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Psychiatric Disorder Incidence Among Adolescents and Young Adults Aged 15-39 With Cancer: Population-Based Cohort

Brianna K. Rosgen, BHSc,[1],[†] Stephana J. Moss, PhD (iD),[1],[†] Kirsten M. Fiest, PhD,[2] Sarah McKillop, MD, MSc,[3] Ruth L. Diaz, MSc,[4] Ronald D. Barr, MB, ChB, MD,[5] Scott B. Patten, MD, PhD (iD),[6] Julie Deleemans, PhD Candidate,[7] Miranda M. Fidler-Benaoudia, PhD[8],[*]

[1]Departments of Community Health Sciences and Critical Care Medicine, O'Brien Institute for Public Health, and Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, AB, Canada; [2]Departments of Community Health Sciences, Critical Care Medicine, and Psychiatry, O'Brien Institute for Public Health, and Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, AB, Canada; [3]Division of Hematology/Oncology, Stollery Children's Hospital, and Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB, Canada; [4]Department of Cancer Epidemiology and Prevention Research, Cancer Care Alberta, Alberta Health Services, Calgary, AB, Canada; [5]Department of Pediatrics, McMaster University, Hamilton, Ontario, Canada Division of Hematology-Oncology, McMaster Children's Hospital, Hamilton, ON, Canada; [6]Departments of Psychiatry and Community Health Sciences, O'Brien Institute for Public Health, and Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada; [7]Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada; and [8]Department of Cancer Epidemiology and Prevention Research, Cancer Care Alberta, Alberta Health Services and Departments of Oncology and Community Health Sciences, Cumming School of Medicine, University of Calgary, AB, Canada

†Authors contributed equally to this work.
*Correspondence to: Miranda Fidler-Benaoudia, PhD, Department of Cancer Epidemiology and Prevention Research, Cancer Care Alberta, Alberta Health Services and Departments of Oncology and Community Health Sciences, Cumming School of Medicine, University of Calgary, Room 508B, Holy Cross Center, 2210 2 St SW, Calgary, AB T2S 3C3, Canada (e-mail: miranda.fidler-benaoudia@albertahealthservices.ca).

Abstract

Background: Adolescent and young adult (AYA) cancer survivors face physical and psychological sequelae related to having cancer decades after treatment completion. It is unclear if AYA cancer survivors are at increased risk for late psychiatric disorders. **Methods:** We used the Alberta AYA Cancer Survivor Study that includes 5-year survivors of cancer diagnosed at age 15-39 years during 1991 to 2013. The primary outcome was incidence of psychiatric disorder (composite outcome) including anxiety, depressive, trauma- and stressor-related, psychotic, and substance use disorders that were identified using coding algorithms for administrative health databases. A validated coding algorithm identified people who experienced a suicide attempt or event of self-harm. Secondary outcomes were incidences of diagnoses by type of psychiatric disorder. **Results:** Among 12 116 AYA 5-year cancer survivors (n = 4634 [38%] males; n = 7482 [62%] females), 7426 (61%; n = 2406 [32%] males; n = 5020 [68%] females) were diagnosed with at least 1 of 5 psychiatric disorders occurring at least 3 years after cancer diagnosis. Survivors of all cancer types were most often diagnosed with anxiety (males: 39.0%, 95% confidence interval [CI] = 37.6% to 40.4%; females: 54.5%, 95% CI = 53.3% to 55.6%), depressive (males: 32.7%, 95% CI = 31.3% to 34.0%; females: 47.0%, 95% CI = 45.8% to 48.1%), and trauma- and stressor-related disorders (males: 13.5%, 95% CI =12.5% to 14.5%; females: 22.5%, 95% CI = 21.6% to 23.5%). **Conclusions:** Anxiety, depressive, and trauma- and stressor-related disorders are common among 5-year survivors of AYA cancer. Primary, secondary, or tertiary preventive strategies for AYAs diagnosed with cancer, particularly at an early age, are needed to mitigate risk of potentially severe outcomes because of psychiatric disorders.

Long-term survival after cancer is common among adolescents and young adults (AYAs) in high-income countries, with approximately 80% of individuals surviving at least 10 years postdiagnosis (1). Despite this, AYA cancer survivors face physical and psychological sequelae related to having cancer even decades after treatment completion (2,3). These late effects exhibit patterns distinct from those in children or older adults (4,5) and often result in impaired quality of life (6). Although long-term, population-based studies in heterogeneous AYA cancer survivors are rare (7), research on psychiatric disorders among AYA cancer survivors reports increased prevalence of anxiety disorders, depressive disorders, and distress compared with the general public or healthy peers (8,9). In a recent meta-analysis of 3 studies, De et al. (10) found that AYA cancer survivors had increased likelihood of experiencing anxiety and depressive disorders but relatively minimal evidence related to other psychiatric outcomes. However, the meta-analysis was limited by the fact that no included study assessed a broad

range of psychiatric disorders (eg, posttraumatic stress disorders), and no study was conducted as a population-based cohort with a representative sample with the ability to conduct subgroup comparisons. Additional limitations to long-term AYA cancer survivor research include loss to follow-up, issues with selection bias, and power limitations related to small sample sizes (10,11).

Consistent data on diverse outcomes for a large patient cohort can be obtained from routinely collected administrative health databases (12,13). We thus conducted a population-based retrospective cohort study to assess the incidence of psychiatric outcomes among 5-year AYA cancer survivors using International Classification of Diseases 9th and 10th Revisions (ICD-9/10) coding algorithms.

