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7

Lymphoma

Executive Summary

In Canada approximately 850 children under the age of 14 years are diagnosed with cancer annually, reflecting an annual age standardized incidence rate (ASIR) of 144–159 per 1 million children.[1] Of these cancers, 12.0% are lymphomas, which represents an ASIR of 16.9 per million. Hodgkin lymphoma (HL) accounts for about 40.0% of the lymphomas diagnosed; non-Hodgkin lymphoma (NHL) accounts for the remainder.

Ontario's statistics reflect the national numbers. Over a period of 20 years (1985–2004), lymphoma incidence data for Ontario were collected and entered into the database of the Pediatric Oncology Group of Ontario Networked Information System (POGONIS). The ASIR of pediatric cancer in Ontario was between 145 and 152.3 per 1 million over that period. During this time, 646 children were diagnosed with lymphoma – 12.0% of all pediatric cancers captured in the database. Approximately 39.5% (255 cases) were HL, and 57.1% (369 cases) were NHL. Age standardized incidence increased with age for all lymphomas, with an increase in particular in the NHL 5–9 year age group. There is also an indication that the incidence for NHL increased overall. There was no increase in the incidence of HL in the younger age groups.

Consistent with the literature, there was a male predominance in lymphoma overall for all age groups combined, with an increasing proportion of females in the older age groups. Overall survival for pediatric lymphoma remains high, with HL survival stable over time. While there was some overall improvement in survival in the NHL group, survival varies across the subtypes. Recognizing that numbers are small in each NHL category, survival for Burkitt lymphoma increased over time, as it did for the mixed category of "other," possibly reflecting the improvement in management of post transplant lymphoproliferative disorder (PTLD). The numbers are small, but patients with anaplastic large cell lymphoma (ALCL) fared less well over time, while lymphoblastic lymphoma (LL) patients had variable survival rates at each of the noted time points.

The trend in therapy showed a decrease in the use of radiation, especially for HL. Reviewing incidence, survival, therapy and development of second malignancies is an important part of overall cancer care and reflecting on these statistics can help in the planning of cancer care services in the province.

Introduction

In Canada almost 850 children 0–14 years of age are diagnosed with cancer every year and around 135 die from their disease. Lymphomas constitute about 12.0% of all cancers in this age group in Canada and are third in frequency after acute leukemias and brain tumours.[1] Lymphomas are clinically and biologically heterogeneous. Approximately 60.0% of newly diagnosed cases are NHL and the rest are HL.[2]

Non-Hodgkin lymphomas

The non-Hodgkin lymphomas are a heterogeneous group of diseases that reflect the differentiation stages of the lymphoid cells from which they originate.[3] Overall, they are rare, with an estimated incidence of 8 or 9 new cases per 1 million children per year.[1] The incidence of NHL increases steadily with age; age-specific incidence varies among the subtypes. The incidence of NHL in male children is almost twice that of female children. NHLs are categorized as low, intermediate or high grade based on their clinical aggressiveness. More than 90% of pediatric NHL cases are considered high grade tumours and comprise 4 main histologic subtypes: Burkitt lymphoma (BL), diffuse large B-cell lymphoma (DLBCL), ALCL and LL.[4] With effective combination chemotherapy and better supportive care, overall survival at 5 years is about 85% for all NHL.[5]

Hodgkin lymphomas

Hodgkin lymphomas are characterized by the presence of rare multinucleated giant cells, or Reed-Sternberg cells, almost always of B-cell derivation. The majority of the tumour is composed of inflammatory cells and fibrosis. The estimated incidence of HL is about 5–6 new cases per 1 million per year.[1] Childhood HL typically affects children 10–14 years of age and has a significant male predominance. HL has a bimodal age peak, occurring in the adolescent/young adult years and at age 55 and over.

Recent large trials report long term survival rates of 85–95% for childhood HL.[6] The main focus of these trials, however, has been to prevent late complications of therapy, including second malignancies, abnormal bone and soft tissue development, sterility and late cardiac and pulmonary disease. Current risk- and response-adapted therapies aim to minimize treatment intensity, therefore reducing toxicity, by omitting involved field radiotherapy among patients who are either at low risk or are rapid early responders.[6]

Classification

The third edition of the International Classification of Childhood Cancer (ICCC-3) classifies tumours coded according to the International Classification of Diseases for Oncology (ICD-O-3) and was designed for use in international population-based cancer registries.[7] The ICCC-3 maintains the division of lymphomas into the 2 major groups, Hodgkin lymphomas (IIa) and non-Hodgkin lymphomas (IIb). NHL in the ICCC-3 includes 4 categories:

- II(b) non-Hodgkin lymphomas (except Burkitt lymphoma)
- II(c) Burkitt lymphoma (including Burkitt-like and other variants)
- II(d) miscellaneous lymphoreticular neoplasms
- II(e) unspecified lymphomas

The ICD-O codes used to classify lymphomas in the ICCC classification have been mapped to the POGONIS fields, ensuring compatibility with ICCC while allowing finer dissection of group IIb as follows:

- Lymphoblastic lymphoma
- Anaplastic large cell lymphoma
- Other, which includes
    a. Large cell lymphoma, B-cell, diffuse not otherwise specified (NOS) and diffuse large cell B-cell lymphoma (DLBCL) [n=47]
    b. Post transplant lymphoproliferative disease [n=23]
    c. Lymphoma non-B non-T cell [n=4]
    d. Primary central nervous system lymphoma [n=5]
    e. Miscellaneous lymphoma (follicular lymphoma, mucosa-associated lymphoid tissue lymphoma and grey zone lymphoma) [n=22]

The reticuloendothelial neoplasms included in the ICCC, disseminated Langerhans cell histiocytosis and identified reticuloendothelial sarcomas (including histiocytic, interdigitating dendritic and follicular dendritic) are included and described in the incidence table and included in all analyses specifying all lymphomas in the following tables, but are not further discussed in this chapter.

Data collection

Lymphoma incidence data for Ontario were obtained from the POGONIS database. Registration in POGONIS is an active process, with cases being registered on confirmation of pathologic diagnosis by the 5 participating institutions that treat all children diagnosed with cancer in Ontario. The database captures 98% of children identified with cancer in the province.

All children aged 0–14 years diagnosed with lymphoma and registered in POGONIS in the categories corresponding to the ICCC definitions during the period 1985–2004 were captured in this analysis. For more information on data sources and methods, refer to Chapter 2 (Survival). The ICCC-defined category comprises 646 cases, including 22 cases of reticuloendothelial neoplasms. The latter are included in all analyses that specify all lymphomas but are not expanded on further. Vital status is based on linkage to Cancer Care Ontario mortality data.

Limitations

Classification systems have changed over time, and cases diagnosed earlier in the cohort will not have been classified according to the latest iteration of the ICD-O. While the POGONIS codes have been mapped to the ICD-O codes used in the ICCC-3 classification, a residual group of miscellaneous cases and cases identified as NOS is found in the category "other"; they do not conform to ICCC-3. However, incidence and mortality data for the NHL group as a whole are compatible with ICCC-3. For example, the subtype currently known as mature B-cell lymphoma should be considered its own category, while in the POGONIS database it is included in the "other" category. Another limitation is that 3.8% of patients did not link in the mortality analysis because they did not have Ontario Health Insurance Numbers, thereby excluding them from the final analyses of survival.

The following discussion provides a population-based overview for Ontario on the age-specific incidence of Hodgkin and non-Hodgkin lymphomas; incidence by NHL subtype and stage; the use of chemotherapy, radiation therapy and hematopoietic stem cell transplantation (HSCT); overall and event free survival (EFS) rates; relapse and survival after relapse; and the incidence of second malignancies for children in Ontario between 1985 and 2004.

Discussion

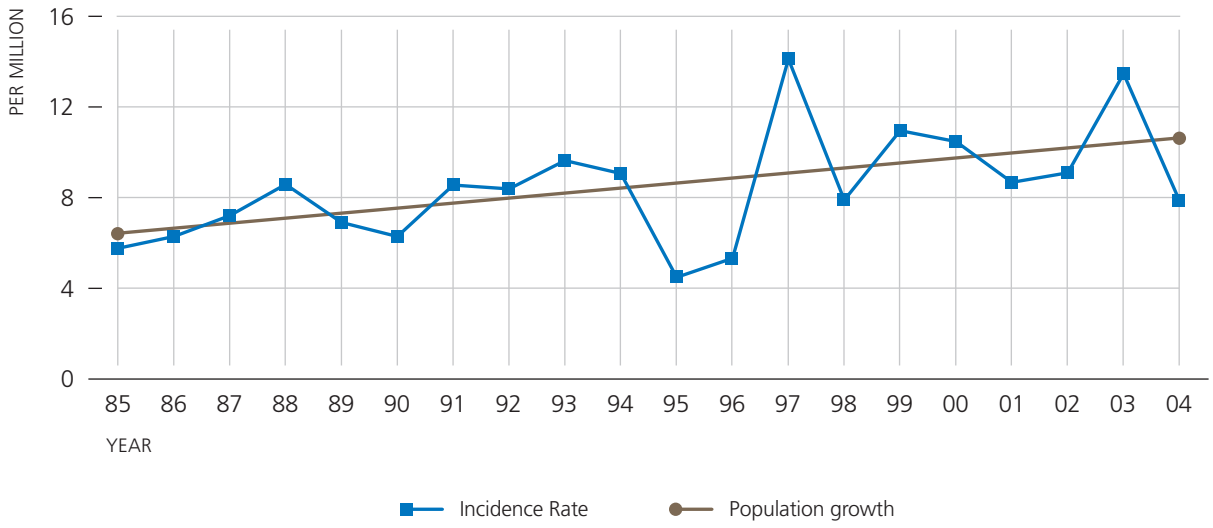
EXHIBIT 7.1a: **Incidence rate per 1 million for all lymphomas by age and period, age 0–14 years, in Ontario, 1985–2004**

