Special Section: Cancer in Adolescents and Young Adults

Overview

In 2020, there will be approximately 89,500 new cancer cases and 9,270 cancer deaths in adolescents and young adults (AYAs) ages 15 to 39 years in the United States (Table S1). These patients are often grouped with younger or older patient populations, which masks important differences in cancer distribution, tumor biology, and survivorship. For example, an increasing body of evidence indicates that several types of cancer in AYAs are molecularly distinct from those that occur in other age groups, suggesting possible differences in how cancers in this age group develop and are most effectively treated.[1,2] In addition, for some cancer types, AYAs are more likely to be diagnosed at a late stage because of both delays in diagnosis due to the rarity of cancer in this age group and higher uninsured rates and higher prevalence of aggressive disease.[3,4] AYA patients also have a high risk of long-term and late effects, including infertility, sexual dysfunction, heart problems, and future cancers.[5-8]

Despite the number of obstacles facing AYA cancer patients, this group was understudied in the US until the mid-2000s, when the National Cancer Institute (NCI), in collaboration with the LIVESTRONG Foundation, convened a group of experts to report on priority areas for AYAs across the cancer continuum.[9] Although this landmark report provided the impetus for rapid progress over the past decade, several challenges remain, including research gaps in basic biology, treatment, and survivorship, as well as persistent disparities in health care access and survival for some common cancers.[10]

Table S1. Estimated Cancer Cases and Deaths in AYAs by Age, US, 2020

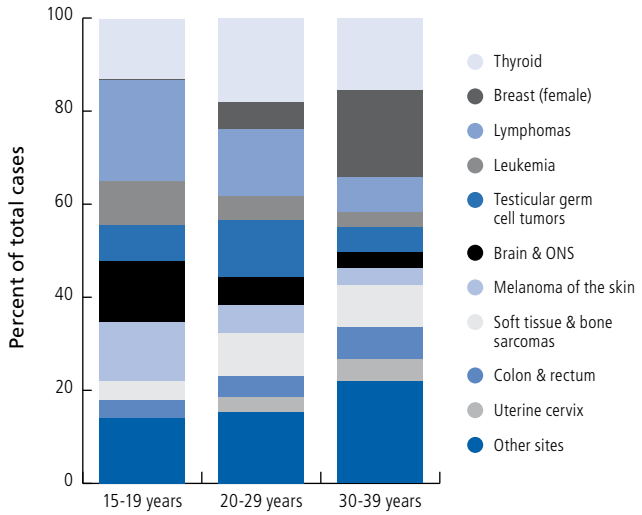
Age	Estimated cases	Estimated deaths
15-19 years	5,800	540
20-29 years	24,900	2,210
30-39 years	58,800	6,520
Total	89,500	9,270

In this special section, we provide an overview of trends in cancer incidence, mortality, and survival and discuss some of the unique challenges among AYAs. In order to fully describe the heterogeneity in the disease burden within AYAs, cancer occurrence is also described separately by age group.

Leading cancers in AYAs

The most common cancers among AYAs vary substantially by age and are shown in Figure S1. Adolescents (15- to 19-year-olds) have a unique cancer profile that includes childhood cancers (e.g., acute lymphocytic leukemia), adult cancers (e.g., thyroid and melanoma of the skin), and a disproportionately high burden of lymphoma. For example, Hodgkin lymphoma accounts for 13% of cancer cases in adolescents compared to 9% in ages 20-29 years and 3% in ages 30-39 years.[11] Conversely, adults 20-39 years have a higher proportion of solid tumors. In 2020, the most commonly

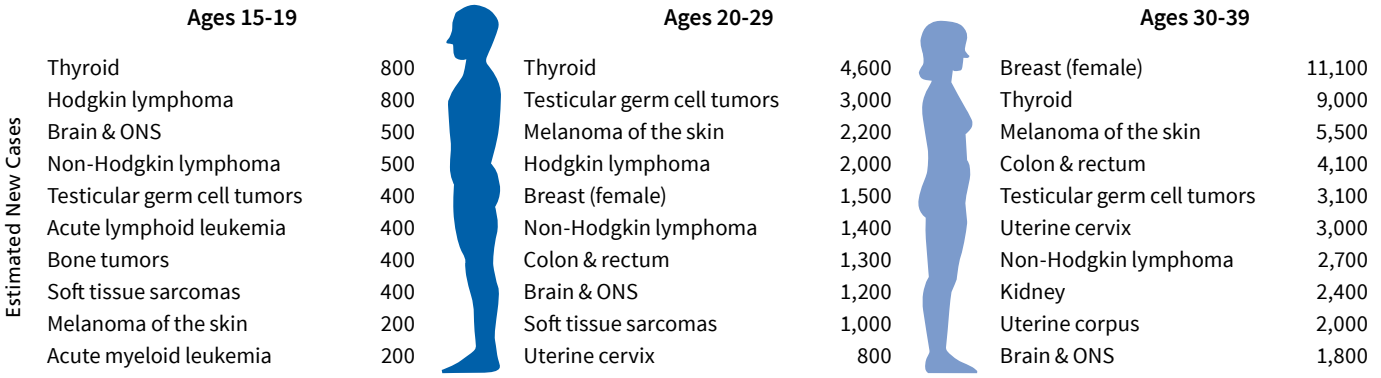
Figure S1. Case Distribution (%) of Leading Cancer Types in AYAs, US, 2012-2016



Coding for cancers of the thyroid, female breast, colon & rectum, and uterine cervix and melanoma of the skin are based on the SEER adult recode variable, excluding a small number of sarcomas.

Source: NAACCR, 2019.

Figure S2. Leading Sites of New Cancer Cases in AYAs, Both Sexes Combined – 2020 Estimates



ONS = other nervous system. Estimates are rounded to the nearest 100 and exclude basal cell and squamous cell skin cancers, benign and borderline brain, and in situ carcinoma of any kind. Ranking is based on modeled progress and may differ from the most recent observed data.

diagnosed cancers will be thyroid, testicular germ cell tumors (GCTs), and melanoma of the skin in ages 20-29 years and female breast, thyroid, and melanoma in ages 30-39 years (Figure S2).

