Young Adult Oncology: The Patients and Their Survival Challenges

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ABSTRACT One in every 168 Americans develops invasive cancer between age 15 to 30 years. During this age interval, cancer is unique in the distribution of types that occur and rarely related to either environmental carcinogens, a recognizable inherited predisposition, or a family cancer syndrome. Patients in this age group have the lowest rate of health insurance coverage, frequent delays in diagnosis, and the lowest accrual to clinical trials. Their psychosocial needs are unique and generally less well attended to than in any other age group. Despite an intrinsically equal ability to tolerate chemotherapy, older adolescents and young adults frequently receive lower dose intensities than do younger patients, and at times less than in older patients. Whereas the 15- to 29-year age group once had a better overall survival rate than either younger or older patients, a relative lack of progress has resulted in the majority of cancers in the age group having a worse overall survival rate than in younger patients, and several of these having a worse prognosis than in older patients. Against this background, young adults with cancer have unique survival challenges—medically, psychosocially, and economically—that are now beginning to be appreciated and addressed with a national initiative. (CA Cancer J Clin 2007;57:242–255.) © American Cancer Society, Inc., 2007.

INTRODUCTION

A quarter of a century ago, the diagnosis of cancer generally had a better prognosis in older adolescents and young adults than in younger or older persons. Today, the situation is reversed relative to younger persons and approaching reversal relative to older persons.1–4 In the 1950s, childhood cancer became a singular focus of treatment and research. In 1971, the National Cancer Act added adults with cancer as a priority. Meanwhile, substantially less attention has been given to the age group in between. As a result, the relative improvement in the survival rate in young adults has not kept pace with that achieved in younger patients. During the past year, this deficit became the subject of a national focus and initiatives.1–4 This review describes these issues relevant and specific to 15- to 29-year-olds5 with cancer and their caregivers. The ultimate goal is to heighten awareness of a relatively neglected group of patients who, during the next half century, deserve better.

EPIDEMIOLOGY

Incidence

Between age 10 years to late adulthood, the incidence of cancer increases exponentially with age (Figure 1). There are nearly 3 times more patients diagnosed during the second 15 years of life than during the first 15 years, accounting respectively for 2% and 0.75% of all invasive cancers.2 Approximately half of the 15- to 29-year-old patients are aged 25 to 29 years. Females demonstrate the exponential risk pattern from age 10 to 50 years; in contrast, males have 2 exponential risk patterns, from age 10 to 40 years and from age 40 to 80 years (Figure 1). The gender pattern of cancer incidence changes steadily as a function of age from a male predominance of 55% between age 5 to 10 years to a female predominance...
between age 40 to 45 years, with the transition from a male predominance in childhood to a female predominance in the middle years of life occurring during late adolescence/early adulthood. In the United States, non-Hispanic Whites have had the highest incidence of cancer among persons aged 15 to 35 years (Figure 2). The lowest incidence, approximately half that of non-Hispanic Whites, has been among American Indians and Native Alaskans (Figure 2), albeit the observed rate may be artificially low due to under-diagnosis or underreporting.

Prior to 1990, cancer increased in incidence for all age groups younger than age 45 years, with most of the increase having occurred in males. The increase in incidence among 25- to 44-year-old males was due in large part to increases in soft tissue sarcoma (notably, Kaposi sarcoma), non-Hodgkin lymphoma, and testicular carcinoma. Among females younger than age 45 years, the greatest increase occurred in germ cell tumors. Since 1992, however, the overall incidence of invasive cancer has not substantially changed in age groups younger than age 30 years (Figure 3). Based on incidence trends during 1975 to 2000, approximately 21,000 persons in the United States aged 15 to 29 years were estimated to be diagnosed with invasive cancer in the year 2000 (Table 1). Based on more recent trends, an estimated 20,260 new cases of invasive cancer can be expected to be diagnosed during 2007 in the United States among 15- to 29-year-olds (Table 1). At the current rate, 1 in every 168 Americans is predicted to develop invasive cancer between the ages of 15 to 30 years.

The types of cancer that occur in 15- to 29-year-olds are unique in their distribution. 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 the age group. Among 15- to 19-year-olds, lymphoma is followed by leukemia, sarcomas, and brain tumors in rank order, whereas in 20- to 29-year-olds, the order is lymphoma, melanoma, thyroid cancer, and testis cancer (Figure 4). Breast cancer and colorectal carcinoma begin to occur with measurable frequency in 20- to 29-year-olds (Figure 4).

