SPECIAL TOPIC: CHILDHOOD CANCER (AGES 0 TO 14)

In Canada close to 850 children (defined as 0 to 14 years of age*) are diagnosed with cancer every year, and around 135 die from their disease (Table 17). In Canadian children over the age of one month, cancer is the leading disease-related cause of death, second only to avoidable injury in overall mortality.[15] While many children with cancer now have the opportunity for cure, a significant proportion of survivors experience life-long adverse effects, as a result either of the cancer itself or of its treatment.[16] Included in these effects are cardiopulmonary, endocrine, renal or pulmonary dysfunction, neurocognitive impairments and the development of second cancers.

Although childhood cancers account for a little over half of one percent of all cancers diagnosed in Canada, they are of significant public health importance. Cancer in children creates a disproportionate impact on health, economic and social welfare systems, as a consequence of the loss of young lives. As well, both child and family are affected by emotional trauma and life-long consequences. Families affected by childhood cancer must often provide care for other young children in the home while attempting, at the same time, to navigate their way through the health and social welfare systems. Parents often work less or stop working altogether, which creates financial stress. Moreover, the impacts of childhood cancer often continue beyond the end of treatment, with both the survivors and their families requiring ongoing emotional, physical and financial support as well as health care.[17]

Cancers in children differ from those occurring in adults in both their site of origin and their behaviour.[18,19] The majority of cancers in adults are carcinomas which start in the glands or tissues that line organs such as the breast, lung, prostate or colon. In children, carcinomas are very rare. Tumours in children have short latency periods, often grow rapidly and are aggressive, invasive and frequently spread to other parts of the body. Relative to adults, cancers in children include a higher proportion of hematopoietic (blood and lymphatic) malignancies, most commonly leukemia. In order to account for the differences in childhood cancers as compared with those in adults, a separate classification scheme of diagnostic groupings has been developed.[20] The International Classification of Childhood Cancers comprises 12 major diagnostic categories, with associated subgroups for additional refinement.

Table 17 presents the number of new cases of childhood cancer with age-standardized incidence rates, and the number of deaths due to cancer with age-standardized mortality rates during 2000-2004. For this period, cancer was diagnosed each year in an average of 850 children aged 0 to 14, and an average of 135 died each year from their disease. Leukemia accounted for 33% of new cases and 27% of deaths due to cancer in children, and remains the most common of the childhood cancers. Cancers of the central nervous system, the second most common group of childhood cancers, constituted approximately 20% of new cases and 30% of deaths, followed by lymphomas, which accounted for 12% of new cases and 5% of deaths.

The overall incidence of childhood cancer has remained relatively stable since 1985, varying from 144 to 159 per 1,000,000 children (Figure 10, all cancers). Estimates of time trends and tests for changes in the trends for age-standardized incidence and mortality rates were conducted using changepoint regression analysis (for details on methods, see *Appendix II: Methods*). The estimated average annual percent change in incidence rates between 1985 and 2004 was not statistically significantly different

* Note: While data in this section are based on children 0 to 14 years of age, most pediatric oncology centres in Canada treat children 0 to 17 years of age.

from zero for all cancers combined or for any of the cancers shown in Figure 10. During the same period, however, there was a dramatic decline in childhood cancer mortality. Linear trends observed statistically significant decreases in the age-standardized mortality rates for all cancers and each of the selected cancers examined ($p<0.05$).

Incidence rates are highest among young children, aged 0 to 4 years (Table 18). Rates are lower and similar for children aged 5 to 9 and 10 to 14. Lymphoma rates increase with age, while rates for neuroblastoma peak prior to age one and become very rare after the age of five. Overall, childhood cancer occurs more commonly in males than in females. For every newly diagnosed female with cancer, there are 1.2 males (Table 19). The largest differences by sex are lymphomas (ratio of male to female new cases, 2.1 to 1) and hepatic tumours (ratio of male to female new cases, 1.4 to 1).

Cancer Control in Children

Cancer control aims not only to prevent and cure cancer, but also to increase both survival and quality of life after diagnosis. Cancer control is strengthened by knowledge gained through research, surveillance, and outcome evaluation, which can then be applied to the development of more effective future strategies and actions.[21] Moreover, all activities that together form the continuum of prevention, early detection, diagnosis, treatment, survivorship, and palliative care are components of cancer control.

Prevention and Screening

Little is known about what causes childhood cancers, thereby limiting opportunities for primary prevention. While many studies have examined possible risk factors, few have been found to be directly related.[22] Certain genetic abnormalities and inherited diseases are associated with a higher risk of childhood cancer (such as Down syndrome). Chemotherapeutic agents, radiotherapy, or maternal (intra-uterine) exposure to diethylstilbestrol (DES) or to ionizing radiation are a few of the better-established risk factors for childhood cancers. However, these risk factors account for only a small percentage of all cases.

Screening for childhood tumours has also proven ineffective, mainly due to short latency periods and cancers that are typically aggressive and fast growing. With the exception of neuroblastoma, no screening methods have been developed to date for childhood cancer. However, screening for neuroblastoma was determined to be ineffective after studies found no decline in mortality related to screening.[23, 24] Moreover, because infant neuroblastoma often regresses naturally, screening resulted in both an increased incidence of the disease and unnecessary treatment.

