |
| | | | | | F | 2.47 | 2.21 | 2.76 | 0.03 | 0.00 | 0.23 | 0.32 | 0.17 | 0.59 | 3.07 | 2.51 | 3.75 | 10.1 | 8.77 | 11.5 | 6.79 | 5.07 | 9.10 |
| | | | | | MF | 3.54 | 3.31 | 3.79 | 0.09 | 0.04 | 0.25 | 0.68 | 0.50 | 0.93 | 4.45 | 3.96 | 5.00 | 13.9 | 12.8 | 15.1 | 9.48 | 7.76 | 11.6 |
| | | | Pilocytic A. | BB | M | 0.50 | 0.36 | 0.68 | 1.22 | 0.84 | 1.78 | 0.32 | 0.17 | 0.61 | 0.18 | 0.08 | 0.39 | 0.00 | | | 0.00 | | |
| | | | | | F | 0.35 | 0.24 | 0.50 | 0.76 | 0.48 | 1.20 | 0.32 | 0.17 | 0.59 | 0.09 | 0.03 | 0.24 | 0.11 | 0.03 | 0.34 | 0.00 | | |
| | | | | | MF | 0.43 | 0.33 | 0.54 | 0.99 | 0.74 | 1.33 | 0.32 | 0.20 | 0.50 | 0.13 | 0.07 | 0.25 | 0.06 | 0.02 | 0.18 | 0.00 | | |
| | | | | BB | M | 0.51 | 0.36 | 0.69 | 1.22 | 0.84 | 1.78 | 0.32 | 0.17 | 0.61 | 0.20 | 0.10 | 0.42 | 0.00 | | | 0.00 | | |
| | | | | | F | 0.39 | 0.27 | 0.54 | 0.88 | 0.57 | 1.34 | 0.32 | 0.17 | 0.59 | 0.11 | 0.05 | 0.27 | 0.11 | 0.03 | 0.34 | 0.00 | | |
| | | | | | MF | 0.45 | 0.35 | 0.57 | 1.05 | 0.79 | 1.40 | 0.32 | 0.20 | 0.50 | 0.16 | 0.09 | 0.28 | 0.06 | 0.02 | 0.18 | 0.00 | | |
| | | | | M | M | 5.87 | 5.43 | 6.33 | 0.69 | 0.41 | 1.14 | 2.32 | 1.83 | 2.94 | 7.23 | 6.36 | 8.23 | 19.9 | 17.9 | 22.1 | 15.0 | 11.5 | 19.7 |
| | | | | | F | 3.15 | 2.84 | 3.49 | 0.48 | 0.26 | 0.88 | 0.93 | 0.64 | 1.36 | 3.79 | 3.16 | 4.55 | 11.2 | 9.82 | 12.8 | 7.09 | 5.33 | 9.44 |
| | | | | | MF | 4.46 | 4.19 | 4.74 | 0.58 | 0.39 | 0.86 | 1.63 | 1.34 | 2.00 | 5.53 | 4.98 | 6.14 | 15.3 | 14.1 | 16.6 | 9.90 | 8.14 | 12.0 |
| | | | | BB | M | 0.79 | 0.62 | 1.00 | 1.22 | 0.84 | 1.78 | 0.82 | 0.54 | 1.23 | 0.41 | 0.24 | 0.70 | 0.61 | 0.33 | 1.13 | 0.34 | 0.05 | 2.38 |
| | | | | | F | 0.63 | 0.48 | 0.82 | 1.04 | 0.70 | 1.55 | 0.58 | 0.36 | 0.91 | 0.40 | 0.23 | 0.69 | 0.40 | 0.20 | 0.81 | 0.00 | | |
| | | | | | MF | 0.71 | 0.59 | 0.85 | 1.13 | 0.86 | 1.49 | 0.70 | 0.51 | 0.95 | 0.40 | 0.27 | 0.59 | 0.50 | 0.32 | 0.80 | 0.12 | 0.02 | 0.84 |
