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ORIGINAL REPORT

Quality of Life Among Long-Term Adolescent and Adult Survivors of Childhood Cancer

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ABSTRACT

Purpose
We assessed effects of childhood or adolescent cancer on quality of life among adolescent and adult cancer survivors, a group who are thought to be at particular risk for adverse late effects.

Patients and Methods
We studied 1,334 survivors and 1,477 age- and sex-matched, general population controls from across Canada using a mailed questionnaire which included the Short Form-36 (SF-36) and measures of self-esteem, optimism, and life satisfaction. General linear models and logistic regression were used. Survivor-control differences corresponding to an effect size (ES) ≥ 0.5 were considered clinically important.

Results
Participants were age 15 years to 37 years. Most survivors (83.8%) were diagnosed ≥ 10 years earlier. Fewer survivors (62.1%) than controls (71.1%) reported very good or excellent general health (adjusted odds ratio, 0.6; 95% CI, 0.5 to 0.7). However, quality of life differences between survivors and controls were small, and for the most part probably not clinically important. Three clinical characteristics—having had CNS or bone cancer, more than one treatment series, and ≥ two organs with a dysfunction at treatment end—were independently associated with poorer quality of life in the physical dimensions. Only survivors with ≥ two organs with dysfunction (8.7%) reported poorer quality of life in both physical and psychosocial domains, with several clinically important ES. The largest ES for the SF-36 physical summary scores were found in the 8% of survivors with two or three of these characteristics simultaneously, compared with those survivors who had none (−0.79 and −1.13, respectively).

Conclusion
Overall, a sizeable majority of adolescent and adult long-term survivors of childhood cancer in Canada appear to have adapted well.

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INTRODUCTION

Cancer is diagnosed in approximately 1,300 children and adolescents, up to 19 years of age, in Canada every year.[1] Seventy-eight percent of children and adolescents now survive at least 5 years after their initial diagnosis.[2] With growing numbers of survivors, it is increasingly important to understand the nature and extent of any late effects on their quality of life.[3] Adolescent and adult survivors of childhood cancers are thought to be particularly at risk[4,5] for poor physical, psychological, and social outcomes as a result of both their cancer and its treatment.[6-15]

Despite several large studies comparing adolescent and young adult survivors' quality of life with that of similar individuals without cancer,[9,11,15] gaps in our knowledge remain. Few studies have been national or population-based in scope.[9,11] While some studies have used population controls,[10,12,16-18] others have compared published population norms[19,20] with unknown age and sex distributions, or used sibling controls[9,11,14] who may themselves have been affected by the survivor's cancer.[21-23] Only two studies with controls, one American and one Dutch, examined clinical characteristics affecting survivors' long-term quality of life.[9,15] Finally, findings from studies conducted in the United States could conceivably differ because of lack of universal health insurance. Lack of health insurance could negatively affect survivors both when they were children (if parents lacked health insurance or lost employment through which insurance was provided because of the child's cancer) or later when survivors were adults and could not obtain health insurance themselves. Thus, long-term quality of life effects of

childhood cancers might differ in countries like Canada, where access to health care is universal.

In this study we assessed the long-term effects of having had cancer during childhood or adolescence on several indicators of quality of life by comparing survivors with controls who have never had cancer. We also examined whether particular groups of these cancer survivors were at risk of poorer quality of life compared with their healthy peers.

PATIENTS AND METHODS

Study Design and Patients

Details of study methodology have been published.[24] Briefly, study data were collected as part of the Canadian Childhood Cancer Surveillance and Control Program.[25] Survivors were identified from patients at 12 pediatric oncology centers and provincial cancer registries from all 10 Canadian provinces. Eligible survivors had survived 5 years after diagnosis, between 1981 and 1990 inclusively, of an incident, primary cancer before age 20. The International Classification of Childhood Cancer was used.[26] In each center, a random sample of potentially eligible patients stratified by diagnosis, age at diagnosis, and calendar year of diagnosis was selected.

General population controls were selected by province using either provincial health insurance records or random digit dialing in provinces where access to health insurance records was not possible. Frequency matching was used to create a control group with a similar overall age and sex distribution as survivors. Individuals previously diagnosed with cancer were ineligible. Research ethics board approval was obtained from all participating centers.

Data Collection

Data collection occurred between January 1997 and February 2000. Except for controls recruited by random digit dialing, potential study participants were sent a letter about the study, and within 2 weeks, telephoned to determine their decision regarding participation. All subjects age $\geq$ 16 years who agreed to participate were mailed the self-administered questionnaire and a consent form and asked to return completed documents using the self-addressed envelope provided. Information on survivors' date of diagnosis, clinical outcome, and therapy came from the medical record.

