Canadian brain cancer survival rates by tumour type and region: 1992–2008

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ABSTRACT

OBJECTIVES: To investigate patterns of survival among brain cancer patients in Canada.

METHODS: Canadian Cancer Registry data were obtained for all patients with first-ever primary malignant brain tumours diagnosed between 1992 and 2008 ($n = 38,095$). Follow-up ended with patient death or December 31, 2008, whichever occurred first. Crude Kaplan–Meier estimates were calculated at one, two and five years post-diagnosis. Cox proportional hazard models were used to obtain adjusted hazard ratios by region for major histology types. A time-specific generalized linear model was used to obtain 5-year survival estimates for specific age group, sex and region for major histology types.

RESULTS: The overall five-year survival rate was 27%. No significant difference in survival rate over time is observed. The highest 5-year survival rate was 65% (95% CI: 62.5%–67.4%) for oligodendrogliomas and the lowest was 4.0% (95% CI: 3.7%–4.3%) for glioblastomas. Compared to Ontario, the adjusted 5-year glioblastoma survival estimates were lower in British Columbia, Alberta and the Prairie provinces (Manitoba and Saskatchewan), while the survival estimates were lower in all other regions for diffuse astrocytoma, and lower in Manitoba and Saskatchewan for anaplastic astrocytomas. Estimates were significantly higher for oligodendrogliomas in Alberta, and for anaplastic oligodendrogliomas in Alberta and Quebec ($p < 0.05$).

CONCLUSION: These data are consistent with previous literature in observing higher survival rates at younger ages, in female patients and for tumours with mixed oligo components. There is a need to further explore the underlying reasons for the observed variation in survival rates by region in an effort to improve the prognosis of brain cancer in the Canadian patient population.

KEY WORDS: Brain neoplasms; survival rate; Canada

La traduction du résumé se trouve à la fin de l'article.

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There is little information available on brain tumour incidence and survival among the Canadian population.[1,2] Available information provides an overall estimate of brain cancer survival without an assessment of patterns by age, sex, region or tumour subtype; these patterns may be influenced by clinical and policy decisions regarding treatment. It is not well recognized by the general population that there is wide variation in the prognosis of patients with brain cancers, depending on the tumour histology type, patient and clinical features, all of which may influence diagnosis and treatment. Based on information from many other countries,[3–7] it is well established that early age at diagnosis is associated with better prognosis for patients with these tumours, largely because the histology types that occur most frequently in younger age groups have a less aggressive nature. Mao[8] demonstrated an improvement in brain cancer survival rates in the Canadian province of Saskatchewan between 1967 and 1986 that was primarily due to survival improvement in patients under the age of 65. The objective of our study is to investigate survival patterns by region and histology among Canadian patients with malignant brain tumours diagnosed between 1992 and 2008, while adjusting for age and sex. Due to the regional nature of health care systems and health care guidelines in Canada, some provincial differences are expected to emerge. This information will allow health care providers and researchers to explore the reasons underlying regional differences in survival rates and make evidence-informed decisions about clinical guidelines and health care policy with this patient population.

METHODS

Cohort selection

Data were acquired after the combined approval of Statistics Canada and the University of Alberta's ethics board. Administrative data were obtained from the Canadian Cancer Registry (CCR, 2012 release) for patients with brain tumours (International Classification of Disease for Oncology (ICD-O) 2nd and 3rd edition topography codes C700–C729 and C751–C753) who were diagnosed between 1992 and 2008 across all Canadian provinces and territories. We excluded patients whose brain tumours are non-malignant (ICD-O-2/3 behaviour code 0/1/2, $n = 10,970$) and whose chronologic sequence numbers of multiple primaries are not one (CCR code TD2, $n = 2185$). Thus our cohort

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consists of patients with first-ever primary malignant brain cancer diagnosis between 1992 and 2008.

Survival time is the outcome of interest and age, sex, geographical region, diagnostic method and tumour histology were independent variables. We collapsed some regions together due to small sample size: the Atlantic provinces (New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador), the Territories (Northwest Territories, Nunavut and Yukon) and two Prairie provinces (Manitoba and Saskatchewan). We used CCR code T25 to categorize diagnostic methods broadly into "microscopically confirmed" and "non-microscopically confirmed" for patients diagnosed between 2004 and 2008. For patients diagnosed between 1992 and 2003, categories (CCR code T11) include "radiology or laboratory diagnosis other than histology, autopsy and cytology", "Surgery (without histology), or clinical diagnosis", "death certificate only" and "method of diagnosis unknown", all of which are classified as "non-microscopically confirmed". Histology types were grouped according to codes outlined by the Central Brain Tumor Registry of the United States (CBTRUS),[9] and the following seven histology types were selected for detailed analysis based on having 800 or more cases: glioblastomas (GBM), diffuse astrocytomas, gliomas (not otherwise specified) – hereinafter referred to as gliomas (NOS), oligodendrogliomas, anaplastic astrocytomas, oligoastrocytic tumours, and anaplastic oligodendrogliomas. All other histology types are collapsed into the "all others" category as an eighth histology type category.

