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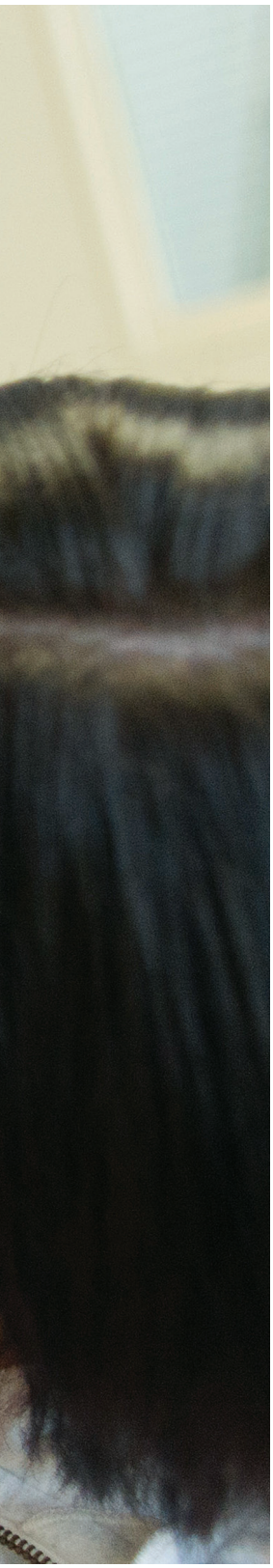
Mark L. Greenberg, OC, MB, ChB, FRCPC
Mohamed Agha, PhD
Jason D. Pole, PhD
Peter Gozdyra, MA
Jack Williams, PhD, FCES
Bruna DiMonte, BScN, RN



3

Incidence Patterns and Trends

Executive Summary

Data concerning 6,193 cases of childhood cancer (in the 0–14 year age group) diagnosed between 1985 and 2004, systematically recorded and grouped according to the International Classification of Childhood Cancer, third edition (ICCC-3), have been analyzed to describe the incidence patterns in Ontario.

Over the majority of the period analyzed, the incidence rate varied between 145 and 152.3 per million children. These incidence rates are comparable to those of most international jurisdictions, including those published in the Surveillance, Epidemiology and End Results (SEER) study and *Canadian Cancer Statistics*. The diseases with the highest incidence rates were leukemia (age standardized incidence rate [ASIR] of 45.5 per million), tumours of the central nervous system (CNS) (31.9 per million) and lymphoma and reticuloendothelial neoplasms (15.9 per million).

Age-specific incidence rates reveal the predominance of acute leukemia, specifically acute lymphoblastic leukemia (ALL), and CNS tumours, specifically astrocytomas, in the 1–4 year age group. By contrast, in children younger than 1 year, neuroblastoma and germ cell and soft tissue tumours predominate. In 10–14 year olds, lymphoma and bone tumours are most frequent. No significant change in incidence rate was detected for the major tumour categories, with the possible exception of astrocytomas, notably juvenile astrocytomas, seen in the late 1980s and early 1990s, after which the rate returned to baseline. This change is thought to represent a higher detection rate of astrocytomas related to neurofibromatosis type 1 resulting from the introduction of computed tomography (CT) and magnetic resonance imaging (MRI) screening.

Analysis of gender distribution reveals that for some malignancies there is male predominance (lymphoma and hepatoblastoma), with quite a remarkable male:female ratio of 4.56:1 in the case of Burkitt lymphoma. By contrast, for renal tumours and germ cell tumours the male:female ratio is reversed. Most remarkably, for thyroid cancers, the male:female ratio dropped dramatically over the observation period, from 0.95:1 in the earliest observation period to 0.22:1 for 2000–2004.

An exploratory mapping exercise tracking childhood cancer incidence across the census divisions of Ontario is presented. The mapping process used both the choropleth method and the Kriging procedure. While there is some variation of distribution across the province, no clear cut geographical pattern emerges.

Introduction

Childhood cancer differs from its adult counterpart in many respects. The spectrum of cancers is different, the biological behaviour is different and the treatment is very intense and most often occurs at a critical stage of physical, emotional and developmental evolution. Because of the severity of the disease and the intensity of treatment, childhood cancer, a relatively rare event, disproportionately affects the health care system.

Childhood cancer was the leading disease cause of death in Canada in the 0–14 year age range over the entire period covered in this Atlas; this continues to be true. While childhood cancer constitutes only 1–1.5% of incident cancers, the high cure rate and longevity of survivors renders it among the most significant contributors to potential years of life saved. Thus on 2 grounds, mortality rate and survival contribution, childhood cancer has impacts apparently disproportionate to its incidence rate.

Descriptive epidemiology may provide useful insights into patterns and trends of occurrence and may influence the study of causation, particularly when combined with contemporary molecular biology. Patterns of geographic distribution lend themselves to studies of etiology and socio-demographic influences on outcomes. Descriptive epidemiology may also enable understanding of health care utilization and system needs, prediction of future needs and health care resource planning.

Over the 20 years covered by this Atlas, 6,193 cases were registered in the Pediatric Oncology Group of Ontario Networked Information System (POGONIS) database, with a consistent registration process over that time. This number reflects a population capture and is larger than many country-specific databases included in the European Automated Childhood Cancer Information System (ACCIS) project. Thus analysis of overall incidence of childhood cancer, and of specific subtypes in the delimited population of Ontario, may be of interest to a range of clinicians, scientists and health planners, in addition to epidemiologists. Combined with an understanding of treatment patterns and health care utilization, the nature of the impact on the current and future health of the population can be estimated. This chapter reports on the analysis of incidence and compares Ontario's incidence with that of other jurisdictions with the hope that doing so will stimulate further study and analysis by interested investigators and planners.

The POGONIS database classifies childhood cancer according to the International Classification of Childhood Cancer, third edition (ICCC-3).[1] This classification divides childhood cancer into 12 groups, each of which has subgroups. Only select subgroups are presented in detail in specific chapters in this Atlas. These subgroups become increasingly important as substantial differences in their basic biology are uncovered.

There is an important caveat, however, regarding the analysis of subgroups in any registry population. Shifts in classification and refining of specificity of diagnoses occur over time as a result of the advent of ever more sophisticated diagnostic tools, including immunohistochemistry and molecular diagnostics. These advances permit finer dissection of categories and re-assignment of some entities to other categories. Some disease entities had not been identified at the time of diagnosis of a proportion of cases in the database. If these cases were diagnosed today, they would be assigned to a different classification category, most frequently within the same major ICCC-3 group but occasionally to a completely different group.

Such reclassification cannot be achieved in retrospect without re-examining tissue specimens using contemporary methodology – an undertaking inappropriate for an Atlas but an opportunity awaiting eager investigators. Thus, as in all registries, individual cases are classified according to the definitive pathology report issued at the time of diagnosis of the malignancy. Since this is a universal practice, comparability among jurisdictions is possible.

Methodology

Incidence rates reported in this chapter are based on all childhood cancer patients (age 0–14 years at time of diagnosis) diagnosed between 1985 and 2004 and registered in POGONIS.

Every occurrence of childhood cancer is considered an incident "case." In subjects diagnosed with a subsequent, different primary cancer during follow up, each cancer was considered an incident case.

The malignancies reported are classified according to ICCC-3. It should be noted that 43 CNS low grade gliomas are included in the CNS chapter of this Atlas but not in the Incidence, Health Service Utilization or Survival chapters. This is because these cases were diagnosed radiologically, without pathologic confirmation, and were detected only by comparison with an imaging database. These cases are therefore not registered in the Ontario Cancer Registry and vital status cannot be confirmed.

