Quantifying treatment delays in adolescents and young adults with cancer at McGill University

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ABSTRACT

Background: Since the end of the 1980s, the magnitude of survival prolongation or mortality reduction has not been the same for adolescents and young adults (AYAS) with cancer as for their older and younger counterparts. Precise reasons for those observations are unknown, but the differences have been attributed in part to delays in diagnosis and treatment. In 2003 at the Jewish General Hospital, we developed the first Canadian multidisciplinary AYA oncology clinic to better serve this unique patient population. The aim of the present study was to develop an approach to quantify diagnosis delays in our AYA patients and to study survival in relation to the observed delay.

Methods: In a retrospective chart review, we collected information about delays, treatment efficacy, and obstacles to treatment for patients seen at our AYA clinic.

Results: From symptom onset, median time to first health care contact was longer for girls and young women (62 days) than for boys and young men (6 days). Median time from symptom onset to treatment was 173 days; time from first health care contact to diagnosis was the largest contributor to that duration. Delays in diagnosis were shorter for patients who initially presented to the emergency room, but compared with patients whose first health contact was of another type, patients presenting to the emergency room were 3 times more likely to die from their disease.

Conclusions: Delays in diagnosis are frequently reported in AYAS with cancer, but the duration of the delay was unrelated to survival in our sample. Application of this approach to larger prospective samples is warranted to better understand the relation between treatment delay and survival in AYAS—and in other cancer patient groups.

Key Words Adolescents, young adults, treatment delay, overall survival

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INTRODUCTION

Between 2002 and 2006 in Canada, 2252 new cases of cancer occurred in adolescents and young adults (AYAS)[1], accounting for about 2% of all newly diagnosed invasive cancers[2–4].

Unfortunately, since the late 1980s, the magnitude of survival prolongation or mortality reduction has not been the same for AYAS with cancer as for their older and younger counterparts[1,2,5]. Precise reasons for the failure to improve survival in this cohort are unknown, but several factors that can be broadly categorized in terms of the patient, the health care system, and the disease and its treatment have been suggested. In terms of the patient, AYAS generally do not seek medical help and do not consider cancer when experiencing nonspecific symptoms[6–9]. Many AYAS do not have access to a family physician—either because of limited availability (Canada) or a lack of insurance (the United States)[10]—making it less likely that they will be referred to a specialist. In terms of the health care system, health professionals often underestimate symptoms of cancer in younger age groups[9,11–30]. Wait times for specialized tests are long in the public sector, and access to specialized medical expertise is limited for AYAS. In terms of the disease and its treatment, distinct tumour biology, lack of participation by AYAS in clinical trials (because of a lack of trials for AYAS, failure to inform AYAS about available trials, or an inability or reluctance of AYAS to participate in trials)[6–9], and financial limitations on the part of both

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the patient and the family or care provider can underlie the lack of progress within this patient population. Taken together, the foregoing factors (although they have not been systematically explored) are thought to result in delays in diagnosis, lack of access to appropriate treatments, and ultimately poorer survival.

In 2003, we developed the first Canadian multidisciplinary AYA oncology clinic at the Jewish General Hospital (affiliated with McGill University, Montreal, QC) to better serve this unique patient population. The aim of the present analysis was to quantify 3 types of treatment delay in the AYA population (patient delay, health care system delay, and treatment delay) and to identify factors contributing to those delays so as to better predict their prognostic effects. Specifically, an association of longer delays with poorer survival or more advanced disease was hypothesized to explain poorer survival rates in the AYA population.

METHODS

Study Design and Data Collection
In a retrospective chart review of 110 AYAs (18–49 years of age) treated for cancer at the Jewish General Hospital during 2010–2011, relevant data related to treatment delays, treatment efficacy, and obstacles to treatment were extracted. A detailed medical history, including timelines for the appearance of symptoms, first appointment with the family doctor and oncologist, date of diagnosis, and participation in clinical trials had been elicited from each patient at the time of first presentation to the AYA clinic. Additional information was gathered from medical charts. Data about sociodemographic parameters such as sex, age, ethnicity, primary residence, marital status, education level, household income, medical insurance, family cancer history, and current life style (Table I) were also collected. French or English versions of the relevant questionnaires (Table II) were provided based on patient preference. Clarification or assistance was provided to patients as needed.