Cancer type	Age group at time of diagnosis (years)	Year of diagnosis: All years N	%	IR	% Female	1985–1989 N	%	IR	% Female
All lymphoma	Overall	**646**	**100.00**	**14.5**	**35.76**	**124**	**100.00**	**12.7**	**32.26**
	0–4	110	17.03	6.9	22.73	18	14.52	5.4	x
	5–9	206	31.89	13.9	31.07	43	34.68	13.4	x
	10–14	330	51.08	22.5	41.21	63	50.81	19.4	41.27
Hodgkin	Overall	**255**	**39.47**	**5.9**	**44.31**	**55**	**44.35**	**5.6**	**47.27**
	0–4	11	4.31	0.8	x	2	3.64	0.6	x
	5–9	49	19.22	3.4	x	14	25.45	4.4	x
	10–14	195	76.47	13.5	48.72	39	70.91	12.0	51.28
Non-Hodgkin	Overall	**369**	**57.12**	**8.7**	**30.35**	**68**	**54.84**	**7.0**	**20.59**
	0–4	86	23.31	6.3	27.91	16	23.53	4.8	x
	5–9	153	41.46	10.7	30.72	28	41.18	8.7	x
	10–14	130	35.23	9.1	31.54	24	35.29	7.4	25.00
Burkitt/Burkitt-like*	Overall	**133**	**36.04**	**3.1**	**18.05**	**33**	**48.53**	**3.4**	**x**
	0–4	30	22.56	2.1	20.00	9	27.27	2.7	x
	5–9	60	45.11	4.1	16.67	11	33.33	3.4	x
	10–14	43	32.33	3.0	18.60	13	39.39	4.0	x
Lymphoblastic	Overall	**95**	**25.75**	**2.2**	**30.53**	**15**	**22.06**	**1.5**	**x**
	0–4	24	25.26	1.7	25.00	3	20.00	0.9	x
	5–9	44	46.32	3.0	36.36	9	60.00	2.8	x
	10–14	27	28.42	1.9	25.93	3	20.00	0.9	x
Anaplastic large cell	Overall	**40**	**10.84**	**0.9**	**40.00**	**2**	**2.94**	**0.2**	**x**
	0–4	7	17.50	0.5	x	0	0.00	0.0	x
	5–9	17	42.50	1.2	41.18	1	50.00	0.3	x
	10–14	16	40.00	1.1	x	1	50.00	0.3	x
Other†	Overall	**101**	**27.37**	**2.3**	**42.57**	**18**	**26.47**	**1.8**	**x**
	0–4	25	24.75	1.8	44.00	4	22.22	1.2	x
	5–9	32	31.68	2.2	43.75	7	38.89	2.2	x
	10–14	44	43.56	3.0	40.91	7	38.89	2.2	x
Miscellaneous reticuloendothelial neoplasms‡	Overall	**22**	**3.41**	**—**	**27.27**	**1**	**0.81**	**—**	**x**
	0–4	13	59.09	—	x	0	0.00	—	x
	5–9	4	18.18	—	x	1	100.00	—	x
	10–14	5	22.73	—	x	0	0.00	—	x

*Burkitt/Burkitt-like includes Burkitt and small non-cleaved cell, non-Burkitt pleomorphic undifferentiated.
†Other includes large cell lymphoma not otherwise specified, post transplant lymphoproliferative disorder, lymphomas not otherwise specified or miscellaneous lymphoma, and central nervous system lymphoma.
‡Miscellaneous reticuloendothelial neoplasms include Langerhans cell histiocytosis/systemic Letterer-Siwe disease, hemophagocytic macrophage related syndrome (familial erythrophagocytic lymphohistiocytosis) and histiocytic lymphoma.
x: For privacy reasons some data have not been reported.

	1990–1994				1995–1999				2000–2004			
	N	%	IR	% Female	N	%	IR	% Female	N	%	IR	% Female
All Cancers	**161**	**100.00**	**15**	**34.16**	**163**	**100.00**	**14.4**	**41.10**	**198**	**100.00**	**17.5**	**31.82**
Leukemias	27	16.77	7.3	x	27	16.56	7.3	33.33	38	19.19	11.3	21.05
Lymphomas	45	27.95	12.6	x	59	36.20	15.3	40.68	59	29.80	15.1	18.64
CNS Tumours	89	55.28	26.1	35.96	77	47.24	20.5	44.16	101	51.01	24.8	43.56
Epithelial Neoplasms	**66**	**40.99**	**6.2**	**40.91**	**62**	**38.04**	**5.4**	**43.55**	**72**	**36.36**	**6.4**	**45.83**
Adrenocortical Carcinoma	2	3.03	0.5	x	5	8.06	1.4	x	2	2.78	0.6	x
Thyroid Carcinoma	10	15.15	2.8	x	14	22.58	3.6	x	11	15.28	2.8	x
Other Epithelial Neoplasms	54	81.82	15.8	42.59	43	69.35	11.5	48.84	59	81.94	14.7	52.54
Germ Cell Tumours	**90**	**55.90**	**8.5**	**31.11**	**97**	**59.51**	**8.9**	**41.24**	**114**	**57.58**	**10.3**	**26.32**
Intracranial Germ Cell Tumours	23	25.56	6.2	x	19	19.59	5.7	42.11	28	24.56	8.7	28.57
Extracranial Germ Cell Tumours	34	37.78	9.8	41.18	45	46.39	11.9	42.22	46	40.35	12.0	19.57
Gonadal Germ Cell Tumours	33	36.67	9.7	x	33	34.02	9.1	39.39	40	35.09	10.1	32.50
Other Neoplasms	**32**	**35.56**	**3.0**	**31.25**	**30**	**30.93**	**2.7**	**x**	**38**	**33.33**	**3.4**	**15.79**
Hepatic Tumours	10	31.25	2.7	x	3	10.00	0.8	x	8	21.05	2.4	x
Bone Tumours	13	40.63	3.6	x	16	53.33	4.1	x	20	52.63	5.1	x
Soft Tissue Sarcomas	9	28.13	2.6	x	11	36.67	2.9	x	10	26.32	2.5	x
Miscellaneous	**22**	**24.44**	**2.1**	**x**	**27**	**27.84**	**2.4**	**40.74**	**31**	**27.19**	**2.7**	**29.03**
Neuroblastoma	6	27.27	1.6	x	6	22.22	1.6	x	9	29.03	2.7	x
Retinoblastoma	8	36.36	2.2	x	14	51.85	3.6	64.29	13	41.94	3.6	x
Other Miscellaneous	8	36.36	2.3	x	7	25.93	1.9	x	9	29.03	2.2	x
Unspecified	**11**	**12.22**	**1.0**	**x**	**9**	**9.28**	**0.8**	**x**	**18**	**15.79**	**1.6**	**38.89**
Unspecified Malignant Tumours	2	18.18	0.5	x	3	33.33	0.8	x	2	11.11	0.6	x
Unspecified Benign Tumours	6	54.55	1.7	x	3	33.33	0.8	x	7	38.89	1.8	x
Unspecified Neoplasms	3	27.27	0.9	x	3	33.33	0.8	x	9	50.00	2.2	x
Non-Neoplastic Disorders	**25**	**27.78**	**2.3**	**x**	**31**	**31.96**	**2.7**	**67.74**	**27**	**23.68**	**2.4**	**29.63**
Histiocytic Disorders	5	20.00	1.3	x	7	22.58	1.9	x	9	33.33	2.7	x
Other Non-Neoplastic Disorders	7	28.00	2.0	x	12	38.71	3.1	x	6	22.22	1.5	x
Unspecified Non-Neoplastic Disorders	13	52.00	3.8	x	12	38.71	3.2	x	12	44.44	2.9	x
Unknown	**5**	**3.11**	**—**	**x**	**4**	**2.45**	**—**	**x**	**12**	**6.06**	**—**	**x**
Unknown Malignant Tumours	2	40.00	—	x	3	75.00	—	x	8	66.67	—	x
Unknown Benign Tumours	1	20.00	—	x	0	0.00	—	x	2	16.67	—	x
Unknown Neoplasms	2	40.00	—	x	1	25.00	—	x	2	16.67	—	x

EXHIBIT 7.2: **Incidence rate per 1 million of non-Hodgkin lymphoma, trend over time, age 0–14 years, in Ontario, 1985–2004**



P-value for trend <0.0001

Exhibits 7.1–7.2

Incidence

The diagnosis of lymphoma accounted for 12% of all cancer cases in children 0–14 years of age between 1985 and 2004 in Ontario, with a total of 646 cases. Incidence rates are reported for each 5 year interval. NHL accounted for the majority of cases (369, or 57.1%), while HL was less common (255 cases, 39.5%). The incidence rate was 14.5 per 1 million per year for all childhood lymphoma – 8.7 for NHL and 5.9 for HL. The incidence rate of all lymphomas increased from 12.7 per 1 million per year in the first reporting period (1985–1989) to 17.5 in the most recent period (2000–2004) (Exhibit 7.1a). This increase was more significant in the NHL group during the last period, with a *P*-value for trend of < 0.0001 (incidence rate increasing from 7.0 in 1985–1989 to 10.3 in the last period) (Exhibit 7.2). The increase was consistent and notable in the 5–9 year age group (Exhibit 7.1a). HL had a modest increase in incidence rate from 5.6 in 1985–1989 to 6.4 in the last period. Although the numbers are small, there was a trend toward an increasing number of stage 4 HL and NHL cases over the 20 year period, possibly reflecting higher detection rates of diffuse disease as a result of better and more sensitive diagnostic tests (data not shown).

EXHIBIT 7.1b: **Incidence rate per 1 million of Hodgkin lymphoma by stage and gender, age 0–14 years, in Ontario, 1985–2004**

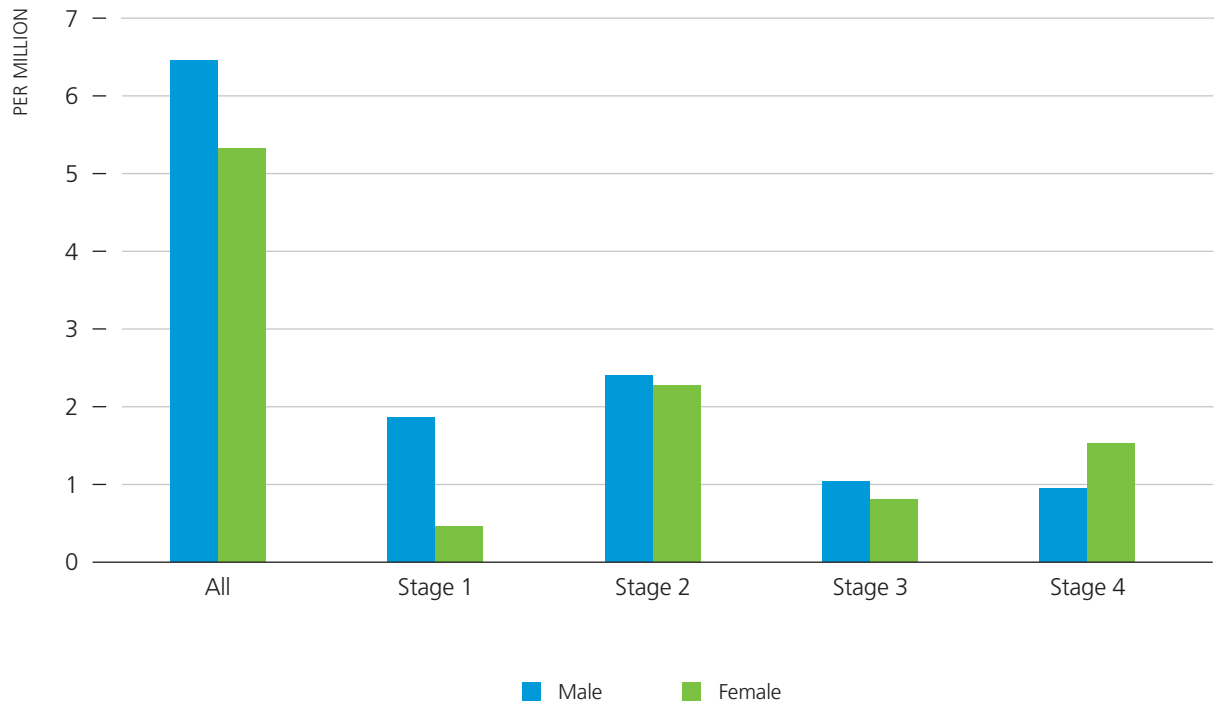


EXHIBIT 7.1c: **Incidence rate per 1 million of non-Hodgkin lymphoma by stage and gender, age 0–14 years, in Ontario, 1985–2004**