Discussion

EXHIBIT 3.1: **Incidence rate (per million) of childhood cancer, by diagnosis, age 0–14 years, in Ontario, 1985–2004**

Diagnostic group	Sub-group	Total no. of cases	Incidence rate/million: Total (1985–2004)	1985–1989	1990–1994	1995–1999	2000–2004
I	**Leukemias, myeloproliferative diseases and myelodysplastic diseases**	**2022**	**46.69**	**45.11**	**47.04**	**49.66**	**44.77**
	a. Lymphoid leukemias*	1591	36.73	36.59	36.49	36.33	36.73
	b. Acute myeloid leukemias†	319	7.37	8.21	9.19	6.08	7.37
	c. Chronic myeloproliferative diseases	22	0.51	0.56	0.35	0.43	0.51
	Other	90	—	—	—	—	—
II	**Lymphomas and reticuloendothelial neoplasms**	**650**	**15.01**	**12.68**	**14.84**	**14.40**	**17.56**
	a. Hodgkin lymphomas	256	5.91	6.16	5.48	6.35	5.91
	b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	219	5.06	5.41	5.30	5.56	5.06
	c. Burkitt lymphoma	110	2.54	2.52	1.77	3.22	2.54
	Other	65	—	—	—	—	—
III	**Central nervous system and miscellaneous intracranial and intraspinal neoplasms**	**1383**	**31.93**	**27.42**	**36.40**	**32.43**	**31.12**
	a. Ependymomas and choroid plexus tumours	119	2.75	2.61	2.21	2.96	2.75
	b. Astrocytomas	761	17.57	21.66	17.41	16.17	17.57
	c. Intracranial and intraspinal embryonal tumours	298	6.88	6.63	7.07	8.17	6.88
	Other	205	—	—	—	—	—
IV	**Neuroblastoma and other peripheral nervous cell tumours**	**446**	**10.30**	**10.13**	**11.20**	**10.69**	**9.21**
	a. Neuroblastomas and ganglioneuroblastomas	438	10.11	11.11	10.43	9.04	10.11
	Other	8	—	—	—	—	—
V	**Retinoblastoma**	**169**	**3.90**	**3.27**	**3.62**	**4.52**	**3.90**
VI	**Renal tumours**	**362**	**8.36**	**8.59**	**8.96**	**9.37**	**6.61**
	a. Nephroblastomas and other nonepithelial renal tumours	339	7.83	8.39	8.49	8.66	5.91
	Other	23	—	—	—	—	—
VII	**Hepatic tumours**	**99**	**2.29**	**2.43**	**2.03**	**2.61**	**2.29**
VIII	**Malignant bone tumours**	**296**	**6.83**	**7.37**	**6.81**	**6.98**	**6.26**
	a. Osteosarcomas	146	3.37	3.27	3.27	2.87	3.37
	b. Ewing tumour and related sarcomas of bone	137	3.16	3.55	3.36	2.69	3.16
	Other	13	—	—	—	—	—

*Almost exclusively acute lymphoblastic leukemia
†Including chronic myeloid leukemia

continued on following page

EXHIBIT 3.1: **Incidence rate (per million) of childhood cancer, by diagnosis, age 0–14 years, in Ontario, 1985–2004** (cont'd)

Diagnostic group	Sub-group	Total no. of cases	Incidence rate/million: Total (1985–2004)	1985–1989	1990–1994	1995–1999	2000–2004
IX	**Soft tissue and other extraosseous sarcomas**	**393**	**9.07**	**7.67**	**8.40**	**8.92**	**11.04**
	a. Rhabdomyosarcomas	165	3.81	4.11	3.09	4.17	3.81
	Other	228	—	—	—	—	—
X	**Germ cell tumours, trophoblastic tumours and neoplasms of gonads**	**185**	**4.27**	**4.09**	**3.17**	**4.68**	**5.04**
	d. Gonadal carcinomas	74	1.71	1.40	1.86	2.35	1.71
	Other	111	—	—	—	—	—
XI	**Other malignant epithelial neoplasms and malignant melanomas**	**128**	**2.96**	**2.86**	**1.12**	**3.18**	**4.52**
	b. Thyroid carcinomas	50	1.15	0.47	1.33	1.39	1.15
	d. Malignant melanomas	20	0.46	0.37	0.09	0.61	0.46
	Other	58	—	—	—	—	—
XII	**Other and unspecified malignant neoplasms**	**60**	**1.39**	**1.12**	**1.86**	**1.13**	**1.39**
	Total	6193					

*Almost exclusively acute lymphoblastic leukemia
†Including chronic myeloid leukemia

Exhibit 3.1

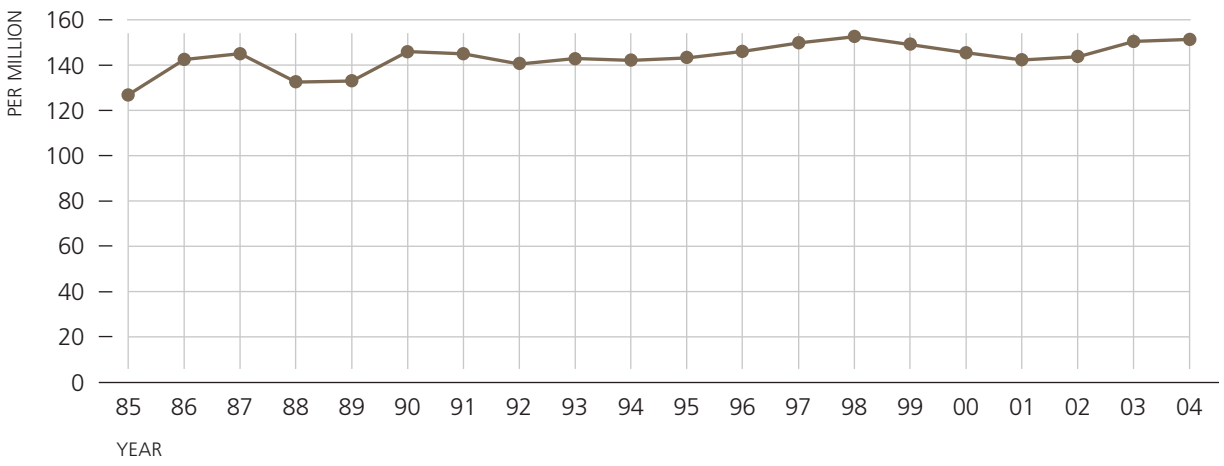
Type-specific incidence rates

Exhibit 3.1 provides the absolute numbers of cases in each of the 12 ICCC-3 categories and in the major subcategories, as well as the resultant incidence rates. The category "other" is used to denote all cases not identified in the major subcategories, and since it is a catch all grouping, incidence rates are not displayed.

For type-specific incidence rates, patients were grouped based on ICCC-3 into diagnosis groups. Patients were further grouped into 5 year intervals (1985–1989, 1990–1994, 1995–1999 and 2000–2004) and cumulative incidence rates are reported for each period.

For the denominator, we used the Ontario population age 0–14 years for the period 1985–2004. For each 5 year period, the 0–14 year old population for that period was determined and used as the denominator. The total number of cases of childhood cancer during the period was used as numerator. The same methodology was used for estimating the incidence rate for all years combined. Incidence rates are reported per million population.[2]

EXHIBIT 3.2: **Age-standardized smoothed incidence rate (per million) of childhood cancer, trend over time, age 0–14 years, in Ontario, 1985–2004**



The reader may note differences in the ASIRs reported in this chapter from those reported in the Survival chapter (Exhibit 4.1). These differences relate to the exclusion of cases from the data set used in the survival chapter that did not link to either the Ontario Cancer Registry or the Ontario Registrar General death file. The incidence rates identified in this chapter are the appropriate rates for quotation.

Exhibit 3.2

To reduce the effect of random variations on incidence trends, we used a 3 year moving average technique to smooth the trend. With this method, the moving average in each year is derived from averaging a weighted incidence value in the index year, the subsequent year and the prior year. The highest weight (0.5) was assigned to the index year and a weight of 0.25 was assigned to the prior and subsequent years. For the tail years, we used 0.75 for the index year and 0.25 for the year before or after it.

Age-specific and age-standardized incidence rates

EXHIBIT 3.3: **Age-specific and age-standardized incidence rates of childhood cancer, by diagnosis, age 0–14 years, in Ontario, 1985–2004**