These analyses are based on 1,334 survivors and 1,477 controls. Specifically, among the 2,229 survivors who met the eligibility criteria, 664 could not be traced or did not return questionnaires, 231 declined participation, and 1,334 returned completed questionnaires giving a response rate of 60% (1,334 of 2,229). Including an estimation of potentially eligible control subjects residing at unanswered telephone numbers,[24] we identified 3,323 eligible control subjects. Of these, 1,477 returned completed questionnaires resulting in a response rate of 44%.[24]

Measures

The eight subscales and two component summaries (physical component summary [PCS] and mental component summary [MCS]) of the Short Form-36 (SF-36; version 1) were used to measure health-related quality of life.[27] The single SF-36 general health question was also used as a stand-alone indicator of perception of overall health. Finally, validated measures of self-esteem,[28] optimism,[29] and life satisfaction[30] were used to assess positive aspects of quality of life. The self-esteem and optimism scales used a 5-point response option (strongly disagree to strongly agree) and the satisfaction with life scale used a 7-point option (same anchors). All scales were transformed to standard scores (0 to 100 scale). For all measures, higher scores represent better function or more positive outcomes.

Physical health problems were evaluated using some questions from the Childhood Cancer Survivor Study.[31] Participants were asked whether they had ever had, or had ever been told by a doctor that they had, a number of different problems. Responses were grouped into cardiovascular, endocrine, hormonal, neurologic, renal, and pulmonary problems. We assumed that health problems occurring before diagnosis would be similar for survivors and similarly aged controls. Thus, if survivors reported more health problems we assumed these problems occurred after diagnosis and were related to cancer and its treatment.[32-35] No information on recurrence or second cancers was collected.

Three indicators of clinical outcome were used: treatment modality, number of treatment series, and organ dysfunction at treatment end. Treatment modality included the different combinations of chemotherapy, radiation therapy, and surgery; a treatment series could include any combination of these modalities. More than one treatment series occurred when the initial planned treatment was extended due to incomplete response or when a new treatment series was initiated after the survivor had relapsed. No other information about relapse subsequent to the end of treatment was available. Organ dysfunction refers to the number of organs or body systems documented in the medical record as impaired at the end of treatment.

Information was obtained on several sociodemographic and personal characteristics including ethnicity, and experience of stressful life events and chronic stressors in the preceding 12-month period.[36-38]

Analysis

General linear models were used to compare mean quality of life scores of either all survivors or survivor subgroups to general population controls, and the beta representing the survivor-control difference in mean scores was the measure of association. All *P* values came from bilateral tests. For categoric outcomes, logistic regression was used to calculate the odds ratio and 95% CI. We first verified potential modifying effects of age at study, sex, stressful life events, and chronic stresses on the size of survivor-control differences in quality of life outcomes by including interaction term(s) in the models, but found little meaningful evidence of interaction. As potential confounders, these variables were not always similarly distributed when comparing survivor subgroups with controls. Thus, for consistency, these four potential confounders were included in all analyses. Stressful life events and chronic stress score (Spearman *r*, 0.28) were not collinear.[39] We also found no evidence that these stress variables were part of the causal pathway, as adjusting for the stress variables increased rather than decreased survivor-control differences.[40]

Because a number of small mean differences were statistically significant given the large sample size, we explored possible clinical significance of survivor-control differences by considering them in relation to effect size (ES).[41] ES is the ratio of the survivor-control difference to the standard deviation among controls. ESs of 0.20 to 0.49 are generally considered to be small, 0.50 to 0.79 medium, and $\geq$ 0.80 large.[41] Recent evidence suggests that an ES of 0.5 corresponds to a minimum perceptible difference and thus could be considered as a clinically important difference.[42]

RESULTS

Participants' characteristics are presented in Table 1. Most participants (88.2%) were younger than 30 years old at study. Just over half of the survivors were adolescents or moving into adolescence when diagnosed (55.0%), and most survivors were 10 or more years past diagnosis (83.5%).

Significantly fewer survivors than controls reported very good or excellent general health (62.3% and 71.2%, respectively; adjusted odds ratio, 0.61; 95% CI, 0.51 to 0.71). Survivors were more likely than controls to report that they had, or been told by a doctor that they had, one or more physical health problems, including endocrine, hormonal, cardiovascular, neurologic, and renal problems (Table 2).