Diagnosis and Treatment

Currently, the most effective methods of cancer control in children are accurate diagnosis and effective treatment. In Canada, definitive diagnosis and treatment for children with cancer is available at one of 17 specialized pediatric cancer treatment centres (Table 23). In general, for Canadian children with cancer, diagnosis and the start of treatment occur rapidly. During 1995-2000, the median interval between first presentation to a health care professional and start of treatment was 17 days (Figure 11). This interval was shortest for children under 1 year of age (median interval of 9 days), and longest for 10- and 14-year olds where the median interval was 26 days; a pattern that is consistent with the biology of tumours that predominate in each age group. The

main factors that affect the time from the onset of symptoms to diagnosis include the biology of the tumour, the site of occurrence, and the patient's age.[25]

Metastasis, the process by which cancer spreads from one part of the body to another through the bloodstream or lymphatic system, is often an important marker to indicate disease severity. Excluding non-applicable cases (i.e. cancers which are systematic in origin, such as leukemia and lymphoma), the proportion of patients with metastatic disease at diagnosis are shown in Table 20. Metastases were present at diagnosis in approximately one quarter of all cancer cases. Sympathetic nervous system tumours, hepatic and renal tumours were most likely to have metastasized before diagnosis (56, 35 and 31% respectively). The lowest proportion of metastasis was for cases of retinoblastoma (5%), followed by cancers of the central nervous system (13%); these findings are consistent with the known biological behaviour of these diseases.

The role of collaborative clinical trials in therapy for children with cancer has been vital in advancing progress. Randomized clinical trials are studies primarily designed to compare the effectiveness of different treatments, with the ultimate aim of increasing survival while minimizing side effects. Clinical trials typically study the best current standard treatment (based on results of previous clinical trials) and an experimental treatment that includes some modification or addition to the standard treatment. The standard treatment of a randomized clinical trial will often also be used as the basis of treatment for children when a clinical trial is not open, they do not meet eligibility criteria, or when a family declines to participate in the research. In Canada, an estimated 80% of children with cancer are either enrolled in a clinical trial or treated according to the standard treatment developed from clinical trial methodologies (Figure 12). Percentages vary widely by type of cancer, from 95% of children with leukemia receiving treatment in a randomized clinical trial or a standardized treatment protocol to 50% of children with central nervous system neoplasms (since a portion are treated by surgery alone, such cases do not get enrolled in a clinical trial or standard treatment protocol).

Late Effects

Progress in the treatment of cancer in children now means that over 82% of children with cancer survive at least 5 years after diagnosis.[26] This has led to an increase in the number of childhood cancer survivors and the need to monitor survivors of childhood cancer for late effects of therapy. Based on U.S. data, it is estimated that 1 in 1000 people in the developed world are survivors of childhood cancer.[27] Late effects are broadly defined as problems that develop after the completion of cancer treatment.

The importance of examining late effects in survivors of childhood cancer relates primarily to concern for the future wellbeing of survivors. Childhood cancer survivors are known to be at increased risk of physical, neurocognitive and psychological health problems, as a result of both their disease and the therapies they have undergone. Chemotherapy, radiation therapy and surgery can all lead to late effects involving any organ or system in the body. In general, adverse effects from radiation may not be apparent for several years. Chemotherapy problems that develop soon after treatment are often temporary, but some may lead to long-term complications.[28] Due to the poor survival rate of childhood cancer in previous decades, knowledge regarding the long-term effects of treatments on childhood cancer survivors as they age beyond midlife is largely unknown. As treatments change, new research will be required to monitor long-term impacts associated with the disease and its treatment.

Owing to the variable nature of late effects and lack of knowledge, management is often difficult. The emergence of late effects depends on many factors: age, exposure to chemotherapy and radiation during treatment (including both the dose and the part of body that was treated), biological predisposition, and the severity of the original disease. Some late effects may be identified relatively early and resolved without consequence; others may not appear until years later and may influence the progression of other age-related diseases.

An estimated two-thirds of survivors have at least one chronic or late-occurring effect from their cancer therapy, while up to one-third have a major, serious or life threatening complication. Endocrine and metabolic complications are the most prevalent late effects among childhood cancer survivors, followed by sensory problems, neurocognitive impairment, cardiopulmonary dysfunction, gastrointestinal disorders and secondary malignant neoplasms.[29] Survivors are also found to be at an increased risk of early death up to 25 years after diagnosis, owing mainly to a relapse of the primary cancer in the early years following the completion of therapy.[30]

Survival

Observed survival proportions (OSP) estimated for children (aged 0 to 14 years) diagnosed from 1999 to 2003 are presented in Table 21. These estimates were derived using period analysis and exclude data from the province of Quebec (see *Appendix II: Methods*). For all childhood cancers combined the five-year OSP was estimated to be 82%. The corresponding one- and three-year survival proportions were 92% and 85%, respectively. Within specific diagnostic groups, the highest five-year OSPs were observed for retinoblastoma (99%), renal tumours (92%), lymphomas (89%), and germ cell tumours (89%) while the lowest were seen in neuroblastoma (70%) and malignant bone tumours (72%).

