

Cancer Statistics for Adolescents and Young Adults, 2020

Kimberly D. Miller, MPH ^(D); Miranda Fidler-Benaoudia, PhD²; Theresa H. Keegan, PhD, MS³; Heather S. Hipp, MD⁴; Ahmedin Jemal, DVM, PhD ^(D); Rebecca L. Siegel, MPH ^(D)

¹Surveillance Research, American Cancer Society, Atlanta, Georgia;
²Department of Cancer Epidemiology and Prevention Research, Calgary, Alberta Canada; ³Hematology and Oncology, University of California at Davis Health, Sacramento, California; ⁴Reproductive Endocrinology and Infertility, Emory University School of Medicine, Atlanta, Georgia.

Corresponding Author: Kimberly D. Miller, MPH, Surveillance Research, American Cancer Society, 250 Williams St, NW, Atlanta, GA 30303-1002 (kimberly. miller@cancer.org).

DISCLOSURES: Rebecca L. Siegel, Kimberly D. Miller, and Ahmedin Jemal are employed by the American Cancer Society, which receives grants from private and corporate foundations, including foundations associated with companies in the health sector for research outside of the submitted work. The authors are not funded by or key personnel for any of these grants, and their salary is solely funded through American Cancer Society funds. Miranda Fidler-Benaoudia, Theresa H. Keegan, and Heather S. Hipp made no disclosures.

doi: 10.3322/caac.21637. Available online at cacancerjournal.com

Abstract: Cancer statistics for adolescents and young adults (AYAs) (aged 15-39 years) are often presented in aggregate, masking important heterogeneity. The authors analyzed population-based cancer incidence and mortality for AYAs in the United States by age group (ages 15-19, 20-29, and 30-39 years), sex, and race/ ethnicity. In 2020, there will be approximately 89,500 new cancer cases and 9270 cancer deaths in AYAs. Overall cancer incidence increased in all AYA age groups during the most recent decade (2007-2016), largely driven by thyroid cancer, which rose by approximately 3% annually among those aged 20 to 39 years and 4% among those aged 15 to 19 years. Incidence also increased in most age groups for several cancers linked to obesity, including kidney (3% annually across all age groups), uterine corpus (3% in the group aged 20-39 years), and colorectum (0.9%-1.5% in the group aged 20-39 years). Rates declined dramatically for melanoma in the group aged 15 to 29 years (4%-6% annually) but remained stable among those aged 30 to 39 years. Overall cancer mortality declined during 2008 through 2017 by 1% annually across age and sex groups, except for women aged 30 to 39 years, among whom rates were stable because of a flattening of declines in female breast cancer. Rates increased for cancers of the colorectum and uterine corpus in the group aged 30 to 39 years, mirroring incidence trends. Five-year relative survival in AYAs is similar across age groups for all cancers combined (range, 83%-86%) but varies widely for some cancers, such as acute lymphocytic leukemia (74% in the group aged 15-19 years vs 51% in the group aged 30-39 years) and brain tumors (77% vs 66%), reflecting differences in histologic subtype distribution and treatment. Progress in reducing cancer morbidity and mortality among AYAs could be addressed through more equitable access to health care, increasing clinical trial enrollment, expanding research, and greater alertness among clinicians and patients for early symptoms and signs of cancer. Further progress could be accelerated with increased disaggregation by age in research on surveillance, etiology, basic biology, and survivorship. CA Cancer J Clin 2020;0:1-17. © 2020 American Cancer Society.

Keywords: adolescent cancer, childhood cancer, epidemiology, pediatric cancer

Introduction

Cancer in adolescents and young adults (AYAs) is defined by the National Cancer Institute as diagnoses occurring among those aged 15 to 39 years¹ and is unique from cancer diagnosed in other age groups because of important differences in the distribution of cancer types, intrinsic and extrinsic risk factors, tumor biology, and prognosis and survivorship. An increasing body of evidence indicates that tumors in AYAs are molecularly distinct from those in both younger and older age groups, possibly suggesting differences in etiology and effective treatment.²⁻⁴ In addition, compared with older patients with cancer, AYAs have a higher risk of long-term and late effects, including infertility, sexual dysfunction, cardiovascular disease, and future cancers,⁵⁻⁸ whereas compared with childhood cancer survivors, the risk of severe late effects is lower.⁹ AYAs are also more likely than older patients with cancer to experience delays in diagnosis for some cancers because of higher uninsured rates, a lack of cost-effective early detection methods, and the rarity of cancer at this age.^{10,11} Despite rapid progress in the scientific understanding of cancer in AYAs, important research gaps in etiology, basic biology, treatment, and survivorship persist, partly because this age group continues to be grouped with children and/ or older adults in many epidemiologic studies. Even within AYA studies, data are often presented in aggregate, masking important differences across AYA age groups. This article summarizes population-based trends in cancer incidence, mortality, and survival among AYAs, with a focus on the heterogeneity within this population, and also briefly reviews survivorship issues.

Materials and Methods

Data Sources

Population-based cancer incidence data in the United States are collected by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program and by the Centers for Disease Control and Prevention's National Program of Cancer Registries (NPCR). Historical incidence and survival trends (1975-2016) were based on data from the 9 oldest SEER registries, representing 9% of the US population.¹² Data from the 18 SEER registries, covering 28% of the US population, were the source for 5-year relative and cancer-specific survival rates.¹³ Combined SEER and NPCR data for 1995 through 2016, as provided by the North American Association of Central Cancer Registries (NAACCR), were the source for the estimated numbers of new cancer cases in 2020, cross-sectional incidence rates (2012-2016), stage distribution (2012-2016), and 10-year average annual percent changes (AAPCs) in incidence rates (2007-2016).^{14,15} Analyses of incidence trends from 1995 through 2016 were based on all available data for the 50 states and the District of Columbia, covering 95% of the US population during that time.

Mortality data covering all 50 states and the District of Columbia were obtained from the National Center for Health Statistics and were the source for death rates in the most recent time period (2012-2016) and long-term trends (1975-2017).^{16,17} Incidence and mortality rates for American Indians/Alaska Natives (AI/ANs) were based on cases and deaths in Preferred/Referred Care Delivery Area counties. The 2018 National Health Interview Survey was used for estimates of self-reported cervical cancer screening.¹⁸

Statistical Analyses

Case estimates were calculated by applying the agespecific proportions of cases diagnosed during 2015 through 2016 from the NAACCR analytic file to the previously published total number of estimated cases in 2020.¹⁹ Similarly, we calculated the estimated number of cancer deaths among AYAs by applying the proportion of

AGE	ESTIMATED CASES	ESTIMATED DEATHS
15-19 years	5800	540
20-29 years	24,900	2210
30-39 years	58,800	6520
Total	89,500	9270

deaths in that age group during 2016 through 2017 to the previously published estimates for total cancer deaths in 2020. Estimates by cancer type for cases are provided for sexes combined for stability and are not provided for cancer deaths because of sparse data.

Incidence and death rates, expressed per 100,000 population, were calculated using SEER*Stat (version 8.3.6) software and were age standardized to the 2000 US standard population.²⁰ In analyses of incidence trends for selected sites using NAACCR data, we applied delay adjustment factors from the US Cancer Statistics data file.²¹ All cases were classified according to the AYA site recode/ World Health Organization 2008 definitions, based on the International Classification of Diseases for Oncology, third edition,^{22,23} with the exception of melanoma of the skin and solid tumors other than brain, which were classified according to SEER site recode/World Health Organization 2008 definitions for comparability to statistics in older age groups as well as differentiation between uterine cervix and uterine corpus. Trends for colorectal cancer incidence excluded the appendix (code C18.1). Causes of death were classified according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision.²⁴ It is important to note that, because of differences in classification, incidence and mortality statistics herein are not directly comparable.

The annual percent change in rates was quantified using the National Cancer Institute's Joinpoint Regression Program (version 4.7.0.0).²⁵ Screening prevalence estimates were calculated using SAS-callable SUDAAN (version 11.0.1; RTI International, Research Triangle Park, North Carolina) and accounted for the complex survey design.

Selected Findings

Expected Cases and Deaths in 2020

In 2020, there will be approximately 89,500 new cancer cases and 9270 cancer deaths in AYAs aged 15 to 39 years in the United States (Table 1). The distribution of cancers among AYAs varies substantially by age (Fig. 1). In particular, adolescents (defined hereafter as individuals aged 15-19 years) have a unique cancer profile that includes a higher proportion of childhood cancers (eg, Hodgkin lymphoma, acute lymphocytic leukemia [ALL]) versus

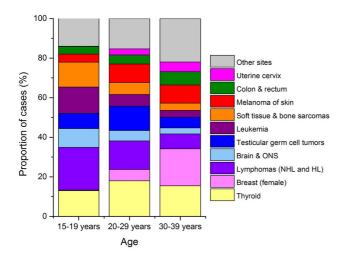


FIGURE 1. Case Distribution (%) of Leading Cancer Types in Adolescents and Young Adults, 2012 to 2016. Coding for cancers of the thyroid, female breast, colon and rectum, and uterine cervix and melanoma of the skin are based on the Surveillance, Epidemiology, and End Results adult recode variable, excluding a small number of sarcomas of the bone and soft tissue. HL indicates Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; ONS, other nervous system.

adult cancers (eg, thyroid cancer and melanoma of the skin) compared with those aged 20 to 39 years. The most commonly diagnosed cancers are thyroid cancer, Hodgkin lymphoma, and brain and other nervous system cancers among adolescents; thyroid cancer, testicular germ cell tumors (GCTs), and melanoma of the skin in the group aged 20 to 29 years and female breast cancer, thyroid cancer, and melanoma in those aged 30 to 39 years (Table 2). Notably, the only commonality among the top 3 sites in each age group is thyroid cancer.