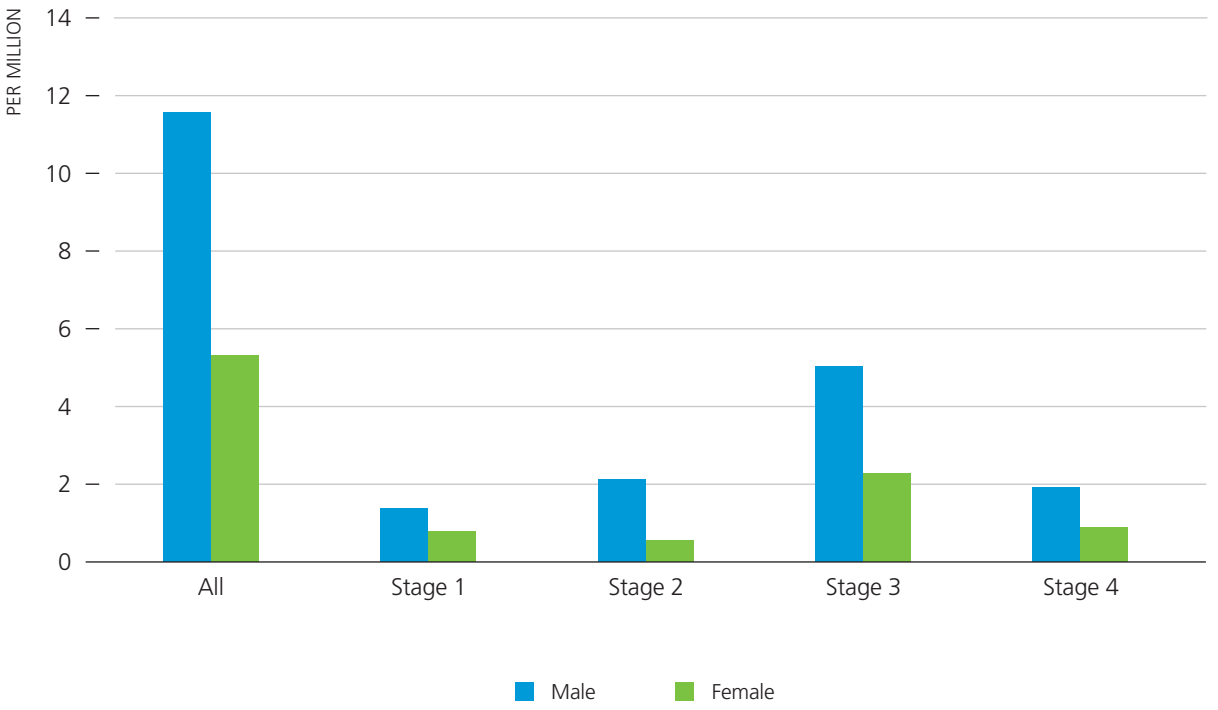
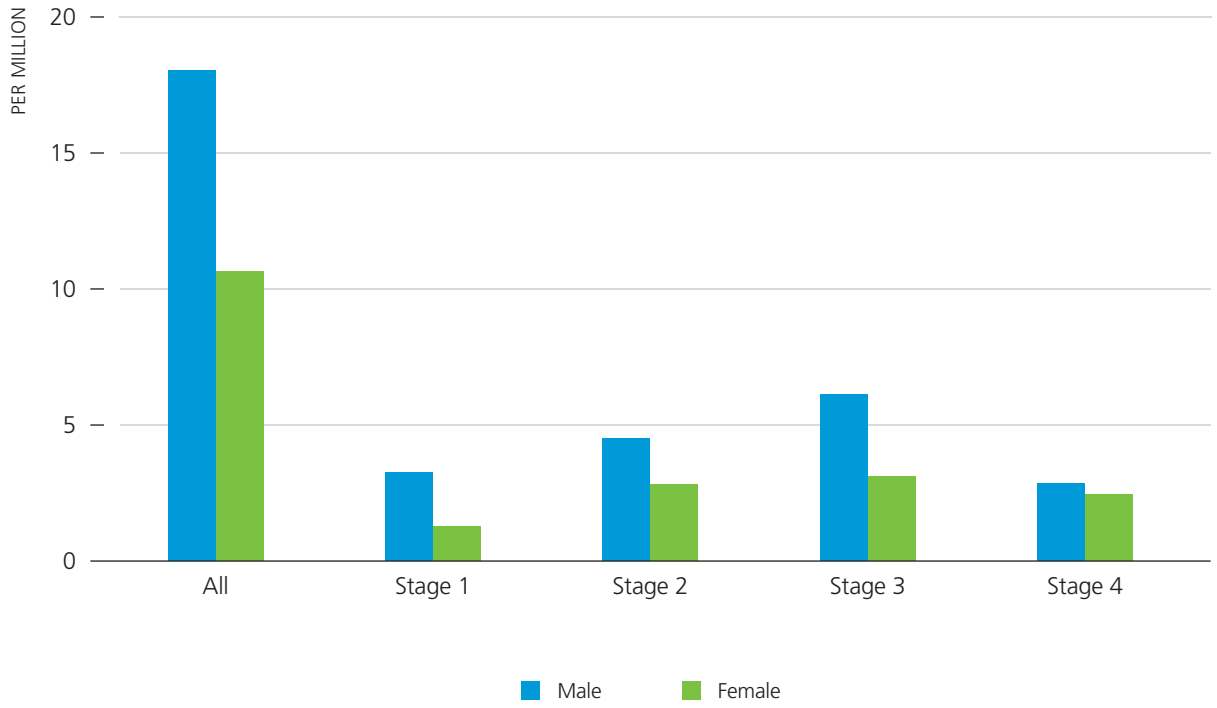


EXHIBIT 7.1d: **Incidence rate per 1 million of Hodgkin and non-Hodgkin lymphoma by stage and gender, age 0–14 years, in Ontario, 1985–2004**



Age-specific incidence

Average incidence increased with age for all lymphomas, with the greatest gradient between age groups in the HL group (incidence rate of 0.8 in children aged 0–4 years, compared with 13.5 in children aged 10–14 years). The incidence pattern of HL is in keeping with that seen in developed countries, where it tends to be more common in adolescents aged 15–19 years. Despite the increase in immigration to Ontario in recent years and recognizing that HL develops at a younger age in less privileged societies, HL was rare among children younger than 5 years. Among the NHL group, the greatest difference was between the 5–9 year group (incidence rate, 10.7) and the 0–4 year group (incidence rate, 6.3) (Exhibit 7.1a).

Gender-specific incidence

Male incidence of lymphoma was predominant in all age groups, particularly in very young children (0–4 years). The overall incidence of lymphoma in females appeared to increase with age. The incidence of stage 4 HL was higher in females, especially in the 10–14 year group (data not shown). In NHL, male incidence was higher for all age groups and among all stages (Exhibit 7.1c). ALCL, however, was more common in females, particularly in children aged 5–14 years (Exhibit 7.1a).

Subtype-specific incidence

When analyzed according to NHL histologic subtype, BL/BL-like were the most frequently diagnosed subtype (133 patients, 36.0%), followed by "other" NHL (101 cases, 27.4%), LL (95 cases, 25.8%) and ALCL (40 cases, 10.8%). BL/BL-like had a peak incidence in the 5–9 year age group, with 60 of 133 (45.1%) patients with BL being diagnosed in this age group. The most striking change over the 20 year period was the appearance of PTLD and primary central nervous system (CNS) lymphoma, which were not reported to the POGONIS database prior to 1995. Regarding ALCL, the number of cases in 1990–1994 was significantly different from the numbers in other periods (chi square = 12.5, $P < 0.01$) and there was a trend toward an increased incidence in children 10–14 years of age.

Regarding NHL subtypes, the incidence rate for BL was stable over the 20 year period, whereas there was a modest increase for both LL (from 1.5 to 2.7) and the "other" category (from 1.8 to 2.4). The increased number of patients diagnosed with ALCL throughout the 20 year period (incidence rate increasing from 0.2 to 1.6) is the result of improved detection of this entity rather than an absolute increase (Exhibit 7.1a).

Risk factors

The reasons for the increasing incidence of NHL are likely a combination of changes in risk factors and improved detection and classification of these lymphomas. The most common risk factor for NHL is immune insufficiency, related to a congenital immunodeficiency syndrome (e.g., X-linked lymphoproliferative disease, ataxia-telangiectasia or Wiskott-Aldrich syndrome), immunosuppressive therapy (e.g., in recipients of solid organ or bone marrow transplants), the human immunodeficiency virus[4] or autoimmune lymphoproliferative syndrome.[8] Although various organic solvents such as pesticides, dioxins and benzene have been implicated in the etiology of NHL, there is no convincing evidence that they represent significant risk factors for childhood lymphomas.[9,10]

Exhibits 7.3a–7.3b

Survival

Overall survival

Among all lymphomas, 1 year overall survival was 91.6% and 3 year overall survival was 85.9%. There was no significant change by 5 years (overall survival, 84.2%). The 1 year overall survival was 87.9% in the first period (1985–1989), improving to 91.9% in the last period (2000–2004); 3 year survival improved from 82.3% in the first period to 87.9% in the last, and 5 year survival improved from 79.8% to 86.4%. Mortality was relatively higher in the 10–14 year age group across all lymphomas. In HL patients (255 in total), overall survival at 1 year was 99.6% (1 death), while 3 and 5 year survival remained stable at approximately 93–94% across the 4 time periods. (One year survival data are not shown.)