Ethics
Ethics approval for the questionnaires was obtained from the Research Ethics Committee of the Jewish General Hospital. The data were analyzed anonymously.

Statistics
The interval between discovery of symptoms and the time at which the patient was diagnosed and received therapy was divided roughly into patient delay, health care system delay, and treatment delay. "Patient delay" was defined as the time elapsed from the initial discovery of symptoms to first contact with a medical provider. "Health care system delay" was defined as the interval from the first provider consultation until the diagnosis was made. "Treatment delay" was defined as the interval between diagnostic tests and the wait time before initiation of treatment.

Relations between the delays and overall survival (the time from cancer diagnosis to death from any cause) were considered by comparing overall survival for each type of delay. Statistical analyses were performed using Stata 12 (StataCorp LP, College Station, TX, U.S.A.). Descriptive statistics consist of proportions for categorical variables and means or medians for continuous variables such as age and delays. Mann–Whitney–Wilcoxon nonparametric tests were used for groups with only two categories. Associations between continuous variables were tested using the Spearman rank correlation. Because of the exploratory nature of this study, a *p* value of 0.05 was chosen as the significance level, and no adjustment was made for multiple comparisons.

RESULTS

Patient Population
Mean age at diagnosis was 30 years. The major ethnicity group (white) accounted for 75% of the patients. In our cohort, 15% had completed high school; 20%, college; 34%, a university degree; and 15%, postgraduate training. Annual income was less than $50,000 for 28% of the sample, and more than $50,000 for 40% (Table I).

Patient reports about their first health care contact fell broadly into 5 categories: 32% had been seen by a public general practitioner, 8% by a private general practitioner, 22% by another specialist or a walk-in clinic, and 24% in an emergency room. The most common cancers were central nervous system tumours (*n* = 33, 30%). Others included gastrointestinal cancer (*n* = 20, 18.2%), sarcoma (*n* = 16, 14.5%), germ-cell tumour (*n* = 14, 12.7%), breast cancer (*n* = 13, 11.8%), lymphoma (*n* = 5, 4.5%), melanoma (*n* = 4, 3.6%), head-and-neck cancer (*n* = 3, 2.7%), lung and renal cancers (*n* = 1 each, 0.9%; Table I).

Delay Analyses
Figure 1 presents the distribution of delays for each patient. The median overall delay (that is, the sum of the patient, health care system, and treatment delays) was 173 days [interquartile range (IQR): 68–410 days]. The median patient delay was 22 days (IQR: 1–214 days). The median health care system delay was 56 days (IQR: 12–174 days), and the median treatment delay was 32 days (IQR: 0–72 days). Table III summarizes the results.

Analyses of Factors Possibly Contributing to Delay
Compared with male patients, female patients experienced significantly longer patient delay (*p* = 0.001, Table III). Age at diagnosis and ethnicity were positively correlated with patient delay (*r* = 0.390, *p* < 0.001 and *p* = 0.041 respectively; Table III). However, a trend toward an inverse correlation of age with treatment delay was observed (*p* = 0.087, Table III). Delays were shorter when the patient's first medical contact was with an emergency room or a private general practitioner (*p* = 0.004 compared with patients having other types of initial health care contact). Of brain cancer patients, 52% went directly to the emergency room; of patients with other cancer types, 16% opted for an emergency room visit (*p* < 0.001). Patients with brain and spinal cancer experienced a significantly longer treatment delay (*p* = 0.001 compared with patients having other types of cancer, Table III). We observed no association of treatment delay with sex and health care contact (*p* = 0.988, Table III).

Survival Analysis
The daily death rate for our sample was estimated at 2463×10^{-4}, equivalent to a 9% annual mortality rate.

