Global surveillance of survival from intrinsic brain tumours diagnosed during 2000-2014: trends by age and histology

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I, Fabio Girardi, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

London, 7 December 2020

We are all responsible for all

Fëdor Dostoevskij

I dedicate this thesis to

my father Mariano and my mother Antonietta

my brother Davide and his wife Valentina

my nephew Elia and my niece Sara

They have been a lifeline

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Abstract

This thesis provides a comprehensive examination of world-wide variation in population-based survival from brain tumours in children and adults, by histology. It comprises five chapters in the form of research papers.

Population-based cancer survival estimates are key to assessing the overall effectiveness of a health care system in managing cancer. The third cycle of the CONCORD programme for the global surveillance of cancer survival (CONCORD-3), which included data for more than 37.5 million cancer patients diagnosed during 2000-2014, highlighted substantial world-wide disparities in survival for all brain tumours combined, in both children and adults.

Survival comparisons for all brain tumours combined, however, are potentially confounded by international variation in histology distribution and the clinical heterogeneity of the various tumour subtypes. Robust comparisons of brain tumour survival require clinically relevant data by histology because histology is the main outcome predictor. Granular survival estimates by histology are therefore warranted.

The first and second chapters, two systematic reviews, appraise the geographical coverage and methodology of studies of brain tumour survival by histology. The first chapter focusses on children, while the second centres on adolescents and young adults. Adolescents and young adults are a transitional age group for which the strategy for presenting epidemiological data by histology is still debated. These reviews show that very little is known about brain tumour survival by histology beyond Europe and North America, and that differences in study design may indeed hamper robust comparisons.

The two systematic reviews inform the scope of the third chapter, in which distinct histology groupings for children and adults are defined. The groupings for children represent an enhanced version of the International Classification of Childhood Cancer (third edition), while those for adults are designed to produce clinically meaningful categories. These groupings schemes form the basis for an examination of the global variation in the histology distribution of brain tumours and for an account of some of the key quality indicators for cancer registration.

The histology distribution of brain tumours varied widely world-wide (2000-2014). In children, the proportion of low-grade astrocytic tumours ranged from less than 10% to more than 30%. In adults, the proportion of glioblastoma varied between 9% and 69%. International comparisons were made difficult by wide differences in the proportion of tumours of unspecified histology, which accounted for up to 52% of diagnoses in children and up to 65% in adults.

These histology groupings are then used to produce up-to-date analyses of global trends in brain tumour survival by histology, for children (chapter 4) and adults (chapter 5), using individual records from CONCORD-3 for 610,710 patients diagnosed with a brain tumour during 2000-2014 in 60 countries. Many of these countries have never previously been included in studies of brain tumour survival by histology. The studies deploy the same protocol for data collection, quality control and statistical methods for all the data sets.

Brain tumour survival in children and adults were examined in two separate analyses. Five-year net survival for low-grade astrocytoma in children was in the range 84-100%, while it varied between 47% and 86% for medulloblastoma. In adults, survival from glioblastoma improved substantially after 2005 in most countries, mainly in the short term (up to two years from diagnosis). The increase in two-year survival between 2000-2004 and 2010-2014 was more remarkable for adults aged 40-70 years than for younger patients (15-39 years). Trends for 2000-2014 were upward for the 40-70 age group, while they were somewhat flat for the 15-39 age group.

To our knowledge, this is the largest study of population-based survival from brain tumours by histology. The geographical breadth, the methodology for data collection and analysis, and the proposed histology groupings are expected to set a benchmark for future global comparisons.

Background

Introduction

Primary central nervous system (CNS) tumours are rare. CNS tumours comprise tumours of the brain, the spinal cord and the meninges. Brain tumours are the largest group. The third cycle of the International Incidence of Childhood Cancer (IICC) study, covering 11% of the world population, reported a world-standardised incidence rate in children (0-14 years) of 28 cases per million person-years during 2001-2010. The incidence rate varied between 6.3 in sub-Saharan Africa to 39 per million person-years in Northern Europe.[1]

Based on data from Cancer Incidence in Five Continents, standardised incidence rates in men (≥15 years) during 2008-2012 varied between 1.0 per 100,000 person years in Seychelles and 11.2 in Croatia, while in women it was lowest in Thailand (Khon Kaen) (1.4) and highest in China (Jiaxing City) (12.2).[2]

The incidence of CNS tumours among children in Europe rose between 1970 and 2001. The magnitude of the increase varied between Western Europe (average annual percentage change (AAPC) +0.8%) and Eastern Europe (AAPC +2.5%).[3] An upward trend in the incidence rate of CNS tumours in adults was observed in some South American countries and in some former Soviet Union countries between 1993 and 2007.[4] The interpretation of these findings is complex. Authors argued that the observed trend was partly attributable to improved access to diagnostic techniques or to more complete cancer registration. The evidence on potential risk factors is weak. Studies assessing the impact of the use of mobile phones on the risk of CNS tumours showed conflicting findings. Radiofrequency electromagnetic fields were classified in 2013 as possibly carcinogenic (2B) in humans by the International Agency for Research on Cancer.[5]

World-wide, primary CNS tumours were estimated to be the second most important cause of cancer-related deaths in children and adolescents in 2012.[6] In patients aged 20 to 39 years CNS tumours were estimated to be the fourth most important cause of cancer-related deaths in high human development index (HDI) and the second most important in very high HDI countries.[6]

Primary CNS tumours vary widely in terms of pathology, clinical behaviour, treatment and outcome. They range from pilocytic astrocytoma, curable with surgery alone, to glioblastoma, which is highly invasive and refractory to treatment.

Tumours of the neuroepithelial tissue are the largest group. They arise from neuronal or glial cells. Glial cells support and maintain the homeostasis of neurons. This group includes several subtypes, depending on the cell of origin. They may be astrocytic, oligodendroglial, ependymal, of the choroid plexus, embryonal, of the pineal gland, or mixed neuronal-glial.[7, 8]

In the EUROCARE-5 study, including 15,281 children diagnosed with a CNS tumour in one of 27 European countries during 2000-2007, the most common brain tumours were astrocytoma (40%) and embryonal tumour (21%). Half of the astrocytic tumours were pilocytic astrocytomas, while two-thirds of the embryonal tumours were medulloblastomas. Five-year observed survival was 95% (95% confidence interval (CI) 94-96%) for pilocytic astrocytoma and 65% (95% CI 62-67%) for medulloblastoma. This study also showed a remarkable international variation. Five-year survival for tumours classified as World Health Organization (WHO) grade I ranged from 70% in Poland (23-92%) to 100% in Finland or Switzerland. Five-year survival for WHO grade III-IV tumours varied from 36% (25-48%) in Bulgaria to 66% (50-78%) in Finland.[9] In a cohort of 2,785 patients in 13 registries from the US Surveillance, Epidemiology, and End Results Program (SEER 13), five-year survival from astrocytoma increased from 69% (64-73%) for children diagnosed during 1975-1979 to 85% (82-89%) for those diagnosed during 1995-1999. Over the same 20-year period, survival at five years from a primary neuroectodermal tumour (PNET) rose from 47% (39-55%) to 65% (59-71%).[10]

Trends in survival by histology have also been examined in adults. In the EUROCARE-5 cohort, including 83,458 adults (15-99 years) diagnosed with a primary CNS tumour during 1999-2007, 50% of the neuroepithelial tumours were glioblastomas and 18% other specified or unspecified astrocytomas and 9% oligodendrogliomas. Five-year relative survival was 6.3% (5.9-6.7%) for glioblastoma and 25% (24-26%) for astrocytoma (other specified or unspecified). These figures suggest a poor prognosis for adults.[11] The same study showed a slight improvement of survival over time. Five-year survival increased from 4.7% (4.1-5.4%) for

glioblastomas diagnosed during 1999-2001 to 6.6% (5.9-7.3%) for those diagnosed during 2005-2007. Over the same eight-year period, five-year survival for astrocytoma rose from 21% (20-22%) to 26% (24-27%).[11] The time frame of this analysis was short, but these findings are clinically relevant, because the oral chemotherapy agent temozolomide started to be used routinely for the treatment of high-grade gliomas from 2005.[12] As with children, survival in adults varied widely between countries. The fourth cycle of the EUROCARE study included 96,167 patients from 22 countries, diagnosed with a CNS tumour during 1988-2002. Five-year survival from glioblastoma was similarly poor in all the five regions (Northern Europe, United Kingdom and Ireland, Central Europe, Eastern Europe and Southern Europe), while survival at 5 years for astrocytoma not otherwise specified (NOS) was lowest in Eastern Europe (28%, 22-34%) and highest in Northern Europe (49%, 43-56%). The same differential was observed for other specified glioma.[13]

Classification of brain tumours

The WHO classification

The World Health Organization (WHO) Classification of Tumours of the Central Nervous System Fourth Edition is the reference for pathological definition.[7, 8] It evolves from the third edition, which introduced genetic profiles as adjuncts for the definition of brain tumours.[14] The fourth edition incorporates eight new tumour entities and further expands the genetic bases of brain tumours. The 2007 WHO classification identifies six categories of primary CNS tumour, plus the metastatic lesions. For each tumour subtype, the classification gives a detailed description of the histological and immunohistochemical hallmarks and guidance for differential diagnosis.

The WHO classification also incorporates a grading scheme, which is a malignancy scale to help predict the biological behaviour of a tumour. Such scheme is cross-sectional because it spans a wide range of morphologies. It represents an important adjunct to clinical decision-making. Tumours are attributed a grade varying from I to IV, depending on their proliferative potential. For instance, astrocytic tumours showing solely cytological atypia are attributed grade II; those showing anaplasia and

mitotic activity are given a grade III, and tumours featuring necrosis and microvascular proliferation are defined as grade IV.

The 2016 revision of the WHO classification revolutionises the taxonomy of CNS tumours by prioritising the molecular profile over histology.[15] For instance, diffuse gliomas, medulloblastomas and other embryonal tumours are now genetically defined. From 2018, the Central Brain Tumor Registry of the United States (CBTRUS) started collecting population-based data from 48 state-wide cancer registries using the 2016 WHO categories.[16] It may take time for other cancer registries world-wide to implement the 2016 WHO classification in brain tumour reporting. Moreover, in some countries, molecular assays are simply not available. For this reason, histology is still relevant to global comparisons of survival from brain tumours.

A summary of the WHO classifications can be found in the appendix.

The ICD-O-3 classification

The International Classification of Diseases for Oncology (ICD-O) is primarily used by cancer registries to code tumours on multiple axes, among which morphology, topography and behaviour are the main ones. The third edition (ICD-O-3) was published in 2000 and revised in 2013.[17]

Morphology is coded as a four-digit number for registration and standardisation purposes. This corresponds to the WHO definitions.[7] For instance, the first three digits for gliomas, originating from neuroepithelial tissue, range from 938 to 948. A further number identifies the subtype (e.g. 9440 for glioblastoma). Two further digits may be used. The fifth digit specifies the behaviour: 0 for benign, 1 for uncertain whether benign or malignant, 2 for *in situ,* 3 for invasive tumours. The sixth digit represents the grade, ranging from 1 to 4 for well, moderately, poorly and undifferentiated tumours, respectively.

The topography axis follows mainly the International Statistical Classification of Diseases and Related Problems (tenth revision, ICD-10).[18] Tumours are defined by four characters: an alphabetical letter, two digits for the main site and one digit for the subsite (e.g. C71.6 identifies a tumour in the cerebellum or C71.2 a tumour in the parietal lobe of the brain).

The ICCC-3

The International Classification of Childhood Cancer (ICCC) is the standard for presenting data on cancer incidence and survival in children. Its implementation was warranted by the conviction that grouping of tumours in children should be grouped primarily on morphology, rather than topography. The third edition (ICCC-3) was published in 2005.[19]

ICCC-3 is based on the ICD-O-3 classification and adopts its codes and definitions. It follows a three-tier system, in which each tier corresponds to a different level of granularity. The main table comprises 12 groups (level 1) and 47 subgroups (level 2). In the extended form, Level 3 further refines selected subgroups. In the first level, group III comprises “CNS tumours and miscellaneous intracranial and intraspinal neoplasms”. It is further divided into 6 subgroups (level 2), denoted with the alphabet: ependymoma and choroid plexus tumour (a), astrocytoma (b), intracranial and intraspinal embryonal tumour (c), other glioma (d), other specified intracranial and intraspinal neoplasm (e) and unspecified intracranial and intraspinal neoplasm (f).[19]

Diagnosis

Magnetic resonance imaging (MRI) is the diagnostic gold standard when a CNS tumour is suspected. The images are the result of the interaction between electro-magnetic fields and hydrogen atoms, which abound in water and fat. For instance, different proportions of these substances in normal and pathological tissue help to identify the tumour and the associated oedema (i.e. swelling). MRI offers high anatomical resolution and allows discrimination between high-grade lesions and low-grade lesions, which usually do not show contrast enhancement. Computerized tomography (CT) adopts X-rays and, similarly to MRI, enables images with or without contrast. It is characterised by shorter execution times, but the spatial resolution is lower.

Common morphologies: clinical presentation and treatment

For the purpose of providing a general background on intrinsic brain tumours, here I will only focus on the main brain tumour subtypes. However, the research project will examine all the relevant histological groupings.

Low-grade gliomas in children

Low-grade gliomas are WHO grade I or II tumours, representing approximately one-third of all CNS tumours in children.[15] These gliomas substantially differ from their adult counterpart: mutations of the isocitrate dehydrogenase gene (*IDH*), encoding for an enzyme involved in the Krebs cycle, are not present, and progression to higher-grade lesions rarely occurs.[20] Low-grade gliomas have a favourable outcome, with an overall survival at 5 years of 95%.[21]

The most frequent low-grade glioma in children is pilocytic astrocytoma. Common sites for this tumour are the cerebellum, the optic nerve, the optic chiasm/hypothalamus and the basal ganglia.[7] Clinical presentation encompasses a range of non-focal signs and symptoms, such as macrocephaly, endocrine dysfunction and raised intracranial pressure (due to obstructive hydrocephalus or oedema), with nausea and vomiting. When located in the optic pathways or in the orbit, it may cause visual impairment or proptosis. Seizures are rare, because pilocytic astrocytoma seldom originates in the cerebral cortex. Genetic hallmarks of pilocytic astrocytoma include mutations in the mitogen-activated protein kinase (MAPK) pathway, which regulates cellular proliferation and differentiation.[22]

Curative surgery is the primary treatment. When total resection is not possible, due to proximity to critical anatomical structures, tumours are likely to progress. In this scenario, chemotherapy with carboplatin or vinca alkaloids (vincristine or vinblastine) is indicated.[23, 24] The role of radiotherapy for unresectable or recurrent tumours is controversial, because of the cognitive sequelae that may affect the growing brain.[25, 26]

Medulloblastoma

Medulloblastoma is an invasive embryonal tumour, occurring most frequently in children. Peak incidence is normally around 7 years of age. When arising in adulthood, it almost exclusively affects young individuals (21-40 years). In children, three-quarters of medulloblastomas are located in the cerebellar vermis. Symptoms at presentation include ataxia, disrupted gait and hydrocephalus.[8] Because of the tendency to metastasise via the cerebrospinal fluid, staging encompasses MRI of the whole neuroaxis and a lumbar puncture.[27]

Treatment includes a combination of surgery, radiotherapy and chemotherapy and may vary depending on risk stratification. High-risk patients (older than 3-5 years) are defined as those having post-operative residual disease larger than 1.5 cm^2 or metastases. These patients should receive craniospinal irradiation (36-39 Gray (Gy)) plus a 55 Gy boost to the tumour bed in the posterior fossa, followed by chemotherapy with cyclophosphamide and cisplatin.[28] Average-risk patients should be treated with lower-dose craniospinal irradiation (23.4 Gy), a radiation boost to the posterior fossa, and adjuvant chemotherapy.[29] Infants are usually spared radiotherapy in consideration of the potentially severe neurological sequelae.[30]

Medulloblastoma can be further defined based on the molecular profile.[31] Four subgroups have been identified, each with peculiar clinical traits. (1) Wingless-related integrated site (*WNT*) activated tumours: they have a longer pre-diagnostic phase, rarely disseminate, occur in older children and show a more favourable outcome. (2) Sonic Hedgehog (*SHH*) activated tumours: they are usually localised, their incidence does not vary with age and the pre-diagnostic phase is shorter; outcome is age-dependent: excellent in infants and poor in children in whom a Tumour Protein 53 gene (*TP53*) mutation is also present. (3) Group 3 tumours: they are characterised by the activation of the GABAergic (GABA: gamma-aminobutyric acid) and photoreceptor pathways; they are more frequent in boys, are located in the fourth ventricle close to the brainstem, have a short pre-diagnostic phase and in half of the cases present metastases at diagnosis; the prognosis is poor, especially for infants who do not receive radiotherapy. (4) Group 4 tumours: their genetic hallmark is the activation of neuronal and glutaminergic pathways; they are the most frequent subgroup in children older than 3 years, and one-third of the cases are metastatic at onset; the prognosis is intermediate. Such molecular stratification may be used to tailor treatment.[32-34] and it has been incorporated in the latest WHO classification of CNS tumours.[15] Relapse of medulloblastoma is associated with a poor outcome. Salvage therapy includes repeat surgery, re-irradiation and high-dose chemotherapy.[35]

Diffuse and anaplastic astrocytoma in adults

Diffuse astrocytoma (WHO grade II) and anaplastic astrocytoma (WHO grade III) are relatively common in adolescents and young adults. These tumours harbour a mutation in the isocitrate dehydrogenase 1 (*IDH*1) gene in approximately two-thirds of

cases.[36] Tumours with a mutation in the *IDH* gene often show a more favourable outcome. Surgical resection, when feasible, represents the best initial management.

For WHO grade II astrocytic tumours, post-operative radiotherapy should only be considered after incomplete surgical removal or in patients aged 40 years or more.[37] These patients may also benefit from subsequent chemotherapy with lomustine, procarbazine and vincristine.[38]

For WHO grade III astrocytic tumours, the treatment protocol includes maximal surgical resection followed by radiotherapy. The randomised controlled NOA-04 trial showed that chemotherapy with lomustine, procarbazine and vincristine, or temozolomide alone, was as effective as radiotherapy.[39] In the randomised controlled CATNON trial, patients whose tumours had a methylation of the O-6-methylguanine-DNA-methyltransferase gene (*MGMT*) promoter and did not have an *IDH* mutation, experienced improved survival if 12 months of temozolomide chemotherapy were added.[40] Methylation of the *MGMT* promoter silences the transcription of a gene implicated in the repair of damages from alkylating agents such as temozolomide.

Treatment at progression depends on performance status, previous therapies and extent of relapse. Surgical re-excision should always be considered, followed by radiotherapy in patients who were not previously irradiated, or chemotherapy.

Glioblastoma

Adult glioblastoma is the most common astrocytic tumour, with the highest incidence in individuals 45-75 years old. Ionizing radiation is the only recognized aetiological factor.[41] Due to its aggressiveness and rapid growth, the onset of symptoms usually occurs only a few months before the diagnosis, unless the disease originates from a previous lower-grade glioma. Glioblastomas originating from a lower-grade lesion are characterized by mutation of the *IDH* gene.[36] Glioblastoma arises most frequently in the subcortical matter of the brain.[7] Symptoms include weakness, visual impairment, memory disorder, speech disruption and change in mood. Headache is common and derives from high intracranial pressure due to direct mass effect or hydrocephalus secondary to ventricle obstruction.[42]

Maximal surgical excision should be offered when the patient's performance status and tumour location permit. Glioblastoma tends to infiltrate surrounding structures, and thus complete removal of all cancer cells is not possible. In adults younger than 70 years, surgery is followed by radiotherapy, concomitant with temozolomide chemotherapy and adjuvant temozolomide. This treatment protocol was implemented in clinical practice after an international randomised controlled trial had shown it was associated with a 36% reduction of the risk of death compared to radiotherapy alone.[12] Patients whose tumours had a methylation of the *MGMT* promoter, experienced an improved outcome.[43] In selected patients with good performance status, chemoradiation may be given over the age of 70 years.[44] None of the treatments investigated in the context of relapsed or progressing disease has proven to be effective in prolonging overall survival. Bevacizumab, a vascular endothelial growth factor (VEGF)-receptor-directed monoclonal antibody, is sometimes used during the disease course. However, despite being beneficial in reducing the use of corticosteroids and improving symptoms arising from cerebral oedema, it only delays disease progression, without affecting overall survival.[45]

Aim and objectives

Aim

This project aims to conduct the first detailed analysis of the world-wide differences in survival from brain tumours, both in children and adults.[46] The project is embedded in the CONCORD programme and represents an extension of its main research question.

The CONCORD programme was the first to establish global surveillance of cancer survival. The third cycle (CONCORD-3) included 18 cancers, including brain. It drew individual-level information on more than 37 million cancer patients from 322 population-based cancer registries in 71 countries.

Cancer registration is the backbone for estimating population-based cancer survival. For a given cancer, the survival of all patients in the population reflects the overall effectiveness of a health care system in managing that cancer. Access to care

is the main differential accounting for between-country disparities in survival. It depends on primary care, referral pathways, availability of diagnostic facilities and equitable provision of adequate treatment.[47, 48] Ecological or socioeconomic descriptors may also play a role. Relevant variables include distance from treatment facilities, health insurance status or the population density of neuro-oncology specialists.

CONCORD-3 included 656,659 adults (15-99 years) and 66,814 children (0-14 years) diagnosed with a primary brain tumour during 2000-2014. Five-year net survival from all brain tumours combined varied widely between countries. During 2010-2014, it ranged between 15% in Thailand (13-17%) and 42% in Croatia (40-44%) in adults, and from 29% in Brazil (16-42%) to about 80% in some European countries, in children.[46]

I will analyse novel data from CONCORD-3 to estimate survival by all the available patient-related and tumour-related factors. Survival analyses will not account for societal factors, but these should be incorporated in future studies to help explain the international disparities in survival.

Diagnosis of brain tumours is complex, and its timeliness depends on prompt recognition of symptoms,[49-51] imaging confirmation and accessibility of a neurosurgical facility to provide a biopsy or surgery. Furthermore, while radiotherapy is the mainstay of treatment, the world-wide distribution of linear accelerators is highly uneven. Low-income and middle-income countries, in which 50% of childhood CNS tumours arise, possess only 30% of all the world's linear accelerators, and in many countries, radiotherapy is simply not available.[52] Inequalities in access to these treatment modalities may impact survival, and the extent of variation is different between morphologies.[9, 13, 46]

Especially in children and young adults, a thorough analysis of international survival gaps by histology is warranted. This would enable the estimation of specific care needs to help inform cancer control plans. The project is expected to become the reference for international comparisons of brain tumour survival.

Objectives

Specific objectives of the project are:

1. To perform the first systematic review of the literature on population-based survival from brain tumours.

2. To produce frequency distributions of brain tumours by histology and country, separately for children and adults.

3. To estimate net survival from brain tumours by histology and country, separately for children and adults.

4. To describe survival trends for the most common histological subtypes by five-year calendar period of diagnosis (i.e. 2000-2004, 2005-2009 and 2010-2014) and country, separately for children and adults.

Methods

Systematic reviews

I queried six databases for relevant literature: Dissertation and Theses Global, Embase, Medline, Open Grey, Scopus and Web of Science. Search strategies were database-specific and were reviewed by the LSHTM librarian. They included a combination of free-text keywords and, whenever possible, exploded medical subject headings (MeSH). Wildcard (?) and truncation (*) operators were used to account for variations in spelling or word endings.

Entries from each source were combined and duplicates were removed. The relevance of the remaining records was assessed through a step-wise process, based firstly on the title and then the abstract. The full text of the potentially eligible publications was appraised based on pre-specified inclusion criteria. Studies were eligible if they:

1. included children (0-14 years of age), adolescents (15-19 years of age) or young adults (20-39 years of age), affected by a primary brain tumour;
2. were observational and longitudinal;
3. the outcome of interest was five-year survival;
4. follow-up started at cancer diagnosis and ended at the earliest of death (regardless of the cause), end of study or last known vital status;
5. survival estimates based on data from population-based cancer registries.

For the purposes of the systematic reviews, I only focussed on survival at five years because it is the most commonly used time landmark. Hospital-based studies were also eligible if no population-based estimates were available for that country. A time restriction was set to improve comparability. Studies published before 1995 adopted earlier morphological or topographical classifications, which were substantially different from the more recent versions, so studies published before 1995 were excluded.

I followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines and the study protocol was validated by the international prospective registry of systematic reviews PROSPERO.[53] I used modified forest plots to graphically display international trends in survival.

Analyses of population-based data for patients diagnosed with a brain tumour, included in the CONCORD-3 data base

I performed a secondary analysis of anonymised data collected as part of the CONCORD-3 study. The aim of the CONCORD-3 summary article was to update trends in five-year population-based survival for 18 cancers to 2014. However, CONCORD-3 collected information on the full range of descriptors commonly adopted for cancer registration (e.g. morphology).

I used a data set comprising 67,331 children and 671,085 adults diagnosed with a primary brain tumour in 60 countries during 2000-2014. Data were collected using the same protocol, and centrally validated for protocol adherence and consistency through a rigorous 3-phase data quality control procedure (details published elsewhere).[46, 54] In brief, registrations based on a death certificate or autopsy, age out of range and those with invalid date sequences were excluded. Possible errors included implausible combinations of age, sex, site and morphology. Each registry was invited to confirm or correct records with possible errors.

Data quality was examined using the proportion of histologically verified tumours, the proportion of brain tumours of unspecified histology and the proportion of patients lost to follow-up or censored within 5 years of diagnosis. Registries had to submit data with follow-up for at least 5 years or, for patients diagnosed during 2010–14, until December 31, 2014. Cancer registries use different techniques to assess the vital status of patients registered with cancer. Passive follow-up entails that records are linked to regional or national vital statistics systems. Active follow-up is also widely adopted: registries routinely contact treating physicians, family doctors or hospitals to record the vital status for each cancer patient. The proportion of patients lost to follow-up is relevant to countries using active follow-up; alternatively, the proportion of patients censored alive before five years from diagnosis pertains to countries where passive follow-up techniques are in place.

The London School of Hygiene and Tropical Medicine's Ethics Committee approved the proposed research (determination 14654 on the 19 December 2017).

The study considered children (0-14 years) and adults (15-99 years) who were diagnosed with a brain tumour (ICD-O-3 topography code C71) between 2000 and 2014. Both malignant (ICD-O-3 behaviour code 3) and non-malignant neoplasms (ICD-O-3 behaviour code 0 or 1) were eligible. The analysis incorporated both patient- and tumour-related variables. The variables defining the patient were: person code, country, registry, sex, full date of birth and race/ethnicity where relevant. The variables defining the disease were: full date of cancer diagnosis, full date of death or last known vital status and histology. Complete dates (day, month, year) are needed for comparison of cancer survival estimates.[55]

All brain tumours were included, regardless of their order, to allow for survival to vary after a first primary tumour at a different site. The probability for a brain tumour to be correctly identified as the first primary tumour depends on the time the cancer registry has been operating for. A long-standing cancer registry will be likely to detect both first and subsequent primary tumours, while a more recently established cancer registry will not be able to confidently attribute the right order to a given cancer. If only first malignancies were included, survival for a given population would partly depend on the "age" of a given cancer registry, resulting in bias. Assuming that a prior tumour diagnosis could affect treatment (and therefore survival) for the subsequent malignancy, survival for populations with long-standing registries where tumours were correctly identified as first-in-order would potentially be longer than in populations with recently established registries where both "true" first and higher order primaries were included.[56, 57]

Follow-up for survival estimation begins from the date of diagnosis of the brain tumour and ends at the earliest of death, last known vital status or the end of the study (in this case, 31 December 2014). What can be practically observed is the overall survival, because the cause of death is not available. The cause of death cannot be safely used in international comparisons of cancer survival, because it may be not available, or it may be based on unreliable information from the death certificate,[58, 59] or its recording may vary between countries and over time.[60, 61] What we are interested in, however, is net survival. Net survival is the survival attributable exclusively to

cancer and it is estimated by removing the effects of competing risks of death (i.e.: background mortality). Background mortality is the mortality due to causes other than cancer.

Background mortality in the general population is extracted from life-tables. Complete life tables are tables of mortality rates by single year of age, sex and calendar year. They may also be specific for region, deprivation status and ethnicity. Life tables were constructed as part of the CONCORD programme and made publicly available (**http://csg.lshtm.ac.uk/tools-analysis/life-tables/**).

Until recently, relative survival has been used as the best approximation of net survival. Relative survival is the ratio between the observed survival and the survival that would be expected if the patients were subject only to the mortality rates observed in the general population. This method, however, does not correct for "informative censoring". Informative censoring occurs when the probability of dying from cancer is not independent of the probability of dying from other causes. This is likely to occur with increasing age, when the potential impact of competing risks is greater. If not properly accounted for, the presence of informative censoring leads to bias in the estimation of net survival.

Net survival can be directly obtained using the non-parametric Pohar Perme estimator, which allows us to take into account the fact that older patients are more likely than younger patients to die from causes other than cancer (i.e. informative censoring is more frequent in the elderly).[62]

The age distribution of cancer patients may vary between countries and over time, and net survival varies with age. Therefore, valid comparison of all-ages survival estimates requires age standardisation to correct for these differences. The age-standardised estimate is a weighted average of the age-specific estimates. The International Cancer Survival Standard (ICSS) weights have been widely adopted.[63] Age is grouped in five categories: 15-44, 45-54, 55-64, 65-74 and ≥75 years. ICSS weights are attributed to each category within three clusters of cancers defined by their pattern of age-incidence: increasing with age (cluster 1, most cancers); broadly stable with age (cluster 2), and decreasing with age (cluster 3). Brain tumours belong to the

second cluster, but the incidence rates of medulloblastoma and glioblastoma are more strongly age-dependent.

For children, age-standardised estimates are derived by attributing equal weights to the three age groups (0-4, 5-9, 10-14 years).[64] Age standardisation may result in unstable values when data for a given age group are sparse.

The cohort approach was used to estimate net survival for patients diagnosed during 2000-2004 and 2005-2009, while the period approach was adopted for the latest calendar period (2010-2014). For five-year net survival to be estimated, the cohort approach requires that all the patients included in the analysis were followed up for at least 5 years. The period approach allows estimation of five-year survival when adequate follow-up (in this case, five years) is not available for all cancer patients. This approach combines the most recent follow-up data for cancer patients diagnosed during a specified year or calendar period and the follow-up data for patients diagnosed up to five years earlier, who were still alive at the start of the specified year or calendar period of diagnosis. The survival prediction derived from this approach is conditional, because it incorporates the survival probabilities matured over the preceding years, when most of the individuals were diagnosed. The key assumption is that the conditional probabilities of survival that were observed in the period remain stable over the next few years. Such an assumption may not hold if survival has been improving over time. In this situation, “period estimates” are inherently conservative, and will be slightly lower than the corresponding cohort estimates when complete follow-up is available for all patients. Nevertheless, empirical evidence shows that they are a good approximation to the cohort estimates.[65-68]

Preface to Research Papers 1 and 2

The histology of brain tumours is a key factor in the selection of treatment, and thus a predictor of outcome. Population-based survival reflects the overall effectiveness of a health care system in managing cancer. To my knowledge, no systematic review of world-wide variation and time trends in survival from brain tumours, by histology, is currently available. I set out to fill this gap by conducting two systematic reviews, to help define the strategy for defining the histology groupings, discussed in chapter 3, and for conducting the survival analyses, presented in chapters 4 and 5.

The first review is focussed on children. Brain tumours in children differ from those occurring in adults, both in genetic hallmarks and in clinical behaviour,[20] so children have been considered separately throughout the doctoral project.

The distribution of brain tumour histology varies with age. Low-grade subtypes are more common in children, while high-grade subtypes are predominant in adults.[16] The transition in the histology distribution mainly occurs among adolescents and young adults, making it difficult to define informative histology groupings for this age group.

It is still debated how epidemiological data for adolescents and young adults should be presented, using childhood classifications or analysed as for older adults. In the second systematic review, therefore, I chose to restrict the attention to individuals aged 15-39 years, rather than including all adults, in order to address the relevant methodological issues more thoroughly.

I considered children diagnosed with astrocytic and embryonal tumours, and adolescents and young adults diagnosed with astrocytic tumours. I did not consider other, rarer subtypes, because data were too scanty to allow meaningful comparisons. Both non-malignant and malignant tumours were eligible for inclusion. The two systematic reviews focused on tumours of the brain, by far the most common site of origin, excluding other central nervous system tumours.

Both systematic reviews follow the same methods. Each chapter is self-contained, so there is some repetition of the methods. I searched six electronic

databases, using complex search strategies, to identify longitudinal, observational studies based on primary data from cancer registries. The estimator was five-year survival, obtained through a time-to-event analysis.

For children, I retrieved 5,244 potentially eligible studies. Forty-seven articles, collectively providing 228 survival estimates, are included in the systematic review. All but five of these studies were conducted in high-income countries (Canada, the United States, South Korea, European countries and Australia). Five-year survival from embryonal tumours rose from 37% in 1980 to around 60% in 2009. While survival for medulloblastoma improved substantially (from 29% to 73% during 1959-2009), survival for primitive neuroectodermal tumours wavered over time (1973-2009) and between countries. Five-year survival for astrocytomas increased slightly over the 28 years between 1982 and 2009 (from 78% to 89%).

For adolescents and young adults, among 5,640 retrieved records, only 20 studies fulfilled the inclusion criteria. All but one study focused on high-income countries. Five-year survival from astrocytoma (broad histology group) mostly varied between 48% and 71% (1973-2004), with no clear trends and little international variation. During 2002-2007, five-year survival for WHO grade I-II tumours was in the range 73-89% in England, Germany and the US, but lower in South-Eastern Europe (59%). Five-year survival for anaplastic astrocytoma varied between 40% and 55% (2002-2007). Five-year survival from glioblastoma was in the range 14-23% (1991-2009).

Interpretation of the literature was made difficult by the heterogeneity of study designs, both for children and for adolescents and young adults. Discrepancies in the definition of histology groupings represented the main challenge.

I found a striking gap in research on survival from brain tumours in low-income and middle-income countries. Data for Africa, Asia and Oceania are scanty, while no data are available for Central and South America.

The International Classification of Childhood Cancer (ICCC) is the standard classification for categorising histology in epidemiological studies of childhood cancer.[19] For childhood brain tumours, however, I found that ICCC may not properly account for international differences in the ascertainment and registration of non-malignant

astrocytic tumours. As a result, the interpretation of international comparisons of survival from astrocytoma (broad histology group) may be complicated if WHO grade is not considered.

The ICCC has often been extended to adolescents and young adults.[69] For this age range, the shortcomings of ICCC are even more apparent than in children, because the histology distribution is substantially different. Barr and Birch proposed a bespoke classification incorporating WHO grade.[70, 71] As yet, Barr's and Birch's classification has been implemented in the Surveillance Epidemiology End Results Adolescents and Young Adults Site Recode, but it has not been widely adopted in epidemiological studies.

In conclusion, the analyses of brain tumour survival by histology, derived from the CONCORD-3 data, are expected to be novel because the data were collected with a standardised protocol and prepared with stringent, centralised data quality checks, and the analyses will include data for countries that have not previously been represented in survival studies. Based on the limitations of previous study designs, I have defined separate histology groupings for children and adults. The histology groupings for childhood astrocytic tumours are more granular than those in ICCC-3. For adults, the larger proportion of higher-grade tumours in this age group is considered.

Research Paper 1 has been published in the Journal of Global Oncology (2019), now JCO Global Oncology. Research Paper 2 has been published in JNCI Cancer Spectrum (2020).

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed <u>for each</u> research paper included within a thesis.

<u>SECTION A – Student Details</u>

Student ID Number	1701655	**Title**	Dr
First Name(s)	Fabio		
Surname/Family Name	Girardi		
Thesis Title	Global surveillance of survival from brain tumours diagnosed during 2000-2014: trends by age and histology		
Primary Supervisor	Dr Claudia Allemani		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

<u>SECTION B – Paper already published</u>

Where was the work published?	Journal of Global Oncology, now JCO Global Oncology		
When was the work published?	October 2019		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**No**	Was the work subject to academic peer review?	**Yes**

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

<u>SECTION C – Prepared for publication, but not yet published</u>

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	Choose an item.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Conception and design, collection and assembly of data, data analysis and interpretation, manuscript writing

SECTION E

Student Signature	[redacted]
Date	7 December 2020

Supervisor Signature	[redacted]
Date	7 December 2020

Research Paper 1: a systematic literature review on survival from brain tumours in children

World-wide trends in survival from common childhood brain tumours: a systematic review

Introduction

Primary tumours of the central nervous system (CNS) in children are rare. The estimated world-standardised incidence rate in 2018 was 12 cases per million, ranging from 1.8 in Melanesia to 36.0 in North America.[72] Despite their rarity, primary CNS tumours were estimated to be the second most important cause of childhood cancer-related deaths after leukaemia. The estimated world-standardised mortality rate in 2018 was 0.7 deaths per million, varying between 0.04 in Tanzania and 2.4 in Honduras.[72]

Incidence and mortality are essential indicators of the cancer burden in a given population, but the duration of survival also accounts for the dynamic nature of the process between diagnosis and death. Therefore, population-based survival is the most appropriate measure to assess the overall effectiveness of a health care system in managing a given cancer.[47, 48] The third cycle of the CONCORD programme (CONCORD-3) found wide disparities in survival among more than 700,000 patients who were diagnosed with a primary brain tumour in 58 countries world-wide during the 15-year period 2000-2014. Five-year net survival for all childhood brain tumours combined ranged from 29% in Brazil to about 80% in several European countries.[46] International disparities in survival may result from obstacles in access to surgery, radiotherapy and chemotherapy.[52, 73-75] Such inequalities will inevitably result in failure to diagnose and treat brain tumours adequately, ultimately leading to premature deaths.[76]

CNS tumours comprise tumours of the brain, the spinal cord and the meninges, but brain tumours are by far the largest group. Brain tumours vary widely in terms of histology and clinical behaviour. Histology plays a pivotal role in treatment planning,

and treatment needs are specific to each tumour sub-type. Therefore, a breakdown of the observed disparities in survival by histology is warranted to help shape cancer control plans. In the EUROCARE-5 study, covering children diagnosed during 2000-2007 in 27 European countries, average five-year observed survival was 95% for children diagnosed with pilocytic astrocytoma and 65% for those affected by medulloblastoma. This study showed very wide international disparities. For instance, among children diagnosed with a brain tumour defined as World Health Organisation (WHO) grade III-IV, five-year survival ranged from 36% in Bulgaria to 66% in Finland.[9]

To date, no summary of the scientific evidence on population-based survival for the main sub-types of brain tumour is available. We aimed to fill this gap in knowledge by conducting the first systematic review on time trends and geographical variation in survival from brain tumours.

Methods

We considered longitudinal, observational studies that provided estimates of population-based survival, by histology, for children (mainly those aged 0-14 years) diagnosed with primary brain tumours, either malignant or non-malignant. We excluded studies that only included patients with a CNS tumour in anatomical sites other than the brain, because of their rarity and the paucity of data. We also excluded studies that only presented survival estimates for all histologies combined. Studies had to be based on primary data drawn from population-based cancer registries. In order to maximise geographical coverage, we did not discard studies presenting hospital-based estimates, if those estimates were likely to be representative of a given country or territory (e.g. a single referral centre or a comprehensive network of referral centres), and no population-based estimate was available. We also excluded clinical trials or clinical series, because these study designs only include selected patients. Studies were eligible if they included estimates of the survival probability from a time-to-event analysis. To improve comparability between studies, only those presenting survival estimates at five years following the diagnosis were included.

We searched six databases (Dissertation and Theses Global, Embase, Medline, Open Grey, Scopus and Web of Science) from database inception to 30 September 2018, using pre-defined search strategies that included terms related to

the disease under study, the statistical method and the study design. A professional librarian at the London School of Hygiene and Tropical Medicine reviewed the search strategies. (Supplementary Table 1.1)

There were no restrictions relating to language or publication status, but we excluded studies published before 1995, because the versions of the reference classifications were too early to allow comparability with subsequent editions.

Countries were defined based on their United Nations name and continent.

Based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) approach,[53] potentially eligible studies were evaluated at three progressive levels: title, abstract, and full text. Where eligibility was unclear, we reached an agreement through discussion.

For each eligible study, we extracted data on the tumour sub-types included and the reference classification used for tumour definitions (e.g. International Classification of Diseases for Oncology Third Edition, ICD-O-3).[17] Where available, we collected specifications of data quality indicators: the proportions of microscopically verified tumours, poorly specified/unspecified morphologies and patients lost to follow-up, and whether diagnoses based on death certificate only (DCO) or autopsy were excluded. We recorded five-year survival probabilities for each eligible sub-type and, where available, the corresponding survival estimates for each calendar period. Lastly, for each cancer registry, we sought information on the proportion of the population covered and on the completeness of ascertainment.

For studies considering several calendar periods, we abstracted each survival estimate separately. The calendar periods examined varied widely between studies, so we described trends by using the middle year of the corresponding time interval. Given the sparseness of data for some very rare sub-types, we focussed on the most frequent morphologies, namely astrocytic and embryonal tumours. Morphological groupings and definitions also differed between studies. We combined different definitions for the same sub-type under a common descriptor. (Supplementary Table 1.2)

This systematic review is registered with **PROSPERO, number CRD42018111981**.

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for submission for publication.

Results

We assessed 5,244 records for eligibility. Forty-seven studies were included in the systematic review. (Figure 1.1) For each study, we detailed: location, completeness of ascertainment, population covered, calendar period for incident cases, age range, quality indicators available, reference classification, and outcome measure. (Table 1.1)

In thirty studies (64%) patients were aged 0-14 years, 0-15 years in four studies, and two years or less in three studies. Nine studies (19%) included individuals aged 20 years or less, and in one study the upper age limit was 24 years. Studies using non-standard age definitions were included here because the study populations comprised mainly children.

Nineteen studies (40%) had regional population coverage, ten (21%) were based on nation-wide registries, eight (17%) were international studies based on both regional and national registries, and in ten studies, the information was not available. Only five studies were entirely or partially conducted in low-income or middle-income countries.[77-80] The calendar period for incident cases ranged from 1954 to 2014. (Table 1.1) The eligible studies collectively provided 228 survival estimates.

For patients diagnosed with embryonal tumours as a broad histology group, five-year survival rose substantially during the 30 years between 1980 and 2009, from 37% in 1980 to around 60% in 2009.[78, 81-90] In most countries, the survival probability was 50% or lower until 1997.[81-90] Despite this positive trend, there were remarkable geographical disparities. Around 2000, there was a 26% gap in five-year survival between the Southern and Eastern Europe (SEE) consortium, including middle-income countries such as Belarus, Bulgaria and Ukraine (40%),[78] and the

EUROCARE-5 consortium, which includes all the most affluent European countries (66%).[87] (Figure 1.2)

Five-year survival from medulloblastoma rose from 29% to 73% during the 50 years between 1959 and 2009.[91-110] In Denmark, Italy, and Slovakia survival was 10% or less until 1972. In Denmark and Italy, survival increased sharply during the following decade (around 40% in 1982), while in Slovakia, survival was still 26% in 1985.[92-94] In most of the European countries, the survival probability was 60% or more after 1992,[9, 69, 91, 99, 102-106] while in the United States, similar or higher values were observed in 1977.[95] Five-year survival from medulloblastoma in Tunisia was below 27% in 1997, while it was zero in Uganda in 2007 (14 patients).[77, 80] Survival in children younger than two years was 50% or lower, and did not change over time.[109-112] (Figure 1.2)

Five-year survival from primitive neuro-ectodermal tumours (PNET) fluctuated in the range 27-52% in most European countries (1973-2009), without a monotonic trend.[9, 10, 99, 100, 102-106, 109, 113, 114] In two studies conducted in England and France, survival values were not in line with those observed in other European countries, but confidence intervals were wide.[103, 113] In the United States, five-year survival ranged between 47% and 81% during 1977-2009.[10, 106, 109, 114] These values were higher than those observed in Europe during the four decades between 1973 and 2009 (24-47%). Five-year survival from PNET in infants (one year or less) varied between zero and 33% (1990-2004), but data were scant and inconsistent.[109, 112, 115] (Figure 1.3)

For children diagnosed with atypical teratoid/rhabdoid tumour, a rare sub-type of embryonal tumour, five-year survival in Germany rose from 21% to 42% during 2001-2009, but confidence intervals overlapped.[103] In the United States[116] and the EUROCARE-5 consortium,[9] the survival probability during 2004-2008 was 30% or less. (Figure 1.3)

Astrocytoma as a broad histology group was the most commonly adopted definition. Five-year survival was 71% or lower during 1970-1980,[10, 93, 94, 96, 113] and it rose slightly over three decades, from 78% in 1982 to 89% in 2009.[10, 69, 78, 81, 83, 84, 86-89, 93-96, 99, 101, 113, 117] During 1982-1996, when ICD-O-2 was in force,[118] five-year survival for astrocytoma ranged between 72% and 82% in most countries.[10, 83, 85, 94-96, 99, 102, 113] In the EUROCARE-4 study[87] (ICD-O-3[17]), five-year survival for astrocytoma (1995-

2002) in Central Europe, Northern Europe, Southern Europe, and the UK and Ireland, was also around 75% when all behaviours were considered, but it fell by 10% when non-malignant tumours were excluded. In Eastern Europe, the survival probability was around 65%, regardless of tumour behaviour.[87] Similarly, in the EUROCARE-5 study, five-year survival for malignant astrocytoma was in the range 60-65% during 2000-2007.[69] Five-year survival from astrocytoma in India was 39% in 1996, while survival in the SEE consortium was similar to other European regions.[78, 79] (Figure 1.4)

Five-year survival for low-grade astrocytoma (World Health Organization (WHO) grades I and II combined) was 80% or more in Europe, the United States and Israel,[89, 100, 104, 108] while it was slightly below 80% in Tunisia.[77] For patients diagnosed with pilocytic astrocytoma during 1981-1991, five-year survival was in in the range 88-91% in England, Wales, the United States, and South-Eastern Europe. During 1995-2004, five-year survival from pilocytic astrocytoma rose to 95% or more in the United States, Israel and in the EUROCARE-5 consortium,[9, 106, 108, 114, 119] while it remained unchanged in South-Eastern Europe.[119] Five-year survival for diffuse astrocytoma was in the range 60-78% in Europe and Japan during 1981-2004.[9, 97, 120] (Figure 1.5)

Five-year survival for high-grade astrocytoma (WHO grades III and IV combined) was 20-30% in France, Germany, and Sweden (1990-2004).[89, 100, 104] The five-year survival probability for anaplastic astrocytoma was 30% or lower in Europe,[9, 97, 106] Japan,[120] South Korea and the United States,[106, 117] while it was 55% in Israel.[108] Five-year survival for glioblastoma was in the range 8-20% in Europe,[9, 97] Israel,[108] Japan,[120] South Korea and the United States.[95, 106, 117] (Figure 1.5). For high-grade astrocytoma, there was no improvement in the observed outcomes during the 25 years between 1981 and 2004.

Among 47 studies, only 11 (23%) specified the completeness of case ascertainment. One-third (36%) did not provide details on data quality. Twenty-six studies (55%) specified at least the proportion of microscopically verified tumours, and seven of them only included patients with microscopically verified tumours (Appendix, page 4). Four of the eight international studies specified the proportion of histologically confirmed brain tumours,[9, 78, 106, 119] while the others reported a proportion for all childhood tumours combined (Appendix, page 4).[69, 82, 83, 87] Seven studies (15%) did not specify the reference classification and two did not clarify the version of the ICD-

O or the International Classification of Childhood Cancer (ICCC) that was used. (Table 1.1) Five of the 22 studies using the definition “astrocytoma” (broad histology group) did not elucidate whether they included only malignant tumours, or both malignant and non-malignant tumours (Appendix, page 4).[79, 81, 84, 93, 99] Thirty-nine studies (83%) provided estimates of all-cause survival (“observed”). Only eight provided relative survival estimates, adjusted for background mortality. (Table 1.1)

Discussion

To our knowledge, this is the first systematic review synthesising trends and geographical variation in survival for the most common morphologic sub-types of brain tumour in children. Five-year survival for embryonal tumours rose remarkably during the 1980s and the 2000s, and the change was mostly driven by an improvement in the outcome of patients diagnosed with medulloblastoma. Survival from astrocytic tumours changed very little, regardless of WHO grade.

Only five studies included patients diagnosed in low-income or middle-income countries (Belarus, Bulgaria, India, Montenegro, Romania, Serbia, Tunisia, Turkey, Uganda, Ukraine).[77-80] In this setting, the magnitude of the survival gap depended on country and histology, albeit the largest deficit was seen for embryonal tumours. In high-income countries, where nearly all the studies were conducted, outcomes were similar. However, in the United States, survival from the most common embryonal tumours improved earlier than elsewhere.

Low-grade gliomas represent approximately one-third of all CNS tumours in children. They are biologically distinct from low-grade gliomas seen in adults, and progression to higher-grade lesions rarely occurs.[20] Pilocytic astrocytoma is the most common glioma sub-type in children.[7] We adopted different levels of granularity in the histology definitions, but data for specified astrocytic tumours were sparse. Most studies presented survival estimates based on the second tier of the ICCC, group IIIb (i.e. astrocytoma).[19] For tumours defined as astrocytoma (broad group), corresponding to the ICCC group IIIb, five-year survival was around 90% during 2004-2009. Over a comparable period, survival from pilocytic astrocytoma (WHO grade I) was nearly 100%. Pilocytic astrocytoma is therefore likely to be responsible for the favourable outcome observed in the broader group, since diffuse astrocytoma,

anaplastic astrocytoma and glioblastoma, combined, only comprised about 30% of astrocytic tumours in children.[9]

The current recommendation is to present survival in children separately for each ICCC group. Even though pilocytic astrocytoma is predominant in children, we believe that the adoption of a broad category such as astrocytoma (ICCC-3 group IIIb) does not fully account for international variations in survival, and it may actually attenuate the observed trends and differences. We chose to report survival at five years because it is the most commonly reported time landmark, and to facilitate comparisons between studies. Low-grade gliomas are often indolent tumours that progress slowly, even following partial resection or biopsy.[21] In a large US study including nearly 3,500 children (aged 0-20 years) diagnosed with low-grade gliomas during 1973-2005, the survival probability at 10 years for WHO grade I and grade II tumours was around 90% and 80%, respectively.[121] Therefore, outcomes for this cancer subtype may be better described with longer-term survival estimates.

A remarkable proportion of studies adopting the definition “astrocytoma” (as a broad histology group) did not clarify the tumour behaviour. This information is necessary to interpret trends correctly. In the second edition of ICD-O (in force from 1990),[118] pilocytic astrocytoma was coded as malignant (behaviour code 3), while in the third edition (in force from 2000) it was attributed a borderline behaviour (code 1).[17] In studies considering patients diagnosed during 1982-1996, which used ICD-O-2, survival from astrocytoma was likely to be high due to the inclusion of pilocytic astrocytoma, which was defined at that time as a malignant tumour. In brain tumours, location is more important than for tumours at other anatomic sites, because it affects clinical presentation, diagnosis, treatment, and morbidity. Therefore, even though pilocytic astrocytoma was re-classified as a non-malignant tumour in ICD-O-3, most studies published after 2000, adopting ICD-O-3, included all brain tumours, regardless of behaviour. As a result, survival estimates from these studies were in fact comparable to those in earlier reports, based on ICD-O-2. In EUROCARE-5, however, survival from astrocytoma in Eastern Europe was similar, regardless of whether tumours with borderline behaviour were included or not.[87] This finding suggests under-registration of non-malignant brain tumours in Eastern Europe.

Medulloblastoma is the most common embryonal tumour, with a peak incidence around 7 years of age. Treatment includes a combination of surgery, cranio-spinal irradiation and chemotherapy. In this review, the steepest gain in survival from medulloblastoma occurred before 1992, possibly reflecting improvement in radiotherapy techniques.[122] The effect of adding chemotherapy with lomustine, cisplatin and vincristine after radiotherapy was first assessed in a phase II trial in the 1990s.[123] In the light of the observed benefit, the use of chemotherapy became standard. In the 1990s and 2000s, five-year survival rose from about 60% to 70%. This finding may be the joint result of improved surgical management and routine incorporation of chemotherapy into clinical practice.[29] Survival from medulloblastoma was much lower in low-income and middle-income countries than in high-income countries. This may reflect the lack of access to optimal multi-modality treatment.[52, 73-75]

In three studies, medulloblastoma was grouped with primitive neuro-ectodermal tumours (PNET), even though ICD-O-3 was given as the reference classification.[10, 113, 114] As a result, survival estimates were higher than those for PNET only.[99, 102, 105, 106] Infra-tentorial medulloblastoma and supra-tentorial PNET are distinct entities, described as separate morphologies in the second edition of the WHO classification of CNS tumours (2002).[124] Since medulloblastoma has a more favourable outcome than PNET, their inclusion in a wider group mislabelled as PNET will bias the survival estimates upwards.

Two studies defined astrocytoma, not otherwise specified (NOS), as a separate morphological entity, perhaps to allow for a generic diagnosis of unspecified astrocytic tumour.[9, 97] In the US, the proportion of astrocytic tumours registered as “astrocytoma NOS” decreased from 47% to 13% during 1973-2005.[121] The WHO classification does not recognise astrocytoma NOS as a distinct definition. Diffuse astrocytoma and astrocytoma NOS share the same ICD-O-3 code, but the WHO classification retains only the first of the two descriptors.[7, 17] Therefore, we grouped together the survival estimates, which proved comparable (70-80%).[9, 97]

In most of the studies reviewed here, indicators of data quality were often missing or incomplete. The proportion of tumours that had been microscopically verified was the most widely available parameter. Few studies reported any additional

descriptors, such as the proportion of patients who were lost to follow-up before the end of the study. The proportion of microscopically verified tumours pertains to disease management, namely whether surgery or biopsy was performed, but also to whether the cancer registry had access to pathology reports.[125] The proportion of microscopically verified brain tumours was in the range 73-93% in the SEE consortium (1983-2014), and 71-100% in the EUROCARE-5 study (2000-2007).[9, 78]

The proportion of brain tumours that are microscopically verified is typically lower than for other types of cancer, because brain tumours are more lethal, and patients are often too unwell to undergo an invasive diagnostic procedure; advanced surgical expertise is also required. If the proportion of tumours that are histologically unclassified is high, survival estimates for specific morphologies may be biased, because patients with histologically confirmed disease are likely to have higher survival than those whose tumours could not be pathologically confirmed.

Similarly, information on the completeness of ascertainment of brain tumours was very often missing. In most of the studies where this information was available, it was usually reported as nearly complete (95% or more). This parameter is important to assess whether the patients included in the study are representative of all brain tumour patients in the population of a given region or country.[126]

In most of the studies (83%), survival was reported only as observed survival, without taking account of death from causes other than the brain tumour (background mortality). If competing risks of death are not properly accounted for, survival estimates will be biased downwards. Background mortality also varies widely between countries and over time, so valid international comparisons require that background mortality is incorporated in the survival estimates. However, nearly all the studies were conducted in affluent countries, where background mortality in children has generally been very low for several decades. The distortion in international comparisons of brain tumour survival in children is likely to be small.

This systematic review was affected by several limitations. First, we aimed to give a comprehensive account of variations in brain tumour survival by including all the relevant histology categories. However, very few studies were available for some categories, precluding robust conclusions on time trends and geographical variations

in survival. Second, almost all the studies were based on regional rather than national data. Assuming that regional survival estimates are applicable to the whole country may not be wise in the presence of regional disparities in access to or provision of treatment within a given country. However, data from most of these regions were later included in wider studies, with national or international coverage. Survival estimates from those studies were in line with those previously reported at regional level, suggesting that findings from the earlier, smaller studies were indeed generalisable to the country. Finally, the dates and the length of calendar periods in which the patients had been diagnosed also varied widely between studies. To allow an orderly presentation of time trends, we referred to the central year for any given time interval, but we were not able to compare the average annual increment or decrement in survival between calendar periods of different lengths, and often overlapping. Improvements in survival were nevertheless mainly limited to embryonal tumours, and they occurred over an extended period, so the international comparisons may be considered reasonably informative.

In conclusion, there is a staggering gap in evidence on survival from the most common types of childhood brain tumour in low-income and middle-income countries. Interpretation of the literature is hampered by the very wide heterogeneity between the designs of the various studies, and by the quality of the available data.

We highlight the fact that ICCC does not allow accurate description of variation in survival from astrocytic tumours, because it does not encompass stratification by grade. The goal of the WHO Global Initiative for Childhood Cancer is to raise survival world-wide for six cancer subtypes, including low-grade gliomas.[127] In the context of brain tumours, future assessment of the progress of this global effort will require that an informative, up-to-date survival benchmark for low-grade gliomas is set. Ultimately, ICCC should be revised.

The 2016 WHO classification of Tumours of the Central Nervous System has redefined or replaced several diagnostic entities or subgroups by incorporating molecular classifiers.[15] For instance, PNET is no longer included in the diagnostic dictionary and medulloblastoma is now genetically defined. Future comparisons of survival will have to account for these changes, but capacity-building and resources

are needed to extend the use of this classification, both in clinical practice and in cancer registries, especially in low-income and middle-income countries.

Larger international studies including currently under-represented countries are warranted, and robust survival estimates are only possible through using the same protocol for data collection, centralised and stringent data quality checks and the same statistical methodology, including appropriate life tables to correct for the risk of death due to causes other than cancer.

Figure 1.1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.

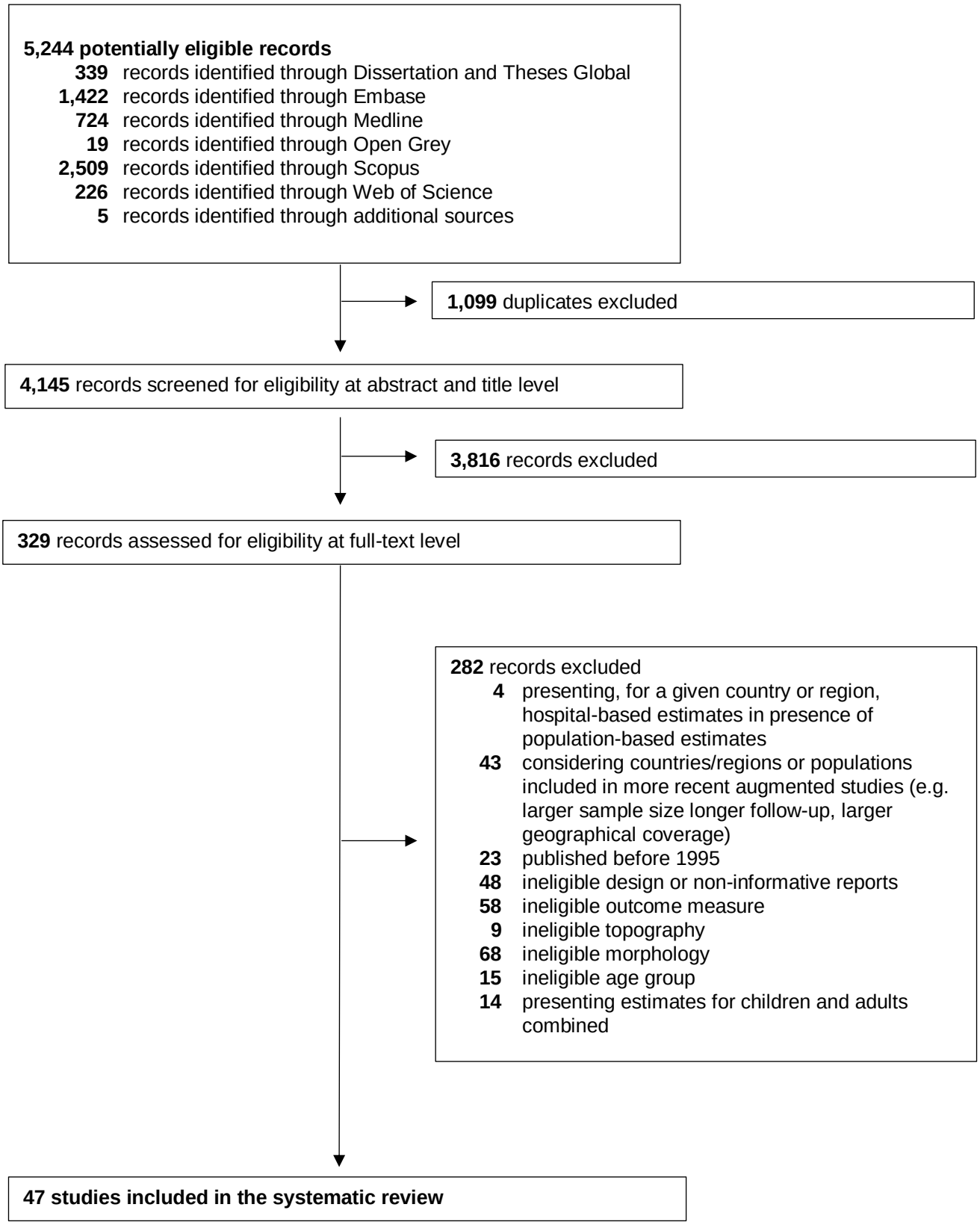
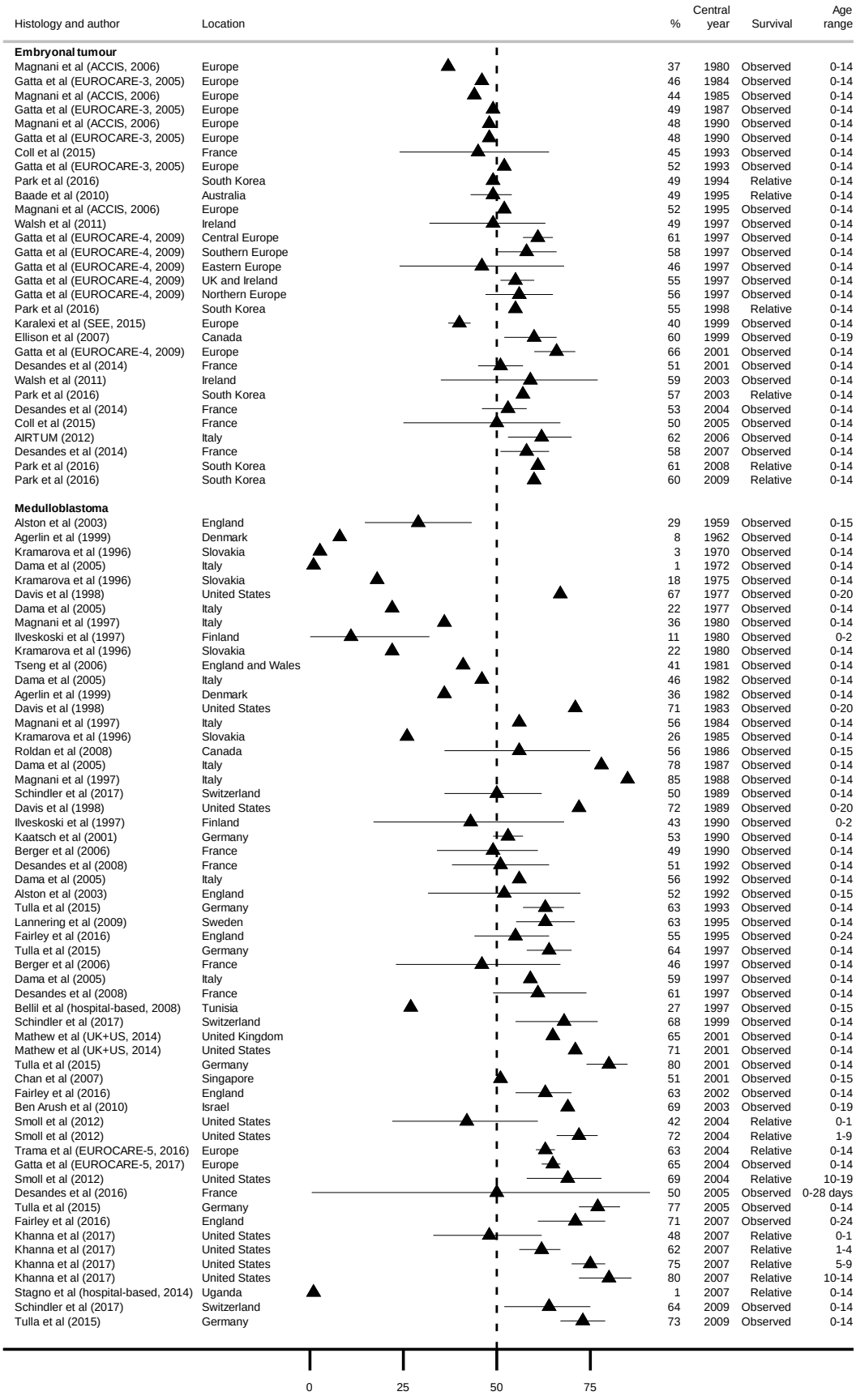


Figure 1.2. Five-year survival (%) from embryonal tumours and medulloblastoma.



Automated Childhood Cancer Information System (ACCIS) consortium: Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Italy, Netherlands, Slovakia, Slovenia, Spain, Switzerland, UK, Norway

EUROCARE-3 consortium: Austria, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Italy, Malta, Netherlands, Norway, Poland, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales.

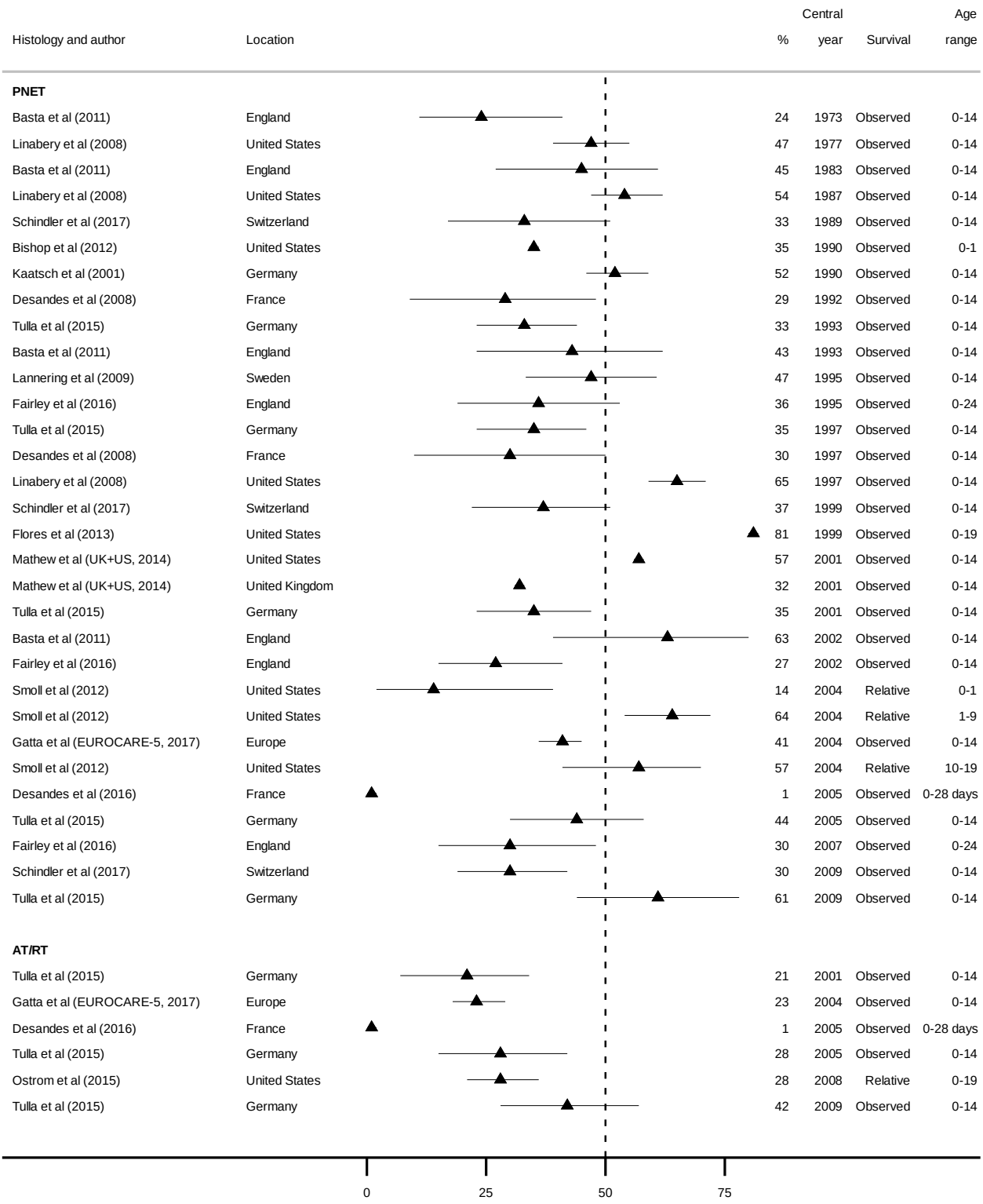
EUROCARE-4 consortium: Austria, Belgium, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

Southern and Eastern Europe (SEE) consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine

AIRTUM: Associazione Italiana Registri Tumori

Figure 1.3. Five-year survival (%) from primitive neuro-ectodermal tumour (PNET) and atypical teratoid/rhabdoid tumour (ATRT).

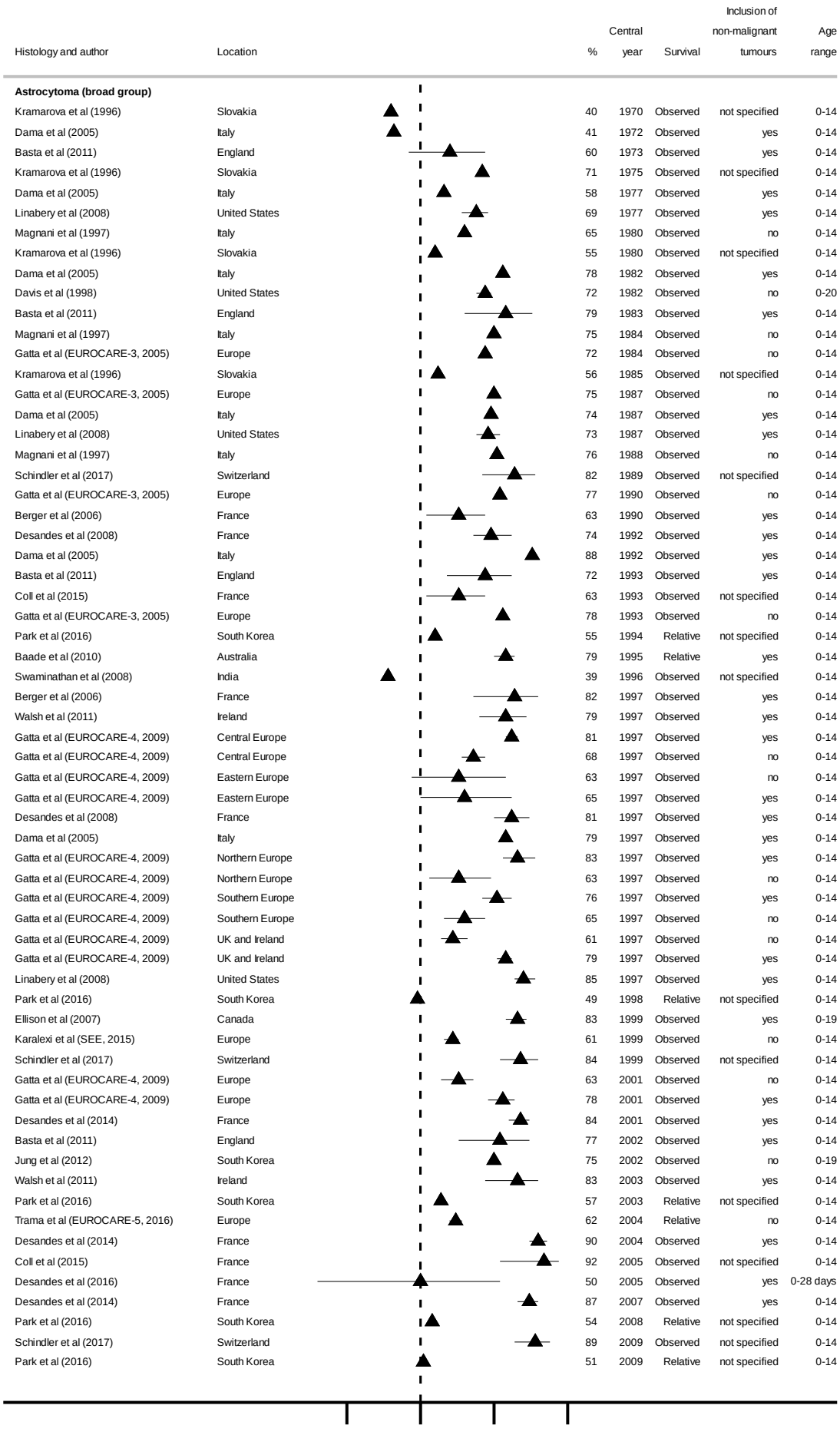


PNET: primitive neuro-ectodermal tumour

EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

AT/RT: atypical teratoid/rhabdoid tumour

Figure 1.4. Five-year survival (%) from astrocytoma (broad group).



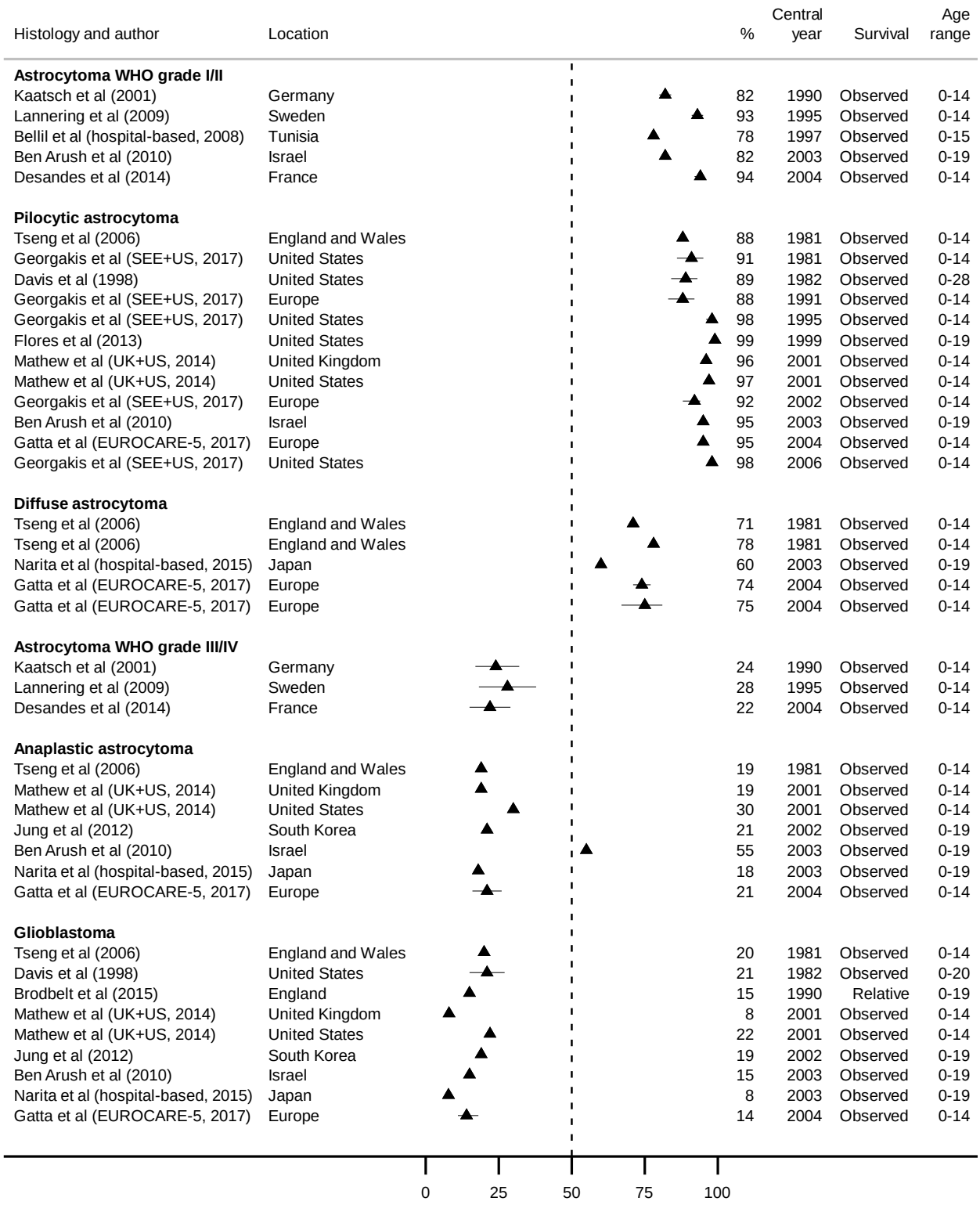
EUROCARE-3 consortium: Austria, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Italy, Malta, Netherlands, Norway, Poland, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

EUROCARE-4 consortium: Austria, Belgium, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

Southern and Eastern Europe (SEE) consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine

Figure 1.5 Five-year survival (%) from astrocytoma WHO grade I/II, pilocytic astrocytoma, diffuse astrocytoma, astrocytoma WHO grade III/IV, anaplastic astrocytoma, and glioblastoma



WHO: World Health Organization

EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

Southern and Eastern Europe (SEE) consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine

Table 1.1. Studies included in the systematic review.

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
Kramarova et al., 1996	Slovakia	Not specified	National	1968-1987, 1988	0-14	Proportion of microscopically verified tumours, proportion of patients lost to follow-up	Birch and Marsden	Observed survival
Ilveskoski et al., 1997	Finland	Not specified	Not specified	1975-1993, not specified	0-2	Not specified	Rorke and Kernohan	Observed survival
Magnani et al., 1997	Italy	Not specified	Not specified	1978-1989, 1994	0-14	Proportion of microscopically verified tumours, exclusions, proportion of patients lost to follow-up	ICD-O[1], not further specified	Observed survival
Davis et al., 1998	United States	Not specified	Regional (9.5%, SEER[2] 9)	1973-1991, not specified	0-20	Not specified	ICD-O-2	Observed survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
Agerlin et al., 1999	Denmark	Not specified	Not specified	1960-1984, 1996	0-14	Proportion of microscopically verified tumours	Not specified	Observed survival
Kaatsch et al., 2001	Germany	95%	Not specified	1980-1999, not specified	0-14	Not specified	ICCC[3]-2	Observed survival
Alston et al., 2003	England	95%	Regional: Manchester	1954-1997, not specified	0-15	Not specified	Not specified	Observed survival
Dama et al., 2005	Italy	Not specified	Regional (Piemonte)	1970-2001, 2004	0-14	Proportion of microscopically verified tumours, exclusions, proportion of patients lost to follow-up	ICCC-2	Observed survival
Gatta et al., 2005	EUROCARE-3 consortium[4]	Not specified	Regional and national (12-100%)	1983-1994, not specified	0-14	Proportion of microscopically verified tumours, exclusions, proportion of	ICCC-2	Observed survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
						patients lost to follow-up, proportion of unspecified morphologies		
Berger et al., 2006	France	Not specified	Regional (Rhone-Alpes)	1987-1999, 2004	0-14	Not specified	ICD-O-2	Observed survival
Magnani et al., 2006	ACCIS consortium[5]	Not specified	Regional and national	1978-1997, not specified	0-14	Proportion of microscopically verified tumours, exclusions, proportion of patients lost to follow-up/censored before 5 years, proportion of unspecified morphologies	ICCC-2	Observed survival
Tseng et al., 2006	England, Wales	95%	National	1971-1990, 1995	0-14	Exclusions	ICD-O, not further specified	Observed survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
Chan et al., 2007	Singapore	Not specified	National	1997-2005, not specified	0-15	Proportion of microscopically verified tumours	Not specified	Observed survival
Ellison et al., 2007	Canada	Not specified	Regional (Quebec excluded)	1994-2003, 2003	0-19	Proportion of microscopically verified tumours, exclusions	ICCC-3	Observed survival
Bellil et al., 2008	Tunisia	Not specified	Regional (Institute of Neurosurgery of Tunis)	1990-2004, not specified	0-15	Not specified	WHO[6], 4th edition	Observed survival
Desandes et al., 2008	France	Not specified	Regional (24%, Auvergne-Limousin, Bretagne, Lorraine, Rhone-Alpes, Valde-Marne)	1990-1999, 2006	0-14	Proportion of patients lost to follow-up	ICCC-3	Observed survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
Linabery et al., 2008	United States	98%	Regional (14%, SEER 13)	1975-1999, not specified	0-14	Proportion of microscopically verified tumours, proportion of patients lost to follow-up	ICD-O-3	Observed survival
Roldan et al., 2008	Canada	Not specified	Regional (Alberta)	1975-1996, not specified	0-15	Proportion of microscopically verified tumours	ICD-O-2	Observed survival
Swaminathan et al., 2008	India	Not specified	Regional (Chennai)	1990-2001, 2003	0-14	Proportion of microscopically verified tumours, exclusions, proportion of patients lost to follow-up	ICD-O-2	Observed survival
Gatta et al, 2009	EUROCARE-4 consortium[7]	Not specified	Regional and national	1995-2002, 2003	0-14	Proportion of microscopically verified	ICCC-3	Observed survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
						tumours, exclusions, proportion of unspecified morphologies		
Lannering et al., 2009	Sweden	Not specified	Not specified	1984-2005, 2007	0-14	Not specified	ICCC-3	Observed survival
Baade et al., 2010	Australia	Not specified	National	1983-2006, 2006	0-14	Proportion of microscopically verified tumours, exclusions	ICCC-3	Relative survival
Ben Arush et al., 2010	Israel	Not specified	Not specified	1998-2007, not specified	0-19	Not specified	ICCC, not further specified	Observed survival
Basta et al., 2011	England	98%	Regional (Northumberland, Tyne and Wear, Durham, Teesside and Cumbria)	1968-2005, not specified	0-14	Proportion of patients lost to follow-up	ICCC-3	Observed survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
Walsh et al., 2011	Ireland	Not specified	National	1994-2005, 2006	0-14	Proportion of microscopically verified tumours, exclusions, proportion of patients lost to follow-up/censored before 5 years, proportion of unspecified morphologies	ICCC-3	Observed survival
Associazione Italiana Registri Tumori, 2012	Italy	Not specified	Regional (11 registries)	2003-2008, 2008	0-14	Proportion of microscopically verified tumours	ICCC-3	Observed survival
Bishop et al., 2012	United States	Not specified	Regional (SEER 17)	1973-2006, 2008	0-1	Not specified	Not specified	Observed survival
Jung et al., 2012	South Korea	Not specified	National	1999-2004, 2009	0-19	Proportion of microscopically	ICD-O-3	Observed survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
						verified tumours		
Smoll et al., 2012	United States	98%	Regional (25%, SEER 17)	2000-2006, not specified	0-19	Not specified	ICD-O-3	Relative survival
Flores et al., 2013	United States	Not specified	Regional: California	1988-2009, not specified	0-19	Not specified	Not specified	Observed survival
Desandes et al., 2014	France	Not specified	Not specified	2000-2009, 2013	0-14	Proportion of patients lost to follow-up	ICCC-3	Observed survival
Mathew et al., 2014	United Kingdom, United States	99%	United Kingdom: national; United States: regional (SEER 18)	1996-2005, not specified	0-14	Proportion of microscopically verified tumours	ICCC-3	Observed survival
Stagno et al., 2014	Uganda	Not specified	Not specified	2002-2012, not specified	0-14	Proportion of microscopically verified tumours	Not specified	Relative survival
Brodbelt et al., 2015	England	Not specified	National	2007-2011, not specified	0-19	Proportion of microscopically	ICD-O-2	Relative survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
						verified tumours		
Coll et al., 2015	France	Not specified	Regional (Auvergne-Limousin)	1986-2009, not specified	0-14	Not specified	ICCC-3	Observed survival
Karalexi et al., 2015	SEE consortium	Not specified	Regional and national	1983-2014, 2014	0-14	Proportion of microscopically verified tumours, exclusions, proportion of patients lost to follow-up, proportion of unspecified morphologies	ICCC-3	Observed survival
Narita et al., 2015	Japan	Not specified	Not specified	2001-2004, not specified	0-19	Not specified	Not specified	Observed survival
Ostrom et al., 2015	United States	98%	Regional (26%, SEER 18)	2001-2010, 2011	0-19	Not specified	ICD-O-3	Relative survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
Tulla et al., 2015	Germany	Not specified	National	1991-2010, 2010	0-14	Proportion of microscopically verified tumours, proportion of patients lost to follow-up	ICCC-3	Observed survival
Desandes et al., 2016	France	Not specified	Not specified	2000-2009, 2011	0-28 days	Proportion of microscopically verified tumours, proportion of patients lost to follow-up	ICCC-3	Observed survival
Fairley et al., 2016	England	100%	Regional (Yorkshire, Northumberland, Tyne and Wear, Durham, Teesside and Cumbria)	1990-2013, 2014	0-24	Not specified	ICCC-3	Observed survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
Park et al., 2016	South Korea	80-90%	National	1993-2011, 2012	0-14	Not specified	ICCC-3	Relative survival
Trama et al., 2016	EUROCARE-5 consortium[9]	Not specified	Regional and national (12-100%)	2000-2007, 2008	0-14	Proportion of microscopically verified tumours, exclusions, proportion of lost to follow-up, proportion of unspecified morphologies	ICD-O-3	Relative survival
Gatta et al., 2017	EUROCARE-5 consortium	Not specified	Regional and national	2000-2007, 2008	0-14	Proportion of microscopically verified tumours, exclusions, proportion of patients lost to follow-up/censored before 5 years,	ICD-O-3	Observed survival

Author	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span	Quality indicators	Reference classification	Estimator
						proportion of unspecified morphologies		
Georgakis et al., 2017	SEE consortium[8], United States	Not specified	SEE consortium: regional and national; United States: regional (29%, SEER 18)	SEE: 1983-2014, not specified; SEER: 1973-2012, not specified	0-14	Proportion of microscopically verified tumours	ICCC-3	Observed survival
Khanna et al., 2017	United States	Not specified	Regional (28%, SEER 18)	2001-2013, not specified	0-14	Not specified	ICD-O-3	Relative survival
Schindler et al., 2017	Switzerland	91%	National	1984-2013, 2013	0-14	Proportion of microscopically verified tumours, proportion of unspecified morphology	ICCC-3	Observed survival

[1] ICD-O: International Classification of Diseases for Oncology

[2] SEER: Surveillance, Epidemiology, and End Results Program

[3] ICCC: International Classification of Childhood Cancer

[4] EUROCARE-3 consortium: Austria, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Italy, Malta, Netherlands, Norway, Poland, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

[5] ACCIS consortium: Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Italy, Netherlands, Slovakia, Slovenia, Spain, Switzerland, UK, Norway

[6] WHO: World Health Organization

[7] EUROCARE-4 consortium: Austria, Belgium, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

[8] SEE consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine

[9] EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

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SECTION A – Student Details

Student ID Number	1701655	**Title**	Dr
First Name(s)	Fabio		
Surname/Family Name	Girardi		
Thesis Title	Global surveillance of survival from brain tumours diagnosed during 2000-2014: trends by age and histology		
Primary Supervisor	Dr Claudia Allemani		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	JNCI Cancer Spectrum		
When was the work published?	June 2020		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
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SECTION E

Student Signature	[redacted]
Date	7 December 2020

Supervisor Signature	[redacted]
Date	7 Decem er 2020

Research Paper 2: a systematic literature review on survival from brain tumours in adolescents and young adults

Global trends in survival from astrocytic tumours in adolescents and young adults: a systematic review.

Introduction

Primary tumours of the central nervous system (CNS) are rare. In adolescents and young adults (15-39 years), the estimated world-standardised incidence rate was 15 new cases per million in 2018, ranging from 29 in Western Europe to 4.4 in Eastern Africa.[72] Although uncommon, in 20-39 year-olds, CNS tumours ranked second among the leading causes of cancer-related deaths in countries with very high human development index.[6] Adolescents and young adults are patients with distinct needs, and services provided for children and older adults may not be adequate.[128]

Globally, almost 80% of CNS tumours in adolescents and young adults (15-39 years) are diagnosed in low-income and middle-income countries, where most people in this age group live.[72] Where the burden of CNS tumours is highest, however, patients may encounter obstacles in being diagnosed and treated for their disease. For instance, access to radiotherapy is extremely unequal world-wide. Density of radiotherapy machines varies between 4.9 or more per million population in Western Europe, North America, Australia and Japan, and 0.4 per million in the rest of the world.[52] The divide between the number of diagnoses and the availability of treatment facilities will inevitably translate to missed opportunities of care (and cure), years of life lost, and financial hardship in families where patients are the breadwinners.

Mortality is a key indicator in epidemiological surveillance, but it does not provide information on the course of the disease following a cancer diagnosis. By contrast, population-based survival incorporates the follow-up component, and reflects the overall effectiveness of a health care system in managing that cancer.[47, 48]

The CNS comprises brain, spinal cord and meninges. Brain tumours are, by far, the most important group. In the third cycle of the CONCORD programme (CONCORD-3), broad disparities in survival emerged among more than 650,000 adults who were diagnosed with a primary brain tumour in 58 countries world-wide during 2000-2014. Age-standardised five-year net survival for all brain tumour subtypes and all ages combined (15-99 years) ranged between 14.7% in Thailand and 42.2% in Croatia.

Brain tumour morphology is the most important predictor of clinical outcome. In patients aged 15-44 years, the European average five-year relative survival during 2000-2007 was 14.2% for glioblastoma, but 56.1% for lower-grade astrocytic tumours.[11]

For adolescents and young adults diagnosed with a given brain tumour subtype, it is currently not known how survival varies around the world, and whether it has improved over time.

As age increases from childhood to early adulthood, the morphology distribution shifts progressively from a predominance of low-grade gliomas (e.g. pilocytic astrocytoma) to a higher proportion of more aggressive tumours. The use of the International Classification of Childhood Cancer (ICCC) has been often extended to adolescents and young adults,[19, 129] but in the light of the differences in the morphology distribution, it is unclear whether alternative strategies should be adopted.

We aimed to address these questions by systematically synthesising the scientific evidence pertaining to population-based survival from brain tumours in adolescents and young adults.

Methods

This systematic review focussed on prospective, observational studies presenting survival from brain tumours in adolescents and young adults.

