Closing the Gap: *Research and Care Imperatives for Adolescents and Young Adults with Cancer*

Report of the Adolescent and Young Adult Oncology Progress Review Group

U.S. DEPARTMENT OF
HEALTH AND HUMAN SERVICES
National Institutes of Health
National Cancer Institute

LIVE**STRONG**™ Young Adult Alliance

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FROM THE ADOLESCENT AND YOUNG ADULT ONCOLOGY PROGRESS REVIEW GROUP

It is our great privilege to submit this Report of the Adolescent and Young Adult Oncology Progress Review Group (AYAO PRG) to the Advisory Committee to the Director of the National Cancer Institute (NCI). This document is the product of an innovative, collaborative effort, the first public-private partnership of its kind, between NCI and the Lance Armstrong Foundation (LAF). The nation's leading researchers and clinicians in adolescent and young adult oncology joined with cancer survivors, advocates, pediatricians, gerontologists, disease-specific experts, statisticians, and insurance and pharmaceutical industry representatives to develop recommendations for a national agenda to advance adolescent and young adult oncology. The AYAO PRG is only the second PRG not to be disease-specific, and the cross-disciplinary nature of this collaboration is reflected in the diversity of its membership.

We hope this report will raise the awareness of the health care and research communities and the general public to the reality of cancer as a major health problem in this population and the unique challenges faced by adolescents and young adults diagnosed with cancer. We fully expect the recommendations in the report to act as catalysts for future programs and initiatives. An implementation meeting, sponsored by the LIVE**STRONG**™ Young Adult Alliance, has been arranged to discuss how these recommendations can most effectively and efficiently be realized to improve the outcomes and quality of life for adolescents and young adults with cancer. We look forward eagerly to this discussion and the development of concrete strategies for action.

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ACKNOWLEDGMENTS

The Adolescent and Young Adult Oncology Progress Review Group (AYAO PRG) process has been a collaborative effort of the National Cancer Institute (NCI) and the Lance Armstrong Foundation (LAF) involving contributions from numerous people with different backgrounds, skills, and talents. The AYAO PRG wishes to acknowledge and extend special thanks to the following groups and individuals:

- The many scientists, clinicians, advocates, and other professionals who generously gave of their time and knowledge. Without their participation, this report would not have been possible. In particular, we acknowledge the participants in our AYAO PRG Roundtable meeting and the extraordinary efforts of not only the PRG members and Co-Chairs but the non-PRG Co-Chairs of our Roundtable Breakout Groups—Marjorie Kagawa Singer, Kimberly Calder, Smita Bhatia, William Carroll, Robert Comis, Jennifer Ford, Carolyn Gotay, Brandon Hayes-Lattin, Robert Hiatt, Sandra Horning, Ian Lewis, Joan McClure, Kevin Oeffinger, Joseph San Filippo, and Carol Somkin.
- The staff of the NCI Office of Science Planning and Assessment, under the leadership of Cherie Nichols, who provided ongoing guidance, technical support, and encouragement throughout the process. In particular, we acknowledge the hard work and dedication of Anne Tatem, Joy Wiszneauckas, Jamelle Banks, and Julie Mendelsohn.
- The staff at LAF, led by Doug Ulman, who provided coordination and ongoing support in all phases of the AYAO PRG process. We would like to recognize the hard work of David Lyon, Tina Hamilton, Claire Neal, Schlonge Dermody, and Devon McGoldrick. We look forward to their efforts in moving the recommendations into action through the work of the LIVE**STRONG**™ Young Adult Alliance and by convening the Implementation meeting with experts of the oncology community.
- Beth Mathews-Bradshaw at Science Applications International Corporation (SAIC) for her hard work, dedication, and meticulous attention to detail while coordinating this effort to keep the PRG focused and on target.
- The staff of SAIC who assisted in logistics, documentation, and breakout session report preparation: Karen Rulli and Adeyinka Smith for preparing portfolio analyses and resource materials; Rob Watson for conference support; Deborah Berlyne, Adam Book, Greg Cole, Maneesha James, Eric Levine, Sabina Robinson, Karen Rulli, Anita Sabourin, Heather Sansbury, and Pamela Zingeser for serving as science writers; and Jennifer Secula and Julie Jessup for their expertise related to the design, layout, and editing of the report.
- Suzanne Reuben of Progressive Health Systems, who, as lead science writer, worked steadfastly in crafting this report.
- Janis Mullaney at the Foundation for the National Institutes of Health (NIH) for her help in establishing the NCI/LAF public-private partnership.
- NOVA Research, in particular, Ben Neal, for developing and maintaining the AYAO PRG Web site.
- Lynn Ries of the NCI Division of Cancer Control and Population Sciences for her tireless efforts generating Surveillance, Epidemiology, and End Results (SEER) data for the report.

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EXECUTIVE SUMMARY

Relatively little is known about biologic, genetic, epidemiologic, therapeutic, psychosocial, and economic factors that affect the incidence, disease outcomes, and quality of life of adolescents and young adults (AYAs) diagnosed with cancer. However, it is known that compared with younger and older age groups, this population—defined as those ***diagnosed with cancer at ages 15 through 39***—has seen little or no improvement in cancer survival rates for decades.

In 2005-2006, the National Cancer Institute (NCI) partnered with the Lance Armstrong Foundation (LAF) to conduct a Progress Review Group (PRG) to address the special research and cancer care needs of the AYA age group and solicit recommendations for a national agenda to improve cancer prevention, early detection, diagnosis, treatment (including survivorship care), and outcomes among these patients. An Adolescent and Young Adult Oncology Progress Review Group (AYAO PRG) was convened, drawing together more than 100 experts from diverse disciplines across the research enterprise, the cancer control continuum, and the advocacy and survivor communities. Further, the PRG leadership sought the input of individuals whose work in areas not related directly to AYA cancer research and care might offer important insights for addressing AYA-specific concerns.

Cancers Affecting the Adolescent and Young Adult Population

Nearly 68,000 people aged 15 to 39 years were diagnosed with cancer in 2002, approximately 8 times more than children under age 15. These cases represent about 6 percent of all new cancer diagnoses. Excluding homicide, suicide, and unintentional injury, cancer is the leading cause of death among 15 to 39 year-olds. It is the most common cause of death among females in this age group, and among males in this group only heart disease claims more lives annually than cancer.

The most common tumors in 15 to 39 year-olds (accounting for 86 percent of cancers in the age range) are breast cancer, lymphoma, germ cell tumors (including testicular cancer), thyroid carcinoma, sarcoma (bone and soft tissue), cervical carcinoma, leukemia, colorectal carcinoma, and central nervous system tumors. However, the incidence of specific cancer types varies considerably across the AYA age continuum. For example, among younger AYAs (15 to 19 year-olds), lymphomas, germ cell tumors, and leukemias account for the largest percentages of all cancers. Between ages 20 and 39, these and other cancers decline as a percentage of all cases, while carcinomas (particularly breast cancer) comprise an increasing share of cancers in the AYA age cohort. Non-Hispanic whites in the AYA age group have the highest incidence of cancer, but also have the highest overall 5-year survival. American Indians/Alaska Natives have the lowest cancer incidence, but also have poor survival rates. African Americans, however, have the lowest 5-year survival rate across the age range.

Factors Limiting Progress Against Cancer in Adolescents and Young Adults

Overall, progress in AYA oncology has been hampered because cancer risk and adverse cancer outcomes have been under-recognized in this population. Several closely interrelated factors may have contributed to the failure to improve the outcomes of AYAs with cancer. Access to care can be restricted or delayed, in part because AYAs have the highest uninsured rate of any age group in the country. Diagnosis can be delayed because AYAs typically see themselves as invulnerable to serious disease or injury, causing them to ignore or minimize symptoms and delay seeking medical attention. Delayed diagnosis also is common because providers tend to have a low suspicion of cancer in this population. Symptoms of cancer may be attributed to fatigue, stress, or other causes. AYAs with first symptoms of cancer may see a variety of health care providers, including pediatricians, internists, family physicians, emergency room physicians, gynecologists, dermatologists, gastroenterologists, neurologists, surgeons, orthopedists, and other specialists.

Once seen, referral patterns for AYAs with suspected or diagnosed cancers vary widely. These patients too frequently fall into a “no man’s land” between pediatric and adult oncology; they may be treated by pediatric, adult medical, radiation, surgical, or gynecologic oncologists. Most AYAs are treated in the community

rather than in cancer centers, but a robust community oncology and primary care infrastructure currently does not exist to enable patient data collection and aggregation that would support research efforts. In addition, contact with many AYA patients is lost following treatment, complicating collection of late effects and outcome data in this highly mobile population.

Research on AYAs has been further constrained by their exceedingly low participation in the relatively few clinical trials available to them, in part because diagnosing physicians seldom refer these patients to trials. Poor understanding of patient and tumor biology that distinguishes cancers in this population has contributed to minimal advances in treatment.

Inconsistency in treatment and follow-up care, coupled with insufficient research data, has prevented the development of guidelines for treating and monitoring AYAs with cancer, and few tools exist to measure the efficacy of treatment and psychosocial interventions delivered in diverse settings.

Psychosocial and support services available to AYAs with cancer (and their families/caregivers) are limited, although their needs for such services tend to be broader in scope and intensity than among younger and older patients because of the many emotional, developmental, and social changes and transitions that occur during this stage of life. Lastly, cancer prevention and early detection receive little emphasis in health care for the AYA population.

Recommendations

The AYAO PRG identified five imperatives for improving the outcomes of adolescents and young adults with cancer.

Recommendation 1: Identify the characteristics that distinguish the unique cancer burden in the AYAO patient.

A significantly more robust research effort is needed to better understand tumor and human factors that contribute to AYAs' susceptibility to cancer, their response to treatment, and their disease outcomes. Among the cancers affecting AYAs, the PRG identified as particularly high priorities basic and other biologic research on aging and patient/host-related factors in non-Kaposi's sarcoma, leukemia, lymphoma, and breast and colorectal carcinomas. Additionally, increased resources are needed for studies of AYAs' genetic susceptibility to cancer.

AYA cancer patients and survivors face developmental challenges that both exceed significantly those faced by other young people and are distinct from the challenges faced by other age groups with cancer. Research is needed to better understand patient and survivor life stage and developmental characteristics across six principal domains—intellectual, interpersonal, emotional, practical, existential/spiritual, and cultural—that singly or in combination may have profound effects on individuals' medical outcomes and quality of life.

In addition, the factors that characterize and account for disparities experienced by AYA cancer patients and survivors are understood only in the broadest terms and may include human and disease biology, pharmacogenetics, socioeconomic factors, and the appropriateness and accessibility of health services (especially clinical trials). Therefore, research is needed to elucidate in detail the factors contributing to under-service and poorer outcomes among AYAs as a whole and among racial and ethnic subgroups within the AYA population.

Recommendation 2: Provide education, training, and communication to improve awareness, prevention, access, and quality cancer care for AYAs.

The AYAO PRG recognized an urgent need for a variety of education, training, and communication activities to raise awareness and recognition of the AYA population at both public and professional levels as a first step toward increasing national focus and resource allocation to address the AYA cancer problem. To be effective, all education, training, and communications must be culturally appropriate and delivered by individuals who are culturally competent.

Educational and other interventions to modify the exposure of AYAs in the general population to potentially modifiable cancer risk factors (e.g., human papillomavirus, ultraviolet light, poor diet, lack of physical activity, obesity, tobacco use) offer the opportunity to reduce cancer risk during the AYA years as well as risk for cancers in older adulthood. Efforts

also are needed to promote the importance of health insurance in this population, since neither AYAs nor their families may place a high priority on maintaining coverage for young people who typically are healthy. For those diagnosed with cancer and their families, targeted education and online resources for cancer information, insurance resources, peer support, and other information needs will help empower AYAs to understand and manage their own care.

Current health care provider training programs generally do not address AYA-specific issues, resulting in poor recognition of AYAs' cancer risk and inadequate response to their medical and psychosocial needs. Core competency curricula are needed for inclusion in appropriate initial training and continuing education programs to ensure that all providers who work with adolescents and young adults have the requisite understanding of the cancers that either peak or occur more commonly in this age group, post-treatment surveillance for late effects, and the specific psychosocial, economic, educational, and communication needs of the population. Programs also are needed to train patient navigators, advocates, and other lay persons who conduct outreach to and represent AYA interests. It was the consensus of the PRG that physician involvement is the key factor in the patient's decision to participate in a clinical trial. Thus, targeted education to raise referring physicians' and medical oncologists' awareness of the potential benefit of AYAO relevant trials provides a means to improve patient outcomes.

Recommendation 3: Create the tools to study the AYA cancer problem.

The existing research infrastructure is inadequate to support needed AYA-focused research. Appropriate research tools to enable such studies must be developed if they do not exist, and strengthened if potentially useful infrastructure already is in place.

The most pressing needs are to: (1) create a prospective database on all AYA cancer patients; (2) increase the number of annotated AYA tumor, normal tissue, and other biospecimens; (3) create or modify assessment tools specific to AYA cancer issues; (4) improve grant coding and search term standardization; and (5) expand the number of clinical trials appropriate for and available to AYAs.

Recommendation 4: Ensure excellence in service delivery across the cancer control continuum (i.e., prevention, screening, diagnosis, treatment, survivorship, and end of life).

The AYAO PRG urges the implementation of two principal strategies to improve service delivery to AYAs with or at risk for cancer and ensure excellence in care across the cancer control continuum. First, standards of care for AYA cancer patients must be developed, evaluated, and disseminated. This enormous task must be undertaken with the understanding that standards are dynamic and must be updated as advances in care are achieved. Excellence in care may vary not only by cancer diagnosis but by multiple other variables (e.g., age and gender, race/ethnicity/culture, socioeconomic status, access to/source of care, insurance status) that must be addressed to meet the complete spectrum of patient needs.

Second, establishing, disseminating, and reinforcing standards of cancer care for AYAs will require the ongoing and concerted collaboration of a diverse array of stakeholders. Health care providers, research sponsors, investigators, regulators, insurers, and patient advocates should expand existing collaborations and establish a national network or coalition committed to improving the quality of life and outcomes for AYAs with cancer.

Recommendation 5: Strengthen and promote advocacy and support of the AYA cancer patient.

In addition to raising public and professional awareness of AYAs as a distinct understudied and underserved age group, advocacy and support services for AYA cancer patients and survivors need to be strengthened. Such effective support of AYAs with cancer must be predicated on an understanding of how cancer may affect young peoples' self-identity, self-esteem, spiritual perspectives, body image, perception of their future possible life goals, distress levels, need for information and communication, and numerous other subjective components of experiencing a life-threatening disease. Empirical research is needed to explore these aspects of the cancer experience among AYAs and inform intervention development and health care provider training.

Numerous advocacy, patient support, social service, religious, fraternal, social, and health professional organizations currently have some focus on AYA cancer patients and survivors. Training and fiscal support are needed to expand the capacity of these established entities to address the psychosocial needs of this population. In addition to building the capacity of existing resources to address the psychosocial needs of AYAs, evaluation is needed to assess the efficacy (i.e., effect on outcomes) of existing programs. These evaluations should be used to inform the development of new AYA-specific interventions.

Conclusion

Cancer in adolescents and young adults is an important problem that has gone unrecognized or is only a peripheral concern among numerous research, medical, health services payor, patient support and advocacy, funding, and cancer surveillance constituencies, as well as healthy teenagers and young adults who do not know they are at risk for cancer. This limited focus has had severe consequences—a lack of cancer survival progress spanning more than two decades and persistent diminution of young cancer survivors' quality of life.

The AYAO PRG believes that a major, ongoing AYAO-specific research initiative emphasizing AYA clinical trials and outcomes research is urgently needed. Collaboration and support from numerous governmental, academic, public health, community-based, and other private sector entities will be essential to its success. The AYAO PRG offers this report as a blueprint for a focused and structured approach to improving cancer prevention, cancer care, and the duration and quality of life for this vital segment of our society.

INTRODUCTION

Impetus for the Adolescent and Young Adult Oncology Progress Review Group (AYAO PRG)

In recent years, the research, clinical care, and patient advocacy communities increasingly have recognized a significant lack of attention and resources directed to adolescent and young adult (AYA) cancer patients and survivors. Compared with other age groups, relatively little is known about basic biologic, genetic, epidemiologic, therapeutic, psychosocial, and economic factors that affect the incidence, disease outcomes, and cancer-related quality of life in this population. It is known, however, that compared with younger patients, AYAs with cancer have seen little or no improvement in their survival rates for decades.

In 2005-2006, the National Cancer Institute (NCI) partnered with the Lance Armstrong Foundation (LAF) to conduct a PRG to address the special research and cancer care needs of the AYA age group and solicit recommendations for a national agenda to improve cancer prevention, early detection, diagnosis, treatment (including survivorship care), and outcomes among these patients. Previous PRGs have addressed specific tumor types and cancer-related health disparities experienced by people of all ages with any form of cancer.

The AYAO PRG's principal focus was to identify priorities for improving the outcomes of people diagnosed with cancer as adolescents and young adults. The survivorship care needs of adolescents and young adults who were diagnosed and treated as children, while important, were not the PRG's central focus.

The PRG Process

As Figure 1 illustrates, the PRG process entails a comprehensive, collaborative, and integrated approach with three phases: (1) developing recommendations with input from the clinical care, research, and advocacy communities; (2) planning for and implementing strategies to achieve scientific advances based on PRG recommendations; and (3) reporting on progress made in addressing PRG recommendations. Thus, the PRG process offers the opportunity to continually evaluate progress by tracking current and future research trends and provides a framework for a national effort to control and eliminate disease. This report documents Phase I of the AYAO PRG process.

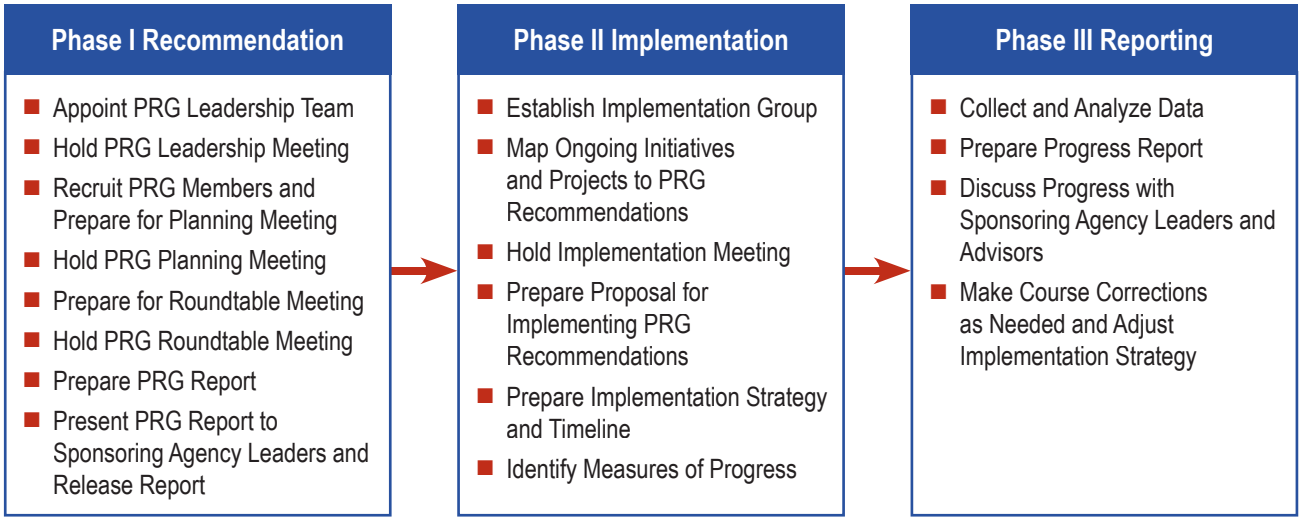


Figure 1. PRG Three-phase Approach

The AYAO PRG

Following selection of the AYAO PRG leadership group, individuals were nominated to become PRG members and/or to participate in the Roundtable meeting at which the recommendations for AYA research and cancer care priorities contained in this report were developed. The PRG and Roundtable participants were drawn from diverse disciplines across the research enterprise, the cancer control continuum, and the advocacy community. Further, the PRG leadership sought the input of individuals whose work in areas not related directly to AYA cancer research and care might offer important insights for addressing AYA concerns.

On December 6-7, 2005, the PRG leadership and 22 PRG members met in Austin, Texas to plan the Roundtable meeting and identify key issues to be explored in Breakout Group sessions. The Roundtable meeting was held on April 24-26, 2006 in Denver, Colorado. Appendix A provides a roster of all AYAO PRG participants. Appendix B includes the reports of the 11 Roundtable Breakout Groups, and Appendix C specifies the charge to the PRG. Additional appendices (D and E, respectively) include survival rates by selected cancer type and a glossary of terms and acronyms used in this report.

CANCER IN THE ADOLESCENT AND YOUNG ADULT (AYA) POPULATION

AYAs Defined

Empirical and observational research to date indicates that AYAs with cancer are distinguished by physiologic, developmental, and societal characteristics and less improvement in survival that set them apart from younger and older age groups. In prioritizing research and health care needs of adolescents and young adults with cancer, the AYAO PRG chose to define the AYA population by upper and lower age limits to facilitate clarity, consensus, and data collection and comparison. After considerable discussion and with some caveats, the PRG defined the AYA population as comprising individuals aged ***15 through 39 years at cancer diagnosis***. Ideally, the population should be defined as narrowly as possible by tumor biology, physiologic characteristics, psychodevelopmental stage of life, and cancer-related challenges. The AYAO PRG sought a range that was inclusive rather than exclusive, since the entire age range continues to experience a relative lack of improvement in survival and because a chief concern of AYAs with cancer is the lack of a "home" in research and health care.

