VALUE IN HEALTH 20 (2017) 345–356

Available online at www.sciencedirect.com

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Costs for Childhood and Adolescent Cancer, 90 Days Prediagnosis and 1 Year Postdiagnosis: A Population-Based Study in Ontario, Canada

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ABSTRACT

Background: Childhood and adolescent cancers are uncommon, but they have important economic and health impacts on patients, families, and health care systems. Few studies have measured the economic burden of care for childhood and adolescent cancers. **Objectives:** To estimate costs of cancer care in population-based cohorts of children and adolescents from the public payer perspective. **Methods:** We identified patients with cancer, aged 91 days to 19 years, diagnosed from 1995 to 2009 using cancer registry data, and matched each to three noncancer controls. Using linked administrative health care records, we estimated total and net resource-specific costs (in 2012 Canadian dollars) during 90 days prediagnosis and 1 year postdiagnosis. **Results:** Children (≤14 years old) numbered 4,396: 36% had leukemia, 21% central nervous system tumors, 10% lymphoma, and 33% other cancers. Adolescents (15–19 years old) numbered 2,329: 28.9% had lymphoma. Bone and soft tissue sarcoma, germ cell tumor, and thyroid carcinoma each comprised 12% to 13%. Mean net prediagnosis costs were $5,810 and $1,127 and mean net postdiagnosis costs were $136,413 and $62,326 for children and adolescents, respectively; the highest were for leukemia ($157,764 for children and $172,034 for adolescents). In both cohorts, costs were much higher for patients who died within 1 year of diagnosis. Inpatient hospitalization represented 69% to 74% of postdiagnosis costs. **Conclusions:** Treating children with cancer is costly, more costly than treating adolescents or adults. Substantial survival gains in children mean that treatment may still be very cost-effective. Comprehensive age-specific population-based cost estimates are essential to reliably assess the cost-effectiveness of cancer care for children and adolescents, and measure health system performance.

Keywords: adolescent cancer, Canada, childhood cancer, costs and cost analysis.

Introduction

Children aged 0 to 14 years represent less than 1% of patients newly diagnosed with cancer in North America [1,2], but the burden of cancer on patients and their families is very high. Treatment is resource-intensive and costly for health care systems and families [3–6].

Incidence and survival statistics provide information concerning disease burden and the effects of improved diagnosis and treatments [7,8]. Studies describing the cost of care are analogues of descriptive epidemiological studies. They characterize disease burden as the financial burden borne by patients, families, and health systems. This information is useful for hypothesis generation, and to plan budgets, prioritize research, and report financial indicators for cancer system performance [9,10]. Most importantly, costing studies provide a scientific foundation for robust and reliable inputs for cost-effectiveness studies of cancer treatments [11,12].

Conflicts of interest: The authors have no conflicts of interest. Parts of this material are based on data and information compiled and provided by the Canadian Institute for Health Information as well as by Cancer Care Ontario. Nevertheless, the analyses, conclusions, opinions, and statements expressed herein are those of the authors, and not necessarily of either of these organizations. No endorsement is intended or should be inferred.

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http://dx.doi.org/10.1016/j.jval.2016.10.010

Most studies of the costs of childhood and adolescent cancer therapy are outdated, use small samples, or include only one type of cancer or health care service [4,13–17]. Consistent methods and standards of reporting are required for the interpretation and practical application of cost estimates [9,10].

Also, existing studies often group patients aged 15 to 19 years with children or older adults. This age group is, however, unique in that embryonal and hematological cancers are less common than in young children, and few patients have tumors typical of adults [2,18,19]. Although centers for adolescents and young adults exist in some areas, these patients often receive care at either a pediatric or an adult facility, frequently receiving different treatment protocols and supportive care depending on the locus of care [20–22].

In Canada, universal health care insurance is publicly funded, mostly through taxation, and provides coverage for almost all medically necessary health care (including the direct medical costs of cancer therapy) for all permanent residents (including children) regardless of medical history or personal income. Each province administers its own insurance plan within guidelines set by the federal government under the Canada Health Act [23]. The Ontario Health Insurance Plan (OHIP) covers all residents of Ontario, Canada's most populous province, under the direction of the Ontario Ministry of Health and Long-Term Care. Private health insurance is not available or required for the medically necessary services covered by OHIP, but can be obtained for services not covered by OHIP, such as most dental care, allied health, and outpatient prescription drugs (covered for only those aged 65 years and older, on social assistance, or with high drug costs relative to their income).

We developed costing methods using linked cancer registry and health care administrative data in adults in Canada [24–26]. The objective of this study was to use this published costing methodology to estimate total and net health care costs for 90 days prediagnosis (to capture tests and procedures before the definitive cancer diagnosis) and for 1 year postdiagnosis (when initial treatment is provided) in children and adolescents diagnosed with cancer in Ontario.

Methods

We conducted the analysis from the perspective of the public payer, the Ontario Ministry of Health and Long-Term Care. Our primary outcome measures were total and net direct medical costs borne by the public payer. The study was approved by the Research Ethics Boards of the University of Toronto and Sunnybrook Health Sciences Centre.

Data

We used health care administrative databases containing information on all Ontario residents, held at the Institute for Clinical Evaluative Sciences (ICES). We also used the Pediatric Oncology Group of Ontario Network Information System (POGONIS), which contains demographic, clinical, and treatment data from Ontario's five pediatric cancer centers, to which almost all Ontario children with cancer are referred. POGONIS has been shown to capture 96% of all patients diagnosed with cancer at ages 0 to 14 years [27]. There are no specialized adolescent or young adult cancer centers in Ontario, and POGONIS was shown to capture only 48% of adolescents diagnosed at ages 15 to 17 years [27]. Therefore, we used the population-based Ontario Cancer Registry, which includes records of 98% of all newly diagnosed cancers in Ontario, except for nonmelanoma skin cancer [28,29], to complete the identification of patients aged 15 years and older. Cancer Care Ontario provided additional data on radiation therapy and chemotherapy. All data sets were linked using unique encoded identifiers and analyzed at ICES.