Methods

Study Population

The Alberta AYA Cancer Survivor Study is a retrospective, population-based cohort study of 24 460 individuals diagnosed with cancer between the ages of 15 and 39 years from 1983 to 2017 in Alberta, Canada. The cohort was established in collaboration with the Alberta Cancer Registry using the Barr et al. AYA cancer classification system (14). Additional details on cohort development have been published previously (15). For this study, we assessed 5-year cancer survivors as defined by the National Cancer Institute: the percentage of people in a study or treatment group who are alive 5 years after they were diagnosed with cancer (16). The exclusion criteria for this study were 1) unable to link to administrative databases because of missing Alberta Health Care Insurance Plan number; 2) not a 5-year cancer survivor; and 3) not alive on January 1, 1994 (the start of follow-up via administrative databases described below) (17,18). Details on used databases and outcome ascertainment are provided in Supplementary Methods (available online).

Psychiatric Disorders

Patients were classified as being identified with a psychiatric disorder if they had 1 or more incident psychiatric disorders documented through ICD-9 and ICD-10 codes captured in the Discharge Abstract Database (DAD), National Ambulatory Care Reporting System (NACRS), or Physician Claims databases. We excluded psychiatric disorders diagnosed within the first 3 years of follow-up after the first cancer diagnosed to avoid bias because of the inclusion of psychiatric conditions associated with the symptoms of cancer or short-term side effects of treatment of the disease (17,18). Validated coding algorithms were used to identify and classify anxiety disorders (19), depressive disorders (20), psychotic disorders (21), and substance use disorders (21). A coding algorithm for trauma- and stressor-related disorders was developed in consultation with a psychiatrist and neuropsychiatrist, described in detail elsewhere (22). Past suicide or self-harm events were identified through a validated coding algorithm for physician-documented ICD-9 and ICD-10 codes (sensitivity 44.8%; specificity 96.6%) (23). The primary outcome measure was risk of a psychiatric disorder (composite outcome) including anxiety, depressive, trauma- and stressor-related, psychotic, and substance use disorders. Secondary outcomes were diagnostic types of individual psychiatric disorders.

Potential Risk Factors

We examined multiple potential risk factors for incidence of psychiatric disorders among AYA 5-year cancer survivors based on prior literature (24). Demographic and cancer-related variables included sex, age at first cancer diagnosis, calendar year of cancer diagnosis, time since cancer diagnosis (ie, attained age), cancer type, and initial treatment type (ie, surgery, radiotherapy, chemotherapy, or hormonotherapy [excluding glucocorticosteroids]).

Statistical Analyses

Follow-up for psychiatric disorders began at 3-year survival, and participants were censored at the earliest of subsequent cancer diagnosis, death, move out of province, or the study exit date (March 31, 2018). Baseline characteristics are presented as frequencies and percentages for categorical variables. Incidence of psychiatric disorders are presented as percentages with 95% confidence intervals (CIs). A priori identified potential demographic and cancer-related risk factors associated with psychiatric disorders were explored using stratified analyses. Cumulative incidence of psychiatric disorders overall, and by diagnostic types, were investigated as a function of attained age in which subsequent cancer diagnosis and death were treated as competing risks. Recognizing that the DAD and NACRS databases were not available for the entire follow-up period, sensitivity analyses were undertaken when outcomes ascertained only through these 2 administrative health databases were excluded. Statistical analyses were conducted using the Stata ICV.16 software (StataCorp LLC); tests were considered statistically significant at $P < .05$ or via nonoverlapping 95% confidence intervals.

Ethics Approval

This study was approved by the health research ethics board of Alberta Cancer Committee (HREBA.CC-18-0712). Given the use of administrative data, requirement for informed consent was waived.