| | | | | M | M | 7.54 | 7.04 | 8.07 | 1.61 | 1.15 | 2.24 | 3.87 | 3.22 | 4.64 | 9.11 | 8.12 | 10.2 | 22.5 | 20.4 | 24.8 | 20.3 | 16.0 | 25.7 |
| | | | | | F | 4.33 | 3.95 | 4.73 | 1.30 | 0.90 | 1.88 | 1.88 | 1.44 | 2.45 | 5.21 | 4.47 | 6.08 | 12.9 | 11.4 | 14.6 | 9.15 | 7.09 | 11.8 |
| | | | | | MF | 5.87 | 5.56 | 6.19 | 1.46 | 1.14 | 1.87 | 2.88 | 2.48 | 3.35 | 7.18 | 6.55 | 7.87 | 17.4 | 16.2 | 18.8 | 13.1 | 11.0 | 15.6 |
| | | | | BB | M | 1.19 | 0.98 | 1.44 | 1.74 | 1.28 | 2.37 | 1.16 | 0.82 | 1.63 | 0.96 | 0.67 | 1.37 | 0.68 | 0.37 | 1.22 | 0.34 | 0.05 | 2.38 |
| | | | | | F | 0.92 | 0.73 | 1.14 | 1.25 | 0.87 | 1.82 | 1.00 | 0.70 | 1.42 | 0.67 | 0.44 | 1.03 | 0.65 | 0.38 | 1.13 | 0.00 | | |
| | | | | | MF | 1.06 | 0.91 | 1.22 | 1.50 | 1.19 | 1.91 | 1.08 | 0.84 | 1.38 | 0.82 | 0.62 | 1.08 | 0.66 | 0.45 | 0.99 | 0.12 | 0.02 | 0.84 |
| | | | | M | M | 7.78 | 7.27 | 8.32 | 2.29 | 1.75 | 3.01 | 3.98 | 3.33 | 4.77 | 9.14 | 8.16 | 10.3 | 22.5 | 20.4 | 24.8 | 20.3 | 16.0 | 25.7 |
| | | | | | F | 4.53 | 4.14 | 4.95 | 1.70 | 1.23 | 2.34 | 2.08 | 1.62 | 2.68 | 5.31 | 4.56 | 6.18 | 12.9 | 11.4 | 14.6 | 9.15 | 7.09 | 11.8 |
| | | | | | MF | 6.09 | 5.77 | 6.43 | 2.00 | 1.63 | 2.47 | 3.04 | 2.63 | 3.52 | 7.25 | 6.61 | 7.94 | 17.4 | 16.2 | 18.8 | 13.1 | 11.0 | 15.6 |
| Tumours of Cranial and Spinal Nerves | | | | BB | M | 1.24 | 1.04 | 1.47 | 0.18 | 0.07 | 0.49 | 0.57 | 0.35 | 0.94 | 2.11 | 1.65 | 2.71 | 3.20 | 2.44 | 4.19 | 1.55 | 0.64 | 3.72 |
| | | | | | F | 1.49 | 1.27 | 1.74 | 0.19 | 0.07 | 0.52 | 0.80 | 0.53 | 1.19 | 2.55 | 2.03 | 3.20 | 3.55 | 2.78 | 4.54 | 0.73 | 0.28 | 1.95 |
| | | | | | MF | 1.37 | 1.21 | 1.53 | 0.19 | 0.09 | 0.38 | 0.68 | 0.50 | 0.93 | 2.33 | 1.97 | 2.75 | 3.39 | 2.83 | 4.06 | 1.02 | 0.53 | 1.96 |
| Meningioma | | | | BB | M | 2.83 | 2.54 | 3.15 | 0.06 | 0.02 | 0.25 | 0.80 | 0.53 | 1.19 | 3.66 | 3.04 | 4.39 | 9.63 | 8.28 | 11.2 | 14.3 | 10.8 | 18.9 |
| | | | | | F | 8.61 | 8.09 | 9.15 | 0.09 | 0.02 | 0.35 | 2.69 | 2.15 | 3.36 | 13.3 | 12.0 | 14.6 | 26.9 | 24.7 | 29.3 | 26.6 | 22.8 | 31.1 |
