Abstract: There are nearly 70,000 new cancer diagnoses made annually in adolescents and young adults (AYAs) in the United States. Historically, AYA patients with cancer, aged 15 to 39 years, have not shown the same improved survival as older or younger cohorts. This article reviews the contemporary cancer incidence and survival data through 2015 for the AYA patient population based on the National Cancer Institute’s Surveillance, Epidemiology, and End Results registry program and the North American Association of Central Cancer Registries. Mortality data through 2016 from the Centers for Disease Control and Prevention’s National Center for Health Statistics are also described. Encouragingly, absolute and relative increases in 5-year survival for AYA cancers have paralleled those of childhood cancers since the year 2000. There has been increasing attention to these vulnerable patients and improved partnerships and collaboration between adult and pediatric oncology; however, obstacles to the care of this population still occur at multiple levels. These vulnerabilities fall into 3 significant categories: research efforts and trial enrollment directed toward AYA malignancies, access to care and insurance coverage, and AYA-specific psychosocial support. It is critical for providers and health care delivery systems to recognize that the AYA population remains vulnerable to provider and societal complacency.

Introduction

Approximately 70,000 new cases of invasive cancer diagnosed annually are among adolescents and young adults (AYAs) aged 15 to 39 years. Historically, this age group has not shown the same improved survival as either older or younger cohorts. There are many unique aspects of care to consider in this population that may influence outcomes both during and after therapy. These include developmental status of the age group, research focus of age-based cooperative groups, socioeconomic impact of health insurance and access to care, and biologic differences in cancer types. Many of these issues are unique to the AYA population, which may complicate medical care and require additional support compared with either older adults or younger children.

In this article, we review contemporary cancer incidence, survival, and mortality data for the AYA patient population based on the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program and compare the most recent SEER data for AYA patients with data from previous reports. The discussion focuses on the improvements made over the past 10 to 15 years, specifically, improved AYA enrollment in clinical trials, extended access to care, and age-appropriate psychosocial supports. Finally, we discuss the future of AYA oncology care in the United States.
Perspective on the AYA Gap
In 2006, the NCI, the Children's Oncology Group (COG), and the SEER database worked in collaboration to release a detailed publication regarding cancer incidence and survival in AYA patients. This analysis by Bleyer et al highlighted reduced improvement in AYA patients with cancer compared with pediatric and adult patients. The lower percentage improvement in AYA cancer survival in recent decades compared with other age groups was termed the AYA gap. Acknowledgment of this gap provided the impetus for much of the recent research and activism focused on this population, although, in retrospect, more recent publications have noted how time trends in the HIV/acquired immunodeficiency syndrome (AIDS) epidemic contributed to the AYA gap.

Concurrently, the NCI and the Lance Armstrong Foundation (subsequently renamed the LIVESTRONG Foundation) created an Adolescent and Young Adult Progress Review Group to identify gaps in care and to develop strategies to improve survival disparities. The review group described the unique cancer-related medical, biological, and psychosocial issues that affect the AYA population. In addition, the authors reviewed programs, policies, and research initiatives that might directly benefit AYAs and published recommendations to improve the outcomes of AYA patients with cancer. Since the publication of these recommendations and the landmark report by Bleyer et al, efforts to address the disparity between the AYA population and other age groups have been ongoing within the medical community. This early work has highlighted several issues that are unique to this age group and can be applied in the context of current epidemiological trends.

Contemporary AYA Epidemiology Trends
Methods and Materials
Contemporary cancer incidence data (2011-2015) to calculate AYA case distribution were obtained from the North American Association of Central Cancer Registries (NAACCR) public use database. NAACCR compiles high-quality data from population-based central cancer registries that participate in the NCI's SEER program and/or the Centers for Disease Control and Prevention's National Program of Cancer Registries. Combined, SEER and the National Program of Cancer Registries provide complete cancer registration coverage for the entire United States. Data for 2011 through 2015 include cases from 45 states that consented and met NAACCR high-quality data standards for those years. Trends in population-based cancer survival (1975-2014, with follow-up through 2015) and historical cancer incidence rates (1975-2015) were calculated using data from the 9 SEER cancer registries, covering approximately 8% of the US population. Contemporary trends in survival since the early 2000s were obtained using data from all 18 SEER registries, providing coverage for 28% of the US population. Mortality data from 1970 to 2016 were obtained from the Centers for Disease Control and Prevention's National Center for Health Statistics.