Results

Participants

A total of 12 116 AYA 5-year cancer survivors from the full cohort were included in analyses (Figure 1; 9123 patients were not 5-year survivors; 90 patients were not alive on January 1, 1994; and 2770 patients were diagnosed with a psychiatric disorder within the first 3 years post initial cancer diagnosis). Demographic and cancer-related characteristics are shown in Table 1. AYA cancer survivors were frequently aged 35-39 years at first cancer diagnosis (n = 4624, 38%), and 62% (n = 7482) were female. Survivors were commonly diagnosed with carcinomas and other malignant epithelial neoplasms (n = 5579, 46%), followed by gonadal and related tumors (n = 1701, 14%). Most survivors (n = 9472, 78%) underwent surgery as an initial treatment, and 4120 (34%) received chemotherapy as an initial treatment. The incidence of psychiatric disorders by first cancer diagnosis during follow-up among survivors who did not receive any cancer treatment is provided in Supplementary Table 1 (available online).
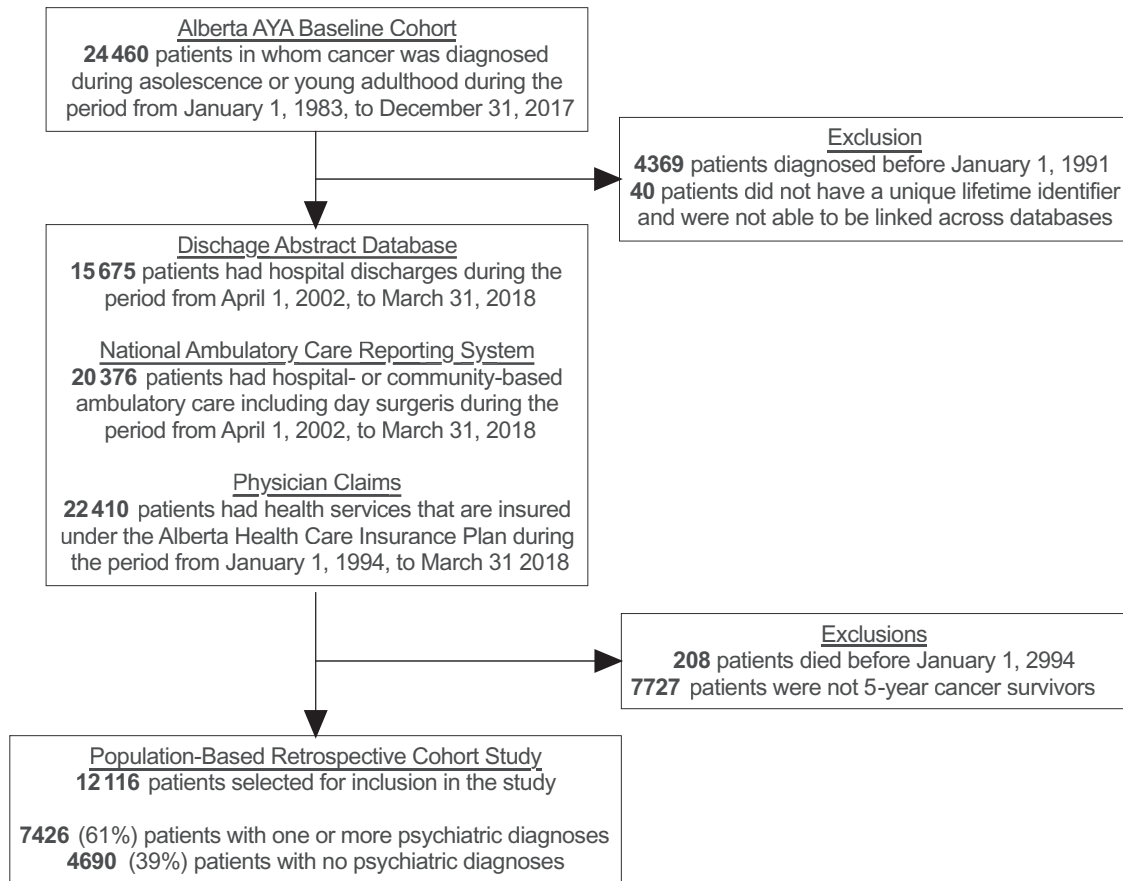
Figure 1. Flow through study of psychiatric disorder diagnoses among 12 116 survivors of cancer in adolescence or young adulthood in Alberta, Canada, 1994-2013.

Psychiatric Disorders

Among AYA cancer survivors included in the study, 7426 (61%; n = 2406 [32%] males; n = 5020 [68%] females) were diagnosed with at least 1 of the 5 types of psychiatric disorders between 1994 and 2013, 38% of whom (n = 4654) were diagnosed with more than 1 psychiatric disorder (Table 2). The incidence of any psychiatric disorder was 61.3% (95% CI = 60.4% to 62.2%; n = 7426) overall and was statistically significantly higher among females, at 67.1% (95% CI = 66.0% to 68.2%) compared with males (51.9%, 95% CI = 50.5% to 53.3%) (Table 3). Statistically significant variation in the incidence of psychiatric disorders by age at cancer diagnosis was not observed, except for substance use disorder where incidence decreased with each 5-year increase in the age at cancer diagnosis.

When investigated by psychiatric disorder subgroup, AYA cancer survivors were most often diagnosed with anxiety disorders (48.5%, 95% CI = 47.6% to 49.4%), depressive disorders (41.5%, 95% CI = 40.6% to 42.4%), and trauma- and stressor-related disorders (19.1%, 95% CI = 18.4% to 19.8%)—all of which were statistically significantly higher in females compared with males (Table 3). Conversely, males had a statistically significantly higher incidence of substance use disorders (males: 9.8%, 95% CI = 9.0% to 10.7% vs females: 6.2%, 95% CI = 5.7% to 6.8%) and suicide attempts and self-harm (males: 3.7%, 95% CI = 3.2% to 4.3% vs females: 2.9%, 95% CI = 2.5% to 3.2%). When further stratified by age at diagnosis, a higher burden of anxiety, depressive, and trauma and stressor-related disorders in

females compared with males was observed across all 5-year bands of age at first cancer diagnosis. There was also an indication of a lower burden of substance use disorders in females compared with males in all bands except among those diagnosed with cancer at ages 20-24 years. Notably, the incidence of suicide and self-harm was 9.8% (95% CI = 7.3% to 13.1%) in males who were diagnosed with cancer at ages 15-19 years, which was statistically significantly greater than their female counterparts (5.3%, 95% CI = 3.5% to 8.0%) and all other male age at diagnosis bands, with incidence decreasing when age at diagnosis increased for males.

The incidence of any psychiatric disorder in males ranged from 46% in AYA survivors of melanoma and skin carcinomas to 59% in AYA survivors of nerve sheath tumors (Figure 2). In females, the overall incidence of any psychiatric disorder ranged from 61% in AYA survivors of sarcomas to 71% in AYA survivors of unspecified malignant neoplasms. When the carcinomas and other malignant epithelial neoplasms group were further stratified into major categories, the overall incidence of any psychiatric disorder varied but was consistently high; for example, 69% (n = 1106) of AYA survivors of breast carcinomas and 53% (n = 168) and 63% (n = 826) of AYA survivors of thyroid carcinomas for males and females, respectively, had at least 1 psychiatric disorder (Supplementary Table 2, available online).