Incidence

Among AYAs, incidence increases with advancing age for all cancer types except for ALL, bone tumors, and Hodgkin lymphoma, for which rates are highest in adolescents (Table 3). Cancer incidence rates for all sites combined are similar by sex in AYAs aged 15 to 19 years (23 vs 24 cases per 100,000 population in females and males, respectively, during 2012-2016). Rates in women compared with men, however, are 30% higher in AYAs aged 20 to 29 years (55 vs 42 per 100,000 population) and nearly double in those aged 30 to 39 years (161 vs 84 per 100,000 population) (Table 3),¹⁹ primarily because of the substantially higher incidence of breast and thyroid cancers and melanoma of the skin in women. For example, thyroid cancer incidence rates among women in their 20s are greater than 5-fold higher than those among men (15 vs 3 per 100,000 population during 2012-2016, respectively).¹⁹ Notably, although lung cancer is rare in AYAs, rates among women in their 30s are higher than those among men despite lower smoking prevalence in women; research is ongoing to elucidate the causes of this pattern.²⁶

Long-term trends in cancer incidence rates among AYAs by age group are shown in Figure 2. Rates among men aged 20 to 39 years rapidly increased in the late 1980s and subsequently declined in the early 1990s in parallel with the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) epidemic, primarily reflecting a peak in the occurrence of Kaposi sarcoma (Fig. 3). During the past decade of available data (2007-2016), overall incidence rates increased in all AYAs, but may be stabilizing among men in their 20s (Fig. 2). Rising rates in AYAs, especially among women, are largely driven by the increased detection of thyroid cancer, for which rates rose by almost 3% annually among adults aged 20 to 39 years and 4% annually among adolescents during 2007 through 2016 (Table 4).¹³ Indeed, when thyroid cancer is excluded from overall trends, rates in women during 2007 through 2016 were stable. Increases in thyroid cancer incidence

AGES 15 TO 19 YEARS		AGES 20 TO 29 YEARS	5	AGES 30 TO 39 YEAF	RS
CANCER TYPE	NO.	CANCER TYPE NO.		CANCER TYPE	NO.
Thyroid	800	Thyroid	4600	Breast (female)	11,100
Hodgkin lymphoma	800	Testicular germ cell tumors	3000	Thyroid	9000
Brain and ONS	500	Melanoma of the skin	2200	Melanoma of the skin	5500
Non-Hodgkin lymphoma	500	Hodgkin lymphoma	2000	Colon and rectum	4100
Testicular germ cell tumors	400	Breast (female)	1500	Testicular germ cell tumors	3100
Acute lymphoid leukemia	400	Non-Hodgkin lymphoma	1400	Uterine cervix	3000
Bone tumors	400	Colon and rectum	1300	Non-Hodgkin lymphoma	2700
Soft-tissue sarcomas	400	Brain and ONS	1200	Kidney	2400
Melanoma of the skin	200	Soft-tissue sarcomas	1000	Uterine corpus	2000
Acute myeloid leukemia	200	Uterine cervix	800	Brain and ONS	1800

TABLE 2. Leading Sites of New Cancer Cases in Adolescents and Young Adults, Both Sexes Combined: 2020 Estimates^a

Abbreviation: ONS, other nervous system.

^aEstimates are rounded to the nearest 100 and exclude basal cell and squamous cell skin cancers, benign and borderline brain tumors, and in situ carcinoma of any site except urinary bladder. Ranking is based on modeled progress and may differ from the most recent observed data.

OCCC TYC ICCD FICT ICCD FICT <th< th=""><th></th><th></th><th>15 TO 19 YEARS</th><th></th><th></th><th>20 TO 29 YEARS</th><th></th><th></th><th>30 TO 39 YEARS</th><th>S</th></th<>			15 TO 19 YEARS			20 TO 29 YEARS			30 TO 39 YEARS	S
All carcer type ³ 235 236 85% 423 53<	CANCER TYPE	INCIDENCE RATE	DEATH RATE	AR SURVIVAL,	INCIDENCE RATE	DEATH RATE	5-YEAR SURVIVAL, %	INCIDENCE RATE	DEATH RATE	5-YEAR SURVIVAL, %
Mele 240 33 82% 42.4 5.4 83% 833 13.4 73% Finale 239 23 88% 54.9 44 68% 613 122 86% Binn and ONS* 16 0.5 73% 53 0.3 66% 66% Binn and ONS* 2.2 0.5 73% 0.3 66% 66% 66% Binn and ONS* 2.2 0.5 75% 0.3 66% 67% 66% Color and rectum 0.1 -d" 85% 5.7 0.4 83% 46.6 48 86% Color and rectum 2.1 0.1 2.4% 0.2 0.3 66% 11 10	All cancer types ^b	23.5	2.8	85%	48.5		86%	122.5	15.3	83%
Fendle 229 23 88% 549 44 88% 112 124 86% Boin et untrot ¹ 16 0.5 67% 0.3 66% 0.3 123 124 86% Boin et untrot ¹ 116 0.5 67% 0.3 0.3 66% 135 12 66% 135 125 66% Boin et untrot ¹ 0.1 -0 137 61% 135 12 13 66% 135 13 12 66% <t< td=""><td>Male</td><td>24.0</td><td>3.3</td><td>82%</td><td>42.4</td><td>5.4</td><td>83%</td><td>83.8</td><td>13.4</td><td>79%</td></t<>	Male	24.0	3.3	82%	42.4	5.4	83%	83.8	13.4	79%
Bothe tunori 16 05 67% 08 03 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 73% 66% 74% 75% 74% 75% 74% 74% 74% 73% 73% 73% 74% 74% 74% 74% 74% 74% 74% 74	Female	22.9	2.3	88%	54.9	4.4	88%	161.3	17.2	86%
Brain ard ON ^{4/c} 22 0.5 7% 2.5 0.6 73% 3.7 1.5 66% Breat (frame) 0.1 -d 8% 3.7 1.6 1.6 66% Groen and rectum 1.1 -d 1.2 8% 3.7 1.6 1.8 66% Hodgrin lymphoma 3.1 -d 1.9 9.7% 0.1 9.5% 3.4 0.2 9.6% Hodgrin lymphoma 1.1 0.1 9.7% 0.1 9.5% 1.1 0.1 9.5% 1.1 0.1 1.1 0.1 0.2 0.4 0.2 0.4 0.1 0.2 0.4 0.2 0.4 0.2 0.2 0.2 0.3 0.4 0.2 0.2 0.3 0.4 0.3	Bone tumors ^c	1.6	0.5	67%	0.8	0.3	68%	0.8	0.2	74%
Breast (femel) 0.1 -d SS% 5.7 0.4 SS% 4.6 4.8 8.8 <	Brain and ONS ^{b,c}	2.2	0.5	77%	2.5	0.6	73%	3.7	1.5	66%
Colon and return09<0182%220366%83131866%Hodyin ymphona31<01	Breast (female)	0.1	р 	85%	5.7	0.4	83%	46.6	4.8	86%
Hotolprin 3.1 < 0.1 9.7 < 1.1 < 0.1 < 9.7 < 9.4 < 0.2 < 9.1 < 0.1 < 9.1 < 0.2 < 0.1 < 0.1 < 0.1 < 0.2 < 0.1 < 0.2 < 0.1 < 0.2 < 0.1 < 0.2 < 0.1 < 0.2 < 0.1 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2 < 0.2	Colon and rectum	0.9	<0.1	82%	2.2	0.3	68%	8.3	1.8	68%
Kdney and renal pelvis 0.2 <0.1 73% 0.9 0.1 83% 49 0.3 90% Leukemia 3.1 0.7 73% 2.9 0.9 64% 4.1 1.1 69% Acute bymployofic leukemia 1.7 0.3 74% 0.9 0.3 55% 57% 57% Acute bymployofic leukemia 1.0 0.3 66% 1.1 0.3 56% 1.16 0.3 55% 57% Acute bymployofic leukemia 1.0 0.1 6.0% 1.1 0.3 56% 1.12 0.3 56% 58% 58% 58% 58% 58% 58% 58% 58% 58% 58% 58% 58% 58% 56% 117 0.0 58% 58	Hodgkin lymphoma	3.1	<0.1	97%	4.1	0.1	95%	3.4	0.2	94%
Letelemia 3.1 0.7 73% 2.9 0.9 64% 4.1 1.1 69% Acute lymphogric leukemia 1.7 0.3 74% 0.9 0.3 52% 0.7 0.3 51% Acute lymphogric leukemia 1.0 0.3 66% 1.1 0.3 56% 1.1 0.3 51% 0.3 51% 51% 0.3 51% 0.3 51% 0.3 54% 0.3 54% 51% 0.3 51% 51% 0.3 54% 0.3 54% 54% 0.3 54% 54	Kidney and renal pelvis	0.2	<0.1	73%	0.9	0.1	83%	4.9	0.3	%06
Actue hymphocycic leukemia 1.7 0.3 74% 0.9 0.3 52% 0.7 0.3 51% Actue myeloid leukemia 10 0.3 66% 1.1 0.3 59% 1.6 0.5 57% Lung and bronchus 0.1 <0.1	Leukemia	3.1	0.7	73%	2.9	0.9	64%	4.1	1.1	%69
Acute myeloid leukeria 10 0.3 66% 1.1 0.3 59% 1.6 0.5 57% Lung and bronchus 0.1 <0.1 81% 0.4 0.1 60% 2.0 0.8 39% Melanoma of the skin 1.0 <0.1 81% 0.4 0.1 60% 2.0 0.8 39% Melanoma of the skin 1.0 <0.1 85% 2.9 0.2 96% 11.2 0.6 34% Non-Hodykin ymphoma 1.9 0.1 83% 2.9 0.3 83% 5.8 0.6 34% Soft-tissue sarcoma 1.3 0.3 6.9% 2.1 0.4 6.9% 35 74% Thyoid 3.1 $-d$ 9.11 0.4 6.1 5.9% 17% Thyoid 3.1 $-d$ 1.1 0.3 8.7 2.1 9.9% Thyoid 3.1 $-d$ 1.1 0.3 8.7 2.1 1.4% <td>Acute lymphocytic leukemia</td> <td>1.7</td> <td>0.3</td> <td>74%</td> <td>0.9</td> <td>0.3</td> <td>52%</td> <td>0.7</td> <td>0.3</td> <td>51%</td>	Acute lymphocytic leukemia	1.7	0.3	74%	0.9	0.3	52%	0.7	0.3	51%
Lung and bronchus 0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <0.1 <t< td=""><td>Acute myeloid leukemia</td><td>1.0</td><td>0.3</td><td>66%</td><td>1.1</td><td>0.3</td><td>59%</td><td>1.6</td><td>0.5</td><td>57%</td></t<>	Acute myeloid leukemia	1.0	0.3	66%	1.1	0.3	59%	1.6	0.5	57%
Melanoma of the skin10 $(01$ 95% 4.5 0.2 96% 11.2 0.6 94% Non-Hodgkin lymphoma19 0.1 88% 2.9 0.3 83% 5.8 0.6 83% Non-Hodgkin lymphoma19 0.1 88% 2.9 0.3 83% 2.4 0.2 82% Oral cavity and pharynx 0.5 <0.1 90% 0.8 0.1 84% 2.4 0.2 82% Softsisue sarcoma 1.3 0.3 69% 2.1 0.4 69% 3.5 7.4 0.2 87% Testicular gem cell tumors 3.5 <0.1 96% 11.7 0.2 95% 13.0 0.2 96% Thyroid 3.1 $-d$ 99% 11.7 0.2 95% 13.1 1.9 0.2 Uterine cervix 0.1 $-d$ $-d$ 3.1 0.2 95% 12.1 1.9 90% Uterine corpus 0.1 $-d$ $-d$ 3.1 0.3 82% 7.8 0.1 1.9 90% Uterine corpus 0.1 $-d$ $-d$ $-d$ 3.1 0.3 82% 7.8 0.1 1.9 90% Uterine corpus 0.1 $-d$ $-d$ $-d$ $-d$ 0.1 8% 7.8 0.1 1.9 80% Uterine corpus 0.1 $-d$ $-d$ $-d$ $-d$ $-d$ 1.3 1.0 1.0 1.0 1.0 1.0	Lung and bronchus	0.1	<0.1	81%	0.4	0.1	60%	2.0	0.8	39%
Non-Hodgkin lymphoma1.90.188%2.90.383%5.80.683%Oral cavity and pharynx0.5 <0.1 90%0.80.184%2.40.282%Soft-tissue sarcoma1.30.369%2.10.469%3.60.574%Soft-tissue sarcoma1.30.369%2.10.469%3.60.574%Testicular germ cell tumors3.5 <0.1 96%11.70.295%13.00.296%Thyroid3.1 $-d$ 99%8.7 <0.1 $>99\%$ 18.70.1 $>99\%$ 18.7Uterine cervix0.1 $-d$ $-d$ 3.10.1 $>99\%$ 12.11.980%Uterine corpus0.1 $-d$ $-d$ 1.30.188%7.80.1 $>99\%$ Uterine corpus0.1 $-d$ $-d$ $-d$ 1.30.1 $=96\%$ 90% 90% Uterine corpus0.1 $-d$ $-d$ $-d$ $-d$ $-d$ $-d$ 90% 90% Uterine corpus0.1 $-d$ $-d$ $-d$ $-d$ $-d$	Melanoma of the skin	1.0	<0.1	95%	4.5	0.2	96%	11.2	0.6	94%
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Non-Hodgkin lymphoma	1.9	0.1	88%	2.9	0.3	83%	5.8	0.6	83%
Soft-tissue sarcoma1.30.369%2.10.469%3.60.574%Testicular germ cell tumors3.5<0.1	Oral cavity and pharynx	0.5	<0.1	%06	0.8	0.1	84%	2.4	0.2	82%
Testicular germ cell tumors3.5<0.196%11.70.295%13.00.296%Thyroid3.1 $-d$ 99%8.7<0.1	Soft-tissue sarcoma	1.3	0.3	69%	2.1	0.4	69%	3.6	0.5	74%
Thyoid 3.1 $-d$ 99% 8.7 <0.1 $>99\%$ 18.8 <0.1 $>99\%$ Uterine cervix 0.1 $-d$ $-d$ 3.1 0.3 82% 12.1 1.9 80% Uterine cervix 0.1 $-d$ $-d$ 3.1 0.3 82% 12.1 1.9 80% Uterine corpus 0.1 $-d$ $-d$ 1.3 0.1 88% 7.8 0.5 91% Abbreviation: ONS, other nervous system 0.1 $-d$ $-d$ 1.3 0.1 88% 7.8 0.5 91% Abbreviation: ONS, other nervous system 0.1 $-d$ $-d$ 1.3 0.1 88% 7.8 0.5 91% Abbreviation: ONS, other nervous system 0.1 $-d$ $-d$ 1.3 0.1 88% 7.8 0.5 91% Abbreviation: on one should reader are aper 100,000 population and are age adjusted to the 2000 US standard population. Mortality and incidence are not directly comparable for some cancer types for which cases are defined using the reserved code reader and soft-tissue sarcomas.These exclude being mather of these correspond to the following adolescent and young adult site recode/World Health Organization 2008 definitions: bone tumors, including osseous and chrondomatou.The one shown because there were fewer than 16 cases or deaths or could not be calculated because of data limitations.Data are not shown because there were fewer than 16 cases or deaths or could not be calculated because of data limitations.	Testicular germ cell tumors	3.5	<0.1	96%	11.7	0.2	95%	13.0	0.2	96%
Uterine cervix 0.1 $-d$ $-d$ 3.1 0.3 82% 12.1 1.9 80% Uterine corpus 0.1 $-d$ $-d$ $-d$ 1.3 0.1 82% 0.5 91% Abbreviation: ONS, other nervous system. ¹ Incidence and death rates are per 100,000 population and are age adjusted to the 200 US standard population. Mortality and incidence are not directly comparable for some cancer types for which cases are defined using information, including testicular germ cell tumors. ¹ These exclude benign and borderline brain tumors. ¹ For incidence and borderline brain tumors. ¹ For incidence and solution and are equivated to the 2000 US standard population. Mortality and incidence are not directly comparable for some cancer types for which cases are defined using transmation, including testicular germ cell tumors. ¹ For incidence and summa borderline brain tumors. ¹ For incidence and summa borderline brain tumors. ¹ For incidence and summa borderline transmation that and intraspinal tumors.	Thyroid	3.1	٩	%66	8.7	<0.1	>99%	18.8	<0.1	>66
Uterine corpus 0.1 — 0.1 — 0.5 91% Abbreviation: ONS, other nervous system. Abbreviation: ONS, other nervous system. Incidence and death rates are per 100,000 population and are age adjusted to the 2000 US standard population. Mortality and incidence are not directly comparable for some cancer types for which cases are defined using this exclude brain tumors, brain and ONS tumors, bone tumors, and soft-tissue sarcomas. For incidence and benefined nervous system tumors, and other intracranial and intraspinal tumors. These exclude benefined nervous contral nervous system tumors, and other intracranial and intraspinal tumors. For incidence and surval, coding for these cancer types correspond to the following adolescent and young adult site recode/World Health Organization 2008 definitions: bone tumors, including osseous and chrondomatous tumors, brain and ONS tumors, central nervous system tumors, and other intracranial and intraspinal tumors. Data are not shown because there were fewer than 16 cases or deaths or could not be calculated because of data limitations.	Uterine cervix	0.1	٩	β	3.1	0.3	82%	12.1	1.9	80%
Abbreviation: ONS, other nervous system. Incidence and death rates are per 100,000 population and are age adjusted to the 2000 US standard population. Mortality and incidence are not directly comparable for some cancer types for which cases are defined using information, including testicular germ cell tumors, brain and ONS tumors, bone tumors, and soft-tissue sarcomas. These exclude benign and borderline brain tumors. For incidence and survival, coding for these cancer types correspond to the following adolescent and young adult site recode/World Health Organization 2008 definitions: bone tumors, including osseous and chrondomatous tumors, brain and ONS tumors, and intraspinal tumors.	Uterine corpus	0.1	р 	۹ ا	1.3	0.1	88%	7.8	0.5	91%
^c For incidence and survival, coding for these cancer types correspond to the following adolescent and young adult site recode/World Health Organization 2008 definitions: bone tumors, including osseous and chrondomatous tumors, bene tumors, and other intracranial and intraspinal tumors. ^d Data are not shown because there were fewer than 16 cases or deaths or could not be calculated because of data limitations.	Abbreviation: ONS, other nervous ^a lncidence and death rates are pe histology information, including te ^b These exclude benign and border	system. rr 100,000 population sticular germ cell tum line brain tumors.	and are age adju ors, brain and ON	sted to the 2000 US star IS tumors, bone tumors,	ndard population. Mor and soft-tissue sarcon	tality and incidence nas.	e are not directly compar-	able for some cancer	r types for which	i cases are defined using
	^c For incidence and survival, codir. tumors, brain and ONS tumors, cc ^d Data are not shown because then	g for these cancer typ entral nervous system e were fewer than 16	tumors, and other cases or deaths c	the following adolescen r intracranial and intrasp or could not be calculated	t and young adult site inal tumors. because of data limit	recode/World Hea ations.	Ith Organization 2008 def	initions: bone tumor	s, including osse	eous and chrondomatou.

