
Chapter 15

Highlights and Challenges



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HIGHLIGHTS AND CHALLENGES

Summary

- Cancer patients diagnosed when 15 to 29 years of age are at the interface of pediatric and young adult oncology.
- In this age group, cancer is unique in the distribution of the types that occur; at no other age is the distribution similar.
- Cancer occurring at 15 to 29 years of age accounts for only 2 to 3 percent of all invasive cancer, but is nearly three times more frequent in incidence than cancer during the first 15 years of life.
- In the 15- to 29-year age group, males are at higher risk than females of developing cancer and have a lower likelihood of survival, with the risks directly proportional to age.
- Over a span of just 15 years, from age 15 to 29, the frequency distribution of cancer types changes substantively, such that the pattern at the youngest age does not resemble the one at the oldest.
- The vast majority of cases of cancer diagnosed before age 30 appear to be spontaneous and unrelated to either carcinogens in the environment or inherited factors. Exceptions are those melanomas due to ultraviolet light, cervical carcinoma caused by the human papillomavirus infection, Kaposi sarcoma and certain non-Hodgkin lymphoma related to the human immunodeficiency virus; and Hodgkin and Burkitt lymphomas associated with the Epstein-Barr virus.
- Hodgkin lymphoma, Ewing sarcoma, osteosarcoma, and testis cancer peak in incidence within this age range. Melanoma, female genital tract malignancies, thyroid cancer, soft-tissue sarcomas, non-Hodgkin lymphoma, leukemia, central nervous system tumors, breast cancer, and non-gonadal germ cell tumors account for 95% of the remaining cancers in this age group.
- Among the races/ethnicities evaluated, the incidence of cancer in this age group is highest among non-Hispanic whites and lowest in Asians, American Indians and Alaska Natives. Survival has been worse among African Americans/blacks, American Indians, and Alaska Natives than among the other races and ethnicities.
- The incidence of cancer in the 15- to 29-year age group increased steadily during the past quarter century. The rate of increase is now slowing, and at the older end of the age range the overall incidence appears to be returning to the incidence of the 1970s. Reasons for these changes remain speculative.
- 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 in 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, and the deficit is increasing with longer follow-up.
- The deficit in survival improvement is not limited to the United States; it appears to be a global problem.

Challenges

- Adolescent and young adult oncology patients belong to a distinct age group and, like pediatric, adult, and geriatric patients, have unique medical and psychosocial needs.
- Challenges in treating the 15- to 29-year age group include understanding the complex psychosocial environment of this age group, particularly during diagnosis and treatment, managing chronic and delayed adverse sequelae, overcoming a lack of progress in prolonging survival, improving the quality of survival, and addressing the economic costs associated with diagnosis, treatment and long-term follow-up.
- The single greatest current challenge in young adults and older adolescents with cancer is to overcome the lack of progress in their survival improvement, a deficit that has spanned nearly a quarter of a century.
- There are multiple reasons for the lack of progress. These may be categorized into personal/patient (older adolescents and young adults), family/community (family members, colleagues/friends, educators, employers, politicians, legislators, knowledge workers), health professional (physicians, nurses, allied health professionals), and societal/cultural (healthcare system) factors.

- The features common to the above factors are lack of awareness, inadequate health insurance coverage, lack of clinical trial participation, and a deficit in translational research of the cancers in older adolescents and young adults.
- Solutions to the survival deficit include raising awareness about the problem, improving healthcare access and insurance, enhancing understanding of the biology of cancers that occur in this age group, developing national and international organizations to address the deficits, and ultimately, creating a formal discipline of adolescent/young adult oncology.
- In particular, resources should be devoted to educating the public, health professionals, insurers, and legislators about cancer during this phase of life and about the special needs of these patients.
- Specific attention should be paid to longer delays in diagnosis that occur in older adolescents and young adults relative to younger patients. These are correlated with the quality of health insurance coverage.
- Also of special importance is the facility where diagnosis and treatment take place. For several of the pediatric type of malignancies (acute lymphoblastic leukemia, acute myelogenous leukemia, Ewing sarcoma, rhabdomyosarcoma), there is evidence that the therapeutic approach taken by pediatric oncologists has led to better survival rates than those applied by medical oncologists and hematologists.
- Meanwhile, older adolescents and young adults with cancer should be encouraged to report symptoms without delay, to seek care at a comprehensive health care center, to not “age out” of insurance, to understand that what is done at the time of diagnosis is most important, and to ask about and find clinical trials for their age.

INTRODUCTION

Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975-2000 includes 15 chapters contributed and reviewed by more than 50 authors, editors and reviewers from a wide variety of disciplines across the spectrum of pediatric and adult oncology. In this chapter, the senior editors offer their perspectives on the monograph's highlights, elucidate challenges, and offer recommendations for the future. The opinions expressed by the editors are theirs alone, and do not officially represent the opinions of any of the chapter authors per se, nor of their organizations, including the U.S. government, the National Cancer Institute, or the National Institutes of Health.

CURRENT STATUS

Despite the well-known and characterized childhood cancer incidence peak, malignant disease diagnosed from 15 to 29 years of age is nearly three times more frequent in the U.S. and Canada than cancer during the first 15 years of life. It is nonetheless uncommon, relative to cancer at older ages, and accounts for just 2% of all invasive cancer. The vast majority of cases of cancer diagnosed before age 30 appear to be spontaneous

and unrelated to either carcinogens in the environment or inherited factors. Exceptions are melanoma induced by ultraviolet light, cervical carcinoma ascribed to human papillomavirus, Kaposi sarcoma and non-Hodgkin lymphoma related to human immunodeficiency virus, and Hodgkin and Burkitt lymphomas associated with Epstein-Barr virus. These six cancers account for the vast majority of malignancies known to be environmentally-induced in this age group. In aggregate, they represent more than one-third of cases, with the remainder not known to be either caused by environmental agents or inherited (familial) factors.