We queried six electronic databases (Dissertation and Theses Global, Embase, Medline, Open Grey, Scopus and Web of Science) from database inception to 31 December 2019. Search strategies were specific to each database, and included terms referring to four domains: disease, statistical method, study design, and

outcome. A professional librarian at the London School of Hygiene and Tropical Medicine reviewed the search strategies. (Supplementary Table 1.1)

There is no consensus on the definition of “young adults”, and in most studies the upper age boundary varied between 24 and 39 years. We adopted a comprehensive approach by including patients aged 15-39 years. However, studies including individuals who overlapped this age range were still eligible.

We extracted data from published reports. Eligible studies had to include survival estimates from primary data collected in population-based cancer registries. For a given country or region, hospital-based estimates were retained only if no population-based estimates were available.

Studies were eligible if they included estimates derived from a time-to-event analysis and survival probabilities up to at least five years. More specifically, survival probabilities had to be estimated as observed survival, relative survival or net survival.[62] These outcome measures do not require knowledge of the cause of death.

We did not put restrictions relating to language and we considered both published articles and grey literature, such as conference abstracts and statistical reports. However, because morphology classifications changed substantially after 1995, we did not include earlier reports.

Countries were defined based on their United Nations name and continent.

If a study did not clearly meet the eligibility criteria, we decided on inclusion or exclusion through discussion.

We were interested in both non-malignant and malignant brain tumours. We focussed on astrocytic tumours, because data for rarer subtypes, such as oligodendrogliomas, were too scanty to allow robust comparisons.

Since morphological groupings differed between studies, we combined similar definitions (e.g. anaplastic astrocytoma and astrocytoma World Health Organisation (WHO) grade III) under a common descriptor (Supplementary Table 2.2) but, where possible, without combining morphologies with different clinical behaviour (i.e. WHO grade). Definitions sharing the same code in the International Classification of Diseases for Oncology (ICD-O) Third Edition were merged.[17] Then we conducted a

sensitivity analysis by re-grouping morphologies according to SEER AYA Site Recode, to explore whether less granular categories were equally informative.[130] SEER AYA Site Recode is based on the classification proposed by Birch and Barr for tumours diagnosed in adolescents and young adults.[70, 71] SEER AYA Site Recode subdivides astrocytic tumours into three categories: low-grade tumours, glioblastoma plus anaplastic astrocytoma, and astrocytoma not otherwise specified (NOS).[130]

From each eligible study, we abstracted five-year survival probabilities by morphology. When studies provided survival estimates for more than one calendar period or considered more than one age group (e.g. patients aged 15-19 years and 20-24 years), each estimate was considered separately. Where available, we collected specifications on the reference classification used for morphology definitions, data quality indicators (e.g. proportion of microscopically verified tumours, patients lost to follow-up and poorly specified/unspecified morphologies), and completeness of ascertainment.

Calendar periods differed between studies, and their length also varied. Therefore, we have presented the results labelled with the middle year of the calendar period.

The systematic review is registered with PROSPERO, number CRD42018111981.

Results

The database search yielded 5,640 records. We screened these records for eligibility from the title and the abstract. We then assessed the full text of the remaining 356 publications for eligibility. This process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[53] Twenty studies were included in the systematic review. (Figure 2.1)

The calendar period for incident cases ranged from 1968 to 2014. Twelve studies (60%) were conducted in one or more European countries, four in the US, two in Asia (South Korea and Japan), one comprised patients from the US and Germany, and one international study was carried out in Europe, but including also Cyprus and Turkey, and the US. Only one study included any data from middle-income countries.[131] (Table 2.1)

Young adults were defined as individuals up to the age of 24 years in six studies, up to age 39 in seven studies, and up to age 44 in three studies. Two studies adopted alternative age definitions of the upper boundary (29 or 40 years). The eligible studies collectively provided 75 survival estimates: 14 for adolescents only (15-19 years), 23 for young adults (20 years or more) only, and 38 estimates for adolescents and young adults combined. (Table 2.1)

Eight of the 20 studies had a regional population coverage, four were based on national registries, seven were international studies drawing data from both regional and national registries, and in one study the information was not available. (Table 2.1)

The completeness of ascertainment was only specified in four of the 20 studies.[10, 132-134] Twelve (60%) of the 20 studies provided details on data quality indicators: two studies only specified the criteria for exclusions (e.g. diagnoses based on death certificate only or autopsy), and ten reported at least the proportion of microscopically verified tumours. (Table 2.1)

The proportion of microscopically verified tumours referred specifically to brain tumours in four studies,[11, 16, 131, 135] while in five the parameter was for all tumours combined.[10, 64, 69, 87, 136] In the two international comparisons, the proportion of microscopically verified tumours varied between 57.2% and 96.4% (South-Eastern European (SEE) consortium, plus US), and between 61.0% and 100% in the EUROCARE-5 study, covering adolescents and young adults diagnosed during 1999-2007 in 27 European countries.[11, 131] One study comprised exclusively patients with microscopically verified tumours.[117] (Supplementary Table 2.3)

Five studies did not clarify the reference classification. In the remaining 15 studies, the second or third editions of the International Classification of Diseases for Oncology (ICD-O) were the reference classification.[17, 118] (Table 2.1)

Ten of the 20 eligible studies grouped all astrocytic morphologies under the broad definition “astrocytoma”, but two of these studies did not clarify the behaviour of eligible tumours (only malignant, or both malignant and non-malignant).[137, 138] (Supplementary Table 2.3) Ten studies considered either subgroups (i.e. low-grade astrocytoma or high-grade astrocytoma) or single morphologies (e.g. diffuse astrocytoma, glioblastoma).

In 13 studies (65%), the outcome measure was observed survival (i.e. all-cause survival), while in seven studies it was relative survival. (Table 2.1)

For astrocytoma as a broad morphology group, survival estimates referred mostly to patients aged 15-24 years. No studies were available from low-income or middle-income countries. Nearly all estimates of five-year survival fell within the range 48.0-71.0% during 1973-2004, with little variation in survival between countries or over time. [69, 87, 117, 132-134, 136, 137, 139, 140] In the only US study, however, five-year survival was higher than in Europe: 73.1% versus 65.0% around 1988, and 81.3% versus 64.2% around 2000.[10] In the EUROCARE-5 study for diagnoses during 2000-2007, five-year survival from astrocytoma was 50.8% in adolescents (15-19 years), similar (47.6%) in patients up to age 34, but lower (38.7%) in the 35-39 age group.[69] (Figure 2.2). One study from Portugal, however, found that five-year survival from astrocytoma was remarkably higher in young adults (20-24 years) than in adolescents (81.3% versus 55.5%), but confidence intervals were wide and largely overlapping due to the very small study population (51 patients overall).[137]

Among the studies using the broad definition “astrocytoma”, we identified four possible combinations of age (adolescents (15-19 years), or adolescents and young adults combined (15-44 years)), and tumour behaviour (all behaviours or malignant only). Five-year survival from non-malignant and malignant astrocytoma combined was slightly higher in adolescents (15-19 years, 60.1-81.3%) than in the broader age group (15-44 years, 48.0-68.4%), except in Eastern Europe and France, where values were lower (52.0%).[139, 140] Conversely, five-year survival for malignant astrocytoma in adolescents was very similar to the values observed in adolescents and young adults combined. (Figure 2.3)

Five-year survival from low-grade astrocytoma (WHO grade I and II combined), was 87.0% or more for patients aged 16-29 years, in England, Germany, and the US (2002-2005). In the same countries, survival was lower (72.6-76.0%) when individuals up to age 39 were also included.[131, 138, 141] In the SEE consortium, five-year survival for patients diagnosed in 2005 was much lower (59.0%, 15-39 year-olds).[131] (Figure 2.4)

Five-year survival from high-grade astrocytoma (WHO grade III and IV combined) was 18.0% in England, in 1997,[138] while it varied between 27.3% and

39.2% in Germany, United States and the SEE consortium, during 2002-2005.[131, 141] (Figure 2.4)

Five-year survival from diffuse astrocytoma was in the range 62.9-75.9% in Germany and the US, during 2002-2007.[16, 131, 141] In the EUROCARE-5 consortium (27 European countries combined) and the SEE consortium (Southern and Eastern Europe), average five-year survival was 56.1% (2003) and 55.0% (2005), respectively.[11, 131] (Figure 2.4)

The survival probability at five years for South-Korean patients diagnosed with anaplastic astrocytoma in 2002 was 39.6%.[117] In the US, five-year survival was higher, 50.4% in 2003 and 55.4% in 2007.[16, 142] (Figure 2.4)

Five-year survival from glioblastoma was in the range 14.2-23.1% in England, the EUROCARE-5 consortium, the US and South Korea, without improvements in the 20 years between 1991 and 2009.[11, 16, 117, 135, 143] (Figure 2.4)

Lastly, studies were grouped according to SEER AYA Site Recode.[130] Such system does not adopt the broad definition “astrocytoma”, so studies using this definition were excluded from the analysis. None of the studies focussed solely on adolescents (15-19 years). Five-year survival from low-grade astrocytic tumours was in the range 71.4-93.4%.[16, 120, 131, 138, 141] Five-year survival from high-grade astrocytic tumours varied between 14.2% and 55.4%.[11, 16, 117, 131, 135, 138, 141-143]. Five-year survival for astrocytoma not otherwise specified was in the range 55.0-75.9%.[11, 131, 141] (Supplementary Figure 2.1)

Discussion

To our knowledge, this is the first systematic review summarising international trends in survival from astrocytic tumours in adolescents and young adults (15-39 years).

Five-year survival for all astrocytic tumours combined was mostly in the range 48.0-71.0%. Survival was much lower in studies only including patients with malignant astrocytoma or considering broader age groups. Outcomes changed very little during the 30 years between 1973 and 2004. However, differences in study design hampered the appraisal of possible changes in survival over time.

Five-year survival was in the range 55.0-75.9% for diffuse astrocytoma, but it rose up to 89.1% when WHO grade I and II tumours were combined. The survival probability at five years was 23.1% or less for glioblastoma, in the range 39.6-55.4% for anaplastic astrocytoma, and mostly between 27.3% and 39.2% when the two morphologies were jointly considered. For a given morphology, older patients experienced poorer outcomes.

Nearly all the studies were conducted in high-income countries, noticeably in high-income countries in Europe, and in the US. In these settings, survival was similar. Only one international study included patients diagnosed in middle-income countries (Belarus, Bulgaria, Montenegro, Romania, Serbia, Turkey, Ukraine). In this study (SEE consortium) the average five-year survival for low-grade astrocytic tumours was at least 15% lower than in more affluent countries (England, Germany and the US), but the gap in survival was smaller (around 10%) for high-grade astrocytic tumours, for which little can be done.[131]

Eleven out of 20 studies (55%) extended the use of ICCC to adolescents and young adults, using the broad definition “astrocytoma”. We were obliged to retain such definition in our analyses because these 11 studies did not stratify survival estimates by tumour subtype (e.g. diffuse astrocytoma, glioblastoma) or WHO grade (i.e. low-grade and high-grade), leading to a loss of precision and hampering the interpretation of results. The distribution of astrocytic tumours with different clinical behaviour varies widely with age. Pilocytic astrocytoma, the most common non-malignant astrocytic tumour, accounts for 60% of all astrocytic tumours in children, compared to 47% in adolescents (15-19 years), and 19% in the 15-39 age group.[16] Pilocytic astrocytoma is associated with a survival probability at five years of around 90%, while survival for higher-grade astrocytoma is 50% or less.[16] Therefore, any grouping strategy combining morphologies with very different outcomes will result in inflated, misleading survival estimates.

When we stratified the 11 studies using the information they provided on the eligible tumour behaviours, survival trends in adolescents (15-19 years) became slightly clearer, with lower five-year survival when non-malignant astrocytic tumours were excluded. When broader age groups were considered (upper age limit 24 years or more), however, survival was similar after inclusion or exclusion of patients with

non-malignant astrocytic tumours. These tumours are rare in older adults, and their impact on survival estimates for the broad morphology “astrocytoma” is likely to be smaller with increasing age. Yet, in Eastern European adolescents, survival for all-behaviour astrocytoma was in line with the values observed for malignant-only astrocytoma.[139, 140] Such finding suggests under-registration of non-malignant tumours.

We found that five-year survival from astrocytoma in adolescents and young adults mostly varied between 48.0% and 71.0% during 1973-2004. Conversely, in children (0-14 years), survival from astrocytoma varied between 71.0% and 89.0% in most countries during 1970-2009.[144] Differences in survival between the two age groups, however, were less remarkable when more granular morphology definitions, instead of ICCC, were used, but studies adopting such strategy were few.[144] Such discrepancy emphasises the limitations of ICCC in accounting for the substantial differences in the morphology distribution of astrocytic tumours between children, and adolescents and young adults.

The classification proposed by Birch and Barr for tumours diagnosed in adolescents and young adults formed the basis of SEER AYA Site Recode,[70, 71, 130] which implemented a bespoke classification scheme for adolescents and young adults in a large, population-based cancer registry. This classification scheme aimed to address the ICCC limitations by using WHO grade to further subdivide astrocytic tumours. We tried to re-group the studies based on SEER AYA Site Recode. (Supplementary Figure 2.1) Only one study adopted this classification, so we were obliged to mainly use the original morphology definitions.[138] Five-year survival from low-grade astrocytic tumours was mostly in the range 71.4-93.4% during 1997-2007, and five-year survival from high-grade astrocytic tumours varied between 14.2% and 55.4% during 1991 and 2009. Survival for low-grade astrocytic tumours was remarkably higher than for anaplastic astrocytoma and glioblastoma, suggesting that SEER AYA Site Recode may be more appropriate than ICCC in describing survival in adolescents and young adults. The variation in survival within each morphology group, however, implies that combining different morphologies may still result in some loss of information. This seems particularly relevant to high-grade morphologies, namely anaplastic astrocytoma and glioblastoma. Anaplastic astrocytoma often recurs as glioblastoma, but outcomes at five years are remarkably different.[16] (Supplementary Figure 2.1) Further research is needed to understand whether SEER AYA Site Recode

may replace ICCC in studies exploring survival disparities between children, and adolescents and young adults.[130]

SEER AYA Site Recode comprises also the category astrocytoma NOS. In most of the studies using such definition, survival estimates were in the range 55.0-75.9%.[11, 131, 141] These values are in line with those observed for diffuse astrocytoma (WHO grade II).[16] In ICD-O-3, diffuse astrocytoma is one of the alternative descriptors of astrocytoma not otherwise specified.[17] Conversely, in the WHO classification (4th edition), astrocytoma not otherwise specified is not a separate definition and the corresponding ICD-O-3 code is attributed to diffuse astrocytoma.[7] Given that the definitions “astrocytoma not otherwise specified” and “diffuse astrocytoma” refer to the same entity, we recommend against using the definition “astrocytoma NOS” as a synonym for unspecified astrocytic tumours. (Supplementary Figure 2.1)

Overall, there were no clear trends in five-year survival from astrocytoma as a broad morphology group. In the US, however, survival for adolescents (15-19 years of age) rose from 60.1% to 81.3% during the two decades between 1977 and 1997.[10] Conversely, survival for adolescents in Europe persisted in the range 64.2-66.0% during 1988-2001.[87, 136, 139] These findings may suggest that in the US outcomes for adolescents improved earlier than elsewhere, possibly due to the implementation of dedicated health services.

In adolescents and young adults, more than one fourth of astrocytic tumours are glioblastomas.[16] In 2005, a randomised clinical trial showed that two-year survival was 26.5% in patients treated with radiotherapy plus temozolomide chemotherapy, and only 10.4% in those receiving radiotherapy.[12] Since, the concomitant treatment has become the standard of care for adults younger than 70 years. We could not explore the benefit of this treatment protocol at population level, because very few survival estimates are available for patients diagnosed after 2005. In this systematic review, five-year survival was in the range 14.2-23.1%. In older adults (40 years or more), five-year survival is below 10%. Glioblastoma may arise as a WHO grade IV lesion, or develop from a lower-grade glioma. Glioblastomas arising from a lower-grade glioma are characterised by mutation of the isocitrate dehydrogenase (*IDH*) gene. Patients with *IDH*-mutated glioblastomas are younger than those affected by *IDH* wild-type glioblastomas (median age at diagnosis 32 years versus 59 years), and have a more favourable outcome.[36] We chose to report only five-year survival to

improve comparability between studies, because it was the most commonly adopted outcome measure. For glioblastoma, however, shorter-term survival estimates may be more informative.

Information on data quality indicators was inadequately reported, and often totally missing (42% of studies). Data quality indicators tell us about cancer registry practices (e.g. sources of data, type of follow-up), and affect the reliability of the data.[125] Most frequently, studies indicated the proportion of microscopically verified tumours. Histological confirmation of brain tumours may not be possible if the patient is clinically unfit to surgery or a biopsy, or if tumour location bars a diagnostic procedure. In each of the two large international studies reviewed here, the proportion of microscopically verified tumours varied widely between the participating registries. The average proportion of microscopically verified tumours in these two studies was similar (around 80%), but the SEE consortium also included middle-income countries, where access to care may be sub-optimal.[11, 131] In some of the more affluent European countries, however, the proportion of microscopic verification was also rather low (e.g. 63.3% in Italy).[11] Proportions which are very high may indicate over-reliance on pathology reports, and, therefore, a restricted number of data sources, leading to incompleteness of case ascertainment. Furthermore, patients with microscopically verified brain tumours may not necessarily represent the whole population, because they were at least able to undergo an invasive diagnostic procedure. If only these patients are included in the study, survival estimates may be higher. The overall completeness of case ascertainment was specified only in four studies, where it was 95% or more. Lower levels may suggest that a cancer registry fails to capture all the data within its catchment area, and this may lead to under-ascertainment of brain tumours.[126]

Two-thirds of the studies estimated survival as all-cause survival (i.e. observed survival). The cause of death is not used in international comparisons of cancer survival, because it may be unavailable, or based on unreliable information from the death certificate.[58-60] Observed survival can be readily obtained, but it is biased downwards because it includes death from other causes (i.e. background mortality). Background mortality varies between populations and over time, and it can be derived from life tables.[145] Once competing risks of death are properly accounted for, the estimate will reflect net survival, which is the survival attributable exclusively to cancer. Net survival permits robust international comparisons, and it can now be directly

estimated with the non-parametric, unbiased Pohar Perme estimator.[62] Until recently, relative survival has been used as the best approximation of net survival, but this indicator does not allow for informative censoring. Informative censoring arises when the probability of dying from cancer is not independent of the probability of dying from other causes, and this is more frequent in the elderly. We have been obliged to compare studies that used different survival estimators, which may reduce the validity of some comparisons. Nevertheless, given that we considered relatively young patients and nearly all were diagnosed in affluent countries, failing to account for the rather low background mortality is unlikely to lead to substantial bias.

This systematic review presents some limitations. We adopted a wide range of morphology definitions in order to summarise survival variation in as much detail as possible. However, the number of survival estimates in some categories was small, hindering robust comparisons.

Many studies (75%) were partly or entirely based on regional data. We assumed that regional survival estimates applied to the whole country, but this assumption may not hold if provision of cancer care is unequally distributed. However, these regions were often also included in national or international studies. Estimates from studies with different geographical coverage did not differ substantially, so findings from smaller studies were fairly generalisable.

We were obliged to present trends using the central year of the calendar period covered by a given study, regardless of its length. Although this strategy improved clarity, when two or more calendar periods overlapped, we could not use differences in length to explore non-linear changes in survival. However, there were no substantial gains in survival for any of the morphologies, so comparisons referring to the central year may be acceptable.

In conclusion, there is a striking gap in knowledge about survival trends in middle-income and low-income countries, where disparities in access to care are reported.[52] Studies with a wider scope, extending to currently under-represented geographical regions, could fill this gap. Moreover, standardised data collection, data quality control, and data analysis using the same statistical methods are required in order to reduce heterogeneity and enable robust international comparisons. ICCC does not allow accurate reporting of survival from astrocytic tumours in adolescents and young adults because it does not account for the substantial differences in the

histology distribution of brain tumours between adolescents and young adults, and children. Ultimately, ICCC should be revised. SEER AYA Site Recode, which proposes granular morphology groupings based on WHO grade, may inform such revision. Future studies should use improved classification systems to properly explore potential outcome disparities in adolescents and young adults, and to inform cancer control plans.

Figure 2.1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.

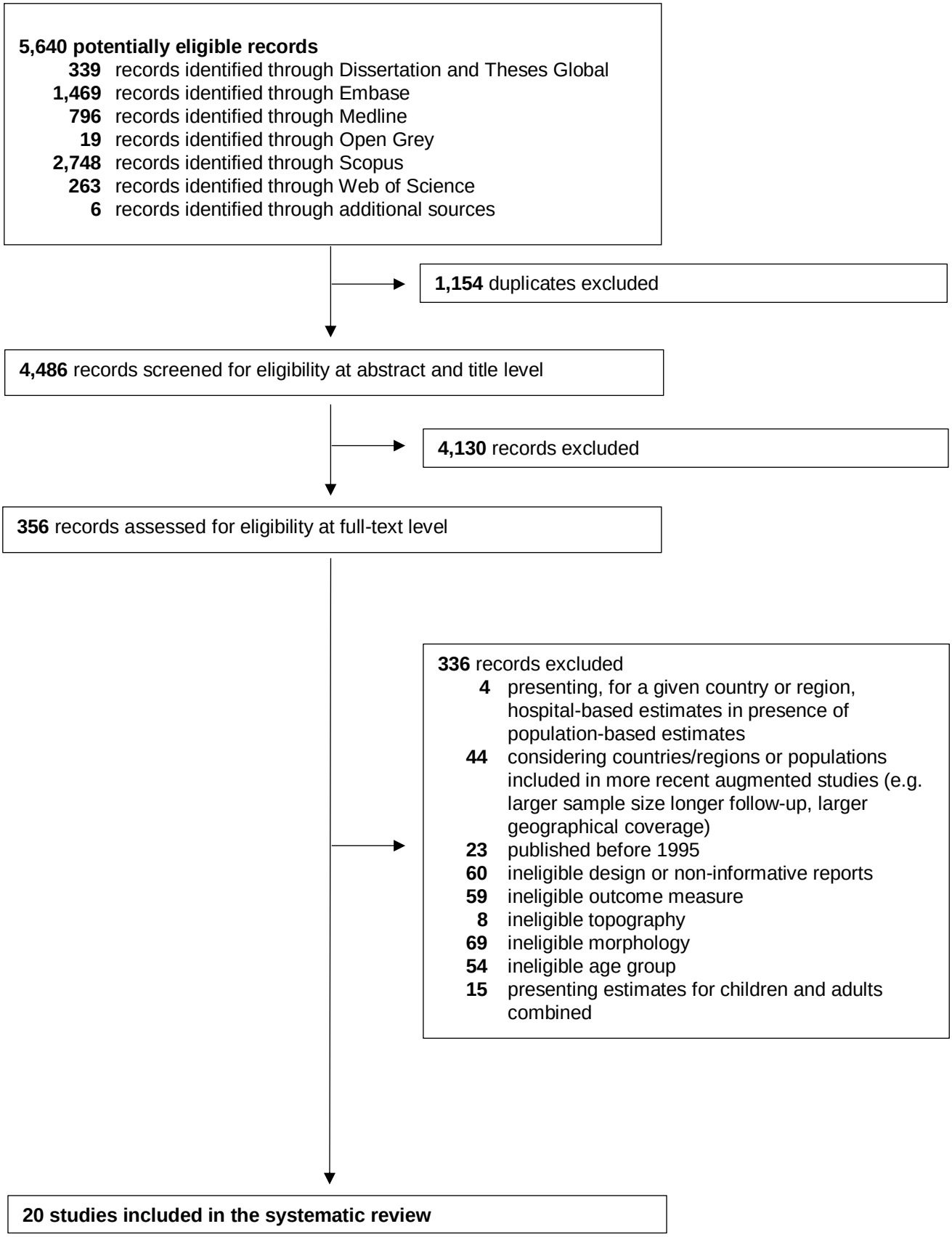
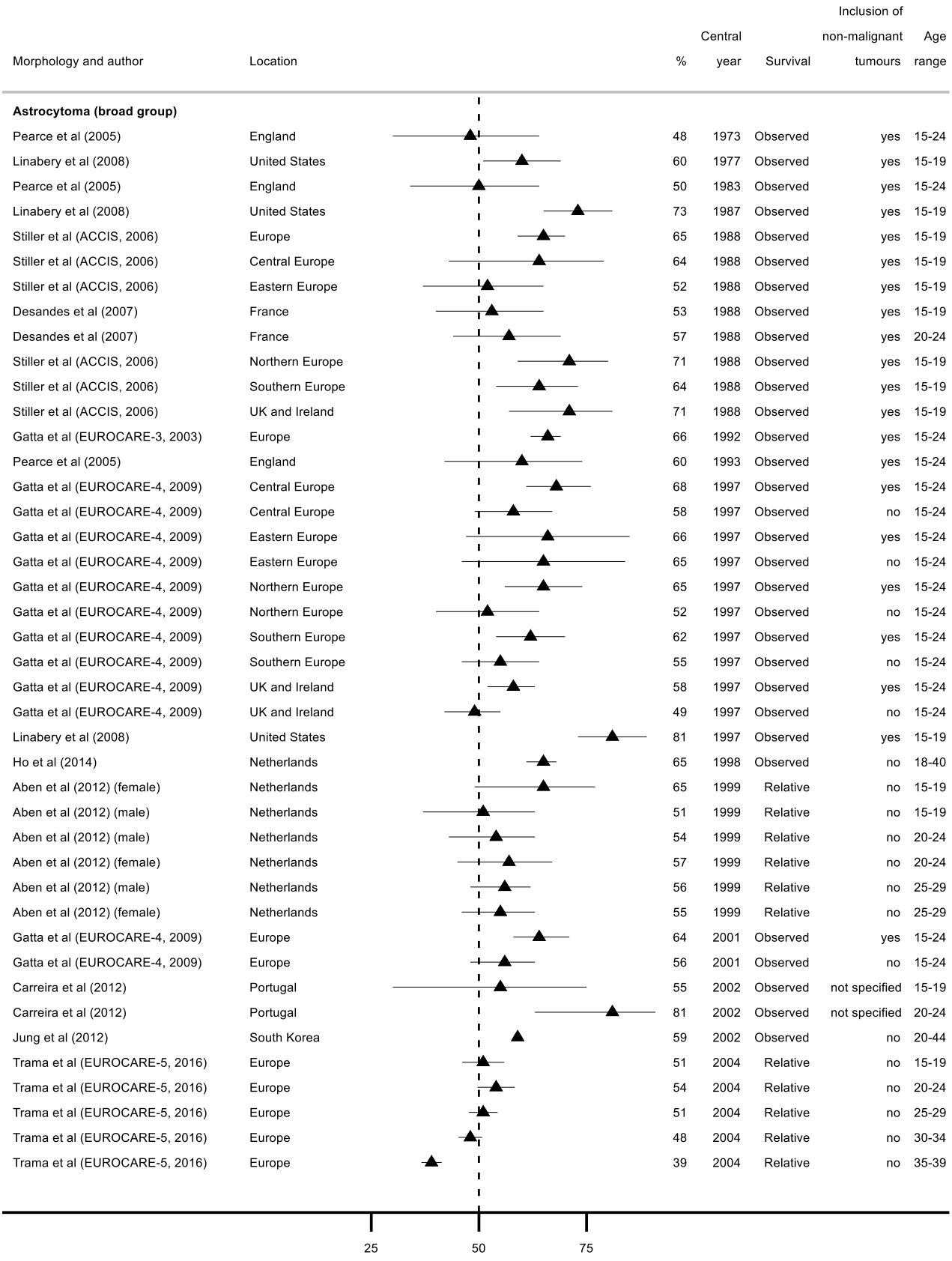


Figure 2.2. Five-year survival (%) from astrocytoma (broad morphology group).



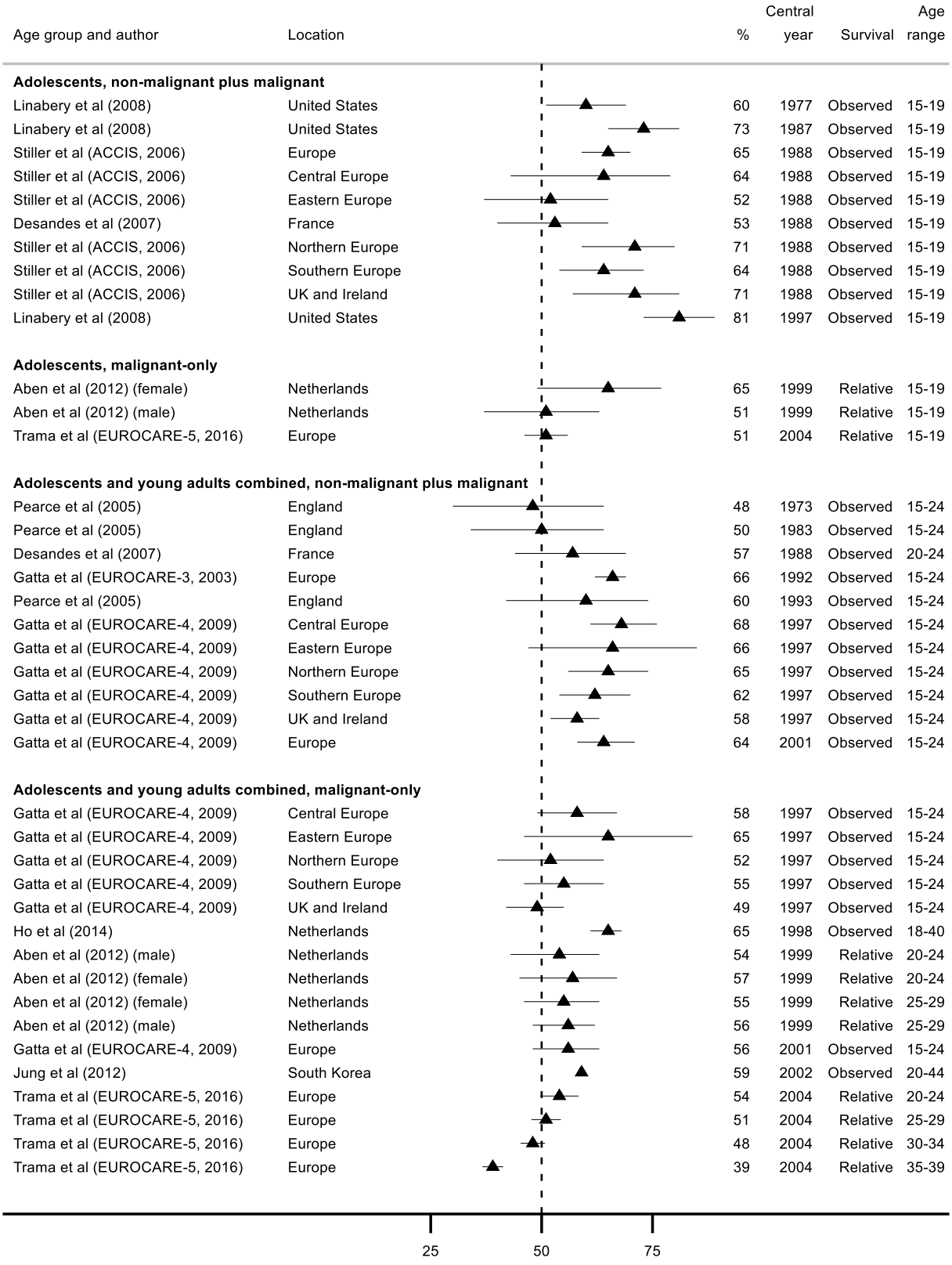
Automated Childhood Cancer Information System (ACCIS) consortium: Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Italy, Netherlands, Slovakia, Slovenia, Spain, Switzerland, UK, Norway

EUROCARE-3 consortium: Austria, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Italy, Malta, Netherlands, Norway, Poland, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales.

EUROCARE-4 consortium: Austria, Belgium, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

Figure 2.3. Five-year survival (%) from astrocytoma (broad morphology group), by age group (adolescents, or adolescents and young adults combined) and tumour behaviour (non-malignant plus malignant, or malignant-only).



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EUROCARE-4 consortium: Austria, Belgium, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

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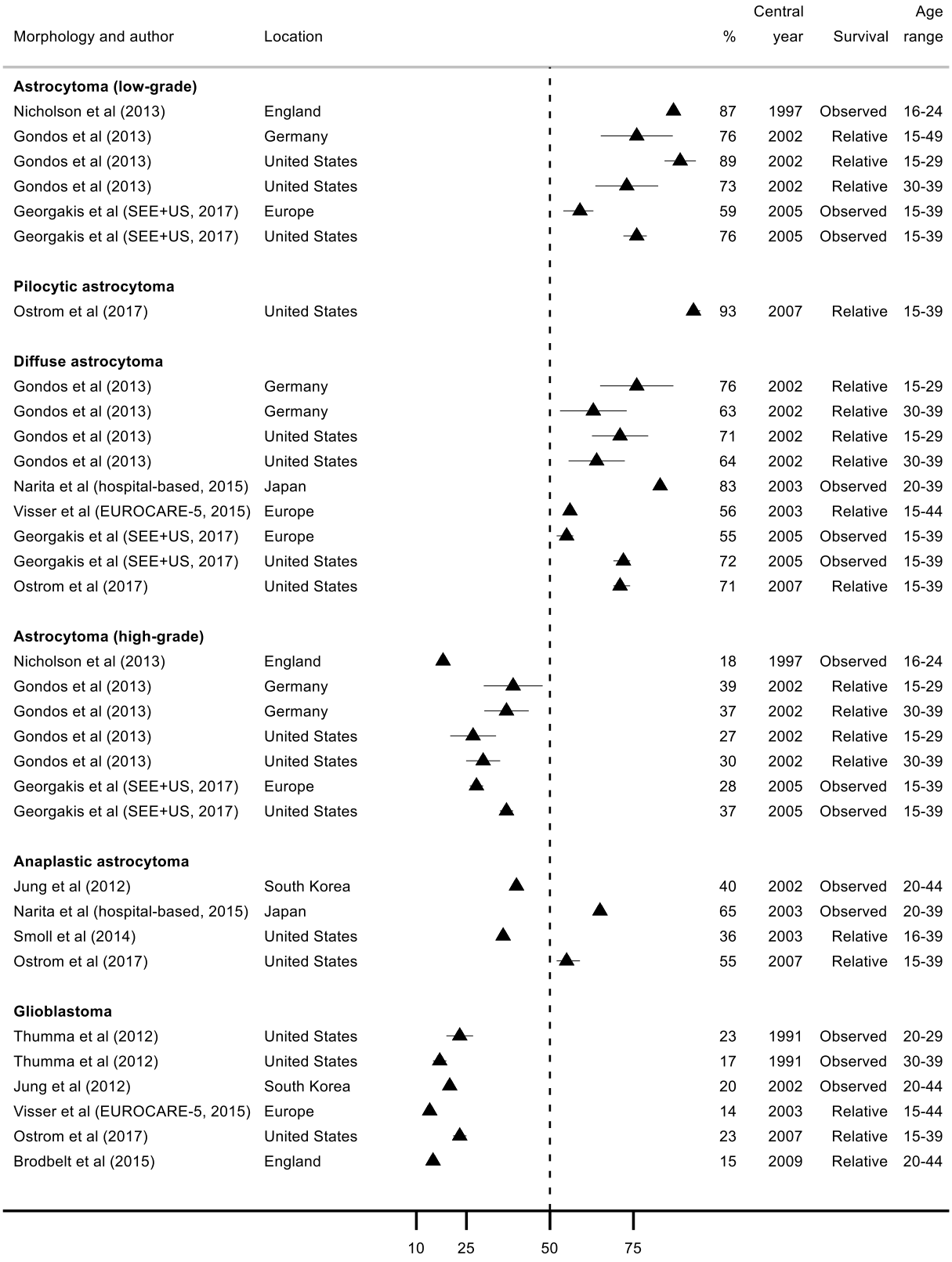
Figure 2.4. Five-year survival (%) from astrocytoma (low-grade), pilocytic astrocytoma, diffuse astrocytoma, astrocytoma (high-grade), anaplastic astrocytoma, and glioblastoma.



EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

Southern and Eastern Europe (SEE) consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine

Table 2.1. Studies included in the systematic review.

Study	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span, y	Quality indicators	Reference classification	Estimator
Gatta et al., 2003	EUROCARE-3[1] consortium	Not specified	Regional and national	1990-1994, not specified	15-24	Proportion of microscopically verified tumours, exclusions, proportion of patients censored before 5 years, proportion of unspecified morphologies	ICD-O[2]-3	Observed survival
Pearce et al., 2005	England	98%	Regional: Northern Region	1968-1997, not specified	15-24	Not specified	Not specified	Observed survival
Stiller et al., 2006	ACCIS[3]	Not specified	Regional and national	1978-1997, 2001	15-19	Proportion of microscopically verified tumours, exclusions, proportion of unspecified morphologies	ICD-O-2	Observed survival

Study	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span, y	Quality indicators	Reference classification	Estimator
Desandes et al., 2007	France	Not specified	Regional (10%): 9 registries	1978-1997, 2002	15-24	Not specified	ICD-O-2	Observed survival
Linabery et al., 2008	United States	98%	Regional (14%): SEER[4] 13	1975-1999, not specified	15-19	Proportion of microscopically verified tumours, proportion of patients lost to follow-up	ICD-O-3	Observed survival
Gatta et al., 2009	EUROCARE-4[5] consortium	Not specified	Regional and national	1995-2002, 2003	15-24	Proportion of microscopically verified tumours, exclusions, proportion of unspecified morphologies	ICD-O-3	Observed survival
Aben et al., 2012	Netherlands	95%	National	1989-2009, 2010	15-29	Exclusions	ICD-O -1,2,3	Relative survival
Carreira et al., 2012	Portugal	Not specified	Regional (30%): 5 districts	1997-2006, 2010	15-24	Not specified	ICD-O-3	Observed survival

Study	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span, y	Quality indicators	Reference classification	Estimator
Jung et al., 2012	South Korea	Not specified	National	1999-2004, 2009	20-44	Proportion of microscopically verified tumours	ICD-O-3	Observed survival
Thumma et al., 2012	United States	Not specified	Regional: SEER	1973-2008, not specified	20-39	Not specified	Not specified	Observed survival
Gondos et al., 2013	Germany, United States	Not specified	Germany: regional (41%); United States: regional (14%)	1997-2006, not specified	15-39	Exclusions	ICD-O-3	Relative survival
Nicholson et al., 2013	England	Not specified	Regional: Yorkshire	1990-2004, 2009	16-24	Not specified	Not specified	Observed survival
Ho et al., 2014	Netherlands	98%	National	1989-2010, not specified	18-40	Not specified	ICD-O-3	Observed survival
Smoll et al., 2014	United States	Not specified	Regional: SEER 18	2000-2006, not specified	16-39	Not specified	Not specified	Relative survival
Brodbelt et al., 2015	England	Not specified	National	2007-2011, not specified	20-44	Proportion of microscopically verified tumours	ICD-O-2	Relative survival

Study	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span, y	Quality indicators	Reference classification	Estimator
Narita et al., 2015	Japan	Not specified	Not specified	2001-2004, not specified	20-39	Not specified	Not specified	Observed survival
Visser et al., 2015	EUROCARE-5[6] consortium	Not specified	Regional and national	2000-2007, 2008	15-44	Proportion of microscopically verified tumours, proportion of unspecified morphologies	ICD-O-3	Relative survival
Trama et al., 2016	EUROCARE-5 consortium	Not specified	Regional and national (12-100%)	2000-2007, 2008	15-39	Proportion of microscopically verified tumours, exclusions, proportion of lost to follow-up, proportion of unspecified morphologies	ICD-O-3	Relative survival

Study	Countries	Completeness of ascertainment	Population coverage	Calendar period for incident cases and end of follow-up	Age span, y	Quality indicators	Reference classification	Estimator
Georgakis et al., 2017	South Eastern Europe (SEE[7]) consortium, United States	Not specified	SEE consortium: regional and national (5-100%); United States: regional (28%): SEER 18	2001-2009, 2016	15-39	Proportion of microscopically verified tumours, exclusions, proportion of unspecified morphologies	ICD-O-3	Observed survival
Ostrom et al., 2017	United States	Not specified	Regional (26%): SEER 18	2000-2014, not specified	15-39	Proportion of microscopically verified tumours	ICD-O-3	Relative survival

[1] EUROCARE-3 consortium: Austria, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Italy, Malta, Netherlands, Norway, Poland, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

[2] ICD-O: International Classification of Diseases for Oncology

[3] ACCIS consortium: Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Italy, Netherlands, Slovakia, Slovenia, Spain, Switzerland, UK, Norway

[4] SEER: Surveillance, Epidemiology, and End Results Program

[5] EUROCARE-4 consortium: Austria, Belgium, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

[6] EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

[7] SEE consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed <u>for each</u> research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1701655	**Title**	Dr
First Name(s)	Fabio		
Surname/Family Name	Girardi		
Thesis Title	Global surveillance of survival from brain tumours diagnosed during 2000-2014: trends by age and histology		
Primary Supervisor	Dr Claudia Allemani		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Choose an item.	Was the work subject to academic peer review?	Choose an item.

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	Neuro-Oncology
Please list the paper's authors in the intended authorship order:	Fabio Girardi, Brian Rous, Charles A Stiller, Gemma Gatta, Naomi Fersht, Hans H Storm, Jessica R Rodrigues, Christian Herrmann, Rafael Marcos-Gragera, Rafael Peris-Bonet, Mikhail Valkov, Hannah K Weir, Ryan R Woods, Hui You, Patricia A Cueva, Prithwish De, Veronica Di Carlo, Tom

	Børge Johannesen, Carlos A Lima, Charles F Lynch, Michel P Coleman, Claudia Allemani, CONCORD Working Group
Stage of publication	**Undergoing revision**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Conception and design, data analysis and interpretation, manuscript writing

SECTION E

Student Signature	[redacted]
Date	7 December 2020

Supervisor Signature	[redacted]
Date	7 December 2020

Preface to Research Paper 3

I have appraised the geographical coverage and methodology of the evidence available to date in chapters 1 and 2 (Research Paper 1 and Research Paper 2). The conclusions of this preparatory work were two-fold. (1) Larger studies on survival from brain tumours by histological subtype are warranted, since little is known beyond Europe and North America. (2) The currently available histology classifications, such as the International Classification of Childhood Cancer (third edition, ICCC-3),[19] do not properly account for variations in the histology distribution by age and country, and may hinder the interpretation of survival estimates by brain tumour subtype. Therefore, improved histology groupings are required, to allow robust and informative global comparisons in brain tumour survival by histology. Survival analyses based on these histology groupings may also be expected to help explain the wide global variations in survival from brain tumours that are seen when all histological types are considered as a whole.

In the following chapter, I have laid the foundation for the survival analyses in chapters 4 and 5 by defining 12 histology groups for children and 11 histology groups for adults. In children, the key innovation is the incorporation of WHO grade in the subgroup for astrocytoma, while preserving the overall ICCC-3 framework. In adults, for whom a bespoke classification is not available, I have developed a scheme that accounts for the predominance of higher-grade subtypes. In this scheme, I have attempted to incorporate the most recent advances in the understanding of the genetics of brain tumours, even though I could not include molecular data. The attribute “not otherwise specified” (NOS) can be used by cancer registries for ill-defined histological entities. The 6th digit of the morphology code in the International Classification of Diseases for Oncology (third edition, ICD-O-3) defines the tumour grade as assigned by the pathologist.[17] I used such information to reclassify astrocytic tumours, whenever possible, into the relevant, specific histological subtypes.

The source for these analyses is the CONCORD-3 data base.[46] I have considered the individual records of all patients aged 0-99 years who were diagnosed with a primary brain tumour during 2000-2014, whether malignant or non-malignant. I present the histology distribution of these tumours, by country, for patients diagnosed during 2000-2004, 2005-2009, and 2010-2014.

The analyses include 60,783 children and 602,112 adults who were diagnosed with a primary brain tumour in 60 countries on five continents. In children (0-14 years), the proportion of low-grade astrocytomas ranged between 6% and 50%. Medulloblastoma was the most common subtype in countries where low-grade astrocytoma was less commonly reported. In adults (15-99 years), the proportion of glioblastomas varied between 9% and 69%. The proportion of unspecified astrocytomas was in the range 0-21% in children, and 0-34% in adults. Unspecified gliomas were rarely reported in children or adults. International comparisons were made difficult by wide differences in the proportion of tumours with unspecified histology, which accounted for up to 52% of diagnoses in children and up to 65% in adults.

To my knowledge, this is the first report on the global distribution of brain tumour histology among both children and adults. The findings provide insights into the practices and the quality of cancer registration of brain tumours world-wide. This study will inform the survival analyses for children and adults, presented in chapters 4 and 5, respectively.

Research Paper 3 has been reviewed and cleared by more than 600 collaborators in the CONCORD Working Group and their comments have been examined and incorporated in the manuscript where relevant. The manuscript has been provisionally accepted for publication in Neuro-Oncology, depending on submitting a revised version (October 2020).

Research Paper 3: the global histology distribution of brain tumours (CONCORD-3)

The histology of brain tumours for 67,331 children and 671,085 adults diagnosed in 60 countries during 2000-2014: a global, population-based study (CONCORD-3)

Introduction

Central Nervous System (CNS) tumours encompass more than fifty subtypes, with distinct genetic hallmarks, clinical behaviour and survival.[15] In Europe, age-standardised five-year observed survival was 95% for children diagnosed with pilocytic astrocytoma during 2000-2007, while age-standardised five-year relative survival for adults diagnosed with glioblastoma during the same period was only 6.3%.[9, 11] Primary CNS tumours can arise in the brain, the meninges and the spinal cord, but the brain is by far the most common site.

CNS tumours were the most important cause of cancer-related deaths in children diagnosed with a solid tumour in 2018.[72] In countries with a very high Human Development Index, they represented the second most important cause of cancer-related deaths in young adults in 2012.[6]

The formal diagnosis of a brain tumour requires imaging, surgery or biopsy, and pathology. The lack of adequate diagnostic facilities may lead to under-diagnosis of brain tumours, and may hamper correct identification and the delivery of optimal treatment.[146, 147]

In order to make a robust international comparison of the frequency of the various histological types of brain tumour, it is first necessary to define suitable histology groupings. The framework for presenting data on tumours in children is the International Classification of Childhood Cancer (third edition: ICCC-3[19]), based on the International Classification of Diseases for Oncology (3rd edition, ICD-O-3). A separate framework for adolescents and young adults was devised by Birch and

Barr.[70] Further schemes for grouping brain tumours by their histology include those used in Cancer Incidence in Five Continents (CI5), the Central Brain Tumour Registry of the United States (CBTRUS), and the Information Network on Rare Cancers (RARECARENet).[2, 16, 148] Such strategies are not specific to children or adults, however, and the level of granularity varies.

The evidence on global disparities in incidence and survival for all brain tumours combined is robust, but little is known on variation by histology.[1, 4, 46] Differences in incidence and survival should be interpreted in the light of the histology distribution in each country, but a world-wide account of the histology distribution of brain tumours is currently not available.

The distribution of brain tumours by histology has been only described as part of analyses of incidence or survival by histology in a given country, region or territory,[144] but differences in study design do not allow valid comparisons. Large international population-based studies, such as the Automated Childhood Cancer Information System (ACCIS) and the European Cancer Registry-based study on survival and care of cancer patients (EUROCARE), used standardised data collection, but they only include European countries.[3, 9, 11] African, Central and South American, and Asian countries are substantially under-represented in brain tumour studies by histology.[144]

The CONCORD programme established global surveillance of cancer survival trends in 2015.[46] The third cycle, in 2018 (CONCORD-3), included individual data for more than 37 million patients from 71 countries, diagnosed with one of 18 common tumours during 2000-2014. CONCORD-3 highlighted wide global disparities in survival from all brain tumours combined.

Here, we have examined the CONCORD-3 data to describe the international distribution of brain tumour histology in children and adults. We aimed to inform future global comparisons of survival from brain tumours and to appraise some of the indicators of data quality in cancer registration.

Methods

Records were obtained from population-based cancer registries participating in CONCORD-3. Data were collected using the same protocol, and centrally validated for protocol adherence and consistency through a rigorous 3-phase data quality control procedure (details published elsewhere).[46, 54]

The study population comprised children (0-14 years) or adults (15-99 years), diagnosed during 2000-2014 with a tumour originating in the brain (ICD-O-3 topography code C71), and for whom a morphology code was available. We included both primary, malignant tumours (ICD-O-3 behaviour code 3) and non-malignant tumours, whether benign or of uncertain behaviour (code 0 or 1, respectively).

We used ICD-O-3 to select the morphology codes and the World Health Organisation (WHO) Classification of Tumours of the Central Nervous System (4th edition) for the definition of pathology.[7, 17]

Morphology codes in ICD-O-3 such as 9400/3 with the attribute “not otherwise specified” (NOS) can be used in cancer registration. Rule G of ICD-O-3 allows the use of a 6th digit in the morphology code to define the histology grading, or degree of differentiation.[17] We used this rule to re-classify tumours coded to “astrocytoma NOS” (ICD-O-3 code 9400/3) to one of the more specific astrocytic subtypes. For example, a moderately differentiated astrocytoma NOS (grade 2) was re-classified as a diffuse astrocytoma, while an undifferentiated astrocytoma NOS (grade 4) was assumed to be a glioblastoma. We did not recode “astrocytoma NOS” with an undetermined grade (grade 9); these were analysed separately. The 6th digit of the morphology code is assigned by the pathologist or the registrar while the WHO grade is part of the tumour subtype definition.

We describe the distribution of brain tumour histology by calendar period of diagnosis (2000-2004, 2005-2009 and 2010-2014, in conformity with CONCORD-3). We categorised the basis of diagnosis as histologically verified; not histologically verified but clinically confirmed (e.g. with an MRI scan), and not available.

Results

We defined distinct histology groupings for children and adults. For children, we mainly followed ICCC-3,[19] but we made three changes: (1) we introduced a third, more granular tier for astrocytic tumours; (2) three of the four ICCC-3 subgroups of embryonal tumours (atypical teratoid/rhabdoid tumour, medulloepithelioma, and primitive neuroectodermal tumour) were grouped together, and (3) oligoastrocytoma was included in the "oligodendroglial tumour" histology group. For adults, there are no bespoke classification systems, so we based our definitions on advice from expert pathologists. Differences between children and adults were mainly for astrocytic tumours. In children, astrocytic tumours were divided into low-grade (WHO grades I and II) and high-grade tumours (WHO grades III and IV). This grouping reflects the predominance of low-grade subtypes in children. Conversely, in adults, we merged diffuse and anaplastic astrocytomas, and considered other specified low-grade tumours and glioblastomas separately. The 12 histology groupings adopted for children, and the 11 groupings adopted for adults are set out in Supplementary Tables 3.1 and 3.2, respectively.

CONCORD-3 included 67,331 children and 671,085 adults diagnosed with a primary brain tumour in 60 countries during 2000-2014. We excluded from analysis 6,548 children (9.7% of eligible tumour records) and 68,973 adults (10.3%) because the morphology code was (1) not consistent with the WHO classification; (2) consistent with the WHO classification but relevant only for the meninges or the pituitary gland), or (3) missing. (Supplementary Tables 3.3 and 3.4)

The final study population comprised 60,783 children (90.3% of eligible submissions) and 602,112 adults (89.7%). Table 3.1 and Table 3.2 present detailed trends for 2000-2004, 2005-2009, and 2010-2014, by country and histology group.

We focus our comments mainly on the histology distribution for 2005-2009, when proportions were more robust than for 2000-2004 and 2010-2014 because more registries contributed data for the central period. Our comments, however, are broadly applicable to earlier and later periods. In the interest of clarity, we only refer to individual countries where data for at least 50 children or adults were available for 2005-2009. If none of the countries in a given continent had 50 patients or more, we

report the average proportion for that continent. Countries are listed in alphabetical order within continental order.

Children (0-14 years) – 2005-2009

The proportion of brain tumours classified as low-grade astrocytoma (WHO grade I and II) varied from less than 10% to more than 30%. The proportion was below 10% in African countries, Brazil, Costa Rica, Ecuador, China, Korea, Thailand, the Russian Federation and New Zealand; in the range 10-19% in Argentina, Colombia, Japan, Jordan, Taiwan, Poland and Australia, and in the range 20-29% in Chile, Canada, Israel, Singapore, Turkey, Croatia, Denmark, France, Germany, Italy, Norway, Portugal, Spain and Sweden. These tumours accounted for more than 30% of brain tumours in Puerto Rico, the United States, Belarus, Czech Republic, Finland, Ireland, the Netherlands, Slovakia, Switzerland and the United Kingdom. (Table 3.1 and Figure 3.1)

High-grade astrocytomas (WHO grade III and IV) comprised less than 10% of all brain tumours in Argentina, Colombia, Costa Rica, Puerto Rico, Canada, the United States, China, Israel, Japan, Korea, Singapore, Turkey, and in 17 of 28 participating European countries. The proportion was in the range 10-20% in African countries, Brazil, Ecuador, Jordan, Taiwan, Thailand, Germany, Poland, the Russian Federation, Australia and New Zealand. (Table 3.1 and Figure 3.1)

Unspecified astrocytomas (ICD-O-3 code 9400/39) accounted for less than 10% of brain tumours in 30 of 59 countries, but the proportion was in the range 10-19% in African countries, Argentina, Colombia, Thailand, Croatia, Finland, Poland, the Russian Federation and Sweden. The highest levels were seen in Ecuador (20.6%) and the Russian Federation (27.0%). Unspecified astrocytoma was ungraded (6^{th} digit of the ICD-O-3 morphology code) in less than 50% of the cases in Puerto Rico, Israel, Belarus, Belgium, Germany, the Netherlands, Slovakia and New Zealand; in 50-99% of the cases in African countries, Ecuador, Canada, the United States, China, Japan, Jordan, Taiwan, Turkey, Czech Republic, Italy, Norway, Poland, Portugal, the Russian Federation, Spain, Switzerland, the United Kingdom and Australia; 100% ungraded elsewhere. Most cases with known grade were assigned grade 1 or 2 in the United States, Israel, Taiwan, Turkey, France, Germany, the Netherlands, the United

Kingdom and Australia. In Jordan, however, there were slightly more grade 3-4 than 1-2. (Table 3.1 and Figure 3.1, Supplementary Table 3.5)

Medulloblastomas represented less than 10% of brain tumours in African countries, China and Ireland. The proportion was in the range 10-19% in 21 of 59 countries; in the range 20-29% in Argentina, Brazil, Korea, Thailand, Poland and New Zealand; the proportion was 30.1% in Ecuador, 30.8% in Jordan and 31.2% in Taiwan. (Table 3.1 and Figure 3.1)

Unspecified gliomas accounted for less than 10% of brain tumours in 27 countries, but the proportion was in the range 10-21% in Canada, the United States, Israel, Japan, Korea, Singapore, Thailand, Turkey, the Netherlands, the United Kingdom, Australia and New Zealand. (Table 3.1 and Figure 3.1)

Unspecified tumours represented less than 10% of brain tumours in most countries. The proportion was in the range 10-20% in Argentina, Brazil, Ecuador, Japan, Korea, Thailand, Belarus, Italy and New Zealand. The proportion was 40.9% in African countries, 32.7% in Costa Rica, 52.4% in China and 31.4% in Denmark. (Table 3.1 and Figure 3.1)

Adults (15-99 years) – 2005-2009

Diffuse and anaplastic astrocytomas accounted for less than 10% or brain tumours in 26 of 59 countries. The proportion was in the range 10-19% in Argentina, Brazil, Chile, Ecuador, Puerto Rico, the United States, Cyprus, Israel, Jordan, Qatar, Singapore, Taiwan, Austria, Belgium, Czech Republic, Germany, Latvia, Malta, the Netherlands, Poland, Romania, the Russian Federation, Slovakia, Slovenia, Spain, Switzerland and New Zealand; the proportion was 21.3% in Estonia. (Table 3.2 and Figure 3.2)

The proportion of brain tumours classified as glioblastoma varied from less than 10% to more than 50%. In countries with low proportions of glioblastoma, the proportion of tumours of unspecified histology was often remarkably higher than elsewhere. The proportion of glioblastoma was below 10% only in China; in the range 10-29% in Algeria, Nigeria, Costa Rica, Ecuador, India, Malaysia, Thailand, Malta, and the Russian Federation; in the range 30-49% in Argentina, Brazil, Chile, Colombia,

Japan, Korea, Qatar, Singapore, Taiwan, Turkey, Denmark, Iceland, Italy, Latvia, Romania, Slovakia, and Spain; in the range 50-70% in Martinique, Puerto Rico, North America, Cyprus, Israel, Jordan, Kuwait, in 21 of 28 participating European countries and in Oceania (Table 3.2 and Figure 3.2).

Unspecified astrocytoma encompassed less than 10% of brain tumours in 43 countries. The proportion was in the range 10-19% in Algeria, Argentina, Brazil, Colombia, Finland and Lithuania; in the range 20-29% in Costa Rica, Malaysia, Thailand and the Russian Federation. The highest level was seen in Ecuador (34.3%). Unspecified astrocytoma was ungraded (6^{th} digit of the ICD-O-3 morphology code) in less than 50% of the cases in Puerto Rico, the United States, Cyprus, Israel, Jordan, Qatar, Singapore, Turkey, Belgium, Czech Republic, the Netherlands, Slovakia, Slovenia, Spain, Switzerland, the United Kingdom and New Zealand; in 50-99% of the cases in 23 countries; 100% ungraded in Nigeria, Brazil, Costa Rica, Martinique, Korea, Malaysia, Croatia, Denmark, Estonia, Finland, France, Iceland, Ireland, Latvia and Sweden. Most cases with known grade were assigned grade 1 in Norway and the Russian Federation, grade 2 or 3 in 30 countries, and grade 4 in Canada. (Table 3.2 and Figure 3.2, Supplementary Table 3.6)

Oligodendroglial tumours accounted for less than 10% of brain tumours in 32 countries. The proportion was in the range 10-19% in Costa Rica, Canada, Korea, Malaysia, Singapore, Taiwan, Turkey, Belgium, Estonia, Finland, Iceland, Ireland, the Netherlands, Norway, Poland, Sweden, Switzerland and Australia; the levels were highest in Qatar (20.2%), France (24.3%) and Portugal (21.8%). (Table 3.2 and Figure 3.2)

Unspecified gliomas were overall uncommon, with proportions below 10% in most countries. The proportion was in the range 11-19% only in China, India, Kuwait, Qatar, Malta and the United Kingdom. (Table 3.2 and Figure 3.2)

Brain tumours of unspecified histology accounted for less than 10% of brain tumours in 28 countries. The proportion was in the range 10-19% in Brazil, Costa Rica, Ecuador, Canada, Turkey, the Netherlands, Romania, the Russian Federation, Sweden and the United Kingdom; in the range 30-50% in Nigeria, Chile, Colombia,

India, Thailand, Denmark, Italy and Latvia. The highest levels were seen in Algeria (64.8%) and China (64.4%). (Table 3.2 and Figure 3.2)

Basis of diagnosis – 2000-2014

In children, the vast majority of low-grade astrocytomas were histologically verified. The proportion was in the range 90-94% in Canada and Australia; in the range 95-99% in the United States, Israel, Japan, Singapore, Turkey, Belgium, Croatia, France, Germany, Italy, the Netherlands, Spain and the United Kingdom; and 100% in the remaining 38 countries. (Supplementary Table 3.7)

The proportion of childhood unspecified gliomas with a histological verification varied between 24% in Oceania and 87% in Africa. For childhood unspecified neoplasms, a diagnostic confirmation was mostly not available in Central and South America, North America, Asia, Europe and Oceania (10-25%), while diagnoses were largely confirmed in Africa (74.5%). (Supplementary Table 3.7)

In adults, glioblastomas were mostly histologically verified. The proportion was 78.7% in Malta; in the range 80-89% in Canada, Croatia, Norway, United Kingdom and New Zealand; in the range 90-94% in the United States, Israel, Korea, Kuwait, Austria, Germany, Switzerland and Australia; in the range 95-99% in 26 countries; glioblastomas were reported as 100% histologically verified in the remaining 13 countries. (Supplementary Table 3.8)

Unspecified gliomas in adults were mainly histologically unverified in North America, Europe and Oceania (33-48%), while a diagnostic confirmation was overall available in Africa, in Central and South America and Asia (62-84%). The proportion of histological verification for unspecified neoplasms, in adults, varied between 4% in Oceania and 65% in Africa. (Supplementary Table 3.8)

Time trends

The proportion of low-grade astrocytomas in children was fairly stable in all continents during the 15 years between 2000 and 2014. Increasing trends for unspecified glioma in Asia and Oceania were offset by a decline in the proportion of

unspecified neoplasms. The proportion of unspecified neoplasms rose from 2% to 6% in North America. (Table 3.1)

In adults, the proportion of glioblastomas during 2000-2014 rose only in Europe (from 46% to 56%) and Oceania (from 57% to 65%). Increasing trends for both unspecified gliomas and unspecified neoplasms were observed in Central and South America, while the proportions for both subtypes subsided in Europe and Oceania. In North America, the proportion of unspecified neoplasms rose from 6% to 12%. (Table 3.2)

Discussion

To our knowledge, this is the first global study of the distribution of brain tumour histology. It spans 59 countries in five continents and including countries, regions or territories not previously represented in international comparisons. We analysed individual patient records from 286 population-based cancer registries. Data were collected using the same study protocol and checked using the same data quality procedures to ensure high-quality and robustly comparable information.

In the interest of clarity, we have mainly commented on the histology distribution during 2005-2009, when proportions were slightly more robust because more diagnoses were available. For most categories, international differences in the distribution of histological subtypes were much more marked than any changes in those distributions over time.

There is wide international variation in the distribution of brain tumour around the world. There were striking international differences in the proportion of low-grade astrocytomas in children (ranging from 6% to 50% in 2005-2009). The proportion of childhood medulloblastomas also varied widely between countries, in several of which it offset the low proportion of low-grade astrocytomas. In adults, the largest international variation was for glioblastomas (from 9% to 69%).

We found wide international disparities in some of the quality indicators, such as the proportion of tumours with an unspecified histology, up to 52% in children and 65% in adults, and the proportion of histologically verified tumours. Such variation in some of the common data quality indicators calls for caution when interpreting the

histology distribution itself, but also the survival inequalities for individual brain tumour subtypes or for all brain tumour combined.

Non-malignant brain tumours should be recorded because tumour location is a determinant of the outcome. Here we provided compelling evidence that remarkable international differences exist in the registration of non-malignant brain tumours. This was mostly seen in children for low-grade astrocytomas, and childhood neuronal and mixed neuronal-glial tumours, both of which are mainly non-malignant subtypes. For instance, Ecuador started recording non-malignant brain tumours in 2011, while in New South Wales, Australia, only malignant brain tumour sub-types are registered, by law.

ICCC-3 is a well-established standard for conducting studies on childhood tumours, but it does not allow for stratification of astrocytic tumours by WHO grade.[19] Studies on survival from childhood brain tumours published to date widely adopted ICCC-3, but interpretation of time trends and international differences was made difficult by changes in coding over time and the inconsistent registration of non-malignant tumours between countries or regions.[144] ICD-O underwent a major change in 2000, coinciding with the release of the third edition. Pilocytic astrocytoma was attributed a behaviour code of 3 (malignant) in ICD-O-2 and a behaviour code of 1 (borderline) in ICD-O-3.[17, 118] In the US, where registration of non-malignant tumours is mandatory since 2004,[149] pilocytic astrocytoma (WHO grade I) represented alone 30% of all childhood gliomas (2007-2011).[150] In countries where non-malignant tumours are inconsistently recorded, pilocytic astrocytoma has become potentially ineligible for cancer registration since 2000. Failing to record pilocytic astrocytoma, the most common, single childhood brain tumour, and any other non-malignant tumours would potentially result in underestimation of survival and incidence when all childhood astrocytic tumours are combined, regardless of behaviour. The CONCORD-3 protocol required data to be submitted according to ICD-O-3, and both malignant and non-malignant brain tumours were eligible. In this study, however, pilocytic astrocytoma was still coded as malignant (ICD-O-3 behaviour code equal to 3) in 7,194 children and 5,344 adults. For instance, the proportion of miscoded childhood pilocytic astrocytoma was 70% in Czech Republic and 100% in Canada, the United States, Israel and Taiwan (data not shown). EUROCARE-5 examined survival for children

diagnosed with a brain tumour in 27 European countries during 2000-2007, dividing CNS tumours by WHO grade to understand survival variation across Europe.[9] We decided to stratify by grade only astrocytic tumours because they are by far the largest histology group and to avoid pooling very different tumour entities.

CONCORD-3 showed wide international disparities in survival from childhood brain tumours. For instance, among children diagnosed during 2005-2009, age-standardised five-year net survival varied from less than 40% in Brazil, 60% in Australia, and close to 80% in Sweden.[46] Those disparities persisted substantially unchanged among children diagnosed during 2010-2014. In our study, during 2005-2009, the proportion of low-grade astrocytoma in Brazil, Australia, and Sweden were 9%, 17%, and 26%, respectively.

Limited access to care is likely to be the main reason for the global disparities in survival. If survival analyses include both malignant and non-malignant tumours, international differences could also arise by confounding if the distribution of histological subtypes varies world-wide and there are differences in survival between the histological subtypes.

Here glioblastomas comprised 80% of astrocytic tumours in the 40-99 years age group in North America, Europe and Oceania, but only 60% or less in Central and South America, during 2000-2014 (data not shown). Glioblastoma incidence was remarkably higher in non-Hispanic Whites than in other ethnicities in the United States during 2000-2014, suggesting that risk alleles are more common in populations of predominantly European ancestry.[16, 151] Alternatively, a higher proportion of cases in a given population could reflect an older population, because incidence of glioblastoma increases with age. Socioeconomic factors, such as impaired access to optimal diagnostic and treatment facilities for ethnic minorities, may also play a role. In countries where glioblastomas were more frequently reported in 2010-2014 than in 2000-2004 and 2005-2009, we found a concurrent decline in the proportion of unspecified astrocytomas (e.g. Croatia, Poland, Portugal, and the United Kingdom) or the proportion of diffuse and anaplastic astrocytomas (e.g. Belgium, France, the Netherlands, and Korea). These findings may suggest improved quality in cancer registration but also a refinement in the pathology workup of astrocytic tumours enabling identification of clinically aggressive subtypes.

We combined diffuse astrocytoma and anaplastic astrocytoma in adults into a single group. Sub-optimal reproducibility of the pathological diagnosis of glioma has been clearly established, with an estimated 20-30% of gliomas re-classified at independent review.[152, 153] Mutations in the isocitrate dehydrogenase (*IDH*) gene 1 or 2 were recognised to be a genetic hallmark of glioblastoma.[154] These mutations were later found to characterise 70-80% of WHO grade II and III gliomas.[36] Tumours harbouring an *IDH* mutation have a more favourable outcome.[155, 156] The classification of central nervous system tumours issued by WHO in 2016 substantially revised the neuropathology taxonomy, with several tumour subtypes being genetically defined.[15] Grade II or III gliomas with the same genetic profile have a similar clinical behaviour, regardless of the pathological grading.[153]

The definition “astrocytoma NOS” was used in previous studies for ill-defined astrocytic tumours which could not be assigned a more precise descriptor (e.g. glioblastoma).[9, 11] “Astrocytoma NOS”, however, is a standalone definition in ICD-O-3, rather than a category for astrocytic tumours which could not be otherwise specified, and it shares the same morphology code with “diffuse astrocytoma” (WHO grade II).[7, 17] In 2005-2009, the proportion of brain tumours that were coded as astrocytoma NOS varied widely between countries, suggesting different practices and interpretations among cancer registries. The quality of cancer registration, however, seemed to improve during 2000-2014, because the use of “astrocytoma NOS” subsided in several countries (e.g. from 41% to 23% in Ecuador, or from 29% to 5% in Thailand). We supposed that recording of grade (rule G in ICD-O) was accurate. For a given record, if the grade (6^{th} digit of histology) was coded in the range 1-4, the use of the definition “astrocytoma NOS” was assumed to be a random error at coding level; if the grade was not available (coded to 9), we assumed that the tumour could not be defined more precisely. Such a strategy should control for randomly misclassified astrocytic tumours.

We included both histologically confirmed and histologically unconfirmed brain tumours, in line with previous studies.[9, 11, 16] The diagnosis of a brain tumour may pose challenges due to anatomical constraints for safely performing biopsy or surgery, or the poor clinical condition of the patient. These hurdles may be more relevant for adults, who are frequently diagnosed at an advanced age. Brain tumours often show

appearances at neuroimaging that may potentially suggest a clinical diagnosis.[157, 158] Nevertheless, the differential diagnosis between a solitary metastasis and a high-grade glioma may be challenging in clinical practice if advanced imaging techniques are not available.[159] International coding guidelines currently restrict the use of a specific morphology code in the absence of histological verification to certain clinical situations (e.g. neoplasms located in the brain stem). In all other cases, the morphology code for a tumour of unspecified morphology (i.e. 8000-8005) should be preferred if the diagnosis cannot be histologically proven. However, with the refinement of neuroimaging, these guidelines may need to be updated.[160] Here, the proportion of histological verification for specified tumour subtypes was around 100% in children, while in adults it was slightly lower, but still in the range 90-100%. The higher proportion of histological confirmation in children than in adults may point to increased diagnostic intensity in children or to the existence of specialist paediatric cancer registries. Very high proportions of histological confirmation, however, may also suggest over-reliance on pathology records for cancer registration, or under-ascertainment of brain tumours.[161] The selective recording of only histologically verified brain tumours may ultimately bias survival estimates upward, because patients receiving a biopsy or surgery are more likely to present in better clinical condition and because the availability of these procedures may reflect better access to treatment in general. Surprisingly, in several countries, most or even 100% of brain tumours with an unspecified histology were reported as histologically confirmed. One would expect that histologically confirmed tumours could be assigned a specific morphology code. This suggests that the basis of diagnosis may be mis-coded and its use as an indicator of data quality requires caution.

In this study, the proportion of tumours of unspecified histology (ICD-O-3 codes 8000-8005) was generally low, but some countries had high proportions, particularly in adults. Interestingly, in countries where the proportion of unspecified tumours was 30% or more, the quality of data was consistently poor across all participating sub-national registries (data not shown). Survival estimates for specific tumour subtypes are likely to be biased if histology is fully known for only a subset of records. Overall, we found a decline in the proportions of unspecified neoplasms during 2000-2014, but increasing trends were observed in North America for both children and adults, although both the values and the changes were small.

We proposed distinct histology groupings for international comparisons of brain tumour survival in children and adults, because brain tumours in these two children and adults are very different in biology and clinical behaviour. In children, the ICCC-3 framework was largely retained, but astrocytic tumours were stratified by WHO grade to account for different registration practices world-wide.[19] For adults, the histology groupings we propose are slightly more granular than those in CI5, where the WHO grade was not implemented for astrocytic tumours.[2] Conversely, CBTRUS and RARECARENet adopted a multi-tier system comprising individual tumour subtypes.[16, 148] Global comparisons of brain tumour survival for specific histology subtypes may be compromised if numbers are small, so we have grouped entities with similar clinical behaviour.

In CONCORD-3, we only collected data for tumours of the brain (ICD-O topography code C71). Diagnoses for histological subtypes in other parts of the central nervous system, such as germ-cell tumours of the pineal gland or optic nerve gliomas, were excluded because they were likely to be misclassified or to represent a minority of the true population of patients for that subtype. For instance, germ cell tumours and optic nerve gliomas accounted for 4% and 6% of all childhood CNS tumours, respectively, in England, during 2001-2010.[162] These tumours are uncommon, but they should ideally be included in future iterations of CONCORD.

Our study only provided insights on some of the data quality indicators world-wide, questioning the accuracy of neuropathology reports or cancer registration. However, we could not explore other important quality measures, for instance whether multiple data sources were used to capture or validate a brain tumour diagnosis. Ascertainment of non-malignant brain tumours is likely to be incomplete in several countries. While this finding may suggest impaired access to care, it is likely to reflect mainly disparities in underlying, local health regulations, for which we could not take account.

In conclusion, this study population will be used for further global comparisons of brain tumour survival by histology. International disparities in survival can only be interpreted if a detailed analysis of the histology distribution in the same cancer population is available. The quality of data is sub-optimal in several countries and, ultimately, needs to improve. Our study should prompt the international associations

of both cancer registries (**IACR**) and pathologists (**IAP**) to promote harmonisation of data collection. Ultimately, this would enable clinicians, policy-makers and other stakeholders to use these data for public health purposes with greater confidence.

Figure 3.1. Histology distribution (%) by country. Children (0-14 years) diagnosed with a brain tumour, 2005-2009.
Numbers in brackets are counts (all brain tumours combined). * Data with 100% coverage of the national population.

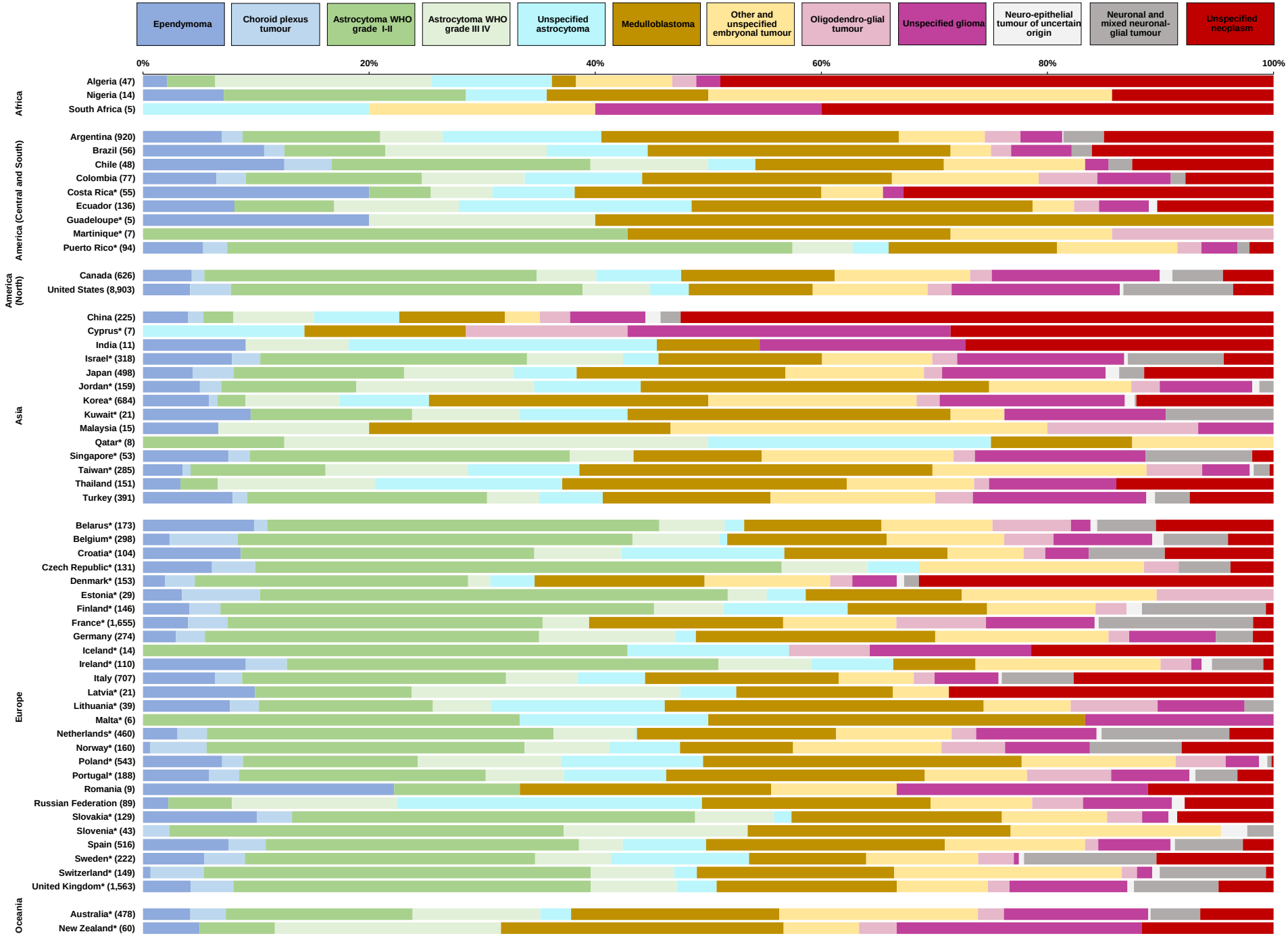


Figure 3.2. Histology distribution (%) by country. Adults (15-99 years) diagnosed with a brain tumour, 2005-2009.
Numbers in brackets are counts (all brain tumours combined). * Data with 100% coverage of the national population.

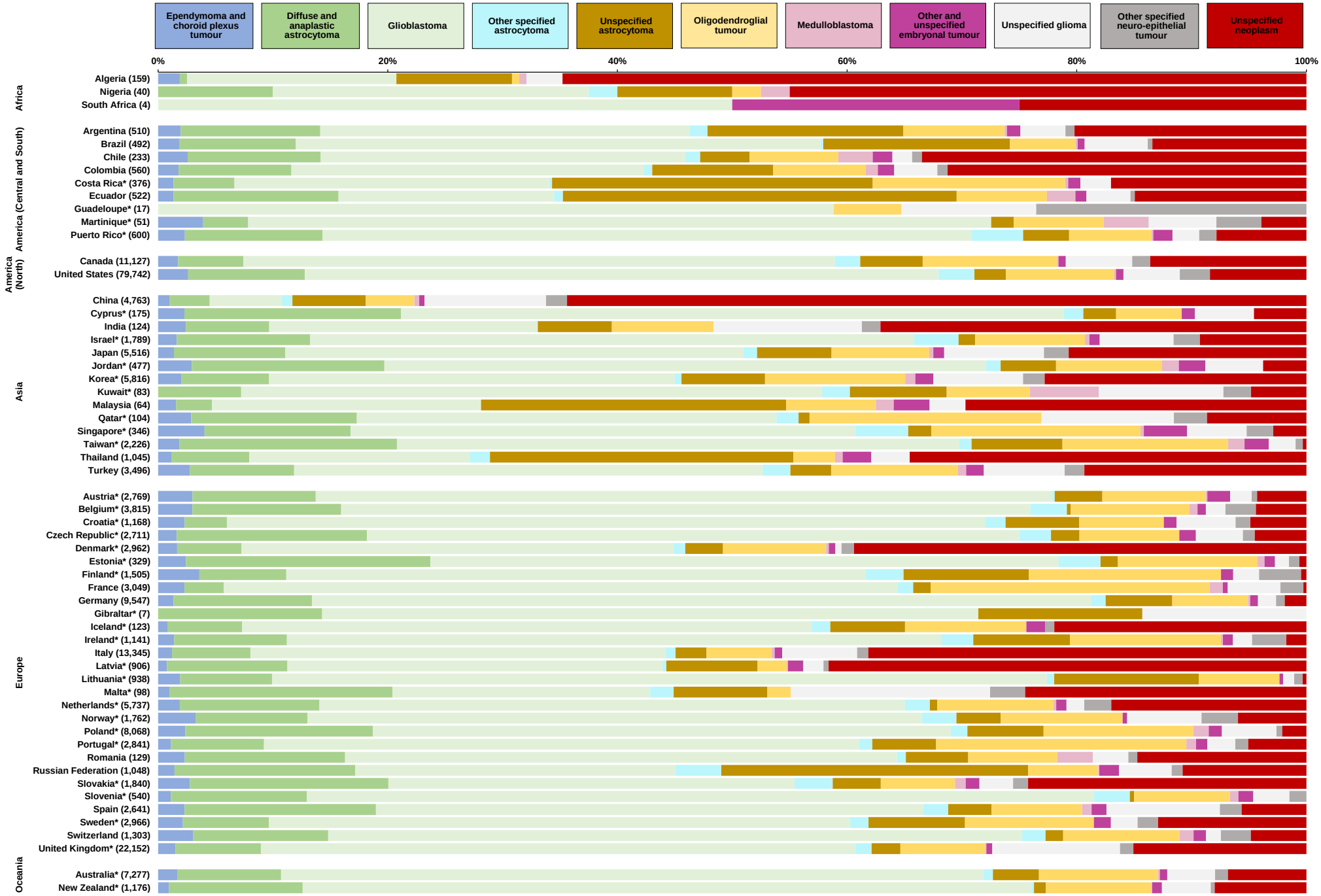


Table 3.1. Histology distribution, by continent, country and calendar period. Children (0-14 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependymoma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medulloblastoma		Other and unspecified embryonal tumour		Oligodendroglial tumour		Unspecified glioma		Neuroepithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Africa	2000-2004	26	-	-	-	-	2	**7.7**	8	**30.8**	1	**3.8**	1	**3.8**	5	**19.2**	-	-	4	**15.4**	-	-	-	-	5	**19.2**
	2005-2009	66	2	**3.0**	-	-	5	**7.6**	9	**13.6**	7	**10.6**	3	**4.5**	10	**15.2**	1	**1.5**	2	**3.0**	-	-	-	-	27	**40.9**
	2010-2014	69	4	**5.8**	-	-	6	**8.7**	2	**2.9**	6	**8.7**	12	**17.4**	21	**30.4**	1	**1.4**	2	**2.9**	-	-	-	-	15	**21.7**
Algeria	2000-2004	16	-	-	-	-	1	**6.3**	6	**37.5**	-	-	-	-	2	**12.5**	-	-	4	**25.0**	-	-	-	-	3	**18.8**
	2005-2009	47	1	**2.1**	-	-	2	**4.3**	9	**19.1**	5	**10.6**	1	**2.1**	4	**8.5**	1	**2.1**	1	**2.1**	-	-	-	-	23	**48.9**
	2010-2014	34	1	**2.9**	-	-	1	**2.9**	2	**5.9**	4	**11.8**	3	**8.8**	11	**32.4**	1	**2.9**	1	**2.9**	-	-	-	-	10	**29.4**
Mauritius*	2010-2014	3	-	-	-	-	-	-	-	-	2	**66.7**	1	**33.3**	-	-	-	-	-	-	-	-	-	-	-	-
Nigeria	2005-2009	14	1	**7.1**	-	-	3	**21.4**	-	-	1	**7.1**	2	**14.3**	5	**35.7**	-	-	-	-	-	-	-	-	2	**14.3**
	2010-2014	26	2	**7.7**	-	-	5	**19.2**	-	-	-	-	7	**26.9**	8	**30.8**	-	-	1	**3.8**	-	-	-	-	3	**11.5**
South Africa	2000-2004	10	-	-	-	-	1	**10.0**	2	**20.0**	1	**10.0**	1	**10.0**	3	**30.0**	-	-	-	-	-	-	-	-	2	**20.0**
	2005-2009	5	-	-	-	-	-	-	-	-	1	**20.0**	-	-	1	**20.0**	-	-	1	**20.0**	-	-	-	-	2	**40.0**
	2010-2014	6	1	**16.7**	-	-	-	-	-	-	-	-	1	**16.7**	2	**33.3**	-	-	-	-	-	-	-	-	2	**33.3**
America (Central and South)	2000-2004	1,217	90	**7.4**	34	**2.8**	155	**12.7**	91	**7.5**	128	**10.5**	303	**24.9**	112	**9.2**	32	**2.6**	42	**3.5**	1	**0.1**	26	**2.1**	203	**16.7**
	2005-2009	1,398	109	**7.8**	24	**1.7**	205	**14.7**	95	**6.8**	179	**12.8**	354	**25.3**	107	**7.7**	40	**2.9**	53	**3.8**	2	**0.1**	37	**2.6**	193	**13.8**
	2010-2014	1,204	105	**8.7**	33	**2.7**	163	**13.5**	76	**6.3**	175	**14.5**	264	**21.9**	98	**8.1**	29	**2.4**	55	**4.6**	6	**0.5**	25	**2.1**	175	**14.5**
Argentina	2000-2004	900	63	**7.0**	31	**3.4**	85	**9.4**	58	**6.4**	87	**9.7**	237	**26.3**	84	**9.3**	25	**2.8**	29	**3.2**	-	-	25	**2.8**	176	**19.6**
	2005-2009	920	64	**7.0**	17	**1.8**	112	**12.2**	51	**5.5**	129	**14.0**	242	**26.3**	70	**7.6**	29	**3.2**	34	**3.7**	1	**0.1**	33	**3.6**	138	**15.0**
	2010-2014	791	71	**9.0**	25	**3.2**	102	**12.9**	42	**5.3**	128	**16.2**	172	**21.7**	60	**7.6**	20	**2.5**	39	**4.9**	4	**0.5**	18	**2.3**	110	**13.9**
Brazil	2000-2004	79	3	**3.8**	3	**3.8**	13	**16.5**	9	**11.4**	15	**19.0**	21	**26.6**	4	**5.1**	-	-	7	**8.9**	-	-	-	-	4	**5.1**
	2005-2009	56	6	**10.7**	1	**1.8**	5	**8.9**	8	**14.3**	5	**8.9**	15	**26.8**	2	**3.6**	1	**1.8**	3	**5.4**	-	-	1	**1.8**	9	**16.1**
	2010-2014	48	7	**14.6**	2	**4.2**	2	**4.2**	4	**8.3**	2	**4.2**	15	**31.3**	5	**10.4**	1	**2.1**	3	**6.3**	-	-	-	-	7	**14.6**
Chile	2000-2004	13	5	**38.5**	-	-	-	-	1	**7.7**	1	**7.7**	3	**23.1**	-	-	-	-	-	-	-	-	-	-	3	**23.1**
	2005-2009	48	6	**12.5**	2	**4.2**	11	**22.9**	5	**10.4**	2	**4.2**	8	**16.7**	6	**12.5**	-	-	1	**2.1**	-	-	1	**2.1**	6	**12.5**
	2010-2014	14	-	-	-	-	3	**21.4**	2	**14.3**	-	-	3	**21.4**	1	**7.1**	1	**7.1**	2	**14.3**	-	-	-	-	2	**14.3**
Colombia	2000-2004	72	5	**6.9**	-	-	12	**16.7**	11	**15.3**	13	**18.1**	10	**13.9**	4	**5.6**	4	**5.6**	1	**1.4**	-	-	1	**1.4**	11	**15.3**
	2005-2009	77	5	**6.5**	2	**2.6**	12	**15.6**	7	**9.1**	8	**10.4**	17	**22.1**	10	**13.0**	4	**5.2**	5	**6.5**	-	-	1	**1.3**	6	**7.8**
	2010-2014	88	4	**4.5**	-	-	16	**18.2**	13	**14.8**	10	**11.4**	11	**12.5**	13	**14.8**	2	**2.3**	5	**5.7**	1	**1.1**	1	**1.1**	12	**13.6**
Costa Rica*	2000-2004	15	1	**6.7**	-	-	3	**20.0**	-	-	1	**6.7**	4	**26.7**	2	**13.3**	1	**6.7**	-	-	-	-	-	-	3	**20.0**
	2005-2009	55	11	**20.0**	-	-	3	**5.5**	3	**5.5**	4	**7.3**	12	**21.8**	3	**5.5**	-	-	1	**1.8**	-	-	-	-	18	**32.7**
	2010-2014	80	11	**13.8**	1	**1.3**	10	**12.5**	5	**6.3**	9	**11.3**	19	**23.8**	8	**10.0**	1	**1.3**	1	**1.3**	-	-	-	-	15	**18.8**
Ecuador	2000-2004	42	5	**11.9**	-	-	2	**4.8**	4	**9.5**	10	**23.8**	13	**31.0**	3	**7.1**	1	**2.4**	3	**7.1**	1	**2.4**	-	-	-	-
	2005-2009	136	11	**8.1**	-	-	12	**8.8**	15	**11.0**	28	**20.6**	41	**30.1**	5	**3.7**	3	**2.2**	6	**4.4**	1	**0.7**	-	-	14	**10.3**
	2010-2014	139	11	**7.9**	-	-	18	**12.9**	9	**6.5**	24	**17.3**	35	**25.2**	8	**5.8**	3	**2.2**	4	**2.9**	-	-	-	-	27	**19.4**
Guadeloupe	2005-2009	5	1	**20.0**	-	-	-	-	1	**20.0**	-	-	3	**60.0**	-	-	-	-	-	-	-	-	-	-	-	-
	2010-2014	8	-	-	-	-	1	**12.5**	-	-	1	**12.5**	1	**12.5**	2	**25.0**	-	-	-	-	-	-	3	**37.5**	-	-
Martinique*	2000-2004	6	1	**16.7**	-	-	2	**33.3**	-	-	-	-	3	**50.0**	-	-	-	-	-	-	-	-	-	-	-	-
	2005-2009	7	-	-	-	-	3	**42.9**	-	-	-	-	2	**28.6**	1	**14.3**	1	**14.3**	-	-	-	-	-	-	-	-
	2010-2014	4	1	**25.0**	-	-	1	**25.0**	-	-	-	-	1	**25.0**	-	-	-	-	-	-	-	-	1	**25.0**	-	-
Puerto Rico*	2000-2004	90	7	**7.8**	-	-	38	**42.2**	8	**8.9**	1	**1.1**	12	**13.3**	15	**16.7**	1	**1.1**	2	**2.2**	-	-	-	-	6	**6.7**
	2005-2009	94	5	**5.3**	2	**2.1**	47	**50.0**	5	**5.3**	3	**3.2**	14	**14.9**	10	**10.6**	2	**2.1**	3	**3.2**	-	-	1	**1.1**	2	**2.1**
	2010-2014	32	-	-	5	**15.6**	10	**31.3**	1	**3.1**	1	**3.1**	7	**21.9**	1	**3.1**	1	**3.1**	1	**3.1**	1	**3.1**	2	**6.3**	2	**6.3**

