Cancer in 15- to 29-Year-Olds by Primary Site

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Learning Objectives
After completing this course, the reader will be able to:

1. Define the cancers most common in 15- to 29-year-olds.
2. Identify the variations in cancer histology in this age group according to age, sex, and race/ethnicity.
3. Understand survival trend differences during the past quarter century.
4. Perceive incidence and survival according to sex, race/ethnicity, and age groups.
5. Discuss areas where progress has been suboptimal in managing cancer in 15- to 29-year-olds.

Abstract
Incidence. Cancer occurring between the ages of 15 and 30 years is 2.7 times more common than cancer occurring during the first 15 years of life, yet is much less common than cancer in older age groups, and accounts for just 2% of all invasive cancer. Cancer in adolescents and young adults is unique in the distribution of the types that occur. Hodgkin lymphoma, melanoma, testis cancer, female genital tract malignancies, thyroid cancer, soft-tissue sarcomas, non-Hodgkin lymphoma, leukemia, brain and spinal cord tumors, breast cancer, bone sarcomas, and nongonadal germ cell tumors account for 95% of the cancers in this age group. The frequency distribution of cancer types changes dramatically from age 15–30, such that the pattern at the youngest age does not resemble the one at the oldest. The incidence of cancer in this age group increased steadily during the past quarter century. This increase is declining and at the older end of the age range appears to be returning to the incidence of the 1970s. Males in the 15- to 29-year age group have been at higher risk of developing cancer, with the risk directly proportional to age. Non-Hispanic whites have had the highest risk of developing cancer during this phase of life, and Asians, American Indians and Native Alaskans the lowest. Males had a worse prognosis than females. African-Americans, American Indian/Alaska Natives had a worse prognosis than white non-Hispanics and Asians.

Mortality & Survival. At the beginning of the last quarter century, the diagnosis of cancer in 15- to 29-year-olds carried a more favorable prognosis, on the average, relative to cancer at other ages. Since then, there has been a lack of progress in survival improvement among older adolescents and young adults relative to all other ages. Survival improvement trends portend a worse prognosis for young adults diagnosed with cancer today than 25 years ago. The survival deficit is increasing with longer follow-up of the survivors, and is worse in males. Among 15- to 29-year-olds, non-
Hispanic whites had the best survival and African Americans/blacks had the worst survival, with a 20% difference apparent by 5 years. Asians/Pacific Islanders had the second best survival, with Hispanics and American Indians/Alaska Natives next in sequence.

Risk Factors. In general, there are relatively scant data to support either an environmental causation or an inherited predisposition to cancer in this age group. The majority of cases of cancer occurring before age 30 appear to be spontaneous and unrelated to either carcinogens in the environment or family cancer syndromes. Overall, family cancer syndromes appear to account for less than 5% of the cases of cancer in the age group. Melanoma, cervical carcinoma and Kaposi sarcoma, non-Hodgkin lymphoma, Hodgkin and Burkitt lymphomas accounting for the majority of environmentally induced malignancies (ultraviolet light, human papillomavirus, human immunodeficiency virus, and Epstein-Barr virus, respectively). Ultimately, a larger proportion of cases may be attributable to specific factors or genetic predisposition, but at present, most cancer in this age group appears to be sporadic and random. The Oncologist 2006;11:590–601

INTRODUCTION
To our knowledge, this is the first treatise devoted exclusively to cancer in adolescents and young adults 15- to 29-years of age. A prior monograph from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NCI) of the United States reported the epidemiology of cancer in children younger than 15 years of age [1]. For many of the analyses in the current report, data for the age groups 0–15 years and 30–44 years are included for comparison. The SEER incidence data included in this introductory chapter were collected mainly between 1975 and 2001. As in the prior monograph, and as routinely available in the SEER database [2], five year increments (15–19 years, 20–24 years, 25–29 years, etc.) are utilized in most analyses. Only recently have data from SEER become available in shorter age intervals, but with the exception of this introductory chapter, these data are not presented in this monograph. Although the pediatric cancer monograph included a chapter about 15- to 19-year-olds [3], the current monograph contains new and more varied analyses.

Each disease-based chapter follows a standard outline, beginning with incidence and followed by death rates, survival information and risk factors/etiology, in that sequence. Each of the disease-based chapters is authored by an expert epidemiologist, at least one pediatric oncologist, and at least one academic oncologist who is an expert in the care of adult patients with cancer (medical oncologist, surgical oncologist, radiation oncologist).