**ETIOLOGY AND RISK FACTORS**

Overall, the vast majority of cases of cancer diagnosed before age 30 years appear to be spontaneous and unrelated to either carcinogens in the environment or family cancer syndromes. This contrasts with known etiologies and contributing factors in older adults in whom many cancers have been strongly linked to environmental causes. Rare exceptions include clear cell adenocarcinoma of the vagina or uterine...
cervix and breast cancer caused by prenatal diethylstilbestrol,6,8 second malignant neoplasms in patients treated with chemotherapy and/or radiotherapy for a prior cancer, melanoma induced by ultraviolet light, cervical carcinoma resulting from human papillomavirus, Kaposi sarcoma and non-Hodgkin lymphoma arising in persons infected with human immunodeficiency virus, and Hodgkin and Burkitt lymphomas resulting from Epstein-Barr virus.9

Given that the duration of exposure to potential environmental carcinogens is directly proportional to age, it is not surprising that tobacco-, sunlight-, or diet-related cancers are less likely to occur in older adolescents and young adults than in older persons. Skin cancer, lymphoma, sarcoma, thyroid cancer, and hepatic cancers may also occur at higher frequency during this period of life in persons with inherited conditions. In total, however, cancers attributable to environmental or inherited factors account for only a small proportion of the cancers that occur during adolescence and early adulthood.

Nonetheless, adolescents and young adults should be particularly aware of environmental carcinogens, including tobacco, ultraviolet rays from the sun and tanning lamps, recreational drugs, alcohol, and sexually transmitted diseases, since exposure to these agents starts or intensifies during this age period, and lifestyles are often established during adolescence and early adulthood. Cancer control efforts to reduce exposure to these carcinogens are unlikely to affect rates of cancers in young adults, but should decrease their rates as older adults.

TABLE 1 Incidence of Invasive Cancer Before Age 45 Years, Incidence Trends Since 1975 and Estimated Cases of New Cancer in 2006, by 5-year Age Intervals, US SEER*

| Age at Diagnosis (Years) | <5   | 5 to 9 | 10 to 14 | 15 to 19 | 20 to 24 | 25 to 29 | 30 to 34 | 35 to 39 | 40 to 44 |
|-------------------------|------|--------|----------|----------|----------|----------|----------|----------|----------|
| US population, year 2007 census, in millions* | 20.436 | 19.384 | 21.446 | 19.396 | 20.394 | 18.809 | 19.905 | 21.756 | 22.127 |
| Incidence of all invasive cancer per million per year, 1975 to 2000, SEER | 206 | 111 | 125 | 203 | 352 | 547 | 833 | 1,289 | 2,094 |
| Average annual % increase in invasive cancer, 1975 to 2000, SEER | 1.0 | 0.4 | 0.9 | 0.7 | 1.0 | 1.9 | 1.6 | 1.1 | 0.4 |
| Average annual % increase in invasive cancer, 1993 to 2003, SEER | −0.3 | 0.6 | 0.3 | 0.9 | 0.4 | −0.5 | −0.8 | −0.7 | −0.3 |
| Estimated incidence of invasive cancer per million, year 2007, United States | 206.4 | 116.4 | 125.1 | 212.5 | 336.5 | 493.3 | 737.5 | 1,154.5 | 1,979.5 |
| Estimated no. persons diagnosed with invasive cancer, year 2007, United States | 4,218 | 2,257 | 2,684 | 4,121 | 6,862 | 9,278 | 14,680 | 25,118 | 43,801 |

* Estimated from linear regression of 2001 to 2005 data from the US Census Bureau (www.census.gov/popest/states/NST-ann-est.html).7
As would be expected from the uniqueness of the types of cancer that occur in the adolescent and young adult age group, the signs and symptoms differ from the typical set promulgated for older adults and for children. Common symptoms of cancer in adolescents and young adults are masses in the neck, testis, breast, abdomen, or elsewhere; persistent or progressive fatigue and lethargy; abnormal discharge from an orifice; lymph gland swelling; unilateral knee/shoulder pain/swelling; change in mole; or a specific neurologic deficit or symptom of increased intracranial pressure.