When investigated by attained age, the cumulative incidence of any psychiatric disorder was observed to steadily rise with time, though the rate was slower for males compared with females (Figure 3). In female AYA survivors, anxiety, depressive,

Table 1. Characteristics of 12 116 survivors of cancer in adolescence or young adulthood in Alberta, Canada, 1994-2013

Characteristic	No. (%)
Sex	
Male	4634 (38)
Female	7482 (62)
Type of cancer[a]	
Leukemias	544 (5)
Lymphomas	1548 (13)
Tumor of the central nervous system	833 (7)
Sarcomas	326 (3)
Nerve sheath tumors	140 (1)
Gonadal and related tumors	1701 (14)
Melanoma and skin carcinomas	1341 (11)
Carcinomas and other malignant epithelial neoplasms	5579 (46)
Blood and lymphatic vessel tumors	62 (0.5)
Miscellaneous specified neoplasms	33 (0.3)
Unspecified malignant neoplasms	9 (0.1)
Initial cancer treatment	
Surgery	9472 (78)
Radiotherapy	3485 (29)
Chemotherapy	4120 (34)
Hormone therapy	1857 (15)
Age at first cancer diagnosis, y	
15-19	815 (7)
20-24	1233 (10)
25-29	2203 (18)
30-34	3241 (27)
35-39	4624 (38)
Year of first cancer diagnosis	
1991-1995	2252 (19)
1996-2000	2535 (21)
2001-2005	2681 (22)
2006-2010	3062 (25)
2011-2013	1586 (13)
Psychiatric diagnosis	
No psychiatric diagnosis	4690 (39)
Three or more years after initial cancer diagnosis	7426 (61)

[a]Cancers are grouped according to the classification scheme for tumors diagnosed in adolescents and young adults by Barr and colleagues (14). The first cancer diagnosed was counted.

and trauma- and stressor-related disorders exhibited a sharp rise in cumulative incidence between 40 and 50 years attained age, ultimately reaching 54.4% (95% CI = 53.2% to 55.5%), 46.9% (95% CI = 45.7% to 48.0%), and 22.5% (95% CI = 21.5% to 23.4%), respectively, at 65 years attained age. In contrast, substance use disorders, psychotic disorders, and suicide attempts and self-harm events exhibited a steady rise up to 65 years attained age, ultimately reaching 6.2% (95% CI = 5.6% to 6.7%), 5.2% (95% CI = 4.7% to 5.8%), and 2.9% (95% CI = 2.5% to 3.3%), respectively, at 65 years attained age. No sharp rise in any of the types of psychiatric disorders was exhibited in male AYA survivors; psychotic disorders and suicide attempts and events of self-harm exhibited the slowest increase in cumulative incidence with time.

Sensitivity Analyses

When restricted to only psychiatric disorders obtained from the Physician Claims database, for which there was complete ascertainment across the entire study period, the results did not meaningfully vary (Supplementary Table 3, available online).

Discussion

This large, population-based, retrospective study of 12 116 AYA 5-year cancer survivors is the most contemporary study to determine the risk for psychiatric disorders among AYA cancer survivors, providing comprehensive results for the 15-39 years diagnosis age range and all tumor diagnoses. Our findings highlight the substantial burden of psychiatric disorders among AYA cancer survivors, which was consistently high across all tumor groups, even among those for which survival is relatively favorable such as thyroid cancer (25), in which incidence rates of 53.6% (males) to 62.5% (females) were observed. When assessed by 5 types of psychiatric disorders, we found that AYA cancer survivors experienced a high burden of anxiety disorders (49%), depressive disorders (42%), and trauma- and stressor-related disorders (19%). Compared with females, males of all ages were diagnosed more frequently with substance use disorders, whereas females more frequently experienced trauma- and stressor-related disorders. Substance use disorders and psychotic disorders, as well as suicide attempts and self-harm, were most common among AYA cancer survivors aged 15-19 years at first cancer diagnosis, highlighting the complex and dynamic needs of these young survivors. Based on these findings, there is a critical need for targeted preventive strategies that will mitigate the risk of potentially severe outcomes due to long-term psychiatric disorders. Given that most survivors in our study were diagnosed with multiple psychiatric disorders, initiatives focusing on comorbidity of multiple psychiatric disorders among AYA cancer survivors might be most effective (26).

Our results are comparable with earlier reports that suggest age-specific rates of mental illness among children and young adolescents in the general population increase with time (27,28). There is a paucity of studies investigating psychiatric disorders in AYA-onset cancer survivors (10), and our results highlight that the incidences of anxiety, depression, and psychological distress in this priority population (29) are high (30-32) in comparison to adult survivor populations (33). Although the incidence of any psychiatric disorder does not appear to differ substantially when stratified by sex (29), it is important to consider sex differences in coping strategies and their association with psychiatric problems, which underscore differences in the clinical presentation of psychiatric disorders between males and females (34). High incidence of psychiatric disorders in females may be due to several factors including differences in help-seeking behaviors, as females have been shown to have more positive help-seeking attitudes related to mental health services than males (35). In addition, several biological processes, including hormonal fluctuations related to various aspects of reproductive function that may affect certain neural processes that mediate depressive states, are thought to predispose females to depression more than males (36,37). Our results add compelling evidence to support the call for action for providing more accessible and age-appropriate psychological resources to AYA cancer survivors.