Survival for those diagnosed with acute myeloid leukaemia (five-year OSP 67%) was considerably less than for those diagnosed with a lymphoid leukaemia (five-year OSP 90%). The outlook for those diagnosed with Hodgkin lymphoma (93% five-year OSP) was better than those diagnosed with non-Hodgkin lymphoma (84% five-year OSP). Similarly, the five-year prognosis for certain types of brain cancers such as astrocytoma (87%) was found to be higher than intracranial and intraspinal embryonal tumours (60%). Thyroid carcinomas (98% five-year OSP) and malignant melanomas (92% five-year OSP), the two most common subgroups of the other malignant epithelial neoplasms and malignant melanomas diagnostic group, had better survival than the diagnostic group as a whole (86%). Similarly, survival for malignant gonadal germ cell tumour cases (95% five-year OSP) was better than within its diagnostic group as a whole (89%).

Progress in cancer survival among children in Canada over the last decade or longer is difficult to quantify due to the lack of previously published results. Such information is, however, available for those aged 0 to 19 years at diagnosis. A 2007 study[26] found that the most current estimate (1999-2003) of the overall five-year OSP for children and adolescents in Canada of 82% was 11% higher than the 71% that was reported previously using cases diagnosed from 1985 to 1988.[31] Among diagnostic groups, the largest survival increases were observed for hepatic tumours (20%), leukaemias (15%), and central nervous system neoplasms (14%). There were also substantial improvements in survival in most subgroups studied. Improvements in five-year OSPs in the range of 12% to 14% were observed for lymphoid leukaemias, non-Hodgkin lymphomas, and astrocytomas.

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Tumours of the central nervous system are the leading cause of death due to childhood cancer (Table 17). These tumours have historically been very difficult to treat due to their location in vital structures. Chemotherapy has had disappointing results in the majority of central nervous system tumours, while the use of radiation therapy is avoided in young children due to the significant risks of intellectual impairments caused by radiating the developing brain. Other tumour groups that have disappointing survival rates include metastatic solid tumours such as Ewing's sarcoma, rhabdomyosarcoma, osteosarcoma, and neuroblastoma.

Palliative Care

While the majority of children with cancer become long-term survivors, significant numbers continue to die from the disease. Results from a Canadian study that examined cases in eight dedicated pediatric palliative care programs in 2002 found variability in disease referrals, with cancer diagnosis accounting for 22% of all referrals.[32] While care at the end of life is a key component of comprehensive cancer control for children, knowledge about palliative care in pediatric oncology, as well as how such care is to be monitored, remains underdeveloped.[33]

Progress and Application of Research in Childhood Cancer

Significant progress has been achieved through research in childhood cancers, most notably in the decline in mortality rates. Understanding the biology of cancers in children and the overall ability of children to tolerate more intense treatments than adults are also significant factors in this success. The coordination of successive cooperative clinical trials across North America since the 1950s is also a fundamental component in the progress against childhood cancers (see Table 22). Early research, first supported by the U.S. National Cancer Institute, allowed several hospitals to cooperate in clinical trials to study new drugs which had been developed to treat acute leukemia. The success of this early research demonstrated the benefits of a collaborative multi-centre approach, as the organization of cooperative research groups provided sufficient numbers of cases to conduct clinical trials and achieve results in a timely fashion.

Advances in treatment through cooperative group clinical trials eventually led to the identification of chemotherapy drugs that could eliminate leukemia cells from blood and bone marrow. The achievements of this early cooperative group investigating leukemia subsequently lead to the development and support of multi-disciplinary teams for the treatment of solid tumours in children. Other successes came when it was determined that the combined use of different therapies, such as radiation, surgery and chemotherapy, could provide successful treatments. After fifty years of cooperative research groups the treatment of children with cancer using treatment protocols derived from cooperative, multi-disciplinary clinical trials, has become the standard of care.[34]

Ongoing research in children has yielded an increased understanding of the basic biology of cancer, particularly in the role of genetics and tumour suppressor genes. Studies on children have assisted with advances in treatments (such as chemotherapy), the development of team management in patient care, and the demonstration of the significant advantages of multi-centred cooperative clinical research.

Currently, the majority of pediatric clinical trials in North America are operated through the Children's Oncology Group (COG). COG represents the largest multi-centre trial group for childhood cancer in the world. All 17 Canadian pediatric

oncology centres belong to COG. As such, each individual pediatric oncology centre has access to the clinical trials, biology and late- effects studies in order to enroll patients and gather information on children in these research studies. Efforts to obtain national data have been through the Canadian Childhood Cancer Surveillance and Control Program, which aims to monitor trends in diagnosis, treatment, and outcomes.[35]

Several years ago, directors of the 17 pediatric cancer centres in Canada formally established the Council of Canadian Pediatric Hematology/Oncology Directors or C^{17} Council through support from the Childhood Cancer Foundation – Candlelighters Canada. The C^{17} Council's aim is to promote excellence in clinical care, education and research for children and adolescents with cancer and serious disorders of the blood, as well as to advocate on behalf of such children and their families at the national level. The research arm of the Council, the C^{17} Research Network was created in 2004, and has enabled two to four pan-Canadian studies a year to be funded in order to undertake multi-disciplinary and multi-centre research projects in pediatric hematology, oncology and hematopoietic stem cell transplantation.

Although childhood cancer is rare, it remains of significant public health importance.