Because of psychological and social factors in adolescents and young adults, patients in this age range may be at higher risk for a delay in diagnosis, which in turn may impact cancer survival. In a study of the interval between symptom onset and diagnosis in 2,665 children participating in Pediatric Oncology Group therapeutic protocols between 1982 to 1988, Pollock and colleagues found by multivariate analysis that for all solid tumors except Hodgkin lymphoma, cancer-specific lag times were longer in adolescents than in children. In addition, data from the University of Texas MD Anderson Cancer Center indicate that among 15- to 29-year-olds with newly diagnosed, previously untreated cancer, the lag time to diagnosis was correlated with the quality of health insurance. Those with public or no health insurance had statistically longer lag times in most of the cancers evaluated. In multivariate analysis, only the type of cancer and quality of health insurance were significantly correlated with lag time. Gender, age subgroup, race/ethnicity, religion, marital status, rural versus urban residence, median household income, and population density of the zip code of residence were not correlated.

Among a variety of explanations for young adults delaying to seek medical care and obtain a correct diagnosis are their sense of invincibility, lack of routine medical care, physicians poorly trained or unwilling to care for adolescents, under-recognition by medical professionals of cancer or its symptoms and signs in the age group, and lack of health insurance. Given the lack of routine care, empowering young adults and older adolescents for self-care and detection is important, particularly learning how to perform self-examination of the skin and, in females, being able to recognize any changes of the breasts, as recommended by the American Cancer Society (ACS) and the University of Texas MD Anderson Cancer Center. The ACS promotes awareness of testicular cancer in young men, but not routine testicular self-examination.

**Diagnostic Imaging and Pathology Considerations**

Many of the established procedures for diagnostic imaging, biopsies, pathologic evaluation, and staging have been derived from the more common malignancies in older adults, especially from the carcinomas that predominate in older patients. Older adolescents and young adults are typically referred to diagnosticians based on the patient’s age rather than on the disease. Yet, the workup for cancer is nearly always disease specific and usually not patient-age dependent. Hence, consults may be better undertaken by those who specialize in the age group (pediatric versus adult) to which the patient is referred. Knowing the most common sites and histology of malignancies in the age group assists in evaluating symptoms and in selecting the most appropriate imaging and biopsy procedures. Also, noninvasive imaging without the need for sedation, endoscopy, and minimally invasive surgery, all of which are available to patients in this age group.
group, may be underutilized in the age group because of a lack of health insurance and other economic constraints, difficulty taking off from work, transportation limitations, and a lack of understanding on the part of the professional staff as to what diagnostic and staging procedures are appropriate.

**DIAGNOSIS AND TREATMENT**

**Pediatric Versus Adult-care Specialists and Facilities**

The choice of cancer specialists most often depends on the decision of the referring physician. Young adult and older adolescent patients are seen by a breadth of specialists, including internists, family physicians, gynecologists, emergency room physicians, dermatologists, gastroenterologists, neurologists, and other specialists. These physicians may have very different referral patterns. And when the referral of a young adult or adolescent patient is made to an oncologist, it may be to a medical, radiation, surgical, gynecologic, or other oncologic specialist. The majority of 15- to 19-year-olds diagnosed with cancer are treated at adult facilities. In the end, the health care facility decision should be based in large part on which setting will provide the patient with the best outcome. If these are equivalent, “social” or “supportive” factors should next weigh into the decision. For some diseases, data support a particular site or specialist. In North America, France, the Netherlands, Denmark, Italy, and the United Kingdom, older adolescents with acute lymphoblastic leukemia (ALL) treated on pediatric clinical trials have fared considerably better than those treated on adult leukemia trials. In Germany, older adolescents with Ewing sarcoma who were treated at pediatric cancer centers had a better outcome than those treated at other centers. In Italy, young adults with rhabdomyosarcoma fared better if they were treated according to pediatric standards of therapy than when treated ad hoc or on an adult sarcoma regimen.

At the University of Texas MD Anderson Cancer Center, results of treatment for ALL in adults improved substantively after treatment derived from pediatric trials was introduced into the institution’s series of clinical trials. The analysis of data from the US National Cancer Data Base revealed that adolescents aged 15 to 19 years with non-Hodgkin lymphoma, leukemia, liver cancer, and bone tumors had a survival advantage if treated at a National Cancer Institute (NCI) pediatric group institution. Thus, for these pediatric types of cancer, the pediatric specialist/facility is favored.

For other cancers, adult-treating medical/surgical/radiation oncologists are more appropriate providers. Young adults with malignant melanoma, colorectal carcinoma, breast cancer, or epithelial ovarian cancer should be better served by medical oncologists, gynecologic oncologists, and surgical oncologists familiar with the cancers of adults. That most adult oncology centers have access to few services dedicated to older adolescent and young adult patients limits the comprehensiveness of care of the age group in the adult oncology setting.