Patients

We identified and analyzed two groups of patients with cancer diagnosed between January 1, 1995, and December 31, 2009: children, diagnosed at age 91 days (to have data for 90 days prediagnosis) to 14 years, and adolescents, diagnosed at age 15 to 19 years. Both cohorts received an initial diagnosis of 1 of the 12 groups of the International Classification of Childhood Cancer, Third Edition [30] (ICCC). Children were identified from POGONIS, and adolescents were identified from POGONIS and the Ontario Cancer Registry. When duplicate records were found for adolescents, we selected the record from the Ontario Cancer Registry over the POGONIS record for data related to diagnosis, because this resulted in most patients being selected from the same source. We excluded patients with identical dates of diagnosis and death, or with missing or invalid OHIP number, histology code, or sex. We followed patients for 1 year after diagnosis, or from diagnosis to death if they died within the year. We stratified patients into those who survived for less than a year and those who survived for a year or longer, because previous work in adults indicated that costs of care differ by postdiagnosis survival [26].

Patients were described in terms of cancer type, comorbidity, and demographic characteristics. We described comorbidity by categorizing all *International Classification of Diseases* (*Ninth Revision, Ninth Revision-Clinical Modification, and Tenth Revision*) diagnostic codes in hospital records and physicians' billing data in the year before diagnosis, or from birth to diagnosis for patients diagnosed when aged less than 1 year, into 1 of 29 aggregated diagnosis groups (ADGs), a unit in a population-patient case-mix adjustment system [31] that relates to health care costs in patients of all ages [32]. We classified the total number of ADGs assigned to each patient into the following groups: 0, 1 to 4, 5 to 9, and 10 or more. We used the Statistics Canada Postal Code Conversion file and data from the 2001 Canada Census to obtain neighborhood-level median household income (measured in quintiles) and rurality of residence (rural/urban). Communities with a population of less than 10,000 were defined as rural [33,34].

We classified children into the three most common diagnostic groups (leukemia, lymphoma, and central nervous system [CNS] tumors), and a fourth category for "other" cancers, for most of our analyses. In addition, we examined net costs in the 12 ICCC groups. We distinguished seven major diagnostic groups in adolescents: leukemia, lymphoma, CNS tumors, bone tumors and soft tissue sarcomas, germ cell tumors, thyroid carcinomas, and other cancers. In addition, we examined net costs in adolescents with acute lymphoblastic leukemia (ALL) [35], and those with other types of leukemia, as well as those in the other ICCC groups.

Controls

We used the Ontario Registered Persons Database, which contains information on all persons registered for OHIP coverage, to select controls without cancer. We estimated net cancer-related costs by subtracting the total health care costs of controls from the total health care costs of patients with cancer [25,36,37]. Potential controls were matched on birth year and month, and assigned an index date corresponding to the diagnosis date of the patient. We computed the propensity score (probability of being a patient with cancer) for each patient and potential control using logistic regression, with sex, rurality, and number of ADGs as predictors [38]. Greedy matching was used to select three controls

with the closest propensity scores that fell within 0.1 SD of each patient's propensity score [38–40].

Estimating Costs

Utilization of the following health care resources for patients and controls in the 90 days before diagnosis and the 1 year after diagnosis was measured and costed (Table 1): inpatient hospitalizations, emergency department (ED) visits, same-day surgeries (including biopsies, lumbar punctures, and blood transfusions), outpatient chemotherapy, radiation therapy, outpatient diagnostic and laboratory tests, physician services, home care services, and outpatient prescription drugs covered under the provincial health care plan. Out-of-pocket costs and time costs for patients and caregivers were not included.

Each record of an inpatient hospitalization, ED visit (April 2003 onward), same-day surgery visit, and outpatient chemotherapy visit (October 2003 onward) was assigned a resource intensity weight (RIW) associated with its case-mix group [24]. The RIW includes the intensity of use of drugs, chemotherapy, procedures, tests, and personnel (excluding physicians) associated with the visits. Following standard costing procedures, we multiplied the RIW by the cost per weighted case (CPWC) for the year of use [24,41]. The CPWC is the cost of treating an average patient at each hospital [41]. Because of the complex needs of children and adolescents, pediatric hospitals have higher CPWC values than do adult general hospitals. The CPWC values in 2010 for the Hospital for Sick Children and the Children's Hospital of Eastern Ontario were approximately $14,000 and $10,000, respectively, versus $6,200 for nonpediatric hospitals. Our base-case analysis used hospital-specific CPWC for the two pediatric hospitals in Ontario and the three large acute care general hospitals with pediatric oncology facilities, and the mean provincial CPWC of all other hospitals for all other hospital visits. A sensitivity analysis applying the mean CPWC for the two pediatric hospitals to all other hospital visits increased costs by moderate amounts, relative to their mean costs. We believed that potential small underestimations were preferable to overestimations and reported only the base-case analysis.

We identified ED visits before April 2003 and outpatient chemotherapy visits before October 2003 from the OHIP Claims History database using physicians' billing codes. We applied the mean costs for visits in the first 6 months after April 2003 or October 2003 to all earlier ED and outpatient chemotherapy visits, respectively. We also included chemotherapy drug costs from the New Drug Funding Program data [42] for completeness, although this program mainly reimburses adult chemotherapy regimens.

The OHIP Claims History database includes records of inpatient and outpatient physician services. Most records were billed fee-for-service and include the cost. Nevertheless, many Ontario

Table 1 – Data and costing methods.