Physiologic Characteristics and Possible Biologic Influences on Cancers in AYAs

Clearly, post-pubertal adolescents and young adults are physiologically distinct from younger children. Their body conformation, hormonal milieu, and organ function approximate those of a "full-grown" adult. However, in terms of oncology, the distribution of tumor types across the AYA age range overlaps somewhat with both the common list of pediatric cancers and those commonly occurring in older adults. Though pediatric embryonal tumors and carcinomas common to older adults occur in AYAs, neither makes up a significant percentage of cancers in this age group. The cancers that span this age range—leukemias, lymphomas, sarcomas, and brain tumors—vary in incidence and survival rates by age. It is becoming increasingly understood that the survival differences are as much due to variations in tumor biology as to variations in either patient physiology or the health services received. For example, acute lymphoblastic leukemia (ALL) in a 6-year-old may differ with regard to key biologic factors compared to ALL in a 19-year-old. Likewise, breast cancer in a 30-year-old woman or colon cancer in a 35-year-old man may have biologic characteristics not found in patients with what appear to be the same diseases at 65 years of age. These biologic differences likely interact with or may be due to genetic, metabolic, hormonal, environmental, pharmacokinetic, social, and other human factors that affect disease susceptibility, treatment response, and outcome.

Heterogeneity of the AYA Population

It is crucial to consider more than chronological age with regard to research and care delivery recommendations for AYA cancer patients and survivors and to expect not only some overlap with both older and younger age groups but also marked heterogeneity within the age range. In addition to biologic and physiologic changes, numerous psychological, developmental, and social changes make this a significant period of transition for AYAs. AYAs possess both developmental similarities and important differences across the 15 to 39 year age range that often affect their care-seeking patterns, adherence to recommended treatment and follow-up care, and ultimately, disease outcomes.

- **Shared Developmental Characteristics**

Among the characteristics AYAs share are a sense of invincibility and a limited awareness of their own mortality that can make a cancer diagnosis particularly devastating. For most AYAs, the personal experience of disease has been limited to brief bouts of infectious disease, sports-related injuries, or other non-life-threatening illnesses. Individuals in the lower range of this age group are reaching important social milestones and achieving some measure of autonomy from parents—getting a driver's license, living on their own, establishing financial independence, graduating from high school or college, seeking employment, and gaining voting privileges and legal independence. Young adults in their 20s and 30s are seeking and forming intimate and long-term relationships and are either planning or establishing their careers and families. A cancer diagnosis abruptly derails these important developmental processes, thrusting the individual back into uncertainty and sometimes an

unwelcome or uncomfortable dependent state. At the same time, an AYA with cancer, particularly an individual at the younger end of the age range, often must "grow up" quickly to understand his or her disease and become an active participant in cancer treatment. In addition, since the AYA age range encompasses the reproductive years, family planning and fertility preservation are key concerns of both women and men.

- **Developmental Differences**

These similarities notwithstanding, AYAs can vary widely in terms of their emotional age and maturity and in their life stage and related needs, and these differences may not correlate with chronologic age. The psychosocial needs of a 20-year-old living at home while attending college are very different from those of a 35-year-old with two young children. However, there are 35-year-olds living at home with parents and there are 20-year-olds with young children. Likewise, cultural differences may influence attitudes about disease and health, customary life tasks during this period, or other factors that may contribute directly or indirectly to cancer risk, disease management, and outcome. Just as pediatric providers must adapt to the developmental stage of the child from infancy through early adolescence and the adult practitioner must provide age-appropriate care to individuals over a span of many decades, the provider of oncology services to AYAs must adapt to and meet both the medical and the psychosocial needs of the patients in this age range.

Rationale for Selecting the Lower Age Limit

Some AYA cancer patients may be undergoing some of the life transitions described previously in early adolescence and will feel out of place in a pediatric setting. Others do not start these transitions until after the teenage years but may find themselves in adult-oriented settings that do not recognize their psychosocial immaturity. Our health care system is split in a binary fashion between pediatric and adult medicine, particularly among the subspecialties and certainly in oncology. But the point of transition between the two is blurry—no rules dictate where AYA patients should receive care. Pediatric hospitals increasingly have upper age limits of 21 and beyond and non-pediatric hospitals often accept patients as young as 15. Studies of care patterns for adolescent cancer patients show that provision of care at pediatric hospitals begins to drop at age 14, and by ages 16 to 17 is less than 50 percent. Therefore, the PRG felt an inclusive lower age limit of 15 was reasonable in considering the research and care needs of AYAs.

Rationale for Selecting the Upper Age Limit

The biologic and physiologic maturity that occurs around the time of puberty and achievement of full stature remains relatively stable during the 20s and 30s. Between ages 15 and 39, patients have passed puberty but have not yet experienced the effects of hormonal decline (menopause for females) or immune response decline. Few have developed the chronic medical conditions (e.g., atherosclerosis, hypertension, type II diabetes, alcoholism) that cause organ dysfunction and the need for concomitant medications that can influence oncologic decision-making and the care of older patients. The PRG concluded that from a psychosocial perspective, the majority of patients up to age 40 are more likely to feel they have more in common with other younger patients than with middle aged or older patients. For these reasons and other important similarities across the age range described, the PRG determined that individuals through age 39 should be considered part of the AYA population.

The AYA Cancer Survival Improvement Gap

In addition to the reasons noted for classifying this group as a distinct, understudied—and underserved—population, further support for the distinction is found in an analysis of data from the NCI's Surveillance, Epidemiology, and End Results (SEER) program. These data reveal that improvement in overall 5-year cancer survival in this age cohort has lagged far behind that achieved in other age groups. While dramatic survival improvements (expressed as average annual percent change, or AAPC) have been achieved in patients diagnosed at age 15 or younger and steady improvement has been made against a number of cancers common among those over age 40, little or no progress has been seen in the AYA population (Figure 2). In fact, among those aged 25 to 35 years, survival has not improved in more than two decades. As Figure 3 illustrates, 15 to 39 year-olds diagnosed with cancer in 1975-1980 had dramatically better survival than most other age groups; however, survival rates for this population have stagnated while survival improvements achieved in younger and older age groups have now—or will soon—eclipse AYAs'

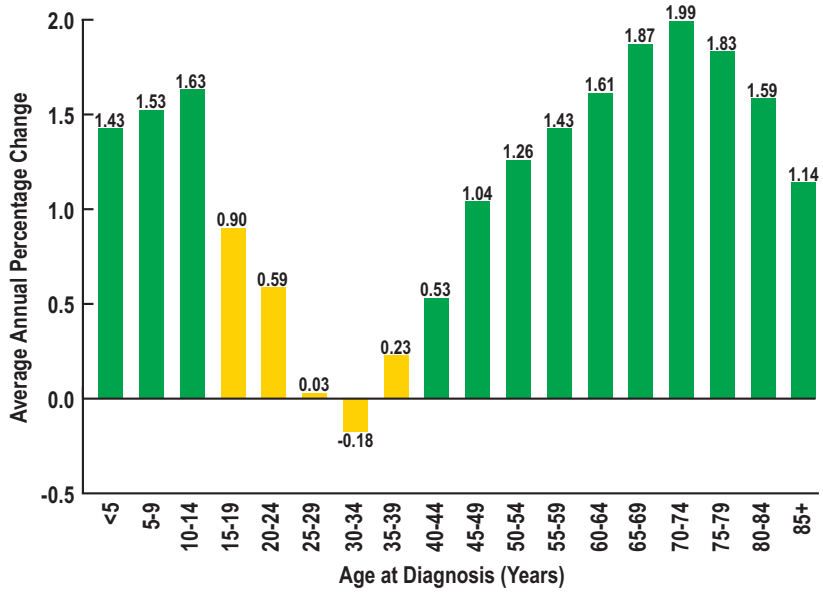


Figure 2. Improvement in 5-Year Relative Survival, Invasive Cancer, SEER 1975-1997

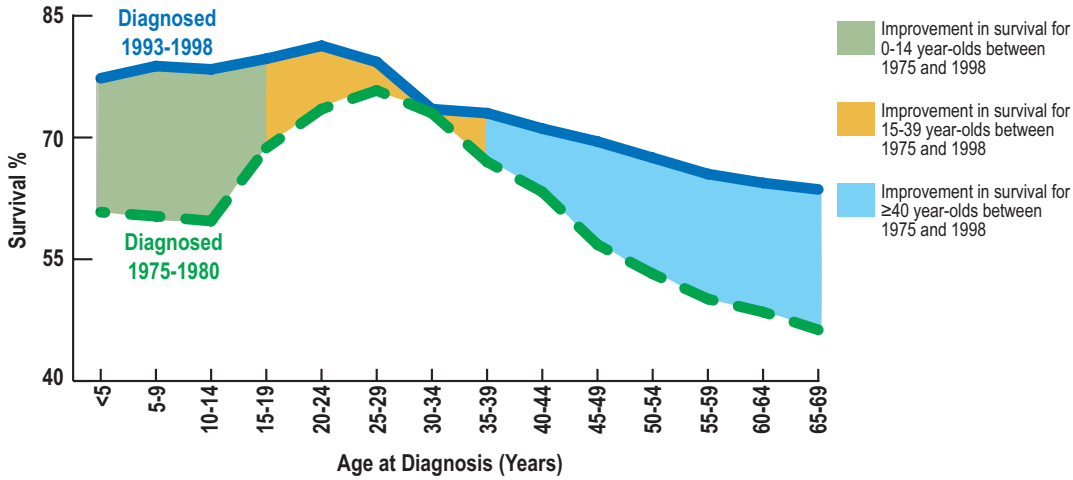


Figure 3. 5-Year Survival of Patients with Cancer by Era, SEER, 1975-1998

previously superior survival rates. Given the variability in survival rates by diagnosis (and the very high survival rates in some cancers common in the AYA age range), these data have been further analyzed for selected diagnoses (see Appendix D). The two HIV-related cancers (Kaposi's sarcoma and non-Hodgkin's lymphoma) in this era certainly contributed to the declining trend; conversely, survival rates for several diagnoses increased (especially ALL). However, most of the other cancers showed the same pattern of lack of survival improvement as the overall trend.

Cancers Affecting the AYA Population

Excluding homicide, suicide, and unintentional injury, cancer is the leading cause of death among those aged 15 to 39 years. It is the most common cause of death due to disease among females in this age group, and among males in this group only heart disease claims more lives annually than cancer.[1]

Other statistics illustrate the generally underappreciated cancer problem in the AYA population:

- Nearly 68,000 people aged 15 to 39 years were diagnosed with cancer in 2002, approximately 8 times more than children under age 15.[2] These cases represent about 6 percent of all new cancer diagnoses.
- Cancer incidence among males aged 15 to 19 years is slightly higher than among females of the same age, but from ages 20 to 39, incidence is higher among females. At each 5-year interval, the incidence gap between the genders increases; by ages 35 to 39, cancer incidence among females is more than 80 percent higher than among males.[3] However, after age 40, this trend reverses (in large part due to increasing numbers of prostate cancer diagnoses) and overall cancer incidence among men exceeds that of women.
- The average annual increase in the incidence rate of invasive cancer is higher in people aged 25 to 29 years and 30 to 34 years than for other 5-year age intervals under age 45.[4]

The most common tumors in 15 to 39 year-olds (accounting for 86 percent of cancers in the age range) are breast cancer, lymphoma, germ cell tumors (including testicular cancer), thyroid carcinoma, sarcoma (bone and soft tissue), cervical carcinoma, leukemia, colorectal carcinoma, and central nervous system tumors.[5] As Figure 4 illustrates, the incidence of specific cancer types varies across the AYA age continuum. For example, among younger AYAs (15 to 19 year-olds), lymphomas, germ cell tumors, and leukemias account for the largest percentages of all AYA cancers. Between ages 20 and 39, these and other cancers decline as a percentage of all cases, while carcinomas (particularly breast cancer) comprise an increasing share of cancers in the AYA age cohort.

Non-Hispanic whites in the AYA age group have the highest incidence of cancer, but also have the highest overall 5-year survival (Figures 5 and 6). American Indians/Alaska Natives have the lowest cancer incidence, but also have poor survival rates. Blacks have intermediate incidence rates, but the lowest 5-year survival rate across the age range.

Factors Limiting Progress Against Cancer in the AYA Population

Several closely interrelated factors may have contributed to the failure to improve the outcomes of AYAs with cancer.

- **Access and Limited Insurance Coverage**

Young adults have the highest percentage of uninsured or underinsured individuals of any age group. In 2004, 13.7 million young adults aged 19 to 29 years lacked coverage, an increase of 2.5 million since 2000.[6] Lack of insurance is a major cause of access limitations

[1] Total U.S. Deaths 2003, ages 15-39, data from SEER and the National Center for Health Statistics.

[2] American Cancer Society data for 2002.

[3] Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Mariotto A, Feuer EJ, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2002. National Cancer Institute, Bethesda, MD; at: http://seer.cancer.gov/csr/1975_2002/, based on November 2004 SEER data submission, posted to the SEER Web site 2005.

[4] Bleyer A, O'Leary M, Barr R, Ries LAG (eds). Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, including SEER Incidence and Survival, 1975-2000. National Cancer Institute, NIH Pub. No. 06-5767, Bethesda, MD, June 2006; at: www.seer.cancer.gov/publications/aya.

[5] SEER 17, 2000-2003.

[6] Collins SR, Schoen C, Kriss JL, et al. Rite of Passage? Why Young Adults Become Uninsured and How New Policies Can Help. The Commonwealth Fund, updated May 24, 2006.

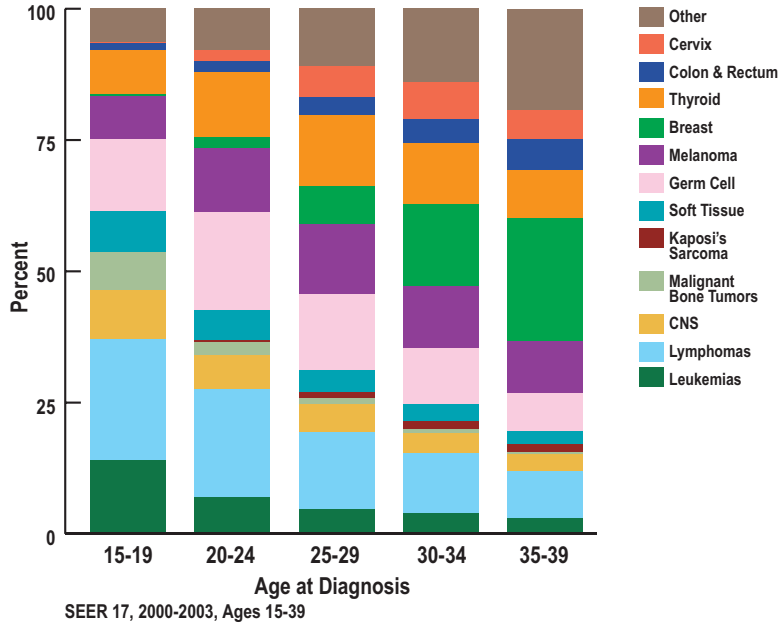


Figure 4. Types of Cancer in Older Adolescents and Young Adults (% cases/disease)

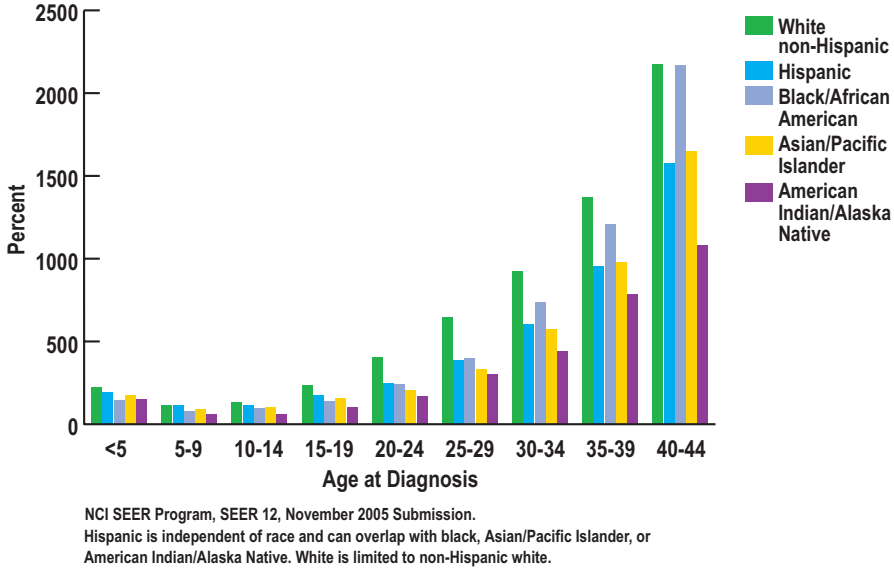
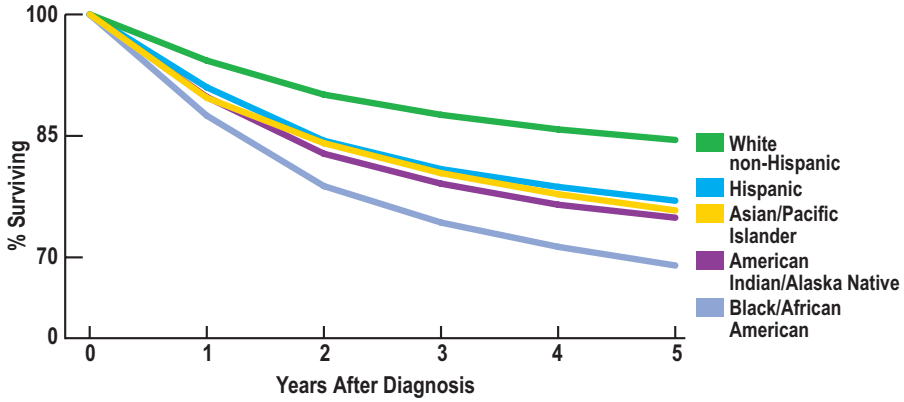


Figure 5. Incidence of All Invasive Cancer by Race/Ethnicity SEER, 1994-2003



Hispanic is independent of race and can overlap with black, Asian/Pacific Islander, or American Indian/Alaska Native. White is limited to non-Hispanic white.

Cause-specific based on any cancer death was used for this analysis.

Figure 6. Survival, All Invasive Cancer Sites Combined, Aged 15-39 Years, Both Sexes, All Races, SEER 13 Areas, 1992-2002

in this population. Unless they are disabled, young adults rarely are covered by their parents' health insurance policies after age 23, and many policies cease covering dependents at age 19 or when they no longer are full-time students. Medicaid and its state child health insurance component, SCHIP, also cease coverage at age 19. Many of the jobs held by AYAs offer either limited or no health benefits. Those in jobs that offer health coverage may decline it or choose high deductible, narrow benefit plans due to cost. If cancer subsequently is diagnosed, AYAs may find themselves with limited access to care and may incur high levels of debt for the cost of care not covered by insurance. Even those with relatively comprehensive insurance may be liable for substantial out-of-pocket treatment and non-treatment costs and may forgo recommended follow-up testing due to cost. Further, a cancer diagnosis affects the AYA's insurability and insurance rates (for health, life, and disability coverage) for the rest of his or her life and may cause individuals to remain in unsatisfactory jobs or choose jobs because of their health benefits.

- **Delayed Diagnosis**

Anecdotes abound among AYA cancer survivors who describe the misdiagnosis of their cancer symptoms and the months—in some cases years—that elapsed before a correct diagnosis of cancer was made. Both provider and patient factors may contribute to late diagnosis. Health care providers' level of suspicion of cancer as a cause of symptoms in this population generally is low, contributing to delayed diagnosis of primary cancers, second cancers, and late effects due to cancer treatment. Cancer symptoms in AYAs may be attributed to fatigue, stress, or other causes. In addition, many primary care providers lack the unique skills and/or are unwilling to care for adolescents. American and Canadian studies of pediatric and adolescent cancer patients have shown that the number of days from symptom onset to diagnosis increases with patient age, as much as double the number of days for older adolescents compared with patients 14 and under.[7,8] Diagnosis also is delayed because AYAs typically see themselves as invulnerable to serious disease or injury, causing them to ignore or minimize symptoms and delay seeking medical attention. Some also may be embarrassed or afraid to seek treatment for symptoms that involve the genitalia or bowel function. Personal preferences and cultural taboos may prevent some patients from receiving needed routine examinations (e.g., pelvic or breast examinations, in some cases particularly if performed by male health care providers). Many AYAs have no primary care provider and do not receive routine care; they may delay seeking care because they do not know where to go (e.g., clinic, private physician, emergency room) for help. When they do seek care, they may give incomplete health histories because they are unaware

[7] Pollock B, Krischer JP, Vietti TJ. Interval between symptom onset and diagnosis of pediatric solid tumors. *Journal of Pediatrics* 1991;119(5):725-732.

[8] Klein-Geltink J, Pogany L, Mery LS, Barr RD, Greenberg ML. Impact of age and diagnosis on waiting times between important treatment events among children 0 to 19 years cared for in pediatric units: The Canadian Childhood Cancer Surveillance and Control Program. *Journal of Pediatric Hematology Oncology* 2006;28(7):433-439.

of (or not asked about) relevant personal or family history or because they choose to withhold information. In addition, for some AYA women, an obstetrician/gynecologist may be their only primary care provider; these providers may have a lower level of suspicion about non-gynecologic cancers in their AYA patients.

- **Treatment Practices and Treatment Setting**

AYAs with first symptoms of cancer may see a variety of health care providers, including pediatricians, internists, family physicians, emergency room physicians, gynecologists, dermatologists, gastroenterologists, neurologists, surgeons, orthopedists, and other specialists. As a result, referral patterns for AYAs with suspected or diagnosed cancers vary widely. AYAs with cancer too frequently fall into a "no man's land" between pediatric and adult oncology. They may be treated by pediatric, adult medical, radiation, surgical, or gynecologic oncologists. Little comparative outcome data exist to guide the cancer care of these patients with respect to treatment setting, treatment provider, or treatment regimen. For younger AYAs and those with tumors also seen in the pediatric population, it often is unclear whether pediatric or adult dosages or dosing schedules of chemotherapeutic agents or radiotherapy are most appropriate for AYAs with cancer. Differences in biology and physiology may affect AYAs' tolerance of therapy but are poorly understood. Treatment of AYAs can be complicated by their treatment regimen adherence issues, which may contribute to their poorer outcomes.