In this age group, cancer is unique in the distribution of the types that occur—at no other age is the distribution similar. 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 non-gonadal germ cell tumors account for 95% of the cancers in 15- to 29-year-olds. Over a span of just 15 years—from age 15 through 29—the frequency distribution of cancer types changes dramatically, such that the pattern at the youngest age does not resemble that at the oldest. The incidence of cancer in the 15- to 29-year age group increased steadily during the past

quarter century. However, the rate of increase is slowing and at the older end of the age range the overall incidence appears to be returning to the rate of the 1970s. Compared to females, males in the 15- to 29-year age group are at higher risk of developing cancer and have a lower likelihood of survival, with the risks directly proportional to age. Among the races/ethnicities evaluated, the incidence of cancer in this age group is highest among non-Hispanic whites and lowest in Asians, Pacific Islanders, American Indians and Alaska Natives. Survival has been worse among African Americans/blacks, American Indians, and Alaska Natives than among the other races and ethnicities.

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, compared to a cancer diagnosis at other ages. Since then, there has been a relative lack of progress in survival improvement among older adolescents and young adults. In the U.S., the 15- to 19-year age group showed some progress in the early 1980s, but progress has remained relatively static since 1986 (Figure 15.1, upper panel). In the 20- to 24-year age group, there has been no improvement since 1980 (Figure 15.1, middle panel). The 25- to 29-year age group actually had a decline in the overall survival rate in the mid- to late 1980s, likely due to HIV-related cancers, primarily Kaposi sarcoma and non-Hodgkin lymphoma (Figure 15.1; lower panel). In the latter age group, the decrease abated as HIV-induced cancers were prevented during the 1990s; there is evidence that a modicum of overall survival improvement has been achieved subsequently (Figure 15.1; lower panel).

Paramount among other challenges is improving the quality of survival of cancer patients in this age group. This includes enhancing the psychosocial environment during diagnosis and treatment, reducing and preventing acute, chronic and delayed adverse sequelae, and abrogating the financial costs associated with diagnosis, treatment and long-term follow-up.

REASONS FOR LACK OF PROGRESS

The relative lack of survival improvement for older adolescent and young adult cancer patients is a complex

issue. In this section, probable explanations and contributing factors are specified and potential solutions are suggested. Contributing factors were derived from workshops and discussion groups hosted by the U.S. National Cancer Institute (NCI),¹ the Children’s Oncology Group (COG), the International Society of Pediatric Oncology (SIOP),² and from preliminary studies in the U.S. Proposed explanations were categorized according to whether they applied to individuals (potential patients or patients diagnosed to have cancer), family/community members, the health care profession or society/culture in general.³ In turn, each category was subdivided into factors that were likely (primary determinants) or unlikely (secondary determinants) to explain the survival deficit (Table 15.1).

Personal/Patient

The personal/patient category includes the individual adolescent and young adult before, during and after a cancer diagnosis. Importantly, it includes persons before they are diagnosed with cancer—because of the importance of early diagnosis in an age group for which prevention is largely ineffective. Factors within this category can be further subdivided into those that are biologic/physical, psychologic/emotional/spiritual, economic/financial, and social. Biologic factors include the unique physiologic and pharmacologic characteristics of adolescent and young adult patients and their cancers, many of which are unique to their age group.

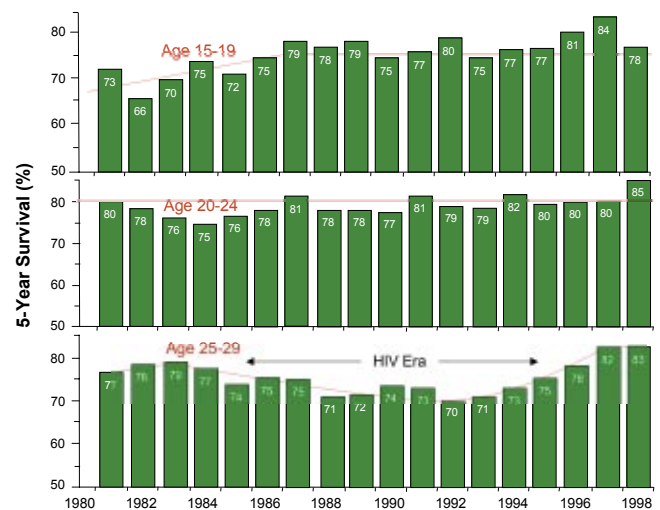


Figure 15.1: 5-Year Survival Rate for All Invasive Cancer Since 1980 by Age Group, U.S., SEER

A primary factor in the personal/patient category is the overarching goal for those in this age group to learn how to become independent and autonomous. To a large extent, making one’s way in the world does not lend itself to concern about the risk of cancer. The individual is much more challenged by tasks of daily living and the immediate future. Another factor is the characteristic, age-specific feeling of immortality and invulnerability, which at no other time in life is more prominent. It is striking how few adolescents and young adults are aware that cancer can and does occur in their age group, or that the risk of developing cancer increases exponentially with age.

and external pressures that mitigate adherence. The former has been well characterized in adolescents, not only with respect to expectations but also with regard to compliance with chemotherapy.⁴⁻⁷ Once in college or in the workforce, many young adults face restrictions about taking time for medical concerns. Having to attend class, complete homework, or be on the job make it difficult to adhere to the rigors of diagnosis and treatment, especially when teachers, school administrators and employers are not aware of, or won’t accommodate, their student’s or employee’s needs with respect to cancer management (see *Family/ Community* section below).