Resource	Data	Costing method
Inpatient hospitalization	Canadian Institute for Health Information-Discharge Abstract Database [60]	Multiply the RIW by the cost per weighted case in Ontario for the year of use [24,41]
ED visits	April 1, 2003, onward: Canadian Institute for Health Information-National Ambulatory Care Reporting System Data [61]	Multiply the RIW by the cost per weighted case in Ontario for the year of use [24,41]
	Before April 1, 2003: OHIP Claims History Database	Identify ED visits by physicians' billing codes; apply the mean cost for ED visits from April 1, 2003, to December 31, 2003, to all OHIP-identified visits
Same-day surgery procedures	Database compiled at ICES from the Canadian Institute for Health Information-Discharge Abstract Database [60] and National Ambulatory Care Reporting System Data [61]	Multiply the RIW by the cost per weighted case in Ontario for the year of use [24,41]
Outpatient chemotherapy visits	October 1, 2003, onward Canadian Institute for Health Information-National Ambulatory Care Reporting System Data [61]	Multiply the RIW by the cost per weighted case in Ontario for the year of use [24,41]
	Before October 1, 2003: OHIP Claims History Database	Identify chemotherapy visits by physicians' billing codes; apply the mean cost for chemotherapy visits from October 1, 2003, to March 31, 2004, to all OHIP-identified visits
	New Drug Funding Program data [42]	Drug costs are in the data
Radiation therapy	Cancer Care Ontario Activity Level Reporting System	National Health Productivity Improvement Program codes [62] and cost per unit [26,58]
	POGONIS radiation therapy data	Applied age-specific costs per fraction for children estimated as described earlier
Outpatient diagnostic and laboratory tests	OHIP Claims History Database	Costs are in the data
Physician services	OHIP Claims History Database	Fee-for-service (in the data) and shadow billings (see text)
Home care services	Home Care Database; Ontario Home Care Administrative System data	Average service costs from Community Care Access Centres in Toronto [63]
Outpatient prescription drugs	Ontario Drug Benefit program data	Costs are in the data

ED, emergency department; ICES, Institute for Clinical Evaluative Sciences; OHIP, Ontario Health Insurance Plan; POGONIS, Pediatric Oncology Group of Ontario Network Information System; RIW, resource intensity weight.

physicians receive all or some of their income through alternative funding plans [43]. Physicians record "shadow" billings with zero costs for services provided under these plans. We estimated the costs for shadow-billed records from the mean cost of the fee-for-service records with the same year and fee code.

Families on social assistance or whose drug costs are high relative to their income are eligible for coverage of outpatient prescription drugs listed in the provincial formulary under the Ontario Drug Benefit program [44]. We obtained these drug costs only for patients and controls whose families were eligible.

All costs were adjusted to 2012 Canadian dollars using the Statistics Canada Consumer Price Index for health [41,45].

Analysis

We computed total (observed) and net (difference between patients with cancer and controls) direct medical costs [37], stratified by resource type and for all resources combined, in the 90 days before diagnosis/index date and 1 year after, for patients and their matched controls [37]. All controls lived for at least as long as the patients to whom they were matched. For patients who survived less than 1 year after diagnosis, we estimated costs for their controls for the time that the patient was alive.

We used generalized estimating equation models to estimate net costs and their 95% confidence intervals [25,46]. The outcome was the cost for an individual, patient or control status was the predictor variable, and patient-control sets were treated as clusters [25].

Results

Patients and Controls

We identified 4420 patients aged 91 days to 14 years at diagnosis and 2339 patients aged 15 to 19 years who met our inclusion criteria. We excluded 24 patients younger than 14 years and 10 patients aged 15 to 19 years because they could not be matched to 3 controls, leaving 4396 children and 2329 adolescents. The selection processes for the childhood and adolescent cohorts are shown in Appendix Figures 1 and 2, respectively, in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.10.010.

Table 2 presents their baseline characteristics. For children, the mean age at diagnosis was 6 years, and 92.5% survived at least 1 year after diagnosis. Approximately 36% had leukemia, 21% had a CNS tumor, 10% had lymphoma, and 33% had other cancers. Adolescents had a mean age of 17 years at diagnosis, and 93.4% survived at least 1 year. Their most common diagnostic groups were lymphoma (29%), germ cell tumors (13%), and thyroid carcinoma (12%).

Patients and controls were exactly matched on age and sex. The patient and control cohorts were almost identical in terms of rurality of residence. Among adolescents, 2% more controls than patients were in the lowest income quintile; hence, fewer controls were in higher income quintiles. Patients in both cohorts had slightly higher comorbidity than their controls (Table 2).

Prediagnosis Costs

Children

The mean total cost for all resources for all children in the prediagnosis period was $6316. Costs were higher for those who died within 1 year than for survivors ($8948 vs. $6103, respectively) (Table 3).

The mean 90-day cost per control was only $506 (see Appendix Table 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.10.010), indicating that most of the patients' costs were related to investigating early symptoms of cancer. Patients' mean net cost in the 90 days before diagnosis was $5810; costs were higher for patients who died within 1 year after diagnosis ($8351) than for those who survived ($5605) (Table 3). Overall (nonsurvivors and survivors), the mean net costs were the highest for patients with CNS tumors ($7441) and other cancers ($6337). Approximately 76% of mean net costs before diagnosis were for hospitalization.

Adolescents

Prediagnosis costs for adolescents were much lower than for children. The mean total cost for all adolescents in the prediagnosis period was $1442 (Table 3).

The mean 90-day cost per control was only $315 (see Appendix Table 1 in Supplemental Materials). Patients' mean net cost in the 90 days before diagnosis was $1127; costs were higher for patients who died within 1 year after diagnosis ($1749) than for those who survived ($1083) (Table 3). Among survivors, the highest mean cost was for CNS tumors ($2305) and the lowest was for thyroid carcinoma ($207).

Postdiagnosis Costs

Children

The mean total cost for children in the year after diagnosis was $137,693; costs were higher among nonsurvivors ($173,202) than among survivors ($134,820) (Table 4; see also Appendix Tables 2 and 3 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.10.010).

The mean first-year cost for controls was only $1280 (see Appendix Table 5 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.10.010). Therefore, net costs were very similar to total costs and exhibited the same trends (Table 4). The most costly resources were hospitalization, physician services, chemotherapy, and radiation therapy (Fig. 1).