| | | | | | MF | 5.80 | 5.50 | 6.12 | 0.07 | 0.03 | 0.20 | 1.73 | 1.43 | 2.10 | 8.42 | 7.72 | 9.17 | 18.8 | 17.4 | 20.2 | 22.3 | 19.5 | 25.5 |
| Unspecified tumours | | | | BB | M | 1.00 | 0.83 | 1.19 | 0.10 | 0.03 | 0.41 | 0.33 | 0.18 | 0.61 | 0.95 | 0.66 | 1.35 | 3.18 | 2.45 | 4.12 | 9.37 | 6.66 | 13.2 |
| | | | | | F | 1.36 | 1.16 | 1.57 | 0.19 | 0.07 | 0.52 | 0.51 | 0.30 | 0.86 | 1.24 | 0.89 | 1.71 | 4.64 | 3.80 | 5.67 | 11.4 | 9.08 | 14.3 |
| | | | | | MF | 0.18 | 1.05 | 1.32 | 0.15 | 0.07 | 0.33 | 0.42 | 0.28 | 0.62 | 1.09 | 0.86 | 1.39 | 3.95 | 3.37 | 4.63 | 10.7 | 8.84 | 12.9 |
| | | | | M | M | 0.42 | 0.32 | 0.55 | 0.22 | 0.09 | 0.52 | 0.04 | 0.01 | 0.27 | 0.14 | 0.06 | 0.34 | 1.04 | 0.67 | 1.61 | 8.65 | 6.18 | 12.1 |
| | | | | | F | 0.37 | 0.28 | 0.48 | 0.03 | 0.00 | 0.23 | 0.04 | 0.01 | 0.28 | 0.19 | 0.08 | 0.45 | 1.32 | 0.92 | 1.91 | 6.60 | 4.96 | 8.79 |
| | | | | | MF | 0.39 | 0.32 | 0.47 | 0.13 | 0.06 | 0.28 | 0.04 | 0.01 | 0.16 | 0.16 | 0.09 | 0.31 | 1.19 | 0.90 | 1.57 | 7.33 | 5.90 | 9.12 |
| Total | | | | BB | M | 6.59 | 6.11 | 7.08 | 2.19 | 1.66 | 2.89 | 3.20 | 2.61 | 3.92 | 7.97 | 7.04 | 9.04 | 17.4 | 15.5 | 19.5 | 26.2 | 21.3 | 32.2 |
| | | | | | F | 12.63 | 11.99 | 13.29 | 1.84 | 1.35 | 2.51 | 5.14 | 4.38 | 6.02 | 18.2 | 16.7 | 19.7 | 36.2 | 33.6 | 39.0 | 38.9 | 34.2 | 44.1 |
| | | | | | MF | 9.69 | 9.29 | 10.10 | 2.02 | 1.64 | 2.48 | 4.16 | 3.67 | 4.71 | 13.0 | 12.1 | 13.9 | 27.3 | 25.7 | 29.1 | 34.4 | 30.9 | 38.3 |
| | | | | M | M | 8.37 | 7.84 | 8.93 | 2.65 | 2.06 | 3.41 | 4.11 | 3.44 | 4.90 | 9.43 | 8.43 | 10.6 | 23.9 | 21.7 | 26.2 | 29.8 | 24.6 | 36.1 |
| | | | | | F | 5.05 | 4.65 | 5.48 | 1.73 | 1.26 | 2.38 | 2.25 | 1.77 | 2.87 | 5.61 | 4.84 | 6.50 | 14.8 | 13.2 | 16.5 | 16.6 | 13.8 | 19.9 |
| | | | | | MF | 6.64 | 6.31 | 6.99 | 2.20 | 1.81 | 2.68 | 3.19 | 2.77 | 3.68 | 7.54 | 6.90 | 8.25 | 19.1 | 17.7 | 20.5 | 21.3 | 18.6 | 24.3 |

