ELSEVIER

European Journal of Cancer 41 (2005) 404–410

European Journal of Cancer

www.ejconline.com

Use of paediatric *versus* adult oncology treatment centres by adolescents 15–19 years old: the Canadian Childhood Cancer Surveillance and Control Program☆

J. Klein-Geltink [a,*], A.K. Shaw [a], H.I. Morrison [a], R.D. Barr [b], M.L. Greenberg [c,d,e]

[a] *Chronic Disease Control and Management Division, Population and Public Health Branch, 120 Colonnade Road, AL: 6702A Ottawa, Ont., Canada, K1A 0K9*

[b] *McMaster University, Hamilton, Ont., Canada*

[c] *The Hospital for Sick Children, Toronto, Ont., Canada*

[d] *The University of Toronto, Toronto, Ont., Canada*

[e] *Pediatric Oncology Group of Ontario, Toronto, Ont., Canada*

Received 30 June 2004; received in revised form 4 October 2004; accepted 22 October 2004
Available online 15 December 2004

Abstract

The aim of this study was to evaluate the treatment patterns of adolescents with cancer in Canada to ensure this population is receiving the most appropriate care. The Treatment and Outcome Surveillance (TOS) system was compared with the Canadian Cancer Registry (CCR) to estimate the proportion of adolescents (15–19 years) treated in Canadian paediatric oncology centres from 1995 to 2000 inclusive. Using TOS, the demographic, disease, and clinical characteristics of adolescents treated in paediatric *versus* adult centres in the Prairies were compared and differences were tested statistically. Approximately 30% of Canadian adolescents with cancer were treated in a paediatric centre. Adolescents treated in an adult centre were older at diagnosis and more likely to have carcinoma or germ cell tumours. The time between symptom onset and first treatment was longer for these adolescents, primarily due to the time between first health-care contact and assessment by a treating oncologist or surgeon. They were less likely to be enrolled in a clinical trial. These results suggest that care for adolescents with cancer in Canada is less satisfactory than for younger children, and can be improved.

Keywords: Neoplasms; Health-care delivery; Adolescents; Young adults; Cancer care units

1. Introduction

Approximately 400 adolescents, 15–19 years old, are diagnosed with cancer in Canada each year [1,2]. Although cancer in adolescents is relatively rare, it remains the leading cause of disease-related death in this age group [3]. Improvements in therapy and supportive care have led to a dramatic increase in the overall survival rate among children and adolescents with cancer, with more than 75% now surviving 5 years past diagnosis [4–7]. However, the improvement in 5-year survival among adolescent cases has lagged behind the increase

☆ Ms. Klein-Geltink contributed to the conception of the project, analysis, and drafting of the manuscript. Ms. Shaw contributed to the analysis and manuscript writing. Dr. Morrison contributed to the conception of the project, and revision of the draft. Dr. Barr and Dr. Greenberg contributed to the interpretation of data, and revision of the draft. All authors gave final approval of the paper. Please note that Dr. Greenberg holds the POGO Chair in Childhood Cancer Control at the University of Toronto.

* Corresponding author. Tel.: +1 613 957 0275; fax: +1 613 941 5497.

E-mail address: julia_klein-geltink@phac-aspc.gc.ca (J. Klein-Geltink).

0959-8049/$ - see front matter.
doi:10.1016/j.ejca.2004.10.023

seen in children with cancer. Between 1975 and 1998, the survival rate among childhood cancer cases in the United States (US) rose by nearly 40% compared with 23% among adolescents with cancer [5].

Several factors may account for the relatively smaller improvement in survival among adolescent compared with childhood cancer cases [8–10]. The spectrum of cancers in adolescents differs from that in younger children, they have different tolerances for therapy, and the pattern of care they receive often differs [8,10]. In particular, the locus of therapy varies among adolescent cancer cases with some cases attending adult oncology centres and others using paediatric facilities, as specialised adolescent cancer units do not exist currently in Canada [10]. For a number of reasons, adolescents treated in paediatric compared with adult oncology centres generally have better survival prospects. Paediatric oncology specialists are more familiar with childhood cancers, age-appropriate supportive care is more readily available in paediatric centres, and the chance of being enrolled in a clinical trial is higher in a paediatric centre [4,9–12]. In fact, several childhood cancer care task forces have recommended recently that adolescents with cancer always be treated in a paediatric rather than an adult setting [10,13]. However, two small regional studies in North America found that over half of adolescents with cancer were treated at adult oncology centres [10–12]. The treatment patterns of adolescents with cancer in Canada are not clear at present and need to be evaluated to ensure that this population is receiving the most appropriate care [13].