Adherence to treatment regimens is another major factor, both in terms of an intrinsic antagonism towards compliance (as a result of the need to become autonomous)

Also important is the frequent lack of, or utilization of, health insurance in adolescents and young adults. As described below, this is more problematic in this age

Table 15.1: Factors Likely (Primary) or Unlikely (Secondary) to Explain the Survival Deficit

GENERAL CATEGORY	PRIMARY FACTORS*	SECONDARY FACTORS
Personal/Patient (older adolescents and young adults)	Independence/Autonomy Feelings of Invincibility Under-utilization of Healthcare Services <i>Awareness</i> <i>Delays in Diagnosis</i> <i>Health Insurance</i> Adherence Financial Limitations <i>Participation in Clinical Trials</i> <i>Tumor Specimens</i> <i>Translational Research</i>	Embarrassment Psychosomatic Emphasis Transportation Limitations Psychosocial Environment during Diagnosis and Treatment Pharmacokinetic Differences
Family/Community (family members, colleagues/friends, educators, employers, politicians, legislators, knowledge workers)	<i>Awareness</i> Lack of Education Lack of Guidance Inadequate Community Resources	Constituency Influence
Health Professional (physicians, nurses, allied health professionals)	<i>Awareness</i> <i>Delays in Diagnosis</i> Healthcare Teams Education/Training Reimbursement <i>Health Insurance</i> <i>Participation in Clinical Trials</i> <i>Tumor Specimens</i> <i>Translational Research</i> Lack of Specialty/Discipline	Communication Skills Facilities Turf Conflicts Lack of Dedicated Researchers
Societal/Cultural (healthcare system)	<i>Awareness</i> (by Employers, School Personnel, Associates, Neighbors, Community) <i>Health Insurance</i> <i>Delays in Diagnosis</i>	Focus on Young and Middle Age Competing Challenges

*Items in italics appear in multiple categories

group than in any other. In the U.S., young adults are the most underinsured age group, falling in the gap between parental coverage and programs designed to provide universal health insurance to children (Medicaid and Children’s Health Insurance Programs) on the one hand, and the coverage supplied by a full-time, secure job on the other. Nearly one-third of all 18- to 24-year-olds in the United States are uninsured, and more than 40% are either uninsured (Figure 15.2) or have Medicaid (state government) assistance (Figure 15.3).⁸ More than twice as many 18- to 24-year-olds are uninsured or underinsured as 45- to 54-year-olds (Figures 15.2 and 15.3).

Young adults and older adolescents also have the lowest rate of primary care use of any age group in the United States.⁹ Regardless of health insurance status, adolescents and young adults are more likely than younger children to lack a usual source of care. Without a primary physician with knowledge of the patient’s baseline health status, the symptoms of cancer can be missed.

Cancer patients in the 15- to 29-year age group are at the interface between pediatric and adult oncology (Figure 15.4). They have cancers that peak in incidence within their age range (Figure 15.4) and a mix of tumor types (Figure 15.5) unique to their age. As a result, patients in the 15- to 29-year age group present a special challenge to those trained to care for younger and older persons (see *Health Professional* factors below).

Family/Community

The family/community category includes family members, colleagues/friends, educators, employers, politicians and knowledge workers, who in general also lack awareness of the cancer problem in the adolescent and young adult group. Despite often being the first source of information and guidance for a young person, they almost always lack education and guidance themselves. Patient navigator programs conducted by community volunteers and cancer survivors—for prostate, lung, breast or colorectal cancer, for example—have been formed in many communities because of this need. However, such programs, when they do exist, are rarely applicable to adolescents or young adults. Community resources that exist at the local level are generally devoted to younger and older patients.

Health Professional

Health professional factors include a lack of awareness about cancer in the adolescent and young adult, in part due to a lack of training and in part to the absence of continuing medical education programs on the topic. Oncology specialists and allied health professionals have less knowledge about treating this age group than children or adults with cancer. Approximately one half of the cancers in the 20- to 29-year age group constitute those ordinarily treated by adult oncologists (medical, radiation, gynecologic, surgical); the other half are more familiar to pediatric oncologists and their specialized pediatric diagnostic, therapeutic and supportive care teams (oncology nurses, radiologists, pathologists, infectious disease specialists, endocrinologists, nephrologists, psychologists,

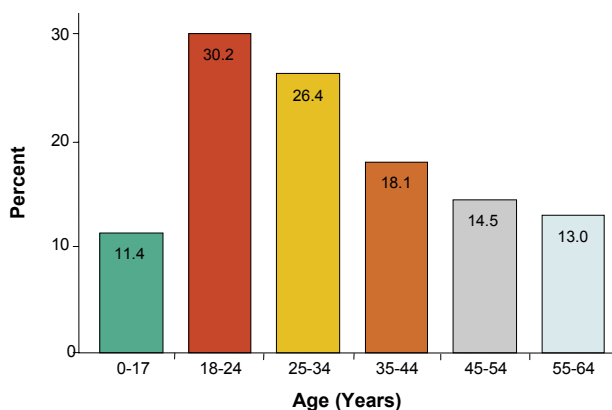


Figure 15.2: Percent without Health Insurance, Under 65 Years of Age, U.S., 2003

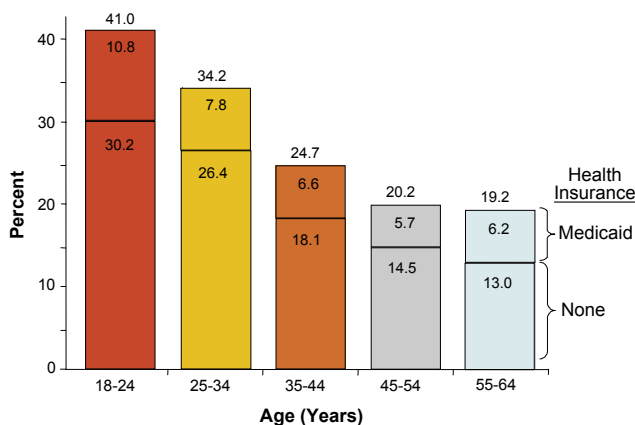


Figure 15.3: Percent without Health Insurance, 18 to 65 Years of Age, U.S., 2003

psychiatrists, and social workers) (Figure 15.5; lower pie diagram). The pediatric approach is favored for 15- to 19-year-olds, because two-thirds to three-fourths of the malignancies that occur in this age group are well known by the pediatric oncology team (Figure 15.5; upper pie diagram).