Common cancer risk factors in AYAs

Little is known about the causes of many pediatric cancers that occur in AYAs, and established risk factors for adult cancers are based on studies conducted among older populations. Although the majority of cases in AYAs occur in the absence of a known hereditary predisposition,[12-14] certain genetic syndromes are strongly linked to early-onset cancers, such as:

- Lynch syndrome and colorectal, ovarian, and endometrial cancers[15]
- Familial adenomatous polyposis and colorectal cancer[16]
- Li-Fraumeni syndrome and several cancer types, including breast, sarcoma, brain, and leukemia[17]
- MEN2 familial syndrome and medullary thyroid cancer[18]

In addition, a history of cancer in a parent or sibling increases the risk of being diagnosed with cancer at a younger age, especially if the relative was diagnosed at a young age.[13, 19, 20] For example, men with a first-degree relative with a history of a testicular GCT are four times more likely to develop the disease compared to those without this medical history.[12, 21]

Research is still ongoing to describe the complex interactions between environmental exposures, health behaviors, and/or genetic susceptibility that likely precipitate the development of cancer in AYAs. For example, melanoma of the skin in AYAs appears to occur among susceptible individuals through genetic interactions with early-life UV exposure, whereas melanoma in older adults likely reflects cumulative lifetime UV exposure among those with less susceptibility.[22] However, some exposures may be linked to early-onset disease regardless of heredity. In one study, excess body weight was associated with an increased risk of early-onset colorectal cancer among women regardless of family history of the disease.[23]

Exposure to infectious agents is another important risk factor among AYAs. Infections associated with cancers in AYAs include human papillomavirus, Epstein-Barr virus, human immunodeficiency virus (HIV), and human herpesvirus 8. Importantly, although smoking-related cancers other than cervical are generally uncommon in AYAs, cigarette smoking increases susceptibility to these cancer-related infections.[24]

Cancer in AYAs by sex and race/ethnicity

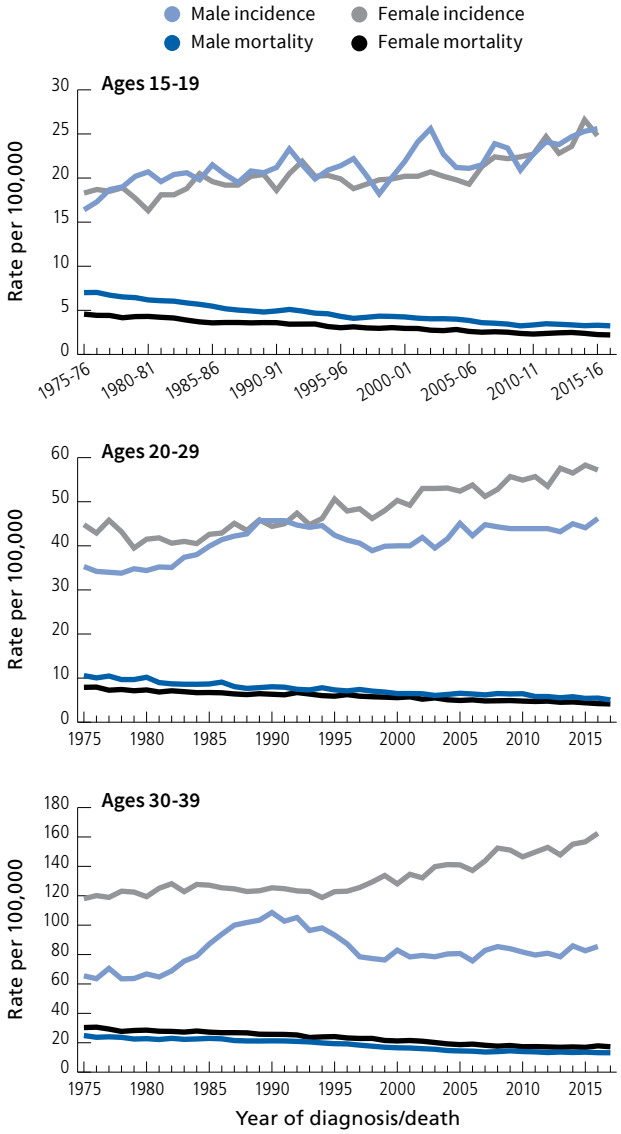
Sex

During 2012-2016, cancer incidence rates for all sites combined were similar in females and males ages 15-19 years (23 versus 24 cases per 100,000, respectively) but 30% higher in females compared to males ages 20-29 years (55 versus 42 per 100,000) and nearly double in females ages 30-39 years (161 versus 84 per 100,000).[11] Higher incidence rates in women ages 20-39 years are primarily driven by breast cancer, as well as higher rates of thyroid cancer and melanoma of the skin. For example, thyroid cancer incidence rates among women in their 20s are more than fivefold those among men (15 versus 3 per 100,000 during 2012-2016, respectively).[11] Notably, although lung cancer is rare in AYAs, incidence rates in women in their 30s are higher than those in men, in contrast to higher rates among men compared to women 50 years of age and older.[25] Higher lung cancer rates in young women are not fully explained by smoking prevalence.

Despite lower overall rates, incidence is higher in males than females for a number of cancers in AYAs. In particular, gonadal GCTs are substantially more common in males than females across all age groups, for reasons that are largely unknown but may reflect sex-specific interactions between genetic factors and maternal hormones prior to birth.[26] Testicular GCTs are the most commonly diagnosed cancer among young adult men, with rates peaking in the 30-39 age group (13 per 100,000 during 2012-2016).[11] Conversely, ovarian GCTs are rare and rates peak during adolescence (0.8 per 100,000).

In contrast to incidence, cancer mortality in males is slightly higher than in females among adolescents and young adults in their 20s (Figure S3), primarily reflecting higher incidence rates among males for cancers with lower survival (e.g., brain tumors and soft tissue and bone sarcomas).[27] Notably, melanoma and thyroid cancer death rates in females are similar to or lower than those in males despite higher incidence rates because much of the overall case burden is due to overdiagnosis (i.e., the detection of cancers that would never have progressed or caused harm), and males are slightly more likely to be diagnosed with distant-stage disease. Leukemia is the leading cause of cancer death in both males and females ages 15-29 years, whereas brain and breast cancers are the leading causes of death in males and females, respectively, ages 30-39 years. Although cervical cancer is highly preventable, it is the second-leading cause of cancer death among women ages 20-39 years.

Figure S3. Trends in AYA Cancer Incidence and Mortality Rates for All Cancers Combined by Age and Sex, US, 1975-2017



Rates are age adjusted to the 2000 US standard population and incidence rates are adjusted for reporting delays. Rates for 15- to 19-year-olds are two-year moving averages.

Sources: Incidence – SEER 9 registries; Mortality – National Center for Health Statistics (NCHS), 2019.