TABLE I Sociodemographic characteristics of the 110 study patients

Characteristic	Value	
	Overall [*n* (%)]	Ignoring missing data (%)
Status		
Alive	81 (73.64)	73.64
Deceased	29 (26.36)	26.36
Sex		
Women and girls	56 (50.91)	50.91
Men and boys	54 (49.09)	49.09
Mean age (years)	30.39±0.55	
Age group		
<30 Years	56 (50.91)	50.91
30–39 Years	40 (36.36)	36.36
40–49 Years	14 (12.73)	12.73
>49 Years	0 (0.0)	0.0
Marital status		
Single	41 (37.27)	39.42
Partnered or married	54 (49.09)	51.92
Separated, divorced, or widowed	9 (8.18)	8.65
Not stated	6 (5.45)	—
Ethnicity		
White	76 (69.10)	74.51
Other	26 (23.64)	25.49
Not stated	8 (7.27)	—
Education		
High school or less	16 (14.55)	17.39
College	22 (20.00)	23.91
University	37 (33.64)	40.22
Postgraduate studies	17 (15.45)	18.48
Not stated	18 (16.36)	—
Insurance		
Provincial health care	41 (37.27)	41.84
Private insurance	57 (51.82)	58.16
Not stated	12 (10.91)	—
Family history of cancer		
Yes	45 (40.91)	48.91
No	47 (42.73)	51.09
Not stated	18 (16.36)	—
Level of exercise		
Sedentary	18 (16.36)	20.00
Mild	19 (17.27)	21.11
Vigorous, occasional	19 (17.27)	21.11
Vigorous, regular	34 (30.91)	37.78
Not stated	20 (18.18)	—
Alcohol consumption (weekly)		
None	57 (51.82)	63.33
1–5	29 (26.36)	32.22
6–10	4 (3.64)	4.44
11–20	0 (0.0)	0.0
Not stated	20 (18.18)	—
Tobacco consumption		
Never smoker	36 (32.73)	75.00
Current or former smoker	12 (10.91)	25.00
Not stated	62 (56.36)	—
Annual income		
Mean	$80,296.88	
Median	$70,000.00	
Income group		
<$50,000	31 (28.18)	41.33
$50,000–$70,000	13 (11.82)	17.33
>$70,000	31 (28.18)	41.33
Not stated	35 (31.82)	—
First health care contact		
Emergency room	26 (23.64)	27.66
General practitioner (public)	35 (31.82)	37.23
General practitioner (private)	9 (8.18)	9.57
Other	24 (21.82)	25.53
Not stated	16 (14.55)	—
Has a general practitioner		
No	33 (30.00)	35.87
Yes	59 (53.64)	64.13
Not stated	18 (16.36)	—
Trouble finding a general practitioner?		
No	51 (46.36)	62.20
Yes	31 (28.18)	37.80
Not stated	28 (25.45)	—
Type of cancer		
Brain or spinal	33 (30.0)	30.00
Other	77 (70.0)	70.00

Median survival for the cohort overall was 3.76 years. No variable except emergency room presentation was significantly associated with survival (Table IV). And although there was an association between first health care contact and cancer type, patients with a specific type of cancer were not significantly more likely to die (*p* = 0.807, Table IV).

DISCUSSION

In this study, we tried to quantify cancer diagnosis delays and to uncover any association of those delays with survival.

Although our work was conducted within the framework of issues specific to AYAs, the same approach could be used to address concerns within and across disease sites and age ranges.

We found that the total delay from presentation to treatment at our institution was almost 6 months for patients treated at the AYA oncology clinic. The period from first health care contact to diagnosis was the greatest contributor to the total delay, which is consistent with other reports[3]. Interestingly, we found a very mild positive correlation of age with patient delay, suggesting that older

TABLE II McGill Adolescent and Young Adult Oncology Program: Good Clinical Practice Questionnaire

Thank you for taking the time to fill out this questionnaire. As you may be aware, there is a lack of knowledge, understanding, and awareness when it comes to cancer in the adolescent and young adult population. In fact, the National Cancer Institute of Canada and the National Cancer Institute (U.S.A.) have called for the creation of specialized programs to care for such patients so that we can accrue information about the challenges this very special population faces. By taking the time to fill out this questionnaire, you will give us an idea of not only how we can help you, but also the thousands of adolescent and young adults diagnosed with a malignancy each year. Rest assured, all of this information will remain strictly confidential.

Thank you for taking the time to help us help you.