Table 3.1. Histology distribution, by continent, country and calendar period. Children (0-14 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependy-moma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medullo-blastoma		Other and unspecified embryonal tumour		Oligodendro-glial tumour		Unspecified glioma		Neuro-epithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
America (North)	2000-2004	8,206	480	**5.8**	110	**1.3**	2,902	**35.4**	581	**7.1**	341	**4.2**	1,041	**12.7**	915	**11.2**	269	**3.3**	1,185	**14.4**	33	**0.4**	210	**2.6**	139	**1.7**
	2005-2009	9,529	398	**4.2**	328	**3.4**	2,954	**31.0**	565	**5.9**	351	**3.7**	1,061	**11.1**	980	**10.3**	201	**2.1**	1,417	**14.9**	35	**0.4**	893	**9.4**	346	**3.6**
	2010-2014	7,925	297	**3.7**	258	**3.3**	2,377	**30.0**	551	**7.0**	327	**4.1**	787	**9.9**	797	**10.1**	124	**1.6**	1,155	**14.6**	30	**0.4**	782	**9.9**	440	**5.6**
Canada	2000-2004	596	32	**5.4**	7	**1.2**	183	**30.7**	32	**5.4**	37	**6.2**	92	**15.4**	83	**13.9**	21	**3.5**	63	**10.6**	1	**0.2**	18	**3.0**	27	**4.5**
	2005-2009	626	27	**4.3**	7	**1.1**	184	**29.4**	33	**5.3**	47	**7.5**	85	**13.6**	75	**12.0**	12	**1.9**	93	**14.9**	7	**1.1**	28	**4.5**	28	**4.5**
	2010-2014	810	31	**3.8**	23	**2.8**	183	**22.6**	43	**5.3**	31	**3.8**	92	**11.4**	82	**10.1**	6	**0.7**	96	**11.9**	3	**0.4**	73	**9.0**	147	**18.1**
United States	2000-2004	7,610	448	**5.9**	103	**1.4**	2,719	**35.7**	549	**7.2**	304	**4.0**	949	**12.5**	832	**10.9**	248	**3.3**	1,122	**14.7**	32	**0.4**	192	**2.5**	112	**1.5**
	2005-2009	8,903	371	**4.2**	321	**3.6**	2,770	**31.1**	532	**6.0**	304	**3.4**	976	**11.0**	905	**10.2**	189	**2.1**	1,324	**14.9**	28	**0.3**	865	**9.7**	318	**3.6**
	2010-2014	7,115	266	**3.7**	235	**3.3**	2,194	**30.8**	508	**7.1**	296	**4.2**	695	**9.8**	715	**10.0**	118	**1.7**	1,059	**14.9**	27	**0.4**	709	**10.0**	293	**4.1**
Asia	2000-2004	2,077	130	**6.3**	27	**1.3**	251	**12.1**	225	**10.8**	186	**9.0**	467	**22.5**	220	**10.6**	70	**3.4**	172	**8.3**	14	**0.7**	26	**1.3**	289	**13.9**
	2005-2009	2,826	158	**5.6**	45	**1.6**	333	**11.8**	259	**9.2**	207	**7.3**	581	**20.6**	389	**13.8**	72	**2.5**	364	**12.9**	21	**0.7**	68	**2.4**	329	**11.6**
	2010-2014	2,500	112	**4.5**	50	**2.0**	334	**13.4**	248	**9.9**	124	**5.0**	506	**20.2**	369	**14.8**	45	**1.8**	371	**14.8**	15	**0.6**	60	**2.4**	266	**10.6**
China	2000-2004	84	3	**3.6**	-	**-**	9	**10.7**	1	**1.2**	6	**7.1**	9	**10.7**	-	**-**	2	**2.4**	5	**6.0**	1	**1.2**	-	**-**	48	**57.1**
	2005-2009	225	9	**4.0**	3	**1.3**	6	**2.7**	16	**7.1**	17	**7.6**	21	**9.3**	7	**3.1**	6	**2.7**	15	**6.7**	3	**1.3**	4	**1.8**	118	**52.4**
	2010-2014	181	3	**1.7**	4	**2.2**	11	**6.1**	6	**3.3**	9	**5.0**	28	**15.5**	15	**8.3**	1	**0.6**	13	**7.2**	4	**2.2**	4	**2.2**	83	**45.9**
Cyprus*	2000-2004	3	1	**33.3**	1	**33.3**	-	**-**	-	**-**	1	**33.3**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	2005-2009	7	-	**-**	-	**-**	-	**-**	-	**-**	1	**14.3**	1	**14.3**	-	**-**	1	**14.3**	2	**28.6**	-	**-**	-	**-**	2	**28.6**
	2010-2014	4	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**25.0**	-	**-**	-	**-**	3	**75.0**	-	**-**	-	**-**	-	**-**
India	2000-2004	3	-	**-**	-	**-**	1	**33.3**	1	**33.3**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**33.3**
	2005-2009	11	1	**9.1**	-	**-**	-	**-**	1	**9.1**	3	**27.3**	1	**9.1**	-	**-**	-	**-**	2	**18.2**	-	**-**	-	**-**	3	**27.3**
	2010-2014	11	-	**-**	-	**-**	1	**9.1**	1	**9.1**	2	**18.2**	1	**9.1**	-	**-**	1	**9.1**	4	**36.4**	-	**-**	-	**-**	1	**9.1**
Israel*	2000-2004	260	12	**4.6**	3	**1.2**	90	**34.6**	15	**5.8**	7	**2.7**	50	**19.2**	21	**8.1**	7	**2.7**	33	**12.7**	1	**0.4**	12	**4.6**	9	**3.5**
	2005-2009	318	25	**7.9**	8	**2.5**	75	**23.6**	27	**8.5**	10	**3.1**	46	**14.5**	31	**9.7**	7	**2.2**	47	**14.8**	1	**0.3**	27	**8.5**	14	**4.4**
	2010-2014	246	12	**4.9**	8	**3.3**	69	**28.0**	11	**4.5**	6	**2.4**	43	**17.5**	30	**12.2**	4	**1.6**	40	**16.3**	1	**0.4**	9	**3.7**	13	**5.3**
Japan	2000-2004	277	19	**6.9**	3	**1.1**	25	**9.0**	33	**11.9**	29	**10.5**	46	**16.6**	28	**10.1**	3	**1.1**	38	**13.7**	2	**0.7**	9	**3.2**	42	**15.2**
	2005-2009	498	22	**4.4**	18	**3.6**	75	**15.1**	48	**9.6**	28	**5.6**	92	**18.5**	61	**12.2**	8	**1.6**	72	**14.5**	6	**1.2**	11	**2.2**	57	**11.4**
	2010-2014	358	12	**3.4**	12	**3.4**	53	**14.8**	34	**9.5**	18	**5.0**	57	**15.9**	43	**12.0**	4	**1.1**	56	**15.6**	1	**0.3**	13	**3.6**	55	**15.4**
Jordan*	2000-2004	145	13	**9.0**	-	**-**	13	**9.0**	26	**17.9**	21	**14.5**	39	**26.9**	14	**9.7**	5	**3.4**	11	**7.6**	-	**-**	-	**-**	3	**2.1**
	2005-2009	159	8	**5.0**	3	**1.9**	19	**11.9**	25	**15.7**	15	**9.4**	49	**30.8**	20	**12.6**	4	**2.5**	13	**8.2**	1	**0.6**	2	**1.3**	-	**-**
	2010-2014	171	7	**4.1**	3	**1.8**	27	**15.8**	21	**12.3**	4	**2.3**	41	**24.0**	18	**10.5**	2	**1.2**	28	**16.4**	1	**0.6**	1	**0.6**	18	**10.5**
Korea*	2000-2004	726	53	**7.3**	12	**1.7**	16	**2.2**	73	**10.1**	49	**6.7**	197	**27.1**	89	**12.3**	26	**3.6**	50	**6.9**	6	**0.8**	-	**-**	155	**21.3**
	2005-2009	684	40	**5.8**	5	**0.7**	17	**2.5**	57	**8.3**	54	**7.9**	169	**24.7**	126	**18.4**	14	**2.0**	112	**16.4**	6	**0.9**	1	**0.1**	83	**12.1**
	2010-2014	591	24	**4.1**	9	**1.5**	14	**2.4**	74	**12.5**	39	**6.6**	142	**24.0**	138	**23.4**	15	**2.5**	89	**15.1**	5	**0.8**	6	**1.0**	36	**6.1**
Kuwait*	2000-2004	18	2	**11.1**	-	**-**	2	**11.1**	2	**11.1**	1	**5.6**	6	**33.3**	1	**5.6**	-	**-**	3	**16.7**	1	**5.6**	-	**-**	-	**-**
	2005-2009	21	2	**9.5**	-	**-**	3	**14.3**	2	**9.5**	2	**9.5**	6	**28.6**	1	**4.8**	-	**-**	3	**14.3**	-	**-**	2	**9.5**	-	**-**
	2010-2014	9	1	**11.1**	-	**-**	-	**-**	1	**11.1**	-	**-**	2	**22.2**	-	**-**	1	**11.1**	4	**44.4**	-	**-**	-	**-**	-	**-**
Malaysia	2005-2009	15	1	**6.7**	-	**-**	-	**-**	2	**13.3**	-	**-**	4	**26.7**	5	**33.3**	2	**13.3**	1	**6.7**	-	**-**	-	**-**	-	**-**
	2010-2014	25	2	**8.0**	-	**-**	1	**4.0**	2	**8.0**	3	**12.0**	6	**24.0**	5	**20.0**	1	**4.0**	4	**16.0**	1	**4.0**	-	**-**	-	**-**
Qatar*	2000-2004	12	-	**-**	-	**-**	2	**16.7**	1	**8.3**	-	**-**	2	**16.7**	1	**8.3**	-	**-**	4	**33.3**	-	**-**	-	**-**	2	**16.7**
	2005-2009	8	-	**-**	-	**-**	1	**12.5**	3	**37.5**	2	**25.0**	1	**12.5**	1	**12.5**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	2010-2014	11	-	**-**	-	**-**	5	**45.5**	1	**9.1**	-	**-**	1	**9.1**	2	**18.2**	-	**-**	-	**-**	-	**-**	-	**-**	2	**18.2**

Table 3.1. Histology distribution, by continent, country and calendar period. Children (0-14 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependy-moma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medullo-blastoma		Other and unspecified embryonal tumour		Oligodendro-glial tumour		Unspecified glioma		Neuro-epithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Singapore*	2000-2004	51	5	**9.8**	1	**2.0**	16	**31.4**	7	**13.7**	-	**-**	10	**19.6**	3	**5.9**	1	**2.0**	4	**7.8**	-	**-**	1	**2.0**	3	**5.9**
	2005-2009	53	4	**7.5**	1	**1.9**	15	**28.3**	3	**5.7**	-	**-**	6	**11.3**	9	**17.0**	1	**1.9**	8	**15.1**	-	**-**	5	**9.4**	1	**1.9**
	2010-2014	59	2	**3.4**	2	**3.4**	18	**30.5**	9	**15.3**	5	**8.5**	5	**8.5**	7	**11.9**	-	**-**	7	**11.9**	-	**-**	3	**5.1**	1	**1.7**
Taiwan*	2000-2004	321	15	**4.7**	1	**0.3**	51	**15.9**	44	**13.7**	51	**15.9**	79	**24.6**	49	**15.3**	17	**5.3**	9	**2.8**	3	**0.9**	2	**0.6**	-	**-**
	2005-2009	285	10	**3.5**	2	**0.7**	34	**11.9**	36	**12.6**	28	**9.8**	89	**31.2**	54	**18.9**	14	**4.9**	12	**4.2**	1	**0.4**	4	**1.4**	1	**0.4**
	2010-2014	247	16	**6.5**	2	**0.8**	39	**15.8**	38	**15.4**	15	**6.1**	73	**29.6**	44	**17.8**	6	**2.4**	12	**4.9**	-	**-**	1	**0.4**	1	**0.4**
Thailand	2000-2004	91	3	**3.3**	-	**-**	2	**2.2**	15	**16.5**	20	**22.0**	20	**22.0**	3	**3.3**	2	**2.2**	4	**4.4**	-	**-**	-	**-**	22	**24.2**
	2005-2009	151	5	**3.3**	-	**-**	5	**3.3**	21	**13.9**	25	**16.6**	38	**25.2**	17	**11.3**	2	**1.3**	17	**11.3**	-	**-**	-	**-**	21	**13.9**
	2010-2014	103	3	**2.9**	1	**1.0**	8	**7.8**	7	**6.8**	11	**10.7**	32	**31.1**	12	**11.7**	1	**1.0**	12	**11.7**	-	**-**	-	**-**	16	**15.5**
Turkey	2000-2004	86	4	**4.7**	6	**7.0**	24	**27.9**	7	**8.1**	1	**1.2**	9	**10.5**	11	**12.8**	7	**8.1**	11	**12.8**	-	**-**	2	**2.3**	4	**4.7**
	2005-2009	391	31	**7.9**	5	**1.3**	83	**21.2**	18	**4.6**	22	**5.6**	58	**14.8**	57	**14.6**	13	**3.3**	60	**15.3**	3	**0.8**	12	**3.1**	29	**7.4**
	2010-2014	484	30	**6.2**	9	**1.9**	88	**18.2**	43	**8.9**	12	**2.5**	74	**15.3**	55	**11.4**	9	**1.9**	99	**20.5**	2	**0.4**	23	**4.8**	40	**8.3**
Europe	2000-2004	7,289	393	**5.4**	200	**2.7**	2,079	**28.5**	451	**6.2**	462	**6.3**	1,352	**18.5**	676	**9.3**	295	**4.0**	513	**7.0**	34	**0.5**	438	**6.0**	396	**5.4**
	2005-2009	7,931	384	**4.8**	253	**3.2**	2,246	**28.3**	547	**6.9**	359	**4.5**	1,364	**17.2**	824	**10.4**	307	**3.9**	567	**7.1**	39	**0.5**	606	**7.6**	435	**5.5**
	2010-2014	6,927	278	**4.0**	228	**3.3**	1,977	**28.5**	566	**8.2**	211	**3.0**	1,195	**17.3**	802	**11.6**	176	**2.5**	538	**7.8**	30	**0.4**	579	**8.4**	347	**5.0**
Belarus*	2000-2004	214	12	**5.6**	4	**1.9**	72	**33.6**	12	**5.6**	5	**2.3**	49	**22.9**	15	**7.0**	27	**12.6**	3	**1.4**	-	**-**	8	**3.7**	7	**3.3**
	2005-2009	173	17	**9.8**	2	**1.2**	60	**34.7**	10	**5.8**	3	**1.7**	21	**12.1**	17	**9.8**	12	**6.9**	3	**1.7**	1	**0.6**	9	**5.2**	18	**10.4**
	2010-2014	192	18	**9.4**	5	**2.6**	79	**41.1**	11	**5.7**	-	**-**	22	**11.5**	19	**9.9**	5	**2.6**	8	**4.2**	-	**-**	8	**4.2**	17	**8.9**
Belgium*	2000-2004	60	4	**6.7**	7	**11.7**	21	**35.0**	6	**10.0**	-	**-**	8	**13.3**	3	**5.0**	3	**5.0**	3	**5.0**	-	**-**	5	**8.3**	-	**-**
	2005-2009	298	7	**2.3**	18	**6.0**	104	**34.9**	23	**7.7**	2	**0.7**	42	**14.1**	31	**10.4**	13	**4.4**	26	**8.7**	3	**1.0**	17	**5.7**	12	**4.0**
	2010-2014	377	8	**2.1**	18	**4.8**	119	**31.6**	29	**7.7**	6	**1.6**	60	**15.9**	40	**10.6**	12	**3.2**	37	**9.8**	2	**0.5**	34	**9.0**	12	**3.2**
Croatia*	2000-2004	108	6	**5.6**	1	**0.9**	11	**10.2**	4	**3.7**	18	**16.7**	25	**23.1**	12	**11.1**	1	**0.9**	11	**10.2**	-	**-**	-	**-**	19	**17.6**
	2005-2009	104	9	**8.7**	-	**-**	27	**26.0**	8	**7.7**	15	**14.4**	15	**14.4**	7	**6.7**	2	**1.9**	4	**3.8**	-	**-**	7	**6.7**	10	**9.6**
	2010-2014	87	4	**4.6**	-	**-**	10	**11.5**	10	**11.5**	8	**9.2**	19	**21.8**	17	**19.5**	2	**2.3**	12	**13.8**	-	**-**	4	**4.6**	1	**1.1**
Czech Republic*	2000-2004	126	10	**7.9**	3	**2.4**	39	**31.0**	20	**15.9**	8	**6.3**	14	**11.1**	14	**11.1**	5	**4.0**	6	**4.8**	1	**0.8**	-	**-**	6	**4.8**
	2005-2009	131	8	**6.1**	5	**3.8**	61	**46.6**	10	**7.6**	6	**4.6**	-	**-**	26	**19.8**	4	**3.1**	-	**-**	-	**-**	6	**4.6**	5	**3.8**
	2010-2014	139	7	**5.0**	3	**2.2**	56	**40.3**	15	**10.8**	1	**0.7**	17	**12.2**	24	**17.3**	2	**1.4**	3	**2.2**	-	**-**	6	**4.3**	5	**3.6**
Denmark*	2000-2004	168	8	**4.8**	2	**1.2**	43	**25.6**	8	**4.8**	13	**7.7**	29	**17.3**	16	**9.5**	2	**1.2**	4	**2.4**	1	**0.6**	15	**8.9**	27	**16.1**
	2005-2009	153	3	**2.0**	4	**2.6**	37	**24.2**	3	**2.0**	6	**3.9**	23	**15.0**	17	**11.1**	3	**2.0**	6	**3.9**	1	**0.7**	2	**1.3**	48	**31.4**
	2010-2014	158	-	**-**	2	**1.3**	21	**13.3**	8	**5.1**	2	**1.3**	18	**11.4**	13	**8.2**	4	**2.5**	-	**-**	-	**-**	3	**1.9**	87	**55.1**
Estonia*	2000-2004	38	2	**5.3**	2	**5.3**	23	**60.5**	1	**2.6**	-	**-**	4	**10.5**	3	**7.9**	1	**2.6**	-	**-**	-	**-**	2	**5.3**	-	**-**
	2005-2009	29	1	**3.4**	2	**6.9**	12	**41.4**	1	**3.4**	1	**3.4**	4	**13.8**	5	**17.2**	3	**10.3**	-	**-**	-	**-**	-	**-**	-	**-**
	2010-2014	20	3	**15.0**	1	**5.0**	5	**25.0**	-	**-**	2	**10.0**	6	**30.0**	3	**15.0**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Finland*	2000-2004	159	7	**4.4**	3	**1.9**	66	**41.5**	12	**7.5**	7	**4.4**	16	**10.1**	20	**12.6**	3	**1.9**	1	**0.6**	1	**0.6**	20	**12.6**	3	**1.9**
	2005-2009	146	6	**4.1**	4	**2.7**	56	**38.4**	9	**6.2**	16	**11.0**	18	**12.3**	14	**9.6**	4	**2.7**	-	**-**	2	**1.4**	16	**11.0**	1	**0.7**
	2010-2014	178	8	**4.5**	12	**6.7**	67	**37.6**	10	**5.6**	9	**5.1**	22	**12.4**	23	**12.9**	4	**2.2**	1	**0.6**	1	**0.6**	21	**11.8**	-	**-**
France	2000-2004	1,621	73	**4.5**	58	**3.6**	518	**32.0**	40	**2.5**	-	**-**	309	**19.1**	140	**8.6**	114	**7.0**	150	**9.3**	3	**0.2**	183	**11.3**	33	**2.0**
	2005-2009	1,655	66	**4.0**	58	**3.5**	461	**27.9**	68	**4.1**	-	**-**	284	**17.2**	166	**10.0**	131	**7.9**	159	**9.6**	6	**0.4**	226	**13.7**	30	**1.8**
	2010-2014	1,050	34	**3.2**	38	**3.6**	303	**28.9**	61	**5.8**	-	**-**	188	**17.9**	108	**10.3**	46	**4.4**	109	**10.4**	5	**0.5**	150	**14.3**	8	**0.8**
Germany	2000-2004	149	6	**4.0**	4	**2.7**	34	**22.8**	13	**8.7**	16	**10.7**	31	**20.8**	25	**16.8**	5	**3.4**	8	**5.4**	1	**0.7**	4	**2.7**	2	**1.3**
	2005-2009	274	8	**2.9**	7	**2.6**	81	**29.6**	33	**12.0**	5	**1.8**	58	**21.2**	42	**15.3**	5	**1.8**	21	**7.7**	-	**-**	9	**3.3**	5	**1.8**
	2010-2014	199	5	**2.5**	4	**2.0**	42	**21.1**	35	**17.6**	4	**2.0**	34	**17.1**	37	**18.6**	3	**1.5**	24	**12.1**	1	**0.5**	9	**4.5**	1	**0.5**

Table 3.1. Histology distribution, by continent, country and calendar period. Children (0-14 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependy-moma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medullo-blastoma		Other and unspecified embryonal tumour		Oligodendro-glial tumour		Unspecified glioma		Neuro-epithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Greece*	2010-2014	226	5	**2.2**	7	**3.1**	66	**29.2**	11	**4.9**	-	**-**	57	**25.2**	35	**15.5**	6	**2.7**	18	**8.0**	1	**0.4**	18	**8.0**	2	**0.9**
Iceland*	2000-2004	10	-	**-**	-	**-**	5	**50.0**	1	**10.0**	1	**10.0**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	2	**20.0**	1	**10.0**
	2005-2009	14	-	**-**	-	**-**	6	**42.9**	-	**-**	2	**14.3**	-	**-**	-	**-**	1	**7.1**	2	**14.3**	-	**-**	-	**-**	3	**21.4**
	2010-2014	8	-	**-**	-	**-**	3	**37.5**	-	**-**	-	**-**	2	**25.0**	1	**12.5**	1	**12.5**	1	**12.5**	-	**-**	-	**-**	-	**-**
Ireland*	2000-2004	105	3	**2.9**	4	**3.8**	46	**43.8**	1	**1.0**	17	**16.2**	4	**3.8**	22	**21.0**	3	**2.9**	3	**2.9**	-	**-**	2	**1.9**	-	**-**
	2005-2009	110	10	**9.1**	4	**3.6**	42	**38.2**	9	**8.2**	8	**7.3**	8	**7.3**	18	**16.4**	3	**2.7**	1	**0.9**	1	**0.9**	5	**4.5**	1	**0.9**
	2010-2014	103	2	**1.9**	-	**-**	38	**36.9**	10	**9.7**	4	**3.9**	12	**11.7**	13	**12.6**	8	**7.8**	2	**1.9**	1	**1.0**	12	**11.7**	1	**1.0**
Italy	2000-2004	524	33	**6.3**	12	**2.3**	112	**21.4**	36	**6.9**	36	**6.9**	90	**17.2**	31	**5.9**	10	**1.9**	37	**7.1**	4	**0.8**	22	**4.2**	101	**19.3**
	2005-2009	707	45	**6.4**	17	**2.4**	165	**23.3**	45	**6.4**	42	**5.9**	121	**17.1**	47	**6.6**	13	**1.8**	40	**5.7**	2	**0.3**	45	**6.4**	125	**17.7**
	2010-2014	309	15	**4.9**	5	**1.6**	66	**21.4**	20	**6.5**	19	**6.1**	50	**16.2**	23	**7.4**	3	**1.0**	19	**6.1**	1	**0.3**	25	**8.1**	63	**20.4**
Latvia*	2000-2004	59	0	**0.0**	0	**0.0**	2	**3.4**	5	**8.5**	25	**42.4**	1	**1.7**	1	**1.7**	2	**3.4**	1	**1.7**	2	**3.4**	0	**0.0**	20	**33.9**
	2005-2009	21	2	**9.5**	0	**0.0**	3	**14.3**	5	**23.8**	1	**4.8**	3	**14.3**	1	**4.8**	0	**0.0**	0	**0.0**	0	**0.0**	0	**0.0**	6	**28.6**
	2010-2014	49	1	**2.0**	0	**0.0**	7	**14.3**	13	**26.5**	10	**20.4**	7	**14.3**	3	**6.1**	0	**0.0**	2	**4.1**	0	**0.0**	0	**0.0**	6	**12.2**
Lithuania*	2000-2004	51	3	**5.9**	-	**-**	5	**9.8**	6	**11.8**	15	**29.4**	14	**27.5**	3	**5.9**	2	**3.9**	2	**3.9**	1	**2.0**	-	**-**	-	**-**
	2005-2009	39	3	**7.7**	1	**2.6**	6	**15.4**	2	**5.1**	6	**15.4**	11	**28.2**	3	**7.7**	3	**7.7**	3	**7.7**	-	**-**	1	**2.6**	-	**-**
	2010-2014	14	2	**14.3**	-	**-**	3	**21.4**	3	**21.4**	-	**-**	3	**21.4**	1	**7.1**	-	**-**	1	**7.1**	-	**-**	1	**7.1**	-	**-**
Malta*	2000-2004	10	1	**10.0**	-	**-**	3	**30.0**	2	**20.0**	-	**-**	2	**20.0**	1	**10.0**	-	**-**	-	**-**	-	**-**	1	**10.0**	-	**-**
	2005-2009	6	-	**-**	-	**-**	2	**33.3**	-	**-**	1	**16.7**	2	**33.3**	-	**-**	-	**-**	1	**16.7**	-	**-**	-	**-**	-	**-**
	2010-2014	8	1	**12.5**	-	**-**	-	**-**	-	**-**	3	**37.5**	1	**12.5**	-	**-**	-	**-**	2	**25.0**	-	**-**	1	**12.5**	-	**-**
Netherlands*	2000-2004	453	32	**7.1**	9	**2.0**	142	**31.3**	40	**8.8**	1	**0.2**	76	**16.8**	50	**11.0**	18	**4.0**	44	**9.7**	3	**0.7**	26	**5.7**	12	**2.6**
	2005-2009	460	14	**3.0**	12	**2.6**	141	**30.7**	33	**7.2**	1	**0.2**	81	**17.6**	47	**10.2**	10	**2.2**	49	**10.7**	2	**0.4**	52	**11.3**	18	**3.9**
	2010-2014	475	13	**2.7**	18	**3.8**	152	**32.0**	29	**6.1**	-	**-**	80	**16.8**	54	**11.4**	8	**1.7**	53	**11.2**	1	**0.2**	46	**9.7**	21	**4.4**
Norway*	2000-2004	165	7	**4.2**	11	**6.7**	52	**31.5**	6	**3.6**	4	**2.4**	18	**10.9**	16	**9.7**	7	**4.2**	11	**6.7**	-	**-**	18	**10.9**	15	**9.1**
	2005-2009	160	1	**0.6**	8	**5.0**	45	**28.1**	12	**7.5**	10	**6.3**	16	**10.0**	21	**13.1**	9	**5.6**	12	**7.5**	-	**-**	13	**8.1**	13	**8.1**
	2010-2014	130	3	**2.3**	4	**3.1**	45	**34.6**	10	**7.7**	2	**1.5**	8	**6.2**	17	**13.1**	1	**0.8**	15	**11.5**	1	**0.8**	18	**13.8**	6	**4.6**
Poland*	2000-2004	573	41	**7.2**	5	**0.9**	88	**15.4**	56	**9.8**	91	**15.9**	162	**28.3**	82	**14.3**	23	**4.0**	17	**3.0**	4	**0.7**	2	**0.3**	2	**0.3**
	2005-2009	543	38	**7.0**	10	**1.8**	84	**15.5**	69	**12.7**	68	**12.5**	153	**28.2**	74	**13.6**	24	**4.4**	16	**2.9**	4	**0.7**	2	**0.4**	1	**0.2**
	2010-2014	435	41	**9.4**	16	**3.7**	42	**9.7**	53	**12.2**	29	**6.7**	138	**31.7**	70	**16.1**	19	**4.4**	24	**5.5**	1	**0.2**	1	**0.2**	1	**0.2**
Portugal*	2000-2004	173	3	**1.7**	8	**4.6**	44	**25.4**	9	**5.2**	20	**11.6**	39	**22.5**	11	**6.4**	11	**6.4**	19	**11.0**	1	**0.6**	2	**1.2**	6	**3.5**
	2005-2009	188	11	**5.9**	5	**2.7**	41	**21.8**	13	**6.9**	17	**9.0**	43	**22.9**	17	**9.0**	14	**7.4**	13	**6.9**	1	**0.5**	7	**3.7**	6	**3.2**
	2010-2014	139	6	**4.3**	2	**1.4**	43	**30.9**	16	**11.5**	6	**4.3**	20	**14.4**	22	**15.8**	-	**-**	8	**5.8**	1	**0.7**	14	**10.1**	1	**0.7**
Romania	2005-2009	9	2	**22.2**	-	**-**	1	**11.1**	-	**-**	-	**-**	2	**22.2**	1	**11.1**	-	**-**	2	**22.2**	-	**-**	-	**-**	1	**11.1**
	2010-2014	10	-	**-**	-	**-**	2	**20.0**	-	**-**	-	**-**	2	**20.0**	1	**10.0**	2	**20.0**	2	**20.0**	-	**-**	-	**-**	1	**10.0**
Russian Federation	2000-2004	67	2	**3.0**	-	**-**	2	**3.0**	9	**13.4**	26	**38.8**	14	**20.9**	2	**3.0**	7	**10.4**	1	**1.5**	2	**3.0**	-	**-**	2	**3.0**
	2005-2009	89	2	**2.2**	-	**-**	5	**5.6**	13	**14.6**	24	**27.0**	18	**20.2**	8	**9.0**	4	**4.5**	7	**7.9**	1	**1.1**	-	**-**	7	**7.9**
	2010-2014	124	6	**4.8**	3	**2.4**	5	**4.0**	20	**16.1**	32	**25.8**	27	**21.8**	15	**12.1**	5	**4.0**	6	**4.8**	1	**0.8**	-	**-**	4	**3.2**
Slovakia*	2000-2004	139	7	**5.0**	2	**1.4**	62	**44.6**	4	**2.9**	1	**0.7**	23	**16.5**	11	**7.9**	7	**5.0**	3	**2.2**	-	**-**	5	**3.6**	14	**10.1**
	2005-2009	129	13	**10.1**	4	**3.1**	46	**35.7**	9	**7.0**	2	**1.6**	24	**18.6**	12	**9.3**	4	**3.1**	3	**2.3**	1	**0.8**	-	**-**	11	**8.5**
	2010-2014	36	2	**5.6**	1	**2.8**	10	**27.8**	7	**19.4**	1	**2.8**	8	**22.2**	2	**5.6**	2	**5.6**	1	**2.8**	-	**-**	1	**2.8**	1	**2.8**
Slovenia*	2000-2004	34	-	**-**	1	**2.9**	11	**32.4**	4	**11.8**	-	**-**	9	**26.5**	3	**8.8**	2	**5.9**	2	**5.9**	-	**-**	2	**5.9**	-	**-**
	2005-2009	43	-	**-**	1	**2.3**	15	**34.9**	7	**16.3**	-	**-**	10	**23.3**	8	**18.6**	-	**-**	-	**-**	1	**2.3**	1	**2.3**	-	**-**
	2010-2014	26	-	**-**	2	**7.7**	4	**15.4**	4	**15.4**	-	**-**	10	**38.5**	3	**11.5**	1	**3.8**	1	**3.8**	-	**-**	1	**3.8**	-	**-**

Table 3.1. Histology distribution, by continent, country and calendar period. Children (0-14 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependy-moma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medullo-blastoma		Other and unspecified embryonal tumour		Oligodendro-glial tumour		Unspecified glioma		Neuro-epithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Spain	2000-2004	389	28	**7.2**	9	**2.3**	102	**26.2**	21	**5.4**	50	**12.9**	88	**22.6**	42	**10.8**	4	**1.0**	23	**5.9**	1	**0.3**	9	**2.3**	12	**3.1**
	2005-2009	516	39	**7.6**	17	**3.3**	143	**27.7**	20	**3.9**	38	**7.4**	109	**21.1**	64	**12.4**	6	**1.2**	33	**6.4**	2	**0.4**	31	**6.0**	14	**2.7**
	2010-2014	417	29	**7.0**	13	**3.1**	117	**28.1**	26	**6.2**	17	**4.1**	93	**22.3**	55	**13.2**	5	**1.2**	19	**4.6**	2	**0.5**	33	**7.9**	8	**1.9**
Sweden*	2000-2004	219	13	**5.9**	5	**2.3**	67	**30.6**	11	**5.0**	20	**9.1**	27	**12.3**	31	**14.2**	6	**2.7**	6	**2.7**	1	**0.5**	11	**5.0**	21	**9.6**
	2005-2009	222	12	**5.4**	8	**3.6**	57	**25.7**	15	**6.8**	27	**12.2**	23	**10.4**	22	**9.9**	7	**3.2**	1	**0.5**	1	**0.5**	26	**11.7**	23	**10.4**
	2010-2014	250	7	**2.8**	10	**4.0**	78	**31.2**	22	**8.8**	19	**7.6**	33	**13.2**	27	**10.8**	10	**4.0**	5	**2.0**	-	**-**	19	**7.6**	20	**8.0**
Switzerland*	2000-2004	167	5	**3.0**	2	**1.2**	70	**41.9**	11	**6.6**	3	**1.8**	33	**19.8**	21	**12.6**	5	**3.0**	-	**-**	1	**0.6**	15	**9.0**	1	**0.6**
	2005-2009	149	1	**0.7**	7	**4.7**	51	**34.2**	11	**7.4**	3	**2.0**	26	**17.4**	30	**20.1**	2	**1.3**	2	**1.3**	1	**0.7**	14	**9.4**	1	**0.7**
	2010-2014	155	3	**1.9**	5	**3.2**	66	**42.6**	17	**11.0**	2	**1.3**	26	**16.8**	23	**14.8**	2	**1.3**	2	**1.3**	-	**-**	9	**5.8**	-	**-**
United Kingdom*	2000-2004	1,508	87	**5.8**	48	**3.2**	439	**29.1**	113	**7.5**	85	**5.6**	267	**17.7**	101	**6.7**	27	**1.8**	158	**10.5**	7	**0.5**	84	**5.6**	92	**6.1**
	2005-2009	1,563	66	**4.2**	59	**3.8**	494	**31.6**	119	**7.6**	55	**3.5**	249	**15.9**	126	**8.1**	30	**1.9**	163	**10.4**	9	**0.6**	117	**7.5**	76	**4.9**
	2010-2014	1,613	55	**3.4**	59	**3.7**	528	**32.7**	126	**7.8**	35	**2.2**	232	**14.4**	153	**9.5**	25	**1.5**	163	**10.1**	11	**0.7**	145	**9.0**	81	**5.0**
Oceania	2000-2004	545	49	**9.0**	7	**1.3**	81	**14.9**	61	**11.2**	29	**5.3**	87	**16.0**	66	**12.1**	24	**4.4**	64	**11.7**	1	**0.2**	18	**3.3**	58	**10.6**
	2005-2009	538	23	**4.3**	15	**2.8**	83	**15.4**	66	**12.3**	13	**2.4**	103	**19.1**	88	**16.4**	13	**2.4**	74	**13.8**	1	**0.2**	21	**3.9**	38	**7.1**
	2010-2014	510	31	**6.1**	13	**2.5**	80	**15.7**	49	**9.6**	10	**2.0**	94	**18.4**	80	**15.7**	14	**2.7**	78	**15.3**	1	**0.2**	29	**5.7**	31	**6.1**
Australia*	2000-2004	453	41	**9.1**	4	**0.9**	61	**13.5**	53	**11.7**	26	**5.7**	70	**15.5**	58	**12.8**	18	**4.0**	51	**11.3**	1	**0.2**	18	**4.0**	52	**11.5**
	2005-2009	478	20	**4.2**	15	**3.1**	79	**16.5**	54	**11.3**	13	**2.7**	88	**18.4**	84	**17.6**	11	**2.3**	61	**12.8**	1	**0.2**	21	**4.4**	31	**6.5**
	2010-2014	445	23	**5.2**	12	**2.7**	78	**17.5**	42	**9.4**	9	**2.0**	86	**19.3**	68	**15.3**	13	**2.9**	59	**13.3**	1	**0.2**	28	**6.3**	26	**5.8**
New Zealand*	2000-2004	92	8	**8.7**	3	**3.3**	20	**21.7**	8	**8.7**	3	**3.3**	17	**18.5**	8	**8.7**	6	**6.5**	13	**14.1**	-	**-**	-	**-**	6	**6.5**
	2005-2009	60	3	**5.0**	-	**-**	4	**6.7**	12	**20.0**	-	**-**	15	**25.0**	4	**6.7**	2	**3.3**	13	**21.7**	-	**-**	-	**-**	7	**11.7**
	2010-2014	65	8	**12.3**	1	**1.5**	2	**3.1**	7	**10.8**	1	**1.5**	8	**12.3**	12	**18.5**	1	**1.5**	19	**29.2**	-	**-**	1	**1.5**	5	**7.7**

* Data with 100% coverage of the national population.

Table 3.2. Histology distribution, by continent, country and calendar period. Adults (15-99 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Africa	2000-2004	32	-	-	2	6.3	13	40.7	-	-	1	3.1	1	3.1	-	-	-	-	1	3.1	-	-	14	43.7
	2005-2009	203	3	1.5	5	2.5	42	20.7	1	0.5	20	9.9	2	1.0	2	1.0	1	0.5	5	2.5	-	-	122	60.1
	2010-2014	338	10	3.0	6	1.8	105	31.1	4	1.2	17	5.0	6	1.8	-	-	8	2.4	19	5.6	1	0.3	162	47.9
Algeria	2000-2004	31	-	-	1	3.2	13	41.9	-	-	1	3.2	1	3.2	-	-	-	-	1	3.2	-	-	14	45.2
	2005-2009	159	3	1.9	1	0.6	29	18.2	-	-	16	10.1	1	0.6	1	0.6	-	-	5	3.1	-	-	103	64.8
	2010-2014	187	5	2.7	1	0.5	66	35.3	-	-	9	4.8	5	2.7	-	-	2	1.1	11	5.9	-	-	88	47.1
Mauritius*	2010-2014	36	1	2.8	1	2.8	17	47.2	-	-	6	16.7	-	-	-	-	-	-	1	2.8	-	-	10	27.8
Nigeria	2005-2009	40	-	-	4	10.0	11	27.5	1	2.5	4	10.0	1	2.5	1	2.5	-	-	-	-	-	-	18	45.0
	2010-2014	104	3	2.9	3	2.9	22	21.2	4	3.8	1	1.0	1	1.0	-	-	6	5.8	5	4.8	1	1.0	58	55.8
South Africa	2000-2004	1	-	-	-	-	1	100.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2005-2009	4	-	-	-	-	2	50.0	-	-	-	-	-	-	-	-	1	25.0	-	-	-	-	1	25.0
	2010-2014	11	1	9.1	1	9.1	-	-	-	-	1	9.1	-	-	-	-	-	-	2	18.2	-	-	6	54.5
America (Central and South)	2000-2004	1,933	40	2.1	262	13.6	660	34.1	33	1.7	342	17.7	173	8.9	17	0.9	17	0.9	56	2.9	8	0.4	325	16.8
	2005-2009	3,361	63	1.9	363	10.8	1,218	36.2	48	1.4	545	16.2	288	8.6	32	1.0	40	1.2	121	3.6	30	0.9	613	18.2
	2010-2014	2,792	68	2.4	282	10.1	958	34.3	44	1.6	364	13.0	280	10.0	41	1.5	30	1.1	124	4.4	23	0.8	578	20.7
Argentina	2000-2004	110	2	1.8	15	13.6	30	27.3	-	-	23	20.9	17	15.5	-	-	4	3.6	3	2.7	-	-	16	14.5
	2005-2009	510	10	2.0	62	12.2	164	32.2	8	1.6	87	17.1	45	8.8	1	0.2	6	1.2	20	3.9	4	0.8	103	20.2
	2010-2014	465	13	2.8	41	8.8	159	34.2	9	1.9	61	13.1	35	7.5	2	0.4	9	1.9	34	7.3	3	0.6	99	21.3
Brazil	2000-2004	322	9	2.8	51	15.8	133	41.3	3	0.9	62	19.3	15	4.7	2	0.6	5	1.6	10	3.1	-	-	32	9.9
	2005-2009	492	9	1.8	50	10.2	225	45.7	1	0.2	80	16.3	28	5.7	1	0.2	3	0.6	27	5.5	2	0.4	66	13.4
	2010-2014	327	11	3.4	28	8.6	149	45.6	2	0.6	38	11.6	29	8.9	3	0.9	2	0.6	18	5.5	-	-	47	14.4
Chile	2000-2004	40	-	-	8	20.0	5	12.5	-	-	3	7.5	5	12.5	1	2.5	1	2.5	-	-	-	-	17	42.5
	2005-2009	233	6	2.6	27	11.6	74	31.8	3	1.3	10	4.3	18	7.7	7	3.0	4	1.7	4	1.7	2	0.9	78	33.5
	2010-2014	111	1	0.9	13	11.7	33	29.7	4	3.6	6	5.4	5	4.5	2	1.8	-	-	6	5.4	1	0.9	40	36.0
Colombia	2000-2004	433	10	2.3	49	11.3	132	30.5	6	1.4	52	12.0	37	8.5	4	0.9	3	0.7	14	3.2	1	0.2	125	28.9
	2005-2009	560	10	1.8	55	9.8	172	30.7	4	0.7	59	10.5	45	8.0	6	1.1	8	1.4	21	3.8	5	0.9	175	31.3
	2010-2014	481	18	3.7	52	10.8	155	32.2	8	1.7	39	8.1	47	9.8	2	0.4	12	2.5	20	4.2	4	0.8	124	25.8
Costa Rica*	2000-2004	260	4	1.5	21	8.1	68	26.2	1	0.4	64	24.6	43	16.5	2	0.8	-	-	1	0.4	1	0.4	55	21.2
	2005-2009	376	5	1.3	20	5.3	103	27.4	1	0.3	105	27.9	63	16.8	1	0.3	4	1.1	10	2.7	-	-	64	17.0
	2010-2014	424	10	2.4	19	4.5	162	38.2	1	0.2	64	15.1	76	17.9	4	0.9	1	0.2	8	1.9	3	0.7	76	17.9
Ecuador	2000-2004	251	4	1.6	30	12.0	48	19.1	-	-	104	41.4	20	8.0	6	2.4	-	-	11	4.4	1	0.4	27	10.8
	2005-2009	522	7	1.3	75	14.4	98	18.8	4	0.8	179	34.3	41	7.9	13	2.5	5	1.0	20	3.8	2	0.4	78	14.9
	2010-2014	650	9	1.4	114	17.5	111	17.1	8	1.2	151	23.2	61	9.4	27	4.2	2	0.3	21	3.2	2	0.3	144	22.2
Guadeloupe	2005-2009	17	-	-	-	-	10	58.8	-	-	-	-	1	5.9	-	-	-	-	2	11.8	4	23.5	-	-
	2010-2014	37	1	2.7	-	-	28	75.7	-	-	-	-	2	5.4	-	-	1	2.7	1	2.7	4	10.8	-	-

Table 3.2. Histology distribution, by continent, country and calendar period. Adults (15-99 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Martinique*	2000-2004	46	-	-	3	6.5	17	37.0	1	2.2	14	30.4	5	10.9	1	2.2	-	-	-	-	4	8.7	1	2.2
	2005-2009	51	2	3.9	2	3.9	33	64.7	-	-	1	2.0	4	7.8	2	3.9	-	-	3	5.9	2	3.9	2	3.9
	2010-2014	38	-	-	-	-	32	84.2	1	2.6	-	-	1	2.6	-	-	-	-	1	2.6	2	5.3	1	2.6
Puerto Rico*	2000-2004	471	11	2.3	85	18.0	227	48.2	22	4.7	20	4.2	31	6.6	1	0.2	4	0.8	17	3.6	1	0.2	52	11.0
	2005-2009	600	14	2.3	72	12.0	339	56.5	27	4.5	24	4.0	43	7.2	1	0.2	10	1.7	14	2.3	9	1.5	47	7.8
	2010-2014	259	5	1.9	15	5.8	129	49.8	11	4.2	5	1.9	24	9.3	1	0.4	3	1.2	15	5.8	4	1.5	47	18.1
America (North)	2000-2004	78,607	1,163	1.5	9,412	12.0	44,298	56.4	2,472	3.1	2,003	2.5	9,087	11.6	103	0.1	560	0.7	4,019	5.1	600	0.8	4,890	6.2
	2005-2009	90,869	2,287	2.5	8,729	9.6	49,748	54.7	2,730	3.0	2,781	3.1	8,833	9.7	139	0.2	583	0.6	4,559	5.0	2,271	2.5	8,209	9.0
	2010-2014	78,267	1,967	2.5	6,545	8.4	43,568	55.7	1,996	2.6	2,605	3.3	6,282	8.0	105	0.1	443	0.6	3,644	4.7	1,998	2.6	9,114	11.6
Canada	2000-2004	9,829	127	1.3	621	6.3	5,078	51.7	215	2.2	588	6.0	1,278	13.0	10	0.1	70	0.7	554	5.6	60	0.6	1,228	12.5
	2005-2009	11,127	194	1.7	633	5.7	5,730	51.5	247	2.2	604	5.4	1,302	11.7	15	0.1	70	0.6	644	5.8	174	1.6	1,514	13.6
	2010-2014	12,922	200	1.5	512	4.0	5,656	43.8	167	1.3	357	2.8	1,011	7.8	11	0.1	66	0.5	501	3.9	288	2.2	4,153	32.1
United States	2000-2004	68,778	1,036	1.5	8,791	12.8	39,220	57.0	2,257	3.3	1,415	2.1	7,809	11.4	93	0.1	490	0.7	3,465	5.0	540	0.8	3,662	5.3
	2005-2009	79,742	2,093	2.6	8,096	10.2	44,018	55.2	2,483	3.1	2,177	2.7	7,531	9.4	124	0.2	513	0.6	3,915	4.9	2,097	2.6	6,695	8.4
	2010-2014	65,345	1,767	2.7	6,033	9.2	37,912	58.0	1,829	2.8	2,248	3.4	5,271	8.1	94	0.1	377	0.6	3,143	4.8	1,710	2.6	4,961	7.6
Asia	2000-2004	14,498	254	1.8	1,663	11.5	4,935	34.0	237	1.6	1,334	9.2	1,499	10.3	143	1.0	175	1.2	859	5.9	210	1.4	3,189	22.0
	2005-2009	26,024	458	1.8	2,354	9.0	8,839	34.0	369	1.4	1,755	6.7	2,457	9.4	176	0.7	337	1.3	1,975	7.6	445	1.7	6,859	26.4
	2010-2014	26,019	504	1.9	2,145	8.2	9,832	37.8	369	1.4	1,216	4.7	2,663	10.2	147	0.6	252	1.0	1,890	7.3	475	1.8	6,526	25.1
China	2000-2004	1,413	7	0.5	63	4.5	45	3.2	28	2.0	133	9.4	35	2.5	5	0.4	5	0.4	185	13.1	39	2.8	868	61.4
	2005-2009	4,763	47	1.0	167	3.5	298	6.3	45	0.9	304	6.4	202	4.2	20	0.4	22	0.5	504	10.6	87	1.8	3,067	64.4
	2010-2014	4,552	55	1.2	190	4.2	409	9.0	37	0.8	167	3.7	220	4.8	15	0.3	19	0.4	399	8.8	123	2.7	2,918	64.1
Cyprus*	2000-2004	25	1	4.0	6	24.0	9	36.0	-	-	3	12.0	3	12.0	-	-	-	-	1	4.0	-	-	2	8.0
	2005-2009	175	4	2.3	33	18.9	101	57.7	3	1.7	5	2.9	10	5.7	-	-	2	1.1	9	5.1	-	-	8	4.6
	2010-2014	189	3	1.6	28	14.8	129	68.3	1	0.5	4	2.1	15	7.9	-	-	1	0.5	5	2.6	-	-	3	1.6
India	2000-2004	34	1	2.9	9	26.5	6	17.6	-	-	1	2.9	-	-	1	2.9	-	-	3	8.8	-	-	13	38.2
	2005-2009	124	3	2.4	9	7.3	29	23.4	-	-	8	6.5	11	8.9	-	-	-	-	16	12.9	2	1.6	46	37.1
	2010-2014	85	1	1.2	12	14.1	18	21.2	1	1.2	6	7.1	7	8.2	-	-	-	-	8	9.4	-	-	32	37.6
Israel*	2000-2004	1,581	30	1.9	214	13.5	829	52.4	57	3.6	43	2.7	168	10.6	4	0.3	11	0.7	58	3.7	37	2.3	130	8.2
	2005-2009	1,789	29	1.6	208	11.6	941	52.6	69	3.9	26	1.5	171	9.6	7	0.4	16	0.9	115	6.4	41	2.3	166	9.3
	2010-2014	1,552	20	1.3	175	11.3	817	52.6	54	3.5	28	1.8	143	9.2	2	0.1	7	0.5	69	4.4	23	1.5	214	13.8
Japan	2000-2004	2,693	44	1.6	250	9.3	1,068	39.7	27	1.0	242	9.0	153	5.7	11	0.4	23	0.9	245	9.1	32	1.2	598	22.2
	2005-2009	5,516	76	1.4	535	9.7	2,201	39.9	65	1.2	358	6.5	469	8.5	20	0.4	52	0.9	479	8.7	119	2.2	1,142	20.7
	2010-2014	4,481	60	1.3	359	8.0	1,700	37.9	70	1.6	206	4.6	404	9.0	10	0.2	39	0.9	343	7.7	97	2.2	1,193	26.6

Table 3.2. Histology distribution, by continent, country and calendar period. Adults (15-99 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Jordan*	2000-2004	463	15	**3.2**	111	**24.0**	162	**35.0**	14	**3.0**	45	**9.7**	36	**7.8**	11	**2.4**	9	**1.9**	34	**7.3**	2	**0.4**	24	**5.2**
	2005-2009	477	14	**2.9**	80	**16.8**	250	**52.4**	6	**1.3**	23	**4.8**	44	**9.2**	7	**1.5**	11	**2.3**	24	**5.0**	-	**-**	18	**3.8**
	2010-2014	515	12	**2.3**	60	**11.7**	262	**50.9**	6	**1.2**	13	**2.5**	49	**9.5**	16	**3.1**	7	**1.4**	36	**7.0**	3	**0.6**	51	**9.9**
Korea*	2000-2004	4,581	75	**1.6**	468	**10.2**	1,369	**29.9**	30	**0.7**	358	**7.8**	618	**13.5**	56	**1.2**	80	**1.7**	195	**4.3**	66	**1.4**	1,266	**27.6**
	2005-2009	5,816	117	**2.0**	445	**7.7**	2,054	**35.3**	35	**0.6**	423	**7.3**	710	**12.2**	51	**0.9**	92	**1.6**	454	**7.8**	109	**1.9**	1,326	**22.8**
	2010-2014	6,693	171	**2.6**	526	**7.9**	2,845	**42.5**	49	**0.7**	416	**6.2**	875	**13.1**	29	**0.4**	81	**1.2**	599	**8.9**	131	**2.0**	971	**14.5**
Kuwait*	2000-2004	64	3	**4.7**	12	**18.8**	28	**43.8**	1	**1.6**	4	**6.3**	4	**6.3**	3	**4.7**	-	**-**	6	**9.4**	1	**1.6**	2	**3.1**
	2005-2009	83	-	**-**	6	**7.2**	42	**50.6**	2	**2.4**	7	**8.4**	6	**7.2**	5	**6.0**	-	**-**	9	**10.8**	2	**2.4**	4	**4.8**
	2010-2014	77	-	**-**	7	**9.1**	42	**54.5**	1	**1.3**	7	**9.1**	11	**14.3**	-	**-**	1	**1.3**	5	**6.5**	-	**-**	3	**3.9**
Malaysia	2005-2009	64	1	**1.6**	2	**3.1**	15	**23.4**	-	**-**	17	**26.6**	5	**7.8**	1	**1.6**	2	**3.1**	2	**3.1**	-	**-**	19	**29.7**
	2010-2014	67	2	**3.0**	4	**6.0**	20	**29.9**	-	**-**	15	**22.4**	7	**10.4**	1	**1.5**	2	**3.0**	3	**4.5**	-	**-**	13	**19.4**
Qatar*	2000-2004	48	2	**4.2**	8	**16.7**	15	**31.3**	1	**2.1**	3	**6.3**	4	**8.3**	-	**-**	-	**-**	6	**12.5**	1	**2.1**	8	**16.7**
	2005-2009	104	3	**2.9**	15	**14.4**	38	**36.5**	2	**1.9**	1	**1.0**	21	**20.2**	-	**-**	-	**-**	12	**11.5**	3	**2.9**	9	**8.7**
	2010-2014	126	3	**2.4**	22	**17.5**	50	**39.7**	1	**0.8**	1	**0.8**	34	**27.0**	1	**0.8**	1	**0.8**	2	**1.6**	3	**2.4**	8	**6.3**
Singapore*	2000-2004	242	7	**2.9**	32	**13.2**	111	**45.9**	8	**3.3**	12	**5.0**	38	**15.7**	-	**-**	5	**2.1**	3	**1.2**	6	**2.5**	20	**8.3**
	2005-2009	346	14	**4.0**	44	**12.7**	152	**43.9**	16	**4.6**	7	**2.0**	63	**18.2**	1	**0.3**	13	**3.8**	18	**5.2**	8	**2.3**	10	**2.9**
	2010-2014	445	17	**3.8**	31	**7.0**	211	**47.4**	18	**4.0**	21	**4.7**	68	**15.3**	-	**-**	9	**2.0**	23	**5.2**	18	**4.0**	29	**6.5**
Taiwan*	2000-2004	2,076	45	**2.2**	326	**15.7**	940	**45.3**	34	**1.6**	294	**14.2**	307	**14.8**	34	**1.6**	32	**1.5**	50	**2.4**	13	**0.6**	1	**0.0**
	2005-2009	2,226	41	**1.8**	422	**19.0**	1,090	**49.0**	24	**1.1**	176	**7.9**	321	**14.4**	32	**1.4**	47	**2.1**	52	**2.3**	14	**0.6**	7	**0.3**
	2010-2014	2,606	48	**1.8**	413	**15.8**	1,382	**53.0**	39	**1.5**	166	**6.4**	399	**15.3**	20	**0.8**	39	**1.5**	55	**2.1**	30	**1.2**	15	**0.6**
Thailand	2000-2004	625	8	**1.3**	53	**8.5**	124	**19.8**	13	**2.1**	180	**28.8**	29	**4.6**	10	**1.6**	4	**0.6**	14	**2.2**	-	**-**	190	**30.4**
	2005-2009	1,045	12	**1.1**	71	**6.8**	201	**19.2**	18	**1.7**	276	**26.4**	38	**3.6**	7	**0.7**	26	**2.5**	35	**3.3**	-	**-**	361	**34.5**
	2010-2014	909	13	**1.4**	59	**6.5**	239	**26.3**	5	**0.6**	50	**5.5**	53	**5.8**	5	**0.6**	9	**1.0**	23	**2.5**	7	**0.8**	446	**49.1**
Turkey	2000-2004	653	16	**2.5**	111	**17.0**	229	**35.1**	24	**3.7**	16	**2.5**	104	**15.9**	8	**1.2**	6	**0.9**	59	**9.0**	13	**2.0**	67	**10.3**
	2005-2009	3,496	97	**2.8**	317	**9.1**	1,427	**40.8**	84	**2.4**	124	**3.5**	386	**11.0**	25	**0.7**	54	**1.5**	246	**7.0**	60	**1.7**	676	**19.3**
	2010-2014	3,722	99	**2.7**	259	**7.0**	1,708	**45.9**	87	**2.3**	116	**3.1**	378	**10.2**	48	**1.3**	37	**1.0**	320	**8.6**	40	**1.1**	630	**16.9**
Europe	2000-2004	75,155	1,320	**1.8**	8,295	**11.0**	34,550	**46.0**	1,226	**1.6**	4,638	**6.2**	7,031	**9.4**	285	**0.4**	639	**0.9**	5,007	**6.7**	868	**1.2**	11,296	**15.0**
	2005-2009	95,440	1,747	**1.8**	9,551	**10.0**	48,974	**51.3**	1,541	**1.6**	3,885	**4.1**	8,890	**9.3**	364	**0.4**	795	**0.8**	5,156	**5.4**	1,259	**1.3**	13,278	**13.9**
	2010-2014	84,238	1,642	**1.9**	8,065	**9.6**	47,537	**56.4**	1,464	**1.7**	2,597	**3.1**	6,897	**8.2**	243	**0.3**	627	**0.7**	4,247	**5.0**	1,333	**1.6**	9,586	**11.4**
Austria*	2000-2004	2,310	43	**1.9**	159	**6.9**	1,437	**62.2**	2	**0.1**	213	**9.2**	133	**5.8**	2	**0.1**	29	**1.3**	77	**3.3**	19	**0.8**	196	**8.5**
	2005-2009	2,769	83	**3.0**	297	**10.7**	1,776	**64.1**	6	**0.2**	115	**4.2**	249	**9.0**	4	**0.1**	55	**2.0**	52	**1.9**	13	**0.5**	119	**4.3**
	2010-2014	2,479	53	**2.1**	178	**7.2**	1,736	**70.0**	-	**-**	117	**4.7**	208	**8.4**	1	**0.0**	24	**1.0**	50	**2.0**	5	**0.2**	107	**4.3**
Belgium*	2000-2004	733	17	**2.3**	111	**15.1**	385	**52.5**	21	**2.9**	6	**0.8**	100	**13.6**	3	**0.4**	8	**1.1**	19	**2.6**	18	**2.5**	45	**6.1**
	2005-2009	3,815	114	**3.0**	494	**12.9**	2,290	**60.0**	121	**3.2**	13	**0.3**	394	**10.3**	27	**0.7**	28	**0.7**	65	**1.7**	101	**2.6**	168	**4.4**
	2010-2014	4,016	110	**2.7**	409	**10.2**	2,557	**63.7**	94	**2.3**	25	**0.6**	393	**9.8**	29	**0.7**	36	**0.9**	61	**1.5**	113	**2.8**	189	**4.7**

Table 3.2. Histology distribution, by continent, country and calendar period. Adults (15-99 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Croatia*	2000-2004	1,049	26	**2.5**	48	**4.6**	593	**56.5**	9	**0.9**	127	**12.1**	88	**8.4**	1	**0.1**	17	**1.6**	73	**7.0**	8	**0.8**	59	**5.6**
	2005-2009	1,168	27	**2.3**	43	**3.7**	771	**66.0**	21	**1.8**	75	**6.4**	86	**7.4**	-	**-**	13	**1.1**	60	**5.1**	15	**1.3**	57	**4.9**
	2010-2014	1,046	20	**1.9**	31	**3.0**	743	**71.0**	23	**2.2**	72	**6.9**	76	**7.3**	2	**0.2**	8	**0.8**	45	**4.3**	23	**2.2**	3	**0.3**
Czech Republic*	2000-2004	2,532	50	**2.0**	561	**22.2**	1,352	**53.4**	64	**2.5**	81	**3.2**	229	**9.0**	4	**0.2**	23	**0.9**	91	**3.6**	13	**0.5**	64	**2.5**
	2005-2009	2,711	44	**1.6**	449	**16.6**	1,540	**56.8**	75	**2.8**	67	**2.5**	236	**8.7**	-	**-**	39	**1.4**	111	**4.1**	28	**1.0**	122	**4.5**
	2010-2014	2,824	57	**2.0**	464	**16.4**	1,732	**61.3**	83	**2.9**	87	**3.1**	186	**6.6**	2	**0.1**	34	**1.2**	77	**2.7**	29	**1.0**	73	**2.6**
Denmark*	2000-2004	2,463	37	**1.5**	119	**4.8**	873	**35.4**	34	**1.4**	161	**6.5**	239	**9.7**	10	**0.4**	21	**0.9**	39	**1.6**	32	**1.3**	898	**36.5**
	2005-2009	2,962	49	**1.7**	166	**5.6**	1,114	**37.6**	31	**1.0**	97	**3.3**	266	**9.0**	7	**0.2**	17	**0.6**	16	**0.5**	32	**1.1**	1,167	**39.4**
	2010-2014	3,186	28	**0.9**	148	**4.6**	1,355	**42.5**	30	**0.9**	72	**2.3**	164	**5.1**	12	**0.4**	18	**0.6**	25	**0.8**	16	**0.5**	1,318	**41.4**
Estonia*	2000-2004	316	3	**0.9**	72	**22.8**	191	**60.4**	11	**3.5**	4	**1.3**	23	**7.3**	2	**0.6**	4	**1.3**	1	**0.3**	4	**1.3**	1	**0.3**
	2005-2009	329	8	**2.4**	70	**21.3**	180	**54.7**	12	**3.6**	5	**1.5**	40	**12.2**	2	**0.6**	3	**0.9**	4	**1.2**	3	**0.9**	2	**0.6**
	2010-2014	202	2	**1.0**	34	**16.8**	124	**61.4**	3	**1.5**	3	**1.5**	21	**10.4**	2	**1.0**	7	**3.5**	-	**-**	5	**2.5**	1	**0.5**
Finland*	2000-2004	1,317	29	**2.2**	133	**10.1**	629	**47.8**	64	**4.9**	145	**11.0**	201	**15.3**	1	**0.1**	14	**1.1**	30	**2.3**	52	**3.9**	19	**1.4**
	2005-2009	1,505	54	**3.6**	114	**7.6**	759	**50.4**	50	**3.3**	164	**10.9**	252	**16.7**	-	**-**	16	**1.1**	34	**2.3**	55	**3.7**	7	**0.5**
	2010-2014	1,658	54	**3.3**	94	**5.7**	894	**53.9**	59	**3.6**	128	**7.7**	276	**16.6**	1	**0.1**	14	**0.8**	59	**3.6**	65	**3.9**	14	**0.8**
France	2000-2004	2,342	34	**1.5**	118	**5.0**	1,178	**50.3**	35	**1.5**	102	**4.4**	620	**26.5**	23	**1.0**	12	**0.5**	156	**6.7**	43	**1.8**	21	**0.9**
	2005-2009	3,049	70	**2.3**	104	**3.4**	1,790	**58.7**	41	**1.3**	46	**1.5**	741	**24.3**	35	**1.1**	13	**0.4**	140	**4.6**	61	**2.0**	8	**0.3**
	2010-2014	661	14	**2.1**	13	**2.0**	433	**65.5**	7	**1.1**	5	**0.8**	138	**20.9**	6	**0.9**	2	**0.3**	19	**2.9**	22	**3.3**	2	**0.3**
Germany	2000-2004	6,733	92	**1.4**	812	**12.1**	4,302	**63.9**	88	**1.3**	470	**7.0**	552	**8.2**	14	**0.2**	61	**0.9**	163	**2.4**	44	**0.7**	135	**2.0**
	2005-2009	9,547	129	**1.4**	1,150	**12.0**	6,480	**67.9**	119	**1.2**	554	**5.8**	630	**6.6**	17	**0.2**	65	**0.7**	151	**1.6**	72	**0.8**	180	**1.9**
	2010-2014	8,685	147	**1.7**	857	**9.9**	6,289	**72.4**	92	**1.1**	344	**4.0**	570	**6.6**	17	**0.2**	42	**0.5**	121	**1.4**	83	**1.0**	123	**1.4**
Gibraltar*	2000-2004	3	-	**-**	-	**-**	2	**66.7**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**33.3**	-	**-**	-	**-**
	2005-2009	7	-	**-**	1	**14.3**	4	**57.1**	-	**-**	1	**14.3**	-	**-**	-	**-**	-	**-**	1	**14.3**	-	**-**	-	**-**
Iceland*	2000-2004	106	1	**0.9**	8	**7.5**	49	**46.2**	9	**8.5**	7	**6.6**	6	**5.7**	-	**-**	-	**-**	4	**3.8**	1	**0.9**	21	**19.8**
	2005-2009	123	1	**0.8**	8	**6.5**	61	**49.6**	2	**1.6**	8	**6.5**	13	**10.6**	-	**-**	2	**1.6**	-	**-**	1	**0.8**	27	**22.0**
	2010-2014	106	1	**0.9**	7	**6.6**	52	**49.1**	2	**1.9**	15	**14.2**	4	**3.8**	1	**0.9**	-	**-**	2	**1.9**	-	**-**	22	**20.8**
Ireland*	2000-2004	947	12	**1.3**	135	**14.3**	507	**53.5**	30	**3.2**	91	**9.6**	101	**10.7**	1	**0.1**	16	**1.7**	19	**2.0**	11	**1.2**	24	**2.5**
	2005-2009	1,141	16	**1.4**	112	**9.8**	650	**57.0**	32	**2.8**	96	**8.4**	150	**13.1**	2	**0.2**	10	**0.9**	19	**1.7**	34	**3.0**	20	**1.8**
	2010-2014	1,049	22	**2.1**	92	**8.8**	594	**56.6**	30	**2.9**	64	**6.1**	183	**17.4**	1	**0.1**	5	**0.5**	12	**1.1**	28	**2.7**	18	**1.7**
Italy	2000-2004	9,016	138	**1.5**	693	**7.7**	3,076	**34.1**	63	**0.7**	232	**2.6**	457	**5.1**	41	**0.5**	34	**0.4**	642	**7.1**	43	**0.5**	3,597	**39.9**
	2005-2009	13,345	162	**1.2**	910	**6.8**	4,824	**36.1**	118	**0.9**	359	**2.7**	758	**5.7**	34	**0.3**	88	**0.7**	871	**6.5**	129	**1.0**	5,092	**38.2**
	2010-2014	5,195	96	**1.8**	391	**7.5**	1,844	**35.5**	68	**1.3**	102	**2.0**	292	**5.6**	22	**0.4**	36	**0.7**	329	**6.3**	74	**1.4**	1,941	**37.4**
Latvia*	2000-2004	721	7	**1.0**	89	**12.3**	114	**15.8**	-	**-**	79	**11.0**	22	**3.1**	4	**0.6**	7	**1.0**	38	**5.3**	9	**1.2**	352	**48.8**
	2005-2009	906	7	**0.8**	95	**10.5**	296	**32.7**	3	**0.3**	72	**7.9**	23	**2.5**	1	**0.1**	12	**1.3**	16	**1.8**	4	**0.4**	377	**41.6**
	2010-2014	889	14	**1.6**	46	**5.2**	292	**32.8**	-	**-**	68	**7.6**	33	**3.7**	-	**-**	8	**0.9**	12	**1.3**	3	**0.3**	413	**46.5**

Table 3.2. Histology distribution, by continent, country and calendar period. Adults (15-99 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Lithuania*	2000-2004	858	15	**1.7**	53	**6.2**	500	**58.3**	6	**0.7**	194	**22.6**	71	**8.3**	-	**-**	3	**0.3**	6	**0.7**	10	**1.2**	-	**-**
	2005-2009	938	18	**1.9**	75	**8.0**	633	**67.5**	6	**0.6**	118	**12.6**	66	**7.0**	-	**-**	3	**0.3**	9	**1.0**	7	**0.7**	3	**0.3**
	2010-2014	575	9	**1.6**	76	**13.2**	388	**67.5**	13	**2.3**	28	**4.9**	34	**5.9**	1	**0.2**	5	**0.9**	7	**1.2**	12	**2.1**	2	**0.3**
Malta*	2000-2004	104	2	**1.9**	15	**14.4**	30	**28.8**	4	**3.8**	4	**3.8**	2	**1.9**	1	**1.0**	-	**-**	7	**6.7**	1	**1.0**	38	**36.5**
	2005-2009	98	1	**1.0**	19	**19.4**	22	**22.4**	2	**2.0**	8	**8.2**	2	**2.0**	-	**-**	-	**-**	17	**17.3**	3	**3.1**	24	**24.5**
	2010-2014	106	3	**2.8**	25	**23.6**	42	**39.6**	1	**0.9**	7	**6.6**	4	**3.8**	-	**-**	-	**-**	8	**7.5**	-	**-**	16	**15.1**
Netherlands*	2000-2004	5,059	110	**2.2**	775	**15.3**	2,220	**43.9**	138	**2.7**	42	**0.8**	525	**10.4**	9	**0.2**	40	**0.8**	110	**2.2**	97	**1.9**	993	**19.6**
	2005-2009	5,737	108	**1.9**	698	**12.2**	2,925	**51.0**	125	**2.2**	37	**0.6**	581	**10.1**	13	**0.2**	51	**0.9**	89	**1.6**	135	**2.4**	975	**17.0**
	2010-2014	6,033	114	**1.9**	701	**11.6**	3,373	**55.9**	159	**2.6**	27	**0.4**	481	**8.0**	12	**0.2**	35	**0.6**	108	**1.8**	152	**2.5**	871	**14.4**
Norway*	2000-2004	1,579	37	**2.3**	162	**10.3**	808	**51.2**	45	**2.8**	59	**3.7**	202	**12.8**	2	**0.1**	12	**0.8**	84	**5.3**	40	**2.5**	128	**8.1**
	2005-2009	1,762	58	**3.3**	171	**9.7**	943	**53.5**	53	**3.0**	68	**3.9**	187	**10.6**	-	**-**	7	**0.4**	114	**6.5**	56	**3.2**	105	**6.0**
	2010-2014	1,920	61	**3.2**	218	**11.4**	1,083	**56.4**	59	**3.1**	46	**2.4**	185	**9.6**	1	**0.1**	15	**0.8**	83	**4.3**	46	**2.4**	123	**6.4**
Poland*	2000-2004	6,297	147	**2.3**	1,073	**17.0**	2,556	**40.6**	69	**1.1**	768	**12.2**	893	**14.2**	73	**1.2**	91	**1.4**	370	**5.9**	71	**1.1**	186	**3.0**
	2005-2009	8,068	192	**2.4**	1,317	**16.3**	4,060	**50.3**	117	**1.5**	535	**6.6**	1,052	**13.0**	109	**1.4**	92	**1.1**	384	**4.8**	40	**0.5**	170	**2.1**
	2010-2014	8,577	224	**2.6**	1,305	**15.2**	4,790	**55.8**	139	**1.6**	355	**4.1**	911	**10.6**	81	**0.9**	103	**1.2**	423	**4.9**	67	**0.8**	179	**2.1**
Portugal*	2000-2004	1,971	28	**1.4**	195	**9.9**	963	**48.9**	45	**2.3**	176	**8.9**	388	**19.7**	10	**0.5**	28	**1.4**	65	**3.3**	8	**0.4**	65	**3.3**
	2005-2009	2,841	32	**1.1**	230	**8.1**	1,472	**51.8**	33	**1.2**	158	**5.6**	619	**21.8**	24	**0.8**	28	**1.0**	69	**2.4**	32	**1.1**	144	**5.1**
	2010-2014	1,876	27	**1.4**	153	**8.2**	1,131	**60.3**	47	**2.5**	62	**3.3**	292	**15.6**	6	**0.3**	15	**0.8**	47	**2.5**	28	**1.5**	68	**3.6**
Romania	2005-2009	129	3	**2.3**	18	**14.0**	62	**48.1**	1	**0.8**	7	**5.4**	10	**7.8**	4	**3.1**	-	**-**	4	**3.1**	1	**0.8**	19	**14.7**
	2010-2014	150	5	**3.3**	21	**14.0**	72	**48.0**	3	**2.0**	8	**5.3**	17	**11.3**	1	**0.7**	-	**-**	1	**0.7**	3	**2.0**	19	**12.7**
Russian Federation	2000-2004	451	8	**1.8**	43	**9.5**	148	**32.8**	2	**0.4**	160	**35.5**	29	**6.4**	1	**0.2**	14	**3.1**	8	**1.8**	10	**2.2**	28	**6.2**
	2005-2009	1,048	15	**1.4**	165	**15.7**	292	**27.9**	42	**4.0**	280	**26.7**	64	**6.1**	1	**0.1**	18	**1.7**	48	**4.6**	10	**1.0**	113	**10.8**
	2010-2014	1,331	21	**1.6**	239	**18.0**	477	**35.8**	15	**1.1**	334	**25.1**	83	**6.2**	-	**-**	30	**2.3**	65	**4.9**	12	**0.9**	55	**4.1**
Slovakia*	2000-2004	1,299	37	**2.8**	317	**24.4**	427	**32.9**	53	**4.1**	27	**2.1**	85	**6.5**	13	**1.0**	21	**1.6**	21	**1.6**	8	**0.6**	290	**22.3**
	2005-2009	1,840	51	**2.8**	318	**17.3**	651	**35.4**	61	**3.3**	77	**4.2**	119	**6.5**	17	**0.9**	22	**1.2**	54	**2.9**	24	**1.3**	446	**24.2**
	2010-2014	408	9	**2.2**	81	**19.9**	170	**41.7**	2	**0.5**	13	**3.2**	16	**3.9**	3	**0.7**	8	**2.0**	11	**2.7**	1	**0.2**	94	**23.0**
Slovenia*	2000-2004	483	2	**0.4**	44	**9.1**	308	**63.8**	25	**5.2**	2	**0.4**	62	**12.8**	10	**2.1**	7	**1.4**	10	**2.1**	5	**1.0**	8	**1.7**
	2005-2009	540	6	**1.1**	64	**11.9**	370	**68.5**	17	**3.1**	2	**0.4**	45	**8.3**	4	**0.7**	7	**1.3**	17	**3.1**	8	**1.5**	-	**-**
	2010-2014	471	6	**1.3**	42	**8.9**	337	**71.5**	9	**1.9**	-	**-**	54	**11.5**	2	**0.4**	2	**0.4**	16	**3.4**	3	**0.6**	-	**-**
Spain	2000-2004	2,273	53	**2.3**	375	**16.5**	1,056	**46.5**	51	**2.2**	123	**5.4**	165	**7.3**	23	**1.0**	18	**0.8**	236	**10.4**	36	**1.6**	137	**6.0**
	2005-2009	2,641	61	**2.3**	440	**16.7**	1,258	**47.6**	58	**2.2**	100	**3.8**	208	**7.9**	22	**0.8**	34	**1.3**	261	**9.9**	50	**1.9**	149	**5.6**
	2010-2014	1,588	38	**2.4**	233	**14.7**	889	**56.0**	29	**1.8**	44	**2.8**	111	**7.0**	9	**0.6**	17	**1.1**	134	**8.4**	42	**2.6**	42	**2.6**
Sweden*	2000-2004	2,522	64	**2.5**	456	**18.1**	1,013	**40.2**	66	**2.6**	218	**8.6**	235	**9.3**	-	**-**	42	**1.7**	109	**4.3**	53	**2.1**	266	**10.5**
	2005-2009	2,966	64	**2.2**	222	**7.5**	1,501	**50.6**	48	**1.6**	249	**8.4**	333	**11.2**	-	**-**	44	**1.5**	69	**2.3**	53	**1.8**	383	**12.9**
	2010-2014	3,404	82	**2.4**	205	**6.0**	1,828	**53.7**	60	**1.8**	211	**6.2**	400	**11.8**	-	**-**	34	**1.0**	69	**2.0**	70	**2.1**	445	**13.1**

Table 3.2. Histology distribution, by continent, country and calendar period. Adults (15-99 years) diagnosed with a brain tumour, 2000-2014.

Country	Period of diagnosis	All tumour types combined	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Switzerland	2000-2004	1,084	29	**2.7**	163	**15.0**	619	**57.1**	25	**2.3**	18	**1.7**	116	**10.7**	11	**1.0**	4	**0.4**	22	**2.0**	30	**2.8**	47	**4.3**
	2005-2009	1,303	40	**3.1**	153	**11.7**	787	**60.4**	27	**2.1**	20	**1.5**	132	**10.1**	16	**1.2**	14	**1.1**	17	**1.3**	34	**2.6**	63	**4.8**
	2010-2014	1,265	50	**4.0**	122	**9.6**	770	**60.9**	35	**2.8**	11	**0.9**	116	**9.2**	6	**0.5**	18	**1.4**	31	**2.5**	41	**3.2**	65	**5.1**
United Kingdom*	2000-2004	20,587	299	**1.5**	1,566	**7.6**	9,214	**44.8**	267	**1.3**	1,129	**5.5**	1,487	**7.2**	26	**0.1**	113	**0.5**	2,606	**12.7**	202	**1.0**	3,678	**17.9**
	2005-2009	22,152	334	**1.5**	1,648	**7.4**	11,463	**51.7**	320	**1.4**	554	**2.5**	1,634	**7.4**	25	**0.1**	114	**0.5**	2,464	**11.1**	258	**1.2**	3,338	**15.1**
	2010-2014	24,538	375	**1.5**	1,880	**7.7**	13,542	**55.2**	402	**1.6**	349	**1.4**	1,649	**6.7**	25	**0.1**	111	**0.5**	2,432	**9.9**	390	**1.6**	3,383	**13.8**
Oceania	2000-2004	7,602	114	**1.5**	830	**10.9**	4,343	**57.1**	72	**0.9**	375	**4.9**	807	**10.6**	11	**0.1**	53	**0.7**	398	**5.2**	47	**0.6**	552	**7.3**
	2005-2009	8,453	135	**1.6**	792	**9.4**	5,196	**61.5**	64	**0.8**	304	**3.6**	863	**10.2**	12	**0.1**	57	**0.7**	353	**4.2**	86	**1.0**	591	**7.0**
	2010-2014	8,281	134	**1.6**	741	**8.9**	5,359	**64.7**	76	**0.9**	190	**2.3**	800	**9.7**	23	**0.3**	46	**0.6**	322	**3.9**	104	**1.3**	486	**5.9**
Australia*	2000-2004	6,463	99	**1.5**	691	**10.7**	3,713	**57.5**	55	**0.9**	340	**5.3**	696	**10.8**	11	**0.2**	44	**0.7**	312	**4.8**	42	**0.6**	460	**7.1**
	2005-2009	7,277	124	**1.7**	655	**9.0**	4,450	**61.2**	61	**0.8**	292	**4.0**	755	**10.4**	11	**0.2**	47	**0.6**	303	**4.2**	82	**1.1**	497	**6.8**
	2010-2014	6,884	118	**1.7**	574	**8.3**	4,422	**64.2**	67	**1.0**	180	**2.6**	702	**10.2**	22	**0.3**	42	**0.6**	237	**3.4**	97	**1.4**	423	**6.1**
New Zealand*	2000-2004	1,139	15	**1.3**	139	**12.2**	630	**55.3**	17	**1.5**	35	**3.1**	111	**9.7**	-	**-**	9	**0.8**	86	**7.6**	5	**0.4**	92	**8.1**
	2005-2009	1,176	11	**0.9**	137	**11.6**	746	**63.4**	3	**0.3**	12	**1.0**	108	**9.2**	1	**0.1**	10	**0.9**	50	**4.3**	4	**0.3**	94	**8.0**
	2010-2014	1,397	16	**1.1**	167	**12.0**	937	**67.1**	9	**0.6**	10	**0.7**	98	**7.0**	1	**0.1**	4	**0.3**	85	**6.1**	7	**0.5**	63	**4.5**

* Data with 100% coverage of the national population.

Preface to Research Papers 4 and 5

In chapter 3, I defined distinct histology groupings for brain tumours in children and adults. I then used these categories to examine the world-wide histology distribution of brain tumours. International differences in the histological make-up of brain tumours are sharp and data quality also varies widely (Girardi F et al., manuscript under review).

Because brain tumour subtypes have distinct clinical behaviour, international comparisons of survival for all brain tumours combined may be confounded when the histology distribution of brain tumours differs between countries. As a result, for comparisons of brain tumour survival to be robust, stratification by histology is required. For brain tumours, histology is key to the choice of treatment, so accurate monitoring of outcomes can only be possible if survival estimates by histology are available.

In chapters 4 and 5, I present a detailed, global analysis of brain tumour survival by histology. Chapter 4 is focussed on children, while chapter 5 is centred on adults. In summary, I analysed all brain tumours included in the CONCORD-3 database, using the same methods for both studies. I considered children (0-14 years) and adults (15-99 years) diagnosed with a brain tumour during 2000-2014, regardless of tumour behaviour. Data underwent a rigorous, three-phase quality control as part of CONCORD-3.[46] Data were analysed using the histology groupings defined in chapter 3.

I estimated net survival using the unbiased non-parametric Pohar Perme estimator.[62] Net survival is the cumulative probability for cancer patients to survive their cancer up to a given time since diagnosis (e.g. five years), after correcting for other causes of death (background mortality). Data on background mortality are derived from life tables of all-cause mortality by single year of age, sex and single calendar year, in the general population of each participating country or territory.[145]

The childhood study (chapter 4) includes data for 54,473 children. Age-standardised five-year net survival for low-grade astrocytoma ranged between 84% and 100% world-wide during 2000-2014. In most countries, five-year survival was 90%

or more during 2000-2004, 2005-2009 and 2010-2014. Global variation in survival for medulloblastoma was much wider than for low-grade astrocytoma, with age-standardised five-year net survival between 47% and 86% for children diagnosed during 2010-2014. Increasing trends in survival were observed in Eastern Europe for low-grade astrocytoma, and in Korea, Taiwan and the Netherlands for medulloblastoma.

The study in chapter 5 includes data for 556,237 adults. In 2010-2014, the global range in age-standardised five-year net survival for the most common subtypes was broad: in the range 20-38% for diffuse and anaplastic astrocytoma, from 4% to 17% for glioblastoma and between 32% and 69% for oligodendroglioma. For patients with glioblastoma, the largest gains in survival occurred between 2000-2004 and 2005-2009. These improvements were more noticeable among adults diagnosed aged 40-70 years than among younger adults (15-39 years).

To the best of my knowledge, these studies provide the largest account to date of global trends in population-based survival for brain tumours by histology, in children and adults. For children, I have implemented, for the first time in an international comparison of survival, a revised version of the International Classification of Childhood Cancer (3rd edition).[19] This new scheme controls for under-registration of non-malignant astrocytic tumours by stratifying on World Health Organization (WHO) grade: low-grade and high-grade. This strategy may have public health implications, because low-grade glioma (i.e. low-grade astrocytoma) is one of the six index childhood cancers included by WHO in the Global Initiative for Childhood Cancer, which is aimed at attaining a 60% survival for all children diagnosed with one of these cancer types by 2030.

In adults, I have highlighted the remarkable gains in five-year survival from glioblastoma since 2005, providing large-scale empirical evidence on the uptake of chemoradiation at population level. World-wide, survival improvements have been extensive, but some countries still lag behind. A breakdown of survival by age, the first to my knowledge, emphasises disparities in survival from glioblastoma between adolescents and young adults (15-39 years), and older adults. Further research is needed to explore whether hurdles to optimal cancer care may exist for these younger adults, who represent a vulnerable age group with distinct needs.

Research Papers 4 and 5 have been prepared, but not yet submitted for publication.

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed <u>for each</u> research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1701655	**Title**	Dr
First Name(s)	Fabio		
Surname/Family Name	Girardi		
Thesis Title	Global surveillance of survival from brain tumours diagnosed during 2000-2014: trends by age and histology		
Primary Supervisor	Dr Claudia Allemani		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	Neuro-Oncology
Please list the paper's authors in the intended authorship order:	Fabio Girardi, (additional authors), Veronica Di Carlo, Michel P Coleman, Claudia Allemani, CONCORD Working Group
Stage of publication	**Not yet submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Conception and design, data analysis and interpretation, manuscript writing

SECTION E

Student Signature	[redacted]
Date	7 December 2020

Supervisor Signature	[redacted]
Date	7 December 2020

Research Paper 4: global trends in survival from brain tumours in children (CONCORD-3)

World-wide trends in survival from brain tumours, by histology: analysis of individual records for 67,331 children diagnosed in 60 countries during 2000-2014 (CONCORD-3)

Introduction

Tumours of the central nervous system (CNS) rank second after leukaemia among the leading causes of cancer-related death in children.[1] CNS tumours may originate in the brain, the meninges or the spinal cord, but the brain is by far the most common site. The estimated age-standardised (world) incidence rate, in 2018, ranged from 1 per 100,000 person-years in Polynesia to 6.1 in Southern Europe.[72] Health care disparities, however, may lead to substantial under-diagnosis or under-registration. Up to 57% of childhood cancer diagnoses may be missed in Western Africa, compared with 3% in North America and Western Europe.[163]

Health care facilities are unevenly distributed world-wide.[74, 147, 164] In some countries, for instance, radiotherapy facilities are simply not available. Unmet opportunities for treatment due to sub-optimal access to care will translate to many years of life lost and extended periods of disability.[165] Given that only 10% of children live in high-income countries, the social burden of childhood cancer in low-income and middle-income countries is disproportionately great in countries that are generally least well equipped to deal with that burden.[76, 166]

Population-based survival is a key metric to evaluate the performance of the health care system in a given country in managing cancer.[47, 48, 167] In 2015, the CONCORD programme began global surveillance of trends in cancer survival with data for patients diagnosed during the 15-year period 1995-2009.[168] The third cycle (CONCORD-3), covering 71 countries, comprised more than 37 million patients diagnosed during 2000-2014 with one of 18 common cancer types, including childhood brain tumours.[46] Global differences in age-standardised five-year net survival for all

brain tumours combined were very wide, ranging between 29% in Brazil and 89% in Sweden.

Intrinsic brain tumours represent a disparate group of subtypes, with more than 50 histological entities.[7] Histology is an important determinant of outcome, so international comparisons in brain tumour survival can be more meaningful for health care planning if they account for histology. Survival estimates that take account of histology enable better interpretation of international differences in survival for all brain tumours combined, since these differences are confounded by the heterogeneity of clinical behaviour and the global variation in the distribution of histological types (Girardi F et al., Research Paper 3, under review).

The third edition of the International Classification of Childhood Cancer (ICCC-3) has become established as the standard tool for categorising childhood tumours by histology.[19] ICCC-3 is a scheme with three progressively more granular tiers. However, the third tier is not available for astrocytoma, so it is not possible to analyse low-grade and high-grade astrocytic tumours separately using data classified with ICCC-3, but alternative approaches are seldom used.[144] The third edition of the International Classification of Diseases for Oncology defines as non-malignant (ICD-O-3 behaviour code 0 or 1) most of the low-grade brain tumours, including pilocytic astrocytoma,[17] which alone comprises 70% of all childhood astrocytic tumours.[169]

This has important implications for international comparisons of brain tumour survival. Non-malignant tumours are not consistently recorded world-wide, due to differences in health regulations and cancer registration practice. Registration of non-malignant brain tumours is important because not only tumour behaviour, but also anatomical site, has an effect on diagnosis, treatment choices and outcome. As a result, World Health Organisation (WHO) grade must be incorporated in survival analyses for astrocytic tumours in children, because international comparisons are otherwise uninterpretable with data coded to ICCC-3, owing to the very different proportions of low-grade and high-grade astrocytic tumours in cancer registry data.

To date, studies of survival from childhood brain tumours by histology have not been readily comparable because of differences in study design, especially as to the inclusion or exclusion of non-malignant brain tumours.[144] Nearly all these studies have

been conducted in high-income countries. No data are currently available for Africa, Central and South America, and most of Asia.

We set out to conduct a world-wide study of population-based survival from childhood brain tumours, using data collected with a central protocol, checked for quality using standardised rules and analysed with the same robust statistical methods.

Methods

For CONCORD-3, individual tumour registrations for 71,040 children (0-14 years) diagnosed with a non-malignant or malignant brain tumour (ICD-O-3 topography code C71) during 2000-2014 were provided by 260 cancer registries in 60 countries.

Each tumour record was subjected to rigorous quality checks for eligibility and definite or possible errors.[54] Registrations based on a death certificate or autopsy, age out of range and those with invalid date sequences were excluded. Possible errors included implausible combinations of age, sex, site and morphology. Each registry was invited to confirm or refute records with possible errors.

The proportion of records with incomplete dates was less than 1% in North America, Asia, Europe and Oceania, 2.4% in Central and South America and 10.7% in Africa. Overall, children registered through a death certificate only (DCO) comprised 1.1% of all submissions. DCO proportions for Africa (6.8%) and Central and South America (5.9%) were higher than in other continents (2% or less). The proportion of brain tumours with a histological confirmation was generally high, in the range 88-97%. Brain tumours registered with a non-specific histology (ICD-O-3 morphology code 8000-8005) only represented 3.2% of all brain tumour diagnoses in North America, but they accounted for 26.3% of diagnoses in Africa (Table 4.1). Following quality checks, 67,331 (94.8%) records were retained for analysis.

We defined 12 histology groups, each comprising a set of relevant ICD-O-3 codes. The groups were based on ICCC-3, but we devised more granular categories for astrocytic tumours, and merged some entities within the embryonal tumour

category. The methodology and the principles for selecting the ICD-O-3 codes in each category are explained elsewhere (Girardi F et al., Research Paper 3, under review).

Net survival at five years after diagnosis was estimated using the unbiased, non-parametric Pohar Perme estimator.[62] Net survival is the cumulative probability for cancer patients to survive their cancer up to a given time since diagnosis (e.g. five years), after accounting for competing risks of death (background mortality). Data on background mortality are derived from life tables of all-cause mortality specific for single year of age, sex and single calendar year, in the general population of each participating country or territory.[145]

Survival was not estimated if fewer than ten patients were available for a given histology group, calendar period and country or region. If 10–49 patients were available, we produced unstandardised estimates of survival for all ages combined. We attempted age standardisation if 50 children or more were available. Standardisation was obtained by applying equal weights to the age-specific survival estimates for children aged 0-4, 5-9 and 10-14 years.[64] If a single age-specific estimate could not be computed, we pooled the records for two adjacent age groups and attributed the aggregated estimate to both age groups before age standardisation. We did not combine data for consecutive calendar periods.[46]

We used the cohort approach for patients diagnosed during 2000-2004 and 2005-2009, because at least five years of follow-up were available for all patients. For children diagnosed during 2010-2014, we adopted the period approach, since five years of follow-up were not available for most patients.[65, 68] The period approach allows estimation of five-year survival for patients diagnosed in 2010-2014 using the available follow-up data and the survival probabilities of patients diagnosed in previous years who are still alive at the beginning of 2010.

We produced five-year survival estimates for each histology group by country and calendar period. For selected tumour types, we also examined longer-term survival, up to 10 years from diagnosis.

We regarded survival estimates as less reliable if they were based on a cancer registry with 15% or more of patients registered with incomplete dates; or with a registration based solely on a death certificate or autopsy; or lost to follow-up or

censored alive within five years. Unreliable estimates were not included in pooled national survival estimates unless they were the only estimates available from that country, in which case the estimate is flagged.

Results

Children potentially eligible for survival analyses were 67,331. We excluded 6,548 (9.7%) records of tumours that were otherwise eligible for inclusion in the survival analyses because the morphology code did not fall within the histology groups selected for this study. We also excluded 6,310 (9.4%) records from 57 registries for which survival estimates were deemed less reliable. The analyses included 54,473 tumour records (80.9% of eligible submissions).

Our comments are focussed on reliable, age-standardised survival estimates. When examining time trends, we only considered countries for which reliable, age-standardised survival estimates were available for 2000-2004, 2005-2009 and 2010-2014. For each continent, countries are listed in alphabetical order. Trends in survival for the 12 histology groupings in successive five-year calendar periods are presented in Table 4.2.

Data for ependymoma were scanty (2,685 records). Age-standardised five-year net survival for children diagnosed during 2010-2014 was 54.0% in Turkey, 59.7% in Korea, 79.3% in Poland and in the range 80-90% in the United States, France, Italy and the United Kingdom. (Table 4.2).