Among NHL patients, mortality was higher in the 10–14 year age group, particularly in the BL/BL-like and "other" categories. There was a trend toward improved overall survival in all NHL patients across the 4 periods: 1 year overall survival increased from 77.9% in the first period to 88.6% in the last, 3 year survival from 72.1% to 86.0% and 5 year survival from 69.1% to 84.2%.

Overall survival at 1 year for all BL patients over the 20 year period was 86.4%; as expected, it plateaued at 85.0% at 3 years. The 1, 3 and 5 year overall survival for BL patients was essentially constant at 72.7–69.7% in the first period, increasing to a stable 5 year survival of 89.5% during the last period.

For all patients with LL over the 20 year period, overall survival dropped slightly from 94.7% at 1 year to 86.3% at 5 years. Over the 4 consecutive periods, there was no substantial change in 1, 3 or 5 year overall survival. There is a suggestion that mortality was higher in younger children with LL, with 3 of 5 deaths by 1 year occurring in children under 4 years of age, and 8 of 12 deaths by 3 years occurring in children younger than 10 years.

The 5 year overall survival for ALCL throughout the 20 year period was 70.0% and remained relatively stable at 66.7% during the last 2 periods. In the "other" category, overall survival improved significantly from 50.0% to 85.2% at 3 years and from 44.4% to 81.5% at 5 years (Exhibits 7.3a and 7.3b).

Across all lymphoma types, mortality was, not surprisingly, higher in patients with stage 3 or 4 disease (with 66 deceased out of 314, or 21.0%) as opposed to those with stage 1 or 2 cancer (19 deceased out of 257, or 7.4%). Overall survival for stages 1 and 2 remained the same (92.1%–95.7%) throughout the 4 periods, while survival for stages 3 and 4 improved from 73.4% in the first period to 84.5% in the last.

EXHIBIT 7.3a: **3 year survival rates for lymphoma by tumour type, age at diagnosis and year of diagnosis, age 0–14 years, in Ontario, 1985–2004**

Cancer type	Age group at time of diagnosis (years)	Year of diagnosis: All years N	All years Deaths	All years % Survived	1985–1989 N	1985–1989 Deaths	1985–1989 % Survived
All lymphoma	Overall	**646**	**91**	**85.91**	**124**	**22**	**82.26**
	0–4	110	18	83.64	18	5	72.22
	5–9	206	29	85.92	43	9	79.07
	10–14	330	44	86.67	63	8	87.30
Hodgkin	Overall	**255**	**15**	**94.12**	**55**	**3**	**94.55**
	0–4	11	0	100.00	2	0	100.00
	5–9	49	2	95.92	14	1	92.86
	10–14	195	13	93.33	39	2	94.87
Non-Hodgkin	Overall	**369**	**69**	**81.30**	**68**	**19**	**72.06**
	0–4	86	14	83.72	16	5	68.75
	5–9	153	26	83.01	28	8	71.43
	10–14	130	29	77.69	24	6	75.00
Burkitt/Burkitt-like*	Overall	**133**	**20**	**84.96**	**33**	**9**	**72.73**
	0–4	30	4	86.67	9	3	66.67
	5–9	60	6	90.00	11	3	72.73
	10–14	43	10	76.74	13	3	76.92
Lymphoblastic	Overall	**95**	**12**	**87.37**	**15**	**1**	**93.33**
	0–4	24	3	87.50	3	0	100.00
	5–9	44	5	88.64	9	1	88.89
	10–14	27	4	85.19	3	0	100.00
Anaplastic large cell	Overall	**40**	**10**	**75.00**	**2**	**0**	**100.00**
	0–4	7	1	85.71	0	0	—
	5–9	17	5	70.59	1	0	100.00
	10–14	16	4	75.00	1	0	100.00
Other†	Overall	**101**	**27**	**73.27**	**18**	**9**	**50.00**
	0–4	25	6	76.00	4	2	50.00
	5–9	32	10	68.75	7	4	42.86
	10–14	44	11	75.00	7	3	57.14
All		**576**	**76**	**86.81**	**115**	**21**	**81.74**
Stage 1 & 2		258	15	94.19	51	4	92.16
Stage 3 & 4		318	61	80.82	64	17	73.44

The total for stages may not be the same as reported in Exhibit 7.3b because all individuals may not have linked successfully to Cancer Care Ontario mortality data.
*Burkitt/Burkitt-like includes Burkitt and small non-cleaved cell, non-Burkitt pleomorphic undifferentiated.
†Other includes large cell lymphoma not otherwise specified, post transplant lymphoproliferative disorder, lymphomas not otherwise specified or miscellaneous lymphoma, and central nervous system lymphoma.

22 reticuloendothelial neoplasms not shown separately on this table are included in the overall total for all lymphomas.
7 deaths occurred in this group and are included in the survival calculations for the "all lymphomas" category.

	1990–1994			1995–1999			2000–2004		
	N	Deaths	% Survived	N	Deaths	% Survived	N	Deaths	% Survived
	161	**22**	**86.34**	**163**	**23**	**85.89**	**198**	**24**	**87.88**
	27	3	88.89	27	6	77.78	38	4	89.47
	45	8	82.22	59	7	88.14	59	5	91.53
	89	11	87.64	77	10	87.01	101	15	85.15
	66	**4**	**93.94**	**62**	**3**	**95.16**	**72**	**5**	**93.06**
	2	0	100.00	5	0	100.00	2	0	100.00
	10	0	100.00	14	1	92.86	11	0	100.00
	54	4	92.59	43	2	95.35	59	5	91.53
	90	**16**	**82.22**	**97**	**18**	**81.44**	**114**	**16**	**85.96**
	23	2	91.30	19	4	78.95	28	3	89.29
	34	7	79.41	45	6	86.67	46	5	89.13
	33	7	78.79	33	8	75.76	40	8	80.00
	32	**4**	**87.50**	**30**	**3**	**90.00**	**38**	**4**	**89.47**
	10	1	90.00	3	0	100.00	8	0	100.00
	13	2	84.62	16	0	100.00	20	1	95.00
	9	1	88.89	11	3	72.73	10	3	70.00
	22	**3**	**86.36**	**27**	**5**	**81.48**	**31**	**3**	**90.32**
	6	0	100.00	6	1	83.33	9	2	77.78
	8	1	87.50	14	3	78.57	13	0	100.00
	8	2	75.00	7	1	85.71	9	1	88.89
	11	**2**	**81.82**	**9**	**3**	**66.67**	**18**	**5**	**72.22**
	2	0	100.00	3	1	66.67	2	0	100.00
	6	2	66.67	3	1	66.67	7	2	71.43
	3	0	100.00	3	1	66.67	9	3	66.67
	25	**7**	**72.00**	**31**	**7**	**77.42**	**27**	**4**	**85.19**
	5	1	80.00	7	2	71.43	9	1	88.89
	7	2	71.43	12	2	83.33	6	2	66.67
	13	4	69.23	12	3	75.00	12	1	91.67
	147	**19**	**87.07**	**141**	**17**	**87.94**	**173**	**19**	**89.01**
	77	5	93.51	60	3	95.00	70	3	95.71
	70	14	80.00	81	14	82.72	103	16	84.47

EXHIBIT 7.3b: **5 year survival rates for lymphoma by tumour type, age at diagnosis and year of diagnosis, age 0–14 years, in Ontario, 1985–2004**

Cancer type	Age group at time of diagnosis (years)	Year of diagnosis: All years N	All years Deaths	All years % Survived	1985–1989 N	1985–1989 Deaths	1985–1989 % Survived
All lymphoma	Overall	**646**	**102**	**84.21**	**124**	**25**	**79.84**
	0–4	110	22	80.00	18	6	66.67
	5–9	206	31	84.95	43	10	76.74
	10–14	330	49	85.15	63	9	85.71
Hodgkin	Overall	**255**	**18**	**92.94**	**55**	**4**	**92.73**
	0–4	11	0	100.00	2	0	100.00
	5–9	49	2	95.92	14	1	92.86
	10–14	195	16	91.79	39	3	92.31
Non-Hodgkin	Overall	**369**	**76**	**79.40**	**68**	**21**	**69.12**
	0–4	86	17	80.23	16	6	62.50
	5–9	153	28	81.70	28	9	67.86
	10–14	130	31	76.15	24	6	75.00
Burkitt/Burkitt-like*	Overall	**133**	**21**	**84.21**	**33**	**10**	**69.70**
	0–4	30	5	83.33	9	4	55.56
	5–9	60	6	90.00	11	3	72.73
	10–14	43	10	76.74	13	3	76.92
Lymphoblastic	Overall	**95**	**13**	**86.32**	**15**	**1**	**93.33**
	0–4	24	3	87.50	3	0	100.00
	5–9	44	5	88.64	9	1	88.89
	10–14	27	5	81.48	3	0	100.00
Anaplastic large cell	Overall	**40**	**12**	**70.00**	**2**	**0**	**100.00**
	0–4	7	1	85.71	0	0	—
	5–9	17	6	64.71	1	0	100.00
	10–14	16	5	68.75	1	0	100.00
Other†	Overall	**101**	**30**	**70.30**	**18**	**10**	**44.44**
	0–4	25	8	68.00	4	2	50.00
	5–9	32	11	65.63	7	5	28.57
	10–14	44	11	75.00	7	3	57.14
All		**571**	**85**	**85.11**	**115**	**24**	**79.13**
Stage 1 & 2		257	19	92.61	51	5	90.20
Stage 3 & 4		314	66	78.98	64	19	70.31

The total for stages may not be the same as reported in Exhibit 7.3a because all individuals may not have linked successfully to Cancer Care Ontario mortality data.
*Burkitt/Burkitt-like includes Burkitt and small non-cleaved cell, non-Burkitt pleomorphic undifferentiated.
†Other includes large cell lymphoma not otherwise specified, post transplant lymphoproliferative disorder, lymphomas not otherwise specified or miscellaneous lymphoma, and central nervous system lymphoma.

22 reticuloendothelial neoplasms not shown separately on this table are included in the overall total for all lymphomas.
8 deaths occurred in this group and are included in the survival calculations for the "all lymphomas" category.

