Brain Tumour Registry of Canada (BTRC): Incidence Report 2010 - 2015

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In partnership with:
Alberta, British Columbia, Manitoba and Ontario Cancer Registries

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Executive Summary

This report provides the most comprehensive incidence rate information on all primary brain and other central nervous tumours (herein referred to as primary brain tumours) available to date in the Canadian context. This first multi-province Canadian report documents the incidence for all primary brain tumours including the non-malignant portion of brain tumours. The present work is inspired by the surveillance report published by the Central Brain Tumour Registry of the United States (CBTRUS). Incidence rates are presented by sex, age at diagnosis, tumour site, behaviour and histology. In situations of sparse data, groupings have been made to confidentially represent the underlying populations. As data on metastases following a primary cancer diagnosis are not available in cancer registries, metastatic brain tumours are not included in this report.

This BTRC incidence report includes annual average age standardized incidence rates for all primary brain tumours from four Canadian provinces (Alberta, British Columbia, Manitoba, Ontario) using the 2011 Canadian standard population. The annual average age standardized incidence rate (ASIR) of all primary brain tumours was 23.5 per 100,000 population between 2010-2015. About 35.9% of all primary brain tumours were malignant while 64.1% were non-malignant. Figures show that non-malignant tumours were about twice as common as malignant tumours highlighting the importance of recording these tumours in surveillance systems.

The most commonly occurring histology was the primarily non-malignant meningioma (24% of all primary brain tumours) a female predominant tumour not traditionally reported in cancer registries. The second and third most common groupings were unclassified tumours (19%) and glioblastomas (17%). With the exception of meningioma, histology specific incidence rates for primary brain tumours were higher in males compared to females and rates increased with age. It is important to note that tumour histology varies by age and sex. Young children (0-4 years) commonly developed embryonal tumours (ASIR: 1.20 per 100,000 per

year) and children (5-9 years) commonly developed pilocytic astrocytoma (ASIR: 0.97 per 100,000 per year). Pilocytic astrocytoma was also the most common diagnosis among older children aged 10-14 years (ASIR: 0.87 per 100,000 per year) while young adults (15-40 years) commonly developed tumours of the sellar region (ASIR: 1.98 per 100,000 per year). Males commonly developed glioblastoma (ASIR: 5.10 per 100,000 per year) and females commonly developed meningioma (ASIR: 7.58 per 100,000 per year). These incidence rates reflect 67% percent of the Canadian population and allowed us to estimate that approximately 9,800 new cases of primary brain and other central nervous system tumours will be newly diagnosed in 2021.

While this is an important step forward there is much work remaining. These patterns of incidence rates are similar to those reported elsewhere, supporting the validity of the data even though we know that cancer registries tend to underreport non-malignant tumours (Zakaria, Shaw, Woods, De & Davis, 2018). The rates of "*unclassified*" tumours are also higher than expected, a finding that merits further exploration. We anticipate that the data in this report will support provincial cancer registries in their effort to improve data quality and stimulate population-based brain tumour research to better understand potential causes of these tumours. It is our hope that these data will encourage and support histology specific basic science and clinical studies while providing evidence to guide advocacy and policy stakeholders in a joint effort to improve patient outcomes.

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1. Introduction

The Brain Tumour Registry of Canada (BTRC) has been established to ensure that every brain tumour in Canada is counted. Until recently, Canada has relied on data from a number of American and Canadian data resources to guide Canadian research, raise awareness, secure government funding and support treatment programs. However, these data are incomplete and not a true reflection of Canada's brain tumour burden. Our goal is to periodically provide high quality comprehensive data on the incidence, prevalence, and survival rates for all primary brain and other central nervous system (CNS) tumours-both malignant and non-malignant (primary brain tumours) by important patient characteristics to better understand the patterns of occurrence and survival by tumour site, histology, sex, age, region and over time. We anticipate variation in these patterns will stimulate hypothesis about causes, support evidence generation with respect to evaluating treatments and improve patient outcomes within the neuro-oncology research community; these results are needed to inform clinical decision-making and support policy guideline formation.

The collaboration of four provincial cancer registries (Alberta, British Columbia, Manitoba, Ontario) with BTRC has made this first incidence report possible. Our appreciation is extended to every individual that this information represents and to every cancer registry staff member whose work is reflected in this report.

2. Background

In response to advocacy efforts, the Canadian House of Commons passed Bill M235 in February 2007 (Parliament of Canada Vote Number 113, 2007) to create national guidelines for the surveillance of all malignant and non-malignant brain tumours. However, like many private member bills, funds were not aligned to accomplish this task and each provincial registry has been implementing this law as provincial mandates and funds allow. The Brain Tumour Foundation of Canada identified this gap in Canadian brain tumour surveillance information and prioritized development of a Pan-Canadian report on brain tumours, similar to that periodically published by the

Central Brain Tumour Registry of the United States (Ostrom et al., 2016). A collaboration to explore the feasibility of reaching this goal was developed between the Brain Tumour Foundation of Canada and Dr. Faith Davis at the University of Alberta in 2012.

Public Health Agency of Canada (PHAC) undertook an assessment to quantify the counts and rates of non-malignant CNS tumours captured in the Canadian Cancer Registry (CCR) from 2011 to 2015 to evaluate case completeness in response to Bill M 235. They demonstrated that national incidence rates for malignant tumours are similar to that expected, based on US rates, and that these rates vary modestly across provinces. In contrast, coverage of the non-malignant tumours indicated that registration of these tumours is incomplete so that incidence rates based on these data will reflect data limitations that complicate interpretation (Zakaria et al., 2018). The capture of non-malignant CNS tumours varied by province, demographics, tumour characteristic and year suggesting that ways to improve case ascertainment processes need to be explored at the provincial/territorial level. As such, Canadian registries do an excellent job of accruing malignant brain tumours while the transition towards compiling non-malignant brain tumours is currently incomplete and requires continuing attention.

A cancer registration system has been in place in Canada for many years, and provincial/territorial registries have been useful at the regional level for understanding the burden of disease, evaluating trends in disease occurrence and providing an infrastructure for clinical, epidemiologic and health services research, particularly for common cancers such as lung, breast, colorectal and prostate cancer (Canadian Cancer Society's Advisory Committee on Cancer Statistics, 2015). Since 1987, a national report on cancer i.e. Canadian Cancer Statistics (CCS) report is produced annually by the Canadian Cancer Society's Advisory Committee on Cancer Statistics, a joint effort by the Canadian Cancer Society, Statistics Canada, PHAC, and the provincial/territorial cancer registries. The report includes separate incidence rates and mortality rates for all cancers, including brain cancers.

The award of a Brain Canada Platform Support Grant to Dr. Davis and colleagues provided resources to collaborate with

provincial registries (Alberta, British Columbia, Manitoba, Ontario, Quebec,) on the collection of complete and high quality information on all primary brain tumours. This surveillance report includes four provinces and expands information available in CCS reports by incorporating data on all primary brain tumours and reporting it in more detail. As Quebec data were available only for 2011, we did not include that province in the current report, although we anticipate doing so in subsequent reports (personal communication, Christine Bertrand). The four collaborating provinces have generously worked on this Brain Tumour Registry of Canada (BTRC) project to ensure that all tumours are captured in each provincial cancer registry. The integrity of the data presented here is a culmination of each provincial cancer registries' (Alberta, British Columbia, Manitoba, Ontario) work to complete case ascertainment and data abstracting/coding processes for patients diagnosed from 2010 to 2015. Manitoba has a long established practice of including all primary brain tumours in their registry and Ontario had just completed the task of transitioning their case ascertainment procedures to align with bill M235. With the support of this new funding, Alberta and British Columbia reviewed all brain tumour diagnoses since 2010 identified on their respective discharge abstract database and supplemented routine case ascertainment processes of each registry (Normandeau, Mehta, Strother, Hatcher & Davis, 2016; Eckstrand,2018). As such, these data reflect the most complete information from these four provinces at this time. The supplemented incidence information from Alberta and British Columbia will be available through routine data collection processes to CCR users in the spring of 2020.

The current report is an in-depth compilation of cross provincial incidence data reflecting the population experience in four provinces (Alberta, British Columbia, Manitoba, Ontario) for all primary brain tumours since 2010. We recognize that this report is being compiled during a period of transition in brain tumour reporting. In addition to provincial responses to bill M235, evaluating the incorporation of the newer 2016 World Health Organization (WHO) classifications within the Canadian cancer registry system is ongoing (Louis et al., 2016).

A subsequent report compiling survival rate data from these provinces will be released. Plans are progressing to expand future surveillance reports to include information from all provinces and territories in Canada.

Sharing provincial data has allowed BTRC to obtain a better understanding of the originating data and understand the peculiarities of data collection in each province. This collaborative process has allowed for discussions about data completeness and quality and provinces, as required by their regulatory mandate and in conjunction with M235. Individual provincial initiatives are being discussed to further assess data quality. Continued collaboration, examination and use of these data will serve to improve completeness and accuracy over time.

3. Methods

Ethics approval for this project was granted by Health Research Ethics Board of Alberta, Cancer Committee and relevant data custodians in each of the four provinces. Data sharing agreements were approved with cancer registries guiding, confidentiality, data handling and data transfer. Each provincial registry collects patient data under the authority of their respective provincial legislation: The Cancer Act and the Provincial Personal Health Information Protection Act.

