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Antidepressant Use Among Survivors of Childhood, Adolescent and Young Adult Cancer: A Report of the Childhood, Adolescent and Young Adult Cancer Survivor (CAYACS) Research Program

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Background. Although survivors of childhood, adolescent, and young adult (AYA) cancer are at risk for late psychological sequelae, it is unclear if they are more likely to be prescription antidepressant users than their peers. ***Procedure.*** All 5-year survivors of childhood or AYA cancer diagnosed before age 25 years in British Columbia from 1970 to 1995 were identified. Those with complete follow-up in the provincial health insurance registry from 2001 to 2004 were included (n = 2,389). A birth-cohort and gender-matched set of population controls 10 times the size of the survivor group was randomly selected (n = 23,890). All prescriptions filled between 2001 and 2004 were identified through linkage to the provincial prescription drug administrative database. Logistic regression analyses determined the impact of cancer survivorship on the likelihood of ever filling an antidepressant prescription. ***Results.*** After adjusting for sociodemographic factors, survivors of childhood and AYA cancer were more likely to have filled an antidepressant prescription compared to controls (OR 1.21, 95% CI 1.09–1.35). Cancer survivors had an increased likelihood of using all categories of antidepressants, and of using drugs from two or more antidepressant categories, compared to peers (OR 1.31, 95% CI 1.11–1.55 [≥2 antidepressant categories]). Treatment was not a significant predictor of antidepressant use. Female survivors, those in young adulthood and those more than 20 years post-treatment had increased antidepressant use. ***Conclusions.*** Survivors of childhood and AYA cancer are more likely to fill antidepressant prescriptions compared to peer controls. This may indirectly reflect an increased underlying prevalence of mental health conditions among survivors. Pediatr Blood Cancer 2013;60:816–822.

Key words: antidepressants; cancer survivorship; mental health; SSRIs

INTRODUCTION

Outcomes for children and adolescents diagnosed with cancer have improved significantly over the past 30 years with 5-year overall survival rates now exceeding 80% [1,2]. As such, there are an increasing number of childhood and AYA cancer survivors who are at treatment-related risk for second malignant neoplasms, chronic or late-occurring health conditions, and late mortality [3–8]. Almost 20% of survivors report adversely affected mental health status [3]. Specific therapies, neurocognitive and medical sequelae, chronic pain and disability may predispose survivors to mental health conditions after completion of therapy. The Childhood Cancer Survivor Study (CCSS) shows that the odds of reporting poor mental health are 80% higher in survivors of childhood cancer compared to siblings (OR 1.8, 95% CI 1.6–2.1) [3]. Survivors of specific malignancies, including bone and central nervous system (CNS) tumors report more psychological distress, including anxiety and somatization, when compared to siblings [9,10]. The Swiss Survivor Study concludes that mean overall psychological distress scores on validated questionnaires were actually lower in survivors compared to normative population data [11]. However, survivors were more likely to report very high scores for depression, psychotic tendencies, aggression, and interpersonal sensitivity.

Previous studies of mental health outcomes in childhood cancer survivors have been questionnaire-based [3,8–10,12]. Limitations of these studies include selection and self-report biases, especially due to the social stigma of mental health conditions. In addition, tools such as the Brief Symptom Inventory (BSI) or Medical Outcomes Short Form-36 (SF-36) identify symptoms of mental health disorders over a short period, the previous 7 days or 4 weeks respectively, a potentially poor proxy for chronic mental health conditions.

Antidepressants are a class of medications that are commonly prescribed for mental health conditions, including major depression and generalized anxiety disorders [13,14]. In particular, the prescription of multiple antidepressants is strongly associated with major depression; Mojtabai et al. [15] report an OR of 3.44 (99% CI 2.58–4.58). It is unclear if childhood and AYA cancer survivors are more likely to require prescription antidepressants (any or multiple) than their peers. Linkage methodology was used as part of the Childhood, Adolescent and Young Adult Cancer Survivor (CAYACS) Research Program to synthesize de-identified data from population-based registries, administrative databases and medical charts [16]. Our objective was to determine if childhood and AYA cancer survivorship increased the likelihood of filling an antidepressant prescription, after adjusting for sociodemographic variables. Additionally, the impact of sociodemographic, clinical, and treatment-specific characteristics on the likelihood of antidepressant use was determined among survivors.