Data analysis

The incidence of brain cancer and all-causes death was tabulated by sex, age groups, regions, diagnostic method and histology. Crude Kaplan-Meier survival estimates were calculated at one, two and five years for each histology group. We chose the earliest death clearance cut-off date among all provinces, December 31, 2008, as the censoring date. The observed survival (OS) estimates were reported instead of the relative survival (RS) estimates, mainly because these two rates are very close. The five-year survival estimates are 25% (RS) vs. 24% (OS) for brain cancer patients 15 years and older diagnosed in 2006–2008.[10]

Since the proportional hazard (PH) assumption does not hold for the variable age group for any histology type, age-stratified Cox PH models were fitted for each histology type to estimate the adjusted hazard ratios for regions. However, the stratification increases the uncertainty in the estimation of model-based survival rates. To obtain unbiased and efficient model-based age-, sex- and region-specific 5-year survival rate estimates, separate time-specific generalized linear models were used for each of the histology types.[11,12] Our primary analyses used all cases regardless of their diagnosis method.

Estimates for territories were not reported from the crude Kaplan-Meier and model-based analyses due to their small sample sizes. Survival estimates for the <20 years age group from the model-based analyses were not reported, in order to concentrate on the Canadian adult population. All analyses were performed using statistical software SAS 9.4 (SAS Institute, Cary, NC) and R 3.1.3.[13] All frequencies and proportions presented are subject to rounding in accordance with Statistics Canada requirements.

RESULTS

A total of 38,095 patients were diagnosed with first-ever primary malignant brain tumours between 1992 and 2008 in Canada. There is no improvement in survival rates over time during the study period (data not shown). The frequencies and the corresponding observed deaths are summarized in Table 1 for age groups, sex, regions and diagnostic method. Tumours occurred more frequently in males (56%) than in females (44%), and in older than in younger age groups. Patients over the age of 65 years accounted for 37% of the study population and 46% of deaths, while those under age 20 years made up 11% of the study population and accounted for less than 5% of the deaths. The frequency of patients by region reflected the population size in each province; the largest proportion of patients were diagnosed in Ontario (39%) and Quebec (26%), followed by British Columbia (12%). Manitoba and Saskatchewan combined accounted for 7.0% of brain cancers.

Histology type-specific incidence, death and 1-, 2- and 5-year survival estimates are shown in Table 2. The most common histology was GBM (37%) followed by diffuse astrocytomas (15%). In descending order, the estimated 5-year survival rates are: 65% (95% CI: 62.5%–67.4%) for oligodendrogliomas, 46% (95% CI: 42.6%–49.3%) for oligoastrocytic tumours, 41.5% (95% CI: 37.9%–45.0%) for anaplastic oligodendrogliomas, 33.9% (95% CI: 31.6%–36.2%) for gliomas (NOS), 26.6% (95% CI: 25.4%–27.8%) for diffuse astrocytomas, 18.2% (95% CI: 15.8%–20.7%) for anaplastic astrocytomas, and 4.0% (95% CI: 3.7%–4.3%) for GBM.

Figure 1 displays histology type-specific Kaplan-Meier survival curves for brain cancer patients. Long-term prognosis was best for patients with oligodendrogliomas and all other tumours, and poorest for patients with GBM. Survival curves show a poor survival experience within the first few years of diagnosis for gliomas (NOS), diffuse astrocytomas, anaplastic astrocytomas and

Table 1. Frequency of malignant first-ever primary brain tumour diagnosis and death by sex, age, region and diagnostic method during 1992–2008 in Canada

	N	Death
Overall	38,095	28,460
Sex		
Male	21,260	16,140
Female	16,835	12,325
Age (years)		
≤20	4080	1315
21–44	7370	3875
45–64	12,660	10,240
≥65	13,985	13,030
Region		
Ontario	14,700	10,265
Quebec	9920	7570
British Columbia	4705	3775
Alberta	3210	2415
Atlantic provinces*	2950	2340
Prairie provinces†	2550	2060
Territories‡	60	35
Diagnostic method		
Microscopically confirmed	28,720	21,440
Non-microscopically confirmed	9375	7020

* Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador.
† Manitoba and Saskatchewan.
‡ Northwest Territories, Nunavut and Yukon.