	1990–1994			1995–1999			2000–2004		
	N	Deaths	% Survived	N	Deaths	% Survived	N	Deaths	% Survived
	161	**26**	**83.85**	**163**	**24**	**85.28**	**198**	**27**	**86.36**
	27	5	81.48	27	6	77.78	38	5	86.84
	45	9	80.00	59	7	88.14	59	5	91.53
	89	12	86.52	77	11	85.71	101	17	83.17
	66	**5**	**92.42**	**62**	**3**	**95.16**	**72**	**6**	**91.67**
	2	0	100.00	5	0	100.00	2	0	100.00
	10	0	100.00	14	1	92.86	11	0	100.00
	54	5	90.74	43	2	95.35	59	6	89.83
	90	**18**	**80.00**	**97**	**19**	**80.41**	**114**	**18**	**84.21**
	23	3	86.96	19	4	78.95	28	4	85.71
	34	8	76.47	45	6	86.67	46	5	89.13
	33	7	78.79	33	9	72.73	40	9	77.50
	32	**4**	**87.50**	**30**	**3**	**90.00**	**38**	**4**	**89.47**
	10	1	90.00	3	0	100.00	8	0	100.00
	13	2	84.62	16	0	100.00	20	1	95.00
	9	1	88.89	11	3	72.73	10	3	70.00
	22	**3**	**86.36**	**27**	**6**	**77.78**	**31**	**3**	**90.32**
	6	0	100.00	6	1	83.33	9	2	77.78
	8	1	87.50	14	3	78.57	13		100.00
	8	2	75.00	7	2	71.43	9	1	88.89
	11	**3**	**72.73**	**9**	**3**	**66.67**	**18**	**6**	**66.67**
	2	0	100.00	3	1	66.67	2	0	100.00
	6	3	50.00	3	1	66.67	7	2	71.43
	3	0	100.00	3	1	66.67	9	4	55.56
	25	**8**	**68.00**	**31**	**7**	**77.42**	**27**	**5**	**81.48**
	5	2	60.00	7	2	71.43	9	2	77.78
	7	2	71.43	12	2	83.33	6	2	66.67
	13	4	69.23	12	3	75.00	12	1	91.67
	146	**22**	**84.93**	**139**	**18**	**87.05**	**171**	**21**	**87.72**
	77	7	90.91	59	3	94.92	70	4	94.29
	69	15	78.26	80	15	81.25	101	17	83.17

EXHIBIT 7.3c: **5 year survival rates for lymphoma by tumour type, sex and year of diagnosis, age 0–14 years, in Ontario, 1985–2004**

	Year of diagnosis					
	All years			1985–1989		
Cancer type	N	Deaths	% Survived	N	Deaths	% Survived
Female						
All lymphoma	**235**	**44**	**81.28**	**40**	**11**	**72.50**
Hodgkin	113	12	89.38	26	4	84.62
Non-Hodgkin	112	28	75.00	14	7	50.00
Burkitt/Burkitt-like*	24	4	83.33	5	2	60.00
Lymphoblastic	29	5	82.76	4	0	100.00
Anaplastic large cell	16	4	75.00	0	0	—
Other†	43	15	65.12	5	5	0.00
Male						
All lymphoma	**411**	**58**	**85.89**	**84**	**14**	**83.33**
Hodgkin	142	6	95.77	29	0	100.00
Non-Hodgkin	257	48	81.32	54	14	74.07
Burkitt/Burkitt-like*	109	17	84.40	28	8	71.43
Lymphoblastic	66	8	87.88	11	1	90.91
Anaplastic large cell	24	8	66.67	2	0	100.00
Other†	58	15	74.14	13	5	61.54

*Burkitt/Burkitt-like includes Burkitt and small non-cleaved cell, non-Burkitt pleomorphic undifferentiated.
†Other includes large cell lymphoma not otherwise specified, post transplant lymphoproliferative disorder, lymphomas not otherwise specified or miscellaneous lymphoma, and central nervous system lymphoma.

22 reticuloendothelial neoplasms not shown separately on this table are included in the overall total for all lymphomas.
8 deaths occurred in this group and are included in the survival calculations for the "all lymphomas" category.

Exhibit 7.3c

Gender-specific overall survival

The 5 year overall survival in females with any lymphoma was 81.3% during the 20 year period, compared with 85.9% for males. Females showed a trend toward improved overall survival from 72.5% in the first period to 81.2% in the last. Among HL patients, survival in females improved marginally from 84.6% in the first period to 87.9% in the last. In the NHL group, females had a significant increase in survival from 50.0% in the first period to 76.7% in the last. The greatest improvement for females was among BL/BL-like cases, which saw overall survival increase from 60.0% in the first period to 83.3% in the last.

Among males with any lymphoma, 5 year overall survival improved equivalently, from 83.3% in the earliest period to 89.1% in the most recent one. The 5 year survival in males with HL was better, at 100.0% in the first period and 94.9% in the most recent one. Overall survival in males with NHL improved from 74.1% to 86.9%; more specifically, in BL it rose from 71.4% to 90.6% and in ALCL from 57.1% in 1990–1994 to 72.7% in the last period (Exhibit 7.3c).

	1990–1994			1995–1999			2000–2004		
	N	Deaths	% Survived	N	Deaths	% Survived	N	Deaths	% Survived
	56	**9**	**83.93**	**70**	**11**	**84.29**	**69**	**13**	**81.16**
	27	2	92.59	27	2	92.59	33	4	87.88
	28	6	78.57	40	8	80.00	30	7	76.67
	10	1	90.00	3	0	100.00	6	1	83.33
	5	1	80.00	11	3	72.73	9	1	88.89
	4	0	100.00	5	1	80.00	7	3	57.14
	9	4	55.56	21	4	80.95	8	2	75.00
	105	**17**	**83.81**	**93**	**13**	**86.02**	**129**	**14**	**89.15**
	39	3	92.31	35	1	97.14	39	2	94.87
	62	12	80.65	57	11	80.70	84	11	86.90
	22	3	86.36	27	3	88.89	32	3	90.63
	17	2	88.24	16	3	81.25	22	2	90.91
	7	3	57.14	4	2	50.00	11	3	72.73
	16	4	75.00	10	3	70.00	19	3	84.21

EXHIBIT 7.4a: **3 year event free survival rates for lymphoma by tumour type, age at diagnosis and year of diagnosis, age 0–14 years, in Ontario, 1995–2004**

Cancer type	Age group at time of diagnosis (years)	Year of diagnosis								
		All years			1995–1999			2000–2004		
		N	Event	% Event free survival	N	Event	% Event free survival	N	Event	% Event free survival
All lymphoma	Overall	**361**	**85**	**76.45**	**163**	**36**	**77.91**	**198**	**49**	**75.25**
	0–4	54	13	75.93	27	8	70.37	38	12	68.42
	5–9	116	25	78.45	59	15	74.58	59	11	81.36
	10–14	175	37	78.86	77	13	83.12	101	26	74.26
Hodgkin	Overall	**134**	**19**	**85.82**	**62**	**6**	**90.32**	**72**	**13**	**81.94**
	0–4	7	0	100.00	5	0	100.00	2	0	100.00
	5–9	25	3	88.00	14	2	85.71	11	1	90.91
	10–14	102	16	84.31	43	4	90.70	59	12	79.66
Non-Hodgkin	Overall	**211**	**56**	**73.46**	**98**	**27**	**72.45**	**114**	**29**	**74.56**
	0–4	47	13	72.34	19	5	73.68	28	8	71.43
	5–9	91	22	75.82	46	13	71.74	46	9	80.43
	10–14	73	21	71.23	33	9	72.73	40	12	70.00
Burkitt/ Burkitt-like*	Overall	**68**	**9**	**86.76**	**30**	**3**	**90.00**	**38**	**6**	**84.21**
	0–4	11	1	90.91	3	0	100.00	8	1	87.50
	5–9	36	2	94.44	16	0	100.00	20	2	90.00
	10–14	21	6	71.43	11	3	72.73	10	3	70.00
Lymphoblastic	Overall	**58**	**16**	**72.41**	**27**	**7**	**74.07**	**31**	**9**	**70.97**
	0–4	15	5	66.67	6	1	83.33	9	4	55.56
	5–9	27	6	77.78	14	4	71.43	13	2	84.62
	10–14	16	5	68.75	7	2	71.43	9	3	66.67
Anaplastic large cell	Overall	**27**	**12**	**55.56**	**9**	**4**	**55.56**	**18**	**8**	**55.56**
	0–4	5	3	40.00	3	2	33.33	2	1	50.00
	5–9	10	4	60.00	3	1	66.67	7	3	57.14
	10–14	12	5	58.33	3	1	66.67	9	4	55.56
Other†	Overall	**58**	**19**	**67.24**	**31**	**13**	**58.06**	**27**	**6**	**77.78**
	0–4	16	4	75.00	7	2	71.43	9	2	77.78
	5–9	18	10	44.44	12	8	33.33	6	2	66.67
	10–14	24	5	79.17	12	3	75.00	12	2	83.33

*Burkitt/Burkitt-like includes Burkitt and small non-cleaved cell, non-Burkitt pleomorphic undifferentiated.
†Other includes large cell lymphoma not otherwise specified, post transplant lymphoproliferative disorder, lymphomas not otherwise specified or miscellaneous lymphoma, and central nervous system lymphoma.

16 reticuloendothelial neoplasms not shown separately on this table are included in the overall total for all lymphomas.