Diagnostic group	Sub-group	Age-specific incidence rate per million per year, 1985–2004					
		Age < 1	Age 1–4	Age 5–9	Age 10–14	All ages	Age-standardized rate
I	**Leukemias, myeloproliferative diseases and myelodysplastic diseases**	**38.13**	**87.44**	**38.01**	**24.94**	**46.69**	**45.50**
	a. Lymphoid leukemias*	18.34	74.41	30.67	16.67	36.73	35.70
	b. Acute myeloid leukemias†	13.67	10.23	5.28	5.99	7.37	7.46
	c. Chronic myeloproliferative diseases	—	0.44	0.34	0.83	0.51	1.18
II	**Lymphomas and reticuloendothelial neoplasms**	**4.32**	**8.13**	**14.27**	**23.08**	**14.96**	**15.93**
	a. Hodgkin lymphomas	—	0.96	3.36	13.50	5.91	7.44
	b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	0.72	3.41	6.17	6.06	5.06	5.41
	c. Burkitt lymphoma	—	2.45	3.50	2.14	2.54	2.91
III	**Central nervous system and miscellaneous intracranial and intraspinal neoplasms**	**28.42**	**39.17**	**32.38**	**26.45**	**31.93**	**31.94**
	a. Ependymomas and choroid plexus tumours	5.40	4.90	1.65	1.65	2.75	3.07
	b. Astrocytomas	10.79	21.51	18.45	14.88	17.57	17.73
	c. Intracranial and intraspinal embryonal tumours	7.55	9.01	7.75	4.20	6.90	7.08
IV	**Neuroblastoma and other peripheral nervous cell tumours**						
	a. Neuroblastomas and ganglioneuroblastomas	55.39	19.50	3.36	0.83	10.11	10.88
V	**Retinoblastoma**	**26.60**	**7.90**	**0.30**	—	**3.90**	**5.30**
VI	**Renal tumours**	**14.00**	**20.30**	**5.00**	**1.20**	**8.40**	**8.80**
	a. Nephroblastomas and other nonepithelial renal tumours	14.03	19.59	4.66	0.55	7.83	8.65
VII	**Hepatic tumours**	**11.15**	**3.50**	**1.10**	**0.83**	**2.29**	**2.86**
VIII	**Malignant bone tumours**	**1.08**	**1.49**	**5.90**	**13.09**	**6.80**	**8.06**
	a. Osteosarcomas		0.44	2.61	7.10	3.40	4.31
	b. Ewing tumour and related sarcomas of bone	0.36	0.96	3.16	5.44	3.20	3.83
IX	**Soft tissue and other extraosseous sarcomas**	**15.11**	**9.97**	**7.61**	**8.68**	**9.10**	**9.24**
	a. Rhabdomyosarcomas	3.24	5.77	4.18	2.00	3.81	4.10
X	**Germ cell tumours, trophoblastic tumours and neoplasms of gonads**	**12.95**	**4.02**	**2.13**	**4.96**	**4.30**	**4.61**
	d. Gonadal carcinomas	3.24	1.22	1.10	2.41	1.71	2.24
XI	**Other malignant epithelial neoplasms and malignant melanomas**	**1.08**	**0.79**	**2.40**	**5.58**	**3.00**	**3.77**
	b. Thyroid carcinomas	—	0.09	1.10	2.27	1.15	1.83
	d. Malignant melanomas	0.72	0.09	0.21	0.96	0.46	1.15
XII	**Other and unspecified malignant neoplasms**	**4.00**	**1.00**	**0.80**	**1.80**	**1.40**	**1.90**

*Almost exclusively acute lymphoblastic leukemia
†Including chronic myeloid leukemia

Exhibit 3.3

The age-specific incidence rate is the number of cases found in a given age group divided by the number of children in that age group in the general population in the same time period, expressed as rate per million. The population used for each age group was the corresponding population for Ontario for the years 1985–2004. Age-specific incidence rates (ASIR) are reported for age groups of less than 1 year, 1–4, 5–9 and 10–14 years.

The ASIR is a weighted average of the age-specific incidence rate, where the weights are the proportions of persons in the corresponding age groups in a standard population. This statistic reduces the potential confounding effect of age. The standard populations used in the calculations were the Ontario population in 1996 and the world population in 2000. Since there was no substantive difference in these rates, only the Ontario adjusted rate is shown. Direct standardization was used in estimating ASIRs.

Between 1985 and 1990 the ASIR increased from 126.8 per million to 145.8 per million, an increase of 15%. A sharp increase occurs between 1985 and 1986 and while the data have been verified, some of this increase may represent underreporting in 1985. The subsequent rise between 1988 and 1990 may in part be accounted for by more ready access to CT and MRI screening for low grade gliomas in patients with neurofibromatosis.

Since 1990, the overall incidence rate of childhood cancer among 0–14 year olds in Ontario has remained stable, varying between 145.8 and 152.3 per million. This rate is very close to reported rates for Canada during the same period,[3] which ranged from 144 to 159 per million with an ASIR for 2000–2004 of 149.7 per million.[4] Since Ontario's population constitutes over 40% of the Canadian population, the impact of Ontario's incidence rate on the Canadian incidence data is substantial.

Comparative data from international jurisdictions include SEER, which reports ASIRs for the same age group from 1985 to 2002 ranging from 139 to 155 per million, comparable to Ontario data reported here.[5] Australian population-based data for 1997–2006 show an equivalent ASIR of 157.5 per million. The incidence rate for Europe as a whole between 1988 and 1997, derived from registries from many European countries from the ACCIS, is reported as 139 per million. Rates varied from 130 to 160 per million among regions and from 116 to 173 per million among countries.[6] Similar regional and geographic variations in incidence have been reported for different regions of the U.S.[7] using data from both SEER and the National Program of Cancer Registries for diagnoses during the period 2001–2003. French national data for the period 2000–2004 show an ASIR of 155 per million.[8]

Approaches to and reliability of registration procedures vary by region and over time. The degree of consistency of ASIRs across most registries is thus reassuring. It is acknowledged, however, that differences exist both in overall incidence rates among countries and regions and in distribution of specific diagnostic groups across geographic regions. An example of such a difference is the dramatically increased incidence of thyroid carcinoma documented in the Belarus registry in ACCIS.[9]

When adjusted for age, leukemia (45.5 per million), central nervous system tumours (CNS) tumours (31.9 per million) and lymphoma and reticuloendothelial neoplasms (15.9 per million) were the most common incident malignancies. With respect to age-specific rates, rates for leukemia, specifically ALL, and for CNS tumours peak in the 1–4 year age group. Within the CNS category, astrocytoma is the most frequent type, with the majority of cases occurring in the 1–4 year old group.

Peak incidence for neuroblastoma and germ cell and soft tissue tumours occurred in the less than 1 year age group. Lymphoma and bone tumours are most prevalent in the 10–14 year age group.

Both the age-specific and age standardized rates reported in Exhibit 3.3 are similar to incidence rates reported in other jurisdictions, such as the U.S.[10]

Disease-specific analyses are reported below for the 5 most frequently occurring cancers, for which sample size permits detailed analysis.

Leukemia

Leukemias, myeloproliferative diseases and myelodysplastic diseases have an ASIR of 45.5 per million for the entire period. This rate is comparable to rates in other reporting jurisdictions. The rate overwhelmingly represents ALL, with an ASIR of 35.7 per million, compared with 7.5 for acute myeloblastic leukemia (AML). Age-specific rates demonstrate an expected higher rate of 74.4 per million in the 1–4 year age group for ALL. The incidence rate for all leukemias over the period 1985–2004 differs little by 5 year period. While the incidence rate for AML fluctuates between 6.08 per million for 1995–1999 and 9.19 per million for 1990–1994, the total number of cases is small and the confidence intervals are wide.

Canadian national data reveal a marginally higher rate of 49.3 per million in the period 2000–2004.[4] SEER reports an ASIR over the period 1985–2002 of between 37 and 44 per million. The French ASIR for 2000–2004 was comparable at 45.9 per million,[8] as are Swiss data: 47.2 per million for all leukemias, 38.1 per million for ALL and 6.7 per million for AML in the period 1995–2004.[11] In Ontario there is a consistently elevated male:female ratio in the ASIR for ALL not seen in AML. Other jurisdictions report similar data.[8,12]

It is not possible on the basis of the Ontario data to determine subtypes of ALL by lineage classification.

A caveat to interpretation is important: the latest version of the International Classification of Diseases for Oncology (ICD-O),[13] implemented in 2001, incorporates myelodysplastic disorders of the bone marrow in the leukemia category and therefore assigns them a malignant behaviour code. Myelodysplastic disorders were not considered malignant in prior versions; comparison of data collected in earlier and later periods is therefore complicated by inclusion of these rare entities, the data for which are inconsistently collected.

Lymphoma and Reticuloendothelial Neoplasms

ICCC-3 group 2 includes Hodgkin lymphoma, non-Hodgkin lymphoma, Burkitt lymphoma and miscellaneous reticuloendothelial neoplasms, limited to true malignant histiocytic entities and systemic variants of Langerhans histiocytosis. Since the inclusion of these latter entities in ICCC-3 is recent, there is inconsistency over the sequential time periods reported in the literature; comparability with reports from other jurisdictions is thus complicated. Additionally, nosology and classification systems of lymphoma have changed over the period reported here, further complicating comparison of subgroups.

The ASIR for lymphoma in Ontario over the 20 year period is 15.0 per million. The reported incidence in the U.S. in the period 2001–2003 is 15.6 per million.[7] National incidence data for France in the period 2000–2004 show a higher rate, at 17.1 per million.[8] The incidence in Ontario over the same period is equivalent at 17.6 per million (Exhibit 3.1). There is no obvious change in the Ontario incidence rate over the entire period (data not shown).

The ASIR for Hodgkin lymphoma is 7.4 per million, comparable to French and U.S. data for 1985–2002 (5 per million). The age-specific incidence is substantially higher in the 10–14 year age group at 13.5 per million, compared with 3.4 per million in the 5–9 year group. Equivalent incidence figures for the U.S. for 2001–2003 are 11.8 and 3.93 per million.

Non-Hodgkin lymphoma, excluding Burkitt lymphoma, has an incidence rate of 5.4 per million, with higher age-specific rates in the 2 older quartile age groups. No incidence trend over time is discernible. These incidence data are similar to French rates. U.S. data reported for 1985–2002, which do not separate Burkitt lymphoma, show rates ranging from 6 to 10 per million, with a rate of 10 per million for 1998–2002.