Table 2. Histology type-specific incidence, death and Kaplan-Meier survival estimates at one, two and five years post diagnosis for brain cancer patients

Histology	*N*	Death	Kaplan-Meier survival estimate		
			1-year % (95% CI)	2-year % (95% CI)	5-year % (95% CI)
Glioblastoma (GBM)	14,120	13,340	26.5 (25.7–27.2)	9.5 (9.0–10.0)	4.0 (3.7–4.3)
Diffuse astrocytoma	5680	4475	48.9 (47.6–50.2)	36.1 (34.8–37.4)	26.6 (25.4–27.8)
Glioma, NOS	1845	1245	49.5 (47.1–51.8)	40.5 (38.2–42.8)	33.9 (31.6–36.2)
Oligodendroglioma	1715	785	87.5 (85.8–89.0)	80.7 (78.7–82.5)	65.0 (62.5–67.4)
Anaplastic astrocytoma	1100	900	47.9 (44.9–50.9)	33.1 (30.3–36.0)	18.2 (15.8–20.7)
Oligoastrocytic tumour	1030	590	78.0 (75.3–80.4)	63.0 (59.9 – 66.0)	46.0 (42.6–49.3)
Anaplastic oligodendroglioma	885	580	76.5 (73.6–79.2)	61.1 (57.7–64.3)	41.5 (37.9 – 45.0)
All others	11,725	6545	59.9 (59.0–60.8)	54.6 (53.7–55.6)	46.8 (45.8–47.7)
Overall	38,095	28,460	47.0 (46.5–47.5)	35.2 (34.7–35.6)	26.9 (26.5–27.4)

Note: NOS = not otherwise specified.

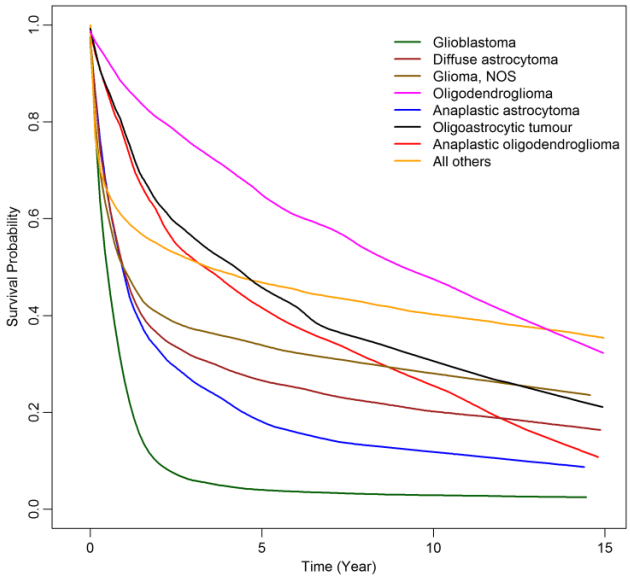

Figure 1. Kaplan-Meier survival curves for brain cancer patients, stratified by histology.

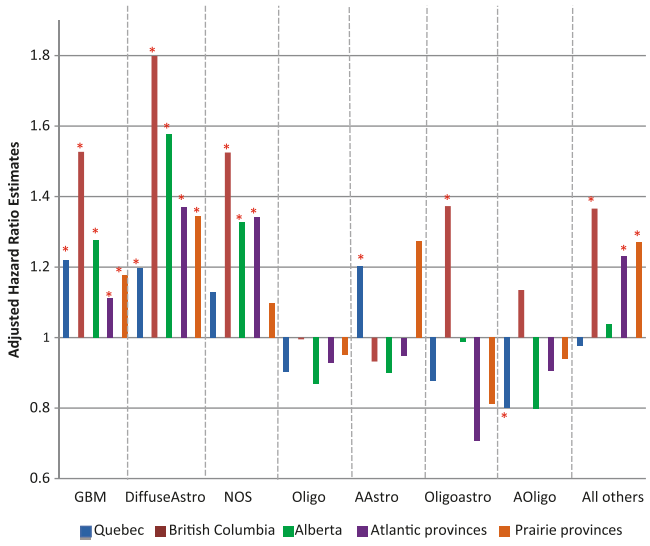

Figure 2. Adjusted hazard ratio estimates of regions by histological types, using stratified Cox proportional hazard models. The asterisk indicates that the hazard rate estimate of the corresponding province is statistically significantly different from the hazard rate of Ontario, which is the reference region ($p < 0.05$). GBM: glioblastoma; DiffuseAstro: diffuse astrocytoma; NOS: gliomas, NOS; Oligo: oligodendroglioma; AAstro: anaplastic astrocytoma; Oligoastro: oligoastrocytic tumour; AOligo: anaplastic oligodendroglioma. All others: all other histology types.