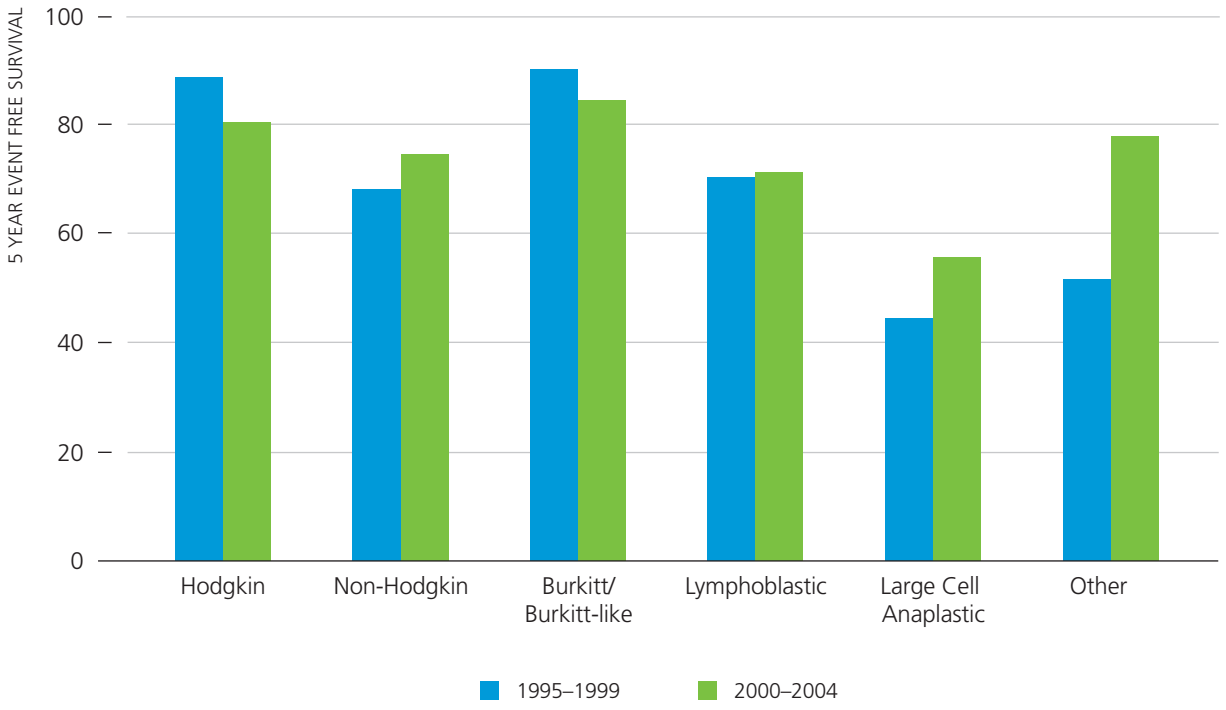
EXHIBIT 7.4b: **5 year event free survival rates for lymphoma by tumour type, age at diagnosis and year of diagnosis, age 0–14 years, in Ontario, 1995–2004**

Cancer type	Age group at time of diagnosis (years)	Year of diagnosis								
		All years			1995–1999			2000–2004		
		N	Event	% Event free survival	N	Event	% Event free survival	N	Event	% Event free survival
All lymphoma	**Overall**	**361**	**91**	**74.79**	**163**	**41**	**74.85**	**198**	**50**	**74.75**
	0–4	54	15	72.22	27	10	62.96	38	12	68.42
	5–9	116	25	78.45	59	15	74.58	59	11	81.36
	10–14	175	41	76.57	77	16	79.22	101	27	73.27
Hodgkin	**Overall**	**134**	**21**	**84.33**	**62**	**7**	**88.71**	**72**	**14**	**80.56**
	0–4	7	0	100.00	5	0	100.00	2	0	100.00
	5–9	25	3	88.00	14	2	85.71	11	1	90.91
	10–14	102	18	82.35	43	5	88.37	59	13	77.97
Non-Hodgkin	**Overall**	**211**	**60**	**71.56**	**98**	**31**	**68.37**	**114**	**29**	**74.56**
	0–4	47	15	68.09	19	7	63.16	28	8	71.43
	5–9	91	22	75.82	46	13	71.74	46	9	80.43
	10–14	73	23	68.49	33	11	66.67	40	12	70.00
Burkitt/ Burkitt-like*	**Overall**	**68**	**9**	**86.76**	**30**	**3**	**90.00**	**38**	**6**	**84.21**
	0–4	11	1	90.91	3	0	100.00	8	1	87.50
	5–9	36	2	94.44	16	0	100.00	20	2	90.00
	10–14	21	6	71.43	11	3	72.73	10	3	70.00
Lymphoblastic	**Overall**	**58**	**17**	**70.69**	**27**	**8**	**70.37**	**31**	**9**	**70.97**
	0–4	15	6	60.00	6	2	66.67	9	4	55.56
	5–9	27	6	77.78	14	4	71.43	13	2	84.62
	10–14	16	5	68.75	7	2	71.43	9	3	66.67
Anaplastic large cell	**Overall**	**27**	**13**	**51.85**	**9**	**5**	**44.44**	**18**	**8**	**55.56**
	0–4	5	3	40.00	3	2	33.33	2	1	50.00
	5–9	10	4	60.00	3	1	66.67	7	3	57.14
	10–14	12	6	50.00	3	2	33.33	9	4	55.56
Other†	**Overall**	**58**	**21**	**63.79**	**31**	**15**	**51.61**	**27**	**6**	**77.78**
	0–4	16	5	68.75	7	3	57.14	9	2	77.78
	5–9	18	10	44.44	12	8	33.33	6	2	66.67
	10–14	24	6	75.00	12	4	66.67	12	2	83.33

*Burkitt/Burkitt-like includes Burkitt and small non-cleaved cell, non-Burkitt pleomorphic undifferentiated.
†Other includes large cell lymphoma not otherwise specified, post transplant lymphoproliferative disorder, lymphomas not otherwise specified or miscellaneous lymphoma, and central nervous system lymphoma.

16 reticuloendothelial neoplasms not shown separately on this table are included in the overall total for all lymphomas.

EXHIBIT 7.4c: **5 year event free survival among lymphoma cases, by type and period, age 0–14 years, in Ontario, 1995–2004**



Exhibits 7.4a – 7.4c

Event free survival

EFS rates were reportable for only the 1995–2004 period. The 3 and 5 year EFS rates for all lymphomas were very similar at 76.5% and 74.8%, respectively, and were relatively stable from 1995–1999 to the most recent period (77.9 % and 75.3% for 3 year EFS in the 2 periods, and 74.8% throughout the 10 year period for 5 year EFS) (Exhibits 7.4a and 7.4b). HL patients had 3 and 5 year EFS that was stable at 85.8% and 84.3%, respectively. The 3 year EFS for HL decreased from 90.3% during the 1995–1999 period to 81.9% in the most recent one, while 5 year EFS decreased from 88.7% to 80.6%. Interestingly, the small number (7) of younger patients with HL (age 0–4 years) had 100.0% 3 and 5 year EFS. The drop in EFS was more obvious among teenagers with HL, with 3 year EFS dropping from 90.7% in the first period to 79.7% in the last, and 5 year EFS dropping from 88.4% to 78.0%.

Among NHL patients, 3 and 5 year EFS was very similar at 73.5% and 71.5%, respectively, again implying that any significant events occurred within the first 3 years. The 3 year EFS was 72.5% in 1995–1999 and remained relatively stable at 74.6% in the most recent period, while 5 year EFS was 68.4% in 1995–1999 and 74.6% in 2000–2004. From 1995 until 2004, the 3 and 5 year EFS rates for patients with BL/BL-like disease were identical at 86.8%, with a mild decrease in EFS from 90.0% to 84.2% in the most recent period. Patients with BL/BL-like disease aged 0–4 and 5–9 years had 5 year EFS of 90.9% and 94.4%, respectively, compared with 71.4% for patients aged 10–14 years (Exhibits 7.4a and 7.4b).

Overall 5 year EFS for LL patients was 70.7%, with younger and older children having worse EFS (60.0% and 68.8%, respectively) while the 5–9 year old group had better EFS at 77.8%. In addition, 5 year EFS decreased from 66.7% during 1995–1999 to 55.6% in the most recent period for younger patients (0–4 years) and from 71.4% to 66.7% in the 10–14 year group. EFS improved from 71.4% to 84.6% for the 5–9 year group. Throughout the 1995–2004 period, 5 year EFS for ALCL patients was only 51.9%, with a slight improvement from 44.4% in the first period to 55.6% in the last. The sample size, however, is small. The 5 year EFS for the "other" group was 51.6% in 1995–1999, improving to 77.8% in 2000–2004 (Exhibits 7.4a–c).

EXHIBIT 7.5a: **3 year relapse free survival rates for lymphoma by tumour type, age at diagnosis and year of diagnosis, age 0–14 years, in Ontario, 1995–2004**

Cancer type	Age group at time of diagnosis (years)	Year of diagnosis								
		All years			1995–1999			2000–2004		
		N	Relapse	% Relapse free survival	N	Relapse	% Relapse free survival	N	Relapse	% Relapse free survival
All lymphoma	**Overall**	**361**	**53**	**85.32**	**163**	**21**	**87.12**	**198**	**32**	**83.84**
	0–4	54	11	79.63	27	4	85.19	38	7	81.58
	5–9	116	16	86.21	59	11	81.36	59	5	91.53
	10–14	175	26	85.14	77	6	92.21	101	20	80.20
Hodgkin	**Overall**	**134**	**17**	**87.31**	**62**	**5**	**91.94**	**72**	**12**	**83.33**
	0–4	7	0	100.00	5	0	100.00	2	0	100.00
	5–9	25	2	92.00	14	1	92.86	11	1	90.91
	10–14	102	15	85.29	43	4	90.70	59	11	81.36
Non-Hodgkin	**Overall**	**211**	**30**	**85.78**	**101**	**15**	**85.15**	**114**	**15**	**86.84**
	0–4	47	7	85.11	21	3	85.71	28	4	85.71
	5–9	91	13	85.71	46	10	78.26	46	3	93.48
	10–14	73	10	86.30	34	2	94.12	40	8	80.00
Burkitt/ Burkitt-like*	**Overall**	**68**	**5**	**92.65**	**30**	**0**	**100.00**	**38**	**5**	**86.84**
	0–4	11	1	90.91	3	0	100.00	8	1	87.50
	5–9	36	2	94.44	16	0	100.00	20	2	90.00
	10–14	21	2	90.48	11	0	100.00	10	2	80.00
Lymphoblastic	**Overall**	**58**	**8**	**86.21**	**27**	**6**	**77.78**	**31**	**2**	**93.55**
	0–4	15	1	93.33	6	0	100.00	9	1	88.89
	5–9	27	4	85.19	14	4	71.43	13	0	100.00
	10–14	16	3	81.25	7	2	71.43	9	1	88.89
Anaplastic large cell	**Overall**	**27**	**7**	**74.07**	**9**	**3**	**66.67**	**18**	**4**	**77.78**
	0–4	5	2	60.00	3	2	33.33	2	0	100.00
	5–9	10	2	80.00	3	1	66.67	7	1	85.71
	10–14	12	3	75.00	3	0	100.00	9	3	66.67
Other†	**Overall**	**58**	**10**	**82.76**	**31**	**6**	**80.65**	**27**	**4**	**85.19**
	0–4	16	3	81.25	7	1	85.71	9	2	77.78
	5–9	18	5	72.22	12	5	58.33	6	0	100.00
	10–14	24	2	91.67	12	0	100.00	12	2	83.33

*Burkitt/Burkitt-like includes Burkitt and small non-cleaved cell, non-Burkitt pleomorphic undifferentiated.
†Other includes large cell lymphoma not otherwise specified, post transplant lymphoproliferative disorder, lymphomas not otherwise specified or miscellaneous lymphoma, and central nervous system lymphoma.