A limitation of previous studies is that AYA cancer survivors are frequently grouped with children or older adults (38). As shown by our results, the burden of psychiatric disorders varies by age among AYA cancer survivors, with the highest incidence

Table 2. Characteristics of 7426 patients in whom cancer was diagnosed during adolescence or young adulthood with an incident psychiatric disorder during the period from 1994 to 2013, grouped by calendar period corresponding to first cancer diagnosis[a]

Characteristic	All years (n = 7426)	Year of cancer diagnosis[b] No. of patients (%)				
		1991-1995 (n = 1663)	1996-2000 (n = 1780)	2001-2005 (n = 1695)	2006-2010 (n = 1607)	2011-2013 (n = 681)
Sex						
Male	2406 (32)	543 (33)	582 (33)	549 (32)	505 (31)	227 (33)
Female	5020 (68)	1120 (67)	1198 (67)	1146 (68)	1102 (69)	454 (67)
Type of cancer						
Leukemias	325 (4)	44 (3)	53 (3)	88 (5)	106 (7)	34 (5)
Lymphomas	893 (12)	199 (12)	237 (13)	203 (12)	182 (11)	72 (11)
Tumor of the central nervous system	529 (7)	116 (7)	112 (6)	119 (7)	126 (8)	56 (8)
Sarcomas	188 (3)	46 (3)	30 (2)	50 (3)	45 (3)	17 (3)
Nerve sheath tumors	86 (1)	16 (1)	16 (1)	23 (1)	21 (1)	10 (2)
Gonadal and related tumors	943 (13)	256 (15)	264 (14)	180 (11)	172 (11)	71 (10)
Melanoma and skin carcinomas	784 (11)	208 (13)	246 (14)	158 (9)	130 (8)	42 (6)
Carcinomas and other malignant epithelial neoplasms	3615 (49)	766 (46)	804 (45)	860 (51)	810 (50)	375 (55)
Blood and lymphatic vessel tumors	38 (1)	4 (1)	9 (1)	11 (1)	10 (1)	4 (1)
Miscellaneous specified neoplasms	19 (1)	4 (1)	8 (1)	3 (1)	4 (1)	0 (0)
Unspecified malignant neoplasms	6 (1)	4 (1)	1 (1)	0 (0)	1 (1)	0 (0)
Age at cancer diagnosis, y[b]						
15-19	496 (7)	105 (6)	117 (7)	125 (7)	102 (6)	47 (7)
20-24	708 (10)	123 (7)	153 (9)	181 (11)	189 (12)	62 (9)
25-29	1289 (17)	288 (17)	288 (16)	290 (17)	300 (19)	123 (18)
30-34	2002 (27)	475 (29)	468 (26)	439 (26)	442 (27)	178 (26)
35-39	2931 (39)	672 (40)	754 (42)	660 (39)	574 (36)	271 (40)
Cancer treatment[c]						
Surgery	5858 (78)	1356 (82)	1420 (80)	1320 (78)	1221 (76)	541 (79)
Radiotherapy	2243 (30)	570 (34)	604 (34)	549 (32)	375 (23)	145 (21)
Chemotherapy	2526 (34)	499 (30)	585 (33)	595 (35)	603 (38)	244 (36)
Hormonotherapy	1031 (15)	38 (2)	83 (5)	210 (12)	470 (29)	230 (34)
Age at psychiatric disorder diagnosis, y						
15-19	6 (1)	0 (0)	0 (0)	1 (1)	2 (1)	3 (1)
20-24	97 (1)	3 (1)	12 (1)	18 (1)	27 (2)	37 (5)
25-29	237 (3)	13 (1)	23 (1)	46 (3)	106 (7)	49 (7)
30-34	513 (7)	17 (1)	57 (4)	145 (9)	197 (12)	97 (14)
35-39	981 (13)	79 (5)	167 (9)	228 (13)	338 (21)	169 (25)
40-44	1498 (20)	200 (12)	272 (15)	354 (21)	434 (27)	238 (35)
45-49	1554 (21)	259 (16)	371 (21)	402 (24)	434 (27)	88 (13)
50-54	1044 (14)	218 (13)	334 (19)	423 (25)	69 (4)	0 (0)
55-59	922 (12)	385 (23)	459 (26)	78 (5)	0 (0)	0 (0)
60-64	507 (7)	422 (25)	85 (5)	0 (0)	0 (0)	0 (0)
65-69	67 (1)	67 (4)	0 (0)	0 (0)	0 (0)	0 (0)

[a]Any psychiatric disorder denotes at least 1 of anxiety disorders, depressive disorders, substance use disorders, trauma- and stressor-related disorders, and psychotic disorders. Percentages 0%-1% are rounded to 1%.
[b]The age and year of the first cancer diagnosed was counted.
[c]More than 1 type of cancer treatment per patient may be counted.

of suicide and self-harm observed among survivors diagnosed at ages 15-19 years—consistent with a common age of onset of most psychiatric disorders (39). As these individuals are generally treated at pediatric hospitals and are eligible to attend long-term survivor clinics that monitor physical and psychosocial sequelae throughout their life (40), our findings highlight a potential gap in existing resources. This study emphasizes that additional supportive care at these ages is needed as psychiatric disorders during adolescence and young adulthood impact developmental trajectories and long-term functional outcomes. For example, even in noncancer populations, psychiatric disorders at young ages can make it problematic for individuals to complete higher education, secure and maintain employment,

avoid illegal and risky health behaviors, and develop a fundamental social support network (41-44). As AYA cancer survivors are already at an increased risk of poorer educational outcomes, work instability, financial toxicity, and risky behaviors (45-49), there is a critical need for psycho-oncological strategies to improve mental health in AYAs with cancer at all stages of medical care (50,51). The majority of resources for AYA cancer survivors is invested in acute cancer treatments, however, much of the burden for these individuals may come later in the form of psychiatric problems.