For low-grade astrocytomas (WHO grade I and II), age-standardised five-year net survival during 2010-2014 was in the range 80-89% in Taiwan, Turkey and Spain; 90-94% in eight of 20 European countries (Belarus, Belgium, France, Greece, Italy, the Netherlands, Slovakia and Switzerland) and in Australia. Survival was highest (95-100%) in Canada, the United States, Israel, Japan, two Eastern European countries (Czech Republic and Poland), Germany, six Northern European countries (Denmark, Finland, Ireland, Norway, Sweden and the United Kingdom), and Portugal. (Table 4.2, Figure 4.1).

For children diagnosed with a low-grade astrocytoma during the 15 years between 2000 and 2014, age-standardised five-year net survival remained above

90%, and largely unchanged, in North America, Israel, Northern Europe (Finland, Sweden and the United Kingdom), Western Europe (France, the Netherlands and Switzerland) and Italy. Survival in Spain, above 90% during 2000-2004, later subsided to level off in the range 85-90%. Marked survival improvements occurred in Eastern Europe: survival rose from 78.1% to 92.4% in Belarus and from 86.5% to 95.1% in Poland. Survival in Australia, around 87% during 2000-2009, reached 90.9% during 2010-2014 (Table 4.2 and Figure 4.2).

Outcomes for high-grade astrocytomas (WHO grade III and IV) were rather poor. Reliable, age-standardised estimates were only available for eight countries. Five-year survival during 2010-2014 was 6.3% in France, 17.1% in the United Kingdom, in the range 20-29% in the United States, Korea, Taiwan, Italy and Australia; and 31.2% in Poland (Table 4.2). In recent years, molecular biology has been implemented at neuro-pathology level to correctly identify astrocytic tumours with more aggressive behaviour. The relatively broad variation in survival suggests that in some countries these strategies may have been implemented earlier than elsewhere.

In the CONCORD-3 data for children diagnosed with a brain tumour during 2000-2014, malignant tumours (ICD-O-3 behaviour code 3) accounted for 80% of all tumour records in Australia (but 100% in New South Wales, which comprises 45% of the national population), and the totality of cases in Korea, Taiwan and New Zealand (data not shown).

Wide variation in survival was seen for medulloblastoma, the most common embryonal CNS tumour. Age-standardised five-year net survival between 2010 and 2014 was less than 50% in Belarus and Spain; it ranged between 50% and 59% in Turkey and Greece; between 60% and 69% in Taiwan and seven of 20 European countries (Belgium, France, Italy, the Netherlands, Poland, Switzerland and the United Kingdom). Survival was in the range 70-79% in Canada, the United States, Japan, Korea, Denmark, Germany and Australia. The highest survival was observed in Israel (81.0%), Portugal (80.6%) and Sweden (88.0%) (Table 4.2 and Figure 4.1).

Fifteen-year trends in age-standardised five-year net survival from medulloblastoma were only available for nine countries. Survival was stable, or fluctuating slightly, in Poland (in the range 55-60%), in France, Italy and Australia (64-

72%), and in the United States (70-75%). Survival from medulloblastoma rose from 60.5% to 70.0% in Korea, from 56.4% to 62.7% in Taiwan, and from 51.8% to 63.3% in the Netherlands, while it fell from 68.8% to 61.5% in the United Kingdom (Table 4.2 and Figure 4.2).

The subgroup “other and unspecified embryonal tumours” includes some rare entities, such as primitive neuroectodermal tumour and atypical teratoid/rhabdoid tumour. Age-standardised five-year net survival (2010-2014) ranged between 30% and 39% in Canada and Israel; between 40% and 49% in Japan, Taiwan, Turkey, France, the Netherlands and Australia, and between 50% and 59% in the United States, Korea, Poland, Sweden and the United Kingdom. Survival was 65.6% in Belgium, 83.5% in Germany and 84.5% in Germany (Table 4.2).

Age-standardised five-year net survival for children diagnosed during 2010-2014 with glioma, otherwise unspecified (ICD-O-3 morphology code 9380/3) varied between 30% and 39% in Japan, France, the Netherlands and Australia; between 40% and 49% in Canada, Korea, Turkey and the United Kingdom, and in the range 50-61% in the United States, Israel, Belgium and Italy (Table 4.2).

During 2010-2014, at least 10 children were diagnosed with a brain tumour labelled as unspecified (ICD-O-3 morphology codes 8000-8005) in 21 of 45 countries from which suitable data were available. Variation in age-standardised five-year net survival for these poorly specified neoplasms was remarkable: 35.8% in China, 58.5% in Korea, 72.3% in Italy, 77.9% in the United Kingdom and in the range 80-89% in the United States, Japan, Turkey, Denmark and Australia (Table 4.2).

Discussion

To our knowledge, this is the largest study on survival from childhood brain tumours to date. Individual records for over 50,000 children were collected from 260 population-based cancer registries in 60 countries using a central protocol and the same rigorous quality checks, and analysed with the same, robust statistical methodology.

Age-standardised five-year net survival for low-grade astrocytoma (WHO grade I and II) was 90% or more during the whole period between 2000 and 2014 in most

countries. World-wide variation in survival for medulloblastoma was much more broad than for low-grade astrocytoma, with age-standardised five-year net survival in the range 47-86% during 2010-2014.

Most previous international comparisons of survival from childhood brain tumours, in compliance with ICCC-3, adopted the broad definition “astrocytoma”.[69, 78, 83, 87, 144] Such survival estimates cannot be safely compared with those presented here, since we did not merge low-grade and high-grade astrocytic tumours.

More than two-thirds of childhood low-grade tumours are pilocytic astrocytomas.[169] ICD-O-3 classifies pilocytic astrocytoma as a non-malignant entity (ICD-O-3 behaviour code 1).[17] In the fourth cycle of the European cancer registry based study on survival and care of cancer patients (EUROCARE-4), during 1995-1999, five-year observed survival for astrocytoma (broad group) was rather poor in Eastern Europe, around 60%, irrespective of exclusion of non-malignant tumours, and lower than in other European regions. These findings suggest under-registration of non-malignant brain tumours.[87] In EUROCARE-5, survival from childhood brain tumours was presented for malignant tumours only, but this design is not consistent with the histology distribution of childhood brain tumours.[69] Alternatively, EUROCARE-5 provided survival estimates for the whole of Europe combined, by single ICD-O-3 morphology code, but this more granular approach cannot be readily implemented in large international comparisons of survival by histology.[9]

Non-malignant tumours are recorded inconsistently, not only in Europe, but world-wide. For instance, health regulations in New South Wales mandate registration of malignant tumours only, while Ecuador started recording non-malignant tumours only from 2010. If these international differences in cancer registration practices are not properly considered, global disparities in survival for all astrocytic tumours may be wrongly interpreted. Survival in countries or regions that only include malignant brain tumours will be systematically lower in countries where non-malignant tumours are also registered. We conducted a sensitivity analysis. Age-standardised five-year net survival for all astrocytic tumours combined (ICCC-3 category) ranged from 43% to 88% world-wide during 2010-2014 (Supplementary Table 1). By contrast, survival was in the range 84-100% for low-grade tumours and in the range 6-30% for high-grade tumours. The remarkable reduction in global disparities in survival with the more

granular categories confirms that international comparisons of survival for astrocytic tumours should take account of confounding by tumour grade. Where possible, estimates for low-grade and high-grade tumours should be reported separately.

Five-year survival for medulloblastoma during 2010-2014 was in the range 70-80% in several affluent countries. These values were in line with those from recent national studies assessing survival for 2000-2010 or so in Germany (72-80%) and the United States (72-80%), but higher than the survival levels for the 1990s.[9, 69, 91, 94, 99-105, 108-111, 144] This may reflect recent advances in treatment protocols for children with medulloblastoma that revolve around two main pillars: reduction of the radiotherapy dose to minimise long-term neurological sequelae, and treatment intensification only for high-risk patients.[27] Other reasons for these survival gains may be the implementation of volumetric radiotherapy, better surgery with removal of larger tumour volumes and fewer complications, and more timely referral for post-surgical treatment.[27, 170] However, the wide global inequalities in survival strongly suggest that in some countries, children may still not have access to optimal treatment for medulloblastoma.

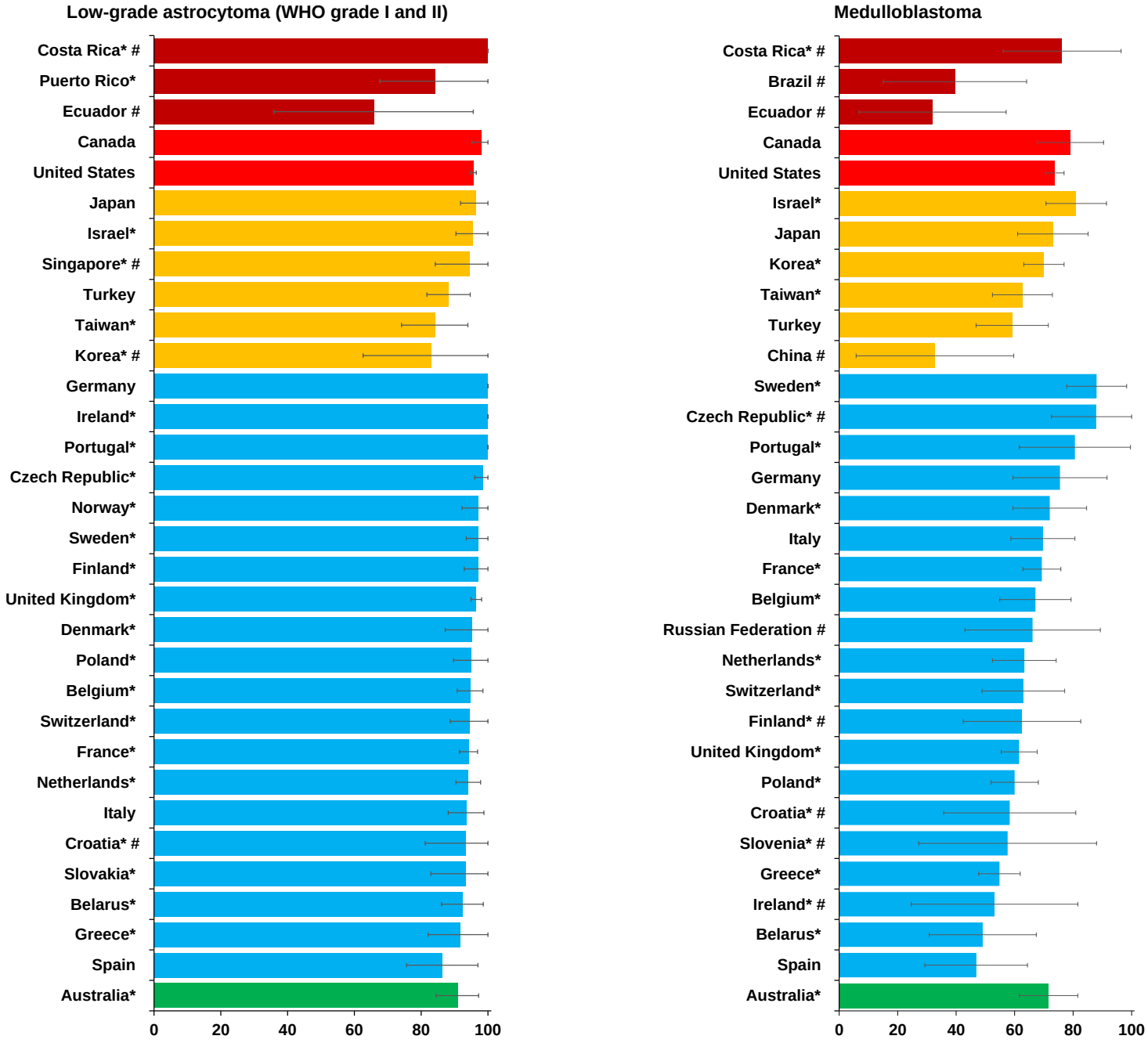
Most childhood brain tumour subtypes have a favourable outcome, but timely surveillance for relapse and survivorship care are both crucial.[171] We assessed survival at 10 years for low-grade astrocytoma and medulloblastoma during 2000-2004 (Supplementary Table 2). For low-grade astrocytoma, age-standardised ten-year survival and five-year survival differed by less than 3% in 10 of the 14 countries for which suitable data were available, while reductions were slightly larger (3% or more) in Argentina, Taiwan, Belarus and Australia. The absolute difference between five-year and 10-year net survival for medulloblastoma was in the range 0-4% in Argentina, the United States, Korea, Italy, the Netherlands and Australia, but in the range 6-10% in Israel, Taiwan, France, Poland and the United Kingdom. These findings should be interpreted with caution, because the changes are still small. However, it would seem that net survival tends to plateau after five years in some countries, suggesting low excess mortality among survivors to that point, whereas in other countries, brain tumour survivors may continue to be at higher long-term risk of death than children in the general population.

Up to two-thirds of pilocytic astrocytomas originate in the cerebellum. The most common supra-tentorial sites are the optic nerve and the optic chiasm. When pilocytic astrocytoma involves the optic pathways, it is also called “optic nerve glioma”.[7] These tumours are usually not biopsied, because of the high risk of visual loss, and the diagnosis is made through a combination of imaging and testing of the visual fields. These tumours may be thus labelled in the cancer registry with the ICD-O-3 descriptor “glioma not otherwise specified (NOS)” (ICD-O-3 morphology code 9380/3).[9] CONCORD-3 only collected information for tumours originating in the brain. Nevertheless, we cannot exclude that, given the close anatomical proximity, some optic nerve gliomas may have been submitted with the ICD-O-3 topography code used for brain (C71), instead of the code for optic pathways (C75.2). We considered that some of the gliomas NOS might in fact have been pilocytic astrocytomas of the optic pathways, but the data did not support this hypothesis. Five-year survival for unspecified glioma was much lower than for pilocytic astrocytoma, and for 87% of these records, the tumour grade was unspecified (6th digit 9), so we could not confirm the non-malignant behaviour.

The Lancet Oncology Commission on Sustainable Care for Children with Cancer has recently presented evidence for the implementation of cost-effective interventions to reduce the clinical and economic burden of childhood cancer.[172] The evidence included projections of survival for children diagnosed during 2015-2019, by histology, for over 200 countries and territories. Survival was modelled from CONCORD-3 estimates for 2000-2014. The commission adopted ICCC-3 to classify childhood tumours, so it could not present any data for low-grade astrocytoma. This was also a major limitation of the Global Burden of Disease study, that could not account for histology because it was based on topography descriptors from the International Classification of Diseases (ICD).[76, 165] In this thesis, we have presented, for the first time to our knowledge, survival estimates for low-grade astrocytoma at global level. In the US CONCORD data set, where registration of non-malignant tumours is statutory,[149] low-grade astrocytomas accounted for 63.7% of all low-grade gliomas during 2000-2014. If the revised ICCC-3 framework proposed in this thesis were to be widely adopted, survival estimates from low-grade astrocytoma may represent a suitable surrogate for survival from low-grade glioma.

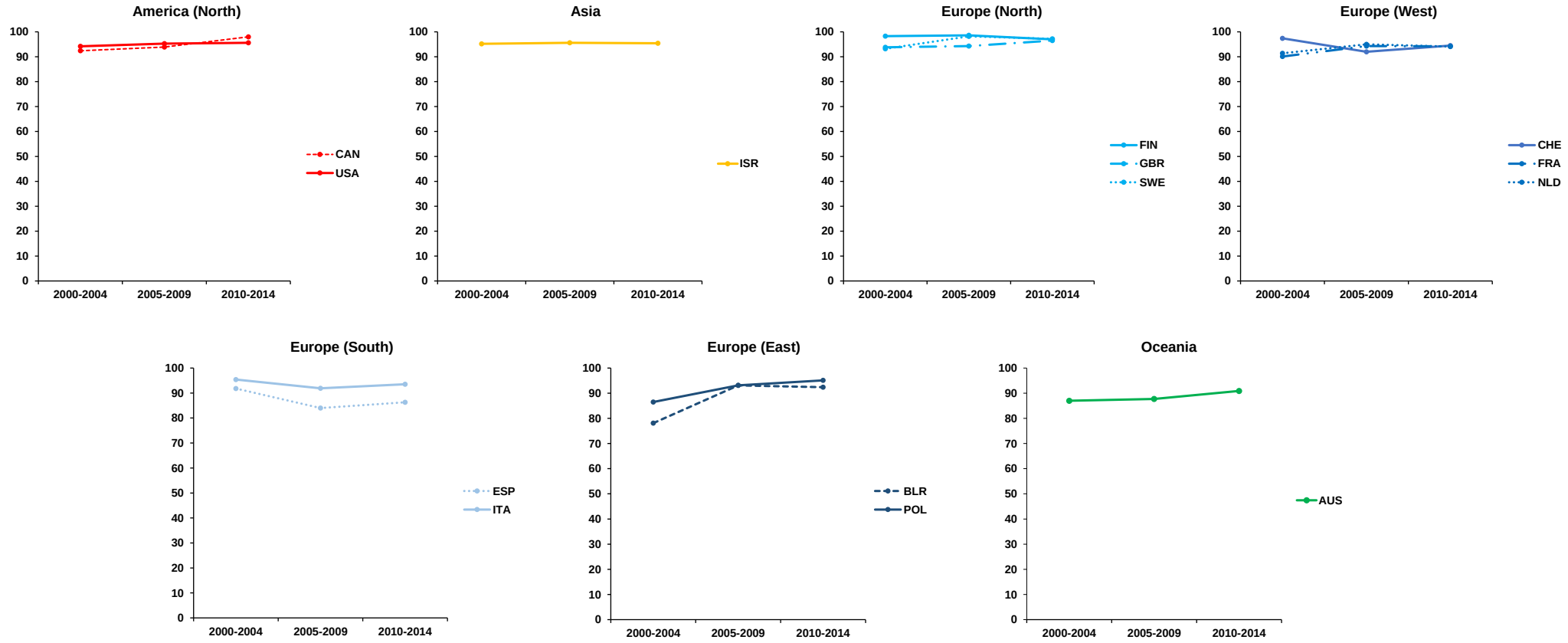
The WHO Global Initiative for Childhood Cancer aims to attain five-year survival of 60% for six types of childhood cancer combined by 2030.[127] Low-grade glioma is one of these six cancers. Here we provide a methodological framework for future global survival comparisons, in which it will be important to include data from more low-income and middle-income countries. Those studies will be instrumental for monitoring progress toward the global targets for better control of childhood cancer.

Figure 4.1. Age-standardised five-year net survival (%) with 95% confidence interval, by country. Children (0-14 years) diagnosed with low-grade astrocytoma or medulloblastoma during 2010-2014.



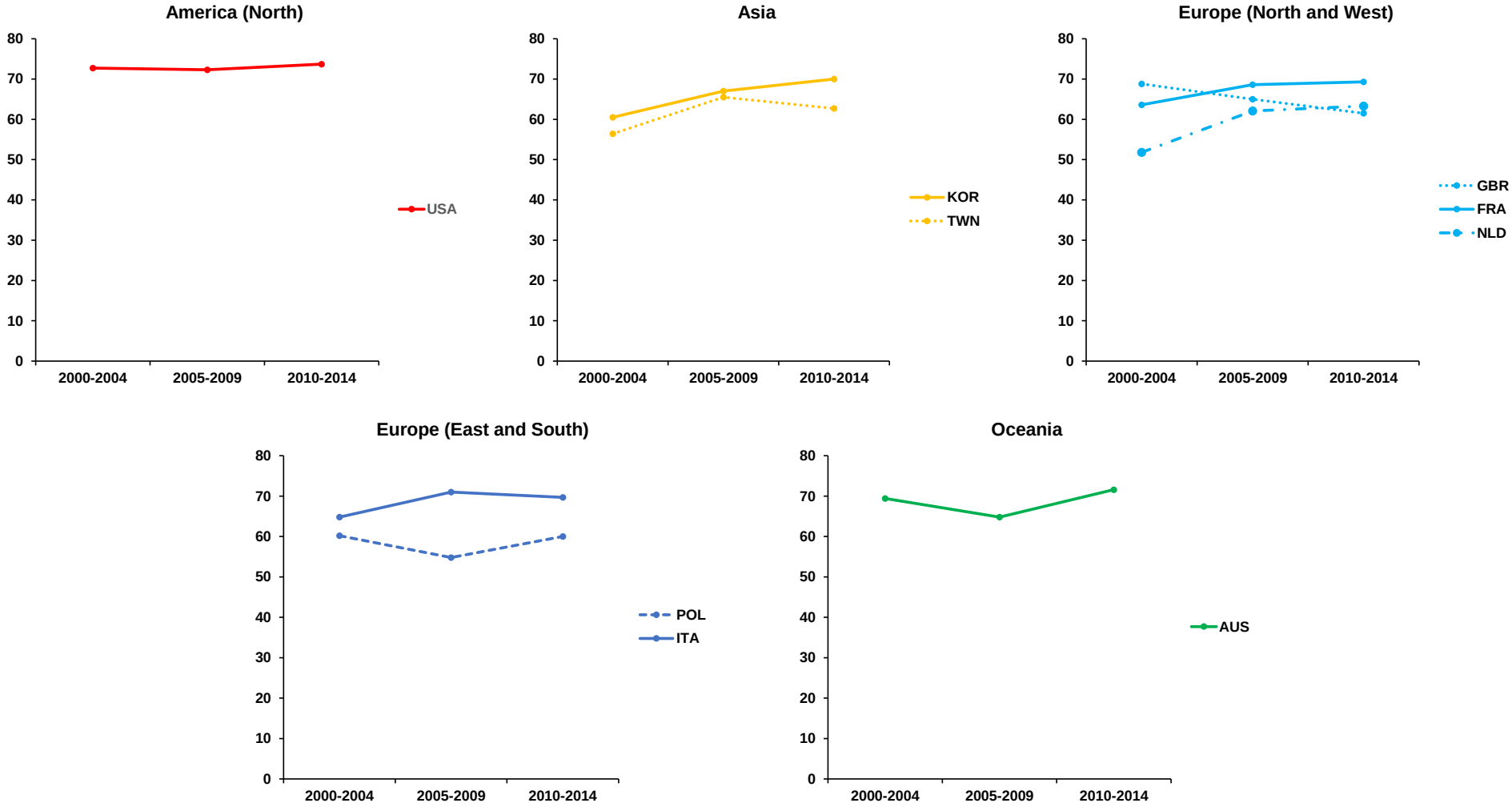
* Countries with 100% coverage of the national population. # Survival estimates are not age-standardised. X-axis: age-standardised five-year net survival.

Figure 4.2. Trends in age-standardised five-year net survival (%) from WHO grade I and II astrocytoma, 2000-2014, by world region. Children (0-14 years).



Countries were included if age-standardised survival estimates were available for patients diagnosed during 2000-2004, 2005-2009 and 2010-2014. X-axis: period of diagnosis; Y-axis: age-standardised five-year net survival (%). Australia=AUS; BLR=Belarus; Canada=CAN; Finland=FIN; France=FRA; Israel=ISR; Italy=ITA; Netherlands=NLD; Poland=POL; Spain=ESP; Sweden=SWE; Switzerland=CHE; UK=GBR; USA=USA.

Figure 4.3. Trends in age-standardised five-year net survival (%) from medulloblastoma, 2000-2014, by world region. Children (0-14 years).



Countries were included if age-standardised survival estimates were available for patients diagnosed during 2000-2004, 2005-2009 and 2010-2014. X-axis: period of diagnosis; Y-axis: age-standardised five-year net survival (%). Australia=AUS; France=FRA; Italy=ITA; Netherlands=NLD; Korea: KOR; Poland: POL; Taiwan: TWN; UK=GBR; USA=USA.

Table 4.1. Data quality indicators, children (0-14 years) diagnosed with a brain tumour during 2000-2014, by continent and country.

			Ineligible (%)ϒ				Exclusions (%)ǂ			Data quality indicators (%)ϕ			
	Calendar period	Patients submitted	Incomplete dates	In situ	Other	Eligible patients	DCO	Other	Available for analysis	MV	Non-specific morphology	Lost to follow-up	Censored
AFRICA		**440**	**10.7**	**0.0**	**39.3**	**220**	**6.8**	**11.8**	**179**	**88.8**	**26.3**	**1.1**	**36.9**
Algerian registries	2000-2014	**323**	2.5	0.0	53.6	**142**	7.7	15.5	**109**	90.8	33.0	0.0	17.4
Mauritius*	2010-2012	**5**	0.0	0.0	0.0	**5**	0.0	40.0	**3**	100.0	0.0	0.0	0.0
Nigeria (Ibadan)	2005-2014	**89**	43.8	0.0	0.0	**50**	8.0	2.0	**45**	88.9	11.1	0.0	71.1
South Africa (Eastern Cape)	2002-2014	**23**	0.0	0.0	0.0	**23**	0.0	4.3	**22**	77.3	27.3	9.1	68.2
AMERICA (CENTRAL AND SOUTH)		**5,526**	**2.4**	**0.0**	**1.2**	**5,328**	**5.9**	**1.1**	**4,958**	**91.1**	**11.5**	**2.6**	**12.6**
Argentinian registries	2000-2013	**2,958**	0.0	0.0	0.0	**2,957**	9.2	0.7	**2,662**	88.2	15.9	0.0	16.7
Brazilian registries	2000-2014	**202**	0.0	0.0	0.0	**202**	5.0	1.0	**190**	93.2	10.5	0.0	1.6
Chilean registries	2000-2012	**88**	0.0	0.0	0.0	**88**	1.1	4.5	**83**	78.3	13.3	0.0	16.9
Colombian registries	2000-2014	**267**	1.9	0.0	1.5	**258**	2.7	3.1	**243**	88.5	11.9	0.0	17.3
Costa Rica*	2002-2014	**163**	0.0	0.0	0.6	**162**	1.9	3.7	**153**	82.4	23.5	0.0	0.0
Ecuadorian registries	2000-2013	**389**	10.3	0.0	0.3	**348**	4.0	2.9	**324**	88.9	12.7	0.9	9.6
Guadeloupe (France)	2008-2013	**14**	0.0	0.0	0.0	**14**	0.0	0.0	**14**	100.0	0.0	0.0	50.0
Martinique (France)	2000-2012	**20**	0.0	0.0	0.0	**20**	0.0	0.0	**20**	100.0	0.0	0.0	25.0
Mexico*	2008-2014	**1,185**	6.6	0.0	5.0	**1,048**	0.0	0.1	**1,047**	99.7	0.0	12.1	7.4
Puerto Rico*	2000-2011	**240**	3.8	0.0	0.0	**231**	2.6	1.3	**222**	99.1	4.5	0.0	0.0
AMERICA (NORTH)		**29,121**	**0.6**	**0.0**	**0.4**	**28,848**	**0.5**	**3.7**	**27,643**	**97.5**	**3.3**	**2.8**	**0.1**
Canadian registries	2000-2014	**2,268**	0.1	0.0	0.2	**2,260**	0.5	2.3	**2,196**	91.1	9.2	0.0	0.0
US registries	2000-2014	**26,853**	0.6	0.0	0.4	**26,588**	0.5	3.8	**25,447**	98.1	2.8	3.0	0.1
ASIA		**8,994**	**0.5**	**0.0**	**0.5**	**8,909**	**1.7**	**3.1**	**8,481**	**88.0**	**10.4**	**0.9**	**1.0**
Chinese registries	2003-2013	**540**	0.0	0.2	0.2	**538**	2.0	0.2	**526**	57.0	47.3	7.4	0.2
Cyprus*	2004-2014	**20**	0.0	0.0	0.0	**20**	10.0	20.0	**14**	85.7	14.3	0.0	0.0
Indian registries	2000-2014	**31**	0.0	0.0	0.0	**31**	0.0	19.4	**25**	80.0	20.0	4.0	0.0
Israel*	2000-2013	**879**	0.0	0.0	0.9	**871**	2.8	0.5	**843**	96.7	4.3	0.0	0.0
Japanese registries	2000-2014	**1,409**	0.6	0.0	0.6	**1,392**	6.4	0.7	**1,293**	88.3	11.9	0.0	2.4
Jordan*	2000-2014	**534**	0.0	0.0	0.2	**533**	0.6	7.7	**489**	98.4	4.3	6.1	0.0
Korea*	2000-2014	**2,381**	0.6	0.0	0.0	**2,366**	0.0	1.4	**2,333**	89.0	11.7	0.0	0.0
Kuwait*	2000-2013	**57**	0.0	0.0	0.0	**57**	8.8	5.3	**49**	100.0	0.0	2.0	0.0
Malaysia (Penang)	2000-2013	**53**	0.0	0.0	0.0	**53**	0.0	15.1	**45**	100.0	0.0	0.0	0.0
Qatar*	2000-2014	**44**	0.0	2.3	0.0	**43**	0.0	23.3	**33**	93.9	12.1	0.0	33.3
Singapore*	2000-2014	**224**	0.0	0.0	0.0	**224**	0.4	12.1	**196**	92.3	2.6	0.0	0.0
Taiwan*	2000-2014	**1,215**	0.1	0.0	0.0	**1,214**	0.0	0.2	**1,211**	83.9	0.2	0.0	0.1
Thai registries	2000-2014	**469**	0.0	0.0	0.0	**469**	3.6	14.3	**385**	84.7	15.3	0.0	2.3
Turkish registries	2000-2013	**1,138**	1.4	0.0	2.1	**1,098**	0.2	5.2	**1,039**	93.6	7.0	0.6	2.7
EUROPE		**25,120**	**0.0**	**0.0**	**0.7**	**24,940**	**0.4**	**1.9**	**24,357**	**92.8**	**4.8**	**1.3**	**3.3**
Belarus*	2000-2014	**626**	0.0	0.0	0.0	**626**	0.8	6.5	**580**	93.8	7.2	1.7	0.0
Belgium*	2004-2014	**782**	0.0	0.0	0.0	**782**	0.1	0.0	**781**	97.3	3.1	2.8	0.0
Croatia*	2000-2014	**414**	0.0	0.0	0.2	**413**	1.0	1.5	**403**	74.9	7.4	0.0	0.0
Czech Republic*	2000-2014	**555**	0.0	0.0	0.0	**555**	2.9	9.0	**489**	84.0	3.3	0.0	0.0
Denmark*	2000-2014	**494**	0.0	0.0	0.2	**493**	0.0	0.0	**493**	88.4	32.9	0.8	0.0
Estonia*	2000-2012	**108**	0.0	0.0	0.0	**108**	0.0	4.6	**103**	87.4	0.0	1.9	0.0
Finland*	2000-2014	**519**	0.8	0.0	0.2	**514**	0.6	1.6	**503**	98.0	0.8	0.8	0.0
French registries	2000-2010	**4,483**	0.0	0.0	0.1	**4,477**	0.0	0.0	**4,477**	98.8	1.6	0.0	2.7
German registries	2000-2014	**757**	0.0	0.0	3.0	**734**	2.9	3.0	**691**	94.5	1.2	0.0	20.1
Greece*	2010-2014	**246**	0.8	0.0	0.0	**244**	0.0	2.9	**237**	99.2	0.8	4.6	0.0
Iceland*	2000-2014	**35**	0.0	0.0	0.0	**35**	0.0	0.0	**35**	88.6	11.4	0.0	0.0
Ireland*	2000-2013	**417**	0.0	0.0	0.2	**416**	0.2	4.6	**396**	83.8	0.5	0.0	0.0
Italian registries	2000-2014	**1,642**	0.0	0.2	0.0	**1,638**	0.1	1.4	**1,613**	83.3	17.9	1.2	1.7
Latvia*	2000-2014	**157**	0.0	0.0	13.4	**136**	0.0	2.9	**132**	76.5	24.2	0.0	0.0
Lithuania*	2000-2012	**143**	0.0	0.0	0.7	**142**	3.5	0.7	**136**	80.1	0.0	0.0	0.0
Malta*	2000-2013	**28**	0.0	0.0	0.0	**28**	7.1	7.1	**24**	100.0	0.0	0.0	0.0
Netherlands*	2000-2014	**1,447**	0.0	0.0	0.1	**1,445**	0.3	0.9	**1,428**	96.5	3.6	1.2	0.0
Norway*	2000-2014	**560**	0.0	0.0	8.0	**515**	0.2	5.8	**484**	97.5	7.0	0.4	0.0
Poland*	2000-2014	**2,128**	0.0	0.0	0.0	**2,128**	0.9	1.8	**2,071**	89.1	0.2	0.0	0.0
Portugal*	2000-2014	**563**	0.2	0.0	0.7	**558**	0.0	1.6	**549**	93.1	2.4	1.6	0.0
Romania (Cluj)	2006-2012	**21**	0.0	0.0	0.0	**21**	0.0	9.5	**19**	89.5	10.5	0.0	0.0
Russian registries	2000-2014	**443**	0.0	0.0	12.0	**390**	0.5	15.6	**327**	91.7	4.0	3.4	4.9
Slovakia*	2000-2010	**330**	0.0	0.0	0.0	**330**	2.1	0.0	**323**	92.0	8.0	0.0	0.0
Slovenia*	2000-2013	**116**	0.0	0.0	1.7	**114**	0.0	0.0	**114**	93.0	0.0	0.0	0.0
Spanish registries	2000-2013	**1,546**	0.1	0.0	0.1	**1,544**	0.2	0.7	**1,530**	88.4	2.2	0.1	32.5
Sweden*	2000-2014	**813**	0.0	0.0	0.2	**811**	0.5	5.7	**761**	92.9	8.4	0.5	0.1
Swiss registries	2000-2014	**577**	0.0	0.0	0.3	**575**	0.0	1.7	**565**	85.7	0.4	0.7	1.9
United Kingdom*	2000-2014	**5,170**	0.0	0.0	0.0	**5,168**	0.2	1.2	**5,093**	95.0	4.9	3.8	0.0
OCEANIA		**1,839**	**0.4**	**0.0**	**0.4**	**1,825**	**0.4**	**5.7**	**1,713**	**92.8**	**7.4**	**0.0**	**0.0**
Australia*	2000-2014	**1,567**	0.4	0.0	0.4	**1,553**	0.5	3.9	**1,484**	92.8	7.3	0.0	0.0
New Zealand*	2000-2014	**272**	0.0	0.0	0.0	**272**	0.0	15.8	**229**	93.0	7.9	0.0	0.0
Total		**71,040**	**0.6**	**0.0**	**0.8**	**70,070**	**1.1**	**2.9**	**67,331**	**94.0**	**5.5**	**1.9**	**2.4**

DCO: death certificate only. MV: microscopic verification. * Data with 100% coverage of the national population. ϒ Incomplete dates: records in which the year of birth is unknown; or the month or year of diagnosis is unknown; or the year of last known vital status is unknown. Other: records with incomplete data or for tumours that are metastatic from another organ (behaviour code 6), or unknown if primary or metastatic (behaviour code 9); or for patients with age outside the range 0–14 years (chidren); or other conditions. ǂ DCO: tumours registered only from a death certificate or detected at autopsy. Other: vital status or sex unknown; invalid date or sequence of dates; inconsistency of sex–site, site-morphology, age–site, age-morphology, or age–site-morphology. ϕ Non-specific morphology: ICD-O-3 morphology code in the range 8000–8005. Censored: patients whose last known vital status is "alive" and who were censored within 5 years of diagnosis.

Table 4.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Ependymoma			Choroid plexus tumour			Astrocytoma, WHO grade I and II			Astrocytoma, WHO grade III and IV			Astrocytoma, unspecified			Medulloblastoma		
		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	
AFRICA																			
Algeria	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-			-			-			-			-			-	
AMERICA (CENTRAL AND SOUTH)																			
Argentina*	2000-2004	**51.4**	38.8 -	63.9	*67.8*	*51.7 -*	*84.0*	**82.7**	74.8 -	90.5	**4.6**	0.0 -	9.5	**61.3**	51.1 -	71.5	**48.2**	41.7 -	54.7
	2005-2009	**63.2**	51.8 -	74.7	*65.0*	*43.0 -*	*87.0*	**90.6**	85.1 -	96.0	**22.8**	11.8 -	33.9	**73.6**	65.9 -	81.2	**51.1**	44.5 -	57.6
	2010-2014	**72.8** §	62.3 -	83.4	*79.9 §*	*61.8 -*	*98.0*	**87.5** §	80.2 -	94.7	**40.3** §	25.8 -	54.9	**76.3** §	69.2 -	83.5	**57.5** §	49.9 -	65.0
Brazil	2000-2004		-			-		*92.3*	*78.4 -*	*100.0*		-		*71.5*	*48.8 -*	*94.2*	*50.1*	*27.9 -*	*72.3*
	2005-2009		-			-			-			-			-		*53.9*	*28.2 -*	*79.7*
	2010-2014		-			-			-			-			-		*39.6*	*15.1 -*	*64.1*
Colombia	2000-2004		-			-		*72.9 §*	*47.8 -*	*97.9*	*37.6 §*	*8.7 -*	*66.5*	*61.8 §*	*36.5 -*	*87.0*		-	
	2005-2009		-			-		*63.8 §*	*36.9 -*	*90.7*		-			-		*16.8 §*	*0.0 -*	*33.9*
	2010-2014		-			-		*92.6 §*	*78.6 -*	*100.0*	*0.0 §*	*0.0 -*	*0.0*	*43.8 §*	*13.3 -*	*74.3*	*45.4 §*	*15.9 -*	*74.9*
Costa Rica*	2000-2004		-			-			-			-			-			-	
	2005-2009	*91.1*	*74.8 -*	*100.0*		-			-			-			-		*33.4*	*8.8 -*	*58.0*
	2010-2014	*91.0*	*74.8 -*	*100.0*		-		*100.0*	*100.0 -*	*100.0*		-			-		*76.2*	*56.1 -*	*96.4*
Ecuador	2000-2004		-			-			-			-		*45.1 §*	*15.3 -*	*74.9*	*46.3 §*	*21.3 -*	*71.4*
	2005-2009		-			-			-			-		*50.0*	*25.2 -*	*74.9*	*15.8*	*0.9 -*	*30.8*
	2010-2014		-			-		*65.8*	*36.0 -*	*95.6*		-		*66.3*	*43.2 -*	*89.4*	*31.9*	*6.8 -*	*57.1*
Puerto Rico*	2000-2004		-			-		*97.4*	*92.4 -*	*100.0*		-			-		*58.4*	*32.0 -*	*84.8*
	2005-2009		-			-		*85.2*	*75.2 -*	*95.2*		-			-		*64.3*	*40.3 -*	*88.3*
	2010-2014		-			-		**84.2**	67.6 -	100.0		-			-			-	
AMERICA (NORTH)																			
Canada	2000-2004	*81.0*	*64.6 -*	*97.4*		-		**92.4**	87.1 -	97.6	*33.4*	*11.0 -*	*55.7*	*58.4*	*32.0 -*	*84.8*	*65.8*	*50.3 -*	*81.3*
	2005-2009	*76.6*	*57.1 -*	*96.1*		-		**93.9**	89.3 -	98.6	*23.6*	*4.8 -*	*42.3*	*47.1*	*24.4 -*	*69.8*	*74.3*	*60.1 -*	*88.6*
	2010-2014	*81.8*	*63.5 -*	*100.0*		-		**98.0**	95.2 -	100.0	*11.7*	*0.8 -*	*22.6*		-		**79.0**	67.7 -	90.4
United States	2000-2004	**75.8**	71.3 -	80.3	**75.8**	64.2 -	87.3	**94.2**	93.3 -	95.1	**28.9**	24.9 -	32.8	**80.0**	75.2 -	84.8	**72.7**	69.6 -	75.8
	2005-2009	**81.1**	76.7 -	85.4	**89.1**	84.4 -	93.8	**95.3**	94.4 -	96.1	**25.0**	21.1 -	28.9	**83.3**	78.8 -	87.9	**72.3**	69.3 -	75.3
	2010-2014	**85.8**	81.8 -	89.9	**93.5**	90.2 -	96.8	**95.6**	94.8 -	96.5	**23.1**	19.4 -	26.7	**84.6**	80.3 -	88.9	**73.7**	70.6 -	76.9
ASIA																			
China	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-			-			-			-			-		*32.8*	*5.8 -*	*59.7*
Israel*	2000-2004	*83.4*	*63.1 -*	*100.0*		-		**95.2**	90.7 -	99.7	*13.3*	*0.0 -*	*28.4*		-		**71.1**	60.4 -	81.7
	2005-2009	*80.1*	*64.7 -*	*95.4*		-		**95.6**	90.9 -	100.0	*33.4*	*16.2 -*	*50.5*	*100.0*	*69.2 -*	*100.0*	*56.6*	*42.4 -*	*70.7*
	2010-2014	*82.4*	*64.9 -*	*100.0*		-		**95.4**	90.4 -	100.0	*47.1*	*23.3 -*	*70.9*		-		**81.0**	70.7 -	91.4
Japan	2000-2004	*56.3*	*33.0 -*	*79.6*		-		*87.5*	*71.8 -*	*100.0*	*13.1*	*0.5 -*	*25.6*	*85.1*	*69.8 -*	*100.0*	*76.5*	*62.5 -*	*90.6*
	2005-2009	*49.2*	*25.6 -*	*72.9*	*88.2*	*73.2 -*	*100.0*	**95.7**	91.2 -	100.0	*9.4*	*0.1 -*	*18.7*	*75.0*	*58.1 -*	*92.0*	**63.7**	53.2 -	74.2
	2010-2014		-		*76.2*	*49.2 -*	*100.0*	**96.5**	91.8 -	100.0	*16.4*	*0.8 -*	*31.9*		-		**73.1**	61.0 -	85.1
Jordan*	2000-2004	*100.0 §*	*100.0 -*	*100.0*		-		*89.0 §*	*69.6 -*	*100.0*	*61.7 §*	*42.5 -*	*80.9*	*78.4 §*	*60.1 -*	*96.8*	*78.2 §*	*64.9 -*	*91.5*
	2005-2009		-			-		*79.1 §*	*61.3 -*	*96.9*	*67.9 §*	*49.9 -*	*85.9*	*80.1 §*	*60.6 -*	*99.6*	*69.4 §*	*56.7 -*	*82.2*
	2010-2014		-			-		*82.9 §*	*69.3 -*	*96.4*	*35.8 §*	*16.0 -*	*55.7*		-		**70.7** §	56.8 -	84.7
Korea*	2000-2004	**71.7**	60.6 -	82.7	*33.4*	*8.8 -*	*58.0*	*93.8*	*82.3 -*	*100.0*	**20.7**	11.0 -	30.5	*83.8*	*73.5 -*	*94.0*	**60.5**	53.6 -	67.4
	2005-2009	*72.6*	*58.9 -*	*86.2*		-		*82.4*	*64.9 -*	*100.0*	**21.3**	11.5 -	31.1	**72.0**	60.5 -	83.4	**67.0**	59.5 -	74.5
	2010-2014	**59.7**	43.5 -	75.9		-		*83.1*	*62.6 -*	*100.0*	**26.9**	15.1 -	38.6	**66.7**	54.4 -	78.9	**70.0**	63.1 -	76.9
Singapore*	2000-2004		-			-		*100.0*	*79.4 -*	*100.0*		-			-		*50.0*	*21.2 -*	*78.8*
	2005-2009		-			-		*100.0*	*78.2 -*	*100.0*		-			-			-	
	2010-2014		-			-		*94.5*	*84.2 -*	*100.0*		-			-			-	
Taiwan*	2000-2004	*46.7*	*22.7 -*	*70.7*		-		**91.4**	84.4 -	98.3	*38.7*	*24.6 -*	*52.8*	**82.8**	73.2 -	92.5	**56.4**	45.6 -	67.3
	2005-2009	*80.0*	*56.6 -*	*100.0*		-		*85.4*	*73.7 -*	*97.1*	*30.6*	*16.0 -*	*45.2*	*82.2*	*68.3 -*	*96.1*	**65.5**	55.9 -	75.0
	2010-2014	*60.1*	*33.8 -*	*86.3*		-		**84.1**	74.1 -	94.0	**21.7**	9.4 -	34.1	**70.6**	53.8 -	87.3	**62.7**	52.4 -	72.9
Thailand	2000-2004		-			-			-		*13.4 §*	*0.0 -*	*28.4*	*30.1 §*	*12.5 -*	*47.7*	*36.9 §*	*16.2 -*	*57.7*
	2005-2009		-			-			-		*17.7*	*1.2 -*	*34.2*	*41.8*	*22.9 -*	*60.7*	*50.2*	*33.2 -*	*67.2*
	2010-2014		-			-			-			-			-		**49.6** §	32.8 -	66.3
Turkey	2000-2004		-			-		*82.5*	*67.1 -*	*97.8*		-			-			-	
	2005-2009	*43.1*	*24.7 -*	*61.6*		-		**83.3**	75.4 -	91.3	*17.7*	*1.2 -*	*34.2*	*90.9*	*79.2 -*	*100.0*	**53.1**	39.8 -	66.5
	2010-2014	**54.0**	36.3 -	71.7		-		**88.2**	81.7 -	94.7	*34.5*	*19.2 -*	*49.8*	*80.0*	*62.7 -*	*97.2*	**59.2**	46.8 -	71.5
EUROPE																			
Belarus*	2000-2004	*50.1*	*23.5 -*	*76.7*		-		**78.1**	68.4 -	87.7	*8.4*	*0.0 -*	*20.7*		-		*65.4*	*52.2 -*	*78.6*
	2005-2009	*58.9*	*36.4 -*	*81.5*		-		**93.1**	86.7 -	99.5	*30.0*	*5.3 -*	*54.7*		-		*52.4*	*31.8 -*	*73.1*
	2010-2014	*57.4*	*35.8 -*	*79.0*		-		**92.4**	86.1 -	98.6	*21.7*	*1.4 -*	*42.0*	*100.0*	-		**49.1**	30.8 -	67.4
Belgium*	2000-2004		-			-		*95.3*	*86.4 -*	*100.0*		-			-			-	
	2005-2009		-		*70.7*	*49.8 -*	*91.6*	**95.0**	91.3 -	98.8	*17.4*	*3.0 -*	*31.8*		-		*57.2*	*42.4 -*	*71.9*
	2010-2014		-		*86.3*	*69.1 -*	*100.0*	**94.7**	90.8 -	98.5	*10.8*	*0.2 -*	*21.5*		-		**67.1**	54.9 -	79.3
Croatia*	2000-2004		-			-		*81.8*	*60.2 -*	*100.0*		-		*72.3*	*52.2 -*	*92.3*	*64.1*	*45.7 -*	*82.4*
	2005-2009		-			-		*96.3*	*89.3 -*	*100.0*		-		*80.0*	*60.5 -*	*99.5*	*53.4*	*29.3 -*	*77.4*
	2010-2014		-			-		*93.4*	*81.2 -*	*100.0*	*0.0*	*0.0 -*	*0.0*		-		*58.3*	*35.7 -*	*80.9*
Czech Republic*	2000-2004	*70.0*	*43.3 -*	*96.8*		-		*87.3*	*76.9 -*	*97.6*	*30.0*	*11.0 -*	*49.1*		-		*50.0*	*25.2 -*	*74.9*
	2005-2009		-			-		**95.0**	89.7 -	100.0	*10.0*	*0.0 -*	*24.6*		-			-	
	2010-2014		-			-		**98.6**	96.0 -	100.0	*15.7*	*0.0 -*	*31.4*		-		*87.9*	*72.6 -*	*100.0*

Table 4.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Ependymoma			Choroid plexus tumour			Astrocytoma, WHO grade I and II			Astrocytoma, WHO grade III and IV			Astrocytoma, unspecified			Medulloblastoma		
		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	
Denmark*	2000-2004		-			-		*95.4*	*89.1*	*100.0*		-		*53.9*	*28.2*	*79.6*	*65.5*	*48.7*	*82.4*
	2005-2009		-			-		*97.3*	*92.1*	*100.0*		-			-		*69.6*	*51.4*	*87.8*
	2010-2014		-			-		**95.2**	87.2	100.0		-			-		**72.0**	59.4	84.6
Estonia*	2000-2004		-			-		*100.0*	*85.2*	*100.0*		-			-			-	
	2005-2009		-			-		*100.0*	*73.5*	*100.0*		-			-			-	
	2010-2014		-			-			-			-			-			-	
Finland*	2000-2004		-			-		**98.3**	95.2	100.0	*25.0*	*2.9*	*47.1*		-		*75.0*	*54.6*	*95.5*
	2005-2009		-			-		**98.6**	96.0	100.0		-		*56.3*	*33.0*	*79.6*	*77.8*	*59.4*	*96.2*
	2010-2014		-		*76.5*	*48.6*	*100.0*	**97.0**	92.9	100.0	*9.2*	*0.0*	*22.7*		-		*62.5*	*42.4*	*82.6*
France*	2000-2004	**68.6**	57.7	79.6	*61.9*	*49.5*	*74.4*	**90.1**	87.6	92.7	*15.0*	*4.5*	*25.6*		-		**63.6**	58.4	68.8
	2005-2009	**82.3**	73.8	90.7	*86.1*	*77.2*	*95.0*	**94.3**	92.2	96.5	**15.5**	7.2	23.9		-		**68.6**	63.2	74.1
	2010-2014	**89.9**	83.2	96.6	**100.0**	100.0	100.0	**94.2**	91.5	96.9	**6.3**	0.1	12.5		-		**69.3**	62.8	75.8
Germany	2000-2004		-			-		*85.3*	*73.7*	*97.0*	*15.4*	*0.0*	*31.1*	*68.8*	*46.9*	*90.6*	*74.2*	*59.1*	*89.4*
	2005-2009		-			-		*94.7*	*87.5*	*100.0*	*17.4*	*3.1*	*31.8*		-		*67.8*	*52.9*	*82.6*
	2010-2014		-			-		**100.0**	100.0	100.0	*32.1*	*8.9*	*55.4*		-		**75.5**	59.4	91.6
Greece*	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-			-		**91.8**	82.1	100.0	*43.2*	*8.6*	*77.9*		-		**54.8**	47.7	61.9
Ireland*	2000-2004		-			-		*89.2*	*80.3*	*98.1*		-		*76.5*	*57.0*	*96.0*		-	
	2005-2009	*60.0*	*31.6*	*88.5*		-		*92.9*	*85.2*	*100.0*		-			-			-	
	2010-2014		-			-		**100.0**	100.0	100.0	*36.8*	*8.3*	*65.3*		-		*53.1*	*24.6*	*81.6*
Italy	2000-2004	*74.3*	*59.1*	*89.4*	*75.1*	*51.8*	*98.5*	**95.4**	91.5	99.3	*20.6*	*7.8*	*33.4*	*77.8*	*64.5*	*91.2*	**64.8**	55.1	74.4
	2005-2009	*81.3*	*69.8*	*92.9*	*78.7*	*58.0*	*99.4*	**91.9**	87.5	96.4	*44.2*	*29.7*	*58.8*	*67.8*	*53.5*	*82.1*	**71.0**	63.0	79.1
	2010-2014	**80.8**	69.7	91.8		-		**93.5**	88.1	98.8	**29.8**	13.5	46.2	**71.5**	53.9	89.1	**69.7**	58.7	80.6
Latvia*	2000-2004		-			-			-			-		*80.2*	*64.8*	*95.5*		-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-			-			-		*55.4*	*26.1*	*84.7*	*100.0*	*100.0*	*100.0*		-	
Lithuania*	2000-2004		-			-			-			-		*66.8*	*43.8*	*89.7*	*35.8*	*12.3*	*59.3*
	2005-2009		-			-			-			-			-		*45.5*	*18.1*	*73.0*
	2010-2014		-			-			-			-		*75.0*	*38.2*	*100.0*		-	
Netherlands*	2000-2004	*71.7*	*56.3*	*87.0*		-		**91.4**	86.6	96.1	*25.0*	*12.1*	*38.0*		-		**51.8**	41.6	62.0
	2005-2009	*78.6*	*57.9*	*99.2*	*75.1*	*51.7*	*98.4*	**95.0**	91.4	98.6	*9.1*	*0.1*	*18.1*		-		**62.1**	52.2	72.0
	2010-2014	*80.4*	*61.1*	*99.6*	*88.7*	*74.1*	*100.0*	**94.1**	90.4	97.8	*9.3*	*0.1*	*18.5*		-		**63.3**	52.4	74.2
Norway*	2000-2004		-		*82.0*	*60.3*	*100.0*	**92.3**	85.2	99.4		-			-		*72.3*	*52.2*	*92.3*
	2005-2009		-			-		*91.2*	*83.0*	*99.4*	*0.0*	*0.0*	*0.0*	*50.1*	*21.3*	*78.8*	*87.5*	*71.8*	*100.0*
	2010-2014		-			-		**97.2**	92.2	100.0	*0.0*	*0.0*	*0.0*		-			-	
Poland*	2000-2004	*65.9*	*51.6*	*80.2*		-		**86.5**	79.6	93.4	**31.3**	20.1	42.5	**72.4**	63.3	81.4	**60.2**	52.7	67.6
	2005-2009	*71.1*	*56.9*	*85.3*	*80.1*	*56.6*	*100.0*	**93.1**	87.8	98.3	**24.5**	14.7	34.3	**76.7**	67.0	86.3	**54.8**	47.1	62.5
	2010-2014	**79.3**	65.7	92.8	*66.9*	*44.0*	*89.9*	**95.1**	89.7	100.0	**31.2**	19.1	43.3	**83.1**	73.1	93.0	**60.0**	51.9	68.1
Portugal*	2000-2004		-			-		*86.5*	*76.4*	*96.5*		-		*60.1*	*39.3*	*80.9*	*59.0*	*43.9*	*74.2*
	2005-2009	*45.5*	*18.1*	*72.9*		-		*90.3*	*81.3*	*99.3*	*7.7*	*0.0*	*19.1*	*88.3*	*73.4*	*100.0*	*69.2*	*55.4*	*82.9*
	2010-2014		-			-		**100.0**	100.0	100.0	*25.0*	*0.0*	*56.9*		-		**80.6**	61.6	99.6
Russian Federation	2000-2004		-			-			-			-		*83.4*	*69.0*	*97.8*		-	
	2005-2009		-			-			-		*38.6*	*13.8*	*63.3*	*74.6*	*57.4*	*91.8*	*70.7*	*49.8*	*91.7*
	2010-2014		-			-			-		*40.2*	*16.7*	*63.7*	**81.1**	65.8	96.4	*66.1*	*43.0*	*89.3*
Slovakia*	2000-2004		-			-		**86.2**	77.6	94.9		-			-		*47.9*	*28.1*	*67.7*
	2005-2009	*69.3*	*45.3*	*93.3*		-		*91.0*	*82.6*	*99.4*		-			-		*66.7*	*48.3*	*85.1*
	2010-2014		-			-		**93.4**	82.9	100.0		-			-			-	
Slovenia*	2000-2004		-			-		*81.8*	*60.2*	*100.0*		-			-			-	
	2005-2009		-			-		*100.0*	*78.2*	*100.0*		-			-		*40.0*	*12.2*	*67.9*
	2010-2014		-			-			-			-			-		*57.6*	*27.2*	*88.0*
Spain	2000-2004	*35.7*	*12.3*	*59.2*		-		**91.8**	85.0	98.5		-		*88.9*	*77.3*	*100.0*	*54.8*	*40.0*	*69.6*
	2005-2009	*76.5*	*57.0*	*96.0*	*70.1*	*43.3*	*96.9*	**84.0**	76.1	91.9	*16.7*	*0.0*	*35.1*	*82.4*	*64.9*	*100.0*	**56.4**	44.5	68.3
	2010-2014	*100.0*	*100.0*	*100.0*		-		**86.3**	75.6	97.0		-			-		**46.9**	29.3	64.4
Sweden*	2000-2004	*84.6*	*65.8*	*100.0*		-		**93.2**	86.1	100.0	*20.5*	*0.0*	*42.3*	*85.0*	*69.8*	*100.0*	*74.1*	*57.9*	*90.3*
	2005-2009	*100.0*	*73.5*	*100.0*		-		**98.2**	94.7	100.0	*20.0*	*1.7*	*38.4*	*85.2*	*72.1*	*98.3*	*65.2*	*46.4*	*84.1*
	2010-2014		-		*100.0*	*100.0*	*100.0*	**97.2**	93.5	100.0	*26.5*	*7.7*	*45.3*	**80.6**	66.2	94.9	**88.0**	77.8	98.3
Switzerland*	2000-2004		-			-		**97.4**	93.9	100.0	*9.1*	*0.0*	*22.4*		-		*66.7*	*50.9*	*82.5*
	2005-2009		-			-		**92.0**	83.8	100.0	*54.6*	*27.0*	*82.2*		-		*61.6*	*43.3*	*79.8*
	2010-2014		-			-		**94.5**	88.7	100.0	*34.1*	*10.3*	*57.9*		-		**63.0**	48.8	77.1
United Kingdom*	2000-2004	**65.1**	54.4	75.8	*58.9*	*44.9*	*72.9*	**93.8**	91.5	96.1	**13.3**	6.8	19.9	**79.1**	70.6	87.7	**68.8**	63.3	74.3
	2005-2009	**79.1**	71.0	87.2	*81.2*	*71.3*	*91.2*	**94.3**	92.2	96.4	**13.4**	7.7	19.1	**68.1**	55.8	80.4	**65.0**	59.0	71.1
	2010-2014	**81.3**	72.2	90.5	**90.6**	83.6	97.6	**96.5**	94.9	98.1	**17.1**	11.2	23.0	**68.3**	54.8	81.9	**61.5**	55.4	67.7
OCEANIA																			
Australia*	2000-2004	*68.3*	*54.3*	*82.4*		-		**87.0**	78.8	95.2	**19.2**	9.3	29.0	*80.9*	*66.0*	*95.7*	**69.4**	59.7	79.1
	2005-2009	*79.5*	*61.9*	*97.0*	*73.5*	*51.9*	*95.0*	**87.7**	80.7	94.6	**25.0**	13.6	36.5	*92.4*	*78.4*	*100.0*	**64.8**	54.7	75.0
	2010-2014	*76.7*	*59.1*	*94.2*	*58.5*	*36.0*	*80.9*	**90.9**	84.5	97.2	**21.5**	11.0	32.0		-		**71.6**	61.6	81.6
New Zealand*	2000-2004		-			-		*85.0*	*69.8*	*100.0*		-			-		*76.5*	*57.0*	*96.0*
	2005-2009		-			-			-		*16.7*	*0.0*	*35.0*		-		*66.8*	*43.8*	*89.7*
	2010-2014		-			-			-			-			-			-	

* Countries with 100% coverage of the national population. § Survival estimates considered less reliable because the proportion of patients lost to follow-up or censored alive prior to five years, or the proportion of diagnoses based on a death certificate or autopsy, or the proportion of patients registered with incomplete dates, was 15% or more. Survival estimates in italics are not age-standardised.

Table 4.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Other and unspecified embryonal tumour			Oligodendroglial tumour			Unspecified glioma			Neuroepithelial glial tumour of uncertain origin		Neuronal and mied neuronal-glial tumour			Unspecified neoplasm		
		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	NS	95% CI		NS	95% CI	
AFRICA																		
Algeria	2000-2004		-			-			-			-		-			-	
	2005-2009		-			-			-			-		-		*47.9 §	*28.2 -	*67.6*
	2010-2014		-			-			-			-		-		*62.1 §	*37.1 -	*87.1*
AMERICA (CENTRAL AND SOUTH)																		
Argentina*	2000-2004	**44.8**	35.6 -	54.1	*60.2*	*41.4 -	*78.9*	*38.0*	*21.0 -	*55.1*		-	*92.1*	*81.7 -	*100.0*	**16.7**	11.2 -	22.2
	2005-2009	**47.5**	35.6 -	59.3	*72.7*	*56.7 -	*88.7*	*50.1*	*33.6 -	*66.6*		-	*88.2*	*77.2 -	*99.2*	**26.7**	19.6 -	33.7
	2010-2014	**44.0** §	29.9 -	58.0	**88.3** §	78.3 -	98.4	**89.2** §	77.3 -	100.0		-	**94.7** §	88.2 -	100.0	**37.6** §	28.8 -	46.4
Brazil	2000-2004		-			-			-			-		-			-	
	2005-2009		-			-			-			-		-			-	
	2010-2014		-			-			-			-		-			-	
Colombia	2000-2004		-			-			-			-		-			-	
	2005-2009	*22.9 §	*0.0 -	*46.8*		-			-			-		-			-	
	2010-2014	*44.5 §	*16.4 -	*72.6*		-			-			-		-		*30.3 §	*3.4 -	*57.3*
Costa Rica*	2000-2004		-			-			-			-		-			-	
	2005-2009		-			-			-			-		-		*77.9	*59.2 -	*96.5*
	2010-2014		-			-			-			-		-		*71.8	*51.5 -	*92.1*
Ecuador	2000-2004		-			-			-			-		-			-	
	2005-2009		-			-			-			-		-		*18.2	*0.0 -	*38.0*
	2010-2014		-			-			-			-		-		*39.6	*19.0 -	*60.2*
Puerto Rico*	2000-2004	*46.7*	*22.7 -	*70.7*		-			-			-		-			-	
	2005-2009	*80.2*	*56.7 -	*100.0*		-			-			-		-			-	
	2010-2014		-			-			-			-		-			-	
AMERICA (NORTH)																		
Canada	2000-2004	*41.5*	*26.7 -	*56.3*	*72.7*	*47.8 -	*97.7*	*59.3*	*41.2 -	*77.4*		-	*100.0*	*79.4 -	*100.0*		-	
	2005-2009	*33.4*	*18.4 -	*48.4*		-		*58.6*	*43.8 -	*73.4*		-	*92.6*	*82.9 -	*100.0*		-	
	2010-2014	**38.5**	21.8 -	55.2		-		**49.8**	36.2 -	63.3		-	**96.7**	90.8 -	100.0		-	
United States	2000-2004	**52.5**	48.3 -	56.7	**83.8**	78.9 -	88.7	**48.6**	45.5 -	51.7	*52.1*	*33.0 -	*71.1*	**91.3**	86.6 -	96.1	**56.1**	46.2 -	65.9
	2005-2009	**53.8**	49.4 -	58.2	**82.5**	76.7 -	88.2	**52.9**	50.0 -	55.7	*66.7*	*48.3 -	*85.1*	**95.6**	94.0 -	97.1	**81.0**	76.4 -	85.5
	2010-2014	**56.5**	51.7 -	61.4	**83.0**	76.1 -	89.9	**56.8**	54.0 -	59.7	**67.1**	49.6 -	84.6	**95.6**	93.9 -	97.2	**86.7**	82.6 -	90.7
ASIA																		
China	2000-2004		-			-			-			-		-		*19.1	*7.6 -	*30.5*
	2005-2009		-			-		*30.8*	*7.6 -	*53.9*		-		-		**27.2**	17.3 -	37.1
	2010-2014		-			-			-			-		-		**35.8**	23.6 -	48.0
Israel*	2000-2004	*52.5*	*31.8 -	*73.1*		-		*42.5*	*26.0 -	*58.9*		-	*83.4*	*63.3 -	*100.0*		-	
	2005-2009	*51.7*	*34.5 -	*68.9*		-		*53.2*	*39.2 -	*67.3*		-	*92.6*	*82.9 -	*100.0*	*71.5	*48.8 -	*94.2*
	2010-2014	**32.0**	19.3 -	44.6		-		**55.2**	40.0 -	70.4		-		-		*69.9	*42.6 -	*97.2*
Japan	2000-2004	*56.3*	*33.0 -	*79.6*		-		*20.7*	*6.7 -	*34.7*		-		-		*84.4	*72.1 -	*96.7*
	2005-2009	*46.4*	*33.0 -	*59.8*		-		**31.0**	19.9 -	42.0		-	*91.0*	*74.8 -	*100.0*	*70.5	*56.6 -	*84.4*
	2010-2014	**48.1**	41.4 -	54.8		-		**33.4**	19.2 -	47.5		-	*100.0*	*100.0 -	*100.0*	**87.7**	77.3 -	98.2
Jordan*	2000-2004	*54.0 §	*28.3 -	*79.7*		-		*50.0 §	*21.3 -	*78.8*		-		-			-	
	2005-2009	*50.1 §	*29.0 -	*71.3*		-		*30.8 §	*7.6 -	*54.0*		-		-			-	
	2010-2014	*31.5 §	*12.7 -	*50.4*		-		*18.6 §	*5.4 -	*31.7*		-		-		*83.5 §	*66.8 -	*100.0*
Korea*	2000-2004	**52.4**	41.2 -	63.5	*92.3*	*82.3 -	*100.0*	**33.4**	20.9 -	45.8		-		-		**40.1**	32.7 -	47.5
	2005-2009	**53.3**	43.2 -	63.5	*85.7*	*68.1 -	*100.0*	**41.4**	32.3 -	50.6		-		-		**64.2**	54.1 -	74.2
	2010-2014	**55.5**	45.8 -	65.2	**73.4**	58.0 -	88.8	**43.2**	33.6 -	52.7		-		-		**58.5**	45.1 -	72.0
Singapore*	2000-2004		-			-			-			-		-			-	
	2005-2009		-			-			-			-		-			-	
	2010-2014		-			-			-			-		-			-	
Taiwan*	2000-2004	*38.8*	*25.4 -	*52.2*	*76.7*	*57.1 -	*96.2*		-			-		-			-	
	2005-2009	**57.5**	46.9 -	68.1	*57.2*	*32.5 -	*81.9*	*33.3*	*8.8 -	*57.9*		-		-			-	
	2010-2014	**49.4**	33.3 -	65.5		-		*12.1*	*0.0 -	*28.9*		-		-			-	
Thailand	2000-2004		-			-			-			-		-		*23.6 §	*4.9 -	*42.3*
	2005-2009	*43.9*	*20.8 -	*67.0*		-		*6.3*	*0.0 -	*15.7*		-		-		*47.3	*23.2 -	*71.4*
	2010-2014	*41.8 §	*19.9 -	*63.7*		-		*37.6 §	*13.0 -	*62.2*		-		-		*30.8 §	*7.0 -	*54.6*
Turkey	2000-2004	*21.2*	*0.0 -	*43.6*		-		*22.2*	*0.0 -	*44.8*		-		-			-	
	2005-2009	**50.4**	36.3 -	64.6		-		**40.9**	28.1 -	53.8		-	*91.0*	*74.8 -	*100.0*	*64.2	*45.9 -	*82.6*
	2010-2014	**47.6**	35.7 -	59.5		-		**47.3**	37.8 -	56.9		-	*85.3*	*70.1 -	*100.0*	**88.9**	79.2 -	98.6
EUROPE																		
Belarus*	2000-2004	*33.4*	*11.0 -	*55.7*	*85.3*	*72.2 -	*98.5*		-			-		-			-	
	2005-2009	*41.3*	*19.0 -	*63.5*	*91.8*	*76.8 -	*100.0*		-			-		-		*33.4	*12.7 -	*54.0*
	2010-2014	*30.0*	*9.2 -	*50.7*		-			-			-		-		*42.1	*21.2 -	*63.1*
Belgium*	2000-2004		-			-			-			-		-			-	
	2005-2009	*64.6*	*48.1 -	*81.1*	*69.3*	*45.3 -	*93.3*	*68.1*	*50.3 -	*85.9*		-	*100.0*	*80.5 -	*100.0*	*90.9	*74.7 -	*100.0*
	2010-2014	**65.6**	50.1 -	81.1	*75.7*	*52.6 -	*98.9*	**52.1**	37.2 -	67.0		-	**94.2**	86.9 -	100.0	*91.7	*76.7 -	*100.0*
Croatia*	2000-2004	*41.7*	*16.3 -	*67.1*		-		*81.8*	*60.1 -	*100.0*		-		-		*63.2	*42.4 -	*84.1*
	2005-2009		-			-			-			-		-		*60.0	*31.6 -	*88.4*
	2010-2014	*69.9*	*46.0 -	*93.7*		-		*43.7*	*19.1 -	*68.2*		-		-			-	
Czech Republic*	2000-2004	*50.0*	*25.2 -	*74.9*		-			-			-		-			-	
	2005-2009	*23.1*	*7.8 -	*38.4*		-			-			-		-			-	
	2010-2014	*31.1*	*15.6 -	*46.5*		-			-			-		-			-	

Table 4.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Other and unspecified embryonal tumour			Oligodendroglial tumour			Unspecified glioma			Neuroepithelial glial tumour of uncertain origin			Neuronal and mied neuronal-glial tumour			Unspecified neoplasm		
		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	
Denmark*	2000-2004	*18.8*	*1.5*	*36.1*		-			-			-		*93.4*	*81.2*	*100.0*	*66.7*	*49.4*	*84.0*
	2005-2009	*53.0*	*30.2*	*75.7*		-			-			-			-		*83.4*	*72.9*	*93.8*
	2010-2014	*62.3*	*37.6*	*87.1*		-			-			-			-		**88.3**	81.9	94.7
Estonia*	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-			-			-			-			-			-	
Finland*	2000-2004	*55.0*	*34.0*	*76.1*		-			-			-		*100.0*	*83.2*	*100.0*		-	
	2005-2009	*57.2*	*32.5*	*81.8*		-			-			-		*100.0*	*79.4*	*100.0*		-	
	2010-2014	*38.4*	*18.3*	*58.5*		-			-			-		**100.0**	100.0	100.0		-	
France*	2000-2004	**40.7**	30.7	50.8	**54.5**	45.8	63.2	**20.1**	13.8	26.4		-		**95.0**	91.7	98.2	*54.6*	*38.1*	*71.0*
	2005-2009	**51.6**	42.2	60.9	**44.6**	36.1	53.1	**35.4**	27.8	43.0		-		**96.9**	94.6	99.2	*56.7*	*39.7*	*73.7*
	2010-2014	**48.6**	35.9	61.2	**51.3**	38.7	64.0	**30.9**	22.6	39.2		-		**95.3**	92.2	98.5		-	
Germany	2000-2004	*68.0*	*50.2*	*85.9*		-			-			-			-			-	
	2005-2009	*62.5*	*46.1*	*79.0*		-		*52.7*	*31.1*	*74.3*		-			-			-	
	2010-2014	**84.5**	74.8	94.3		-		*42.8*	*23.2*	*62.4*		-			-			-	
Greece*	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014	*43.8*	*25.2*	*62.5*		-		*29.9*	*7.8*	*52.1*		-		*100.0*	*100.0*	*100.0*		-	
Ireland*	2000-2004	*45.5*	*25.4*	*65.6*		-			-			-			-			-	
	2005-2009	*66.7*	*45.6*	*87.7*		-			-			-			-			-	
	2010-2014	*55.6*	*30.2*	*81.0*		-			-			-		*80.0*	*48.7*	*100.0*		-	
Italy	2000-2004	*42.0*	*25.1*	*58.9*	*80.1*	*56.6*	*100.0*	*46.0*	*30.3*	*61.7*		-		*100.0*	*83.2*	*100.0*	**58.4**	49.0	67.8
	2005-2009	*49.6*	*34.9*	*64.2*	*77.0*	*55.0*	*98.9*	*42.0*	*26.3*	*57.8*		-		*100.0*	*100.0*	*100.0*	**79.3**	72.4	86.1
	2010-2014	**83.5**	70.2	96.8		-		**60.9**	42.8	78.9		-		**96.3**	89.9	100.0	**72.3**	61.7	82.9
Latvia*	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-			-			-			-			-			-	
Lithuania*	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-			-			-			-			-			-	
Netherlands*	2000-2004	**33.5**	22.3	44.8	*61.2*	*39.5*	*82.9*	*31.1*	*17.7*	*44.5*		-		*96.2*	*89.0*	*100.0*	*41.7*	*16.2*	*67.1*
	2005-2009	*40.5*	*26.7*	*54.2*	*60.0*	*31.6*	*88.5*	*20.4*	*9.5*	*31.3*		-		**91.4**	83.5	99.2	*55.6*	*33.8*	*77.3*
	2010-2014	**46.2**	32.9	59.5		-		**32.1**	19.1	45.0		-		**94.8**	89.3	100.0	*59.8*	*40.7*	*78.9*
Norway*	2000-2004	*56.3*	*33.3*	*79.4*		-		*45.5*	*18.4*	*72.5*		-		*94.4*	*84.2*	*100.0*	*93.3*	*81.1*	*100.0*
	2005-2009	*47.7*	*27.1*	*68.2*		-		*58.4*	*32.0*	*84.8*		-		*100.0*	*75.3*	*100.0*	*100.0*	*75.3*	*100.0*
	2010-2014	*47.0*	*26.7*	*67.4*		-		*41.5*	*18.4*	*64.5*		-		*100.0*	*100.0*	*100.0*		-	
Poland*	2000-2004	**56.2**	45.6	66.8	*87.0*	*73.6*	*100.0*	*64.8*	*42.9*	*86.7*		-			-			-	
	2005-2009	**51.9**	40.1	63.7	*62.6*	*43.7*	*81.4*	*56.3*	*33.0*	*79.6*		-			-			-	
	2010-2014	**52.6**	39.7	65.4	**72.4**	56.9	87.9	*75.9*	*57.6*	*94.2*		-			-			-	
Portugal*	2000-2004	*54.6*	*27.0*	*82.2*	*54.6*	*27.0*	*82.3*	*52.7*	*31.1*	*74.3*		-			-			-	
	2005-2009	*41.2*	*19.0*	*63.5*	*57.2*	*32.5*	*81.9*	*46.2*	*20.7*	*71.7*		-			-			-	
	2010-2014	*64.1*	*28.6*	*99.6*	*50.0*	*1.0*	*99.1*		-			-		*100.0*	*100.0*	*100.0*		-	
Russian Federation	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014	*18.2*	*0.0*	*38.3*		-			-			-			-			-	
Slovakia*	2000-2004	*54.8*	*27.1*	*82.5*		-			-			-			-		*21.4*	*2.0*	*40.9*
	2005-2009	*25.0*	*2.9*	*47.2*		-			-			-			-		*54.6*	*27.0*	*82.3*
	2010-2014		-			-			-			-			-			-	
Slovenia*	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-			-			-			-			-			-	
Spain	2000-2004	*14.3*	*0.6*	*28.0*		-		*31.6*	*11.8*	*51.4*		-			-		*36.4*	*10.2*	*62.5*
	2005-2009	*34.2*	*20.0*	*48.4*		-		*37.5*	*18.9*	*56.2*		-		*80.1*	*60.6*	*99.6*		-	
	2010-2014	*38.0*	*14.3*	*61.6*		-			-			-		*80.1*	*48.7*	*100.0*		-	
Sweden*	2000-2004	*51.7*	*34.5*	*68.8*		-			-			-		*90.9*	*74.7*	*100.0*	*52.4*	*31.8*	*73.0*
	2005-2009	*63.7*	*44.1*	*83.2*		-			-			-		*88.5*	*76.5*	*100.0*	*52.2*	*32.4*	*72.0*
	2010-2014	**58.3**	39.1	77.5	*60.6*	*27.9*	*93.4*		-			-		**89.8**	80.4	99.1	*58.9*	*39.0*	*78.7*
Switzerland*	2000-2004	*47.7*	*27.1*	*68.3*		-			-			-		*100.0*	*78.2*	*100.0*		-	
	2005-2009	*43.4*	*26.1*	*60.6*		-			-			-		*100.0*	*100.0*	*100.0*		-	
	2010-2014	*64.6*	*43.7*	*85.6*		-			-			-			-			-	
United Kingdom*	2000-2004	**53.1**	42.6	63.6	*58.1*	*39.7*	*76.6*	**37.8**	30.3	45.3		-		**98.1**	94.4	100.0	**72.9**	64.7	81.1
	2005-2009	**48.6**	39.3	57.8	*63.4*	*46.5*	*80.2*	**49.8**	42.4	57.3		-		**93.8**	89.5	98.2	**62.7**	51.9	73.4
	2010-2014	**53.5**	44.2	62.8	**70.4**	59.7	81.2	**49.4**	41.8	57.0	*54.6*	*27.0*	*82.2*	**97.0**	94.2	99.9	**77.9**	68.8	87.0
OCEANIA																			
Australia*	2000-2004	**29.9**	20.4	39.4	*83.4*	*66.7*	*100.0*	**48.7**	35.1	62.2		-		*100.0*	*81.5*	*100.0*	**69.3**	57.2	81.4
	2005-2009	**48.4**	36.7	60.2	*81.9*	*60.2*	*100.0*	**32.4**	21.2	43.7		-		*85.8*	*71.2*	*100.0*	*58.1*	*41.1*	*75.1*
	2010-2014	**48.2**	34.6	61.8	*70.2*	*46.6*	*93.9*	**36.9**	24.3	49.5		-		**96.3**	89.9	100.0	**89.2**	78.6	99.8
New Zealand*	2000-2004		-			-		*30.8*	*7.6*	*53.9*		-			-			-	
	2005-2009		-			-		*30.8*	*7.6*	*53.9*		-			-			-	
	2010-2014	*60.8*	*32.0*	*89.7*		-		*44.1*	*23.1*	*65.1*		-			-			-	

* Countries with 100% coverage of the national population. § Survival estimates considered less reliable because the proportion of patients lost to follow-up or censored alive prior to five years, or the proportion of diagnoses based on a death certificate or autopsy, or the proportion of patients registered with incomplete dates, was 15% or more. Survival estimates in italics are not age-standardised.

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed <u>for each</u> research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1701655	**Title**	Dr
First Name(s)	Fabio		
Surname/Family Name	Girardi		
Thesis Title	Global surveillance of survival from brain tumours diagnosed during 2000-2014: trends by age and histology		
Primary Supervisor	Dr Claudia Allemani		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	Neuro-Oncology
Please list the paper's authors in the intended authorship order:	Fabio Girardi, (additional authors), Melissa Matz, Michel P Coleman, Claudia Allemani, CONCORD Working Group
Stage of publication	**Not yet submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Conception and design, data analysis and interpretation, manuscript writing

SECTION E

Student Signature	[redacted]
Date	7 December 2020

Supervisor Signature	[redacted]
Date	7 December 2020

Research Paper 5: global trends in survival from brain tumours in adults (CONCORD-3)

World-wide survival trends for brain tumours, by histology: analysis of individual records for 671,085 adults diagnosed in 59 countries during 2000-2014 (CONCORD-3)

Introduction

Tumours originating in the central nervous system are rare: projections to 2018 of the age-standardised (World) incidence rates for adult patients (15-99 years) varied between 1.4 per 100,000 person-years in Western Africa and 12 in Southern Europe.[72] In England, the age-standardised (Europe) incidence rate for glioblastoma, the most common tumour subtype in adults, was 5 per 100,000 person-years, in 2015.[173]

Only a few treatment protocols of proven efficacy are available for brain tumours.[12, 38-40] Patients may receive different combinations of radiotherapy and chemotherapy, depending on histology. For instance, the standard therapeutic regimen for glioblastoma is maximal safe resection (when feasible), a course of radiotherapy given concomitantly with temozolomide and, subsequently, chemotherapy with temozolomide for six months.[12]

Data from all patients registered by national or regional population-based cancer registries are the backbone of population-based cancer survival estimates. Survival for all patients in the population reflects the overall effectiveness of a health care system in managing cancer.[47] World-wide disparities in survival can only be explored through large studies using the same protocol for data collection, the same data quality control procedures and the same statistical methods.

The third cycle of the CONCORD programme for global surveillance of cancer survival (CONCORD-3) obtained individual tumour records from 322 population-based cancer registries in 71 countries, for 37.5 million patients diagnosed during 2000-2014 with one of 18 common cancer types, including 723,473 brain tumours. Age-

standardised five-year survival for all brain tumours combined ranged from 15% in Thailand to 42% in Croatia for patients diagnosed during 2010-2014.[46]

Access to care is inequitable world-wide. Radiotherapy is critical to brain tumour management, but only 65% of middle-income countries and 76% of upper middle-income countries have operating facilities.[74, 174] The neurosurgical workforce has been increasing in low-income and middle-income countries, but it is still largely suboptimal.[164] Distribution of pathology services is uneven and, in many countries, they are simply not available.[147]

Survival for all brain tumours combined is likely to vary world-wide because of health care inequalities, but there is known confounding by the histology composition and the clinical heterogeneity of the tumours under study.

Brain tumours represent a heterogeneous group of entities that have distinct clinical behaviour and survival. In the United States, five-year relative survival in young adults (15-39 years of age) diagnosed during 2001-2015 was 76% for diffuse astrocytoma and 26% for glioblastoma. For older adults (40 years or more), five-year relative survival was 32% and 5%, respectively.[169]

The histology distribution of brain tumours widely varies between countries. In CONCORD-3, the proportion of glioblastoma was less than 10% in China, but more than 50% in Europe and North America, during 2000-2014 (Girardi F et al., Research Paper 3, under review). There may be true geographical differences in incidence for some brain tumour subtypes,[175] but these findings may also point to international differences in cancer registration practices and in the quality of data.

Treatment of brain tumours depends on histology and grade, thus for health systems aiming to improve and monitor cancer outcomes, relying on clinically relevant survival analyses by histology is crucial. Data on population-based survival from brain tumours by histology, however, are limited to Europe and North America. Hardly any studies have been conducted in low-income and middle-income countries, and study designs vary widely. In addition, up-to-date recent international comparisons of survival trends by histology are not currently available.[176] We aimed to address this gap by conducting a study of population-based survival trends with global coverage and up-to-date follow-up for vital status.

Methods

For CONCORD-3, 286 cancer registries in 59 countries submitted 742,145 individual records for adults (15-99 years) diagnosed with a primary brain tumour (International Classification for Diseases in Oncology, third edition (ICD-O-3),[17] topography code C71) during 2000-2014. Non-malignant tumours were also included in the analysis because anatomical location has an impact on treatment choices and morbidity.

Data underwent a stringent, three-phase quality control, which is described elsewhere.[46] In brief, diagnoses based on a death certificate or autopsy were excluded. Tumour records were also discarded if they contained errors in the date sequence or mistakes in various combinations of age, sex, site and morphology.

The proportion of records with incomplete dates was low in most continents (0-2%), but relatively high in Africa (26.2%). Patients registered only from a death certificate (DCO) accounted for more than 10% of records in Africa (10.3%) and Central and South America (14.6%). Data quality indicators are summarised in Table 5.1. Subsequent to quality checks, 671,085 (90.4%) were deemed potentially eligible for analysis.

We selected a set of relevant ICD-O-3 codes. (Girardi F et al., Research Paper 3, under review) using the World Health Organisation Classification of Central Nervous System Tumours (4th edition).[8] ICD-O-3 codes were then categorised into 11 histology groups, compliant with the WHO Classification taxonomy, but more granular.

We estimated net survival using the unbiased non-parametric Pohar Perme estimator. Net survival is the probability for cancer patients to survive their cancer, after controlling for competing risks of death (background mortality), which are higher in the elderly. Information on background mortality is obtained from life tables specific for single year of age, sex, and single calendar year in each country or territory.

We estimated net survival by age (15-44, 45-54, 55-64, 65-74 and 75-99 years). We then used the International Cancer Survival Standard (ICSS) weights (group 2, tumours with age-independent incidence) to produce age-standardised survival estimates for all ages combined.[63] Age standardisation was attempted if 50 patients

or more were available for a given histology group and calendar period. If patients for a given age group were fewer than ten, we merged the records for two adjacent age groups and attributed the same, combined survival estimate to both age groups before performing age standardisation. We did not combine data if survival could not be estimated for two or more age groups. If 10–49 patients were available for analysis, we only produced survival estimates for all ages combined, while we did not estimate survival if fewer than ten patients were available for a given histology group and calendar period. We did not combine data for consecutive calendar periods.[46]

We used the cohort approach for patients diagnosed in 2000-2004 and 2005-2009, because in most data sets all the patients were followed up for at least 5 years. We adopted the period approach for patients diagnosed in 2010-2014, because 5 years of follow-up were not available for all patients. This approach allowed estimation of five-year net survival for patients diagnosed in 2010-2014, by combining the survival probabilities from the most recent follow-up data for patients diagnosed during 2010-2014 with the survival probabilities for patients diagnosed over the preceding five years who were still alive on 1 January 2010.[65, 68]

We produced age-standardised five-year survival estimates by histology group, country and calendar period. For glioblastoma, we also estimated five-year survival by age, to examine the remarkable differences in tumour biology and outcome between different age groups. For this purpose, we identified three age groups: 15-39, 40-70 and 71-99 years. The age boundaries for the 15-39 age group were chosen to match the methods used in previous studies. The age range for adults aged 40-70 years was chosen to be in line with most treatment guidelines, which recommend radiotherapy up to this age. For patients diagnosed with glioblastoma, we also estimated two-year survival by age, in the light of the very poor prognosis for this subtype.

Survival estimates from a given cancer registry were deemed less reliable if the proportion of patients lost to follow-up or censored alive prior to five years, or the proportion of diagnoses based on a death certificate or autopsy, or the proportion of patients registered with incomplete dates, was 15% or more. These estimates were not included in the pooled survival estimate for a country with more than one registry, unless they were the only available survival estimates for that country, in which case they were flagged in tables and figures

Results

Patients potentially eligible for survival analyses were 671,085. Records with morphology codes different from those selected for study (No. 68,973, 10.3% of eligible records) or from cancer registries in which the information was deemed less reliable for the purpose of survival analyses (No. 45,887, 6.8%) were also excluded. The final study population comprised 556,225 adults (82.9% of eligible submissions).

We focus our comments on diffuse and anaplastic astrocytoma, glioblastoma, oligodendroglioma and unspecified astrocytoma. We comment only on countries for which age-standardised, reliable survival estimates were available. Countries are listed in alphabetical order within each continent. Table 5.2 presents detailed five-year survival trends by calendar period of diagnosis (2000-2004, 2005-2009 and 2010-2014) for the 11 histology groups.

Age-standardised five-year survival for patients diagnosed with diffuse and anaplastic astrocytoma during 2010-2014 was in the range 20-29% in China, Israel, Korea, Singapore, Taiwan, Turkey and in nine of 26 European countries; in the range 30-39% in Canada, the United States, nine European countries (Austria, Belgium, Czech Republic, Germany, the Netherlands, Norway, Spain, Sweden and the United Kingdom), Australia and New Zealand. (Table 5.2 and Figure 5.1)

Age-standardised five-year survival from diffuse and anaplastic astrocytoma improved remarkably in Canada, most North European countries, Belgium and the Netherlands (Western Europe), Spain (Southern Europe), Czech Republic (Eastern Europe), and in Australia. Trends were substantially stable elsewhere. Overall, the largest differential occurred between 2000-2004 and 2005-2009. (Figure 5.2)

During 2010-2014, age-standardised five-year survival for glioblastoma was generally poor, nowhere exceeding 17%. Survival was 4.4 % in Ecuador; in the range 5-9% in Puerto Rico, Israel, Thailand, Turkey, Singapore and in 20 of 27 European countries; between 10 and 15% in Canada, the United States, Korea, Singapore, Taiwan, Germany, Latvia, Australia and New Zealand; five-year survival was 16.9% in China. (Table 5.2 and Figure 5.1)

Overall, age-standardised five-year survival for glioblastoma improved over time, mainly between 2000-2004 and 2005-2009. Survival fluctuated or declined over time in Israel, Austria, Belgium, Croatia, Germany, Ireland, Latvia and Norway, while it remained substantially unchanged in Poland. (Figure 5.3)

Outcomes for glioblastoma were further analysed at two years since diagnosis, by age group. Two-year survival in young adults (15-39 years) varied between 30% and 70% world-wide. For patients diagnosed during 2010-2014, two-year survival was in the range 31-42% in Central and South American countries, 30-62% in Asian countries and 27-72% in European countries; survival was around 48% in Canada, the United States, Australia and New Zealand. For patients diagnosed aged 40-70 years during 2010-2014, two-year survival was 24% or lower in nearly all countries. Only in China, Korea, Kuwait, Singapore and Taiwan were outcomes more favourable (31-42%). In patients older than 70 years, two-year survival rarely exceeded 10%. (Supplementary Table 5.1)

In young adults, two-year survival for glioblastoma changed slightly during the 15-year period from 2010 to 2014. Steady, upward trends were observed in only nine countries: Canada, Korea, Denmark, Sweden, the United Kingdom, France, Germany, the Netherlands and Slovenia. In a further 11 countries, early improvements in survival were offset by a decline during 2010-2014. (Supplementary Figure 5.1)

During 2000-2014, remarkable improvements in two-year survival for adults aged 40-70 years occurred in nearly all regions. The steepest increases were observed between 2000-2004 and 2005-2009, but more recently, trends were still upward. The differential was slightly smaller in North America, and in Western and Southern European countries. In Israel, Singapore, Denmark, Sweden, Australia and New Zealand, two-year survival rose from around 10% to more than 20%. In Eastern Europe, however, two-year survival was somewhat stable during 2000-2014 and much lower than 20%. (Supplementary Figure 5.2) During 2000-2014, survival at five years since diagnosis for patients aged 40-70 years improved only slightly and values were below 10% in almost all countries. (Supplementary Table 5.2)

For patients diagnosed with an oligodendroglioma during 2010-2014, age-standardised five-year survival varied widely, from less than 40% to 70%. Survival was

less than 40% in Turkey, Denmark, Poland and Portugal; it ranged between 40% and 49% in Taiwan and in nine out of 25 European countries. Survival varied between 50 and 59% in Canada, China, Israel, Korea, the United Kingdom, Australia and New Zealand. The highest values (60-70%) were seen in Austria, Finland, Germany, the Netherlands, Norway and Slovenia. (Table 5.2 and Figure 5.1)

Steady improvements in age-standardised five-year survival for oligodendroglioma were observed in North America, Israel, Korea, most North European countries, in France and the Netherlands (Western Europe), Croatia and Spain (Southern Europe), in East European countries and in Australia. Survival wavered over time, or declined, in Taiwan, Finland, Austria and New Zealand. (Figure 5.4)

Global disparities in five-year survival from unspecified astrocytoma (namely, astrocytoma without further specification of the histology) were striking. Survival was 27.2% in Ecuador and around 40% in Canada and the United States. In Asia it ranged between 13.1% (Thailand) and 45.5% (Turkey), while in Europe it varied between 25.7% (Czech Republic) and 45.7% (Sweden). Five-year survival was 41.8% in Australia. (Table 5.2)

Discussion

To our knowledge, this is the largest study to date of population-based survival from brain tumours by histology. Many of the countries represented here have never previously been included in international comparisons. We analysed more than half a million individual patient records using the same protocol for data collection, the same standardised data quality controls and the same robust statistical methodology, accounting for international differences in background mortality and in the age profile of cancer patients.