GBM, and a better survival experience for oligoastrocytic tumours, anaplastic oligodendrogliomas, oligodendrogliomas and all other tumours.

The region-specific Kaplan-Meier survival curves are shown in supplementary materials (Supplementary Figure A – see ARTICLE TOOLS section on journal website). Using Ontario as the reference province, the adjusted hazard ratio estimates of regions are shown in Figure 2 for the eight histological types. The patterns of hazard ratios were not consistent by region across the histology types. Compared to Ontario, the estimated hazard rates were significantly higher in all other provinces for GBM and diffuse astrocytomas ($p < 0.001$), and higher for gliomas (NOS) in British Columbia, Alberta and the Atlantic provinces ($p < 0.01$). Hazard rate estimate was significantly higher for anaplastic astrocytomas in Quebec ($p < 0.05$), for oligoastrocytic tumours in British Columbia ($p < 0.01$), and for all other tumours in British Columbia, the Atlantic provinces and the Prairie provinces ($p < 0.01$) when compared to Ontario. Estimated hazard rates were significantly lower for anaplastic oligodendrogliomas in Quebec ($p < 0.05$) and marginally lower for oligoastrocytic tumours in the Atlantic provinces ($p < 0.10$) when compared to Ontario. When we restricted the analyses to microscopically-confirmed cases only, the regional survival patterns remain largely unchanged in all histology types except for gliomas (NOS) and "all others".

Table 3 shows 5-year region-, age group- and sex-specific survival rate estimates for selected histology types – i.e., excluding the gliomas (NOS) and "all others" – obtained from the time-specific generalized linear models using all cases. The estimates for gliomas

Table 3. Estimated five-year survival probability (95% confidence interval) for selected histology types by region, age group, and sex when sex effect is significant ($p < 0.05$),* based on all cases (including non-microscopically confirmed)