3a: Brain and Other CNS Tumour Definition and Classification

Primary brain tumours (malignant and non-malignant) were defined as brain and other CNS tumours occurring at the following ICD-O3 sites: C700-C709, C710-C719, C720-C729, C751-C753, and C300. Tumours were classified into topography groups, based on ICD-O-3 topography codes, and histology groups based on both ICD-O-3 histology codes and ICD-O-3 behaviour codes. Topography and histology groups were based on classifications used in the CBTRUS report (Ostrom et al., 2016). Tumours located in the brain that were incongruent with CBTRUS classification due to a combination of histology and behaviour codes that were placed in a new histology category "not classified in CBTRUS". For example, codes 8010/0; 8050/1 were placed in this group. The ICDO-3 codes used to create major and specific histological categories are shown in Appendix A. The classification system

used here reflects what is available in the cancer registry system. Data on biomarkers as used in the recent WHO diagnostic classification are not available in the cancer registry (Louis et al., 2016). We anticipate that biomarkers are being used in establishing the underlying diagnoses reflected here, but we are unable to present information by specific biomarkers.

3b. Data Collection

Each of the participating provinces have case ascertainment procedures identify primary brain tumour diagnoses that guide their work. Manitoba has a history of collecting information on all malignant and non-malignant tumours and Ontario has completed a project focused on identifying and incorporating information on brain tumours from 2010 forward. Knowing this, we considered Manitoba an Ontario data to be "*complete*" and focused on supporting Alberta and British Columbia in supplementing their routine case ascertainment processes. Building on a pilot project conducted in British Columbia (Ryan Woods, personal communication), historical case ascertainment activities in Alberta and British Columbia were enhanced using discharge abstract database records within each province as a new case-reporting source.

The discharge abstract database contains in-hospital discharge records for all Canadian hospitals excluding Quebec. This database includes demographic and clinical information on for acute care facilities (Canadian Institute for Health Information, 2019). Potential primary brain tumours with diagnosis from 2010 forward were identified in the discharge abstract database by each provincial cancer registry. Each identified record was reviewed by internal staff who then assessed eligibility for inclusion in their provincial cancer registry. Information on finalized cases, with specified variables were compiled for this project.

3c. Data Management

Patients diagnosed with all primary brain tumours registered in the four provincial cancer registries (Alberta, British Columbia, Manitoba, Ontario) between 2010 and 2015 were identified within each registry and data files, as approved, were shared with project analysts at the University of Alberta.

Multiple provincial datasets were combined into one file and all data elements were harmonized to facilitate calculating standardized estimates.

3d: Data Analysis

Descriptive epidemiology analysis was conducted to calculate average cases per year and annual average age standardized incidence rates (ASIR).

Annual average age standardized incidence rates (ASIR)[1] and 95% confidence intervals (CI) were calculated using the 2011 Canadian population as a reference. Denominator data was obtained for the four provinces providing data and was stratified by age and sex. Denominator data and frequency of cases were averaged over the six years (2010-2015) of data received to obtain an average annual estimate of the population at risk. Reference population data and denominator data were obtained from Statistics Canada (Canadian Socio-Economic Information Management System [CANSIM] Table: 17-10-0005-01). Post-censal and inter-censal estimates were used for each year by age and sex. For calculation of incidence rate by gender, data was standardized to the entire 2011 population using indirect standardization method. However, for age groups, data were standardized exclusively to the portion of the 2011 population that contained the age group being examined. Cases, denominator data and the reference population were all separated in to five-year age stratums with 0-4 years of age being the youngest and with 100+ years of age being the oldest. In general, the stability or confidence we had in the incidence rates estimated increased as the actual case count increased. Data harmonization and analysis was done using SAS version 9.4. Figures were made using Microsoft Excel 2010.

[1] *Note on Incidence Rates:*

*Incidence rates provide a measure of the occurrence of disease in a specific population for a specific period of time. This report includes two types of rate estimates: age-specific and age standardized. All incidence rates are presented per 100,000 population by convention for readability.
*Age Specific Incidence Rate – Age specific incidence rates reflect are defined as the number of new cases diagnosed within a specific time period and age category over the total population within the same time period and same age category.
*Annual Age Standardized Incidence Rate (ASIR)- ASIR are the weighted averages of age-specific incidence rates, when applied to the distribution of a reference population. All ASIRs in this report are standardized to the 2011 Canadian Population. This adjustment procedure allows the reader to compare rates within the same category (total, sex, age) based on the same population.

Projected cases for 2021 were calculated using age-specific incidence rates generated and the projected population numbers from CANSIM. Age specific rates were first calculated using data obtained from the provinces and denominator data from CANSIM. Then expected values for 2012 were estimated using the "*medium-growth*" estimate stratified by age and sex from Statistic Canada's population projections for Canadian provinces and territories, 2010 to 2036 (CANSIM, Table 11-1). To ensure confidentiality of individuals underlying these data, average annual estimates were censored in tables when based on fewer than 5 cases. Furthermore, cells that could result in residual disclosure were also censored as per the guidelines recommended by Statistics Canada (Canadian Cancer Registry, 2019).

4. Results

These data reflect at total of 32,593 individuals (Table 1) diagnosed between 2010 and 2015 with primary brain tumours whose information is a part of their provincial cancer registry system. Incidence rates are reported by tumour location and both major and specific histology groupings. Histology groupings, both major and specific subtypes, are reported by sex, age group at diagnoses and tumour behaviour. Data are unavailable in the provincial registry systems for individuals diagnosed with metastatic brain tumours so the information included here does not reflect this population. There was one patient with "Unclassified" histology that was categorized as " Not Classified in CBTRUS" due to an error. The error did not effect estimates and will be corrected in future reports.

Please note that the incidence rates presented here cannot be directly compared to rates from external reports. For example, one can compare the rates by tumour location of histology within males or females or within the same age category, but not across sex or age categories, because each rate is based on a unique subset of the Canadian population. When assessing rates across countries, for example BTRC and CBTRUS publications, any difference observed may have multiple explanations: 1) differences in the age distribution, or 2) varying occurrence rates of the disease in the two populations.

4a. Incidence Rates by Tumour Site and Sex

The incidence counts and rates for each tumour site and its associated topography code are shown in Table 2 for all cases, males and females.

- Overall, the most common location for primary brain tumours was cerebral meninges with average of about 1,299 cases per year (Figure 1).
- Within the lobes of the brain itself frontal lobe tumours (ASIR: 2.5/100,000/year) were the most common followed by tumours in the brain not otherwise specified categories ([NOS], ASIR: 2.3/100,000/year).
- The location where brain tumours appeared most commonly in both males and females were cerebral meninges (ASIR: 5.6/100,000/year) followed by pituitary gland tumours (ASIR: 3.3/100,000/year) (Table 2, Figure 2).
- Incidence rates for males were found to be slightly higher than their female counterparts for most tumour locations (Table 2 and Figure 2). Cerebral meninges are the major exception, with female rates (ASIR: 7.4/100,000/year) almost double compared to male rates (ASIR: 3.7/100,000/year.

Figure 1: Primary brain and other central nervous system (CNS) tumours by tumour site and sex: total number of cases for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies)