The ASIR for Burkitt lymphoma over the timeframe of the study is 2.9 per million. The French rate for the period 2000–2004 is substantially higher at 4 per million. Age-specific incidence rates show no differences across age groups.

Central Nervous System and Miscellaneous Intracranial and Intraspinal Neoplasms

The ASIR for this group is 31.9 per million, comparable to that reported for Germany (31.9), the U.S. (32.0) and Switzerland (30.4), but lower than that reported for France (36.2).

The ICCC-3 includes in this category certain neoplasms not considered malignant in adult populations. In particular, juvenile pilocytic astrocytoma and other low grade astrocytomas, classified in ICD-O as neoplasms of uncertain behaviour and allocated a behaviour code of 1, are included in the ICCC-3. (ICD-O assigns a behaviour code of 3 to malignant neoplasms, 0 to benign neoplasms and 1 to neoplasms of indeterminate behaviour.) This group constitutes about 45% of astrocytomas[14] among people under 20 years of age, and an active decision was made to include them in ICCC-3. Other included entities are craniopharyngioma and pituitary adenomata – the data collection for both is less reliable because these tumours are frequently treated by neurosurgical services only and not identified by pathology reports as malignant. They are thus incompletely recorded in the Ontario dataset, but in the French report constitute less than 2% of ICCC-3 group 3.

Astrocytomas, including juvenile astrocytomas, constitute by far the largest proportion of group 3 tumours, followed by intracranial and spinal embryonal tumours and ependymomas, with ASIRs of 17.7, 7.1 and 3.1 per million, respectively. The comparable ASIRs for the French group in its 2000–2004 data are 13.6, 7.8 and 3.8 per million. The difference in the ASIR for astrocytoma stands out. The increase in the absolute numbers of astrocytomas diagnosed in the late 1980s and early 1990s may account for this difference, postulated to be the consequence of the widespread introduction of screening CT and MRI in patients with neurofibromatosis type 1 during that period, resulting in the pre-symptomatic identification of juvenile astrocytomas.[15] These rates dropped to baseline levels by 1996 and have remained at that level since. Across the age quartiles, astrocytomas have the highest ASIR, maximal in the 1–4 year age group.

The ASIR for non-astrocytic tumours remained constant across the periods under analysis.

Embryonal tumours, including intracranial and spinal embryonal tumours, constitute approximately 20% of the cases recorded over the 20 year period.

Neuroblastoma and Other Peripheral Nervous Cell Tumours

The ASIR of 10.9 per million is in line with data reported from Germany (12.0), the U.S. (10.8)[7] and Switzerland (10.4).[11] The rate reported for France of 14.5 is higher than rates in most other jurisdictions.

As expected, the age-specific rate is substantially higher in the youngest age group than in any other – with a rate in the first year of life of 55.4 per million. No significant variation is noted over the successive periods, in contrast to reports from Piedmont, Italy,[16] and the French data, which demonstrate an increasing rate from the first year of life over time, suggesting the influence either of screening programs or of improved access to care. The Ontario rates are virtually identical to those reported for the U.S., suggesting that access to care is not the reason for rate increases in the early years of life.

Nephroblastoma and Other Nonepithelial Kidney Tumours

Since only a small number of renal cell carcinomas are represented in the renal tumour category, this discussion focuses on nephroblastoma and variants, as classified in ICCC-3.

Nephroblastoma, group 6a in ICCC-3, encompasses clear cell sarcoma and renal rhabdoid tumours, which together constitute less than 5% of renal tumours in most registries. The overall ASIR for the 20 year period of 8.7 per million is consistent across periods, with a small decline in the last 5 year period. This ASIR compares closely to the reported European incidence for all renal tumours of 8.5 per million[17,18] in the period 1988–1997. In the European study, the incidence demonstrated an annual increase of 0.8%, with variation by geographic zone. The sample size in Ontario does not permit such granular analysis. SEER data for 2001–2003 demonstrate an ASIR for this age group of 8.5 per million.[7]

The age-specific incidence data demonstrate a peak incidence in the 1–4 year age group, followed by the less than 1 year age group. Similar trends are seen in the European and SEER datasets.

EXHIBIT 3.4: **Incidence rate (per million) of childhood cancer, by diagnosis, males, age 0–14 years, in Ontario, 1985–2004**

Diagnostic group	Sub-group	Total (1985–2004) No. of cases	Incidence rate/million	95% CI	1985–1989 Incidence rate/million	95% CI
I	**Leukemias, myeloproliferative diseases and myelodysplastic diseases**	**1114**	**50.21**	**47.74-52.69**	**48.46**	**43.35-53.57**
	a. Lymphoid leukemias*	892	40.21	37.99-42.42	40.88	36.19-45.58
	b. Acute myeloid leukemias†	166	7.48	6.53-8.44	6.18	4.36-8.01
	c. Chronic myeloproliferative diseases	8	0.36	0.15-0.57	0.60	0.03-1.17
	Other	48	—	—	—	—
II	**Lymphomas and reticuloendothelial neoplasms**	**415**	**18.70**	**17.15-20.17**	**16.80**	**13.75-19.76**
	a. Hodgkin lymphomas	143	6.45	5.56-7.33	5.78	4.02-7.55
	b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	147	6.63	5.73-7.53	5.98	4.19-7.78
	c. Burkitt lymphoma	91	4.10	3.39-4.81	4.19	2.68-5.69
	Other	34	—	—	—	—
III	**Central nervous system and miscellaneous intracranial and intraspinal neoplasms**	**772**	**34.80**	**32.74-36.86**	**30.71**	**26.64-34.78**
	a. Ependymomas and choroid plexus tumours	65	2.93	2.33-3.53	2.99	1.72-4.26
	b. Astrocytomas	401	18.08	16.59-19.56	15.95	13.02-18.89
	c. Intracranial and intraspinal embryonal tumours	202	9.11	8.05-10.16	7.18	5.21-9.15
	Other	104	—	—	—	—
IV	**Neuroblastoma and other peripheral nervous cell tumours**	**255**	**11.49**	**10.31-12.68**	**11.57**	**9.07-14.07**
	a. Neuroblastomas and ganglioneuroblastomas	250	11.27	10.10-12.44	11.37	8.89-13.84
	Other	5	—	—	—	—
V	**Retinoblastoma**	**89**	**4.01**	**3.31-4.71**	**2.99**	**1.72-4.26**
VI	**Renal tumours**	**161**	**7.26**	**6.32-8.20**	**7.58**	**5.56-9.60**
	a. Nephroblastomas and other nonepithelial renal tumours	149	6.72	5.81-7.62	7.38	5.38-9.37
	Other	12	—	—	—	—
VII	**Hepatic tumours**	**61**	**2.75**	**2.17-3.33**	**2.79**	**1.56-4.02**
VIII	**Malignant bone tumours**	**155**	**6.99**	**6.06-7.91**	**8.77**	**6.60-10.95**
	a. Osteosarcomas	83	3.74	3.07-4.42	4.79	3.18-6.39
	b. Ewing tumour and related sarcomas of bone	69	3.11	2.49-3.73	3.79	2.36-5.22
	Other	3	—	—	—	—
IX	**Soft tissue and other extraosseous sarcomas**	**222**	**10.01**	**8.90-11.11**	**9.97**	**7.65-12.29**
	a. Rhabdomyosarcomas	99	4.46	3.72-5.20	5.19	3.51-6.86
	Other	123	—	—	—	—

*Almost exclusively acute lymphoblastic leukemia
†Including chronic myeloid leukemia
CI = confidence interval

1990–1994		1995–1999		2000–2004	
Incidence rate/million	95% CI	Incidence rate/million	95% CI	Incidence rate/million	95% CI
52.23	**47.16-57.30**	**51.03**	**46.15-55.91**	**49.02**	**44.27-53.77**
40.58	36.11-45.05	38.27	34.05-42.50	41.19	36.83-45.55
9.65	7.47-11.82	8.62	6.61-10.63	5.45	3.86-7.03
0.55	0.03-1.06	0.69	0.12-1.26	0.34	-0.06-0.74
—	—	—	—	—	—
18.90	**15.87-21.98**	**16.20**	**13.46-18.96**	**22.50**	**19.25-25.68**
7.10	5.23-8.97	6.21	4.50-7.91	6.64	4.89-8.39
7.10	5.23-8.97	6.03	4.36-7.71	7.32	5.48-9.16
3.82	2.45-5.19	3.10	1.90-4.31	5.28	3.72-6.84
—	—	—	—	—	—
37.13	**32.85-41.40**	**36.20**	**32.09-40.31**	**34.72**	**30.72-38.72**
2.37	1.29-3.45	2.24	1.22-3.26	4.09	2.71-5.46
21.29	18.05-24.53	18.27	15.35-21.19	16.68	13.91-19.45
8.74	6.66-10.81	10.00	7.84-12.16	10.21	8.04-12.38
—	—	—	—	—	—
11.10	**8.76-13.44**	**11.72**	**9.38-14.06**	**11.57**	**9.27-13.88**
10.92	8.60-13.24	11.38	9.07-13.68	11.40	9.11-13.70
—	—	—	—	—	—
4.73	**3.21-6.26**	**3.79**	**2.46-5.12**	**4.43**	**3.00-5.85**
9.28	**7.14-11.42**	**6.55**	**4.80-8.30**	**5.79**	**4.15-7.42**
8.92	6.82-11.01	5.86	4.21-7.52	4.94	3.43-6.44
—	—	—	—	—	—
3.09	**1.86-4.33**	**2.07**	**1.09-3.05**	**3.06**	**1.88-4.25**
6.55	**4.76-8.35**	**7.59**	**5.70-9.47**	**5.28**	**3.72-6.84**
3.46	2.15-4.76	3.79	2.46-5.12	3.06	1.88-4.25
3.09	1.86-4.33	3.62	2.32-4.92	2.04	1.07-3.01
—	—	—	—	—	—
9.28	**7.14-11.42**	**9.65**	**7.53-11.78**	**11.06**	**8.81-13.32**
4.91	3.36-6.47	3.79	2.46-5.12	4.09	2.71-5.46
—	—	—	—	—	—