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METHODS

Identification of the Survivor Cohorts and General Population Comparison Groups

The study received ethical approval from the University of British Columbia, BC Cancer Agency and BC Children's Hospital research ethics boards. Approval for access, use and linkage of data was obtained from the BC Cancer Registry, BC College of Pharmacists and the BC Ministry of Health. All BC residents younger than 25 years who were diagnosed with a primary malignancy, as defined by the International Classification of Childhood Cancers (ICCC) [17] or the Adolescent and Young Adult Cancer Classification (AYACC) [18,19], between January 1, 1970 and December 31, 1995 who survived 5 or more years from diagnosis, were identified as described previously [16]. Those alive on December 31, 2004 (n = 3,225) were considered eligible for this analysis. Of these, 2,389 (74.1%) linked to the provincial health insurance client registry for the entire period between January 1, 2001 and December 31, 2004 and were included in this study. Failure to link was most likely related to relocation outside the province for any amount of time during the 4 year study period. A general population comparison group was selected randomly from the health insurance registry and frequency-matched 10:1 to survivors (n = 23,890).

Data Sources, Data Collection, and Modifying Variables

For survivors, birth date, gender, diagnosis date, cancer diagnostic code [17–19] and date of second cancer diagnosis were obtained from the BC Cancer Registry. Clinical and treatment data were abstracted from patient health records at the pediatric tertiary care facility in the province and from provincial adult cancer centers. Sociodemographic variables including gender and birth date for the comparison groups, as well as postal code of residence at start of follow-up and health insurance coverage dates, were obtained from the BC Health Insurance Plan Client Registry. Statistics Canada methodology was used to determine urban or rural residential status and socio-economic status (SES), assigned as a neighborhood-specific income quintile based on the average income per person equivalent, from residential postal code [20].

Outcome Measures

Prescription drug information was obtained for all study subjects from PharmaNet, the administrative database that captures all outpatient prescriptions filled in the province. Medications were classified according to the American Hospital Formulary Service (AHFS) system [21]. Antidepressant categories were monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), serotonin modulators, tricyclic antidepressants (TCAs) and other norepinephrine-reuptake inhibitors and miscellaneous antidepressants. Individuals who had ever filled an antidepressant prescription during the period of January 1, 2001 to December 31, 2004 were considered antidepressant users.

Statistical Analyses

Descriptive statistics were used to describe the characteristics of the survivor and comparison cohorts, and the chi-square test was used to identify differences in baseline characteristics. The effect of cancer survivorship on the likelihood of ever filling an antidepressant prescription, both overall and by antidepressant drug class, during the study period was determined using logistic regression. Odds ratios (OR) with 95% confidence intervals adjusting for age, gender, SES quintile and residential status were calculated. Likelihood ratio tests were used to assess the significance of fitted models. For ordered categorical variables, trend tests were calculated by including the variable as continuous in the model and reporting the resulting *P*-value.

A secondary, survivor-only logistic regression analysis was completed to determine the impact of cancer diagnosis and treatment variables on the likelihood of ever filling an antidepressant prescription during follow-up. Among cancer diagnostic categories, leukemia was selected as the reference group due to its large size (n = 401) and because we anticipated minimal late mental health sequelae in this group based on previous reports. Adjusted ORs with 95% confidence intervals were computed to estimate the effect of age at diagnosis (5 year categories), elapsed time since diagnosis (5 year categories) and attained age at start of follow-up (10 year categories). Clinical factors included chemotherapy (yes/no), treatment-related cancer surgery (yes/no), radiation therapy (cranial irradiation, other irradiation or none), second cancer diagnosis prior to end of follow-up (yes/no) and relapse within 5 years of diagnosis (yes/no). Secondary analyses to determine the impact of treatment modality and specific chemotherapeutic agents were performed.