All cases were classified using the International Classification of Diseases for Oncology, third edition. Cases were grouped according to the SEER AYA definitions, which use both topographical site and histology information. The only exception was for sex-specific cancers and those of the breast, kidney (including renal pelvis), colorectum, and thyroid, which were grouped according to the SEER/World Health Organization 2008 recode. Deaths were coded according to the International Classification of Diseases, 10th revision. Because histology is considered in the classification scheme for AYAs, survival and incidence data based on SEER AYA definitions are not directly comparable to mortality data based on the International Classification of Diseases, 10th revision. Historical cancer incidence rates based on SEER 9 registries were adjusted to account for delays in case reporting, which has the greatest effect on the most recent data years. Annual percent changes in mortality rates were calculated using Joinpoint (version 4.6.0.0; NCI), which fits a series of log-linear regression lines to observed data using the permutation test method. All tests were 2-sided and a P value <.05 was considered significant.

Cancer Occurrence in AYAs
AYA cancers accounted for 5% of all newly diagnosed invasive cancers in the United States between 2011 and 2015. Although overall cancer incidence rates during the most recent 10 years of available data (2006-2015) declined in men and were stable in women, pediatric and AYA cases per 100,000 during the most recent time period (2011-2015) were nearly 30% higher than the rates during 1975 through 1979. Recent data suggest that these increases may be caused in part by rising obesity rates and obesity-related cancers in the AYA population.

The distribution of different cancers varies dramatically across AYA age groups, defined herein as ages 15 to 19 years, 20 to 29 years, and 29 to 39 years (Fig. 1). For example, hematologic malignancies are the most common cancers in adolescents (ages 15-19 years), with lymphoma accounting for 22% of all cases (Hodgkin lymphoma, 14%; non-Hodgkin lymphoma, 8%) and leukemia accounting for 14% (acute lymphocytic leukemia [ALL], 7%; acute myeloid leukemia, 4%). In addition, brain tumors account for a larger percentage of all cancers in the group aged 15 to 19 years (10.4%) relative to other age groups. However, hematologic malignancies and brain tumors are less common among older...
AYAs, among whom melanoma, breast, and colorectal cancers are more common. Among those aged 30 to 39 years, lymphomas and leukemias account for just 7.7% and 3.4% of cases, respectively.

Regarding sex-specific cancers, males have a higher percentage of gonadal tumors than females overall and especially during their third decade of life. Among females, the proportion of cases because of non–germ-cell ovarian cancer (ie, sex cord stromal and epithelial tumors) remains relatively constant across AYA age groups. However, both breast and cervical cancer become substantially more common with older age, accounting for less than 1% of cases in adolescent females but 29.0% and 7.7% of cases, respectively, in those aged 30 to 39 years (Table 1).