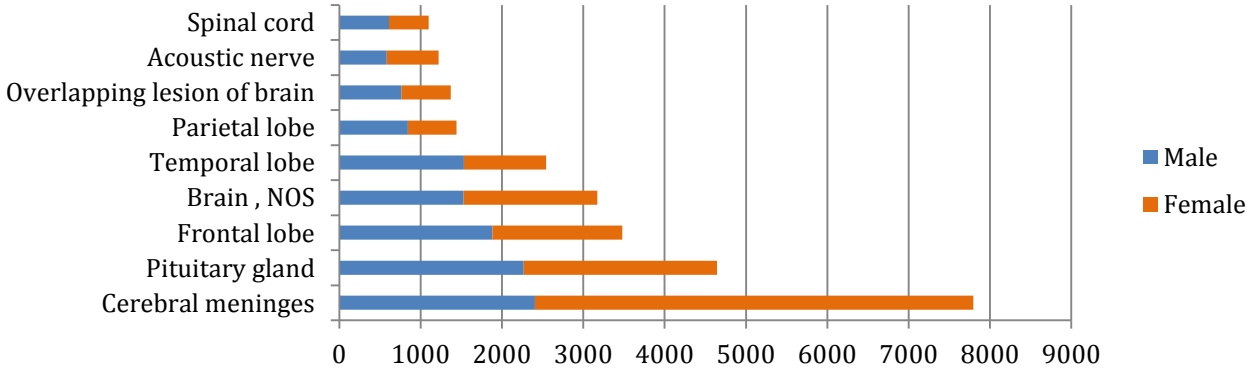
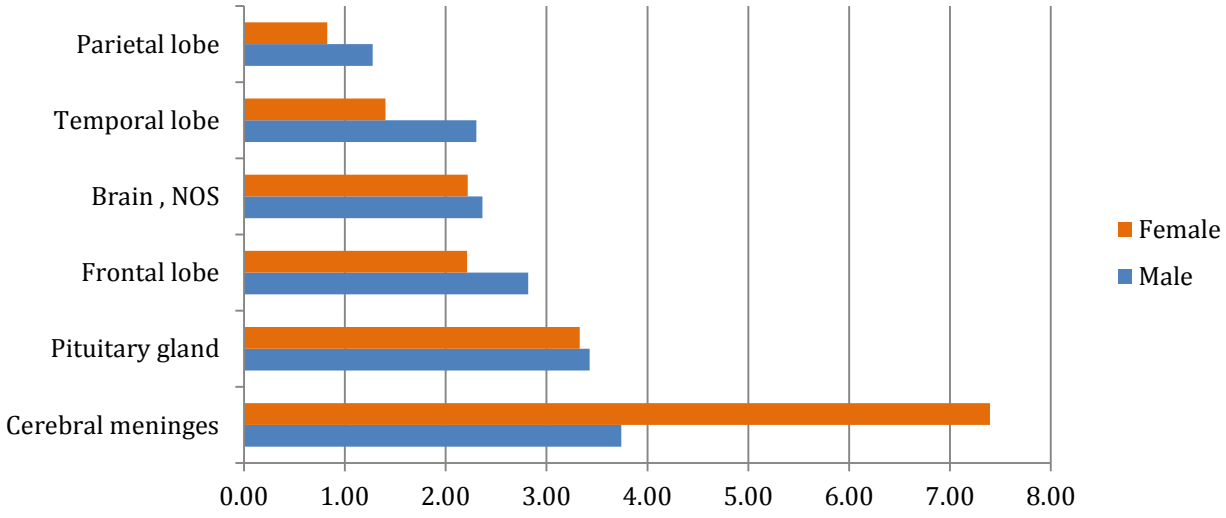
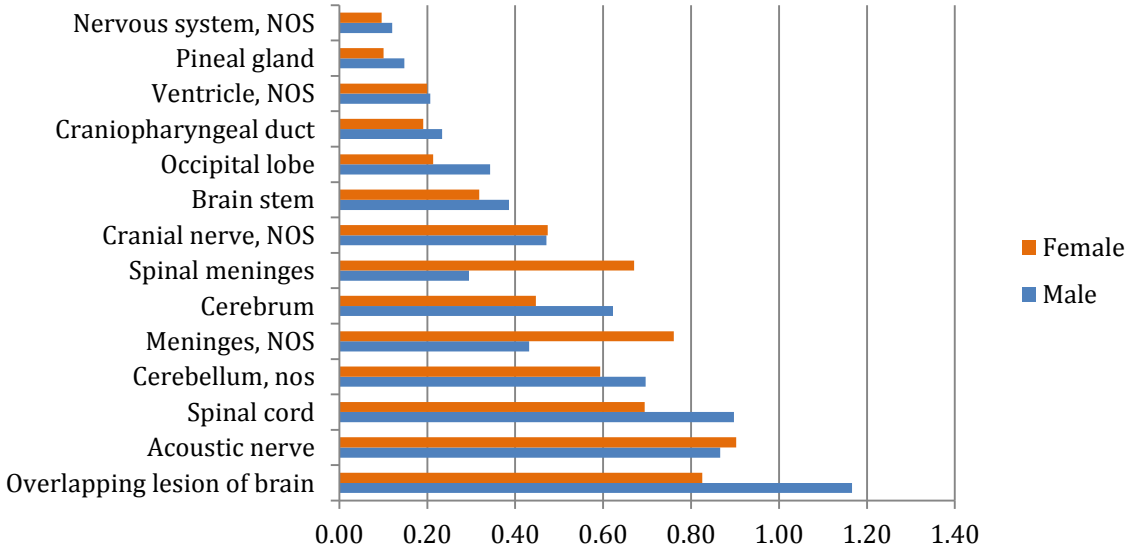


Figure 2: Primary brain and other central nervous system (CNS) tumours by tumour site and sex: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies)

a. ASIR greater than 1



b. ASIR greater than 0.1 but less than 1



4b. Incidence Rates by Tumour Histology and Sex

The case counts and rates for each tumour histology grouping (major and specific categories) are shown in Table 3, and Figures 3-6 for all cases, males and females. Table 3 shows major histology groupings in **bold** and specific histology groupings under the appropriate major grouping. Table 3 describes the cases combined across provinces that subsequent incidence rates are based on. Incidence rates estimated using this underlying population will be more robust for those categories with larger numbers.

- With respect to major histology groupings, neuroepithelial tumours had the highest number of cases (total number of cases: 10,467, annual average number of cases: 1744.5) incidence rate (ASIR: 7.5/100,000/year) followed by tumours of meninges (total cases: 8,349, annual average number of cases: 1391.5, ASIR: 6.0/100,000/year) (Tables 1,3; Figures 3,4).
- With respect to specific histology groupings, meningioma had the highest number of cases and incidence rate (total number of cases: 7,822, average cases per years: 1303.7, ASIR: 5.7/100,000/year) followed by unclassified tumours (total number of cases: 6,223, average cases per years: 1037.17, ASIR: 4.5/100,000/year) and glioblastoma (total number of cases: 5,691, average cases per years: 948.5, ASIR: 4.1/100,000/year) (Tables 1, 3).
- The rate of most specific histology categories was higher in males compared to females; exceptions were meningioma and unclassified tumours. The average cases per years and ASIR of all primary brain tumours by tumour histology and sex are shown in Table 3.
- The most commonly diagnosed specific histology among males was glioblastoma (total count: 3.371, average annual count: 562, ASIR: 5.1/100,000/year) while the most commonly diagnosed histology in females was meningioma (total count: 5,482, average annual count:914, ASIR:7.6/100,000/year) (Table 1,3 and Figures 5,6)

Figure 3: Primary brain and other central nervous system (CNS) tumours by major histology groups and sex: total number of cases for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies with total number of cases greater than 1000)

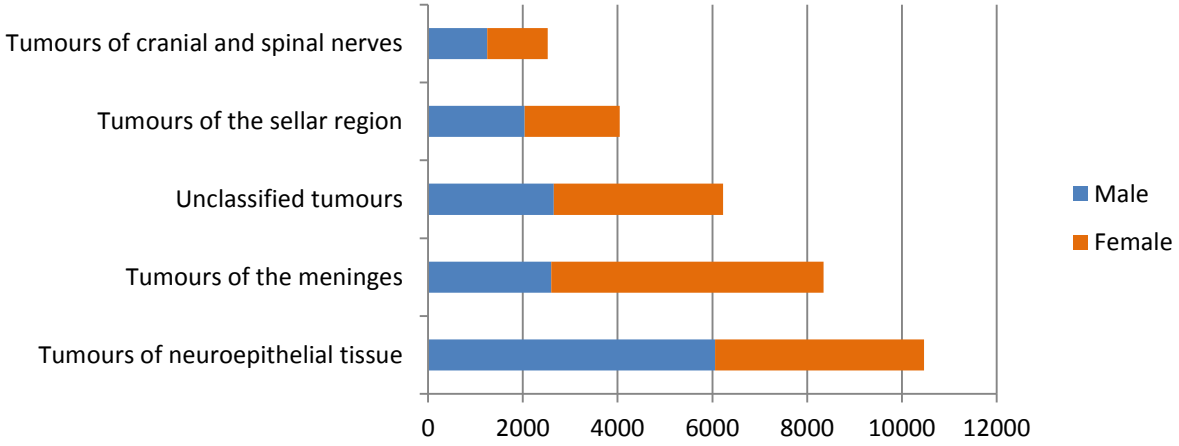


Figure 4: Primary brain and other central nervous system (CNS) tumours by major histology groups and sex: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies with ASIR greater than 1)

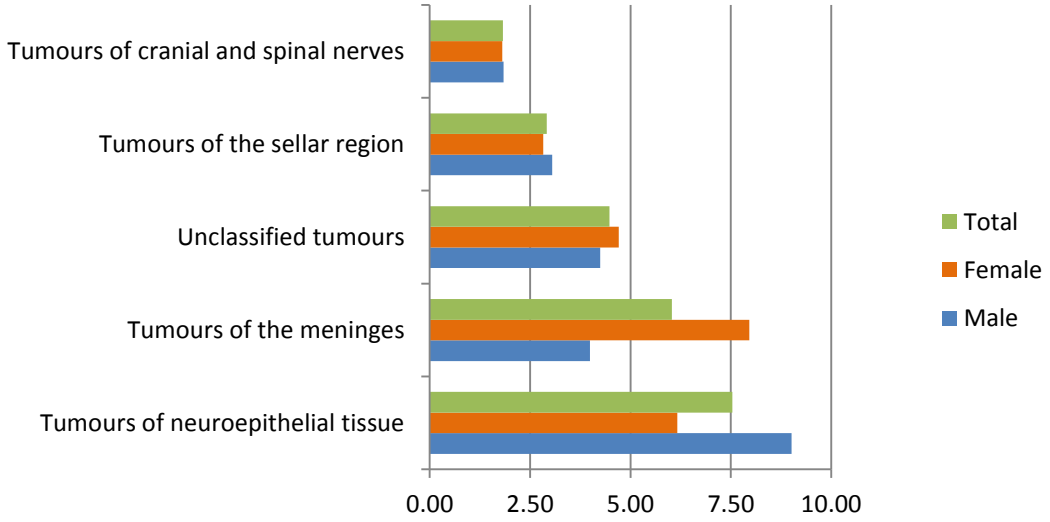


Figure 5: Primary brain and other central nervous system (CNS) tumours by specific histology groups and sex: total number of cases for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies total number of cases than 1000)