- **Understudied Population**

Research on AYAO has been limited in part because cancer risk and adverse cancer outcomes have been under-recognized in this population. Poor understanding of patient and tumor biology distinguishing cancers in this population (e.g., ALL cytogenetics, breast cancer hormone status, colorectal cancer microsatellite instability) has contributed to limited advances in treatment. In addition, the percentage of AYA cancers that are due to hereditary predisposition is unknown. However, several environmental risk factors have been identified, such as human papillomavirus (HPV) infection for cervical cancer, sun exposure for melanoma, HIV for AIDS-related malignancies, hepatitis B for liver cancer, and other linkages to malignancy have been hypothesized (e.g., Epstein-Barr virus for some cases of Hodgkin's disease and nasopharyngeal carcinoma).

- **Capture of Patients and Patient Data**

Most AYAs are treated in the community rather than in cancer centers. A robust community oncology and primary care infrastructure currently does not exist to enable patient data collection and aggregation that would support research efforts. In addition, contact with many AYAs is lost following treatment, complicating collection of late effects and outcome data. The AYA population is highly mobile and patients may leave the geographic area in which they were initially treated to pursue educational or career opportunities. Further, some AYAs shun continued contact with their treatment providers and the health care system in general as they attempt to move on with their lives after cancer.

- **Number of Clinical Trials/Participation Levels**

Unlike pediatric cancer patients, few AYAs participate in treatment clinical trials. More than 90 percent of patients with cancer under age 15 are treated at institutions that participate in NCI-sponsored clinical trials, and as many as two-thirds of these children are enrolled in clinical trials. This high level of trial participation has been a principal reason for the dramatic improvements in cancer survival among children. By contrast, only 20 to 35 percent of older adolescents (15 to 19 years old) are treated at institutions that participate in NCI-sponsored treatment clinical trials, and only 10 percent of this group is enrolled in trials.[9,10] Only 1 to 2 percent of 20 to 39 year-olds are entered into clinical trials of pediatric or adult NCI Cooperative Groups.[11] This low level of participation may occur because few clinical trials are available for AYA patients or because physicians fail

[9] Bleyer WA, Tejeda H, Murphy SM, Robison LL, Ross JA, Pollock BH, Severson RK, Brawley OW, Smith MA, Ungerleider RS. National cancer clinical trials: children have equal access; adolescents do not. *Journal of Adolescent Health* 1997;21:366-373.

[10] Albritton K, Bleyer A. The management of cancer in the older adolescent. *European Journal of Cancer* 2003;39:2548-2548; at: http://authors.elsevier.com/sd/article/S0959804903008098.

[11] Bleyer WA, Barr R. Highlights and challenges. In: Bleyer WA, O'Leary M, Barr R, Reis LAG (eds). Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, including SEER Incidence and Survival 1975-2000. National Cancer Institute, NIH Pub. No. 06-5767, Bethesda, MD, June 2006; at: www.seer.cancer.gov/publications/aya.

to enroll patients in trials for which they are eligible. Patients aged 15 to 18 years are unlikely to have tumor biology or host physiology that is different from those over age 18, yet they usually are excluded from first-line adult drug development studies. Further, while nearly all pediatric cancer treatment trials include patients at least to age 18, a 15-year-old may have a disease that is not covered by pediatric trials but is ineligible for adult trials focused on his or her disease. Similarly, a 35-year-old may have a disease not covered by adult trials.

- **Psychosocial and Supportive Care**

The psychosocial and supportive care needs of AYAs with cancer tend to be broader in scope and intensity than such needs in younger and older patients because of the many emotional, developmental, and social changes and transitions that occur during this stage of life. For example, because adolescents and individuals in their 20s often are self-consciousness (e.g., concerned about body changes and body image), these patients may experience greater difficulty than younger or older patients in coping with treatment side effects such as hair loss, weight gain or loss, acne, and growth disturbances. For most AYAs, a cancer diagnosis is the first time they have confronted their mortality. Many AYA patients also experience feelings of isolation and have difficulty finding peers among other patients.

AYAs may want or need to maintain work, school, and social aspects of their lives during treatment. Moreover, some AYAs, including but not limited to those at the older end of the age range, may be responsible for young children of their own. Lingering cognitive effects may make it difficult for AYAs to return to school or work following treatment, and educational or career plans may have to be altered. School systems and employers may not recognize these treatment effects as real or may resist accommodating them. Though health provider awareness of potential treatment-related fertility damage may be improving, these issues still are not discussed routinely with patients prior to treatment. Younger AYAs and their families may experience conflicts concerning who should be responsible for medical decisions and AYAs of all ages may experience difficulties navigating the health care system. Because of the complexity and intensity of their emotional and other needs, AYA patients would benefit from psychosocial and supportive care. Services available in pediatric-oriented settings (which tend to be more numerous) or adult-oriented settings (where they are more scarce) still may not be appropriately focused on the needs of this age group. Lack of psychosocial support during and after treatment may be a factor in AYAs' decreased adherence to treatment and follow-up care regimens compared with other age groups.

- **Treatment/Follow-up Care Guidelines**

Inconsistency in treatment and follow-up and insufficient research data have prevented the development of guidelines for treating and monitoring AYAs with cancer, and few tools exist to measure the efficacy of treatment and psychosocial interventions. Guidelines for fertility preservation, a vital concern of the AYA population, recently were published and will be disseminated to the oncology community.[12]

- **Prevention and Early Detection Emphasis**

Cancer prevention and early detection in the AYA population usually are limited to Papanicolaou testing (Pap smear) for precancerous cervical abnormalities and cervical cancer. Physicians do not consistently recommend that AYA patients perform regular skin self-examination for early detection of melanoma, or breast or testicular self-examination, in part due to controversy about the efficacy of the latter two examinations. Similarly, these topics typically are not discussed in school health education programs. Adherence levels among patients whose physicians do recommend self-examination for breast or testicular cancer or malignant melanoma are unknown. Because many physicians are unaware of specific cancer risks in AYAs, they may not recommend early surveillance when it is warranted (e.g., for individuals with strong family histories of cancer). Of note, a new test for HPV now is available and covered by insurance (including nearly all Medicaid programs) in conjunction with a Pap smear for those over 30 or at high risk for cervical cancer (such as women of any age with an abnormal Pap smear), and an HPV vaccine recently was approved by the U.S. Food and Drug Administration.

[12] Lee SJ, Schover LR, Partridge AH, et al. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *Journal of Clinical Oncology* 2006;24(18):2917-2931; at: http://www.jco.org/cgi/doi/10.1200/JCO.2006.06.5888.

RECOMMENDATIONS

This section describes five imperatives for improving the outcomes of adolescents and young adults with cancer. These overarching recommendations encompass the chief concerns expressed in the research and care priorities identified by the 11 AYAO PRG Roundtable Breakout Groups (Table 1). In addition, the AYAO PRG strongly emphasizes that the detailed Breakout Group reports provided in Appendix B are integral components of this report and urges that those responsible for implementing the PRG's recommendations give these documents full consideration in developing implementation strategies.

Recommendation 1: Identify the characteristics that distinguish the unique cancer burden in the AYAO patient.

The limited research to date on older adolescents and young adults with cancer has only just begun to elucidate distinguishing biologic and life stage/developmental characteristics of this population and, further, to reveal the disparities in cancer care and outcomes that mark AYAs as an underserved population.

Elucidate unique biologic characteristics of AYA cancers and AYA patients that affect disease outcome in this population. A significantly more robust research effort is needed to better understand tumor and human factors (e.g., the tumor microenvironment) that contribute to AYAs' susceptibility to cancer, their response to treatment, and their disease outcomes. For example, the correlation between poorer prognosis and older age in ALL has been established (more than 80 percent survival in young children compared with survival below 40 percent in 20 to 39 year-olds). However, little is known about genotypic variability by age for other cancers affecting AYAs or the role of the gene environment in the etiology of malignancies or late effects. Similarly, the effect of age-related physical and hormonal changes on drug metabolism and adverse treatment effects (e.g., neuropathies, glucose intolerance, avascular necrosis of bone, toxicity-related death) is poorly understood. Among the cancers affecting AYAs, the PRG identified as particularly high priorities basic and other biologic research on aging and patient/host-related factors in non-Kaposi's sarcoma, leukemias, lymphomas, and breast and colorectal carcinomas. In addition, increased resources are needed for studies of AYAs' genetic susceptibility to cancer, including both malignancies common to this age cohort and cancers most common in older adults that occasionally occur in AYAs (e.g., lung cancer in an 18-year-old).

Elucidate AYA life stage/developmental characteristics that influence care seeking, adherence to treatment, and medical and psychosocial outcomes. Adolescence and young adulthood are times of increased vulnerability to stress under normal circumstances. AYA cancer patients and survivors face developmental challenges that both significantly exceed those faced by other young people and are distinct from other age groups with cancer. The empirical literature, however, is limited with respect to the causes

Table 1. Adolescent and Young Adult Oncology Progress Review Group Roundtable Meeting Breakout Groups

Core Topics	Cross-cutting Areas
• Biology • Prevention/Cancer Control/ Epidemiology/Risk • Insurance • Clinical Care Models • Psychosocial/Behavioral Factors • Long-term Effects	• Access • Clinical Trials/Research • Health-related Quality of Life • Special Populations • Awareness

and correlates of specific psychosocial outcomes. Previous psychosocial research has combined the AYA population with either pediatric or adult patients and survivors, which has obscured the unique needs of this population. In addition, researchers typically do not have access to a representative population of AYAs due to small numbers of cases, gatekeepers' (e.g., referring physicians) lack of knowledge that their referral choices may affect outcomes, limited research resources in community centers where most AYAs are treated, and limited research funding to support this area of behavioral research. Research is needed to better understand patient and survivor life stage and developmental characteristics across six principal domains—intellectual, interpersonal, emotional, practical, existential/spiritual, and cultural—that singly or in combination may have profound effects on individuals' medical outcomes and quality of life.

Cancer health disparities are differences in the incidence, prevalence, mortality, and burden of cancer and related adverse health conditions that exist among specific population groups in the United States. These population groups may be characterized by gender, age, ethnicity, education, income, social class, disability, geographic location, or sexual orientation.

– National Cancer Institute, Division of Cancer Control and Population Sciences

Identify and ameliorate health disparities experienced by AYA cancer patients and survivors. Numerous factors (e.g., age, gender, race/ethnicity/culture, geographic location, education), singly or in combination characterize specific populations affected by cancer health disparities (see inset, for definition). The type and severity of disparities may result from inequalities in access to health care, receipt of quality health care, and/or differences in co-morbidities, including psychosocial morbidities. Little data exist to explain outcome disparities by race/ethnicity even for the most common pediatric cancers. In the adult literature, particularly regarding breast and prostate cancers, non-Caucasians appear to have markedly worse outcomes. However, ongoing research is clarifying that race often is a proxy measure for disparities such as socioeconomic position, geographic access to care, health insurance status, education, and living conditions. These findings are instructive for research on AYA cancer disparities, which likewise are influenced by factors other than patient age.

The factors that characterize and account for disparities experienced by AYA cancer patients and survivors are understood only in the broadest terms and may include human and disease biology, pharmacogenetics, socioeconomic factors, and the appropriateness and accessibility of health services (especially clinical trials). Therefore, research is needed to elucidate in detail the factors contributing to under-service and poorer outcomes among AYAs as a group and among racial and ethnic subgroups within the AYA population. Community involvement and partnership (including the oncology/medical community and community-based organizations) in research design and implementation should be sought to develop and test hypotheses to ascertain the critical factors influencing AYA cancer disparities, their relative impact, and possible potentiating interrelationships. Such studies are essential to designing and implementing treatment and other interventions with a high likelihood of success.

Efforts to eliminate disparities also may benefit from studies of the military model for AYA oncology care. All AYAs in the military have equal access to primary and tertiary care, longitudinal care throughout treatment and requisite follow-up care, and either continued employment after treatment or continued health benefits as veterans. This model effectively eliminates many of the access and insurance barriers to care experienced in the civilian population.

Recommendation 2: Provide education, training, and communication to improve awareness, prevention, access, and quality cancer care for AYAs.

The AYAO PRG recognized an urgent need for a variety of education, training, and communication activities to raise awareness and recognition of the AYA population at both public and professional levels. To be effective, all education, training, and communications must be culturally appropriate and delivered by individuals who are culturally competent.

Raise awareness of AYA cancer issues as a first step toward increasing national focus and resource allocation to address the AYA cancer problem. Limited awareness of the AYA population as one having specific cancer risk, treatment, and other care

needs distinct from younger and older age groups has hampered targeted research and education, training, and communication activities designed for this population. Raising awareness of these needs and achieving broad acceptance of AYAs as a distinct demographic group are crucial steps toward addressing them. Efforts to raise awareness of the AYA population have been complicated by its heterogeneity, varying perceptions of the group by different stakeholders depending on their relationship to the population, and difficulty establishing standard descriptive terminology among government agencies, funding organizations, and professional groups.

Further, it is not widely known among the general public, policy makers, the news and entertainment media, the military, educational institutions, philanthropic and other funding organizations, and the business world that cancer is the leading cause of disease-related death among adolescents and young adults. Each of these components of the non-clinical public requires tailored messaging and focused outreach to improve awareness of cancer risk among AYAs and encourage funding for AYA oncology research and resources. Awareness of the AYA cancer problem also has been limited by a relative lack of spokespersons/champions for this population in the public and professional arenas.

Provide targeted education to patients, families/caregivers, and the public about AYA cancer issues. Educational and other interventions to modify the exposure of AYAs in the general population to potentially modifiable cancer risk factors (e.g., HPV, hepatitis B virus, ultraviolet light, poor diet, lack of physical activity, obesity, tobacco use, other environmental carcinogens) offer the opportunity to reduce cancer risk during the adolescent and young adult years as well as risk for future cancers in older adulthood. In addition, efforts are needed to promote the importance of health insurance in this population, since neither AYAs nor their families may place a high priority on maintaining coverage for young people who typically are healthy. Greater public awareness of AYA cancer risk and care may be expected to increase enrollment in health insurance plans and reduce delays in diagnosis.

For those diagnosed with cancer and their families, online resources for cancer information, insurance resources, peer support, and other information needs will help to empower AYAs to understand and manage their own care. Educational programs developed and led by advocacy groups and patient support organizations that specifically focus on AYA issues across the spectrum of care are needed for patients and their families and caregivers.

Educate multidisciplinary providers who work with AYAs to improve referrals and services to this population. In general, current health care provider training programs do not address AYA-specific issues, resulting in poor recognition of AYAs' cancer risk and an inadequate response to their medical and psychosocial needs. Subsequently, AYAs often experience delayed diagnosis that may contribute to the population's lack of survival rate improvement. Core competency curricula must be developed and incorporated into appropriate initial training and continuing education programs to ensure that all providers who work with adolescents and young adults—including but not limited to primary care practitioners, oncology and other medical specialists, nurses, rehabilitative care providers, other allied health professionals, and mental health and social workers—have the requisite understanding of characteristics unique to or of particular importance to AYAs. Curricula should address the cancers that either peak or occur more commonly in this age group, post-treatment surveillance for late effects, and the specific psychosocial, economic, educational, and communication needs of the population. Similarly, programs are needed to train "expert" patients (including patient navigators) and advocates who conduct outreach to and represent AYA interests.

Based on data from recent surveys,[13] it was the consensus of the PRG that physician involvement is the key factor in the patient's decision to participate in a clinical trial. Therefore, targeted education to raise referring physicians' and medical oncologists' awareness of the potential benefit of AYAO-relevant trials may be an effective strategy to improve outcomes for these patients.

[13] Comis RL, Colaizzi DD, Miller JD. Cancer Clinical Trials Awareness and Attitudes in Cancer Survivors. Coalition of Cancer Cooperative Groups, poster presentation, American Society of Clinical Oncology Annual Meeting, June 5, 2006.

Recommendation 3: Create the tools to study the AYA cancer problem.

The existing research infrastructure is inadequate to support needed AYA-focused research. Research tools to enable AYA-specific studies must be developed if they do not exist and strengthened if potentially useful infrastructure already is in place.

Create a large prospective database of AYA cancer patients to facilitate research on this age group. Although several sources of data exist on this population, each has significant shortcomings. SEER and population-based cancer registries are well suited for studies of incidence, survival, and second cancers but are limited by a lack of detailed treatment exposure data. The NCI Cooperative Groups provide an established data collection infrastructure; however, most AYAO patients are not enrolled in these protocols, survivor studies are a lower priority, and many patients are lost to follow-up. Some AYA-specific data may exist at individual institutions. Neither clinical trial groups nor individual institutions have the resources to track patients who are geographically mobile. The Childhood Cancer Survivor Study (CCSS) describes late effects in AYA patients treated as children and adolescents, but it is not known to what extent these findings are relevant to adolescents treated outside of a pediatric setting, to young adults (over age 21 at diagnosis), or to people with cancers not included in the CCSS because they typically are young adult or adult cancers (e.g., testicular, cervical, and breast cancers; melanoma).

The Medicaid database should be explored for the applicability and feasibility of its use in developing an AYA prospective database. Further, the well-established active military and veterans health databases, which include a comprehensive electronic medical record for each individual, allow easy access and transfer of data. Because of the skewed age of its population, approximately 2.3 percent of all new AYA cancers in the United States are diagnosed within the military.

Whether a new database is created or existing data sources are enhanced, standardized, linked, and aggregated, establishing the necessary data resources for AYA research is a long-term project that will require substantial ongoing funding. Privacy concerns (including restrictions related to Health Insurance Portability and Accountability Act provisions) must be addressed, and professional/advocacy partnerships will be needed to promote participation by health providers and patients.

Increase the number of annotated specimens to support research progress. A significant lack of infrastructure limits the acquisition and distribution of AYA tumor samples. Specimens of tumors that occur in adolescents and young adults are scarce, in part because some of these cancers are rare and also because most AYAs are treated in the community and preserved specimens are not centrally collected or documented. Even those specimens that exist may lack sufficient clinical annotation to make them useful for many research purposes. As is true in other age groups and for specific cancers, few samples of normal tissue are available to support research aimed at improving understanding of cancer etiology, the role of the tumor microenvironment, mechanisms of progression and metastasis, and other influences that may affect treatment and outcome. Efforts should be undertaken to optimize the effectiveness of existing infrastructure (e.g., Cooperative Human Tissue Network) and to establish standard operating procedures for tissue collection, preservation, storage, and distribution that will help improve AYA tumor, normal tissue, and other biospecimen resources.

Create/modify needed assessment tools specific to AYA cancer issues. The AYAO PRG noted the paucity of assessment and other measurement tools relevant to AYA cancer patients and survivors. For example, numerous instruments for assessing health-related quality of life (HRQL) are available for use in adult respondents. Only a few such measures have been developed more or less specifically for adolescents, and few of these have been employed in assessing HRQL in young adults with cancer. HRQL measures may be used to distinguish the burden of morbidity among groups or individuals at a particular point in time, to assess changes in morbidity over time, in longitudinal/prospective studies such as clinical trials, to predict the score on another measure, or to predict clinical outcome. The need for appropriate HRQL measures for AYAs with cancer is great and should be a subject of increased research. Such measures should

span the survivorship continuum, be developmentally appropriate, include co-morbidity assessment and family well-being, and be usable with patients with varying literacy levels and cultural identities.

Improve grant coding and search term standardization to enable evaluation of research efforts and progress. Consistent research award coding across Federal and non-Federal funding organizations and standardized keyword search terminology are essential to enable researchers and funding organizations to adequately evaluate the type and extent of research on a population. AYAs lack recognition as a defined population, making it extremely difficult, except in obvious cases, to determine whether and to what extent many National Institutes of Health (NIH) and other research awards include AYA subjects, address research questions relevant to them, or conduct separate data analyses on this age group. The AYAO PRG encountered this problem first hand in attempting to assess the NCI research portfolio on AYA oncology.

Expand clinical trials for AYAs to increase treatment choices and accelerate treatment advances. More clinical trials designed specifically for AYAs are needed, as are more trials that include AYAs in the accepted patient age range. Young adults diagnosed with cancers that most commonly occur in younger children should not be excluded from pediatric trials that address those malignancies, nor should adolescents diagnosed with cancers more commonly occurring in older adults routinely be excluded from trials of treatments for those diseases. New or expanded existing clinical trial networks, particularly community-based networks, are needed to enhance AYAs' access to appropriate clinical trials and to aggregate data on AYAs with specific cancers to better understand their treatment responses and outcomes. When AYAs are enrolled in trials that include a wide age range, separate analyses, and reporting of outcomes by age cohort should be conducted whenever possible.

The AYAO PRG recommends that expanded cancer treatment trials for AYAs should focus on malignancies in which treatment improvements will have the greatest potential impact on the AYA cancer problem: sarcoma, lymphoma, early breast cancer, early colorectal carcinoma, germ cell tumors, and leukemia. Further, increased research is needed on interventions to prevent or ameliorate the sequelae of cancer therapy (e.g., second cancers, infertility, cardiotoxicity, hearing loss, cognitive dysfunction, obesity) in the AYA population. HRQL should be routinely incorporated as a primary outcome measure in clinical trials, as well as in health services research focused on models of care, prospective studies of late effects, and studies of palliative and end of life care. Trial designs that accommodate factors such as work, school, and child care demands may improve AYAs' ability to adhere to treatment protocols.

Recommendation 4: Ensure excellence in service delivery across the cancer control continuum (i.e., prevention, screening, diagnosis, treatment, survivorship, and end of life).

The AYAO PRG urges the implementation of two principal strategies to improve service delivery to AYAs with or at risk for cancer and ensure excellence in care across the cancer control continuum.

Develop, evaluate, and disseminate standards of care for AYA cancer patients and survivors to improve outcomes. No consistent standards exist for delivery of cancer-related care to AYAs, and the evidence base needed to establish standards across the continuum of care is weak. The inconsistent approach to cancer diagnosis and treatment delivery among AYAs often results in poor patient experiences in many aspects of care and may be a factor in the lack of survival improvements seen in this population compared with pediatric and older adult counterparts. Excellence in care may vary not only by cancer diagnosis, but by multiple other variables (e.g., age and gender, race/ethnicity/culture, socioeconomic status, source of care) that must be addressed to meet the complete spectrum of patient needs. Developing, disseminating, and evaluating clinical care guidelines are complex endeavors. Standards of care are dynamic; they must be continually evaluated and updated to reflect advances in screening, diagnostic techniques and technologies, treatment, and supportive and palliative care.