Additionally, the annual prevalence of prescription antidepressant users among cancer survivors and the general population was determined using prescription medication data for an expanded period of January 1, 1996 to December 31, 2004. This period was chosen to incorporate all available prescription drug data, and annual period prevalence of drug users could be assessed without requiring each subject to be present for the entire 9 year period, as opposed to the logistic regression analysis described above. Of the study cohort and comparison groups, all individuals who were linked to the Health Insurance Registry for each complete calendar year were included and prevalent users were defined as all individuals who filled $\geq$1 prescription for any antidepressant medication during each year. To address confidentiality concerns, the Ministry of Health requires that numbers less than five be masked in tables and text.

RESULTS

Of 2,389 cancer survivors diagnosed before age 25, 1,225 (51.3%) were male and the majority were adolescents or young adults at the start of follow-up, with a mean age of 28.8 ($\pm$10.9) years. Survivors were slightly, but significantly, more likely to live in an urban center than comparators (85.8% vs. 83.9%) and slightly more likely to belong to a higher SES quintile (Table I). The most frequent cancer diagnoses were lymphoma in 485 (20.3%) followed by carcinoma in 454 (19.0%) and leukemia in 401 (16.8%). Mean age at diagnosis was 6.3 ($\pm$4.6) years, 568 (23.8%) were diagnosed before age 5 years and mean time from diagnosis to start of follow-up was 15 (range 5–31) years.

Overall, 515 (21.6%) of the cancer survivors filled an antidepressant prescription during follow-up and 169 (7.1%) filled prescriptions for drugs from more than one antidepressant category (Table II). Survivors were significantly more likely to be

TABLE I. Characteristics of Cancer Survivors and General Population Comparison Groups

	Survivor cohort, N (%) (n = 2,389)	Comparison group, N (%) (n = 23,890)	*P*-value[a]
Gender			
Female	1,164 (48.7)	11,640 (48.7)	NA[c]
Male	1,225 (51.3)	12,250 (51.3)	
Attained age (years)[b]			
5 to <15	308 (12.9)	3,093 (12.9)	0.995[d]
15 to <25	567 (23.7)	5,668 (23.7)	
25 to <35	787 (32.9)	7,820 (32.7)	
35 to <45	550 (23.0)	5,481 (22.9)	
45 to 60	177 (7.4)	1,828 (7.7)	
Residential status			
Rural	307 (12.9)	3,270 (13.7)	0.002
Urban	2,050 (85.8)	20,044 (83.9)	
Unknown	32 (1.3)	576 (2.4)	
SES quintile			
5 (Highest)	445 (18.6)	4,273 (17.9)	0.008
4	463 (19.4)	4,533 (19.0)	
3	442 (18.5)	4,464 (18.7)	
2	448 (18.8)	4,698 (19.7)	
1	454 (19.0)	4,910 (20.6)	
Unknown	137 (5.7)	1,012 (4.2)	
Age at diagnosis (years)			
0 to <5	568 (23.8)		
5 to <10	278 (11.6)		
10 to <15	306 (12.8)		
15 to <20	450 (18.8)		
20 to <25	787 (32.9)		
Diagnosis			
Leukemia	401 (16.8)		
Lymphoma	485 (20.3)		
CNS	338 (14.1)		
Bone	95 (4.0)		
Germ cell	257 (10.8)		
Soft tissue sarcoma	129 (5.4)		
Carcinoma	454 (19.0)		
Other	230 (9.6)		
Time since diagnosis (years)			
5 to <10	697 (29.2)		
10 to <15	599 (25.1)		
15 to <20	519 (21.7)		
20 to <25	337 (14.1)		
≥25	237 (9.9)		
Relapse status			
No	2,154 (90.2)		
Yes	235 (9.8)		
Second cancer			
No	2,254 (94.3)		
Yes	135 (5.7)		

SES, socioeconomic status. [a]Chi-square test. [b]Attained age at the beginning of follow-up (2001). [c]The comparison group was frequency matched by gender to survivors. [d]Birth-year, but not exact birth date, was matched resulting in small, non-significant differences in attained age.

prescription antidepressant users than comparators, after adjusting for sociodemographic variables (OR 1.21, 95% CI 1.09–1.35). When analyzed by antidepressant category, survivors had a significantly higher likelihood of using each category compared to their peers. They were also more likely to fill prescriptions for drugs from more than one antidepressant category (OR 1.31, 95% CI 1.11–1.55).