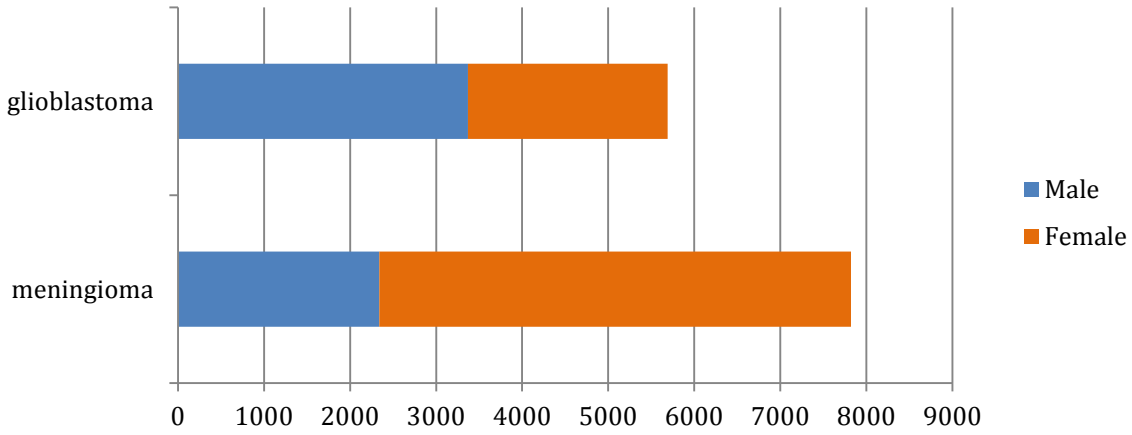
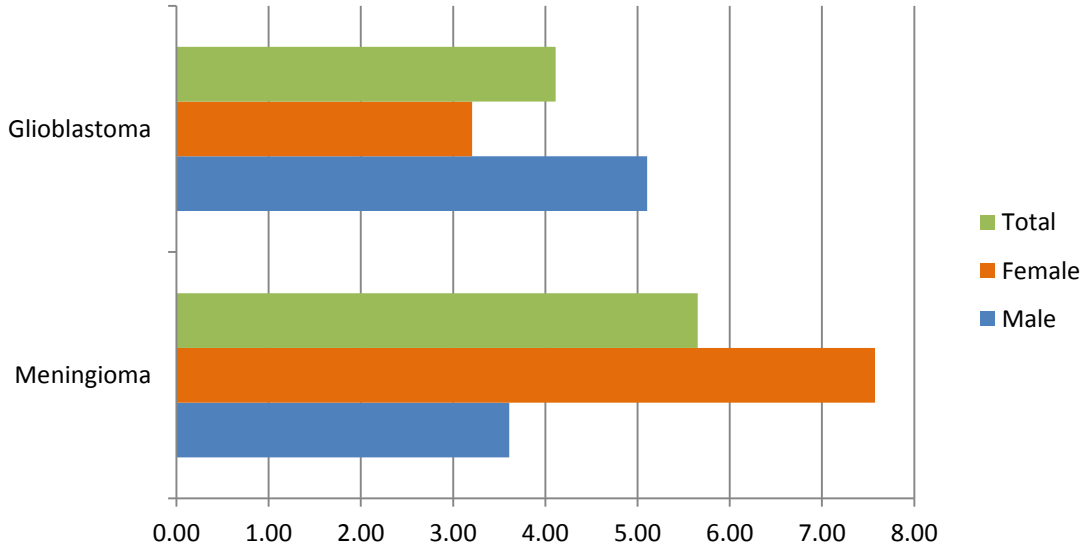


Figure 6: Primary brain and other central nervous system (CNS) tumours by specific histology groups and sex: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies with ASIR greater than 1)

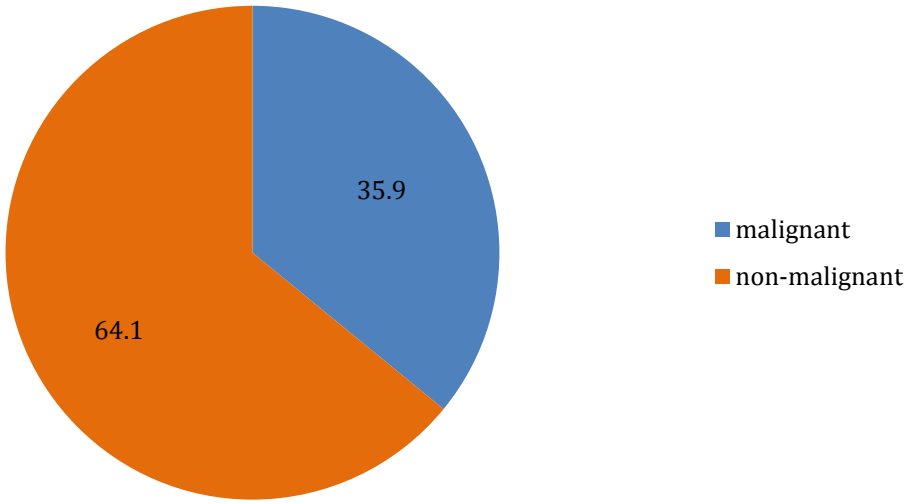


4c. Incidence Rates by Tumour Histology and Behaviour

The average incidence counts, rates for each tumour major and specific histology category and percent malignant cases are shown in Tables 1, 4 and Figures 7,8,9, for all cases by tumour behaviour. The addition of the non-malignant tumours in the data provided by participating registries allowed reporting of incidence rate patterns for all primary brain tumours. For example, 4044 tumours of the sellar region were reported. This is the third most common major histology grouping with a median age of 55 years at diagnosis which reflects 12.4 percent of all primary brain tumours (Table 1). All but 18 (0.5%) of these tumours were classified as non-malignant (therefore 99.5% are malignant) and they occurred fairly evenly between males (n=2,041) and females (n=2,003). In contrast, the specific histology category of embryonal tumours are quite rare (n=310), primarily malignant in nature (98%) and present with a median age of 9 years. Data for these tumours are too sparse to report further breakdowns by sex.

- About 36% of all primary brain tumours presented as malignant and 64% as non-malignant tumours in this population (Figure 7).
- With respect to major histological groupings, neuroepithelial tumours were the most common (32.1% of all primary brain tumours) and 93% of these tumours had malignant behaviour (Table 1).
- Non-malignant tumours made up more than 85% of the tumours in four major histological groupings: tumours of the meninges, tumours of the sellar regions, cranial and spinal nerves and unclassified tumours (Figure 8).
- Lymphomas was the only category with almost all malignant tumours (Tables 1, 4).
- Among malignant tumours glioblastoma had the highest incidence rate (ASIR: 4.1/100,000/year) while among non-malignant tumours meningioma had the highest incidence rate (ASIR: 5.5/100,000/year) (Table 4, Figure 9).
- About 44% of all cases occurring in males were malignant compared to 28.9% in females (Table 1)

Figure 7: Primary brain and other central nervous system (CNS) tumours: pie chart showing percent malignant and non-malignant tumours



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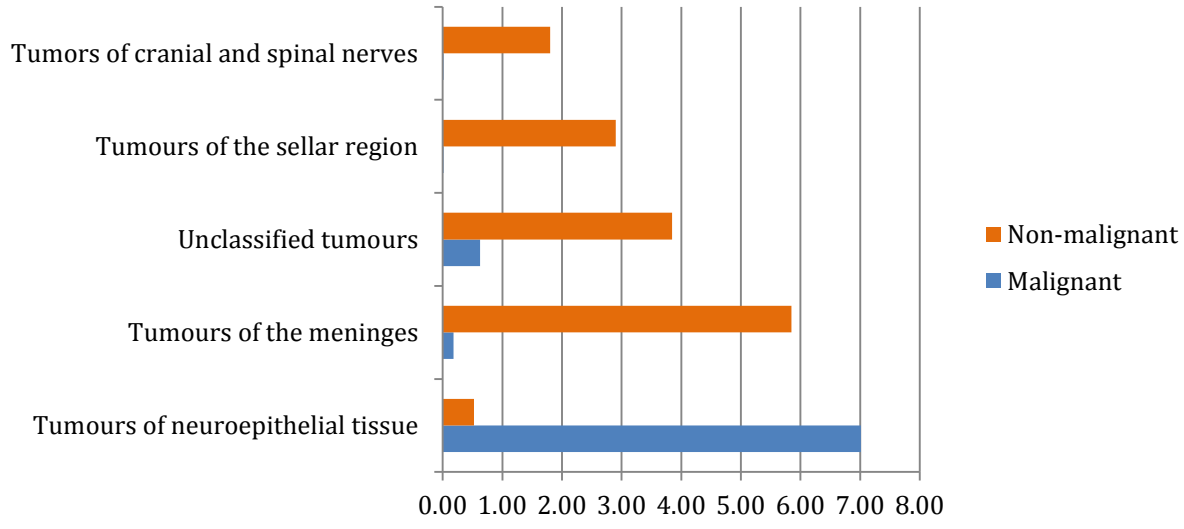
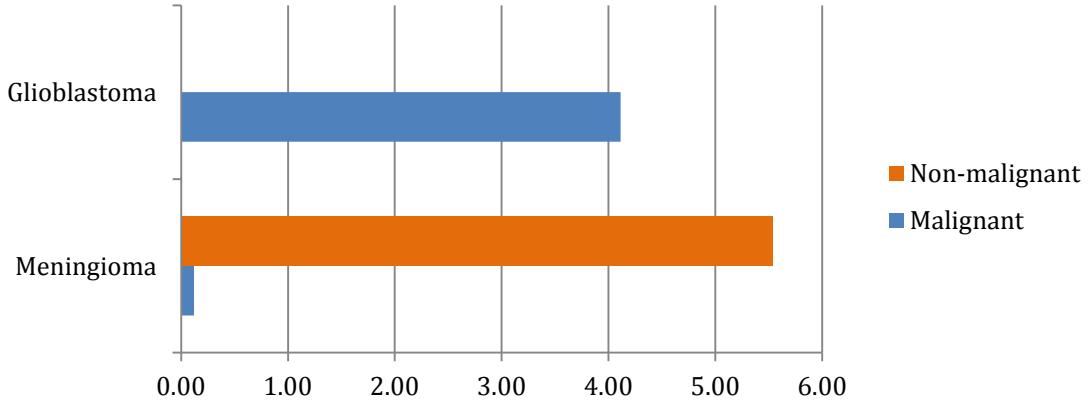


Figure 9: Primary brain and other central nervous system (CNS) tumours by specific histology groups by behaviour: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies)



4d. Incidence Rates by Tumour Histology and Age at Diagnosis

The average incidence counts and rates for each tumour (major and specific histology) category are shown by age at diagnosis in Tables 5 and 6 and Figures10-15 for all ages. Broader categories of age are shown in Table 5 and narrower categories of age are shown in Table 6. The most common tumours presenting in different age groups is summarized in Table 7. Children and adolescent tumours are addressed separately in Tables 8 and 9. Median age at diagnosis is presented in Table 1.