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EXHIBIT 3.4: **Incidence rate (per million) of childhood cancer, by diagnosis, males, age 0–14 years, in Ontario, 1985–2004** (cont'd)

Diagnostic group	Sub-group	Total (1985–2004) No. of cases	Incidence rate/million	95% CI	1985–1989 Incidence rate/million	95% CI
X	**Germ cell tumours, trophoblastic tumours and neoplasms of gonads**	**83**	**3.74**	**3.07-4.42**	**4.19**	**2.68-5.69**
	d. Gonadal carcinomas	30	1.35	0.95-1.76	1.20	0.39-2.00
	Other	53	—	—	—	—
XI	**Other malignant epithelial neoplasms and malignant melanomas**	**49**	**2.21**	**1.69-2.73**	**2.39**	**1.26-3.53**
	b. Thyroid carcinomas	16	0.72	0.42-1.02	1.40	0.53-2.26
	d. Malignant melanomas	6	0.27	0.09-0.45	0.40	-0.07-0.86
	Other	27	—	—	—	—
XII	**Other and unspecified malignant neoplasms**	**25**	**1.13**	**0.76-1.50**	**1.40**	**0.53-2.26**

*Almost exclusively acute lymphoblastic leukemia
†Including chronic myeloid leukemia
CI = confidence interval

EXHIBIT 3.5: **Incidence rate (per million) of childhood cancer, by diagnosis, females, age 0–14 years, in Ontario, 1985–2004**

Diagnostic group	Sub-group	Total (1985–2004) No. of cases	Incidence rate/million	95% CI	1985–1989 Incidence rate/million	95% CI
I	**Leukemias, myeloproliferative diseases and myelodysplastic diseases**	**908**	**42.98**	**40.63-45.33**	**41.59**	**36.72-46.45**
	a. Lymphoid leukemias*	699	33.09	31.03-35.15	34.23	29.82-38.65
	b. Acute myeloid leukemias†	153	7.24	6.28-8.21	5.46	3.70-7.22
	c. Chronic myeloproliferative diseases	14	0.66	0.37-0.95	0.84	0.15-1.53
	Other	42	—	—	—	—
II	**Lymphomas and reticuloendothelial neoplasms**	**235**	**11.08**	**9.89-12.27**	**8.40**	**6.22-10.59**
	a. Hodgkin lymphomas	113	5.35	4.52-6.18	5.46	3.70-7.22
	b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	72	3.41	2.75-4.07	1.47	0.56-2.38
	c. Burkitt lymphoma	19	0.90	0.56-1.24	1.05	0.28-1.82
	Other	31	—	—	—	—
III	**Central nervous system and miscellaneous intracranial and intraspinal neoplasms**	**611**	**28.92**	**27.00-30.85**	**23.94**	**20.25-27.63**
	a. Ependymomas and choroid plexus tumours	54	2.56	1.98-3.13	3.57	2.15-5.00
	b. Astrocytomas	360	17.04	15.56-18.52	13.86	11.06-16.67
	c. Intracranial and intraspinal embryonal tumours	96	4.54	3.78-5.31	3.57	2.15-5.00
	Other	101	—	—	—	—

*Almost exclusively acute lymphoblastic leukemia
†Including chronic myeloid leukemia
CI = confidence interval

	1990–1994		1995–1999		2000–2004	
	Incidence rate/million	95% CI	Incidence rate/million	95% CI	Incidence rate/million	95% CI
	2.73	**1.57-3.89**	**3.62**	**2.32-4.92**	**4.43**	**3.00-5.85**
	1.27	0.48-2.07	1.03	0.34-1.73	1.87	0.94-2.80
	—	—	—	—	—	—
	0.55	**0.03-1.06**	**2.07**	**1.09-3.05**	**3.74**	**2.43-5.06**
	0.18	-0.12-0.48	0.86	0.23-1.50	0.51	0.03-1.00
	0.73	0.13-1.33	0.17	-0.11-0.46	0.68	0.12-1.24
	—	—	—	—	—	—
	1.27	**0.48-2.07**	**1.03**	**0.34-1.73**	**0.85**	**0.22-1.48**

	1990–1994		1995–1999		2000–2004	
	Incidence rate/million	95% CI	Incidence rate/million	95% CI	Incidence rate/million	95% CI
	41.58	**36.94-46.23**	**48.21**	**43.35-53.07**	**40.33**	**35.92-44.73**
	32.38	28.29-36.48	34.62	30.50-38.74	31.27	27.39-35.14
	6.71	4.84-8.57	9.79	7.60-11.98	6.75	4.95-8.55
	0.57	0.03-1.12	0.72	0.13-1.32	0.53	0.03-1.04
	—	—	—	—	—	—
	10.54	**8.20-12.88**	**12.51**	**10.03-14.98**	**12.44**	**9.99-14.88**
	5.17	3.54-6.81	4.71	3.19-6.23	6.04	4.34-7.74
	3.64	2.27-5.01	4.53	3.04-6.02	3.73	2.39-5.07
	1.15	0.38-1.92	0.36	-0.06-0.78	1.07	0.35-1.78
	—	—	—	—	—	—
	35.64	**31.34-39.94**	**28.46**	**24.72-32.19**	**27.36**	**23.73-30.98**
	2.87	1.65-4.10	2.17	1.14-3.21	1.78	0.85-2.70
	22.04	18.66-25.42	16.49	13.65-19.34	15.63	12.89-18.37
	4.41	2.90-5.92	3.99	2.59-5.39	6.04	4.34-7.74
	—	—	—	—	—	—

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EXHIBIT 3.5: **Incidence rate (per million) of childhood cancer, by diagnosis, females, age 0–14 years, in Ontario, 1985–2004** (cont'd)

Diagnostic group	Sub-group	Total (1985–2004) No. of cases	Total (1985–2004) Incidence rate/million	Total (1985–2004) 95% CI	1985–1989 Incidence rate/million	1985–1989 95% CI
IV	**Neuroblastoma and other peripheral nervous cell tumours**	**191**	**9.04**	**7.96-10.12**	**8.61**	**6.40-10.82**
	a. Neuroblastomas and ganglioneuroblastomas	188	8.90	7.83-9.97	8.40	6.22-10.59
	Other	3	—	—	—	—
V	**Retinoblastoma**	**80**	**3.79**	**3.09-4.48**	**5.46**	**3.70-7.22**
VI	**Renal tumours**	**201**	**9.51**	**8.41-10.62**	**9.66**	**7.32-12.00**
	a. Nephroblastomas and other nonepithelial renal tumours	190	9.00	7.90-10.10	9.50	7.10-11.80
	Other	11	—	—	—	—
VII	**Hepatic tumours**	**38**	**1.80**	**1.32-2.28**	**1.26**	**0.41-2.11**
VIII	**Malignant bone tumours**	**141**	**6.67**	**5.75-7.60**	**5.88**	**4.05-7.71**
	a. Osteosarcomas	63	2.98	2.36-3.60	3.57	2.15-5.00
	b. Ewing tumour and related sarcomas of bone	68	3.22	2.58-3.86	2.31	1.16-3.46
	Other	10	—	—	—	—
IX	**Soft tissue and other extraosseous sarcomas**	**171**	**8.09**	**7.08-9.11**	**5.25**	**3.52-6.98**
	a. Rhabdomyosarcomas	66	3.12	2.49-3.76	2.52	1.32-3.72
	Other	105	—	—	—	—
X	**Germ cell tumours, trophoblastic tumours and neoplasms of gonads**	**102**	**4.83**	**4.04-5.61**	**3.99**	**2.48-5.50**
	d. Gonadal carcinomas	44	2.08	1.57-2.60	1.05	0.28-1.82
	Other	58	—	—	—	—
XI	**Other malignant epithelial neoplasms and malignant melanomas**	**79**	**3.74**	**3.05-4.43**	**3.36**	**1.98-4.74**
	b. Thyroid carcinomas	34	1.61	1.16-2.06	1.47	0.56-2.38
	d. Malignant melanomas	14	0.66	0.37-0.95	1.26	0.41-2.11
	Other	31	—	—	—	—
XII	**Other and unspecified malignant neoplasms**	**35**	**1.66**	**1.20-2.12**	**1.47**	**0.56-2.38**