It is important to note that incidence among AYAs differs by sex for some cancer types that occur in both males and females. For example, compared with males, females have a nearly 5-fold greater incidence rate of thyroid carcinoma.
| CANCER TYPE | OVERALL, AGES 15-39 YEARS | 15-19 AGES YEARS | 20-29 AGES YEARS | 30-39 AGES YEARS |
|-------------|--------------------------|-----------------|-----------------|-----------------|
|             | % CASES, 2011-2015 | 5-YEAR SURVIVAL (SE) 2008-2014, % | % CASES, 2011-2015 | 5-YEAR SURVIVAL (SE) 2008-2014, % | % CASES, 2011-2015 | 5-YEAR SURVIVAL (SE) 2008-2014, % | % CASES, 2011-2015 | 5-YEAR SURVIVAL (SE) 2008-2014, % |
| Males       |                       |                 |                 |                 |
| All cancers combinedb | 80.2 (0.2) | 81.9 (0.6) | 82.5 (0.3) | 78.6 (0.3) |
| Testicular germ cell/trophoblastic neoplasms | 20.0 | 94.7 (0.2) | 92.9 (0.9) | 94.2 (0.4) | 95.7 (0.4) |
| Lymphoma    | 15.6 | 86.0 (0.4) | 92.5 (0.9) | 87.0 (0.7) | 83.3 (0.7) |
| Non-Hodgkin lymphoma | 8.4 | 79.9 (0.7) | 88.2 (1.7) | 78.6 (1.2) | 79.0 (0.9) |
| Hodgkin lymphoma | 7.2 | 93.4 (0.5) | 95.8 (1.0) | 93.8 (0.7) | 91.7 (0.9) |
| Melanoma (skin)c | 8.4 | 91.4 (0.5) | 92.2 (2.2) | 91.8 (0.9) | 91.2 (0.6) |
| Colorectal cancer | 7.6 | 64.9 (1.0) | 60.0 (7.2) | 64.0 (2.2) | 65.3 (1.1) |
| Thyroid cancer | 7.5 | 99.3 (0.2) | 99.4 (0.8) | 99.2 (0.4) | 99.2 (0.3) |
| Leukemia | 7.1 | 65.7 (0.9) | 72.9 (1.8) | 60.9 (1.6) | 55.6 (1.3) |
| Acute myeloid | 2.4 | 59.2 (1.6) | 75.0 (2.3) | 50.2 (2.8) | 46.6 (3.3) |
| Acute lymphoid | 2.3 | 53.8 (1.6) | 63.6 (3.8) | 53.8 (2.7) | 50.6 (2.4) |
| CNS and other intracranial/intraspinal neoplasmsb | 6.2 | 67.0 (1.0) | 75.6 (2.3) | 69.5 (1.7) | 62.7 (1.4) |
| Astrocytoma | 3.5 | 56.5 (1.4) | 72.1 (3.2) | 61.8 (2.4) | 48.3 (2.0) |
| Glioblastoma and anaplastic astrocytoma | 1.8 | 31.4 (2.0) | 17.0 (5.6) | 40.3 (1.8) | 33.2 (2.5) |
| Soft-tissue sarcoma | 5.4 | 69.4 (1.0) | 62.7 (3.2) | 66.3 (1.6) | 52.6 (1.2) |
| Kidney cancer | 4.8 | 86.8 (0.9) | 67.0 (7.2) | 80.1 (2.5) | 88.5 (0.9) |
| Osseous and chondromatous neoplasms | 2.1 | 66.0 (1.7) | 64.1 (2.7) | 65.1 (2.8) | 70.8 (3.2) |
| Osteosarcoma | 0.8 | 61.8 (2.8) | 62.1 (3.8) | 61.0 (5.2) | 62.6 (7.7) |
| Females     |                       |                 |                 |                 |
| All cancers combinedb | 86.4 (0.1) | 87.5 (0.6) | 88.0 (0.3) | 85.8 (0.2) |
| Breast cancer | 22.8 | 85.8 (0.3) | 86.4 (6.4) | 83.6 (1.0) | 86.1 (0.3) |
| Thyroid cancer | 21.7 | 99.9 (0.0) | 99.1 (0.5) | 99.8 (0.1) | 99.9 (0.1) |
| Melanoma (skin)c | 9.5 | 69.6 (0.3) | 97.5 (1.1) | 97.3 (0.4) | 96.7 (0.3) |
| Lymphoma    | 7.7 | 91.6 (0.4) | 94.7 (0.8) | 92.0 (0.6) | 90.2 (0.6) |
| Non-Hodgkin lymphoma | 3.5 | 87.5 (0.7) | 90.5 (1.0) | 87.6 (1.2) | 87.0 (0.9) |
| Hodgkin lymphoma | 4.2 | 95.1 (0.4) | 96.4 (0.9) | 94.0 (0.7) | 95.8 (0.8) |
| Uterine cervix cancer | 6.8 | 80.3 (0.6) | 84.7 (7.1) | 82.3 (1.2) | 79.7 (0.7) |
| Colorectal cancer | 4.6 | 72.0 (0.9) | 85.5 (4.3) | 71.1 (2.1) | 71.8 (1.1) |
| Uterine corpus cancer | 4.0 | 89.7 (0.7) | 86.9 (8.7) | 88.3 (1.8) | 90.0 (0.7) |
| Leukemia     | 3.3 | 67.7 (1.0) | 70.5 (2.3) | 66.2 (1.8) | 67.6 (1.5) |
| Acute lymphoid | 0.8 | 57.8 (2.2) | 71.4 (3.4) | 48.6 (4.1) | 51.8 (3.8) |
| Acute myeloid | 1.6 | 61.6 (1.5) | 64.9 (3.8) | 64.2 (2.5) | 58.6 (2.2) |
| CNS and other intracranial/intraspinal neoplasmsb | 3.1 | 74.9 (1.0) | 80.5 (2.2) | 75.7 (1.7) | 72.3 (1.6) |
| Astrocytoma | 1.6 | 66.3 (1.6) | 78.7 (2.9) | 69.0 (2.6) | 58.2 (2.5) |
| Glioblastoma and anaplastic astrocytoma | 0.8 | 40.9 (2.6) | 26.0 (6.9) | 52.6 (4.3) | 35.8 (3.5) |
| Soft-tissue sarcoma | 2.5 | 74.1 (1.1) | 74.0 (3.0) | 72.7 (1.9) | 74.9 (1.5) |
| Ovarian cancer | 3.2 | 80.0 (0.9) | 89.7 (2.1) | 85.8 (1.4) | 74.9 (1.3) |
| Excluding germ cellc | 2.4 | 90.6 (1.1) | 82.6 (7.2) | 85.7 (3.0) | 76.0 (2.4) |
| Germ cell/trophoblastic neoplasms | 0.7 | 92.2 (0.9) | 96.4 (1.4) | 92.0 (1.4) | 89.2 (1.9) |
| Kidney cancer | 2.2 | 89.5 (0.9) | 81.8 (7.0) | 86.5 (2.1) | 90.6 (1.0) |
| Osseous and chondromatous neoplasms | 0.9 | 74.9 (1.9) | 74.3 (3.3) | 74.2 (2.9) | 75.9 (3.4) |
| Osteosarcoma | 0.4 | 70.7 (3.2) | 72.9 (4.8) | 65.1 (5.3) | 78.1 (6.4) |