Race/Ethnicity

While AYAs account for 5% of cancer cases in the US overall, they represent about 1 in 10 cases among Hispanics and Asians/Pacific Islanders,[11] reflecting the young age structure of these populations. AYA cancer incidence rates are highest in non-Hispanic whites (83 per 100,000), followed by non-Hispanic blacks (63 per 100,000), and are lowest in Asians/Pacific Islanders (54 per 100,000) (Figure S4). However, non-Hispanic blacks have the highest cancer mortality rates (11 per 100,000) despite 25% lower incidence rates than those in non-Hispanic whites. In women, this largely reflects substantial disparities in breast cancer; breast cancer mortality rates in non-Hispanic black women in their 30s are nearly double those in non-Hispanic whites (8.5 versus 4.5 deaths per 100,000, respectively).[28]

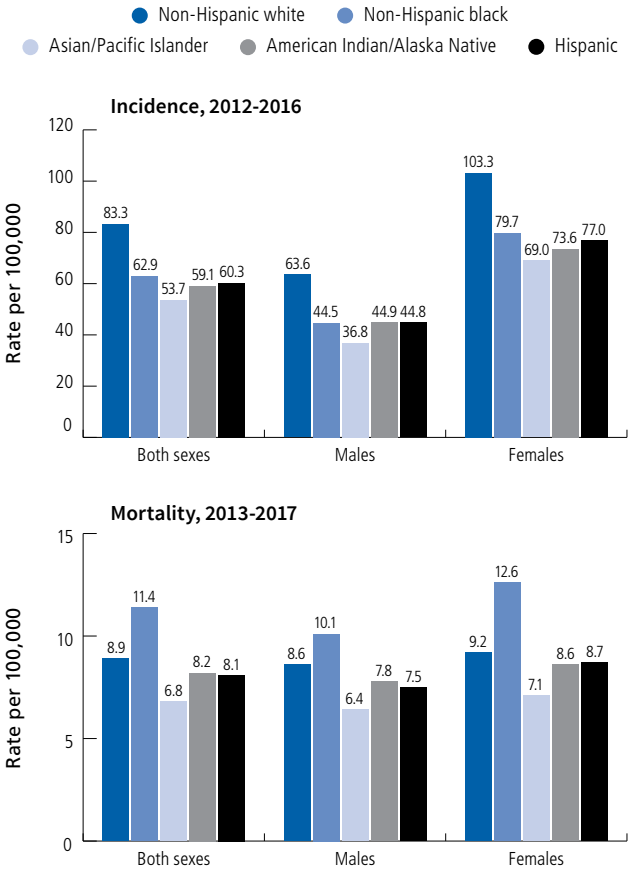
Trends in AYA cancer occurrence

Trends in incidence rates

In contrast to steadier trends among adolescents and young adult women, cancer incidence among young adult men increased rapidly in the late 1980s and declined in the early 1990s in parallel with the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) epidemic (Figure S3). This pattern primarily reflects a peak in the occurrence of Kaposi sarcoma (Figure S5). The HIV/AIDS epidemic did not contribute substantially to trends in female AYAs or male adolescents.

During the past decade of available data (2007-2016), rates in men ages 20-39 years were largely stable, whereas incidence rates increased by about 1% annually in

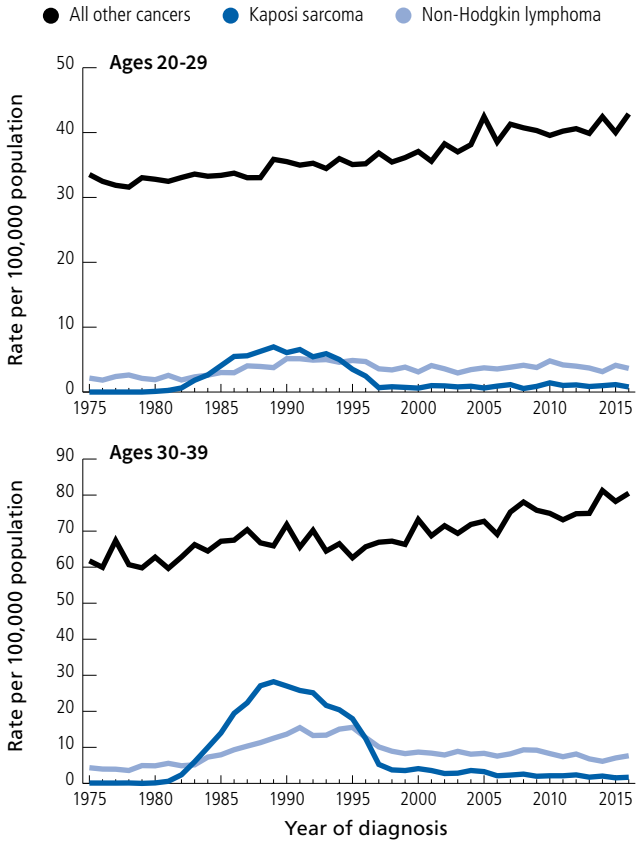
Figure S4. AYA Cancer Incidence and Mortality Rates by Sex and Race/Ethnicity, US, 2012-2017



Rates are per 100,000 and age adjusted to the 2000 US standard population. Rates for AIs/ANs are based on Preferred/Referred Delivery Care Area counties.

Sources: Incidence – NAACCR, 2019. Mortality – NCHS, 2019.