In survivor-control comparisons stratified by sex, survivors of both genders reported significantly poorer scores in the PCS, general health, role-physical, and social function relative to their respective controls (Table 3). Although the effect of having had cancer during childhood was, or almost was, significantly greater for females than for males for the first three of these scores (interaction *P* values were .11, .048, and .08, respectively), differences comparing female survivors with controls on these outcomes were small (ES ≤ -0.30) and those

Table 1. Sociodemographic, Psychosocial, and Health Characteristics of Survivors and Controls

Characteristic	Survivors (n = 1,334) No.	Survivors (n = 1,334) %*	Controls (n = 1,477) No.	Controls (n = 1,477) %*
Sex				
Male	641	48.1	668	45.2
Female	693	52.0	809	54.8
Current age, years				
15 to 19	443	33.2	441	29.9
20 to 24	383	28.7	422	28.6
25 to 29	335	25.1	370	25.1
30 to 37	173	13.0	244	16.5
Mean ± SD	23.0 ± 5.2		23.6 ± 5.4	
Ethnic background				
One or both parents white	1199	91.0	1284	88.0
Neither parent white	119	9.0	175	12.0
Unknown	16		18	
No. of reported life stressors				
0	481	36.3	457	31.0
1	385	29.0	464	31.5
2	223	16.8	300	20.4
3 to 8	237	17.9	253	17.2
Unknown	8		3	
Mean ± SD	1.3 ± 1.4		1.0 ± 2.0	
Chronic stress (score out of 60)				
0 to 4	363	27.3	329	22.3
5 to 9	421	31.6	466	31.6
10 to 14	282	21.2	348	23.6
15 to 45	266	20.0	333	22.6
Unknown	2		1	
Mean ± SD	9.4 ± 7.0		10.1 ± 6.8	
Diagnosis				
Leukemia	333	25.0		
Lymphoma	312	23.4		
Central nervous system tumors	238	17.8		
Carcinoma	95	7.1		
Soft tissue cancer	89	6.7		
Bone	78	5.9		
Germ cell and other gonadal cancer	75	5.6		
Kidney	66	5.0		
Other†	48	3.6		
Age at diagnosis, years				
0 to 4	326	24.4		
5 to 9	275	20.6		
10 to 14	196	14.7		
15 to 19	537	40.3		
Length of survival, years				
5 to 9	220	16.5		
10 to 14	684	51.3		
15 to 19	430	32.2		
No. of treatment series				
1	1,178	88.3		
2 to 3	156	11.7		
No. of organs with dysfunction at the end of treatment				
0	958	71.8		
1	261	19.6		
2 to 7	115	8.6		
Treatment modalities				
Chemotherapy only	123	9.2		
AK	78	5.9		
Other CT	45	3.4		
Surgery only	224	16.8		
Radiation only	38	2.9		
CRT	7	0.5		
Other RT	31	2.3		
Chemotherapy + surgery	216	16.2		
AK + surgery	166	12.4		
Other CT + surgery	50	3.8		
Chemotherapy + radiation	272	20.4		
AK + CRT	104	7.8		
AK + Other RT	76	5.7		
Other CT + CRT	82	6.2		
Other CT + other RT	10	0.8		
Surgery + radiation	174	13.0		
Surgery + CRT	97	7.3		
Surgery + other RT	77	5.8		
Chemotherapy + surgery +radiation	263	19.7		
AK + surgery + CRT	74	5.6		
AK + surgery + other RT	138	10.3		
Other CT + surgery + CRT	19	1.4		
Other CT + surgery + other RT	32	2.4		
No treatment or missing	24	1.4		

(continued in next column)

Abbreviations: SD, standard deviation; AK, alkylating agent; CT, chemotherapy agent; CRT, cranial radiation therapy; RT, radiation therapy.

*Individuals with unknown values not considered in the calculation of percentages. Percentages may not add to 100% because of rounding.

†Other includes retinoblastoma, neuroblastoma, and hepatic cancer.

for male survivors and controls were negligible (ES ≤ -0.18). For the other outcomes, among both females and males, survivor-control differences were even smaller. Thus considered overall, there were no survivor-control sex differences that might be considered clinically important (ES for general health, -0.25; all others ranged from -0.03 to -0.19; data not shown).

Compared with controls, survivors of CNS and bone cancers had significantly poorer quality of life in several domains (Table 4). Among CNS survivors, general health, physical function, and role limitations due to physical health problems all showed relatively large absolute differences compared with controls, although ESs were small. CNS survivors also reported poorer quality of life in the psychosocial dimensions, but again ESs were small. For bone cancer survivors, negative and clinically important effects on quality of life compared with controls were found in the physical domain, with a large ES in physical function (ES, -1.02) and medium one for role limitations due to physical health problems (ES, -0.60). Twenty-three of 78 bone cancer survivors had an amputation.