The AYAO PRG believes steps toward establishing standards of excellence in AYA cancer care must be taken now. The standards should be based on available evidence, best practices, and expert opinion, with the expectation that they will evolve as the evidence base

matures. Assessment of HRQL should be routinely incorporated as a part of the standard of quality cancer care. Existing clinical practice guidelines for cancers common in AYAs (e.g., leukemia, Hodgkin's disease), supportive care (e.g., pain and distress management), and post-treatment surveillance such as those developed by the National Cancer Comprehensive Network and the Children's Oncology Group provide a starting point for this work. In addition, the American Society of Clinical Oncology is developing evidence-based guidelines for the long-term care of adult survivors, including AYAs.

Likewise, new AYA-specific clinical programs should be developed based on current knowledge and successful existing programs. These AYA programs should be evaluated rigorously through a program of health services research to strengthen the evidence base and guide future program development. Specifically, research is needed to investigate the benefits and drawbacks of treating AYAs as a distinct group with special clinical and psychosocial care needs, the value of creating organizational structures to support these needs, and the impact of such programs on patient outcomes. Despite the need for research, the PRG concurs with the consensus that has emerged among health professionals, health care organizations, patients, and advocates that services for AYAs should be based on a patient-centered model of care. Such a model includes system-related elements (e.g., rapid access, competent assessment, timely and accurate diagnosis, evidence-based treatment, access to clinical trials, minimal treatment and late treatment effects, psychosocial and other support) and other patient-valued elements (e.g., clear, accurate, and empathetic communication; expertise specific to young people and disease; appropriate facilities; peer support).

In addition, the impact of access to care on the ability of AYAs to receive quality care must be considered across the care continuum. As the age group most likely to be uninsured or underinsured, the lack of or insufficient medical insurance coverage is a significant impediment to AYAs developing a primary care relationship, obtaining appropriate referrals and second opinions, and receiving the best possible care. For the best possible outcomes, AYA patients need access to oncology centers of excellence, access to clinical trials, and a means to obtain appropriate counseling, peer support, and patient navigation/health coaching. Moreover, some services (e.g., patient navigation, psychosocial care) may not be reimbursed, creating a further barrier to access. Establishing standards of care/treatment guidelines for AYA oncology will provide the basis for insurance coverage determinations and should secure or improve reimbursements for needed services.

Establish a national network or coalition of providers and advocates seeking to achieve a standard of excellence in AYA cancer care. Establishing, disseminating, and reinforcing standards of cancer care for AYAs will require the ongoing and concerted collaboration of a diverse array of stakeholders including health care providers, research sponsors, investigators, regulators, insurers, and patient advocates who are committed to improving the quality of life and outcomes for AYAs with cancer. Currently, limited collaborative agreements exist among specific stakeholders to advance a particular aspect of AYA care or to fulfill individual organizational missions. To achieve excellence in care across the cancer control continuum, ways must be found to better coordinate the activities of these numerous stakeholders toward common goals and to measure and communicate progress.

Recommendation 5: Strengthen and promote advocacy and support of the AYA cancer patient.

In addition to raising public and professional awareness of AYAs as a distinct understudied and underserved age group (see also Recommendation 2), advocacy and support services for AYA cancer patients and survivors need to be strengthened. To do so, it will be necessary to better understand and address the subjective experience of AYA patients, expand the capacity of existing resources to address AYA psychosocial needs, and develop new resources and interventions designed to meet these needs.

Address the subjective experience of AYA patients. Effective support of AYAs with cancer must be predicated on an understanding of how cancer may affect young peoples' self-identity, self-esteem, spiritual perspectives, body image, perception of their future possible life goals, distress levels, peer relationships, family dynamics, need for information and communication, and numerous other subjective

components of experiencing a life-threatening disease. Empirical research is needed to explore these aspects of the cancer experience among AYAs and inform intervention development and health care provider training.

Build the capacity of existing resources to address AYA psychosocial needs. Some resources exist to address psychosocial needs of AYA cancer patients/survivors and their caregivers. For example, a small number of online communities (such as Planet Cancer) have been started with limited resources by young adult survivors; these communities are serving a substantial number of AYAs but need more support to evaluate, refine, and expand their programs. Other existing AYA-specific resources include print materials, telephone information services, and in-person counseling/educational activities. Many general and disease-oriented patient support organizations are in place but have a variable level of focus on the AYA population. Community clinical oncology practices and other medical, social service, and rehabilitative care providers could be more effective providers of AYA psychosocial care or could be assisted to become more effective in making appropriate referrals. These providers also could become involved in developing, testing, and evaluating AYA-specific psychosocial interventions in various community settings.

Social, professional, religious, and fraternal organizations with established ties to their communities also could build their capacity to assist AYAs with cancer and their families and caregivers. In addition, such organizations offer the possibility of community partnerships to better design, test, and evaluate psychosocial interventions targeting defined subgroups of AYAs. Further, with appropriate training, community organizations can be an important resource for addressing AYA psychosocial needs outside of the traditional insurance system until reimbursement policies more fully cover these services.

Evaluate existing programs and develop new interventions. In addition to building the capacity of existing resources to address the psychosocial needs of AYAs, evaluation is needed to assess the efficacy (i.e., effect on outcomes) of existing interventions. These evaluations should be used to inform the development of new AYA-specific interventions. For example, funding should be obtained to support efforts such as testing and refining existing peer navigation models and developing new AYA-specific navigation programs, conducting longitudinal and/or multi-method theory-based approaches to evaluating peer support and family-based interventions, and developing and testing interventions (e.g., to reduce social isolation, improve family communication, increase health promoting behaviors) to ameliorate negative psychosocial outcomes.

CONCLUSION

Cancer in adolescents and young adults is an important problem that has gone unrecognized or is only a peripheral concern among numerous constituencies, including but not limited to healthy teenagers and young adults who do not know they are at risk; primary care providers; pediatric and adult medical, radiation, and gynecologic oncologists; basic scientists; psychosocial, behavioral, and health services researchers; many cancer patient support providers and advocates; cancer registries; and funding sources for research and cancer-related care. The unfortunate results of this lack of focus have been severe—a lack of cancer survival progress spanning more than two decades and persistent diminution of young cancer survivors' quality of life.

The Adolescent and Young Adult Oncology Progress Review Group (AYAO PRG) drew together more than 100 researchers, health care providers, advocates, insurers, industry representatives, and health services and health policy experts to consider the state of cancer-related science and care for this population and develop recommendations to accelerate progress and improve outcomes across the research and cancer care continuum. The AYAO PRG believes that a major, ongoing AYAO-specific research initiative emphasizing AYA clinical trials and outcomes research is urgently needed. Collaboration and support from numerous governmental, academic, public health, community-based, and other private sector entities will be essential to its success. The AYAO PRG offers this report as a blueprint for a focused and structured approach to improving cancer prevention, cancer care, and the duration and quality of life for this vital segment of our society.

APPENDIX A
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APPENDIX B
BREAKOUT GROUP REPORTS

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Background

Adolescents and young adults (AYAs) with cancer have "fallen through the cracks" when it comes to treatment, clinical research, resources, and support services. The Adolescent and Young Adult Oncology Progress Review Group (AYAO PRG) has defined the AYA age group as those 15 to 39 years old. This definition was based on data showing a "gap" that occurs in this age range: In the past 30 years, improvement in survival rates for AYAs has not kept pace with that experienced by their older and younger counterparts.

For AYA issues to be addressed effectively, the first, critical step is broad acceptance of AYAs as a distinct demographic group with unique needs related to their age and stage of life. Awareness and acceptance of AYAs as a unique group must increase among AYA stakeholders, including clinicians, researchers, advocates, and patients and their families/caregivers to achieve the goal of increasing awareness among funding agencies, policy makers, publishers, medical societies, and the general public.

An initial step toward achieving this goal will be identifying key groups among these stakeholders that can significantly effect change for AYAs. Messages and outreach strategies then must be developed to increase awareness about AYAs as a separate population with unique characteristics.

Another key to defining AYAs as a distinct group will be highlighting those points in the cancer care continuum where AYAs fall through the cracks. For example, compared to the general population, AYAs are more likely to experience delayed diagnoses, they are the least represented population in clinical trials, and they are the most likely non-elderly group to be under- or uninsured. Increased awareness that problems such as these exist is essential to begin addressing them.

Descriptions of the unique epidemiology of AYA cancer patients have only begun to appear in the past decade. Only this year (2006) was the first-ever Surveillance, Epidemiology, and End Results (SEER) program monograph on AYAs published. Little published research exists that pertains specifically to AYA patients. The current state of the AYA oncology literature remains largely descriptive; research projects and publications may involve patients in the AYA age range, but questions directly relating biologic and psychosocial AYA factors to outcomes rarely have been addressed.

AYA research is difficult to identify because it lacks standardized language for keyword searches. The lack of recognition of AYAs as a distinct group was illustrated by the difficulty in extracting relevant information from the National Cancer Institute's (NCI's) research portfolio for the purposes of this PRG. An initial keyword search for "young," "teen," or "adolescent" retrieved 585 studies; however, the majority of the studies were not focused on AYA cancers and were therefore eliminated from consideration. In addition, projects that focused specifically on cancers that predominately strike AYAs (e.g., testicular cancer) were not retrieved by this search strategy unless the abstract specifically included the previously noted keywords. NCI's indexing and coding systems need to be adapted to recognize AYAs as a distinct group for the purposes of effective research and data compilation.

With AYAs established as a discrete demographic group, the essential prospective research specifically designed or stratified for AYAs can be conducted.

Well-designed studies addressing AYA-specific biologic and psychosocial factors will require identification of programs with adequate numbers of AYA patients in treatment and follow-up and dedicated, funded researchers.

Priority 1

Establish AYA as a distinct group of cancer patients based on unique needs and issues, institutionalize the definition, and gain broad acceptance among stakeholders in AYA care.

Rationale

The AYA group shares common needs and issues that differentiate them from other cancer cohorts. To effectively and appropriately address these needs, they must be accorded recognition as a separate demographic group. The lack of recognition of AYAs as a distinct group is illustrated by the difficulty in extracting relevant information from the NCI research portfolio so that neither a specific nor sensitive search for AYA investigations was possible in preparation for this PRG as detailed earlier. Education, research, career development, clinical care, and support services focused on the distinct AYA group cannot occur without appropriate, broad recognition of their definition.

Implementation Barriers

- AYAs are a previously undefined, heterogeneous group of patients.
- AYAs may be viewed differently by various stakeholders according to their relationship to the group.
- The term "adolescent" may have a negative connotation for older adolescent patients.
- Limited data exist to support the current definition of AYAs as comprising patients aged 15 to 39 years.
- Establishing standardized terminology among government agencies, funding organizations, and professional societies is difficult.

Potential Partnerships and Resources

- Funding agencies
- Health care professional organizations
- Advocacy groups
- Federal agencies
- National Library of Medicine
- International Committee of Medical Journal Editors
- International Cancer Research Portfolio

Concrete Actions in the Next Three Years

- NCI should establish/coordinate search terms, keywords, and coding specific to AYAs.
- Key stakeholders should be convened at the November 2006 meeting of the LIVE**STRONG**™ Young Adult Alliance to demonstrate unified acceptance of the AYA definition.

Priority 2

Increase awareness in the clinical sphere (e.g., patients, caregivers, providers) regarding the significance and unique aspects of AYA oncology.

Rationale

To this point, AYA cancer patients have fallen through the cracks in medical, psychosocial, and support services, resulting in a relative lack of improvement in survival rates. Because the prevalence of cancer in this age group is not widely appreciated, clinical suspicion in AYA patients, caregivers, and providers is low. Once diagnosed, there is a lack of awareness as to the elements of appropriate care for AYA patients. In addition to the greater likelihood of delayed diagnoses, AYAs face unique issues with regard to their education, financial, and insurance status; fertility; social support; and psychological issues. Spotlighting these issues and the under-representation of AYAs in clinical trials are the first steps toward addressing them.

Implementation Barriers

- Getting the attention of stakeholders is difficult.
- AYAs are a previously undefined cohort.
- Clinical care providers are fragmented between pediatric and adult oncology and between academic and community centers.
- AYAs lack spokespeople/champions.

- Feelings of invincibility among AYAs contribute to awareness problems.
- Different messages will be required to effectively reach different segments in the clinical care sphere: health care professionals, patients, and caregivers.

Potential Partnerships and Resources

- Professional organizations
- Academic institutions
- Community cancer centers
- Advocacy organizations
- Medical journals
- Mass media
- American Medical Writers Association
- Military and educational institutions

Concrete Actions in the Next Three Years

- Encourage professional societies and publications to develop AYA-specific forums.
- Stimulate development of AYA-specific curricula in oncology professional training programs.
- Encourage the Lance Armstrong Foundation (LAF), CancerCare, and other partner organizations to host teleconferences for patients/caregivers on AYA issues.
- Encourage the LIVE**STRONG**™ Young Adult Alliance to coordinate a comprehensive public relations campaign on AYA needs and issues.
- Encourage NCI to develop AYA-specific patient, provider, and caregiver materials.

Priority 3

Increase awareness in the non-clinical sphere (e.g., public, media, corporations, and policy makers) regarding the significance and unique aspects of AYA oncology.

Rationale

The general public, funding organizations, policy makers, and the business world are largely unaware that cancer is a leading cause of death among adolescents and young adults. Increased awareness about the prevalence and burden of AYA cancer may increase enrollment in health insurance plans, promote timely diagnoses, and encourage funding of research and resources for AYA oncology, thereby reducing AYAs' suffering and improving outcomes.

Implementation Barriers

- Significant competition with other health-related messages targeting AYAs, such as drunk driving and drug abuse.
- Lack of high-profile spokespeople to champion AYA cause.
- Lack of messaging and focus.
- Small size and political weakness of AYAs as a group.
- Competition for funding.
- AYA sense of invincibility.

Potential Partnerships and Resources

- Large corporations/employers
- Military
- Educational institutions
- Community organizations
- Advocacy groups
- Insurance industry
- Youth-oriented media outlets
- Professional organizations
- Government policy makers
- Celebrities, entertainment industry

Concrete Actions in the Next Three Years

- Identify and recruit high-profile, credible AYA spokespeople.
- Approach Health in Hollywood and other youth-oriented media to encourage them to highlight this problem.
- Schedule briefings for policy makers on Capitol Hill.
- Encourage the LIVE**STRONG**™ Young Adult Alliance to coordinate a comprehensive public relations campaign on AYA needs and issues.
- Approach the Ad Council for a national media campaign highlighting AYAs.

Conclusion

A lack of awareness exists among all stakeholders and the general public about the significance of cancer in the AYA population and the unique needs and issues of AYA patients related to their age and stage of life. Until now, the AYA population has not been officially defined. Broad recognition and acceptance of the AYA definition are critical first steps to improving outcomes and quality of life for AYA patients.

Awareness must increase in both the clinical and non-clinical arenas. Within these spheres of influence, key stakeholders who can significantly effect change for AYAs must be identified and, through appropriately tailored messaging and outreach, these stakeholders must be energized to recognize and promote AYAs as a distinct demographic population.

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Background

Etiology

The etiology of AYA cancers remains largely understudied. Without an understanding of the etiology of these malignancies, developing effective cancer preventive interventions is challenging. Substantial resources have been directed at studying the causes of childhood cancer, which collectively represent less than 1 percent of all new cancer cases annually. Cancer incidence in the 15 to 39 year-old age group is 4.3 times higher than for children under age 15. Six types of cancer account for 67 percent of all cancers in the AYA population: breast (15.4 percent), lymphoma (12.1 percent), melanoma (11.0 percent), thyroid (10.7 percent), female genital system (9.9 percent), and male genital system (8.1 percent).[1]

Little research has focused on the etiology of malignancies that occur primarily in AYAs. The research that has been done indicates that cancer family syndromes (e.g., germline mutations) account for less than 5 percent of the overall incidence of cancers in this age group. Environmental factors are thought to play a minimal but undefined role in the etiology of childhood malignancies. The etiologies of cancers in the adolescent and young adult years represent a mix of the genetic and environmental factors.

Adolescents and young adults in the general population often are exposed to known risk factors for adult malignancies (e.g., human papillomavirus, hepatitis B virus, poor diet, lack of physical activity, obesity, tobacco use). Therefore, an important opportunity exists in this age group to develop and implement interventions that can reduce the risk of future adult malignancies. In addition, the occurrence of treatment-related sequelae in AYA survivors may be modified by interventions during or after cancer therapy. Currently, little evidence is available to indicate that these interventions alter long-term outcomes. A number of intervention strategies for adult cancer involve altering exposure to potentially modifiable risk factors. It is likely that understanding the interplay between environmental exposures and genetic factors, or gene-environment interactions, will guide the way to developing effective preventive interventions for AYAs.

Prevention

Very little prevention research has been targeted at this age group because the AYA cancer problem is under-appreciated and because researchers may anticipate problems with AYAs' adherence to research protocols. AYAs with cancer also are unlikely to be treated in research centers. Because of these barriers and those imposed by gaps in health care use and insurance, few preventive interventions have been aimed at this age group.

Cancer prevention strategies are aimed at reducing the incidence of new cancers. These strategies can be grouped into those aimed at blocking the initial onset of disease (primary prevention), those aimed at detecting disease in the earliest stages of development (secondary prevention), and interventions targeting the post-diagnosis period (tertiary prevention).

An overall prevention strategy should focus on identifying etiologic factors for cancers that affect AYAs. However, primary prevention focused on the AYA population will also affect cancer incidence later in life, given the long latency of most cancers following exposure. For example, tobacco use is not likely to significantly increase the burden of cancers in the adolescent and young adult years, but will do so later in life. Likewise, sun exposure at early ages is strongly associated with skin cancers, including malignant melanomas, that occur most frequently later

[1] SEER 17, 2000-2003.

in adulthood. Reduced exposure to direct sunlight and increased use of sun block decrease cancer incidence later in life. Infectious agents are strongly implicated in the etiology of some adult malignancies, such as cervical cancer. Human papillomavirus (HPV) vaccines have been shown to be extremely effective at blocking new HPV infection in adolescent girls, thus reducing cervical cancer incidence later in life. Other AYA cancer preventive strategies might focus on increasing physical activity and maintaining appropriate energy balance.

Secondary preventive methods in early detection are non-existent in this population with the exception of Pap smears for cervical cancer. The low incidence of common adult cancers (e.g., breast, colon, prostate) in AYAs make efficacy trials of established early detection procedures such as mammography and colonoscopy impractical. However, identifying high-risk AYAs based on their genetic predisposition may provide an acceptable and cost-effective strategy for targeted early detection interventions. Improved access to and use of diagnostic imaging and screening tests that use highly sensitive biomarker assays may also reduce the cancer burden.

Tertiary prevention is aimed at reducing subsequent cancer risk and adverse treatment effects following a primary cancer diagnosis. Survivors of AYA cancer are at risk for many treatment-related, long-term sequelae, such as second primary cancers, heart failure, hearing loss, and cognitive dysfunction. Prognostic factors for these outcomes must be elucidated to formulate strategies for reducing their incidence. Relevant interventions may involve manipulations of primary cancer therapies, such as using continuous instead of bolus infusion of anthracyclines to decrease the risk of cardiotoxicity, chemoprotectants designed to decrease myocardial damage during anthracycline administration, or otoprotectants during platinum administration. Other interventions may be targeted at survivors, such as increasing physical exercise to prevent obesity among AYAs who are completing their cancer therapy.

Identified Action Areas

The Prevention/Cancer Control/Epidemiology/Risk Breakout Group identified the need for action in 10 areas:

1. Tobacco control: postponement of smoking initiation; potential long-term health effects of environmental tobacco smoke exposure; adverse effects on offspring of tobacco smoke exposure during pregnancy; genetic variation in addiction susceptibility; cessation efforts in AYAs.
2. Cancer prevention vaccines: HPV vaccine implementation issues; hepatitis B vaccine; Epstein-Barr virus vaccine.
3. Genetic susceptibility: importance in AYA cancer etiology; potential use of genetic screening to identify high-risk populations and in monitoring for second cancers; privacy and data access concerns; use of genetic testing to identify populations for chemoprevention; possibility of including an AYA cancer in The Cancer Genome Atlas (TCGA).
4. Sequelae of cancer treatment in AYAs: second primary cancers; ototoxicity; cardiotoxicity; social integration and educational reentry; fertility issues; dietary interventions to modify risk of sequelae.
5. Sun exposure risk (increased education for prevention and early detection of malignant melanoma, squamous cell carcinoma): awareness of risk among AYAs, educators, and parents; possible viable screening alternatives; access to early detection services.
6. Surveillance of AYA cancer patterns: greater depth and breadth of traditional surveillance activities; more detailed information on risk behaviors, treatment/tumor characterization, quality of care, economic factors, and patient-centered outcomes.
7. Early-onset breast cancer: research on epidemiology; chemoprevention (e.g., raloxifene, COX-2 inhibitors); special population issues including higher incidence in African American and Asian women; relation of risk to diet, obesity, and energy balance.
8. Chemoprevention
9. Lifestyle interventions: behavior modification to improve diet (e.g., 5-A-Day); education on benefits of healthy lifestyle; healthy lifestyle interventions in AYA survivors.

10. Early detection of AYA cancers: efficacy of using genetic susceptibility markers to identify high-risk populations with special attention to testicular cancer, breast cancer, cervical dysplasia, and melanoma.

The top three priorities were selected based on these criteria:

- Importance with respect to the level of cancer burden in the AYA population or to the potential for intervening with AYAs to reduce adult cancer risk
- Lack of resources currently devoted to the issue
- Potential for actual implementation

Priority 1

Increase research on interventions to prevent or ameliorate the sequelae of cancer therapy in the AYA population.