All Ages

- In general, rates for brain tumour subtypes increase with age at diagnosis (Tables 5,6; Figures 10,11).
- Meningioma and gliobastoma both increased with age (Figure 12).
- Pilocytic astrocytoma, embryonal and choroid plexus tumours were most common in childhood and declined with age (Table 5, Figure 12).
- Neuronal and mixed neuronal glial tumours had higher incidence rates in the adolescents and young adult group (ASIR: 0.5/100,000/year) than in the children (ASIR:0.4/100,000/year) or adult

groups (ASIR: 0.2/100,000/year) (Table 5).

- Table 7 summarizes the three most common tumours within selected age groups. In the very young (0-4 years) embryonal tumours predominated while in 5-14 year olds, pilocytic astrocytomas were the most common diagnosis. Among 15-34 year olds tumours of the sellar region dominated, while after 35 years of age meningioma and glioblastoma emerged as the most common tumours.

Childhood and Adolescence

Table 8 and 9 and figures 13 to 16 provide information on children and adolescents (0-19 years) for all primary brain tumours by histology (major and specific groupings) and sex:

- Tumours of neuroepithelial tissue had the highest incidence rate among children and adolescents (ASIR: 3.7/100,000/year).
- Among specific histology categories unclassified tumours (ASIR: 0.8/100,000/year) had incidence rates similar to pilocytic astrocytomas (ASIR: 0.8/100,000/year) and embryonal tumours (ASIR: 0.7/100,000/year).
- There were no major differences in primary brain tumours incidence by histology (major or specific groupings) and sex in children and adolescents aged 0-19 years at diagnosis. (Table 8, Figures 13,14)
- In children and adolescents, the pattern by age was more subtle than in adults; all major groupings, except for neuroepithelial tumours, increased with age. (Figure 15).
- Majority of neuroepithelial tumours were observed to be more common among the very young (0-4 years) children. (Table 9, Figure 16)

Median Age at Diagnosis

- The median age at diagnosis was lowest for embryonal tumours (9 years) and highest for unclassified tumour (69 years)
- The median age for the most common malignant histology glioblastoma was 64 years while the median age for most common non-malignant histology meningioma was 62 years (Table 1).

Figure 10: Primary brain and other central nervous system (CNS) tumours by children, adolescents/young adults (AYA) and adults by major histology groups: total number of cases for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies with total number of cases greater than 1000)

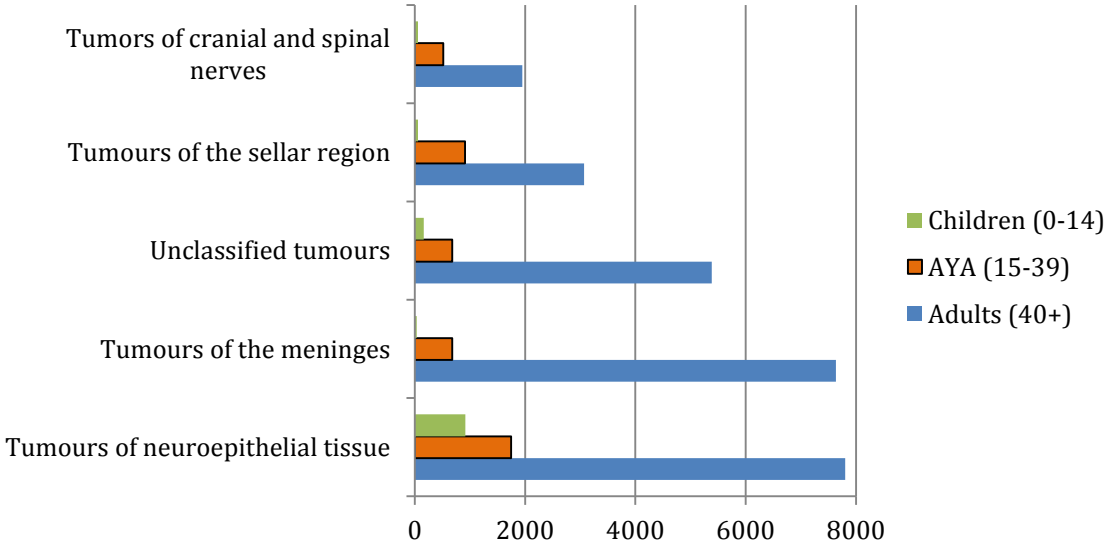


Figure 11: Trends for primary brain and other central nervous system (CNS) tumours by age groups and major histology groups: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies)

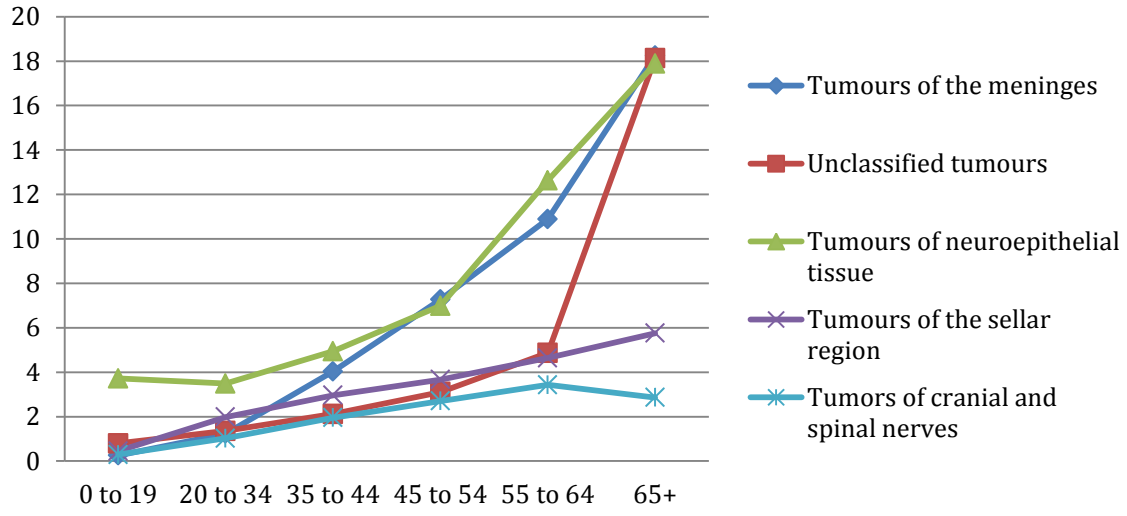


Figure 12: Trends for primary brain and other central nervous system (CNS) tumours by age groups and selected specific histology groups: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies)

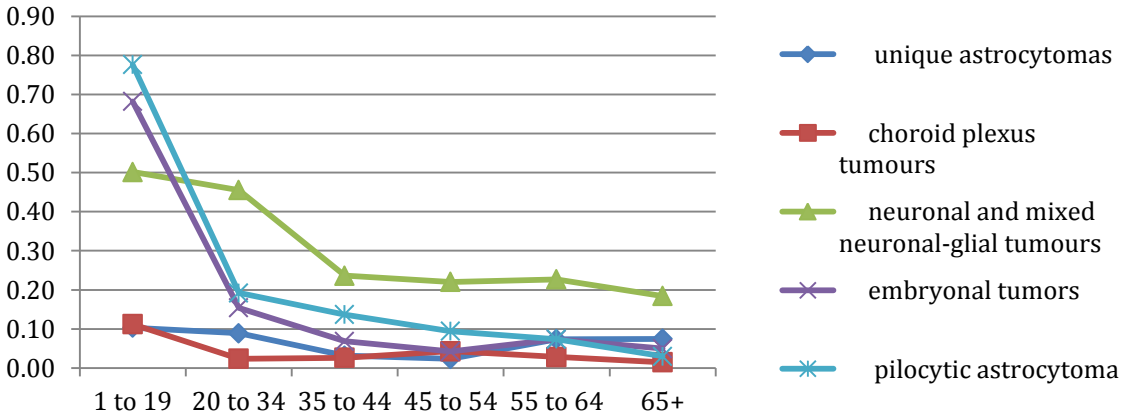


Figure 13: Primary brain and other central nervous system (CNS) tumours in children and adolescents (aged 0-19 years) by major histology groups and by sex: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies with ASIR >0.4)