* Age-adjustment (EU standard population). $ Incidence rate (N per 100'000 person-years). # Lower (UB) and upper bound (UB) of the 95% confidence interval.

Tab. 2. Incidence rates for major brain/CNS tumours in Switzerland during 2010-2014 with benign/borderline (BB) and malignant (M) behaviour.

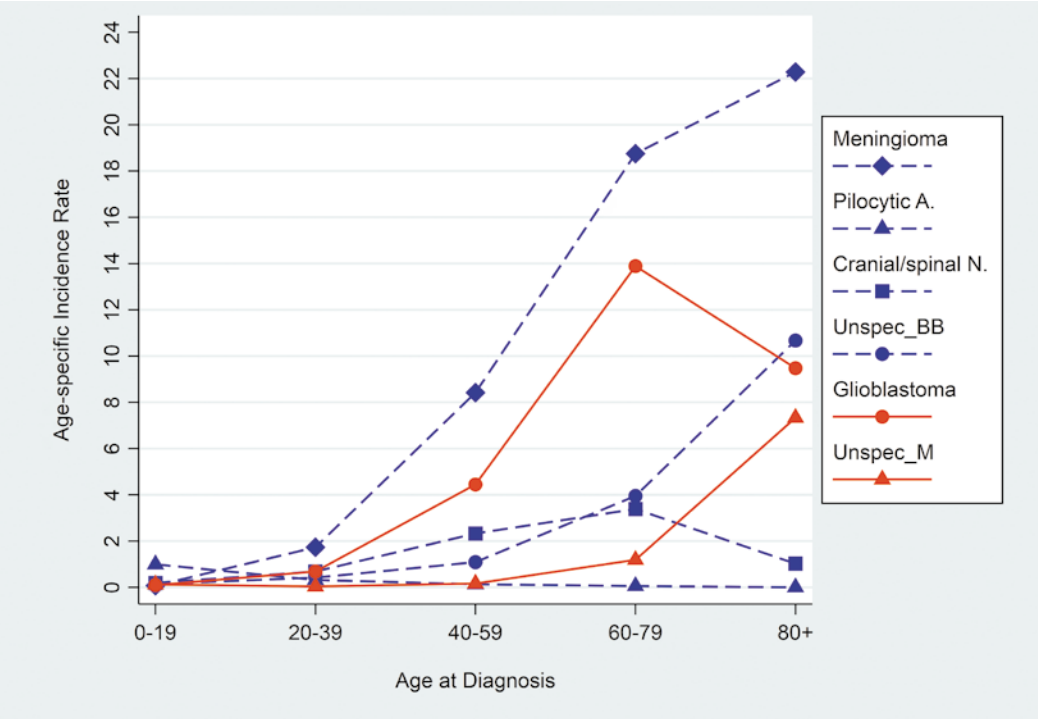



Fig. 1. Age-specific incidence rates for selected brain/CNS tumours. Tumours with benign/borderline (BB) behaviour in blue and dashed lines. Cancers with malignant (M) behaviour in red and straight lines. Both sexes were combined. Period of diagnosis 2010-2014.

*Diagnostic context and procedures*

**Figure 2A** shows that the large majority of brain/CNS M tumours at all ages were symptomatic at time of detection and diagnosis, whereas BB tumours are often discovered incidentally. The proportion of incidentally detected BB tumours rose from less than 10% at age 0-19 to about 50% at age 80+.

**Figure 2B** shows that the proportion of less precise clinical (non-microscopic) methods as confirmation of the diagnosis is much higher with respect to BB tumours, as compared with M tumours, except for the youngest age group. The proportion of clinical diagnostic procedures in BB tumours increased steadily from 20% at age 0-19 to over 70% at age 80+ (**Fig. 2B**). In contrast, more accurate microscopic methods form the basis of diagnosis in over 80% of M tumours at all ages below 80, while for age 80 and higher, they were used in only 40% of the cases.