Region	Age (years)	Histology										
		GBM	DiffuseAstro		Oligo		AAstro		Oligoastro		AOligo
			Male	Female	Male	Female	Male	Female	Male	Female	
Ontario	21–44	17.3 (15.2–19.6)	61.0 (57.2–64.5)	66.4 (62.8–69.7)	69.6 (64.9–73.8)	76.6 (72.3–80.4)	37.3 (30.3–44.2)	44.4 (36.8–51.8)	56.8 (49.4–63–6)	63.6 (56.3–69.9)	56.9 (50.2–63.0)
	45–64	3.5 (2.9–4.2)	24.5 (20.7–28.5)	31.2 (26.9–35.5)	47.6 (41.5–53.5)	58.0 (51.7–63.7)	7.7 (4.6–11.7)	12.1 (7.8–17.4)	29.8 (22.5–37.5)	37.9 (29.7–46.1)	27.1 (21.1–33.4)
	≥65	1.9 (1.5–2.4)	7.7 (5.4–10.4)	11.9 (9.0–15.2)	15.9 (9.9–23.2)	25.9 (18.4–34.1)	3.3 (1.4–6.6)	6.1 (3.2–10.3)	1.4 (0.3–4.5)	3.2 (0.9–8.1)	2.2 (0.6–6.0)
Quebec	21–44	18.7 (16.4–21.1)	56.4 (52.6–60.1)	62.2 (58.5–65.7)	72.6 (67.3–77.1)	79.0 (74.4–82.9)	35.7 (28.5–42.9)	42.9 (35.0–50.5)	63.8 (55.8–70.6)	69.7 (62.2–76.0)	68.2 (61.8–73.8)
	45–64	4.1 (3.4–4.8)	19.7 (16.4–23.1)	26.0 (22.2–29.9)	51.8 (44.3–58.9)	61.7 (54.4–68.1)	6.8 (4.0–10.8)	11.0 (6.9–16.3)	38.2 (29.0–47.2)	46.2 (36.5–55.3)	41.3 (33.6–48.7)
	≥65	2.3 (1.8–2.8)	5.1 (3.5–7.1)	8.5 (6.3–11.1)	19.6 (12.2–28.4)	30.2 (21.3–39.6)	2.9 (1.1–5.9)	5.4 (2.7–9.6)	3.3 (0.8–9.0)	6.5 (2.2–14.2)	7.6 (3.1–14.9)
British Columbia	21–44	7.7 (4.0–13.0)	37.3 (33.6–41.0)	44.2 (40.2–48.0)	69.0 (62.2–74.8)	76.1 (70.2–81.0)	51.0 (36.1–64.1)	57.5 (42.6–69.9)	54.8 (46.0–62.7)	61.7 (53.2–69.2)	49.8 (38.2–60.3)
	45–64	0.7 (0.2–2.0)	6.1 (4.8–7.5)	9.8 (7.9–11.9)	46.7 (37.6–55.3)	57.1 (48.2–65.1)	17.4 (7.4–30.9)	23.7 (11.4–38.5)	27.6 (19.9–35.8)	35.6 (26.9–44.4)	19.9 (11.4–30.1)
	≥65	0.3 (0.1–1.0)	0.6 (0.3–1.0)	1.4 (0.9–2.2)	15.2 (8.2–24.2)	25.0 (15.9–35.1)	9.9 (3.0–21.7)	14.9 (5.5–28.6)	1.0 (0.2–4.0)	2.6 (0.6–7.4)	0.9 (0.1–4.2)
Alberta	21–44	9.0 (6.4–12.0)	44.6 (39.7–49.3)	51.2 (46.3–55.9)	82.5 (76.7–87.0)	86.8 (82.0–90.4)	43.9 (31.3–55.7)	50.8 (37.8–62.4)	61.3 (52.5–69.0)	67.5 (58.8–74.8)	71.5 (59.9–80.3)
	45–64	1.0 (0.5–1.7)	10.1 (7.4–13.3)	14.9 (11.4–18.9)	67.4 (58.2–75.0)	74.8 (66.6–81.3)	11.7 (5.1–21.4)	17.2 (8.4–28.6)	35.1 (24.5–45.8)	43.2 (31.6–54.2)	46.0 (30.8–59.9)
	≥65	0.4 (0.2–0.8)	1.5 (0.8–2.6)	3.1 (1.8–4.9)	37.6 (24.7–50.5)	48.8 (35.5–60.8)	5.9 (1.7–13.8)	9.7 (3.5–19.7)	2.5 (0.4–8.1)	5.1 (1.3–13.3)	10.5 (2.7–24.4)
Atlantic provinces†	21–44	15.0 (12.0–18.4)	53.9 (48.7–58.8)	59.9 (54.9–64.5)	75.9 (66.4–83.1)	81.7 (73.8–87.4)	38.9 (27.3–50.4)	46.1 (34.0–57.3)	67.3 (55.5–76.5)	72.8 (62.2–80.8)	61.1 (49.9–70.6)
	45–64	2.7 (1.8–3.7)	17.3 (13.2–21.8)	23.3 (18.5–28.5)	56.9 (43.3–68.3)	66.0 (53.7–75.8)	8.6 (3.6–16.4)	13.3 (6.4–22.8)	42.8 (28.2–56.6)	50.6 (36.0–63.5)	32.0 (20.1–44.5)
	≥65	1.4 (0.9–2.1)	4.0 (2.3–6.4)	7.0 (4.5–10.2)	24.7 (11.8–40.0)	35.8 (20.8–51.0)	3.9 (1.1–9.8)	6.9 (2.5–14.6)	5.0 (0.8–15.2)	9.0 (2.2–21.8)	3.6 (0.6–11.5)
Prairie provinces‡	21–44	11.7 (8.7–15.2)	53.2 (47.4–58.7)	59.3 (53.7–64.4)	75.5 (67.9–81.5)	81.3 (74.9–86.2)	23.5 (12.4–36.7)	30.4 (17.6–44.3)	61.6 (49.3–71.7)	67.8 (56.2–76.9)	62.5 (46.3–75.1)
	45–64	1.7 (1.0–2.6)	16.6 (12.1–21.8)	22.6 (17.3–28.3)	56.1 (45.4–65.6)	65.4 (55.6–73.6)	2.3 (0.4–7.4)	4.5 (1.1–12.0)	35.4 (21.9–49.2)	43.5 (29.2–57.0)	33.7 (16.7–51.7)
	≥65	0.8 (0.4–1.4)	3.8 (2.0–6.3)	6.6 (4.0–10.0)	23.9 (13.4–36.2)	35.0 (22.8–47.4)	0.7 (0.1–3.5)	1.7 (0.2–6.3)	2.5 (0.3–9.6)	5.3 (1.0–15.1)	4.2 (0.5–15.6)

Note: "Glioma, NOS" and "all others" are not included because the survival estimates are different between all-cases analysis and microscopically-confirmed only cases analysis. GBM, glioblastoma; DiffuseAstro, diffuse astrocytoma; Oligo, oligodendroglioma; AAstro, anaplastic astrocytoma; Oligoastro, oligoastrocytic tumour; AOligo, anaplastic oligodendroglioma.

* Based on the time-specific generalized linear models. All numbers reported are in percentages.

† Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador.

‡ Manitoba and Saskatchewan.