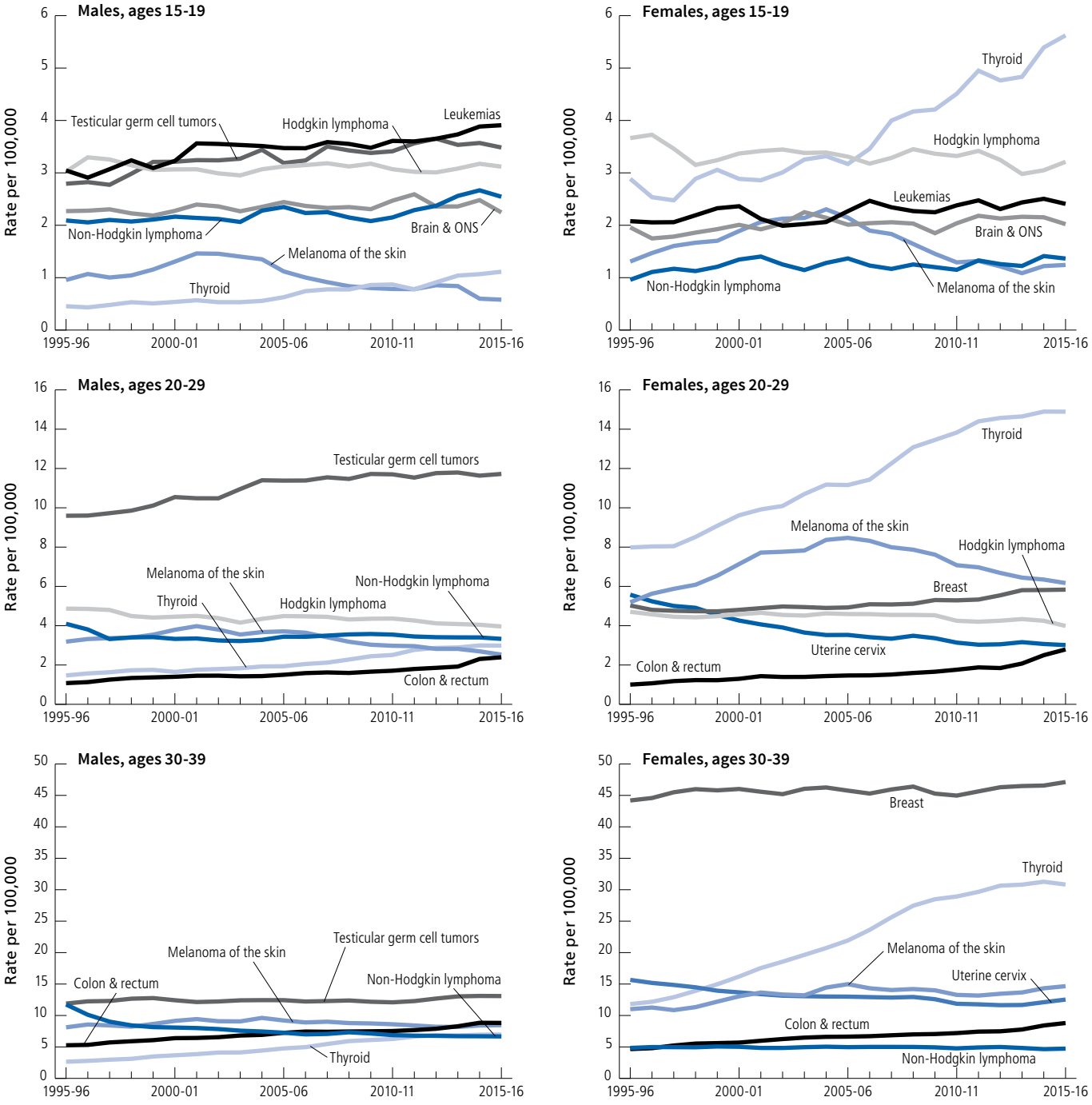
Figure S5. Kaposi Sarcoma and Non-Hodgkin Lymphoma Incidence Rates in Comparison to All Other Cancers Combined among Young Adult Men, US, 1975-2016



Incidence rates are age adjusted to the 2000 US standard population and are adjusted for reporting delays.

Sources: SEER 9 registries, 2019.

Figure S6. Trends in AYA Cancer Incidence Rates by Site and Age, US, 1995-2016

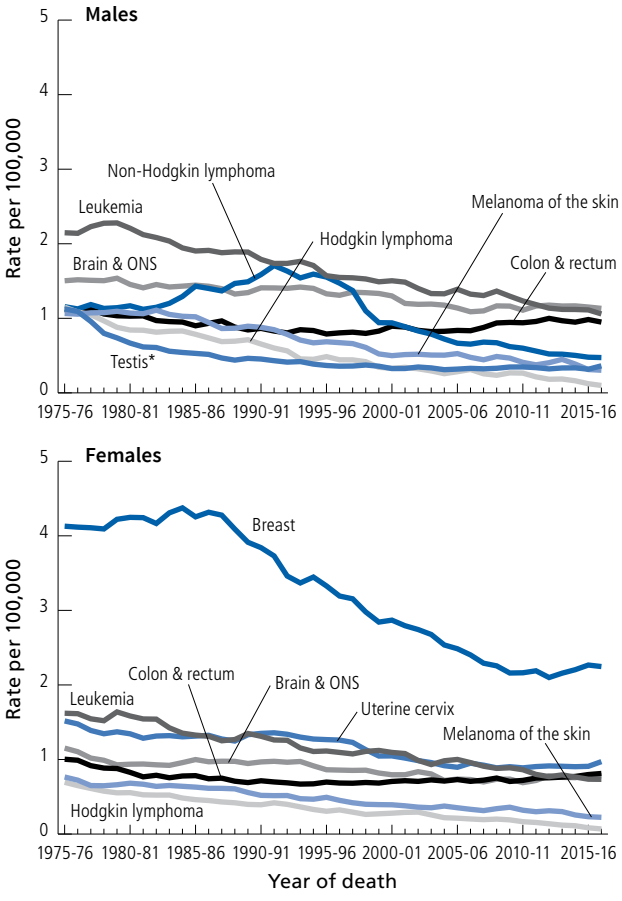


Rates are age-adjusted to the 2000 US standard population and are two-year moving averages.
Source: NAACCR, 2019.

adolescents and 0.4% to 1.1% annually in women ages 20-39 years. Contemporary trends, especially among women, are driven by rapid increases in thyroid cancer incidence rates as a result of rising detection of papillary thyroid tumors (Figure S6).[29] During 2007-2016, the steepest increases in thyroid cancer incidence rates occurred among adolescents, 4.9% per year among males and 4.1% per year among females. In adults ages 20-39

years, rates increased for cancers of the colorectum (3%-6% per year), uterine corpus (3%), kidney (3%), and female breast (0.2%-2%), with more rapid increases occurring among those in their 20s. While rates are also increasing in older adults for kidney and uterine corpus cancers, increases in AYAs are steeper.[30] Increasing attention has been given to the possible contribution of the obesity epidemic and related factors (e.g., poor diet) to rising incidence rates of many cancers in young adults, such as colorectal and uterine corpus.[23, 30] Increasing kidney cancer rates may partly reflect increased detection via advances in imaging. Rates also increased in all AYA age groups for leukemia in both sexes and testicular GCTs in men. Increases in leukemia may be linked to increased exposure to radiation and chemotherapy for the treatment of previous cancers, as well as obesity, although it is unclear to what extent each of these factors contributes.[30-32] Little is known about the causes of rising incidence rates of testicular GCTs, but trends may reflect changes in prenatal hormonal exposures, as well as other environmental exposures.[33, 34]

Figure S7. Trends in AYA Cancer Mortality Rates by Site and Sex, US, 1975-2017



Rates are age-adjusted to the 2000 US standard population and are two-year moving averages. *Includes all tumors of the testis or ovaries, as histological information is unavailable on death certificates.

Source: NCHS, 2019.