Among cancer survivors, female gender was strongly predictive of ever filling an antidepressant prescription (OR 2.02, 95% CI 1.63–2.50; Table III). Survivors who were 15–34 years at start of follow-up were more likely than younger survivors to use antidepressants (OR 2.33, 95% CI 1.33–4.16 [age 15–24 years], OR 2.52, 95% CI 1.18–5.36 [age 25–34 years]). Survivors diagnosed between ages 15 and 20 years had nearly twice the odds of an antidepressant prescription than those diagnosed before age 5 (OR 1.89, 95% CI 1.04–3.45). There was an increasing trend of antidepressant use with increasing time since diagnosis (trend *P*-value = 0.026), after adjusting for other variables including attained age. Specific cancer diagnostic category and SES quintile were not predictive of antidepressant use among survivors.

Cancer treatment with chemotherapy, radiation or surgery did not significantly impact the likelihood of antidepressant use compared to those survivors who did not receive that treatment modality (OR 1.12, 95% CI 0.84–1.50 [chemotherapy]; OR 0.91, 95% CI 0.69–1.19 [cranial radiotherapy]; OR 0.96, 95% CI 0.70–1.31 [surgery]). Similarly, we were unable to identify treatment modality combinations that were associated with an increased likelihood of antidepressant use, compared to surgery alone. Analysis by specific chemotherapeutic agent, including anthracyclines, alkylators and intrathecal chemotherapy, did not show an effect on the likelihood of being an antidepressant user. Similarly, survivors who were diagnosed with a second malignant neoplasm (n = 135) or had disease relapse (n = 235) were not at significantly increased risk of antidepressant use (OR 1.25, 95% CI 0.84–1.90 [second cancer]; OR 1.10, 95% CI 0.79–1.54 [relapse]).

Prevalence of Antidepressant Users in Survivors and the General Population

Among survivors, the annual prevalence of antidepressant users increased from 5.8% in 1996 to 12.6% in 2004 (Fig. 1). Annual prevalence increased in both male and female survivors and across all age groups. This trend was paralleled in the comparison sample, in which there were 5.0% and 10.1% antidepressant users in 1996 and 2004, respectively.

DISCUSSION

In general, the ability of childhood and AYA cancer survivors diagnosed to demonstrate resilience and psychosocial adjustment is well documented [9,11,22]. However, a proportion of survivors remain at risk for psychological sequelae, and it is unclear if this has resulted in an increased prevalence of mental health conditions requiring medical intervention. The CCSS reports an increased prevalence of self-reported symptoms of depression or anxiety among childhood cancer survivors compared to siblings, but no difference in reported prevalence of antidepressant users [23]. We show that survivors are more likely to be prescription antidepressant users than their peers, but it is notable that the impact of cancer survivorship on this outcome is not large. Survivors of childhood and AYA cancer are 21% more likely to use any antidepressant than age and gender-matched controls in our study. Survivors were 31% more likely to use multiple

TABLE II. Prevalence and Likelihood of Antidepressant Users Among Cancer Survivors and General Population Comparators

	Survivors (n = 2,389)		Comparators (n = 23,890)		
Anitdepressant drug category	N	% of antidepressant users	N	% of antidepressant users	Adjusted[a] OR (95% CI)
Any antidepressant	515	—	4,436	—	1.21 (1.09–1.35)
MAOIs	6	1.2	21	0.5	2.82 (1.14–7.00)
SSRIs	298	36.7	2,533	36.4	1.20 (1.06–1.37)
Serotonin modulators	91	15.0	601	11.9	1.54 (1.23–1.93)
TCAs	141	21.5	1,148	20.6	1.25 (1.05–1.50)
Miscellaneous	218	29.7	1,870	29.7	1.19 (1.02–1.38)
≥2 antidepressant drug categories	169	32.8	1,325	29.9	1.31 (1.11–1.55)