Rationale

AYA survivors suffer from a broad spectrum of treatment-related sequelae (e.g., second malignancies, infertility, cardiotoxicity, hearing loss, cognitive dysfunction, obesity). Although adolescents and young adults have a sense of immortality prior to having cancer, awareness of their vulnerability and motivation to participate in prevention research may be heightened after being treated. Opportunities therefore exist to conduct effective research aimed at improving survival and preventing or ameliorating the late effects of cancer therapy.

Implementation Barriers

- More than 75 percent of adolescents aged 15 to 19 years are not seen at a cooperative group institution.
- People in this age range often have difficulty in adhering to prescribed regimens.
- Funding in this area is inadequate.
- Researcher interest is low due to lack of awareness of the AYA cancer problem.
- This population often falls through the cracks with respect to access to health services, including prevention services.

Potential Partnerships and Resources

- Expanded biospecimen repositories to facilitate research
- New and enhanced infrastructure for conducting longitudinal studies and interventions and tracking long-term outcomes
- Potential partners: National Institutes of Health (NIH), Lance Armstrong Foundation (LAF), college health groups, American Cancer Society (ACS), American Society of Clinical Oncology (ASCO), Centers for Disease Control and Prevention (CDC)

Concrete Actions in the Next Three Years

- Fund sequelae prevention research.
- Increase awareness of need for research in this area (e.g., conferences, publications, workshops).

Priority 2

Increase resources for studies of genetic susceptibility in AYA cancers, including designation of an AYA cancer-specific component in The Cancer Genome Atlas (TCGA).

Rationale

Cancers that occur in younger persons (children and adolescents) are thought to be related more to genetic etiologies than to environmental etiologies. In the general AYA population, opportunities exist to identify subsets at high risk of adult cancers using genetic screening and new technologies, such as high-throughput genomic and proteomic assessments. The new TCGA needs to include at least one cancer that is common in the AYA population.

Implementation Barriers

- Privacy, medicolegal, and insurability issues may restrict more widespread use of genetic screening.

Potential Partnerships and Resources

- Genetic counselors
- Biotechnology industry
- NIH/NCI

Concrete Actions in the Next Three Years

- Sponsor conferences and workshops focused on genetic susceptibility and the use of genetic markers to identify high-risk subsets of AYAs.
- Increase research funding (e.g., through Requests for Applications and Program Announcements) to assess the use of genetic screening to reduce the cancer burden.

Priority 3

Increase education in the AYA population on the risks of sun exposure to reduce the risk of malignant melanoma.

Rationale

It is known that sun exposure at younger ages greatly increases the risk of malignant melanoma and other skin cancers in adulthood. Melanoma accounts for 93 percent of invasive skin cancers (excluding basal and squamous cell carcinoma and Kaposi's sarcoma) in the 15 to 39 year-old age group.

Implementation Barriers

- Adolescents and young adults consider themselves at minimum risk of disease and therefore feel that they do not need to protect themselves from sun exposure.
- Even though AYAs have some knowledge about the effects of sun exposure, physical appearance in this population remains an overriding high priority. Being sun tanned is considered attractive among most Caucasians, who are at highest risk for melanoma.

Potential Partnerships and Resources

- Cosmetic industry
- Pharmaceutical industry
- Schools and health educators
- NCI, ACS, CDC

Concrete Actions in the Next Three Years

- Develop and implement school curricula (elementary through college) on the dangers of sun exposure and on practices that can reduce skin cancer risk.
- Support behavioral research to develop more effective interventions to reduce sun exposure.
- Identify AYAs in the general population who are at relatively high risk of skin cancers due to genetic predisposition.

Conclusion

There are many prevention opportunities to dramatically reduce the burden of cancer in both the AYA population and older adult populations. Some of the common barriers to achieving prevention goals are related to the sense of invulnerability and immortality common among adolescents and young adults, the lack of scientific interest in developing preventive measures for this population, and providers' lack of concern about the need to recommend preventive measures. In addition, it is not clear which health care specialists should be responsible for implementing preventive measures. By implementing the three top priorities described along with the research and programs listed in the Breakout Group's other identified action areas, the incidence of cancer and cancer-related morbidity among AYAs would be markedly decreased.

BIOLOGY

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Background

The stark lack of improvement in survival outcomes for adolescent and young adult cancer patients over the past few decades contrasts sharply with dramatic improvements in childhood cancer cure rates and the recent, steady improvement in overall cancer survival rates for adults. Many of the advances in cancer survival in children and adults have been achieved through an integrated understanding of tumor biology and the normal biology of the patient, which has far outpaced the state of this knowledge about the AYA population, even for cancers with a high prevalence in adults (e.g., breast and colon cancers). To improve outcomes for AYA cancer patients, this knowledge gap must be closed.

The lack of progress in AYA cancer biology research is partly explained by the relative rarity of AYA cancers, the small number of AYA patients entering clinical trials, and the scarcity of normal and tumor tissue samples. Therefore, the many AYA cancer research stakeholders must pool their resources and cooperate to more effectively study normal and tumor biology in the AYA population.

Sequencing of the human genome and new technologies for global molecular analysis (e.g., global gene expression[1]) are creating opportunities to study molecular differences among AYA, childhood, and adult cancers in greater detail than previously has been possible. Much of the data showing that age-related biologic factors probably do play a role in cancer outcomes result from studies comparing the genetics of acute lymphoblastic leukemia (ALL) in children and adults.

Researchers know that different age groups tend to develop characteristic genetic subtypes of ALL, and the relationship of ALL subtype to prognosis is well established. For example, children with ALL blast cells[2] having a genetic mutation known as the TEL-AML1 fusion transcript have an unusually good prognosis. In contrast, patients with a particular BCR-ABL mutation[3] have an unfavorable prognosis. Researchers have found that up to 50 percent of children between 1 and 9 years of age, but only 10 percent or fewer of children ages 10 or older, have blast cells harboring a favorable genotype such as TEL-AML1. Less than 2 percent of younger children have the unfavorable BCR-ABL genotype, compared with approximately 12 percent of young adult ALL patients.

Less is known about age-related genetic differences in other tumor types. However, one study showed that gastrointestinal stromal tumors in children tend not to have a c-kit mutation that is commonly seen in adults with this disease. Other research suggests that the type of genetic mutations found in Ewing's sarcoma tumors may differ considerably between children and adult patient populations.

Some studies point to the role of epigenetics, including methylation of cancer-causing genes, in age-related differences in cancer outcomes. In one study for example, several key cancer-causing genes, including LATS-1, CDH1, p57, p14, and p15, were more likely to be methylated in adults than in children. Age-related changes in epigenetic regulation also may affect the expression of genes involved in drug metabolism and account for some of the characteristic differences in outcome and drug toxicity documented in AYAs. Side effects that AYA patients experience more than other populations include higher induction death

[1] Global gene expression measures the patterns of expression of up to thousands of genes in a sample.

[2] Immature cells that normally comprise 5 percent of the bone marrow.

[3] t(9;22) BCR-ABL translocation.

rate,[4] pancreatitis, treatment-related neuropathy,[5] and glucose intolerance. An understanding of the biologic mechanisms underlying treatment toxicities will help researchers design equally effective but less toxic treatment regimens for AYA patients. For example, one group of researchers found that the maturing bone of AYA patients treated with dexamethasone may be particularly susceptible to osteonecrosis. This finding led to a modified dexamethasone dosage schedule for adolescents 13 years and older.

Further, developmental and hormonal differences may influence drug metabolism and increase the risk of drug toxicity and relapse. The increased incidence of obesity in AYA patients compared with younger patients has been associated with poorer outcomes. Data from another study suggest that obese patients can tolerate therapy, although an acute myeloid leukemia (AML) study reported increased side effects in obese AML patients. Further research is needed to elucidate the relationship among obesity, drug toxicity, and outcomes. The effects of pregnancy on cancer development and response to therapy in AYAs also are not well understood.

In summary, emerging data, much of it from ALL studies, indicate that differences in host/patient and tumor biology play a role in the poorer prognosis of AYA patients. Further studies in ALL and other tumors are likely to lead to important observations that can be translated into better therapies and improved outcomes for the AYA population.

Major Challenges in Studying Tumor Biology in the AYA Population

- The biology of tumors in AYAs is poorly understood.
- Host/patient differences as a function of age are understudied.
- Infrastructure to support acquisition and distribution of samples is lacking.

[4] The rate of patient death due to toxic effects of chemotherapy given to treat the tumor.

[5] Functional disturbance or pathologic changes in the peripheral nervous system.

Priority 1

Improve basic biologic research in AYA non-Kaposi's sarcomas.

Rationale

Although sarcomas are an important group of diseases in the AYA population, the basic biology of AYA non-Kaposi's sarcomas is poorly understood. In many respects sarcomas are an orphan disease, but the opportunity exists to significantly enhance knowledge about AYA sarcoma biology. Although some investigators already are collecting biological samples for AYA sarcoma research, establishing a network to share samples is the top priority. Building on existing infrastructure, such as the Cooperative Human Tissue Network (CHTN), to obtain more AYA sarcoma samples would be an expedient way to accomplish this goal.

Implementation Barriers

- Sarcoma is a relatively rare disease.
- Limited funding is available to study sarcoma biology.
- The number, size, and quality of annotated AYA non-Kaposi's sarcoma biological samples are limited.
- AYA sarcoma patients are diagnosed and treated by a diverse group of providers, mostly in community medical settings where collection of fresh tissue samples is not valued.
- The incentive for investigators to collect samples is low. There is no mandatory sample collection, best practice collection guidelines, or infrastructure for accessing samples. Regulatory barriers to sample collection also exist.

Potential Partnerships and Resources

- Sarcoma Alliance for Research through Collaboration (SARC)
- National Cancer Institute (NCI) Cooperative Groups and Cancer Centers
- American Association for Cancer Research (AACR)
- CHTN—infrastructure for sample collection, maintenance, and distribution

- Lance Armstrong Foundation (LAF)—AYA non-Kaposi's sarcoma research advocacy
- American College of Surgeons—partnerships for tissue collection

Concrete Actions in the Next Three Years

- NCI, SARC, and the cooperative groups should issue a directive requiring submission of AYA sarcoma samples to CHTN for sharing with other investigators. For example, SARC membership could be made dependent on providing an agreed upon number of samples for submission. NCI and/or SARC also should develop and require compliance with a standard operating procedure for sample processing, annotation, and access. Both tumor and normal tissues are needed. Scientific review for proper sample distribution already exists through CHTN.
- NCI and others should identify funding sources for and implement collection of tissues with a required minimum of annotation data, building on the CHTN infrastructure.
- NCI, AACR, and/or other funders should issue a Request for Applications (RFA) for basic biologic research in AYA non-Kaposi's sarcomas. Research areas should not be limited by the RFA; however, important areas include epigenetics, developmental biology, stem cell research, and preclinical models. Cross-disciplinary studies (e.g., stem cell research, developmental biology) should be encouraged.

Priority 2

Improve understanding of host/patient biology of aging and cancers, including sarcomas, leukemias, lymphomas, and breast and colorectal carcinomas, in the AYA population.

Rationale

The biology of aging in this population has been understudied yet may have cross-cutting relevance to many AYA cancers. This population may have unique genetic and epigenetic differences compared to either younger or older age groups, as well as important hormonal and physiologic differences (e.g., effects of pregnancy, increased prevalence of obesity in adolescence). An understanding of how these differences may affect cancer development, drug metabolism, and response to treatment is needed to improve survival in AYA cancer patients. Achieving this understanding will require focused collaboration and optimal utilization of resources. The availability of normal tissues is essential.

Implementation Barriers

- Few normal tissue samples are available to perform this research.
- Collaboration among oncologists studying AYA cancer and biologists studying aging is limited.
- Funding for host/patient biologic research in the AYA population is insufficient.

Potential Partnerships and Resources

- National Institute on Aging (NIA), LAF, Leukemia & Lymphoma Society, and AACR—promote research collaboration and provide funding
- Cooperative groups, cancer centers, and CHTN—provide infrastructure for tissue collection

Concrete Actions in the Next Three Years

- AACR/NCI/NIA should convene a multidisciplinary meeting of investigators to discuss hypotheses and experimental approaches to understanding the effects of AYA development and aging on cancer. This meeting will serve as a springboard for creating a network of experts and potential collaborators interested in this research topic.
- NCI, NIA, and other funders should issue an RFA for the study of biologic aging in the AYA population in both the normal and cancer contexts. The RFA should encourage investigation of all AYA cancers, including sarcomas, leukemias, lymphomas, and carcinomas.
- NCI, SARC, and/or other research sponsors should provide funding to create incentives for banking and sharing normal and all types of AYA tumor samples using mechanisms similar to those described in Priority 1.

Priority 3

Investigate a potential biologic basis of age-related differences in outcome for AYA cancers, beginning with leukemias and lymphomas.

Rationale

Evidence suggests that for certain cancers such as leukemia and lymphoma, disease biology is different in AYA patients compared with their younger or older counterparts. These differences could be due to variations in host/patient physiology (see Priority 2) or age-related differences in tumor biology. Understanding how basic aspects of disease biology, including the role of the tumor microenvironment, change with aging in AYA individuals is needed. Leukemias and lymphomas are AYA cancers for which a substantial body of biologic knowledge already exists. Furthermore, pediatric and medical oncologists studying leukemia and lymphoma already have formed effective collaborative infrastructures. Thus, these diseases provide a good starting point for implementing this priority.

Implementation Barriers

- The number and quality of biologic samples in the AYA population for leukemia and lymphoma are limited.
- Funding for studies of tumor biology related to outcomes in the AYA population is limited.
- Because accrual of AYA patients to protocols is limited, the collection of samples and clinical information on disease presentation, laboratory features, stage, and outcome also is limited.

Potential Partnerships and Resources

- NCI, AACR, Leukemia & Lymphoma Society, LAF—funding
- Cooperative groups—clinical trials, samples, and annotated data

Concrete Actions in the Next Three Years

NCI and/or other funders should issue an RFA to study age-related biologic differences in lymphoma and/or leukemia, focusing on the AYA population. The RFA should fund examination of samples from both adult and pediatric clinical trials and address the biologic basis of outcome differences. Progress in lymphoma and leukemia studies will serve as a model for investigating other cancers in this population.

Conclusion

Preliminary research indicates that significant differences in AYA tumor and host biology compared with other age groups account for some of the corresponding differences in outcome for this population. Researchers are beginning to identify some differences in biology that will serve as a lead to more detailed studies. Relevant technical and scientific breakthroughs are being made in fields such as genomics, stem cell research, and aging research. Investigators increasingly are developing collaborative networks and encouraging clinical trial participation and tumor banking. The following will be critical to the success of research in this area: (1) improved funding for AYA cancer research (especially in understudied cancers such as non-Kaposi's sarcoma), (2) tissue samples (normal and tumor), and (3) consideration of both host/patient physiology and tumor biology in the AYA population.

ACCESS

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Background

Access, as defined by the Institute of Medicine Committee on Monitoring Access to Personal Health Care Services,[1] is the "timely use of personal health services to achieve the best possible health outcomes." An individual with cancer should have access to an oncologist who offers the most experience and best survival outcome for a given diagnosis, participation in clinical trials, and support services appropriate for the needs of the patient. Adolescents and young adults (AYAs) with cancer should have the same opportunity as older or younger patients to achieve their best possible outcome. Population data document poorer outcomes in AYA patients compared with their younger counterparts, and studies in Ewing's sarcoma, rhabdomyosarcoma, synovial sarcoma, and acute lymphoblastic leukemia have shown that this difference is due in part to health services delivery and access barriers and not solely to biology. Outcome differentials such as these are alarming and highlight the need to identify factors that affect access to therapy for these different populations.

In assessing access issues of the AYA population, the entire continuum of care must be considered, beginning with evaluation of first symptoms, the diagnostic process, therapy, supportive care, post-treatment surveillance, and survivorship issues. To minimize delays in diagnosis and to ensure appropriate referral, patients should have access, regardless of financial and insurance status, to a consistent primary care provider who provides a developmentally appropriate, welcoming environment that maximizes adherence and communication. The provider should be knowledgeable about AYA cancers to have an appropriate level of suspicion regarding cancer in these patients and allow referral to the appropriate oncologist.

Upon diagnosis, a patient should have access to oncologic professionals who can provide high quality care based on experience or specialized training. AYAs also should have access to developmentally appropriate psychosocial support and counseling regarding issues such as fertility preservation, education, employment, disability, insurance, and other financial and legal concerns. Further, AYAs should have access to peer support and sufficient information to make informed decisions about treatment. To ensure the best quality of treatment, AYAs should have access to an evidence-based standard of care (where it exists) and clinical trials, including biologically appropriate novel agents. Following completion of therapy, AYA survivors should be provided with a portable follow-up plan of care that takes into account their stage of life and mobility and includes information about long-term and late effects, insurance, self-advocacy, and health maintenance.

The challenges to optimal access are substantial:

- Practical and Financial Barriers
  - Lack of adequate insurance decreases therapeutic options for patients (e.g., second opinions, choice of specialists, access to expensive treatments and medication).
  - Lack of a primary care physician may be a deterrent to seeking timely attention for early symptoms of cancer.
  - Concerns about missing school or work or getting child care for young children may

[1] Millman M (ed). Access to Health Care in America. Committee on Monitoring Access to Personal Health Care Services, Institute of Medicine, Washington DC, National Academies Press, 1993.

keep AYA patients from making or keeping appointments during normal clinic hours and otherwise impede access to care.

  - Location of treatment may limit access to clinical trials.
  - AYAs may not be willing or able to travel long distances to centers of AYA excellence for specialty care.
- Provider Issues
  - The clinical suspicion of cancer is low for patients of this age.
  - Because AYAs do not need or receive routine medical care, physicians may be unaware of the patients' baseline medical status and therefore may miss signs of cancer.
  - Coordination of care issues among multidisciplinary providers is a challenge to both providers and patients.
  - Treatment setting may limit access to clinical trials.
- Personal Beliefs, Knowledge, and Behavior
  - AYAs are a generally healthy population with a strong sense of immortality and invincibility that may limit their ability to acknowledge the possibility of a cancer diagnosis and the necessity of intervention.
  - For AYAs, the rigors of therapy may interfere with meeting the developmental milestones of independence and socialization and can lead to non-adherence with treatment and follow-up recommendations.

Priority 1

Explore models and pilot programs that use health coaches/navigators to facilitate full access to and utilization of optimal AYA oncology care.

Rationale

AYA patients must navigate a complex health care system composed of multiple specialists and uncoordinated resources. The health care system is unfamiliar to this generally healthy population that previously has not needed to access these services. In addition, the system is not focused on the special needs of younger cancer patients and most available resources are not developmentally appropriate. Many AYA patients lack the built-in advocacy of family or community. A patient navigator can provide information and guidance regarding the treatment center, clinical trials, and supportive care services.

Implementation Barriers

- Navigator services are not billable and require institutional or long-term philanthropic support.
- Efficacy of cancer patient navigators is not yet established.
- AYAs are relatively few in number and are scattered throughout the country, making service programs difficult to implement.

Potential Partnerships and Resources

- Potential funding sources—National Cancer Institute (NCI), including the Cancer Disparities Research Program/Patient Navigator Research Program; Lance Armstrong Foundation (LAF); American Cancer Society (ACS); public and private payors
- Potential models—Foundation for Informed Medical Decision Making, Cancer Information Service (CIS), Ulman Cancer Fund for Young Adults, NCI Patient Navigator Academy
- Potential implementers—Academic cancer centers, Community Clinical Oncology Programs (CCOPs), CIS

Concrete Actions in the Next Three Years

- Evaluate existing models of patient navigation/ health coaching and explore their applicability in the AYA setting.
- Pilot and assess models of AYAO health coaching/navigation including virtual navigators accessed through existing patient information programs such as CIS and ACS.

Priority 2

Develop an AYA-specific educational portal (Web-based and CD-ROM/DVD) for patients, caregivers, and health care providers.

Rationale

Due to the rarity of AYA cancers and limited evidenced-based care guidelines, no central information resource exists that is developmentally and clinically appropriate for AYAs. Such a resource, maintained and updated for use by diverse groups, is needed to ensure access to the most up-to-date diagnostic, treatment, follow-up, and survival information.

Implementation Barriers

- A variety of groups are working to develop such resources; however, these groups generally have limited financial resources and personnel to dedicate to this effort, and duplication of effort should be avoided.
- Funding is needed to develop and maintain an integrated Web portal.

Potential Partnerships and Resources

- NCI, including CIS and www.cancer.gov
- ACS
- Patient advocacy groups
- Professional organizations, e.g., American Society of Clinical Oncology (ASCO), Oncology Nursing Society (ONS)
- CureSearch
- Association of Cancer Online Resources (www.acor.org)
- LIVE**STRONG**™ Young Adult Alliance

Concrete Actions in the Next Three Years

- Identify the most appropriate parent organization or establish a coalition for the Web portal.
- Identify current sources of content and contributors who will collaborate to develop a comprehensive and integrated site.
- Build a developmentally appropriate Web-based user interface.
- Market the portal to user communities.
- Negotiate linkage to and from medical information Web sites used by primary care providers.

Priority 3

Develop standards of excellence that document best practices for access to diagnostic, treatment, and follow-up care for AYAs.

Rationale

An essential element of providing access to quality care is defining what constitutes that care so that organizations and institutions can have a standard by which to develop their programs and by which to measure success. These standards also will help empower patients to participate actively in planning care with their providers. Because AYA oncology is a relatively new field, it is anticipated that these standards will begin as a consensus process informed by current evidence, and the levels of evidence on which recommendations are based will be identified explicitly. The limitations of this evidence will inform future research priorities and standards will evolve as additional evidence is developed.

Implementation Barriers

- Limited evidence is available to inform best practices.
- Small numbers of experts are available to develop and update standards of care.
- The wide age range and the diversity of diagnoses, many of which are low incidence cancers, will make it difficult to develop recommendations that apply to the entire AYA population.
- Compliance with guidelines may not be achievable by all providers.