In contrast to the breadth of the pediatric oncology team, healthcare teams available to the young adult patient in an adult care program pale by comparison. It is rare that an adult patient has access to the services provided to a patient at a pediatric cancer center (Figure 15.6).

In general, specific communication skills are needed to relate to adolescents. Neither adult nor pediatric oncologists are trained with these skills, and difficult topics of conversation, such as sexuality and fertility, are often not addressed.

There is no other patient age group for which the time period to diagnosis is longer, clinical trial participation is lower,¹⁰ and fewer tumor specimens are available for translational research (Figure 15.7). The lack of clinical trial participation is particularly problematic. Only one to two percent of all 20- to 29-year-olds with cancer can be identified as participating in a therapeutic clinical trial sometime during their cancer experience. A correlation exists between the level of clinical trial activity and improvement in survival prolongation and mortality reduction.¹¹⁻¹³ These factors explain much of the deficit in translational research and the lack of tumor specimens available for studies assessing molecular and cellular mechanisms of cancer in this age group. There is also a shortage of laboratory-based and clinical researchers dedicated to the study of cancers in the adolescent and young adult age group.

Patterns of care delivered to adolescents and young adults differ from those delivered to younger and older patients. Children are treated almost always in pediatric facilities where the specialists are familiar with their diseases, where they receive age-appropriate therapy, and where they are frequently enrolled in clinical trials.¹⁴⁻¹⁶ By contrast, some adolescents receive care in adult facilities where certain diagnostic and treatment events take longer to accomplish than in

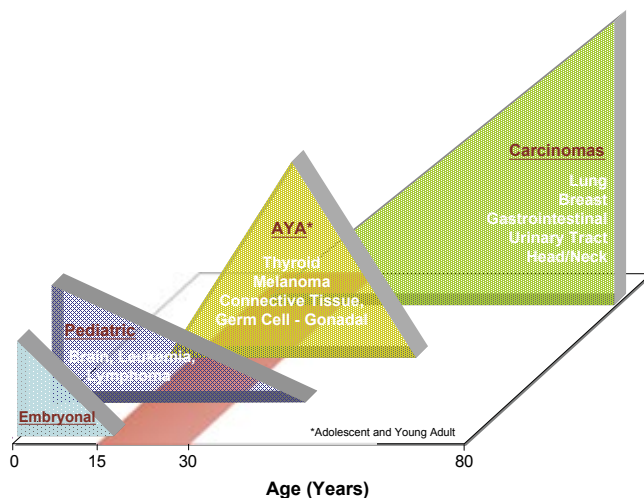
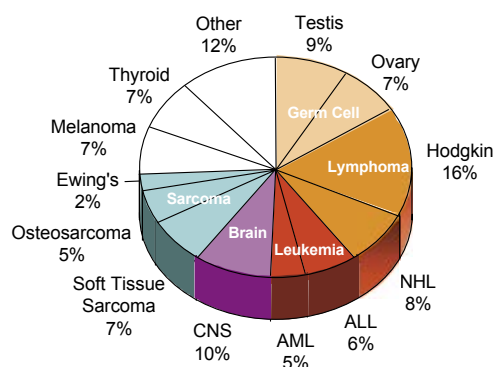
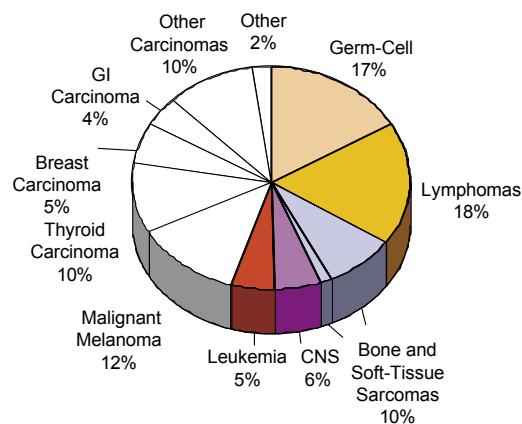


Figure 15.4: The Interface Between Pediatric and Adult Oncology

15- to 19-Year-Olds



20- to 29-Year-Olds



Segments in color represent "pediatric malignancies"

Figure 15.5: Cancers in 15- to 29-Year-Olds, U.S. SEER, 1975-2001

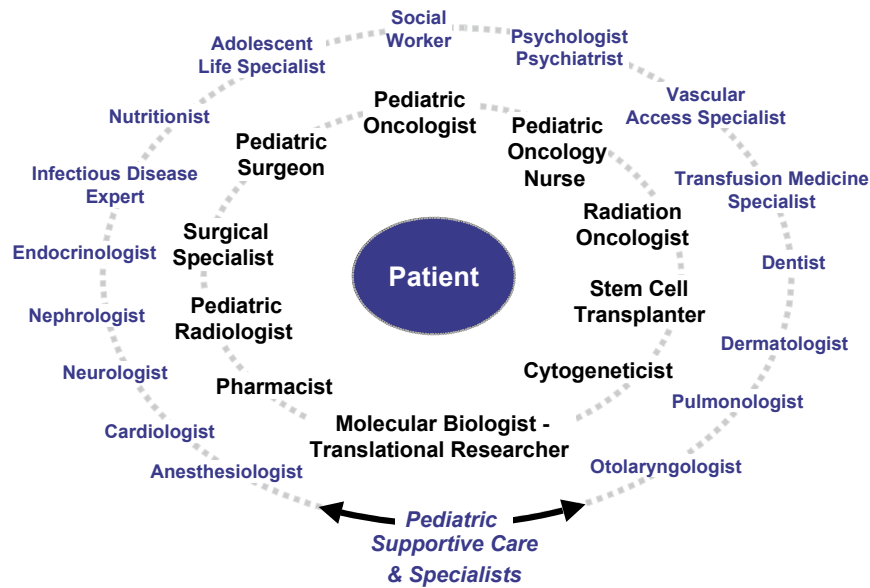


Figure 15.6: Pediatric Oncology Team

pediatric centers.¹⁷ Also, adolescents are more likely to delay contact with the health care system, behavior likely related to their increasing autonomy.¹⁸⁻²⁰ Finally, types of cancer differ between children and adolescents, and the two groups have different tolerances for therapy.^{21,22} These factors, taken together, contribute to delays in diagnosis and treatment for adolescents and young adults with cancer. When their care is managed less efficiently and effectively than that of other age groups, decreased survival is the likely outcome.