For both survivors and nonsurvivors, the highest mean net costs were for leukemia ($157,764) and other cancers ($142,644). Chemotherapy costs were the highest for patients with leukemia and other cancers, and radiation therapy costs were the highest for patients with CNS tumors (see Appendix Tables 2 and 3 in Supplemental Materials).

Adolescents

The mean total cost for adolescents in the year after diagnosis was $63,258; costs were much higher among nonsurvivors ($151,724) than among survivors ($56,994) (Table 4). The highest mean costs were for patients with leukemia, both for patients who died ($229,011) and for those who survived ($162,174). The lowest mean cost was $10,419 for patients with thyroid carcinoma, all of whom survived for 1 year or longer after diagnosis. Hospitalization was the most costly resource, comprising 66% and 82% of total costs in survivors and nonsurvivors, respectively (see Appendix Tables 4 and 5 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.10.010).

The mean net cost during the 1-year postdiagnosis was $62,326, and costs were much higher for the patients who died within 1 year ($151,187) than for those who survived ($56,034) (Table 4). After hospitalization, the most costly resources were physician services, followed by chemotherapy and radiation therapy (Fig. 1).

Patients with leukemia had the highest net costs ($228,585 and $161,398) for nonsurvivors and survivors and the lowest mean net cost ($9,499) was for patients with thyroid carcinoma. Among patients who survived, the highest chemotherapy costs were for patients with leukemia and the highest radiation

Table 2 – Characteristics of patients diagnosed from January 1, 1995, to December 31, 2009, at age 91 d to 14 y (children) and 15 to 19 y (adolescents).

Characteristic	Children aged 91 d to 14 y at diagnosis (N = 4,396) and controls (N = 13,188)					Adolescents aged 15–19 y at diagnosis (N = 2,329) and controls (N = 6,987)				
	Patients		Controls (%)	Survived ≥1 y (N = 4,067)	Survived <1 y (N = 329)	Patients		Controls (%)	Survived ≥1 y (N = 2,175)	Survived <1 y (N = 154)
	N	%				N	%			
Age (y) at diagnosis										
Mean ± SD	6.1 ± 4.4		6.1 ± 4.4	6.2 ± 4.3	5.4 ± 4.5	17.1 ± 1.4		17.1 ± 1.4	17.1 ± 1.4	17.1 ± 1.4
Median (IQR)	5 (2–10)		5 (2–10)	5 (2–10)	4 (1–9)	17 (16–18)		17 (16–18)	17 (16–18)	17 (16–18)
91 d to 2 y	1,144	26.0	26.0	25.1%	36.8%					
3–5	1,132	25.7	25.7	26.0%	22.5%					
6–8	735	16.7	16.8	16.9%	14.9%					
9–11	630	14.3	14.3	14.7%	9.7%					
12–14	755	17.2	17.1*	17.3%	16.1%			0.2*		
15–17						1,291	55.4	55.2	55.4%	55.8%
18–19						1,038	44.6	44.6*	44.6%	44.2%
Sex										
Female	2,025	46.1	46.1	45.6%	51.7%	1,100	47.2		48.2%	33.8%
Male	2,371	53.9	53.9	54.4%	48.3%	1,229	52.8		51.8%	66.2%
Residence										
Urban	3,913	89.0	89.1	89.0%	88.8%	2,041	87.6		87.7%	87.0%
Rural	483	11.0	10.9	11.0%	11.25	288	12.4		12.3%	13.0%
Income quintile										
1 (low)	827	18.8	21.0	18.5%	22.8%	387	16.6		16.5%	18.2%
2	841	19.1	19.5	19.1%	19.5%	442	19.0		18.7%	23.4%
3	849	19.3	19.9	19.6%	15.8%	455	19.5		19.7%	16.9%
4	978	22.2	20.9	22.3%	21.6%	526	22.6		22.5%	24.0%
5 (high)	894	20.3	18.4	20.4%	20.1%	≥515†	≥22.1†		≥22.4%†	17.5%
Missing	7	0.2	0.2	0.1%	0.3%	≤5†	≤0.2		≤0.1%†	0%
Number of collapsed ambulatory diagnosis groups										
Mean ± SD	4.97 ± 2.4		4.35 ± 2.5	4.93 ± 2.4	5.41 ± 2.7	4.1 ± 2.4		3.6 ± 2.4	4.1 ± 2.4	4.3 ± 2.4
Median (IQR)	5 (3–6)		5 (2–6)	5 (3–6)	5 (4–7)	4 (2–5)		3 (2–5)	4 (2–5)	4 (3–6)
	N	%		N*	N*	N*	%		N*	N*
Year of diagnosis										
1995	295	6.7		270	25	147	6.3		131	16
1996	291	6.6		264	27	144	6.2		133	11
1997	297	6.8		270	27	139	6.0		131	8
1998	313	7.1		294	19	113	4.8		107	6
1999	276	6.3		252	24	140	6.0		129	11
2000	296	6.7		271	25	160	6.9		149	11