Potential Partnerships and Resources

- National Comprehensive Cancer Network
- Professional societies, e.g., ASCO
- Agency for Healthcare Research and Quality
- Coalition of Cooperative Oncology Groups

Concrete Actions in the Next Three Years

- Review the existing evidence.
- Identify a parent organization for the standards development process.
- Identify experts who will write the standards.
- Identify groups that will disseminate the standards.
- Convene a meeting and develop a draft standard.
- Develop an implementation plan including ongoing updates and expansion.

Conclusion

Because AYA patients appear to be lagging behind in survival improvements and quality of survival, the extent to which access issues are barriers to the best outcome must be assessed and better understood. Research is needed to analyze and ameliorate the impact of provider (e.g., site, specialist, treatment regimen, level of supportive care), logistic, and patient barriers so that care can be provided equally to all patients. In the interim, concrete steps can be taken to improve care provided today: developing guidelines that establish a standard of care, making this and other guidance available to AYA patients through a coordinated Web portal, and providing patient navigator assistance to AYA cancer patients. These steps should alleviate some of the disparities that AYAs suffer in accessing quality cancer care.

INSURANCE

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Background

Adolescence and young adulthood are periods of great change for most individuals. The transition from being a "dependent" to an independent and autonomous functioning member of the "real world" has important implications for all aspects of adolescents' and young adults' (AYAs') lives.

For AYAs with health insurance, this transition includes an evolution in health insurance as coverage is transferred from parent or school to a new employer or spouse. For others, however, the transition is not nearly so smooth. Lack of health insurance due to "aging out" of parent's coverage, the end of full-time student coverage, unemployment, or an initial job that does not offer health insurance can be an outcome of the current employer-based health insurance system that underpins the health care system in the United States. Young adults are the most underinsured age group in the United States. Recent data reveal that over 49 percent of young adults aged 18 to 24 years were uninsured for at least 1 month over a 24-month period (2001-2002), and 29.6 percent were uninsured for an entire year.[1] Even when purchasing health insurance is an option, many young adults forgo many optional forms of insurance in favor of other necessities. Unfortunately for some, when major health problems arise, the lack of health care coverage becomes a major obstacle to treatment and recovery. There appear to be multiple reasons that young adults place such low priority on health coverage. These include the following:

- A perception of invulnerability and the presence of good health
- Competing financial priorities such as education, transportation, housing costs, and entertainment
- The high cost of health insurance premiums

One of the well-worn tenets of insurance is that "you can't get fire insurance on a house when smoke is coming out of the windows." The same generally holds true for health insurance—individual coverage generally is not available if one has developed a major health condition prior to application, and if available, its cost can be prohibitive.

Group health insurance holds more promise for AYAs with pre-existing conditions because little if any underwriting is required. Most employer-sponsored health insurance is of this nature, but rising premiums have caused many employers to limit this popular employee benefit by decreasing the employer's contribution and offering less comprehensive plans with higher employee copayments. Some smaller employers have discontinued health insurance as a benefit and recent surveys indicate a strengthening of this trend.

Most employers who extend coverage to dependents do so only until age 19, unless the child is enrolled as a full-time student. Coverage typically ceases at age 23 unless the individual is disabled and remains dependent upon the parent. In employer and other group health plans, pre-existing conditions are not covered unless there has been continuous "creditable" health insurance coverage prior to application (i.e., no gap in coverage for more than 63 days). In the AYA age group, breaks in coverage occur frequently for numerous reasons, as noted previously. These issues, coupled with the individual's (and perhaps family's) perception that health insurance for adolescents and young adults is not a high priority need, may pose major problems in obtaining health insurance at an affordable rate in

[1] Mills R, Bhandari S. Health Insurance Coverage in the United States: Current Population Reports, U.S. Census Bureau P60-223, 2003; at: http://www.census.gov/prod/2003pubs/p60-223.pdf.

the future, particularly if the young person develops a major health condition such as cancer that requires costly extended treatment.

Provisions of Federal laws such as the Consolidated Omnibus Budget Reconciliation Act (COBRA) and the Health Insurance Portability and Accountability Act (HIPAA) provide important legal protections that guarantee continued insurability provided that the individual previously was covered under a group health insurance plan and maintained creditable coverage without an extended disruption. In addition, COBRA and HIPAA provide for a transition period during which alternative coverage can be obtained. These provisions are particularly important for those with pre-existing conditions and other "high risks," as a significant break in coverage may subject the individual to a pre-existing condition exemption clause, higher premiums, or outright declination of coverage. Although these laws guarantee continuous eligibility during a transition period, under COBRA, employer contributions to premiums cease and premiums rise considerably as the individual assumes both employee and employer portions of the cost. Further, when COBRA and HIPAA protections cease, unless group coverage can be obtained, individual coverage often is financially out of reach for AYAs with pre-existing conditions. These principles and scenarios apply similarly to disability insurance and to a certain extent to life insurance.

States have served as the nation's laboratories for developing and testing insurance programs for individuals at high risk, yet no standard model exists. Unaffordable premiums, waiting periods, and other barriers often place these programs out of reach for many individuals and families. Nationwide, Medicaid continues to serve as the insurer of last resort, although eligibility, benefits, and administration vary widely among the states. Further, many consider state budget cutbacks and Federal deficit reduction measures major threats to meaningful Medicaid coverage.

Priority 1

Develop a public relations campaign using high-profile individuals to promote the need for health insurance.

Rationale

AYAs must be encouraged to take responsibility for their own health care needs as they enter adulthood. They must be educated about the fact that they are at risk for serious illnesses, particularly cancer. Unless AYAs are covered under a parent's health insurance as an eligible dependent, employed with health benefits, or a full-time student, they need to include health insurance among their high priorities. However, convincing typically healthy AYAs that health insurance is an important priority is a challenge. Well-known public figures such as athletes and entertainers should be enlisted to bring this important issue to light. This approach has been successful in changing AYA behavior, as evidenced by public campaigns to reduce tobacco use and teenage drinking and driving, and should be employed to promote the need for health care coverage in this population.

Implementation Barriers

- Persuading young adults to purchase health insurance is difficult because of their perception of invincibility. In addition, limited income (if any), finishing education, career pursuits, housing expenses, starting a family, and other priorities tend to take precedence over health insurance concerns.
- It is important to recognize that the AYA group is a heterogeneous population and, therefore, targeted marketing is necessary. A variety of media messages and approaches will be needed, taking into account "language," cultural, and ethnic differences in the AYA population. Further, AYAs must be approached on their level, using their language, values, and technology.
- AYAs lack an understanding of the complex health insurance marketplace, particularly regarding "transition issues," insurance rating practices, exclusions for pre-existing conditions, waiting periods, variation in benefit packages, regulatory variation among states, and policy

costs. It will be a challenge to convey the message that insurance is important to a population with limited knowledge of the issues and a lack of experience.

Potential Partnerships and Resources

- National Cancer Institute
- Centers for Medicare and Medicaid Services
- Lance Armstrong Foundation
- National Coalition of Cancer for Survivorship
- American Cancer Society (ACS)/cancer advocacy community (young adults)
- Insurance industry
- America's Health Insurance Plans

Concrete Actions in the Next Three Years

- Contact insurance industry representatives to share available information/descriptive data regarding numbers of uninsured AYAs and causal factors to document the extent of the problem and to determine the focus of the campaign.
- Encourage public-private partnerships to promote the value and importance of maintaining continuous health insurance coverage utilizing marketing plans focused on the AYA target audience.
- Identify successful health education campaign models for the AYA population.
- Identify potential spokespeople and organizations to launch the campaign.
- Determine funding sources.

Priority 2

Convene stakeholders and experts to create and disseminate a centralized repository of resources and best practices regarding available health coverage options.

Rationale

AYAs lack sufficient knowledge of the issues associated with obtaining and maintaining insurance coverage, including rules and regulations governing guaranteed insurability and the multitude of potential public and private health insurance/health care coverage options. It is difficult for consumers generally, and particularly for inexperienced AYAs, to navigate the complex insurance and health care system and obtain concise, relevant, and easily understandable information. A centralized repository of information on potential sources of coverage, eligibility criteria, policy options, benefits and limitations, premiums and copayments, insurer contact information, and other key elements would be extremely useful to consumers seeking insurance coverage. Such an information source also would be helpful to AYAs who may be insured but need assistance in identifying providers or understanding benefits, coverage restrictions, and reimbursement. The repository also would be available to benefits counselors who provide support to AYAs and their families.

In concert with this priority, the PRG endorses the development of a curriculum to train AYA advocates in identifying sources of health insurance and navigating the system to make best use of available coverage.

Implementation Barriers

- No centralized source for this information exists at present; therefore, stakeholder cooperation is essential for success.
- Stakeholders need to be made aware of the magnitude of the problem and be willing to provide and update the relevant data.
- Content must be identified, and information must be presented in a consistent fashion to enable meaningful assessment of alternatives.
- Insurance-related information is complex and may be difficult for many to comprehend.
- Sources of leadership and funding for this effort are unclear.

Potential Partnerships and Resources

- Cancer Information Service
- ACS
- Cancer and insurance advocacy groups
- Academic institutions
- Insurance industry
- Private foundations

Concrete Actions in the Next Three Years

- Identify minimum data set for dissemination.
- Determine strategy for collecting and disseminating information.
- Identify and convene key stakeholders.
- Obtain information and resources within 12 months.
- Implement information dissemination strategy within 18 months.

Priority 3

Challenge oncology experts to develop AYA oncology treatment guidelines upon which coverage determinations can be made for this population.

Rationale

No universally accepted payment guidelines exist for AYA oncology patients. Health plans vary significantly with regard to benefit packages and associated treatment costs. This situation results in patient and provider frustration, time spent pursuing appeals, and delays or interruptions in treatment. Establishing guidelines will support a more consistent approach to coverage for AYA treatment modalities, including psychosocial support and rehabilitative services.

Implementation Barriers

- It is difficult to arrive at consensus.
- No current guidelines exist upon which to base coverage.
- Guideline development is a lengthy, complex, and costly process.
- Technology advances often outpace clinical guideline development.

Potential Partnerships and Resources

- American Society of Clinical Oncology
- Oncology Nursing Society
- Association of Clinical Oncology Social Workers
- Insurance industry technology assessment groups
- National Association of Insurance Commissioners
- Advocates

Concrete Actions in the Next Three Years

- Establish consensus regarding the need to develop coverage guidelines.
- Convene a panel of leaders in oncology practice and care to draft guidelines.
- Obtain endorsement by nationally recognized professional cancer organizations.
- Identify funding sources including public, private, and industry organizations.
- Obtain support of the health insurance industry.

Conclusion

The need for health insurance coverage for AYAs is generally unappreciated as AYAs typically view themselves as healthy individuals who are invulnerable. With limited resources and competing priorities, health insurance often is not considered a necessity.

Lack of awareness of viable options for insuring this population group exacerbates the problem of coverage loss among AYAs. No centralized source of information exists regarding viable health coverage options for AYAs. A centralized repository of health coverage information will improve consumer information access and enhance decision-making regarding health care coverage.

It is crucial to help AYAs understand that individual insurance coverage must be purchased and maintained when the AYA is in good health so that coverage can be obtained at a reasonable cost and to ensure that the plan is in place if and when the need for care arises. Sports figures and popular entertainers have proven most successful in changing youth behavior and should be recruited to help communicate the importance of health coverage for AYAs.

The absence of universal coverage guidelines currently results in confusion and frustration among providers, payors, and patients; national coverage guidelines would provide the basis for agreement about coverage for AYA cancer care.

CLINICAL CARE MODELS

Co-Chairs

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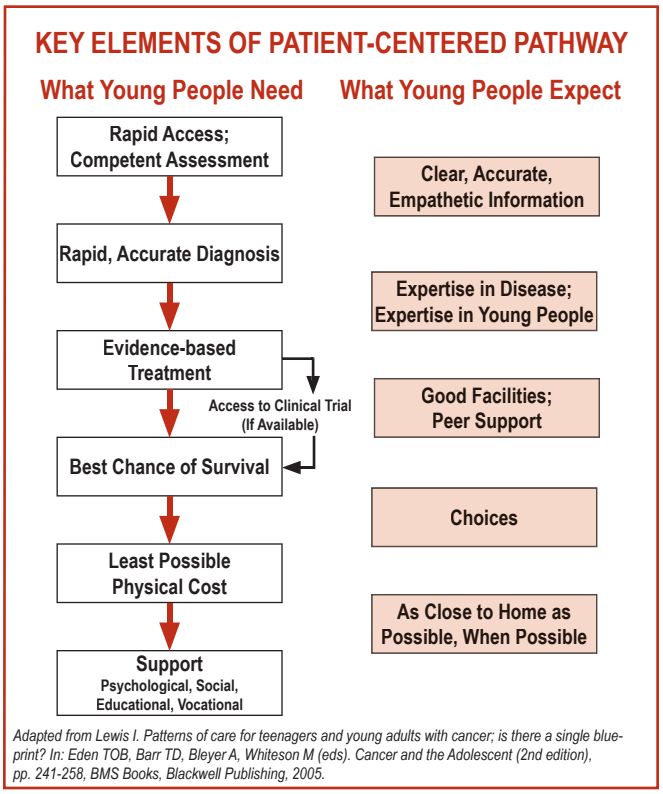
Background

Adolescents and young adults (AYAs) with cancer have not benefited comparably from the increased survival and reduced mortality experienced in recent years by both older and younger cancer patients.[1] Tremendous gaps in our knowledge exist concerning the factors that account for poor outcomes in this age group and how best to treat AYA patients with cancer.

AYAs with cancer face multiple clinical and social challenges that affect their outcomes and which may vary not only by cancer site, but also by multiple other variables, including age, gender, race/ethnicity, socioeconomic status, and source of care. For example, concerns about school, work, family, pregnancy, sexuality, and insurance are likely to affect adherence to treatment. Yet little data exist to address these issues.

Considerable interest has emerged recently in developing innovative specialized programs for AYAs with cancer. Research is needed to investigate the benefits and drawbacks of treating AYAs as a distinct group with special needs for clinical care and psychosocial support services, and the consequent value of creating organizational structures to support these needs. Currently, most AYAs are treated by either pediatric or adult oncologists and few studies have evaluated how the organization of clinical care affects an individual's survival and quality of life. Further, little is known about what additional specialized training health professionals need to improve treatment for AYA patients with cancer.

In the United Kingdom, the first inpatient unit to care specifically for teenagers and young adults with cancer was established in 1990. Since then, an additional eight units have been established, with more planned. AYA-specific multidisciplinary teams have started to evolve alongside the inpatient units, but with no clearly consistent model of practice. Each unit and team has responded to local circumstances. Early indications are that outcomes for patients with cancer treated in areas with these centers have improved, but the data are preliminary and the methodology has not been validated. Recently, a broad consensus has emerged among health care professionals, health care organizations, patients, and advocates regarding the key elements required to deliver a patient-centered model of care (see figure that follows).



Adapted from Lewis I. Patterns of care for teenagers and young adults with cancer; is there a single blue-print? In: Eden TOB, Barr TD, Bleyer A, Whiteson M (eds). Cancer and the Adolescent (2nd edition), pp. 241-258, BMS Books, Blackwell Publishing, 2005.

[1] Bleyer A, O'Leary M, Barr R, Ries LAG (eds). Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, including SEER Incidence and Survival: 1975-2000. National Cancer Institute, NIH Pub. No. 06-5767, Bethesda, MD, 2006.

These elements now have been incorporated into formal national guidelines for improving outcomes in children and young people with cancer in the United Kingdom.[2] This model is conceptual and implementation requires practical elements such as AYA-specific multidisciplinary teams, dedicated units, navigators (called key workers in the United Kingdom), good informatics, a registry system, appropriate clinical trials and protocols, and the development of local and national networks. These developments have specific implications for training and research.

The AYAO PRG Clinical Care Models Breakout Group agreed that the core elements of this model were relevant to the United States health care system but required local modification. Key aspects of the AYA clinical cancer care problem in the United States include the following:

- AYAs are an underserved population.
- Underservice to AYAs with cancer is poorly recognized. Delayed diagnosis occurs frequently.
- AYA patients are treated disparately; no agreed upon standards/protocols of care exist.
- Access to clinical trials is poor.
- Recognition of the need for peer and psychosocial support is limited, and little such support is provided.
- Knowledge about AYA clinical care needs is limited.
- Service development in the United States is embryonic.

The Breakout Group recommends the following priorities.

Priority 1

Develop patient-centered and needs-led AYA programs after first defining core elements and standards.

Rationale

To improve care for AYA cancer patients, it is necessary to establish protocols, to improve recognition of the population, clinical trial access, peer and psychosocial support, and knowledge of AYA clinical care needs.

Implementation Barriers

- Lack of clarity and definition of the population (15 to 39 years of age).
- Multiple cancer sites.
- Lack of advocacy.
- Lack of recognition by many oncology professionals that AYAs need both site-specific and age-specific care, leading to treatment and patient "ownership" conflicts.
- Existing National Cancer Institute (NCI) Cooperative Group self-interest.
- Lack of funding.

Potential Partnerships and Resources

- Patient advocacy organizations, e.g., Lance Armstrong Foundation (LAF)
- National Institutes of Health (NIH), e.g., NCI, National Heart, Lung, and Blood Institute (NHLBI)
- Health care organizations
- American Society of Clinical Oncology (ASCO) and other professional societies
- American Cancer Society (ACS)
- International partners
- NCI Cooperative Groups
- Department of Defense (DoD)
- National Comprehensive Cancer Network (NCCN)
- Academic institutions
- Robert Wood Johnson Foundation (RWJF)

Concrete Actions in the Next Three Years

- Create a national network of stakeholders to deliver this agenda.
- Develop agreed upon service standards with NCCN.
- Identify champions to develop and promote local multidisciplinary networks to share practice and develop local responses to national guidelines.

[2] National Institute of Health and Clinical Excellence—Improving Outcomes Guidance, United Kingdom.

- Issue a Request for Applications (RFA) for service development and evaluation programs.
- Convene a national patient meeting to collect feedback.

Priority 2

Develop core competency-based curricula to incorporate appropriate training programs for multidisciplinary professionals and develop expert patient and advocate programs.

Rationale

Current training programs do not address AYA-specific issues, resulting in poor recognition of the needs of this group, delayed diagnosis, and no improvement in outcome for decades. The AYA population has a specific set of cancers that either peak or occur more commonly in this age range (e.g., bone sarcomas, germ cell tumors, lymphomas, leukemias, melanoma, certain less common/early-onset epithelial tumors). AYAs have specific psychosocial, economic, and educational needs. The AYA population also does not fit easily into either the classic pediatric or the adult paradigms of communication and interaction with health professionals. The challenges of working within a focused multidisciplinary group must be addressed through training programs for health professionals.

Implementation Barriers

- Lack of recognition by many oncology professionals that AYAs need both site-specific and age-specific care, leading to treatment and patient "ownership" conflicts.
- Lack of awareness/understanding among practitioners about why AYA-specific curriculum development and training are needed.
- Competition for time and funding.
- Lack of awareness of the existence of this population.
- Scarcity of trainers.

Potential Partnerships and Resources

- Patient advocacy organizations, e.g., LAF
- NIH institutes, e.g., NCI, NHLBI
- Health care organizations
- ASCO and other professional societies
- ACS
- International partners
- NCI Cooperative Groups
- DoD
- NCCN
- Academic institutions
- RWJF
- Accreditation Council for Graduate Medical Education (ACGME)
- Aflac

Concrete Actions in the Next Three Years

- Create AYA-specific modules or tracks within existing health professional training programs.
  - Identify AYA educators to develop necessary curricula.
  - Discuss with ACGME and the Oncology Nursing Society the need to incorporate AYA curricula as a requirement.
  - Obtain funding for training through the following:
    - NIH K-type training grants specific for AYA
    - Other organizations such as Aflac, RWJF, American Association for Cancer Research, and ASCO
  - Develop educational programs for AYA patients and families led by advocacy groups.

Priority 3

Develop AYA-focused health services research capacity to evaluate service delivery programs.

Rationale

(see Background)

Implementation Barriers

- Health Insurance Portability and Accountability Act privacy provisions

- Need to identify funding and champions
- Lack of consistent and validated methodologies

Potential Partnerships and Resources

- Patient advocacy organizations, e.g., LAF
- NIH institutes, e.g., NCI, NHLBI
- Health care organizations
- ASCO and other professional societies
- ACS
- International partners
- NCI Cooperative Groups
- DoD
- NCCN
- Academic institutions
- RWJF

Concrete Actions in the Next Three Years

- Convene a working group to develop research methods and establish collaborations to evaluate different models of care. It is imperative to include all relevant stakeholders, including researchers, providers, patients, advocacy groups, insurance representatives, and NIH (NCI and other institutes).

Conclusion

No consistent standard exists for delivery of care to the AYAO population. This deficit has resulted in poor patient experiences and likely is associated with the lack of recent improvement in survival compared to the pediatric or adult populations. Similarly, educational programs are lacking that address directly the needs of the AYA group and those who provide service to them.

To address these issues, the AYAO PRG Clinical Care Models Breakout Group recommends the adoption of patient-centered approaches to care, which requires the development of a standard of care and AYA-specific programs. These standards and programs will require evaluation through a program of health service research. In addition, core competency programs for professionals, patients, and advocates should be developed.

CLINICAL TRIALS/RESEARCH

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Background

The Clinical Trials/Research Breakout Group considered the following background information in formulating its priority recommendations:

- Excluding homicide, suicide, and unintentional injury, cancer is the leading cause of death in Americans aged 15 to 39 years. In females it ranks as the number one cause of death, whereas in males it ranks as number two, following heart disease.
- The average annual increase in the incidence rate of invasive cancer is higher in people aged 25 to 29 years and 30 to 34 years than for all other 5-year age groups under 45 years old.
- Among the 703 active, applicable National Cancer Institute (NCI)-sponsored trials, only 26 Phase III trials do not have age limitations that exclude a portion of the adolescent and young adult (AYA) patient population. No Phase III melanoma, hepatic cancer, or thyroid cancer trials are accessible to this group.
- The average annual percent change (AAPC) in 5-year survival rate among 15 to 39 year-olds decreases in correspondence with the rate of clinical trial participation in this age group.
- It is possible to estimate the impact of a specific cancer type in the AYA patient population by combining three factors: survival progress (AAPC in 5-year survival), cancer incidence rate, and mortality rate.