Abbreviation: CNS, central nervous system.

aAll patients were followed through 2015.

bThese exclude benign and borderline brain cancers.

cCoding for these cancers is based on Surveillance, Epidemiology, and End Results (SEER) site recode International Classification of Diseases for Oncology, third edition/World Health Organization 2008 definitions. Kidney includes the renal pelvis. Sources: Case distribution, North American Association of Central Cancer Registries public use database, 2018; survival, SEER 18 registries, 2018.
(19.4 vs 4.1 per 100,000 during 2011–2015) and a 2-fold greater rate for melanoma of the skin (8.4 vs 4.7 per 100,000 during 2011–2015). The female-to-male cancer incidence rate ratio for AYAs aged 15 to 39 years is 1.67, driven largely by breast cancer incidence rates (21.7 per 100,000 population among females vs 0.1 per 100,000 population for males) and by thyroid cancer to a smaller degree (19.4 vs 4.1 per 100,000 population for females and males, respectively) (Table 2).

Current Trends in AYA Cancer Survival and Mortality

Overall 5-year relative survival among AYAs increased from 71% for those patients diagnosed in the mid-1970s to 86% for those diagnosed during 2008 through 2014 (Fig. 2). These figures illustrate the impact of HIV-related malignancies in the 1980s and 1990s and the subsequent increase in overall AYA cancer survival. Since 2000, survival gains have been similar overall among AYAs and pediatric patients with cancer (Table 3). Within the AYA population, survival varies by age subgroup (15-19 years, 20-29 years, and 30-39 years) and sex for several cancer types. For example, the 5-year survival rate for patients diagnosed with acute myeloid leukemia during 2008 through 2014 was 81.2% for males aged 14 to 19 years but only 60.3% and 62.7% for males aged 20 to 29 years and 30 to 39 years, respectively. Similarly, the 5-year colorectal cancer survival rate among males was 66% or 67% across age groups but was substantially higher in females, especially those aged 15 to 19 years (90.3%) (see Table 1).

Mortality rates among pediatric, AYA, and adult populations have been significantly declining since at least 1970. During the most recent 10 years of mortality data (2007-2016), mortality rates among AYAs declined by about 0.8% per year. By cancer type, mortality rates declined similarly among males and females for leukemia, non-Hodgkin lymphoma, and melanoma of the skin, while rates for Hodgkin lymphoma declined more rapidly in females (10% per year) compared with males (5% per year) (Table 4). Rates also declined among females for ovarian cancer. However, these declines have been somewhat offset by stable or increasing mortality rates for several common AYA cancers, including those of the colorectum, bones and joints, and uterine corpus.

Biologic Features of AYA Cancer Types

AYA cancers have unique biological/genomic characteristics, and analysis of driver mutations in AYA cancer is a new but growing field of research. In breast and colorectal cancer, the mutational burden of AYA cancers appears to be higher, and less favorable histology, such as mucinous colon cancer or triple-negative breast cancer, is overrepresented in the adolescent population. In colorectal cancer, mismatch repair genes appear to be disproportionately affected in AYA patients compared with older adults, even excluding patients with the genetic predisposition hereditary nonpolyposis colon cancer syndrome (Lynch syndrome), and mutations in the MUC gene seem to be correlated with the higher incidence of mucinous colorectal cancer. In addition, recent studies have suggested that the rising incidence of colorectal cancer in young adults may be related to the parallel increase in obesity. In melanoma, mutations associated with sun exposure are present at similar rates in AYAs and older adults, but AYAs have a different distribution of nonultraviolet-associated DNA damage, potentially linked to mismatch gene repair, which may contribute to AYA melanoma development. Thyroid carcinoma, in contrast, shows similar driver mutations but demonstrates differences in secondary gene mutations. ALL shows a significant heterogeneity in driver mutations, with a prevalence of higher risk mutations, such as Philadelphia chromosome-like leukemia, increasing as age of diagnosis increases.
The relationship between these genetic differences in cancer and the poorer prognosis of the AYA population is not fully elucidated. Thus, the implications of these biologic differences for therapeutic intervention are only hypothetical for most tumor types. However, tumors with high-risk histological or genetic signatures can affect treatment recommendations. High-risk breast cancer, for example, may alter the use of long-term hormone suppression in women of childbearing age, and increased dose intensity of pediatric ALL protocols has improved survival in higher risk ALL.29 As such, further research is necessary to explore these fundamental differences in AYA cancer.10

FIGURE 2. Trends in 5-Year Relative Survival (%) by Sex and Age, From 1975 to 2014, (A,B) With and (C,D) Without Including Kaposi Sarcoma (KS) and Non-Hodgkin Lymphoma (NHL). Source: Surveillance, Epidemiology, and End Results 9 registries, 2018.