In contrast, melanoma incidence rates have rapidly declined in adolescents (6% annually during 2007-2016) and adults in their 20s (3% annually) after peaking in the early- to mid-2000s. Among adults in their 30s, melanoma rates remained stable in females and slightly declined among males. Recent declines in younger AYAs may reflect successful interventions to increase sun-protective behaviors and reduce indoor tanning.[35] Similarly, cervical cancer incidence rates decreased by 2% annually during 2007-2016 among women in their 20s but appear to have stabilized among women in their 30s. The stable trend in women ages 30-39 years largely reflects attenuating declines in squamous cell cervical cancer rates due to recent slight declines in cervical cancer screening with the Pap test.[36, 37] Incidence rates have largely declined or remained stable for other common AYA cancers, including Hodgkin lymphoma, non-Hodgkin lymphoma, soft tissue sarcomas, bone and joint tumors, and brain cancer.

Trends in mortality rates

Cancer mortality rates in AYAs have been declining in all age/sex groups since at least 1975 (Figure S3). However, these trends do not reflect the impact of the HIV/AIDS-related cancers because these deaths 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 about 1% per year in men but appear to have stabilized in recent years among women. In contrast to declines for many common cancers, death rates in AYAs during 2008-2017 increased for colorectal and uterine corpus cancer and were stable for cervical, thyroid, and testicular cancer (Figure S7).[27] Female breast cancer death rates have also stabilized in recent years after more than two decades of declines.

Cancer survival in AYAs

Overall 5-year survival has increased since the mid-1970s among AYAs with the exception of a decline during the HIV/AIDS epidemic among young adult men. Five-year relative survival rates for AYA patients diagnosed during 2009-2015 were generally similar across age groups (83%-86%) and comparable to that in children (84%), but substantially higher than that in adults 40 years of age and older (66%).[38] High overall survival in AYAs reflects 5-year relative survival rates of 94% or greater for many of the most common cancers, such as thyroid and testicular cancer, melanoma, and Hodgkin lymphoma, but masks lower rates for leukemias, brain tumors, and bone and soft tissue sarcomas (Table S2). Importantly, overall AYA cancer survival may be artificially inflated as a result of overdetection of thyroid cancer, which has >99% 5-year survival.[39]

Notably, there are some cancer types for which survival progress in AYAs has lagged behind that in children.[39] For example, AYAs have substantially worse 5-year relative survival than children for acute lymphocytic leukemia overall (60% versus 91%, respectively) and in every AYA age group (Table S2),[38] which may reflect differences in biology and/or clinical trial participation.[40] Similarly, the 5-year survival rate in AYAs for non-Kaposi soft tissue sarcoma was lower than that in children for patients diagnosed during 2009-2015 (73% versus 81%) despite a higher rate during 1975-77 (70% versus 58%).[41] This is partly due to the higher occurrence of aggressive clinical characteristics among non-Kaposi sarcomas in AYAs compared to those in children, but also reflects lower clinical trial participation among AYAs.[42]

AYAs have better 5-year relative survival for most cancers compared to older adults, with the exception of female breast (86% in AYAs versus 91% in ages 45-64 years).[38] AYA female breast cancer patients are less likely than older adults to be diagnosed with early-stage disease (47% versus 60% in ages 45-54 years, 65% in ages 55-64 years, and 68% in ages 65+ respectively),[11] which likely reflects diagnostic delays, as well as a higher prevalence of aggressive molecular subtypes.[43, 44] (See *Breast Cancer*

Table S2. Cancer Incidence (2012-2016), Mortality (2013-2017), and 5-year Relative Survival (2009-2015) Rates in AYAs by Age, US

	15-19 years			20-29 years			30-39 years		
	Incidence rate	Death rate	5-year survival, %	Incidence rate	Death rate	5-year survival, %	Incidence rate	Death rate	5-year survival, %
All cancer types	23.5	2.8	85%	48.5	4.9	86%	122.5	15.3	83%
Acute lymphocytic leukemia	1.7	0.3	74%	0.9	0.3	52%	0.7	0.3	51%
Acute myeloid leukemia	1.0	0.3	66%	1.1	0.3	59%	1.6	0.5	57%
Bone tumors	1.6	0.5	67%	0.8	0.3	68%	0.8	0.2	74%
Brain & ONS*	2.2	0.5	77%	2.5	0.6	73%	3.7	1.5	66%
Breast (female)	0.1	–	85%	5.7	0.4	83%	46.6	4.8	86%
Colon & rectum	0.9	<0.1	82%	2.2	0.3	68%	8.3	1.8	68%
Hodgkin lymphoma	3.1	<0.1	97%	4.1	0.1	95%	3.4	0.2	94%
Kidney & renal pelvis	0.2	<0.1	73%	0.9	0.1	83%	4.9	0.3	90%
Melanoma of the skin	1.0	<0.1	95%	4.5	0.2	96%	11.2	0.6	94%
Non-Hodgkin lymphoma	1.9	0.1	88%	2.9	0.3	83%	5.8	0.6	83%
Soft tissue sarcoma	1.3	0.3	69%	2.1	0.4	69%	3.6	0.5	74%
Testicular germ cell tumors	3.5	<0.1	96%	11.7	0.2	95%	13.0	0.2	96%
Thyroid	3.1	–	99%	8.7	<0.1	>99%	18.8	<0.1	>99%
Uterine cervix	0.1	–	–	3.1	0.3	82%	12.1	1.9	80%
Uterine corpus	0.1	–	–	1.3	0.1	88%	7.8	0.5	91%

– Data not shown due to fewer than 16 cases or deaths. ONS: Other nervous system. Incidence and death rates are per 100,000 and are age adjusted to the 2000 US standard population. *Excludes benign and borderline brain. Mortality and incidence are not directly comparable for some cancer types for which cases are defined using histology information, including testicular germ cell tumors, brain & ONS, bone tumors, and soft tissue sarcomas.

Source: Incidence – NAACCR, 2019. Mortality – NCHS, 2019. Survival – SEER 18 registries, 2019.