Thus, the objectives of this analysis are to estimate the proportion of adolescents with cancer in Canada treated in paediatric compared with adult oncology centres, and to compare the demographic, disease and clinical characteristics of these two groups.

2. Patients and methods

Data for this study were obtained from the Treatment and Outcome Surveillance (TOS) system of the Canadian Childhood Cancer Surveillance and Control Program [2,14,15]. The TOS system was a national, population-based surveillance mechanism conducted in paediatric oncology centres and selected provincial cancer registries across Canada between 1995 and 2000. Information on all children (0–14 years) and adolescents (15–19 years) diagnosed and/or treated with cancer in a paediatric oncology centre in Canada was included in the system. In addition, during the same period, information on adolescents treated at adult oncology centres was collected in three of the 10 Canadian provinces (the Prairies). Previous analyses have shown that TOS captures 99% of all child and adolescent (0–19 years) cancer cases and 96% of adolescent cancer cases (15–19 years) treated in paediatric oncology centres in Canada [2,14]. For this analysis, cases were assumed to have been treated at the same centre in which they were initially seen and diagnosed.

Child and adolescent cancer cases in TOS were classified according to the International Classification of Childhood Cancer (ICCC) [16]. Information gathered included: demographics, diagnostic data, treatments used, and short-term outcomes. Data were extracted from medical charts by Clinical Research Associates at diagnosis and every 6 months for up to 5 years. The Research Ethics Board of each paediatric oncology centre and/or provincial cancer registry approved the protocol and the parent or legal guardian of each patient provided informed consent prior to data collection.

The proportion of adolescents treated in paediatric *versus* adult oncology centres by age at diagnosis and diagnostic category for all geographical regions in Canada was assessed by comparing incidence counts in the TOS system to those in the Canadian Cancer Registry (CCR). The CCR compiles basic diagnostic information for all cases of cancer in Canada from the provincial and territorial cancer registries. Given that TOS has nearly complete coverage of cancer cases treated in paediatric oncology centres, it was assumed that adolescent cases included in the CCR but not in TOS were not diagnosed or treated in a paediatric oncology centre. For this table only, the eligibility criteria for the CCR were applied to the TOS data, so patients diagnosed with Langerhans cell histiocytosis, myelodysplastic syndromes, skin carcinomas and benign brain tumours were excluded.

To evaluate the demographic, disease and clinical characteristics of adolescent cancer cases treated in paediatric compared with adult oncology centres, cases from the Prairie region were used as this was the only region in Canada where information on almost all adolescents with cancer was gathered, irrespective of treatment location (422/423 = 99.8%). Out of 422 adolescent cancer cases included in TOS from the Prairie region, 204 consented to participate and are included in this analysis (204/422 = 48.3%). Sensitivity analyses found no difference between adolescents who consented to participate compared with those who did not consent based on gender, age at diagnosis, and diagnostic category (data not shown).

Outcomes compared between adolescents treated in paediatric and adult centres included diagnosis, age at diagnosis, time (in days) between consecutive health-care events, type of health-care practitioner first contacted and enrolment in a clinical trial. Date of onset of symptoms and date of initial health-care contact were often estimated by the patient or their parents (58% of dates of onset and 81% of dates of initial health-care contact). Outlying dates were reviewed on a case-by-case basis for their clinical plausibility.

The Statistical Analysis System, version 8.01 for Windows (SAS Institute, Inc., Cary, NC), was used for all of the analyses. Differences between adolescents treated in

paediatric compared with adult oncology centres were evaluated using χ^2 tests, Fisher's exact tests, or Wilcoxon non-parametric tests, as appropriate [17]. All tests of significance were two-sided ($P < 0.05$).