The alternative is for adult-care specialists/facilities to adopt a pediatric approach, which may be difficult for a variety of historical, sociopolitical, economic, and infrastructure reasons. For example, the 3 major adult cooperative groups in the United States (Cancer and Acute Leukemia Group B, Southwest Oncology Group, and the Eastern Cooperative Oncology Group) are starting a trial of a pediatric regimen taken directly from the Children’s Oncology Group that will treat 15- to 29-year-old patients with ALL. A number of obstacles have been encountered in planning this approach, including differences in treatment philosophy (eg, when to resume therapy after myelosuppression relative to the platelet and absolute phagocyte counts and when to transfuse platelets and red cells), health insurance coverage, adherence of patients to treatment schedules and regimens, and the availability of supportive care and allied health professionals. Nonetheless, these obstacles are expected to be surmounted and the outcomes of young adult patients improved in the process.

Determining which specialist/facility is most appropriate certainly will vary from cancer to cancer and from case to case. Patients at any age who have a “pediatric” tumor, such as rhabdomyosarcoma, Ewing sarcoma, and osteosarcoma, will probably benefit from the expertise of a pediatric oncologist, at least in the form of
consultation. Individuals between the ages of 16 to 24 years may have varying levels of maturity and independence, and the choice of physician and setting for their care should be individually determined. Historically, medical oncologists have based the dose intensity of their chemotherapy regimens on their most common patients who, with a median age at cancer diagnosis of 68 years, have more coexisting morbid conditions and tolerate less therapy than their healthiest patients in the young adult age range. They may be less aggressive with chemotherapy dosing than the pediatric oncologist whose patients, like young adults, can tolerate higher doses. Pediatric oncologists have also pioneered risk-adapted therapies to preserve fertility and reduce adverse effects on body image. On the other hand, services to facilitate gamete preservation are usually more limited in pediatric than in adult centers.

Ideally, centers and oncologists devoted to the care of this group of patients could be available to provide age-specific nursing care, recreation therapy, and peer companionship. In the United Kingdom, “teenage cancer units” have been established that are staffed by physicians and nurses with expertise in adolescent and young adult cancer-patient management. The government has recognized their initial success and has decided to replicate the model nationally. Ultimately, there should be a discipline of adolescent and young adult oncology with its own training programs, science, translational research, clinical trials, and oversight organizations.

Treatment Differences

Surgery

In general, surgery is more readily performed in young adults or older adolescents than in younger or older patients because young adults are generally healthier than older patients, with fewer coexisting morbidities, and anesthesia is easier to administer and surgery more feasible than in children. A disadvantage relative to children and younger patients is that fully grown patients generally have fewer compensatory mechanisms to overcome deficits and disabilities resulting from the surgical resection of large tumors.

Radiation Therapy

Remarkably little is actually known about the differential normal tissue effects of radiotherapy in patients between age 15 to 30 years. Adolescents and young adults are generally less vulnerable to most adverse effects of ionizing radiation, as exemplified by the central nervous system, the cardiovascular system, connective tissue, and the musculoskeletal system, each of which may be irradiated to higher doses and/or larger volumes with less long-term morbidity than in younger patients. Exceptions are those sites and tissues that are still undergoing development, such as the breast and gonads. Infertility is of greater concern if the testes or ovaries are in the irradiated volume in adolescents or young adults. Breast cancer, for example, is more likely in women who received radiation for Hodgkin lymphoma if the radiation was administered between the onset of puberty and age 30 years. 

Chemotherapy

Adherence to therapeutic regimens, particularly oral chemotherapy, is often more problematic in teenagers and young adults than in younger and older patients, either because of the lack of parental or spousal oversight; feelings of invincibility on the part of the patient; or impediments to compliance because of transportation, financial limitations, or conflicts with work or school. Teenagers and young adults often display anticipatory vomiting when younger or older patients do not. For some chemotherapies, the adolescent and young adult is more resistant to the delayed or chronic adverse effects. Examples are anthracycline-induced cardiomyopathies and central nervous system dysfunction from neurotoxic chemotherapies like intrathecal methotrexate.

Treatment Intensity

On the other hand, the acute toxicities of radiation and chemotherapy are generally less problematic than in older patients who have coexisting morbidities, decreased tissue reserve, or are on medications or other drugs (eg, alcohol) that adversely affect the toxicity profile or treatment efficacy of chemotherapy. Adolescents and young adults better tolerate more intensive
therapy than older adults because of better organ function, especially marrow reserve. They typically recover more rapidly from myelosuppressive therapy and can tolerate higher dose-intensive regimens without dose delays or modifications required in older patients. For autologous rescue transplant regimens, they usually have more stem cells available in their peripheral blood than older patients. This should encourage those treating patients in this age group to push the limits of dose intensification.