Table 17

New Cases and Deaths and Average Annual Age-Standardized Cancer Incidence and Mortality Rates by Diagnostic Group, Ages 0-14, Canada, 2000-2004*

Diagnostic Group and Subgroup	New cases	ASIR (per 1,000,000) per year	Deaths	ASMR (per 1,000,000) per year
I. Leukemia	**1,380**	**49.3**	**184**	**6.4**
a. Lymphoid	1,091	39.0	71	2.4
b. Acute myeloid	176	6.3	51	1.8
III. Central Nervous System	**828**	**28.9**	**201**	**6.9**
a. Ependymoma	88	3.2	19	0.7
b. Astrocytoma	365	12.5	41	1.4
c. Intracranial & intraspinal embryonal	207	7.3	57	2.0
II. Lymphoma	**506**	**16.9**	**32**	**1.1**
a. Hodgkin lymphoma	172	5.5	4	0.1
b. Non-Hodgkin lymphoma	155	5.2	10	0.3
c. Burkitt lymphoma	93	3.1	8	0.3
IV. Neuroblastoma & Other PNC	**295**	**11.4**	**82**	**2.9**
a. Neuroblastoma	292	11.3	82	2.9
IX. Soft Tissue	**262**	**9.0**	**45**	**1.5**
a. Rhabdomyosarcoma	135	4.7	28	1.0
VI. Renal Tumours	**230**	**8.5**	**34**	**1.2**
a. Nephroblastoma	214	7.9	27	0.9
XI. Other Malignant Epithelial	**184**	**6.1**	**9**	**0.3**
b. Thyroid	63	2.0	0	0.0
d. Malignant Melanoma	45	1.5	1	0.0
VIII. Malignant Bone Tumours	**183**	**6.0**	**47**	**1.5**
a. Osteosarcoma	88	2.8	16	0.5
c. Ewing's sarcoma	79	2.6	28	0.9
X. Germ Cell and Other Gonadal	**137**	**4.7**	**10**	**0.3**
c. Malignant gonadal germ cell	53	1.8	2	0.1
V. Retinoblastoma	**100**	**3.9**	**2**	**0.1**
VII. Hepatic Tumours	**68**	**2.6**	**12**	**0.4**
XII. Other and unspecified Cancers	**57**	**2.1**	**9**	**0.3**
Total (5 years)**	**4,242**	**149.8**	**676**	**23.3**
Average Per Year	**848**		**135**	

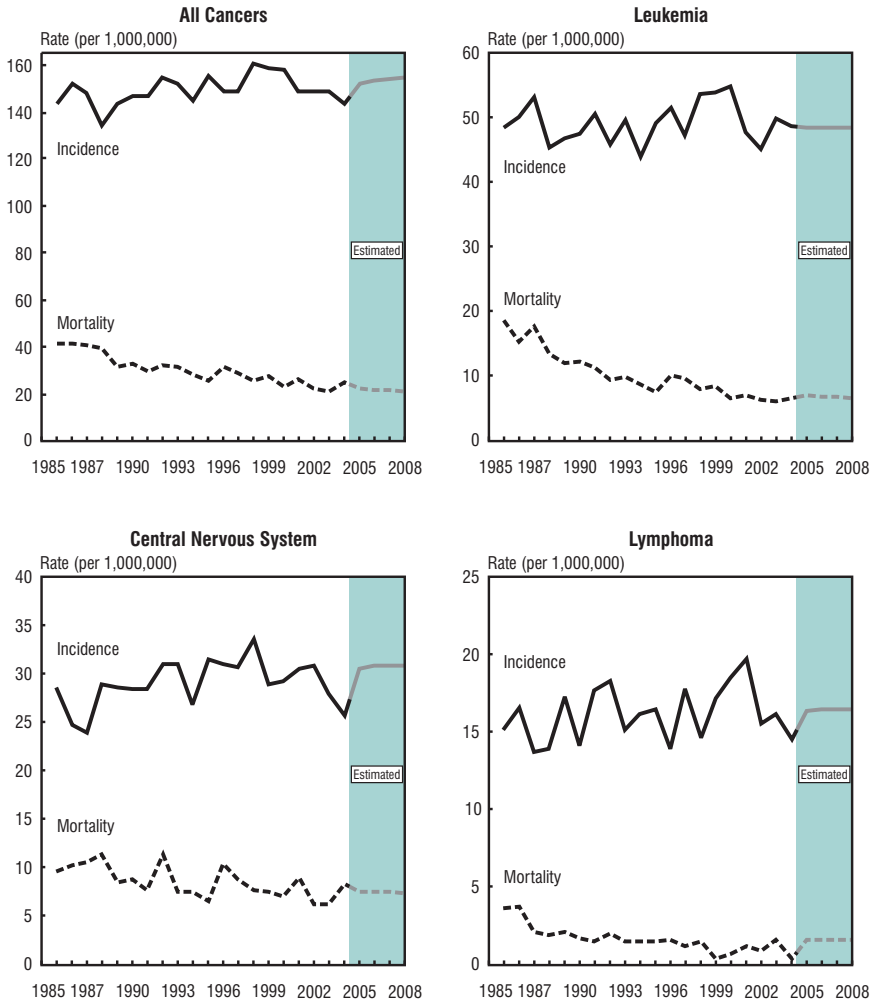
* Rates are age-standardized to the 1991 Canadian population and are expressed per million per year due to disease rarity. Diagnostic groups are listed according to frequency of occurrence. Cases were classified according to the third edition of the International Classification of Childhood Cancer.[20] Non-malignant intracranial and intraspinal tumours were excluded. Only selected subgroups within each diagnostic group are listed. PNC denotes peripheral nervous cell tumours.