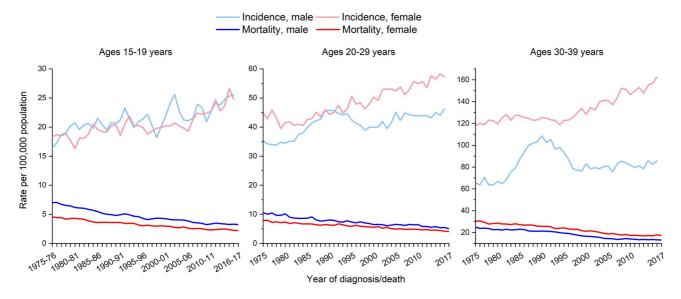


FIGURE 2. Trends in Adolescent and Young Adult Cancer Incidence and Mortality Rates for All Cancers Combined by Age and Sex, 1975 to 2017. Rates are age adjusted to the 2000 US standard population, and incidence rates are adjusted for reporting delays. Rates for those aged 15 to 19 years are 2-year moving averages.

rates have occurred across all age groups (Fig. 4), largely reflecting increased detection because of advances in imaging.²⁷ Other cancers for which rates are increasing in AYAs include those that have similarly been linked to increased detection (eg, kidney), as well as those cancers associated with the obesity epidemic (eg, colorectal, kidney, uterine corpus, and possibly leukemia).^{28,29} However, the extent to which known risk factors contribute specifically to the rising incidence in AYAs is unclear, and further research is needed. For example, the increase in kidney cancer, which is the most rapidly increasing cancer across all AYA age groups, is largest for high-grade, aggressive tumors and renal cell carcinoma; renal pelvic cancer rates have not similarly increased, as would be expected from increased detection.³⁰

By race/ethnicity, cancer incidence rates among AYAs are highest in non-Hispanic Whites (83 per 100,000 population) and lowest in Asian/Pacific Islanders (APIs) (54 per 100,000 population) for both sexes (Fig. 5). This reflects generally higher rates in non-Hispanic Whites for thyroid cancer, testicular GCTs, and melanoma compared with other major racial/ethnic groups. Overall incidence rates during 2007 through 2016 increased among AYA women for all racial/ethnic groups except AI/ANs (Table 5), among whom rates were stable. Incidence was generally stable among men across all racial/ethnic groups except for APIs and Hispanics, among whom rates increased annually by 1.5% and 0.8%, respectively. These increases largely reflect rates for testicular GCT and thyroid cancer, especially among Hispanics, among whom testicular GCT incidence rates rose by nearly 3% annually, for reasons that are unknown.¹⁵

Cancer Survival and Stage Distribution

Except for a decline during the HIV/AIDS epidemic from the mid-1980s to the mid-1990s among men aged 20 to 39 years, overall 5-year survival among AYAs has increased since the mid-1970s.^{12,13} Five-year relative survival rates for AYA patients diagnosed during 2009 through 2015 were generally similar across age groups (range, 83%-86%) (Table 3) and were comparable to the rate in children (84%) but were substantially higher than that in adults aged ≥ 40 years (66%).¹³ However, overall AYA cancer survival is largely influenced by the high survival rates of thyroid cancer,³¹ which has a 5-year survival rate >99%. In addition, many other common cancers in young adults have high 5-year survival rates (eg, \geq 94% for testicular GCTs, melanoma, and Hodgkin lymphoma) because of highly effective treatment for testicular GCTs, Hodgkin lymphoma, and early-stage melanoma (Table 3). AYAs are diagnosed at earlier stages than older adults for most cancers except colorectal and female breast cancers, which is due not only to screening differences but also to diagnosis delays resulting from less access to health care.³²

Despite comparable cancer survival in AYAs and children, survival in AYAs is lower for some cancer types.^{33,34} For example, the 5-year relative survival rate for patients with ALL who were diagnosed during 2009 through 2015 was higher in children (91%) than in AYAs overall (60%) and in every age group (Table 3).¹³ Similarly, the 5-year survival rate for patients with non-Kaposi soft-tissue sarcoma was lower in AYAs than in children (73% vs 81%) despite higher survival during 1975 through 1977 (70% vs 58%).¹²

Five-year cancer-specific survival in AYAs for all cancer types combined is lower in racial/ethnic minorities, especially