Psychosocial and Supportive Care

Perhaps the greatest difference between patients in the adolescent/early adulthood age range and other ages is in supportive care, particularly psychosocial care. Adolescents and young adults have special needs that are unique, broader in scope, and often more intense than those at any other time in life. Cancer therapy causes practical problems in social arenas. The dependence of adolescent and young adult patients on peer-group approval poses greater challenges when confronted with a diagnosis of cancer. Self-image, a critical determinant during this phase of life, is compromised by many of the adverse effects of therapy, such as alopecia, weight gain or loss, mucositis and dermatitis (acne, mouth sores), bleeding, infection and contagiousness, susceptibility to infection and need for isolation, impaired sexuality (intimacy, impotency, tetragenicity risk), and mutilating surgery. Other challenges include the loss of time from school, work, and community and the financial hardships that occur at an age when economic independence from family is an objective. A wide range of financial challenges occurs in the age group. In addition to the health insurance challenge described above, there are the usual limitations in affording life, much more once confounded by the costs of cancer treatment. There may be guilt if not attending to these responsibilities or stress and fatigue if trying to keep up a semblance of normal activity. Partner relationships are tested by the strain of the cancer diagnosis and its therapy. Whether a partner stays in the relationship is challenged by fear of relapse or infertility and may be influenced unduly in either direction by guilt or sympathy. Those contemplating having children may fear passing on a genetic predisposition to cancer. Medical professionals are often poorly equipped to deal with the psychosocial challenges within the age group and are often stymied by the need in these patients to increase compliance, reduce stress, and improve the quality of life during cancer therapy.

Lack of Clinical Trials and Participation in Clinical Trials

Cancer patients between age 15 to 35 years have had the lowest proportion of patients accrued to clinical trials (Figure 5). When expressed as a proportion of all patients in the age group, more than 90% of children younger than age 15 years with cancer are managed at institutions that participate in NCI-sponsored clinical trials, and most of these young patients are entered onto clinical trials. In contrast, only 20% to 35% of 15- to 19-year-olds with cancer are seen at such institutions, and only approximately 10% are entered into a clinical trial. Among 20- to 29-year-olds, the participation rate is even lower, with fewer than 10% being seen at member institutions of the cooperative groups, and only approximately 1% of 20- to 29-year-olds entering clinical trials of the pediatric or adult cooperative groups. Among older patients, the trial-participation rate is higher, estimated to be between 3% to 5%. The reasons for the gap include a lack of available trials, lack of informing the young adult patient about clinical trials, inability or reluctance of the patient to participate in the trial, and financial limitations by both the patient/family and care provider.

Outcome

Duration of Survival

Twenty to 30 years ago, older adolescent and young adult cancer patients had a better overall survival from cancer than either younger or older patients (Figure 6, red segment of lower curve), primarily as a manifestation of having more favorable types of cancer like thyroid cancer, melanoma, testicular carcinoma, and seminoma. By the mid 1990s, this advantage was lost (Figure 6, upper curve), as younger and older patients benefited from survival improvement far more than did older adolescent and young adult patients. When patients with the major favorable types
of cancer are excluded from the survival-by-age analysis, the advantage of the older adolescent/young adult age range during the 1970s is still apparent, but it was converted to a relative deficit by the mid 1990s. Fourteen individual types of cancers in adolescent and young adult patients now have 5-year relative survival rates that are lower in the age group than in younger patients (Figures 7 and 8), 6 of which now have rates that are lower than in either younger or older patients (Figure 7).

The disparity in 5-year cancer survival between non-Hispanic Whites and each of the following is greater in 15- to 29-year-olds than in younger or older patients: African Americans, Hispanics, Asians/Pacific Islanders, and Native Americans/Alaska natives. The greatest difference is between African Americans and non-Hispanic Whites, among males, and particularly among male African Americans.