Efforts to develop a mental health guideline for the follow-up of childhood and AYA cancer survivors are underway by the International Guidelines Harmonization Group (52). It is

Table 3. Incidence of psychiatric disorders during follow-up by age group at first cancer diagnosis among 12 116 survivors of cancer in adolescence or young adulthood in Alberta, Canada, 1994-2013

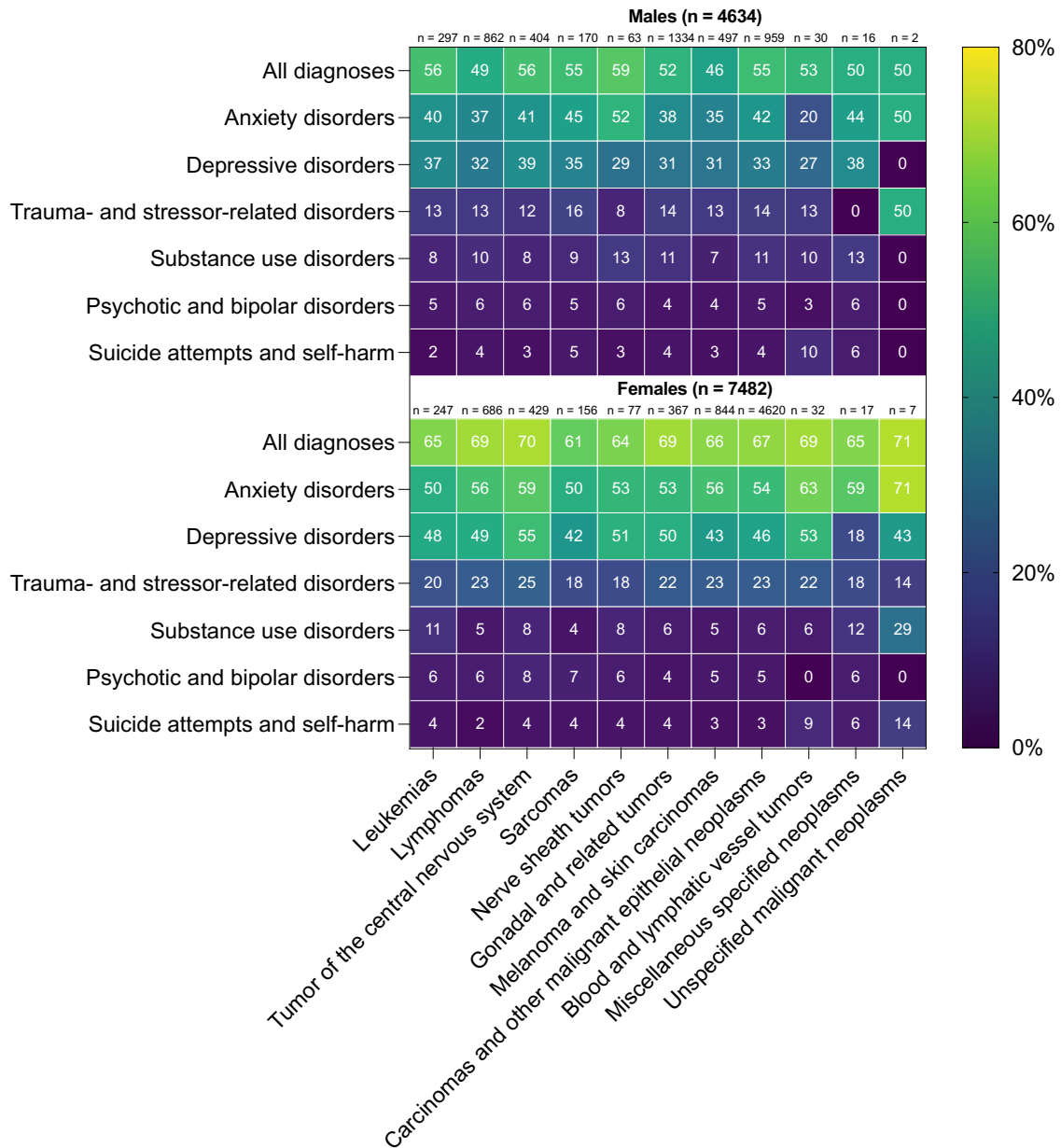| Psychiatric disorder diagnosis	Total % participants (95% CI)	Age at diagnosis of cancer[a]				
		15-19 y % participants (95% CI)	20-24 y % participants (95% CI)	25-29 y % participants (95% CI)	30-34 y % participants (95% CI)	35-39 y % participants (95% CI)
Males, No.	4634	418	620	940	1216	1440
All diagnoses[b]	51.9 (50.5 to 53.3)	55.0 (50.2 to 59.8)	49.7 (45.7 to 53.6)	49.0 (45.8 to 52.2)	53.6 (50.8 to 56.4)	52.4 (49.8 to 55.0)
Anxiety disorders	39.0 (37.6 to 40.4)	41.1 (36.5 to 46.0)	37.1 (33.3 to 41.0)	36.9 (33.9 to 40.1)	40.4 (37.6 to 43.2)	39.2 (36.7 to 41.8)
Depressive disorders	32.7 (31.3 to 34.0)	35.6 (31.2 to 40.4)	29.5 (26.0 to 33.2)	31.1 (28.2 to 34.1)	33.7 (31.1 to 36.4)	33.3 (30.9 to 35.8)
Trauma- and stressor-related disorders	13.5 (12.5 to 14.5)	15.6 (8.2 to 14.3)	11.5 (9.2 to 14.2)	11.9 (10.0 to 14.2)	12.8 (11.1 to 14.8)	15.3 (13.5 to 17.2)
Substance use disorders	9.8 (9.0 to 10.7)	16.7 (12.4 to 19.4)	10.3 (8.2 to 13.0)	10.5 (8.7 to 12.7)	8.9 (7.4 to 10.6)	7.8 (6.6 to 9.4)
Psychotic disorders	4.9 (4.3 to 5.6)	7.9 (5.7 to 10.9)	3.5 (2.3 to 5.3)	4.7 (3.5 to 6.2)	5.3 (4.1 to 6.7)	4.5 (3.6 to 5.7)
Suicide attempts or self-harm	3.7 (3.2 to 4.3)	9.8 (7.3 to 13.1)	3.7 (2.5 to 5.5)	3.7 (2.7 to 5.1)	3.6 (2.7 to 4.8)	2.1 (1.5 to 3.0)
Females, No.	7482	397	613	1263	2025	3184
All diagnoses[b]	67.1 (66.0 to 68.2)	67.0 (62.2 to 71.5)	65.3 (61.4 to 68.9)	65.6 (62.9 to 68.1)	66.7 (64.6 to 68.7)	68.3 (66.7 to 69.9)