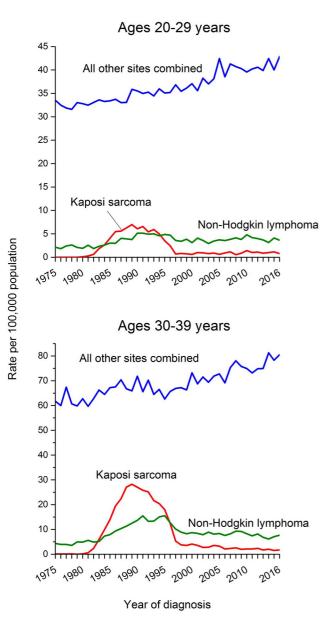


FIGURE 3. Kaposi Sarcoma and Non-Hodgkin Lymphoma Incidence Rates Compared With All Other Cancers Combined Among Young Adult Men, 1975 to 2016. Incidence rates are age adjusted to the 2000 US standard population and are adjusted for reporting delays.

individuals who are non-Hispanic Black (75%) compared with those who are non-Hispanic White (88%) (Fig. 6).¹³ Some of the largest disparities occur among those who are non-Hispanic Black and Hispanic compared with non-Hispanic Whites for ALL (57% and 58% vs 71%, respectively) and female breast cancer (78% and 85% vs 89%, respectively) and among AI/ANs compared with non-Hispanic Whites for colorectal cancer (59% vs 72%, respectively). These disparities are not only driven by differences in the timeliness and quality of diagnosis and treatment as a result of inequities in insurance status and access to care but also by differences in tumor characteristics, such as estrogen receptor status for female breast cancer.^{10,35}

Mortality

The leading causes of cancer death differ substantially by age group (Table 6). In 2017, leukemia and brain tumors were among the leading cancer causes of death in all sex and age groups except women aged 30 to 39 years, among whom breast, cervical, and colorectal cancers were the leading cancer causes of death. Importantly, leukemia continues to be the leading cause of cancer death in both adolescents and adults aged 20 to 29 years, a point that is masked when adolescents are combined with children, among whom brain cancer is the leading cancer cause of death.³⁶

In contrast to incidence, cancer death rates among AYAs aged 15 to 29 years are higher in males than in females (Table 3) because of differences in case distribution and lower survival in males for some common cancers (eg, melanoma).¹⁶ By race/ethnicity, non-Hispanic Black AYAs have the highest cancer mortality rates (11 per 100,000 population) despite 25% lower incidence rates than those in non-Hispanic Whites. In women, this largely reflects substantial disparities in breast cancer mortality; breast cancer death rates in non-Hispanic Black women in their 30s are nearly double those in non-Hispanic White women (8.5 vs 4.5 deaths per 100,000 population, respectively).¹⁷

Cancer mortality rates in AYAs have been steadily declining in all age and sex groups since at least 1975 (Fig. 2). Notably, these trends do not reflect the impact of the HIV/ AIDS epidemic because deaths from HIV/AIDS-related cancers are often attributed to the underlying viral infection. In addition, Kaposi sarcoma was not a separate reportable cause of death until 1999. During the most recent 10 years of available data (2008-2017), mortality rates for all cancers combined declined on average by approximately 1% per year in both men and women but leveled off in recent years among women aged 30 to 39 years, likely reflecting stable rates for breast cancer mortality after more than 2 decades of decline (Table 4). By race/ethnicity, mortality declines over the past decade were steepest in non-Hispanic White and Black AYAs and were stable in Hispanics, AI/AN men, and API women (Table 5).

Selected sites

Brain and other nervous system tumors

Malignant brain and other nervous system tumors (also referred to as brain cancer) are a substantial cause of morbidity and mortality in AYAs. An estimated 3700 cases of malignant brain tumors are expected to be diagnosed among AYAs in 2020 (Table 2). Brain cancer is the most common cause of cancer death in AYA men and the second leading cause overall after breast cancer (Table 6). Gliomas account for the majority of cases in AYAs, similar to other age groups. Among AYAs, however, there is substantial heterogeneity in the distribution of other brain tumor subtypes by age: adolescents have a higher TABLE 4. Ten-Year Fixed-Interval Trends in Incidence (2007-2016) and Mortality (2008-2017) Rates for Selected Cancers in Adolescents and Young Adults^a

CANCER TYPE 15 TO 19 YEARS All cancer types 0.9 ^b Male 1.2 ^b Female 1.0 ^b							
	20 TO 29 YEARS	30 TO 39 YEARS	15 TO 39 YEARS	15 TO 19 YEARS	20 TO 29 YEARS	30 TO 39 YEARS	15 TO 39 YEARS
	0.5 ^b	1.0 ^b	1.0 ^b	-1.7 ^b	-1.5 ^b	-0.6 ^b	de.0–
	0.7 ^b	0.8 ^b	0.5 ^b	-1.7 ^b	-1.4 ^b	-0.7 ^b	-1.0 ^b
	1.1 ^b	1.3 ^b	1.2 ^b	-1.8 ^b	-1.7 ^b	-0.5	-0.7 ^b
	-0.1	0.3	-0.1	-0.1	-2.2	0.8 ^b	-0.8
Brain and ONS 0.4	-1.6 ^b	-0.5 ^b	-0.8 ^b	-1.0	-0.8 ^b	1.1 ^b	0.5
Breast (female) -2.1	1.9 ^b	0.2 ^b	0.2 ^b	Ŭ	0.7	-0.4	-0.3
Colon and rectum ^d 0.6	0.9 ^b	1.5 ^b	1.4 ^b	⁰	-0.0	1.0 ^b	0.8 ^b
Hodgkin lymphoma —0.2 ^b	-0.7 ^b	-1.2 ^b	-1.1 ^b	J	-9.9 ^b	-10.7 ^b	-10.5 ^b
Kidney and renal pelvis	2.6 ^b	3.2 ^b	3.1 ^b	Ŭ	2.3 ^b	-1.2 ^b	1.4
Leukemia 1.0 ^b	1.0 ^b	1.3 ^b	0.6	—2.3 ^b	-3.1 ^b	-2.0 ^b	—1.9 ^b
Acute lymphocytic leukemia 0.7 ^b	1.4 ^b	1.9 ^b	1.3 ^b	-2.7 ^b	-1.5 ^b	-0.1	-1.8 ^b
Acute myeloid leukemia 1.1 ^b	0.4 ^b	1.2 ^b	0.9 ^b	-1.1 ^b	– 3.8 ^b	-2.1 ^b	-2.8 ^b
Lung and bronchus 0.3	0.3	–3.3 ^b	-2.8 ^b	Ŭ	-4.8	-5.1 ^b	-4.8 ^b
Melanoma of the skin —6.2 ^b	-3.5 ^b	-0.7	-1.5 ^b	J	-7.5 ^b	-4.8 ^b	-5.2 ^b
Non-Hodgkin lymphoma 0.9 ^b	-0.2	-0.8 ^b	-0.5 ^b	-4.8 ^b	—5.0 ^b	—3.3 ^b	-4.0 ^b
Oral cavity and pharynx 0.6	0.5	0.1	0.2	Ŭ	-1.0 ^b	-1.5 ^b	-1.5 ^b
Soft-tissue sarcoma	-0.5 ^b	-1.1 ^b	-0.8 ^b	-0.5 ^b	-0.4 ^b	0.7	-0.3 ^b
Kaposi sarcoma	2.5 ^b	–5.9 ^b	-4.3 ^b	Ŭ	J	Ŭ	Ĭ
Testicular germ cell tumors	0.4 ^b	0.9 ^b	0.6 ^b	Ŭ	0.6	2.3	0.5
Thyroid 4.3 ^b	2.5b	2.8 ^b	2.8 ^b	Ŭ	Ŭ	-0.8 ^b	-0.5 ^b
Uterine cervix —4.8 ^b	-1.6 ^b	-0.0	-0.3	Ŭ	1.2	0.2	0.4
Uterine corpus 0.9	2.5 ^b	3.0 ^b	2.9 ^b	J	0.5	2.3 ^b	2.3 ^b
Abbreviations: AAPC, average annual percent change; ONS, other nervous system. [#] Fixed-interval trends represent the 10-year AAPC based on 1995 to 2016 incidence rates and 1975 to 2017 mortality rates. AAPCs were calculated allowing up to 4 joinpoints for incidence trends and 5 joinpoints for mortality trends. Trends.	ONS, other nervous system. ed on 1995 to 2016 incidenc and (P < 05)	se rates and 1975 to 201	17 mortality rates. AAPC	s were calculated allowi	ng up to 4 joinpoints for	r incidence trends and 5	joinpoints for mor
©Data were too sparse in some data spears to calculate trends.	trends.						

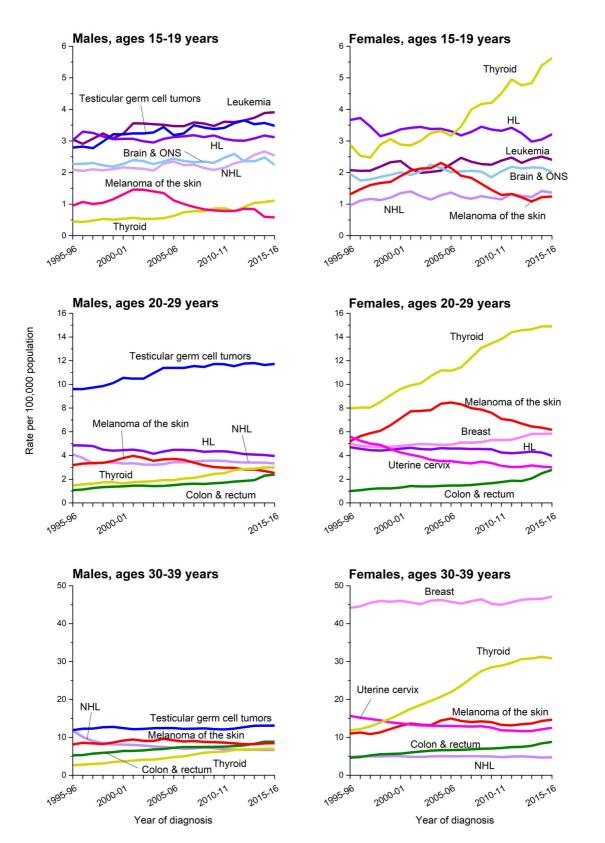


FIGURE 4. Trends in Adolescent and Young Adult Cancer Incidence Rates by Site and Age, 1995 to 2016. Rates are age adjusted to the 2000 US standard population and are 2-year moving averages. HL indicates Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; ONS, other nervous system.

proportion of intracranial GCTs and other brain tumors associated with childhood, such as medulloblastoma, than those aged 20 to 39 years.³⁷ For example, during 2012 through 2016, medulloblastoma accounted for 9% of brain and other nervous system tumors in adolescents compared with 3% of tumors in the group aged 30 to 39 years.