Facts & Figures 2019-2020, available on cancer.org, for more information.) In contrast, 5-year relative colorectal cancer survival in AYAs is higher than that in screening-age adults ages 50+ (68% versus 64%, respectively) despite a greater likelihood of being diagnosed with distant-stage disease (24% versus 20% during 2012-2016, respectively).[38]

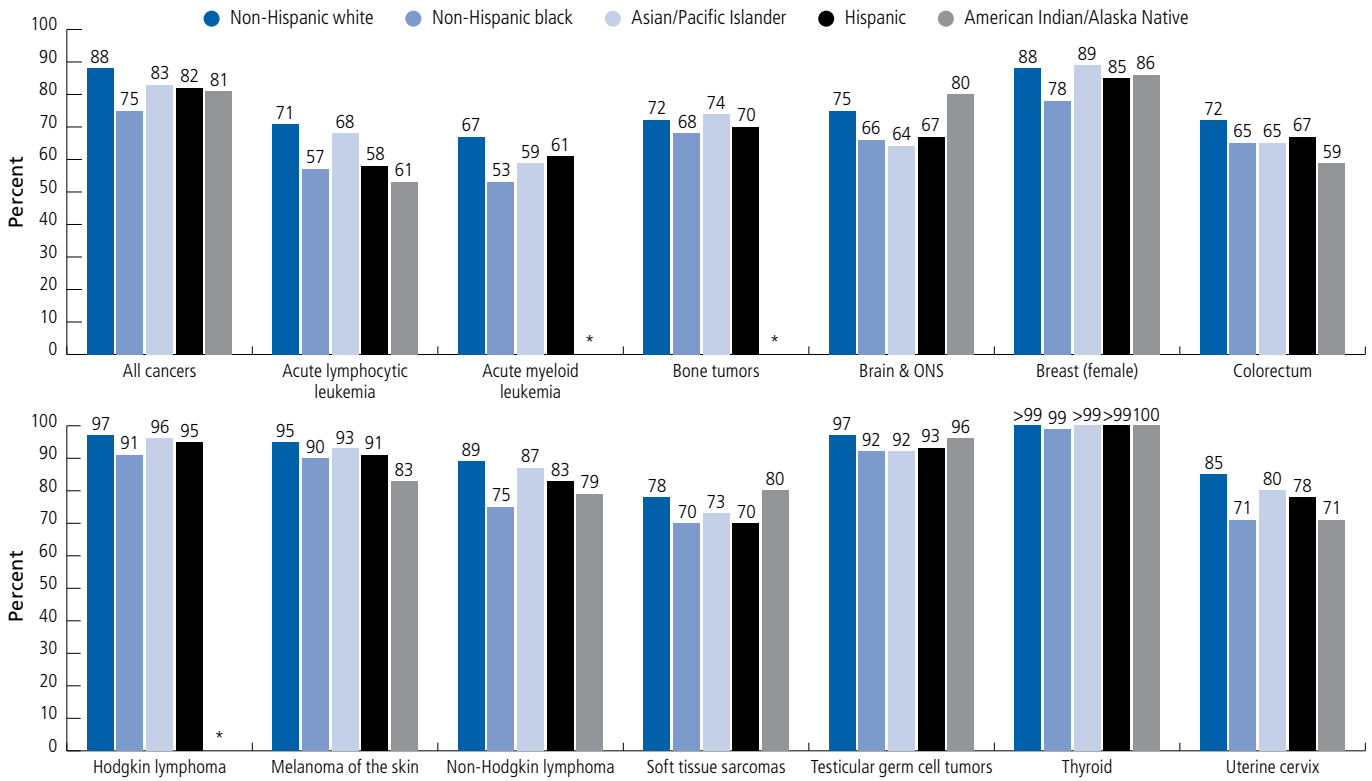
Compared to non-Hispanic whites, 5-year cause-specific survival in AYAs for all cancer types combined is lower in racial/ethnic minorities, especially non-Hispanic blacks (75% versus 88%, respectively) (Figure S8).[38] By cancer type, some of the largest black-white racial disparities occur for acute lymphocytic leukemia (57% versus 71%, respectively), melanoma (90% versus 95%), and female breast cancer (78% versus 88%). These disparities are largely driven by delays in diagnosis and treatment as a result of differences in insurance status and access to care, but also by differences in tumor characteristics, such as estrogen-receptor status for female breast cancer.[3,45]

Prevention and early detection of cancer in AYAs

Stage distribution for selected common cancers in AYAs is shown in Figure S9. Compared to screening-age adults, AYAs are more likely to be diagnosed at a distant stage for female breast and colorectal cancers.[3,4] Although routine cancer screening in individuals younger than 40 years of age is only recommended for cervical cancer (beginning at age 21; see page 70), increased awareness through self-examination could alert AYAs to changes in the skin, breasts, and testicles. In 2018, 74% of adults ages 21-29 years and 90% of those ages 30-39 years were up-to-date with cervical cancer screening, compared to 86% of adults ages 40-65 years.[46]

Several cancers in AYAs could potentially be prevented. For example, almost all cervical cancers can be prevented through screening, which allows for the removal of precancerous lesions, as well as human papillomavirus

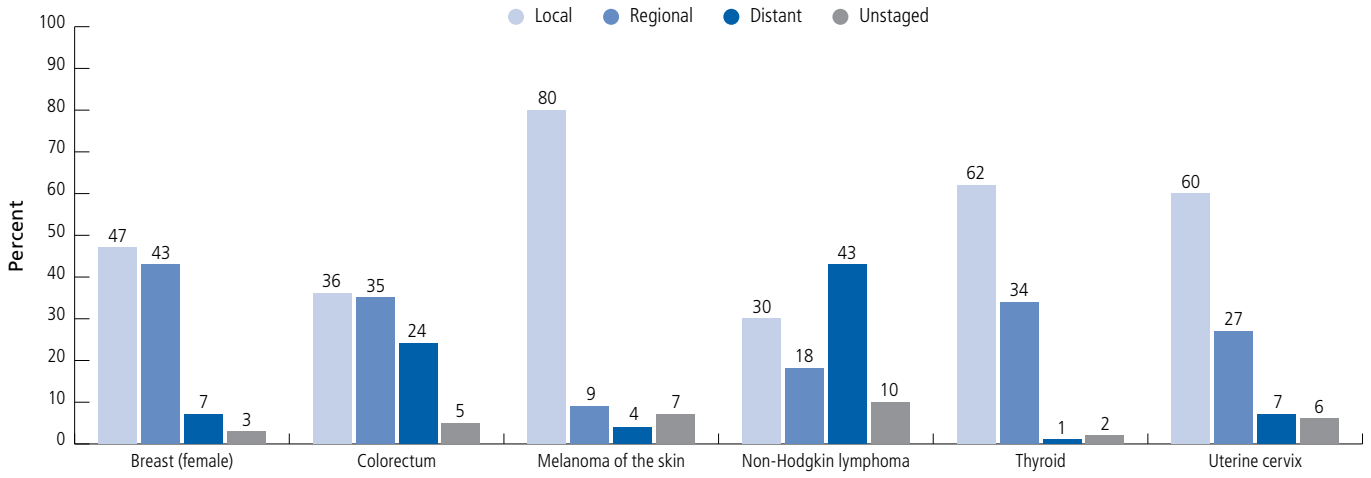
Figure S8. Five-year Cause-specific Survival by Race/Ethnicity for Selected Cancers in AYAs, US, 2009-2015



*Data are suppressed for American Indians/Alaska Natives for acute myeloid leukemia, bone tumors, and Hodgkin lymphoma due to sparse case numbers (<25 cases). Patients were diagnosed during 2009-2015 and followed through 2016.