Brain tumour survival in adults varies very widely between groups defined by their histology. Among the most common subtypes, the best outcomes were observed for oligodendroglioma. During 2010-2014, the global range in age-standardised five-year survival within each histology group was also remarkable: between 4% and 17% for glioblastoma, in the range 20-38% for diffuse and anaplastic astrocytoma, and

between 32% and 69% for oligodendroglioma. For patients diagnosed with glioblastoma, survival gains were steepest between 2000-2004 and 2005-2009; these improvements were more pronounced in adults aged 40-70 years than in adolescents and young adults (15-39 years).

Diffuse astrocytoma (WHO grade II) and anaplastic astrocytoma (WHO grade III) harbour a mutation in the isocitrate dehydrogenase 1 (*IDH*1) gene in approximately two-thirds of cases.[36] Such a genetic hallmark has been found to be a more powerful predictor of outcome than the WHO grade,[155, 156] and it has been formally incorporated in the 2016 WHO Classification of Central Nervous System Tumours.[15] Extent of resection, age and performance status now drive choice of subsequent treatment, rather than the tumour histology.[177] Moreover, inter-observer variability in the pathological definition of WHO grade II or III astrocytic tumours is well established.[152, 153] Based on such evidence, we chose to pool tumours defined as diffuse astrocytoma or anaplastic astrocytoma. In a sensitivity analysis in which these two entities were kept separate, international variation in survival within the diffuse astrocytoma subgroup or the anaplastic astrocytoma subgroup was more pronounced than with the combined category. This finding suggests that non-uniform practices in the pathology definition of WHO grade II or III astrocytic tumours may amplify disparities in population-based survival for each of these tumour subtypes, hampering international comparisons. (Supplementary Table 5.3)

In many countries, a steady decline in the proportion of diffuse astrocytoma and anaplastic astrocytoma during 2000-2014 was offset by increasing proportions of glioblastoma (data not shown). Refinements in brain tumour pathology may have led to a progressive reclassification of lower-grade astrocytic tumours with a more aggressive phenotype into glioblastoma.[178-182] As a result, survival from diffuse and anaplastic astrocytoma may have improved during 2000-2014. Treatment options for diffuse and anaplastic astrocytoma are not yet widely agreed and the definition of a standard is still under way,[38-40] so reclassification of diffuse astrocytic tumours (WHO grade II or III) with features of glioblastoma may be the main reason for the observed survival gains. Improvements in surgical techniques, timely surveillance for recurrence and higher rates of repeated surgeries may also play a role.

Glioblastoma is the most common brain tumour subtype in adults. The outcome is generally poor, and most tumours relapse or progress shortly after diagnosis and initial treatment. The current standard of care for glioblastoma was established in 2005, following the results of a large phase 3 randomised clinical trial: two-year survival for adults up to age 70 years receiving radiotherapy concomitant with chemotherapy was 26%, but only 10% for those treated with radiotherapy alone.[12] Here, we have aimed to assess whether the implementation of that treatment protocol in clinical practice has had any impact at population level. We assumed that most patients up to age 70 years were likely to receive concomitant chemo-radiotherapy. That age boundary was used in the 2005 trial, and it has been implemented in clinical guidelines. We explored whether the survival benefit from treatment, barely visible at five years, was more pronounced in shorter-term survival. We considered adolescents and young adults separately, because they may encounter barriers to optimal treatments due to the lack of age-appropriate psychosocial support services or centralised cancer care.[128, 183] Improvements in two-year survival for adults aged 40-70 years were striking, with survival increasing markedly to values in the range 20-30% in several countries over the period 2000-2014. However, trends were somewhat flat in countries such as Poland and Czech Republic, suggesting that constraints in the uptake of modern treatment protocols may still exist. In patients aged 15-39 years, outcomes were more favourable than in those aged 40-70 years, as expected in the light of the biological differences.[36] In absolute terms, however, survival gains during 2000-2014 were much smaller than in patients 40-70 years and limited to a few, affluent countries (Canada, the Netherlands, Korea). Clinical trials have not yet explored outcomes in adolescents and young adults, so it is still unclear whether the potential treatment benefit varies with age. However, the strikingly different trends in survival between patients aged 15-39 and those aged 40-70 years underline the age-related disparities in outcome, as well as the geographical disparities. The prevalence of *IDH* mutations in the 15-39 age group may also account for the favourable outcome in younger patients. Survival gains for glioblastoma were more remarkable in two-year survival than in five-year survival, suggesting that improvements in early diagnosis or the quality of initial treatment may not have had a substantial effect on the longer-term prognosis.

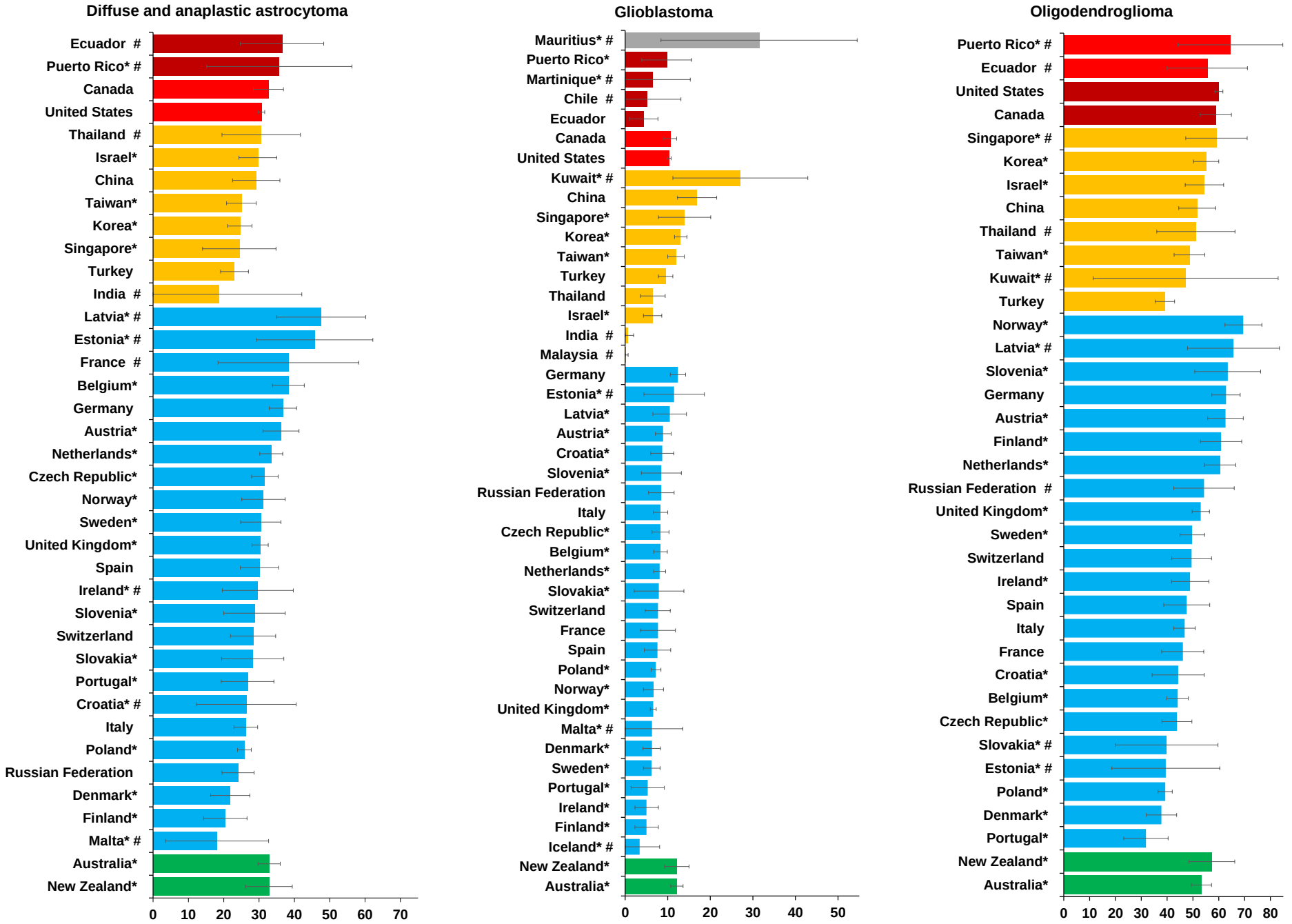
CONCORD-3 asked participating registries to submit treatment data, including the full date of the first course of chemotherapy or radiotherapy.[46] For brain tumours, only 22 US cancer registries provided the full date of the first course of radiotherapy for at least 70% of the patients. The American Society for Radiation Oncology (ASTRO) and the American Society of Clinical Oncology (ASCO) recommend starting radiotherapy as soon as safely permissible.[184] Patients enrolled in clinical trials usually start radiotherapy three to six weeks after surgery,[43, 185] but for patients not in trials, who are the great majority, the time between diagnosis and the initiation of treatment may be much longer, if access to care is suboptimal. In the US CONCORD data set, the 76% of patients received the first course of radiotherapy within six weeks of surgery or biopsy (2000-2014), varying between 70% and 86% (data not shown). More detailed data are needed to explore the impact of treatment delay on survival.

The proportion of brain tumours with non-specific histology (ICD-O-3 codes 8000-8005) varied widely around the world. These neoplasms accounted for 64% and 41% of all brain tumour diagnoses in countries such as China and Denmark, respectively. In China and Italy, the proportion of unspecified tumours was larger than 30% in all the participating regional registries (Girardi et al., Research Paper 3, under review). Strikingly, during 2010-2014, age-standardised five-year survival for brain tumours with non-specific histology ranged from 7% in Puerto Rico to 82% in Norway. Very low survival may imply that the histology of these tumours could not be further specified because the patients were too unwell to undergo surgery or biopsy safely. Nevertheless, the proportion of unspecified tumours recorded as histologically verified was relatively high, which seems counterintuitive. It is difficult to draw firm conclusions, because the broad range of survival values suggests that barriers to the accurate reporting of a brain tumour may intervene at all levels between diagnosis and cancer registration. In countries where the proportion of unspecified brain tumours is very high, age-standardised five-year net survival for tumours in specific histology groups should be interpreted with caution.

Although we could not incorporate world-wide analyses of treatment, we have been able to provide robust population-based evidence that some countries may have failed to implement the current therapeutic standard for glioblastoma, the most common subtype in adults. Importantly, the wide disparities in brain tumour survival

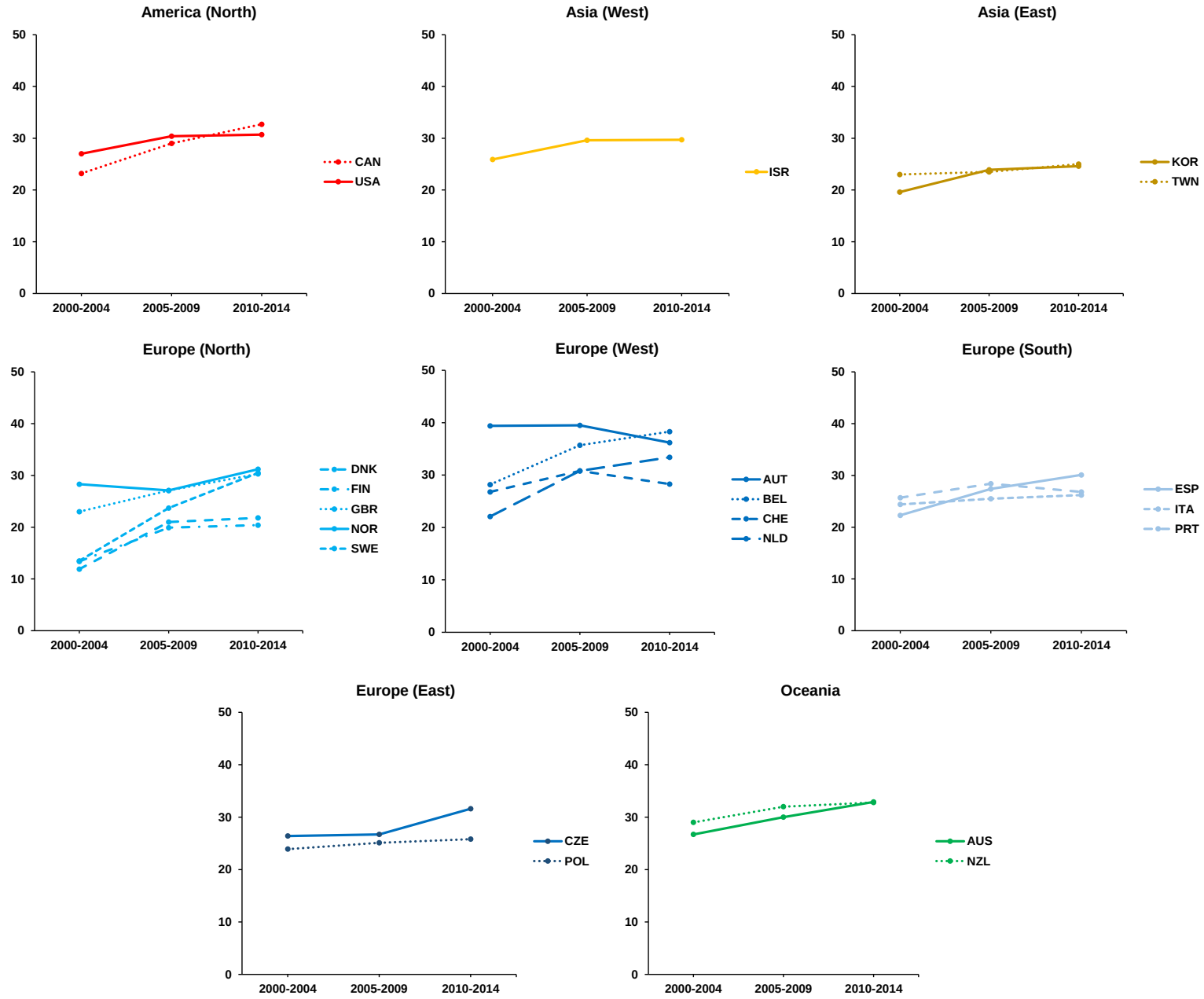
among adolescents and young adults warrant larger efforts to attain equitable access to care for this vulnerable age group. Our findings may also enable clinicians involved in national and international tumour pathway boards to promote initiatives aiming for an extensive uptake of clinical guidelines. In some countries, data quality was still sub-optimal, but we hope that participation in such a large collaborative study will also encourage improvements in cancer registration.

Figure 5.1. Age-standardised five-year net survival (%) with 95% confidence interval, by country. Adults (15-99 years) diagnosed with diffuse and anaplastic astrocytoma, glioblastoma or oligodendroglioma during 2010-2014.



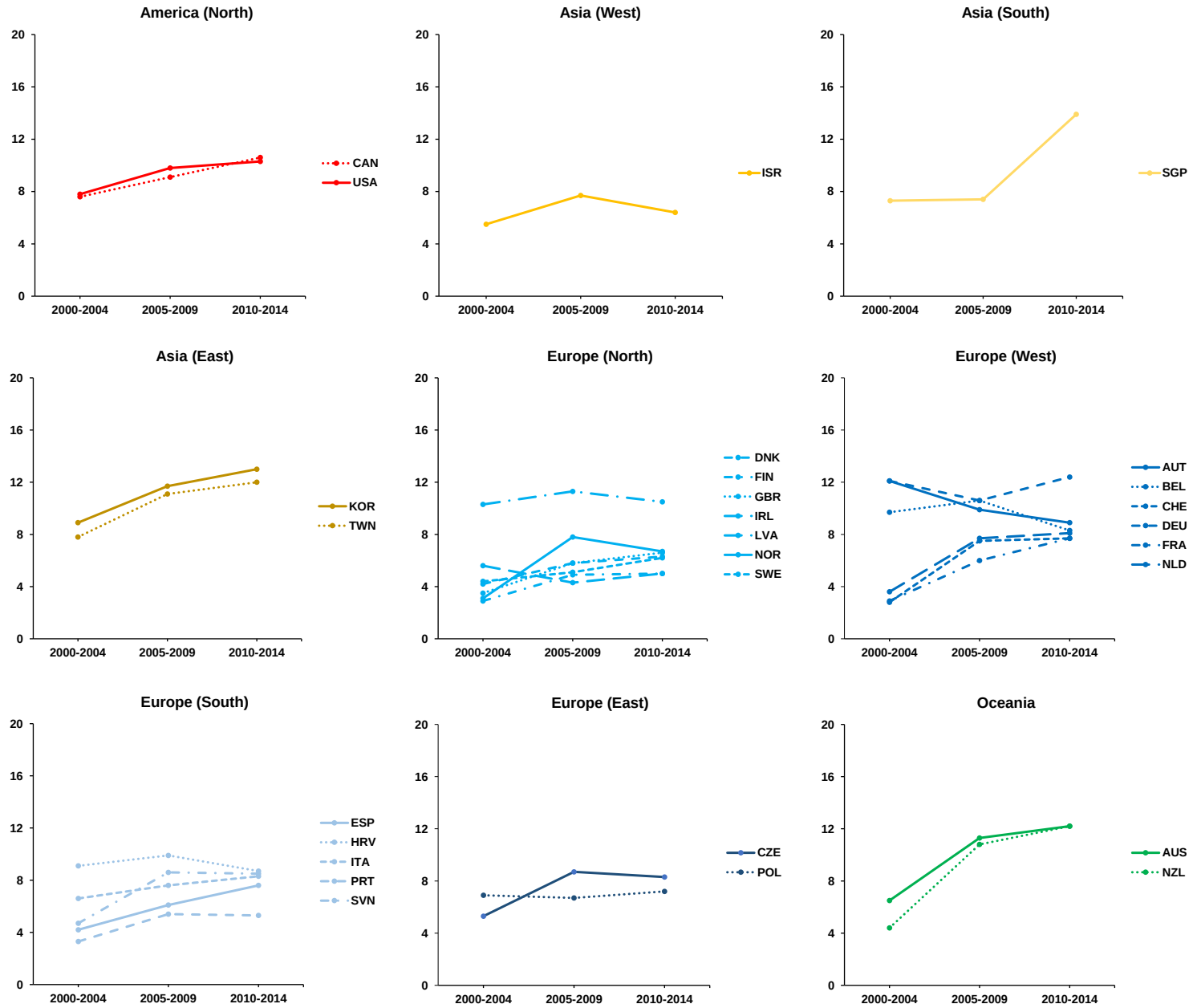
* Countries with 100% coverage of the national population. # Survival estimates are not age-standardised.

Figure 5.2. Trends in age-standardised five-year net survival (%) from diffuse and anaplastic astrocytoma, 2000-2014, by world region. Adults (15-99 years).



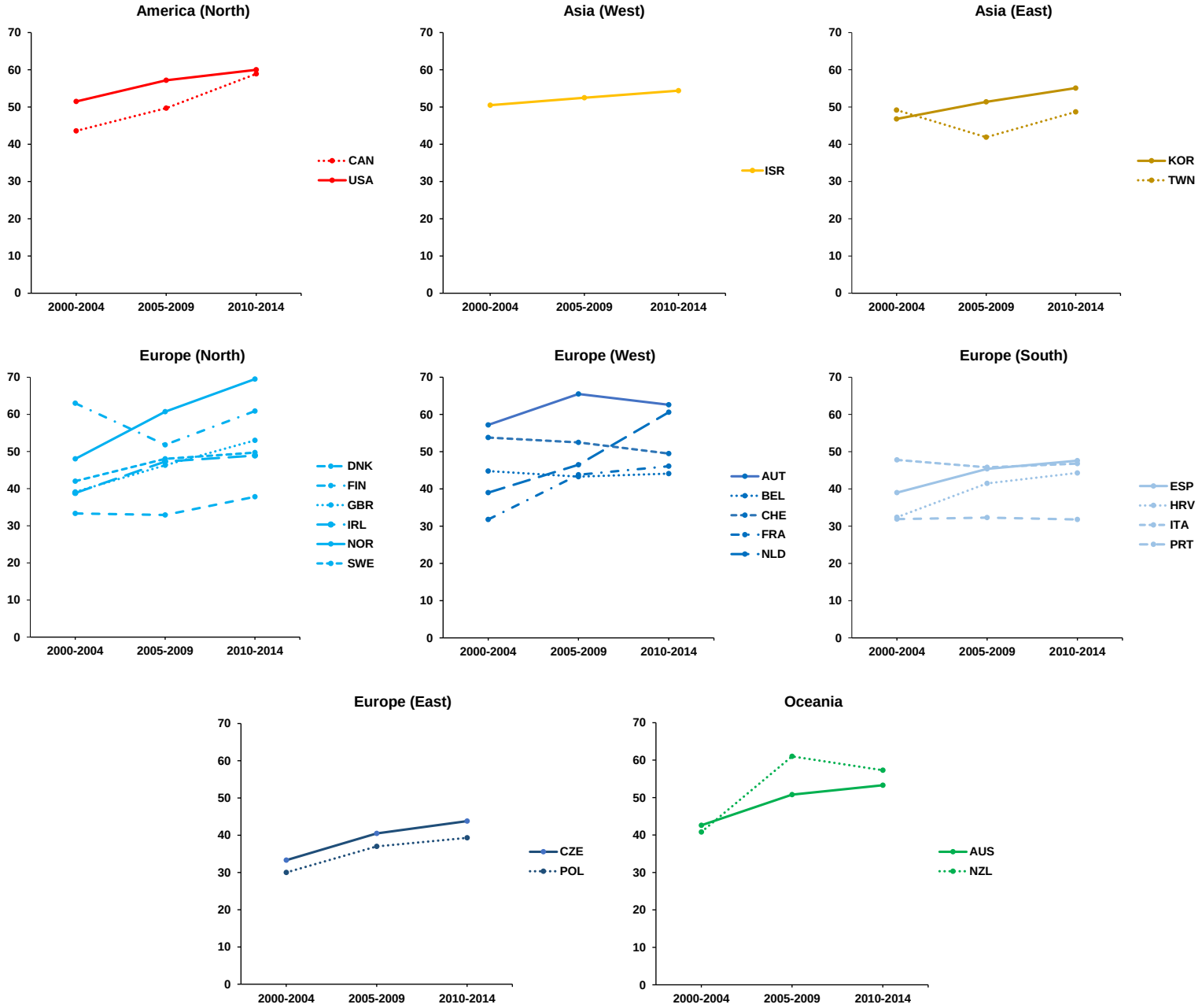
Countries were included if age-standardised survival estimates were available for patients diagnosed during 2000-2004, 2005-2009 and 2010-2014. X-axis: period of diagnosis; Y-axis: age-standardised five-year net survival (%). Australia=AUS; Austria=AUT; Belgium=BEL; Canada=CAN; Czech Republic=CZE; Denmark=DNK; Finland=FIN; Israel=ISR; Italy=ITA; Netherlands=NLD; New Zealand=NZL; Norway=NOR; Poland=POL; Portugal=PRT; South Korea=KOR; Spain=ESP; Sweden=SWE; Switzerland=CHE; Taiwan=TWN; UK=GBR; USA=USA.

Figure 5.3. Trends in age-standardised five-year net survival (%) from glioblastoma, 2000-2014, by world region. Adults (15-99 years).



Countries were included if age-standardised survival estimates were available for patients diagnosed during 2000-2004, 2005-2009 and 2010-2014. X-axis: period of diagnosis; Y-axis: age-standardised five-year net survival (%). Australia=AUS; Austria=AUT; Belgium=BEL; Canada=CAN; Croatia=HRV; Czech Republic=CZE; Denmark=DNK; Finland=FIN; France=FRA; Germany=DEU; Ireland=IRL; Israel=ISR; Italy=ITA; Latvia=LVA; Netherlands=NLD; New Zealand=NZL; Norway=NOR; Poland=POL; Portugal=PRT; Singapore=SGP; Slovenia=SVN; South Korea=KOR; Spain=ESP; Sweden=SWE; Switzerland=CHE; Taiwan=TWN; UK=GBR; USA=USA.

Figure 5.4. Trends in age-standardised five-year net survival (%) from oligodendroglioma, 2000-2014, by world region. Adults (15-99 years).



Countries were included if age-standardised survival estimates were available for patients diagnosed during 2000-2004, 2005-2009 and 2010-2014. X-axis: period of diagnosis; Y-axis: age-standardised five-year net survival (%). Australia=AUS; Austria=AUT; Belgium=BEL; Canada=CAN; Croatia=HRV; Czech Republic=CZE; Denmark=DNK; Finland=FIN; France=FRA; Ireland=IRL; Israel=ISR; Italy=ITA; Netherlands=NLD; New Zealand=NZL; Norway=NOR; Poland=POL; Portugal=PRT; South Korea=KOR; Spain=ESP; Sweden=SWE; Switzerland=CHE; Taiwan=TWN; UK=GBR; USA=USA.

Table 5.1: Data quality indicators, adults (15-99 years) diagnosed with a brain tumour during 2000-2014, by continent and country.

			Ineligible (%)ϒ			Exclusions (%)ǂ			Data quality indicators (%)ϕ			
	Calendar period	Patients submitted	Incomplete dates	Other	Eligible patients	DCO	Other	Available for analysis	MV	Non-specific morphology	Lost to follow-up	Censored
AFRICA		**988**	**26.2**	**0.9**	**720**	**10.3**	**7.5**	**592**	**81.8**	**50.3**	**0.3**	**21.6**
Algerian registries	2000-2014	**632**	22.6	1.3	**481**	12.5	6.0	**392**	93.9	52.3	0.0	3.1
Mauritius*	2010-2012	**46**	0.0	0.0	**46**	0.0	21.7	**36**	77.8	27.8	0.0	0.0
Nigeria (Ibadan)	2005-2014	**293**	39.6	0.0	**177**	7.9	8.5	**148**	53.4	51.4	0.0	72.3
South Africa (Eastern Cape)	2002-2014	**17**	0.0	5.9	**16**	0.0	0.0	**16**	56.3	43.8	12.5	56.3
AMERICA (CENTRAL AND SOUTH)		**11,434**	**2.2**	**2.3**	**10,923**	**14.6**	**5.8**	**8,695**	**84.1**	**17.4**	**0.2**	**4.6**
Argentinian registries	2000-2013	**1,918**	1.1	1.1	**1,875**	22.0	13.1	**1,217**	85.2	17.9	0.0	0.0
Brazilian registries	2000-2014	**1,642**	0.2	1.0	**1,623**	24.8	3.8	**1,159**	89.8	12.5	0.0	0.8
Chilean registries	2000-2012	**600**	0.0	1.3	**592**	17.1	2.7	**475**	59.6	28.4	0.0	6.5
Colombian registries	2000-2014	**1,976**	2.3	2.4	**1,884**	7.6	7.4	**1,601**	76.6	26.5	0.0	20.5
Costa Rica*	2002-2014	**1,411**	0.0	6.9	**1,314**	14.8	4.0	**1,067**	84.4	18.3	0.0	0.0
Ecuadorian registries	2000-2013	**1,767**	7.0	0.5	**1,634**	7.9	1.5	**1,481**	84.4	16.8	0.1	2.0
Guadeloupe (France)	2008-2013	**56**	0.0	0.0	**56**	0.0	1.8	**55**	100.0	0.0	0.0	10.9
Martinique (France)	2000-2012	**186**	0.0	0.0	**186**	0.0	2.2	**182**	78.6	2.2	7.1	0.0
Puerto Rico*	2000-2011	**1,878**	3.1	3.2	**1,759**	12.0	5.1	**1,458**	94.5	10.0	0.0	0.0
AMERICA (NORTH)		**296,096**	**0.6**	**4.7**	**280,326**	**3.1**	**2.7**	**263,989**	**92.6**	**8.4**	**0.8**	**0.0**
Canadian registries	2000-2014	**38,758**	0.1	1.9	**37,990**	1.9	4.7	**35,491**	80.5	19.4	0.0	0.0
US registries	2000-2014	**257,338**	0.7	5.2	**242,336**	3.3	2.4	**228,498**	94.4	6.7	0.9	0.1
ASIA		**84,027**	**0.7**	**2.7**	**81,189**	**8.3**	**1.5**	**73,240**	**77.5**	**22.6**	**0.5**	**1.2**
Chinese registries	2003-2013	**11,797**	0.5	0.3	**11,703**	3.0	0.1	**11,341**	44.2	60.4	2.8	0.1
Cyprus*	2004-2014	**503**	0.6	2.8	**486**	16.0	2.9	**394**	97.7	3.3	0.0	0.0
Indian registries	2000-2014	**295**	0.0	0.3	**294**	5.1	10.5	**248**	64.1	36.7	2.0	7.3
Israel*	2000-2013	**6,358**	0.0	6.3	**5,959**	9.8	2.4	**5,235**	91.5	9.7	0.0	0.0
Japanese registries	2000-2014	**21,939**	0.7	7.4	**20,156**	24.8	0.8	**15,007**	80.2	19.5	0.0	1.9
Jordan*	2000-2014	**1,625**	0.1	1.9	**1,593**	0.5	6.4	**1,483**	95.5	6.3	3.4	0.0
Korea*	2000-2014	**17,946**	0.8	0.0	**17,797**	0.0	0.5	**17,701**	80.7	20.1	0.0	0.0
Kuwait*	2000-2013	**259**	0.0	0.0	**259**	8.9	2.3	**230**	96.5	3.9	0.9	0.0
Malaysia (Penang)	2000-2013	**163**	1.2	0.0	**161**	4.3	10.6	**137**	77.4	23.4	0.0	0.0
Qatar*	2000-2014	**316**	0.0	2.5	**307**	2.0	4.6	**287**	92.0	8.7	0.0	62.0
Singapore*	2000-2014	**1,300**	0.0	0.5	**1,293**	3.2	3.9	**1,202**	90.2	4.9	0.0	0.0
Taiwan*	2000-2014	**8,492**	0.1	0.0	**8,482**	0.0	0.8	**8,410**	87.8	0.3	0.0	0.0
Thai registries	2000-2014	**3,606**	0.0	1.7	**3,545**	11.5	10.1	**2,779**	64.3	35.9	0.1	2.2
Turkish registries	2000-2013	**9,428**	1.9	1.0	**9,154**	2.3	1.7	**8,786**	88.8	15.6	0.1	4.1
EUROPE		**322,910**	**0.1**	**1.4**	**318,064**	**4.4**	**1.5**	**299,275**	**80.1**	**11.4**	**0.6**	**0.8**
Austria*	2000-2014	**9,591**	0.0	9.2	**8,706**	9.7	2.9	**7,615**	97.2	5.5	0.0	0.0
Belgium*	2004-2014	**9,072**	0.0	0.0	**9,072**	0.1	0.1	**9,057**	96.1	4.4	1.9	0.0
Croatia*	2000-2014	**8,115**	0.0	0.0	**8,115**	6.5	0.9	**7,515**	44.4	1.6	0.0	0.0
Czech Republic*	2000-2014	**11,755**	0.0	0.2	**11,731**	2.9	3.3	**11,007**	75.0	2.4	0.0	0.0
Denmark*	2000-2014	**8,991**	0.0	0.4	**8,951**	0.0	0.0	**8,951**	70.7	37.8	0.3	0.0
Estonia*	2000-2012	**1,425**	0.0	3.4	**1,376**	5.5	0.4	**1,295**	68.5	0.3	0.3	0.0
Finland*	2000-2014	**6,874**	0.9	6.7	**6,355**	5.7	0.6	**5,953**	87.1	0.7	0.2	0.0
French registries	2000-2010	**7,656**	0.4	0.6	**7,580**	0.0	0.6	**7,532**	82.5	0.4	1.2	0.0
German registries	2000-2014	**34,337**	0.4	2.6	**33,327**	16.3	0.7	**27,683**	91.0	1.6	0.3	7.9
Gibraltar*	2000-2009	**18**	16.7	5.6	**14**	0.0	21.4	**11**	100.0	0.0	0.0	9.1
Iceland*	2000-2014	**362**	0.0	2.5	**353**	0.8	0.6	**348**	79.9	20.1	0.0	0.0
Ireland*	2000-2013	**4,763**	0.0	0.0	**4,763**	1.6	1.7	**4,605**	72.7	1.3	0.0	0.0
Italian registries	2000-2014	**29,270**	0.0	0.2	**29,205**	0.9	2.1	**28,325**	63.6	37.5	0.7	0.7
Latvia*	2000-2014	**2,654**	0.0	0.7	**2,635**	0.0	3.1	**2,552**	56.5	44.7	0.0	0.0
Lithuania*	2000-2012	**3,514**	0.0	3.0	**3,407**	12.2	1.5	**2,942**	83.4	0.2	0.0	0.4
Malta*	2000-2013	**366**	0.0	1.9	**359**	8.1	4.2	**315**	76.5	24.8	0.0	0.0
Netherlands*	2000-2014	**17,411**	0.0	0.0	**17,407**	0.2	0.7	**17,261**	84.2	16.4	0.6	0.0
Norway*	2000-2014	**6,739**	0.0	0.0	**6,738**	2.3	0.8	**6,528**	83.4	5.5	0.4	0.0
Poland*	2000-2014	**39,723**	0.0	0.3	**39,612**	4.2	0.4	**37,794**	78.4	1.4	0.0	0.0
Portugal*	2000-2014	**8,158**	0.5	3.9	**7,796**	0.2	5.5	**7,348**	92.2	3.8	1.9	0.0
Romania (Cluj)	2006-2012	**449**	0.0	1.8	**441**	32.4	1.6	**291**	88.0	13.1	0.0	0.0
Russian registries	2000-2014	**4,989**	0.0	0.3	**4,973**	1.1	9.5	**4,449**	65.6	4.4	2.4	0.9
Slovakia*	2000-2010	**4,304**	0.0	2.9	**4,180**	11.6	0.0	**3,695**	77.8	22.5	0.0	0.0
Slovenia*	2000-2013	**2,271**	0.0	12.9	**1,979**	1.8	0.0	**1,943**	78.5	0.4	0.2	0.0
Spanish registries	2000-2013	**9,507**	0.2	2.0	**9,301**	3.2	1.0	**8,910**	72.9	3.7	0.4	0.0
Sweden*	2000-2014	**9,559**	0.0	0.1	**9,554**	1.2	1.2	**9,327**	88.8	11.7	0.2	0.0
Swiss registries	2000-2014	**4,372**	0.0	3.3	**4,227**	1.8	1.1	**4,102**	89.8	4.3	3.6	2.4
United Kingdom*	2000-2014	**76,665**	0.1	0.8	**75,907**	3.4	1.9	**71,921**	83.5	14.5	1.0	0.0
OCEANIA		**26,690**	**0.3**	**1.5**	**26,199**	**1.9**	**1.5**	**25,294**	**92.4**	**6.4**	**0.0**	**0.0**
Australia*	2000-2014	**22,797**	0.4	1.7	**22,306**	1.6	1.7	**21,569**	92.2	6.4	0.0	0.0
New Zealand*	2000-2014	**3,893**	0.0	0.0	**3,893**	3.6	0.7	**3,725**	93.7	6.7	0.0	0.0
Total		**742,145**	**0.4**	**2.9**	**717,421**	**4.4**	**2.1**	**671,085**	**85.2**	**11.4**	**0.6**	**0.6**

DCO: death certificate only. MV: microscopic verification. * Data with 100% coverage of the national population. ϒ Incomplete dates: records in which the year of birth is unknown; or the month or year of diagnosis is unknown; or the year of last known vital status is unknown. Other: records with incomplete data or for tumours that are metastatic from another organ (behaviour code 6), or unknown if primary or metastatic (behaviour code 9); or for patients with age outside the range 15–99 years (adults); or other conditions. ǂ DCO: tumours registered only from a death certificate or detected at autopsy. Other: vital status or sex unknown; invalid date or sequence of dates; inconsistency of sex–site, site-morphology, age–site, age-morphology, or age–site-morphology. ϕ Non-specific morphology: ICD-O-3 morphology code in the range 8000–8005. Censored: patients whose last known vital status is "alive" and who were censored within 5 years of diagnosis.

Table 5.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Ependymoma and choroid plexus tumour			Diffuse and anaplastic astrocytoma			Glioblastoma			Other specified astrocytoma			Unspecified astrocytoma			Oligodendroglial tumour		
		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	
AFRICA																			
Algeria	2000-2004		-			-		*0.0* §	*0.0* -	*0.0*		-			-			-	
	2005-2009		-			-		*48.8* §	*29.9* -	*67.7*		-		*77.2* §	*56.3* -	*98.1*		-	
	2010-2014		-			-		*13.9* §	*5.8* -	*22.0*		-			-			-	
Mauritius*	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-			-		*31.5*	*8.4* -	*54.5*		-			-			-	
Nigeria (Ibadan)	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-		*95.6* §	*76.8* -	*100.0*		-			-			-	
	2010-2014		-			-		*0.1* §	*0.0* -	*0.2*		-			-			-	
AMERICA (CENTRAL AND SOUTH)																			
Argentina	2000-2004		-		*27.1* §	*5.9* -	*48.4*	*6.9* §	*0.0* -	*15.1*		-		*39.8* §	*20.3* -	*59.3*	*48.7* §	*25.0* -	*72.3*
	2005-2009	*42.0* §	*13.3* -	*70.8*	*34.4* §	*22.4* -	*46.3*	**12.5** §	7.2 -	17.9		-		**27.2** §	20.4 -	34.1	*61.4* §	*46.7* -	*76.2*
	2010-2014	*60.7* §	*31.1* -	*90.3*	*47.4* §	*31.1* -	*63.6*	**9.7** §	5.0 -	14.3		-		*33.4* §	*22.0* -	*44.9*	*57.3* §	*40.4* -	*74.2*
Brazil	2000-2004		-		*32.8* §	*19.8* -	*45.8*	**13.1** §	7.4 -	18.9		-		*48.0* §	*35.3* -	*60.6*	*61.0* §	*36.9* -	*85.1*
	2005-2009		-		*50.9* §	*36.9* -	*65.0*	**10.5** §	6.3 -	14.6		-		*56.2* §	*45.0* -	*67.4*	*62.0* §	*43.9* -	*80.0*
	2010-2014	*64.7* §	*36.6* -	*92.8*	*50.1* §	*32.3* -	*67.9*	**18.0** §	11.1 -	25.0		-		*47.8* §	*33.6* -	*61.9*	*68.4* §	*50.3* -	*86.6*
Chile	2000-2004		-			-			-			-			-			-	
	2005-2009		-		*25.5*	*3.0* -	*48.0*	*4.4*	*0.0* -	*11.2*		-			-			-	
	2010-2014		-			-		*5.1*	*0.0* -	*13.1*		-			-			-	
Colombia	2000-2004	*80.5*	*56.9* -	*100.0*	*44.6*	*28.6* -	*60.7*	*3.8*	*0.4* -	*7.3*		-		*50.8*	*31.0* -	*70.5*	*68.1*	*50.2* -	*86.1*
	2005-2009	*36.8*	*8.0* -	*65.6*	*33.9*	*19.9* -	*48.0*	**8.5**	4.1 -	12.8		-		*39.7*	*25.1* -	*54.2*	*56.4*	*39.8* -	*73.1*
	2010-2014	*50.3* §	*18.7* -	*81.9*	**27.2** §	16.2 -	38.2	**6.6** §	2.0 -	11.1		-		*32.8* §	*16.1* -	*49.5*	*51.5* §	*32.3* -	*70.7*
Costa Rica*	2000-2004		-		*48.2* §	*27.3* -	*69.2*	*17.3* §	*8.2* -	*26.3*		-		*44.7* §	*32.4* -	*56.9*	*47.3* §	*32.5* -	*62.2*
	2005-2009		-		*40.5* §	*19.7* -	*61.4*	**12.7** §	6.6 -	18.9		-		**22.8** §	16.3 -	29.3	*41.9* §	*29.7* -	*54.1*
	2010-2014	*71.9* §	*39.6* -	*100.0*	*40.7* §	*21.4* -	*59.9*	**12.6** §	7.0 -	18.1		-		**24.9** §	16.0 -	33.7	*45.6* §	*34.2* -	*57.0*
Ecuador	2000-2004		-		*17.5*	*4.3* -	*30.8*	*5.1*	*0.0* -	*11.2*		-		*38.5*	*28.8* -	*48.2*	*45.7*	*23.6* -	*67.9*
	2005-2009		-		*28.3*	*17.3* -	*39.2*	**1.2**	0.0 -	2.8		-		**22.3**	17.0 -	27.6	*54.4*	*38.3* -	*70.6*
	2010-2014		-		*36.5*	*24.7* -	*48.3*	**4.4**	1.0 -	7.7		-		**27.2**	20.6 -	33.8	*55.6*	*40.0* -	*71.1*
Guadeloupe	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-		*0.0* §	*0.0* -	*0.1*		-			-			-	
	2010-2014		-			-		*0.0* §	*0.0* -	*0.1*		-			-			-	
Martinique*	2000-2004		-			-		*7.1*	*0.0* -	*17.7*		-		*21.7*	*1.9* -	*41.4*		-	
	2005-2009		-			-		*4.2*	*0.0* -	*10.4*		-			-			-	
	2010-2014		-			-		*6.4*	*0.0* -	*15.3*		-			-			-	
Puerto Rico*	2000-2004	*65.7* §	*36.3* -	*95.0*	**32.1** §	25.2 -	38.9	**10.8** §	5.2 -	16.3	*69.0* §	*49.2* -	*88.7*	*52.3* §	*30.4* -	*74.2*	*53.2* §	*35.3* -	*71.1*
	2005-2009	*86.3*	*67.9* -	*100.0*	*46.7*	*35.0* -	*58.3*	**7.3**	4.5 -	10.0	*78.1*	*62.6* -	*93.6*	*47.2*	*27.3* -	*67.2*	*79.0*	*66.2* -	*91.9*
	2010-2014		-		*35.7*	*15.2* -	*56.3*	**9.8**	3.9 -	15.6	*84.7*	*64.8* -	*100.0*		-		*64.5*	*44.2* -	*84.8*
AMERICA (NORTH)																			
Canada	2000-2004	**65.5**	57.3 -	73.6	**23.2**	20.0 -	26.4	**7.6**	6.3 -	8.9	*83.4*	*77.0* -	*89.8*	**24.0**	20.5 -	27.5	**43.6**	40.1 -	47.1
	2005-2009	**84.7**	78.1 -	91.3	**29.0**	25.4 -	32.7	**9.1**	7.7 -	10.5	*87.4*	*82.1* -	*92.7*	**30.4**	26.4 -	34.4	**49.7**	46.1 -	53.3
	2010-2014	**79.8**	72.4 -	87.2	**32.7**	28.4 -	36.9	**10.6**	9.1 -	12.1	*88.7*	*82.8* -	*94.5*	**36.6**	31.8 -	41.4	**58.9**	52.8 -	64.9
United States	2000-2004	**71.9**	68.2 -	75.5	**27.0**	26.1 -	27.8	**7.8**	7.4 -	8.1	**57.9**	54.3 -	61.5	**35.4**	33.1 -	37.7	**51.5**	50.2 -	52.9
	2005-2009	**81.8**	79.3 -	84.3	**30.4**	29.5 -	31.2	**9.8**	9.4 -	10.3	**67.6**	63.7 -	71.5	**40.1**	38.1 -	42.1	**57.2**	55.8 -	58.7
	2010-2014	**82.9**	80.5 -	85.3	**30.7**	29.8 -	31.6	**10.3**	9.9 -	10.8	**67.7**	63.6 -	71.8	**42.4**	40.4 -	44.5	**60.0**	58.5 -	61.6
ASIA																			
China	2000-2004		-		*42.5*	*30.1* -	*54.9*	*18.1*	*7.0* -	*29.2*	*18.5*	*4.6* -	*32.5*	**27.6**	20.7 -	34.5	*73.0*	*57.7* -	*88.4*
	2005-2009	*75.9*	*63.3* -	*88.6*	**31.0**	24.7 -	37.3	**15.1**	10.8 -	19.3	*32.1*	*18.4* -	*45.8*	**35.3**	30.4 -	40.3	**48.3**	42.1 -	54.6
	2010-2014	*78.4*	*65.3* -	*91.5*	**29.2**	22.5 -	35.9	**16.9**	12.3 -	21.5	*62.8*	*45.9* -	*79.7*	**38.9**	32.6 -	45.1	**51.7**	44.5 -	58.8
Cyprus*	2000-2004		-			-			-			-			-			-	
	2005-2009		-		*30.8* §	*15.1* -	*46.5*	**6.7** §	1.7 -	11.6		-			-		*70.7* §	*43.7* -	*97.8*
	2010-2014		-		*29.2* §	*13.8* -	*44.5*	**10.1** §	4.0 -	16.2		-			-		*62.0* §	*37.5* -	*86.4*
India	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-			-			-			-			-	
	2010-2014		-		*18.7*	*0.0* -	*42.1*	*0.6*	*0.0* -	*2.0*		-			-			-	
Israel*	2000-2004	*77.7*	*62.5* -	*92.9*	**25.9**	21.5 -	30.4	**5.5**	3.4 -	7.6	*85.2*	*75.7* -	*94.7*	*35.5*	*21.3* -	*49.8*	**50.5**	43.0 -	58.1
	2005-2009	*81.1*	*66.0* -	*96.2*	**29.6**	24.5 -	34.7	**7.7**	5.2 -	10.2	*84.6*	*75.9* -	*93.2*	*38.7*	*20.3* -	*57.1*	**52.5**	45.5 -	59.5
	2010-2014	*90.5*	*75.1* -	*100.0*	**29.7**	24.3 -	35.0	**6.4**	4.3 -	8.6	*89.1*	*80.3* -	*97.8*	*47.5*	*28.1* -	*66.9*	**54.4**	47.0 -	61.9
Japan	2000-2004	*62.8* §	*47.8* -	*77.8*	**28.5** §	23.5 -	33.5	**8.4** §	6.4 -	10.4	*60.2* §	*41.2* -	*79.2*	**35.5** §	30.3 -	40.7	**54.5** §	47.5 -	61.6
	2005-2009	*76.0* §	*65.8* -	*86.2*	**30.5** §	26.7 -	34.3	**10.9** §	9.1 -	12.6	*72.8* §	*61.1* -	*84.4*	**38.8** §	34.1 -	43.4	**58.2** §	53.4 -	62.9
	2010-2014	**91.2** §	84.3 -	98.1	**29.2** §	25.2 -	33.2	**11.2** §	9.3 -	13.1	**65.6** §	52.7 -	78.4	**47.1** §	41.0 -	53.2	**62.3** §	57.3 -	67.3

Table 5.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Ependymoma and choroid plexus tumour			Diffuse and anaplastic astrocytoma			Glioblastoma			Other specified astrocytoma			Unspecified astrocytoma			Oligodendroglial tumour		
		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	
Jordan*	2000-2004	*87.7 §	*71.0 -	*100.0*	**70.2** §	59.9 -	80.5	**37.1** §	29.6 -	44.5	*92.8 §	*77.6 -	*100.0*	*67.1 §	*52.2 -	*81.9*	*84.6 §	*71.9 -	*97.3*
	2005-2009	*93.1 §	*79.8 -	*100.0*	*53.2 §	*41.8 -	*64.7*	**38.5** §	31.7 -	45.3		-		*70.9 §	*52.3 -	*89.5*	*68.0 §	*53.9 -	*82.2*
	2010-2014	*83.3 §	*65.9 -	*100.0*	**36.7** §	24.2 -	49.2	**23.1** §	15.2 -	31.1		-		*35.8 §	*12.0 -	*59.5*	*55.9 §	*41.0 -	*70.8*
Korea*	2000-2004	*75.6*	*64.9 -	*86.3*	**19.6**	16.7 -	22.6	**8.9**	7.6 -	10.3	*84.0*	*70.7 -	*97.3*	**32.4**	27.7 -	37.0	**46.8**	42.7 -	51.0
	2005-2009	**74.9**	66.7 -	83.1	**23.9**	20.5 -	27.3	**11.7**	10.2 -	13.1	*68.8*	*53.5 -	*84.1*	**44.2**	39.8 -	48.6	**51.4**	47.1 -	55.8
	2010-2014	**82.7**	75.3 -	90.1	**24.6**	21.1 -	28.0	**13.0**	11.6 -	14.5	*74.3*	*61.5 -	*87.1*	**42.9**	38.5 -	47.4	**55.1**	50.2 -	60.0
Kuwait*	2000-2004		-		*33.5 §	*8.8 -	*58.3*	*11.6 §	*0.2 -	*23.0*		-			-			-	
	2005-2009		-			-		*7.2*	*0.0 -	*14.5*		-			-			-	
	2010-2014		-			-		*27.1*	*11.2 -	*42.9*		-			-		*47.2*	*11.4 -	*83.0*
Malaysia (Penang)	2000-2004		-			-			-			-			-			-	
	2005-2009		-			-		*14.7*	*0.0 -	*31.2*		-		*29.7*	*8.9 -	*50.4*		-	
	2010-2014		-			-		*0.2*	*0.0 -	*0.7*		-		*17.7*	*0.0 -	*40.4*		-	
Qatar*	2000-2004		-			-		*35.6 §	*2.8 -	*68.4*		-			-			-	
	2005-2009		-		*54.7 §	*18.5 -	*90.9*	*13.3 §	*0.0 -	*27.1*		-			-		*62.6 §	*25.2 -	*100.0*
	2010-2014		-		*84.0 §	*56.5 -	*100.0*	*10.0 §	*0.0 -	*23.7*		-			-		*26.7 §	*0.0 -	*60.0*
Singapore*	2000-2004		-		*38.2*	*21.6 -	*54.8*	**7.3**	2.9 -	11.7		-		*33.6*	*8.8 -	*58.4*	*66.9*	*51.5 -	*82.4*
	2005-2009	*87.3*	*68.9 -	*100.0*	*35.1*	*21.1 -	*49.1*	**7.4**	2.9 -	11.9	*81.3*	*62.8 -	*99.8*		-		*51.4*	*39.0 -	*63.8*
	2010-2014	*82.1*	*62.7 -	*100.0*	**24.4**	14.0 -	34.8	**13.9**	7.8 -	20.1	*87.1*	*73.4 -	*100.0*	*40.7*	*18.0 -	*63.5*	*59.1*	*47.2 -	*71.0*
Taiwan*	2000-2004	*67.2*	*52.7 -	*81.6*	**23.0**	18.7 -	27.3	**7.8**	6.1 -	9.6	*74.0*	*59.3 -	*88.7*	**27.9**	23.4 -	32.4	**49.2**	42.3 -	56.1
	2005-2009	*77.2*	*63.6 -	*90.7*	**23.5**	19.8 -	27.1	**11.1**	9.1 -	13.1	*72.2*	*53.6 -	*90.7*	**37.7**	31.2 -	44.1	**41.9**	36.6 -	47.2
	2010-2014	*81.1*	*68.8 -	*93.4*	**25.0**	20.8 -	29.2	**12.0**	10.0 -	13.9	*60.3*	*43.4 -	*77.1*	**42.8**	34.9 -	50.8	**48.7**	42.7 -	54.6
Thailand	2000-2004		-		*17.7 §	*5.8 -	*29.6*	**5.2** §	1.4 -	8.9	*8.5 §	*0.0 -	*19.5*	**8.4** §	4.9 -	11.9	*19.5 §	*6.4 -	*32.7*
	2005-2009	*46.0*	*18.0 -	*74.1*	*32.4*	*20.6 -	*44.2*	**5.7**	2.8 -	8.7	*42.3*	*19.4 -	*65.3*	**15.9**	11.4 -	20.3	*46.0*	*27.9 -	*64.2*
	2010-2014	*31.1*	*9.6 -	*52.5*	*30.6*	*19.5 -	*41.7*	**6.5**	3.6 -	9.4		-		**13.1**	7.5 -	18.8	*51.1*	*36.0 -	*66.3*
Turkey	2000-2004	*56.4 §	*31.2 -	*81.6*	*27.3 §	*17.7 -	*37.0*	**5.2** §	1.7 -	8.7	*84.5 §	*67.6 -	*100.0*	*50.7 §	*23.0 -	*78.3*	*53.7 §	*42.7 -	*64.7*
	2005-2009	**75.9**	66.7 -	85.1	**21.3**	17.5 -	25.1	**7.4**	5.9 -	8.9	*79.0*	*70.0 -	*87.9*	*57.6*	*48.7 -	*66.5*	**40.8**	35.6 -	45.9
	2010-2014	**83.0**	73.3 -	92.7	**23.0**	19.1 -	27.0	**9.5**	7.8 -	11.2	*81.6*	*73.1 -	*90.0*	**45.5**	34.1 -	56.9	**39.2**	35.4 -	42.9
EUROPE																			
Austria*	2000-2004	*82.4*	*69.4 -	*95.4*	**39.4**	32.8 -	46.0	**12.1**	10.0 -	14.2		-		**32.4**	26.6 -	38.3	**57.2**	49.7 -	64.8
	2005-2009	**97.5**	92.5 -	100.0	**39.5**	34.3 -	44.8	**9.9**	8.0 -	11.8		-		**43.2**	36.0 -	50.5	**65.5**	58.8 -	72.3
	2010-2014	**86.0**	76.1 -	95.9	**36.2**	31.1 -	41.3	**8.9**	7.1 -	10.8		-		**38.2**	31.3 -	45.0	**62.6**	55.7 -	69.5
Belgium*	2000-2004	*72.9*	*46.2 -	*99.7*	**28.2**	21.1 -	35.3	**9.7**	5.6 -	13.7	*95.3*	*86.4 -	*100.0*		-		**44.8**	37.1 -	52.5
	2005-2009	**79.2**	70.5 -	88.0	**35.7**	31.9 -	39.6	**10.6**	8.8 -	12.4	*78.4*	*70.7 -	*86.2*	*33.6*	*8.5 -	*58.6*	**43.3**	39.1 -	47.5
	2010-2014	**90.7**	81.2 -	100.0	**38.3**	33.8 -	42.8	**8.3**	6.7 -	9.9	**64.6**	53.7 -	75.5	*31.7*	*4.5 -	*58.8*	**44.1**	39.9 -	48.2
Croatia*	2000-2004	*74.7*	*57.7 -	*91.7*	*44.3*	*30.3 -	*58.3*	**9.1**	6.1 -	12.0		-		**30.0**	24.2 -	35.7	**32.4**	26.6 -	38.3
	2005-2009	*78.8*	*63.1 -	*94.6*	*33.6*	*19.4 -	*47.7*	**9.9**	7.1 -	12.7	*81.7*	*64.9 -	*98.4*	*49.7*	*38.3 -	*61.1*	**41.5**	33.4 -	49.5
	2010-2014	*66.0*	*46.2 -	*85.9*	*26.4*	*12.3 -	*40.5*	**8.7**	6.0 -	11.4	*67.3*	*49.2 -	*85.4*	**30.7**	23.2 -	38.2	**44.3**	34.2 -	54.4
Czech Republic*	2000-2004	*59.8*	*45.9 -	*73.8*	**26.4**	23.5 -	29.3	**5.3**	3.7 -	7.0	*61.3*	*49.3 -	*73.3*	**21.6**	14.3 -	29.0	**33.3**	28.6 -	37.9
	2005-2009	*58.1*	*43.5 -	*72.7*	**26.7**	23.5 -	29.9	**8.7**	6.5 -	10.9	*53.6*	*42.3 -	*64.8*	*40.8*	*28.8 -	*52.7*	**40.5**	35.4 -	45.7
	2010-2014	**50.4**	38.8 -	62.1	**31.6**	27.9 -	35.4	**8.3**	6.3 -	10.3	*67.6*	*56.9 -	*78.4*	**25.7**	18.3 -	33.0	**43.8**	38.0 -	49.6
Denmark*	2000-2004	*74.8*	*60.4 -	*89.3*	**11.9**	7.0 -	16.8	**4.2**	2.2 -	6.1	*88.5*	*77.8 -	*99.2*	**23.6**	18.0 -	29.2	**33.3**	28.5 -	38.0
	2005-2009	*84.4*	*74.1 -	*94.7*	**21.0**	15.8 -	26.2	**5.8**	3.8 -	7.8	*81.2*	*67.4 -	*95.0*	**34.4**	27.0 -	41.7	**32.9**	27.5 -	38.3
	2010-2014	**73.4**	61.9 -	85.0	**21.8**	16.3 -	27.4	**6.3**	4.2 -	8.3	*85.1*	*72.3 -	*97.8*	**34.7**	27.2 -	42.2	**37.8**	31.9 -	43.7
Estonia*	2000-2004		-		*29.9*	*19.2 -	*40.6*	**5.4**	1.0 -	9.8	*81.9*	*60.2 -	*100.0*		-		*48.9*	*27.9 -	*70.0*
	2005-2009		-		**24.4**	18.4 -	30.5	**7.5**	2.4 -	12.7	*75.1*	*51.4 -	*98.8*		-		*36.2*	*21.1 -	*51.3*
	2010-2014		-		*45.8*	*29.3 -	*62.2*	*11.5*	*4.4 -	*18.6*		-			-		*39.5*	*18.6 -	*60.4*
Finland*	2000-2004	*78.9*	*62.9 -	*95.0*	**13.4**	8.7 -	18.2	**2.9**	1.0 -	4.7	*89.8*	*81.9 -	*97.7*	**46.1**	38.9 -	53.3	**63.0**	55.6 -	70.4
	2005-2009	*83.9*	*73.2 -	*94.5*	**19.9**	14.0 -	25.7	**4.9**	2.5 -	7.4	*80.6*	*69.4 -	*91.8*	**41.4**	35.0 -	47.8	**51.8**	45.5 -	58.1
	2010-2014	**74.9**	65.2 -	84.6	**20.4**	14.3 -	26.6	**5.0**	2.3 -	7.8	*81.7*	*70.9 -	*92.5*	**42.3**	34.4 -	50.1	**60.9**	52.9 -	68.9
France	2000-2004	*69.6*	*53.8 -	*85.4*	**24.0**	17.2 -	30.8	**2.9**	1.4 -	4.3	*80.5*	*67.3 -	*93.7*	**23.5**	16.4 -	30.7	**31.8**	28.5 -	35.2
	2005-2009	*81.3*	*71.2 -	*91.4*	**22.5**	15.7 -	29.2	**6.0**	4.2 -	7.9	*88.0*	*77.9 -	*98.1*	*24.8*	*10.7 -	*38.9*	**43.8**	40.0 -	47.6
	2010-2014	*81.6*	*56.8 -	*100.0*	*38.3*	*18.4 -	*58.2*	**7.7**	3.6 -	11.8		-			-		**46.1**	37.9 -	54.2
Germany	2000-2004		-		*10.1*	*0.0 -	*24.6*	**12.1**	6.9 -	17.4		-		*40.9*	*16.8 -	*64.9*	*78.1*	*65.2 -	*91.1*
	2005-2009	**90.2**	80.8 -	99.6	**37.2**	33.6 -	40.7	**10.6**	9.1 -	12.1	*91.3*	*84.8 -	*97.7*	**33.2**	29.0 -	37.3	**59.9**	54.4 -	65.3
	2010-2014	**78.3**	67.7 -	88.9	**36.7**	32.9 -	40.6	**12.4**	10.6 -	14.2	*91.3*	*83.7 -	*98.9*	**37.8**	32.4 -	43.1	**62.8**	57.3 -	68.3
Iceland*	2000-2004		-			-		*0.0*	*0.0 -	*0.2*		-			-			-	
	2005-2009		-			-		*3.4*	*0.0 -	*7.5*		-			-		*54.4*	*28.5 -	*80.4*
	2010-2014		-			-		*3.4*	*0.0 -	*8.1*		-		*24.6*	*0.0 -	*53.3*		-	
Ireland*	2000-2004	*83.6*	*63.3 -	*100.0*	**17.7**	12.4 -	23.0	**5.6**	2.9 -	8.4	*87.1*	*75.0 -	*99.3*	**27.8**	21.7 -	33.9	**38.8**	31.3 -	46.2
	2005-2009	*87.6*	*71.9 -	*100.0*	**19.4**	13.7 -	25.0	**4.3**	2.3 -	6.3	*90.9*	*80.9 -	*100.0*	**31.2**	24.1 -	38.4	**47.3**	40.2 -	54.4
	2010-2014	*97.7*	*89.0 -	*100.0*	*29.6*	*19.6 -	*39.7*	**5.0**	2.3 -	7.8	*89.8*	*78.6 -	*100.0*	**38.9**	28.1 -	49.7	**48.9**	41.7 -	56.2
Italy	2000-2004	**71.5**	64.2 -	78.9	**24.4**	21.6 -	27.1	**6.6**	5.1 -	8.0	*59.7*	*47.0 -	*72.5*	**27.2**	22.3 -	32.1	**47.8**	42.7 -	52.9
	2005-2009	**69.8**	62.4 -	77.2	**25.5**	23.1 -	27.9	**7.6**	6.4 -	8.8	*72.8*	*64.1 -	*81.5*	**32.5**	28.4 -	36.7	**45.8**	42.6 -	49.0
	2010-2014	**78.2**	68.3 -	88.0	**26.2**	22.9 -	29.6	**8.3**	6.6 -	10.0	*75.5*	*64.7 -	*86.4*	**33.9**	27.7 -	40.0	**46.8**	42.6 -	50.9

Table 5.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendroglial tumour	
		NS	95% CI	NS	95% CI	NS	95% CI	NS	95% CI	NS	95% CI	NS	95% CI
Latvia*	2000-2004		-	**26.7**	19.0 - 34.4	**10.3**	4.7 - 16.0		-	*44.6*	*33.4 - 55.8*	*48.5*	*26.7 - 70.2*
	2005-2009		-	*45.2*	*35.0 - 55.4*	**11.3**	7.1 - 15.4		-	*57.2*	*45.4 - 69.0*	*59.0*	*38.2 - 79.8*
	2010-2014	*32.9*	*4.1 - 61.8*	*47.6*	*35.0 - 60.2*	**10.5**	6.5 - 14.4		-	*58.9*	*46.9 - 70.9*	*65.7*	*47.9 - 83.5*
Lithuania*	2000-2004	*33.7*	*10.7 - 56.8*	*40.7*	*27.3 - 54.0*	**2.5**	0.6 - 4.4		-	**25.2**	20.9 - 29.5	*59.8*	*47.9 - 71.8*
	2005-2009	*61.5*	*37.9 - 85.0*	*55.1*	*43.3 - 66.9*	**5.7**	3.1 - 8.3		-	**33.7**	27.2 - 40.2	*48.1*	*35.3 - 60.9*
	2010-2014		-	*58.8 §*	*45.1 - 72.5*	*3.6 §*	*1.7 - 5.5*	*82.6 §*	*59.6 - 100.0*	*45.5 §*	*30.0 - 60.9*	*48.4 §*	*29.7 - 67.2*
Malta*	2000-2004		-	*20.2*	*1.6 - 38.8*	*3.7*	*0.0 - 9.4*		-		-		-
	2005-2009		-	*31.8*	*11.8 - 51.9*	*0.0*	*0.0 - 0.1*		-		-		-
	2010-2014		-	*18.1*	*3.5 - 32.7*	*6.3*	*0.0 - 13.5*		-		-		-
Netherlands*	2000-2004	**64.7**	57.2 - 72.3	**22.1**	19.6 - 24.6	**3.6**	2.5 - 4.6	*79.7*	*72.6 - 86.8*	*19.2*	*7.7 - 30.8*	**39.0**	34.8 - 43.2
	2005-2009	**80.3**	73.2 - 87.4	**30.8**	27.8 - 33.9	**7.7**	6.4 - 9.1	*82.8*	*76.0 - 89.5*	*24.7*	*10.8 - 38.6*	**46.5**	42.6 - 50.4
	2010-2014	**95.2**	89.8 - 100.0	**33.4**	30.2 - 36.7	**8.1**	6.7 - 9.5	**66.7**	57.3 - 76.0	*22.0*	*8.4 - 35.5*	**60.6**	54.5 - 66.6
Norway*	2000-2004	*85.0*	*67.9 - 100.0*	**28.3**	22.1 - 34.4	**3.1**	1.2 - 5.1	*84.7*	*74.2 - 95.2*	*58.2*	*45.5 - 70.8*	**48.0**	41.0 - 54.9
	2005-2009	*96.7*	*89.8 - 100.0*	**27.1**	21.7 - 32.5	**7.8**	5.0 - 10.7	*85.6*	*76.0 - 95.2*	*50.6*	*38.6 - 62.6*	**60.7**	54.1 - 67.4
	2010-2014	**88.9**	81.3 - 96.4	**31.2**	25.1 - 37.4	**6.7**	4.3 - 9.0	*83.5*	*73.2 - 93.8*	*51.1*	*38.6 - 63.6*	**69.5**	62.4 - 76.7
Poland*	2000-2004	*65.8*	*55.1 - 76.4*	**23.9**	21.1 - 26.7	**6.9**	5.4 - 8.3	*84.3*	*73.0 - 95.5*	**23.1**	19.8 - 26.5	**30.0**	27.0 - 32.9
	2005-2009	**53.6**	46.8 - 60.4	**25.1**	23.2 - 27.0	**6.7**	5.6 - 7.8	*67.5*	*58.7 - 76.3*	**27.4**	24.2 - 30.7	**37.0**	34.4 - 39.6
	2010-2014	**68.8**	62.6 - 74.9	**25.8**	23.9 - 27.8	**7.2**	6.1 - 8.4	*70.6*	*62.2 - 79.0*	**30.8**	26.6 - 35.0	**39.3**	36.5 - 42.0
Portugal*	2000-2004	*80.5*	*64.7 - 96.2*	**25.7**	20.5 - 30.9	**3.3**	1.7 - 5.0	*71.7*	*58.1 - 85.2*	**22.9**	17.8 - 27.9	**31.9**	28.3 - 35.5
	2005-2009	*70.3*	*53.9 - 86.6*	**28.4**	23.7 - 33.1	**5.4**	3.6 - 7.3	*75.3*	*60.2 - 90.4*	**24.4**	18.8 - 30.0	**32.3**	29.1 - 35.4
	2010-2014	**80.5**	63.1 - 97.9	**26.8**	19.3 - 34.2	**5.3**	1.4 - 9.2	*75.0*	*43.0 - 100.0*	**29.4**	17.9 - 40.8	**31.8**	23.2 - 40.4
Romania (Cluj)	2000-2004		-		-		-		-		-		-
	2005-2009		-	*11.2 §*	*0.0 - 24.2*	*5.6 §*	*0.0 - 11.3*		-		-	*52.0 §*	*22.2 - 81.7*
	2010-2014		-	*43.9 §*	*22.6 - 65.1*	*8.4 §*	*1.9 - 15.0*		-		-	*16.6 §*	*0.0 - 33.7*
Russian Federation	2000-2004		-	*31.7*	*17.6 - 45.8*	*13.9*	*7.9 - 19.9*		-	*46.7*	*38.2 - 55.2*	*43.0*	*24.7 - 61.4*
	2005-2009	*21.5*	*1.9 - 41.1*	**24.9**	20.1 - 29.7	**10.6**	6.9 - 14.3	*17.7*	*6.3 - 29.1*	**33.3**	27.7 - 39.0	*60.9*	*48.2 - 73.6*
	2010-2014	*24.2*	*5.9 - 42.5*	**24.1**	19.5 - 28.6	**8.5**	5.5 - 11.5	*35.8*	*10.9 - 60.7*	**36.3**	29.3 - 43.3	*54.3*	*42.6 - 66.0*
Slovakia*	2000-2004	*60.3 §*	*44.0 - 76.5*	**21.8** §	18.3 - 25.3	**4.4** §	2.1 - 6.6	*53.0 §*	*39.6 - 66.5*	*15.6 §*	*2.6 - 28.7*	*43.9 §*	*33.1 - 54.8*
	2005-2009	*66.5*	*52.8 - 80.2*	**24.9**	21.3 - 28.5	**4.7**	2.3 - 7.1	*64.7*	*52.6 - 76.9*	**31.2**	23.9 - 38.5	**39.7**	32.6 - 46.7
	2010-2014		-	**28.2**	19.4 - 37.0	**7.9**	2.1 - 13.8		-	*54.6*	*29.9 - 79.2*	*39.8*	*19.9 - 59.7*
Slovenia*	2000-2004		-	*34.1*	*20.1 - 48.1*	**4.7**	0.9 - 8.4	*82.0*	*66.0 - 98.0*		-	*56.4*	*43.9 - 69.0*
	2005-2009		-	*49.2*	*36.8 - 61.6*	**8.6**	5.0 - 12.2	*88.3*	*73.3 - 100.0*		-	*67.5*	*53.7 - 81.3*
	2010-2014		-	**28.7**	20.0 - 37.4	**8.5**	3.8 - 13.2		-		-	**63.5**	50.7 - 76.2
Spain	2000-2004	*60.7*	*47.2 - 74.3*	**22.3**	19.2 - 25.3	**4.2**	2.6 - 5.7	*79.3*	*67.6 - 91.1*	**21.5**	16.1 - 26.8	**39.0**	32.5 - 45.4
	2005-2009	*81.3*	*70.7 - 91.8*	**27.4**	24.0 - 30.9	**6.1**	4.2 - 8.0	*83.9*	*74.1 - 93.7*	**35.7**	28.3 - 43.0	**45.4**	39.6 - 51.2
	2010-2014	**58.7**	45.6 - 71.7	**30.1**	24.7 - 35.5	**7.6**	4.5 - 10.7	*63.1*	*42.5 - 83.8*	*42.7*	*26.7 - 58.7*	**47.6**	38.7 - 56.5
Sweden*	2000-2004	**78.2**	69.9 - 86.5	**13.5**	10.5 - 16.4	**4.4**	2.6 - 6.1	*85.2*	*76.6 - 93.8*	**32.0**	27.4 - 36.6	**42.0**	36.6 - 47.3
	2005-2009	*83.9*	*74.0 - 93.9*	**23.7**	19.1 - 28.4	**5.1**	3.4 - 6.8	*86.8*	*76.7 - 96.9*	**43.9**	38.8 - 49.0	**48.0**	43.1 - 52.8
	2010-2014	**80.9**	73.6 - 88.1	**30.5**	24.8 - 36.2	**6.2**	4.3 - 8.2	*85.7*	*76.1 - 95.2*	**45.7**	40.2 - 51.3	**49.7**	45.0 - 54.5
Switzerland	2000-2004	*76.0*	*56.1 - 95.9*	**26.8**	20.9 - 32.6	**2.8**	0.8 - 4.8	*78.1*	*60.2 - 96.1*	*27.1*	*7.3 - 47.0*	**53.8**	44.4 - 63.2
	2005-2009	*89.6*	*78.1 - 100.0*	**30.8**	24.4 - 37.1	**7.5**	4.6 - 10.5	*65.7*	*47.1 - 84.3*	*36.3*	*13.4 - 59.3*	**52.5**	44.4 - 60.6
	2010-2014	**85.6**	79.5 - 91.8	**28.3**	21.9 - 34.7	**7.7**	4.7 - 10.6	*78.5*	*62.2 - 94.8*	*35.0*	*10.5 - 59.5*	**49.5**	41.8 - 57.2
United Kingdom*	2000-2004	**63.8**	58.0 - 69.6	**23.0**	21.2 - 24.8	**3.5**	2.9 - 4.1	**54.5**	46.8 - 62.1	**22.3**	20.1 - 24.4	**39.1**	36.6 - 41.7
	2005-2009	**69.8**	64.0 - 75.6	**27.1**	25.2 - 29.1	**5.8**	5.1 - 6.4	**65.5**	56.5 - 74.5	**30.3**	27.1 - 33.5	**46.3**	43.9 - 48.7
	2010-2014	**73.3**	68.2 - 78.5	**30.3**	28.0 - 32.6	**6.6**	5.9 - 7.3	**66.5**	58.9 - 74.2	**31.1**	27.4 - 34.9	**53.0**	49.7 - 56.4
OCEANIA													
Australia*	2000-2004	*84.2*	*76.3 - 92.2*	**26.7**	24.0 - 29.4	**6.5**	5.3 - 7.6	*80.2*	*69.7 - 90.7*	**34.1**	29.6 - 38.7	**42.6**	39.2 - 46.1
	2005-2009	**88.1**	81.0 - 95.2	**30.0**	27.2 - 32.8	**11.3**	9.9 - 12.7	*77.8*	*67.1 - 88.4*	**39.2**	33.7 - 44.7	**50.8**	47.0 - 54.5
	2010-2014	**89.1**	80.8 - 97.4	**32.9**	29.7 - 36.0	**12.2**	10.7 - 13.6	*80.7*	*70.0 - 91.4*	**41.8**	35.3 - 48.2	**53.3**	49.4 - 57.2
New Zealand*	2000-2004	*68.4*	*45.0 - 91.7*	**29.0**	23.0 - 35.0	**4.4**	2.1 - 6.6	*83.0*	*65.2 - 100.0*	*17.3*	*5.2 - 29.4*	**40.8**	33.5 - 48.2
	2005-2009	*64.2*	*36.0 - 92.4*	**32.0**	24.5 - 39.6	**10.8**	8.0 - 13.7		-	*33.7*	*8.8 - 58.6*	**61.0**	53.0 - 68.9
	2010-2014	*83.3*	*63.3 - 100.0*	**32.8**	26.2 - 39.4	**12.2**	9.3 - 15.0		-	*14.0*	*0.0 - 31.5*	**57.3**	48.5 - 66.2

* Countries with 100% coverage of the national population. § Survival estimates considered less reliable because the proportion of patients lost to follow-up or censored alive prior to five years, or the proportion of diagnoses based on a death certificate or autopsy, or the proportion of patients registered with incomplete dates, was 15% or more. Survival estimates in italics are not age-standardised.

Table 5.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Medulloblastoma			Other and unspecified embryonal tumour			Unspecified glioma			Other specified neuro-epithelial tumour			Unspecified tumour		
		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI		NS	95% CI	
AFRICA																
Algeria	2000-2004		-			-			-			-			-	
	2005-2009		-			-			-			-		**48.8** §	39.8	57.8
	2010-2014		-			-		*57.5* §	*25.8*	*89.1*		-		**59.4** §	47.4	71.3
Mauritius*	2000-2004		-			-			-			-			-	
	2005-2009		-			-			-			-			-	
	2010-2014		-			-			-			-		*55.8*	*18.6*	*92.9*
Nigeria (Ibadan)	2000-2004		-			-			-			-			-	
	2005-2009		-			-			-			-			-	
	2010-2014		-			-			-			-		*34.2* §	*9.0*	*59.4*
AMERICA (CENTRAL AND SOUTH)																
Argentina	2000-2004		-			-			-			-		*26.1* §	*4.2*	*48.1*
	2005-2009		-			-		*26.8* §	*7.4*	*46.2*		-		**24.7** §	16.6	32.8
	2010-2014		-			-		*23.1* §	*6.9*	*39.2*		-		**33.0** §	23.3	42.7
Brazil	2000-2004		-			-		*60.6* §	*31.9*	*89.2*		-		*25.4* §	*10.5*	*40.4*
	2005-2009		-			-		*41.5* §	*23.1*	*59.8*		-		**15.8** §	7.8	23.8
	2010-2014		-			-		*33.5* §	*14.5*	*52.5*		-		**24.6** §	4.1	45.2
Chile	2000-2004		-			-			-			-		*17.6*	*0.0*	*37.2*
	2005-2009		-			-			-			-		*3.3*	*0.0*	*9.1*
	2010-2014		-			-			-			-		*28.9*	*5.0*	*52.9*
Colombia	2000-2004		-			-		*29.1*	*5.6*	*52.6*		-		**23.4**	16.4	30.3
	2005-2009		-			-		*38.8*	*14.9*	*62.6*		-		**28.9**	21.9	36.0
	2010-2014		-		*21.8* §	*0.0*	*45.1*	*13.8* §	*0.0*	*29.9*		-		**15.3** §	8.7	22.0
Costa Rica*	2000-2004		-			-			-			-		*58.4* §	*44.6*	*72.2*
	2005-2009		-			-		*20.9* §	*0.0*	*43.1*		-		*41.3* §	*28.6*	*54.0*
	2010-2014		-			-			-			-		**61.4** §	50.4	72.5
Ecuador	2000-2004		-			-		*20.5*	*0.0*	*42.1*		-		*34.3*	*16.0*	*52.6*
	2005-2009	*75.1*	*51.7*	*98.4*		-		*38.0*	*16.8*	*59.2*		-		*9.9*	*2.6*	*17.1*
	2010-2014	*70.1*	*51.5*	*88.7*		-		*26.0*	*5.4*	*46.6*		-		**15.8**	9.4	22.3
Guadeloupe	2000-2004		-			-			-			-			-	
	2005-2009		-			-			-			-			-	
	2010-2014		-			-			-			-			-	
Martinique*	2000-2004		-			-			-			-			-	
	2005-2009		-			-			-			-			-	
	2010-2014		-			-			-			-			-	
Puerto Rico*	2000-2004		-			-		*41.8* §	*19.2*	*64.4*		-		*48.3* §	*34.2*	*62.4*
	2005-2009		-		*20.3*	*0.0*	*42.1*	*53.2*	*27.2*	*79.2*		-		*20.4*	*7.1*	*33.6*
	2010-2014		-			-		*51.6*	*20.5*	*82.6*		-		**6.8**	1.2	12.3
AMERICA (NORTH)																
Canada	2000-2004		-		*31.5*	*18.5*	*44.5*	**32.4**	27.5	37.4	*39.1*	*25.7*	*52.5*	**41.9**	36.7	47.1
	2005-2009		-		*35.5*	*20.8*	*50.1*	**40.0**	35.1	44.9	**51.7**	44.7	58.6	**34.9**	30.8	39.0
	2010-2014		-		*40.2*	*24.8*	*55.6*	**38.8**	33.7	43.9	**51.7**	41.7	61.7	**35.4**	30.6	40.3
United States	2000-2004	*63.7*	*53.8*	*73.6*	**28.6**	24.4	32.9	**37.1**	35.4	38.8	**49.6**	45.3	54.0	**36.3**	34.3	38.3
	2005-2009	*73.1*	*65.0*	*81.2*	**26.0**	22.0	29.9	**42.3**	40.7	43.9	**64.9**	61.4	68.3	**52.6**	51.2	54.0
	2010-2014	*81.0*	*73.6*	*88.4*	**25.3**	21.0	29.5	**45.7**	44.0	47.4	**65.8**	62.4	69.3	**54.9**	53.5	56.4
ASIA																
China	2000-2004		-			-		**20.4**	15.1	25.6	*28.8*	*14.8*	*42.9*	**16.2**	13.5	18.8
	2005-2009	*45.3*	*24.3*	*66.4*	*41.8*	*21.6*	*62.0*	**24.7**	21.1	28.4	**27.5**	18.9	36.1	**21.6**	20.0	23.2
	2010-2014	*36.2*	*11.9*	*60.6*	*31.0*	*12.0*	*50.0*	**27.1**	22.6	31.5	**39.8**	30.6	49.1	**27.6**	25.6	29.5
Cyprus*	2000-2004		-			-			-			-			-	
	2005-2009		-			-			-			-			-	
	2010-2014		-			-			-			-			-	
India	2000-2004		-			-			-			-		*10.6* §	*0.0*	*25.9*
	2005-2009		-			-			-			-		*9.4*	*0.1*	*18.8*
	2010-2014		-			-			-			-		*16.7*	*1.7*	*31.7*

Table 5.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Medulloblastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		NS	95% CI	NS	95% CI	NS	95% CI	NS	95% CI	NS	95% CI
Israel*	2000-2004	-		*37.0*	*10.5 - 63.6*	*29.6*	*17.8 - 41.3*	*87.4*	*76.4 - 98.5*	**57.2**	47.6 - 66.7
	2005-2009	-		*32.8*	*10.9 - 54.7*	**25.3**	17.1 - 33.5	*80.7*	*68.6 - 92.9*	**62.1**	54.7 - 69.5
	2010-2014	-		-		**37.1**	28.0 - 46.3	*81.2*	*66.1 - 96.2*	**52.5**	45.3 - 59.7
Japan	2000-2004	*63.7* §	*36.8 - 90.6*	*31.1* §	*12.8 - 49.4*	**23.2** §	18.0 - 28.4	*65.5* §	*48.6 - 82.3*	**29.4** §	24.9 - 33.9
	2005-2009	*55.5* §	*33.8 - 77.3*	*23.1* §	*11.2 - 35.0*	**25.2** §	20.8 - 29.5	*61.3* §	*51.8 - 70.8*	**50.2** §	46.7 - 53.8
	2010-2014	*63.3* §	*38.1 - 88.6*	*24.5* §	*11.8 - 37.3*	**24.5** §	19.9 - 29.1	**57.8** §	47.9 - 67.6	**68.9** §	65.7 - 72.1
Jordan*	2000-2004	*71.1* §	*44.5 - 97.7*	-		*79.9* §	*57.0 - 100.0*	-		*62.1* §	*39.9 - 84.4*
	2005-2009	-		*45.8* §	*18.0 - 73.6*	*38.0* §	*19.1 - 56.9*	-		*52.4* §	*29.3 - 75.5*
	2010-2014	*62.7* §	*28.5 - 97.0*	-		*50.5* §	*33.0 - 67.9*	-		*34.4* §	*20.8 - 48.1*
Korea*	2000-2004	*66.3*	*54.0 - 78.6*	*40.8*	*30.0 - 51.6*	**31.4**	25.2 - 37.5	*23.2*	*13.0 - 33.3*	**34.6**	32.0 - 37.3
	2005-2009	*67.2*	*54.4 - 80.1*	*34.2*	*24.5 - 43.9*	**44.3**	39.9 - 48.7	**16.7**	11.0 - 22.5	**40.4**	37.6 - 43.3
	2010-2014	*61.1*	*46.7 - 75.4*	**33.7**	24.4 - 43.1	**46.6**	42.4 - 50.8	**19.6**	13.3 - 25.8	**46.4**	43.2 - 49.6
Kuwait*	2000-2004	-		-		-		-		-	
	2005-2009	-		-		-		-		-	
	2010-2014	-		-		-		-		-	
Malaysia (Penang)	2000-2004	-		-		-		-		-	
	2005-2009	-		-		-		-		*10.9*	*0.0 - 23.6*
	2010-2014	-		-		-		-		*38.6*	*12.2 - 64.9*
Qatar*	2000-2004	-		-		-		-		-	
	2005-2009	-		-		*53.4* §	*12.4 - 94.4*	-		-	
	2010-2014	-		-		-		-		-	
Singapore*	2000-2004	-		-		-		-		*10.3*	*0.0 - 22.7*
	2005-2009	-		*54.2*	*28.1 - 80.3*	*39.8*	*17.9 - 61.7*	-		*31.1*	*4.6 - 57.6*
	2010-2014	-		-		*35.1*	*16.7 - 53.5*	*69.4*	*44.2 - 94.6*	*27.0*	*9.7 - 44.4*
Taiwan*	2000-2004	*65.3*	*49.4 - 81.2*	*41.9*	*24.9 - 58.9*	*49.2*	*35.2 - 63.2*	*69.5*	*45.2 - 93.8*	-	
	2005-2009	*63.3*	*46.6 - 79.9*	*46.7*	*31.9 - 61.5*	*37.7*	*24.0 - 51.3*	*57.7*	*32.7 - 82.8*	-	
	2010-2014	*59.5*	*41.2 - 77.7*	*36.3*	*21.3 - 51.4*	**26.7**	18.2 - 35.3	*27.1*	*11.3 - 42.9*	*42.4*	*16.4 - 68.5*
Thailand	2000-2004	-		-		*11.4* §	*0.0 - 27.4*	-		*38.5* §	*25.3 - 51.6*
	2005-2009	-		*23.2*	*6.4 - 39.9*	*30.1*	*15.0 - 45.2*	-		**17.9**	13.6 - 22.3
	2010-2014	-		-		*24.7*	*10.1 - 39.2*	-		**11.1**	7.9 - 14.3
Turkey	2000-2004	-		-		*47.3* §	*32.9 - 61.6*	*73.7* §	*48.4 - 99.1*	**44.2** §	32.0 - 56.4
	2005-2009	*70.4*	*52.2 - 88.6*	*32.4*	*20.0 - 44.9*	**31.5**	26.8 - 36.3	*68.3*	*55.9 - 80.7*	**54.3**	50.3 - 58.3
	2010-2014	*73.6*	*57.0 - 90.3*	*44.8*	*30.3 - 59.2*	**32.9**	28.6 - 37.2	*62.0*	*48.2 - 75.7*	**57.2**	53.3 - 61.1
EUROPE											
Austria*	2000-2004	-		*44.0*	*25.7 - 62.2*	**31.9**	23.1 - 40.6	*10.6*	*0.0 - 22.9*	**26.7**	18.9 - 34.6
	2005-2009	-		*35.3*	*22.6 - 48.1*	*29.3*	*16.5 - 42.1*	*23.3*	*2.1 - 44.5*	**33.7**	24.5 - 43.0
	2010-2014	-		*36.3*	*20.7 - 51.9*	*33.3*	*19.6 - 47.0*	-		**34.1**	23.5 - 44.6
Belgium*	2000-2004	-		-		*37.3*	*16.1 - 58.5*	*77.8*	*58.0 - 97.6*	*25.5*	*10.9 - 40.1*
	2005-2009	*59.5*	*41.3 - 77.6*	*22.3*	*7.3 - 37.3*	**57.2**	48.2 - 66.1	*81.2*	*73.2 - 89.1*	**64.7**	58.1 - 71.3
	2010-2014	*68.0*	*51.7 - 84.3*	*19.5*	*6.2 - 32.9*	**53.6**	41.7 - 65.5	*85.7*	*78.7 - 92.6*	**68.8**	61.4 - 76.2
Croatia*	2000-2004	-		*41.3*	*18.9 - 63.8*	*15.9*	*7.4 - 24.4*	-		*36.1*	*23.8 - 48.4*
	2005-2009	-		*15.4*	*0.0 - 32.6*	*12.0*	*3.8 - 20.1*	*73.6*	*51.7 - 95.6*	*15.9*	*6.8 - 25.0*
	2010-2014	-		-		**13.5**	7.1 - 19.8	*44.7*	*20.3 - 69.1*	-	
Czech Republic*	2000-2004	-		*57.0*	*37.2 - 76.7*	**14.0**	7.7 - 20.3	*39.0*	*13.9 - 64.1*	**15.6**	7.3 - 23.9
	2005-2009	-		*23.3*	*10.3 - 36.3*	**19.0**	11.9 - 26.1	*61.4*	*43.5 - 79.4*	**26.9**	20.9 - 32.8
	2010-2014	-		*29.5*	*14.5 - 44.6*	**17.0**	9.1 - 24.9	*45.8*	*27.9 - 63.6*	**25.2**	17.1 - 33.3
Denmark*	2000-2004	*90.6*	*72.9 - 100.0*	*24.2*	*6.8 - 41.5*	*15.5*	*4.6 - 26.4*	*82.0*	*68.5 - 95.4*	**52.8**	49.3 - 56.3
	2005-2009	-		*11.8*	*0.0 - 25.3*	*18.9*	*1.7 - 36.2*	*84.9*	*72.4 - 97.4*	**60.5**	57.8 - 63.3
	2010-2014	*58.8*	*28.5 - 89.2*	*16.1*	*0.0 - 33.6*	*24.2*	*7.0 - 41.4*	*82.9*	*64.4 - 100.0*	**67.1**	64.5 - 69.7
Estonia*	2000-2004	-		-		-		-		-	
	2005-2009	-		-		-		-		-	
	2010-2014	-		-		-		-		-	

Table 5.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Medulloblastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		NS	95% CI	NS	95% CI	NS	95% CI	NS	95% CI	NS	95% CI
Finland*	2000-2004		-	*28.8*	*6.8 - 50.8*	*14.3*	*2.2 - 26.3*	*90.4*	*81.5 - 99.2*	*37.2*	*16.3 - 58.1*
	2005-2009		-	*31.6*	*10.0 - 53.2*	*27.3*	*12.4 - 42.3*	*93.1*	*86.2 - 100.0*		-
	2010-2014		-	*21.5*	*3.9 - 39.0*	*32.1*	*19.4 - 44.8*	*87.7*	*79.6 - 95.9*	*57.6*	*26.4 - 88.9*
France	2000-2004	*61.2*	*41.7 - 80.7*	*33.6*	*8.7 - 58.6*	**11.1**	6.2 - 16.0	*58.5*	*43.7 - 73.3*	*29.0*	*10.2 - 47.9*
	2005-2009	*73.8*	*57.4 - 90.2*	*23.5*	*2.5 - 44.6*	**16.4**	10.3 - 22.5	*69.9*	*57.8 - 81.9*		-
	2010-2014		-		-	*8.8*	*0.0 - 17.8*	*64.2*	*38.6 - 89.8*		-
Germany	2000-2004		-		-	*20.4*	*3.7 - 37.1*		-	*7.9*	*0.0 - 17.3*
	2005-2009	*71.0*	*44.5 - 97.6*	*43.3*	*27.5 - 59.1*	**31.9**	24.5 - 39.3	*69.7*	*56.2 - 83.3*	**51.6**	42.3 - 60.8
	2010-2014		-	*54.8*	*33.9 - 75.6*	*30.9*	*18.7 - 43.1*	*70.2*	*55.6 - 84.8*	**47.7**	35.1 - 60.3
Iceland*	2000-2004		-		-		-		-	*31.0*	*11.2 - 50.8*
	2005-2009		-		-		-		-	*22.6*	*7.5 - 37.7*
	2010-2014		-		-		-		-	*29.8*	*11.1 - 48.5*
Ireland*	2000-2004		-	*56.5*	*33.0 - 79.9*	*37.0*	*16.1 - 57.9*	*54.6*	*26.8 - 82.4*	*21.0*	*5.3 - 36.8*
	2005-2009		-	*30.1*	*4.4 - 55.7*	*37.6*	*16.4 - 58.9*	*80.3*	*66.7 - 93.8*	*15.5*	*0.0 - 31.3*
	2010-2014		-		-	*56.5*	*26.3 - 86.8*	*77.1*	*60.5 - 93.7*	*18.9*	*1.4 - 36.5*
Italy	2000-2004	*73.4*	*59.3 - 87.6*	*34.6*	*18.6 - 50.7*	**21.8**	17.9 - 25.8	*57.4*	*41.5 - 73.3*	**25.7**	23.7 - 27.8
	2005-2009	*61.6*	*44.7 - 78.5*	**15.6**	8.8 - 22.4	**21.9**	18.3 - 25.4	**47.3**	38.9 - 55.7	**29.6**	27.8 - 31.5
	2010-2014	*67.2*	*47.5 - 86.8*	*21.9*	*8.9 - 34.9*	**20.3**	15.5 - 25.1	*77.6*	*67.1 - 88.1*	**29.5**	26.9 - 32.1
Latvia*	2000-2004		-		-	*13.3*	*2.9 - 23.6*		-	**11.0**	7.5 - 14.5
	2005-2009		-	*26.0*	*2.9 - 49.0*	*6.3*	*0.0 - 15.8*		-	**10.9**	6.4 - 15.4
	2010-2014		-		-	*40.0*	*11.5 - 68.6*		-	**23.9**	17.4 - 30.3
Lithuania*	2000-2004		-		-		-	*10.5*	*0.0 - 26.0*		-
	2005-2009		-		-		-		-		-
	2010-2014		-		-		-	*76.7 §*	*37.7 - 100.0*		-
Malta*	2000-2004		-		-		-		-	*8.0*	*0.0 - 16.0*
	2005-2009		-		-	*5.9*	*0.0 - 14.8*		-	*0.1*	*0.0 - 0.3*
	2010-2014		-		-		-		-	*16.9*	*0.0 - 35.8*
Netherlands*	2000-2004		-	*27.7*	*14.2 - 41.3*	**21.3**	14.9 - 27.7	*73.8*	*64.9 - 82.7*	**18.7**	14.7 - 22.8
	2005-2009	*69.4*	*45.4 - 93.4*	*27.3*	*15.1 - 39.5*	**23.8**	15.4 - 32.2	*81.2*	*74.5 - 88.0*	**27.9**	23.8 - 31.9
	2010-2014	*84.1*	*64.5 - 100.0*	*21.7*	*10.0 - 33.4*	**29.8**	20.5 - 39.1	**56.0**	46.0 - 66.0	**30.9**	25.9 - 35.9
Norway*	2000-2004		-	*25.1*	*4.3 - 46.0*	*41.6*	*30.6 - 52.5*	*85.3*	*74.3 - 96.3*	**76.2**	69.9 - 82.4
	2005-2009		-		-	**45.2**	37.7 - 52.7	*87.0*	*77.5 - 96.5*	*91.8*	*85.7 - 98.0*
	2010-2014		-	*43.6*	*18.3 - 68.8*	**41.9**	32.4 - 51.3	*89.5*	*80.3 - 98.6*	**81.8**	75.1 - 88.6
Poland*	2000-2004	*60.9*	*46.8 - 75.0*	*38.9*	*26.2 - 51.7*	**12.2**	8.1 - 16.3	*24.6*	*13.9 - 35.2*	**24.8**	17.6 - 31.9
	2005-2009	*60.2*	*50.9 - 69.5*	*39.4*	*29.1 - 49.7*	**20.2**	16.1 - 24.2	*34.5*	*19.4 - 49.6*	**8.4**	3.8 - 12.9
	2010-2014	*58.1*	*47.4 - 68.8*	**24.6**	17.7 - 31.5	**16.6**	12.5 - 20.6	**26.6**	16.1 - 37.1	**9.5**	2.7 - 16.4
Portugal*	2000-2004	*45.5*	*15.4 - 75.7*	*40.1*	*22.3 - 58.0*	*22.7*	*12.4 - 33.0*		-	**27.4**	18.6 - 36.2
	2005-2009	*54.5*	*35.0 - 74.0*	*30.7*	*5.7 - 55.8*	*12.0*	*4.3 - 19.8*	*52.1*	*34.7 - 69.5*	**38.8**	30.5 - 47.1
	2010-2014		-	*0.0*	*0.0 - 0.0*	*3.9*	*0.0 - 9.9*	*41.6*	*11.3 - 72.0*	**32.6**	16.8 - 48.4
Romania (Cluj)	2000-2004		-		-		-		-		-
	2005-2009		-		-		-		-	*5.5 §*	*0.0 - 14.1*
	2010-2014		-		-		-		-	*45.8 §*	*14.3 - 77.3*
Russian Federation	2000-2004		-	*44.3*	*18.0 - 70.5*		-	*30.8*	*4.6 - 57.0*	*31.1*	*13.5 - 48.7*
	2005-2009		-	*30.5*	*9.4 - 51.5*	**7.4**	1.5 - 13.3	*22.8*	*0.0 - 47.2*	**17.3**	10.7 - 23.8
	2010-2014		-	*26.9*	*10.9 - 43.0*	**5.6**	1.4 - 9.9	*17.1*	*0.0 - 36.4*	**12.9**	4.2 - 21.7
Slovakia*	2000-2004	*69.6 §*	*45.4 - 93.8*	*20.0 §*	*3.7 - 36.3*	*14.4 §*	*0.6 - 28.2*		-	**24.9** §	18.4 - 31.4
	2005-2009	*65.2*	*43.1 - 87.2*	*15.6*	*1.0 - 30.2*	*26.0*	*14.0 - 38.0*	*51.2*	*31.1 - 71.3*	**32.7**	27.3 - 38.1
	2010-2014		-		-	*23.5*	*2.6 - 44.4*		-	**35.8**	24.1 - 47.4
Slovenia*	2000-2004	*40.2*	*12.2 - 68.2*		-	*20.3*	*0.0 - 42.2*		-		-
	2005-2009		-		-	*17.8*	*1.1 - 34.4*		-		-
	2010-2014		-		-	*27.8*	*6.1 - 49.5*		-		-

Table 5.2. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with a brain tumour, by country, calendar period and histology group.