1. Your name (last, first, middle initial): _____

2. Date of birth (dd/mm/yyyy): _____

3. Your age at diagnosis: _____

4. Gender: ☐ Male ☐ Female

5. Ethnicity: _____

6. Primary residence:

    ☐ Montreal ☐ Quebec (outside Montreal) ☐ Canada (outside Quebec) ☐ Outside Canada

7. Marital Status: ☐ Single ☐ Partnered ☐ Married ☐ Separated ☐ Divorced ☐ Widowed

8. If applicable, how long have you been with your current partner? _____

9. If you are divorced or separated, do you feel your illness was the cause of separation? ☐ Yes ☐ No

10. Do you have children? ☐ Yes ☐ No

11. If so, how many? _____ And how old? _____

12. Your highest education level:

    ☐ High school ☐ Professional/ technical school ☐ CEGEP ☐ Bachelor's degree ☐ Graduate degree

    ☐ Other (please specify) _____

13. The type of work/study you are doing now _____

14. Your work/study status right now:

    ☐ On temporary sick leave ☐ On permanent sick leave ☐ Full-time ☐ Part-time

15. Household income per year (prior to diagnosis):

    ☐ <$30,000 ☐ $30,000– $50,000 ☐ $50,000– $70,000 ☐ $70,000– $100,000 ☐ >$100,000

16. Did your household income decrease after diagnosis? ☐ Yes ☐ No

    If yes, how much did it decrease per year?

    ☐ <$5,000 ☐ $5,000– $10,000 ☐ $10,000– $20,000 ☐ $20,000– $30,000 ☐ $30,000– $40,000 ☐ >$40,000

17. Are you covered by RAMQ (Quebec insurance)? ☐ Yes ☐ No

18. Do you have private insurance? ☐ Yes ☐ No

19. Current life style:

    Alcohol ☐ None _____/day _____/week _____/month _____/year

    Cigarettes ☐ None _____/day _____/week _____/month _____/year

    Drugs ☐ None _____/day _____/week _____/month _____/year

    Exercise ☐ None _____/day _____/week _____/month _____/year

    Do you think your sex life is affected by your cancer? ☐ Yes ☐ No

20. Did you take care of your health before diagnosis? ☐ Yes ☐ No

21. Did you have a general practitioner before diagnosis? ☐ Yes ☐ No

22. Were you being followed by your general practitioner regularly (at least once per year)? ☐ Yes ☐ No

23. Do you have a general practitioner now? ☐ Yes ☐ No

24. Have you had trouble finding a general practitioner? ☐ Yes ☐ No

25. What were the first symptoms you had?

    _____

26. What was the approximate date of symptom onset (dd/mm/yyyy)? _____

27. At the time your symptoms started, did you think they were suggesting a serious illness? ☐ Yes ☐ No
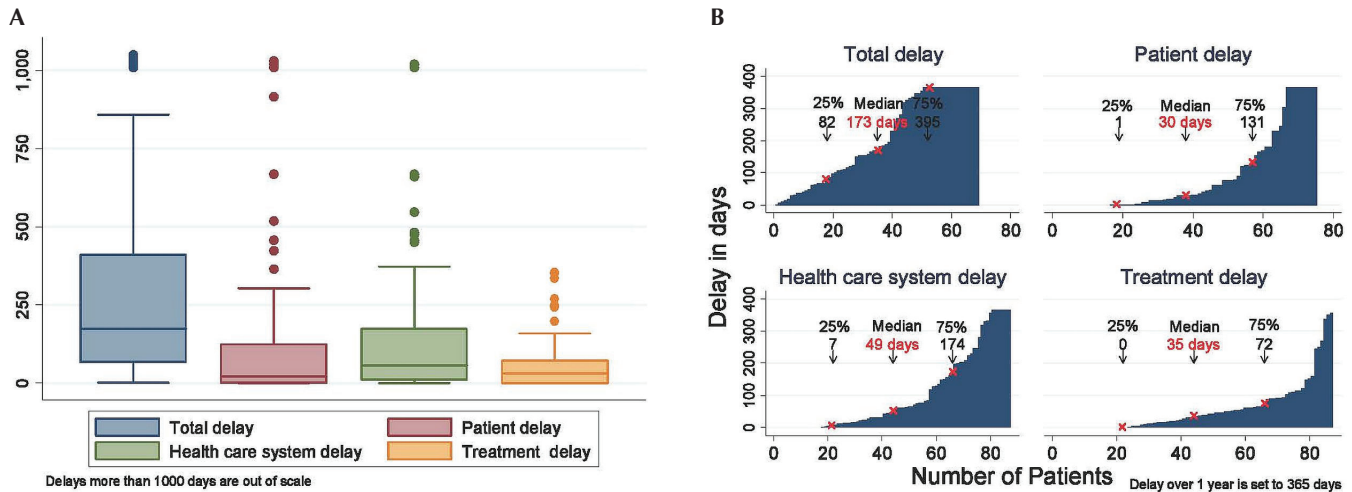
TABLE II   Continued