(NOS) and "all others" were not provided because we observed large discrepancy between estimates from the all-case analysis and the microscopically-confirmed cases only analysis. Survival estimates were significantly higher for females than for males in all histology groups with the exception of GBM and anaplastic oligodendroglioma, where survival rate differences by sex were not statistically significant. Estimated survival decreased significantly as age-at-diagnosis increased from 21–44 years to 45–64 years, and to 65 years and over, in all histology groups studied. Compared to Ontario, the age- and sex-adjusted 5-year GBM survival estimates were lower in British Columbia, Alberta and the Prairie provinces ($p < 0.01$), and lower in the Prairies for anaplastic astrocytomas ($p < 0.05$). Survival estimates were significantly higher for oligodendrogliomas in Alberta ($p < 0.001$), and for anaplastic oligodendrogliomas in Alberta and Quebec ($p < 0.05$). The patterns of these 5-year survival rates by province(s) were similar but not the same when compared to the patterns of hazard rates by province(s) estimated from the Cox proportional hazard model. This is to be expected, as the Cox model assumes proportion hazard throughout the entire follow-up time while the time-specific generalized linear model takes a snap shot of the survival status at 5 years post diagnosis. Repeating Table 3 restricted to microscopically-confirmed cases provided estimates that were similar to those reported here, except for diffuse astrocytomas of all age groups in Quebec and oligoastrocytic tumours for age group 45–64 in Quebec and the Prairie provinces (lower by 2 percentage points or more in the microscopically-confirmed cases only analysis).

DISCUSSION

As expected, observed brain cancer survival rates tend to be higher in females than in males and in younger than in older age groups. These data are limited to patients with malignant brain tumours. Information on non-malignant tumours has not historically been available in most provinces,[1] so survival rates for these tumour categories await the accrual of prospective data.

Survival and hazard rate patterns by region and histology type suggest that there may be a number of underlying reasons for variation. There are known differences in how Quebec vs. other provinces records date of diagnosis,[14] but we anticipate this survival underestimate to be rather small in the context of the long-term rates presented. It is possible that variation in clinical presentation, diagnostic classification, patient care and treatment decisions (by the patient, the physician and/or due to system differences) may explain some of the variation in provincial rates. No treatment variables were available in the CCR data, which is a limitation of the data sources. Thus we were not able to assess its effect on survival and whether it confounds the relationship of survival rate and region. Other clinical factors, including tumour size and other prognostic factors, have not been considered in this analysis. We know that the health care system is driven by provincial policy and that clinical guidelines and chemotherapy drug coverage vary across provinces, factors that will be indirectly reflected in these data. For example, in current clinical practice, Avastin is a relatively new drug used for GBM treatment that is covered by insurance in Manitoba but not in Alberta. We also know that factors in the cancer care continuum may be present, such as access to primary care, access to medical specialist and/or

technology, delay in the referral process during cancer diagnostics and/or treatment phase, lack of care coordination, and adherence to treatment guidelines. Similar regional variation for other cancers in health care has been reported in Canada, the Netherlands and Italy,[15–17] indicating a need for routine monitoring across provinces/insurance providers.

We recognize that if histology is not classified consistently across provinces, then analyses by histology may be subject to measurement error and bias, contributing to the observed variable regional survival rates. The data did suggest possible variation in histology classification across regions. For example, British Columbia has a much higher proportion of diffuse astrocytomas and a much lower proportion of GBM than the rest of the country. It is possible that the BC survival rates reflect more advanced GBM tumours (classified as GBM) and less advanced GBM tumours (classified in the diffuse astrocytoma category) that would lower the estimated survival rates in both categories. Ontario has a much lower proportion of diffuse astrocytomas and a higher proportion of all other tumours. It is possible that some diffuse astrocytomas were classified into the all other tumours category, which could distort the true survival rates of both categories. The variation in microscopic confirmation, particularly for "all others" and gliomas (NOS) categories, also suggests some diagnostic variation which would be reflected in the histological classifications. Further assessment is needed to understand the variation in classification across regions. Going forward, surveillance data may need to incorporate the new molecular classification systems emerging for this type of information, which is expected to be increasingly clinically relevant.[18]

As the most populated provinces – Ontario and Quebec – tended to have the better survival rates, one might speculate that providing patient care for a rare disease is more effective when the number of patients is larger; but the better survival rates for the mixed tumours with oligo features outside of Ontario suggests that other health system factors may also be at play. Provinces with populations over large geographic regions may have urban/rural or socio-economic level factors that indirectly influence disease outcomes that have not been addressed in our analyses.