** Total includes 12 malignant new cases and 9 deaths which were unclassifiable.

Source: Health Statistics Division, Statistics Canada

Figure 10

Age-Standardized Incidence and Mortality Rates for Selected Cancers for Children and Youth Ages 0-14, Canada, 1985-2008



Note: Cases and deaths were classified according to the groupings found in the *Glossary*. The range of rate scales differ widely between the cancers. Incidence figures exclude non-melanoma skin cancer (basal and squamous). Actual incidence data are available to 2005 except for Quebec, Ontario, Manitoba and Alberta where 2005 incidence is estimated. Please refer to *Appendix II: Methods* for further details.

Source: Chronic Disease Surveillance Division, CCDPC, Public Health Agency of Canada

Table 18

Age-specific Average Annual Incidence Rates by Diagnostic Group, Canada, 2000-2004*

Diagnostic Group and Subgroup	Cases per 1,000,000 per year			
	< 1 year	1-4 years	5-9 years	10-14 years
All Diagnostic Groups**	**226.3**	**213.9**	**115.0**	**116.5**
I. Leukemias, Myeloproliferative Diseases and Myelodysplastic Diseases	**48.6**	**90.6**	**39.6**	**25.7**
a. Lymphoid leukaemias	17.4	78.5	32.7	17.7
b. Acute myeloid leukaemias	16.2	7.3	4.6	5.0
II. Lymphomas and Reticuloendothelial Neoplasms	**7.8**	**11.1**	**14.8**	**25.6**
a. Hodgkin lymphomas	–	–	3.0	13.2
b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	3.0	4.8	4.6	6.7
c. Burkitt lymphoma	–	2.0	4.3	3.4
III. CNS and Miscellaneous Intracranial and Intraspinal Neoplasms	**22.2**	**38.5**	**29.4**	**21.7**
a. Ependymoma	6.6	5.7	1.5	2.1
b. Astrocytomas	6.6	13.8	13.7	11.5
c. Intracranial and intraspinal embryonal tumours	7.2	11.2	8.2	3.3
IV. Neuroblastoma and Other Peripheral Nervous Cell Tumours	**58.8**	**21.9**	**3.2**	**1.0**
a. Neuroblastoma	58.8	21.8	3.1	1.0
V. Retinoblastoma	**16.8**	**9.4**	**0.5**	**–**
VI. Renal Tumours	**16.2**	**17.8**	**6.5**	**1.3**
a. Nephroblastoma and other non-epithelial renal tumours	15.6	17.2	6.1	0.7
VII. Hepatic Tumours	**12.0**	**5.1**	**0.7**	**0.5**
VIII. Malignant Bone Tumours	**–**	**2.3**	**4.6**	**11.4**
a. Osteosarcomas	–	0.9	2.0	5.9
c. Ewing tumour and related sarcomas of bone	–	1.0	2.2	4.8
IX. Soft-tissue and Other Extraosseous Sarcomas	**12.0**	**8.4**	**7.5**	**10.4**
a. Rhabdomyosarcomas	4.2	6.5	4.8	3.2
X. Germ Cell Tumours, Trophoblastic Tumours, and Neoplasms of Gonads	**13.2**	**3.3**	**2.6**	**6.3**
c. Malignant gonadal germ cell tumours	–	1.0	1.5	2.6
XI. Other Malignant Epithelial Neoplasms and Malignant Melanomas	**10.2**	**1.8**	**4.1**	**10.8**
b. Thyroid carcinomas	–	–	2.0	4.0
d. Malignant melanomas	–	–	1.1	2.6
XII. Other and Unspecified Malignant Neoplasms	**6.0**	**3.0**	**1.1**	**1.4**

– Rates based on fewer than five cases were suppressed.

* Cases were classified and itemized according to the third edition of the International Classification of Childhood Cancer.[20] Non-malignant intracranial and intraspinal tumours were excluded. Only selected subgroups within each diagnostic group are listed. CNS denotes central nervous system.

** All diagnostic groups combined includes 12 malignant new cases which were unclassifiable.

Source: Health Statistics Division, Statistics Canada

Table 19

Average Annual Incidence Rates by Sex and Diagnostic Group, Ages 0-14, Canada, 2000-2004*