As alluded to above, few—if any—health care centers have dedicated units for adolescents and young adults. One of the most frequent complaints from patients in this age group is that they have little in common with other patients in the waiting room, outpatient clinic, or hospital environment.

Reimbursement is a factor for both pediatric and adult oncology treatment teams. The lower rate of health insurance coverage in young adults lowers the reimbursement rate of services rendered and tends to diminish incentives for providers and limit diagnostic evaluation, treatment interventions, and supportive care.

That patients in the adolescent and young adult age group are at the interface between pediatric and adult medicine may lead to uncoordinated care, to uncertainties about

who is responsible for their management, and, in worse case scenarios, to conflicts of turf.

Societal/Cultural

The societal/cultural category consists of the challenges societies face in providing for the healthcare needs of older adolescents and young adults. The general public is largely unaware of cancer as a significant health care problem among young adults in the U.S. Even health-care providers at universities and colleges do not have cancer in their curricula. High schools and universities do not have cancer awareness as an essential educational or health evaluation component. It is not surprising, therefore, that the time to diagnosis in older adolescent and young adult patients is not only delayed relative to the time to diagnosis in younger patients, but that it is also correlated with health insurance status, as discussed below.

PRIORITIZATION OF CHALLENGES AND POTENTIAL SOLUTIONS

Primary factors (Table 15.1) contributing to the deficit in survival for older adolescents and young adults should be prioritized over secondary factors, and those factors that appear in more than one category are likely to be more important targets for change. *Lack of awareness*, for example, appears in all of the four major categories.

Inadequate health insurance coverage appears in three categories, as does *low participation in clinical trials*. A *deficit in translational research* and *lack of tumor specimens for research* appear in two categories. These four factors—*awareness, health insurance, participation in clinical trials, and translational research*—may be regarded as paramount and are emphasized in the prioritization review below.

Personal/Patient

Awareness is a primary goal. Older adolescents and young adults not only believe they are immune to the risks of disease and accident, they do not realize the risk of cancer is one in 210 for those between 15 and 29 years of age in the U.S. Overcoming ideation of invincibility will require local and national educational efforts. The importance of healthcare availability and healthcare insurance coverage will also need more emphasis, while the availability and goals of clinical trials will require particular attention. Moreover, the approaches used to educate and recruit adolescent and young adult cancer patients to clinical trials and translational research efforts will likely need to be quite different from those utilized for older adults.

Family/Community

Those who associate with older adolescents or young adults should be aware that cancer occurs in this age group and be able to advise and encourage a medical evaluation for symptoms and signs of malignant disease. This applies to family members, friends, neighbors, classmates, teachers, fellow employees, employers, and clergy.

Health Professional

Health professionals must become more aware of cancer occurring during early adulthood, and professional training and continuing education should emphasize the risk of cancer and its common symptoms and signs. Health professionals should become advocates for affordable health insurance. Oncologists should become more cognizant of the gaps in clinical trial activity and translational research in the adolescent and young adult group. They should make available more clinical trials for the adolescent and young adult population and seek ways to increase clinical trial participation specific to this age group.

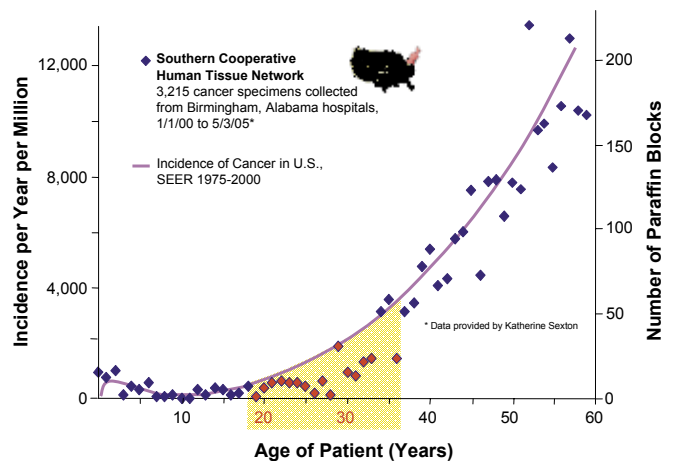


Figure 15.7: Number of Tumor Bank Specimens Compared with Incidence of Cancer by Age

Societal/Cultural

The lack of awareness of the adolescent and young adult cancer problem should be overcome with public information and education programs. Legislators, health policy administrators, insurance company directors, national medical organization leaders, and leaders of institutions of higher learning should be particularly informed and educated. The role of healthcare insurance should be emphasized, as should the risk of cancer in educational curricula. In the U.S., cancer organizations such as the American Society of Clinical Oncology, the American Cancer Society, the National Cancer Institute, the National Comprehensive Cancer Network, C-Change, and the national cancer cooperative groups should make adolescent and young adult oncology a priority. They should be joined in this effort by private cancer foundations that have a responsibility for young adults or older adolescents, such as Planet Cancer, Fertile Hope, Young Survival Coalition, and The Leukemia and Lymphoma Society (see *Appendix I*). Ideally, universal healthcare insurance should be available to all persons in the 18- to 29-year age range, until private insurance is provided by an employer or young people can afford or supplement it on their own.