METHODS, CLASSIFICATION SYSTEMS, AND DATABASES
Invasive cancer refers to any malignancy except squamous and basal cell carcinoma skin cancer, in situ cancers of any organ except bladder, or ovarian cancers of borderline significance. It does include juvenile pilocytic astrocytoma, a low-grade brain tumor with little metastatic potential. There are two primary site and histology groupings based on the International Classification of Diseases for Oncology (ICD-O); the SEER site recode (http://www.seer.cancer.gov/siterecode/icdo3_d01272003/) and the International Classification of Childhood Cancers (ICCC). The ICD-O evolved as an expansion of the International Classification of Diseases for Oncology [4] in order to code both primary site and histologic type, and has been through a number of iterations [5]. The SEER site recode was developed mainly to group adult cancers by primary site. The ICCC was developed later [6] to better characterize pediatric cancers. The SEER site recode was based primarily on the site in the body where cancer arises (e.g. gastrointestinal tract, genitourinary system, respiratory system, and the breast). The majority of pediatric cancers are disseminated when they are diagnosed and only the tissue of origin can be determined. The SEER site recode is therefore mainly topographic and the ICCC is primarily based on histology. A further refinement has been proposed for adolescents and young adults to allow categorization of the epithelial tumors (carcinomas) that are much more common in this age group than in children [7]. The Methods chapter that follows provides more information on classification and explains which SEER and national mortality databases were used and how the analyses were conducted.

INCIDENCE
In the U.S., as in most economically advantaged countries of the world, 2% of all invasive cancer occurs in the 15-year interval between the ages of 15 and 30 years. This compares with cancer diagnosed before age 15, which accounts for 0.75% of all cancers. There are 2.7 times more patients diagnosed during the second 15 years of life than during the first 15 years. At the turn of the millennium—in the year 2000—nearly 21,400 persons in the United States from 15- to 29-years of age were diagnosed with invasive cancer (Table 1). Because the incidence of cancer increases exponentially as a function of age (Fig. 1), approximately half of the 15- to 29-year-old patients are 25–29 years of age.
Age-Specific Incidence

Figure 1 shows the incidence of all invasive cancer in the U.S. from 1975 to 2000 as a function of 5-year age intervals from birth to 85+ years. The upper panel displays a linear ordinate and the lower panel uses semilogarithmic coordinates. The straight line in the lower panel indicates that the incidence is exponentially correlated with age from 10–60 years. That adolescents and young adults have an exponential risk of developing cancer as they age suggests a basic carcinogenic exposure that is age-dependent, such as telomerase shortening or a mutation-to-malignancy rate that increases constantly with age. This pattern is consistent with acquired mutations from increasing carcinogenic exposures with age and also implies that most cancer in adolescents and young adults is not due to environmental carcinogens since they have not had enough time to accrue the mutations that lead to overt cancer.

Table 1. Incidence of invasive cancer in persons younger than 45 years of age

<table>
<thead>
<tr>
<th>Age at Diagnosis (Years)</th>
<th>&lt; 5</th>
<th>5–9</th>
<th>10–14</th>
<th>15–19</th>
<th>20–24</th>
<th>25–29</th>
<th>30–34</th>
<th>35–39</th>
<th>40–44</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. population, year 2000 census, in millions</td>
<td>19.175</td>
<td>20.549</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence of all invasive cancer per million per year, 1975–2000, SEER</td>
<td>206</td>
<td>111</td>
<td>125</td>
<td>203</td>
<td>352</td>
<td>547</td>
<td>833</td>
<td>1,289</td>
<td>2,094</td>
</tr>
<tr>
<td>Average annual % increase in invasive cancer, 1975–2000, SEER</td>
<td>1.0</td>
<td>0.4</td>
<td>0.9</td>
<td>0.7</td>
<td>1.0</td>
<td>1.9</td>
<td>1.6</td>
<td>1.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Estimated incidence of invasive cancer per million, year 2000, U.S.</td>
<td>217</td>
<td>113</td>
<td>129</td>
<td>216</td>
<td>365</td>
<td>662</td>
<td>983</td>
<td>1,462</td>
<td>2,156</td>
</tr>
<tr>
<td>Estimated number of persons diagnosed with invasive cancer, year 2000, U.S.</td>
<td>4,153</td>
<td>2,314</td>
<td>2,638</td>
<td>4,374</td>
<td>6,928</td>
<td>12,830</td>
<td>20,162</td>
<td>33,197</td>
<td>48,385</td>
</tr>
</tbody>
</table>

Figure 1. Incidence of all invasive cancer, SEER 1975–2000.