Compared with controls, survivors with organ dysfunction in $\geq$ two organs had consistent evidence of poorer quality of life (Table 5). Large effects were observed for general health and physical function (ES, -0.87 and -0.96 respectively), and medium effects for role-physical, social function, and life satisfaction (ES, -0.57 to -0.64).

Table 2. Physical Health Problems Among Survivors and Controls

	Survivors (n = 1,334) %	Controls (n = 1,477) %	Adjusted OR	95% CI
Very good or excellent general health*	62.1	71.1	0.6	0.5 to 0.7
≥ 1 physical health problem†	73.4	52.5	2.7	2.3 to 3.2
Health problems†				
Endocrine (diabetes, osteoporosis)	29.2	5.7	7.7	6.0 to 9.9
Hormonal (pituitary/growth, thyroid)	18.1	4.1	5.5	4.1 to 7.4
Neurological	43.9	28.9	2.0	1.7 to 2.4
Cardiovascular	12.7	8.0	1.8	1.4 to 2.3
Renal	11.5	8.7	1.4	1.1 to 1.9
Pulmonary	23.8	22.3	1.1	0.9 to 1.3

Abbreviation: OR, odds ratio.
*Adjusted for age at interview (16 to 19, 20 to 24, 25 to 29, 30 to 37 years), sex, number of stressful life events in past year (0, 1, 2, 3 to 8), chronic stress score (0 to 4, 5 to 9, 10 to 14, 15 to 45). Missing values: four for survivors, seven for controls.
†Adjusted only for age at interview (16 to 19, 20 to 24, 25 to 29, 30 to 37 years) and sex. The two stressor variables were not included because they referred only to the 12 months prior to the study and thus likely occurred after most of the health problems.

This was the only survivor group that had small to borderline clinically important effects in all other outcomes assessed including psychosocial ones (ES, −0.27 to −0.49). Survivors who had undergone ≥ two treatment series also reported poorer general health and role function related to physical health (ES, −0.53 for each; Table 5).

Considering treatment modality, survivor-control differences in mean PCS were generally largest and sometimes of borderline clinical importance among survivors who had all three treatment modalities (ESs, −0.31 to −0.49; Table 6). In absolute terms, the largest treatment ESs seen were in survivors who had cranial radiation alone or cranial radiation combined with other treatments (although the ES estimate for cranial radiation alone, based on only seven survivors, might be unstable). ESs for different treatment modalities on the MCS were small or negligible.

When the five important clinical characteristics were assessed together (CNS or bone cancer, more than one treatment series, ≥ two organs with dysfunction, all three treatment modalities and cranial radiation [CRT]) in relation to the PCS and MCS, the most important for predicting poorer quality of life among survivors were CNS or bone cancer, more than one treatment series, and ≥ two organs with dysfunction. Only these three variables remained independently associated with the PCS in the model containing all five clinical characteristics (data not shown). While only a minority of survivors (27%) had one of the three characteristics and few had two (7%) or three (1%) of them simultaneously, large ESs consistent with clinical importance were found for the PCS comparing survivors with two and three problems to those with none (−0.79 and −1.13, respectively).

Table 3. Quality of Life and Other Psychosocial Outcomes Among Childhood Cancer Survivors and Controls by Sex

	Females (n = 1,502)				Males (n = 1,309)			
Outcome	Survivor Mean* (smallest n = 674)	Control Mean* (smallest n = 797)	Mean Difference*	Effect Size	Survivor Mean* (smallest n = 629)	Control Mean* (smallest n = 656)	Mean Difference*	Effect Size
SF-36 summary scores								
Physical component	51.6	53.4	−1.9 (< 0.0001)	−0.25†	53.2	54.0	−0.9 (0.042)	−0.11
Mental component	46.4	46.7	−0.3 (0.52)	−0.03	48.8	49.2	−0.5 (0.36)	−0.05
SF-36 subscales								
General health	68.5	74.4	−5.9 (< 0.0001)	−0.30†	74.6	78.2	−3.6 (0.0011)	−0.18
Physical function	88.4	92.3	−3.9 (< 0.0001)	−0.24†	91.7	93.1	−1.5 (0.11)	−0.09
Role: physical	82.5	87.3	−4.8 (0.0005)	−0.18	87.7	91.1	−3.4 (0.019)	−0.13
Bodily pain	77.7	78.8	−1.1 (0.29)	−0.06	80.6	80.6	0.1 (0.96)	0.0
Vitality	56.1	58.0	−1.9 (0.051)	−0.10	63.4	63.5	0.0 (0.96)	0.0
Social function	79.5	81.7	−2.2 (0.026)	−0.12	83.8	86.0	−2.2 (0.037)	−0.12
Role: emotional	75.1	76.9	−1.9 (0.25)	−0.06	81.7	82.7	−1.0 (0.54)	−0.03
Mental health	70.2	71.2	−1.0 (0.22)	−0.06	73.6	74.7	−1.1 (0.20)	−0.07
Self-esteem	81.5	82.2	−0.6 (0.47)	−0.04	84.8	86.0	−1.2 (0.21)	−0.07
Optimism	65.0	65.8	−0.8 (0.39)	−0.04	65.6	65.8	−0.2 (0.87)	−0.01
Satisfaction with life	62.9	63.7	−0.8 (0.50)	−0.04	59.9	62.9	−3.0 (0.018)	−0.13