*Almost exclusively acute lymphoblastic leukemia
†Including chronic myeloid leukemia
CI = confidence interval

Gender patterns in incidence

Exhibits 3.4 and 3.5

Overall, from 1985 to 2004 in Ontario, childhood cancers occurred more frequently in males than in females, with a male:female ratio of 1.16:1. The largest differences are seen in the lymphoma and reticuloendothelial neoplasms group, where the ratio is 1.69:1, and hepatic tumours, where the ratio is 1.53:1. Within the lymphoma and reticuloendothelial neoplasms grouping, sub-group differences in the male:female ratio are even more striking. Among the non-Hodgkin lymphoma group (not including Burkitt lymphoma) the male:female ratio is 1.94:1. Among those diagnosed with Burkitt lymphoma the male:female ratio is 4.56:1. U.S. and French data show equivalent gender ratios, as do data derived from the Berlin Frankfurt Munster Group. There is

	1990–1994		1995–1999		2000–2004	
	Incidence rate/million	95% CI	Incidence rate/million	95% CI	Incidence rate/million	95% CI
	11.31	**8.88-13.73**	**9.61**	**7.44-11.78**	**6.75**	**4.95-8.55**
	11.31	8.88-13.73	9.42	7.27-11.57	6.57	4.80-8.35
	—	—	—	—	—	—
	1.72	**0.78-2.67**	**3.44**	**2.14-4.74**	**4.62**	**3.13-6.11**
	8.62	**6.51-10.74**	**12.32**	**9.87-14.78**	**7.46**	**5.57-9.36**
	8.05	6.01-10.09	11.60	9.21-13.99	6.90	5.10-8.80
	—	—	—	—	—	—
	1.72	**0.78-2.67**	**1.99**	**1.00-2.98**	**2.13**	**1.12-3.14**
	7.09	**5.17-9.01**	**6.34**	**4.58-8.11**	**7.28**	**5.41-9.15**
	3.07	1.81-4.33	2.72	1.56-3.87	2.66	1.53-3.80
	4.02	2.58-5.47	3.08	1.85-4.31	3.38	2.10-4.65
	—	—	—	—	—	—
	7.47	**5.50-9.44**	**8.16**	**6.16-10.16**	**11.01**	**8.71-13.32**
	3.26	1.96-4.56	2.36	1.28-3.43	4.26	2.83-5.70
	—	—	—	—	—	—
	3.64	**2.27-5.01**	**5.80**	**4.11-7.49**	**5.68**	**4.03-7.34**
	1.53	0.64-2.42	2.72	1.56-3.87	2.84	1.67-4.01
	—	—	—	—	—	—
	1.72	**0.78-2.67**	**4.35**	**2.89-5.81**	**5.33**	**3.73-6.93**
	0.77	0.14-1.40	1.81	0.87-2.76	2.31	1.26-3.36
	0.77	0.14-1.40	0.18	-0.12-0.48	0.53	0.03-1.04
	—	—	—	—	—	—
	0.96	**0.25-1.66**	**2.72**	**1.56-3.87**	**1.42**	**0.59-2.25**

a less dramatic ratio of 2.5:1 for T cell lymphoblastic lymphoma in the latter series.[19] Similar data were observed for mature B cell leukemia in the French report. While there are no obvious explanations for this gender difference, it has been suggested that it may reflect a suppressor gene on the X chromosome.[19]

In several diagnostic groups females have higher incidence rates, including renal tumours (male:female ratio, 0.76:1). In the European data, sex differences were not noted. However, SEER data for 2001–2003 noted higher incidence rates in females than in males, with a male:female ratio of 0.87:1. Other tumours demonstrating female predominance include germ cell tumours (0.77:1) and other epithelial tumours (0.59:1).

Although the incidence trends by gender are generally stable over the entire period from 1985 to 2004, some changes have occurred. Among ependymoma and choroid plexus tumours the male:female ratio for the entire period is 1.15:1, although in the earliest period, 1985–1989, the male:female ratio was 0.84:1 and steadily climbed to the last period, 2000–2004, when it was 2.30:1. In contrast, among thyroid tumours the male:female ratio for the entire period was 0.45:1, although in the earliest period, 1985–1989, the ratio was 0.95:1 and steadily decreased to 2000–2004, when it was 0.22:1. A similar dramatic rise in average incidence rate of 5% per year between 1981 and 2009 has been described in young women aged 15–29 years between 1981 and 2009 in Ontario.[20]

Mapping and Spatial Distribution

The POGONIS database contains the 6 character postal code of the addresses of registered cases at the date of diagnosis. These postal codes can be linked to the 2001 Census Divisions for Ontario, permitting mapping of the variations of ASIRs across the province and exploration of differences in incidence.

A search of the literature revealed no reports of mapping of incidence rates for childhood cancer in Canada, either across provinces and territories or within any of these jurisdictions.

For the U.S., tables of incidence rates and maps displaying incidence rates are available for all cancers, including childhood cancers, across counties for each state.[21] We followed the methods described in this publication for reporting data by census division and mapping the incidence rates.

To obviate potential methodologic problems that would be caused by changes in population density and census definitions over the 20 years covered by this chapter, only the cases recorded in the 10 year period 1995–2004 were used for this exercise. For each census division we reviewed the number of incident cases of childhood cancer and recorded the incidence rate for the 10 years per 100,000 children, along with the lower and upper limits of the confidence intervals for the reported rates. The incidence rates are adjusted to the age distribution of children in Ontario as reported for the 2001 census.

We report the data for the 24 census divisions that had at least 30 incident cases of childhood cancer during the 10 year period. Census divisions with fewer than 30 incident cases were excluded for 2 reasons: 1) the estimates of incidence rates for census divisions with small numbers of cases may not be stable and 2) we wished to avoid the possibility of indirect identification of the individual children diagnosed with cancer.

EXHIBIT 3.6: **Ontario census divisions with ≥ 30 childhood cancer incident cases, age 0–14 years, in Ontario, 1995–2004**

Census division number	Census division name (alphabetically)	No. of children aged 0–14 years (2001)	No. of incident cases of cancer	Incidence rate per million	95% CI
57	Algoma District	21,025	35	166.50	114.10-221.60
28	Brant County	23,840	35	146.80	98.20-195.40
18	Durham Regional Municipality	115,565	170	147.10	125.00-169.20
37	Essex County	75,580	82	108.50	85.00-132.00
10	Frontenac County	23,235	62	255.80	192.20-319.40
53	General Sudbury Division	28,380	48	169.10	121.30-216.90
28	Haldimand-Norfolk Regional Municipality	20,970	45	214.60	152.00-277.20
24	Halton Regional Municipality	77,000	118	153.20	125.60-180.90
25	Hamilton Division	94,390	148	156.80	131.60-182.00
12	Hastings County	23,835	32	134.30	87.80-180.70
39	Middlesex County	78,780	125	158.70	130.90-186.50
26	Niagara Regional Municipality	74,915	114	152.20	124.30-180.10
48	Nipissing District	15,425	31	201.00	130.30-271.60
6	Ottawa Division	146,145	259	177.00	155.70-198.80
32	Oxford County	50,595	33	160.20	105.60-214.90
21	Peel Regional Municipality	217,290	367	168.90	151.60-186.20
15	Peterborough County	22,465	32	142.40	93.10-191.80
43	Simcoe County	80,245	125	155.80	128.50-183.10
1	Stormont, Dundas and Glengarry United Counties	21,395	30	140.20	90.10-190.40
58	Thunder Bay District	28,310	36	127.20	85.60-168.70
20	Toronto Division	433,810	662	152.60	141.00-164.20
30	Waterloo Regional Municipality	91,000	138	151.60	126.40-176.90
23	Wellington County	38,730	75	193.60	149.90-237.40
19	York Regional Municipality	155,715	255	163.80	143.70-183.80

CI = confidence interval

EXHIBIT 3.7: **Ontario census divisions with < 30 childhood cancer incident cases excluded from analysis, age 0–14 years, in Ontario, 1995–2004**

Census division number	Census division name (alphabetically)	No. of children aged 0–14 years (2001)
41	Bruce County	11,685
36	Chatham-Kent County	21,205
56	Cochrane District	17,730
22	Dufferin County	12,200
34	Elgin County	17,450
42	Grey County	16,315
40	Huron County	12,090
16	Kawartha Lakes Division	12,850
38	Lambton County	24,180
9	Lanark County	12,305
7	Leeds and Grenville United Counties	18,085
11	Lennox and Addington County	7,435
44	Muskoka District Municipality	9,180
14	Northumberland County	14,535
49	Parry Sound District	6,580
31	Perth County	15,435
2	Prescott and Russell United Counties	16,275
13	Prince Edward Division	4,170
47	Renfrew County	18,470
52	Sudbury District	4,220
54	Timiskaming District	6,410

Exhibits 3.6 and 3.7

Exhibit 3.6 displays the data of the 24 census divisions that had 30 or more incident cases of childhood cancer over the 10 year period, listed alphabetically. In the 2001 census data, the numbers of children ranged from just over 20,000 for Oxford County and Haldimand-Norfolk Regional Municipality to 433,810 in the Toronto Division. The numbers of incident cases ranged from 30 in Stormont, Dundas and Glengarry United Counties to 662 in the Toronto Division.