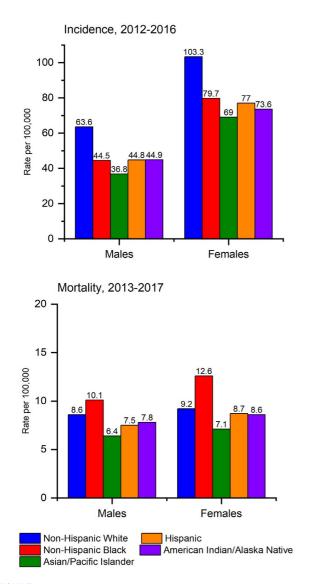


FIGURE 5. Cancer Incidence and Mortality Rates by Sex and Race/Ethnicity, Ages 15 to 39 Years, 2012 to 2017. Rates are per 100,000 population and age adjusted to the 2000 US standard population. Rates for American Indians/Alaska Natives are based on Preferred/Referred Delivery Care Area counties.

From 2007 to 2016, brain cancer incidence rates were stable in adolescents and declined among adults aged 20 to 39 years (Table 4). Reasons for these trends are unknown, as there are few established risk factors for brain tumors other than exposure to ionizing radiation.³⁸ Current trends may be influenced by recent changes in reporting after an improved understanding of tumor biology, as has been hypothesized for younger age groups.³⁹ The 5-year relative survival rate for malignant brain tumors ranges from 77% in adolescents to 66% in the group aged 30 to 39 years, largely reflecting differences in the aggressiveness of glioma subtypes by age.¹³ For example, the 5-year relative survival rate for patients with astrocytoma who were diagnosed during 2009 through 2015 was 76% in adolescents compared with 50% in the group aged 30 to 39 years.

TABLE 5.Ten-Year Fixed-Interval Trends in Cancer
Incidence (2007-2016) and Mortality (2008-2017)
Rates by Race/Ethnicity in Adolescents and
Young Adults^a

	INCIDE	NCE AAPC	MORTAI	.ITY AAPC
RACE/ETHNICITY	MALE	FEMALE	MALE	FEMALE
Non-Hispanic White	0.2	0.8 ^b	-1.3 ^b	-1.6 ^b
Non-Hispanic Black	0.0	0.5 ^b	-1.2 ^b	-2.0 ^b
Asian/Pacific Islander	1.5 ^b	1.4 ^b	-1.7 ^b	0.6
American Indian/Alaska Native	0.4	0.3	-0.7	-1.1 ^b
Hispanic	0.8 ^b	1.5 ^b	-0.1	0.9

Abbreviation: AAPC, average annual percent change.

^aFixed-interval trends represent the 10-year AAPC based on 1995 to 2016 incidence rates and 1990 to 2017 mortality rates. AAPCs were calculated allowing up to 4 joinpoints for incidence trends and 5 joinpoints for mortality trends. ^bThe AAPC is statistically significantly different from zero (*P* < 0.05).

Benign and borderline brain tumors account for a large proportion of overall cases of brain tumors in all age groups; among AYAs in particular, this percentage ranges from 48% in adolescents to 63% in the group aged 30 to 39 years.¹⁴ Incidence rates for these cancers, which were not reportable until 2004, have increased in recent years largely because of improvements in reporting.⁴⁰ The overall 5-year relative survival rate for benign and borderline tumors is relatively high, at approximately 97%, in all AYA age groups.⁴¹

Female breast

Breast cancer is the most commonly diagnosed cancer among women aged 30 to 39 years, with an estimated 11,100 cases expected in 2020 (Table 2). It is the leading cancer cause of death in AYA women, accounting for 22% of cancer deaths in 2017 (Table 6). The risk of developing breast cancer at a young age is higher for women with a family history of the disease, particularly a diagnosis in a relative aged younger than 50 years and in those with heritable mutations in cancer susceptibility genes (eg, BRCA1/BRCA2) or certain other genetic syndromes (eg, Li-Fraumeni syndrome).42 However, most AYA women who are diagnosed with breast cancer do not have these risk factors.⁴³ Reproductive risk factors generally do not appear to differ long-term by age or menopausal status.^{44,45} However, among younger women, the risk of breast cancer is temporarily increased after first birth.

Incidence rates in non-Hispanic Black AYAs are 14% higher than those in non-Hispanic White AYAs (25.9 vs 22.3 per 100,000 population during 2012-2016)¹⁹ in contrast to older women, among whom rates are highest in Whites. However, higher incidence rates in non-Hispanic Black AYAs are confined to hormone receptor–negative disease; in particular, triple-negative rates are >50% higher than those in non-Hispanic Whites (6.1 vs 3.9 per 100,000 population during 2012-2016, respectively).¹⁹ Notably, the

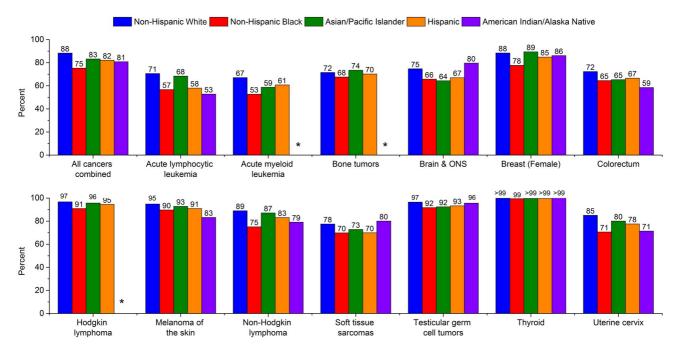


FIGURE 6. Five-Year Cause-Specific Survival by Race/Ethnicity for Selected Cancers in Adolescents and Young Adults, 2009 to 2015. Patients were diagnosed from 2009 to 2015 and followed through 2016. *Data are suppressed for American Indians/Alaska Natives because of sparse case numbers (<25 cases). ONS indicates other nervous system.

15 TO 39 YEARS			15 TO 19	9 YEARS		20 TO 29	9 YEARS		30 TO 39	YEARS	
					Ν	IALE					
CANCER TYPE	NO.	%		NO.	%		NO.	%		NO.	%
All sites	4303		All sites	332		All sites	1182		All sites	2789	
Brain and ONS	594	14%	Leukemia	87	26%	Leukemia	225	19%	Colon and rectum	388	14%
Leukemia	556	13%	Bone tumors	64	19%	Brain and ONS	169	14%	Brain and ONS	377	14%
Colon and rectum	467	11%	Brain and ONS	48	14%	Testis	100	8%	Leukemia	244	9%
					FE	MALE					
CANCER TYPE	NO.	%		NO.	%		NO.	%		NO.	%
All sites	4791		All sites	228		All sites	933		All sites	3630	
Breast	1063	22%	Leukemia	58	25%	Leukemia	118	13%	Breast	968	27%
Uterine cervix	514	11%	Brain and ONS	49	21%	Brain and ONS	117	13%	Uterine cervix	437	12%
Brain and ONS	407	8%	Bone tumors	40	18%	Breast	95	10%	Colon and rectum	338	9%

TABLE 6. Leading Cancer Causes of Death Among Adolescents and Young Adults by Age and Sex, 2017

Black-White disparity in breast cancer mortality is largest in AYAs and declines with age.⁴⁶ Death rates in non-Hispanic Black AYAs compared with those who are White are nearly double (3.9 vs 2.0 per 100,000 population, respectively, during 2013-2017),¹⁷ reflecting in part the higher rates of aggressive tumors with a poorer prognosis combined with inequities in access to high-quality cancer care.

During the most recent 10 years of available data, breast cancer incidence rates increased by nearly 2% annually among women aged 20 to 29 years and by 0.2% annually among women in their 30s; rates in adolescents were stable. The overall increase in female breast cancer is largely driven by non-Hispanic Whites, among whom rates have increased since at least 1995.¹⁵ Factors thought to be driving the increase include changes in reproductive patterns, such as declines in the fertility rate and older age at first birth. Breast cancer mortality rates are no longer decreasing in AYA women after more than 2 decades of continuous decline, likely reflecting increased incidence (Table 4) (Fig. 7).

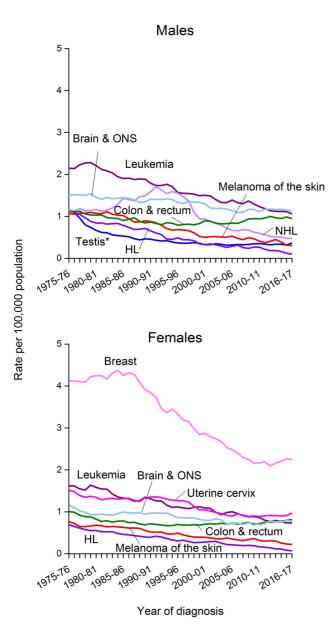


FIGURE 7. Trends in Adolescent and Young Adult Cancer Mortality Rates by Site, Ages 15 to 39 Years, 1975 to 2017. Rates are age adjusted to the 2000 US standard population and are 2-year moving averages. *These include all tumors of the testis and is not limited to germ cell tumors, because histologic information is unavailable on death certificates. HL indicates Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; ONS, other nervous system.

AYA patients with breast cancer are more commonly diagnosed at an advanced stage than older patients; less than one-half (47%) are diagnosed at a localized stage compared with 60% in patients aged 45 to 54 years and 65% in those aged 55 to 64 years.¹⁹ In addition to mammographic screening not being recommended for AYAs at average breast cancer risk, this also reflects diagnostic delays and a higher proportion of aggressive disease (eg, triple-negative breast cancer) at younger ages.^{16,47} As a result, the 5-year relative survival rate for female breast cancer is lower in AYAs than in older, screening-aged women (86% vs 91% in women aged 45-64 years).¹⁹

Colon and rectum (colorectum)

Colorectal cancer is the fourth most commonly diagnosed cancer among adults aged 30 to 39 years, with 4100 cases expected in 2020 (Table 2). In 2017, it was the leading cancer cause of death among men in this age group and the third among women (Table 6). Increasing evidence suggests that colorectal cancer in adults aged <30 years is unique from that diagnosed in older adults, in part because of a higher frequency of tumors occurring in the distal colon or rectum and exhibiting microsatellite instability and mucinous and signet ring cell histologies.⁴⁸ A family history of young-onset diagnosis and certain hereditary conditions (eg, Lynch syndrome, familial adenomatous polyposis) are associated with a higher risk of colorectal cancer before age 40 years.^{49,50}

During 2007 through 2016, colorectal cancer incidence rates increased by 0.9% and 1.5% annually among the groups aged 20 to 29 years and 30 to 39 years, respectively (Table 4). Mirroring incidence, colorectal cancer mortality rates likewise increased by approximately 1% annually among those aged 30 to 39 years during 2008 through 2017. These patterns reflect a birth cohort effect in which colorectal cancer risk has been increasing in subsequent generations since 1950.⁵¹ In contrast, rates in adults aged ≥ 65 years are continuing to rapidly decline, largely reflecting the widespread uptake of screening with colonoscopy since 2000.⁵² Reasons for the increases in young adults are not clear but may be associated with obesity and changes in dietary factors.²⁹ Similar trends among young adults have been observed in many other high-income countries.⁵³

The 5-year relative survival rate in the group aged 20 to 39 years for patients diagnosed during 2009 through 2015 was 68% (Table 3), similar to that in screening-aged adults.⁵²