continued on next page

Table 2 – *continued*

Characteristic	Children aged 91 d to 14 y at diagnosis (N = 4,396) and controls (N = 13,188)					Adolescents aged 15–19 y at diagnosis (N = 6,987)				
	Patients		Controls (%)	Survived ≥1 y (N = 4,067)	Survived <1 y (N = 329)	Patients		Controls (%)	Survived ≥1 y (N = 2,175)	Survived <1 y (N = 154)
	N	%				N	%			
2001	278	6.3		252	26	159	6.8		149	10
2002	276	6.3		258	18	150	6.4		141	9
2003	301	6.8		274	27	152	6.5		144	8
2004	285	6.5		264	21	166	7.1		153	13
2005	287	6.5		275	12	153	6.6		145	8
2006	297	6.8		273	24	170	7.3		161	9
2007	288	6.6		268	20	184	7.9		171	13
2008	316	7.2		299	17	184	7.9		173	11
2009	300	6.8		283	17	168	7.2		158	10
ICCC diagnostic group										
I. Leukemia	1,566	35.6		1,476	90	259	11.1		218	40
Acute lymphoid leukemia (subset of leukemia in adolescents)						103	4.4		15	See XII[†]
II. Lymphoma	446	10.1		426	20	673	28.9		643	30
III. CNS	938	21.3		800	138	207	8.9		183	24
All other cancers (specified below)	1,446	32.9		1,365	81	1,190	51.1		1,131	
IV. Neuroblastoma	306	6.9		284	22	See XII[‡]			See XII[‡]	0
V. Retinoblastoma	91	2.1		≥86[†]	≤5[†]	See XII[‡]			See XII[‡]	0
VI. Renal tumors	249	5.7		≥244[†]	≤5[†]	18	0.8		17	See XII[‡]
VII. Hepatic tumors	73	1.7		60	13	14	0.6		10	See XII[‡]
VIII. Bone tumors	187	4.2		175	12	160	6.9		141	19
IX. Soft tissue sarcomas	277	6.3		260	17	138	5.9		123	15
X. Germ cell tumors	110	2.5		≥105[†]	≤5[†]	299	12.8		289	10
XI. Other malignant epithelial neoplasms and malignant melanomas	117	2.7		≥112[†]	≤5[†]	545	23.4		535	10
XIb. Thyroid carcinoma (subset of XI in adolescents)						287	12.3		287	0
XII. Other and unspecified malignant neoplasms	36	0.8		≥31[†]	≤5[†]	16	0.7		16	6

CNS, central nervous system; IQR, interquartile range.

* A few controls were aged 1 year younger or older on the diagnosis date of their matched patient. We matched on month and year of birth, but not day. A patient born on May 31, 1986, and diagnosed on May 10, 2000, was 14 y old at diagnosis. If his or her matched control was born on May 1, 1986, the control was aged 15 y on May 10, 2000.

† Cell sizes of five or fewer patients cannot be reported or able to be calculated in compliance with privacy policy at the Institute for Clinical Evaluative Sciences.

‡ Included in the number for group XII because at least one diagnostic group had five or fewer patients.

Table 3 – Mean (95% CI) total and net direct costs in the 90 d before diagnosis by cohort, major ICCG group, and survivor group.

ICCG group		Children (aged 91 d to 14 y at diagnosis) (N = 4,396)				Adolescents (aged 15 to19 y at diagnosis) (N = 2,329)			
		Patients who lived <1 y after diagnosis		Patients who lived ≥1 y after diagnosis		Patients who lived <1 y after diagnosis		Patients who lived ≥1 y after diagnosis	
		Total cost ($)	Net cost ($)	Total cost ($)	Net cost ($)	Total cost ($)	Net cost ($)	Total cost ($)	Net cost ($)
Leukemia	Mean cost 95% CI	5,236 3,776 to 6,697	4,789 3,372 to 6,206	4,883 4,518 to 5,247	4,468 4,118 to 4,818	3,127 117 to 6,136	2,578 −390 to 5,546	1,168 805 to 1,530	1,011 648 to 1,375
Lymphoma	Mean cost 95% CI	7,111 3,481 to 10,742	5,662 2,277 to 19,047	5,835 4,878 to 6,791	5,305 4,330 to 6,280	1,927 876 to 2,978	1,408 411 to 2,406	1,410 978 to 1,842	1,101 664 to 1,538
CNS	Mean cost 95% CI	7,979 6,150 to 9,809	7,712 5,906 to 9,872	7,819 7,103 to 8,535	7,935 6,675 to 8,114	1,908 742 to 3,075	1,754 654 to 2,853	2,591 1,382 to 3,800	2,305 1,105 to 3,505
Bone and soft tissue	Mean cost 95% CI					1,389 568 to 2,210	1,148 359 to 1,937	1,580 1,123 to 2,036	1,396 952 to 1,842
Germ cell	Mean cost 95% CI					2,940 236 to 5,643	2,696 499 to4,893	1,195 900 to1,490	957 660 to 1,253
Thyroid	Mean cost 95% CI					– –	– –	773 554 to 991	207 −261 to 676
Other	Mean cost 95% CI	15,178 7,946 to 22,410	14,062 7,011 to 21,114	6,501 5,848 to 7,155	5,878 5,321 to 6,435	1,118 447 to 1,788	889 309 to 1,469	1,421 933 to 1,908	1,031 537 to1,525
All cancers	Mean cost 95% CI	8,948 6,946 to 10,951	8,351 6,371 to 10,331	6,103 5,793 to 6,414	5,605 5,217 to 5,892	2,111 1,252 to 2,971	1,749 880 to 2,618	1,394 1,200 to 1,588	1,083 880 to 1,286
All cancers and survivor groups	Mean total cost (95% CI)	6,316 (5,992 to 6,640)				1,442 (1,252 to 1,632)			
	Mean net cost (95% CI)	5,810 (5,505 to 6,115)				1,127 (928 to 1,325)			

Note. All total and net costs are in 2012 Canadian dollars.
CI, confidence interval; CNS, central nervous system; ICCG, International Classification of Childhood Cancer, Third Edition.

Table 4 – Mean (95% CI) total and net direct costs in 1 y after diagnosis by cohort, major ICCG group, and survivor group.