Quality of Survival

The quality of survival, both during and after therapy, is always a critical issue, but it is particularly problematic during adolescence and early adulthood. Certain acute toxicities of therapy such as alopecia; weight gain or loss; acne; bleeding; and sores of the mouth, urethra, and anus are harder for adolescents and young adults to cope with than for either younger or older patients. The same may be true for nausea, vomiting, and mucositis at sites other than the mouth, anus, and genitourinary tract. With emancipation for parental influences, patients in the age group may decide to forego therapy on an emotional rather than a rational basis. There is a higher rate of risk-taking behavior in young adult cancer survivors, such as tobacco use in 18- to 40-year-olds, compared with survivors of cancer who are diagnosed at a later age. Oligospermia and ovarian damage due to radiation or high doses of alkylating agents and decreased production of luteinizing and follicle-stimulating hormones may occur as a result of radiation of the mid brain. Fertility is a primary concern to many adolescent and young adult cancer survivors. Yet, most young adult cancer survivors do not recall an adequate discussion with their physician at the initiation of therapy of the risks of infertility or methods to decrease the risks. Persistent anxiety over relapse, death, or late effects is likely to be higher in adolescents and young adults who are cognitively aware of the severity of their illness than in those treated in early childhood (the Damocles syndrome). There is some evidence that suggests that adolescent and young adult cancer survivors show better attendance and performance at school and work.

Mortality

In the United States, cancer is the fourth most common cause of death among 15- to 24-year-old...
olds and the second most common cause of death due to disease (nonaccidental death), after suicide. Among 20- to 39-year-olds, cancer causes more deaths than heart disease, human immunodeficiency virus infection, diabetes mellitus, chronic liver disease (including cirrhosis), cerebrovascular disease, and congenital anomalies combined. In females, deaths caused by cancer occur at more than twice the frequency of the second leading cause of death caused by disease. Since 1970, when the cancer mortality rate in children was nearly twice the rate in 15- to 19-year-olds, their death rate has declined steadily and more rapidly than in 15- to 29-year-olds, such that the nation is now losing more 15- to 29-year-olds to cancer than children younger than age 15 years (Figure 9). Also, the death rate has a peak between age 15 to 25 years (Figure 10), which is in contrast to the incidence profile that has no peak in this age range (Figure 1). Also, between 1981 and 1999, the lowest reduction in the national cancer mortality rate over all age groups was in the 15- to 40-year-old group (Figure 10). Only since 1999 is there evidence that the rate in reduction in the death rate in this age group has begun to match other ages.

The national cancer death rate declined by 67% between 1970 and 2003 in both boys and girls younger than age 15 years (Figure 9). Also, the death rate has a peak between age 15 to 25 years (Figure 10), which is in contrast to the incidence profile that has no peak in this age range (Figure 1). Also, between 1981 and 1999, the lowest reduction in the national cancer mortality rate over all age groups was in the 15- to 40-year-old group (Figure 10). Only since 1999 is there evidence that the rate in reduction in the death rate in this age group has begun to match other ages. The national cancer death rate declined by 67% between 1970 and 2003 in both boys and girls younger than age 15 years. In 15- to 29-year-olds, the corresponding rate declined by 40% and 35% in males and females, respectively.

CONCLUSIONS, RECOMMENDATIONS, AND RECENT PROGRESS

The incidence of cancer in 15- to 29-year-olds is nearly 3 times of that during the first 15 years of life, the latter of which has received far more attention during the past half century. Cancer kills more 20- to 30-year-olds than any other disease except depression-induced suicide, and in young women, cancer outranks all other disease killers by a wide margin. Yet cancer in young adults has been under-recognized and frequently not considered by internists, family practitioners, pediatricians, gynecologists, other health professionals, and even, at times, oncologists.

 Whereas many cancers that develop later in life are due to health risk behaviors (tobacco use, poor diet and physical inactivity leading to obesity, sexually transmitted infections, etc.) and environmental carcinogens, cancers that arise in young adults are rarely preventable. Screening and the earliest possible detection of cancer in young adults are, therefore, especially critical. A singular exception may be carcinoma of the uterine cervix, which with the new human papillomavirus vaccines could be significantly reduced. Otherwise, the primary role of cancer prevention strategies in adolescents and young adults is to prevent their cancer in later adulthood by instilling lifestyles and preventive practices during formative years.

That one of the most favorable ages to have cancer, in terms of long-term survival expectations, is no longer the older adolescent/young
adult age group is unacceptable. In older adults, the average survival after cancer diagnosis is 10 years. Among 15- to 29-year-olds, the number of years of life that can be spared is obviously much longer. The 20-year-old who survives cancer can live another 40 to 60 years longer—that is, 4 to 6 times greater in terms of patient years affected or lost. And if one considers the potential long-term economic impact of health and attention to healthy behaviors in this age group—they are or can become the most productive members of society—the benefits of improving the duration and quality of survival in young adults is all the more obvious.