Leukemia

ALL and acute myeloid leukemia (AML) account for the majority of leukemia cases in AYAs, with ALL comprising most cases in adolescents and AML becoming the predominant subtype among older AYAs (Table 2). Leukemia is among the most commonly diagnosed cancers in adolescents, with approximately 600 cases of ALL and AML combined expected in 2020. Overall, despite progress in optimizing cytotoxic chemotherapy regimens and, more recently, in molecularly targeted agents and immunotherapies, leukemia continues to be the leading cancer cause of death in the group aged 15 to 29 years (Table 6).⁵⁴

From 2007 through 2016, incidence rates increased by 0.7% to 1.9% annually for ALL and by 0.4% to 1.2% for AML. Increases in leukemia may be linked to increased exposure to radiation (including computed tomography exposure) and chemotherapy, although it is unclear to what extent each of these factors contributes.⁵⁵⁻⁵⁷ Obesity has also been

proposed as a contributing factor,²⁹ although this is based on prospective cohort studies that are largely confined to older adults.⁵⁷ The 5-year relative survival rate for ALL and AML is substantially higher in adolescents (74% and 66%, respectively) compared with older AYA age groups (Table 3), which may reflect inequities in access to care, differences in the receipt of adult versus pediatric treatment regimens, and more aggressive disease in older AYAs.⁵⁸ In one population-based study of AYA patients with ALL, higher overall survival was associated with pediatric regimens delivered in front-line pediatric oncology settings, regardless of age.⁵⁸

Lymphoma

Approximately 4200 cases of Hodgkin lymphoma and 4600 cases of non-Hodgkin lymphoma are expected to be diagnosed among AYAs in 2020. Whereas Hodgkin lymphoma accounts for the majority of lymphomas diagnosed in AYAs aged 15 to 29 years, non-Hodgkin lymphoma is more common in the group aged 30 to 39 years (Table 2). Non-Hodgkin lymphoma includes a constellation of subtypes that vary in occurrence by age. For example, Burkitt lymphoma accounts for a higher proportion of cases in adolescents than in older AYAs (15% vs 4% in those aged 30-39 years).¹⁴ Established risk factors for both Hodgkin lymphoma and some types of non-Hodgkin lymphoma (eg, Burkitt lymphoma) include prior infection with Epstein-Barr virus (EBV) as well as immunocompromising conditions, such as infection with HIV and immunosuppression after organ transplantation.^{59,60} Notably, although EBVassociated Hodgkin lymphoma cases appear to peak in AYAs aged 15 to 24 years, non-EBV-associated Hodgkin lymphoma is more common among older AYAs.⁵⁹ The risk for Hodgkin lymphoma and some non-Hodgkin lymphoma subtypes has also been linked to a family history of disease, particularly in siblings.^{61,62} Diffuse large B-cell lymphoma may also be linked to obesity.⁶³

Incidence rates for Hodgkin lymphoma declined by 0.2% to 1% annually across age groups from 2007 through 2016, while death rates declined even more dramatically, by 10% per year, during 2008 through 2017 (Table 4). Conversely, non-Hodgkin lymphoma incidence trends differ directionally by age, increasing by 1% annually in adolescents but declining in the group aged 30 to 39 years by 1% annually. However, overall non-Hodgkin lymphoma death rates are declining across AYA age groups. The 5-year relative survival rates for Hodgkin lymphoma and non-Hodgkin lymphoma exceeds 94% and 83%, respectively, across all AYA age groups but are slightly higher for adolescents than for older AYAs (Table 3).

Melanoma of the skin

Melanoma is the third most commonly diagnosed cancer in the group aged 20 to 39 years. An estimated 7900 cases are expected in 2020 among all AYAs combined. It is substantially more common in AYA women than in AYA men, in contrast to older adults, among whom rates are higher in men. Spitzoid malignant melanomas, some of which can be difficult to distinguish from benign Spitz nevi because of similarities in some clinical and histologic features, are rare but account for a higher proportion of melanoma cases in younger individuals compared with older adults.⁶⁴ In general, melanoma of the skin in AYAs appears to occur among susceptible individuals through genetic interactions with ultraviolet light exposure in early life, whereas melanoma in older adults likely reflects cumulative lifetime ultraviolet light exposure among those with comparatively less susceptibility.⁶⁵ Although indoor tanning has decreased in the United States,⁶⁶ its prevalence in young adult women remains substantially higher than that in older women and in men overall.¹⁸ Indoor tanning use is particularly important for AYAs, as the risk of melanoma is approximately 60% higher for people who begin use before age 35 years, and the risk increases with duration and intensity of use.^{67,68}

Melanoma incidence rates have rapidly declined in adolescents (6.2% annually during 2007-2016) and adults in their 20s (3.5% annually) after peaking in the early to middle 2000s (Table 4). Among the group aged 30 to 39 years, melanoma rates were stable among women in the most recent time period but slightly declined among men. Recent declines in younger AYAs may reflect successful interventions to reduce indoor tanning and increase sun-protective behaviors.⁶⁶ Mirroring incidence, mortality in AYAs has rapidly declined by approximately 5% annually. The 5-year relative survival rate is generally high for melanoma in AYAs (ie, >94%), reflecting the high proportion of cases (80%) diagnosed at an early stage (Fig. 8). Although the higher proportion of spitzoid melanoma cases in younger patients has been proposed to confer a survival advantage compared with older patients, existing research has largely focused on pediatric cases, and further research specific to AYAs is needed.⁶⁴

Testicular germ cell tumors

Gonadal GCT rates are substantially higher in AYA men than in AYA women for reasons that are largely unknown but may reflect sex-specific interactions between genetic factors and maternal hormones before birth.¹⁷ An estimated 6500 cases of testicular GCT are expected to be diagnosed in AYA men in 2020 (Table 2). Testicular GCTs are the most commonly diagnosed cancer among men aged 20 to 39 years, with rates peaking at ages 30 to 39 years (13 per 100,000 population during 2012-2016).¹⁹ Testicular GCT rates are highest in non-Hispanic Whites (13 per 100,000 population), followed by Hispanics (10 per 100,000 population), and AI/ANs (10 per 100,000 population), and are lowest in non-Hispanic Black AYAs (2.4 per 100,000 population).¹⁹ With the exception of cryptorchidism and Klinefelter syndrome, risk factors

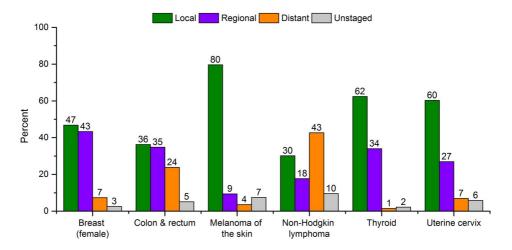


FIGURE 8. Stage Distribution for Selected Cancers in Adolescents and Young Adults, 2012 to 2016.

for testicular GCT are not well described, although a family history of testicular GCT in a first-degree relative has been shown to increase risk 4-fold.^{12,18}

During the most recent 10 years of available data, incidence rates for testicular GCTs increased in all AYA age groups by 0.4% to 1.1% annually, whereas mortality rates were stable (Table 4). Little is known about the causes of the rising incidence rates of testicular GCTs, but trends may reflect changes in *in utero* exposures to maternal hormones as well as other environmental exposures.^{69,70} A strong birth cohort effect in testicular GCTs has been described in the United States and several northern European countries, where rates are likewise increasing.⁵³ The 5-year relative survival rate is generally high for testicular GCTs, exceeding 95% in all age groups (Table 3)

Thyroid

Thyroid cancer is the most commonly diagnosed cancer in adolescents and in AYAs aged 20 to 29 years in both sexes combined. An expected 14,400 cases are projected to be diagnosed in 2020 among all AYAs (Table 2); most of these cases will occur among women. Similar to older adults, papillary thyroid cancer accounts for most cases of thyroid cancer in AYAs. During the most recent 10 years of available data, thyroid cancer incidence rates rose rapidly in all AYA age groups, whereas mortality rates declined slightly by 0.5% annually (Table 4). Although much of the increase in incidence rates has been attributed to increased detection, it is increasingly recognized that there may be a true rise in the burden of advanced-stage papillary thyroid cancer;²⁷ however, data for AYAs are sparse. In one study, exposure to tomographic scans substantially increased the risk of subsequent thyroid cancer by greater than 2-fold.⁵⁵ The 5-year relative survival rate for thyroid cancer is generally high and exceeds 99% in AYAs aged 20 to 39 years (Table 3). Previous studies have found that, although AYAs are more likely to be diagnosed with larger thyroid cancers or with locoregional lymph node involvement compared with older patients, they are less likely to be diagnosed with distant metastases and continue to have a better prognosis than their older counterparts.⁷¹

Uterine cervix

In 2020, an estimated 3800 cases of cervical cancer are expected among women aged 20 to 39 years (Table 2). Cervical cancer is the second leading cancer cause of death among women aged 30 to 39 years and among AYA women overall. All cases of cervical cancer are attributable to persistent infection with human papillomavirus, although susceptibility may be increased by cigarette smoking and immunocompromising factors.⁷² Recent use of oral contraceptives has also been shown to slightly increase risk.⁷³ However, the cancer can be prevented through vaccination against HPV infection or removal of precancerous lesions detected via screening. From 2013 through 2018, the percentage of women aged 18 to 26 years who reported ever initiating human papillomavirus vaccination (≥ 1 dose) increased from 37% to 54%, while series completion (≥ 2 doses) increased from 26% to 35%.⁷⁴ Squamous cell carcinoma is the most common histologic type for all age groups, although childhood cancers that are not detectable through routine screening, such as embryonal rhabdomyosarcoma, occur among young AYAs.⁷⁵

Cervical cancer incidence rates decreased by 1.6% annually during 2007 through 2016 among women in their 20s but appear to have stabilized among women in their 30s. The stable trend in women aged 30 to 39 years in part reflects attenuating declines in squamous cell cervical cancer rates combined with slight increases in adenocarcinoma rates.^{76,77} The 5-year relative survival rate for patients diagnosed during 2009 through 2015 was 82% for patients aged 20 to 29 years and 80% for those aged 30 to 39 years (Table 3). Nearly one-third of cases (34%) are diagnosed at the regional or distant stage, which may reflect screening delays or more aggressive histologic subtypes, particularly in younger AYA women. In 2018, approximately 74% of AYAs aged 21 to 29 years were up to date with cervical cancer screening, compared with 90% of adults aged 30 to 39 years and 86% of adults aged 40 to 65 years.¹⁸

Survivorship

AYA cancer survivors are at risk of several late and long-term effects that can influence cognitive, psychosocial, and physical functioning as well as financial prospects.^{78,79} Although cancer treatment regimens in AYAs can be tailored to minimize long-term and late effects, there is a paucity of data from clinical trials to support modifications.⁸⁰ In addition, similar to childhood cancer survivors, AYA cancer survivors have a notably higher risk of developing subsequent cancers compared to the general population. In one population-based study, approximately 14% of AYA cancer survivors developed a subsequent cancer 30 years postdiagnosis, with melanoma and breast, gastrointestinal, and genitourinary cancers being the most common subsequent malignancies.⁶ Another recent analysis of population-based data found that, whereas all-cause late mortality among 5-year AYA cancer survivors declined from 8% among those diagnosed during 1975 through 1984 to 5% among those diagnosed during 2005 through 2011, little improvement in late mortality from the original cancer was observed for several cancer types, including colorectal cancer, bone and soft-tissue sarcomas, and cervical cancer.⁸¹