In preparation for the Breakout Group session, each group member was asked to complete a survey of factors that may explain the AYA clinical trial participation gap. The integrated results of this survey are shown in Table 1.

Priority 1

Focus on increasing referring physician and oncologist awareness.

Rationale

More than 60 percent of children with cancer participate in clinical trials, compared with 3 to 5 percent of adults. Only 1 to 2 percent of adolescent and young adult oncology (AYAO) patients participate in clinical trials.[1] Many differences exist between the pediatric and adult clinical trials environment that may explain the trial participation dichotomy, including an integrated clinical trials educational approach in pediatrics training and the fact that pediatric oncology is largely academic/medical center-based. Adult oncology is carried out primarily in the community, where 80 percent of cancer patients receive their care. Many excellent community-based oncology practices exist and approximately 60 percent of adult patients entered into NCI Cooperative Group studies are referred from community-based practices. Clinical trials participation is generally underfunded and takes significant resources in both time and personnel.

The Breakout Group members agreed that physician involvement and influence are key factors in the patient's decision to participate in a clinical trial. This impression is confirmed by recent surveys evaluating the role of the physician, conducted by the Coalition of Cancer Cooperative Groups (CCCG).[2] According

[1] Bleyer A, Budd T, Montello M. Lack of clinical trial participation and of progress in older adolescents and young adults with cancer. *Current Problems in Pediatric and Adolescent Health Care* 2005;35(5):186-195.

[2] Comis RL, Colaizzi DD, Miller JD. Cancer clinical trials awareness and attitudes in cancer survivors. Coalition of Cancer Cooperative Groups, poster presentation, American Society of Clinical Oncology Annual Meeting, June 5, 2006.

to the surveys, 6 percent of Americans rely exclusively on their physician in health care decision-making, and an additional 53 percent rely on both their physician and their own research into their health problem. Physicians and/or organizations of physicians and researchers are the most trusted information sources concerning health issues in general, and clinical trials in particular. Approximately 20 percent of Americans indicate that they would be very willing to participate in clinical trials, but would rely on their physician for guidance.

Only 10 percent of cancer survivors report being aware that they could have participated in a clinical trial as part of their cancer treatment. Among the survivors who know about clinical trials, over 70 percent were made aware of this opportunity through a physician; no other information source category had a significant impact on patients' awareness of clinical trials. Three percent of survivors participated in a clinical trial and an identical proportion declined to participate, primarily because they were not sure that the clinical trial would provide an outcome at least equivalent to standard care. Lastly, there was a direct and statistically significant relationship between patient clinical trial participation and the physician's encouragement to participate, the oncology team's efforts to educate the patient about clinical trials, and the oncology team's assistance to the patient to find a trial.

Table 1. Potential Reasons for the AYA Clinical Trials Participation Gap

Health Professional (physicians, nurses, allied health professionals)	• Lack of clinical trials for AYAO patients • Arbitrary clinical trial age criteria excludes AYAs • Lack of awareness of clinical trials available to the AYAO population • Referral patterns dictate the centers to which AYAO patients go • Medical and pediatric oncologists may not be aware of each other's clinical trials • Most experienced medical team not providing care to AYAO patients with specific diagnoses • Adult oncologists have few patients with "AYA cancers" • Lack of access to oncologist/cancer center • More business-like models of medical oncology practice vs. academic model of pediatric oncology practice • Money/time commitment to initial and continuing education • Location/hours not amenable to hours required for clinical trials • Expected poor patient adherence to protocol • Loss of patients – turf conflicts, expected good outcome • Lower reimbursement expected • Lack of facility conducive to AYA care and clinical trial requisites • Clinical trial not available via medical oncologist's practice • Reluctance of medical oncologists and pharmaceutical companies to develop clinical trials for young patients
Societal/Cultural (health care system, socioeconomics, cultural dynamics)	• Age – denial of disease • Patient unprepared for illness, much less clinical trials • Health insurance gap • Insurance guides referral patterns • For "emancipated" adolescent or young adult, entry into quality health care system may be a major issue • Time constraints – school, work, and late or multiple appointments • Clinic hours not friendly to student or working adult schedules • Language barrier • Educational level • Trial groups not "cross-cutting" for diseases (e.g., Children's Oncology Group vs. intergroups) • Lack of social support for transportation, cost of care • Lack of awareness by employers, school personnel, associates, neighbors, and community • Clinical trials not a priority • Financial – physicians want reimbursement for themselves • Physician ego – can do things as well or better than a trial • Adolescents may be less compliant than adults • Lack of clinical niche (e.g., adult vs. child cooperative group)

Table 1. Potential Reasons for the AYA Clinical Trials Participation Gap (cont.)

Personal/Patient (older adolescents and young adults)	**15 to 19 year-olds:** • Dependency on parents/system – lack of independence • Parental lack of education • Age group least expected to take ownership of their own health care • Not wishing to assume responsibility • Unsure of best treatment setting (medical vs. pediatric oncology center) **20 to 29 year-olds:** • Access – not offered • Intermediate likelihood of taking ownership of own health care • School/work/family responsibilities **30 to 39 year-olds:** • Access – not offered • Group most expected to take ownership of own health care • Work/family responsibilities **All three AYA age groups:** • Lack of awareness of trials or their importance • Not advocates for themselves • Health insurance; financial burden of premiums and out-of-pocket costs • Body image • Transportation/housing • Financial limitations • Travel restrictions • Distrust – "guinea pig" issues (afraid of being experimented on) • Distrust – delays in diagnosis • Adherence • Independence/autonomy • Concern about time commitment and extra tests/studies associated with trial participation for young adults with job/family concerns • Preference to stay close to home and peers • Less motivated
Family/ Community (family members, colleagues/ friends, educators, employers, politicians, legislators, knowledge workers)	• Family – distance, responsibilities • Want patients close to home/family • Colleagues – isolation • Educators – home schooling • Employees – lost hours • Politicians – lack of knowledge of impact • Lack of awareness of clinical trial importance • Lack of education • Lack of guidance • Inadequate community resources • Lack of advocate within health care system • Too much input from too many people • Conflicting opinions offered by family members and/or others • Isolation – lack of knowledgeable support group • Afraid of experimental nature of trials • Difficult dynamics – patients have both parents and children

Therefore, since most AYAO patients are cared for in the community medical oncology system, increasing referring physician and oncologist awareness of the availability and potential value of clinical trials to AYA cancer patients should be a top priority to increase AYA participation in trials.

Implementation Barriers

- Need to change referring physician and oncologist attitudes about AYA participation in clinical trials and the most appropriate treatment setting for AYAO patients.
- Lack of health provider education regarding clinical trials in general and trials available for AYAO patients.
- Need to address barriers to the transition of primary cancer treatment responsibility for AYAO patients from a predominantly academically based, clinical research-oriented pediatric oncology environment to the more private practice-oriented adult oncology environment.
- Need to overcome barriers to AYAO patient referral from practice-oriented adult oncology environments to tertiary cancer center programs.

Potential Partnerships and Resources

- CCCG, representing the various components of the publicly funded clinical trials structure, and the individual NCI-supported Cooperative Groups
- Community and academic cancer organizations, networks, and societies that reflect the spectrum of providers involved in caring for AYA cancer patients
- General medical societies, including family practice, internal medicine, surgery and surgical specialties, gynecology, dermatology, and local/state medical societies
- Nursing societies, which represent an integral and indispensable component of the health care and clinical trials continuum

Concrete Actions in the Next Three Years

- Develop a syllabus on AYAO for presentations by oncology experts to professional societies.
- Develop syllabi (slide libraries) on AYAO adapted for local/regional presentations.
- Have professional societies endorse the AYAO clinical trials awareness concept.
- Request that the American Society of Clinical Oncology (ASCO) conduct a targeted educational session at its annual meeting.
- Disseminate a "Dear Physician" letter from NCI.

Priority 2

Target malignancies that have the greatest potential impact on the AYA[3] cancer problem for increased clinical trial involvement: sarcomas, lymphomas, breast cancer, colorectal carcinoma, germ cell tumors, leukemia, malignant melanoma, bone sarcomas, and brain tumors.

Rationale

The AAPC in 5-year survival rate for all invasive cancers shows the least amount of progress in patients between 15 and 39 years of age at diagnosis.[4] The AYA survival improvement deficit is a general AYA cancer problem, with 18 of 26 cancers/cancer groups evaluated demonstrating a deficit. By equally considering the AAPC in 5-year survival rate, the absolute survival rate during 1975-1998, and the proportion of all malignancies that the cancer represents, a list of the cancers that could provide the greatest potential impact on AYA outcome can be estimated and would include non-Kaposi's soft-tissue sarcoma, non-Hodgkin's lymphoma, hepatic cancer, germ cell tumors (males and females combined), colorectal carcinoma, breast cancer, malignant melanoma, and brain tumors. If one weights the AAPC more than the absolute 5-year survival rate and cancer prevalence, the cancer priority list changes to include non-Kaposi's soft-tissue sarcomas, non-Hodgkin's lymphomas, hepatic cancer, germ cell tumors, colorectal carcinoma, breast cancer, Hodgkin's lymphoma, and bone sarcoma (see Table 2). The least common of these cancers is hepatocellular carcinoma and is therefore not considered a high priority. Although leukemia does not appear in the list, the AYAO PRG opted to include leukemia as a second

[3] Ages 15 to 39 years, inclusive.

[4] Hampton T. Cancer treatment's trade-off. *Journal of the American Medical Association* 2005;294:167-168.

Table 2. Top 8 Cancers in 15-39 Year-Olds in Order of National Deficit, with Emphasis on Lack of Progress

	5-Yr Survival AAPC*	Mean 5-Yr Survival*	% of All Cancer+	Impact Factor
Impact Weighting	50%	25%	25%	
Non-Kaposi's Soft Tissue Sarcoma	5.2%	21%	4%	10.0
Non-Hodgkin's Lymphoma	2.1%	60%	6%	4.7
Hepatic Cancer	0%	13%	1%	4.6
Germ Cell Tumors	2.1%	87%	10%	3.5
Colorectal Carcinoma	0.6%	58%	5%	3.1
Breast Cancer	0.4%	74%	15%	3.0
Hodgkin's Lymphoma	1.4%	88%	6%	2.5
Bone Sarcoma	0.1%	74%	11%	2.2

*1975-1998
+In age group

Source: SEER 1975-1998.

tier priority because of the now well-known difference in outcome among 15 to 21 year-olds with acute lymphoblastic leukemia when treated with adult and pediatric therapies.[5,6,7]

Therefore, the AYAO PRG recommends that the first tier of high priority cancers should be non-Kaposi's soft tissue sarcoma, non-Hodgkin's lymphoma, germ cell tumors, colorectal carcinomas, and breast cancer. The second tier includes Hodgkin's lymphoma, bone sarcomas, melanoma, brain tumors, and leukemia.

Implementation Barriers

- Lack of awareness: The cancers with the greatest potential to address the AYA cancer survival deficit are not generally known.
- Inadequate and variable clinical trial availability: Too few NCI Cancer Therapy Evaluation Program (CTEP)-sponsored clinical trials are available to AYA cancer patients, ranging from 0 to 6 for each of the individual cancers targeted.
- Limited focus within the clinical trials enterprise: The high-impact AYA cancers and the AYA clinical trials deficit are underrepresented in the high-profile 2006 NCI Clinical Trials Working Group (CTWG) report.[8] The pharmaceutical industry has little incentive to focus on this group of malignancies.

Potential Partnerships and Resources

- NCI and pharmaceutical industry support will be essential to provide a portfolio of clinical trials to address these cancers.
- Intergroup mechanisms, e.g., cooperative groups, cancer centers, and Community Clinical Oncology Programs (CCOPs), as these cancers will need CTEP guidance and incentives. CCOPs can assume responsibility for accruing patients to these trials.
- Community networks such as U.S. Oncology, Kaiser Permanente, and Tennessee Oncology should focus on accruing AYA patients with these cancers to clinical trials.
- Military medical facilities that treat AYAs with the high priority cancers should be encouraged to participate in intergroup trials.
- The U.S. Food and Drug Administration (FDA) can encourage new agent development for AYA patients with the selected cancers, including providing orphan drug status and other incentives to the pharmaceutical industry.

[5] Stock W, Sather H, Dodge RK, Bloomfield CD, Larson A, Nachman J. Outcome of adolescents and young adults with ALL: a comparison of Children's Cancer Group and Cancer and Leukemia Group B regimens. *Blood* 2000;96:467a (Abstract).

[6] Boissel N, Auclerc MF, Lheritier V, et al. Should adolescents with acute lymphoblastic leukemia be treated as old children or young adults? Comparison of the French FRALLE-93 and LALA-94 trials. *Journal of Clinical Oncology* 2003;21:774-780.

[7] Ramanujachar R, Richards S, Hann I, Goldstone A, Mitchell C, Vora A, Rowe J, Webb D. Adolescents with acute lymphoblastic leukaemia: outcome on UK national paediatric (ALL97) and adult (UKALLXII/E2993) trials. *Pediatric Blood Cancers* 2006, in press, online at: http://www3.interscience.wiley.com/cgi-bin/abstract/112264430.

[8] Accessed at: http://www.cancer.gov/dctd/report.pdf on April 26, 2006.

- The National Cancer Comprehensive Network can both set guidelines for the management of these cancers in AYA patients and conduct clinical trials in this age group.
- The Association of Community Cancer Centers can make clinical trials in these diseases in AYA patients a priority.
- Advocacy organizations and professional societies can inform constituents of the age group and its high priority cancers and identify programs/resources to address the challenge. Examples include ASCO, AACR, Lance Armstrong Foundation (LAF), American Cancer Society, American Society of Hematology, Leukemia & Lymphoma Society, Oncology Nursing Society, and the Association of Pediatric Oncology Nurses.
- The Cooperative Human Tissue Network and cancer center tissue repositories can target these cancers for tissue collection for AYA patients to facilitate translational research.

Concrete Actions in the Next Three Years

- NCI should designate selected clinical trials in these cancers in AYA patients as "high priority" and establish appropriate per-case reimbursement.
- Through its Pediatric Exclusivity mechanism, the Best Pharmaceuticals for Children Act,[9] and its Office of Orphan Products Development,[10] the FDA should encourage orphan disease status for high priority AYA cancers that meet the criteria.
- The Cancer Center Support Grant (CCSG) mechanism should be used to evaluate cancer center performance in AYA oncology and thereby promote clinical research in the targeted cancers in AYA patients.
- Encourage and mentor young investigators in AYA oncology to focus on the targeted cancers.

[9] http://www.fda.gov/cder/pediatric/index.htm.

[10] http://www.fda.gov/orphan.

Priority 3

Create a NCI Adolescent and Young Adult Oncology Initiative including a scientific/clinical liaison position, supported through public-private partnership, to facilitate the development and implementation of AYA clinical trials and to focus NCI efforts on AYA cancer-related health care delivery and outcomes research.

Rationale

NCI-supported cancer clinical trial Cooperative Groups and Cancer Centers currently lack incentives to encourage the necessary collaboration among institutions and investigators to enroll AYA patients on clinical trials or to generate AYA relevant clinical trials and related research. NCI lacks personnel to champion AYA clinical trial implementation and to oversee other AYA cancer-related research efforts. Developing an Adolescent and Young Adult Oncology Initiative would demonstrate NCI's commitment to the AYA cancer research effort and provide leverage for advancing AYA cancer initiatives. The United Kingdom National Cancer Research Institute's Teenage and Young Adults Clinical Studies Development Group,[11] a public-private partnership, drives clinical trial activity for 15 to 25 year-old cancer patients and has successfully increased accrual to clinical trials among this group. The Adolescent and Young Adult Oncology Initiative and its scientific/clinical liaison should be housed in the Office of the NCI Director to increase the position's profile and authority.

Implementation Barriers

- Insufficient personnel for clinical trial support mechanisms within NCI to accommodate the additional work necessary to appropriately address AYA clinical trial and research needs.
- Insufficient NCI funds to readily support personnel for an Adolescent and Young Adult Oncology Initiative.
- Relatively high cost of implementing clinical trials affecting small numbers of patients at the central and local level; lack of non-governmental resources to conduct these trials successfully.

[11] Accessed at: http://www.ncrn.org.uk/csg/groups.asp?groupID=23 on April 26, 2006.

Potential Partnerships and Resources

- NCI Office of the Director, NCI CTEP; National Institute on Aging; National Center for Child Health and Human Development; National Heart, Lung, and Blood Institute
- CCCG, cooperative groups, and CCOPs
- FDA
- Pharmaceutical companies
- Department of Defense
- LAF

Concrete Actions in the Next Three Years

- Devote resources from the NCI Center to Reduce Cancer Health Disparities to fund an Adolescent and Young Adult Oncology Initiative.
- Facilitate the access of AYA patients to all disease-appropriate adult or pediatric cooperative group trials by actively promoting intergroup collaboration and increasing awareness of available studies among medical and surgical oncologists.
- Increase the number of clinical trials (cooperative group and cancer center) that target malignancies diagnosed in AYA patients and that are designed to answer specific biologic, treatment-related, quality of life, and late effect questions relevant to the AYA age group.
- Provide incentives for oncologists to enroll AYA patients in trials by increasing reimbursement rates for enrolling an AYA patient in the more complex Phase III trials.
- Increase the overall number of clinical trials relevant for AYA patients.
- Consider establishing AYA Centers of Excellence.

Conclusion

Low accrual into clinical trials is a critical factor affecting the poor rate of improvement in AYA survival. Because referring physicians and oncologists play a key role in directing patients into clinical trials, it is important that they be fully informed of the availability and potential benefits of trials for which AYA patients are eligible. A key finding of the Breakout Group is that even when AYA patients are aware of and willing to participate in clinical trials, relatively few trials are open to them because of age restrictions or the absence of trials for the cancer types that are diagnosed in this age group. A public-private partnership, managed within NCI, can ensure that the AYA patient population has equal access to clinical trials and the progress in outcome that results from them.

The cancers that have the highest likelihood of national impact on AYA outcome are non-Kaposi's soft tissue sarcoma, non-Hodgkin's lymphomas, germ cell tumors, colorectal carcinomas, and breast cancer. The second tier of priority includes Hodgkin's lymphoma, bone sarcomas, melanoma, brain tumors, and leukemia. Improving treatment for these targeted malignancies through clinical trials will have the greatest potential to reduce cancer-induced death and suffering in the AYA population.

SPECIAL POPULATIONS

Co-Chairs

- William Hicks
- Marjorie Kagawa Singer
- Smita Bhatia*

Participants

- Lucile Adams-Campbell
- Kimlin Ashing-Giwa
- Cheryl Boyce
- William Carroll
- Jacqueline Casillas
- Stella Davies
- Robert Hiatt
- Marion Lee
- Steven Lipkin
- Kevin Oeffinger
- Grace Powers-Monaco
- Lynn Ries
- Barbara Schwerin
- Susan Shinagawa

*Named co-chair but unable to attend Roundtable

Background

Significant disparities in cancer incidence, prevalence, and mortality exist among specific populations in the United States. These populations, often referred to as "special populations," can be defined by gender, age, ethnicity, race, culture, education, income, and social class, among other parameters.[1] Historically, special populations, particularly racial and ethnic minority groups, have been understudied and underserved. In recent years, the U.S. Department of Health and Human Services (HHS) has launched several initiatives to address and eliminate health disparities among population subsets, such as Healthy People 2010 and the Cancer Health Disparities Progress Review Group. Because our nation is still faced with and committed to eliminating the unequal burden of cancer among different racial and ethnic minority groups, the Special Populations Breakout Group focused primarily on cancer disparities that exist among racial and ethnic groups within the AYA population, while recognizing that our strategies need to be explored across all of the special populations.

The statistics are daunting—among 15 to 39 year-olds, non-Hispanic whites have the highest risk of developing cancer, while Asians, American Indians, and Native Alaskans have lower risk. African Americans and American Indian/Alaska Natives, however, have worse outcomes compared with non-Hispanic whites and Asians. Data are extremely scarce, however, on outcome by race/ethnicity within the AYA population for individual cancer types.

Disparities may result from inequalities in access to health care, in receipt of quality health care, and/or from differences in co-morbidities. Other factors known to contribute to racial disparities in cancer mortality include differences in exposure (e.g., *Helicobacter pylori* for stomach cancer), access to high-quality regular screening (for breast, cervical, and colorectal cancers), and timely treatment. The extent to which these factors individually or collectively contribute to overall differential survival is unclear. However, limited findings suggest that blacks who receive cancer treatment and medical care equivalent to whites experience similar outcomes.[2]

In 1993, Congress responded to concerns about unequal access to clinical trials and enacted the National Institutes of Health (NIH) Revitalization Act, which encouraged representation of women and minority patients in NIH-sponsored research.[3] HHS has responded to this call to enhance the heterogeneity of trial populations through multiple mechanisms, including creating the National Cancer Institute (NCI) Minority Community Clinical Oncology Programs, developing focused initiatives in partnership with the Centers for Disease Control and Prevention (CDC) and academic and medical centers, and emphasizing trials that focus specifically on the elderly.[4]

Investigations of race- and sex-based disparities in cancer treatment trial participation have yielded conflicting results. A study of black, Hispanic, and white participation in NCI cancer treatment trials between 1991 and 1994 concluded that these groups

[1] Trans-HHS Cancer Health Disparities Progress Review Group. Making Cancer Health Disparities History, a Report of the Trans-HHS Cancer Health Disparities Progress Review Group, Department of Health and Human Services, March 2004.

[2] Bach PB, Schrag D, Brawley OW, et al. Survival of blacks and whites after a cancer diagnosis. *Journal of the American Medical Association* 2002;287:2106-2112.

[3] NIH Revitalization Act of 1993, P.L. 103-43.