Figure 2. Incidence of all invasive cancer, SEER 1975–2000.
Gender-Specific Incidence

Figure 2 shows the corresponding incidence in females (upper panel) and males (lower panel), each expressed on semi-logarithmic coordinates. Females demonstrate the exponential risk pattern from age 10–50 years. Males instead have two exponential risk patterns, from 10–40 years and 40–80 years. This suggests that another age-dependent mechanism is operative in young adult males. This pattern may be attributable also to the cancers that occurred in males during the 1980s and early 1990s as a result of the human immunodeficiency virus, namely Kaposi sarcoma and HIV-related lymphoma.

Figure 3 demonstrates how dependent on age is the relative risk of being diagnosed with cancer in males versus females. The male:female ratio has a nadir at 40–44 years, during which females are almost twice as likely as males to be diagnosed with invasive cancer. At both ends of the age spectrum—in children and older adults—the ratio is reversed. Boys are 10%–25% more likely than girls to be diagnosed with cancer, and older adult males are much more likely to develop cancer than females. The transition from a male predominance in childhood to a female predominance in the middle years of life occurs during late adolescence/early adulthood. The male:female ratio declines linearly from the 10- to 14-year age group to the 40- to 44-year age group.

Racial/Ethnic Differences in Incidence

The dependence of cancer incidence on race and ethnicity as a function of age is shown in Figure 4 for all ages in 15-year intervals up to age 44 and as one group for older persons. In Figure 5, it is shown for 5-year age intervals up to age 44. Non-Hispanic whites had the highest incidence during the first 45 years of life. Over age 45, African Americans/blacks had the highest incidence, followed by white non-Hispanics and Americans of Hispanic/Latino, Asian, and Pacific Islander descent. American Indians/Alaska Natives had the lowest cancer incidence at all ages. Males and females follow similar race/ethnicity-incidence patterns to those described above up to age 40 (Fig. 6). The conversion to a higher incidence in African Americans/blacks occurs in males between age 40 and 44 and in females at an older age (Fig. 4 and Fig. 6).

Types of Cancer

The common types of cancer and their relative proportion of all invasive cancers that occurred in 60,824 15- to 29-year-old Americans registered by SEER during 1975–2000 are shown in Figure 7, according to the SEER site recode. Lymphoma accounted for the largest proportion, 20% of all cases, with Hodgkin lymphoma alone accounting for 12% of all cases. Next in frequency were invasive skin cancer (15%) and male genital system cancer (11%), followed in rank order by endocrine tumors.
The distribution of the most frequent cancers in the U.S. among 15- to 29-year-olds according to gender is shown in Figure 8. The most striking difference between males and females in the 15- to 29-year age range is the much higher frequency of thyroid cancer in females. In both males and females, malignancies of the genital tract are the most frequent type of cancer followed closely by lymphomas (and thyroid for females).

The distribution of the most frequent cancers by 5-year age intervals within the 15- to 29-year age range is shown in figures 9, 10, and 11. The most dramatic changes in the types of cancer as a function of age (15–29 years) occurred in melanoma (from fifth most frequent in the 15- to 19-year age group to first most frequent in the 25- to 29-year age group, when gender is not considered), leukemia (from second most frequent to ninth), and CNS tumors (third–seventh).

Figure 6. Incidence of all invasive cancer by race/ethnicity, SEER 1990–1999.

Figure 7. Cancer in 15- to 29-years-olds by primary site (SEER Site Recode) U.S., SEER 1975–2000.

Trends in Incidence
Between 1975 and 2000, cancer increased in incidence for all age groups younger than 45 years (Fig. 12). Between 25 and 45 years of age, most of the increase in overall cancer incidence occurred in males (Fig. 13). Those cancers with the greatest change in incidence during this interval are shown in Figures 14 and 15.

The increase in incidence among 25- to 44-year-old males (Fig. 13) was due in large part to increases in soft tissue sarcoma (notably Kaposi sarcoma), non-Hodgkin lymphoma, and testicular carcinoma (Fig. 14). Among females younger than 45 years of age, the greatest increase occurred in germ cell tumors (Fig. 15).

There is evidence that the increase in incidence has declined for 15- to 29-year-olds, with a leveling off of incidence among 15- to 24-year-olds and a decrease in 25- to 29-year-olds (after a peak in the late 1980s and early 1990s)
That sarcoma and lymphoma accounted for most of the increase in cancer in males between 25 and 40 years of age (Fig. 14) suggests that the peak in incidence in this age group was primarily due to Kaposi sarcoma and non-Hodgkin lymphoma as a result of the human immunodeficiency virus epidemic.

**OUTCOME**

**Age- and Gender-Specific Mortality**

National mortality of all invasive cancer as a function of age at death is shown in Figure 17. By and large, the age-dependent cancer death rate reflects the incidence profile (Fig. 1). More males than females die of cancer over age 45 (Fig. 17, Inset). From 30–44 years of age, deaths among females predominate. In patients younger than 30 years, mortality is higher in males (Fig. 17).