Country	Period of diagnosis	Medulloblastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		NS	95% CI	NS	95% CI	NS	95% CI	NS	95% CI	NS	95% CI
Spain	2000-2004	*77.6*	*60.6 - 94.6*	*33.7*	*12.9 - 54.6*	**19.7**	13.7 - 25.8	*59.4*	*43.4 - 75.5*	**25.1**	15.5 - 34.7
	2005-2009	*73.0*	*54.8 - 91.2*	*20.7*	*7.6 - 33.8*	**22.0**	15.9 - 28.1	*52.3*	*38.4 - 66.1*	**19.8**	10.2 - 29.3
	2010-2014		-	*27.8*	*6.1 - 49.5*	**13.3**	5.9 - 20.7	*56.8*	*38.0 - 75.6*	*8.5*	*0.0 - 17.8*
Sweden*	2000-2004		-	*19.6*	*8.0 - 31.3*	**24.4**	17.5 - 31.4	*83.2*	*72.9 - 93.5*	**39.7**	32.5 - 46.8
	2005-2009		-	*34.4*	*20.6 - 48.2*	*11.8*	*4.3 - 19.4*	*86.0*	*76.4 - 95.6*	**40.2**	33.5 - 46.8
	2010-2014		-	*57.7*	*41.2 - 74.2*	**20.3**	11.2 - 29.3	*83.3*	*74.1 - 92.5*	**46.6**	40.4 - 52.8
Switzerland	2000-2004	*91.5*	*75.3 - 100.0*		-	*24.0*	*6.5 - 41.5*	*69.7*	*52.3 - 87.2*	*10.8*	*2.3 - 19.3*
	2005-2009	*72.7*	*50.6 - 94.9*	*30.9*	*7.6 - 54.3*	*7.3*	*0.0 - 18.2*	*78.6*	*64.2 - 93.1*	*28.4*	*17.0 - 39.9*
	2010-2014		-	*36.2*	*13.3 - 59.1*	*21.3*	*3.7 - 38.9*	*92.9*	*84.0 - 100.0*	*25.9*	*14.8 - 36.9*
United Kingdom*	2000-2004	*89.3*	*77.1 - 100.0*	*25.3*	*17.2 - 33.3*	**18.2**	16.1 - 20.3	**49.5**	41.7 - 57.3	**24.4**	22.3 - 26.5
	2005-2009	*60.3*	*41.5 - 79.1*	**16.4**	11.2 - 21.6	**21.3**	19.2 - 23.5	**45.8**	38.8 - 52.8	**29.5**	27.3 - 31.6
	2010-2014	*81.3*	*64.8 - 97.7*	**19.8**	13.2 - 26.4	**23.7**	21.4 - 26.0	**48.8**	43.4 - 54.2	**36.1**	34.0 - 38.3
OCEANIA											
Australia*	2000-2004	*100.0*	*71.5 - 100.0*	*27.4*	*14.5 - 40.3*	**33.6**	28.0 - 39.2	*57.5*	*42.6 - 72.5*	**43.1**	37.5 - 48.6
	2005-2009	*73.0*	*48.0 - 98.0*	*31.6*	*18.1 - 45.1*	**35.6**	30.0 - 41.2	*66.5*	*56.1 - 76.9*	**53.2**	48.1 - 58.4
	2010-2014	*80.9*	*61.6 - 100.0*	*30.3*	*15.8 - 44.7*	**39.1**	33.0 - 45.2	*75.8*	*66.8 - 84.8*	**52.6**	46.8 - 58.3
New Zealand*	2000-2004		-		-	**18.9**	10.0 - 27.9		-	*10.2*	*4.0 - 16.4*
	2005-2009		-	*40.2*	*12.3 - 68.2*	*6.1*	*0.0 - 12.4*		-	*14.2*	*7.1 - 21.4*
	2010-2014		-		-	**20.9**	13.3 - 28.6		-	*14.9*	*6.0 - 23.8*

* Countries with 100% coverage of the national population. § Survival estimates considered less reliable because the proportion of patients lost to follow-up or censored alive prior to five years, or the proportion of diagnoses based on a death certificate or autopsy, or the proportion of patients registered with incomplete dates, was 15% or more. Survival estimates in italics are not age-standardised.

Discussion

Critical summary of the main findings

With my doctoral project, I set out to provide a comprehensive examination of world-wide variation in survival from brain tumours in children and adults, by histology. The project revolved around five standalone studies, which together form a coherent body of research.

First, I conducted two systematic reviews of survival from brain tumours by histology, one for children and one for adolescents and young adults. Adolescents and young adults constitute a transitional age group for which it is still unclear whether epidemiological data by histology should be presented using the childhood classifications or analysed as for older adults. These systematic reviews collectively included 303 survival estimates, amounting, to my knowledge, to the largest studies of this kind to date.[144, 176] Nearly the entirety of the available evidence was obtained in high-income countries, especially in Europe and North America. My doctoral project, covering 60 countries in five continents, was designed to fill this gap in knowledge.

Most childhood studies have adopted the third edition of the International Classification of Childhood Cancer (ICCC-3),[19] published in 2005. Comparison of these studies was complicated by inconsistencies in the inclusion of non-malignant astrocytic tumours, both between countries and over time. ICCC-3 is a well-established scheme for analyses of childhood cancer by histology, but in the current form, it may not properly account for the international differences in registration practice for non-malignant (low-grade) tumours.[19] In children, pilocytic astrocytoma is the most common low-grade tumour, accounting for 70% of astrocytic tumours.[169] Under-registration of pilocytic astrocytoma leads to lower survival estimates for all astrocytic tumours combined than if all pilocytic astrocytomas were registered and included in the estimates. International survival disparities will then appear wider as a result of this bias. Failure to adjust survival estimates for tumour grade may therefore hinder firm conclusions about international disparities of childhood brain tumour survival.

In adolescents and young adults (15-39 years), malignant, higher-grade astrocytic tumours are predominant, and their proportion increases rapidly with age. In the US CONCORD data set, the proportion of WHO grade III and IV astrocytoma during 2010-2014 was 16.9% in children (0-14 years), 25.9% in adolescents (15-19 years) and 55.6% in young adults (20-39 years) (data not shown). The use of ICCC-3 has often been extended to adolescents and young adults, but survival estimates have proved to be uninformative.[69] I therefore decided to estimate survival for brain tumours in this age group together with older adults (40-99 years).

In the second part of my project, I built upon the findings from the two systematic reviews to define novel histology groupings, separately for children and adults. I deployed these schemes in the last part of my research, in which I used the CONCORD-3 data to conduct granular analyses of brain tumour survival by histology. I examined the global variation in the histology distribution of brain tumours, and provided an extensive account of some of the quality indicators for cancer registration (Girardi F et al., Research Paper 3, under review). Knowledge of the histology distribution in cohorts of cancer patients used for population-based survival analyses is key to interpreting global disparities in survival for all brain tumour subtypes combined.

Overall, the histology distribution of brain tumours varied widely world-wide. In children, the proportion of low-grade astrocytic tumours (World Health Organisation grade I and II) ranged from less than 10% to more than 30% (Girardi F et al., Research Paper 3, under review). This finding firmly supports my argument that the use of WHO grade may help explain part of the observed international disparities in survival from astrocytic tumours. The strategy adopted here is expected to be implemented in future international comparisons and it could inform a revision of the definition of the ICCC-3 IIIb subgroup (astrocytoma).

In adults, I found that the proportion of glioblastoma varied between countries, but also that it changed during the 15 years between 2000 and 2014 (Girardi F et al., Research Paper 3, under review). Low proportions of glioblastoma in regions other than North America, Europe and Oceania, are consistent with the evidence that this tumour subtype is less frequent in populations of non-European ancestry.[151] The increasing trend in the proportion of glioblastoma, however, suggests a shift in the

pathological reporting of astrocytic tumours, favouring glioblastoma (WHO grade IV) over lower-grade subtypes (diffuse and anaplastic astrocytoma, WHO grades II and III). This may partly mirror the understanding that some WHO grade II and III astrocytic tumours should be classified as glioblastoma because they present an aggressive molecular phenotype.[180, 182] We could not confirm this hypothesis, because molecular data were not available.

In the third and last part of the project, I conducted novel, up-to-date analyses of brain tumour survival, using the histology groupings I have defined. Children and adults were examined in two separate studies. Many of the countries covered here had never previously been included in international comparisons of brain tumour survival by histology. Five-year net survival for low-grade (WHO grade I and II) astrocytoma in children was in the range 84-100%, while it varied between 47% and 86% for medulloblastoma. These findings suggest that in some countries, brain tumours in children may be diagnosed at a more advanced stage, or that initiation of treatment may be delayed. The survival inequalities persisted, or broadened, at 10 years after diagnosis. Timely surveillance for disease relapse and equitable access to rehabilitation services for treatment or cancer-related disabilities, may affect longer-term outcomes.[171]

In adults, I found that survival from glioblastoma improved substantially after 2005 in most countries, mainly in the short term (up to two years from diagnosis). This is likely to be attributable to the more widespread implementation of chemoradiation in clinical practice, following the results of a large randomised clinical trial.[12] The survival gains were widespread, but some countries still seem to lag behind. Strikingly, the increase in two-year survival between 2000-2004 and 2010-2014 was much larger for adults aged 40-70 years than for younger patients (15-39 years). In some countries, population-based outcomes for patients aged 40-70 years were similar to those observed in the highly selected population enrolled in the clinical trial. Trends for 2000-2014 were clearly upward for the 40-70 age group, while they were somewhat flat for the 15-39 age group. Outcomes for younger patients are still more favourable than in older patients because the genetic makeup of the tumours differs between the two age groups.[36] It remains unclear, however, whether the smaller gains in survival for adolescents and young adults may be the result of

differences in the biological response to chemo-radiation or whether the difference reflects that younger adults have no access to dedicated health care services.[183] The 2005 study of chemoradiation in glioblastoma did not provide results by age, so a clinical benchmark is not available.[12] To our knowledge, this thesis provides the first large-scale evidence for age-related disparities for adults diagnosed with glioblastoma and it should prompt further research.

I could not incorporate ecological or socioeconomic descriptors in the survival analyses. Relevant variables may be distance from treatment facilities, health insurance status or the population density of neuro-oncology specialists. Distribution of health care is inequitable world-wide.[74, 147, 164] Societal factors should be incorporated in future analyses to help identify the underlying reasons for the observed disparities.

Methodological considerations

The third cycle of the CONCORD study included individual records for over 37 million patients diagnosed during 2000-2014 with one of 18 common cancer types, including brain tumours, provided by 322 population-based cancer registries in 71 countries. The geographical coverage of CONCORD-3 was broader than any previous international comparison of cancer survival.[46] Standardised protocol for data collection ensured that information was collected based on the same set of patient-related and tumour-related variables.[54] This strategy enabled robust comparisons of survival, overcoming the obstacles to data interpretation posed by survival assessments using different study designs. As part of CONCORD-3, data underwent a stringent, stepwise quality control, including variable-by-variable assessment of adherence to the study protocol, and detection of records with logical inconsistencies (e.g. sex/topography mismatch, mistakes in the sequence of dates).

CONCORD-3 adopted the same, robust statistical methodology for analysis of almost 5,000 data sets. Net survival was estimated with the non-parametric Pohar Perme estimator, ensuring that variations in background mortality by age, sex, calendar year and country were properly accounted for.[62] Survival is a key metric to evaluate the capacity of a given country to manage cancer.[47]

The complement of the mortality-to-incidence ratio has recently been used in large epidemiological studies to model survival and, based on these modelled survival estimates, to derive measures of the cancer burden such as disability-adjusted life years (DALYs).[165] However, incidence and mortality rates do not refer to the same individuals, while survival allows an unequivocal connection between the cancer diagnosis and the outcome (i.e. death or alive at a given point in time), by incorporating the time component, through follow-up of each registered patient. The validity of mortality rates may also be questionable because civil registration systems in low-income and middle-income countries may not record all deaths. In settings with limited resources, however, cancer registries may still be able to reliably update vital status by performing active follow-up.[186] Furthermore, mortality rates require the use of the cause of death stated on the death certificate, which may not be accurate or comparable between countries.[58-60] Net survival does not require knowledge of the cause of death, because background mortality is accounted for by using life tables specific to country, sex, single year of age at death and single calendar year.[145] Taken together, net survival estimated with the Pohar Perme estimator is unbiased; the M/I ratio is not a valid surrogate.

This study only included tumours of the brain (International Classification of Diseases for Oncology (ICD-O-3) topography code C71), by far the most common site for central nervous system (CNS) tumours. CONCORD-3 did not collect data for CNS tumours arising in the meninges (C70), the spinal cord or the cranial nerves, including the optic chiasma (C72), or the pituitary gland (C75.1) or pineal gland (C75.3). For the sake of consistency, I excluded tumour records coded to the topography of brain (C71) but to a morphology that is generally found in other intracranial sites (e.g. pineal gland), because these tumours were likely to be misclassified (Girardi F et al., Research Paper 3, under review). I believe this approach improved comparability of data, but future analyses should aim to include the full range of CNS sites. The rationale for broadening the scope of future international comparisons is two-fold: to enable estimation of survival for clinically important entities, mainly in children, such as germ cell tumours and optic chiasma gliomas; and to help define comprehensive classification systems or to appraise and validate existing ones (e.g. the International Classification of Childhood Cancer).

I have provided a detailed examination of some of the data quality indicators. I assessed the proportion of tumours with poorly specified histology (ICD-O-3 morphology codes 8000-8005) by country, and the proportion of histological verification, by country and histology group (Girardi F et al., Research Paper 3, under review). Overall, the data quality was good, but in some countries the proportion of unspecified tumours was remarkably high. These findings suggest that barriers to the accurate reporting of a brain tumour may intervene at all stages, including formulation and clinical recording of the diagnosis, data transmission and data extraction for the cancer registry. If the accuracy of neuropathology reports is called into question, it is important to measure the effect on patient outcomes, which may be poorer if treatment is not appropriate for the specific histology. Furthermore, survival estimates for specific tumour sub-types are likely to be biased if the histology is fully known for only a subset of records; those estimates may not be robustly generalisable to the entire population of a given country or territory. In some countries, tumours of unspecified histology were labelled as histologically verified in a relatively high proportion of cases, which calls into question the reliability of the information on the basis of diagnosis as histologically confirmed, because one would expect biopsy of a brain tumour to be followed by a specific histological diagnosis. These findings should prompt audits at local and national level on the quality of pathological diagnosis, as well as cancer registration.

Future perspectives

The CONCORD-3 protocol included the date of the first course of each major treatment modality as optional variables. In the brain tumour dataset, information on whether a patient underwent radiotherapy was available for a few countries, but only the United States provided the date of the first course of radiotherapy for at least 70% of the patients. In an exploratory analysis, a remarkable proportion (up to 30.4%) of patients in the United States experienced delays in treatment initiation during 2000-2014 (data not shown). Further research, with equivalent data from more countries, will be needed to understand the impact of these delays on survival. In this context, granular, high-resolution treatment data, such as the dose of radiotherapy, may be used to assess adherence to treatment guidelines. These data, mostly in children, may be also used to examine potential modifiers of survival, such as abandonment

of treatment due to financial toxicity, or distance from treatment centres.[166]

In this research, the definition of the histology groupings, and the selection of the relevant ICD-O-3 morphology codes, was based on the WHO Classification of Tumours of the Central Nervous System (4th edition, 2007).[8] In 2016, however, a revision of the WHO classification revolutionised the taxonomy of CNS tumours by genetically defining tumour entities and prioritising the molecular profile over the traditional WHO grading system.[15] ICD-O-3 was updated accordingly. The Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy (cIMPACT) has been issuing recommendations on how to revise future WHO classifications in the light of advances in understanding of the molecular biology of brain tumours.[179] From 2018, the Central Brain Tumor Registry of the United States (CBTRUS) started collecting population-based data from 48 state-wide cancer registries using the 2016 WHO categories.[16] It may take time for other cancer registries world-wide to follow suit, and in some countries molecular assays may simply be unavailable. Notwithstanding these obstacles, international associations of cancer registries should promote transition to the new neuropathology lexicon for data collection, paving the way for modern, informative international comparisons in brain tumour survival by histology.

The Lancet Oncology Commission on Sustainable Care for Children with Cancer offered robust evidence to invest in scaling-up interventions for childhood cancer control in low-income and middle-income countries.[172] Such research was inscribed in the global effort to attain universal health coverage by 2030, as set out in the United Nations Sustainable Developments Goals.[187] The CONCORD Programme was instrumental in this work, because it produced novel survival estimates for tumours in children, by histology. These detailed estimates were then deployed to build and calibrate a micro-simulation model to simulate childhood cancer survival for 200 countries and territories during 2015-2019. The reference classification scheme for the new CONCORD survival estimates was the second tier of ICCC-3.[19] As previously described, ICCC-3 does not incorporate stratification by WHO grade for astrocytomas, the most common brain tumour entity in children. The Global Initiative for Childhood Cancer was launched by WHO in 2018, aiming to achieve a five-year overall survival of 60% for six childhood tumour subtypes

combined, including low-grade glioma.[127] However, global survival estimates for low-grade glioma are currently not available. The impossibility of teasing out low-grade, non-malignant tumours from the broader astrocytoma group was a major limitation of studies on the childhood cancer burden, including the Global Burden of Disease study.[165] Here, I presented what are, to the best of my knowledge, the first global survival estimates for low-grade astrocytoma in children, inclusive of detailed population counts by country and calendar period. In the US CONCORD data set, more than half of low-grade gliomas were low-grade astrocytomas during 2000-2014.(Girardi F et al., Research Paper 3, under review) Therefore, survival estimates for low-grade astrocytoma may be a proxy for survival from low-grade glioma. The data presented in this thesis could become a benchmark to monitor progress against the objectives established by the Global Initiative for Childhood Cancer.

Brain tumours in children entail a particularly heavy population burden in terms of disability and premature death, and they have a substantial long-term impact due to the loss of persons' economic contribution. In the population as a whole, these brain tumours are rare, and they tend not to be prioritised by public health officials and stakeholders involved in planning interventions to improve cancer control. My research will increase awareness of the importance of brain tumours, by shining a light on the wide survival disparities that exist world-wide. By focussing on vulnerable age groups, my research findings should also promote better interventions to safeguard the right of children and young adults to achieve the best possible outcome, and to lead rewarding and fruitful lives.

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Appendices

Research Paper 1

Research Paper 2

Research Paper 3

Supplementary Table 3.5. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Children (0-14 years) diagnosed with an astrocytic tumour, 2000-2014.

Supplementary Table 3.6. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Adults (15-99 years) diagnosed with an astrocytic tumour, 2000-2014.

Supplementary Table 3.7. Basis of diagnosis by histology group and country, children (0-14 years of age).

Supplementary Table 3.8. Basis of diagnosis by histology group and country, adults (15-99 years of age).

Research Paper 4

Supplementary Table 4.1. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with astrocytoma (broad group), by country and calendar period.

Supplementary Table 4.2. Age-standardised 10-year net survival (%) with 95% confidence interval (CI), 2000-2004. Children (0-14 years) diagnosed with low-grade astrocytoma (WHO grade I and II) or medulloblastoma, by country.

Research Paper 5

Supplementary Figure 5.1. Trends in age-specific two-year net survival (%) from glioblastoma, 2000-2014, by world region. Adults (15-39 years of age).

Supplementary Figure 5.2. Trends in age-specific two-year net survival (%) from glioblastoma, 2000-2014, by world region. Adults (40-70 years of age).

Supplementary Table 5.1. Age-specific two-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Supplementary Table 5.2. Age-specific five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Supplementary Table 5.3. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with diffuse astrocytoma or anaplastic astrocytoma, by country and calendar period.

Other supplementary materials

WHO Classification of Tumours of the Central Nervous System, Fourth Edition, 2007

WHO Classification of Tumours of the Central Nervous System, Revised Fourth Edition, 2016

Supplementary Table 1.1. Strategy for searching Embase.

Exposure domain: central nervous system tumour	
#1	“central nervous system tumo?r*".mp[1].
#2	"central nervous system cancer*".mp.
#3	"central nervous system neoplasm*".mp.
#4	"brain cancer*".mp.
#5	"brain tumo?r*".mp.
#6	"brain neoplasm*".mp.
#7	"cns cancer*".mp.
#8	"cns tumo?r*".mp.
#9	exp[2] central nervous system neoplasms
#10	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9
Outcome domain: survival	
#11	"survival".mp.
#12	“survival analysis”.mp.
#13	exp survival rate
#14	#11 or #12 or #13
Study design domain: longitudinal observational studies	
#15	"cancer registr*".mp.
#16	“international comparison*”.mp.
#17	exp epidemiology
#18	exp life tables
#19	exp registries
#20	#15 or #16 or #17 or #18 or #19
#21	exp clinical trial, phase i or exp clinical trial, phase ii or exp clinical trial, phase iii or exp clinical trial, phase iv or exp controlled clinical trial or exp randomized controlled trial or exp double-blind method or exp random allocation or exp single-blind method
#22	“randomized controlled trial”.mp.
#23	"clinical trial".mp.
#24	"clinical trial, phase i".pt[3].
#25	"clinical trial, phase ii".pt.
#26	"clinical trial, phase iii".pt.
#27	"clinical trial, phase iv".pt.
#28	"controlled clinical trial".pt.
#29	"randomized controlled trial".pt.

#30	"clinical trial".pt.
#31	#21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30
#32	#20 not #31
Combination of the above domains	
#33	#10 and #14 and #32
#34	"comment".pt.
#35	"letter".pt.
#36	"editorial".pt.
#37	exp case reports
#38	exp comment
#39	exp letter
#40	exp editorial
#41	#34 or #35 or #36 or #37 or #38 or #39 or #40
#42	#33 not #41
#43	Animals
#44	Humans
#45	#43 not #44
#46	#42 not #45

[1] mp: multi-purpose. The database looks for the keywords in the default set of fields.

[2] exp: explosion. The database searches not only for the medical subject heading, but also for many related terms.

[3] pt: publication type.

Hashes are only used to improve reading.

Supplementary Table 1.2. Morphology groupings adopted in the systematic review of population-based survival from brain tumours in children.

Grouping strategy in the systematic review	Definitions as adopted in the studies
Embryonal tumour	Embryonal tumour
Medulloblastoma	Medulloblastoma
	Ependymoma and medulloblastoma
PNET[1]	PNET
	Supra-tentorial PNET
AT/RT[2]	AT/RT
Astrocytoma (broad group)	Astrocytoma
	Astrocytoma + pilocytic astrocytoma
	IIIb (ICCC-3[3])
Astrocytoma WHO[4] grade I/II	Astrocytoma WHO grade I/II
	Astrocytoma low-grade
Pilocytic astrocytoma	Astrocytoma WHO grade I
	Pilocytic astrocytoma
Diffuse astrocytoma	Astrocytoma WHO grade II
	Diffuse astrocytoma
	Fibrillary astrocytoma
	Astrocytoma NOS[5]
Astrocytoma WHO grade III/IV	Astrocytoma WHO grade III/IV
	Astrocytoma high-grade
	Glioblastoma and anaplastic astrocytoma
Anaplastic astrocytoma	Anaplastic astrocytoma
	Astrocytoma WHO grade III
Glioblastoma	Glioblastoma

[1] PNET: primitive neuro-ectodermal tumour

[2] AT/RT: atypical teratoid/rhabdoid tumour

[3] ICCC-3: International Classification of Childhood Cancer, Third Edition

[4] WHO: World Health Organization

[5] NOS: not otherwise specified

Supplementary Table 1.3. Studies included in the systematic review of population-based survival from brain tumours in children.

Author	Quality indicators	Estimator	5-year survival
Agerlin et al., 1999	MV[1]: 100%	Observed survival	Medulloblastoma: 1960-1964: 8%; 1980-1984: 36%
Associazione Italiana Registri Tumori, 2012	MV: 90-94% DCO[2] and autopsy only excluded	Observed survival	Embryonal tumour: 62% (95% CI[3] 53-70%)
Alston et al., 2013	Not specified	Observed survival	Medulloblastoma: 1954-1964: 29% (SE[4] 7.3%); 1987-1997: 52% (10.4%)
Baade et al., 2010	MV: 95% DCO and autopsy only excluded	Relative survival	Astrocytoma: 79% (75-82%) Embryonal tumour: 49% (43-54%)
Basta et al., 2011	Lost to follow-up <1%	Observed survival	Astrocytoma: 1968-1977: 60% (46-72%); 1978-1987: 79% (65-88%); 1988-1997: 72% (59-81%); 1998-2005: 77% (63-87%) PNET[5]: 1968-1977: 24% (11-41%); 1978-1987: 45% (27-61%); 1988-1997: 43% (23-62%); 1998-2005: 63% (39-80%)
Bellil et al., 2008	Not specified	Observed survival	Astrocytoma (low-grade): 78% Medulloblastoma: 27% *Hospital-based estimates*
Ben Arush et al., 2010	Not specified	Observed survival	Astrocytoma (WHO[6] grade I/II): 82% Astrocytoma (WHO grade III): 55% Pilocytic astrocytoma: 95% Medulloblastoma: 69% Glioblastoma multiforme: 15%
Berger et al., 2006	Not specified	Observed survival	Astrocytoma: 1987-1993: 63% (52-72%); 1994-1999: 82% (68-90%) Medulloblastoma: 1987-1993: 49% (34-61%); 1994-1999: 46% (23-67%)
Bishop et al., 2012	Not specified	Observed survival	Supra-tentorial PNET: 35%
Brodbelt et al., 2015	MV: 90%	Relative survival	Glioblastoma: 15%

Author	Quality indicators	Estimator	5-year survival
Chan et al., 2007	MV: 100%	Observed survival	Medulloblastoma: 51%
Coll et al., 2015	Not specified	Observed survival	Astrocytoma*: 1986-1999: 63% (52-72%); 2000-2009; 92% (77-97%) Embryonal tumour: 1986-1999: 45% (24-64%); 2000-2009: 50% (25-70%) * *Behaviour not specified*
Dama et al., 2005	MV: 79% DCO excluded Lost to follow-up: 0.9%	Observed survival	Astrocytoma: 1970-1974: 41%; 1975-1979: 58%; 1980-1984: 78%; 1985-1989: 74%; 1990-1994: 88%; 1995-1999: 79% Medulloblastoma: 1970-1974: 0%; 1975-1979: 22%; 1980-1984: 46%; 1985-1989: 78%; 1990-1994: 56%; 1995-1999: 59%
Davis et al., 1998	Not specified	Observed survival	Glioblastoma: 21% (15-27%) Astrocytoma*: 72% (69-74%) Pilocytic astrocytoma: 89% (84-93%) Medulloblastoma: 1973-1980: 67% (66-68%); 1981-1985: 71% (70-72%); 1986-1991: 72% (71-73%) * *Only malignant*
Desandes et al., 2008	Lost to follow-up: 2.6%	Observed survival	Astrocytoma: 1990-1994: 74% (68-81%); 1995-1999: 81% (68-81%) Medulloblastoma: 1990-1994: 51% (38-64%); 1995-1999: 61% (49-74%) PNET: 1990-1994: 29% (9-48%); 1995-1999: 30% (9.9-50%)
Desandes et al., 2014	Lost to follow-up: 7.5%	Observed survival	Astrocytoma: 2000-2002: 84% (80-87%); 2003-2005: 90% (87-93%); 2006-2008: 87% (83-90%) Astrocytoma (low-grade): 94% (92-95%) Astrocytoma (high-grade): 22% (15-29%) Embryonal tumour: 2000-2002: 51% (45-57%); 2003-2005: 53% (46-58%); 2006-2008: 58% (51-64%)
Desandes et al., 2016	MV: 80% Lost to follow-up: 0.3%	Observed survival	Astrocytoma: 50% (15-77%) Medulloblastoma: 50% (0.5-91%) PNET: 0%

Author	Quality indicators	Estimator	5-year survival
			AT/RT[7]: 0%
Ellison et al., 2007	MV: 89% DCO and autopsy only excluded	Observed survival	Astrocytoma: 83% (79-86%) Embryonal tumour: 60% (52-66%)
Fairley et al., 2016	Not specified	Observed survival	Medulloblastoma: 1990-1999: 55% (44-64%), 2000-2013: 71% (61-79%) Medulloblastoma: 0-14 years: 63% (55-70%) PNET: 1990-1999: 36% (19-53%), 2000-2013: 30% (15-48%) PNET: 0-14 years: 27% (15-41%);
Flores et al., 2013	Not specified	Observed survival	Pilocytic astrocytoma: 99% PNET: 81%
Gatta et al., 2005	MV: 95% DCO and autopsy only excluded Lost to follow-up: 1.5% <4 years of follow-up: 4% Unspecified morphology: 3.5%	Observed survival	Astrocytoma*: 1983-1985: 72%; 1986-1988: 75%; 1989-1991: 77%; 1992-1994: 78% Embryonal tumour: 1983-1985: 46%; 1986-1988: 49%; 1989-1991: 48%; 1992-1994: 52% * *Only malignant*
Gatta et al., 2009	MV: 95% DCO and autopsy only excluded <5 years of follow-up: 2.6%	Observed survival	Astrocytoma*: 1995-1999: Northern Europe: 63% (53-74%), UK and Ireland: 61% (57-66%), Central Europe: 68 (64-72%), Southern Europe: 65% (58-72%); Eastern Europe: 63% (47-79%); 2000-2002: 63% (57-68%) Astrocytoma (including pilocytic astrocytoma): 1995-1999: Northern Europe: 83% (78-89%), UK and Ireland: 79% (76-81%), Central Europe: 81% (79-83%), Southern Europe: 76% (71-81%), Eastern Europe: 65% (50-81%); 2000-2002: 78% (73-82%)

Author	Quality indicators	Estimator	5-year survival
	Unspecified morphologies: 3.8%		Embryonal tumour: 1995-1999: Northern Europe: 56% (47-65%), UK and Ireland: 55% (51-60%), Central Europe: 61% (57-65%), Southern Europe: 58% (50-66%), Eastern Europe: 46% (24-68%); 2000-2002: 66% (60-71%) * *Only malignant*
Gatta et al., 2017	MV: 87% DCO and autopsy only excluded <5 years of follow-up: < 4% Unspecified morphology: 5.6%	Observed survival	Pilocytic astrocytoma: 95% (94-96%) Diffuse astrocytoma: 75% (67-81%) Astrocytoma NOS[8]: 74% (71-77%) Anaplastic astrocytoma: 21% (16-26%) Glioblastoma: 14% (11-18%) Medulloblastoma: 65% (62-67%) PNET: 41% (36-45%) AT/RT: 23% (18-29%)
Georgakis et al., 2017	MV: 97%	Observed survival	Pilocytic astrocytoma: SEE[9]: 1983-1999: 88% (83-92%), 2000-2004: 92% (88-94%); SEER[10]: 1973-1989: 91% (86-95%), 1990-1999: 98% (96-99%), 2000-2012: 98% (97-98%)
Ilveskoski et al., 1997	Not specified	Observed survival	Medulloblastoma: 1975-1985: 11% (0-32%); 1986-1993: 43% (17-68%)
Jung et al., 2012	MV: 100%	Observed survival	Astrocytoma*: 75% Anaplastic astrocytoma: 21% Glioblastoma: 19% * *Only malignant*
Kaatsch et al., 2001	Not specified	Observed survival	Astrocytoma (WHO grade I/II): 82% (80-84%) Astrocytoma (WHO grade III/IV): 24% (17-32%) Medulloblastoma: 53% (49-57%) Supra-tentorial PNET: 52% (46-59%)

Author	Quality indicators	Estimator	5-year survival
Karalexi et al., 2015	MV: 58-91% DCO excluded Lost to follow-up: 0-3.6% Unspecified morphology: 0-37%	Observed survival	Astrocytoma*: 61% (58-63%) Embryonal tumour: 40% (37-43%) * *Only malignant*
Khanna et al., 2017	Not specified	Relative survival	Medulloblastoma: < 1 year: 48% (33-62%); 1-4 years: 62% (56-67%); 5-9 years: 75% (70-79%); 10-14 years: 80% (72-86%)
Kramarova et al., 1996	MV: 98% Lost to follow-up: 6.5%	Observed survival	Ependymoma and medulloblastoma: 1968-1972: 2.7%; 1973-1977: 18%; 1978-1982: 22%; 1983-1987: 26% Astrocytoma*: 1968-1972: 40%; 1973-1877: 71%; 1978-1982: 55%; 1983-1987: 56% * *Behaviour not specified*
Lannering et al., 2009	Not specified	Observed survival	Astrocytoma (low-grade): 93% (1%) Astrocytoma (high-grade): 28% (5%) Medulloblastoma: 63% (4%) Supratentorial PNET: 47% (7%)
Linabery et al., 2008	MV: 95% Lost to follow-up: 14%	Observed survival	Astrocytoma: 1975-1979: 69% (64-73%); 1985-1989: 73% (69-77%); 1995-1999: 85% (82-89%) PNET: 1975-1979: 47% (39-55%); 1985-1989: 54% (47-62%); 1995-1999: 65% (59-71%)
Magnani et al., 1997	MV: 64-94% DCO and autopsy only excluded Lost to follow-up: 1.3%	Observed survival	Astrocytoma*: 1978-1981: 65%; 1982-1985: 75%; 1986-1989: 76% Medulloblastoma: 1978-1981: 36%; 1982-1985: 56%; 1986-1989: 85% * *Only malignant*

Author	Quality indicators	Estimator	5-year survival
Magnani et al., 2006	MV: 86% DCO excluded <5 years of follow-up: 1-74% Lost to follow-up: 4% Unspecified morphology: 0-16%	Observed survival	Embryonal tumour: 1978-1982: 37%; 1983-1987: 44%; 1988-1992: 48%; 1993-1997: 52%
Mathew et al., 2014	MV: 100%	Observed survival	Pilocytic astrocytoma: NRCT[11]: 96%; SEER: 97% Anaplastic astrocytoma: NRCT: 19%; SEER: 30% Glioblastoma: NRCT: 8%; SEER: 22% Medulloblastoma: NRCT: 65%; SEER: 71% PNET: NRCT: 32%; SEER: PNET: 57%
Narita et al., 2015	Not specified	Observed survival	Diffuse astrocytoma: 60% Anaplastic astrocytoma: 18% Glioblastoma: 7.8 % *Hospital-based estimates*
Ostrom et al., 2015	Not specified	Relative survival	AT/RT: 28% (21-36%)
Park et al., 2016	Not specified	Relative survival	Astrocytoma*: 1993-1995: 55%; 1996-2000: 49%; 2001-2005: 57%; 2006-2010: 54%; 2007-2011: 51% Embryonal tumour: 1993-1995: 49%; 1999-2000: 55%; 2001-2005: 57%; 2006-2010: 61%; 2007-2011: 60% ** Behaviour not specified*
Roldan et al., 2008	MV: 100%	Observed survival	Medulloblastoma: 56% (36-75%)

Author	Quality indicators	Estimator	5-year survival
Schindler et al., 2017	MV: 94% Unspecified morphology: 1.4%	Observed survival	Astrocytoma*: 1984-1993: 82% (71-89%); 1994-2003: 84% (77-90%); 2004-2013: 89% (82-94%) Medulloblastoma: 1984-1993: 50% (36-62%): 1994-2003: 68% (55-77%); 2004-2013: 64% (52-75%) PNET: 1984-1993: 33% (17-51%); 1994-2003: 37% (22-51%); 2004-2013: 30% (19-42%) ** Behaviour not specified*
Smoll et al., 2012	Not specified	Relative survival	Medulloblastoma: < 1 year: 42% (22-61%); 1-9 years: 72% (66-77%); 10-19 years: 69% (58-78%) PNET: < 1 year: 14% (2-39%); 1-9 years: 64% (54-72%); 10-19 years: 57% (41-70%)
Stagno et al., 2014	MV: 100%	Relative survival	Medulloblastoma: 0% *Hospital-based estimates*
Swaminathan et al., 2008	MV: 95% DCO excluded Lost to follow-up: 15%	Observed survival	Astrocytoma*: 39% ** Behaviour not specified*
Tseng et al., 2006	DCO and autopsy only excluded	Observed survival	Pilocytic astrocytoma: 88% Astrocytoma NOS: 71% Diffuse astrocytoma: 78% Anaplastic astrocytoma: 19% Glioblastoma: 20% Medulloblastoma: 41%
Trama et al., 2016	MV: 84-100% DCO, autopsy only or zero survival excluded	Relative survival	Astrocytoma*: 62% (1.1%) Medulloblastoma*:* 63% (1.3%) ** Only malignant*

Author	Quality indicators	Estimator	5-year survival
	Lost to follow-up: 0-9.7% Unspecified morphologies: 0.0-18%		
Tulla et al., 2015	MV: 100% Lost to follow-up: 4%	Observed survival	Medulloblastoma: 1991-1994: 63% (57-68%); 1995-1998: 64% (58-70%); 1999-2002: 80% (74-85%); 2003-2006: 77% (72-83%); 2007-2010: 73% (67-79%) PNET: 1991-1994: 33% (23-44%); 1995-1998: 35% (23-46%); 1999-2002: 35% (23-47%); 2003-2006: 44% (30-58%); 2007-2010: 61% (44-78%) AT/RT: 1999-2002: 21% (7-34%); 2003-2006: 28% (15-42%); 2007-2010: 42% (28-57%)
Walsh et al., 2011	MV: 93% DCO and autopsy only excluded Lost to follow-up: 0% Follow-up < 5 years: 35% Unspecified morphology: 5.1%	Observed survival	Astrocytoma: 1994-1999: 79% (70-86%); 2000-2005: 83% (72-90%) Embryonal tumour: 1994-1999: 49% (32-63%); 2000-2005: 59% (35-77%)

[1] MV: microscopic verification

[2] DCO: death certificate only

[3] CI: confidence interval

[4] SE: standard error

[5] PNET: primitive neuro-ectodermal tumour

[6] WHO: World Health Organization

[7] AT/RT: atypical teratoid/rhabdoid tumour

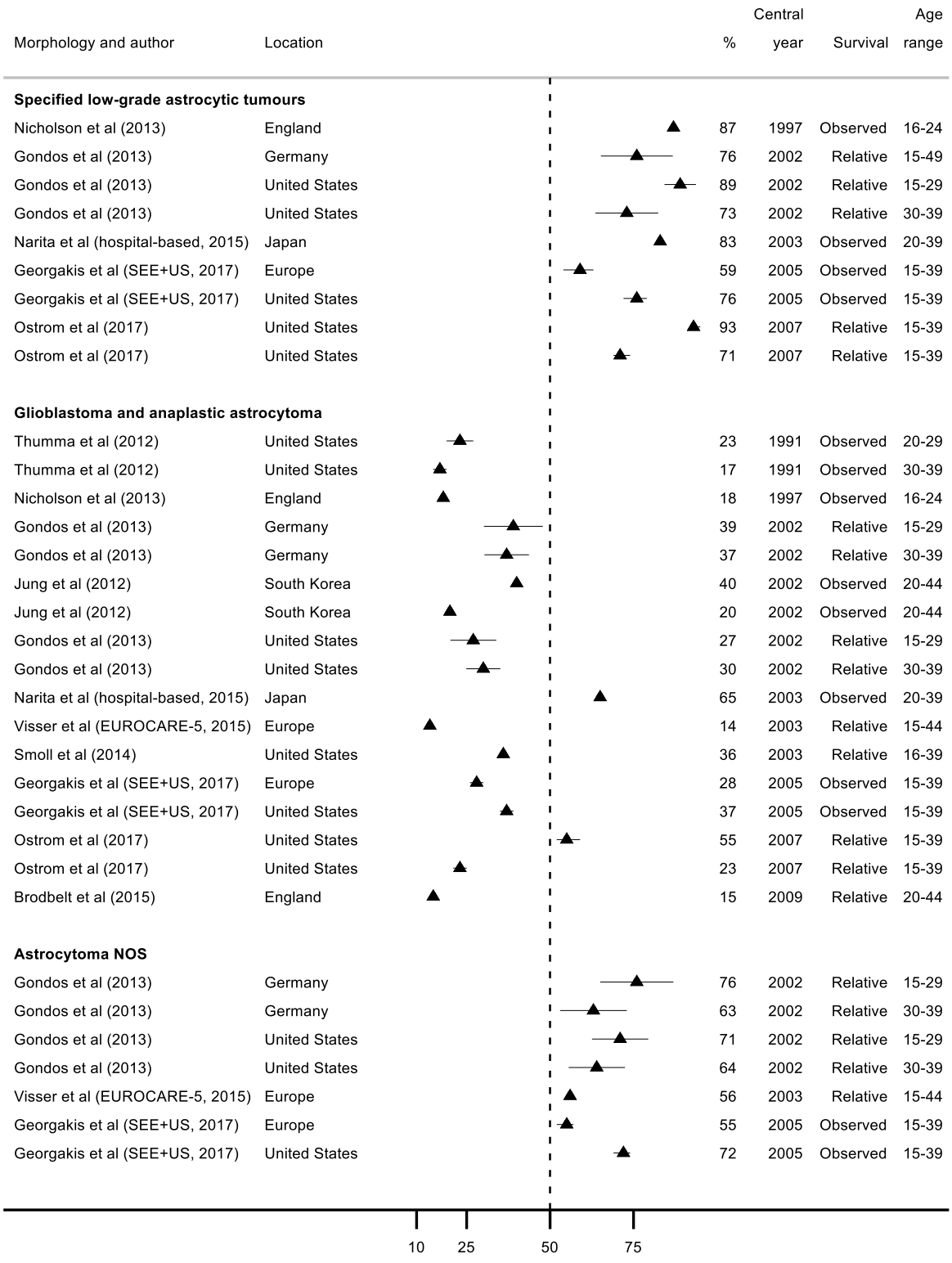
[8] NOS: not otherwise specified

[9] SEE consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine

[10] SEER: Surveillance, Epidemiology and End Results

[11] NCRT: National Registry of Childhood Tumours

Supplementary Figure 2.1. Five-year survival (%) from specified low-grade astrocytic tumours, glioblastoma and anaplastic astrocytoma, and astrocytoma not otherwise specified (NOS) (Surveillance Epidemiology and End Results Adolescents and Young adults Site Recode).



EUROCARE-5 consortium: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Northern Ireland, Norway, Poland, Portugal, Scotland, Slovakia, Slovenia, Spain, Sweden, Switzerland, Wales

Southern and Eastern Europe (SEE) consortium: Belarus, Bulgaria, Croatia, Cyprus, Greece, Malta, Portugal, Romania, Serbia, Slovenia, Turkey, Ukraine

Supplementary Table 2.2. Morphology groupings adopted in the systematic review of population-based survival from brain tumours in adolescents and young adults.

All relevant definitions	
Definitions adopted in the studies	**Definitions adopted the systematic review**
Astrocytoma Astrocytoma + pilocytic astrocytoma	Astrocytoma (broad group)
Astrocytoma low-grade	Astrocytoma low-grade
Astrocytoma NOS[1] Astrocytoma NOS and other Diffuse astrocytoma	Diffuse astrocytoma
Astrocytoma high-grade Glioblastoma and anaplastic astrocytoma	Astrocytoma high-grade
Anaplastic astrocytoma	Anaplastic astrocytoma
Glioblastoma	Glioblastoma
SEER AYA[2] Site Recode	
Definitions adopted in the studies	**Definitions adopted the systematic review**
Astrocytoma low-grade Diffuse astrocytoma	Specified low-grade astrocytic tumours
Anaplastic astrocytoma Astrocytoma high-grade Glioblastoma Glioblastoma and anaplastic astrocytoma	Glioblastoma and anaplastic astrocytoma
Astrocytoma NOS Astrocytoma NOS and other	Astrocytoma, NOS
Astrocytoma Astrocytoma + pilocytic astrocytoma	Unclassified

[1] NOS: not otherwise specified

[2] SEER AYA: Surveillance Epidemiology and End Results Adolescents and Young adults

Supplementary Table 2.3. Studies included in the systematic review of population-based survival from brain tumours in adolescents and young adults.

Author	Quality indicators	Estimator	5-year survival
Aben et al., 2012	DCO[1] excluded	Relative survival	Astrocytoma (male)*: 15-19 years: 51% (37-63%); 20-24 years: 54% (43-63%); 25-29 years: 56% (48-62%) Astrocytoma (female)*: 15-19 years: 65% (49-77%); 20-24 years: 57% (45-67%); 25-29 years: 55% (46-63) * *Only malignant*
Brodbelt et al., 2015	MV[2]: 90%	Relative survival	Glioblastoma: 20-44 years: 15%
Carreira et al., 2012	Not specified	Observed survival	Astrocytoma*: 15-19 years: 55% (30-75%); 20-24 years: 81% (63-91%) * *Behaviour not specified*
Desandes et al. 2007	Not specified	Observed survival	Astrocytoma: 15-19 years: 53% (40-65%); 20-24 years: 57% (44-69%)
Gatta et al., 2003	MV: 92% DCO or autopsy with histology excluded <5 years of follow-up: 0.7%	Observed survival	Astrocytoma: 66% (62-69%)

Author	Quality indicators	Estimator	5-year survival
	Unspecified morphologies: 6.5%		
Gatta et al., 2009	MV: 95% DCO and autopsy only excluded <5 years of follow-up: 2.6% Unspecified morphologies: 3.8%	Observed survival	Astrocytoma: 1995-1999: Northern Europe: 52% (40-64%), UK and Ireland: 49% (42-55%), Central Europe: 58% (49-67%), Southern Europe: 55% (46-64%), Eastern Europe: 65% (46-84%); 2000-2002: 56% (48-63%) Astrocytoma (including pilocytic astrocytoma): 1995-1999: Northern Europe: 65% (56-74%), UK and Ireland: 58% (52-63%), Central Europe: 68% (61-76%), Southern Europe: 62% (54-70%), Eastern Europe: 66% (47-85%); 2002-2002: 64% (58-71%)
Georgakis et al., 2017	MV: 92% (SEER[3]); 71-85% (outliers: 57-96%) DCO and lost to follow-up excluded	Observed survival	Astrocytoma (low-grade)*: SEE[4]: 59% (54-63%); US: 76% (72-79%) Glioblastoma and anaplastic astrocytoma: SEE: 28% (26-30%); US: 37% (35-39%) Astrocytoma NOS[5]: SEE: 55% (52-57%); US: 72% (69-74%) * *Only malignant*

Author	Quality indicators	Estimator	5-year survival
	Unspecified morphology: 2.5-35%		
Gondos et al., 2013	DCO or autopsy with histology excluded	Relative survival	Astrocytoma (low-grade)*: SEER: 15-29 years: 89% (2.4%), 30-39 years: 73% (4.8%); Germany: 15-49 years: 76% (5.5%) Glioblastoma and anaplastic astrocytoma: SEER: 15-29 years: 27% (3.5%), 30-39 years: 30% (2.6%); Germany: 15-29 years: 39% (4.5%), 30-39 years: 37% (3.4%) Astrocytoma NOS: SEER: 15-29 years: 71% (4.3%), 30-39 years: 64% (4.3%); Germany: 15-29 years: 76% (5.6%), 30-39 years: 63% (5.1%) * *Only malignant*
Ho et al., 2014	Not specified	Observed survival	Astrocytoma*: 18-40 years: 65% (61-68%) * *Only malignant*
Jung et al., 2012	MV: 100%	Observed survival	Astrocytoma*: 20-44 years: 59% Anaplastic astrocytoma: 20-44 years: 40% Glioblastoma: 20-44 years: 20% * *Only malignant*
Linabery et al., 2008	MV: 95% Lost to follow-up: 14%	Observed survival	Astrocytoma (adolescents): 1975-1979: 60% (51-69%); 1985-1989: 73% (65-81%); 1995-1999: 81% (73-89%)

Author	Quality indicators	Estimator	5-year survival
Narita et al., 2015	Not specified	Observed survival	Diffuse astrocytoma: 20-39 years: 83% Anaplastic astrocytoma: 20-39 years: 65% *Hospital-based estimates*
Nicholson et al., 2013	Not specified	Observed survival	Astrocytoma (low-grade)*: 87% Astrocytoma (high-grade): 18% * *Behaviour not specified*
Ostrom et al., 2017	MV: 89%	Relative survival	Pilocytic astrocytoma: 95% (92-95%) Diffuse astrocytoma: 71% (69-74%) Anaplastic astrocytoma: 55% (52-59%) Glioblastoma: 23% (21-25%)
Pearce et al., 2005	Not specified	Observed survival	Astrocytoma: 1968-1977: 48% (30-64%); 1978-1987: 50% (34-64%); 1988-1997: 60% (42-74%)
Smoll et al., 2014	Not specified	Relative survival	Anaplastic astrocytoma: 16-39 years: 36%
Stiller et al., 2006	MV: 95-96% DCO and zero survival excluded Unspecified morphologies: 6-9%	Observed survival	Astrocytoma: Europe: 65% (59-70%); British Isles: 71% (57-81%); East Europe: 52% (37-65%); North Europe: 71% (59-80%); South Europe: 64% (54-73%); West Europe: 64% (43-79%)

Author	Quality indicators	Estimator	5-year survival
Thumma et al., 2012	Not specified	Observed survival	Glioblastoma: 20-29 years: 23% (19-27%); 30-39 years: 17% (15-19%)
Trama et al., 2016	MV: 84-100% DCO, autopsy only or zero survival excluded Lost to follow-up: 0-9.7% Unspecified morphologies: 0.0-18%	Relative survival	Astrocytoma: 15-19 years: 51% (2.5%); 20-24 years: 54% (2.2%); 25-29 years: 51% (1.7%); 30-34 years: 48% (1.4%); 35-39 years: 39% (1.2%) ** Only malignant*
Visser et al., 2015	MV: 80% Unspecified morphologies: 20%	Relative survival	Glioblastoma: 15-44 years: 14% (13-15%) Astrocytoma (NOS and other): 15-44 years: 56% (55-57%)

[1] DCO: death certificate only

[2] MV: microscopic verification

[3] SEER: Surveillance, Epidemiology and End Results

[4] SEE: Southern and Eastern Europe consortium

[5] NOS: not otherwise specified

Supplementary Table 3.1. Histology groupings for brain tumours in children (0-14 years).

International Classification of Childhood Cancer Third Edition (ICCC-3)		WHO morphology definition and grade		ICD-O-3 morphology definition (sections 938-952)	ICD-O-3 morphology code
Second Tier	**Morphology groupings used in the study (adapted from ICCC-3)**				
Ependymoma and choroid plexus tumour (IIIa)	**Ependymoma**	Subependymoma	I	Subependymoma	9383/1
		Ependymoma	II	Ependymoma, NOS	9391/3
		Papillary ependymoma		Papillary ependymoma	9393/3
		Myxopapillary ependymoma	I	Myxopapillary ependymoma	9394/1
	Choroid plexus tumour	Choroid plexus papilloma	I	Choroid plexus papilloma, NOS	9390/0
		Atypical choroid plexus papilloma	II	Atypical choroid plexus papilloma	9390/1
		Choroid plexus carcinoma	III	Choroid plexus carcinoma	9390/3
Astrocytoma (IIIb)	**Astrocytoma, WHO grade I and II**	Subependymal giant cell astrocytoma	I	Subependymal giant cell astrocytoma	9384/1
		Diffuse astrocytoma	II	Astrocytoma NOS	9400/32
		Protoplasmic astrocytoma		Protoplasmic astrocytoma	9410/3
		Gemistocytic astrocytoma		Gemistocytic astrocytoma	9411/3
		Fibrillary astrocytoma		Fibrillary astrocytoma	9420/3
				Astrocytoma NOS	9400/31
		Pilocytic astrocytoma	I	Pilocytic astrocytoma	9421/1
		Pilomyxoid astrocytoma	II	Pilomyxoid astrocytoma	9425/3
				Polar spongioblastoma	9423/3
		Pleomorphic xanthoastrocytoma	II	Pleomorphic xanthoastrocytoma	9424/3
	Astrocytoma, WHO grade III and IV			Astrocytoma NOS	9400/33
		Astrocytoma, anaplastic	III	Astrocytoma, anaplastic	9401/3
				Astrocytoma NOS	9400/34
		Glioblastoma	IV	Glioblastoma, NOS	9440/3
		Giant cell glioblastoma		Giant cell glioblastoma	9441/3
		Gliosarcoma		Gliosarcoma	9442/3
	Unspecified astrocytoma			Astrocytoma NOS	9400/39
Embryonal tumour (IIIc)	**Medulloblastoma**	Medulloblastoma	IV	Medulloblastoma, NOS	9470/3
		Desmoplastic nodular medulloblastoma		Desmoplastic nodular medulloblastoma	9471/3
		Medulloblastoma with extensive nodularity			9471/3
				Medullomyoblastoma	9472/3
		Anaplastic medulloblastoma		Large cell medulloblastoma	9474/3
		Large cell medulloblastoma		Large cell medulloblastoma	9474/3
				Cerebellar sarcoma, NOS (obs.)	9480/3
	Other and unspecified embryonal tumour			Peripheral neuroectodermal tumour	9364/3
		CNS primitive neuroectodermal tumour	IV	Primitive neuroectodermal tumour, NOS	9473/3
		CNS neuroblastoma		Neuroblastoma, NOS	9500/3
		Ganglioneuroblastoma		Ganglioneuroblastoma	9490/3
		Medulloepithelioma		Medulloepithelioma, NOS	9501/3
		Ependymoblastoma		Ependymoma, anaplastic*	9392/3
		Atypical teratoid / rhabdoid tumour	IV	Atypical teratoid / rhabdoid tumour	9508/3
Other glioma (IIId)	**Oligodendroglial tumour**	Oligoastrocytoma	II	Mixed Glioma	9382/3
		Anaplastic oligoastrocytoma	III	Mixed Glioma	9382/3
		Oligodendroglioma	II	Oligodendroglioma, NOS	9450/3
		Oligodendroglioma, anaplastic	III	Oligodendroglioma, anaplastic	9451/3
				Oligodendroblastoma (obs.)	9460/3
	Unspecified glioma			Glioma, malignant	9380/3
	Neuroepithelial glial tumour of uncertain origin	Gliomatosis cerebri		Gliomatosis cerebri	9381/3
		Astroblastoma		Astroblastoma	9430/3
		Chordoid glioma of the third ventricle	II	Chordoid glioma	9444/1
Other specified neoplasm (IIIe)	**Neuronal and mixed neuronal-glial tumour**	Paraganglioma		Paraganglioma, NOS	8680/1
		Desmoplastic infantile astrocytoma / ganglioglioma		Desmoplastic infantile astrocytoma	9412/1
		Dysembryoblastic neuroepithelial tumour		Dysembryoblastic neuroepithelial tumour	9413/0
		Angiocentric glioma	I	Angiocentric glioma	9431/1
				Gliofibroma	9442/1
		Gangliocytoma	I	Gangliocytoma	9492/0
		Dysplastic gangliocytoma of cerebellum		Dysplastic gangliocytoma of cerebellum	9493/0
		Ganglioglioma	I	Ganglioglioma, NOS	9505/1
		Anaplastic ganglioglioma	III	Ganglioglioma, anaplastic	9505/3
		Central neurocytoma	II	Central neurocytoma	9506/1
		Extraventricular neurocytoma	II	Central neurocytoma	9506/1
		Cerebellar liponeurocytoma	II	Central neurocytoma	9506/1
		Papillary glioneuronal tumour	I	Papillary glioneuronal tumour	9509/1
		Rosette-forming glioneuronal tumour of the fourth ventricle	I	Papillary glioneuronal tumour	9509/1
Unspecified neoplasm (IIIf)	**Unspecified neoplasm**			Neoplasm, benign	8000/0
				Neoplasm, uncertain whether benign or malignant	8000/1
				Neoplasm, malignant	8000/3
				Tumor cells, benign	8001/0
				Tumor cells, uncertain whether benign or malignant	8001/1
				Tumor cells, malignant	8001/3
				Malignant tumor, small cell type	8002/3
				Malignant tumor, giant cell type	8003/3
				Malignant tumor, spindle cell type	8004/3
				Clear cell tumor, NOS	8005/3
				Malignant tumor, clear cell type	8005/3

WHO: World Health Organisation
ICD-O-3: International Classification of Diseases for Oncology
NOS: not otherwise specified

Supplementary Table 3.2. Histology groupings for brain tumours in adults (15-99 years).

Morphology groupings used in the study	WHO morphology definition and grade		ICD-O-3 morphology definition (sections 938-952)	ICD-O-3 morphology code
Ependymoma and choroid plexus tumour	Subependymoma	I	Subependymoma	9383/1
	Ependymoma	II	Ependymoma, NOS	9391/3
	Papillary ependymoma		Papillary ependymoma	9393/3
	Myxopapillary ependymoma	I	Myxopapillary ependymoma	9394/1
	Choroid plexus papilloma	I	Choroid plexus papilloma, NOS	9390/0
	Atypical choroid plexus papilloma	II	Atypical choroid plexus papilloma	9390/1
	Choroid plexus carcinoma	III	Choroid plexus carcinoma	9390/3
Diffuse and anaplastic astrocytoma	Diffuse astrocytoma	II	Astrocytoma, NOS	9400/32
	Protoplasmic astrocytoma		Protoplasmic astrocytoma	9410/3
	Gemistocytic astrocytoma		Gemistocytic astrocytoma	9411/3
	Fibrillary astrocytoma		Fibrillary astrocytoma	9420/3
			Astrocytoma, NOS	9400/33
	Astrocytoma, anaplastic	III	Astrocytoma, anaplastic	9401/3
Glioblastoma			Astrocytoma, NOS	9400/34
	Glioblastoma	IV	Glioblastoma, NOS	9440/3
	Giant cell glioblastoma		Giant cell glioblastoma	9441/3
	Gliosarcoma		Gliosarcoma	9442/3
Other specified astrocytoma	Subependymal giant cell astrocytoma	I	Subependymal giant cell astrocytoma	9384/1
			Astrocytoma, NOS	9400/31
	Pilocytic astrocytoma	I	Pilocytic astrocytoma	9421/1
	Pilomyxoid astrocytoma	II	Pilomyxoid astrocytoma	9425/3
			Polar spongioblastoma	9423/3
	Pleomorphic xanthoastrocytoma	II	Pleomorphic xanthoastrocytoma	9424/3
Unspecified astrocytoma			Astrocytoma, NOS	9400/39
Oligodendroglial tumour	Oligoastrocytoma	II	Mixed Glioma	9382/3
	Anaplastic oligoastrocytoma	III	Mixed Glioma	9382/3
	Oligodendroglioma	II	Oligodendroglioma, NOS	9450/3
	Oligodendroglioma, anaplastic	III	Oligodendroglioma, anaplastic	9451/3
			Oligodendroblastoma (obs.)	9460/3
Medulloblastoma	Medulloblastoma	IV	Medulloblastoma, NOS	9470/3
	Desmoplastic nodular medulloblastoma		Desmoplastic nodular medulloblastoma	9471/3
	Medulloblastoma with extensive nodularity			9471/3
			Medullomyoblastoma	9472/3
	Anaplastic medulloblastoma		Large cell medulloblastoma	9474/3
	Large cell medulloblastoma		Large cell medulloblastoma	9474/3
			Cerebellar sarcoma, NOS (obs.)	9480/3
Other and unspecified embryonal tumour			Peripheral neuroectodermal tumour	9364/3
	CNS primitive neuroectodermal tumour	IV	Primitive neuroectodermal tumour, NOS	9473/3
	CNS neuroblastoma		Neuroblastoma, NOS	9500/3
	Ganglioneuroblastoma		Ganglioneuroblastoma	9490/3
	Medulloepithelioma		Medulloepithelioma, NOS	9501/3
	Ependymoblastoma		Ependymoma, anaplastic	9392/3
	Atypical teratoid / rhabdoid tumour	IV	Atypical teratoid / rhabdoid tumour	9508/3
Unspecified glioma			Glioma, malignant	9380/3
Other specified neuroepithelial tumour	Paraganglioma		Paraganglioma, NOS	8680/1
	Gliomatosis cerebri		Gliomatosis cerebri	9381/3
	Desmoplastic infantile astrocytoma / ganglioglioma		Desmoplastic infantile astrocytoma	9412/1
	Dysembryoblastic neuroepithelial tumour		Dysembryoblastic neuroepithelial tumour	9413/0
	Astroblastoma		Astroblastoma	9430/3
	Angiocentric glioma	I	Angiocentric glioma	9431/1
			Gliofibroma	9442/1
	Chordoid glioma of the third ventricle	II	Chordoid glioma	9444/1
	Gangliocytoma	I	Gangliocytoma	9492/0
	Dysplastic gangliocytoma of cerebellum		Dysplastic gangliocytoma of cerebellum	9493/0
	Ganglioglioma	I	Ganglioglioma, NOS	9505/1
	Anaplastic ganglioglioma	III	Ganglioglioma, anaplastic	9505/3
	Central neurocytoma	II	Central neurocytoma	9506/1
	Extraventricular neurocytoma	II	Central neurocytoma	9506/1
	Cerebellar liponeurocytoma	II	Central neurocytoma	9506/1
	Papillary glioneuronal tumour	I	Papillary glioneuronal tumour	9509/1
	Rosette-forming glioneuronal tumour of the fourth ventricle	I	Papillary glioneuronal tumour	9509/1
Unspecified tumour			Neoplasm, benign	8000/0
			Neoplasm, uncertain whether benign or malignant	8000/1
			Neoplasm, malignant	8000/3
			Tumor cells, benign	8001/0
			Tumor cells, uncertain whether benign or malignant	8001/1
			Tumor cells, malignant	8001/3
			Malignant tumor, small cell type	8002/3
			Malignant tumor, giant cell type	8003/3
			Malignant tumor, spindle cell type	8004/3
			Clear cell tumor, NOS	8005/0
			Malignant tumor, clear cell type	8005/3

WHO: World Health Organisation
ICD-O-3: International Classification of Diseases for Oncology
NOS: not otherwise specified

Supplementary Table 3.3. Excluded ICD-O-3 codes, children (0-14 years).

ICD-O-3 codes								
Digits 1-4	5th digit (behaviour)						Total	
	0 (benign)		1 (uncertain whether benign or malignant)		3 (malignant)			
		No.		No.		No.		
8010					Carcinoma, NOS		1	1
8041					Small cell carcinoma, NOS		1	1
8050	Papilloma, NOS	1						1
8123					Basaloid carcinoma		1	1
8140					Adenocarcinoma, NOS		1	1
8440	Cystadenoma, NOS	1						1
8720					Malignant melanoma, NOS		13	13
8800	Soft tissue tumor, benign	3		1	Sarcoma, NOS		36	40
8801					Spindle cell sarcoma		8	8
8802					Giant cell sarcoma		4	4
8803					Small cell sarcoma		1	1
8804					Epithelioid sarcoma		1	1
8805					Undifferentiated sarcoma		11	11
8806					Desmoplastic small round cell tumor		7	7
8810	Fibroma, NOS	1			Fibrosarcoma, NOS		12	13
8814					Infantile fibrosarcoma		1	1
8815	Solitary fibrous tumor	4						4
8823	Desmoplastic fibroma	1						1
8830					Malignant fibrous histiocytoma		1	1
8834			Giant cell fibroblastoma	1				1
8850	Lipoma, NOS	122	Atypical lipoma	1				123
8861	Angiolipoma, NOS	2						2
8890					Leiomyosarcoma, NOS		4	4
8900	Rhabdomyoma, NOS	2			Rhabdomyosarcoma, NOS		7	9
8910					Embryonal rhabdomyosarcoma, NOS		2	2
8912					Spindle cell rhabdomyosarcoma		1	1
8920					Alveolar rhabdomyosarcoma		1	1
8963					Malignant rhabdoid tumor		191	191
8990					Mesenchymoma, malignant		1	1
9040					Synovial sarcoma, NOS		2	2
9041					Synovial sarcoma, spindle cell		1	1
9043					Synovial sarcoma, biphasic		1	1
9060					Dysgerminoma		18	18
9061					Seminoma, NOS		2	2
9064					Germinoma		1,140	1,140
9065					Germ cell tumor, nonseminomatous		13	13
9070					Embryonal carcinoma, NOS		31	31
9071					Yolc sac tumour		42	42
9080	Teratoma, benign	78	Teratoma, NOS	52	Teratoma, malignant, NOS		217	347
9081					Teratocarcinoma		6	6
9082					Malignant teratoma, undifferentiated		5	5
9084	Dermoid cyst, NOS	219			Teratoma with malignant transformation		3	222
9085					Mixed germ cell tumour		215	215
9100					Choriocarcinoma, NOS		28	28
9101					Choriocarcinoma combined with other germ cell elements		13	13
9120	Hemangioma, NOS	171		1	Hemangiosarcoma		7	179
9121	Cavernous hemangioma	351						351
9122	Venous hemangioma	14						14
9123	Racemose hemangioma	10						10
9130	Hemangioendothelioma, benign	2	Hemangioendothelioma, NOS	2				4
9131	Capillary hemangioma	30						30
9150	Hemangiopericytoma, benign	1	Hemangiopericytoma, NOS	13	Hemangiopericytoma, malignant		16	30
9160	Angiofibroma, NOS	2						2
9161			Hemangioblastoma	119				119
9170	Lymphangioma, NOS	4			Lymphangiosarcoma		3	7
9173	Cystic lymphangioma	4						4
9231					Myxoid chondrosarcoma		4	4
9240					Mesenchymal chondrosarcoma		8	8
9350			Craniopharyngioma	5			1	6
9351			Craniopharyngioma, adamantinomatous	2				2
9362					Pineoblastoma		10	10
9363							1	1
9370					Chordoma, NOS		48	48
9371					Chondroid chordoma		2	2
9373							3	3
9490	Ganglioneuromatosis	31						31
9502					Teratoid medulloepithelioma		13	13
9503		19			Neuroepithelioma, NOS		59	78
9522					Olfactory neuroblastoma		2	2
9530	Meningioma, NOS	2			Meningioma, malignant		7	9
9539			Atypical meningioma	1				1
9540	Neurofibroma, NOS	27	Neurofibromatosis, NOS	417	Malignant peripheral nerve sheath tumor		23	467
9550	Plexiform neurofibroma	11						11
9560	Neurilemoma, NOS	57	Neurinomatosis	2	Neurilemoma, malignant		7	66
9561					Malignant peripheral nerve sheath tumor with rhabdomyoblastic differentiation		3	3
9570	Neuroma, NOS	3						3
9580	Granular cell tumor, NOS	1			Granular cell tumor, malignant		2	3
9999		67		159			2,269	2,495

Combination of morphology code and behaviour as defined by the WHO Classification, for sites other than C71 (brain).

Combination of morphology code and behaviour not found in the WHO Classification, but for which an ICD-O-3 definition is available.

Combination of morphology code and behaviour not found in the WHO Classification, and for which an ICD-O-3 definition is not available.

Cases without a morphology code.

WHO: World Health Organisation
ICD-O-3: International Classification of Diseases for Oncology, third edition
NOS: not otherwise specified

Supplementary Table 3.4. Excluded ICD-O-3 codes, adults (15-99 years).

ICD-O-3 codes								
Digits 1-4	5th digit (behaviour)						Total
	0 (benign)		1 (uncertain whether benign or malignant)		3 (malignant)		
		No.		No.		No.	
8010	Epithelial tumor, benign	2			Carcinoma, NOS	97	99
8011	Epithelioma, benign	2			Epithelioma, malignant	3	5
8020					Carcinoma, undifferentiated, NOS	4	4
8021					Carcinoma, anaplastic, NOS	3	3
8031					Giant cell carcinoma	2	2
8033					Pseudosarcomatous carcinoma	1	1
8041					Small cell carcinoma, NOS	10	10
8050	Papilloma, NOS	8			Papillary carcinoma, NOS	2	10
8070					Squamous cell carcinoma in situ, NOS	13	13
8072					Squamous cell carcinoma, large cell, nonkeratinizing, NOS	1	1
8074					Squamous cell carcinoma, spindle cell	1	1
8083					Basaloid squamous cell carcinoma	1	1
8090					Basal cell carcinoma, NOS	2	2
8121	Schneiderian papilloma, NOS	1					1
8140	Adenoma, NOS	5			Adenocarcinoma, NOS	37	42
8200					Adenoid cystic carcinoma	4	4
8211					Tubular adenocarcinoma	1	1
8246					Neuroendocrine carcinoma, NOS	8	8
8260					Papillary adenocarcinoma, NOS	1	1
8272	Pituitary adenoma, NOS	9			Pituitary carcinoma, NOS	6	15
8310					Clear cell adenocarcinoma, NOS	1	1
8334	Macrofollicular adenoma	2					2
8380	Endometrioid adenoma, NOS	1					1
8381					Endometrioid adenofibroma, malignant	1	1
8400					Sweat gland adenocarcinoma	1	1
8430					Mucoepidermoid carcinoma	1	1
8440	Cystadenoma, NOS	3			Cystadenocarcinoma, NOS	5	8
8450					Papillary cystadenocarcinoma, NOS	1	1
8480					Mucinous adenocarcinoma	1	1
8560					Squamous cell and adenocarcinoma, mixed	1	1
8574					Adenocarcinoma with neuroendocrine differentiation	2	2
8630					Androblastoma, malignant	1	1
8690			Glomus jugulare tumor, NOS	1			1
8693			Extra-adrenal paraganglioma, NOS	1			1
8700					Pheochromocytoma, malignant	1	1
8711	Glomus tumor, NOS	3			Glomus tumor, malignant	2	5
8720					Malignant melanoma, NOS	179	179
8726	Magnocellular nevus	10		1			11
8728			Meningeal melanocytoma	2	Meningeal melanomatosis	2	4
8750	Intradermal nevus	2					2
8761					Malignant melanoma in giant pigmented nevus	1	1
8771					Epithelioid cell melanoma	1	1
8800	Soft tissue tumor, benign	12		1	Sarcoma, NOS	346	359
8801					Spindle cell sarcoma	66	66
8802					Giant cell sarcoma	21	21
8803					Small cell sarcoma	5	5
8804					Epithelioid sarcoma	8	8
8805					Undifferentiated sarcoma	18	18
8806					Desmoplastic small round cell tumor	15	15
8810	Fibroma, NOS	8			Fibrosarcoma, NOS	36	44
8811	Fibromyxoma	1			Fibromyxosarcoma	2	3
8815	Solitary fibrous tumor	89		3	Solitary fibrous tumor, malignant	43	135
8821			Aggressive fibromatosis	8		1	9
8825			Myofibroblastic tumor, NOS	3			3
8830					Malignant fibrous histiocytoma	9	9
8831	Histiocytoma, NOS	2				1	3
8834			Giant cell fibroblastoma	1			1
8836			Angiomatoid fibrous histiocytoma	3			3
8850	Lipoma, NOS	446	Atypical lipoma	5	Liposarcoma, NOS	2	453
8851	Fibrolipoma	1			Liposarcoma, well differentiated	1	2
8852					Myxoid liposarcoma	1	1
8861	Angiolipoma, NOS	2				1	3
8890	Leiomyoma, NOS	4	Leiomyomatosis, NOS	1	Leiomyosarcoma, NOS	24	29
8900					Rhabdomyosarcoma, NOS	13	13
8910					Embryonal rhabdomyosarcoma, NOS	1	1
8940	Pleomorphic adenoma	1					1
8963					Malignant rhabdoid tumor	29	29
8980					Carcinosarcoma, NOS	1	1
8990					Mesenchymoma, malignant	1	1
9040	Synovioma, benign	1			Synovial sarcoma, NOS	10	11
9041					Synovial sarcoma, spindle cell	6	6
9044					Clear cell sarcoma, NOS	4	4
9050					Mesothelioma, malignant	1	1
9060					Dysgerminoma	30	30
9061					Seminoma, NOS	1	1
9064					Germinoma	1,507	1,507
9065					Germ cell tumor, nonseminomatous	10	10
9070					Embryonal carcinoma, NOS	20	20
9071					Yolc sac tumour	4	4
9080	Teratoma, benign	129	Teratoma, NOS	42	Teratoma, malignant, NOS	69	240
9081					Teratocarcinoma	15	15
9082					Malignant teratoma, undifferentiated	8	8

Supplementary Table 3.4. Excluded ICD-O-3 codes, adults (15-99 years).

ICD-O-3 codes							
Digits 1-4	5th digit (behaviour)						Total
	0 (benign)	No.	1 (uncertain whether benign or malignant)	No.	3 (malignant)	No.	
9083					Malignant teratoma, intermediate	2	2
9084	Dermoid cyst, NOS	632		4	Teratoma with malignant transformation	14	650
9085					Mixed germ cell tumour	112	112
9100					Choriocarcinoma, NOS	31	31
9101					Choriocarcinoma combined with other germ cell elements	10	10
9120	Hemangioma, NOS	2,716		6	Hemangiosarcoma	109	2,831
9121	Cavernous hemangioma	4,855		5		2	4,862
9122	Venous hemangioma	488					488
9123	Racemose hemangioma	51					51
9125	Epithelioid hemangioma	1					1
9130	Hemangioendothelioma, benign	6	Hemangioendothelioma, NOS	13	Hemangioendothelioma, malignant	24	43
9131	Capillary hemangioma	66				1	67
9133			Epithelioid hemangioendothelioma, NOS	10	Epithelioid hemangioendothelioma, malignant	12	22
9150	Hemangiopericytoma, benign	56	Hemangiopericytoma, NOS	563	Hemangiopericytoma, malignant	736	1,355
9160	Angiofibroma, NOS	3		1			4
9161	Acquired tufted hemangioma	77	Hemangioblastoma	7,954		90	8,121
9170	Lymphangioma, NOS	5			Lymphangiosarcoma	2	7
9171	Capillary lymphangioma	1					1
9172	Cavernous lymphangioma	4					4
9173	Cystic lymphangioma	65				1	66
9174			Lymphangiomyomatosis	1			1
9180	Osteoma, NOS	4			Osteosarcoma, NOS	1	5
9220	Chondroma, NOS	3			Chondrosarcoma, NOS	5	8
9231					Myxoid chondrosarcoma	13	13
9240					Mesenchymal chondrosarcoma	29	29
9251			Giant cell tumor of soft parts, NOS	2			2
9260					Ewing sarcoma	1	1
9350			Craniopharyngioma	23		1	24
9351			Craniopharyngioma, adamantinomatous	7			7
9352			Craniopharyngioma, papillary	3		1	4
9361			Pineocytoma	1			1
9362					Pineoblastoma	19	19
9370				2	Chordoma, NOS	776	778
9371					Chondroid chordoma	66	66
9372					Dedifferentiated chordoma	3	3
9373						1	1
9432			Pituicytoma	1			1
9490	Ganglioneuroma	86					86
9491	Ganglioneuromatosis	1					1
9503		34			Neuroepithelioma, NOS	118	152
9504					Spongioneuroblastoma	23	23
9520					Olfactory neurogenic tumor	2	2
9522					Olfactory neuroblastoma	156	156
9530	Meningioma, NOS	372	Meningiomatosis, NOS	11	Meningioma, malignant	239	622
9531	Meningothelial meningioma	144					144
9532	Fibrous meningioma	70				1	71
9533	Psammomatous meningioma	11					11
9534	Angiomatous meningioma	20				1	21
9535	Hemangioblastic meningioma	1					1
9537	Transitional meningioma	63				1	64
9538			Clear cell meningioma	3	Papillary meningioma	2	5
9539			Atypical meningioma	28	Meningeal sarcomatosis	7	35
9540	Neurofibroma, NOS	98	Neurofibromatosis, NOS	124	Malignant peripheral nerve sheath tumor	109	331
9550	Plexiform neurofibroma	10		1		1	12
9560	Neurilemoma, NOS	5,012	Neurinomatosis	59	Neurilemoma, malignant	350	5,421
9561					Malignant peripheral nerve sheath tumor w	13	13
9562	Neurothekeoma	5					5
9570	Neuroma, NOS	97				2	99
9571	Perineurioma, NOS	4			Perineurioma, malignant	1	5
9580	Granular cell tumor, NOS	17		1	Granular cell tumor, malignant	14	32
9581					Alveolar soft part sarcoma	2	2
9582	Granular cell tumor of the sellar region	1					1
9999		1,797		2,299		34,327	38,423

Combination of morphology code and behaviour as defined by the WHO Classification, for sites other than C71 (brain).

Combination of morphology code and behaviour not found in the WHO Classification, but for which an ICD-O-3 definition is available.

Combination of morphology code and behaviour not found in the WHO Classification, and for which an ICD-O-3 definition is not available.

Cases without a morphology code.

WHO: World Health Organisation
ICD-O-3: International Classification of Diseases for Oncology, third edition
NOS: not otherwise specified

Supplementary Table 3.5. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Children (0-14 years) diagnosed with an astrocytic tumour, 2000-2014.

Country	Period of diagnosis	Astrocyto-ma, all combined	Astrocytoma NOS									
					grade (6th digit)					basis of diagnosis		
					grade 1	grade 2	grade 3	grade 4	Unknown	MV	not MV	Unknown
		No.	No.	%	%	%	%	%	%	%	%	%
Africa	2000-2004	11	7	**63.6**	-	14.3	-	71.4	14.3	100.0	-	-
	2005-2009	21	14	**66.7**	14.3	-	-	35.7	50.0	100.0	-	-
	2010-2014	14	6	**42.9**	-	-	-	-	100.0	100.0	-	-
Algeria	2000-2004	7	6	**85.7**	-	16.7	-	83.3	-	100.0	-	-
	2005-2009	16	12	**75.0**	16.7	-	-	41.7	41.7	100.0	-	-
	2010-2014	7	4	**57.1**	-	-	-	-	100.0	100.0	-	-
Mauritius*	2010-2014	2	2	**100.0**	-	-	-	-	100.0	100.0	-	-
Nigeria	2005-2009	4	1	**25.0**	-	-	-	-	100.0	100.0	-	-
South Africa	2000-2004	4	1	**25.0**	-	-	-	-	100.0	100.0	-	-
	2005-2009	1	1	**100.0**	-	-	-	-	100.0	100.0	-	-
America (Central and South)	2000-2004	374	132	**35.3**	0.8	2.3	-	-	97.0	99.2	0.8	-
	2005-2009	479	191	**39.9**	1.6	3.1	1.0	0.5	93.7	97.9	2.1	-
	2010-2014	415	182	**43.9**	1.6	1.1	0.5	0.5	96.2	98.4	1.6	-
Argentina	2000-2004	230	87	**37.8**	-	-	-	-	100.0	100.0	-	-
	2005-2009	292	129	**44.2**	-	-	-	-	100.0	100.0	-	-
	2010-2014	273	128	**46.9**	-	-	-	-	100.0	100.0	-	-
Brazil	2000-2004	37	15	**40.5**	-	-	-	-	100.0	100.0	-	-
	2005-2009	18	5	**27.8**	-	-	-	-	100.0	100.0	-	-
	2010-2014	8	2	**25.0**	-	-	-	-	100.0	100.0	-	-
Chile	2000-2004	2	1	**50.0**	-	-	-	-	100.0	100.0	-	-
	2005-2009	18	7	**38.9**	28.6	28.6	14.3	-	28.6	100.0	-	-
	2010-2014	5	1	**20.0**	100.0	-	-	-	-	100.0	-	-
Colombia	2000-2004	36	13	**36.1**	-	-	-	-	100.0	100.0	-	-
	2005-2009	27	8	**29.6**	-	-	-	-	100.0	87.5	12.5	-
	2010-2014	39	10	**25.6**	-	-	-	-	100.0	100.0	-	-
Costa Rica*	2000-2004	4	1	**25.0**	-	-	-	-	100.0	100.0	-	-
	2005-2009	10	4	**40.0**	-	-	-	-	100.0	100.0	-	-
	2010-2014	24	9	**37.5**	-	-	-	-	100.0	100.0	-	-
Ecuador	2000-2004	16	10	**62.5**	-	-	-	-	100.0	90.0	10.0	-
	2005-2009	55	29	**52.7**	-	-	-	3.4	96.6	89.7	10.3	-
	2010-2014	51	30	**58.8**	6.7	6.7	3.3	3.3	80.0	90.0	10.0	-
Guadeloupe	2010-2014	2	1	**50.0**	-	-	-	-	100.0	100.0	-	-
Puerto Rico*	2000-2004	47	5	**10.6**	20.0	60.0	-	-	20.0	100.0	-	-
	2005-2009	55	9	**16.4**	11.1	44.4	11.1	-	33.3	100.0	-	-
	2010-2014	12	1	**8.3**	-	-	-	-	100.0	100.0	-	-
America (North)	2000-2004	3,824	661	**17.3**	19.1	21.3	3.3	4.7	51.6	87.1	12.3	0.6
	2005-2009	3,874	590	**15.2**	14.6	20.5	2.2	3.2	59.5	85.3	13.7	1.0
	2010-2014	3,257	456	**14.0**	7.7	14.9	2.9	2.9	71.7	83.3	14.9	1.8
Canada	2000-2004	252	43	**17.1**	4.7	7.0	2.3	-	86.0	93.0	7.0	-
	2005-2009	264	49	**18.6**	-	4.1	-	-	95.9	81.6	16.3	2.0
	2010-2014	259	33	**12.7**	6.1	-	-	-	93.9	69.7	9.1	21.2
United States	2000-2004	3,572	618	**17.3**	20.1	22.3	3.4	5.0	49.2	86.7	12.6	0.6
	2005-2009	3,610	541	**15.0**	15.9	22.0	2.4	3.5	56.2	85.6	13.5	0.9
	2010-2014	2,998	423	**14.1**	7.8	16.1	3.1	3.1	70.0	84.4	15.4	0.2

Supplementary Table 3.5. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Children (0-14 years) diagnosed with an astrocytic tumour, 2000-2014.

Country	Period of diagnosis	Astrocyto-ma, all combined	Astrocytoma NOS			grade (6th digit)					basis of diagnosis		
						grade 1	grade 2	grade 3	grade 4	Unknown	MV	not MV	Unknown
		No.	No.	%		%	%	%	%	%	%	%	%
Asia	2000-2004	662	235	**35.5**		**3.8**	**13.2**	**3.0**	**0.9**	**79.1**	**98.7**	**1.3**	**-**
	2005-2009	799	279	**34.9**		**5.7**	**14.0**	**5.0**	**1.1**	**74.2**	**96.8**	**3.2**	**-**
	2010-2014	706	161	**22.8**		**9.3**	**9.9**	**3.1**	**0.6**	**77.0**	**93.8**	**5.0**	**1.2**
China	2000-2004	16	12	**75.0**		**8.3**	**33.3**	**8.3**	**-**	**50.0**	**100.0**	**-**	**-**
	2005-2009	39	21	**53.8**		**9.5**	**4.8**	**-**	**4.8**	**81.0**	**100.0**	**-**	**-**
	2010-2014	26	15	**57.7**		**6.7**	**26.7**	**6.7**	**-**	**60.0**	**100.0**	**-**	**-**
Cyprus*	2000-2004	1	1	**100.0**		**-**	**-**	**-**	**-**	**100.0**	**-**	**100.0**	**-**
	2005-2009	1	1	**100.0**		**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
India	2000-2004	2	1	**50.0**		**100.0**	**-**	**-**	**-**	**-**	**100.0**	**-**	**-**
	2005-2009	4	3	**75.0**		**-**	**-**	**-**	**-**	**100.0**	**66.7**	**33.3**	**-**
	2010-2014	4	2	**50.0**		**-**	**-**	**-**	**-**	**100.0**	**-**	**100.0**	**-**
Israel*	2000-2004	112	11	**9.8**		**27.3**	**9.1**	**-**	**-**	**63.6**	**100.0**	**-**	**-**
	2005-2009	112	22	**19.6**		**22.7**	**31.8**	**-**	**-**	**45.5**	**90.9**	**9.1**	**-**
	2010-2014	86	10	**11.6**		**20.0**	**10.0**	**10.0**	**-**	**60.0**	**60.0**	**20.0**	**20.0**
Japan	2000-2004	87	31	**35.6**		**-**	**3.2**	**3.2**	**-**	**93.5**	**100.0**	**-**	**-**
	2005-2009	151	32	**21.2**		**-**	**9.4**	**3.1**	**-**	**87.5**	**100.0**	**-**	**-**
	2010-2014	105	18	**17.1**		**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Jordan	2000-2004	60	29	**48.3**		**6.9**	**17.2**	**3.4**	**-**	**72.4**	**100.0**	**-**	**-**
	2005-2009	59	25	**42.4**		**12.0**	**4.0**	**20.0**	**4.0**	**60.0**	**100.0**	**-**	**-**
	2010-2014	52	9	**17.3**		**44.4**	**-**	**-**	**11.1**	**44.4**	**100.0**	**-**	**-**
Korea*	2000-2004	138	49	**35.5**		**-**	**-**	**-**	**-**	**100.0**	**95.9**	**4.1**	**-**
	2005-2009	128	54	**42.2**		**-**	**-**	**-**	**-**	**100.0**	**92.6**	**7.4**	**-**
	2010-2014	127	39	**30.7**		**-**	**-**	**-**	**-**	**100.0**	**92.3**	**7.7**	**-**
Kuwait	2000-2004	5	1	**20.0**		**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	7	2	**28.6**		**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Malaysia	2010-2014	6	3	**50.0**		**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Qatar*	2000-2004	3	1	**33.3**		**100.0**	**-**	**-**	**-**	**-**	**100.0**	**-**	**-**
	2005-2009	6	4	**66.7**		**-**	**25.0**	**25.0**	**-**	**50.0**	**75.0**	**25.0**	**-**
Singapore*	2010-2014	32	5	**15.6**		**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Taiwan*	2000-2004	146	68	**46.6**		**1.5**	**17.6**	**4.4**	**1.5**	**75.0**	**100.0**	**-**	**-**
	2005-2009	98	48	**49.0**		**2.1**	**35.4**	**2.1**	**2.1**	**58.3**	**100.0**	**-**	**-**
	2010-2014	92	21	**22.8**		**-**	**28.6**	**-**	**-**	**71.4**	**100.0**	**-**	**-**
Thailand	2000-2004	37	22	**59.5**		**-**	**4.5**	**-**	**4.5**	**90.9**	**100.0**	**-**	**-**
	2005-2009	51	31	**60.8**		**-**	**6.5**	**12.9**	**-**	**80.6**	**100.0**	**-**	**-**
	2010-2014	26	13	**50.0**		**7.7**	**7.7**	**-**	**-**	**84.6**	**100.0**	**-**	**-**
Turkey	2000-2004	32	9	**28.1**		**-**	**77.8**	**11.1**	**-**	**11.1**	**100.0**	**-**	**-**
	2005-2009	123	36	**29.3**		**13.9**	**19.4**	**5.6**	**-**	**61.1**	**97.2**	**2.8**	**-**
	2010-2014	143	26	**18.2**		**26.9**	**15.4**	**11.5**	**-**	**46.2**	**96.2**	**3.8**	**-**
Europe	2000-2004	2,994	618	**20.6**		**4.5**	**18.6**	**1.3**	**0.8**	**74.8**	**94.7**	**5.0**	**0.3**
	2005-2009	3,153	514	**16.3**		**8.2**	**19.8**	**1.9**	**0.2**	**69.8**	**95.3**	**4.5**	**0.2**
	2010-2014	2,755	376	**13.6**		**9.3**	**29.8**	**4.3**	**0.5**	**56.1**	**95.7**	**4.3**	**-**
Belarus*	2000-2004	89	9	**10.1**		**11.1**	**33.3**	**-**	**-**	**55.6**	**100.0**	**-**	**-**
	2005-2009	73	7	**9.6**		**14.3**	**42.9**	**-**	**-**	**42.9**	**100.0**	**-**	**-**
	2010-2014	90	9	**10.0**		**-**	**100.0**	**-**	**-**	**-**	**100.0**	**-**	**-**
Belgium*	2000-2004	27	4	**14.8**		**-**	**100.0**	**-**	**-**	**-**	**100.0**	**-**	**-**
	2005-2009	129	11	**8.5**		**-**	**81.8**	**-**	**-**	**18.2**	**100.0**	**-**	**-**
	2010-2014	154	16	**10.4**		**6.3**	**50.0**	**6.3**	**-**	**37.5**	**100.0**	**-**	**-**

Supplementary Table 3.5. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Children (0-14 years) diagnosed with an astrocytic tumour, 2000-2014.