Exhibit 3.7 lists the census divisions with fewer than 30 incident cases of childhood cancer that were excluded from the analysis. They are located throughout Northern and Southern Ontario.

EXHIBIT 3.8: **Incidence rate of childhood cancer per 100,000, by census division, age 0-14 years, in Ontario by tertile,1995-2004**

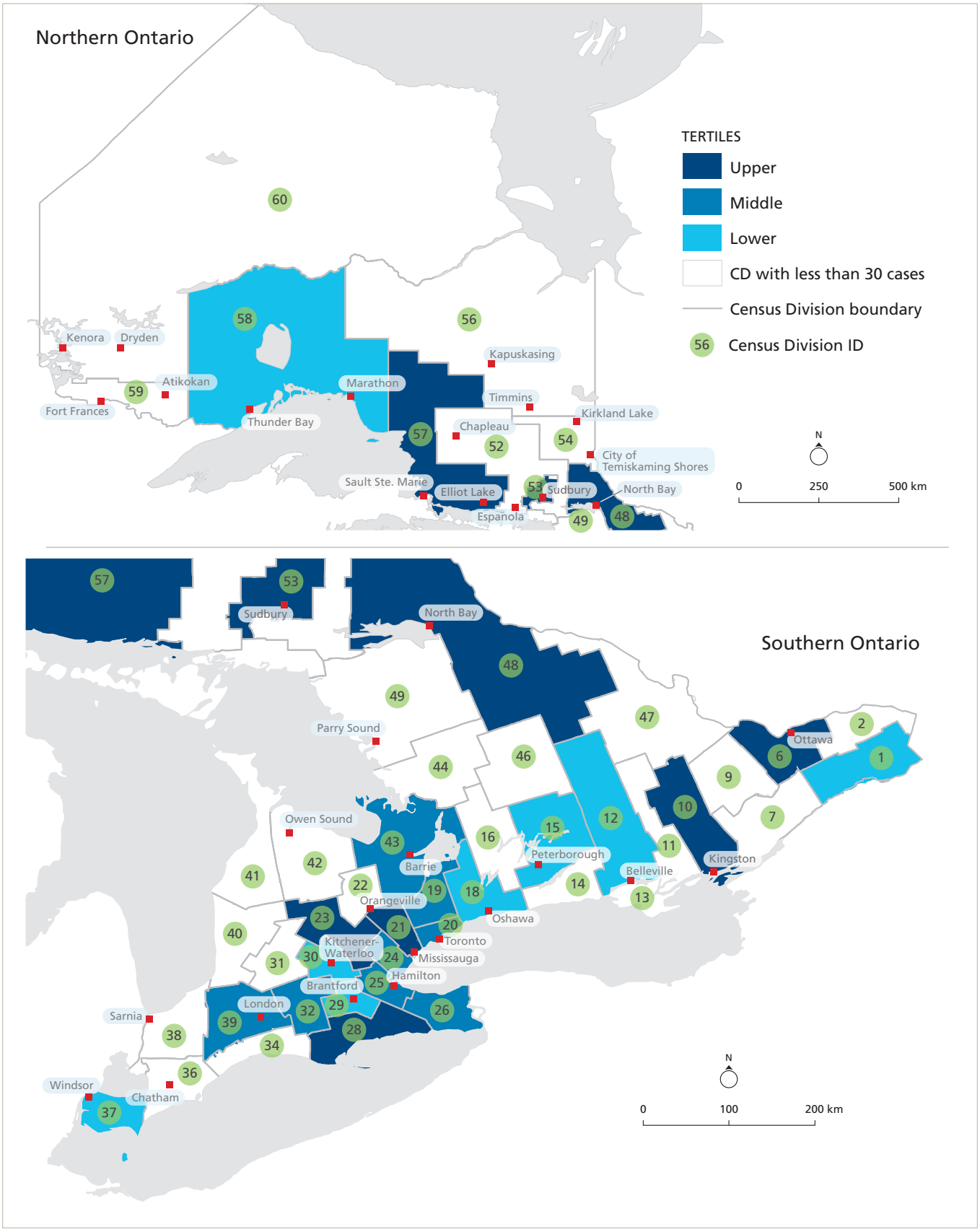

Exhibit 3.8

The incidence rates for the 24 census divisions were divided into lower, middle and upper tertiles; the rankings are displayed on a choropleth map (Exhibit 3.8). The census divisions in the lower and upper tertiles are located in Northern and Southern Ontario; the census divisions in the middle tertiles are located in Southern Ontario, west of Durham Region.

There are limitations to using choropleth maps for large areas, as exhibited on the map. First, the summary of regional variations assumes that if risk factors exist, they are common within each region. Second, there is a presumption that the rates are uniform within each census division, even though they likely vary across given units within divisions. Finally, shifts in colours across tertiles suggest that rates change abruptly between divisions, whereas the divisions are artificial and rates blend between divisions.

EXHIBIT 3.9: **Incidence rates by census division, age 0–14 years, in Ontario, 1995–2004**