Although much regarding AYA cancer survivorship continues to be extrapolated from childhood cancer survivor cohorts,⁸⁰ recent studies have pointed to notable differences between these 2 patient groups, highlighting the need for survivorship studies specific to AYAs. For example, in a retrospective cohort study of childhood and adolescent survivors, patients diagnosed at ages 15 to 20 years had lower long-term risks of severe, chronic health problems than childhood cancer survivors but a 1.5-fold higher risk of dying from recurrence or progression of their primary cancer.⁹ Furthermore, compared with both younger and older patient populations and cancer-free peers, AYA cancer survivors report worse overall psychosocial functioning, which may reflect difficultly in coping with cancer during early life transitions.⁸²⁻⁸⁴

Cancer and its treatment can cause substantial disruptions in school and career, as well as changes in functioning and appearance, leading to further challenges in resuming daily-life activities.⁸⁵ Difficulties with fertility, sexual dysfunction, and body image, particularly among women, are common among AYA cancer survivors.^{8,86} Among AYA survivors who need specific services, a high proportion report a variety of unmet needs within a year after diagnosis, such as access to a mental health professional (56%), cancer rehabilitation (58%), or pain-management services (63%).⁸⁷ Notably, a substantial proportion of AYA patients with cancer, especially women, do not receive adequate information about fertility preservation. In one study of AYA cancer survivors, 18% of males and 38% of females had not made such fertility-preservation arrangements because they were not aware of these options.⁸⁸

Finally, AYA cancer survivors experience more financial hardship than the general population and spend more on out-of-pocket medical costs,⁸⁹ which is compounded by higher uninsured rates among AYAs compared with other age groups. In 2018, uninsured rates in AYAs aged 19 to 25 years were similar to those in the group aged 26 to 34 years (14%), compared with 12% among those aged 34 to 44 years and 9% among those aged 45 to 64 years.⁹⁰ Being uninsured or having public health insurance is associated with significant delays in diagnosis in AYAs, leading to poorer outcomes and more extensive treatment.⁹¹ Compared with older survivors, young survivors have higher rates of bankruptcy and more frequently forgo needed medical care because of cost.⁹²

Conclusions

Although there has been rapid progress in the scientific understanding of cancer in AYAs over the last decade, several research gaps in etiology, basic biology, treatment, and survivorship remain. AYAs diagnosed with cancer also continue to face numerous challenges in health care access during early life transitions, which can negatively impact the timeliness of and adherence to treatment. Although declining mortality rates for hematologic malignancies in AYAs point toward progress in effective treatment for these cancers in recent decades, this progress has lagged behind that for children for some cancers, especially in older AYAs. Further progress in reducing cancer morbidity and mortality among AYAs could be addressed through more equitable access to health care; increasing clinical trial enrollment; expanding research on etiology, basic biology, and survivorship; and greater alertness among clinicians and patients for early symptoms and signs of cancer. Research on cancer in AYAs should also consider the heterogeneity in cancer occurrence within this patient population. In addition, further monitoring of population-based trends for cancers for which mortality rates are increasing, including colorectal and uterine corpus cancers, is warranted.

References

 US Department of Health and Human Services. Closing the Gap: Research and Care Imperatives for Adolescents and Young Adults with Cancer. Report of the Adolescent and Young Adult Oncology Progress Review Group. NIH publication 06-6067. US Department of Health and Human Services; 2006.

- Tricoli JV, Boardman LA, Patidar R, et al. A mutational comparison of adult and adolescent and young adult (AYA) colon cancer. *Cancer.* 2018;124:1070-1082.
- 3. Tricoli JV, Blair DG, Anders CK, et al. Biologic and clinical characteristics of

adolescent and young adult cancers: acute lymphoblastic leukemia, colorectal cancer, breast cancer, melanoma, and sarcoma. *Cancer*. 2016;122:1017-1028.

 Bleyer A, Barr R, Hayes-Lattin B, et al. The distinctive biology of cancer in adolescents and young adults. *Nat Rev Cancer.* 2008;8:288-298.

- Chao C, Bhatia S, Xu L, et al. Incidence, risk factors, and mortality associated with second malignant neoplasms among survivors of adolescent and young adult cancer. *JAMA Netw Open*. 2019;2:e195536.
- Lee JS, DuBois SG, Coccia PF, Bleyer A, Olin RL, Goldsby RE. Increased risk of second malignant neoplasms in adolescents and young adults with cancer. *Cancer.* 2016;122:116-123.
- Chao C, Xu L, Bhatia S, et al. Cardiovascular disease risk profiles in survivors of adolescent and young adult (AYA) cancer: the Kaiser Permanente AYA Cancer Survivors Study. J Clin Oncol. 2016;34:1626-1633.
- Olsson M, Enskar K, Steineck G, Wilderang U, Jarfelt M. Self-perceived physical attractiveness in relation to scars among adolescent and young adult cancer survivors: a population-based study. J Adolesc Young Adult Oncol. 2018;7:358-366.
- Suh E, Stratton KL, Leisenring WM, et al. Late mortality and chronic health conditions in long-term survivors of early-adolescent and young adult cancers: a retrospective cohort analysis from the Childhood Cancer Survivor Study. *Lancet Oncol.* 2020;21:421-435.
- Smith EC, Ziogas A, Anton-Culver H. Delay in surgical treatment and survival after breast cancer diagnosis in young women by race/ethnicity. *JAMA Surg.* 2013;148:516-523.
- Barr RD, Ferrari A, Ries L, Whelan J, Bleyer WA. Cancer in adolescents and young adults: a narrative review of the current status and a view of the future. *JAMA Pediatr.* 2016;170:495-501.
- Greene MH, Kratz CP, Mai PL, et al. Familial testicular germ cell tumors in adults: 2010 summary of genetic risk factors and clinical phenotype. *Endocr Relat Cancer*. 2010;17:R109-R121.
- Davies L, Welch HG. Current thyroid cancer trends in the United States. *JAMA Otolaryngol Head Neck Surg.* 2014;140:317-322.
- 14. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: North American Association of Central Cancer Registries (NAACCR) Incidence Data-Cancer in North America (CiNA) Analytic File, 1995-2016, for Expanded Races, Custom File With County, American Cancer Society Facts and Figures Projection Project (which includes data from the Centers for Disease Control and Prevention's National Program of Cancer Registries, the Canadian Council of Cancer Registries' Provincial and Territorial Registries, and the National Cancer Institute's SEER Registries). National Cancer Institute,

Division of Cancer Control and Population Sciences, Surveillance Research Program; 2018.

- 15. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: North American Association of Central Cancer Registries (NAACCR) Incidence Data-Cancer in North America (CiNA) Analytic File, 1995-2016, for the NAACCR Hispanic Identification Algorithm (NHIA) version 2 Origin, Custom File With County, American Cancer Society Facts and Figures Projection Project (which includes data from the Centers for Disease Control and Prevention's National Program of Cancer Registries, the Canadian Council of Cancer Registries' Provincial and Territorial Registries, and the National Cancer Institute's SEER Registries). National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2018.
- Anders CK, Johnson R, Litton J, Phillips M, Bleyer A. Breast cancer before age 40 years. Semin Oncol. 2009;36:237-249.
- Arora RS, Alston RD, Eden TO, Geraci M, Birch JM. Comparative incidence patterns and trends of gonadal and extragonadal germ cell tumors in England, 1979 to 2003. *Cancer.* 2012;118:4290-4297.
- Nordsborg RB, Meliker JR, Wohlfahrt J, Melbye M, Raaschou-Nielsen O. Cancer in first-degree relatives and risk of testicular cancer in Denmark. *Int J Cancer*. 2011;129:2485-2491.
- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70:7-30.
- 20. Surveillance Research Program, National Cancer Institute. SEER*Stat Software. National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2020.
- 21. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: National Program of Cancer Registries (NPCR) and Surveillance, Epidemiology, and End Results (SEER) Incidence-US Cancer Statistics File for Delay Adjustment-1999-2016-jbk 072919 (created August 3, 2019). National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2019.
- 22. Fritz A, Percy C, Jack A, et al, eds. International Classification of Diseases for Oncology. 3rd ed. World Health Organization; 2000.
- 23. Barr RD, Holowaty EJ, Birch JM. Classification schemes for tumors diagnosed in adolescents and young adults. *Cancer*. 2006;106:1425-1430.
- 24. World Health Organization. International Statistical Classification of Diseases and

Related Health Problems. 10th Revision, Vols I-III. World Health Organization; 2011.

- National Cancer Institute. Joinpoint Regression Program, Version 4.7.0.0. Statistical Research and Applications Branch, National Cancer Institute; 2019.
- 26. Jemal A, Miller KD, Ma J, et al. Higher lung cancer incidence in young women than young men in the United States. *N Engl J Med.* 2018;378:1999-2009.
- Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM. Trends in thyroid cancer incidence and mortality in the United States, 1974-2013. JAMA. 2017;317:1338-1348.
- Liu PH, Wu K, Ng K, et al. Association of obesity with risk of early-onset colorectal cancer among women. *JAMA Oncol.* 2019;5:37-44.
- 29. Sung H, Siegel RL, Rosenberg PS, Jemal A. Emerging cancer trends among young adults in the USA: analysis of a population-based cancer registry. *Lancet Public Health.* 2019;4:e137-e147.
- 30. King SC, Pollack LA, Li J, King JB, Master VA. Continued increase in incidence of renal cell carcinoma, especially in young patients and high grade disease: United States 2001 to 2010. *J Urol.* 2014;191:1665-1670.
- 31. Siegel SE, Coccia PF, Barr R, Hayes-Lattin B, Bleyer A. RE: A reappraisal of sex-specific cancer survival trends among adolescents and young adults in the United States. *J Natl Cancer Inst.* 2019;111:633-634.
- Martin S, Ulrich C, Munsell M, Taylor S, Lange G, Bleyer A. Delays in cancer diagnosis in underinsured young adults and older adolescents. *Oncologist*. 2007;12:816-824.
- 33. Tricoli JV, Seibel NL, Blair DG, Albritton K, Hayes-Lattin B. Unique characteristics of adolescent and young adult acute lymphoblastic leukemia, breast cancer, and colon cancer. *J Natl Cancer Inst.* 2011;103:628-635.
- 34. Bleyer A, Montello M, Budd T, Saxman S. National survival trends of young adults with sarcoma: lack of progress is associated with lack of clinical trial participation. *Cancer.* 2005;103:1891-1897.
- 35. DeRouen MC, Parsons HM, Kent EE, Pollock BH, Keegan THM. Sociodemographic disparities in survival for adolescents and young adults with cancer differ by health insurance status. *Cancer Causes Control.* 2017;28:841-851.
- Curtin SC, Minino AM, Anderson RN. Declines in Cancer Death Rates Among Children and Adolescents in the United States, 1999-2014. NCHS Data Brief, No. 257. National Center for Health Statistics; 2016.
- 37. Zapotocky M, Ramaswamy V, Lassaletta A, Bouffet E. Adolescents and young

adults with brain tumors in the context of molecular advances in neuro-oncology. *Pediatr Blood Cancer*. 2018;65:26861.