The relationship between these genetic differences in cancer and the poorer prognosis of the AYA population is not fully elucidated. Thus, the implications of these biologic differences for therapeutic intervention are only hypothetical for most tumor types. However, tumors with high-risk histological or genetic signatures can affect treatment recommendations. High-risk breast cancer, for example, may alter the use of long-term hormone suppression in women of childbearing age, and increased dose intensity of pediatric ALL protocols has improved survival in higher risk ALL.29 As such, further research is necessary to explore these fundamental differences in AYA cancer.10

Improving Outcomes of AYAs With Cancer
Despite improving survival trends, obstacles to the care of this vulnerable population occur at multiple levels. The AYA age group requires support that is different from that for other age groups in dealing with new cancer diagnoses as well as ongoing long-term and late effects of treatment. These vulnerabilities can be addressed by increasing research efforts and clinical trial enrollment directed toward AYA cancers, expanding access to care and insurance coverage, and providing AYA-specific psychosocial support.

Research Efforts Directed Toward AYA Cancers
Recognizing that clinical trial enrollment in the AYA age group was inferior to pediatric and adult participation, one of the Progress Review Group recommendations was to expand clinical trial access and enrollment.13 While there is evidence that clinical trial enrollment improved clinical outcomes in pediatrics before 2000, there is uncertainty whether or not enrollment in clinical trials since 2000 is causally related to improved survival after adjustment for differences in facility characteristics and patient-level biological, clinical, and sociodemographic characteristics.4,30 Nevertheless, the primary goal of clinical trials is to improve outcomes in target populations in the long term.31 At the time of the review group’s recommendations in 2006,
clinical trial enrollment was 14% of all AYA patients.\textsuperscript{32}
This same analysis demonstrated that uninsured patients, older AYAs, and those not being treated at a pediatric facility were less likely to be treated on a clinical trial.\textsuperscript{32} In the group aged 15 to 19 years, in which care moves from the pediatrician to a wider set of primary care delivery options, including point-of-care clinics and urgent care, only 30% of patients are referred to pediatric institutions at the time of diagnosis.\textsuperscript{33,34} The percentage of patients enrolled in therapeutic trials at pediatric institutions is generally higher than that of patients treated at adult institutions: overall, from 20% to 38% of all patients with cancer in pediatric institutions are enrolled in clinical trials,\textsuperscript{35-38} whereas a similar analysis of adult centers shows approximate enrollment of 5%, with emphasis on cancers that are not represented in the AYA population.\textsuperscript{39} Enrollment of AYA patients in adult centers, whether NCI-designated cancer centers or NCI Community Oncology Research Programs, are at best equal and are usually lower than adult enrollment.\textsuperscript{40} Even in pediatric institutions, AYA enrollment in trials is 10% to 20% lower compared with the enrollment of children.\textsuperscript{36,40} Available trials for this age group are also in short supply. In one institution's review of AYA patients and study enrollment, 57% of AYA patients did not have a therapeutic trial available, reflecting the need for champions of AYA cancers within cooperative trial groups.\textsuperscript{35}

To reduce these age disparities and increase clinical trial enrollment, national organizations and cooperative trial groups have made efforts to bridge the age groups on research protocols. Both the Southwest Oncology Group and the COG have specific committees dedicated to the AYA population. Many of the COG research protocols for leukemia and sarcomas extend the age of eligibility to age ≥30 years. Other cooperative trial groups, such as the Sarcoma Alliance for Research through Collaboration, a national cooperative trial group outside of the National Cooperative Trials Network (NCTN) (sarc_trials.org/), have dropped the minimum ages on their protocols to 12 years, allowing pediatric and AYA enrollment. The NCTN is making a significant effort to allow all 5 national cooperative trials groups, in addition to the NCI Community Oncology Research Programs, access to any trial that addresses the AYA population. For example, 3 adult groups recently collaborated to complete a trial for AYA patients with ALL.\textsuperscript{41} There have also been significant efforts for adult and pediatric intergroup collaboration, as demonstrated by the recently activated intergroup trials for Hodgkins lymphoma (clinicaltrials.gov identifier NCT03907488) and renal cell carcinoma (clinicaltrials.gov identifier NCT03595124). In addition, the COG is also developing local advocates to oversee research efforts related to the AYA population at each institution. Because the majority of AYA patients are treated outside of pediatric institutions,\textsuperscript{32} these local advocates are also increasing collaboration with adult oncology colleagues.