Anxiety disorders	54.5 (53.3 to 55.6)	55.4 (50.5 to 60.2)	53.3 (49.4 to 57.3)	54.9 (52.2 to 57.7)	53.3 (51.1 to 55.5)	55.1 (53.4 to 56.8)
Depressive disorders	47.0 (45.8 to 48.1)	46.3 (41.5 to 51.3)	44.2 (40.3 to 48.2)	46.8 (44.1 to 50.0)	47.2 (45.0 to 49.3)	47.5 (45.8 to 49.3)
Trauma- and stressor-related disorders	22.5 (21.6 to 23.5)	23.2 (19.3 to 27.6)	20.2 (17.2 to 23.6)	20.6 (18.4 to 22.9)	24.0 (22.1 to 25.9)	22.7 (21.3 to 24.2)
Substance use disorders	6.2 (5.7 to 6.8)	7.6 (5.3 to 10.6)	7.2 (5.4 to 9.5)	6.6 (5.3 to 8.1)	6.2 (5.2 to 7.3)	5.7 (5.0 to 6.6)
Psychotic disorders	5.3 (4.8 to 5.8)	5.5 (3.7 to 8.3)	4.7 (3.3 to 6.7)	5.5 (4.3 to 6.9)	5.0 (4.1 to 6.0)	5.4 (4.7 to 6.2)
Suicide attempts or self-harm	2.9 (2.5 to 3.2)	5.3 (3.5 to 8.0)	3.9 (2.6 to 5.8)	4.3 (3.3 to 5.5)	3.0 (2.4 to 3.9)	1.7 (1.3 to 2.2)
Sexes combined, No.	12 116	815	1233	2203	3241	4624
All diagnoses[b]	61.3 (60.4 to 62.2)	60.9 (57.5 to 64.2)	57.4 (54.6 to 60.2)	58.5 (56.4 to 60.6)	61.8 (60.0 to 63.4)	63.3 (62.0 to 64.8)
Anxiety disorders	48.5 (47.6 to 49.4)	48.1 (44.7 to 51.5)	45.2 (42.4 to 48.0)	47.3 (45.2 to 49.3)	48.4 (46.7 to 50.2)	50.2 (48.7 to 51.6)
Depressive disorders	41.5 (40.6 to 42.4)	40.9 (37.5 to 44.3)	36.8 (34.2 to 39.6)	40.1 (38.1 to 42.1)	42.1 (40.4 to 43.8)	43.1 (41.7 to 44.5)
Trauma- and stressor-related disorders	19.1 (18.4 to 19.8)	19.3 (16.7 to 22.1)	15.8 (13.9 to 18.0)	16.9 (15.4 to 18.5)	19.8 (18.4 to 21.2)	20.4 (19.3 to 21.6)
Substance use disorders	7.6 (7.1 to 8.1)	12.3 (10.2 to 14.7)	8.8 (7.3 to 10.5)	8.3 (7.2 to 9.5)	7.2 (6.3 to 8.1)	6.4 (5.7 to 7.1)
Psychotic disorders	5.1 (4.7 to 5.5)	6.7 (5.2 to 8.7)	4.1 (3.2 to 5.4)	5.1 (4.3 to 6.1)	5.1 (4.4 to 5.9)	5.1 (4.5 to 5.8)
Suicide attempts or self-harm	3.2 (2.9 to 3.5)	7.6 (6.0 to 9.6)	3.8 (2.9 to 5.0)	4.0 (3.3 to 4.9)	3.2 (2.7 to 3.9)	1.8 (1.4 to 2.2)