3. Results

Thirty percent of adolescents diagnosed with cancer in Canada between 1995 and 2000 were treated in a paediatric oncology centre (Table 1). The highest proportion of adolescents who underwent treatment in a paediatric centre was found in the Prairie region (52%), while all other regions had similar referral rates, varying between 24% and 33%. The proportion of adolescents treated in a paediatric centre varied by age at diagnosis and diagnostic category. Cases less than 18 years of age were more likely to receive their treatment in a paediatric centre (47%) compared with those aged 18 and 19 years at diagnosis (10%). Only in the Prairie region was a substantial proportion of 18 and 19 year olds treated in a paediatric centre (35%). Adolescents with carcinoma were the least likely to be treated in a paediatric centre (11%), while cases of leukaemia were the most likely (51%). Reconnaissance analysis found little variation in age at diagnosis or diagnostic category between regions based on the CCR data (data not shown).

Table 1
Proportion of adolescent cancer cases, 15–19 years, treated in paediatric centres by region, age at diagnosis and diagnostic category,[a] Canada, 1995–2000

	Adolescents treated in paediatric centres (TOS)[b] (*n*)	Adolescents diagnosed with cancer (CCR) (*n*)	Percent of adolescents with cancer treated in paediatric centres (TOS/CCR) (%)
Region			
Atlantic	63	192	32.8
15–17 years	52	99	52.5
18–19 years	11	93	11.8
Quebec	128	541	23.7
15–17 years	115	290	39.7
18–19 years	13	251	5.2
Ontario	225	918	24.5
15–17 years	215	502	42.8
18–19 years	10	416	2.4
Prairies	218	423	51.5
15–17 years	149	224	66.5
18–19 years	69	199	34.7
BC	69	284	24.3
15–17 years	69	155	44.5
18–19 years	–	129	–
Canada	706	2364	29.9
15–17 years	601	1271	47.3
18–19 years	105	1093	9.6
Diagnostic Category			
Leukaemia	135	265	50.9
Lymphomas	223	675	33.0
CNS	86	218	39.4
Bone	67	175	38.3
Soft tissue	58	164	35.4
Germ cell	62	341	18.2
Carcinoma	52	455	11.4
Other[c]	23	71	32.4

Source: The Canadian Childhood Cancer Surveillance and Control Program (TOS) and The Canadian Cancer Registry (CCR).
Note. Dashes (–) represent fewer than five cases.
CNS, central nervous system.
[a] Malignant neoplasms only, excluding langerhans cell histiocytosis, myelodysplastic syndromes, skin carcinomas, and benign brain tumours.
[b] Adolescents captured through TOS are assumed to represent all adolescents treated in paediatric centres in Canada.
[c] Other includes hepatic tumours, renal tumours, sympathetic nervous system tumours, and other and unspecified malignant neoplasms.

According to the analyses from the Prairie region, adolescents treated in an adult oncology centre were significantly older at diagnosis than those treated in a paediatric oncology centre (17.4 years *versus* 16.5 years) (Table 2). There was no difference in the gender distribution of cases by centre. Adolescents treated in an adult centre were more likely to have a diagnosis of carcinoma (31% *versus* 17%, respectively) or germ cell tumour (19% *versus* 10%, respectively) and less likely to have lymphoma (21% *versus* 32%, respectively) compared with adolescents treated in a paediatric centre. Within the Prairie region, the proportion of adolescents treated in a paediatric *versus* adult oncology centre differed significantly by province. Virtually no adolescents in Saskatchewan were treated in an adult centre, compared with approximately one quarter of adolescents with cancer in Manitoba and over one-third of adolescents with cancer in Alberta. Again reconnaissance analysis found no difference in the distribution of age at diagnosis or diagnosis between the three provinces in the Prairie region (data not shown).

The median number of days between onset of symptoms and first treatment was significantly longer for adolescents treated in an adult compared with a paediatric centre (92 *versus* 57 days), primarily due to the time between first health-care contact and assessment by a treating oncologist or surgeon (Table 3). Adolescents treated in a paediatric centre waited a median of 7 days between first health-care contact and assessment by a treating oncologist or surgeon compared with 34 days for those treated in an adult centre.