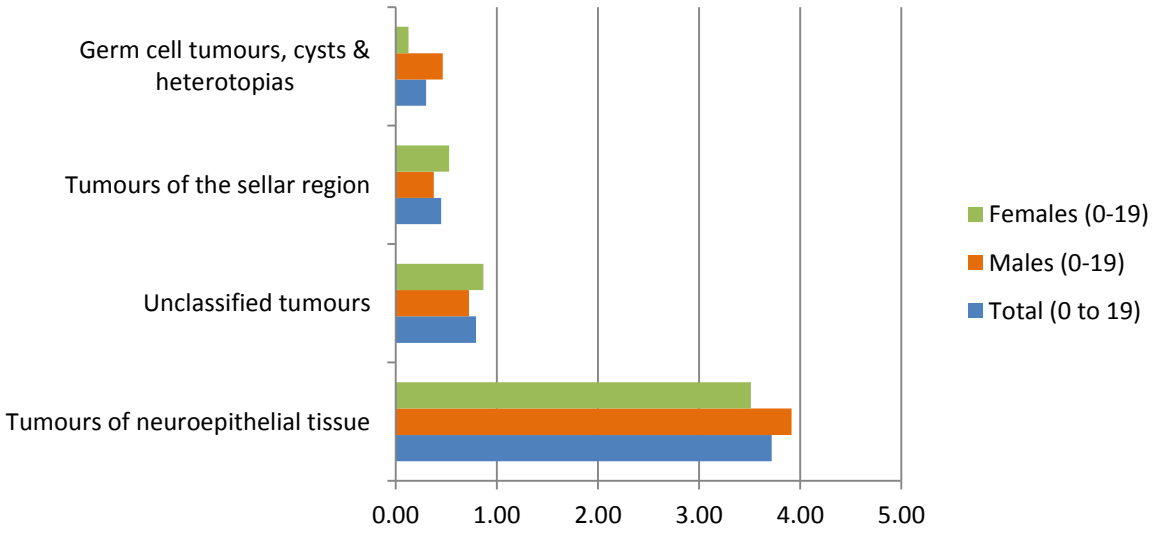


Figure 14: Primary brain and other central nervous system (CNS) tumours in children and adolescents (aged 0-19 years) by specific histology groups and by sex: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies)

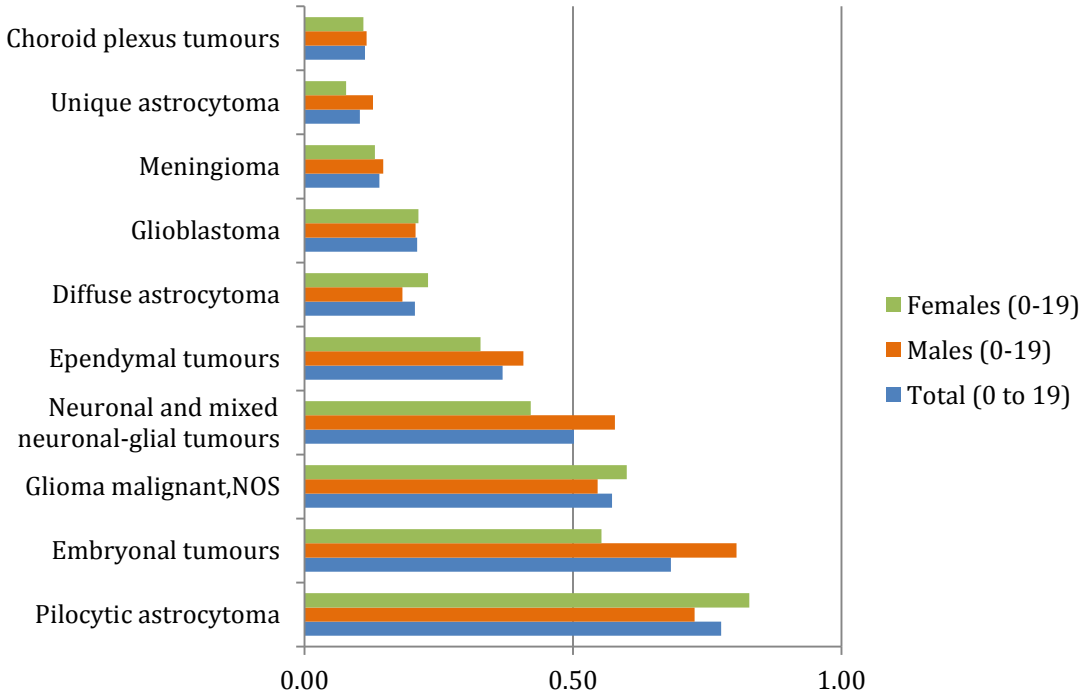


Figure 15: Trends for primary brain and other central nervous system (CNS) tumours in children and adolescents (aged 0-19 years) and major histology groups: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies with ASIR > 0.5)

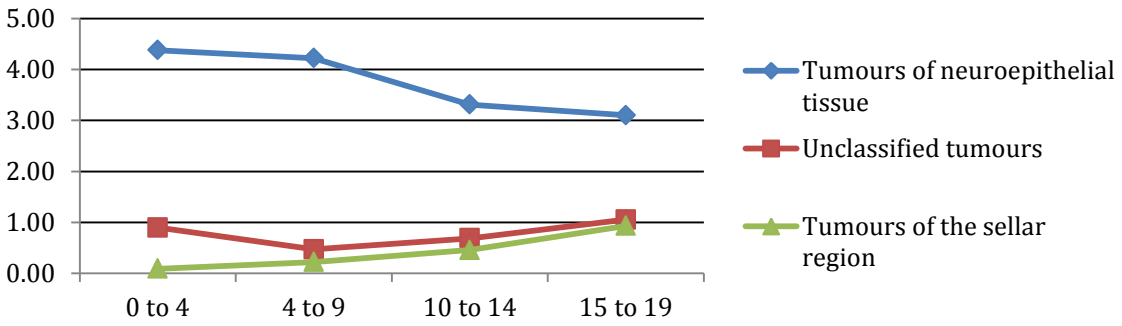
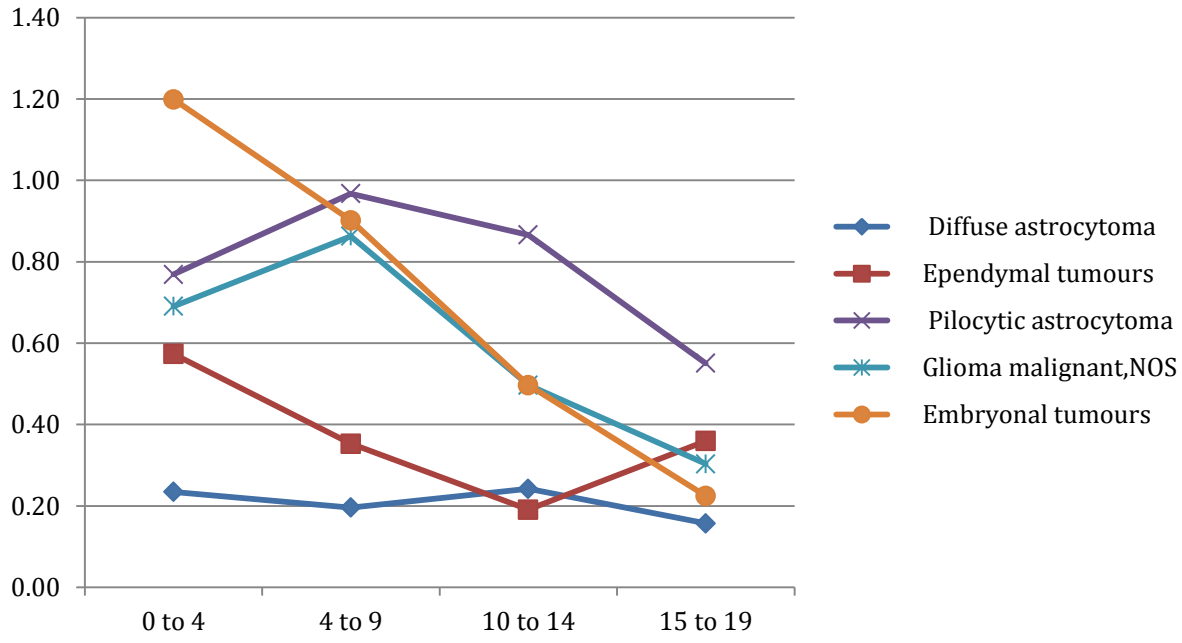


Figure 16: Trends for primary brain and other central nervous system (CNS) tumours in children and adolescents (aged 0-19 years) and specific histology groups: annual average age standardized incidence rates (ASIR) per 100,000 per year for 2010-2015 from four Canadian provinces (AB, BC, MB, ON); (selected histologies)



4e. Expected Number of Primary Brain and Other Central Nervous System Incident Tumour Cases for Canada in 2021

Table 10 provides estimates of the number of expected cases in 2021 in Canada by histology grouping by sex and for children. These estimates are approximations based on population projections provided by Statistics Canada with underlying assumptions: 1) they assume that the incidence rates experienced between 2010-2015 in these four provinces reflect the patterns in all of Canada; 2) that the rates do not change over the projected time period, and 3) there are no changes in case ascertainment and data coding that would affect rates during the projected time period. Should case ascertainment for the non-malignant tumours improve and/or a higher proportion of unclassified tumours receive specific codes, these expected numbers will increase. The number of new primary brain tumours cases

expected to be diagnosed in 2021 in Canada are approximately 9,233; including 1,785 gliobastoma, 2,542 tumours of the meninges, 1,173 tumours of the sellar region and 368 pediatric tumours.

5.Comments on Data Quality

Identifying patterns in the distribution of disease across categories of age and sex can guide research planning and resource allocation. However, the utility of these findings depends on the validity of the data used to estimate them. High quality data will ensure that the patterns themselves are not due to underlying biases in data collection processes. The following discussion to assist the reader in the interpretation of the quantitative information provided in this report and to support the ongoing work within the provincial clinical and registry communities to improve the quality of this data and subsequent information it will generate over time.