Because mortality varies with incidence—the more patients diagnosed with cancer, the higher the death rate would be expected to be—the gender-specific ratio of the death rate to incidence for the era 1975–2000 is shown in Figure 18. Among all age groups—from 10–45 years of age—more males than females have died of cancer when the death rate is considered relative to the variation in incidence. This suggests that the cancers that occurred in adolescent and young adult males during the period 1975–2000 were more lethal than those in women or that the treatment was less effective.
Racial/Ethnic Differences in Mortality
Figures 19 and 20 present mortality data for all invasive cancer according to ethnicity and age of death up to 45 years. The death rate generally reflects incidence (Figs. 4 and 5), with the exception of 15- to 44-year-old African Americans/blacks, who had a higher death rate relative to their incidence than any of the other races/ethnicities.

Trends in Mortality
Mortality from invasive cancer declined between 1975 and 2000 in all age groups younger than age 45, but the least improvement occurred in the 20- to 44-year-olds (Fig. 21). This pattern—less progress in reducing cancer mortality for young adults than for children and young adolescents—is true for males and females (Fig. 22) and for white non-Hispanics and African Americans/blacks (Fig. 23). Among African Americans/blacks, however, the rate of progress in reducing mortality was considerably lower, particularly in 15- to 24-year-olds (Fig. 23).

Survival
Survival up to 20 years after a diagnosis of invasive cancer is shown in Figure 24 for all patients followed by SEER from 1975–1999, and in figures 25 and 26 for females and males, respectively, during this era. Among both female
and male 15- to 29-year-olds, survival after an invasive cancer diagnosis was comparable to that in persons who were younger than age 15 when diagnosed. In males older than 30, survival was worse. Above age 45, survival was considerably worse than for younger age groups, and comparable in men and women. Twenty-nine, 30- to 44-, and 45-plus-year-olds with cancer in the period 1992–1999 are shown in Figure 27. The era is more recent and the follow-up shorter because race/ethnicity data for other than whites and African Americans/blacks were not available until the 1990 census. Among 15- to 29-year-olds, non-Hispanic whites had the best survival and African Americans/blacks had the worst survival, with a 20% difference apparent by 5 years. Hispanics, Asians/Pacific Islanders and American Indians/Alaska natives had an intermediate survival. American Indians/Alaska natives had a more rapid cancer death rate during the first two years than non-Hispanic whites, Hispanics and Asians/Pacific Islanders, and then a relative plateau not seen in the other races/ethnicities. During the 1990s, 27% of American Indians/Alaska natives with cancer died within two years, more than twice the death rate observed among non-Hispanic whites.

When compared to younger and older cancer patients, 15- to 29-year-olds had an intermediate survival for each of the races/ethnicities (Fig. 27). The higher cancer death rate in African American/blacks observed in older adults is equally apparent in 15- to 29-year-olds but not in <15 year-olds, in whom the worst initial survival occurred in American Indians/Alaska natives, and the ultimate survival appeared similar for races/ethnicities other than non-Hispanic whites (Fig. 27). Also, in 30- to 44-year-olds the plateau on the survival curve in 15- to 29-year-old American Indians/Alaska natives was not observed. And in comparison to both <15 and 15- to 29-year age group, the survival curves among 30-to 44-year-olds clearly separated, with the order of best to worst survival being non-Hispanic whites, Asian/Pacific Islanders, Hispanics, American Indians/Alaska natives, and African Americans/blacks.

Figures 28–30 display the average annual percent change in 5-year relative survival of patients diagnosed between 1975 and 1997, inclusive, as a function of age at diagnosis, in 5-year age increments. Relative survival refers to adjustment of the observed survival relative to the survival expected from population norms of the same age and thereby partially corrects for deaths due to causes other than cancer [7]. The average annual percent change in survival for females and males are evaluated separately in Figures 29 and 30.

Steady progress in improving the 5-year survival rate has occurred in children and older adults. For patients between 15 and 45 years of age, however, progress in sur-
vival improvement has been a fraction of that achieved in younger and older patients. For patients between 25 and 35 years of age, in fact, there has been no evidence for an improvement in survival (Fig. 28). Most of the older adolescent/young adult deficit occurred in males (Fig. 29) but females have not been spared (Fig. 30). To determine whether the young adult survival gap was apparent at follow-up time points other than every 5 years, the 1- and 5-year relative survival rates were compared. In this analysis, individual year-to-year age groups were evaluated instead of 5-year age groupings, and the survival rates during the 1995–1999 era were compared with the 1975–1999 era rates and expressed as the percentage improvement since the earlier era.