According to our analyses, adolescents treated in an adult centre were significantly less likely to be enrolled in a clinical trial compared with those treated in a paediatric centre (0% *versus* 21%) and more likely to receive care according to individualised treatment plans (83% *versus* 44%) (Table 4). No difference was found in the type of health-care practitioner first contacted by adolescent cancer cases from paediatric or adult centres (Table 5). Adolescents from both centres were most

Table 2
Demographic and diagnostic characteristics of adolescent cancer cases, 15–19 years, by type of treatment centre, Prairie region, 1995–2000

	Paediatric centre (n = 152)		Adult centre (n = 52)		P value[a]
	n	(%)[b]	n	(%)	
Age at diagnosis (years)					< 0.01
15–17	115	(75.7)	25	(48.1)	
18–19	37	(24.3)	27	(51.9)	
Mean (SD)	16.5 (1.4)		17.4 (1.5)		
Gender					0.80
Female	76	(50.0)	27	(51.9)	
Male	76	(50.0)	25	(48.1)	
Diagnostic category					0.05
Leukaemia	17	(11.2)	–	–	
Lymphomas	49	(32.2)	11	(21.2)	
CNS	20	(13.2)	6	(11.5)	
Bone	14	(9.2)	–	–	
Soft tissue	6	(4.0)	–	–	
Germ cell	15	(9.9)	10	(19.2)	
Carcinoma	25	(16.5)	16	(30.8)	
Other[c]	6	(4.0)	–	–	
Location of centre					< 0.01
Alberta	75	(62.5)	45	(37.5)	
Saskatchewan	58	(98.3)	–	–	
Manitoba	19	(76.0)	6	(24.0)	

Source: The Canadian Childhood Cancer Surveillance and Control Program (TOS).*Note*. Dashes (–) represent fewer than five cases.
SD, standard deviation.
[a] Differences were tested using the χ^2 test.
[b] Column percentages are presented for age at diagnosis, gender, and diagnostic category, while row percentages are presented for location of centre.
[c] Other includes: sympathetic nervous system tumours, renal tumours, hepatic tumours, other and unspecified malignant neoplasms.

Table 3
Time (days) between consecutive health-care events for adolescent cancer cases, 15–19 years, by type of treatment centre, Prairie region, 1995–2000

Consecutive health-care events	Paediatric centre	Adult centre	P value[a]
	Median (IQR)[b] (n = 152)[c]	Median (IQR)[b] (n = 52)[c]	
Onset of symptoms to first treatment	57 (29–138)	92 (56–240)	0.02
Onset of symptoms to first health-care contact	20 (0–70)	25 (0–61)	1.00
First health-care contact to assessment by oncologist	7 (0–35)	34 (4–90)	< 0.01
Assessment by oncologist to first treatment	8 (1–19)	1 (0–19)	0.05

Source: The Canadian Childhood Cancer Surveillance and Control Program (TOS).
[a] Significance of difference was tested using the Wilcoxon non-parametric test.
[b] IQR = Inter-quartile range.
[c] Wait times were not available for all time periods for 21 subjects (n = 10 for paediatric centres, n = 11 for adult centres).

Table 4
Treatment protocol for adolescent cancer cases, 15–19 years, by type of treatment centre, Prairie region, 1995–2000

Initial treatment protocol	Paediatric centre (n = 152)		Adult centre (n = 52)		P value[a]
	n	(%)	n	(%)	
Clinical trial	32	(21.1)	–	–	< 0.01
Non-clinical trial	45	(29.6)	–	–	
Individualised treatment	67	(44.1)	43	(82.7)	
No treatment	–	–	5	(9.6)	
Unknown	8	(5.3)	–	–	

Source: The Canadian Childhood Cancer Surveillance and Control Program (TOS).
Note. Dashes (–) represent fewer than five cases.
[a] Differences were tested using the Fisher's exact χ^2 test.