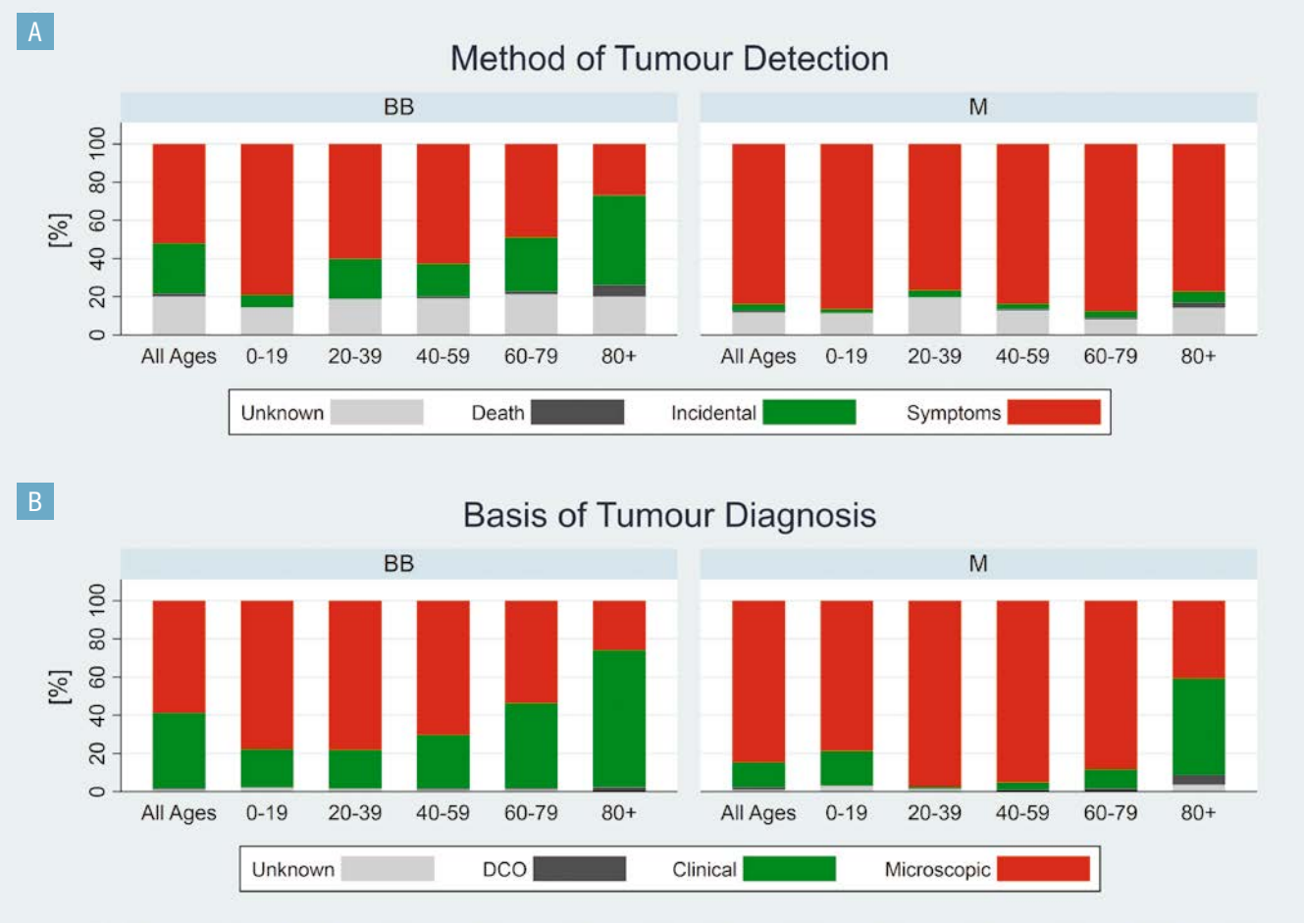
## Discussion

In this report, NICER presents Swiss population-based data on primary brain/CNS tumours with benign/borderline (BB) behaviour for the first time, thus complementing previously published data on primary malignant (M) brain/CNS diagnoses [1]. The plausibility of the NICER tumour dataset was assessed by comparison with the internationally renowned population-based Central Brain Tumor Registry of the United States of America (CBTRUS) [19]. The quality and completeness of the CBTRUS has been supported by national legislation specifically for benign brain tumours since 2004 [20], with boosting effects on incidence rates [21]. There are some differences in case definition: we excluded a number of tumour groups, which made up about 19% of all cases in CBTRUS (17% BB, 2% M), i.e. the ICD-O-3 topographies C75 (pituitary and craniopharyngeal duct) and C30.0 (olfactory tumours of the nasal cavity) as well as all lymphomas and hematopoietic neoplasms in brain/CNS. The Swiss M/F ratio for all brain/CNS tumours of 0.76 (**Tab. 1**) was very close to the CBTRUS ratio of 0.73. The Swiss data also recapitulated the characteristic sex difference with respect to BB and M brain/CNS tumours: Swiss BB M/F ratio of 0.47 (CBTRUS 0.56) and Swiss M M/F ratio of 1.48 (CBTRUS 1.24) [19]. Furthermore, the allocation into different tumour groups was very similar. We reproduced **Figure 4** of the CBTRUS report [19], taking account of the excluded tumour groups in the Swiss data (**Fig. 3**). BB diagnoses made up 215,944 of 333,225, or 63.5%, among brain/CNS diagnoses in the US, whereas there were 4,696 of 7,841, or 59.9%, in Switzerland (**Fig. 3**). The small difference speaks against overt under-registration of BB tumours in Switzerland. In addition to tumour proportions, we compared age-adjusted incidence rates for major morphology groups (**Fig. 4**). The fact that Swiss data was adjusted with the EU standard population [17] and CBTRUS with the 2000 US standard population [22] causes only negligible differences. Overall, M tumour incidence rates were almost identical in Switzerland and the USA,