*Adjusted for age at interview (16 to 19, 20 to 24, 25 to 29, 30 to 37 years), sex, number of stressful life events in past year (0, 1, 2, 3 to 8), and chronic stress score (0 to 4, 5 to 9, 10 to 14, 15 to 45).
†Small effect size: 0.2 to 0.49. (Medium effect size: 0.5 to 0.79. Large effect size: ≥ 0.8. Effect size ≥ 0.5 is considered clinically important).

Table 4. Differences in Mean of Quality of Life and Other Psychosocial Outcomes Comparing Survivors With Controls by Cancer Type

		SF-36 Scales									
		General Health		Physical Function		Role: Physical		Bodily Pain		Vitality	
	No.*	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*
Control†											
Mean	1,462	76.4		92.7		89.1		79.7		60.8	
SE		0.5		0.4		0.7		0.6		0.5	
Survivor difference in means‡											
Leukemia	326	−2.4		−1.3		−3.5	< .05	−1.2		0.9	
Lymphoma	307	−5.6§	< .0001	0.0		0.6		0.2		−0.6	
CNS	232	−6.9§	< .0001	−6.9§	< .0001	−9.7§	< .0001	0.7		−3.4	< .05
Carcinoma	92	−2.0		0.2		−0.1		3.4		−1.4	
Soft tissue	86	−5.6§	< .01	−3.3§		−3.3		−0.1		−1.8	
Bone	77	−4.4§		−16.4‖	< .0001	−15.7¶	< .0001	−7.3§	< .01	−1.0	
Germ cell	72	−6.3§	< .01	−2.6		−3.8		−1.0		−2.2	
Renal	66	−8.8§	< .001	1.9		−4.7		−2.1		−2.5	
Other#	46	−3.3		0.8		−2.2		−2.6		1.2	

	SF-36 Scales									
	Social Function		Role: Emotional		Mental Health		Self-Esteem		Optimism		Satisfaction With Life	
	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*
Control†												
Mean	83.9		79.8		73.0		84.1		65.8		63.2	
SE	0.5		0.9		0.4		0.5		0.5		0.6	
Survivor difference in means‡												
Leukemia	−0.8		−0.8		0.8		0.5		−0.9		0.1	
Lymphoma	−0.9		−1.1		−1.3		0.8		1.1		−0.1	
CNS	−5.5§	< .0001	−3.5		−3.5§	< .01	−5.3§	< .0001	−5.5§	< .0001	−10.3§	< .0001
Carcinoma	−1.5		−0.7		−0.8		−0.2		2.4		1.9	
Soft tissue	−1.4		2.1		−1.0		−0.4		0.6		0.0	
Bone	−5.8§	< .01	−5.3		−0.6		−3.9§	< .05	1.7		−2.0	
Germ cell	−2.9		−1.1		−3.0		−1.3		0.0		−3.3	
Renal	−1.7		−1.2		−0.5		2.1		0.2		1.7	
Other#	−1.2		−1.4		0.8		0.0		1.1		2.4	

*No. columns list the smallest numbers available across all quality of life outcomes.
†Adjusted for age at interview (16 to 19, 20 to 24, 25 to 29, 30 to 37 years), sex, number of stressful life events in past year (0, 1, 2, 3 to 8), and chronic stress score (0 to 4, 5 to 9, 10 to 14, 15 to 45).
‡Survivor mean minus control mean. Higher scores indicate better function on all scales. Thus, negative differences indicate poorer quality of life in survivors compared with controls.
§Small effect size: 0.2 to 0.49.
¶Medium effect size: 0.5 to 0.79.
‖Large effect size: ≥ 0.8. Effect size ≥ 0.5 is considered clinically important.
#Other includes retinoblastoma, neuroblastoma, and hepatic cancer.