ICCG group		Children (aged 91 d to 14 y at diagnosis) (N = 4,396)				Adolescents (aged 15 to 19 y at diagnosis) (N = 2,329)			
		Patients who lived <1 y after diagnosis		Patients who lived ≥1 y after diagnosis		Patients who lived <1 y after diagnosis		Patients who lived ≥1 y after diagnosis	
		Total cost ($)	Net cost ($)	Total cost ($)	Net cost ($)	Total cost ($)	Net cost ($)	Total cost ($)	Net cost ($)
Leukemia	Mean cost	239,563	238,665	154,176	152,831	229,011	228,585	162,174	161,398
	95% CI	191,113–288,012	191,113–286,217	147,828–160,523	146,479–159,182	133,063–324,959	136,732–320,438	142,613–181,734	141,976–180,821
Lymphoma	Mean cost	268,585	265,906	100,521	99,357	187,422	186,683	56,050	54,900
	95% CI	154,185–382,985	160,984–370,827	89,859–111,183	88,836–109,878	127,921–246,923	130,788–242,577	50,261–61,840	49,160–60,641
CNS	Mean cost	112,235	111,863	105,127	104,085	127,105	126,493	61,820	60,951
	95% CI	92,521–131,949	92,406–131,319	94,935–115,319	93,914–114,255	75,797–178,412	78,946–174,040	48,942–74,698	48,206–73,696
Bone and soft tissue	Mean cost					116,809	116,411	109,631	108,811
	95% CI					88,840–144,779	89,898–142,924	96,213–123,049	95,500–122,121
Germ cell	Mean cost					85,878	85,252	37,251	36,355
	95% CI					39,501–132,254	47,272–123,231	31,503–42,999	30,642–42,068
Thyroid	Mean cost					–	–	10,419	9,499
	95% CI					–	–	9,853–10,985	8,913–10,085
Other	Mean cost	179,786	178,999	141,997	140,487	65,393	64,820	29,865	28,901
	95% CI	150,010–209,561	149,988–208,009	134,228–149,767	132,720–148,253	34,149–96,636	37,481–92,158	23,018–36,712	22,093–35,709
All cancers	Mean cost	173,202	172,443	134,820	133,498	151,724	151,187	56,994	56,034
	95% CI	153,962–192,962	153,317–191,570	130,606–139,034	129,286–137,710	121,507–181,941	121,335–181,039	53,214–60,774	52,261–59,807
All cancers and survivor groups	Mean total cost (95% CI)		137,693 (133,528–141,857)			62,326 (58,174–66,477)			
	Mean net cost (95% CI)		136,413 (132,250–140,575)						

Note. All total and net costs are in 2012 Canadian dollars.

CI, confidence interval; CNS, central nervous system; ICCC, International Classification of Childhood Cancer, Third Edition.

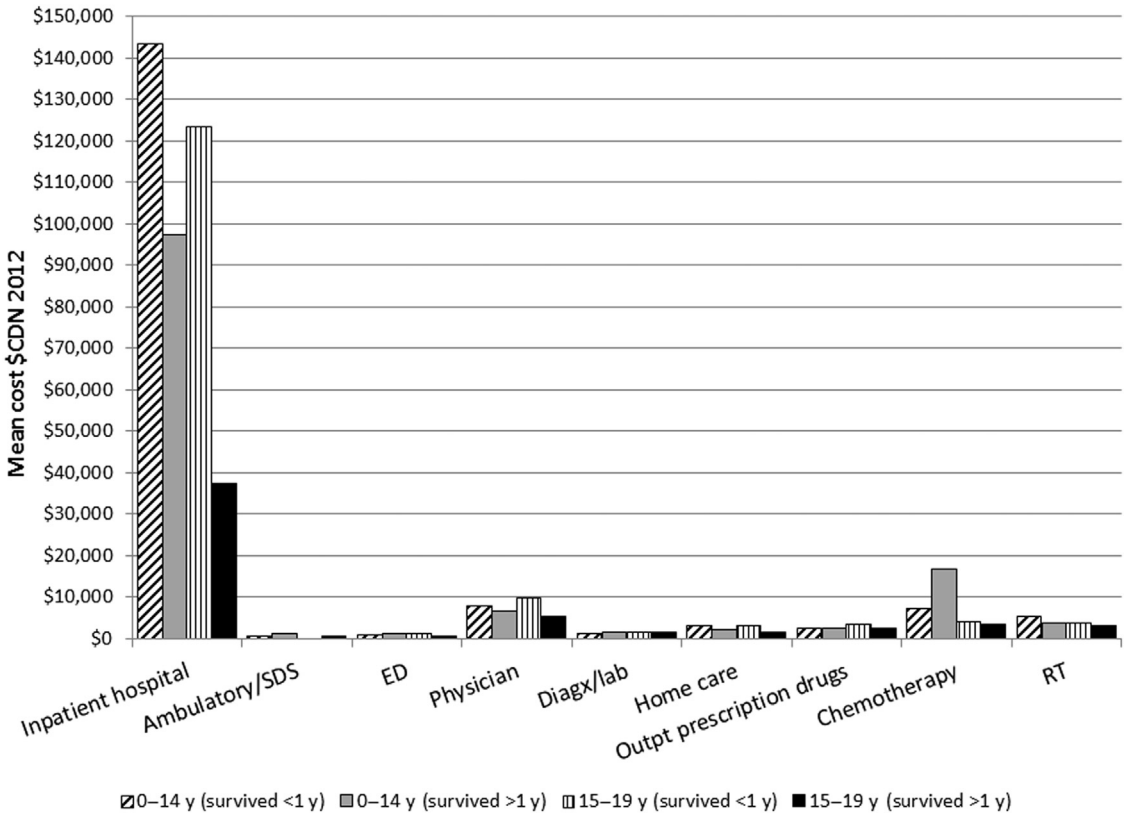

Fig. 1 – Mean net costs in the y after diagnosis by resource type. $CDN, Canadian dollars; ED, emergency department; RT, radiation therapy; SDS, same-day surgery.