i.e. for all M tumours combined: 6.64 versus 6.66, respectively (**Fig.** 4). The incidence rates for BB tumour types ranged somewhat below the US rates, amounting to a 15% lower rate for all BB tumours combined (9.69 versus 11.48, respectively; **Fig.** 4). Restricted to age at diagnosis 0-19 years, our extrapolated value amounted to about 65 (95% CI: 59, 73) brain tumours with BB or M behaviour for Switzerland annually (time period 2010-2014), whereas the Swiss Childhood Cancer Registry, which collects cases nationwide and independent from cantonal cancer registries, counted about 52 cases annually (time period 2007-2016), again speaking against under-registration [23].

Incidence rates are affected by changes in tumour classification, cancer registration procedures (e.g. recognition of international recommendations), public health legislation, or availability of diagnostic technology, among other factors. All of these influences must be considered when comparing different countries. Although most Swiss cancer registries routinely collect all primary brain/CNS tumours, irrespective of behaviour, the extent and completeness of ascertainment of benign or borderline cases may not have been consistent at all times and all areas. We have recently estimated the completeness of ascertainment of all primary malignant tumours in Swiss cancer registration, with very satisfactory results of about 93% completeness for brain/CNS [24]. Our present comparison with CBTRUS did not show overt signs of under-registration or selection bias for recently collected BB diagnoses (2010-2014). The completeness and quality of BB diagnoses in earlier time periods is less certain. BB tumours, such as asymptomatic meningiomas

Fig. 2. Distribution of diagnostic context for benign/borderline (BB) and malignant (M) diagnoses in brain/CNS from 2010 to 2014, by patient age. (A) The method of tumour detection, i.e. the circumstances by which the case came to medical attention. Death: with/without autopsy; Incidental: on occasion of another disease or routine medical consultation; Symptoms: tumour related symptoms. Diagnoses restricted to cantons ZH, FR, VS, and GE. (B) The most valid diagnostic procedure of tumour confirmation. DCO: death certificate based. Clinical: based on neuroradiological imaging. Microscopic: based on bioptic or surgical specimens.