The international literature on overall brain cancer survival comes from a large number of regions: Europe, the UK, the Nordic countries, Australia, the US and Korea, and tends to be consistent in reporting improved survival rates beginning in the 1970s[3–8] through to the present.[19] In Canada, an improvement in survival rates for brain cancer patients between 1967 and 1986 was reported in the province of Saskatchewan which was attributed to patients under the age of 65 years.[8] In contrast, the UK reported an unexpected decline in survival during the late 1980s and 90s, with better survival rates emerging in males and younger age groups a decade later.[20] Histology-specific analysis such as that reported here has begun to explain some of these patterns by age and is needed to monitor changes in the histology-specific treatments now available. A recent analysis of GBM survival in the US suggests that the survival rates for these tumours did not progress much in the past three decades,[21] which agrees with our observation of no overall survival improvement for brain cancers from 1992 to 2008. The benefits of clinical trials, which changed the standard of practice for GBM, may now become apparent at the population level. US patients diagnosed in 2005–2006 had a 30% 2-year survival rate for GBM compared to 18% in 2000–2001.[21] Survival data on a histology-specific basis have not been available for the Canadian population previously.[1]

The ranking of these Canadian survival rates by histology is similar to that reported in CBTRUS for US data between 2005 and 2009.[22] The survival rates reported here are lower than those reported in the US for all histology groups. As noted above, there are differences in patient access to health insurance, access to care, clinical care guidelines and socio-cultural factors that may influence physician and patient decisions, reflecting these between-country survival differences. These data within Canada suggest the need to prioritize how to best approach implementing current evidence to improve brain cancer patient survival within Canada.

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REFERENCES

1. Davis F, Nagamuthu C, Ross J, Megyesi J. Current status of brain tumour surveillance in Canada and why it matters. *J Registry Manage* 2015;42(4): 139–45. PMID: 26938650.
2. Shaw A, Woods R, Semenciw R, Megyesi J. CNS tumours in Canada: Who are we missing? NAACCR 2014 Annual Conference: Capitalizing on Cancer Surveillance Data for Improved Cancer Control. Ottawa, 2014.
3. Shugg D, Allen BJ, Blizzard L, Dwyer T, Roder D. Brain cancer incidence, mortality and case survival: Observations from two Australian cancer registries. *Int J Cancer* 1994;59(6):765–70. PMID: 7989116. doi: 10.1002/(ISSN)1097-0215.
4. Sant M, Van Der Sanden G, Capocaccia R. Survival rates for primary malignant brain tumours in Europe. *Eur J Cancer* 1998;34(14):2241–47. doi: 10.1016/S0959-8049(98)00336-0.
5. Davis FG, Freels S, Grutsch J, Barlas S, Brem S. Survival rates in patients with primary malignant brain tumors stratified by patient age and tumor histological type: An analysis based on Surveillance, Epidemiology, and End Results (SEER) data, 1973–1991. *J Neurosurg* 1998;88(1):1–10. PMID: 9420066. doi: 10.3171/jns.1998.88.1.0001.
6. Bray F, Engholm G, Hakulinen T, Gislum M, Tryggvadóttir L, Storm HH, et al. Trends in survival of patients diagnosed with cancers of the brain and nervous system, thyroid, eye, bone, and soft tissues in the Nordic countries 1964–2003 followed up until the end of 2006. *Acta Oncol* 2010;49(5):673–93. PMID: 20192877. doi: 10.3109/02841861003610200.
7. Jung K, Yoo H, Kong H, Won Y, Park S, Lee SH. Population-based survival data for brain tumors in Korea. *J Neurooncol* 2012;109(2):301–07. PMID: 22660961. doi: 10.1007/s11060-012-0893-5.
8. Mao Y, Desmeules M, Semenciw RM, Hill G, Gaudette L, Wigle DT. Increasing brain cancer rates in Canada. *CMAJ* 1991;145(12):1583–91. PMID: 1742695.
9. Ostrom QT, Bauchet L, Davis FG, Deltour I, Fisher JL, Langer CE, et al. The epidemiology of glioma in adults: A "state of the science" review. *Neuro Oncol* 2014;16(7):896–913. PMID: 24842956.
10. Canadian Cancer Society's Advisory Committee on Cancer Statistics. *Canadian Cancer Statistics 2015*. Toronto, ON: Canadian Cancer Society, 2015.
11. Zhou QM, Zheng Y, Chibnik LB, Karlson EW, Cai T. Assessing incremental value of biomarkers with multi-phase nested case-control studies. *Biometrics* 2015;71(4):1139–49. PMID: 26195245. doi: 10.1111/biom.12344.
12. Uno H, Cai T, Tian L, Wei L. Evaluating prediction rules for t-year survivors with censored regression models. *J Am Stat Assoc* 2007;102(478):527–37. doi: 10.1198/016214507000000149.
13. R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: The R Foundation for Statistical Computing. 2015. Available at: http://www.R-project.org/ (Accessed May 12, 2016).
14. Ellison LF, Gibbons L. Five-year relative survival from prostate, breast, colorectal and lung cancer. *Health Rep* 2001;13(1):21–34.