OR, odds ratio; CI, confidence interval; MAOIs, monoamine oxidase inhibitors; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants. [a]ORs adjusted for urban/rural status, SES quintile, and attained age.

antidepressants than their age and gender-matched peers from the general population; a novel finding among childhood and AYA cancer survivors. Almost one third of survivors who were antidepressant users filled prescriptions for drugs from multiple antidepressant categories. Antidepressant polypharmacy has been found to be significantly associated with underlying psychiatric diagnoses including major depression, other depressive disorders, bipolar disorder and anxiety disorder in the general population [15]. As such, our finding of the increased risk of antidepressant polypharmacy in cancer survivors may be indicative of significant underlying mental health morbidity.

We show that female survivors have an increased likelihood of ever using antidepressants compared to males, as in the general population [13,14,24]. We also found that increasing attained age is an important predictor of antidepressant use in childhood and AYA survivors, as in the general population [13]. As more time passed from diagnosis, we found evidence of a statistical trend ($P = 0.026$) of increasing risk of antidepressant use, independent of attained age. This suggests that the survivor experience may continue to significantly impact mental health outcomes for decades beyond diagnosis and highlights the need for life-long support for these individuals.

SES quintile was not a predictor of antidepressant users among our survivor group. Although SES is a well recognized risk factor of major depression in the general population [25], it has been inconsistently predictive of antidepressant medication use in the Canadian universal health care system [13,26]. We did not evaluate the impact of SES quintile at diagnosis, which is likely more reflective of parental SES in children and adolescents with cancer, and not indicative of the impact of SES on access to, and utilization of, medications as survivors. Treatment modality, including receiving chemotherapy, cancer surgery or radiation, did not have a significant effect on the likelihood of ever filling an antidepressant prescription in the survivor cohort, consistent with results from the CCSS [3,27].

The strengths of our analysis include the use of a population-based cancer registry and administrative databases which provide a comprehensive picture of all survivors in a geographically defined population, eliminating self-selection bias, with essentially complete prescription drug information, removing reporting and recall biases. The ability to utilize linkage methodology to synthesize population-based data from large, administrative databases is powerful methodology that can be used to better understand late morbidity associated with childhood and AYA cancer survivorship and generate new hypotheses [16]. These methods are a cost and time-effective way to assemble and follow essentially complete cancer survivor and comparator cohorts over long periods of time with minimal loss to follow-up.

An important limitation of our study is that the medical indications for prescribed antidepressants are unknown and the number of both approved and off-label indications for these medications is increasing. Specifically, TCAs may be prescribed for migraine headaches and neuropathic pain, and serotonin modulators, such as trazodone, are used as sleep aids [28–30]. To assess prescribing practices by indication, we obtained data from IMS Health Canada, a pharmaceutical market research group that collects information quarterly on the medical indications for prescribed drugs from a representative set of office-based generalist and specialist physicians across Canada. This dataset has been a valuable source of longitudinal drug prescribing trends in Canada [31,32]. These data indicate that for individuals between the ages of 5 and 58 years, as in our study, approximately 80% of SSRIs were prescribed for either depression or anxiety-related indications in Western Canada between 2003 and 2008. The CCSS reports that among childhood cancer survivors who were antidepressant users, almost 70% had impairment detected on the depression/anxiety scale of the Behavior Problem Index [23]. Similarly, among survivors who were antidepressant users but who did not report a major depressive episode (MDE) in the past year, 28% had a previous MDE and 35% had an anxiety disorder [13]. It seems probable that depression and anxiety-related disorders represent the majority of indications for SSRI use among cancer survivors, although this remains to be substantiated. We show that cancer survivors are more likely to use SSRIs than their peers, as well as all other categories of antidepressants.