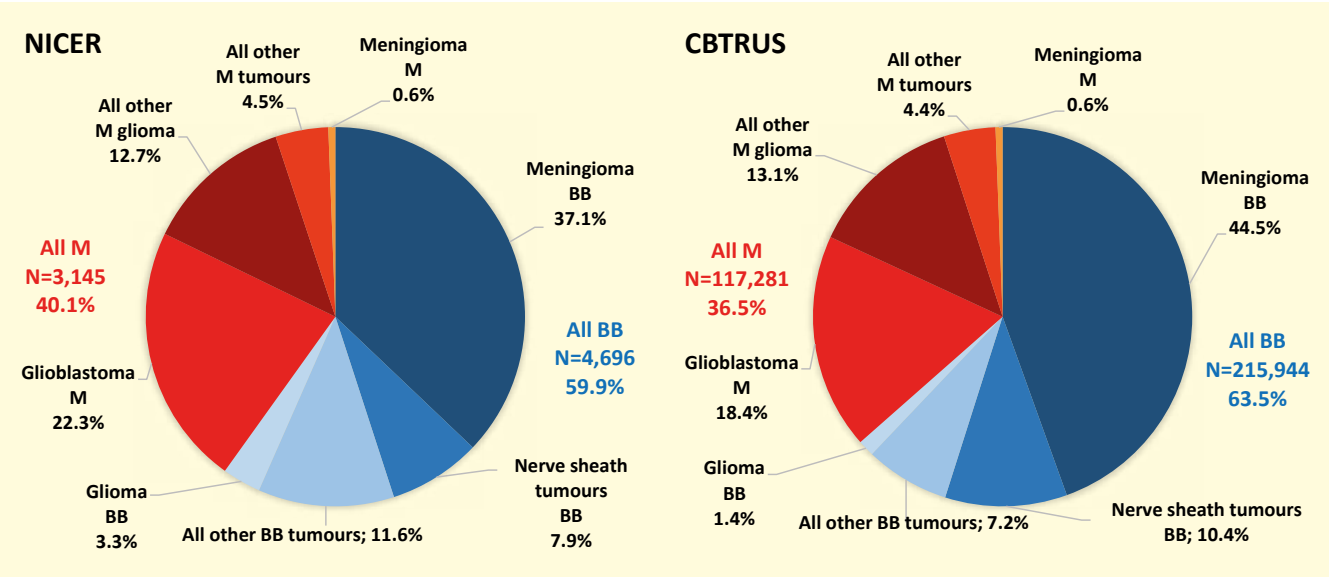



Fig. 3. Similar distribution of primary brain/CNS tumours by behavior in Switzerland, based on the NICER dataset, and in the United States, based on the CBTRUS data, for the same diagnosis period (2010-2014). BB: benign/borderline; M: malignant.

being followed-up clinically by imaging alone, or detected at autopsy, might have been under-registered [25]. Furthermore, since brain metastases (secondary tumours) are observed more frequently than primary tumours in brain/CNS [26], it poses the problem of correctly classifying them, especially when the extracranial primary tumour cannot be identified despite thorough investigation by standard techniques [27].

Radiological methods, e.g. magnetic resonance imaging (MRI) introduced in the 1980s, have improved the abil-