15. Canadian Partnership Against Cancer. *Prostate Cancer Control in Canada: A System Performance Spotlight Report*. Toronto, ON: CPAC, 2015.
16. Wouters MWJM, Siesling S, Jansen-Landheer ML, Elferink MA, Belderbos J, Coebergh JW, Schramel FM. Variation in treatment and outcome in patients with non-small cell lung cancer by region, hospital type and volume in the Netherlands. *Eur J Surg Oncol* 2010;36:S83–92. PMID: 20598845. doi: 10.1016/j.ejso.2010.06.020.
17. Sant M, Minicozzi P, Allemani C, Cirilli C, Federico M, Capocaccia R, et al. Regional inequalities in cancer care persist in Italy and can influence survival. *Cancer Epidemiol* 2012;36(6):541–47. PMID: 22770694. doi: 10.1016/j.canep.2012.06.006.
18. Louis DN, Perry A, Burger P, Ellison DW, Reifenberger G, von Deimling A, et al. International Society of Neuropathology-Haarlem Consensus Guidelines for Nervous System Tumor Classification and Grading. *Brain Pathol* 2014;24(5):429–35. PMID: 25345897. doi: 10.1111/bpa.12171.
19. Kohler BA, Ward E, McCarthy BJ, Schymura MJ, Ries LA, Eheman C, et al. Annual report to the nation on the status of cancer, 1975–2007, featuring tumors of the brain and other nervous system. *J Natl Cancer Inst* 2011;103(9):714–36. PMID: 21454908. doi: 10.1093/jnci/djr077.
20. Rachet B, Mitry E, Quinn MJ, Cooper N, Coleman MP. Survival from brain tumours in England and Wales up to 2001. *Br J Cancer* 2008;99(suppl 1):S98–101. PMID: 18813276. doi: 10.1038/sj.bjc.6604603.
21. Koshy M, Villano JL, Dolecek TA, Howard A, Mahmood U, Chmura SJ, et al. Improved survival time trends for glioblastoma using the SEER 17 population-based registries. *J Neurooncol* 2012;107(1):207–12. PMID: 21984115. doi: 10.1007/s11060-011-0738-7.
22. Dolecek TA, Propp JM, Stroup NE, Kruchko C. CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2005–2009. *Neuro Oncol* 2012;14(suppl 5):v1–49. PMID: 23095881. doi: 10.1093/neuonc/nos218.

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RÉSUMÉ

OBJECTIFS : Étudier les profils de survie des patients atteints d'un cancer du cerveau au Canada.

MÉTHODE : Nous avons obtenu les données du Registre canadien du cancer sur tous les patients atteints d'une première tumeur cérébrale maligne primaire diagnostiquée entre 1992 et 2008 ($n = 38\ 095$). Le suivi s'est terminé au décès des patients ou au 31 décembre 2008, selon la première des deux éventualités. Des estimations de Kaplan-Meier brutes ont été calculées à un, deux et cinq ans après le diagnostic. Nous avons utilisé des modèles des risques proportionnels de Cox pour obtenir des coefficients de danger ajustés par région pour les grands types histologiques, respectivement. Un modèle linéaire généralisé dans le temps a servi à obtenir des estimations de survie après 5 ans par groupe d'âge, par sexe et par région pour les grands types histologiques.

RÉSULTATS : Le taux de survie global était de 27 %. On n'observe aucun écart significatif dans le taux de survie au fil du temps. Le taux de survie le plus élevé après 5 ans était de 65 % (IC de 95 % : 62,5 %–67,4 %) pour les oligodendrogliomes; le plus faible était de 4 % (IC de 95 % : 3,7 %–4,3 %) pour les glioblastomes. Comparativement à l'Ontario, les estimations ajustées de survie au glioblastome après 5 ans étaient inférieures en Colombie-Britannique, en Alberta et dans les provinces des Prairies (Manitoba et Saskatchewan), tandis que les estimations de survie étaient inférieures dans toutes les autres régions pour les astrocytomes diffus, et inférieures au Manitoba et en Saskatchewan pour les astrocytomes anaplasiques. Les estimations étaient sensiblement plus élevées pour les oligodendrogliomes en Alberta, et pour les oligodendrogliomes anaplasiques en Alberta et au Québec ($p < 0,05$).

CONCLUSION : Ces données sont conformes à celles d'études antérieures où l'on a observé des taux de survie supérieurs chez les jeunes patients, chez les femmes et pour les tumeurs mixtes (oligo-astrocytomes). Il faudrait pousser la recherche sur les raisons sous-jacentes de la variation observée des taux de survie par région afin d'améliorer le pronostic du cancer du cerveau dans la population de patients au Canada.

MOTS CLÉS : tumeurs du cerveau; taux de survie; Canada