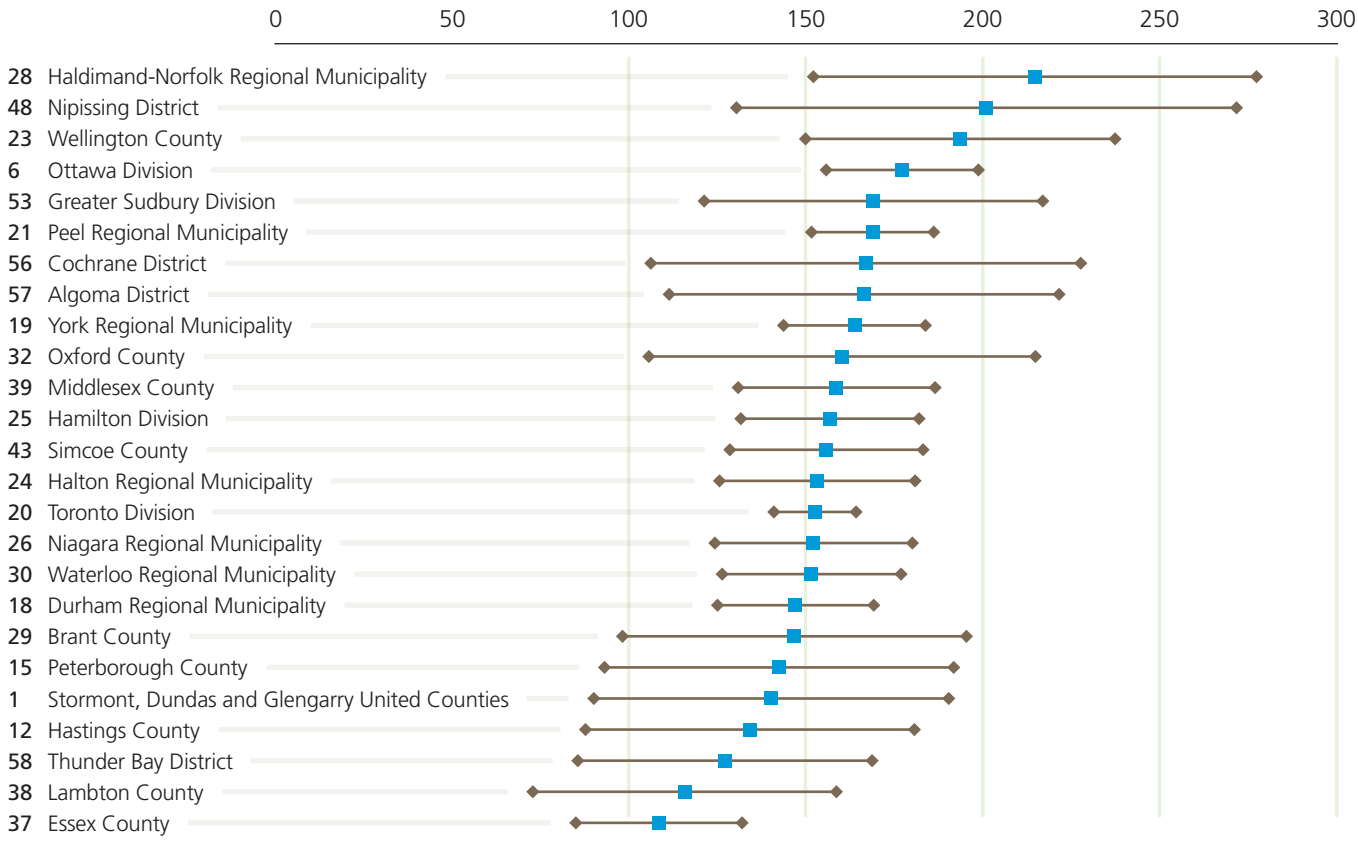

Exhibit 3.9

Exhibit 3.9 displays the variations in incidence rates of childhood cancer across the divisions and the corresponding confidence intervals. The range of the confidence intervals is determined in part by the number of children in each division. Census divisions with fewer children have larger confidence intervals. While the rates show an almost 2-fold difference between the minimum and maximum values, the confidence intervals overlap in most cases, rendering the differences not statistically significant. The variations in rates across the study area thus could have occurred by chance.

It should be noted that the results, statistics and regional variation in the map are comparable to the data and maps reported for Michigan, Ohio and Pennsylvania, the 3 U.S. states south of Ontario.

Another approach to mapping rates of rare cancer is to interpolate regional data onto a continuous surface for the estimating spatial risk function. Kriging is a geostatistical procedure for predicting values of incidence across the entire region from a scattered set of points with known values. The first step to achieving this was to use geographic information systems to define the census divisions as polygons and to place the known incidence rate at the centre of the geographic space for each census division.

The interpolation method for estimating the patterns for incidence rates across the province uses the concept of spatial autocorrelation or similarity of values of incidence rates in locations close to the known data points. The magnitude of the correlations for known points is inversely related to the distance between those points. The method fits a mathematical function for predicting a value (incidence rate) for each location within a specified search radius. Kriging is completed in 2 stages: the creation of variograms and covariance functions to estimate the statistical dependence called spatial correlation, and the prediction of unknown values.

EXHIBIT 3.10: **Incidence rate of childhood cancer per 100,000 by census division, age 0-14 years, in Ontario, 1995-2004**

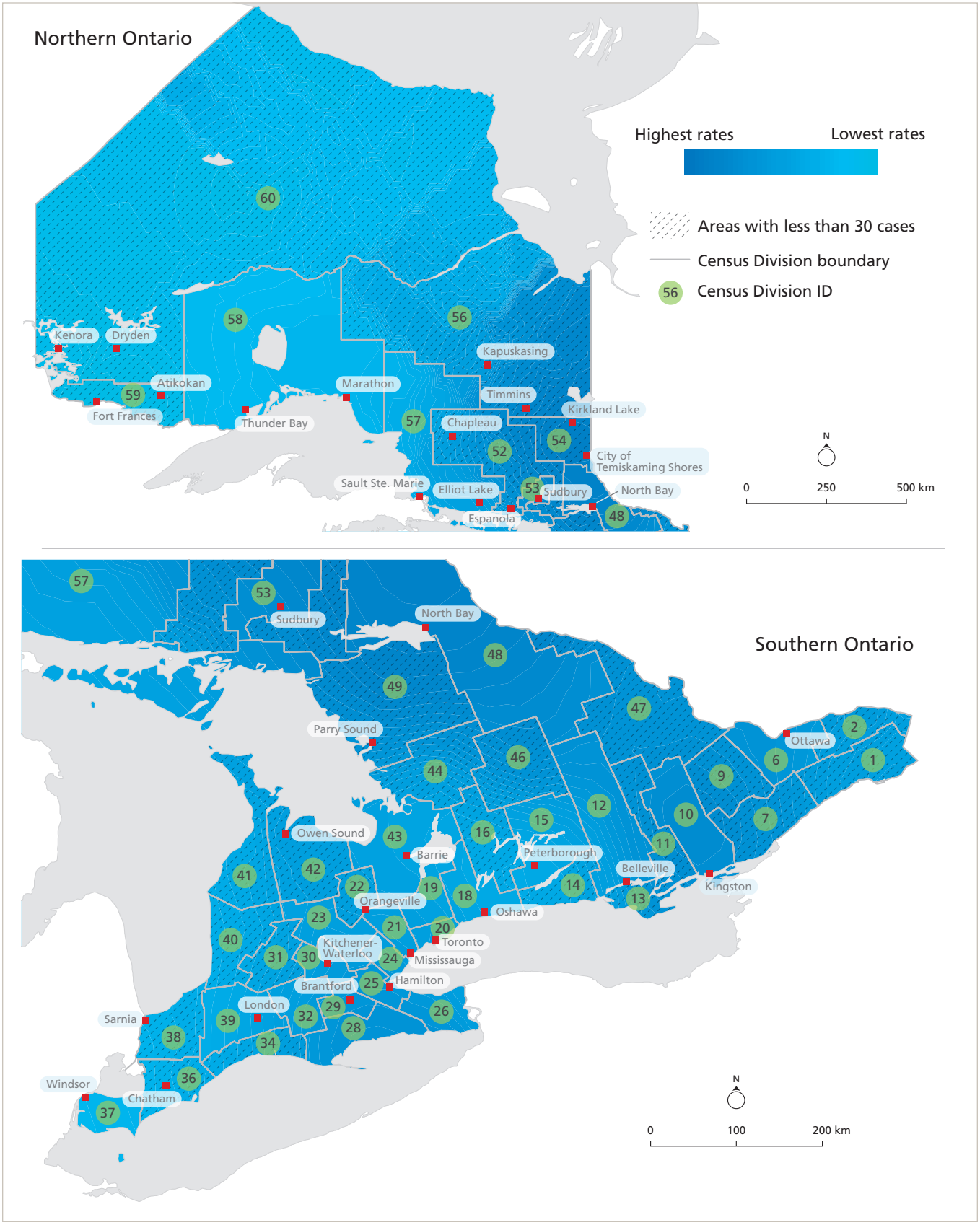

Exhibit 3.10

Exhibit 3.10 displays the map based on the Kriging procedure. To make the estimating of patterns for incidence rates across the province as complete as possible, we included all census divisions. The census divisions with dots are those with fewer than 30 incident cases.

The darkest shades for higher estimates spread from the lower part of Cochrane District down through Timiskaming District, through Nipissing District below North Bay to the Greater Sudbury Division and Parry Sound District. Dark shading is evident for Frontenac County as well. The light shades are evident primarily for census divisions in Northern Ontario and the southwestern parts of the province.

As Berke[22] notes, exploratory disease mapping provides insight into disease distribution, not specific precise estimates of location and spread. The Kriging map serves to generate questions and hypotheses about the epidemiology of childhood cancer.

Summary

A large geographically-defined population cohort of subjects aged 0–14 years diagnosed with childhood cancer in the Province of Ontario between 1985 and 2004, collected in an active database, was analyzed to assess trends in incidence, age distribution and gender. Efforts were made to map incidence rates across census divisions.

Incidence rates in Ontario were largely comparable both to pan-Canadian rates and to rates in international jurisdictions. By far the highest incidence rate was seen for acute leukemia, in particular ALL. This entity occurred predominantly in the 1–4 year age quartile and showed no change in incidence over the 20 year period. Similarly, tumours of the CNS, the second most common diagnostic group, demonstrate the highest rates in the 1–4 year group, largely comprising astrocytomas. While there was an increase in incidence rates in the late 1980s and early 1990s, this is thought to reflect the introduction of imaging screening for asymptomatic low grade gliomas in patients with neurofibromatosis type 1 over that period. Subsequent rates returned to baseline levels.

Lymphoma incidence rates did not demonstrate increases over the period of study. Burkitt lymphoma demonstrated a marked male predominance, a finding reported in other jurisdictions. No clear explanation is known. Substantial changes in male:female ratios were also demonstrated for ependymoma and choroid plexus tumours (which showed an increase in the male:female ratio) and thyroid cancer, which demonstrated both a significant increase in incidence and a steady reduction in the male:female ratio in this age group – a finding similar to that in the older adolescent and young adult group.

Despite meticulous efforts to identify differing geographic distribution, no such finding was established.

The presence of incidence rates similar to those of other jurisdictions both permits comparison and invites re-analysis using contemporary diagnostic tools to clarify sub-group distribution. As such techniques become more sophisticated, it may be possible to demonstrate differing incidence rate trends between molecularly-defined subgroups of childhood cancer acknowledged in the ICCC-3.

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info@pogo.ca

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