Diagnostic Group and Subgroup	Cases per 1,000,000 per year		Ratio of new cases (male to female)†
	Males	Females	
All Diagnostic Groups**	**156.3**	**134.8**	**1.2**
I. Leukemias, Myeloproliferative Diseases and Myelodysplastic Diseases	**51.7**	**43.0**	**1.3**
a. Lymphoid leukaemias	42.6	32.2	1.4
b. Acute myeloid leukaemias	5.2	6.9	0.8
II. Lymphomas and Reticuloendothelial Neoplasms	**23.0**	**11.5**	**2.1**
a. Hodgkin lymphomas	6.3	5.5	1.2
b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	7.6	3.0	2.7
c. Burkitt lymphoma	5.2	1.1	4.8
III. CNS and Miscellaneous Intracranial and Intraspinal Neoplasms	**30.4**	**26.4**	**1.2**
a. Ependymoma	3.4	2.6	1.4
b. Astrocytomas	12.0	13.1	1.0
c. Intracranial and intraspinal embryonal tumours	8.9	5.3	1.8
IV. Neuroblastoma and Other Peripheral Nervous Cell Tumours	**10.9**	**9.4**	**1.2**
a. Neuroblastoma	10.7	9.3	1.2
V. Retinoblastoma	**3.5**	**3.4**	**1.1**
VI. Renal Tumours	**6.8**	**9.1**	**0.8**
a. Nephroblastoma and other non-epithelial renal tumours	6.2	8.6	0.8
VII. Hepatic Tumours	**2.7**	**2.0**	**1.4**
VIII. Malignant Bone Tumours	**6.0**	**6.6**	**0.9**
a. Osteosarcomas	2.8	3.2	0.9
c. Ewing tumour and related sarcomas of bone	2.5	3.0	0.9
IX. Soft-tissue and Other Extraosseous Sarcomas	**9.6**	**8.4**	**1.2**
a. Rhabdomyosarcomas	5.0	4.3	1.2
X. Germ Cell Tumours, Trophoblastic Tumours, and Neoplasms of Gonads	**4.4**	**5.0**	**0.9**
c. Malignant gonadal germ cell tumours	1.1	2.5	0.5
XI. Other Malignant Epithelial Neoplasms and Malignant Melanomas	**5.2**	**7.5**	**0.7**
b. Thyroid carcinomas	1.1	3.2	0.4
d. Malignant melanomas	1.5	1.6	1.0
XII. Other and Unspecified Malignant Neoplasms	**1.7**	**2.2**	**0.8**

* Cases were classified and itemized according to the third edition of the International Classification of Childhood Cancer.[20] Non-malignant intracranial and intraspinal tumours were excluded. Only selected subgroups within each diagnostic group are listed. CNS denotes central nervous system.

** All diagnostic groups combined includes 12 malignant new cases which were unclassifiable.

† Ratio is derived using the number of new cases.

Source: Health Statistics Division, Statistics Canada

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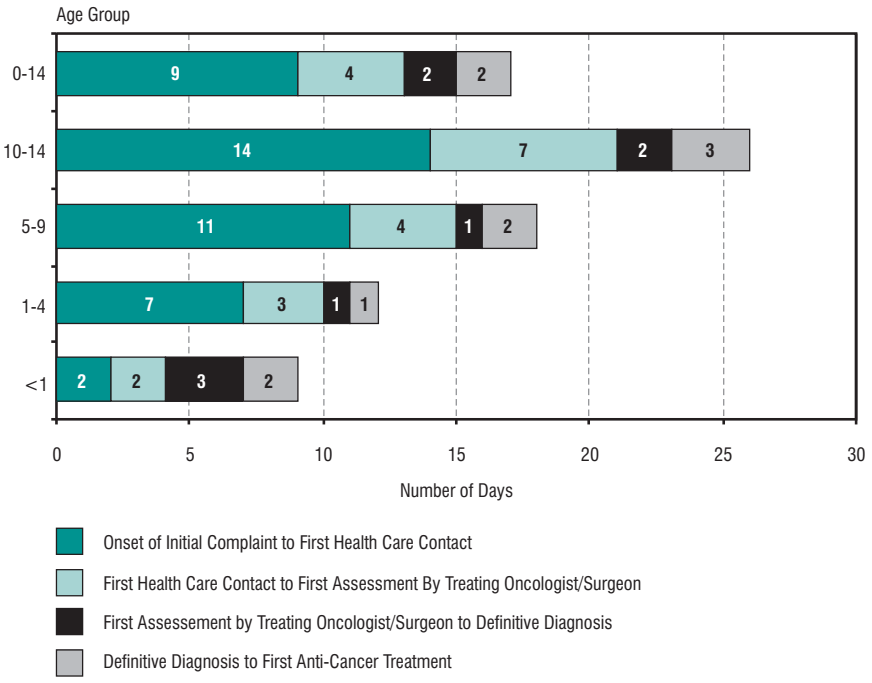
Figure 11

Median Time Between Consecutive Events to Diagnosis and Initiation of Treatment by Age Group, Canada, 1995-2000



Note: Cases were classified according to the second edition of the International Classification of Childhood Cancer.[36] Data presented are for consenting patients and patients with information available on each specific date. Ontario cases were excluded (due to differences in data collection processes) except for results involving the time from diagnosis to initiation of treatment.

Source: The Canadian Childhood Cancer Surveillance and Control Program, Public Health Agency of Canada

The dramatic improvement in childhood cancer has been ascribed to several factors: better diagnostic procedures, the development of multi-modal therapies, and the centralization of care and support services.

Table 20

Percentage of Patients with Metastasis Present at Time of Diagnosis by Cancer*, Ages 0-14, Canada, 1995-2000

Diagnostic Group*	Number of cases	Presence of metastasis at diagnosis, %
III. CNS and miscellaneous intracranial and intraspinal neoplasms	852	12.9
IV. Sympathetic nervous system tumours	315	55.6
V. Retinoblastoma	100	5.0
VI. Renal tumours	280	31.1
VII. Hepatic tumours	65	35.4
VIII. Malignant bone tumours	173	16.8
IX. Soft-tissue sarcomas	233	27.0
X. Germ cell, trophoblastic and other gonadal neoplasms	138	21.7
XI. Carcinomas and other malignant epithelial neoplasms	69	30.4
XII. Other and unspecified malignant neoplasms	39	28.2
All Cancers	2,264	24.5

* Leukemia, lymphomas and reticuloendothelial neoplasms, Langerhans cell histiocytosis and myelodysplastic syndrome have been excluded.