[a]The age at the first cancer diagnosed was counted. CI = confidence interval.

[b]All diagnoses denote at least 1 of anxiety disorders, depressive disorders, substance use disorders, trauma- and stressor-related disorders, and psychotic disorders.

expected that these guidelines will provide evidence-based recommendations on how best to monitor young cancer survivors and prevent adverse psychiatric outcomes. Until then, the Canadian National Standards for Psychological Oncology (53) recommends educational and organizational standards for management of anxiety and depression within all cancer care settings and throughout the cancer trajectory. Documentation of the seriousness of many psychiatric disorders points to a need for professional services; however, cancer care teams often do not include psychiatrists in Canada (54), and where available, it is unclear how often these resources are being offered to AYA cancer patients. Incorporating clinical psychologists or psychiatrists to evaluate psychiatric sequelae of the cancer and its subsequent treatment may allow for targeted recommendations and earlier initiation of preventative interventions to effectively mitigate risk of psychiatric disorders. It is also crucial that all available resources and interventions remain available to AYA cancer survivors regardless of time since diagnosis, given the observed changing burden and profile of psychiatric disorders in this population over time. Indeed, it is likely that what is beneficial in the early years following AYA-onset cancer survival may not be helpful years or decades later as survivors' needs change over time.

Despite the many strengths of our study, we must acknowledge several limitations. First, we do not suggest our statistical models fully explain the incidence of psychiatric disorders among 5-year survivors of AYA-onset cancer. We did not capture psychiatric disorders that were diagnosed by health-care professionals other than physicians (eg, social workers, psychologists) as these services are paid for out-of-pocket and not captured in routine administrative health databases. As well, we identified incident psychiatric diagnoses using validated algorithms for ICD-9 and ICD-10 diagnostic codes; the algorithm used to identify trauma- and stressor-related disorders was developed with a psychiatrist (with face validity) but has not been validated externally. Our coding algorithms may have

Figure 2. Incidence of psychiatric disorders during follow-up by type of first cancer diagnosis among 12 116 survivors of cancer in adolescence or young adulthood in Alberta, Canada, 1994-2013. Data are given as percentages of cancer type. Cancers are grouped according to the classification scheme for tumors diagnosed in adolescents and young adults by Barr and colleagues (14). The first cancer diagnosed was counted. All diagnoses denote 1 or more anxiety disorders, depressive disorders, substance use disorders, trauma- and stressor-related disorders, and psychotic disorders. Diagnoses for psychiatric disorders during the first 3 years after receiving a diagnosis of cancer were excluded from this analysis. More than 1 psychiatric disorder diagnosis per patient may be counted.

excluded some relevant ICD-9 or ICD-10 codes compared with gold-standard physician diagnoses using the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*, though this would lead to an underestimation of the estimates. Second, though we assessed risk factors in stratified analyses, the highly interdependent nature of component causes of psychiatric disorders produces complex interactions with synergistic effects that are lost when disaggregated; this prevents clinical separation of potential risk factors for simplified, tailored interventions. We suggest that the development of targeted strategies for psychiatric disorder prevention and management may be a valuable adjuvant throughout the AYA cancer care continuum. Third, results related to treatment of cancer should be

interpreted with caution given that detailed treatment exposure data are needed to improve the face validity of this variable in the Alberta Cancer Registry. Fourth, information on cancer recurrence is not available in cancer registries, and our results may underestimate the burden of psychiatric disorders for this population. Fifth, we were not able to determine preexisting psychiatric disorders or other potential stressors that an AYA may be more at risk to experience (eg, financial toxicity), and thus our results may be overestimated; however, our data point still to the critical need for targeted preventive strategies among AYA survivors that will mitigate the risk of potentially severe outcomes due to long-term psychiatric disorders regardless of when diagnosis occurred. Sixth, we were also not able to assess
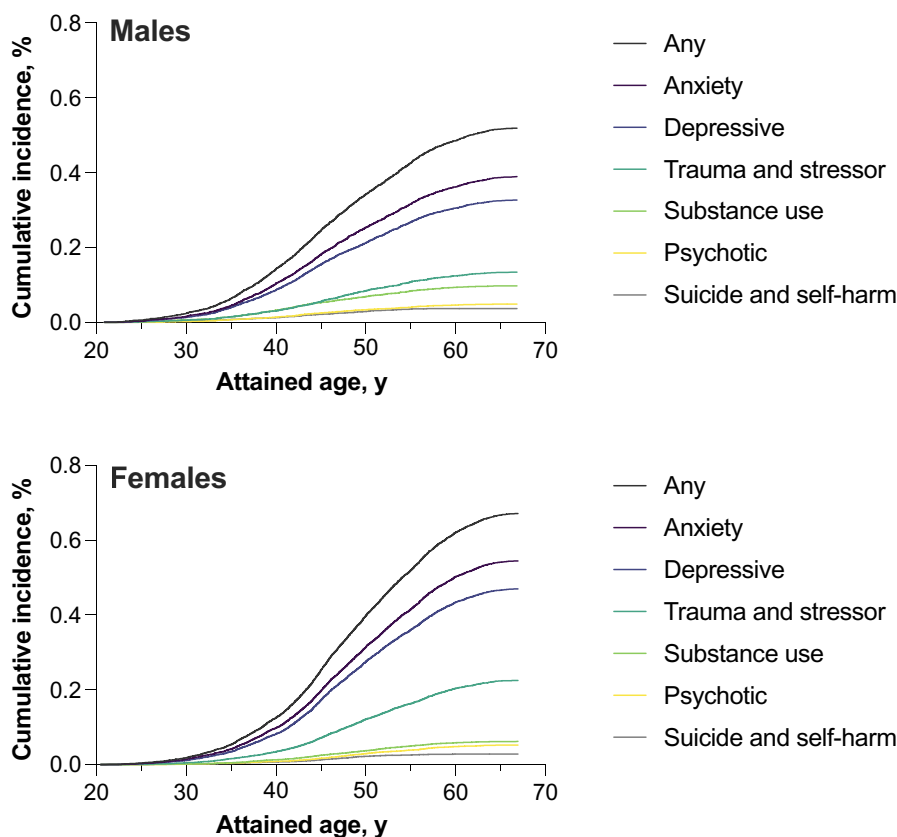
Figure 3. Cumulative incidence of psychiatric disorders diagnosed during follow-up over attained age in years by sex among 12 116 survivors of cancer in adolescence or young adulthood in Alberta, Canada, 1994-2013.

self-reported gender and ethnicity differences as these variables are not captured within the administrative databases that were sourced for this study. Finally, though we conducted a population-based study, our results may not be generalizable to countries without universal access to health care, as AYA cancer survivors in those jurisdictions are likely to face additional barriers to accessing care (55).

The magnitude of psychiatric disorders, mainly anxiety, depressive, and trauma-and stressor-related disorders, is high among 5-year survivors of AYA cancer. Investigation using general population rates with matched controls and multiple comparisons should seek to understand the mechanisms underlying risk factors for comorbid psychiatric disorders among AYA cancer survivors to develop preventive strategies for AYAs diagnosed with cancer that mitigate the risk of psychiatric disorders.

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Notes

Data Availability

The data are not publicly available due to them containing semi-identifiable information that could compromise research participant privacy. Additional summary tables of count data are available from the corresponding author upon request.

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