16 reticuloendothelial neoplasms not shown separately on this table are included in the overall total for all lymphomas.

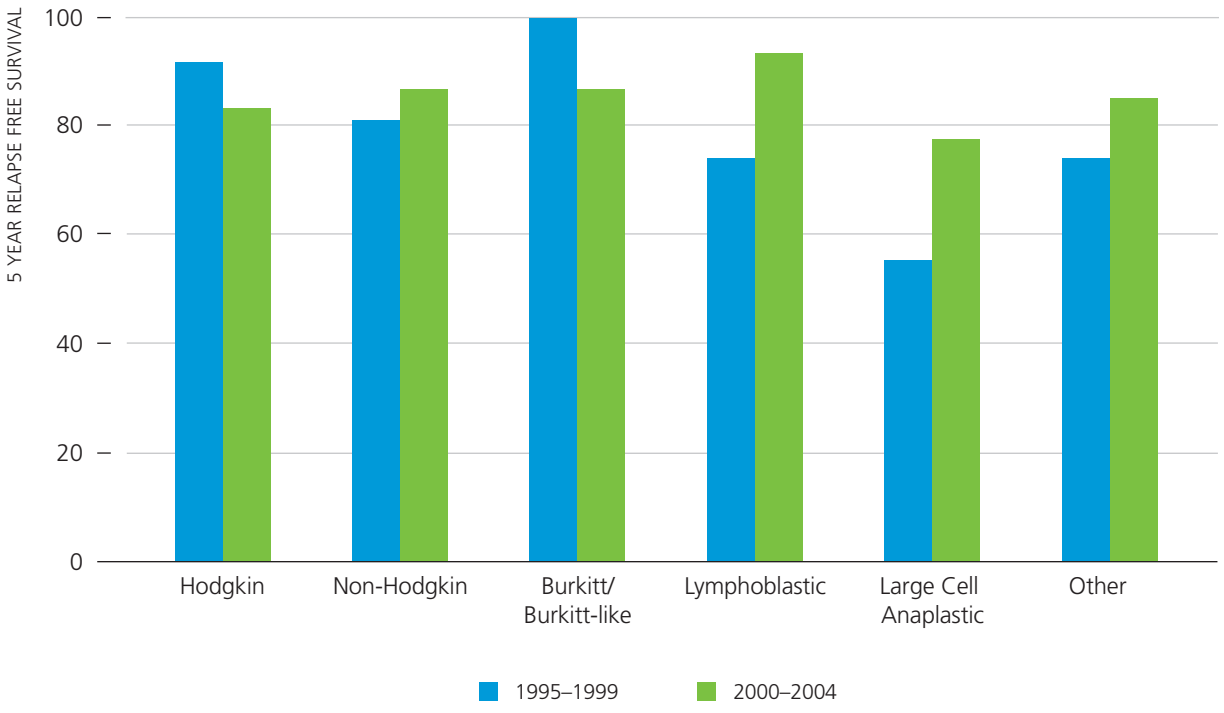
EXHIBIT 7.5b: **5 year relapse free survival rates for lymphoma by tumour type, age at diagnosis and year of diagnosis, age 0–14 years, in Ontario, 1995–2004**

Cancer type	Age group at time of diagnosis (years)	Year of diagnosis								
		All years			1995–1999			2000–2004		
		N	Relapse	% Relapse free survival	N	Relapse	% Relapse free survivall	N	Relapse	% Relapse free survival
All lymphoma	Overall	**361**	**57**	**84.21**	**163**	**25**	**84.66**	**198**	**32**	**83.84**
	0–4	54	13	75.93	27	6	77.78	38	7	81.58
	5–9	116	16	86.21	59	11	81.36	59	5	91.53
	10–14	175	28	84.00	77	8	89.61	101	20	80.20
Hodgkin	Overall	**134**	**17**	**87.31**	**62**	**5**	**91.94**	**72**	**12**	**83.33**
	0–4	7	0	100.00	5	0	100.00	2	0	100.00
	5–9	25	2	92.00	14	1	92.86	11	1	90.91
	10–14	102	15	85.29	43	4	90.70	59	11	81.36
Non-Hodgkin	Overall	**211**	**34**	**83.89**	**97**	**19**	**80.41**	**114**	**15**	**86.84**
	0–4	47	9	80.85	19	5	73.68	28	4	85.71
	5–9	91	13	85.71	45	10	77.78	46	3	93.48
	10–14	73	12	83.56	33	4	87.88	40	8	80.00
Burkitt/ Burkitt-like*	Overall	**68**	**5**	**92.65**	**30**	**0**	**100.00**	**38**	**5**	**86.84**
	0–4	11	1	90.91	3	0	100.00	8	1	87.50
	5–9	36	2	94.44	16	0	100.00	20	2	90.00
	10–14	21	2	90.48	11	0	100.00	10	2	80.00
Lymphoblastic	Overall	**58**	**9**	**84.48**	**27**	**7**	**74.07**	**31**	**2**	**93.55**
	0–4	15	2	86.67	6	1	83.33	9	1	88.89
	5–9	27	4	85.19	14	4	71.43	13	0	100.00
	10–14	16	3	81.25	7	2	71.43	9	1	88.89
Anaplastic large cell	Overall	**27**	**8**	**70.37**	**9**	**4**	**55.56**	**18**	**4**	**77.78**
	0–4	5	2	60.00	3	2	33.33	2	0	100.00
	5–9	10	2	80.00	3	1	66.67	7	1	85.71
	10–14	12	4	66.67	3	1	66.67	9	3	66.67
Other†	Overall	**58**	**12**	**79.31**	**31**	**8**	**74.19**	**27**	**4**	**85.19**
	0–4	16	4	75.00	7	2	71.43	9	2	77.78
	5–9	18	5	72.22	12	5	58.33	6	0	100.00
	10–14	24	3	87.50	12	1	91.67	12	2	83.33

*Burkitt/Burkitt-like includes Burkitt and small non-cleaved cell, non-Burkitt pleomorphic undifferentiated.
†Other includes large cell lymphoma not otherwise specified, post transplant lymphoproliferative disorder, lymphomas not otherwise specified or miscellaneous lymphoma, and central nervous system lymphoma.

16 reticuloendothelial neoplasms not shown separately on this table are included in the overall total for all lymphomas.

EXHIBIT 7.5c: **5 year relapse free survival rates among lymphoma cases by tumour type, and period, age 0–14 years, in Ontario, 1995–2004**



Exhibits 7.5a–7.5c

Relapse free survival

The 3 and 5 year relapse free survival (RFS) rates for all lymphomas were almost identical, at 85.3% and 84.2%, respectively, from 1995 to 2004 (Exhibits 7.5a and 7.5b). Children with HL had similar 3 and 5 year RFS of 87.3% during 1995–2004, while there was a slight decrease in 5 year RFS from 91.9% during 1995–1999 to 83.3% during 2000–2004 (Exhibit 7.5a–c). Children with NHL had 3 year RFS of 85.8% and 5 year RFS of 83.9% for the 10 year period. The 5 year RFS improved from 80.4% during 1995–1999 to 86.8% during the most recent period. For BL patients 1, 3 and 5 year RFS remained stable at 92.7% during 1995–2004, with all events occurring during the first year, as expected; RFS at 5 years was 100.0% for BL patients during 1995–1999 but decreased to 86.8% during 2000–2004 (Exhibit 7.5c). For patients with LL, there was a notable improvement in 5 year RFS from 74.1% during 1995–1999 to 93.6% during 2000–2004. Similarly, patients with ALCL had improved 5 year RFS of 77.8% during 2000–2004, compared with 55.6% during 1995–1999. Those with "other" lymphomas had 5 year RFS of 85.2% in the most recent period and 74.2% during 1995–1999.

EXHIBIT 7.6: **Proportion of patients who received hematopoietic stem cell transplantation, chemotherapy and radiation treatment among lymphoma cases by tumour type, age at diagnosis and year of diagnosis, age 0–14 years, in Ontario, 1995–2004**

Cancer type	Age group at time of diagnosis (years)	Number of cases			Hematopoietic stem cell transplantation					
		1995–2004	1995–1999	2000–2004	All years		1995–1999		2000–2004	
					N	%	N	%	N	%
All lymphoma	Overall	**361**	**163**	**198**	**46**	**12.74**	**19**	**11.66**	**27**	**13.64**
	0–4	65	27	38	10	15.38	4	14.81	6	15.79
	5–9	118	59	59	14	11.86	9	15.25	5	8.47
	10–14	178	77	101	22	12.36	6	7.79	16	15.84
Hodgkin	Overall	**134**	**62**	**72**	**15**	**11.19**	**4**	**6.45**	**11**	**15.28**
	0–4	7	5	2	0	0.00	0	0.00	0	0.00
	5–9	25	14	11	2	8.00	1	7.14	1	9.09
	10–14	102	43	59	13	12.75	3	6.98	10	16.95
Non-Hodgkin	Overall	**211**	**97**	**114**	**28**	**13.27**	**14**	**14.43**	**14**	**12.28**
	0–4	47	19	28	8	17.02	3	15.79	5	17.86
	5–9	91	45	46	12	13.19	8	17.78	4	8.70
	10–14	73	33	40	8	10.96	3	9.09	5	12.50
Burkitt/Burkitt-like*	Overall	**68**	**30**	**38**	**6**	**8.82**	**1**	**3.33**	**5**	**13.16**
	0–4	11	3	8	2	18.18	0	0.00	2	25.00
	5–9	36	16	20	2	5.56	0	0.00	2	10.00
	10–14	21	11	10	2	9.52	1	9.09	1	10.00
Lymphoblastic	Overall	**58**	**27**	**31**	**7**	**12.07**	**6**	**22.22**	**1**	**3.23**
	0–4	15	6	9	2	13.33	1	16.67	1	11.11
	5–9	27	14	13	4	14.81	4	28.57	0	0.00
	10–14	16	7	9	1	6.25	1	14.29	0	0.00
Anaplastic large cell	Overall	**27**	**9**	**18**	**5**	**18.52**	**2**	**22.22**	**3**	**16.67**
	0–4	5	3	2	1	20.00	1	33.33	0	0.00
	5–9	10	3	7	1	10.00	0	0.00	1	14.29
	10–14	12	3	9	3	25.00	1	33.33	2	22.22
Other†	Overall	**58**	**31**	**27**	**10**	**17.24**	**5**	**16.13**	**5**	**18.52**
	0–4	16	7	9	3	18.75	1	14.29	2	22.22
	5–9	18	12	6	5	27.78	4	33.33	1	16.67
	10–14	24	12	12	2	8.33	0	0.00	2	16.67

*Burkitt/Burkitt-like includes Burkitt and small non-cleaved cell, non-Burkitt pleomorphic undifferentiated.
†Other includes large cell lymphoma not otherwise specified, post transplant lymphoproliferative disorder, lymphomas not otherwise specified or miscellaneous lymphoma, and central nervous system lymphoma.