It must also be recognized that factors other than underlying mental health conditions may affect antidepressant prescribing practices. Although many survivors do not fully comply with recommended follow-up guidelines [33,34], childhood cancer survivors are more likely to visit physicians than their peers, which may make antidepressant medications more accessible [35–37]. We found that increasing time since diagnosis was predictive of antidepressant use among our survivor group, with those over 25 years from diagnosis at highest risk. In this Canadian cohort, within a universal health care system, the probability of having a primary or specialist (other than oncologist) physician visit did

TABLE III. Impact of Cancer Diagnosis and Sociodemographic Variables on the Likelihood of Ever Using a Prescription Antidepressant Medication Among Cancer Survivors

Variable	Antidepressant users (n = 515)	Total survivors (n = 2,389)	Adjusted OR (95% CI)	*P*-value	Trend *P*-value[a]
Diagnosis					
Leukemia[b]	69	401	1.00	0.800	—
Lymphoma	106	485	0.86 (0.58–1.27)		
CNS tumor	75	338	1.08 (0.73–1.59)		
Bone	25	95	1.16 (0.66–2.05)		
Germ cell	57	257	1.06 (0.67–1.67)		
Soft tissue sarcoma	31	129	1.15 (0.69–1.91)		
Carcinoma	117	454	0.86 (0.57–1.30)		
Other	35	230	0.96 (0.60–1.54)		
Gender					
Male[b]	195	1,225	1.00	<0.001	—
Female	320	1,164	2.02 (1.63–2.50)		
Residence					
Urban[b]	452	2,050	1.00	0.288	—
Rural	59	307	0.84 (0.61–1.15)		
Unknown	4	32	0.49 (0.15–1.58)		
Diagnosis age (years)					
<5[b]	78	568	1.00	0.215	0.087
5 to <10	49	278	1.07 (0.68–1.68)		
10 to <15	70	306	1.39 (0.83–2.34)		
15 to <20	124	450	1.89 (1.04–3.45)		
20 to <25	194	787	1.78 (0.88–3.59)		
SES quintile					
5[b] (highest)	40	216	1.00	0.607	0.213
4	28	227	1.02 (0.73–1.43)		
3	41	216	1.14 (0.82–1.59)		
2	31	207	1.00 (0.72–1.41)		
1	45	217	1.29 (0.93–1.79)		
Unknown	12	69	1.10 (0.63–1.89)		
Attained age (years)					
<15[b]	22	308	1.00	<0.001	0.849
15 to <25	104	567	2.33 (1.33–4.16)		
25 to <35	198	787	2.52 (1.18–5.36)		
35 to <45	146	550	2.17 (0.81–5.83)		
45 to <60	45	177	1.37 (0.39–4.73)		
Years from diagnosis					
5 to <10[b]	123	697	1.00	0.075	0.026
10 to <15	121	599	1.07 (0.77–1.50)		
15 to <20	110	519	1.13 (0.74–1.74)		
20 to <25	94	337	1.78 (1.04–3.06)		
≥25	67	237	2.05 (1.01–4.14)		

OR, odds ratio; CI, confidence interval; CNS, central nervous system. [a]For all ordered categorical variables, trend tests were calculated by including the variable as continuous in the model and reporting the resulting *P*-value. [b]Reference category.

not decline with increased time since diagnosis, for at least 25 years post-diagnosis, for survivors diagnosed under age 20 years [35], and for those diagnosed at age 20–24 years [38]. Since access to primary care appears stable over time for Canadian survivors, the increased likelihood of filling an antidepressant prescription with increasing time since diagnosis may be reflective of increased morbidity, rather than differential access to care, and highlights the importance of life-long care for survivors who may continue to have late sequelae decades after cancer diagnosis. It is also unknown how the patient's cancer history itself may contribute to each physician's decision to prescribe a medication to a cancer survivor. There is also a possibility for survivor bias, as individuals who were no longer alive in the follow-up period could not be included. There is the potential that some of these excluded individuals may have had serious mental illness and committed suicide. In addition, we would not capture mentally unwell individuals who chose not to or were unable to seek medical care. These limitations would effect both survivors and the general population.