Source: SEER 18 registries, 2019.

Figure S9. Stage Distribution for Selected Cancers in AYAs, US, 2012-2016



Source: NAACCR, 2019.

(HPV) vaccination, which is recommended for females up to age 26 and, depending on risk, males up to age 21.[47] Although studies have been primarily limited to the effectiveness of the HPV vaccine in preventing cervical cancer, the vaccine will likely prevent most other HPV-related cancers. From 2011-2012 to 2015-2016, HPV vaccination prevalence (receipt of ≥2 doses) increased among AYAs ages 18-26 years but remained low overall, especially in males (32% in ages 18-21 years and 17% in ages 22-26 years, compared to 54% in females).[48] This, combined with the comparatively low use of screening in women ages 20-29 years, highlights important targets for decreasing the burden of cervical and other HPV-associated cancers in AYAs. Finally, cervical and other tobacco-related cancers could be prevented through reducing cigarette smoking prevalence in AYAs. In 2018, cigarette smoking prevalence was similar between AYAs and older adults (15% and 16%, respectively).[46]

Reducing exposure to excess UV radiation through sun protective behaviors and not sunbathing or using indoor tanning are important for preventing melanoma and other skin cancers. The risk of melanoma is about 60% higher for people who begin using indoor tanning before the age of 35, and risk increases with duration and intensity of use.[49, 50] Although indoor tanning has decreased in the US,[35] in 2015, indoor tanning prevalence in women was 10% in ages 18-29 years and 7% in ages 30-39 years, compared to 4% in ages 40+; indoor tanning use among men was low (1-2%).[46]

Many additional cancers could be prevented in AYAs by reducing obesity prevalence. Increasing incidence rates for many solid tumors have been linked to rising excess bodyweight. Although trends may have leveled off in children and young adults in the past decade,[51] in 2015-2016, the prevalence of excess body weight (body mass index [BMI] ≥25 kg/m^2) among young adults ages 20-39 years was 65% (68% in men; 62% in women).[52]

Treatment considerations for AYAs with cancer

AYA patients can be treated at pediatric or adult cancer centers depending on cancer type.[53] It is important that the treatment team has experience in AYA oncology, as there are several special considerations for this age group. For example, it may be possible to adjust the treatment regimen to help limit the risk of late effects, such as sexual dysfunction and organ damage, given the long life expectancy of AYA patients. The type of treatment received should consider the patient's health and functional status; cognitive and physical development; and preferences and needs.[54] The possibility of adverse side effects, coupled with the financial and psychosocial challenges of undergoing treatment during several

important early-life transitions, may contribute to delays in treatment and gaps in adherence.[55] The National Comprehensive Cancer Network (NCCN) guidelines for AYA oncology recommend that AYA patients be encouraged to enroll in clinical trials as appropriate because of the substantial knowledge gaps in AYA cancer treatment.[54]

Fertility preservation and sexual function

Fertility counseling and preservation are crucial components in the management of AYA cancer because many cancer treatments directly or indirectly affect fertility.[56, 57] The American Society for Clinical Oncology (ACSO) clinical practice guidelines recommend that fertility preservation be discussed with all new patients at the time of diagnosis because efforts such as sperm banking and embryo/oocyte cryopreservation (the freezing of fertilized or unfertilized eggs) should be started in advance of treatment.[58] 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.[59] Other reasons for not making arrangements included cost; concerns regarding the impact of fertility preservation on outcomes (e.g., delaying cancer treatment, effects on offspring); and physician recommendation against delaying treatment, especially among females.[59]

Semen cryopreservation (sperm banking) is the established method for fertility preservation in men, including those with low sperm counts, and may also be possible in younger adolescents.[60-62] Research is ongoing with regard to cryopreservation (freezing) of stem cells from the testis, which may be an option in the future for prepubescent males.[62]

The established strategy for female fertility preservation in AYA women is egg (oocyte) cryopreservation.[63] Embryo cryopreservation is also an option, but requires that patients either have a partner or donor sperm for fertilization. Oocyte cryopreservation can take 2-3 weeks; the patient's ovaries are first stimulated with injectable hormones to produce mature eggs (oocytes), which are then retrieved in a procedure under anesthesia and cryopreserved in the lab the same day. When the patient desires to use the eggs in the future, they are thawed and fertilized with sperm to create embryos (via in vitro fertilization), and are then transferred into the woman's uterus. When cancer treatment cannot be delayed and/or the patient has not reached puberty, ovarian tissue cryopreservation may be an option for fertility preservation at some institutions.[58, 64, 65]

When female patients are planning to receive radiation therapy to the pelvic or groin area, ovarian transposition (a surgical repositioning of the ovaries) is an option. The procedure helps to preserve ovarian function by surgically positioning the ovaries away from the site of radiation. Typically, one or both ovaries are separated from the uterus and attached to the abdominal wall. Patients who undergo ovarian transposition may want to consider combining it with other fertility preservation options because the ovaries may not be completely protected from radiation exposure. In addition, the ovaries often cannot be reconnected in adults after they have been separated from the uterus, so these patients require referral to a reproductive endocrinologist when they wish to conceive.

Many cancer treatments can also interfere with sexual functioning both during and after treatment; in one study, nearly 50% of pelvic and breast cancer survivors experienced severe, long-term sexual dysfunction.[66] However, cancer patients often receive insufficient counseling and treatment for these concerns.[67] The American Society for Clinical Oncology recommends that problems with sexual health and dysfunction resulting from cancer or its treatment be discussed with all patients.[68] Patients may experience problems such as negative body image, low libido, and/or pain during intercourse, which can be addressed through a combination of psychosocial and/or psychosexual counseling, over-the-counter treatments (e.g., vaginal lubricants), or other medications (e.g., low-dose vaginal estrogen in women or phosphodiesterase type 5 inhibitors in men).

Cancer treatment during pregnancy

Although cancer during pregnancy is extremely rare (1 per 1,000 live births),[69] all women of childbearing potential should receive a pregnancy test before beginning

treatment.[54] Cancer during pregnancy poses significant treatment challenges and should be managed by a multidisciplinary team that includes obstetricians, gynecologic oncologists, and perinatologists in addition to medical, surgical, and radiation oncologists,[70] ideally with expertise in cancer during pregnancy.