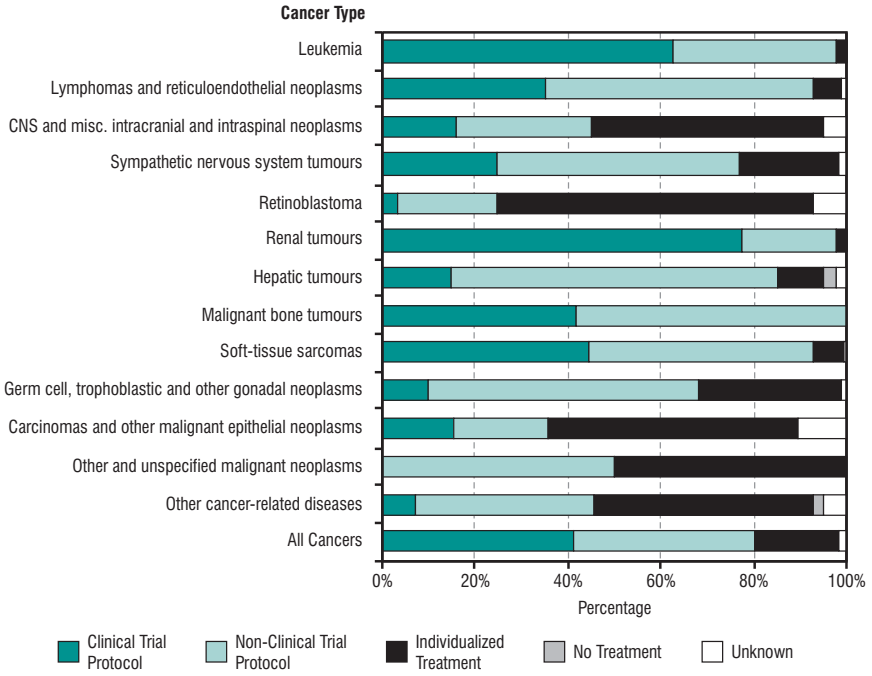
Note: Cases were classified according to the second edition of the International Classification of Childhood Cancer.[36] Data excludes the non-consenting cases and cases with missing information. CNS denotes central nervous system.

Source: The Canadian Childhood Cancer Surveillance and Control Program, Public Health Agency of Canada

Improving survival in childhood cancer (now at 82%), places increasing need for long term follow-up of late effects.

Figure 12

Percent Distribution of Initial Treatment by Cancer Type, Children Ages 0-14, Canada*, 1995-2000



* Excludes Ontario cases due to differences in data collection.

Note: Cases were classified according to the second edition of the International Classification of Childhood Cancer.[36] Data excludes non-consenting and cases with missing information. CNS denotes central nervous system.

Source: The Canadian Childhood Cancer Surveillance and Control Program, Public Health Agency of Canada

In Canada, nearly 80% of children with cancer are either enrolled in a clinical trial or treated according to a registered protocol established by a clinical trial.

Table 21

Observed Survival Proportion (OSP) estimates (%) (and 95% Confidence Intervals (CI)) by Diagnostic Group and Survival Duration, Ages 0-14, Canada excluding Quebec, 1999-2003

Diagnostic Group and Subgroup	Survival duration		
	1-year OSP (95% CI)	3-year OSP (95% CI)	5-year OSP (95% CI)
All Diagnostic Groups	92 (91-93)	85 (83-85)	82 (81-83)
I. Leukemias, Myeloproliferative Diseases, and Myelodysplastic Diseases	93 (91-94)	88 (86-89)	85 (83-87)
a. Lymphoid leukaemias	96 (95-97)	92 (90-94)	90 (88-91)
b. Acute myeloid leukaemias	79 (71-84)	69 (61-76)	67 (59-74)
II. Lymphomas and Reticuloendothelial Neoplasms	94 (91-96)	89 (86-92)	89 (85-92)
a. Hodgkin lymphomas	99 (95-100)	94 (89-97)	93 (88-96)
b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	93 (87-96)	84 (77-90)	84 (77-90)
III. CNS and Miscellaneous Intracranial and Intraspinal Neoplasms	87 (84-89)	78 (75-80)	75 (72-78)
b. Astrocytomas	93 (89-95)	88 (84-91)	87 (82-90)
c. Intracranial and intraspinal embryonal tumours	84 (77-88)	67 (59-73)	60 (52-67)
IV. Neuroblastoma and Other Peripheral Nervous Cell Tumours	92 (88-95)	77 (71-82)	70 (64-75)
V. Retinoblastoma	100 (. - .)	99 (92-100)	99 (92-100)
VI. Renal Tumours	97 (94-99)	93 (88-95)	92 (87-95)
a. Nephroblastoma and other non-epithelial renal tumours	98 (95-99)	93 (89-96)	92 (88-95)
VII. Hepatic Tumours	81 (69-89)	76 (62-85)	76 (62-85)
VIII. Malignant Bone Tumours	93 (88-96)	78 (71-83)	72 (65-78)
a. Osteosarcomas	93 (85-97)	75 (65-83)	70 (59-79)
c. Ewing tumour and related sarcomas of bone	93 (83-97)	79 (68-87)	71 (59-81)
IX. Soft-tissue and Other Extraosseous Sarcomas	94 (90-97)	81 (75-86)	77 (71-83)
a. Rhabdomyosarcomas	95 (89-98)	82 (73-88)	77 (68-84)
X. Germ Cell Tumours, Trophoblastic Tumours, and Neoplasms of Gonads	94 (87-97)	91 (84-95)	89 (81-93)
c. Malignant gonadal germ cell tumours	100 (. - .)	98 (85-100)	95 (83-99)
XI. Other Malignant Epithelial Neoplasms and Malignant Melanomas	94 (88-97)	89 (82-94)	86 (79-91)
b. Thyroid carcinomas	100 (. - .)	98 (84-100)	98 (84-100)
d. Malignant melanomas	96 (75-99)	96 (75-99)	92 (72-98)
XII. Other and Unspecified Malignant Neoplasms	94 (84-98)	94 (84-98)	90 (79-96)