Optimistically, a recent study by Parsons et al aimed to assess whether clinical trial enrollment in the AYA population has increased since 2006.\textsuperscript{32} This study included 1040 AYAs diagnosed in 2006 and 2095 AYAs diagnosed in 2012 and 2013 who had either Hodgkin lymphoma, non-Hodgkin lymphoma, ALL, or sarcoma. The authors found that clinical trial enrollment significantly increased from 14.8% in 2006 to 17.9% in 2012 and 2013. Clinical trial enrollment increases were not uniform across all groups, with patients aged 30 to 34 years and patients with Hodgkin lymphoma declining in clinical trial enrollment. They also found promising trends in patients aged 25 to 29 years, who doubled their enrollment from 6.3% in 2006 to 13.2% in 2012 and 2013. In addition, the authors noted a decrease in uninsured patients and improved trial enrollment among those who were uninsured, from 5.7% in 2006 to 12.8% in 2012 and 2013.\textsuperscript{32}

These efforts by cooperative groups to improve clinical trial enrollment by working collaboratively and expanding the age of eligibility may be effective in improving clinical trial enrollment. Although it is not possible to conclude that

\begin{table}
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\begin{tabular}{|l|cc|cc|}
\hline
\textbf{CANCER TYPE} & \textbf{CANCER DEATHS} & \textbf{AAPC 2007-2016, %} & \textbf{AAPC 2007-2016, %} & \\
& 2012-2016, % & MALES & FEMALES & MALES & FEMALES \\
\hline
Leukemia & & & & \\
Acute lymphocytic & 5.0 & 2.4 & -0.8\textsuperscript{a} & -2.0\textsuperscript{b} \\
Acute myeloid & 5.1 & 4.2 & -0.7\textsuperscript{a} & -1.7\textsuperscript{b} \\
Brain and CNS & 13.8 & 8.4 & 0.6 & 1.0 \\
Colorectal & 11.0 & 8.1 & 1.1\textsuperscript{b} & 0.6\textsuperscript{a} \\
Lymphoma & & & & \\
Non-Hodgkin lymphoma & 6.0 & 3.2 & -4.1\textsuperscript{b} & -4.9\textsuperscript{b} \\
Hodgkin lymphoma & 2.0 & 1.3 & -5.1\textsuperscript{b} & -10.0\textsuperscript{b} \\
Soft tissue & 6.1 & 4.1 & -0.3\textsuperscript{b} & -0.7\textsuperscript{b} \\
Bone and joints & 5.3 & 2.6 & 0.6\textsuperscript{b} & 0.5\textsuperscript{b} \\
Melanoma of the skin & 4.3 & 2.9 & -3.4\textsuperscript{b} & -2.8\textsuperscript{b} \\
Thyroid & 0.3 & 0.3 & -0.6 & -1.0\textsuperscript{b} \\
Kidney and renal pelvis & 2.4 & 2.2 & -2.2 & -1.4\textsuperscript{b} \\
Testis & 4.1 & 0.2 & & \\
Breast & - & 22.2 & -0.2 & \\
Ovary & - & 4.6 & -1.5\textsuperscript{b} & \\
Uterine cervix & - & 9.5 & -0.1 & \\
Uterine corpus & - & 2.3 & 2.8\textsuperscript{b} & \\
\hline
\end{tabular}
\caption{Percent of Adolescent and Young Adult Cancer Deaths (2012-2016) for Patients Ages 15 to 39 Years}
\end{table}

Abbreviations: AAPC, average annual percent change; CNS, central nervous system.
\textsuperscript{a}AAPCs are based on joinpoint models using 1970 to 2016 mortality data, allowing for up to 5 joinpoints.
\textsuperscript{b}Percentages are not shown because of sparse data (<10 deaths during 2012-2016).
\textsuperscript{c}The AAPC is statistically different from zero (P < .05).
increasing clinical trial enrollment has significantly contributed to the improved treatments, as reflected in survival outcomes demonstrated by the recent SEER data, it is certainly encouraging.

Health Insurance and Socioeconomic Status

Young adults have the highest percentage uninsured among Americans by age group, especially among young adults aged ≥26 years. For example, in 2016, the uninsured rate among young adults aged 26 to 34 years was 16% and, among those aged 19 to 25 years, it was 14%. By comparison, the uninsured rate among adults aged 45 to 64 years was 9% and, among those aged ≥65 years, it was 2%. Notably, although the combined uninsured rate among children and adolescents was comparatively low (5%), the uninsured rate spiked in late adolescence, reaching nearly 10% at age 18 years.43,44

For AYA patients with cancer, having public insurance or no insurance has been associated with a greater risk of death for each of 12 most common AYA cancer types.57 Those with public insurance or no insurance present with later stage disease than those with private insurance, and, even among patients who present at the same stage of disease, lack of insurance is an independent risk factor for mortality after a cancer diagnosis.57 Furthermore, many patients with cancer gain public insurance after diagnosis, and it has been shown that those who gain Medicaid only after diagnosis have worse outcomes than those who had continuous coverage.58 In a study of AYA patients with Hodgkin lymphoma, those without insurance were found to have an increased risk of medical illness, such as respiratory or endocrine disease, 2 years after diagnosis, and these medical conditions were associated with a 2-fold increased risk of death.56