5a. Case Ascertainment

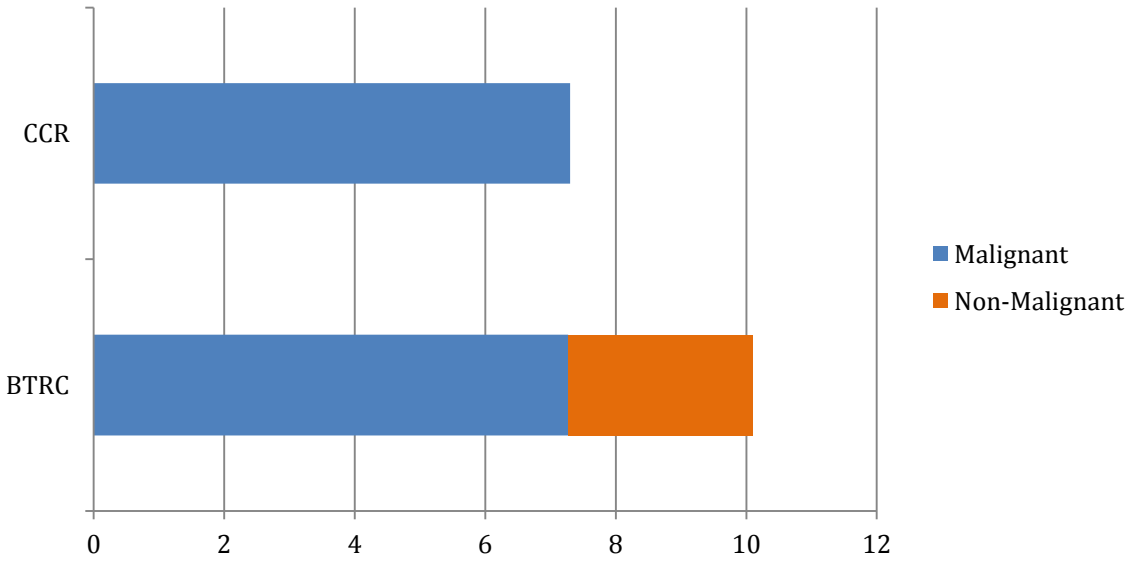
Figure 17 demonstrates that the difference in the total rates of brain and CNS tumours in the CCR (CANSIM; Table: 13-10-0747-01) and all primary brain tumours tumours included in this report is explained by the addition of non-malignant cases. Underrepresentation of nonmalignant tumours in the CCR is known (Zacharia et al, 2018). It is important to note that the case ascertainment work in Alberta and British Columbia that was completed for this project will be incorporated into the CCR files by 2020. This BTRC report represents the most complete primary brain tumours data currently available.

In Alberta, a recent analysis revealed that malignant brain tumours had a 95% or higher completeness of case ascertainment. On the other hand, it was estimated that 38% of non-malignant brain tumours were underreported (Eckstrand, 2018). Until case ascertainment is complete and the reporting of tumours is standardized across provinces, changing incidence rate patterns over time in the Canadian population may not actually reflect true changes.

We support the suggestion of Zakaria and colleagues that new ways to improve case ascertainment processes are needed at the provincial/territorial levels. A 2009 PHAC report suggested that the

unavailability of diagnostic information from radiology reports is one barrier to identifying complete information on brain tumours (Shaw, 2014). Further consideration of this issue by collaborators has resulted in a better understanding of the problem and has provided potential solutions (Yan et al., in press, 2019). As solutions await implementation, it will be important to continue to explore other avenues to improve the identification of the nonmalignant brain tumours for surveillance purposes.

Figure 17. Overall annual age standardized incidence rates (2010) per 100,000 per year for site codes C71.0 to C71.9 comparing Canadian Cancer Registry (CCR) data to data from four Canadian provinces (AB, BC, MB, ON)



*Excludes histology codes 9050 to 9055, 9140, 9530 to 9539, and 9590 to 9992.

5b. Information Quality

In addition to providing direct and detailed incidence rates in the four provinces (Alberta, British Columbia, Manitoba, Ontario) these data provide a snapshot into factors that may reflect information quality for all primary brain tumours; specifically, tumour behaviour, unclassified categories, and tumours

unclassified using the CBTRUS histology groupings (0strom et al., 2016).

Tumour Behaviour

The work of Zakaria and colleagues quantifies the underestimation of non-malignant primary brain tumours in the Canadian registry system and notes that the capture of non-malignant brain tumours varies by province, patient demographics, tumour characteristics and year of diagnosis (Zakaria et al., 2018). As such, the incidence rates for malignant tumours in this report will be most accurate and rates for those histologic groupings that include non-malignant tumours may be less accurate. For example, meningioma, as a primarily non-malignant category, is more likely to be underestimated than glioblastoma, a primarily malignant category of tumours. It is unknown if low grade gliomas are being well captured in the current report.

Unclassified Tumours

Unclassified tumours may be legitimate rare variants of brain tumours, tumours lacking the diagnostic information to classify them more precisely or some coding error made in the data processing. Table 11 shows that the rate of unclassified tumours is higher for 1) non-malignant tumours than malignant tumours; 2) females than in males, and 3) higher in individuals diagnosed at older ages. It is possible that this "*unclassified designation*" is related to clinical decisions reflecting the appropriateness of aggressive/invasive procedures when addressing the complete health status of an individual. For example, elderly patients or female patients (who also tend to live longer than male patients) may not be strong enough to undergo invasive surgical procedures. Tumours that appear non-malignant in presentation may fall into a "*watch and wait*" category for the clinician and end up with an "*Unclassified*" designation.

While these may be legitimate designations it would be useful to better understand the underlying reasons for being unclassified, particularly given that the Canadian unclassified rates are about two times higher than CBTRUS rates. As the proportion of unclassified tumours increases with age, we anticipate that the accuracy of patterns reported in the older age groups may be lower. Similarly, as the proportion of unclassified tumours is slightly higher in females than males we

anticipate that the accuracy of histologic patterns may be lower in females.

Tumours "Not Classified by CBTRUS"

This category was created by BTRC to reflect individuals who have been diagnosed with a tumour coded to a location in the brain, but for which either the tumour histology and/or behaviour code combination is not incorporated in the CBTRUS classification of brain tumours.

We anticipate that this group reflects data transfer or coding errors in the cancer registries. Given that the intent of our work is to count every individual with a brain tumour, we have included this category in our overall estimates and tables. It will be important to work with provincial cancer registries to better understand this category going forward.

6. Concluding Comments

This reports includes the most comprehensive and complete incidence rate patterns on all primary brain and other CNS tumours in the Canadian context available to date. While this is an important step forward there is more work remaining to reach our goal of making all brain tumour patients count in population estimates. The validity of this information is supported by the fact that patterns observed in these data are similar to those reported elsewhere. As each province incorporates revised case ascertainment and quality control procedures for brain and other CNS tumours in their data systems, population estimates will become more complete and accurate. This initial report does allow an estimation of the expected numbers of cases in Canada.

Follow-up national reports utilizing updated CCR data files which incorporate all provinces and territories are planned. We anticipate that the data in this initial report will support provincial registries in their efforts to improve data quality, support researchers.as they plan histologic specific clinical studies and assist epidemiologists in their work to better understand potential causes of these tumours. This evidence may also guide advocacy and policy decisions with the neurooncology community.

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8. Appendices

Appendix A: Brain Tumour Registry of Canada (BTRC), brain and other central nervous system tumour histology groupings

Histology Groups	**ICD-O-3 Histology and Behavior Code***
Tumours of Neuroepithelial Tissue	
pilocytic astrocytoma	9421/1,3; 9425/3
diffuse astrocytoma	9400/3; 9410/3; 9410/3; 9420/3
anaplastic astrocytoma	9401/3
unique astrocytoma	9381/3; 9384/1; 9424/3
glioblastoma	9440/3; 9441/3; 9442/3
oligodendroglioma	9450/3
anaplastic oligoodendroglioma	9401/3
choroid plexus tumours	9390/0,1,3;
oligoastrocytic tumours	9382/3
ependymal tumours	9383/1; 9391/3; 9392/3; 9393/3; 9394/1
glioma malignant, Not otherwise specified	9380/3
neuronal and mixed neuronal-glial tumours	8680/0,1,3; 8681/1; 8690/1; 8693/1,3; 9412/1; ; 9413/0; 9442/1; 9492/0 Site C751 excluded; 9493/0; 9505/1,3; 9506/1; 9509/1; 9522/3; 9523/3
tumors of the pineal region	9360/1; 9361/1; 9362/3; 9395/3;
embryonal tumours	8963/3; 9364/3; 9470-9474/3; 9480/3; 9490/3,0; 9500-9502/3; 9508/3
other neuroepithelial tumours	9363/0, 9423/3, 9430/3, 9444/1