Table 5
Health-care practitioner first contacted by adolescent cancer cases, 15–19 years, by type of treatment centre, Prairie region, 1995–2000

Health-care practitioner first contacted	Paediatric centre ($n = 152$)[b]		Adult centre ($n = 52$)[b]		P value[a]
	n	(%)	n	(%)	
General practitioner	97	(67.8)	34	(79.1)	0.50
Emergency room physician	22	(15.4)	5	(11.6)	
Paediatrician	–	–	–	–	
Other	22	(15.4)	–	–	

Source: The Canadian Childhood Cancer Surveillance and Control Program (TOS).
Note. Dashes (–) represent fewer than five cases.
[a] Differences were tested using the Fisher's exact χ^2 test.
[b] Information on the health-care practitioner first contacted was not available for 18 subjects ($n = 9$ for paediatric centres, $n = 9$ for adult centres).

likely to have first contacted a general practitioner regarding their symptoms (68% and 79%, respectively) and least likely to have first contacted a paediatrician (1% and 0%, respectively).

4. Discussion

Thirty percent of adolescents (15–19 years) with cancer in Canada are treated in paediatric oncology centres, with the remaining majority receiving treatment in an adult setting. Adolescents in the Prairie region are significantly more likely to be treated in a paediatric centre than adolescents in other parts of the country. Based on our national and regional analysis, adolescents treated for cancer in an adult centre are older at diagnosis and are more likely to have an epithelial type of cancer (i.e., carcinoma or germ cell tumour) compared with those treated in a paediatric centre. Adolescents treated in adult centres report longer waiting times between health-care events and are less likely to be enrolled in a clinical trial. These results suggest that care for adolescents with cancer in Canada is less satisfactory than for younger children, and can be improved.

Outcomes for adolescents with cancer are generally more favourable when treatment is provided in a paediatric compared with an adult oncology centre [10–13,18,19]. Comprehensive care provided by specialists in paediatric oncology is more readily available in paediatric centres, and the opportunity for enrollment in clinical trials is higher [10–12]. Furthermore, clinical trials offered in paediatric centres are more appropriate for certain types of cancer in adolescents than those offered in adult centres. Recent data show that survival of adolescents treated on paediatric *versus* adult protocols for some cancers, including acute lymphoblastic leukaemia and Ewing's sarcoma, is higher [18]. Five year survival rates for adolescents treated on paediatric protocols was over 64% in the US and 78% in Europe, compared with 57% for adolescents on adult protocols in the US [10]. This and other evidence has led several childhood cancer task forces to recommend that adolescents always be treated in paediatric rather than adult centres [10,11,13]

However, the large majority of adolescents with cancer are still treated in adult centres with lower access to clinical trials, especially paediatric-specific trials [20]. Similar to our results, two previous studies on adolescents with cancer in Canada and the US found that 54% and 64%, respectively, were treated in adult compared with paediatric centres [10,11]. In most Canadian provinces, more than 60% of adolescents were treated in adult centres between 1995 and 2000; only in the Prairie region were the majority of adolescents with cancer treated in paediatric centres (67%). Age restrictions imposed by the paediatric centres do limit where adolescents with cancer can be treated [2]. Across the country, the oldest age seen at paediatric centres varies from 16 to 19 years. However, there seems to be no consistency between age restrictions and location of treatment for adolescents with cancer in Canada.

Thus, we can only speculate on why the majority of adolescents with cancer attended adult oncology centres for treatment and why the proportion is dramatically different for the Prairie region. Previous studies have postulated that older adolescents often do not feel comfortable attending paediatric clinics as they are child-oriented with lower possibility of contact with peers [12,21,22]. Consistent with our results, adolescents with cancers more common among adults are more likely to be referred to an adult centre [10,12]. However, there was no difference in the distribution of age at diagnosis or diagnostic category between regions in Canada or between provinces in the Prairie region. Although the paediatric centre in Saskatchewan is the only one in Canada to treat patients up to 19 years of age treats only a small percentage of cases in the Prairies. Perhaps in the Prairie region there is a stronger culture of general practitioners referring older adolescents to paediatric centres as opposed to adult centres. Without further investigation into this issue, we are unable to offer more explanation.