DISCUSSION

This retrospective cohort study was conducted among adolescent and adult survivors of childhood and adolescent cancers from all 10 Canadian provinces, the majority of whom had been diagnosed and treated more than 10 years previously. Survivors in general reported more specific physical health problems than population controls with no cancer history. However, quality of life differences between survivors and controls were small, and for the most part probably not clinically important. More detailed analyses of clinical characteristics revealed some clinically important quality of life deficits, mainly in the physical domain, among bone and CNS survivors, those who had more than one treatment series (a proxy for relapse) and who had documented organ dysfunction at the end of treatment, and survivors who had all three modalities or CRT as part of treatment. CNS cancer survivors were the only group found to have consistently poorer physical and psychosocial functioning, but individually many effects were not considered clinically important. Although the case for less than 10% of survivors, clinically important deficits in the physical aspects of quality of life resulted from the clustering of two or three particular clinical characteristics simultaneously, namely diagnosis of CNS or bone cancer, more than one treatment series, and dysfunction in ≥ two organs when treatment was completed. Overall, our findings indicate that the quality of life of a sizeable majority of adolescent and adult long-term survivors of childhood cancer in Canada is comparable with those of their healthy peers.

Analysis of the specific physical health problems indicates that the excess endocrine, hormonal, neurologic, cardiovascular, and renal problems we found is consistent with other reports.[32-35] Our findings that a diagnosis of bone and CNS cancer and that the accumulation of

Table 5. Differences in Mean of Quality of Life and Other Psychosocial Outcomes for Survivors Compared With Controls: Survivors Stratified According to Clinical Characteristics

		SF-36 Scales									
		General Health		Physical Function		Role: Physical		Bodily Pain		Vitality	
	No.*	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*
Controls†	1,462										
Mean		76.4		92.8		89.2		79.7		60.8	
SE		0.5		0.4		0.7		0.6		0.5	
Survivor difference in means											
Years of survival											
5 to 9	217	−4.4§	< .01	−4.6§	< .001	−5.7§	< .01	−0.7		−1.8	
10 to 14	672	−4.3§	< .0001	−2.0	< .01	−2.5	< .05	0.3		−1.1	
15 to 19	421	−5.8§	< .0001	−3.1§	< .001	−5.9§	< .0001	−1.9		−0.5	
No. of treatment series											
1	1,160	−4.1§	< .0001	−2.2	< .001	−2.9	< .01	0.0		−0.7	
2 to 3	153	−10.4¶	< .0001	−6.9§	< .0001	−13.7¶	< .0001	−5.3§	< .01	−3.6	< .05
No. of organs with dysfunction											
0	943	−2.9	< .001	−0.2		−1.9		0.3		0.2	
1	258	−6.8§	< .0001	−6.6§	< .0001	−7.6§	< .0001	−1.2		−2.2	
2 to 7	111	−16.8‖	< .0001	−15.4‖	< .0001	−14.7¶	< .0001	−6.7§	< .001	−9.0§	< .0001

	SF-36 Scales									
	Social Function		Role: Emotional		Mental Health		Self-Esteem		Optimism		Satisfaction With Life	
	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*	Difference	*P*
Controls†												
Mean	83.9		79.8		72.9		84.1		65.8		63.2	
SE	0.5		0.8		0.4		0.5		0.6		0.6	
Survivor difference in means												
Years of survival												
5 to 9	−2.6		−0.6		−0.5		−0.1		1.0		0.5	
10 to 14	−2.1	< .05	−2.7		−1.3		−1.4		−1.0		−3.1	< .01
15 to 19	−2.2	< .05	0.0		−0.9		−0.5		−0.5		−0.9	
No. of treatment series												
1	−1.9	< .05	−1.3		−1.0		−1.0		−0.8		−1.5	
2 to 3	−4.6§	< .01	−2.5		−1.3		−0.1		1.4		−4.6§	< .05
No. of organs with dysfunction												
0	−0.9		0.0		−0.7		−0.3		0.1		0.1	
1	−2.9	< .05	−3.9		−0.6		0.0		−0.1		−3.5	< .05
2 to 7	−11.6¶	< .0001	−8.3§	< .01	−4.9§	< .01	−7.6§	< .0001	−6.9§	< .001	−14.4¶	< .0001

*No. column lists the smallest numbers available across all quality of life outcomes.
†Adjusted for age at interview (16 to 19, 20 to 24, 25 to 29, 30 to 37 years), sex, number of stressful life events in past year (0, 1, 2, 3 to 8), and chronic stress score (0 to 4, 5 to 9, 10 to 14, 15 to 45).
‡Survivor mean minus control mean. Higher scores indicate better function on all scales. Thus, negative differences indicate poorer quality of life in survivors compared to controls.
§Small effect size: 0.2 to 0.49.
¶Medium effect size: 0.5 to 0.79.
‖Large effect size: ≥ 0.8. Effect size ≥ 0.5 is considered clinically important.

all three treatment modalities are associated with poorer physical quality of life have been reported by others,[6,9,14,43-45] as has the association of cranial radiation and surgery.[9,35] To our knowledge, this is the first large population-based study to document the effects of the clustering of these somewhat correlated clinical characteristics. Finally the finding that, despite more health problems and poorer self-rated health, these long-term survivors were functioning as well in the psychosocial sphere as controls has been found in a number of studies,[6,15,18,43,44] but not others.[9,11] Discrepancies here could be related to methodologic differences between studies.