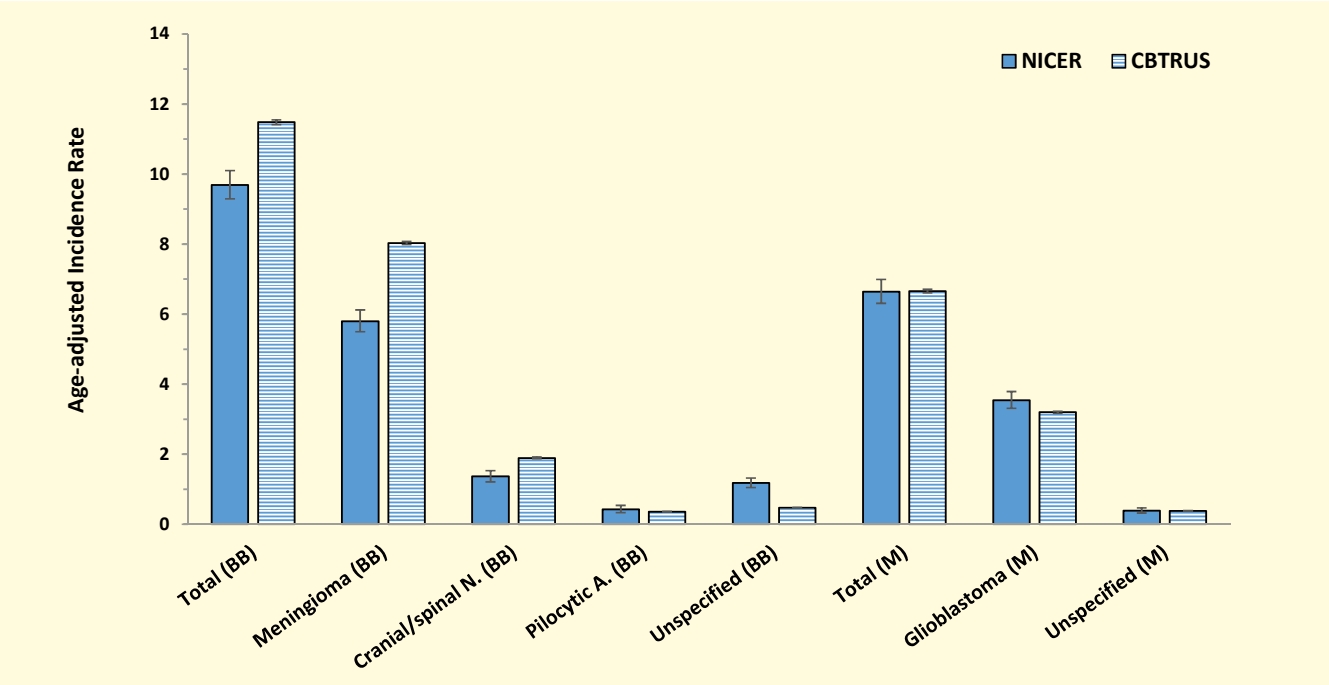



Fig. 4. Age-adjusted incidence rates for benign/borderline (BB) and malignant (M) brain/CNS tumours in Switzerland, based on the NICER dataset, and in the United States, based on CBTRUS data, for identical diagnosis periods (2010-2014).

ity to diagnose diseases and follow-up treatment responses with unprecedented safety and sensitivity. However, it also precipitates incidental findings, mostly asymptomatic brain infarcts, cerebral aneurysms and primary brain/CNS tumours [28, 29]. Incidental findings naturally increase with the age of subjects. Such detected tumours are usually benign and, without relevant symptoms or significant tumour growth, do not require surgery [30, 31]. It is often speculated that the frequently reported increase in benign brain tumour incidence, as well as the large differences between countries, are at least partially related to increased application of neuroradiological imaging methods [32-35]. This would also explain why increases were strongest at higher ages, where physicians had been reluctant to use the older and more invasive diagnostic procedures available before the advent of imaging methods [36]. Furthermore, there has been an increase in cancer survivors over time, in Switzerland and other countries [37, 38]. Cancer survivors are at higher risk for a number of morbidities, among them second primary brain tumours of every behaviour, due to treatment-related irradiation as well as surveillance bias [39]. Finally, the brain is a common site of distant metastasis for high-incidence cancers such as lung or breast cancer [26]. Imaging of the brain for pretreatment clinical staging purposes is routinely performed in these patients [40], further increasing incidental findings of independent primary brain tumours. Our own observations are in accord with the interpretation that BB brain/CNS tumours in Switzerland are often incidental, asymptomatic findings, diagnosed without microscopic verification, especially in older subjects (**Fig. 2**). Although many tumours have unique characteristics that make them identifiable on imaging, it is important to consider the lower level of certainty in specifying the correct morphology. This might underlie the conspicuously high incidence rates of tumours lacking specified morphology, especially with BB behaviour, in patients above 60 years of age at diagnosis (**Fig. 1**).

## Conclusion

Malignant and benign/borderline brain tumours demonstrate differing patterns of occurrence by sex, age, and exhibit considerable diversity with respect to diagnostic context. The NICER dataset appears to be of sufficient quality with respect to benign/borderline brain/CNS diagnoses, at least for the recent time period (2010-2014), to include them in future brain cancer surveillance in Switzerland. The quality and completeness of benign/borderline tumours of brain/CNS in earlier times needs to be assessed. The inclusion of non-malignant brain tumours in cancer surveillance provides a better assessment of disease burden and medical resource needs associated with these unique tumours.

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