The reasons for the deficit in survival improvement span the gamut from patient to providers to society (Table 2).49 The most important factors appear to be a lack of awareness of the cancer problem in the age group, lack of health care insurance coverage and access to health care services, a deficit of clinical and translational research on cancer in older adolescents and young adults, and challenges in psychosocial supportive care and dedicated health care facilities.49

Young adults cannot afford to take their health for granted. Transcending the adolescent and young adult phase of life requires achieving self-sufficiency in health maintenance and screening, detection and prevention of disease, and financial responsibility. Health care requires planning and organization, as well as trust in confidentiality. Trust is essential in being able to negotiate the system and being able to achieve the best care. If young adults don’t trust the health care system, they will be less likely to learn how to navigate the system.

The danger of a delay in diagnosis or treatment because of nontraditional health care is another concern. Most adult cancer patients use complementary and alternative medicines, a practice that has been reported to be most prevalent in young adult cancer patients, especially females or those with a higher education.50,51 The vast majority of them will not reveal that information to their physicians or care providers.52,53 There are risks, including adverse interactions with chemotherapy and radiotherapy, as has been suggested for certain vitamins and antioxidants,52,53 but complementary therapies that are appropriately integrated into the standard of care can have a positive role.

To address the overall problem, the NCI conducted an evaluation in 2005 to 2006 of the current status of a cancer diagnosis in the United States between age 15 to 40 years. Named the Adolescent and Young Adult Oncology Program Review Group and co-funded by the Lance Armstrong Foundation, the review resulted in 5 categories of executive recommendations: (1) identification of the characteristics that distinguish the unique cancer burden in the older adolescent and young adult cancer oncology
patient; (2) education, training, and communication to improve awareness, prevention, access, and quality cancer care to older adolescents and young adults; (3) creation of tools to study the older adolescent and young adult cancer problem; (4) ensuring excellence in service delivery across the cancer control continuum (ie, prevention, screening, diagnosis, treatment, survivorship, and end of life); and (5) strengthening and promoting advocacy and support of the older adolescent and young adult cancer patient.3

In addition, the report contains numerous specific recommendations in each of the aforementioned categories, including a set of actions to improve the clinical trial deficit. Reasons other than poor clinical trial participation, such as undescribed differences in biology, delays in diagnosis, poor compliance or intolerance of therapy, and treatment by physicians less familiar with their diseases and psychosocial needs, may contribute to this outcome disparity, as well, and need to be studied.

A particularly important problem is the lack of clinical trial activity and participation among young adults with cancer. The NCI-sponsored pediatric and adult cooperative groups have launched a national initiative to improve the accrual of adolescents and young adults with cancer into clinical trials. In North America and Australia, the Children’s Oncology Group has taken a leadership role in this effort. In conjunction with the NCI and NCI-sponsored adult cooperative groups, 4 initiatives were identified as priorities for development: (1) improve access to care through understanding barriers to participation; (2) develop a cancer resource network that provides information about clinical trials to patients, families, providers, and the public; (3) enhance adolescent treatment adherence (compliance with protocol-prescribed

| General Category | Primary Factors† |
|------------------|------------------|
| Personal/patient (older adolescents and young adults) | Independence/autonomy, Feelings of invincibility, Underutilization of health care services, Awareness, Delays in diagnosis, Health insurance, Adherence, Financial limitations, Participation in clinical trials, Tumor specimens, Translational research |
| Family/community (family members, colleagues/friends, educators, employers, politicians, legislators, knowledge workers) | Awareness, Lack of education, Lack of guidance, Inadequate community resources |
| Health professional (physicians, nurses, allied health professionals) | Awareness, Delays in diagnosis, Health care teams, Education/training, Reimbursement, Health insurance, Participation in clinical trials, Tumor specimens, Translational research, Lack of specialty/discipline |
| Societal/cultural (health care system) | Awareness (by employers, school personnel, associates, neighbors, community), Health insurance, Delays in diagnosis |

* Modified from Bleyer A, Barr R.49
† Items in italics appear in multiple categories.
therapy); and (4) establish and promote participation in sarcoma trials specifically designed for patients in this age group.

The Children’s Oncology Group Adolescent and Young Adult Committee was formed in 2000 to research the obstacles faced by older adolescents and young adult patients. Working in conjunction with the adult cooperative groups in the United States, an increased number of national clinical trials were opened to older adolescent and young adult cancer patients. A measure of success was achieved in 2003 to 2005, with increased accruals to cancer treatment trials in comparison with the 3 previous years among adolescent and young adult patients in comparison with both younger and older patients (Figure 11). Whereas 20- to 25-year-olds had the lowest estimated proportion of US cancer patients entered onto national cancer treatment trials of all age groups up to age 65 years, there is now evidence that this is no longer true.