In summary, *improving awareness of the cancer problem, providing better healthcare insurance coverage and access to healthcare services, and increasing clinical and translational research on cancer in older adolescents and young adults* are challenges that would benefit patients in

this age group. This is not to say that challenges such as psychosocial supportive care and dedicated healthcare facilities are not important. On the contrary, they are crucial. But tackling problems of highest priority is likely to have downstream effects that will alleviate many of the other problems listed in Table 15.1. The solutions will take a coordinated effort at local, regional, national and international levels. Four additional challenges are discussed in further detail below.

Time to Diagnosis is Longer in Adolescents and Young Adults than in Children

The interval from the onset of the first cancer-specific symptom to the first anti-cancer treatment, known as the *waiting time*, has been shown to be longer in adolescents than in children.²³⁻²⁶ Young children (younger than 5 years of age) have been observed to have the shortest waiting times.²⁷ The waiting time may be influenced by factors related to the individual, to the health care system, and/or to the disease. Variation in waiting times among children has been shown to be due primarily to the type of disease, and secondarily to age. The time from onset of symptoms to initial health care contact is influenced by individual and health care system factors; the time from initial contact to assessment by treating oncologist or surgeon is most likely affected by health care system factors; and the time between that assessment and date of first anti-cancer treatment most likely reflects disease-related factors.²⁸⁻³⁰

The interval from onset of the first cancer-specific symptom to the day of cancer diagnosis is referred to as the *lagtime*. Studies in the United States, Canada, Scotland, and Mexico have demonstrated that lagtimes are longer in adolescents than in children.³¹⁻³⁵ In these studies it is unclear whether the longer lagtime experienced by adolescents—in comparison with younger children—are related to the types of cancers they develop or to other factors related to their age.³⁶

In the U.S., health insurance coverage is a major determinant of lagtimes in patients 15 to 29 years of age.³⁷ The lagtimes in this age group are more closely correlated with health insurance status than race, ethnicity, gender, marital status, religion, urban versus rural home residence, or median household income of the zipcode of residence.^{3,37}

The issue of health insurance coverage is likely a greater factor in 18- to 29-year-olds than in any other age group, since this is the age in the U.S. at which health insurance coverage is the lowest. Countries with national health insurance are also likely affected by this determinant, since health insurance utilization is lower in the young adult age range than in younger or older persons despite the universal availability of health insurance.

Place of Diagnosis and Treatment: Pediatric versus Adult Care Specialists and Facilities

A central, complex issue is the choice of the most appropriate specialist who will manage care for the older adolescent and young adult cancer patient—a pediatric oncologist or an adult oncologist (medical, radiation, surgical or gynecologic oncologist). For older adolescents, the site of diagnosis and treatment may be problematic since, at least in theory, these patients could be treated at either a pediatric or adult care facility. Leonard and his colleagues in the United Kingdom have pointed out that adult oncologists are “untutored in arranging ancillary medical, psychological, and educational supports that are so important to people who are facing dangerous diseases and taxing treatment at a vulnerable time in their lives” and “unpracticed in managing rare sarcomas.” Simultaneously, they have emphasized that pediatric oncologists “have little to no experience in epithelial tumours or some of the other tumours common in late adolescence.”³⁸ In 1997, the (admittedly biased) American Academy of Pediatrics issued a consensus statement in which it indicated that referral to a board-eligible or board-certified pediatric hematologist-oncologist and to pediatric subspecialty consultants was the standard of care for all pediatric and adolescent cancer patients.³⁹ A wider consensus panel that included adult oncologists, the American Federation of Clinical Oncologic Societies, also concluded that “payors must provide ready access to pediatric oncologists, recognizing that childhood cancers are biologically distinct” and that the “likelihood of successful outcome in children is enhanced when treatment is provided by pediatric cancer specialists.”⁴⁰ However, neither of these statements defines an age cutoff in the recommendations.

Currently, the choice of specialist is made haphazardly and most often depends upon the decision of the referring physician. Younger children primarily obtain care

from pediatricians, who refer to pediatric centers and specialists. Young adult and older adolescent patients are seen by a breadth of specialists for their presenting symptoms of cancer. These include internists, family physicians, gynecologists, emergency room physicians, dermatologists, gastroenterologists, neurologists, and other specialists. These physicians may have very different referral patterns.⁴¹ 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 switch from predominantly pediatric to adult medical management tends to occur not at age 21 or even at age 18, as might be expected, but closer to age 15. The majority of 15- to 19-year-olds diagnosed with cancer are treated at adult facilities. A cancer registry review in the state of Utah, which has only one pediatric oncology treatment facility, revealed that only 36% of oncology patients 15 to 19 years of age were ever seen at the pediatric hospital.⁴² In Canada, only 30% of cancer patients in this age group are managed at pediatric centers.¹⁷ A study of the National Cancer Data Base found that, for nearly 20,000 cases of cancer in adolescents aged 15 to 19 years, only 34% were treated at centers that had National Cancer Institute (NCI) pediatric cooperative group affiliation.⁴³

In the end, the healthcare 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, a comparison of 16- to 21-year-olds with acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) showed that the outcome was superior for patients treated on cooperative group trials than for those not entered.⁴⁴ In France, Holland and North America, older adolescents with ALL treated on pediatric clinical trials have fared considerably better than those treated on adult leukemia trials.⁴⁵⁻⁴⁷ In Germany, older adolescents with Ewing sarcoma who were treated at pediatric cancer centers had a better outcome than those treated at other centers.⁴⁸ 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.⁴⁹

At the University of Texas M.D. Anderson Cancer Center, results of treatment for ALL in adults improved substantially after treatment derived from pediatric trials was introduced into the institution’s trials.⁵⁰ The analysis of data from the U.S. National Cancer Data Base revealed that adolescents 15 to 19 years of age with non-Hodgkin lymphoma, leukemia, liver cancer, and bone tumors had a survival advantage if treated at an NCI pediatric group institution.⁴³ Thus, for these *pediatric* types of cancer, the pediatric specialist/facility is favored.