28. Did you consult a doctor right away?   ☐ Yes   ☐ No

29. The first doctor you visited was

    ☐ General practitioner (public)   ☐ General practitioner (private)   ☐ Specialist   ☐ Emergency room   ☐ Walk-in clinic

    ☐ Other (please specify) _____

30. Did you decide to visit emergency because the wait for public health care was too long?   ☐ Yes   ☐ No

31. Did you decide to go private because the wait for public health care was too long?   ☐ Yes   ☐ No

32. When did you visit the doctor for the first time?   Date of first visit (dd/mm/yyyy) _____

33. Did your symptoms progress before you decided to see a doctor for the first time?   ☐ Yes   ☐ No

34. Were your symptoms taken seriously the first time you saw a doctor?   ☐ Yes   ☐ No

35. Did the first doctor you saw request a scan (ultrasound, computed tomography, magnetic resonance imaging)?   ☐ Yes   ☐ No

36. Once a scan was referred for you (even if it was not requested by the first doctor), approximately how long did you wait to get the scan?

    _____ days   _____ week   _____ months

37. Did you go private because the wait was too long?   ☐ Yes   ☐ No

38. Did the first doctor that you saw request a procedure (that is, colonoscopy, gastroscopy, biopsy)?   ☐ Yes   ☐ No

39. Once a procedure was referred for you (even it was not requested by the first doctor), approximately how long did you wait to get the procedure done?   _____ days   _____ week   _____ months

40. Did you go private because the wait was too long?   ☐ Yes   ☐ No

41. Did the first doctor you saw refer you to a surgeon?   ☐ Yes   ☐ No

42. Once referred to a surgeon (even it was not referred by the first doctor), how long did you wait to see the surgeon?

    _____ days   _____ week   _____ months

43. When did you first see an oncologist? Date of visit (dd/mm/yyyy) _____

44. Once referred to an oncologist (even if not referred by the first doctor), how long did you wait to see the oncologist?

    _____ days   _____ week   _____ months

45. From symptom onset, how long did it take until you received your first treatment for cancer (chemotherapy, radiation therapy, surgery)?

    _____ days   _____ week   _____ months   Date of first visit (dd/mm/yr) _____

46. Have you participated in any type of clinical trial?   ☐ Yes   ☐ No

47. If yes, what type of clinical trial?

    ☐ Therapeutic   ☐ Nontherapeutic   ☐ Other (please specify) _____

48. Do you have any family members affected by cancer history?   ☐ Yes   ☐ No

49. If yes, how many first-degree relatives are affected? _____

50. Did you go to cancer genetic testing?   ☐ Yes   ☐ No

51. Did your family cancer history influence your decision to seek care earlier?   ☐ Yes   ☐ No

52. The type(s) of cancer(s) were you diagnosed with and when:

    Type of cancer   Date (dd/mm/yyyy)

    _____   _____

53. The type(s) of cancer treatment(s) you received or are currently receiving:

    ☐ Chemotherapy   ☐ Radiation therapy   ☐ Surgery   ☐ No treatment yet

54. Have you completed your treatment?   ☐ Yes   ☐ No

55. The types of mental health conditions you were diagnosed with and how it was treated (for example, antidepressants with or without psychotherapy)

    Type of mental health condition   Treatment or NA (not applicable)

    _____   _____

56. Have you met our

    ☐ Psychiatrist   ☐ Psychologist   ☐ Social worker   ☐ Nutritionist   ☐ Physiotherapist or exercise specialist

    ☐ Other (please specify) _____

Thank you again for filling out this questionnaire!

patients tended to wait for or to have difficulty with health care contacts, which might be a result of the usually busier schedule of such individuals. A mild inverse correlation between age and treatment delay suggests that, compared with younger patients, those more than 30 years of age received treatment earlier. The reasons for that difference are still unknown. Income was not associated with treatment delay, but the trend has to be investigated further.

A comparator population was available from a poster presented at the 2012 American Society of Clinical Oncology annual meeting. The authors of that poster compared patient and health care system delays from cancer symptom

FIGURE 1 (A) Boxplot of the distribution of delays with marked outliers. (B) Distribution of delays with marked median, and 25% and 75% percentiles.