16 reticuloendothelial neoplasms not shown separately on this table are included in the overall total for all lymphomas.

	Chemotherapy						Radiation						Radiation + chemotherapy					
	All years		1995–1999		2000–2004		All years		1995–1999		2000–2004		All years		1995–1999		2000–2004	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
	344	**95.29**	**152**	**93.25**	**192**	**96.97**	**143**	**39.61**	**77**	**47.24**	**66**	**33.33**	**142**	**39.34**	**76**	**46.63**	**66**	**33.33**
	59	90.77	24	88.89	35	92.11	14	21.54	9	33.33	5	13.16	14	21.54	9	33.33	5	13.16
	114	96.61	57	96.61	57	96.61	31	26.27	21	35.59	10	16.95	31	26.27	21	35.59	10	16.95
	171	96.07	71	92.21	100	99.01	98	55.06	47	61.04	51	50.50	97	54.49	46	59.74	51	50.50
	131	**97.76**	**60**	**96.77**	**71**	**98.61**	**100**	**74.63**	**55**	**88.71**	**45**	**62.50**	**99**	**73.88**	**54**	**87.10**	**45**	**62.50**
	7	100.00	5	100.00	2	100.00	6	85.71	5	100.00	1	50.00	6	85.71	5	100.00	1	50.00
	25	100.00	14	100.00	11	100.00	16	64.00	11	78.57	5	45.45	16	64.00	11	78.57	5	45.45
	99	97.06	41	95.35	58	98.31	78	76.47	39	90.70	39	66.10	77	75.49	38	88.37	39	66.10
	191	**90.52**	**86**	**88.66**	**105**	**92.11**	**37**	**17.54**	**19**	**19.59**	**18**	**15.79**	**37**	**17.54**	**19**	**19.59**	**18**	**15.79**
	39	82.98	15	78.95	24	85.71	6	12.77	3	15.79	3	10.71	6	12.77	3	15.79	3	10.71
	85	93.41	42	93.33	43	93.48	14	15.38	9	20.00	5	10.87	14	15.38	9	20.00	5	10.87
	67	91.78	29	87.88	38	95.00	17	23.29	7	21.21	10	25.00	17	23.29	7	21.21	10	25.00
	66	**97.06**	**28**	**93.33**	**38**	**100.00**	**1**	**1.47**	**1**	**3.33**	**0**	**0.00**	**1**	**1.47**	**1**	**3.33**	**0**	**0.00**
	11	100.00	3	100.00	8	100.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	35	97.22	15	93.75	20	100.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	20	95.24	10	90.91	10	100.00	1	4.76	1	9.09	0	0.00	1	4.76	1	9.09	0	0.00
	58	**100.00**	**27**	**100.00**	**31**	**100.00**	**22**	**37.93**	**14**	**51.85**	**8**	**25.81**	**22**	**37.93**	**14**	**51.85**	**8**	**25.81**
	15	100.00	6	100.00	9	100.00	3	20.00	1	16.67	2	22.22	3	20.00	1	16.67	2	22.22
	27	100.00	14	100.00	13	100.00	10	37.04	8	57.14	2	15.38	10	37.04	8	57.14	2	15.38
	16	100.00	7	100.00	9	100.00	9	56.25	5	71.43	4	44.44	9	56.25	5	71.43	4	44.44
	23	**85.19**	**9**	**100.00**	**14**	**77.78**	**4**	**14.81**	**1**	**11.11**	**3**	**16.67**	**4**	**14.81**	**1**	**11.11**	**3**	**16.67**
	4	80.00	3	100.00	1	50.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	8	80.00	3	100.00	5	71.43	2	20.00	0	0.00	2	28.57	2	20.00	0	0.00	2	28.57
	11	91.67	3	100.00	8	88.89	2	16.67	1	33.33	1	11.11	2	16.67	1	33.33	1	11.11
	44	**75.86**	**22**	**70.97**	**22**	**81.48**	**10**	**17.24**	**3**	**9.68**	**7**	**25.93**	**10**	**17.24**	**3**	**9.68**	**7**	**25.93**
	9	56.25	3	42.86	6	66.67	3	18.75	2	28.57	1	11.11	3	18.75	2	28.57	1	11.11
	15	83.33	10	83.33	5	83.33	2	11.11	1	8.33	1	16.67	2	11.11	1	8.33	1	16.67
	20	83.33	9	75.00	11	91.67	5	20.83	0	0.00	5	41.67	5	20.83	—	0.00	5	41.67

Exhibit 7.6

Type of Treatment

Lymphoma is treated with chemotherapy, radiation, HSCT or a combination of these therapies. For all lymphomas over all years combined, 12.7% were treated with HSCT, 95.3% with chemotherapy and 39.6% with radiation. All but 1 (39.3%) patient undergoing radiation treatment received a combination of radiation and chemotherapy. The use of radiation alone and the combined use of radiation and chemotherapy decreased in the lymphoma group between 1995–1999 and 2000–2004, largely as a result of the reduction in the use of radiation for HL. For all HL patients the proportion receiving radiation dropped from 88.7% to 62.5% between the 2 periods. The NHL group received less radiation than the HL group either alone or in combination with chemotherapy, but the percentages of patients receiving radiation remained constant over time.

Looking at the NHL subtypes, although numbers are small, ALCL patients in the 10–14 year age group were most likely to undergo HSCT (3 of 12, or 25.0%). Virtually all LL patients received chemotherapy or chemotherapy and radiation, but the use of radiation decreased from 51.9% in 1995–1999 to 25.8% in 2000–2004. All patients with BL received chemotherapy and only 1 of 68 patients (1.5%) received radiotherapy during the 1995–1999 period. No BL patient received radiation during 2000–2004 (Exhibit 7.6).

Second Malignancies

The cumulative incidence of second malignancies was 4.3%, or 27 of 624 lymphoma patients, with a median duration of follow up of 10.0 years. Among long term survivors of HL 14 second cancers occurred, for a cumulative rate of 5.4% (3 secondary leukemias, 2 CNS tumours, 2 bone tumours, 1 solid tumour, 1 germ cell tumour and 5 miscellaneous tumours). In survivors of BL, 2 secondary lymphomas and 1 miscellaneous tumour occurred, and 1 miscellaneous secondary tumour developed in a survivor of LL. Eight secondary cancers developed among survivors of "other" lymphomas (2 secondary leukemias, 1 lymphoma, 2 CNS tumours, 2 solid tumours and 2 miscellaneous cancers). The cumulative rate of second malignancies for the entire NHL group was lower than for HL, at 3.5% (data not shown).

Summary

While the overall incidence of pediatric cancer has remained stable over several decades, it is important to assess trends of incidence and patterns of treatment over time to better address the future health needs of the patients and to assess the successes and shortcomings of the care provided. Cancer control mandates that we continue to evaluate outcomes so that future cancer care strategies will be effective.

Ontario has developed a database through POGO that facilitates such endeavours. While the database is not a perfect measure because of changes in categorization over time, it is clear that pediatric lymphoma accounts for 10% of all pediatric cancers in Ontario, which is on par with the rest of the nation. Survival curves and treatment trends parallel reports in the literature and despite an increasing and diverse immigration pattern, there does not seem to be a significant change in the reported numbers and trends. Such statistical analysis remains important in directing future research and appropriately allocating health care resources.

References

1 Canadian Cancer Society, National Cancer Institute of Canada. Canadian cancer statistics 2008. Toronto: CCS/NCIC; 2008.

2 Magrath IT. Malignant non-Hodgkin's lymphoma in children. In: Pizzo PA, Poplack DG, editors. Principles and practice of pediatric oncology. 2nd ed. Philadelphia: J.B. Lippincott; 1993. p. 537-75.

3 Greaves MF. Differentiation-linked leukemogenesis in lymphocytes. Science. 1986 Nov;234(4777):697-704.

4 Sandlund JT, Downing JR, Crist WM. Non-Hodgkin's lymphoma in childhood. N Engl J Med. 1996 May;334(19):1238-48.

5 Burkhardt B, Zimmermann M, Oschlies I, Niggli F, Mann G, Parwaresch R, et al. The impact of age and gender on biology, clinical features and treatment outcome of non-Hodgkin lymphoma in childhood and adolescence. Br J Haematol. 2005 Oct;131(1):39-49.

6 Hodgson DC, Hudson MM, Constine LS: Pediatric Hodgkin lymphoma: maximizing efficacy and minimizing toxicity. Semin Radiat Oncol. 2007 Jul;17(3):230-42.

7 Sterialova-Foucher E, Stiller C, Lacour B, Kaatsch P. International classification of childhood cancer, third edition. Cancer. 2005 Apr;103(7):1457-67.

8 Straus SE, Sneller M, Lenardo MJ, Puck JM, Strober W. An inherited disorder of lymphocyte apoptosis: the autoimmune lymphoproliferative syndrome. Ann Intern Med. 1999 Apr;130(7):591-601.

9 Persson B. Occupational exposure and malignant lymphoma. Int J Occup Med Environ Health. 1996;9(4):309-21.

10 Bertazzi PA, Pesatori AC, Bernucci I, Landi MT, Consonni D. Dioxin exposure and human leukemias and lymphomas. Lessons from the Seveso accident and studies on industrial workers. Leukemia. 1999 Apr;13(Suppl 1):S72-4.

Published by the Pediatric Oncology Group of Ontario (POGO)

Pediatric Oncology Group of Ontario
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Toronto, Ontario M5G 1V2
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Canadian cataloging in publication data:

Atlas of Childhood Cancer in Ontario
Includes bibliographical references.
ISBN: (Print) **978-0-9939255-0-4**
ISBN: (Online) **978-0-9939255-1-1**

How to cite this publication:

The production of *Atlas of Childhood Cancer in Ontario* was a collaborative venture. Accordingly, to give credit to individual authors, please cite individual chapters and title, in addition to editors and book title.

For example: Pole JD, Greenberg ML, Sung L, Agha M, Riehl, M. Survival. In: Greenberg ML, Barnett H, Williams J, editors. Atlas of Childhood Cancer in Ontario. Toronto: Pediatric Oncology Group of Ontario; 2015.

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