While surgery for cancer is usually safe during pregnancy, some treatment options, such as radiotherapy, should generally be avoided, and chemotherapy should be avoided during the first trimester.[71] Limited research suggests chemotherapy during the second and third trimester may be associated with low birth weight and preterm labor,[72] but a multicenter prospective study found no significant adverse cognitive or cardiac effects among children.[73] The safety of hormonal therapies and targeted treatments during pregnancy has not been fully evaluated in humans.[54]

Survivorship concerns in AYA cancer

As of January 1, 2019, there were 678,420 adolescents and young adults (47,760 adolescents ages 15-19 years and 630,660 young adults ages 20-39 years) living in the United States with a history of a cancer diagnosis, some of whom were diagnosed as children.[74] AYA cancer survivors must cope with psychosocial, physical, and financial effects of cancer and its treatment, which range from mild to severe. A high proportion of AYA survivors 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%).[75]

Unfortunately, little is known about the long-term survivorship experience among AYAs compared to those who were diagnosed as children, and much continues to be extrapolated from childhood cancer cohorts.[54] Prospective studies of AYA cancer survivors in the US are still relatively nascent in comparison to decades-long cohort studies in children and older adults. The first national prospective cohort study of AYA cancer survivors in the US, the AYA Health Outcomes and Patient Experience (AYA HOPE) study, was conducted among those diagnosed during 2007-2008.[76]

Long-term and late effects

AYA cancer survivors are at risk of a number of late and long-term effects that can influence cognitive and physical functioning.[77, 78] In particular, they report worse overall psychosocial functioning than other cancer survivors as well as their cancer-free peers, which may reflect difficultly in coping with treatment and recovery during early-life transitions.[79-81] Problems with fertility, sexual dysfunction, and body image, particularly among women, are also common among AYA cancer survivors.[8, 82] Cancer and its treatment can cause substantial disruptions in school and work, as well as changes in functioning and appearance, leading to feelings of shame and isolation that can create further challenges in resuming daily life activities.[83] Cancer rehabilitation or other types of physical therapy may be helpful in some instances.

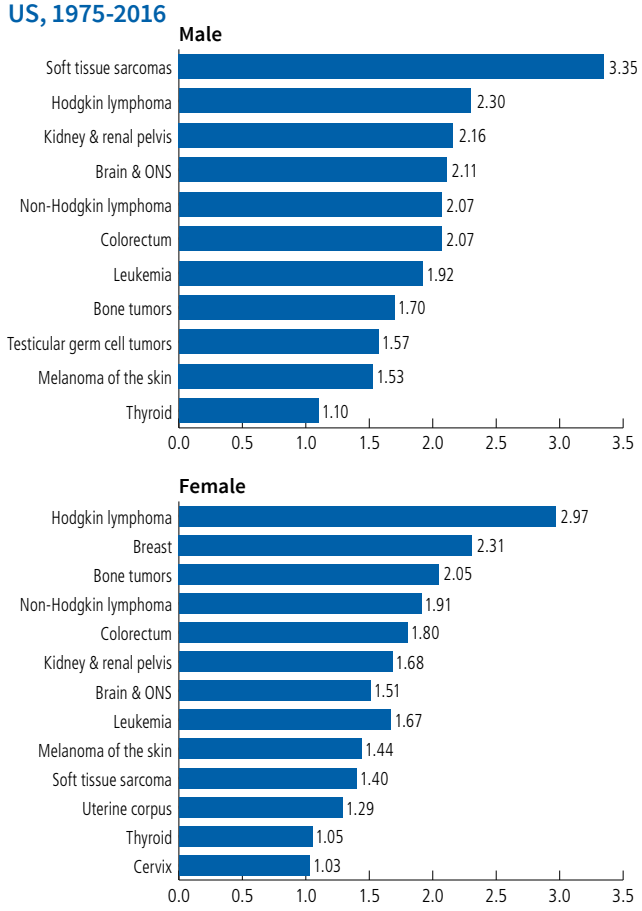
Certain types of chemotherapy used for common AYA cancers, such as anthracyclines for lymphomas, sarcomas, and brain tumors, have been associated with a long-term increased risk of heart problems in AYA cancer survivors.[84, 85] Testicular cancer survivors who were treated with cisplatin-based chemotherapy are at increased risk of heart and neurologic complications, such as numbness and hearing impairment.[86]

See *Cancer Treatment & Survivorship Facts & Figures 2019-2021*, available on cancer.org, for more information on long-term and late effects for common cancers.

Risk of subsequent cancers

The risk of subsequent cancers among AYA survivors can be approximated by comparing the number of new cancers in this population to the number expected in the general population, which is referred to as the observed-to-expected (O/E) ratio. Risk varies by original cancer type and sex and is highest for soft tissue sarcoma (males); Hodgkin lymphoma; and female breast cancer and lowest for thyroid and cervical cancer (Figure S10). The risk of subsequent cancers is related to many factors, including underlying genetic predisposition, adverse health behaviors, and type of initial treatment received. For example, a recent study showed that AYAs had a higher risk of subsequent tobacco-related cancers compared to the general population, likely reflecting

Figure S10. Observed-to-expected (O/E) Ratios for Subsequent Cancers by Primary Site, Ages 15-39, US, 1975-2016



Source: SEER 9 registries, 2019.

their higher historical smoking prevalence compared to the general AYA population.[87] Depending on the type of treatment received and underlying familial risk, some AYA cancer survivors are recommended to initiate screening for colorectal and female breast cancers at a younger age than those at average risk.[54]

Financial concerns

Young adults continue to be the least likely to have health insurance compared to other age groups. In 2017, uninsured rates in 20- to 25-year-olds and 26- to 39-year-olds were 15%, compared to 10% among 40- to 64-year-olds.[88] Lack of health insurance is associated with diagnosis delays, leading to more extensive treatment and poorer outcomes.[89] Not surprisingly, AYA cancer survivors have more financial hardship and out-of-pocket medical costs than the general population.[90] As a result, young adult survivors have higher rates of bankruptcy and more frequently forgo needed medical care due to cost compared to older survivors.[91] Financial distress among AYA survivors is often compounded by nonmedical costs, such as student loans and raising children.

Resources for clinicians and patients

National organizations and websites that provide information and support to adolescents and young adults with cancer:

- The OncoFertility Consortium (https://www.savemyfertility.org/)
- LIVESTRONG (LIVESTRONG Fertility: https://www.livestrong.org/we-can-help/livestrong-fertility)
- Children's Oncology Group (http://www.survivorshipguidelines.org)
- The Samfund: Support for Young Adult Cancer Survivors (https://www.thesamfund.org)
- Teen Cancer America (https://teencanceramerica.org)
- Cancer and Careers (https://www.cancerandcareers.org/en)
- Young Survival Coalition (https://www.youngsurvival.org)

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