* Cases were classified and itemized according to the third edition of the International Classification of Childhood Cancer[20] and include non-malignant intracranial and intraspinal tumours.[26] Observed survival proportions were derived excluding cases diagnosed in Quebec (see Observed and Realtive Survival in *Appendix II: Methods*). Only selected subgroups within each diagnostic group are listed. CNS denotes central nervous system.

(. - .) = confidence interval is undefined.

Source: Health Statistics Division, Statistics Canada

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Table 22
Significant Advances in the History of Childhood Cancer Research

Event	Implication(s)
Multi-Institution Cooperation in Clinical Trials (1955)	Formation of the first group of hospitals that agreed to cooperate in clinical trials of new drugs.
Leukemia Chemotherapy	Introduction of new agents, which were effective in the treatment of acute leukemia.
Treatment of Solid Tumours in Children	Introduction of other medical disciplines to study effects of surgery, radiation and pathology on diagnosis and treatment of solid tumours.
Multi-Disciplinary Team Care	Introduction of multi-modal therapies, conducted through large-scale multi-centre clinical trials.
Laboratory and Translational Research	Knowledge of how cancer cells are affected by improved diagnostic evaluation and treatments.
Concept of Total Cure (1980s)	Incorporation of quality of life determinants as an overall goal for childhood cancer survivors.

Source: CureSearch (Children's Oncology Group) www.curesearch.org

Table 23
Pediatric Oncology Centres in Canada

Alberta Children's Hospital, Calgary, AB	www.calgaryhealthregion.ca
Allan Blair Cancer Centre, Regina, SK	www.saskcancer.ca
British Columbia Children's Hospital, Vancouver, BC	www.bcchildrens.ca
CancerCare Manitoba, Winnipeg, MB	www.cancercare.mb.ca
Children's Hospital of Eastern Ontario, Ottawa, ON	www.cheo.on.ca
Children's Hospital of Western Ontario, London, ON	www.chwo.org
Centre Hospitalier Universitaire de Québec, Québec, QC	www.chuq.qc.ca
Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC	www.chus.qc.ca
Hôpital Sainte-Justine, Montréal, QC	www.chu-sainte-justine.org
IWK Health Centre, Halifax, NS	www.iwk.nshealth.ca
Janeway Children's Health and Rehabilitation Centre, St. John's, NFLD	www.easternhealth.ca
Kingston General Hospital, Kingston, ON	www.kgh.on.ca
McMaster Children's Hospital, Hamilton, ON	www.mcmasterchildrenshospital.ca
The Hospital for Sick Children, Toronto, ON	www.sickkids.ca
The Montreal Children's Hospital, Montreal, QC	www.thechildren.com
Saskatoon Cancer Centre, Saskatoon, SK	www.saskatoonhealthregion.ca
Stollery Children's Hospital, Edmonton, AB	www.stollerykids.com

GLOSSARY

Age — The age of the patient (in completed years) at the time of diagnosis or death.

ICDO-3 — International Classification of Diseases for Oncology, Third Edition.[37]

ICD-10 — International Statistical Classification of Diseases and Related Health Problems, Tenth Revision.[38]

Incidence — The number of new cases of a given type of cancer diagnosed during the year. The basic unit of reporting is a new case of cancer rather than an individual patient.

Mortality — The number of deaths attributed to a particular type of cancer that occurred during the year. Included are deaths of patients whose cancer was diagnosed in earlier years, people with a new diagnosis during the year, and patients for whom a diagnosis of cancer is made only after death.

Observed survival proportion — The proportion of patients alive after a given length of time (e.g., five years) since diagnosis.

Province/Territory — For cancer incidence and mortality data, this is the province/territory of the patient's permanent residence at the time of diagnosis or death, which may or may not correspond to the province/territory in which the new case of cancer or the cancer death was registered.

Relative survival ratio — The ratio of the observed survival for a group of cancer patients to the survival that would be expected for members of the general population, assumed to be practically free of the cancer of interest, who have the same main factors affecting patient survival (e.g., sex, age, area of residence) as the cancer patients. Estimates of the relative survival ratio greater than 100% are possible and indicate that the observed survival of the cancer patients is better than that expected from the general population.

Age-standardized relative survival ratio — The all ages survival estimate that would have occurred if the age distribution of the patient group under study had been the same as that of the standard population (i.e., all patients who were diagnosed with that cancer in Canada between 1992 and 2001).