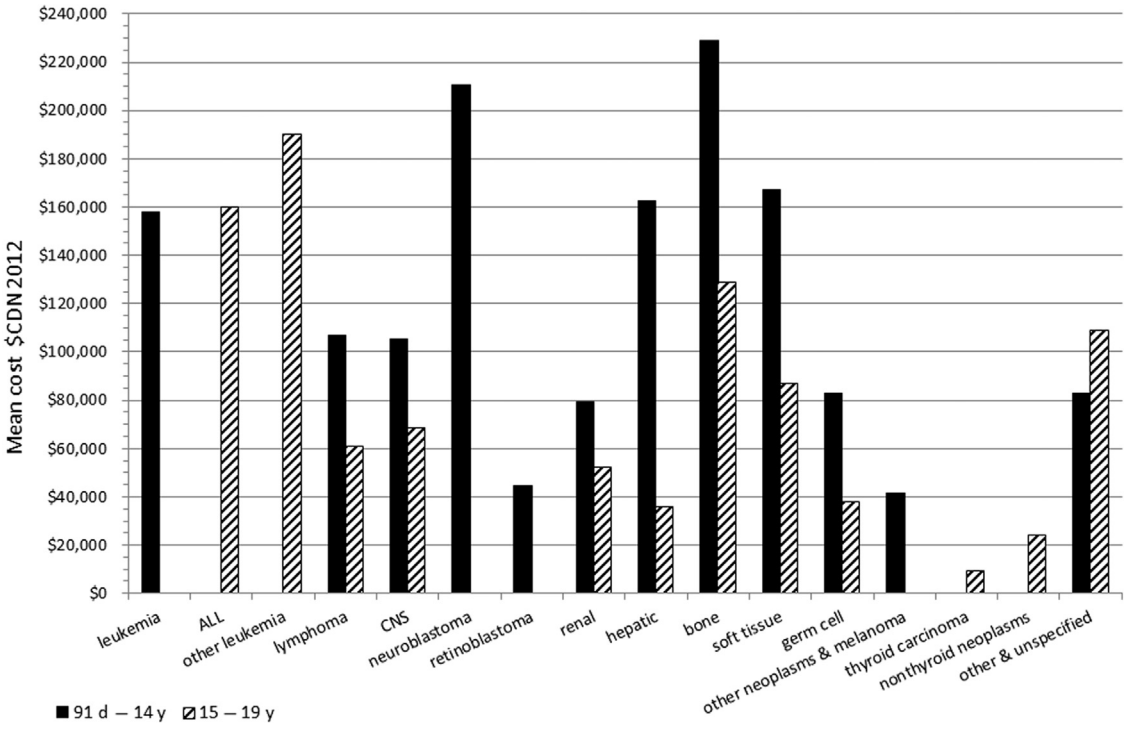

Fig. 2 – Mean net costs in the y after diagnosis for 12 ICCC diagnostic groups. $CDN, Canadian dollars; CNS, central nervous system; ICCC, International Classification of Childhood Cancer, Third Edition.

therapy costs were for patients with lymphoma (see Appendix Tables 4 and 5 in Supplemental Materials).

Costs for Other Cancers

Children

We examined net costs for each of the nine ICCC groups included in other cancers (N = 1446 patients) (Table 2). Because few patients died within 1 year after diagnosis, results by survivorship could not be reported in compliance with ICES privacy policy. Patients with hepatic tumors had the highest mean prediagnosis net costs ($11,186), and patients with retinoblastoma had the lowest ($1,833). In the year after diagnosis, the highest mean costs were for patients with bone tumors ($220,748) and neuroblastoma ($205,747); these were more than twice as high as costs for some other cancers (Fig. 2).

Adolescents

We classified adolescents differently than children because of the numbers and clinical interest in some diagnostic subgroups. We divided patients with leukemia into two groups: those with ALL, on the basis of diagnostic criteria for adolescents and young adults [35], and those with other types of leukemia. We examined patients with thyroid carcinoma separately from those with other carcinomas and malignant melanomas. We combined patients with neuroblastoma, retinoblastoma, and other and unspecified malignant neoplasms because of small numbers (Table 2).

Patients with other and unspecified cancers had the highest mean net prediagnosis cost ($4,074), followed by those with CNS tumors ($2,241). In the year after diagnosis, patients with types of leukemia other than ALL had the highest mean net cost ($190,433) (Fig. 2). ALL was the second most costly type of cancer ($159,879). As reported earlier, the lowest mean cost was for patients with thyroid carcinoma (Fig. 2).

Discussion

Our study provides estimates of the economic burden of care during the 90 days prediagnosis and the first year postdiagnosis for population-based cohorts of children and adolescents diagnosed with cancer. This work fills an important gap in the literature regarding the cancer care provided to these populations. Our main findings can be summarized in three key points, which are described hereafter.

1. *Costs in children and adolescents with cancer are high relative to noncancer populations*: In our study, the mean total cost in the year after diagnosis for children who survived at least 1 year after diagnosis ($138,820) was approximately 100 times the cost for controls in the year after their index date ($1,280). The mean 1-year postdiagnosis cost for adolescents who survived at least 1 year ($56,994) was approximately 60 times the 1-year cost for their controls ($932). Postdiagnosis costs for children and adolescents were approximately 35 times and 15 times, respectively, the average Ontario per capita health expenditure in 2012 ($3,734) [47]. Care for children and adolescents with cancer is, unsurprisingly, quite costly.
2. *Costs are higher in children than in adolescents*: We also found that children had high costs relative to adolescents. For both survivorship groups, both prediagnosis and postdiagnosis, the mean net costs were higher in the younger cohort for almost all diagnostic groups. In addition, some cancers that had very high postdiagnosis costs (such as leukemia and neuroblastoma) were more common in children, whereas some cancers that were less costly to treat (such as lymphoma and thyroid cancer) were more prevalent in adolescents, thus accounting for the overall higher cost in children. Furthermore, we excluded patients diagnosed at age 90 days and younger so that all patients had 90 days of prediagnosis time. These patients, however, may be high users of resources, because of birth defects [48], complex health conditions [49], and short survival [50], and their inclusion might have resulted in even higher costs for the childhood cohort. Higher rates of hospitalization and higher hospitalization costs in children may also explain some of the differences in costs between children and adolescents. Approximately 98% of the younger cohort, but only 79% of the adolescents, had at least one hospitalization in the year after diagnosis. Hospitalization rates were the lowest in adolescents with Hodgkin lymphoma and malignant melanoma, who used higher rates of outpatient services. Studies in the United States reported higher admission rates and cost per admission, and longer length of stay, for children with cancer compared with other pediatric patients or adult patients with cancer [5,51]. In Canada, the average cost per cancer-related hospital stay for children younger than 15 years was reported to be 2 to 3 times the cost for older age groups [52]. Children require extra time, resources, and personnel, which contribute to the higher CPWC for pediatric hospitals as mentioned previously. Some children older than 15 years may be referred to an adult cancer center [27], thus accounting for some proportion of the lower costs in adolescents. With respect to treatment, radiation therapy for young children is resource-intensive and costly because children may require extra time, personnel, and, in many cases, anesthesia to keep them calm [53,54].
3. *Costs are higher for children and adolescents with cancer than for adults*: The mean total costs for adults in Ontario with leukemia, lymphoma, and brain tumors (the most common childhood cancers) who survived at least 1 year postdiagnosis were estimated at approximately $28,000 to $49,000 in the year after diagnosis [26]. Our total costs for children younger than 15 years with these cancers who survived at least 1 year postdiagnosis ranged from $100,521 to $154,176 1 year postdiagnosis, whereas the mean total costs for adolescents ranged from $56,050 to $162,174.