In this geographically defined, population-based cohort, we found that the annual prevalence of antidepressant users tripled among cancer survivors overall, by gender and in all age groups between 1996 and 2004. We found a similar increase in the prevalence of antidepressant users among the general population,

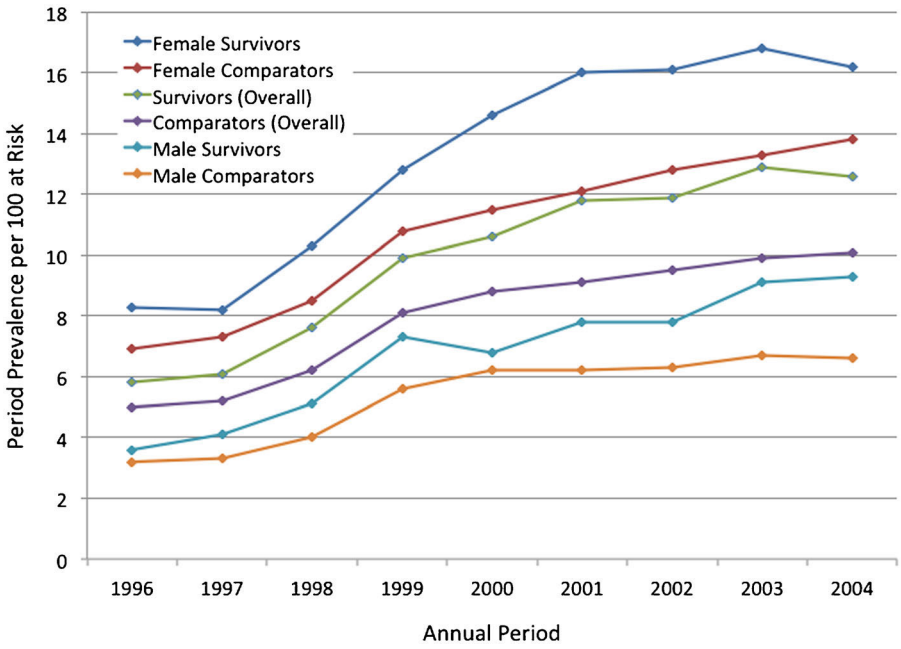

Fig. 1. Prevalence of antidepressant users in childhood and AYA cancer survivors and general population comparators between 1996 and 2004. The annual period prevalence of antidepressant users, individuals who filled at least one prescription during each calendar year, is shown for cancer survivors and general population comparators.

as previously reported [39,40]. Although it is well recognized that major depression is under-treated [24–26], the Canadian National Population Health Survey estimated that the treatment rate improved from less than 15% in 1994 to 30% in 2000, which may largely account for the increasing prevalence of users [14]. Other potential reasons for an increasing prevalence of antidepressant users include improved compliance to therapy with the introduction of newer, more tolerable drugs and the recognition that a longer duration of therapy is often required for major depression. In addition, an increase in the number of medical indications for these drugs, which include treatment of depression and anxiety disorders, neuropathic pain and smoking cessation, and an increase in off-label use may result in increased prevalence of users [13].

The long-term follow up of adult survivors of childhood and AYA cancer is challenging and survivors remain at risk for many chronic medical conditions, second malignancies and late mortality. Emerging evidence suggests that survivors who experience psychological sequelae may also have additional medical morbidity, as do members of the general population [23,41]. In a recent meta-analysis including more than 106,000 members of the general population, the relative risk of mortality was 81% higher in depressed subjects, compared to those who were not depressed [42]. The CCSS reports that survivors who are antidepressant users are three times more likely to be physically inactive and that social withdrawal is a risk factor for obesity [23], another well recognized risk factor for medical morbidity. Recognition of the potentially increased risk of late or chronic mental health conditions in childhood and AYA cancer survivors may promote continuity of primary care, vigilant screening for mental health conditions by health care providers and prompt initiation of therapy when indicated.

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