Both survival parameters (1- and 5-year survival rates) showed the same profile (Fig. 31), with a nadir in progress between age 25 and 40 years (the vertical red band in the figure). The 5-year survival pattern showed a greater disparity than the pattern at 1-year, indicating that the survival deficit gap increased with longer follow-up of the patients. As in the analyses that utilized the average percent change method, young adult males had a more striking deficit than females in the same age group (Fig. 32).

**Risk Factors**

Etiologic mechanisms and risk factors of the most common cancers that occur in the 15- to 29-year age group are considered in the disease-specific chapters. In general, there

![Figure 27](image)

**Figure 27.** Relative survival for all invasive cancer by race/ethnicity, SEER 1992–1999.

![Figure 28](image)

**Figure 28.** Average annual percent change (AAPC) in 5-year relative survival for all invasive cancers, SEER 1975–1997.

![Figure 29](image)

**Figure 29.** Average annual percent change (AAPC) in 5-year relative survival for all invasive cancers in females, SEER 1975–1997.

![Figure 30](image)

**Figure 30.** Average annual percent change (AAPC) in 5-year relative survival for all invasive cancers in males, SEER 1975–1997.
are relatively scant data to support either an environmental causation or an inherited predisposition to cancer in this age group. The vast majority of cases of cancer diagnosed before age 30 appear to be spontaneous and unrelated to either carcinogens in the environment or family cancer syndromes. There are exceptions, covered in each disease chapter, but the exceptions are rare. Clear cell adenocarcinoma of the vagina or cervix in adolescent females has in most cases been caused by diethylstilbestrol taken prenatally by their mothers in an attempt to prevent spontaneous abortion. Radiation-induced cancer may occur in adolescents and young adults after exposure during early childhood. In fact, many of the adolescent and young adult cancers that have been linked to an identifiable cause are second malignant neoplasms in patients who were treated with chemotherapy and/or radiotherapy for a prior cancer. Melanoma, cervical carcinoma, Kaposi sarcoma and non-Hodgkin lymphoma, and Hodgkin and Burkitt lymphomas account for the majority of environmentally induced malignancies (due to ultraviolet light, human papillomavirus, human immunodeficiency virus, and Epstein-Barr virus, respectively). Ultimately, a larger proportion of cases may be attributable to specific factors or genomic predisposition but, at present, most cancers in this age group appear to be sporadic and random. Overall, family cancer syndromes appear to account for less than 5% of the cases of cancer in the 15- to 29-year age group.

**SUMMARY**

A cancer diagnosis between the ages of 15 and 30 years is 2.7 times more common than such a diagnosis during the first 15 years of life, and yet is rare—accounting for just 2% of all invasive cancers—relative to cancer occurring at older ages. Malignant disease in persons 15–29 years of age is unique in the distribution of types that occur, with Hodgkin lymphoma, melanoma, testis cancer, female genital tract malignancies, thyroid cancer, soft-tissue sarcomas, non-Hodgkin lymphoma, leukemia, brain and spinal cord tumors, breast cancer, bone sarcomas, and nongonadal germ cell tumors accounting for 95% of the cancers in this age group. In the brief period from 15 to 30 years of age, the frequency distribution of cancer types changes dramatically, such that the pattern at age 15 does not resemble that at age 30.

A failure to improve length of survival and reduce mortality has occurred in this age group relative to other age groups. Fortunately, the incidence increase observed during the past quarter century is declining, and for those at the older end of the age range appears to be returning to the incidence of the 1970s.

Males in the 15- to 29-year age group have been at higher risk of developing cancer, with the risk directly proportional to age. White non-Hispanics have had the highest risk of developing cancer during this phase of life, and Asians, American Indians and Alaska Natives the lowest. Males have had a worse prognosis, as have African Americans/blacks, American Indians, and Alaska Natives among the races/ethnicities evaluated.

The most disturbing finding is the lack of progress in survival improvement among older adolescents and young adults in contrast to all other ages. Whereas the diagnosis of cancer in this age group used to carry a more favorable prognosis relative to cancer at other ages, current survival improvement trends portend a worse prognosis for today’s young adults diagnosed with cancer.

**AUTHORS’ NOTE**

Adapted and updated from Bleyer WA, O’Leary M, Barr R, Ries LAG (Eds): Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, including SEER Incidence and Survival, 1975-2000. National Cancer
Disclosure of Potential Conflicts of Interest

Dr. Bleyer has acted as a consultant for Enzon Pharmaceuticals within the past two years.

References