Our study represents significant methodological improvements over most of the previous studies of childhood and adolescent cancer costs in Canada and the United States. These include two studies that examined resource use and costs at single hospitals (195 and 223 patients) [16,55]: one was a study that reported 1-month costs in 64 patients at one medical center [4] and the other a chart review study in 159 children and adolescents at a children's hospital [14]. One study included all patients in one state (N = 1651), but included only hospitalization charges [17]. In contrast, we included large, population-based cohorts of children and adolescents covered by a universal health insurance plan. Cost data for cohorts of these age groups are difficult to obtain in many jurisdictions, because their health care is covered by different insurers. Our study is also more comprehensive. We estimated the vast majority of health care costs (in Ontario, patients incur no deductibles or co-payments for publicly insured care), and all major cancer sites.

Despite differences in design and setting, the results of these studies and ours show common trends. Hospitalization is the major cost driver [4,14,56], patients who die within the costing period incur higher costs than those who survive [4,14,55], mean costs are higher for young children than for adolescents [56], and costs vary by cancer type, with leukemia among the most costly and lymphoma and CNS tumors costing less [14,16,17,56].

Study Limitations

Our data and cost estimates have some limitations. The patients with cancer had higher mean costs than the controls but they also had higher mean ADG scores, despite the match on comorbidity. Thus, our net costs may include not only the costs of cancer but also the costs of comorbidities and pathologies that are more common in this population [48]. The controls in our study, however, had higher ADG scores than did children aged 0 to 16 years in several US ambulatory populations. Only 7% to 18% (depending on the population) of those children had four or more ADGs [57], whereas 54% of our younger controls and 38% of the older controls had five or more ADGs.

Ontario's public health care plan does not cover complementary and alternative medicine, or most outpatient physiotherapy, occupational therapy, and social work. Outpatient prescription drugs are covered for patients younger than 65 years only if they, or their families, are on social assistance or have high drug costs relative to their income. We obtained data on outpatient prescription drugs for patients who were eligible for coverage, but we had no information on drugs covered by private insurers. Approximately 50% of children and 35% of adolescents had at least one claim under the public provincial drug plan, but we cannot determine whether more children were covered by the plan or more were prescribed drugs.

Our cost estimates for radiation therapy were largely based on a study published in 1999 [58] but there is, to our knowledge, no recent comprehensive evaluation of radiation therapy costs in Canada. Records of visits to EDs and outpatient chemotherapy clinics were not available until April and October 2003, respectively, and so we relied on physicians' billing data to identify these visits that were before those times. Use and costs for chemotherapy and ED visits fluctuated from 1995 to 2009, but the differences between 2002, 2003, and 2004 were no greater than the differences between many other consecutive years (data not shown). Nonetheless, the reliance on billing data might have underestimated or overestimated total costs, but would have less effect on net costs. We did not include the year of diagnosis in the generalized estimating equation model, and therefore time trends associated with changes in policies or treatment regimens were not captured. We did not attempt to include out-of-pocket costs or time costs, which can be substantial for families even in countries with publicly funded universal health care [3,6,59].

Our results are qualitatively similar to those of the studies in the United States [16,17,55], Europe [56], and other provinces in Canada [14], and are likely generalizable to those of other countries with similar health care systems. Although the direct cost estimates in these and other jurisdictions may differ from those in Ontario, the trends related to age, diagnostic category, and survivorship are common.

Conclusions

Costs of caring for young children are very high relative to those for older children and adults. Accurate estimates of childhood and adolescent cancer costs will provide a valuable scientific foundation for cost-effectiveness analyses of cancer treatments in these patients. Cancer care in children and adolescents may be cost-effective in spite of high costs because of the dramatic effects of cancer treatment on extending survival. Nevertheless, we cannot know this in advance without conducting careful and comprehensive studies. These data will also inform health care and research planning for cancer across the age spectrum. Future research will examine long-term costs and treatment in survivors of childhood and adolescent cancers.

Source of financial support: This work was supported by the Canadian Institutes of Health Research (operating grant no. 259504) and the F. Norman Hughes Chair in Pharmacoeconomics, Faculty of Pharmacy, University of Toronto (career award to Dr Murray Krahn). It was also supported by the Institute for Clinical Evaluative Sciences, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care. The opinions, results, and conclusions reported in this article are those of the authors and are independent from the funding sources. No endorsement by the Institute for Clinical Evaluative Sciences or the Ontario Ministry of Health and Long-Term Care is intended or should be inferred.

Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.jval.2016.10.010 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

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