The Affordable Care Act (ACA) has many provisions that have improved insurance coverage options, including the introduction of marketplace private plans, expansion of parents’ private insurance coverage for dependents until age 26 years, and eliminating preexisting conditions as an exclusion for insurance enrollment. It also provided incentives for states to expand Medicaid eligibility to 138% of the federal poverty level for low-income adults with and without children. These changes reduced the number of uninsured AYA patients by 50% in the first 4 years of the ACA, with the dependent care expansion significantly increasing private insurance coverage among those aged 19 to 25 years and the Medicaid expansion increasing public insurance coverage for all young adults.43,47,48 This coverage, however, has not extended equally to all socioeconomic and racial groups, especially AYA patients with low socioeconomic status (SES) or who are black and/or Hispanic and are less likely to have insurance coverage even after the ACA, especially in states that did not expand Medicaid eligibility.6,49,50

In addition to being underinsured or uninsured, other socioeconomic concerns are a universal consideration for AYA patients, although specific concerns differ based on their age and the presence of dependents.51 There is evidence supporting a relationship between poverty and decreased access to health care, poorer health care utilization, and inferior patient outcomes in multiple medical conditions, including cancer.50,52-54 An association between neighborhood SES and survival has been demonstrated in AYAs with leukemia, lymphoma, melanoma, breast cancer, and colon cancer.55 Lower neighborhood SES was associated with a greater risk of death in AYAs who had private insurance and in those aged 25 to 34 years regardless of insurance type.55 For survivors, cancer-related financial concerns can affect future health care, making patients more likely to delay or forgo medical care.56 In the AYA population, 24% of cancer survivors report forgoing medical care because of cost, compared with 15% of those with no history of cancer.57

Since the implementation of the ACA starting in 2010, there is evidence that the dependent coverage expansion, marketplace insurance, insurance subsidies, and Medicaid expansions have improved insurance coverage and access to care for AYA patients.43,47,58 However, many AYA patients continue to be uninsured or underinsured, and research supports that these individuals may have worse outcomes.6,50 The addition of health insurance alone does not address all socioeconomic concerns that AYA patients face, and future efforts should focus not only on identifying disparities but also on interventions to help improve care for all patients.

Psychosocial Factors

Although the age of legal independence is 18 years, physiologic development of the brain continues until age 30 years, and the psychological development of coping skills arguably continues throughout an individual’s life.7 The hallmark of an adult is the acquisition of mature and healthy coping mechanisms that allow an individual to negotiate the challenges of an adult society.59 AYA patients who are maturing appropriately before a cancer diagnosis report decreased ability to hold a job, complete education, and maintain mature relationships both during and after a cancer diagnosis, indicating that their psychological development may slow, stop, or even regress (Table 5).2,60 Because of these unique developmental considerations, the AYA population has multiple needs that occur during and after therapy.2,61-64 Medical systems and providers must recognize that the AYA age group requires specialized teaching and increased psychological support when discussing therapies and experiencing the rigors and side effects of treatment.64 Much of their anxiety can be alleviated with information developed for their specific concerns.65,66

Young adults with cancer have many sexual and reproductive health-related concerns and unmet needs that can affect future relationships, self-image, health, and quality of life.2,67-70 Females routinely express self-doubt about
their femininity and inherent self-worth when faced with infertility.71 Likewise, males report similar self-doubt perceptions.72 Patients care about the risk of impaired fertility after cancer treatment and desire counseling on risks and preservation options,73-76 yet, in the past, only a minority of AYA patients were approached about reproductive options before chemotherapy.77,78 Since discovering the importance of fertility to young survivors, sexual and reproductive health issues in adolescents with cancer have garnered more recognition from the medical community in the last decade. To help address these concerns, the Oncofertility Consortium was established in 2006. This is a multidisciplinary group of medical and pediatric oncolgists, urologists, gynecologists, psychologists, and researchers dedicated to improving research and access to fertility preservation services for patients with cancer.79

In addition, AYA patients express a need for improved mental health and support group services.14,80 Studies have found that almost one-third of AYA patients with cancer endorse increased depressive symptoms.81,82 Having unmet psychosocial needs is associated with worse health-related quality of life, fatigue, and poor work/school functioning.14 Addressing these needs is difficult with the current mental health infrastructure in the United States, especially when mental health care remains an underserved area of the US health system.83 A review of 209 patients in the Australian AYA cancer treatment system showed that positive experiences during cancer therapy were associated with education and social support the patients received during therapy.84 Patients with chronic medical conditions other than cancer reported improved outcomes when they received psychosocial support.85

### Future Directions

The oncological community has embraced the AYA population in the literature and has worked diligently to address the needs of this population. For the past decade, the number of publications and conferences focused on AYA cancer care has increased dramatically, proving that the AYA population is now recognized as a vulnerable patient group.