Tumors of Cranial and Spinal nerves	9540/0,1,3; 9541,0; 9550/0; 9560/0,1,3; 9561/3, 9570/0; 9571/0,3; 9562/0
Tumours of the Meninges	
meningioma	9530/0,1,3; 9531/0; 9532/0; 9533/0; 9534/0; 9537/0; 9538/1,3; 9539/1,3
mesenchymal tumours	8324/0; 8800/0,3; 8801-8806/3; 8810/0,3; 8815/0,3; 8824/0,1; 8830/0,1,3; 8831/0; 8835/0; 8836/0; 8850/0,1,3; 8851-8852/0,3; 8853/3; 8854/0,3; 8857/0,3; 8861/0; 8870/0; 8880/0; 8890/0,1,3; 8897/1; 8901-8902/3; 8910/3; 8912/3; 8920/1,3; 8921/3; 8935/0,1; 8990/0,1,3; 9040/0,3; 9136/1; 9150/0,1,3; 9170/0,3; 9180/0,3; 9210/0; 9241/0; 9260/3; 9373/0;
primary melanocytic lesions	8720/3; 8728/0,1,3; 8770-8771/0,3;
other neoplasms related to the meninges	9160/1; 9220/0,1,3; 9231/3; 9240/3; 9243/3; 9370-9372/3; 9535/0
Lymphomas & Hematopoietic Neoplasms	
lymphoma	9590-9591/3; 9596/3; 9650-9655/3; 9659/3; 9661-9665/3; 9667/3; 9670/3; 9671/3; 9673/3; 9675/3; 9680/3; 9684/3; 9687/3; 9690/3; 9691/3; 9695/3; 9698-9699/3; 9701/3; 9702/3; 9705/3; 9714/3; 9719/3; 9728/3; 9729/3;
other hematopoietic neoplasms	9727/3; 9731/3; 9733-9734/3; 9740/1,3; 9741/3; 9750/3; 9751-9753/1; 9754-9758/3; 9760/3; 9766/1; 9823/3; 9826/3; 9827/3; 9832/3; 9827/3; 9832/3; 9837/3; 9860/3; 9861/3; 9866/3; 9930/3; 9970/1
Germ Cell Tumors, Cysts and Heterotopias	8020/3; 8440/0,3; 9060-9061/3; 9064-9065/3; 9070-9072/3; 9080/0,1,3; 9081-9083/3; 9084/0,3; 9085/3; 9100/3; 9101/3;
Tumours of the Sellar Region	8040/0,1; 8140/0,1,3; 8146/0; 8246/3; 8260/0,3; 8270/0,3; 8271/0; 8272/0,3; 8280/0,3; 8281/0,3; 8290/0,3; 8300/0,3; 8310/0,3; 8323/0,3; 9492/0 Site C751 only; 9582/0; 9350-9352/1;
Unclassified Tumors	9120/0,3; 9121/0; 9122/0,3; 9123/0; 9125/0; 9130/0,1,3; 9131/0; 9133/1,3; 9140/3; 8000/0,1,3;

	8001/0,1,3; 8002-8004/3; 8005/0,3; 8010/0, 8010/1,3; 8021/3; 8320/3; 8452/1; 8710/3; 8711/0,3; 8713/0; 8811/3; 8840/0,3; 8896/3; 8980/3; 91730/0; 9503/3; 9580/0,3;
Not Classified by Central Brain Tumor Registry of United States (CBTRUS)	8050/1; 8246/0; 8272/1; 8683/3; 8712/0; 8720/0; 8726/0; 8772/0; 8821/1; 8858/3; 9084/1; 9120-9121/1; 9160/0; 9161/0,3; 9172/0; 9350/0,3; 9380/0,1; 9383/3; 9384/0; 9391/0,1; 9393/0; 9394/3; 9400/0,1; 9401/0; 9413/1; 9424/0; 9430/0; 9440/1; 9451/0; 9490/1; 9505/0; 9522/1; 9531/1,3; 9532/1; 9534/1; 9537/1,3; 9538-9539/0; 9571/1; 9581/3; 9688/3; 9712/3; 9751/3; 9971/3

*International Classification of Diseases for Oncology, 3rd Edition, 2000. World Health Organization, Geneva, Switzerland.

Appendix B: Morphology codes (ICD-O-3) by histology grouping observed in four provinces 2010-2015 (AB, BC, MB, ON)

Histology Groups	**ICD-O-3 Histology and Behavior Code***
Tumours of Neuroepithelial Tissue	
pilocytic astrocytoma	9421/3
diffuse astrocytoma	9400/3, 9410/3, 9411/3, 9420/3
anaplastic astrocytom	9401/3
unique astrocytoma	9381/3, 9384/1, 9424/3
glioblastoma	9440/3, 9441/3, 9442/3
oligodendroglioma	9450/3
anaplastic olgiodendroglioma	9451/3, 9460/3
choroid plexus tumour	9390/0, 9390/1, 9390/3
oligoastrocytic tumor	9382/3
ependymal tumours	9383/1, 9391/3, 9392/3, 9393/3, 9394/1
glioma malignant, Not otherwise specified	9380/3
neuronal and mixed neuronal glial tumours	8680/0, 8680/1, 8693/1, 9412/1, 9413/0, 9442/1, 9492/0, 9493/0, 9505/1, 9505/3, 9506/1, 9509/1, 9522/3
tumors of the pineal region	9360/1, 9361/1, 9362/3
embryonal tumours	9470/3, 9471/3, 9472/3, 9473/3, 9474/3, 9490/0, 9490/3, 9500/3, 9501/3, 9508/3
other neuroepithelial tumours	9430/3, 9444/1
Tumors of Cranial and Spinal Nerves	9540/0, 9540/1, 9540/3, 9550/0, 9560/0, 9560/1, 9560/3, 9561/3, 9570/0, 9571/0
Tumours of the Meninges	
meningioma	9530/0, 9530/1, 9530/3, 9531/0, 9532/0, 9533/0, 9534/0, 9537/0, 9538/1, 9538/3, 9539/1, 9539/3
mesenchymal tumours	8800/3, 8802/3, 8803/3, 8804/3, 8805/3, 8806/3, 8810/3, 8815/0, 8815/3, 8830/3, 8850/0, 8861/0, 8890/0, 8900/3, 8910/3, 8990/1, 9040/3, 9150/0, 9150/1, 9150/3, 9170/0
primary melanocytic lesions	8720/3, 8728/0, 8728/1, 8728/3
other neoplasms related to the meninges	9161/1, 9220/0, 9220/3, 9370/3, 9371/3, 9535/0
Lymphomas & Hematopoietic Neoplasms	
lymphoma	9590/3, 9591/3, 9650/3, 9663/3, 9671/3, 9673/3, 9680/3, 9687/3, 9691/3, 9698/3, 9699/3, 9702/3, 9714/3
other hematopoietic neoplasms	9734/3, 9755/3, 9766/1, 9823/3, 9827/3, 9930/3
Germ Cell tumours, Cysts and Hetrotopias	8020/3, 9060/3, 9064/3, 9065/3, 9071/3, 9080/0, 9080/1, 9080/3, 9082/3, 9084/0, 9084/3, 9085/3, 9100/3

Tumours of the Sellar Region	8140/0, 8140/1, 8140/3, 8246/3, 8260/0, 8270/0, 8271/0, 8272/0, 8272/3, 8280/0, 8290/0, 8323/0, 9350/1, 9351/1, 9352/1, 9492/0
Unclassified Tumours	8000/0, 8000/1, 8000/3, 8001/0, 8001/1, 8001/3, 8004/3, 8005/3, 8010/0, 8010/3, 8711/0, 8840/0, 8980/3, 9120/0, 9120/3, 9121/0, 9131/0, 9173/0, 9503/3, 9580/3
Not Classified by Central Brain Tumor Registry of United States (CBTRUS)	8050/1, 8246/0, 8272/1, 8683/3, 8712/0, 8720/0, 8726/0, 8772/0, 8821/1, 8858/3, 9084/1, 9120/1, 9121/1, 9160/0, 9161/0, 9161/3, 9172/0, 9330/0, 9350/0, 9350/3, 9380/0, 9380/1, 9383/3, 9384/0, 9391/0, 9391/1, 9393/0, 9394/3, 9400/0, 9400/1, 9401/0, 9413/1, 9424/0, 9430/0, 9440/1, 9451/0, 9490/1, 9505/0, 9522/1, 9531/1, 9531/3, 9532/1, 9534/1, 9537/1, 9537/3, 9538/0, 9539/0, 9571/1, 9581/3, 9688/3, 9712/3, 9751/3, 9971/3

*International Classification of Diseases for Oncology, 3rd Edition, 2000. World Health Organization, Geneva, Switzerland

Appendix C: Brain Tumour Registry of Canada (BTRC), brain and other central nervous system tumour site groupings

Site	**ICD-O-3 Site Code***
Cerebrum	C710
Frontal lobe	C711
Temporal lobe	C712
Parietal lobe	C713
Occipital lobe	C714
Ventricle, Not otherwise specified	C715
Cerebellum, Not otherwise specified	C716
Brain stem	C717
Overlapping lesion of brain	C718
Brain, Not otherwise specified	C719
Spinal cord	C720
Cauda equina	C721
Olfactory nerve	C722
Optic nerve	C723
Acoustic nerve	C724
Cranial nerve, Not otherwise specified	C725
Overlapping lesion of brain and other central nervous system	C728
Nervous system, Not otherwise specified	C729
Cerebral meninges	C700
Spinal Meninges	C701
Meninges, Not otherwise specified	C709
Pituitary gland	C751
Craniopharyngeal duct	C752
Pineal gland	C753
Nasal cavity**	C300

*International Classification of Diseases for Oncology, 3rd Edition, 2000. World Health Organization, Geneva, Switzerland

*Ostrom, Q. T., Gittleman, H., Truitt, G., Boscia, A., Kruchko, C., & Barnholtz-Sloan, J. S. (2018). CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2011–2015. Neuro-oncology, 20(suppl_4), iv1-iv86

** ICD-O-3 histology codes 9522-9523 only

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