As in a previous study,[15] we found that the long-term effects of childhood cancer on quality of life and other psychosocial outcomes—effects measured by the differences between survivors and controls—did not differ meaningfully among female and male survivors. While female survivors had poorer outcomes than male survivors, these differences were also found between female and male controls in our and other studies,[9,15] and indeed are usually found in the general healthy population. Thus, the sex difference observed in survivors was not an effect specific to having had childhood cancer. In fact, these findings provide further evidence

Table 6. Treatment Modality Mean Differences in Quality of Life and Other Psychosocial Outcomes Comparing Survivors With Controls

		Physical Component Summary			Mental Component Summary		
	No.*	Mean Difference†	*P*	Effect Size	Mean Difference†	*P*	Effect Size
Controls	1,433						
Mean		53.8			48.0		
SE		0.2			0.3		
Treatment modalities							
Chemotherapy only	121	−0.1		−0.01	0.0		0.0
AK	76	0.1		0.02	−0.1		−0.01
Other CT	45	−0.4		−0.05	0.1		0.01
Surgery only	216	−0.2		−0.02	0.0		0.0
Radiation only	37	0.2		0.03	−3.1	< .05	−0.33‡
CRT	7	−5.7	< .05	−0.76§	−0.2		−0.02
Other RT	30	1.6		0.21‡	−3.7	< .05	−0.40‡
Chemotherapy + surgery	212	−1.6	< .01	−0.21‡	0.4		0.04
AK + surgery	163	−1.9	< .01	−0.25‡	0.5		0.05
Other CT + surgery	49	−0.6		−0.07	0.1		0.01
Chemotherapy + radiation	267	−1.2	< .05	−0.16	0.9		0.10
AK + CRT	103	−1.4		−0.19	1.3		0.14
AK + other RT	74	−1.1		−0.15	0.8		0.09
Other CT + CRT	80	−0.8		−0.11	−0.3		−0.03
Other CT+ other RT	10	−2.1		−0.28‡	7.6	< .05	0.80§
Surgery + radiation	169	−2.5	< .0001	−0.33‡	−1.6	< .05	−0.17
Surgery + CRT	93	−2.6	< .01	−0.35‡	−2.2	< .05	−0.24‡
Surgery + other RT	76	−2.3	< .001	−0.30‡	−0.8		−0.08
Chemotherapy + surgery + radiation	257	−3.0	< .0001	−0.39‡	−1.3		−0.13
AK + surgery + CRT	73	−3.7	< .0001	−0.49‡	−2.3	< .05	−0.25‡
AK + surgery + other RT	133	−2.4	< .001	−0.31‡	−0.9		−0.10
Other CT + surgery + CRT	19	−3.7	< .05	−0.48‡	−1.3		−0.14
Other CT + surgery + other RT	32	−3.4	< .05	−0.45‡	−0.1		−0.01
No treatment or missing	24	1.5		0.20‡	−5.7	< .01	−0.60§

Abbreviations: AK, alkylating agent; CT, chemotherapy; CRT, cranial radiation therapy; RT, radiation therapy.
*No. column lists the smallest numbers available across all quality of life outcomes.
†Adjusted for age at interview (16-19, 20-24, 25-29, 30-37 years), sex, No. of stressful life events in past year (0, 1, 2, 3-8), and chronic stress score (0-4, 5-9, 10-14, 15-45).
‡Small effect size: 0.2-0.49.
§Medium effect size: 0.5-0.79; large effect size: ≥ 0.8. Effect size ≥ 0.5 is considered clinically important.

of the extent to which most long-term survivors resemble their healthy peers.

We have considered possible study limitations. Although participation was modest, particularly in controls, several observations about the similarity of survivors and controls who were theoretically targeted compared with those who participated in the study were reassuring about the likely absence of selection bias.[24] First, the long-term survivors who participated in the study had clinical characteristics that were similar to those of survivors who either refused to participate or were lost to follow-up. Second, survivors and population controls had similar distributions of age, sex, and area of residence, and the vast majority of both groups were white. Third, the population controls recruited for our study closely resembled Canadians of the same age and sex based on comparisons with 1996 census information.[24] Other biases are unlikely to have affected our findings. Validated and widely used, self-report instruments suitable for population surveys were used to measure outcomes in our survivors and controls. As well, overall and subgroup comparisons of survivors with controls incorporated the same potential confounding variables.