The results from our regional analyses show that nearly 80% of adolescents with cancer did not participate in a clinical trial, irrespective of locus of treatment. This finding is consistent with a report from the US that more than 75% of adolescents with cancer are not enrolled in clinical trials [12]. Again, given our data, we can not evaluate why adolescents with cancer are not being enrolled in clinical trials as often as children with cancer. Adolescents may be reluctant to participate in clinical trials as they do not want to be separated from their peer group [12,21,22]. Adolescents may not be offered enrolment in trials as often as children [10,12]. Trials specific to their cancer type may not be available, especially in adult centres [23–25]. However, data show that adolescents with cancer are also not being enrolled in adult oncology trials [10,12], meaning that optimum treatment may not be available or offered to this age group.

Finally, the time between first health-care contact and assessment was found to be significantly longer for adolescents treated in adult compared with paediatric centres. This may be due to the types of cancers referred to each centre (e.g., adolescents with epithelial type cancers are more likely to be referred to an adult centre), or it may be due to longer delays experienced in adult centres as a result of higher caseloads and fewer resources per patient [26]. Older adolescents also may be less diligent about obtaining health-care as they become independent from their parents [26]. A large majority of dates of first health-care contact were estimated by the patients or their parents in our study and may not be accurate. Still, other reports found the time between onset of symptoms and treatment was relatively longer for adolescents compared with children treated for cancer within the same paediatric centre [27], which suggests there may be a gap in available health-care for adolescents with cancer. The definitive answer to this question is being explored in an American study by Pollock and colleagues [28] outlined in their recent protocol, "Development of Intervention Strategies to Reduce the Time Between Symptom Onset and Diagnosis of Childhood Cancer".

There are a few limitations to this study. First, clinical information for adolescents treated in adult centres was available in only three of 10 provinces, and a low proportion of these cases consented to participate (204/422 = 48% participation). The adolescents from the Prairies who consented to participate do represent all adolescents with cancer in the region. However, without information on adolescents with cancer from adult centres in other provinces we cannot extrapolate our findings to the whole country. Furthermore, given our data, we are not able to evaluate the reasons for attending an adult compared with a paediatric centre, nor can we determine whether non-participation in a clinical trial was voluntary.

Notwithstanding, the results of this study have potentially important implications. The longer time to diagnosis and lower opportunity to be enrolled in a clinical trial among adolescents treated in adult centres may have a significant impact on the outcome of therapy in this group. Examination of treatments and outcomes for adolescents with cancer by type of treatment centre is the crucial next step being explored in our study.

Conflict of interest statement

None declared.

Acknowledgements

The authors gratefully acknowledge the contributions of study participants, participating paediatric oncology centres, and members of the Canadian Childhood Cancer Surveillance and Control Program (CCCSCP) Management Committee. The CCCSCP is fully funded by Health Canada.

References

1. On L, Semenciw RM, Mao Y. Orius software: calculation of rates and epidemiologic indicators, and preparation of graphical output. *Chronic Dis Can* 2000, **21**(3), 134–136.
2. Canadian Childhood Cancer Surveillance and Control Program. Diagnosis and initial treatment of cancer in Canadian adolescents 15 to19 years, 1995 to 2000. Ottawa: Health Canada; 2004.
3. Health Canada. Measuring up: a health surveillance update on Canadian children and youth. Ottawa: Health Canada; 1999.
4. Huchcroft S, Clarke A, Mao Y, *et al. This battle which I must fight: cancer in Canada's children and teenagers*. Ottawa, Supply and Services Canada, 1996.
5. Bleyer A. Older adolescents with cancer in North America deficits in outcome and research. *Pediatr Clin North Am* 2002, **49**(5), 1027–1042.
6. Ries LAG, Eisner MP, Kosary CL, et al. (Eds). SEER cancer statistics review, 1975–2001. Bethesda, MD: National Cancer Institute; 2004. Available from: www.seer.cancer.gov/csr/1975_2001/.
7. Villeneuve PJ, Raman S, Leclerc JM, *et al*. Survival rates among Canadian children and teenagers with cancer diagnosed between1985 and 1988. *Cancer Prev Control* 1998, **2**(1), 15–22.
8. Bleyer WA. Cancer in older adolescents and young adults: epidemiology, diagnosis, treatment, survival, and importance of clinical trials. *Med Pediatr Oncol* 2002, **38**(1), 1–10.
9. Barr RD. On cancer control and the adolescent. *Med Pediatr Oncol* 1999, **32**(6), 404–410.
10. Albritton K, Bleyer WA. The management of cancer in the older adolescent. *Eur J Cancer* 2003, **39**(18), 2584–2599.
11. Greenberg ML, Barr RD, DiMonte B, *et al*. Childhood cancer registries in Ontario, Canada: lessons learned from a comparison of two registries. *Int J Cancer* 2003, **105**, 88–91.
12. Bleyer WA, Tejeda H, Murphy SB, *et al*. National cancer clinical trials: children have equal access; adolescents do not. *J Adolesc Health* 1997, **21**(6), 366–373.
13. Greenberg ML, Greenberg CM. *A provincial program for childhood cancer control – 1994*. Toronto, Ministry of Health, 1994.