TABLE III Factors possibly influencing the delay

Factor	Patient		*p* Value[a]	Health care system		*p* Value[a]	Treatment		*p* Value[a]
	Median (%)	IQR (%)		Median (%)	IQR (%)		Median (%)	IQR (%)	
Sex			**0.001**			0.988			0.478
Women and girls	61.5	5.5–175.0		60.5	15.0–148.0		38.0	0.0–89.0	
Men and boys	5.5	0.0–30.5		31.0	6.0–319.0		26.0	0.0–56.5	
Age	Rho: 0.390		**<0.001**	Rho: −0.063		0.228	Rho: −0.250		**0.017**
Age group			**0.002**			0.462			0.087
<30 Years	1.5	0.0–40.5		49.0	12.0–246.0		40.0	14.0–92.0	
30–40 Years	30.5	5.0–181.0		31.0	0.0–161.0		15.0	0.0–62.0	
40–50 Years	107.0	62.0–304.0		71.0	18.0–128.0		11.5	0.0–48.0	
Ethnicity			**0.041**			0.126			0.734
White	14.0	0.0–77.0		63.5	9.5–224.5		32.0	0.0–65.0	
Other	53.0	5.5–175.0		31.0	12.0–75.0		32.0	0.0–87.0	
First health care contact			**0.004**			0.920			0.477
Emergency room	1.0	0.0–35.0		56.0	12.0–119.0		20.0	5.0–87.0	
General practitioner (public)	62.0	17.0–165.0		37.5	0.0–179.0		35.0	0.0–65.0	
General practitioner (private)	12.5	2.5–48.5		74.0	45.5–149.0		46.0	0.0–108.0	
Other	30.0	2.0–230.0		28.5	12.0–188.5		16.0	0.0–50.0	
Type of cancer			0.352			0.863			**0.001**
Other	26.5	1.0–124.0		61.0	14.0–161.0		17.5	0.0–50.0	
Brain and spinal	7.5	0.0–123.0		46.5	6.5–200.5		61.0	38.0–111.0	

[a] Boldface type indicates significant values.
IQR = interquartile range.

TABLE IV Factors possibly influencing survival

Factor	HR	5% CI	*p* Value[a]
Sex			
Women and girls		Reference	
Men and boys	1.89	0.82 to 4.35	0.134
Age	1.02	0.97 to 1.07	0.557
Age group	1.04	0.58 to 1.87	0.902
Ethnicity			
White		Reference	
Other	0.65	0.19 to 2.22	0.492
First health care contact			
General practitioner and other		Reference	
Emergency room	3.11	1.08 to 8.90	**0.035**
Type of cancer			
Brain and spinal cord	1.101	0.509 to 2.382	0.807
Patient delay	0.996	0.973 to 1.020	0.751
Health-care system delay	1.013	0.996 to 1.030	0.132
Treatment delay	1.002	0.986 to 1.018	0.818
Oncologist delay	1.000	0.978 to 1.023	0.969
Total delay	1.021	0.991 to 1.052	0.170

[a] Boldface type indicates significant values.
HR = hazard ratio; CI = confidence interval.

onset to diagnosis and treatment for AYA patients and older-adult patients with brain tumours presenting at the McGill University AYA Oncology Centre of the Jewish General Hospital from 1 July 2010 to 22 December 2011. They found that the total delay and the treatment delay were longer for the AYA patients than for the older-adult patients ($p = 0.013$ and $p = 0.048$ respectively).

CONCLUSIONS

Despite limitations to our study (including measurement bias related to the analysis of retrospective data obtained from questionnaires completed for clinical purposes and from medical charts; a small sample size; and collection of data from a single institution in Canada), we quantified delays in diagnosis and treatment for AYAs with cancer. We found that the median overall delay was 173 days from first symptoms to treatment, of which health care system delay accounted for a median of 56 days' delay.

Our analysis is important because it begins to emphasize that delays for AYAs with cancer have been associated with more advanced presentation, a need for more therapy, and a likelihood of worse outcomes. The lengthy observed delay could be shortened with some changes to health care policy. We also noticed a clear disparity in clinical trial participation. A large proportion of our patients were not aware of clinical trials, emphasizing a need for greater promotion and advertisement of such trials.

CONFLICT OF INTEREST DISCLOSURES
We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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