Country	Period of diagnosis	Astrocytoma, all combined	Astrocytoma NOS			grade (6th digit)					basis of diagnosis		
						grade 1	grade 2	grade 3	grade 4	Unknown	MV	not MV	Unknown
		No.	No.	%		%	%	%	%	%	%	%	%
Croatia*	2000-2004	33	18	**54.5**		-	-	-	-	**100.0**	**94.4**	**5.6**	-
	2005-2009	50	15	**30.0**		-	-	-	-	**100.0**	**100.0**	-	-
	2010-2014	28	8	**28.6**		-	-	-	-	**100.0**	**100.0**	-	-
Czech Republic*	2000-2004	67	13	**19.4**		**15.4**	**7.7**	**7.7**	**7.7**	**61.5**	**100.0**	-	-
	2005-2009	77	12	**15.6**		**16.7**	**33.3**	-	-	**50.0**	**100.0**	-	-
	2010-2014	72	13	**18.1**		**53.8**	**30.8**	**7.7**	-	**7.7**	**100.0**	-	-
Denmark*	2000-2004	64	13	**20.3**		-	-	-	-	**100.0**	**92.3**	**7.7**	-
	2005-2009	46	6	**13.0**		-	-	-	-	**100.0**	**100.0**	-	-
	2010-2014	31	2	**6.5**		-	-	-	-	**100.0**	**100.0**	-	-
Estonia*	2005-2009	14	1	**7.1**		-	-	-	-	**100.0**	**100.0**	-	-
	2010-2014	7	2	**28.6**		-	-	-	-	**100.0**	**100.0**	-	-
Finland*	2000-2004	85	7	**8.2**		-	-	-	-	**100.0**	**100.0**	-	-
	2005-2009	81	16	**19.8**		-	-	-	-	**100.0**	**100.0**	-	-
	2010-2014	86	9	**10.5**		-	-	-	-	**100.0**	**100.0**	-	-
France	2000-2004	558	58	**10.4**		-	**100.0**	-	-	-	**84.5**	**13.8**	**1.7**
	2005-2009	529	26	**4.9**		-	**100.0**	-	-	-	**92.3**	**7.7**	-
	2010-2014	364	20	**5.5**		**15.0**	**70.0**	**15.0**	-	-	**95.0**	**5.0**	-
Germany	2000-2004	63	20	**31.7**		**15.0**	**5.0**	-	-	**80.0**	**100.0**	-	-
	2005-2009	119	18	**15.1**		**33.3**	**27.8**	**11.1**	-	**27.8**	**94.4**	-	**5.6**
	2010-2014	81	16	**19.8**		**25.0**	**31.3**	**18.8**	-	**25.0**	**93.8**	**6.3**	-
Greece*	2010-2014	77	13	**16.9**		**15.4**	**84.6**	-	-	-	**100.0**	-	-
Iceland*	2000-2004	7	1	**14.3**		-	-	-	-	**100.0**	**100.0**	-	-
	2005-2009	8	2	**25.0**		-	-	-	-	**100.0**	**100.0**	-	-
Ireland*	2000-2004	64	17	**26.6**		-	-	-	-	**100.0**	**100.0**	-	-
	2005-2009	59	8	**13.6**		-	-	-	-	**100.0**	**100.0**	-	-
	2010-2014	52	4	**7.7**		-	-	-	-	**100.0**	**100.0**	-	-
Italy	2000-2004	185	42	**22.7**		**4.8**	**7.1**	-	**2.4**	**85.7**	**92.9**	**7.1**	-
	2005-2009	252	49	**19.4**		**2.0**	**10.2**	**2.0**	-	**85.7**	**98.0**	**2.0**	-
	2010-2014	105	23	**21.9**		**4.3**	**8.7**	**4.3**	-	**82.6**	**100.0**	-	-
Latvia*	2000-2004	32	25	**78.1**		-	-	-	-	**100.0**	**100.0**	-	-
	2005-2009	9	1	**11.1**		-	-	-	-	**100.0**	**100.0**	-	-
	2010-2014	30	10	**33.3**		-	-	-	-	**100.0**	**100.0**	-	-
Lithuania*	2000-2004	26	15	**57.7**		-	-	-	-	**100.0**	**100.0**	-	-
	2005-2009	14	7	**50.0**		-	**14.3**	-	-	**85.7**	**100.0**	-	-
Malta*	2005-2009	3	1	**33.3**		-	-	-	-	**100.0**	**100.0**	-	-
	2010-2014	3	3	**100.0**		-	-	-	-	**100.0**	**100.0**	-	-
Netherlands*	2000-2004	183	20	**10.9**		**20.0**	**65.0**	-	**10.0**	**5.0**	**90.0**	**10.0**	-
	2005-2009	176	14	**8.0**		-	**85.7**	**7.1**	-	**7.1**	**85.7**	**14.3**	-
	2010-2014	181	19	**10.5**		-	**94.7**	**5.3**	-	-	**78.9**	**21.1**	-
Norway*	2000-2004	62	8	**12.9**		**25.0**	-	**25.0**	-	**50.0**	**87.5**	**12.5**	-
	2005-2009	67	13	**19.4**		**15.4**	**7.7**	-	-	**76.9**	**100.0**	-	-
	2010-2014	57	4	**7.0**		-	**50.0**	-	-	**50.0**	**100.0**	-	-
Poland*	2000-2004	235	95	**40.4**		**2.1**	**2.1**	-	-	**95.8**	**100.0**	-	-
	2005-2009	221	74	**33.5**		**4.1**	**4.1**	-	-	**91.9**	**100.0**	-	-
	2010-2014	124	32	**25.8**		-	**9.4**	-	-	**90.6**	**100.0**	-	-
Portugal*	2000-2004	73	23	**31.5**		-	**13.0**	-	-	**87.0**	**100.0**	-	-
	2005-2009	71	20	**28.2**		**5.0**	**10.0**	-	-	**85.0**	**95.0**	**5.0**	-
	2010-2014	65	11	**16.9**		**36.4**	**9.1**	-	-	**54.5**	**100.0**	-	-

Supplementary Table 3.5. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Children (0-14 years) diagnosed with an astrocytic tumour, 2000-2014.

Country	Period of diagnosis	Astrocyto-ma, all combined	Astrocytoma NOS		grade (6th digit)					basis of diagnosis		
					grade 1	grade 2	grade 3	grade 4	Unknown	MV	not MV	Unknown
		No.	No.	%	%	%	%	%	%	%	%	%
Romania	2010-2014	2	1	**50.0**	**-**	**100.0**	**-**	**-**	**-**	**100.0**	**-**	**-**
Russian Federation	2000-2004	37	26	**70.3**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	42	25	**59.5**	**4.0**	**-**	**-**	**-**	**96.0**	**100.0**	**-**	**-**
	2010-2014	57	36	**63.2**	**-**	**11.1**	**-**	**-**	**88.9**	**100.0**	**-**	**-**
Slovakia*	2005-2009	67	8	**11.9**	**12.5**	**50.0**	**25.0**	**-**	**12.5**	**100.0**	**-**	**-**
	2010-2014	57	5	**8.8**	**20.0**	**20.0**	**20.0**	**-**	**40.0**	**100.0**	**-**	**-**
	2000-2004	18	1	**5.6**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Slovenia*	2000-2004	15	3	**20.0**	**-**	**100.0**	**-**	**-**	**-**	**100.0**	**-**	**-**
	2005-2009	22	1	**4.5**	**-**	**100.0**	**-**	**-**	**-**	**100.0**	**-**	**-**
	2010-2014	8	2	**25.0**	**-**	**50.0**	**50.0**	**-**	**-**	**100.0**	**-**	**-**
Spain	2000-2004	173	59	**34.1**	**3.4**	**11.9**	**-**	**-**	**84.7**	**94.9**	**5.1**	**-**
	2005-2009	201	50	**24.9**	**8.0**	**16.0**	**-**	**-**	**76.0**	**96.0**	**4.0**	**-**
	2010-2014	160	19	**11.9**	**-**	**10.5**	**-**	**-**	**89.5**	**100.0**	**-**	**-**
Sweden*	2000-2004	98	20	**20.4**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	99	27	**27.3**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2010-2014	119	19	**16.0**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Switzerland*	2000-2004	84	7	**8.3**	**14.3**	**42.9**	**-**	**-**	**42.9**	**100.0**	**-**	**-**
	2005-2009	65	4	**6.2**	**-**	**25.0**	**-**	**-**	**75.0**	**100.0**	**-**	**-**
	2010-2014	85	5	**5.9**	**-**	**60.0**	**-**	**-**	**40.0**	**100.0**	**-**	**-**
United Kingdom*	2000-2004	638	107	**16.8**	**7.5**	**9.3**	**2.8**	**0.9**	**79.4**	**87.9**	**11.2**	**0.9**
	2005-2009	668	101	**15.1**	**19.8**	**19.8**	**5.0**	**1.0**	**54.5**	**85.1**	**14.9**	**-**
	2010-2014	690	79	**11.4**	**16.5**	**30.4**	**6.3**	**2.5**	**44.3**	**87.3**	**12.7**	**-**
Oceania	2000-2004	171	34	**19.9**	**2.9**	**2.9**	**5.9**	**2.9**	**85.3**	**94.1**	**5.9**	**-**
	2005-2009	162	27	**16.7**	**7.4**	**37.0**	**3.7**	**3.7**	**48.1**	**88.9**	**11.1**	**-**
	2010-2014	139	20	**14.4**	**10.0**	**40.0**	**-**	**-**	**50.0**	**95.0**	**5.0**	**-**
Australia*	2000-2004	140	31	**22.1**	**3.2**	**3.2**	**6.5**	**3.2**	**83.9**	**93.5**	**6.5**	**-**
	2005-2009	146	23	**15.8**	**8.7**	**26.1**	**4.3**	**4.3**	**56.5**	**87.0**	**13.0**	**-**
	2010-2014	129	18	**14.0**	**11.1**	**38.9**	**-**	**-**	**50.0**	**94.4**	**5.6**	**-**
New Zealand*	2000-2004	31	3	**9.7**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	16	4	**25.0**	**-**	**100.0**	**-**	**-**	**-**	**100.0**	**-**	**-**
	2010-2014	10	2	**20.0**	**-**	**50.0**	**-**	**-**	**50.0**	**100.0**	**-**	**-**

MV: microscopically verified.

* Data with 100% coverage of the national population.

Supplementary Table 3.6. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Adults (15-99 years) diagnosed with an astrocytic tumour, 2000-2014.

Country	Period of diagnosis	Astrocytoma, all combined	Astrocytoma NOS										
					grade (6th digit)					basis of diagnosis		
					grade 1	grade 2	grade 3	grade 4	Unknown	MV	not MV	Unknown
		No.	No.	%	%	%	%	%	%	%	%	%
Africa	2000-2004	26	8	**30.8**	**-**	**12.5**	**-**	**62.5**	**25.0**	**100.0**	**-**	**-**
	2005-2009	68	22	**32.4**	**-**	**-**	**-**	**9.1**	**90.9**	**77.3**	**22.7**	**-**
	2010-2014	132	24	**18.2**	**-**	**-**	**-**	**29.2**	**70.8**	**100.0**	**-**	**-**
Algeria	2000-2004	15	6	**40.0**	**-**	**-**	**-**	**83.3**	**16.7**	**100.0**	**-**	**-**
	2005-2009	46	18	**39.1**	**-**	**-**	**-**	**11.1**	**88.9**	**88.9**	**11.1**	**-**
	2010-2014	76	16	**21.1**	**-**	**-**	**-**	**43.8**	**56.3**	**100.0**	**-**	**-**
Mauritius*	2010-2014	24	6	**25.0**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Nigeria	2005-2009	20	4	**20.0**	**-**	**-**	**-**	**-**	**100.0**	**25.0**	**75.0**	**-**
	2010-2014	30	1	**3.3**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
South Africa	2010-2014	2	1	**50.0**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Tunisia	2000-2004	10	2	**20.0**	**-**	**50.0**	**-**	**-**	**50.0**	**100.0**	**-**	**-**
America (Central and South)	2000-2004	1,297	382	**29.5**	**2.4**	**3.4**	**2.6**	**2.1**	**89.5**	**97.6**	**2.4**	**-**
	2005-2009	2,174	607	**27.9**	**1.8**	**4.6**	**1.8**	**2.0**	**89.8**	**97.4**	**2.6**	**-**
	2010-2014	1,648	439	**26.6**	**2.1**	**6.6**	**5.9**	**2.5**	**82.9**	**96.1**	**3.9**	**-**
Argentina	2000-2004	68	23	**33.8**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	321	98	**30.5**	**5.1**	**1.0**	**-**	**5.1**	**88.8**	**100.0**	**-**	**-**
	2010-2014	270	71	**26.3**	**5.6**	**2.8**	**2.8**	**2.8**	**85.9**	**100.0**	**-**	**-**
Brazil	2000-2004	249	62	**24.9**	**-**	**-**	**-**	**-**	**100.0**	**98.4**	**1.6**	**-**
	2005-2009	356	80	**22.5**	**-**	**-**	**-**	**-**	**100.0**	**98.8**	**1.3**	**-**
	2010-2014	217	38	**17.5**	**-**	**-**	**-**	**-**	**100.0**	**94.7**	**5.3**	**-**
Chile	2000-2004	16	3	**18.8**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	114	17	**14.9**	**5.9**	**23.5**	**11.8**	**-**	**58.8**	**100.0**	**-**	**-**
	2010-2014	56	10	**17.9**	**10.0**	**10.0**	**20.0**	**-**	**60.0**	**100.0**	**-**	**-**
Colombia	2000-2004	239	53	**22.2**	**1.9**	**-**	**-**	**-**	**98.1**	**98.1**	**1.9**	**-**
	2005-2009	290	60	**20.7**	**-**	**-**	**1.7**	**-**	**98.3**	**98.3**	**1.7**	**-**
	2010-2014	254	41	**16.1**	**-**	**-**	**-**	**4.9**	**95.1**	**100.0**	**-**	**-**
Costa Rica*	2000-2004	154	64	**41.6**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	229	105	**45.9**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2010-2014	246	64	**26.0**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Ecuador	2000-2004	182	104	**57.1**	**-**	**-**	**-**	**-**	**100.0**	**97.1**	**2.9**	**-**
	2005-2009	356	181	**50.8**	**-**	**1.1**	**-**	**-**	**98.9**	**93.9**	**6.1**	**-**
	2010-2014	384	202	**52.6**	**1.5**	**12.4**	**9.9**	**1.5**	**74.8**	**93.1**	**6.9**	**-**
Martinique	2000-2004	35	14	**40.0**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	36	1	**2.8**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Puerto Rico*	2000-2004	354	59	**16.7**	**13.6**	**22.0**	**16.9**	**13.6**	**33.9**	**93.2**	**6.8**	**-**
	2005-2009	462	65	**14.1**	**7.7**	**32.3**	**12.3**	**10.8**	**36.9**	**95.4**	**4.6**	**-**
	2010-2014	160	13	**8.1**	**7.7**	**7.7**	**15.4**	**30.8**	**38.5**	**92.3**	**7.7**	**-**
America (North)	2000-2004	58,186	6,308	**10.8**	**8.5**	**25.4**	**14.1**	**20.3**	**31.8**	**90.3**	**8.6**	**1.1**
	2005-2009	63,993	5,797	**9.1**	**7.3**	**18.8**	**10.6**	**15.4**	**48.0**	**89.6**	**9.4**	**1.1**
	2010-2014	54,718	4,011	**7.3**	**4.3**	**14.8**	**5.7**	**10.2**	**64.9**	**91.1**	**8.1**	**0.9**
Canada	2000-2004	6,502	1,287	**19.8**	**0.5**	**3.9**	**8.4**	**41.5**	**45.7**	**88.0**	**11.3**	**0.7**
	2005-2009	7,214	1,020	**14.1**	**0.3**	**3.0**	**6.2**	**31.3**	**59.2**	**85.6**	**13.2**	**1.2**
	2010-2014	6,692	429	**6.4**	**0.2**	**3.0**	**1.4**	**12.1**	**83.2**	**86.2**	**8.4**	**5.4**
United States	2000-2004	51,684	5,021	**9.7**	**10.5**	**30.9**	**15.6**	**14.9**	**28.2**	**90.9**	**7.9**	**1.2**
	2005-2009	56,779	4,777	**8.4**	**8.8**	**22.1**	**11.5**	**12.0**	**45.6**	**90.4**	**8.5**	**1.0**
	2010-2014	48,026	3,582	**7.5**	**4.8**	**16.2**	**6.2**	**10.0**	**62.8**	**91.7**	**8.0**	**0.3**

Supplementary Table 3.6. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Adults (15-99 years) diagnosed with an astrocytic tumour, 2000-2014.

Country	Period of diagnosis	Astrocytoma, all combined	Astrocytoma NOS										
					grade (6th digit)					basis of diagnosis		
					grade 1	grade 2	grade 3	grade 4	Unknown	MV	not MV	Unknown
		No.	No.	%	%	%	%	%	%	%	%	%
Asia	2000-2004	8,169	1,757	**21.5**	**3.0**	**10.5**	**8.1**	**2.6**	**75.9**	**99.3**	**0.7**	**-**
	2005-2009	13,320	2,422	**18.2**	**2.6**	**14.8**	**7.0**	**3.1**	**72.5**	**98.0**	**1.9**	**0.1**
	2010-2014	13,562	1,668	**12.3**	**2.5**	**15.3**	**6.3**	**2.9**	**72.9**	**94.9**	**5.1**	**-**
China	2000-2004	269	154	**57.2**	**1.3**	**3.2**	**7.1**	**1.9**	**86.4**	**100.0**	**-**	**-**
	2005-2009	815	368	**45.2**	**1.6**	**6.0**	**7.9**	**1.9**	**82.6**	**100.0**	**-**	**-**
	2010-2014	803	259	**32.3**	**6.6**	**16.6**	**11.2**	**1.2**	**64.5**	**100.0**	**-**	**-**
Cyprus*	2000-2004	18	6	**33.3**	**-**	**33.3**	**16.7**	**-**	**50.0**	**100.0**	**-**	**-**
	2005-2009	142	31	**21.8**	**9.7**	**41.9**	**29.0**	**3.2**	**16.1**	**96.8**	**3.2**	**-**
	2010-2014	162	21	**13.0**	**-**	**19.0**	**42.9**	**19.0**	**19.0**	**95.2**	**4.8**	**-**
India	2000-2004	16	7	**43.8**	**-**	**42.9**	**42.9**	**-**	**14.3**	**100.0**	**-**	**-**
	2005-2009	46	10	**21.7**	**-**	**10.0**	**10.0**	**-**	**80.0**	**100.0**	**-**	**-**
	2010-2014	37	10	**27.0**	**10.0**	**-**	**20.0**	**10.0**	**60.0**	**100.0**	**-**	**-**
Israel*	2000-2004	1,143	138	**12.1**	**10.1**	**19.6**	**26.1**	**13.0**	**31.2**	**97.8**	**2.2**	**-**
	2005-2009	1,244	116	**9.3**	**7.8**	**27.6**	**29.3**	**12.9**	**22.4**	**97.4**	**1.7**	**0.9**
	2010-2014	1,074	84	**7.8**	**4.8**	**35.7**	**17.9**	**8.3**	**33.3**	**90.5**	**9.5**	**-**
Japan	2000-2004	1,587	267	**16.8**	**1.5**	**5.2**	**2.2**	**0.4**	**90.6**	**100.0**	**-**	**-**
	2005-2009	3,160	433	**13.7**	**0.7**	**9.2**	**5.5**	**1.8**	**82.7**	**99.8**	**-**	**0.2**
	2010-2014	2,335	240	**10.3**	**0.4**	**7.9**	**5.4**	**0.4**	**85.8**	**100.0**	**-**	**-**
Jordan*	2000-2004	332	109	**32.8**	**12.8**	**15.6**	**25.7**	**4.6**	**41.3**	**100.0**	**-**	**-**
	2005-2009	359	61	**17.0**	**6.6**	**19.7**	**16.4**	**19.7**	**37.7**	**100.0**	**-**	**-**
	2010-2014	341	31	**9.1**	**6.5**	**22.6**	**12.9**	**16.1**	**41.9**	**100.0**	**-**	**-**
Korea*	2000-2004	2,225	358	**16.1**	**-**	**-**	**-**	**-**	**100.0**	**98.3**	**1.7**	**-**
	2005-2009	2,957	423	**14.3**	**-**	**-**	**-**	**-**	**100.0**	**91.5**	**8.5**	**-**
	2010-2014	3,836	416	**10.8**	**-**	**-**	**-**	**-**	**100.0**	**83.2**	**16.8**	**-**
Kuwait*	2000-2004	45	13	**28.9**	**-**	**30.8**	**15.4**	**23.1**	**30.8**	**92.3**	**7.7**	**-**
	2005-2009	57	9	**15.8**	**-**	**-**	**11.1**	**11.1**	**77.8**	**77.8**	**22.2**	**-**
	2010-2014	57	8	**14.0**	**-**	**12.5**	**-**	**-**	**87.5**	**100.0**	**-**	**-**
Malaysia	2005-2009	34	17	**50.0**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2010-2014	39	15	**38.5**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Qatar*	2000-2004	27	12	**44.4**	**8.3**	**25.0**	**16.7**	**25.0**	**25.0**	**100.0**	**-**	**-**
	2005-2009	56	13	**23.2**	**7.7**	**38.5**	**38.5**	**7.7**	**7.7**	**92.3**	**7.7**	**-**
	2010-2014	74	18	**24.3**	**5.6**	**66.7**	**16.7**	**5.6**	**5.6**	**100.0**	**-**	**-**
Singapore*	2000-2004	163	15	**9.2**	**-**	**20.0**	**-**	**-**	**80.0**	**100.0**	**-**	**-**
	2005-2009	219	20	**9.1**	**-**	**35.0**	**30.0**	**-**	**35.0**	**100.0**	**-**	**-**
	2010-2014	281	25	**8.9**	**-**	**8.0**	**8.0**	**-**	**84.0**	**92.0**	**8.0**	**-**
Taiwan*	2000-2004	1,594	423	**26.5**	**2.4**	**18.4**	**7.3**	**2.4**	**69.5**	**100.0**	**-**	**-**
	2005-2009	1,712	342	**20.0**	**2.6**	**33.0**	**6.7**	**6.1**	**51.5**	**100.0**	**-**	**-**
	2010-2014	2,000	245	**12.3**	**2.4**	**19.6**	**2.9**	**7.3**	**67.8**	**100.0**	**-**	**-**
Thailand	2000-2004	370	198	**53.5**	**2.0**	**3.5**	**3.5**	**-**	**90.9**	**100.0**	**-**	**-**
	2005-2009	566	324	**57.2**	**4.9**	**7.7**	**1.9**	**0.3**	**85.2**	**100.0**	**-**	**-**
	2010-2014	353	82	**23.2**	**4.9**	**24.4**	**8.5**	**1.2**	**61.0**	**100.0**	**-**	**-**
Turkey	2000-2004	380	57	**15.0**	**5.3**	**36.8**	**26.3**	**3.5**	**28.1**	**96.5**	**3.5**	**-**
	2005-2009	1,953	255	**13.1**	**5.1**	**34.9**	**8.6**	**2.7**	**48.6**	**98.4**	**1.6**	**-**
	2010-2014	2,170	214	**9.9**	**2.8**	**32.7**	**6.5**	**3.7**	**54.2**	**98.1**	**1.9**	**-**

Supplementary Table 3.6. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Adults (15-99 years) diagnosed with an astrocytic tumour, 2000-2014.

Country	Period of diagnosis	Astrocytoma, all combined	Astrocytoma NOS										
					grade (6th digit)					basis of diagnosis		
					grade 1	grade 2	grade 3	grade 4	Unknown	MV	not MV	Unknown
		No.	No.	%	%	%	%	%	%	%	%	%
Europe	2000-2004	48,709	7,514	**15.4**	**1.7**	**14.6**	**9.6**	**12.5**	**61.7**	**94.4**	**4.4**	**1.2**
	2005-2009	63,952	6,479	**10.1**	**2.9**	**23.6**	**8.7**	**4.9**	**60.0**	**94.8**	**4.0**	**1.2**
	2010-2014	59,669	4,802	**8.0**	**2.1**	**33.9**	**7.4**	**2.5**	**54.1**	**94.5**	**4.5**	**1.0**
Austria*	2000-2004	1,811	231	**12.8**	**-**	**3.5**	**4.3**	**-**	**92.2**	**98.7**	**-**	**1.3**
	2005-2009	2,194	161	**7.3**	**-**	**19.3**	**8.7**	**0.6**	**71.4**	**82.6**	**-**	**17.4**
	2010-2014	2,031	168	**8.3**	**-**	**17.9**	**9.5**	**3.0**	**69.6**	**88.1**	**0.6**	**11.3**
Belgium*	2000-2004	523	24	**4.6**	**-**	**70.8**	**-**	**4.2**	**25.0**	**100.0**	**-**	**-**
	2005-2009	2,918	138	**4.7**	**-**	**90.6**	**-**	**-**	**9.4**	**100.0**	**-**	**-**
	2010-2014	3,086	138	**4.5**	**2.2**	**78.3**	**1.4**	**-**	**18.1**	**100.0**	**-**	**-**
Croatia*	2000-2004	777	127	**16.3**	**-**	**-**	**-**	**-**	**100.0**	**91.3**	**8.7**	**-**
	2005-2009	910	75	**8.2**	**-**	**-**	**-**	**-**	**100.0**	**92.0**	**8.0**	**-**
	2010-2014	869	72	**8.3**	**-**	**-**	**-**	**-**	**100.0**	**91.7**	**8.3**	**-**
Czech Republic*	2000-2004	2,058	199	**9.7**	**3.5**	**37.2**	**17.1**	**1.5**	**40.7**	**100.0**	**-**	**-**
	2005-2009	2,132	173	**8.1**	**16.8**	**32.9**	**9.8**	**1.7**	**38.7**	**100.0**	**-**	**-**
	2010-2014	2,368	220	**9.3**	**12.3**	**35.5**	**10.0**	**2.7**	**39.5**	**100.0**	**-**	**-**
Denmark*	2000-2004	1,187	161	**13.6**	**-**	**-**	**-**	**-**	**100.0**	**95.7**	**4.3**	**-**
	2005-2009	1,408	97	**6.9**	**-**	**-**	**-**	**-**	**100.0**	**96.9**	**3.1**	**-**
	2010-2014	1,605	72	**4.5**	**-**	**-**	**-**	**-**	**100.0**	**91.7**	**8.3**	**-**
Estonia*	2000-2004	278	4	**1.4**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	267	5	**1.9**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2010-2014	164	3	**1.8**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Finland*	2000-2004	971	145	**14.9**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	1,087	164	**15.1**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2010-2014	1,175	128	**10.9**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
France	2000-2004	1,433	102	**7.1**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	1,981	46	**2.3**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2010-2014	458	5	**1.1**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Germany	2000-2004	5,672	652	**11.5**	**0.8**	**17.3**	**7.2**	**2.6**	**72.1**	**94.0**	**3.2**	**2.8**
	2005-2009	8,303	723	**8.7**	**0.6**	**15.9**	**6.4**	**0.6**	**76.6**	**92.4**	**3.0**	**4.6**
	2010-2014	7,582	436	**5.8**	**0.5**	**14.4**	**3.9**	**2.3**	**78.9**	**95.4**	**1.1**	**3.4**
Gibraltar*	2005-2009	6	1	**16.7**	**-**	**-**	**-**	**-**	**100.0**	**-**	**100.0**	**-**
Iceland*	2000-2004	73	7	**9.6**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	79	8	**10.1**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2010-2014	76	15	**19.7**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Ireland*	2000-2004	763	91	**11.9**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	890	96	**10.8**	**-**	**-**	**-**	**-**	**100.0**	**99.0**	**-**	**1.0**
	2010-2014	780	64	**8.2**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Italy	2000-2004	4,064	326	**8.0**	**4.3**	**12.0**	**11.0**	**1.5**	**71.2**	**94.5**	**5.5**	**-**
	2005-2009	6,211	552	**8.9**	**2.2**	**17.0**	**11.4**	**4.3**	**65.0**	**94.7**	**5.3**	**-**
	2010-2014	2,406	202	**8.4**	**1.5**	**22.3**	**21.3**	**4.5**	**50.5**	**94.6**	**5.4**	**-**
Latvia*	2000-2004	282	79	**28.0**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2005-2009	466	72	**15.5**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
	2010-2014	406	68	**16.7**	**-**	**-**	**-**	**-**	**100.0**	**100.0**	**-**	**-**
Lithuania*	2000-2004	753	196	**26.0**	**-**	**0.5**	**0.5**	**-**	**99.0**	**100.0**	**-**	**-**
	2005-2009	832	136	**16.3**	**-**	**8.1**	**5.1**	**-**	**86.8**	**100.0**	**-**	**-**
	2010-2014	505	33	**6.5**	**3.0**	**9.1**	**-**	**3.0**	**84.8**	**100.0**	**-**	**-**

Supplementary Table 3.6. Frequency distribution of astrocytoma not otherwise specified (NOS) (ICD-O-3 9400/3) by grade, basis of diagnosis and period of diagnosis. Adults (15-99 years) diagnosed with an astrocytic tumour, 2000-2014.

Country	Period of diagnosis	Astrocyto-ma, all combined	Astrocytoma NOS										
					grade (6th digit)					basis of diagnosis		
					grade 1	grade 2	grade 3	grade 4	Unknown	MV	not MV	Unknown
		No.	No.	%	%	%	%	%	%	%	%	%
Malta*	2000-2004	53	10	**18.9**	**10.0**	**40.0**	**10.0**	**-**	**40.0**	**100.0**	**-**	**-**
	2005-2009	51	13	**25.5**	**-**	**38.5**	**-**	**-**	**61.5**	**92.3**	**7.7**	**-**
	2010-2014	75	9	**12.0**	**-**	**22.2**	**-**	**-**	**77.8**	**77.8**	**22.2**	**-**
Netherlands*	2000-2004	3,175	1,027	**32.3**	**3.1**	**27.9**	**15.9**	**49.0**	**4.1**	**95.4**	**4.6**	**-**
	2005-2009	3,785	555	**14.7**	**2.3**	**53.3**	**14.2**	**23.4**	**6.7**	**92.4**	**7.6**	**-**
	2010-2014	4,260	457	**10.7**	**1.5**	**77.9**	**8.3**	**6.3**	**5.9**	**90.6**	**9.4**	**-**
Norway*	2000-2004	1,074	96	**8.9**	**5.2**	**21.9**	**7.3**	**4.2**	**61.5**	**93.8**	**6.3**	**-**
	2005-2009	1,235	92	**7.4**	**12.0**	**10.9**	**3.3**	**-**	**73.9**	**85.9**	**14.1**	**-**
	2010-2014	1,406	96	**6.8**	**-**	**45.8**	**6.3**	**-**	**47.9**	**93.8**	**6.3**	**-**
Poland*	2000-2004	4,466	798	**17.9**	**0.6**	**2.1**	**1.0**	**-**	**96.2**	**100.0**	**-**	**-**
	2005-2009	6,029	631	**10.5**	**0.8**	**10.1**	**4.0**	**0.3**	**84.8**	**100.0**	**-**	**-**
	2010-2014	6,589	529	**8.0**	**1.7**	**21.7**	**8.7**	**0.8**	**67.1**	**100.0**	**-**	**-**
Portugal*	2000-2004	1,379	223	**16.2**	**2.7**	**8.1**	**4.9**	**5.4**	**78.9**	**100.0**	**-**	**-**
	2005-2009	1,893	216	**11.4**	**1.9**	**15.3**	**3.2**	**6.5**	**73.1**	**100.0**	**-**	**-**
	2010-2014	1,393	108	**7.8**	**5.6**	**21.3**	**10.2**	**5.6**	**57.4**	**94.4**	**-**	**5.6**
Romania	2005-2009	88	9	**10.2**	**-**	**-**	**22.2**	**-**	**77.8**	**100.0**	**-**	**-**
	2010-2014	104	10	**9.6**	**-**	**20.0**	**-**	**-**	**80.0**	**100.0**	**-**	**-**
Russian Federation	2000-2004	353	160	**45.3**	**-**	**-**	**-**	**-**	**100.0**	**98.1**	**1.3**	**0.6**
	2005-2009	779	355	**45.6**	**11.5**	**9.6**	**-**	**-**	**78.9**	**99.4**	**0.3**	**0.3**
	2010-2014	1,065	390	**36.6**	**2.3**	**6.2**	**5.9**	**-**	**85.6**	**100.0**	**-**	**-**
Slovakia*	2005-2009	824	149	**18.1**	**1.3**	**30.2**	**40.3**	**10.1**	**18.1**	**100.0**	**-**	**-**
	2010-2014	1,107	175	**15.8**	**7.4**	**21.7**	**20.0**	**6.9**	**44.0**	**100.0**	**-**	**-**
	2000-2004	266	17	**6.4**	**5.9**	**17.6**	**-**	**-**	**76.5**	**100.0**	**-**	**-**
Slovenia*	2000-2004	379	13	**3.4**	**23.1**	**23.1**	**23.1**	**15.4**	**15.4**	**100.0**	**-**	**-**
	2005-2009	453	16	**3.5**	**12.5**	**75.0**	**-**	**-**	**12.5**	**100.0**	**-**	**-**
	2010-2014	388	21	**5.4**	**14.3**	**66.7**	**19.0**	**-**	**-**	**100.0**	**-**	**-**
Spain	2000-2004	1,605	304	**18.9**	**2.6**	**20.7**	**25.7**	**10.5**	**40.5**	**99.3**	**0.7**	**-**
	2005-2009	1,856	251	**13.5**	**4.4**	**34.7**	**15.9**	**5.2**	**39.8**	**98.0**	**1.6**	**0.4**
	2010-2014	1,195	132	**11.0**	**2.3**	**51.5**	**11.4**	**1.5**	**33.3**	**97.7**	**2.3**	**-**
Sweden*	2000-2004	1,753	218	**12.4**	**-**	**-**	**-**	**-**	**100.0**	**99.5**	**0.5**	**-**
	2005-2009	2,020	249	**12.3**	**-**	**-**	**-**	**-**	**100.0**	**99.2**	**0.8**	**-**
	2010-2014	2,304	211	**9.2**	**-**	**-**	**-**	**-**	**100.0**	**97.2**	**2.8**	**-**
Switzerland	2000-2004	825	59	**7.2**	**6.8**	**20.3**	**32.2**	**10.2**	**30.5**	**94.9**	**5.1**	**-**
	2005-2009	987	63	**6.4**	**1.6**	**36.5**	**25.4**	**4.8**	**31.7**	**92.1**	**7.9**	**-**
	2010-2014	938	39	**4.2**	**-**	**56.4**	**10.3**	**5.1**	**28.2**	**97.4**	**2.6**	**-**
United Kingdom*	2000-2004	12,176	2,113	**17.4**	**1.5**	**17.7**	**11.5**	**15.9**	**53.4**	**86.7**	**10.1**	**3.2**
	2005-2009	13,985	1,407	**10.1**	**2.9**	**34.9**	**15.0**	**7.8**	**39.4**	**90.0**	**9.0**	**1.0**
	2010-2014	16,175	1,159	**7.2**	**2.3**	**54.4**	**9.2**	**4.0**	**30.1**	**88.6**	**10.7**	**0.7**
Oceania	2000-2004	5,620	587	**10.4**	**2.9**	**12.6**	**11.9**	**8.7**	**63.9**	**91.5**	**8.2**	**0.3**
	2005-2009	6,356	523	**8.2**	**1.3**	**25.2**	**9.4**	**5.9**	**58.1**	**89.5**	**10.5**	**-**
	2010-2014	6,366	408	**6.4**	**1.5**	**33.8**	**9.3**	**8.8**	**46.6**	**90.4**	**9.6**	**-**
Australia*	2000-2004	4,799	490	**10.2**	**2.9**	**8.8**	**12.0**	**6.9**	**69.4**	**92.2**	**7.3**	**0.4**
	2005-2009	5,458	452	**8.3**	**1.5**	**19.7**	**8.0**	**6.2**	**64.6**	**90.0**	**10.0**	**-**
	2010-2014	5,243	329	**6.3**	**1.5**	**24.6**	**8.5**	**10.6**	**54.7**	**90.0**	**10.0**	**-**
New Zealand*	2000-2004	821	97	**11.8**	**3.1**	**32.0**	**11.3**	**17.5**	**36.1**	**87.6**	**12.4**	**-**
	2005-2009	898	71	**7.9**	**-**	**60.6**	**18.3**	**4.2**	**16.9**	**85.9**	**14.1**	**-**
	2010-2014	1,123	79	**7.0**	**1.3**	**72.2**	**12.7**	**1.3**	**12.7**	**92.4**	**7.6**	**-**

MV: microscopically verified.

* Data with 100% coverage of the national population.

Supplementary Table 3.7. Basis of diagnosis by histology group and country, children (0-14 years of age).

Country	Period of diagnosis	Ependy-moma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medullo-blastoma		Other and unspecified embryonal tumour		Oligodendro-glial tumour		Unspecified glioma		Neuro-epithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Africa	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**12.5**	-	-	-	-	11	**23.4**
	MV	6	**100.0**	-	-	13	**100.0**	19	**100.0**	14	**100.0**	16	**100.0**	35	**97.2**	2	**100.0**	7	**87.5**	-	-	-	-	35	**74.5**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	1	**2.8**	-	-	-	-	-	-	-	-	1	**2.1**
Algeria	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**2.8**
	MV	2	**100.0**	-	-	4	**100.0**	17	**100.0**	9	**100.0**	4	**100.0**	16	**94.1**	2	**100.0**	6	**100.0**	-	-	-	-	34	**94.4**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	1	**5.9**	-	-	-	-	-	-	-	-	1	**2.8**
Mauritius*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	-	-	-	-	-	-	-	-	2	**100.0**	1	**100.0**	-	-	-	-	-	-	-	-	-	-	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nigeria	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5	**100.0**
	MV	3	**100.0**	-	-	8	**100.0**	-	-	1	**100.0**	9	**100.0**	13	**100.0**	-	-	1	**100.0**	-	-	-	-	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
South Africa	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**100.0**	-	-	-	-	5	**83.3**
	MV	1	**100.0**	-	-	1	**100.0**	2	**100.0**	2	**100.0**	2	**100.0**	6	**100.0**	-	-	-	-	-	-	-	-	1	**16.7**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
America (Central and South)	Not MV	-	-	-	-	-	-	5	**1.9**	8	**1.7**	3	**0.3**	-	-	-	-	23	**15.3**	-	-	-	-	429	**75.1**
	MV	304	**100.0**	91	**100.0**	522	**99.8**	257	**98.1**	474	**98.3**	917	**99.6**	317	**100.0**	100	**99.0**	127	**84.7**	9	**100.0**	88	**100.0**	142	**24.9**
	Unknown	-	-	-	-	1	**0.2**	-	-	-	-	1	**0.1**	-	-	1	**1.0**	-	-	-	-	-	-	-	-
Argentina	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**1.0**	-	-	-	-	314	**74.1**
	MV	198	**100.0**	73	**100.0**	299	**100.0**	151	**100.0**	344	**100.0**	651	**100.0**	214	**100.0**	74	**100.0**	101	**99.0**	5	**100.0**	76	**100.0**	110	**25.9**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Brazil	Not MV	-	-	-	-	-	-	-	-	-	-	1	**2.0**	-	-	-	-	5	**38.5**	-	-	-	-	13	**65.0**
	MV	16	**100.0**	6	**100.0**	20	**100.0**	21	**100.0**	22	**100.0**	50	**98.0**	11	**100.0**	2	**100.0**	8	**61.5**	-	-	1	**100.0**	7	**35.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chile	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**33.3**	-	-	-	-	11	**100.0**
	MV	11	**100.0**	2	**100.0**	14	**100.0**	8	**100.0**	3	**100.0**	14	**100.0**	7	**100.0**	1	**100.0**	2	**66.7**	-	-	1	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Colombia	Not MV	-	-	-	-	-	-	2	**6.5**	1	**3.2**	-	-	-	-	-	-	5	**45.5**	-	-	-	-	26	**89.7**
	MV	14	**100.0**	2	**100.0**	40	**100.0**	29	**93.5**	30	**96.8**	38	**100.0**	27	**100.0**	10	**100.0**	6	**54.5**	1	**100.0**	3	**100.0**	3	**10.3**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Costa Rica*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	27	**75.0**
	MV	23	**100.0**	1	**100.0**	16	**100.0**	8	**100.0**	14	**100.0**	35	**100.0**	13	**100.0**	2	**100.0**	2	**100.0**	-	-	-	-	9	**25.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ecuador	Not MV	-	-	-	-	-	-	3	**10.7**	7	**11.3**	1	**1.1**	-	-	-	-	9	**69.2**	-	-	-	-	36	**87.8**
	MV	27	**100.0**	-	-	32	**100.0**	25	**89.3**	55	**88.7**	88	**98.9**	16	**100.0**	7	**100.0**	4	**30.8**	2	**100.0**	-	-	5	**12.2**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Guadeloupe	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	1	**100.0**	-	-	1	**100.0**	1	**100.0**	1	**100.0**	4	**100.0**	2	**100.0**	-	-	-	-	-	-	3	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Supplementary Table 3.7. Basis of diagnosis by histology group and country, children (0-14 years of age).

Country	Period of diagnosis	Ependy-moma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medullo-blastoma		Other and unspecified embryonal tumour		Oligodendro-glial tumour		Unspecified glioma		Neuro-epithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Martinique*	Not MV	-	-	-	-	-	-	-	-	-	-	1	**16.7**	-	-	-	-	-	-	-	-	-	-	-	-
	MV	2	**100.0**	-	-	5	**83.3**	-	-	-	-	4	**66.7**	1	**100.0**	-	-	-	-	-	-	1	**100.0**	-	-
	Unknown	-	-	-	-	1	**16.7**	-	-	-	-	1	**16.7**	-	-	1	**100.0**	-	-	-	-	-	-	-	-
Puerto Rico*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	**33.3**	-	-	-	-	2	**20.0**
	MV	12	**100.0**	7	**100.0**	95	**100.0**	14	**100.0**	5	**100.0**	33	**100.0**	26	**100.0**	4	**100.0**	4	**66.7**	1	**100.0**	3	**100.0**	8	**80.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
America (North)	Not MV	25	**2.1**	29	**4.2**	314	**3.8**	40	**2.4**	187	**18.4**	19	**0.7**	21	**0.8**	12	**2.0**	2,734	**72.8**	13	**13.3**	82	**4.4**	452	**48.9**
	MV	1,139	**96.9**	661	**95.0**	7,873	**95.6**	1,644	**96.9**	816	**80.1**	2,853	**98.8**	2,648	**98.4**	580	**97.6**	958	**25.5**	84	**85.7**	1,778	**94.3**	252	**27.2**
	Unknown	11	**0.9**	6	**0.9**	46	**0.6**	13	**0.8**	16	**1.6**	17	**0.6**	23	**0.9**	2	**0.3**	65	**1.7**	1	**1.0**	25	**1.3**	221	**23.9**
Canada	Not MV	-	-	1	**2.7**	13	**2.4**	2	**1.9**	14	**12.2**	3	**1.1**	3	**1.3**	4	**10.3**	176	**69.8**	-	-	9	**7.6**	41	**20.3**
	MV	82	**91.1**	30	**81.1**	504	**91.6**	100	**92.6**	95	**82.6**	257	**95.5**	229	**95.4**	34	**87.2**	53	**21.0**	11	**100.0**	88	**73.9**	14	**6.9**
	Unknown	8	**8.9**	6	**16.2**	33	**6.0**	6	**5.6**	6	**5.2**	9	**3.3**	8	**3.3**	1	**2.6**	23	**9.1**	-	-	22	**18.5**	147	**72.8**
United States	Not MV	25	**2.3**	28	**4.2**	301	**3.9**	38	**2.4**	173	**19.1**	16	**0.6**	18	**0.7**	8	**1.4**	2,558	**73.0**	13	**14.9**	73	**4.1**	411	**56.8**
	MV	1,057	**97.4**	631	**95.8**	7,369	**95.9**	1,544	**97.2**	721	**79.8**	2,596	**99.1**	2,419	**98.7**	546	**98.4**	905	**25.8**	73	**83.9**	1,690	**95.7**	238	**32.9**
	Unknown	3	**0.3**	-	-	13	**0.2**	7	**0.4**	10	**1.1**	8	**0.3**	15	**0.6**	1	**0.2**	42	**1.2**	1	**1.1**	3	**0.2**	74	**10.2**
Asia	Not MV	5	**1.3**	-	-	7	**0.8**	7	**1.0**	19	**3.7**	7	**0.5**	16	**1.6**	1	**0.5**	419	**46.2**	3	**6.0**	1	**0.6**	750	**84.8**
	MV	395	**98.8**	122	**100.0**	911	**99.2**	725	**99.0**	496	**95.9**	1,547	**99.5**	961	**98.3**	186	**99.5**	485	**53.5**	47	**94.0**	153	**99.4**	120	**13.6**
	Unknown	-	-	-	-	-	-	-	-	2	**0.4**	-	-	1	**0.1**	-	-	3	**0.3**	-	-	-	-	14	**1.6**
China	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**3.0**	1	**12.5**	-	-	226	**90.8**
	MV	15	**100.0**	7	**100.0**	26	**100.0**	23	**100.0**	32	**100.0**	58	**100.0**	22	**100.0**	9	**100.0**	32	**97.0**	7	**87.5**	8	**100.0**	23	**9.2**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cyprus*	Not MV	-	-	-	-	-	-	-	-	1	**50.0**	-	-	-	-	-	-	3	**60.0**	-	-	-	-	1	**50.0**
	MV	1	**100.0**	1	**100.0**	-	-	-	-	1	**50.0**	2	**100.0**	-	-	1	**100.0**	2	**40.0**	-	-	-	-	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**50.0**
India	Not MV	-	-	-	-	-	-	-	-	3	**60.0**	-	-	-	-	-	-	1	**16.7**	-	-	-	-	5	**100.0**
	MV	1	**100.0**	-	-	2	**100.0**	3	**100.0**	2	**40.0**	2	**100.0**	-	-	1	**100.0**	5	**83.3**	-	-	-	-	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Israel*	Not MV	2	**4.1**	-	-	3	**1.3**	1	**1.9**	4	**17.4**	2	**1.4**	4	**4.9**	-	-	28	**23.3**	-	-	-	-	28	**77.8**
	MV	47	**95.9**	19	**100.0**	231	**98.7**	52	**98.1**	17	**73.9**	137	**98.6**	78	**95.1**	18	**100.0**	92	**76.7**	3	**100.0**	48	**100.0**	8	**22.2**
	Unknown	-	-	-	-	-	-	-	-	2	**8.7**	-	-	-	-	-	-	-	-	-	-	-	-		-
Japan	Not MV	-	-	-	-	2	**1.3**	-	-	-	-	-	-	-	-	-	-	100	**60.2**	-	-	1	**3.0**	124	**80.5**
	MV	53	**100.0**	33	**100.0**	151	**98.7**	115	**100.0**	75	**100.0**	195	**100.0**	131	**99.2**	15	**100.0**	64	**38.6**	9	**100.0**	32	**97.0**	19	**12.3**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	1	**0.8**	-	-	2	**1.2**	-	-	-	-	11	**7.1**
Jordan*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	25	**48.1**	-	-	-	-	8	**38.1**
	MV	28	**100.0**	6	**100.0**	59	**100.0**	72	**100.0**	40	**100.0**	129	**100.0**	52	**100.0**	11	**100.0**	27	**51.9**	2	**100.0**	3	**100.0**	13	**61.9**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Korea*	Not MV	2	**1.7**	-	-	-	-	5	**2.5**	9	**6.3**	5	**1.0**	10	**2.8**	-	-	192	**76.5**	-	-	-	-	257	**93.8**
	MV	115	**98.3**	26	**100.0**	47	**100.0**	199	**97.5**	133	**93.7**	503	**99.0**	343	**97.2**	55	**100.0**	59	**23.5**	17	**100.0**	7	**100.0**	17	**6.2**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Supplementary Table 3.7. Basis of diagnosis by histology group and country, children (0-14 years of age).

Country	Period of diagnosis	Ependy-moma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medullo-blastoma		Other and unspecified embryonal tumour		Oligodendro-glial tumour		Unspecified glioma		Neuro-epithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Kuwait*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6	**60.0**	-	-	-	-	-	-
	MV	5	**100.0**	-	-	5	**100.0**	5	**100.0**	3	**100.0**	14	**100.0**	2	**100.0**	1	**100.0**	4	**40.0**	1	**100.0**	2	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Malaysia	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	**40.0**	-	-	-	-	-	-
	MV	3	**100.0**	-	-	1	**100.0**	4	**100.0**	3	**100.0**	10	**100.0**	10	**100.0**	3	**100.0**	3	**60.0**	1	**100.0**	-	-	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Qatar*	Not MV	-	-	-	-	-	-	-	-	1	**50.0**	-	-	-	-	-	-	-	-	-	-	-	-	2	**50.0**
	MV	-	-	-	-	8	**100.0**	5	**100.0**	1	**50.0**	4	**100.0**	4	**100.0**	-	-	4	**100.0**	-	-	-	-	2	**50.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Singapore*	Not MV	-	-	-	-	1	**2.0**	-	-	-	-	-	-	1	**5.3**	-	-	4	**21.1**	-	-	-	-	3	**60.0**
	MV	11	**100.0**	4	**100.0**	48	**98.0**	19	**100.0**	5	**100.0**	21	**100.0**	18	**94.7**	2	**100.0**	15	**78.9**	-	-	9	**100.0**	2	**40.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Taiwan*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	41	**100.0**	5	**100.0**	124	**100.0**	118	**100.0**	94	**100.0**	241	**100.0**	147	**100.0**	37	**100.0**	33	**100.0**	4	**100.0**	7	**100.0**	2	**100.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thailand	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	1	**3.1**	-	-	5	**15.2**	-	-	-	-	59	**100.0**
	MV	11	**100.0**	1	**100.0**	15	**100.0**	43	**100.0**	56	**100.0**	90	**100.0**	31	**96.9**	5	**100.0**	28	**84.8**	-	-	-	-	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Turkey	Not MV	1	**1.5**	-	-	1	**0.5**	1	**1.5**	1	**2.9**	-	-	-	-	1	**3.4**	52	**30.6**	2	**40.0**	-	-	37	**50.7**
	MV	64	**98.5**	20	**100.0**	194	**99.5**	67	**98.5**	34	**97.1**	141	**100.0**	123	**100.0**	28	**96.6**	117	**68.8**	3	**60.0**	37	**100.0**	34	**46.6**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**0.6**	-	-	-	-	2	**2.7**
Europe	Not MV	17	**1.6**	11	**1.6**	101	**1.6**	19	**1.2**	43	**4.2**	23	**0.6**	19	**0.8**	8	**1.0**	952	**58.8**	7	**6.8**	84	**5.2**	780	**66.2**
	MV	1,035	**98.1**	669	**98.2**	6,194	**98.3**	1,544	**98.7**	987	**95.6**	3,886	**99.4**	2,280	**99.0**	770	**99.0**	639	**39.5**	95	**92.2**	1,537	**94.7**	346	**29.4**
	Unknown	3	**0.3**	1	**0.1**	7	**0.1**	1	**0.1**	2	**0.2**	2	**0.1**	3	**0.1**	-	-	27	**1.7**	1	**1.0**	2	**0.1**	52	**4.4**
Belarus*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5	**35.7**	-	-	-	-	36	**85.7**
	MV	47	**100.0**	11	**100.0**	211	**100.0**	33	**100.0**	8	**100.0**	92	**100.0**	51	**100.0**	44	**100.0**	9	**64.3**	1	**100.0**	25	**100.0**	6	**14.3**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Belgium*	Not MV	-	-	-	-	1	**0.4**	-	-	-	-	-	-	-	-	-	-	63	**95.5**	-	-	-	-	21	**87.5**
	MV	19	**100.0**	43	**100.0**	243	**99.6**	58	**100.0**	8	**100.0**	110	**100.0**	74	**100.0**	28	**100.0**	3	**4.5**	5	**100.0**	56	**100.0**	3	**12.5**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Croatia*	Not MV	1	**5.3**	-	-	2	**4.2**	-	-	1	**2.4**	6	**10.2**	3	**8.3**	-	-	2	**7.4**	-	-	-	-	1	**3.3**
	MV	18	**94.7**	1	**100.0**	46	**95.8**	22	**100.0**	40	**97.6**	53	**89.8**	33	**91.7**	5	**100.0**	25	**92.6**	-	-	11	**100.0**	29	**96.7**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Czech Republic*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	25	**100.0**	11	**100.0**	156	**100.0**	45	**100.0**	15	**100.0**	31	**100.0**	64	**100.0**	11	**100.0**	9	**100.0**	1	**100.0**	12	**100.0**	16	**100.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Denmark*	Not MV	-	-	-	-	6	**5.9**	1	**5.3**	1	**4.8**	-	-	1	**2.2**	-	-	1	**10.0**	-	-	-	-	56	**34.6**
	MV	11	**100.0**	8	**100.0**	95	**94.1**	18	**94.7**	20	**95.2**	70	**100.0**	45	**97.8**	9	**100.0**	9	**90.0**	2	**100.0**	20	**100.0**	105	**64.8**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**0.6**

Supplementary Table 3.7. Basis of diagnosis by histology group and country, children (0-14 years of age).

Country	Period of diagnosis	Ependy-moma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medullo-blastoma		Other and unspecified embryonal tumour		Oligodendro-glial tumour		Unspecified glioma		Neuro-epithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Estonia*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	6	**100.0**	5	**100.0**	40	**100.0**	2	**100.0**	3	**100.0**	14	**100.0**	11	**100.0**	4	**100.0**	-	-	-	-	2	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Finland*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	21	**100.0**	19	**100.0**	189	**100.0**	31	**100.0**	32	**100.0**	56	**100.0**	57	**100.0**	11	**100.0**	2	**100.0**	4	**100.0**	57	**100.0**	4	**100.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
France	Not MV	2	**1.2**	6	**3.9**	31	**2.4**	4	**2.4**	-	-	5	**0.6**	3	**0.7**	6	**2.1**	242	**57.9**	1	**7.1**	46	**8.2**	50	**70.4**
	MV	171	**98.8**	148	**96.1**	1,249	**97.4**	165	**97.6**	-	-	775	**99.2**	411	**99.3**	285	**97.9**	160	**38.3**	13	**92.9**	512	**91.6**	16	**22.5**
	Unknown	-	-	-	-	2	**0.2**	-	-	-	-	1	**0.1**	-	-	-	-	16	**3.8**	-	-	1	**0.2**	5	**7.0**
Germany	Not MV	1	**5.3**	-	-	2	**1.3**	-	-	1	**4.0**	1	**0.8**	1	**1.0**	-	-	35	**66.0**	1	**50.0**	-	-	1	**12.5**
	MV	18	**94.7**	15	**100.0**	153	**97.5**	81	**100.0**	23	**92.0**	122	**99.2**	103	**99.0**	13	**100.0**	17	**32.1**	1	**50.0**	22	**100.0**	7	**87.5**
	Unknown	-	-	-	-	2	**1.3**	-	-	1	**4.0**	-	-	-	-	-	-	1	**1.9**	-	-	-	-	-	-
Greece*	Not MV	-	-	-	-	2	**3.0**	1	**9.1**	-	-	-	-	-	-	-	-	17	**94.4**	1	**100.0**	1	**5.6**	2	**100.0**
	MV	5	**100.0**	6	**85.7**	64	**97.0**	10	**90.9**	-	-	57	**100.0**	35	**100.0**	6	**100.0**	1	**5.6**	-	-	16	**88.9**	-	-
	Unknown	-	-	1	**14.3**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**5.6**	-	-
Iceland*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	**66.7**	-	-	-	-	4	**100.0**
	MV	-	-	-	-	14	**100.0**	1	**100.0**	3	**100.0**	2	**100.0**	1	**100.0**	2	**100.0**	1	**33.3**	-	-	2	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ireland*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	15	**100.0**	8	**100.0**	126	**100.0**	20	**100.0**	29	**100.0**	24	**100.0**	52	**98.1**	14	**100.0**	6	**100.0**	2	**100.0**	19	**100.0**	1	**50.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	1	**1.9**	-	-	-	-	-	-	-	-	1	**50.0**
Italy	Not MV	5	**5.4**	-	-	5	**1.5**	1	**1.0**	4	**4.1**	2	**0.8**	1	**1.0**	-	-	53	**55.2**	1	**14.3**	2	**2.2**	269	**93.1**
	MV	88	**94.6**	34	**100.0**	338	**98.5**	100	**99.0**	93	**95.9**	259	**99.2**	100	**99.0**	26	**100.0**	43	**44.8**	6	**85.7**	90	**97.8**	20	**6.9**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Latvia*	Not MV	-	-	-	-	-	-	1	**4.3**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	28	**87.5**
	MV	3	**100.0**	-	-	12	**100.0**	22	**95.7**	36	**100.0**	11	**100.0**	5	**100.0**	2	**100.0**	3	**100.0**	2	**100.0**	-	-	1	**3.1**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	**9.4**
Lithuania*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	8	**100.0**	1	**100.0**	14	**100.0**	11	**100.0**	21	**100.0**	28	**100.0**	7	**100.0**	5	**100.0**	6	**100.0**	1	**100.0**	2	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Malta*	Not MV	-	-	-	-	1	**20.0**	-	-	-	-	-	-	-	-	-	-	3	**100.0**	-	-	-	-	-	-
	MV	2	**100.0**	-	-	4	**80.0**	2	**100.0**	4	**100.0**	5	**100.0**	1	**100.0**	-	-	-	-	-	-	2	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	50	**98.0**
Netherlands*	Not MV	-	-	1	**2.6**	17	**3.9**	4	**3.9**	-	-	-	-	-	-	-	-	119	**81.5**	-	-	7	**5.6**	1	**2.0**
	MV	59	**100.0**	38	**97.4**	418	**96.1**	98	**96.1**	2	**100.0**	237	**100.0**	151	**100.0**	36	**100.0**	27	**18.5**	6	**100.0**	117	**94.4**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	12	**35.3**
Norway*	Not MV	-	-	1	**4.3**	-	-	-	-	1	**6.3**	-	-	-	-	-	-	24	**63.2**	-	-	4	**8.2**	22	**64.7**
	MV	11	**100.0**	22	**95.7**	142	**100.0**	28	**100.0**	15	**93.8**	42	**100.0**	54	**100.0**	17	**100.0**	14	**36.8**	1	**100.0**	45	**91.8**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Poland*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4	**100.0**
	MV	120	**100.0**	31	**100.0**	214	**100.0**	178	**100.0**	188	**100.0**	453	**100.0**	226	**100.0**	66	**100.0**	57	**100.0**	9	**100.0**	5	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	8	**61.5**

Supplementary Table 3.7. Basis of diagnosis by histology group and country, children (0-14 years of age).

Country	Period of diagnosis	Ependy-moma		Choroid plexus tumour		Astrocytoma WHO grade I and II		Astrocytoma WHO grade III and IV		Unspecified astrocytoma		Medullo-blastoma		Other and unspecified embryonal tumour		Oligodendro-glial tumour		Unspecified glioma		Neuro-epithelial glial tumour of uncertain origin		Neuronal and mixed neuronal-glial tumour		Unspecified neoplasm	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Portugal*	Not MV	-	-	-	-	-	-	-	-	1	**2.3**	-	-	-	-	-	-	17	**42.5**	-	-	-	-	5	**38.5**
	MV	20	**100.0**	15	**100.0**	128	**100.0**	38	**100.0**	42	**97.7**	102	**100.0**	49	**98.0**	25	**100.0**	22	**55.0**	3	**100.0**	23	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	1	**2.0**	-	-	1	**2.5**	-	-	-	-	2	**100.0**
Romania	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	1	**50.0**	-	-	2	**50.0**	-	-	-	-	-	-
	MV	2	**100.0**	-	-	3	**100.0**	-	-	-	-	4	**100.0**	1	**50.0**	2	**100.0**	2	**50.0**	-	-	-	-	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Russian Federation	Not MV	-	-	-	-	-	-	-	-	-	-	1	**1.7**	-	-	-	-	1	**7.1**	-	-	-	-	13	**100.0**
	MV	10	**100.0**	3	**100.0**	12	**100.0**	42	**100.0**	82	**100.0**	58	**98.3**	25	**100.0**	16	**100.0**	13	**92.9**	4	**100.0**	-	-	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	26	**100.0**
Slovakia*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	22	**100.0**	7	**100.0**	118	**100.0**	20	**100.0**	4	**100.0**	55	**100.0**	25	**100.0**	13	**100.0**	7	**100.0**	1	**100.0**	6	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Slovenia*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	-	-	4	**100.0**	30	**100.0**	15	**100.0**	-	-	29	**100.0**	14	**100.0**	3	**100.0**	3	**100.0**	1	**100.0**	4	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	20	**58.8**
Spain	Not MV	1	**1.0**	1	**2.6**	3	**0.8**	-	-	4	**3.8**	2	**0.7**	-	-	-	-	42	**56.0**	1	**20.0**	1	**1.4**	14	**41.2**
	MV	95	**99.0**	38	**97.4**	359	**99.2**	67	**100.0**	101	**96.2**	288	**99.3**	161	**100.0**	15	**100.0**	33	**44.0**	4	**80.0**	72	**98.6**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	54	**84.4**
Sweden*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**8.3**	-	-	-	-	10	**15.6**
	MV	32	**100.0**	23	**100.0**	202	**100.0**	48	**100.0**	66	**100.0**	83	**100.0**	80	**100.0**	23	**100.0**	11	**91.7**	2	**100.0**	56	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Switzerland*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**50.0**
	MV	9	**100.0**	14	**100.0**	187	**100.0**	39	**100.0**	8	**100.0**	85	**100.0**	74	**100.0**	9	**100.0**	4	**100.0**	2	**100.0**	38	**100.0**	1	**50.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	140	**56.2**
United Kingdom*	Not MV	7	**3.4**	2	**1.2**	31	**2.1**	7	**2.0**	30	**17.1**	6	**0.8**	9	**2.4**	2	**2.4**	323	**66.7**	2	**7.4**	23	**6.6**	68	**27.3**
	MV	198	**95.2**	164	**98.8**	1,427	**97.7**	350	**97.8**	144	**82.3**	741	**99.1**	370	**97.4**	80	**97.6**	152	**31.4**	24	**88.9**	323	**93.4**	41	**16.5**
	Unknown	3	**1.4**	-	-	3	**0.2**	1	**0.3**	1	**0.6**	1	**0.1**	1	**0.3**	-	-	9	**1.9**	1	**3.7**	-	-		
Oceania	Not MV	4	**3.9**	2	**5.7**	14	**5.7**	13	**7.4**	6	**11.5**	11	**3.9**	9	**3.8**	-	-	163	**75.5**	-	-	11	**16.2**	94	**74.0**
	MV	99	**96.1**	33	**94.3**	230	**94.3**	163	**92.6**	46	**88.5**	273	**96.1**	225	**96.2**	51	**100.0**	52	**24.1**	3	**100.0**	57	**83.8**	13	**10.2**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**0.5**	-	-	-	-	20	**15.7**
Australia*	Not MV	4	**4.8**	2	**6.5**	14	**6.4**	13	**8.7**	6	**12.5**	11	**4.5**	9	**4.3**	-	-	129	**75.4**	-	-	11	**16.4**	78	**71.6**
	MV	80	**95.2**	29	**93.5**	204	**93.6**	136	**91.3**	42	**87.5**	233	**95.5**	201	**95.7**	42	**100.0**	41	**24.0**	3	**100.0**	56	**83.6**	11	**10.1**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**0.6**	-	-	-	-	20	**18.3**
New Zealand*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	34	**75.6**	-	-	-	-	16	**88.9**
	MV	19	**100.0**	4	**100.0**	26	**100.0**	27	**100.0**	4	**100.0**	40	**100.0**	24	**100.0**	9	**100.0**	11	**24.4**	-	-	1	**100.0**	2	**11.1**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

MV: microscopically verified.

* Data with 100% coverage of the national population.

Supplementary Table 3.8. Basis of diagnosis by histology group and country, adults (15-99 years of age).

Country	Basis of diagnosis	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Africa	Not MV	-	**-**	-	**-**	5	**3.0**	-	**-**	3	**7.7**	1	**11.1**	-	**-**	-	**-**	4	**16.0**	-	**-**	92	**30.8**
	MV	13	**100.0**	14	**100.0**	163	**97.0**	5	**100.0**	36	**92.3**	8	**88.9**	2	**100.0**	10	**100.0**	21	**84.0**	1	**100.0**	195	**65.2**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	12	**4.0**
Algeria	Not MV	-	**-**	-	**-**	2	**1.9**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	7	**3.4**
	MV	8	**100.0**	3	**100.0**	106	**98.1**	-	**-**	26	**100.0**	7	**100.0**	1	**100.0**	2	**100.0**	17	**100.0**	-	**-**	186	**90.7**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	12	**5.9**
Mauritius*	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	8	**80.0**
	MV	1	**100.0**	1	**100.0**	17	**100.0**	-	**-**	6	**100.0**	-	**-**	-	**-**	-	**-**	1	**100.0**	-	**-**	2	**20.0**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Nigeria	Not MV	-	**-**	-	**-**	3	**9.1**	-	**-**	3	**60.0**	1	**50.0**	-	**-**	-	**-**	3	**60.0**	-	**-**	69	**90.8**
	MV	3	**100.0**	7	**100.0**	30	**90.9**	5	**100.0**	2	**40.0**	1	**50.0**	1	**100.0**	6	**100.0**	2	**40.0**	1	**100.0**	7	**9.2**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
South Africa	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**50.0**	-	**-**	7	**100.0**
	MV	1	**100.0**	1	**100.0**	3	**100.0**	-	**-**	1	**100.0**	-	**-**	-	**-**	1	**100.0**	1	**50.0**	-	**-**	-	**-**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
America (Central and South)	Not MV	2	**1.2**	6	**0.7**	66	**2.3**	3	**2.4**	38	**3.0**	1	**0.1**	-	**-**	1	**1.1**	66	**21.9**	-	**-**	1,155	**76.2**
	MV	168	**98.2**	901	**99.3**	2,767	**97.6**	122	**97.6**	1,213	**97.0**	738	**99.6**	90	**100.0**	86	**98.9**	235	**78.1**	60	**98.4**	334	**22.0**
	Unknown	1	**0.6**	-	**-**	3	**0.1**	-	**-**	-	**-**	2	**0.3**	-	**-**	-	**-**	-	**-**	1	**1.6**	27	**1.8**
Argentina	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	95	**43.6**
	MV	24	**96.0**	118	**100.0**	350	**99.2**	17	**100.0**	171	**100.0**	97	**100.0**	3	**100.0**	19	**100.0**	57	**100.0**	6	**85.7**	109	**50.0**
	Unknown	1	**4.0**	-	**-**	3	**0.8**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**14.3**	14	**6.4**
Brazil	Not MV	-	**-**	1	**0.8**	6	**1.2**	-	**-**	4	**2.2**	-	**-**	-	**-**	1	**10.0**	5	**9.1**	-	**-**	113	**77.9**
	MV	29	**100.0**	128	**99.2**	501	**98.8**	6	**100.0**	176	**97.8**	70	**97.2**	6	**100.0**	9	**90.0**	50	**90.9**	2	**100.0**	27	**18.6**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	2	**2.8**	-	**-**	-	**-**	-	**-**	-	**-**	5	**3.4**
Chile	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	132	**97.8**
	MV	7	**100.0**	48	**100.0**	112	**100.0**	7	**100.0**	19	**100.0**	28	**100.0**	10	**100.0**	5	**100.0**	10	**100.0**	3	**100.0**	3	**2.2**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Colombia	Not MV	-	**-**	-	**-**	11	**2.4**	-	**-**	2	**1.3**	-	**-**	-	**-**	-	**-**	7	**12.7**	-	**-**	346	**81.6**
	MV	38	**100.0**	156	**100.0**	448	**97.6**	18	**100.0**	148	**98.7**	129	**100.0**	12	**100.0**	23	**100.0**	48	**87.3**	10	**100.0**	78	**18.4**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Costa Rica*	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**5.3**	-	**-**	166	**85.1**
	MV	19	**100.0**	60	**100.0**	333	**100.0**	3	**100.0**	233	**100.0**	182	**100.0**	7	**100.0**	5	**100.0**	18	**94.7**	4	**100.0**	29	**14.9**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Ecuador	Not MV	2	**10.0**	1	**0.5**	20	**7.8**	1	**8.3**	27	**6.2**	1	**0.8**	-	**-**	-	**-**	29	**55.8**	-	**-**	231	**92.8**
	MV	18	**90.0**	218	**99.5**	237	**92.2**	11	**91.7**	407	**93.8**	121	**99.2**	46	**100.0**	7	**100.0**	23	**44.2**	5	**100.0**	18	**7.2**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**

Supplementary Table 3.8. Basis of diagnosis by histology group and country, adults (15-99 years of age).

Country	Basis of diagnosis	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Guadeloupe	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**33.3**	-	-	-	-
	MV	1	**100.0**	-	-	38	**100.0**	-	-	-	-	3	**100.0**	-	-	1	**100.0**	2	**66.7**	8	**100.0**	-	-
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Martinique*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	2	**100.0**	5	**100.0**	82	**100.0**	2	**100.0**	15	**100.0**	10	**100.0**	3	**100.0**	-	-	4	**100.0**	8	**100.0**	4	**100.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Puerto Rico*	Not MV	-	-	4	**2.3**	29	**4.2**	2	**3.3**	5	**10.2**	-	-	-	-	-	-	23	**50.0**	-	-	72	**49.3**
	MV	30	**100.0**	168	**97.7**	666	**95.8**	58	**96.7**	44	**89.8**	98	**100.0**	3	**100.0**	17	**100.0**	23	**50.0**	14	**100.0**	66	**45.2**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	8	**5.5**
America (North)	Not MV	735	**13.6**	296	**1.2**	10,132	**7.4**	267	**3.7**	1,106	**15.0**	483	**2.0**	1	**0.3**	26	**1.6**	6,838	**55.9**	460	**9.4**	12,633	**56.9**
	MV	4,615	**85.2**	24,290	**98.4**	125,981	**91.5**	6,889	**95.7**	6,145	**83.2**	23,494	**97.1**	340	**98.0**	1,542	**97.2**	5,106	**41.8**	4,322	**88.8**	2,754	**12.4**
	Unknown	67	**1.2**	100	**0.4**	1,501	**1.1**	42	**0.6**	138	**1.9**	225	**0.9**	6	**1.7**	18	**1.1**	278	**2.3**	87	**1.8**	6,826	**30.7**
Canada	Not MV	70	**13.4**	73	**4.1**	2,122	**12.9**	33	**5.2**	296	**19.1**	146	**4.1**	-	-	6	**2.9**	951	**56.0**	85	**16.3**	2,801	**40.6**
	MV	407	**78.1**	1,635	**92.6**	13,637	**82.8**	566	**90.0**	1,222	**78.9**	3,273	**91.1**	32	**88.9**	191	**92.7**	653	**38.4**	369	**70.7**	183	**2.7**
	Unknown	44	**8.4**	58	**3.3**	705	**4.3**	30	**4.8**	31	**2.0**	172	**4.8**	4	**11.1**	9	**4.4**	95	**5.6**	68	**13.0**	3,911	**56.7**
United States	Not MV	665	**13.6**	223	**1.0**	8,010	**6.6**	234	**3.6**	810	**13.9**	337	**1.6**	1	**0.3**	20	**1.4**	5,887	**55.9**	375	**8.6**	9,832	**64.2**
	MV	4,208	**85.9**	22,655	**98.8**	112,344	**92.7**	6,323	**96.3**	4,923	**84.3**	20,221	**98.1**	308	**99.0**	1,351	**97.9**	4,453	**42.3**	3,953	**90.9**	2,571	**16.8**
	Unknown	23	**0.5**	42	**0.2**	796	**0.7**	12	**0.2**	107	**1.8**	53	**0.3**	2	**0.6**	9	**0.7**	183	**1.7**	19	**0.4**	2,915	**19.0**
Asia	Not MV	65	**5.3**	56	**0.9**	720	**3.1**	9	**0.9**	138	**3.2**	88	**1.3**	2	**0.4**	13	**1.7**	1,795	**38.0**	91	**8.1**	14,484	**87.4**
	MV	1,150	**94.6**	6,105	**99.1**	22,883	**96.9**	966	**99.1**	4,167	**96.8**	6,529	**98.6**	464	**99.6**	751	**98.3**	2,913	**61.7**	1,039	**91.9**	1,771	**10.7**
	Unknown	1	**0.1**	1	**0.0**	3	**0.0**	-	-	-	-	2	**0.0**	-	-	-	-	16	**0.3**	-	-	319	**1.9**
China	Not MV	-	-	-	-	-	-	1	**0.9**	-	-	1	**0.2**	-	-	1	**2.2**	128	**11.8**	3	**1.2**	6,321	**92.2**
	MV	109	**100.0**	420	**100.0**	751	**99.9**	109	**99.1**	604	**100.0**	456	**99.8**	40	**100.0**	45	**97.8**	960	**88.2**	246	**98.8**	520	**7.6**
	Unknown	-	-	-	-	1	**0.1**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	12	**0.2**
Cyprus*	Not MV	1	**12.5**	-	-	3	**1.3**	-	-	2	**16.7**	-	-	-	-	-	-	6	**40.0**	-	-	8	**61.5**
	MV	7	**87.5**	67	**100.0**	236	**98.7**	4	**100.0**	10	**83.3**	28	**100.0**	-	-	3	**100.0**	9	**60.0**	-	-	4	**30.8**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**7.7**
India	Not MV	-	-	1	**3.3**	1	**1.9**	-	-	-	-	-	-	-	-	-	-	1	**3.7**	-	-	88	**96.7**
	MV	5	**100.0**	29	**96.7**	52	**98.1**	1	**100.0**	15	**100.0**	18	**100.0**	1	**100.0**	-	-	26	**96.3**	2	**100.0**	2	**2.2**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	**1.1**
Israel*	Not MV	5	**6.3**	11	**1.8**	198	**7.7**	1	**0.6**	13	**13.4**	13	**2.7**	-	-	-	-	44	**18.2**	2	**2.0**	439	**86.1**
	MV	74	**93.7**	585	**98.0**	2,389	**92.3**	179	**99.4**	84	**86.6**	467	**96.9**	13	**100.0**	34	**100.0**	194	**80.2**	99	**98.0**	63	**12.4**
	Unknown	-	-	1	**0.2**	-	-	-	-	-	-	2	**0.4**	-	-	-	-	4	**1.7**	-	-	8	**1.6**
Japan	Not MV	-	-	-	-	17	**0.3**	-	-	-	-	1	**0.1**	-	-	8	**7.0**	414	**38.8**	2	**0.8**	2,375	**81.0**
	MV	179	**99.4**	1,144	**100.0**	4,951	**99.6**	162	**100.0**	806	**100.0**	1,025	**99.9**	41	**100.0**	106	**93.0**	645	**60.4**	246	**99.2**	340	**11.6**
	Unknown	1	**0.6**	-	-	1	**0.0**	-	-	-	-	-	-	-	-	-	-	8	**0.7**	-	-	218	**7.4**
Jordan*	Not MV	-	-	1	**0.4**	5	**0.7**	-	-	-	-	-	-	-	-	-	-	31	**33.0**	-	-	66	**71.0**
	MV	41	**100.0**	250	**99.6**	669	**99.3**	26	**100.0**	81	**100.0**	129	**100.0**	34	**100.0**	27	**100.0**	63	**67.0**	5	**100.0**	27	**29.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Supplementary Table 3.8. Basis of diagnosis by histology group and country, adults (15-99 years of age).

Country	Basis of diagnosis	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Korea*	Not MV	45	**12.4**	35	**2.4**	377	**6.0**	4	**3.5**	112	**9.4**	59	**2.7**	2	**1.5**	4	**1.6**	856	**68.6**	60	**19.6**	3,422	**96.0**
	MV	318	**87.6**	1,404	**97.6**	5,891	**94.0**	110	**96.5**	1,085	**90.6**	2,144	**97.3**	134	**98.5**	249	**98.4**	392	**31.4**	246	**80.4**	141	**4.0**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Kuwait*	Not MV	-	**-**	1	**4.0**	9	**8.0**	1	**25.0**	1	**5.6**	-	**-**	-	**-**	-	**-**	8	**40.0**	-	**-**	7	**77.8**
	MV	3	**100.0**	24	**96.0**	103	**92.0**	3	**75.0**	17	**94.4**	21	**100.0**	8	**100.0**	1	**100.0**	12	**60.0**	3	**100.0**	1	**11.1**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**11.1**
Malaysia	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	2	**40.0**	-	**-**	31	**96.9**
	MV	3	**100.0**	6	**100.0**	35	**100.0**	-	**-**	32	**100.0**	12	**100.0**	2	**100.0**	4	**100.0**	3	**60.0**	-	**-**	1	**3.1**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Qatar*	Not MV	-	**-**	-	**-**	3	**2.9**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	5	**25.0**	-	**-**	22	**88.0**
	MV	8	**100.0**	45	**100.0**	100	**97.1**	4	**100.0**	5	**100.0**	59	**100.0**	1	**100.0**	1	**100.0**	14	**70.0**	7	**100.0**	2	**8.0**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**5.0**	-	**-**	1	**4.0**
Singapore*	Not MV	4	**10.5**	1	**0.9**	22	**4.6**	-	**-**	2	**5.0**	2	**1.2**	-	**-**	-	**-**	18	**40.9**	8	**25.0**	41	**69.5**
	MV	34	**89.5**	106	**99.1**	452	**95.4**	42	**100.0**	38	**95.0**	167	**98.8**	1	**100.0**	27	**100.0**	26	**59.1**	24	**75.0**	18	**30.5**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Taiwan*	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	MV	134	**100.0**	1,161	**100.0**	3,412	**100.0**	97	**100.0**	636	**100.0**	1,027	**100.0**	86	**100.0**	118	**100.0**	157	**100.0**	57	**100.0**	23	**100.0**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Thailand	Not MV	-	**-**	-	**-**	7	**1.2**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	10	**13.9**	-	**-**	990	**99.3**
	MV	33	**100.0**	183	**100.0**	557	**98.8**	36	**100.0**	506	**100.0**	120	**100.0**	22	**100.0**	39	**100.0**	62	**86.1**	7	**100.0**	6	**0.6**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**0.1**
Turkey	Not MV	10	**4.7**	6	**0.9**	78	**2.3**	2	**1.0**	8	**3.1**	12	**1.4**	-	**-**	-	**-**	272	**43.5**	16	**14.2**	674	**49.1**
	MV	202	**95.3**	681	**99.1**	3,285	**97.7**	193	**99.0**	248	**96.9**	856	**98.6**	81	**100.0**	97	**100.0**	350	**56.0**	97	**85.8**	623	**45.4**
	Unknown	-	**-**	-	**-**	1	**0.0**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	3	**0.5**	-	**-**	76	**5.5**
Europe	Not MV	191	**4.1**	240	**0.9**	7,073	**5.4**	95	**2.2**	609	**5.5**	328	**1.4**	3	**0.3**	33	**1.6**	7,128	**49.5**	214	**6.2**	28,032	**82.1**
	MV	4,460	**94.7**	25,507	**98.4**	122,622	**93.6**	4,132	**97.7**	10,315	**92.8**	22,338	**97.9**	888	**99.6**	2,020	**98.0**	6,923	**48.0**	3,224	**93.2**	4,088	**12.0**
	Unknown	58	**1.2**	164	**0.6**	1,366	**1.0**	4	**0.1**	196	**1.8**	152	**0.7**	1	**0.1**	8	**0.4**	359	**2.5**	22	**0.6**	2,040	**6.0**
Austria*	Not MV	-	**-**	-	**-**	4	**0.1**	-	**-**	1	**0.2**	-	**-**	-	**-**	-	**-**	44	**24.6**	-	**-**	148	**35.1**
	MV	136	**76.0**	592	**93.4**	4,650	**94.0**	7	**87.5**	397	**89.2**	529	**89.7**	7	**100.0**	104	**96.3**	118	**65.9**	33	**89.2**	209	**49.5**
	Unknown	43	**24.0**	42	**6.6**	295	**6.0**	1	**12.5**	47	**10.6**	61	**10.3**	-	**-**	4	**3.7**	17	**9.5**	4	**10.8**	65	**15.4**
Belgium*	Not MV	-	**-**	-	**-**	171	**3.3**	2	**0.8**	-	**-**	-	**-**	-	**-**	1	**1.4**	115	**79.3**	-	**-**	353	**87.8**
	MV	241	**100.0**	1,014	**100.0**	5,061	**96.7**	234	**99.2**	44	**100.0**	887	**100.0**	59	**100.0**	71	**98.6**	30	**20.7**	232	**100.0**	49	**12.2**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Croatia*	Not MV	5	**6.8**	12	**9.8**	294	**14.0**	5	**9.4**	23	**8.4**	26	**10.4**	-	**-**	2	**5.3**	25	**14.0**	-	**-**	9	**7.6**
	MV	68	**93.2**	110	**90.2**	1,813	**86.0**	48	**90.6**	251	**91.6**	224	**89.6**	3	**100.0**	36	**94.7**	153	**86.0**	46	**100.0**	110	**92.4**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Czech Republic*	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	MV	151	**100.0**	1,474	**100.0**	4,624	**100.0**	222	**100.0**	235	**100.0**	651	**100.0**	6	**100.0**	96	**100.0**	279	**100.0**	70	**100.0**	259	**100.0**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**

Supplementary Table 3.8. Basis of diagnosis by histology group and country, adults (15-99 years of age).

Country	Basis of diagnosis	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Denmark*	Not MV	7	**6.1**	11	**2.5**	82	**2.5**	13	**13.7**	16	**4.8**	31	**4.6**	-	**-**	1	**1.8**	5	**6.3**	13	**16.3**	2,556	**75.6**
	MV	107	**93.9**	421	**97.2**	3,259	**97.5**	82	**86.3**	314	**95.2**	638	**95.4**	29	**100.0**	55	**98.2**	74	**92.5**	67	**83.8**	764	**22.6**
	Unknown	-	**-**	1	**0.2**	1	**0.0**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**1.3**	-	**-**	63	**1.9**
Estonia*	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	MV	13	**100.0**	176	**100.0**	495	**100.0**	26	**100.0**	12	**100.0**	84	**100.0**	6	**100.0**	14	**100.0**	5	**100.0**	12	**100.0**	4	**100.0**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Finland*	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	MV	137	**100.0**	341	**100.0**	2,282	**100.0**	173	**100.0**	437	**100.0**	729	**100.0**	2	**100.0**	44	**100.0**	123	**100.0**	172	**100.0**	40	**100.0**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
France	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	MV	118	**100.0**	235	**100.0**	3,401	**100.0**	83	**100.0**	153	**100.0**	1,499	**100.0**	64	**100.0**	27	**100.0**	315	**100.0**	126	**100.0**	31	**100.0**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Germany	Not MV	7	**1.9**	8	**0.3**	448	**2.6**	1	**0.3**	45	**3.3**	11	**0.6**	-	**-**	1	**0.6**	70	**16.1**	7	**3.5**	147	**33.6**
	MV	357	**97.0**	2,710	**96.1**	15,976	**93.6**	297	**99.3**	1,258	**92.0**	1,689	**96.4**	48	**100.0**	163	**97.0**	348	**80.0**	183	**92.0**	232	**53.0**
	Unknown	4	**1.1**	101	**3.6**	647	**3.8**	1	**0.3**	65	**4.8**	52	**3.0**	-	**-**	4	**2.4**	17	**3.9**	9	**4.5**	59	**13.5**
Gibraltar*	Not MV	-	**-**	1	**100.0**	5	**83.3**	-	**-**	1	**100.0**	-	**-**	-	**-**	-	**-**	2	**100.0**	-	**-**	-	**-**
	MV	-	**-**	-	**-**	1	**16.7**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Iceland*	Not MV	-	**-**	-	**-**	1	**0.6**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	5	**83.3**	-	**-**	70	**100.0**
	MV	3	**100.0**	23	**100.0**	161	**99.4**	13	**100.0**	30	**100.0**	23	**100.0**	1	**100.0**	2	**100.0**	1	**16.7**	2	**100.0**	-	**-**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Ireland*	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	MV	50	**100.0**	339	**100.0**	1,749	**99.9**	92	**100.0**	250	**99.6**	434	**100.0**	4	**100.0**	31	**100.0**	50	**100.0**	73	**100.0**	21	**33.9**
	Unknown	-	**-**	-	**-**	2	**0.1**	-	**-**	1	**0.4**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	41	**66.1**
Italy	Not MV	23	**5.8**	23	**1.2**	373	**3.8**	2	**0.8**	55	**7.9**	14	**0.9**	1	**1.0**	15	**9.5**	889	**48.3**	29	**11.8**	10,235	**96.3**
	MV	373	**94.2**	1,971	**98.8**	9,369	**96.2**	247	**99.2**	638	**92.1**	1,493	**99.1**	96	**99.0**	143	**90.5**	952	**51.7**	217	**88.2**	324	**3.0**
	Unknown	-	**-**	-	**-**	2	**0.0**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	1	**0.1**	-	**-**	71	**0.7**
Latvia*	Not MV	-	**-**	1	**0.4**	4	**0.6**	-	**-**	-	**-**	1	**1.3**	-	**-**	1	**3.7**	3	**4.5**	1	**6.3**	512	**44.8**
	MV	28	**100.0**	229	**99.6**	698	**99.4**	3	**100.0**	219	**100.0**	77	**98.7**	5	**100.0**	26	**96.3**	61	**92.4**	15	**93.8**	33	**2.9**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	2	**3.0**	-	**-**	597	**52.3**
Lithuania*	Not MV	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
	MV	42	**100.0**	204	**100.0**	1,521	**100.0**	25	**100.0**	340	**100.0**	171	**100.0**	1	**100.0**	11	**100.0**	22	**100.0**	29	**100.0**	5	**100.0**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Malta*	Not MV	-	**-**	1	**1.7**	20	**21.3**	-	**-**	3	**15.8**	-	**-**	-	**-**	-	**-**	26	**81.3**	-	**-**	74	**94.9**
	MV	6	**100.0**	58	**98.3**	74	**78.7**	7	**100.0**	16	**84.2**	8	**100.0**	1	**100.0**	-	**-**	6	**18.8**	4	**100.0**	4	**5.1**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Netherlands*	Not MV	2	**0.6**	79	**3.6**	35	**0.4**	29	**6.9**	29	**27.4**	29	**1.8**	-	**-**	-	**-**	132	**43.0**	13	**3.4**	2,732	**96.2**
	MV	330	**99.4**	2,095	**96.4**	8,483	**99.6**	393	**93.1**	77	**72.6**	1,558	**98.2**	34	**100.0**	126	**100.0**	175	**57.0**	371	**96.6**	107	**3.8**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**
Norway*	Not MV	42	**26.9**	5	**0.9**	330	**11.6**	6	**3.8**	22	**12.7**	3	**0.5**	-	**-**	-	**-**	96	**34.2**	17	**12.0**	218	**61.2**
	MV	114	**73.1**	546	**99.1**	2,504	**88.4**	151	**96.2**	151	**87.3**	571	**99.5**	3	**100.0**	34	**100.0**	185	**65.8**	125	**88.0**	136	**38.2**
	Unknown	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	-	**-**	2	**0.6**

Supplementary Table 3.8. Basis of diagnosis by histology group and country, adults (15-99 years of age).