14. Canadian Childhood Cancer Surveillance and Control Program. Diagnosis and initial treatment of cancer in Canadian children 0 to 14 years, 1995–2000. Ottawa: Health Canada; 2003.
15. Gibbons L, Mao Y, Levy IG, *et al*. The Canadian childhood cancer control program. *CMAJ* 1994, **151**(12), 1704–1709.
16. Kramarova E, Stiller C, Ferlay J, et al. International classification of childhood cancer 1996. IARC technical report; 29. Lyon: International Agency for Research on Cancer; 1996.
17. Pagano M, Gauvreau K. *Principles of biostatistics*. 2nd ed. Pacific Grove, CA, Duxbury, 2000.
18. Rauck AM, Gremgen AM, Hutchison CL, *et al*. Adolescent cancers in the United States: A National Cancer Data Base (NCDB) report. *J Pediatr Hematol Oncol* 1999, **21**, 310.
19. Hoff J, Schymura MJ, McCrea Curren MG. Trends in the incidence of childhood and adolescent cancer in Connecticut, 1935–1979. *Med Pediatr Oncol* 1988, **16**, 78–87.
20. Shochat SJ, Frengen AM, Murphy SB, *et al*. Childhood cancer: patterns of protocol participation in a national survey. *CA Cancer J Clin* 2001, **51**, 119–130.
21. White L, Ewing J, Senner AM, *et al*. Cancer in adolescents and young adults: treatment and outcome in Victoria. *MJA* 2004, **180**, 653–654.
22. Ritchie MA. Sources of emotional support for adolescents with cancer. *J Pediatr Oncol Nurs* 2001, **18**(3), 105–110.
23. Mitchell AE, Scarcella DL, Rigutto GL, *et al*. Cancer in adolescents and young adults: treatment and outcome in Victoria. *MJA* 2004, **180**, 59–62.
24. Goldman S, Stafford C, Weinthal J, *et al*. Older adolescents vary greatly from children in their route of referral to the paediatric oncologist and national trials. In Grunberg SM, ed. *Proceedings of the American Society of Clinical Oncology; 2000, May 20–23*. New Orleans, LA/Alexandria, VA, American Society of Clinical Oncology, 2000. p. 450a.
25. McTiernan A. Issues surrounding the participation of adolescents with cancer in clinical trials in the UK. *Eur J Cancer* 2003, **12**, 233–239.
26. Bleyer WA. Adolescents and young adults with cancer: the great divide. Talk given at the POGO Symposium on Childhood Cancer, Adolescent and Young Adult Oncology: Walking Two Worlds. November 21–22, 2003. Toronto, Ontario.
27. Klein-Geltink J, Pogany L, Mery L, et al. Impact of distance from residence to specialised center on times to diagnosis and treatment of cancer in Canadian children. Pediatr Blood Cancer, 2005 (in press).
28. Pollock BH, Mulhern RK, Ryan B, et al. POG Protocol 9082: Protocol for the development of intervention strategies to reduce the time between symptom onset and diagnosis of childhood cancer. Children's Oncology Group. 2003. 12-8-0030.