Working with the Southwest Oncology Group (for adult patients), the initial focus of the Committee was on sarcomas. Since then, the number of sarcoma patients younger than age 40 years entered on national treatment trials has steadily increased from approximately 320 per year in 1998 to 1999 to over 500 per year in 2004 to 2005 (Figure 12, upper panel). Relative to accruals to all cancer treatment trials, the proportion represented by sarcoma entries nearly doubled (Figure 12, lower panel). Most of the increase was in the 15- to 39-year age group, particularly during the last 2 years. Most of the increase in the latter was not due to clinical trials in gastrointestinal stromal tumors, which is an important differentiating point, since with the discovery in the early 2000s of imatinib as a specific therapy for gastrointestinal stromal tumors, clinical trials of this type of sarcoma were in vogue and could have explained the overall sarcoma accrual increase.

Another relevant initiative in the United States is the formation of a consortium of the Live-Strong Young Adult Alliance, a coalition of organizations dedicated to addressing the care and research of cancers in young adults. The main objective of the Alliance is to help implement the recommendations of the National Cancer Institute Adolescent and Young Adult Oncology Program Review Group.

Eventually, resources will be devoted to educating the public, health professionals, insurers, and legislators about the special needs of the older adolescent and young adult cancer population. Ultimately, schools of medicine, osteopathy, nursing, dentistry, and pharmacy will better address the current lack of formal training in the unique health and health care problems of older adolescents and young adults. Specific training programs in adolescent and...
TABLE 3 Practical Suggestions to Enhance Early Detection of Cancer and Clinical Trial Participation in Older Adolescents and Young Adults*

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| Transcending the adolescent and young adult passage requires the realizations that life is finite; that health is not an entitlement— it must be earned and maintained; and that disease strikes randomly, but regularly. |
| Appreciate that cancer occurs in 1 in every 200 older adolescents and young adults and that everyone is at risk. |
| Know that there are very few known causes of cancer during early adulthood and that "it just happens," regardless of the health of the person. |
| Be aware that young adults often deny symptoms, are too embarrassed to report them, or attribute them to psychosomatic manifestations. In addition to performance or referral for conventional cancer screening tests as appropriate by age and gender beginning at age 20 years, on the occasion of a periodic health examination, the cancer-related check up should include examination for cancers of the thyroid, testicles, ovaries, lymph nodes, oral cavity, and skin, as well as health counseling about tobacco, sun exposure, diet and nutrition, risk factors, sexual practices, and environmental and occupational exposures. |
| Beginning in their early 20s, women should be told about the benefits and limitations of breast self-examination and the importance of prompt reporting of any new breast symptoms to a health professional; for those who choose to perform breast self-examinations, a health professional should teach them how to do it and check their technique during a periodic health examination. |
| Women should undergo cervical cancer screening within 3 years after beginning to have vaginal intercourse, but no later than age 21 years; the Pap test performed in conjunction with the pelvic examination should be performed every year if it is a conventional test or every 2 years if it is a liquid-based test, until age 30 years, when after 3 normal test results the screening can be spaced out to every 2 to 3 years. |
| Before beginning to have sexual intercourse, each female should be immunized against the human papillomavirus by receiving the new vaccine. |
| Males should have a testicular examination during every periodic health examination and should promptly report new scrotal symptoms or masses to a health professional. |
| Illness in older adolescents and young adults is easy to miss—even for skilled and experienced clinicians. |
| Encourage and assist young adults to seek care at a comprehensive health care center. |
| Realize that young adults are least likely to have adequate health insurance and that they should not allow themselves to "age out" of insurance. |
| Convey that what is done at the time of the cancer diagnosis is important and that the best outcome is determined by the initial evaluation and therapy. Optimal cancer management means doing it right from the start! |
| Once diagnosed with cancer, suggest that young adults ask about clinical trials. If none are available on site, help them find centers that participate in clinical trials suitable for their age. |
| Once enrolled on a clinical trial, the adolescent and young adult cancer patient needs understanding and support in order to best adhere to the trial’s requisites. For those who become spouses or parents during the adolescent and young adult years, responsibility for the health of others begins. |

*The National Cancer Institute Adolescent and Young Adult Program Review Group adopted a higher age limit for the definition of young adult: age 39 years.3

Young adult oncology and the development of a formal discipline may eventuate.55 Meanwhile, several practical suggestions should facilitate early detection of cancer in adolescents and young adults and promote referral to a cancer center where clinical trials are a priority (Table 3).

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