To address trial enrollment disparities, the Southwest Oncology Group, the COG, non-NCTN trial groups, and many large research institutions have widened the age of eligibility, increasing both pediatric and AYA enrollment. A few individual institutions across the country have made substantial progress simply by recognizing the need at a local level, initiating collaboration between pediatric and adult centers, addressing the shifting cancers that occur in AYA patients, and offering appropriate clinical trials regardless of the starting institution. The amount of effort that this requires is tremendous, often bridging institutions that are separate in organization and distance, amplified by the need to open protocols at multiple institutions. Those programs and their leaders should be lauded and held as examples to guide other institutions in the future.

The AYA population may also be particularly suited to patient-oriented research, in which patients contribute by helping to select research questions or share results with peers. This level of engagement can help AYA patients become aware of ongoing research and could make novel findings more likely to be implemented.86 A successful example of this patient-oriented process in a retinoblastoma research group was recently described.87

From an economic standpoint, the steps that the ACA has taken have objectively reduced the numbers of uninsured in the US population, which has affected the AYA population more so than any other age group, as a vulnerable population. This is encouraging for AYAs with cancer, who will have significantly increased health care utilization.

One way to systematically address these concerns may be through specialized AYA treatment centers. The Global AYA Cancer Congress, which first met in 2016, is an international meeting focused on how to improve the care for AYA patients.88 This congress is an international, multidiscipline group consisting of pediatric and medical oncologists, scientists, psychologists, nurse navigators, and even young adult survivors and is cosponsored by Teen Cancer America (United States), Teenage Cancer Trust (United Kingdom), and CanTeen Australia (Australia). One of the main missions of Teen Cancer America is to partner with hospitals in the United States to build specialized programs and facilities to improve “AYA-focused” care in the United States, modeled after the experience in the United Kingdom. England has had specialized AYA treatment centers for over 10 years, and currently there is a large cohort study, BRIGHTLIGHT, aimed at

| AGE                  | SOCIAL AND DEVELOPMENTAL CONCERNS                                                                 |
|----------------------|--------------------------------------------------------------------------------------------------|
| Mid-adolescence: <18 y | • Interrupted social skills development  
|                      | • High school achievement/graduation delays  
|                      | • Delays in living independently                                                                |
| Emerging adulthood: 18-25 y | • Delays in higher education  
|                      | • Interruptions in employment                                                                  |
|                      | • Barriers to achieving financial independence                                                   |
|                      | • Difficulties obtaining adequate health insurance                                               |
| Young adulthood: 26-39 y | • Difficulty developing and maintaining relationships with significant others/spouses         |
|                      | • Problems with sexual function and intimate relationships                                        |
|                      | • Fertility issues impacting parenthood                                                           |
|                      | • Barriers to achieving financial independence                                                    |
|                      | • Difficulties obtaining adequate health insurance                                                 |

*Issues are categorized by age. Adapted from: 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.*

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**TABLE 5. Social Issues for Adolescent and Young Adult Patients With Cancer**

| AGE          | SOCIAL AND DEVELOPMENTAL CONCERNS                                                                 |
|--------------|--------------------------------------------------------------------------------------------------|
| Mid-adolescence: <18 y | • Interrupted social skills development  
|                      | • High school achievement/graduation delays  
|                      | • Delays in living independently                                                                |
| Emerging adulthood: 18-25 y | • Delays in higher education  
|                      | • Interruptions in employment                                                                  |
|                      | • Barriers to achieving financial independence                                                   |
|                      | • Difficulties obtaining adequate health insurance                                               |
| Young adulthood: 26-39 y | • Difficulty developing and maintaining relationships with significant others/spouses         |
|                      | • Problems with sexual function and intimate relationships                                        |
|                      | • Fertility issues impacting parenthood                                                           |
|                      | • Barriers to achieving financial independence                                                    |
|                      | • Difficulties obtaining adequate health insurance                                                 |
examining whether these specialized programs have improved the outcomes and experiences of AYA patients with cancer. Data are forthcoming, but these centers may be a mechanism with which to systematically address and coordinate the needs of the AYA patient.

For oncologists caring for AYA patients today, there is an evolving list of available resources (see Supporting Table 1), which aim to address some of the unique needs of this population. This list is not comprehensive but gives an example of the multitude of resources available today. We expect that the efforts to improve AYA care will continue to grow in the next few years. On an individual level, we can continue to advocate for our AYA patients by seeking opportunities for trial enrollment, building collaborations with psychology colleagues, and ensuring that our patients are aware of all financial resources available to them.

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