Despite possible limitations, this study makes several important contributions. First, it is one of the first studies to be based on a large random sample of a diverse childhood cancer survivor population, and the first such study in Canada. Second, given that an important goal of cancer treatment is, after curing or controlling disease, to help those affected regain a quality of life that is, to the extent possible, comparable with that of similarly aged individuals who have not had to face this disease, the inclusion of a population-based control group allowed us to judge the success of treatment in these terms. For the majority of survivors, reported quality of life, self-esteem, optimism, and life satisfaction were comparable with those of their peers. Furthermore, the control group allowed us to see that the effect of childhood cancer on diverse aspects of quality of life was essentially the same in females and males. Third, we identified particular subgroups of survivors more likely to report poor physical quality of life, particularly in the minority of survivors where there was a clustering of clinical characteristics, all known at the end of treatment. This information will be useful for helping identify survivors who need and could benefit from ongoing long-term follow-up.[6,45] Finally, our findings also support the relevance of using such information to tailor follow-up strategies to survivors' likelihood of poor quality of life and late effects.[46] For survivors at lower risk, screening with postal questionnaires may be an effective and economic strategy for identifying those needing additional care.[46] This latter approach might also avoid undermining the positive levels of psychosocial adaptation reported by the majority of long-term adolescent and adult survivors of childhood cancer.

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Appendix

The Appendix is included in the full-text version of this article, available online at www.jco.org. It is not included in the PDF version (via Adobe® Reader®).

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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Over 12,400 children and adolescents younger than 20 years of age are diagnosed with cancer in the United States every year [1]. Survival for many pediatric cancers has improved significantly in the past three decades with improvement in therapies. The surveillance, epidemiology, and end results data estimate that the overall five-year survival rate among children for all cancer sites combined improved from 58% for patients diagnosed in 1975â€“1977 to 80% for those diagnosed in 1996â€“2003 [1].Â There is a considerable variation in quality of life among survivors [82]. Several studies report compromises in mental health among survivors [82]. 3. Prevention of late effects. The Childrenâ€™s Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers (COG LTFU Guidelines) are a resource for healthcare professionals who provide ongoing care to survivors of pediatric malignancies. The screening recommendations in these guidelines are appropriate for asymptomatic survivors of childhood, adolescent, or young adult cancer presenting for routine exposure-based medical follow-up. More extensive evaluations are presumed, as clinically indicated, for survivors presenting with signs and symptoms suggesting illness or organ dys Hormonal replacement is indicated to improve long-term quality of life for adolescents with ovarian insufficiency who have completed the pubertal process. Heavy Menstrual Bleeding and Anemia. Cancer and its treatments place young women at risk of heavy menstrual bleeding and anemia.Â In the largest study of childhood cancer survivors, the relative risk of pregnancy among adult cancer survivors who were not surgically sterilized was 0.81 (95% CI, 0.73â€“0.90) compared with their sibling cohort 6. Reduced fertility was associated with hypothalamic or pituitary irradiation at dose greater than or equal to 30 Gy, ovarianâ€“uterine irradiation at dose greater than 5. Gy, or increased use of alkylating agents 6. See Box 1 for a list of alkylating agents. Posttraumatic stress symptoms and stressful life events predict the long-term adjustment of survivors of childhood cancer and their mothers. Journal of Clinical Psychology in Medical Settings, 7(4), 189-196. Barrera, M., Chung, J. Y. Y., & Fleming, C. F. (2004).Â Advocacy needs of adolescent and young adult cancer survivors: Perspectives of pediatric oncology social workers. Journal of Psychosocial Oncology, 22(2), 75-87. Annie Toro, J.D., M.P.H.; Public Interest Government Relations Office; American Psychological Association; (202) 336-6068; atoro@apa.org. Perceived Health among Adolescent and Young Adult Survivors of Childhood Cancer. by. Morgan Young-Speirs.Â Long-term Survivors of Childhood Cancer: All participants were enrolled in a Long-Term Survivors Clinic (LTSC). The LTSC aims to promote the health and well-being of SCCs by educating and surveilling for the presence of late effects.Â Generally, research has suggested that self-reports of constructs such as quality of life tend to be rated lower than parent-proxy reports [32]. Additionally, survivors â‰¥13 years of age may have filled out the questionnaire in the presence of a parent, which may which may have contributed to the under-reporting of responses to sensitive questions such as alcohol and drug use.