Country	Basis of diagnosis	Ependymoma and choroid plexus tumour		Diffuse and anaplastic astrocytoma		Glioblastoma		Other specified astrocytoma		Unspecified astrocytoma		Oligodendro-glial tumour		Medullo-blastoma		Other and unspecified embryonal tumour		Unspecified glioma		Other specified neuro-epithelial tumour		Unspecified tumour	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Poland*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	563	**100.0**	3,695	**100.0**	11,406	**100.0**	325	**100.0**	1,658	**100.0**	2,856	**100.0**	263	**100.0**	286	**100.0**	1,177	**100.0**	178	**100.0**	535	**100.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Portugal*	Not MV	-	-	-	-	8	**0.2**	-	-	-	-	1	**0.1**	1	**2.5**	-	-	10	**5.5**	-	-	100	**36.1**
	MV	87	**100.0**	578	**100.0**	3,539	**99.2**	125	**100.0**	390	**98.5**	1,295	**99.7**	38	**95.0**	71	**100.0**	167	**92.3**	68	**100.0**	116	**41.9**
	Unknown	-	-	-	-	19	**0.5**	-	-	6	**1.5**	3	**0.2**	1	**2.5**	-	-	4	**2.2**	-	-	61	**22.0**
Romania	Not MV	-	-	-	-	-	-	1	**25.0**	-	-	-	-	-	-	-	-	2	**40.0**	-	-	35	**92.1**
	MV	8	**100.0**	39	**100.0**	134	**100.0**	3	**75.0**	15	**100.0**	27	**100.0**	5	**100.0**	-	-	3	**60.0**	4	**100.0**	3	**7.9**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Russian Federation	Not MV	-	-	1	**0.2**	2	**0.2**	-	-	3	**0.4**	2	**1.1**	-	-	-	-	-	-	2	**6.3**	8	**4.1**
	MV	44	**100.0**	446	**99.8**	912	**99.5**	59	**100.0**	769	**99.4**	174	**98.9**	2	**100.0**	62	**100.0**	121	**100.0**	30	**93.8**	175	**89.3**
	Unknown	-	-	-	-	3	**0.3**	-	-	2	**0.3**	-	-	-	-	-	-	-	-	-	-	13	**6.6**
Slovakia*	Not MV	-	-	-	-	-	-	-	-	-	-	2	**0.9**	-	-	-	-	-	-	-	-	820	**98.8**
	MV	97	**100.0**	716	**100.0**	1,248	**100.0**	116	**100.0**	117	**100.0**	218	**99.1**	33	**100.0**	51	**100.0**	86	**100.0**	33	**100.0**	10	**1.2**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Slovenia*	Not MV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	MV	14	**100.0**	150	**100.0**	1,015	**100.0**	51	**100.0**	4	**100.0**	161	**100.0**	16	**100.0**	16	**100.0**	43	**100.0**	16	**100.0**	8	**100.0**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spain	Not MV	5	**3.3**	6	**0.6**	112	**3.5**	3	**2.2**	3	**1.1**	-	-	-	-	-	-	302	**47.9**	8	**6.3**	287	**87.5**
	MV	147	**96.7**	1,041	**99.3**	3,091	**96.5**	135	**97.8**	264	**98.9**	484	**100.0**	54	**100.0**	69	**100.0**	328	**52.0**	120	**93.8**	29	**8.8**
	Unknown	-	-	1	**0.1**	-	-	-	-	-	-	-	-	-	-	-	-	1	**0.2**	-	-	12	**3.7**
Sweden*	Not MV	3	**1.4**	3	**0.3**	45	**1.0**	1	**0.6**	9	**1.3**	-	-	-	-	-	-	15	**6.1**	2	**1.1**	1,041	**95.2**
	MV	207	**98.6**	880	**99.7**	4,297	**99.0**	173	**99.4**	669	**98.7**	968	**100.0**	-	-	120	**100.0**	232	**93.9**	174	**98.9**	53	**4.8**
	Unknown	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Switzerland	Not MV	18	**15.1**	1	**0.2**	121	**5.6**	3	**3.4**	8	**16.3**	-	-	-	-	-	-	39	**55.7**	10	**9.5**	161	**92.0**
	MV	101	**84.9**	437	**99.8**	2,054	**94.4**	84	**96.6**	41	**83.7**	364	**100.0**	33	**100.0**	36	**100.0**	31	**44.3**	95	**90.5**	14	**8.0**
	Unknown	-	-	-	-	1	**0.0**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
United Kingdom*	Not MV	79	**7.8**	88	**1.7**	5,018	**14.7**	29	**2.9**	391	**19.2**	208	**4.4**	1	**1.3**	12	**3.6**	5,348	**71.3**	112	**13.2**	8,526	**82.0**
	MV	918	**91.1**	4,987	**97.9**	28,805	**84.2**	958	**96.9**	1,566	**77.1**	4,526	**94.9**	75	**98.7**	326	**96.4**	1,838	**24.5**	729	**85.8**	817	**7.9**
	Unknown	11	**1.1**	19	**0.4**	396	**1.2**	2	**0.2**	75	**3.7**	36	**0.8**	-	-	-	-	316	**4.2**	9	**1.1**	1,056	**10.2**
Oceania	Not MV	26	**6.8**	43	**1.8**	1,255	**8.4**	5	**2.4**	134	**15.4**	85	**3.4**	2	**4.3**	1	**0.6**	704	**65.6**	37	**15.6**	1,427	**87.6**
	MV	357	**93.2**	2,319	**98.1**	13,614	**91.4**	207	**97.6**	733	**84.3**	2,383	**96.5**	44	**95.7**	155	**99.4**	352	**32.8**	199	**84.0**	68	**4.2**
	Unknown	-	-	1	**0.0**	29	**0.2**	-	-	2	**0.2**	2	**0.1**	-	-	-	-	17	**1.6**	1	**0.4**	134	**8.2**
Australia*	Not MV	24	**7.0**	38	**2.0**	982	**7.8**	5	**2.7**	111	**13.7**	75	**3.5**	2	**4.5**	1	**0.8**	522	**61.3**	35	**15.8**	1,191	**86.3**
	MV	317	**93.0**	1,881	**98.0**	11,575	**92.0**	178	**97.3**	699	**86.1**	2,076	**96.4**	42	**95.5**	132	**99.2**	313	**36.7**	185	**83.7**	55	**4.0**
	Unknown	-	-	1	**0.1**	28	**0.2**	-	-	2	**0.2**	2	**0.1**	-	-	-	-	17	**2.0**	1	**0.5**	134	**9.7**
New Zealand*	Not MV	2	**4.8**	5	**1.1**	273	**11.8**	-	-	23	**40.4**	10	**3.2**	-	-	-	-	182	**82.4**	2	**12.5**	236	**94.8**
	MV	40	**95.2**	438	**98.9**	2,039	**88.2**	29	**100.0**	34	**59.6**	307	**96.8**	2	**100.0**	23	**100.0**	39	**17.6**	14	**87.5**	13	**5.2**
	Unknown	-	-	-	-	1	**0.0**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

MV: microscopically verified.

* Data with 100% coverage of the national population.

Supplementary Table 4.1. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with astrocytoma (broad group), by country and calendar period.

Country	Period of diagnosis	Astrocytoma (broad group)			
		NS		95% CI	
AFRICA					
Algeria	2000-2004			-	
	2005-2009	*38.2*	§	*14.4* -	*62.0*
	2010-2014			-	
AMERICA (CENTRAL AND SOUTH)					
Argentina*	2000-2004	**54.9**		48.5 -	61.3
	2005-2009	**70.9**		65.7 -	76.1
	2010-2014	**74.1**	§	68.8 -	79.5
Brazil	2000-2004	*62.9*		*47.2* -	*78.6*
	2005-2009	*22.3*		*4.4* -	*40.1*
	2010-2014			-	
Colombia	2000-2004	*58.9*	§	*42.4* -	*75.3*
	2005-2009	*42.5*	§	*24.0* -	*60.9*
	2010-2014	**55.7**	§	40.5 -	70.8
Costa Rica*	2000-2004			-	
	2005-2009	*80.1*		*56.6* -	*100.0*
	2010-2014	*74.7*		*55.8* -	*93.6*
Ecuador	2000-2004	*46.9*	§	*22.9* -	*70.9*
	2005-2009	*53.7*		*35.7* -	*71.8*
	2010-2014	*64.7*		*46.4* -	*82.9*
Puerto Rico*	2000-2004	*87.3*		*77.8* -	*96.7*
	2005-2009	**79.9**		69.6 -	90.3
	2010-2014	**79.3**		62.3 -	96.2
AMERICA (NORTH)					
Canada	2000-2004	**81.2**		74.3 -	88.1
	2005-2009	**79.3**		72.5 -	86.0
	2010-2014	**78.7**		71.8 -	85.6
United States	2000-2004	**82.6**		81.3 -	83.9
	2005-2009	**83.7**		82.5 -	85.0
	2010-2014	**82.6**		81.3 -	84.0

Supplementary Table 4.1. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with astrocytoma (broad group), by country and calendar period.

Country	Period of diagnosis	Astrocytoma (broad group)			
		NS			95% CI
ASIA					
China	2000-2004			-	
	2005-2009	*63.2*	*42.2*	-	*84.1*
	2010-2014			-	
Israel*	2000-2004	**83.9**	77.1	-	90.8
	2005-2009	**81.1**	73.9	-	88.3
	2010-2014	**87.4**	80.4	-	94.3
Japan	2000-2004	**60.6**	49.6	-	71.6
	2005-2009	**67.9**	59.2	-	76.5
	2010-2014	**73.4**	63.6	-	83.2
Jordan*	2000-2004	**72.1** §	59.9	-	84.3
	2005-2009	**74.2** §	63.2	-	85.3
	2010-2014	**64.2** §	52.0	-	76.5
Korea*	2000-2004	**52.3**	43.8	-	60.8
	2005-2009	**49.9**	41.0	-	58.8
	2010-2014	**43.5**	34.4	-	52.6
Singapore*	2000-2004	*73.9*	*56.4*	-	*91.4*
	2005-2009	*88.9*	*74.8*	-	*100.0*
	2010-2014	**69.5**	53.9	-	85.0
Taiwan*	2000-2004	**72.1**	64.9	-	79.2
	2005-2009	**65.8**	57.1	-	74.5
	2010-2014	**53.0**	43.5	-	62.5
Thailand	2000-2004	*21.7* §	*9.1*	-	*34.3*
	2005-2009	*34.9*	*21.4*	-	*48.5*
	2010-2014	**44.8** §	28.6	-	60.9
Turkey	2000-2004	*70.8*	*54.9*	-	*86.6*
	2005-2009	**75.6**	68.1	-	83.1
	2010-2014	**72.8**	65.8	-	79.8

Supplementary Table 4.1. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with astrocytoma (broad group), by country and calendar period.

Country	Period of diagnosis	Astrocytoma (broad group)	
		NS	95% CI
EUROPE			
Belarus*	2000-2004	**67.8**	57.9 - 77.6
	2005-2009	**81.6**	72.8 - 90.4
	2010-2014	**82.2**	73.8 - 90.5
Belgium*	2000-2004	*77.8*	*62.5 - 93.2*
	2005-2009	**81.0**	74.3 - 87.8
	2010-2014	**79.4**	73.1 - 85.8
Croatia*	2000-2004	*72.8*	*57.8 - 87.7*
	2005-2009	**78.4**	67.3 - 89.4
	2010-2014	**71.7**	56.2 - 87.3
Czech Republic*	2000-2004	**66.0**	54.9 - 77.1
	2005-2009	**82.9**	74.6 - 91.1
	2010-2014	**83.9**	76.3 - 91.5
Denmark*	2000-2004	**75.1**	64.7 - 85.5
	2005-2009	*89.2*	*80.3 - 98.1*
	2010-2014	**80.8**	67.1 - 94.5
Estonia*	2000-2004	*95.9*	*88.1 - 100.0*
	2005-2009	*100.0*	*76.8 - 100.0*
	2010-2014		-
Finland*	2000-2004	**84.5**	77.0 - 92.0
	2005-2009	**79.2**	70.5 - 87.9
	2010-2014	**79.7**	71.1 - 88.4
France*	2000-2004	**84.8**	81.8 - 87.8
	2005-2009	**83.7**	80.5 - 86.8
	2010-2014	**79.7**	75.4 - 83.9
Germany	2000-2004	**68.2**	56.7 - 79.7
	2005-2009	**69.3**	58.9 - 79.8
	2010-2014	**74.5**	62.4 - 86.6

Supplementary Table 4.1. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with astrocytoma (broad group), by country and calendar period.

Country	Period of diagnosis	Astrocytoma (broad group)		
		NS	95% CI	
Greece*	2000-2004		-	
	2005-2009		-	
	2010-2014	**86.4**	75.5	- 97.3
Ireland*	2000-2004	**83.7**	74.4	- 93.0
	2005-2009	**83.1**	73.7	- 92.4
	2010-2014	**88.4**	79.9	- 96.9
Italy	2000-2004	**77.3**	71.1	- 83.5
	2005-2009	**79.4**	74.2	- 84.5
	2010-2014	**77.2**	69.8	- 84.6
Latvia*	2000-2004	*78.3*	*64.2*	- *92.4*
	2005-2009		-	
	2010-2014	**80.5**	66.7	- 94.3
Lithuania*	2000-2004	*61.6*	*43.4*	- *79.9*
	2005-2009	*78.7*	*58.0*	- *99.4*
	2010-2014		-	
Netherlands*	2000-2004	**77.1**	71.0	- 83.1
	2005-2009	**78.7**	72.7	- 84.7
	2010-2014	**80.7**	75.1	- 86.4
Norway*	2000-2004	**88.0**	80.4	- 95.6
	2005-2009	**68.4**	57.2	- 79.5
	2010-2014	**77.4**	67.4	- 87.4
Poland*	2000-2004	**67.5**	61.6	- 73.4
	2005-2009	**66.2**	60.0	- 72.4
	2010-2014	**64.3**	56.7	- 71.9
Portugal*	2000-2004	**68.9**	58.5	- 79.3
	2005-2009	**75.3**	66.1	- 84.4
	2010-2014	**66.7**	43.2	- 90.2
Russian Federation*	2000-2004	*82.4*	*69.9*	- *95.0*
	2005-2009	*65.4*	*50.9*	- *79.9*
	2010-2014	**65.6**	51.1	- 80.2

Supplementary Table 4.1. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Children (0-14 years) diagnosed with astrocytoma (broad group), by country and calendar period.

Country	Period of diagnosis	Astrocytoma (broad group)	
		NS	95% CI
Slovakia*	2000-2004	**83.5**	74.5 - 92.5
	2005-2009	**80.9**	71.4 - 90.5
	2010-2014	**84.8**	70.1 - 99.5
Slovenia*	2000-2004	*80.0*	*60.5 - 99.5*
	2005-2009	*81.8*	*66.1 - 97.5*
	2010-2014		-
Spain	2000-2004	**86.7**	80.1 - 93.3
	2005-2009	**76.5**	68.6 - 84.3
	2010-2014	**77.7**	66.3 - 89.2
Sweden*	2000-2004	**85.5**	78.2 - 92.9
	2005-2009	**82.7**	75.3 - 90.0
	2010-2014	**82.9**	76.0 - 89.8
Switzerland*	2000-2004	**86.1**	78.9 - 93.3
	2005-2009	**86.4**	77.7 - 95.0
	2010-2014	**83.6**	75.2 - 91.9
United Kingdom*	2000-2004	**77.8**	74.6 - 81.0
	2005-2009	**77.6**	74.4 - 80.8
	2010-2014	**78.9**	75.8 - 82.0
OCEANIA			
Australia*	2000-2004	**60.6**	52.5 - 68.8
	2005-2009	**64.2**	56.7 - 71.7
	2010-2014	**65.5**	57.4 - 73.5
New Zealand*	2000-2004	*67.8*	*51.6 - 83.9*
	2005-2009	*31.3*	*10.0 - 52.5*
	2010-2014	*46.4*	*17.1 - 75.6*

* Countries with 100% coverage of the national population. § Survival estimates considered less reliable because the proportion of patients lost to follow-up or censored alive prior to five years, and/or the proportion of diagnoses based on a death certificate or autopsy, and/or the proportion of patients registered with incomplete dates, was 15% or more. Survival estimates in italics are not age-standardised.

Supplementary Table 4.2. Age-standardised 10-year net survival (%) with 95% confidence interval (CI), 2000-2004. Children (0-14 years) diagnosed with low-grade astrocytoma (WHO grade I and II) or medulloblastoma, by country.

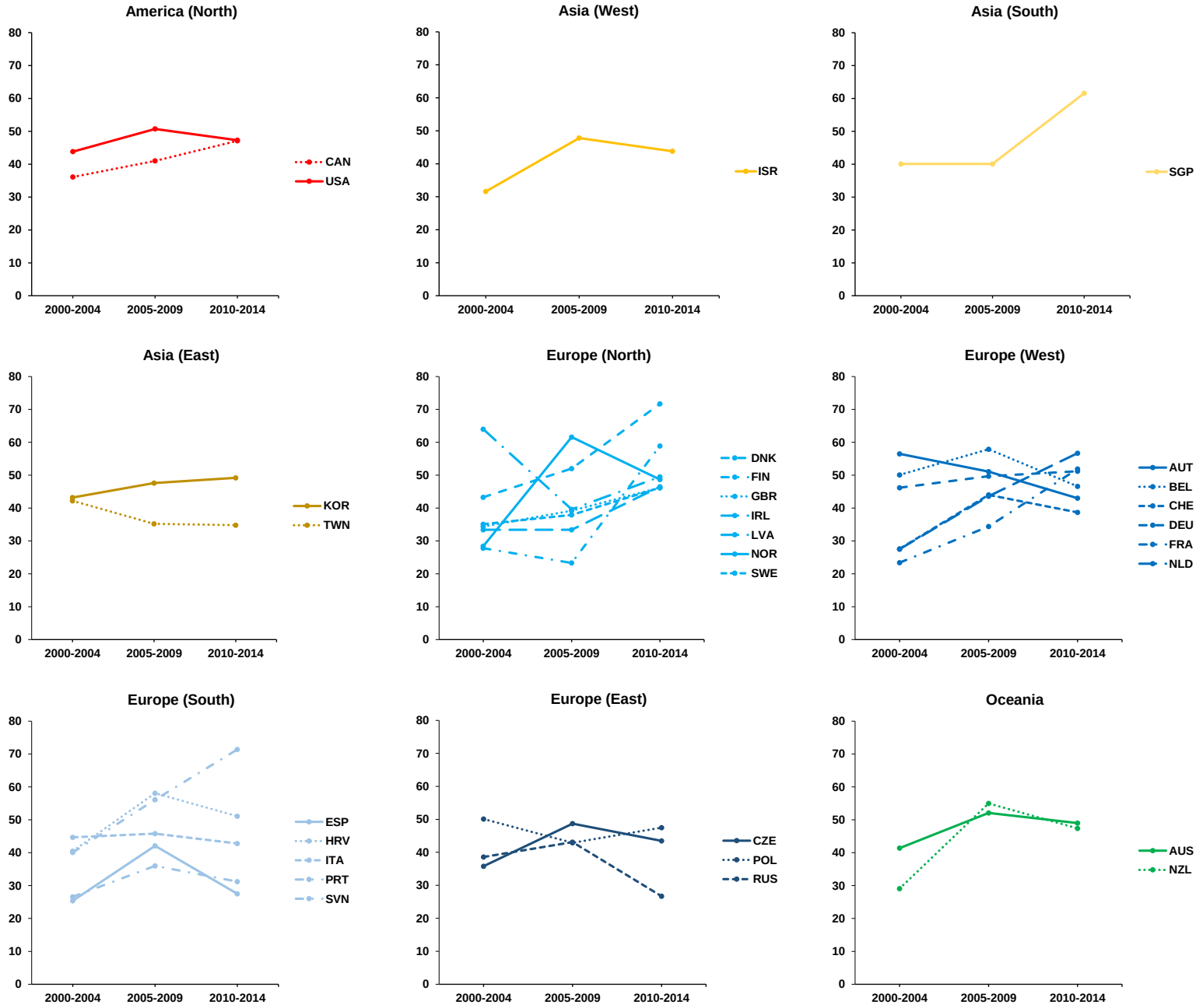
Country	Period of diagnosis	Astrocytoma, WHO grade I and II		Medulloblastoma	
		NS	95% CI	NS	95% CI
AMERICA (CENTRAL AND SOUTH)					
Argentina*	2000-2004	**79.6**	71.2 - 87.9	**44.1**	37.6 - 50.6
Brazil	2000-2004	*92.9*	*78.9 - 100.0*	*50.3*	*28.0 - 72.6*
Colombia	2000-2004	*60.9 §*	*32.0 - 89.7*		-
Ecuador	2000-2004		-	*46.4 §*	*21.3 - 71.5*
Puerto Rico*	2000-2004	*94.9*	*87.9 - 100.0*	*58.4*	*32.0 - 84.8*
AMERICA (NORTH)					
Canada	2000-2004	**92.4**	87.2 - 97.6	*65.8*	*50.4 - 81.3*
United States	2000-2004	**93.9**	92.9 - 94.8	**71.4**	68.2 - 74.5
ASIA					
Israel*	2000-2004	*93.5*	*88.3 - 98.6*	**63.9**	53.1 - 74.8
Japan	2000-2004	*80.9*	*61.9 - 99.8*	*64.4*	*48.5 - 80.4*
Jordan*	2000-2004	*74.3 §*	*45.1 - 100.0*	*75.5 §*	*61.6 - 89.3*
Korea*	2000-2004	*93.8*	*82.3 - 100.0*	**56.5**	49.4 - 63.5
Singapore*	2000-2004		-	*40.0*	*12.2 - 67.9*
Taiwan*	2000-2004	**88.9**	80.5 - 97.3	**46.2**	35.2 - 57.3
Thailand	2000-2004		-	*31.8 §*	*11.9 - 51.7*
EUROPE					
Belarus*	2000-2004	**75.0**	64.9 - 85.1	*57.4*	*43.6 - 71.1*
Belgium*	2000-2004	*85.8*	*71.2 - 100.0*		-
Croatia*	2000-2004	*72.8*	*47.8 - 97.8*	*56.1*	*37.2 - 75.1*
Czech Republic*	2000-2004	*84.7*	*73.5 - 95.9*	*42.9*	*18.5 - 67.4*
Denmark*	2000-2004	*93.1*	*85.6 - 100.0*	*62.2*	*44.9 - 79.4*
Estonia*	2000-2004	*100.0*	*100.0 - 100.0*		-
Finland*	2000-2004	*97.1*	*93.0 - 100.0*	*68.8*	*47.0 - 90.7*
France*	2000-2004	**87.3**	84.3 - 90.2	**55.6**	50.1 - 61.1
Germany	2000-2004	*82.5*	*69.9 - 95.1*	*64.6*	*48.1 - 81.1*
Ireland*	2000-2004	*87.1*	*77.5 - 96.8*		-
Italy	2000-2004	**94.8**	90.6 - 98.9	**59.8**	49.6 - 69.9

Supplementary Table 4.2. Age-standardised 10-year net survival (%) with 95% confidence interval (CI), 2000-2004. Children (0-14 years) diagnosed with low-grade astrocytoma (WHO grade I and II) or medulloblastoma, by country.

Country	Period of diagnosis	Astrocytoma, WHO grade I and II		Medulloblastoma	
		NS	95% CI	NS	95% CI
Lithuania*	2000-2004		-	*35.9*	*12.3 - 59.5*
Netherlands*	2000-2004	**90.1**	85.2 - 95.1	**48.5**	37.9 - 59.1
Norway*	2000-2004	**92.3**	85.2 - 99.4	*66.8*	*45.7 - 87.8*
Poland*	2000-2004	**84.3**	76.9 - 91.8	**53.7**	46.0 - 61.3
Portugal*	2000-2004	*84.2*	*73.6 - 94.9*	*54.0*	*38.6 - 69.3*
Slovakia*	2000-2004	**84.3**	75.2 - 93.5	*34.9*	*16.2 - 53.7*
Slovenia*	2000-2004	*81.8*	*60.2 - 100.0*		-
Spain	2000-2004	**90.0**	82.6 - 97.4	*50.1*	*35.2 - 65.0*
Sweden*	2000-2004	*95.6*	*90.6 - 100.0*	*74.1*	*57.9 - 90.3*
Switzerland*	2000-2004	**95.1**	89.6 - 100.0	*60.4*	*44.0 - 76.9*
United Kingdom*	2000-2004	**92.9**	90.4 - 95.4	**59.3**	53.4 - 65.2
OCEANIA					
Australia*	2000-2004	**84.0**	75.0 - 92.9	**68.6**	58.8 - 78.4
New Zealand*	2000-2004	*80.1*	*63.0 - 97.1*	*70.7*	*49.8 - 91.7*

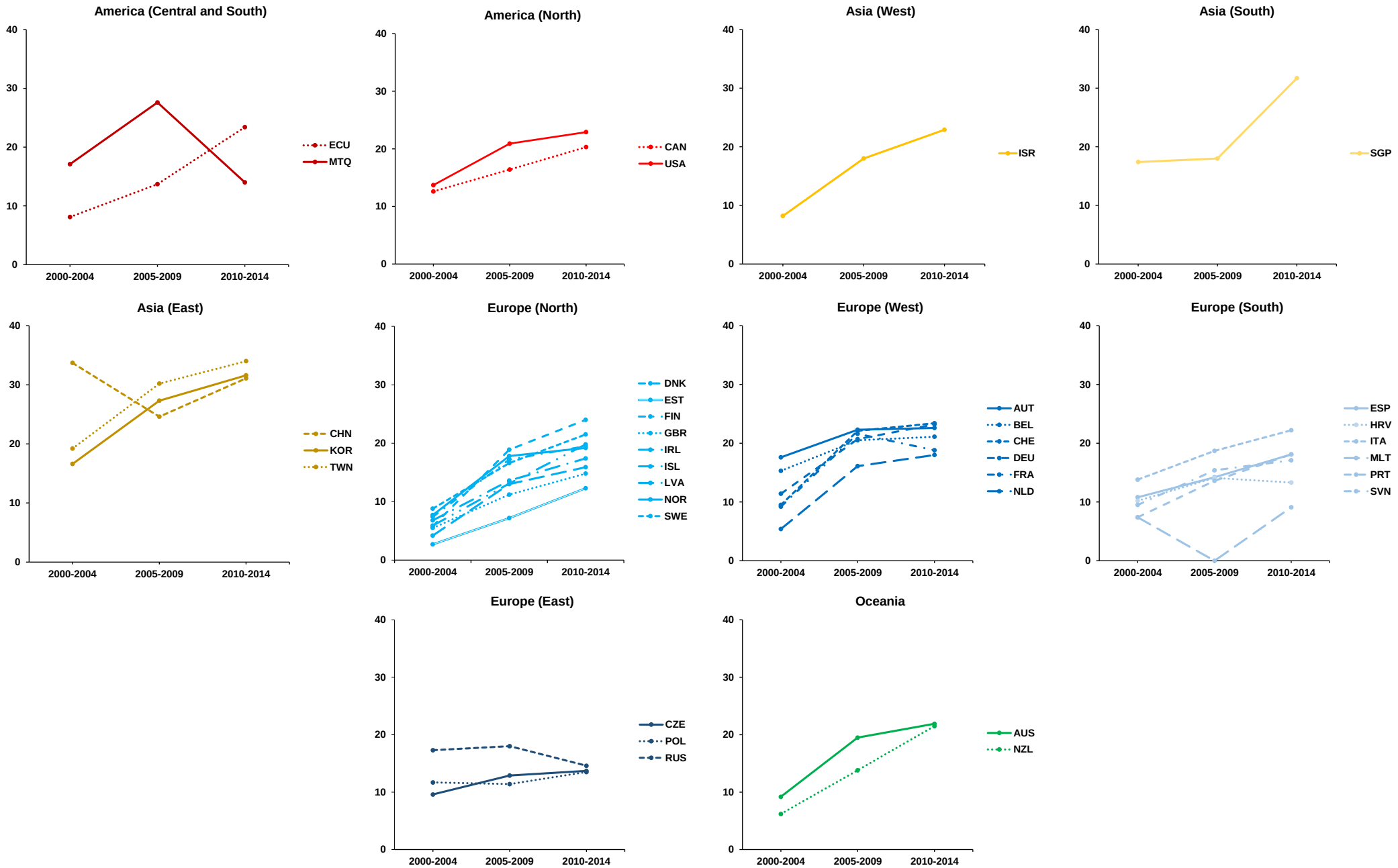
* Countries with 100% coverage of the national population. § Survival estimates considered less reliable because the proportion of patients lost to follow-up or censored alive prior to five years, and/or the proportion of diagnoses based on a death certificate or autopsy, and/or the proportion of patients registered with incomplete dates, was 15% or more. Survival estimates in italics are not age-standardised.

Supplementary Figure 5.1. Trends in age-specific two-year net survival (%) from glioblastoma, 2000-2014, by world region. Adults (15-39 years of age).



Countries were included if age-specific survival estimates were available for patients diagnosed during 2000-2004, 2005-2009 and 2010-2014. X-axis: period of diagnosis; Y-axis: age-specific two-year net survival (%). Australia=AUS; Austria=AUT; Belgium=BEL; Canada=CAN; Croatia=HRV; Czech Republic=CZE; Denmark=DNK; Finland=FIN; France=FRA; Germany=DEU; Ireland=IRL; Israel=ISR; Italy=ITA; Latvia=LVA; Netherlands=NLD; New Zealand=NZL; Norway=NOR; Poland=POL; Portugal=PRT; Russia=RUS; Singapore=SGP; Slovenia=SVN; South Korea=KOR; Spain=ESP; Sweden=SWE; Switzerland=CHE; Taiwan=TWN; UK=GBR; USA=USA.

Supplementary Figure 5.2. Trends in age-specific two-year net survival (%) from glioblastoma, 2000-2014, by world region. Adults (40-70 years of age).



Countries were included if age-specific survival estimates were available for patients diagnosed during 2000-2004, 2005-2009 and 2010-2014. X-axis: period of diagnosis; Y-axis: age-specific two-year net survival (%). Australia=AUS; Austria=AUT; Belgium=BEL; Canada=CAN; China=CHN; Croatia=HRV; Czech Republic=CZE; Denmark=DNK; Ecuador=ECU; Estonia=EST; Finland=FIN; France=FRA; Germany=DEU; Ireland=IRL; Israel=ISR; Italy=ITA; Latvia=LVA; Malta=MLT; Martinique=MTQ; Netherlands=NLD; New Zealand=NZL; Norway=NOR; Poland=POL; Portugal=PRT; Russia=RUS; Singapore=SGP; Slovakia=SVK; Slovenia=SVN; South Korea=KOR; Spain=ESP; Sweden=SWE; Switzerland=CHE; Taiwan=TWN; UK=GBR; USA=USA.

Supplementary Table 5.1. Age-specific two-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Glioblastoma (15-39 years)		Glioblastoma (40-70 years)		Glioblastoma (71-99 years)	
		NS	95% CI	NS	95% CI	NS	95% CI
AFRICA							
Algeria	2000-2004		-		-		-
	2005-2009		-	53.4 §	31.4 - 75.3		-
	2010-2014	36.0 §	12.4 - 59.5	12.1 §	1.9 - 22.4		-
Mauritius*	2000-2004		-		-		-
	2005-2009		-		-		-
	2010-2014		-	30.4	4.5 - 56.3		-
Nigeria (Ibadan)	2000-2004		-		-		-
	2005-2009		-		-		-
	2010-2014		-	0.4 §	0.0 - 1.0		-
AMERICA (CENTRAL AND SOUTH)							
Argentina	2000-2004		-	14.8 §	0.6 - 28.9		-
	2005-2009	63.3 §	42.3 - 84.3	16.2 §	9.5 - 23.0	11.2 §	0.0 - 22.3
	2010-2014	16.7 §	0.0 - 33.6	20.4 §	12.4 - 28.3	10.4 §	0.0 - 21.4
Brazil	2000-2004	41.8 §	15.7 - 67.9	31.9 §	22.7 - 41.0	0.1 §	0.0 - 0.2
	2005-2009	17.1 §	1.1 - 33.1	20.7 §	14.5 - 27.0	10.3 §	1.4 - 19.3
	2010-2014	41.7 §	13.5 - 69.8	21.6 §	12.9 - 30.2	14.8 §	0.3 - 29.3
Chile	2000-2004		-		-		-
	2005-2009		-	0.0	0.0 - 0.0		-
	2010-2014		-	0.0	0.0 - 0.0		-
Colombia	2000-2004	27.4	3.6 - 51.3	5.4	0.6 - 10.2	0.1	0.0 - 0.2
	2005-2009	39.5	15.2 - 63.8	25.4	17.2 - 33.6	3.5	0.0 - 8.9
	2010-2014	46.8 §	18.8 - 74.8	23.6 §	13.8 - 33.4	17.2 §	3.4 - 30.9
Costa Rica*	2000-2004	30.8 §	7.6 - 54.0	19.0 §	7.5 - 30.4	17.9 §	0.0 - 37.7
	2005-2009	35.8 §	12.3 - 59.4	11.4 §	4.6 - 18.2		-
	2010-2014	50.1 §	28.6 - 71.7	19.2 §	11.6 - 26.7	0.2 §	0.0 - 0.5
Ecuador	2000-2004		-	8.1	0.0 - 17.7	0.2	0.0 - 0.6
	2005-2009	11.2	0.0 - 24.0	13.7	4.6 - 22.7	0.1	0.0 - 0.5
	2010-2014	42.5	16.6 - 68.5	23.4	12.4 - 34.3	0.1	0.0 - 0.4
Guadeloupe	2000-2004		-		-		-
	2005-2009		-		-		-
	2010-2014		-	5.4 §	0.0 - 13.5		-
Martinique*	2000-2004		-	17.1	0.0 - 35.7		-
	2005-2009		-	27.6	9.7 - 45.5	21.0	0.0 - 43.6
	2010-2014		-	14.0	0.6 - 27.5		-

Supplementary Table 5.1. Age-specific two-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Glioblastoma (15-39 years)			Glioblastoma (40-70 years)			Glioblastoma (71-99 years)		
		NS	95% CI		NS	95% CI		NS	95% CI	
Puerto Rico*	2000-2004	41.9 §	15.8 -	68.1	11.9 §	6.8 -	16.9	9.0 §	1.8 -	16.1
	2005-2009	30.8	7.6 -	54.0	18.4	13.4 -	23.5	9.5	3.7 -	15.4
	2010-2014		-		23.3	14.2 -	32.3	9.1	0.3 -	17.9
AMERICA (NORTH)										
Canada	2000-2004	36.1	28.4 -	43.7	12.6	11.1 -	14.0	2.1	1.2 -	3.1
	2005-2009	41.0	33.2 -	48.7	16.4	14.9 -	17.9	3.8	2.7 -	5.0
	2010-2014	47.1	38.2 -	56.0	20.3	18.4 -	22.2	4.8	3.3 -	6.3
United States	2000-2004	43.8	41.6 -	46.0	13.7	13.3 -	14.2	2.7	2.5 -	3.0
	2005-2009	50.7	48.4 -	52.9	20.9	20.4 -	21.4	5.4	5.0 -	5.8
	2010-2014	47.3	44.6 -	50.1	22.9	22.2 -	23.5	7.2	6.6 -	7.7
ASIA										
China	2000-2004		-		33.7	17.1 -	50.4		-	
	2005-2009	43.7	28.4 -	58.9	24.6	18.8 -	30.3	10.1	1.4 -	18.7
	2010-2014	48.3	30.6 -	66.0	31.1	25.1 -	37.0	11.6	3.1 -	20.0
Cyprus*	2000-2004		-			-			-	
	2005-2009		-		27.2 §	17.4 -	37.0	5.0 §	0.0 -	12.7
	2010-2014		-		27.5 §	16.7 -	38.4	7.3 §	0.0 -	17.0
India	2000-2004		-			-			-	
	2005-2009		-			-			-	
	2010-2014		-		0.5	0.0 -	1.6		-	
Israel*	2000-2004	31.6	19.8 -	43.5	8.2	5.8 -	10.5	1.3	0.0 -	2.6
	2005-2009	47.8	33.3 -	62.3	18.0	15.0 -	21.1	5.2	2.5 -	7.8
	2010-2014	43.8	29.3 -	58.3	22.9	19.0 -	26.8	6.7	3.3 -	10.2
Japan	2000-2004	38.8 §	29.8 -	47.8	18.0 §	15.1 -	20.9	7.1 §	4.0 -	10.2
	2005-2009	44.6 §	37.7 -	51.5	28.4 §	25.9 -	30.9	11.0 §	8.7 -	13.3
	2010-2014	34.3 §	23.8 -	44.8	33.2 §	29.6 -	36.9	13.3 §	9.8 -	16.8
Jordan*	2000-2004	67.8 §	52.3 -	83.3	34.9 §	25.8 -	44.1	34.8 §	8.3 -	61.2
	2005-2009	50.1 §	37.2 -	63.1	35.7 §	28.5 -	43.0	69.5 §	44.6 -	94.4
	2010-2014	34.4 §	17.6 -	51.1	18.8 §	12.7 -	24.9	19.8 §	4.1 -	35.5
Korea*	2000-2004	43.2	37.4 -	49.0	16.6	14.2 -	18.9	7.9	2.8 -	13.1
	2005-2009	47.6	41.8 -	53.4	27.3	25.0 -	29.6	11.1	7.5 -	14.8
	2010-2014	49.2	42.4 -	55.9	31.6	29.1 -	34.1	14.0	10.7 -	17.3
Kuwait*	2000-2004		-		22.8 §	6.3 -	39.2		-	
	2005-2009		-		15.5	4.0 -	27.0		-	
	2010-2014		-		41.8	25.4 -	58.1		-	

Supplementary Table 5.1. Age-specific two-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Glioblastoma (15-39 years)		Glioblastoma (40-70 years)		Glioblastoma (71-99 years)	
		NS	95% CI	NS	95% CI	NS	95% CI
Malaysia (Penang)	2000-2004		-		-		-
	2005-2009		-		-		-
	2010-2014		-	16.1	0.0 - 35.6		-
Qatar*	2000-2004		-		-		-
	2005-2009	100.0 §	100.0 - 100.0	14.2 §	0.0 - 29.9		-
	2010-2014	80.9 §	58.1 - 100.0	44.2 §	16.4 - 72.1		-
Singapore*	2000-2004	40.1	19.5 - 60.7	17.4	8.6 - 26.1	0.0	0.0 - 0.2
	2005-2009	40.1	12.2 - 68.0	18.0	11.1 - 24.9	13.8	0.6 - 27.0
	2010-2014	61.6	39.8 - 83.5	31.7	23.3 - 40.1	2.5	0.0 - 6.3
Taiwan*	2000-2004	42.2	34.2 - 50.2	19.2	16.0 - 22.5	8.0	4.3 - 11.8
	2005-2009	35.2	27.0 - 43.3	30.2	26.7 - 33.7	10.8	7.1 - 14.6
	2010-2014	34.8	25.0 - 44.5	34.0	30.4 - 37.7	17.8	12.8 - 22.8
Thailand	2000-2004	30.6 §	12.7 - 48.4	6.8 §	0.1 - 13.4	0.3 §	0.0 - 0.9
	2005-2009	33.7	18.0 - 49.5	8.0	3.4 - 12.6	8.2	0.0 - 20.4
	2010-2014	30.5	14.7 - 46.4	15.7	9.5 - 21.9	14.0	1.4 - 26.5
Turkey	2000-2004	25.2 §	3.9 - 46.4	9.8 §	3.8 - 15.8	11.4 §	0.0 - 24.4
	2005-2009	44.0	36.0 - 52.0	18.6	16.2 - 20.9	5.6	2.1 - 9.0
	2010-2014	50.8	43.2 - 58.5	23.5	21.1 - 25.9	7.6	4.1 - 11.1
EUROPE							
Austria*	2000-2004	56.5	47.2 - 65.7	17.6	15.1 - 20.1	4.1	2.1 - 6.0
	2005-2009	51.1	41.1 - 61.2	22.3	19.8 - 24.8	8.1	5.7 - 10.4
	2010-2014	43.0	31.4 - 54.6	22.6	19.7 - 25.6	7.4	4.9 - 10.0
Belgium*	2000-2004	50.1	29.0 - 71.2	15.3	10.7 - 20.0	2.5	0.0 - 5.0
	2005-2009	57.9	49.6 - 66.2	20.5	18.4 - 22.7	5.7	3.9 - 7.4
	2010-2014	46.6	34.4 - 58.9	21.1	18.7 - 23.4	6.9	5.0 - 8.9
Croatia*	2000-2004	40.5	26.0 - 55.1	10.2	7.4 - 13.1	5.8	1.5 - 10.2
	2005-2009	58.1	44.7 - 71.5	14.1	11.1 - 17.1	5.8	2.4 - 9.2
	2010-2014	51.1	35.7 - 66.4	13.3	9.7 - 16.9	5.1	1.7 - 8.6
Czech Republic*	2000-2004	35.8	25.6 - 45.9	9.6	7.8 - 11.5	0.8	0.0 - 1.8
	2005-2009	48.7	37.1 - 60.2	12.9	10.9 - 14.8	2.7	0.9 - 4.5
	2010-2014	43.5	32.1 - 54.9	13.7	11.5 - 15.9	2.9	0.8 - 5.1
Denmark*	2000-2004	43.3	30.0 - 56.6	5.8	4.0 - 7.6	0.0	0.0 - 0.0
	2005-2009	52.0	38.7 - 65.3	18.9	16.2 - 21.6	5.4	2.6 - 8.2
	2010-2014	71.7	57.4 - 86.0	24.0	20.7 - 27.2	6.8	3.6 - 10.0
Estonia*	2000-2004	63.9	36.9 - 90.8	2.7	0.3 - 5.2	0.2	0.0 - 0.6
	2005-2009	27.4	3.6 - 51.2	7.2	2.8 - 11.6	0.1	0.0 - 0.2
	2010-2014		-	12.3	5.3 - 19.3	6.6	0.0 - 14.5

Supplementary Table 5.1. Age-specific two-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Glioblastoma (15-39 years)		Glioblastoma (40-70 years)		Glioblastoma (71-99 years)	
		NS	95% CI	NS	95% CI	NS	95% CI
Finland*	2000-2004	27.8	13.6 - 42.0	7.4	5.0 - 9.8	1.6	0.0 - 3.5
	2005-2009	23.3	8.0 - 38.6	17.2	14.0 - 20.3	3.7	0.9 - 6.5
	2010-2014	58.9	37.1 - 80.8	19.5	15.9 - 23.1	4.0	1.2 - 6.9
France	2000-2004	23.4	11.1 - 35.7	9.2	7.2 - 11.2	2.5	0.7 - 4.3
	2005-2009	34.4	23.0 - 45.9	21.6	19.3 - 24.0	10.8	8.0 - 13.6
	2010-2014	51.9	33.5 - 70.3	18.8	14.2 - 23.3	9.5	4.1 - 15.0
Germany	2000-2004	46.2	20.7 - 71.7	11.4	6.7 - 16.2	4.7	0.0 - 9.6
	2005-2009	49.7	41.7 - 57.7	20.7	19.0 - 22.4	6.4	5.0 - 7.9
	2010-2014	51.2	40.1 - 62.3	23.2	20.9 - 25.5	7.5	5.7 - 9.3
Iceland*	2000-2004		-	5.9	0.0 - 12.9	8.7	0.0 - 21.6
	2005-2009		-	13.1	3.9 - 22.4	9.1	0.0 - 22.3
	2010-2014		-	19.8	6.7 - 32.9	23.6	0.7 - 46.5
Ireland*	2000-2004	33.4	17.1 - 49.7	4.2	2.2 - 6.1	1.2	0.0 - 3.1
	2005-2009	33.4	18.4 - 48.4	13.0	10.1 - 16.0	1.9	0.0 - 4.3
	2010-2014	46.5	28.3 - 64.6	15.9	12.1 - 19.6	7.3	2.7 - 11.8
Italy	2000-2004	44.7	36.4 - 53.0	13.8	12.3 - 15.3	3.1	1.9 - 4.4
	2005-2009	45.8	38.6 - 52.9	18.7	17.4 - 20.1	7.2	5.7 - 8.7
	2010-2014	42.8	30.4 - 55.2	22.2	19.7 - 24.7	6.0	3.8 - 8.2
Latvia*	2000-2004	64.0	37.1 - 91.0	6.8	1.8 - 11.8	0.0	0.0 - 0.1
	2005-2009	39.6	21.9 - 57.2	13.6	9.0 - 18.3	5.5	0.0 - 11.2
	2010-2014	49.5	23.9 - 75.1	17.4	11.4 - 23.4	3.7	0.0 - 8.4
Lithuania*	2000-2004	30.7	16.2 - 45.3	5.6	3.2 - 8.0	0.0	0.0 - 0.0
	2005-2009	44.0	27.1 - 60.8	14.2	10.9 - 17.5	0.7	0.0 - 1.9
	2010-2014	53.6 §	29.4 - 77.8	12.6 §	8.7 - 16.6	4.4 §	0.4 - 8.3
Malta*	2000-2004		-	7.4	0.0 - 16.0		-
	2005-2009		-	0.0	0.0 - 0.1		-
	2010-2014		-	9.1	0.0 - 19.4	0.5	0.0 - 1.7
Netherlands*	2000-2004	27.5	20.3 - 34.7	5.4	4.3 - 6.5	1.3	0.2 - 2.4
	2005-2009	43.6	36.8 - 50.4	16.1	14.5 - 17.6	2.3	1.1 - 3.4
	2010-2014	56.7	48.2 - 65.1	18.0	16.2 - 19.8	4.8	3.0 - 6.7
Norway*	2000-2004	28.4	13.3 - 43.5	7.7	5.4 - 9.9	0.0	0.0 - 0.0
	2005-2009	61.6	46.8 - 76.4	17.8	14.8 - 20.8	2.1	0.5 - 3.7
	2010-2014	48.7	34.9 - 62.4	19.2	15.8 - 22.6	8.1	4.7 - 11.5
Poland*	2000-2004	50.1	41.4 - 58.9	11.7	9.9 - 13.6	4.6	1.9 - 7.4
	2005-2009	42.9	36.8 - 49.0	11.4	10.3 - 12.6	2.6	1.3 - 3.9
	2010-2014	47.5	40.5 - 54.5	13.5	12.1 - 14.9	3.4	2.0 - 4.8

Supplementary Table 5.1. Age-specific two-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Glioblastoma (15-39 years)		Glioblastoma (40-70 years)		Glioblastoma (71-99 years)	
		NS	95% CI	NS	95% CI	NS	95% CI
Portugal*	2000-2004	26.6	14.5 - 38.7	7.4	5.4 - 9.4	2.3	0.4 - 4.1
	2005-2009	36.0	24.4 - 47.6	13.6	11.5 - 15.8	4.3	2.3 - 6.4
	2010-2014	31.2	15.0 - 47.4	18.1	14.9 - 21.3	6.2	3.2 - 9.2
Romania (Cluj)	2000-2004		-		-		-
	2005-2009		-	18.3 §	7.3 - 29.4	29.7 §	6.7 - 52.7
	2010-2014		-	11.4 §	3.2 - 19.6	7.6 §	0.0 - 18.9
Russian Federation	2000-2004	38.6	22.5 - 54.7	17.3	10.1 - 24.4		-
	2005-2009	43.1	27.6 - 58.7	18.0	13.0 - 23.0	7.0	0.0 - 17.5
	2010-2014	26.7	10.4 - 42.9	14.6	10.3 - 19.0	0.0	0.0 - 0.2
Slovakia*	2000-2004	32.3 §	16.5 - 48.1	11.3 §	7.9 - 14.8	4.6 §	0.0 - 9.4
	2005-2009	41.5	26.7 - 56.3	9.9	7.2 - 12.7	2.4	0.0 - 4.9
	2010-2014	40.1	16.6 - 63.6	10.5	5.0 - 16.1	0.1	0.0 - 0.2
Slovenia*	2000-2004	40.1	12.2 - 68.0	9.5	5.8 - 13.1	2.3	0.0 - 6.0
	2005-2009	56.1	37.1 - 75.0	15.4	11.0 - 19.8	2.5	0.0 - 5.6
	2010-2014	71.4	45.2 - 97.5	17.1	12.0 - 22.2	3.3	0.0 - 7.1
Spain	2000-2004	25.4	15.5 - 35.4	10.8	8.5 - 13.0	2.3	0.4 - 4.3
	2005-2009	42.1	28.6 - 55.5	14.2	11.9 - 16.5	4.6	2.3 - 7.0
	2010-2014	27.5	12.0 - 43.0	18.1	14.9 - 21.3	4.8	2.0 - 7.5
Sweden*	2000-2004	35.1	23.0 - 47.3	8.8	6.9 - 10.7	2.8	0.3 - 5.3
	2005-2009	37.9	26.5 - 49.4	16.6	14.5 - 18.8	3.5	1.4 - 5.7
	2010-2014	46.2	31.8 - 60.6	21.5	18.9 - 24.2	5.7	3.2 - 8.1
Switzerland	2000-2004	27.6	12.1 - 43.2	9.5	6.5 - 12.5	3.3	0.6 - 6.0
	2005-2009	44.0	27.6 - 60.3	22.1	18.5 - 25.7	3.8	1.2 - 6.4
	2010-2014	38.7	18.8 - 58.7	23.4	19.1 - 27.6	4.7	1.7 - 7.6
United Kingdom*	2000-2004	34.4	30.4 - 38.3	5.5	4.9 - 6.0	0.9	0.5 - 1.4
	2005-2009	39.2	35.2 - 43.1	11.2	10.5 - 11.9	1.2	0.8 - 1.6
	2010-2014	46.2	41.5 - 50.8	14.8	13.9 - 15.7	1.8	1.3 - 2.3
OCEANIA							
Australia*	2000-2004	41.4	34.3 - 48.5	9.2	8.0 - 10.3	1.7	0.9 - 2.5
	2005-2009	52.1	45.6 - 58.5	19.5	18.0 - 21.0	5.9	4.7 - 7.2
	2010-2014	49.0	41.1 - 57.0	21.9	20.0 - 23.8	5.9	4.4 - 7.4
New Zealand*	2000-2004	29.1	13.6 - 44.5	6.2	4.0 - 8.4	0.7	0.0 - 1.7
	2005-2009	55.0	41.5 - 68.5	13.8	10.7 - 16.8	4.1	1.4 - 6.7
	2010-2014	47.4	31.3 - 63.4	21.5	17.8 - 25.3	8.3	4.4 - 12.3

* Countries with 100% coverage of the national population. § Survival estimates considered less reliable because the proportion of patients lost to follow-up or censored alive prior to five years, or the proportion of diagnoses based on a death certificate or autopsy, or the proportion of patients registered with incomplete dates, was 15% or more.

Supplementary Table 5.2. Age-specific five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Age at diagnosis of glioblastoma					
		15-39 years		40-70 years		71-99 years	
		NS	95% CI	NS	95% CI	NS	95% CI
AFRICA							
Algeria	2000-2004		-		-		-
	2005-2009		-	48.7 §	26.6 - 70.8		-
	2010-2014	3.0 §	0.0 - 8.4	13.9 §	3.6 - 24.2		-
Mauritius*	2000-2004		-		-		-
	2005-2009		-		-		-
	2010-2014		-	0.2	0.0 - 0.5		-
Nigeria	2000-2004		-		-		-
	2005-2009		-		-		-
	2010-2014		-	0.4 §	0.0 - 1.0		-
AMERICA (CENTRAL AND SOUTH)							
Argentina	2000-2004		-	9.9 §	0.0 - 21.3		-
	2005-2009	37.0 §	16.3 - 57.8	7.4 §	2.6 - 12.1	4.5 §	0.0 - 11.4
	2010-2014	15.4 §	0.7 - 30.0	8.7 §	3.1 - 14.4	4.8 §	0.0 - 12.3
Brazil	2000-2004	25.2 §	2.9 - 47.5	20.5 §	12.4 - 28.7	0.1 §	0.0 - 0.2
	2005-2009	11.5 §	0.0 - 24.6	11.2 §	6.3 - 16.1	11.9 §	1.6 - 22.2
	2010-2014	37.3 §	14.0 - 60.6	12.5 §	6.4 - 18.6	14.3 §	1.1 - 27.6
Chile	2000-2004		-		-		-
	2005-2009		-	0.0	0.0 - 0.0		-
	2010-2014		-	0.0	0.0 - 0.0		-
Colombia	2000-2004	18.3	0.0 - 38.3	2.7	0.0 - 6.0	0.1	0.0 - 0.2
	2005-2009	23.9	2.9 - 44.9	9.0	3.6 - 14.5	0.1	0.0 - 0.5
	2010-2014	18.8 §	0.0 - 38.6	4.3 §	0.6 - 8.0	0.2 §	0.0 - 0.7
Costa Rica*	2000-2004	15.4 §	0.0 - 32.6	16.7 §	5.8 - 27.5	17.9 §	0.0 - 37.7
	2005-2009	28.7 §	6.7 - 50.6	6.4 §	1.3 - 11.6		-
	2010-2014	29.8 §	10.3 - 49.2	9.8 §	4.4 - 15.2	5.7 §	0.0 - 14.0
Ecuador	2000-2004		-	8.1	0.0 - 17.7	0.2	0.0 - 0.6
	2005-2009	0.0	0.0 - 0.2	2.0	0.0 - 5.0	0.1	0.0 - 0.5
	2010-2014	0.1	0.0 - 0.5	6.7	0.5 - 13.0	7.6	0.0 - 18.5
Guadeloupe	2000-2004		-		-		-
	2005-2009		-		-		-
	2010-2014		-	0.1 §	0.0 - 0.5		-

Supplementary Table 5.2. Age-specific five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Age at diagnosis of glioblastoma					
		15-39 years		40-70 years		71-99 years	
		NS	95% CI	NS	95% CI	NS	95% CI
Martinique*	2000-2004		-	9.1	0.0 - 22.7		-
	2005-2009		-	0.0	0.0 - 0.0	11.8	0.0 - 29.0
	2010-2014		-	3.7	0.0 - 9.6		-
Puerto Rico*	2000-2004	25.4 §	2.9 - 47.8	6.2 §	2.4 - 10.0	8.3 §	1.0 - 15.6
	2005-2009	0.0	0.0 - 0.0	10.7	6.6 - 14.8	2.3	0.0 - 5.0
	2010-2014		-	10.9	4.7 - 17.1	0.2	0.0 - 0.5
AMERICA (NORTH)							
Canada	2000-2004	19.4	13.1 - 25.7	5.6	4.6 - 6.7	2.0	1.0 - 2.9
	2005-2009	26.7	19.8 - 33.7	6.1	5.1 - 7.0	2.3	1.3 - 3.2
	2010-2014	31.4	24.4 - 38.4	7.1	6.1 - 8.2	1.8	1.0 - 2.6
United States	2000-2004	24.2	22.3 - 26.1	4.8	4.5 - 5.1	1.3	1.1 - 1.5
	2005-2009	27.2	25.2 - 29.1	6.8	6.5 - 7.1	1.8	1.6 - 2.1
	2010-2014	25.8	23.8 - 27.8	7.2	6.8 - 7.5	2.1	1.8 - 2.4
ASIA							
China	2000-2004		-	17.1	4.1 - 30.1		-
	2005-2009	28.3	14.5 - 42.1	12.7	8.2 - 17.2	10.1	1.4 - 18.7
	2010-2014	34.5	18.5 - 50.6	13.8	9.0 - 18.6	10.7	1.7 - 19.7
Cyprus*	2000-2004		-		-		-
	2005-2009		-	6.7 §	1.4 - 12.1	5.0 §	0.0 - 12.7
	2010-2014		-	10.9 §	4.1 - 17.8	0.4 §	0.0 - 1.3
India	2000-2004		-		-		-
	2005-2009		-		-		-
	2010-2014		-	0.6	0.0 - 2.0		-
Israel*	2000-2004	17.6	8.0 - 27.2	3.2	1.7 - 4.7	0.0	0.0 - 0.0
	2005-2009	16.0	5.6 - 26.4	6.5	4.6 - 8.5	1.0	0.0 - 2.2
	2010-2014	10.5	2.2 - 18.8	6.7	4.5 - 8.9	1.5	0.0 - 3.3
Japan	2000-2004	19.9 §	12.5 - 27.2	5.7 §	4.0 - 7.5	2.1 §	0.3 - 3.8
	2005-2009	18.5 §	12.7 - 24.3	9.5 §	7.7 - 11.2	2.2 §	1.1 - 3.4
	2010-2014	17.5 §	11.4 - 23.6	11.1 §	9.0 - 13.2	2.7 §	1.3 - 4.1
Jordan*	2000-2004	50.3 §	33.7 - 66.8	32.3 §	23.2 - 41.4	35.5 §	8.5 - 62.5
	2005-2009	37.5 §	24.9 - 50.1	29.5 §	22.4 - 36.5	69.5 §	44.6 - 94.4
	2010-2014	22.9 §	11.6 - 34.3	12.5 §	7.9 - 17.0	50.5 §	21.6 - 79.3

Supplementary Table 5.2. Age-specific five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Age at diagnosis of glioblastoma					
		15-39 years		40-70 years		71-99 years	
		NS	95% CI	NS	95% CI	NS	95% CI
Korea*	2000-2004	26.6	21.5 - 31.8	5.7	4.2 - 7.2	2.1	0.0 - 4.8
	2005-2009	24.9	19.9 - 30.0	9.8	8.2 - 11.3	3.9	1.6 - 6.3
	2010-2014	25.8	20.8 - 30.8	11.6	10.0 - 13.2	3.5	1.6 - 5.4
Kuwait*	2000-2004		-	13.6 §	0.5 - 26.8		-
	2005-2009		-	9.2	0.1 - 18.3		-
	2010-2014		-	32.2	14.0 - 50.3		-
Malaysia	2000-2004		-		-		-
	2005-2009		-		-		-
	2010-2014		-	0.2	0.0 - 0.8		-
Qatar*	2000-2004		-		-		-
	2005-2009	37.6 §	0.0 - 78.8	7.2 §	0.0 - 17.9		-
	2010-2014	40.5 §	0.0 - 81.8	11.9 §	0.0 - 28.0		-
Singapore*	2000-2004	15.1	0.8 - 29.5	5.9	0.6 - 11.2	0.0	0.0 - 0.2
	2005-2009	20.1	0.0 - 41.6	5.4	1.4 - 9.4	5.3	0.0 - 13.5
	2010-2014	50.5	27.9 - 73.2	9.4	3.8 - 15.0	2.4	0.0 - 6.2
Taiwan*	2000-2004	20.8	14.2 - 27.4	5.4	3.5 - 7.3	2.4	0.3 - 4.6
	2005-2009	19.2	12.5 - 25.9	11.0	8.6 - 13.4	2.7	0.6 - 4.8
	2010-2014	20.1	13.4 - 26.8	12.7	10.3 - 15.1	2.6	0.4 - 4.7
Thailand	2000-2004	17.6 §	3.1 - 32.1	2.3 §	0.0 - 5.8	0.3 §	0.0 - 0.9
	2005-2009	15.4	3.7 - 27.2	4.3	0.8 - 7.7	0.4	0.0 - 1.4
	2010-2014	11.5	2.5 - 20.5	4.9	1.5 - 8.3	15.7	1.5 - 29.8
Turkey	2000-2004	8.4 §	0.0 - 20.6	4.4 §	0.1 - 8.6	6.6 §	0.0 - 16.4
	2005-2009	20.7	14.2 - 27.2	6.0	4.5 - 7.4	2.0	0.0 - 4.0
	2010-2014	24.5	17.4 - 31.6	7.4	5.8 - 9.0	3.7	1.3 - 6.2
EUROPE							
Austria*	2000-2004	30.1	21.6 - 38.7	7.7	5.9 - 9.5	2.7	1.0 - 4.4
	2005-2009	31.0	21.7 - 40.2	6.8	5.3 - 8.3	2.8	1.3 - 4.2
	2010-2014	24.8	16.2 - 33.4	6.0	4.5 - 7.4	2.8	1.2 - 4.3
Belgium*	2000-2004	25.1	7.2 - 43.0	6.5	3.3 - 9.7	0.9	0.0 - 2.4
	2005-2009	32.4	24.5 - 40.3	5.9	4.7 - 7.2	1.2	0.3 - 2.0
	2010-2014	27.0	19.0 - 35.0	5.5	4.3 - 6.7	1.1	0.3 - 1.9

Supplementary Table 5.2. Age-specific five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Age at diagnosis of glioblastoma					
		15-39 years		40-70 years		71-99 years	
		NS	95% CI	NS	95% CI	NS	95% CI
Croatia*	2000-2004	26.3	13.3 - 39.3	5.4	3.2 - 7.6	3.7	0.0 - 7.8
	2005-2009	26.1	14.2 - 38.0	6.4	4.3 - 8.6	3.1	0.5 - 5.6
	2010-2014	19.2	9.3 - 29.1	4.9	3.1 - 6.7	3.0	0.5 - 5.4
Czech Republic*	2000-2004	19.1	10.9 - 27.4	2.7	1.7 - 3.7	0.4	0.0 - 1.1
	2005-2009	34.4	23.4 - 45.4	3.1	2.1 - 4.1	1.8	0.2 - 3.4
	2010-2014	29.2	19.8 - 38.7	3.7	2.6 - 4.8	1.7	0.2 - 3.2
Denmark*	2000-2004	19.7	9.1 - 30.3	1.0	0.2 - 1.7	0.0	0.0 - 0.0
	2005-2009	23.1	12.0 - 34.3	3.3	2.0 - 4.5	0.9	0.0 - 2.1
	2010-2014	26.9	14.2 - 39.6	3.7	2.4 - 5.0	1.5	0.0 - 3.2
Estonia*	2000-2004	36.7	10.3 - 63.0	0.0	0.0 - 0.0	0.2	0.0 - 0.6
	2005-2009	18.3	0.0 - 38.1	5.0	1.3 - 8.7	0.1	0.0 - 0.2
	2010-2014		-	11.4	3.4 - 19.4	0.0	0.0 - 0.1
Finland*	2000-2004	11.2	1.5 - 20.8	1.4	0.3 - 2.4	1.0	0.0 - 2.6
	2005-2009	7.8	0.0 - 16.8	3.2	1.7 - 4.6	0.8	0.0 - 2.0
	2010-2014	17.1	0.1 - 34.0	3.1	1.7 - 4.6	1.1	0.0 - 2.5
France	2000-2004	9.4	1.2 - 17.6	2.0	1.0 - 2.9	0.7	0.0 - 1.6
	2005-2009	12.2	3.7 - 20.6	4.3	2.9 - 5.6	2.2	0.7 - 3.6
	2010-2014	12.8	0.0 - 30.8	6.2	3.1 - 9.4	3.1	0.0 - 7.0
Germany	2000-2004	30.9	7.7 - 54.1	8.7	4.4 - 13.0	4.7	0.0 - 9.6
	2005-2009	26.3	19.2 - 33.4	7.2	6.1 - 8.3	4.8	3.4 - 6.3
	2010-2014	29.9	21.7 - 38.1	7.6	6.4 - 8.8	5.2	3.8 - 6.6
Iceland*	2000-2004		-	0.0	0.0 - 0.0	0.6	0.0 - 2.1
	2005-2009		-	4.4	0.0 - 9.7	0.6	0.0 - 2.0
	2010-2014		-	7.8	0.1 - 15.6	0.3	0.0 - 1.0
Ireland*	2000-2004	26.8	11.5 - 42.0	2.1	0.7 - 3.5	0.0	0.0 - 0.1
	2005-2009	13.9	3.2 - 24.7	2.9	1.4 - 4.3	0.0	0.0 - 0.1
	2010-2014	13.7	0.6 - 26.9	3.4	1.7 - 5.1	0.0	0.0 - 0.1
Italy	2000-2004	22.4	15.4 - 29.4	3.2	2.4 - 4.0	0.6	0.1 - 1.2
	2005-2009	22.8	16.7 - 28.8	4.6	3.9 - 5.4	1.5	0.7 - 2.2
	2010-2014	24.5	16.0 - 32.9	5.6	4.5 - 6.8	1.5	0.5 - 2.5

Supplementary Table 5.2. Age-specific five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Age at diagnosis of glioblastoma					
		15-39 years		40-70 years		71-99 years	
		NS	95% CI	NS	95% CI	NS	95% CI
Latvia*	2000-2004	46.4	18.5 - 74.2	3.7	0.0 - 7.4	0.0	0.0 - 0.1
	2005-2009	32.6	15.7 - 49.6	6.2	2.9 - 9.5	5.5	0.0 - 11.2
	2010-2014	33.4	13.1 - 53.6	7.1	3.5 - 10.6	2.4	0.0 - 5.9
Lithuania*	2000-2004	11.1	1.5 - 20.8	0.6	0.0 - 1.3	0.0	0.0 - 0.0
	2005-2009	12.6	1.8 - 23.4	3.6	1.9 - 5.4	0.0	0.0 - 0.1
	2010-2014	18.4 §	0.0 - 37.9	4.1 §	1.7 - 6.5	0.0 §	0.0 - 0.1
Malta*	2000-2004		-	4.0	0.0 - 10.0		-
	2005-2009		-	0.0	0.0 - 0.1		-
	2010-2014		-	4.9	0.0 - 11.7	13.9	0.0 - 32.9
Netherlands*	2000-2004	13.4	7.9 - 18.9	1.9	1.3 - 2.6	0.3	0.0 - 0.7
	2005-2009	22.9	17.1 - 28.6	4.3	3.4 - 5.2	0.5	0.0 - 1.0
	2010-2014	25.4	19.0 - 31.8	4.3	3.4 - 5.2	1.1	0.1 - 2.2
Norway*	2000-2004	9.5	0.1 - 18.8	1.6	0.5 - 2.6	0.0	0.0 - 0.0
	2005-2009	18.0	6.6 - 29.4	4.4	2.8 - 6.1	0.4	0.0 - 1.0
	2010-2014	15.8	5.7 - 25.9	4.3	2.7 - 5.9	0.8	0.0 - 1.9
Poland*	2000-2004	22.7	15.4 - 30.0	4.6	3.4 - 5.8	1.7	0.0 - 3.4
	2005-2009	18.9	14.1 - 23.8	3.8	3.1 - 4.5	2.0	0.8 - 3.1
	2010-2014	19.5	14.7 - 24.3	4.1	3.4 - 4.9	1.8	0.7 - 2.9
Portugal*	2000-2004	8.2	1.0 - 15.4	2.3	1.2 - 3.5	1.0	0.0 - 2.3
	2005-2009	10.0	2.8 - 17.1	3.5	2.4 - 4.7	1.6	0.3 - 2.9
	2010-2014	7.8	0.0 - 19.2	3.5	1.0 - 6.0	0.0	0.0 - 0.0
Romania (Cluj)	2000-2004		-		-		-
	2005-2009		-	7.3 §	0.1 - 14.5	0.7 §	0.0 - 2.4
	2010-2014		-	5.2 §	0.0 - 11.0	9.2 §	0.0 - 22.8
Russian Federation	2000-2004	16.3	4.2 - 28.4	12.5	5.8 - 19.2		-
	2005-2009	26.5	12.5 - 40.6	8.7	4.9 - 12.4	7.0	0.0 - 17.5
	2010-2014	15.8	5.7 - 25.9	7.8	4.7 - 10.9	0.0	0.0 - 0.2
Slovakia*	2000-2004	9.7 §	0.2 - 19.2	3.9 §	1.8 - 6.0	0.1 §	0.0 - 0.2
	2005-2009	14.7	4.3 - 25.1	2.5	1.1 - 3.9	0.0	0.0 - 0.0
	2010-2014	22.7	0.0 - 48.9	6.5	1.3 - 11.7	0.8	0.0 - 2.3

Supplementary Table 5.2. Age-specific five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with glioblastoma, by country and calendar period.

Country	Period of diagnosis	Age at diagnosis of glioblastoma					
		15-39 years		40-70 years		71-99 years	
		NS	95% CI	NS	95% CI	NS	95% CI
Slovenia*	2000-2004	20.1	0.0 - 41.6	2.5	0.6 - 4.4	0.4	0.0 - 1.3
	2005-2009	36.1	17.9 - 54.3	4.4	1.9 - 7.0	0.0	0.0 - 0.1
	2010-2014	61.7	33.9 - 89.4	4.2	1.6 - 6.9	0.0	0.0 - 0.0
Spain	2000-2004	9.9	3.2 - 16.6	2.6	1.5 - 3.7	0.9	0.0 - 2.1
	2005-2009	16.1	6.2 - 25.9	4.3	3.0 - 5.7	1.7	0.2 - 3.1
	2010-2014	23.1	7.9 - 38.2	5.6	3.1 - 8.1	2.0	0.0 - 4.6
Sweden*	2000-2004	15.0	5.8 - 24.1	2.6	1.5 - 3.6	0.0	0.0 - 0.1
	2005-2009	13.7	5.7 - 21.7	3.6	2.5 - 4.7	0.9	0.0 - 2.1
	2010-2014	17.8	7.9 - 27.6	4.5	3.2 - 5.8	1.3	0.0 - 2.6
Switzerland	2000-2004	12.1	0.8 - 23.5	1.5	0.3 - 2.7	0.7	0.0 - 1.7
	2005-2009	21.3	7.5 - 35.0	4.3	2.5 - 6.1	0.6	0.0 - 1.4
	2010-2014	26.5	10.6 - 42.5	4.1	2.4 - 5.8	1.1	0.0 - 2.3
United Kingdom*	2000-2004	12.9	10.1 - 15.7	1.3	1.0 - 1.6	0.2	0.0 - 0.5
	2005-2009	18.7	15.5 - 21.9	3.0	2.6 - 3.3	0.5	0.2 - 0.8
	2010-2014	19.8	16.5 - 23.1	3.7	3.2 - 4.1	0.6	0.3 - 0.9
OCEANIA							
Australia*	2000-2004	22.4	16.4 - 28.4	3.5	2.8 - 4.3	1.2	0.5 - 1.8
	2005-2009	34.3	28.2 - 40.5	6.7	5.7 - 7.7	2.5	1.6 - 3.4
	2010-2014	35.4	28.8 - 42.0	7.6	6.5 - 8.7	2.1	1.3 - 2.9
New Zealand*	2000-2004	16.2	3.9 - 28.4	2.3	0.9 - 3.7	0.7	0.0 - 1.7
	2005-2009	29.5	17.3 - 41.8	6.7	4.5 - 9.0	1.1	0.0 - 2.5
	2010-2014	27.8	16.1 - 39.5	8.3	5.9 - 10.7	3.6	0.4 - 6.9

* Countries with 100% coverage of the national population. § Survival estimates considered less reliable because the proportion of patients lost to follow-up or censored alive prior to five years, or the proportion of diagnoses based on a death certificate or autopsy, or the proportion of patients registered with incomplete dates, was 15% or more.

Supplementary Table 5.3. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with diffuse astrocytoma or anaplastic astrocytoma, by country and calendar period.

Country	Period of diagnosis	Diffuse astrocytoma			Anaplastic astrocytoma		
		NS	95% CI		NS	95% CI	
AFRICA							
Algeria	2000-2004		-			-	
	2005-2009		-			-	
	2010-2014		-			-	
Mauritius*	2000-2004		-			-	
	2005-2009		-			-	
	2010-2014		-			-	
Nigeria (Ibadan)	2000-2004		-			-	
	2005-2009		-			-	
	2010-2014		-			-	
AMERICA (CENTRAL AND SOUTH)							
Argentina	2000-2004		-		*25.6 §*	*2.7*	*48.6*
	2005-2009	*38.9 §*	*20.2*	*57.5*	*31.1 §*	*16.1*	*46.2*
	2010-2014	*67.7 §*	*43.0*	*92.4*	*35.1 §*	*16.5*	*53.8*
Brazil	2000-2004	*29.5 §*	*7.0*	*52.1*	*34.0 §*	*18.7*	*49.4*
	2005-2009	*50.7 §*	*30.1*	*71.3*	*51.0 §*	*32.3*	*69.8*
	2010-2014	*66.7 §*	*42.8*	*90.6*	*36.3 §*	*13.7*	*58.9*
Chile	2000-2004		-			-	
	2005-2009		-			-	
	2010-2014		-			-	
Colombia	2000-2004		-		*36.8*	*19.9*	*53.7*
	2005-2009	*61.3*	*34.3*	*88.4*	*23.0*	*8.8*	*37.2*
	2010-2014	*57.8 §*	*32.2*	*83.4*	*17.2 §*	*1.4*	*33.0*
Costa Rica*	2000-2004	*81.9 §*	*60.2*	*100.0*	*10.1 §*	*0.0*	*24.8*
	2005-2009	*39.0 §*	*14.0*	*64.0*		-	
	2010-2014		-		*29.1 §*	*5.3*	*52.9*
Ecuador	2000-2004	*28.9*	*6.7*	*51.0*	*6.8*	*0.0*	*17.0*
	2005-2009	*50.6*	*31.7*	*69.6*	*12.7*	*2.8*	*22.6*
	2010-2014	*56.8*	*39.2*	*74.5*	*20.1*	*7.0*	*33.3*
Guadeloupe	2000-2004		-			-	
	2005-2009		-			-	
	2010-2014		-			-	
Martinique*	2000-2004		-			-	
	2005-2009		-			-	
	2010-2014		-			-	

Supplementary Table 5.3. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with diffuse astrocytoma or anaplastic astrocytoma, by country and calendar period.

Country	Period of diagnosis	Diffuse astrocytoma		Anaplastic astrocytoma	
		NS	95% CI	NS	95% CI
Puerto Rico*	2000-2004	*49.4 §*	*34.0 - 64.7*	*39.2 §*	*24.7 - 53.7*
	2005-2009	*68.8*	*51.6 - 86.1*	*32.5*	*18.7 - 46.3*
	2010-2014		-	*24.4*	*3.9 - 45.0*
AMERICA (NORTH)					
Canada	2000-2004	**28.8**	23.3 - 34.2	**19.4**	15.4 - 23.4
	2005-2009	**44.9**	37.2 - 52.5	**23.2**	19.3 - 27.1
	2010-2014	*60.9*	*50.3 - 71.5*	**27.6**	23.0 - 32.1
United States	2000-2004	**35.5**	34.0 - 37.1	**22.0**	21.0 - 22.9
	2005-2009	**38.1**	36.5 - 39.8	**25.6**	24.5 - 26.6
	2010-2014	**38.3**	36.6 - 40.0	**26.7**	25.5 - 27.8
ASIA					
China	2000-2004	*64.5*	*37.4 - 91.6*	*37.9*	*24.6 - 51.3*
	2005-2009	*49.8*	*32.2 - 67.5*	**28.5**	21.7 - 35.2
	2010-2014	*45.0*	*29.6 - 60.3*	**27.3**	19.7 - 34.9
Cyprus*	2000-2004		-		-
	2005-2009	*54.1 §*	*28.0 - 80.3*	*15.6 §*	*0.5 - 30.7*
	2010-2014		-	*20.6 §*	*3.4 - 37.8*
India	2000-2004		-		-
	2005-2009		-		-
	2010-2014		-	*19.9*	*0.0 - 46.1*
Israel*	2000-2004	*49.2*	*37.6 - 60.7*	**19.8**	14.2 - 25.3
	2005-2009	*50.8*	*40.2 - 61.4*	**24.4**	19.0 - 29.8
	2010-2014	**40.4**	30.4 - 50.5	**24.6**	18.3 - 31.0
Japan	2000-2004	*52.7 §*	*39.6 - 65.9*	**24.0** §	18.6 - 29.4
	2005-2009	**48.8** §	40.1 - 57.6	**25.2** §	21.1 - 29.3
	2010-2014	**54.3** §	41.8 - 66.7	**25.5** §	21.2 - 29.8
Jordan*	2000-2004	*91.2 §*	*79.1 - 100.0*	*68.4 §*	*57.2 - 79.7*
	2005-2009	*64.9 §*	*48.3 - 81.4*	*43.1 §*	*28.2 - 58.0*
	2010-2014	*60.3 §*	*43.2 - 77.4*	**33.5** §	18.9 - 48.2
Korea*	2000-2004	*51.7*	*41.9 - 61.5*	**16.2**	13.1 - 19.3
	2005-2009	*58.6*	*48.4 - 68.8*	**18.9**	15.4 - 22.4
	2010-2014	**47.4**	36.7 - 58.2	**20.1**	16.7 - 23.6
Kuwait*	2000-2004		-		-
	2005-2009		-		-
	2010-2014		-		-

Supplementary Table 5.3. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with diffuse astrocytoma or anaplastic astrocytoma, by country and calendar period.

Country	Period of diagnosis	Diffuse astrocytoma		Anaplastic astrocytoma	
		NS	95% CI	NS	95% CI
Malaysia	2000-2004		-		-
	2005-2009		-		-
	2010-2014		-		-
Qatar*	2000-2004		-		-
	2005-2009		-	*51.5 §*	*9.6 - 93.5*
	2010-2014	*100.0 §*	*100.0 - 100.0*		-
Singapore*	2000-2004		-	*34.2*	*15.7 - 52.7*
	2005-2009	*50.2*	*25.1 - 75.3*	*28.0*	*12.2 - 43.7*
	2010-2014		-	*26.1*	*10.5 - 41.7*
Taiwan*	2000-2004	*45.0*	*35.8 - 54.1*	**18.5**	13.8 - 23.1
	2005-2009	**43.1**	34.6 - 51.7	**15.1**	11.5 - 18.6
	2010-2014	**43.2**	33.1 - 53.3	**17.2**	13.5 - 20.9
Thailand (Penang)	2000-2004	*10.1 §*	*0.0 - 24.4*	*20.7 §*	*5.8 - 35.5*
	2005-2009	*54.8*	*36.4 - 73.3*	*12.8*	*1.9 - 23.8*
	2010-2014	*49.7*	*31.8 - 67.6*	*15.2*	*3.6 - 26.7*
Turkey	2000-2004	*51.9 §*	*31.8 - 72.1*	*18.3 §*	*8.5 - 28.2*
	2005-2009	**30.5**	23.7 - 37.3	**13.5**	9.5 - 17.4
	2010-2014	**28.6**	22.1 - 35.0	*28.1*	*20.5 - 35.7*
EUROPE					
Austria*	2000-2004	*71.5*	*60.4 - 82.6*	**30.3**	23.6 - 37.1
	2005-2009	**56.2**	47.3 - 65.2	**32.1**	26.3 - 37.9
	2010-2014	**49.1**	39.8 - 58.4	**28.4**	22.2 - 34.6
Belgium*	2000-2004	*50.9*	*34.2 - 67.7*	*25.0*	*15.0 - 34.9*
	2005-2009	**50.7**	44.2 - 57.2	**22.1**	17.5 - 26.8
	2010-2014	**54.8**	46.9 - 62.7	**23.9**	18.4 - 29.5
Croatia*	2000-2004		-	*43.5*	*29.0 - 57.9*
	2005-2009		-	*37.7*	*22.4 - 53.1*
	2010-2014		-	*34.4*	*17.3 - 51.5*
Czech Republic*	2000-2004	**36.2**	31.5 - 40.8	**14.4**	10.6 - 18.2
	2005-2009	**38.7**	32.9 - 44.5	**17.8**	13.9 - 21.7
	2010-2014	**42.9**	37.5 - 48.4	**17.6**	13.1 - 22.1
Denmark*	2000-2004	*23.4*	*2.4 - 44.3*	**11.3**	6.2 - 16.4
	2005-2009		-	**20.7**	15.5 - 26.0
	2010-2014		-	**21.8**	16.3 - 27.3

Supplementary Table 5.3. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with diffuse astrocytoma or anaplastic astrocytoma, by country and calendar period.

Country	Period of diagnosis	Diffuse astrocytoma		Anaplastic astrocytoma	
		NS	95% CI	NS	95% CI
Estonia*	2000-2004	*40.1*	*25.0 - 55.2*	*16.4*	*3.8 - 28.9*
	2005-2009	*56.7*	*40.1 - 73.4*	*19.6*	*6.9 - 32.2*
	2010-2014	*57.4*	*35.4 - 79.4*	*29.8*	*7.3 - 52.3*
Finland*	2000-2004	*36.8*	*10.4 - 63.2*	**12.6**	7.7 - 17.5
	2005-2009	*45.9*	*18.2 - 73.6*	**18.8**	12.6 - 24.9
	2010-2014		-	**19.4**	13.1 - 25.7
France	2000-2004	*42.8*	*29.2 - 56.5*	**17.3**	9.5 - 25.1
	2005-2009	*38.1*	*19.5 - 56.7*	**19.0**	12.5 - 25.5
	2010-2014		-	*36.6*	*15.2 - 58.0*
Germany	2000-2004		-		-
	2005-2009	**47.3**	40.4 - 54.2	**33.5**	29.4 - 37.7
	2010-2014	**47.7**	40.2 - 55.1	**32.8**	28.4 - 37.2
Iceland*	2000-2004		-		-
	2005-2009		-		-
	2010-2014		-		-
Ireland*	2000-2004	*34.7*	*18.5 - 50.8*	**15.4**	9.0 - 21.9
	2005-2009	*56.7*	*33.1 - 80.3*	**14.1**	8.7 - 19.4
	2010-2014	*68.4*	*48.9 - 87.9*	*17.5*	*8.1 - 26.8*
Italy	2000-2004	**36.7**	31.9 - 41.5	**14.7**	11.4 - 18.1
	2005-2009	**37.2**	32.8 - 41.7	**16.7**	13.7 - 19.7
	2010-2014	**48.8**	38.6 - 58.9	**17.8**	13.7 - 21.8
Latvia*	2000-2004	*35.4*	*18.8 - 52.1*	*33.2*	*20.7 - 45.7*
	2005-2009	*59.7*	*36.8 - 82.6*	*42.0*	*31.0 - 53.1*
	2010-2014		-	*46.7*	*33.3 - 60.0*
Lithuania*	2000-2004	*83.8*	*61.8 - 100.0*	*29.2*	*15.5 - 42.9*
	2005-2009	*64.6*	*48.2 - 81.0*	*47.5*	*31.5 - 63.5*
	2010-2014	*68.4* §	*52.8 - 84.0*	*45.7* §	*25.6 - 65.9*
Malta*	2000-2004		-		-
	2005-2009		-	*18.5*	*0.0 - 38.7*
	2010-2014		-	*13.5*	*0.0 - 27.2*
Netherlands*	2000-2004	**31.9**	27.2 - 36.7	**13.5**	10.8 - 16.3
	2005-2009	**39.3**	34.2 - 44.4	**22.0**	18.3 - 25.7
	2010-2014	**44.7**	39.2 - 50.1	**20.2**	16.5 - 24.0
Norway*	2000-2004	*52.1*	*40.3 - 63.8*	**24.4**	14.9 - 33.9
	2005-2009	*47.2*	*35.9 - 58.6*	**21.3**	15.7 - 27.0
	2010-2014	**43.3**	33.1 - 53.4	**28.2**	21.9 - 34.6

Supplementary Table 5.3. Age-standardised five-year net survival (%) with 95% confidence interval (CI), 2000-2014. Adults (15-99 years) diagnosed with diffuse astrocytoma or anaplastic astrocytoma, by country and calendar period.

Country	Period of diagnosis	Diffuse astrocytoma		Anaplastic astrocytoma	
		NS	95% CI	NS	95% CI
Poland*	2000-2004	**37.1**	31.4 - 42.8	**15.3**	12.6 - 18.0
	2005-2009	**35.7**	32.1 - 39.3	**17.2**	14.9 - 19.5
	2010-2014	**40.4**	36.4 - 44.5	**16.5**	14.2 - 18.8
Portugal*	2000-2004	**41.9**	33.5 - 50.3	**8.8**	3.9 - 13.8
	2005-2009	*49.1*	*38.9 - 59.4*	**18.0**	13.0 - 23.1
	2010-2014	**39.4**	30.4 - 48.4	*11.3*	*0.0 - 22.6*
Romania (Cluj)	2000-2004		-		-
	2005-2009		-	*11.9* §	*0.0 - 25.5*
	2010-2014		-	*29.5* §	*6.4 - 52.6*
Russian Federation	2000-2004		-	*30.5*	*15.7 - 45.3*
	2005-2009	*42.5*	*27.7 - 57.3*	**23.0**	17.6 - 28.4
	2010-2014	*45.4*	*28.6 - 62.1*	**20.2**	15.8 - 24.7
Slovakia*	2000-2004	**28.2** §	23.0 - 33.4	**14.3** §	9.9 - 18.8
	2005-2009	**33.7**	28.0 - 39.3	**14.9**	10.3 - 19.5
	2010-2014	**38.4**	27.0 - 49.7	*18.7*	*5.2 - 32.3*
Slovenia*	2000-2004		-	*32.3*	*17.2 - 47.4*
	2005-2009	*51.6*	*27.7 - 75.5*	*48.4*	*34.1 - 62.7*
	2010-2014	*56.4*	*32.2 - 80.6*	*20.3*	*7.3 - 33.3*
Spain	2000-2004	**31.6**	26.1 - 37.1	**13.7**	9.6 - 17.9
	2005-2009	**33.5**	28.4 - 38.6	**20.5**	15.7 - 25.3
	2010-2014	**34.6**	28.7 - 40.6	**22.1**	14.5 - 29.7
Sweden*	2000-2004	*48.7*	*26.3 - 71.1*	**12.0**	9.0 - 14.9
	2005-2009		-	**23.8**	19.2 - 28.5
	2010-2014	*62.4*	*28.8 - 95.9*	**28.4**	22.6 - 34.1
Switzerland	2000-2004	*54.2*	*41.8 - 66.7*	**14.8**	8.1 - 21.6
	2005-2009	*53.3*	*40.1 - 66.4*	**23.7**	16.8 - 30.6
	2010-2014	*62.0*	*46.7 - 77.4*	**17.1**	10.8 - 23.4
United Kingdom*	2000-2004	**35.3**	30.9 - 39.8	**16.0**	14.1 - 17.9
	2005-2009	**36.7**	32.7 - 40.6	**21.0**	18.8 - 23.1
	2010-2014	**45.0**	39.3 - 50.7	**22.0**	19.8 - 24.2
OCEANIA					
Australia*	2000-2004	**38.6**	32.5 - 44.8	**22.4**	19.4 - 25.3
	2005-2009	**37.7**	32.5 - 42.9	**26.0**	22.7 - 29.4
	2010-2014	**48.5**	38.1 - 58.9	**28.6**	25.0 - 32.3
New Zealand*	2000-2004	*42.4*	*29.4 - 55.4*	**27.8**	20.5 - 35.1
	2005-2009	*61.9*	*49.3 - 74.6*	*33.0*	*22.8 - 43.3*
	2010-2014	*58.8*	*47.1 - 70.4*	**21.6**	14.6 - 28.6

* Countries with 100% coverage of the national population. § Survival estimates considered less reliable because the proportion of patients lost to follow-up or censored alive prior to five years, or the proportion of diagnoses based on a death certificate or autopsy, or the proportion of patients registered with incomplete dates, was 15% or more. Survival estimates in italics are not age-standardised.

WHO Classification of Tumours of the Central Nervous System, Fourth Edition, 2007; intrinsic brain tumours only.

	WHO grade			
	I	**II**	**III**	**IV**
Astrocytic tumours				
Subependymal giant cell astrocytoma	X			
Pilocytic astrocytoma	X			
Pilomyxoid astrocytoma		X		
Diffuse astrocytoma		X		
Pleomorphic xanthoastrocytoma		X		
Anaplastic astrocytoma			X	
Glioblastoma				X
Giant cell glioblastoma				X
Gliosarcoma				X
Oligodendroglial tumours				
Oligodendroglioma		X		
Anaplastic oligodendroglioma			X	
Oligoastrocytic tumours				
Oligoastrocytoma		X		
Anaplastic oligoastrocytoma			X	
Ependymal tumours				
Subependymoma	X			

	Myxopapillary ependymoma	X		
	Ependymoma		X	
	Anaplastic ependymoma			X
Choroid plexus tumours				
	Choroid plexus papilloma	X		
	Atypical choroid plexus papilloma		X	
	Choroid plexus carcinoma			X
Other neuroepithelial tumours				
	Angiocentric glioma	X		
	Chordoid glioma of the third ventricle		X	
Neuronal and mixed neuronal-glial tumours				
	Gangliocytoma	X		
	Ganglioglioma	X		
	Anaplastic ganglioglioma			X
	Desmoplastic infantile astrocytoma and ganglioglioma	X		
	Dysembryoplastic neuroepithelial tumour	X		
	Central neurocytoma		X	
	Extraventricular neurocytoma		X	

	Cerebellar liponeurocytoma		X		
	Paraganglioma of the spinal cord	X			
	Papillary glioneuronal tumour	X			
	Rosette-forming glioneuronal tumour of the fourth ventricle	X			
Embryonal tumours					
	Medulloblastoma				X
	CNS primitive neuroectodermal tumour (PNET)				X
	Atypical teratoid / rhabdoid tumour				X

WHO Classification of Tumours of the Central Nervous System, Revised Fourth Edition, 2016; intrinsic brain tumours only.

	WHO grade			
	I	**II**	**III**	**IV**
Diffuse astrocytic and oligodendroglial tumours				
Diffuse astrocytoma, IDH-mutant		X		
Anaplastic astrocytoma, IDH-mutant			X	
Glioblastoma, IDH-wildtype				X
Glioblastoma, IDH-mutant				X
Diffuse midline glioma, H3 K27M-mutant				X
Oligodendroglioma, IDH-mutant and 1p / 19q codeleted		X		
Anaplastic oligodendroglioma, IDH-mutant and 1p / 19q codeleted			X	
Other astrocytic tumours				
Pilocytic astrocytoma	X			
Subependymal giant cell astrocytoma	X			
Pleomorphic xanthoastrocytoma		X		

Anaplastic pleomorphic xanthoastrocytoma				X
Ependymal tumours				
Subependymoma	X			
Myxopapillary ependymoma	X			
Ependymoma		X		
Ependymoma, *RELA*-fusion positive		X		X
Anaplastic ependymoma				X
Choroid plexus tumours				
Choroid plexus papilloma	X			
Atypical choroid plexus papilloma		X		
Choroid plexus carcinoma				X
Other gliomas				
Angiocentric glioma	X			
Chordoid glioma of the third ventricle		X		
Neuronal and mixed neuronal-glial tumours				
Gangliocytoma	X			
Ganglioglioma	X			
Anaplastic ganglioglioma				X
Desmoplastic infantile astrocytoma and ganglioglioma	X			

	Dysembryoplastic neuroepithelial tumour	X		
	Central neurocytoma		X	
	Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)	X		
	Extraventricular neurocytoma		X	
	Cerebellar liponeurocytoma		X	
	Papillary glioneuronal tumour	X		
	Rosette-forming glioneuronal tumour of the fourth ventricle	X		
Embryonal tumours				
	Medulloblastoma (all subtypes)			X
	Embryonal tumour with multi-layered rosettes C 19MC-altered			X
	Medulloepithelioma			X
	CNS embryonal tumour (NOS)			X
	Atypical teratoid / rhabdoid tumour			X

	CNS embryonal tumour with rhabdoid features		X