- Ostrom QT, Adel Fahmideh M, Cote DJ, et al. Risk factors for childhood and adult primary brain tumors. *Neuro Oncol.* 2019;21:1357-1375.
- Withrow DR, de Gonzalez AB, Lam CJK, Warren KE, Shiels MS. Trends in pediatric central nervous system tumor incidence in the United States, 1998-2013. Cancer Epidemiol Biomarkers Prev. 2019;28:522-530.
- Li XR, Kruchko C, Wu XC, et al. Are benign and borderline brain tumors underreported? *J Registry Manag.* 2016;43: 187-194.
- Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: Incidence-SEER 18 Registries Research Data + Hurricane Katrina Impacted Louisiana Cases, November 2018 Submission (2000-2016) <Katrina/Rita Population Adjustment>-Linked To County Attributes-Total US, 1969-2017 Counties. National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2019.
- 42. Lalloo F, Varley J, Moran A, et al. BRCA1, BRCA2 and TP53 mutations in very early-onset breast cancer with associated risks to relatives. *Eur J Cancer*. 2006;42:1143-1150.
- 43. Mai PL, Best AF, Peters JA, et al. Risks of first and subsequent cancers among TP53 mutation carriers in the National Cancer Institute Li-Fraumeni syndrome cohort. *Cancer*. 2016;122:3673-3681.
- 44. Dartois L, Fagherazzi G, Baglietto L, et al. Proportion of premenopausal and postmenopausal breast cancers attributable to known risk factors: estimates from the E3N-EPIC cohort. *Int J Cancer*. 2016;138:2415-2427.
- 45. Warner ET, Colditz GA, Palmer JR, Partridge AH, Rosner BA, Tamimi RM. Reproductive factors and risk of premenopausal breast cancer by age at diagnosis: are there differences before and after age 40? *Breast Cancer Res Treat*. 2013;142:165-175.
- DeSantis CE, Ma J, Gaudet MM, et al. Breast cancer statistics, 2019. CA Cancer J Clin. 2019;69:438-451.
- Ruddy KJ, Gelber S, Tamimi RM, et al. Breast cancer presentation and diagnostic delays in young women. *Cancer*. 2014;120:20-25.
- Willauer AN, Liu Y, Pereira AAL, et al. Clinical and molecular characterization of early-onset colorectal cancer. *Cancer.* 2019;125:2002-2010.
- 49. Bonadona V, Bonaiti B, Olschwang S, et al. Cancer risks associated with germline mutations in MLH1, MSH2, and

MSH6 genes in Lynch syndrome. *JAMA*. 2011;305:2304-2310.

- Galiatsatos P, Foulkes WD. Familial adenomatous polyposis. *Am J Gastroenterol*. 2006;101:385-398.
- Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal cancer incidence patterns in the United States, 1974-2013. J Natl Cancer Inst. 2017;109:djw322.
- Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. CA Cancer J Clin. 2020;70:145-165.
- 53. Gupta S, Harper A, Ruan Y, et al. International trends in the incidence of cancer among adolescents and young adults. *J Natl Cancer Inst.* Published online February 4, 2020. doi:10.1093/jnci/djaa007
- Kantarjian HM, Keating MJ, Freireich EJ. Toward the potential cure of leukemias in the next decade. *Cancer.* 2018;124: 4301-4313.
- 55. Shao YH, Tsai H, Sinae K, Wu YJ, Demissie K. Exposure to tomographic scans and cancer risk. *JNCI Cancer Spectr.* 2020;4:pkz072.
- 56. Morton LM, Swerdlow AJ, Schaapveld M, et al. Current knowledge and future research directions in treatment-related second primary malignancies. *EJC Suppl.* 2014;12:5-17.
- 57. Castillo JJ, Reagan JL, Ingham RR, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. *Leuk Res.* 2012;36:868-875.
- Muffly L, Alvarez E, Lichtensztajn D, Abrahao R, Gomez SL, Keegan T. Patterns of care and outcomes in adolescent and young adult acute lymphoblastic leukemia: a population-based study. *Blood Adv.* 2018;2:895-903.
- 59. Jarrett RF. Risk factors for Hodgkin's lymphoma by EBV status and significance of detection of EBV genomes in serum of patients with EBV-associated Hodgkin's lymphoma. *Leuk Lymphoma*. 2003;44(suppl 3):S27-S32.
- 60. Teras LR, Rollison DE, Pawlita M, et al. Epstein-Barr virus and risk of non-Hodgkin lymphoma in the Cancer Prevention Study-II and a meta-analysis of serologic studies. *Int J Cancer*. 2015;136:108-116.
- Altieri A, Bermejo JL, Hemminki K. Familial risk for non-Hodgkin lymphoma and other lymphoproliferative malignancies by histopathologic subtype: the Swedish Family-Cancer Database. *Blood.* 2005;106:668-672.
- 62. Linabery AM, Erhardt EB, Richardson MR, et al. Family history of cancer and risk of pediatric and adolescent Hodgkin lymphoma: a Children's Oncology Group study. Int J Cancer. 2015;137:2163-2174.
- 63. Willett EV, Morton LM, Hartge P, et al. Non-Hodgkin lymphoma and

obesity: a pooled analysis from the InterLymph Consortium. *Int J Cancer*. 2008;122:2062-2070.

- Pol-Rodriquez M, Lee S, Silvers DN, Celebi JT. Influence of age on survival in childhood spitzoid melanomas. *Cancer*. 2007;109:1579-1583.
- 65. Anderson WF, Pfeiffer RM, Tucker MA, Rosenberg PS. Divergent cancer pathways for early-onset and late-onset cutaneous malignant melanoma. *Cancer*. 2009;115:4176-4185.
- 66. Holman DM, Freeman MB, Shoemaker ML. Trends in melanoma incidence among non-Hispanic Whites in the United States, 2005 to 2014. *JAMA Dermatol.* 2018;154:361-362.
- Boniol M, Autier P, Boyle P, Gandini S. Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. *BMJ.* 2012;345:e4757.
- 68. Lazovich D, Isaksson Vogel R, Weinstock MA, Nelson HH, Ahmed RL, Berwick M. Association between indoor tanning and melanoma in younger men and women. *JAMA Dermatol.* 2016;152:268-275.
- Bray F, Ferlay J, Devesa SS, McGlynn KA, Moller H. Interpreting the international trends in testicular seminoma and nonseminoma incidence. *Nat Clin Pract Urol.* 2006;3:532-543.
- Morimoto LM, Zava D, McGlynn KA, et al. Neonatal hormone concentrations and risk of testicular germ cell tumors (TGCT). *Cancer Epidemiol Biomarkers Prev.* 2018;27:488-495.
- Vriens MR, Moses W, Weng J, et al. Clinical and molecular features of papillary thyroid cancer in adolescents and young adults. *Cancer.* 2011;117:259-267.
- Syrjanen K, Shabalova I, Petrovichev N, et al. Smoking is an independent risk factor for oncogenic human papillomavirus (HPV) infections but not for high-grade CIN. Eur J Epidemiol. 2007;22:723-735.
- 73. International Collaboration of Epidemiological Studies of Cervical Cancer, Appleby P, Beral V, et al. Cervical cancer and hormonal contraceptives: collaborative reanalysis of individual data for 16,573 women with cervical cancer and 35,509 women without cervical cancer from 24 epidemiological studies. *Lancet*. 2007;370:1609-1621.
- Boersma P, Black LI. Human Papillomavirus Vaccination Among Adults Aged 18-26, 2013-2018. NCHS Data Brief, No. 354. National Center for Health Statistics; 2020.
- Benard VB, Watson M, Castle PE, Saraiya M. Cervical carcinoma rates among young females in the United States. *Obstet Gynecol.* 2012;120:1117-1123.
- Islami F, Fedewa SA, Jemal A. Trends in cervical cancer incidence rates by age, race/ethnicity, histological subtype, and

stage at diagnosis in the United States. *Prev Med.* 2019;123:316-323.

- White A, Thompson TD, White MC, et al. Cancer screening test use—United States, 2015. MMWR Morb Mortal Wkly Rep. 2017;66:201-206.
- Barnett M, McDonnell G, DeRosa A, et al. Psychosocial outcomes and interventions among cancer survivors diagnosed during adolescence and young adulthood (AYA): a systematic review. J Cancer Surviv. 2016;10:814-831.
- 79. Warner EL, Kent EE, Trevino KM, Parsons HM, Zebrack BJ, Kirchhoff AC. Social well-being among adolescents and young adults with cancer: a systematic review. *Cancer*. 2016;122:1029-1037.
- National Comprehensive Cancer Network. Adolescent and Young Adult (AYA) Oncology. NCCN Clinical Practice Guidelines in Oncology. Version 1.2020. National Comprehensive Cancer Network; 2019.
- Anderson C, Nichols HB. Trends in late mortality among adolescent and young adult cancer survivors. J Natl Cancer Inst. Published online March 3, 2020. doi:10.1093/jnci/djaa014

- 82. Lang MJ, Giese-Davis J, Patton SB, Campbell DJT. Does age matter? Comparing post-treatment psychosocial outcomes in young adult and older adult cancer survivors with their cancer-free peers. *Psychooncology*. 2018;27:1404-1411.
- Bellizzi KM, Smith A, Schmidt S, et al. Positive and negative psychosocial impact of being diagnosed with cancer as an adolescent or young adult. *Cancer.* 2012;118:5155-5162.
- Dieluweit U, Debatin KM, Grabow D, et al. Social outcomes of long-term survivors of adolescent cancer. *Psychooncology*. 2010;19:1277-1284.
- Zebrack B, Isaacson S. Psychosocial care of adolescent and young adult patients with cancer and survivors. *J Clin Oncol.* 2012;30:1221-1226.
- Olsson M, Steineck G, Enskar K, Wilderang U, Jarfelt M. Sexual function in adolescent and young adult cancer survivors—a population-based study. *J Cancer Surviv.* 2018;12:450-459.
- 87. Keegan TH, Lichtensztajn DY, Kato I, et al. Unmet adolescent and young adult cancer survivors information and service

needs: a population-based cancer registry study. *J Cancer Surviv.* 2012;6:239-250.

- Shnorhavorian M, Harlan LC, Smith AW, et al. Fertility preservation knowledge, counseling, and actions among adolescent and young adult patients with cancer: a population-based study. *Cancer.* 2015;121:3499-3506.
- 89. Guy GP Jr, Yabroff KR, Ekwueme DU, et al. Estimating the health and economic burden of cancer among those diagnosed as adolescents and young adults. *Health Aff (Millwood)*. 2014;33:1024-1031.
- Berchick ER, Barnett JC, Upton RD. Current Population Reports, P60-267. Health Insurance Coverage in the United States: 2018. US Government Printing Office; 2019.
- Keegan THM, Parsons HM, Chen Y, et al. Impact of health insurance on stage at cancer diagnosis among adolescent and young adults. J Natl Cancer Inst. 2019;111:1152-1160.
- 92. Zheng Z, Jemal A, Han X, et al. Medical financial hardship among cancer survivors in the United States. *Cancer*. 2019;125:1737-1747.