For other cancers, adult-treating medical/surgical/gynecologic/radiation oncologists are more appropriate providers. Adolescent and young adult patients with melanoma, colorectal carcinoma, breast cancer or epithelial neoplasm of the ovary may be better served under the care of physicians who are more familiar with these malignancies, such as medical oncologists or gynecologic oncologists. Until pediatric oncologists demonstrate that they have the expertise to treat these relatively non-pediatric cancers, this referral direction should be a first consideration.

The alternative is for adult care specialists/facilities to adopt a pediatric approach, which may be difficult for a variety of historical, socio-political, economic and infrastructure reasons. For example, two adult cooperative groups in the U.S. (Cancer and Acute Leukemia Group B, and Southwest Oncology Group) are starting a trial of a pediatric regimen taken directly from the Children’s Oncology Group which 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 (e.g. 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. Children younger than 18 years of age—and their parents—may benefit from the social and supportive culture of a pediatric hospital regardless of the diagnosis. Individuals between the ages of 16 and 24 years may have varying levels of maturity and independence, and the choice of physician and setting for their care should be individually determined. Pediatric oncologists may be less adept at a non-paternalistic relationship with the patient (and potentially his or her spouse) and less inclined to consider issues such as sexuality, body image, fertility, and the like. Adult oncologists are more accustomed to dose delays and adjustments, and may be less aggressive with chemotherapy dosing than the pediatric oncologist, whose younger patients can tolerate higher doses. The ultimate challenge would be to develop centers and oncologists devoted solely to the care of this group of patients. Such a dedicated program has been championed in the United Kingdom, at least for older adolescents. A number of unique “teenage cancer units” have been established, staffed by physicians and nurses with expertise in adolescent and young adult cancer patient management.⁵¹ This provides the older adolescent with age-specific nursing care, recreation therapy, and peer companionship. Eventually, there could be a *discipline* of adolescent and young adult oncology with its own training programs, science, translational research, clinical trials and national and international organizations.

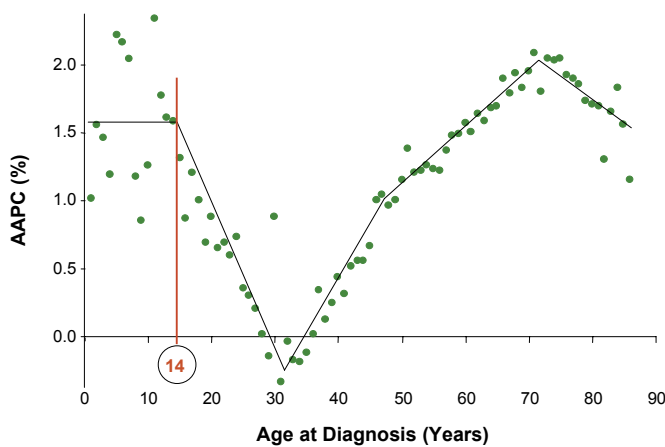


Figure 15.8: Average Annual Percent Change (AAPC) in 5-Year Relative Survival for All Invasive Cancer, U.S. SEER, 1975-1997

IMPLICATIONS FOR OTHER AGE GROUPS

When the average annual percent change in 5-year survival is expressed as a function of specific year of age at diagnosis, the age range affected by adverse trends can be identified more precisely. Such an analysis suggests that the decline in lack of progress versus age over the past quarter century in the United States is linear over the 15- to 29-year age span, with inflections at age 14 and 31 (Figure 15.8). This suggests that the factors that account for the lack of improvement for the adolescent and young adult group relative to children start at age 15, and are increasingly more problematic up to age 30. Between 31 and 47 years of age, the trend is reversed with an analogous, nearly mirror-image linear improvement (Figure 15.8). This observation indicates that the next oldest 15-year age span (30- to 44-years) should be evaluated in a fashion similar to that undertaken for older adolescents and young adults. This analysis also suggests that the greatest progress in prolonging survival from cancer during the past quarter century in the United States has been in the 60- to 80-year age group, with a peak improvement at age 70 (Figure 15.8).

GLOBAL CHALLENGE

The SEER data in this monograph are from the United States, and most of the conclusions herein are derived from these SEER data. Nonetheless, most if not all of the observations are applicable to other countries. Certainly, there is a worldwide lack of awareness about cancer in young adults and older adolescents relative to the recognition of cancer in children and older adults. And it is safe to claim that the deficits in clinical trial participation as well as translational research in early adulthood are universal.

The national survival data for Australia show patterns of outcome similar to those observed in the United States (Figure 15.9; Australian data kindly provided by Stevenson C, Australian Institute of Health and Welfare). During the years 1982 to 1997, 15- to 29-year-old Australians with cancer had the least progress in survival improvement, in comparison with other 15-year groups at younger or older ages. This is consistent with—albeit not as dramatic as—the age pattern in the United States (Figure 15.9). That Australians enjoy universal health insurance—as do most inhabitants of socio-economically

advantaged countries of the world—suggests that lack of national health insurance in the United States does not alone explain the deficit in America. On the other hand, universal health insurance in Australia does not guarantee access to or use of health care services, and is clearly not universally utilized in the young adult age group. Indeed, longer times to a diagnosis of cancer occur in this age group in countries with and without national health insurance, as described above. Most likely, lack of health insurance and of utilization of health care services are global problems in young adults and older adolescents.

FUTURE DIRECTIONS AND INTERIM SOLUTIONS

In North America and Australia, the Children’s Oncology Group (COG) has taken a leadership role in meeting the challenges described in this chapter. In conjunction with the NCI and NCI-sponsored adult cooperative groups, four initiatives were identified as priorities for development: (1) improving access to care through understanding barriers to participation; (2) developing a cancer resource network that provides information about clinical trials to patients, families, providers, and the public; (3) enhancing adolescent treatment adherence (compliance with protocol-prescribed therapy); and (4) increasing adolescent accrual and adult participation in sarcoma trials specifically designed for patients in this age group. The COG Adolescent and Young Adult Committee was formed in 2000 to research the obstacles faced by older adolescents

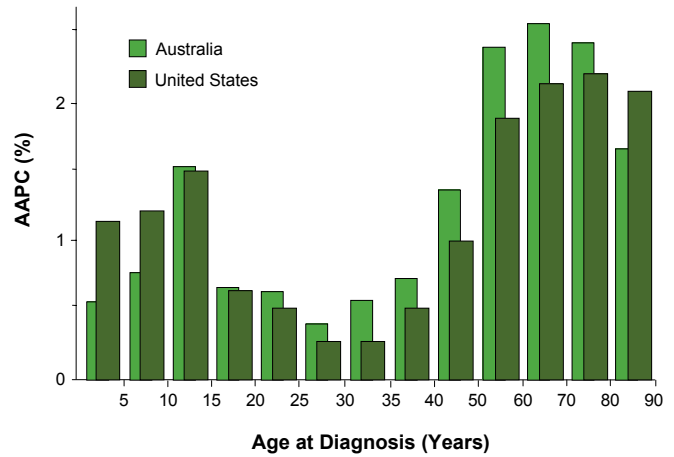


Figure 15.9: Average Annual Percent Change (AAPC) in 5-Year Relative Survival Rate for All Invasive Cancer, by Age, 1982 to 1997

and young adult patients, with the disease focus on sarcomas. The Southwest Oncology Group (for adult patients) subsequently opened the COG trial for metastatic Ewing sarcoma, and thereafter hosted the development of an intergroup sarcoma committee—the Intergroup Consortium Against Sarcoma (ICAS)—with formal representation from all the adult cooperative groups as well as the National Cancer Institute of Canada.

Evidence for improvement in the accruals to NCI-sponsored national sarcoma treatment trials is shown in Table 15.2. The proportion of American sarcoma patients younger than age 40 entered onto the trials has nearly doubled—from 5.1% to 9.8%—during the past five years.

Table 15.2: Accruals to National Cancer Treatment Trials during the Era of National Collaboration to Augment Sarcoma Clinical Trial Development and Participation*

	AGE	1998-9	2000-1	2002-3
All Cancer	All Ages	48,225	57,033	54,717
	<20	9,094	7,791	6,070
	20-39	3,488	3,752	3,411
	40-59	17,403	22,025	22,556
Sarcomas	<40	637	888	929
% of all Entries		5.1%	7.7%	9.8%
Other Cancers	<40	11,945	10,655	8,552

*Clinical trial accrual data from the Cancer Therapy Evaluation Program, National Cancer Institute, courtesy of Michael Montello and Troy Budd

In contrast, and as a control for this observation, the other cancers that occur in this age group (and that have not yet been addressed) showed a decline in patient accrual.

Another initiative in the United States is the formation of a consortium of all the organizations devoted to assisting adolescents and young adults with cancer. Known as the LIVESTRONG™ Young Adult Alliance, this organization is dedicated to improving survival rates and the quality of life of young adults living with cancer by promoting relevant research and the delivery of patient care, generating awareness of the issue, being a voice for young adults with cancer, and advancing helpful community-based programs and services (see *Appendix I*). The Alliance will bring together for the first time key voices in the cancer community to improve results for young adults.

In parallel, the U.S. National Cancer Institute has initiated a Progress Review Group (PRG) to evaluate the national status of young adult cancer outcomes and needs. This PRG will assess the deficits and scientific issues described in this chapter and address others identified by a panel of experts in a year-long process. Specific recommendations for national implementation are expected to be presented in late 2006.

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 15.3).

CONCLUSIONS

The medical literature on cancer during the first 15 years of life—in infants, children, and young adolescents—is vast and burgeoning. This monograph essentially represents the first treatise on cancer during the subsequent 15 years of life. The contrast in available information for each group symbolizes the difficulties that older adolescents and young adults face when they are diagnosed with cancer. With national and international focus on younger and older patients during the past half-century, young adults and older adolescents are orphans, lacking the overall progress made in cancer prevention, diagnosis and treatment. Solutions include raising awareness of the problem, improving healthcare access and insurance, enhancing understanding of the biology of the cancers that occur in the age group, and developing national and international organizations to address the deficits. Ultimately, a formal discipline of adolescent/young adult oncology, dedicated to scientific investigation and replete with training programs, should be developed to address the interface between pediatric and adult oncology. Meanwhile, older adolescents and young adults with cancer should be encouraged to address symptoms, to seek care at a comprehensive healthcare center, to maintain health insurance, to understand that optimal cancer management starts at diagnosis, and to ask about and find clinical trials suitable for them.

Surviving adolescence and young adulthood is difficult enough when all is well and health is robust. Cancer

Table 15.3: *Practical Suggestions to Enhance Early Detection of Cancer and Clinical Trial Participation in Older Adolescents and Young Adults*

- Appreciate that cancer occurs in one in every 200 older adolescents and young adults and that everyone is at risk.
- Be aware that young adults often deny symptoms, are too embarrassed to report them, or attribute them to psychosomatic manifestations.
- Encourage and assist young adults to seek care at a comprehensive healthcare 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.
- 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.
- 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.

makes this phase of life extraordinarily more challenging and demanding. Medical professionals should pay special attention to the unique transitions faced by these patients—at diagnosis, through the process of informed consent, at initiation of therapy, during school and employment re-entrance, at completion of therapy, during post-treatment follow-up, and when switching from pediatric to adult care. Ideally, specialized adolescent and young adult cancer units should be developed with the anticipation that centralization of care and availability of age-targeted clinical trials will lead to improved treatment, survival, and quality of life.

Cancer during adolescence and early adult life is an underestimated challenge that merits specific resources, solutions, and a national focus. Future research should elucidate why survival outcomes for this group have lagged behind those of others and identify the efforts—including better clinical trial accrual—that might remedy the disparity. Lastly, more scholarly and focused attention on the unique psychosocial needs of this population will improve the quality of their cancer care and of their survival. At the very least, those at the interface deserve the same attention and progress that has been achieved in younger and older persons.

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