[4] Stallings FL, Ford ME, Simpson NK, et al. Black participation in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. *Controlled Clinical Trials* 2000;21:379s-389s.

were represented in trial populations in proportions parallel to the incident burden of disease in these groups and suggested that there is equal access to NCI trials.[5] This report was confirmed by a subsequent analysis of enrollment by the Southwest Oncology Group that compared the proportion of blacks and Hispanics enrolled in trials for 15 cancer types with their share of the U.S. cancer population between 1993 and 1996.[6] The authors found that representation of minorities varied substantially by type of cancer. Of the patients with leukemia, head and neck cancer, or prostate cancer, black patients were more likely than white patients to enroll; however, of the lymphoma or ovarian cancer patients, blacks were less likely than whites to enroll. Murthy, et al. characterized the representation of racial and ethnic minorities in cancer trials sponsored by NCI, using a cross-sectional population-based analysis of all participants in therapeutic non-surgical NCI Cooperative Group clinical trials in breast, colorectal, lung, and prostate cancer from 2000 through 2002.[7] In a separate analysis, the ethnic distribution of patients enrolled in 2000 through 2002 was compared with those enrolled in 1996 through 1998, using logistic regression models to estimate the relative risk ratio of enrollment for racial and ethnic minorities to that of white patients during these time periods. The authors concluded that: (1) enrollment in cancer trials is low for all patient groups, (2) racial and ethnic minorities were less likely to enroll in cooperative group cancer trials than were whites, and (3) the proportion of black trial participants has declined in recent years. Again, data specific to the AYA population by race/ethnicity are not available and need to be collected.

The Special Populations Breakout Group examined available data on three of the cancers that significantly affect the AYA population: acute lymphoblastic leukemia (ALL), breast cancer, and rhabdomyosarcoma. The striking variability in outcomes in the AYA population, and more specifically in minorities and other disadvantaged groups within this population, is summarized in the subsequent discussion.

ALL

ALL is the most common childhood malignancy, and children with ALL treated with contemporary therapy have a 5-year survival rate of 80 percent.[8] Several studies have shown highly significant differences in survival among ethnic and racial groups.[9] Remission rates were comparable among the four ethnic and racial groups studied (97 to 99 percent), but relapse rates were significantly different, resulting in the observed differences in event-free survival (EFS). African American children had the poorest outcome and Asian Americans the best outcome. The outcome for Hispanics was intermediate between that of Caucasians and African Americans. Multivariate analysis revealed ethnic background to be independently associated with decreased EFS, even after controlling for known adverse risk factors including age at diagnosis.

Differences in disease biology and clinical presenting features in childhood ALL between whites and African Americans have been examined. African American children present with features indicative of a larger tumor burden including elevated white cell count, adenopathy, and organomegaly; have a higher frequency of T-cell disease (associated with poorer outcome); and display a paucity of hyperdiploid disease (associated with more favorable outcome). However, multivariate analysis demonstrated that neither clinical features nor biologic prognostic factors could explain the poor outcome among African Americans. The literature contains no data examining differences in disease biology among other ethnic and racial groups, let alone in the AYA population.

Breast Cancer

Age-specific breast cancer rates for black women under age 35 are twice that of white women of similar age, and mortality rates are three times higher than among whites. A recent study using SEER data

[5] Tejeda HA, Green SB, Trimble EL, et al. Representation of African-Americans, Hispanics, and whites in National Cancer Institute cancer treatment trials. *Journal of the National Cancer Institute* 1996;88(12):812-816.

[6] Hutchins L, Unger J, et al. Underrepresentation of patients 65 years of age or older in cancer treatment trials. *New England Journal of Medicine* 1999;341:2061-2067.

[7] Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials—race-, sex-, and age-based disparities. *Journal of the American Medical Association* 2004;291:2720-2726.

[8] See note 3.

[9] Clegg LX, Li FP, Hankey BF, et al. Cancer survival among US whites and minorities: a SEER (Surveillance, Epidemiology, and End Results) program population-based study. *Archives of Internal Medicine* 2002;162:1985-1993.

found racial/ethnic variation in clinical presentation, treatment, and survival. Both African American and Hispanic women presented with higher disease stage and a higher prevalence of adverse prognostic indicators compared with white women.[10] African American and Hispanic women were less likely than non-Hispanic white women to receive cancer-directed surgery of any kind and to receive radiation following breast conserving surgery. Racial/ethnic differences in clinical presentation and treatment were associated with poorer overall survival. Native American women included in this study (from the Southwest, Detroit, and Seattle) had the lowest incidence of breast cancer in this age group. In terms of screening, data from the 2000 National Health Interview Survey were analyzed in 2004 to determine the degree to which race/ethnicity remains a predictor of the receipt of mammography screening after adjusting for personal and health characteristics, socioeconomic status, and access to and utilization of care variables.[11] This study found that blacks and Hispanics were significantly less likely to report receipt of nearly all preventive services examined. Among whites, 67 percent reported mammographic screening, as did 60 percent of English-speaking Hispanics. However, only 52 percent of Spanish-speaking Hispanics reported mammographic screening. These findings suggest that some of the differences in socioeconomic status (SES) are indicators of racial/ethnic disparities seen in breast screening, but few studies have been conducted on the racialized aspects of access and care and the interactive effect of race and SES.

Rhabdomyosarcoma

A retrospective analysis of children with rhabdomyosarcoma who were treated on International Rhabdomyosarcoma Group protocols between 1994 and 1997 revealed that African Americans, other ethnic minority groups, and whites experienced similar 5-year EFS despite an exponential increase in non-Kaposi's sarcomas. In addition, African Americans aged 5 to 45 years had the highest incidence of non-Kaposi's sarcoma and Kaposi's sarcoma of any group. Non-white children more often had invasive, larger, stage 2 or 3 tumors, or tumors with positive regional nodes.[12]

Eliminating cancer health disparities is a formidable task that will require multifaceted, multidisciplinary approaches and an understanding of biologic and non-biologic factors that influence clinical outcomes and quality of life. Based upon the current literature, disease biology; pharmacogenetic differences; social, cultural, and economic factors; and participation in clinical trials will likely be key factors in incidence and survival disparities among racial and ethnic groups, particularly with respect to the AYA population. The following three recommendations were developed to eliminate health disparities in cancer care in adolescent and young adult populations across the cancer care continuum (prevention, screening, diagnosis, treatment, survivorship, and end of life). In some instances, the recommendations will extend to subgroups other than ethnic/racial minorities within the AYA population, such as legal immigrants.

Priority 1

Identify specific biologic mechanisms that contribute to variations in cancer incidence and outcomes in racial/ethnic groups within the AYA population.

Rationale

Differences in incidence and outcomes between different racial and ethnic groups have been observed (see Background section).

Implementation Barriers

- Inaccuracy of race/ethnicity designation by both patients and providers.
- Low accrual of clinical trial participants (aversion to clinical trials both in minority and AYA populations).
- Population heterogeneity (e.g., age, gender, SES, race/ethnicity, high variation within the OMB Directive 15 categories for race/ethnicity).

[10] Shavers VL, Harian LC, Stevens JL. Racial/ethnic variation in clinical presentation, treatment, and survival among breast cancer patients under age 35. *Cancer* 2003;97:134-137.

[11] Lees KA, Wortely PM, Coughlin SS. Comparison of racial/ethnic disparities in adult immunizations and cancer screening. *American Journal of Preventive Medicine* 2005;29:404-411.

[12] Baker KS, Anderson JA, Lobe TE, et al. Children from ethnic minorities have benefited equally as other children from contemporary therapy for rhabdomyosarcoma: a report from the Intergroup Rhabdomyosarcoma Study Group. *Journal of Clinical Oncology* 2002;20(22):4428-4433.

Potential Partnerships and Resources

- Ethnic medical associations—e.g., National Medical Association (NMA)
- Community and cancer advocacy groups, including children's cancer advocates
- Urban/regional hospitals
- NIH/NCI/CDC
- Community nonmedical professional organizations
- Churches/minority-based organizations
- State cancer plans
- Historically Black Colleges and Universities (HBCU)/minority-serving institutions (MI), tribal colleges, Hispanic educational institutions, Asian American and Pacific Islander Health Forum
- State offices of minority health
- NCI-designated Comprehensive Cancer Centers (CCCs)
- NCI Community Network Programs (CNPs)
- AYA survivors

Concrete Actions in the Next Three Years

- Encourage funding organizations to develop and release specific Requests for Applications (RFAs) and Program Announcements that focus on underlying biologic mechanisms of ethnic differences in the AYA cancer population.
- Promote the use of existing biorepositories (e.g., NCI-designated CCC and Veterans Administration repositories) by the research community to explore racial/ethnic differences.

Priority 2

Improve access and quality of care across the cancer care continuum (i.e., standard of care, prevention, screening, diagnosis, treatment, survivorship, and end of life) for the AYA population.

Rationale

A more comprehensive, integrated approach to cancer care is needed. Many minority groups do not have the same access and quality of care as whites, thereby affecting their cancer outcomes adversely. The AYA population must have access to comprehensive, integrated state-of-the-art health care, including insurance coverage.

Implementation Barriers

- Lack of insurance.
- Dearth of education/awareness among patients and health care professionals about the cultural needs of diverse racial/ethnic groups.
- Lack of cultural competency.
- Paucity of minority providers that can provide and model appropriate and acceptable care for patients from diverse cultural groups.

Potential Partnerships and Resources

- Ethnic medical associations (e.g., NMA)
- Community and cancer advocacy groups
- Urban/regional hospitals
- NIH/NCI/CDC
- Community nonmedical professional organizations
- Churches/minority-based organizations
- State cancer plans
- HBCU/MI, tribal colleges, Hispanic educational institutions, Asian American and Pacific Islander Health Forum
- State offices of minority health
- CCCs
- CNPs
- AYA survivors

Concrete Actions in the Next Three Years

- Encourage meaningful partnerships between cancer centers and community physicians/hospitals/other community providers to evaluate the standard of care for AYAs from diverse race/ethnic/cultural/socioeconomic groups.
- Implement patient navigator programs for racial/ethnic/cultural/socioeconomic subgroups within the AYA population (see also other Breakout Group recommendations that focus on navigators/coaches).

- Provide community incentives for recruiting patients to clinical and cancer control trials (i.e., funded resources within the community to focus on the AYA population, including media promotion). Examples may include establishing centers of learning and developing and implementing school curricula (beginning in elementary school and continuing through college) to improve understanding among AYAs of cancer risk and appropriate cancer screening and care.
- Require cancer centers to adhere to established and emerging culturally and linguistically appropriate standards and skills and integrate them into education and practice.
- Develop programs for AYA survivors to serve as health care informants, providers, and researchers (e.g., National Breast Cancer Coalition's Project LEAD).

Priority 3

Integrate existing community assets (religious, social, professional, and fraternal organizations) to decrease disparities in AYA populations.

Rationale

The most straightforward and practical approach to gaining the necessary knowledge and confidence of the community is by joining forces with existing community assets and organizations. The positive impact of community support and collaborative efforts has been demonstrated (e.g., the NCI-funded, ethnic-specific Community Partners Network). This recommendation is intended to engage and expand community participation and develop sustainable infrastructure within communities. Similar recommendations were made by the Trans-HHS Cancer Health Disparities Progress Review Group and can be cross-referenced in its report.[13]

Implementation Barriers

- Lack of community education.
- Awareness deficits.
- Acceptance of the status quo; lack of age-appropriate innovative outreach efforts that are culturally relevant and acceptable.
- Nascent stage of scientific inquiry into the actual effects of culture variation and the racialization of our society and its impact on practice.

Potential Partnerships and Resources

- Ethnic medical associations (e.g., NMA)
- Community and cancer advocacy groups
- Urban/regional hospitals
- NIH/NCI/CDC
- Community nonmedical professional organizations
- Churches/minority-based organizations
- State cancer plans
- HBCU/MI, tribal colleges, Hispanic educational institutions, Asian American and Pacific Islander Health Forum
- State offices of minority health
- CCCs
- CNPs
- AYA survivors

Concrete Actions in the Next Three Years

- Encourage funding organizations to prepare and release RFAs that develop and sustain community-based participatory education and research (e.g., Continuing Medical Education accreditation for professionals involved in AYAO care) in which investigators will work with the community across the cancer care continuum.
- Promote cooperation and networks between existing AYA advocacy groups and the community.
- Advocate for more sophisticated social and behavioral scientific paradigms that are inclusive of cultural differences beyond the crude distal measures of race/ethnicity currently used.

[13] See note 1.

Conclusion

The AYA oncology population is an understudied group. Within this group, special populations as defined by gender, age, ethnicity, race, education, income, social class, and other parameters are even less well studied. By implementing these priorities, a substantial improvement in racial and ethnic disparities within the AYA population will be achieved. A multifaceted approach is necessary, including the participation of communities of affected individuals. Individuals and communities must be empowered to undertake and solve the problem together. Included in this approach is a better understanding of the biologic and nonbiologic factors that contribute to cancer disparities in the AYA population.

PSYCHOSOCIAL/BEHAVIORAL FACTORS

Co-Chairs

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Participants

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- Kimlin Ashing-Giwa
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- Ernie Katz
- David Osoba
- Randi Rosenberg
- Lydia Shrier
- Carol Sienche

Background

Adolescence and young adulthood are times of increased vulnerability to stress, presenting adolescent and young adult (AYA) cancer patients and survivors with major developmental challenges beyond those faced by other young people.[1] Thus, they have unique health and psychosocial needs when compared with childhood cancer patients or older adults diagnosed and treated for cancer during later stages of life. Yet empirical literature is limited regarding specific psychosocial outcomes, causes, and correlates for patients and survivors diagnosed as older adolescents and young adults.

Contemporary research trends in pediatric psychosocial oncology are relevant to an AYA population. These trends encompass: (1) a stress-coping model/framework, recently amended with a focus on post-traumatic effects; (2) a family systems approach emphasizing interactive responses and interpersonal influences within families; and (3) a developmental approach in which the issues experienced by children of various ages are treated in the context of their normative physical and psychosocial maturation. Assessing psychosocial and behavioral issues across six dimensions will help identify patient and survivor needs and inform the development of interventions that address both psychopathologic disease prevention and health promotion.

Intellectual Issues

Often, adolescents and young adults with cancer lack critical information regarding their disease and its treatment, including information about types and dosages of treatment and in some cases, even the type of cancer they have, along with knowledge about potential long-term late physical effects.[2,3] As a result, many patients/survivors seek educational and support resources that are relevant to their age group. Communicating information about diagnosis, prognosis, treatment, and long-term effects to AYA cancer patients can be a sensitive issue and it is crucial that information is targeted toward each patient's age and cognitive abilities. Furthermore, these resources must be culturally relevant and disseminated with a high level of cultural competence (i.e., communicating with messages of hope and compassion relative to each unique culture).

Interpersonal Issues

Relating with family, peers, and health professionals is an important aspect of life for AYAs with cancer. As young people try to deal with or discuss cancer with their parents they sometimes discover that they have quite different coping strategies. For instance, parents may want to discuss issues with their child that the child does not wish to discuss, or vice versa. Family member support is a critical component of health, well-being, and adjustment to cancer, and studies suggest that most young adult survivors report improved family relationships. With regard to peer relations, it is not uncommon for adolescents and young adults with cancer to experience changes in friendships and/or a sense of isolation from friends due to lengthy periods away from home, school, or work during treatment. Some friendships may founder over time.

[1] Hobbie WL, Stuber M, Meeske K, Wissler K, Rourke MT, Ruccione K, et al. Symptoms of posttraumatic stress in young adult survivors of childhood cancer. *Journal of Clinical Oncology* 2000;18(24):4060-4066.

[2] Bashore L. Childhood and adolescent cancer survivors' knowledge of their disease and effects of treatment. *Journal of Pediatric Oncology Nursing* 2004;21(2):98-102.

[3] Kadan-Lottick NS, Robison LL, Gurney JG, Neglia JP, Yasui Y, Hayashi R, et al. Childhood cancer survivors' knowledge about their past diagnosis and treatment: Childhood Cancer Survivor Study. *Journal of the American Medical Association* 2002;287:1832-1839.

The impact of cancer treatment on sexuality, intimacy, and formation of mature, committed relationships is particularly salient to this population. Finally, while a trusting and therapeutic relationship between a doctor and a patient is an important component of care, health care professionals and young adults may find it difficult or intimidating to communicate with one another and poor communication of important clinically relevant information may result.

Emotional Issues

Though varying substantially in their theoretical frames, inquiry methods, and samples of informants, studies of AYAs suggest the following: (1) some patients and survivors have managed to grow in positive ways as a result of their cancer experience, (2) most patients and survivors are probably relatively average in psychosocial terms and on most psychosocial/quality of life measures, and (3) some patients experience ongoing psychological and/or social adjustment problems, including depression and other mood disorders, and anxiety, including post-traumatic stress symptoms. Risk factors for these and other associated psychosocial stressors identified in the research literature include but are not limited to temporal clustering of stressful medical and life events, poverty, prior experiences with poor coping resources, pre-existing emotional problems or family discord, extent of disease and treatment severity, degree of distress or residual disability, and lack of social support. Additionally, cancer requires individuals to renegotiate their identity.[4] Changes in body image, disruption of normal activities, and adverse reactions to the effects of cancer and its treatment may affect the sense of self in adolescents and young adults with cancer.[5]

Some AYA survivors actively seek to improve or adjust their physical, psychological, and social status and view themselves as involved in a process of accepting their cancer and getting back to normal. Yet even these young people may still worry about their physical health status and bodies, their self-esteem and identity, their immediate family's welfare, relating with the social world and being "different," re-integrating with the school system or work environment, possibilities for the future (including access to life and health insurance, jobs and career options, understanding genetic compromises stemming from treatment), and ensuring continued care from a skilled and attentive medical system. Opportunities for peer involvement often provide adolescents and young adults a chance to address these areas of concern.

Practical Issues

AYA patients often are subject to painful procedures and treatments. They also experience a lack of "fit" in a health care system that distinguishes pediatric from adult care. As a direct result of cancer diagnosis and treatment, they confront myriad disruptions in their lives, particularly with regard to school, work, and family life. Many families lack resources to pay for increased needs for transportation, child care, copayments for health care and drugs, and food or housing expenses. After treatment ends, AYAs face a complex system of health care delivery and financing, and they may have difficulty locating and accessing primary care providers. As maturing and developing young people, they remain challenged by peer and other pressures regarding tobacco, alcohol, or drug use, and these challenges may be more pronounced in underserved groups. All of these factors may influence AYAs' adherence to treatment protocols and their sense of independence or control over their lives.

Existential/Spiritual Issues

Young people with cancer define uncertainty both as living with the unknown and as not knowing what to expect. Survivors in their teens and young adult years further suggest that while uncertainty can be a source of distress, it also can be a catalyst for personal growth, a deepened appreciation for life, greater awareness of life purpose, development of confidence and resilience, and optimism. A significant proportion of people with cancer acknowledge the support they receive through God, faith, religious practices, and involvement in their place of worship, although some young people indicate that having cancer challenges their current religious beliefs and values.

[4] Mathieson CM, Stam HJ. Renegotiating identity: cancer narratives. *Sociology of Health and Illness* 1995;17(3):283-306.

[5] Zebrack BJ. Cancer survivor identity and quality of life. *Cancer Practice* 2000;8(5):238-242.

Cultural Relevance

Understanding the needs, risks, and lifestyles of adolescent and young adult cancer patients and survivors necessitates an awareness of the strong, often covert influences of culture, race/ethnicity, and socioeconomic status in shaping reactions and responses to health problems. Literature suggests that culturally different views of the meanings of health, illness, and treatment exert strong influence on both patients' and care providers' behaviors. At the same time, unintentional and often institutionalized forms of discrimination in the provision of care (e.g., unconscious bias; poverty; and racial inequalities in education, financial resources, transportation facilities, insurance) often determine the level of care available to whole groups of patients and families. As a result, neither equitable nor adequate access to quality cancer care is ensured for everyone in today's health care environment.

Methodologic Considerations

The majority of research combines adolescents and young adults into a single or more heterogeneous sample. This is true in many studies of patients on treatment as well as in studies of off-treatment survivors. Literature searches utilizing the keywords "cancer" and "young adults" or "cancer" and "adolescents" most often turn up research studies that include AYA survivors of childhood cancer, and young adults as part of samples consisting of a wide range of ages. For example, less than 1 percent of cancer-related citations in the National Library of Medicine's PubMed database between 1993 and 2003 were specific to survivorship issues among the adolescent and young adult population.[6] Since data on adolescents and young adults often are not reported separately, little is known about the specific needs, concerns, and psychosocial development of AYA cancer patients and survivors.[7]

Priority 1

Develop and apply appropriate methodologic approaches to better understand AYA health care and psychosocial needs.

Rationale

AYAs share a set of universal needs with cancer patients of all ages, including the need for evidence-based clinical care and family/social support. In addition, AYAs have unique health care and psychosocial needs that are influenced by developmental, sociocultural, and cancer-specific contexts. Existing methods for assessing psychosocial outcomes in either pediatric or adult populations may not be sufficient for capturing the full AYA experience. Appropriate approaches for assessing AYA health care and psychosocial needs must be founded on methods of investigation that address the impacts of cancer as they are influenced by normative developmental challenges (e.g., peer involvement, establishing a world view, identity development) and sociocultural factors (e.g., values and beliefs about cancer/illness, socioeconomic status, education). Current research limits our ability to draw specific conclusions about the unique needs of AYAs.

Implementation Barriers

- AYAs currently are not recognized as a distinct or diverse population.
- Researchers typically do not have access to a representative population of AYAs, due in part to small numbers, lack of recognition among gatekeepers (e.g., providers) that AYAs are a unique and understudied cohort, and limited research resources in community centers where most AYAs are treated.
- Few researchers possess training in both developmental psychology and research methodologies that could advance our understanding of the unique needs of this population. In addition, few funding mechanisms exist to support this area of behavioral research.

[6] Bleyer A, O'Leary M, Barr RD, Ries LAG (eds). Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, including SEER Incidence and Survival:1975-2000. Bethesda, MD, National Cancer Institute, 2006.

[7] Reuben SH. Living Beyond Cancer: Finding a New Balance, President's Cancer Panel, 2003-2004 Annual Report. National Institutes of Health, National Cancer Institute, May 2004.

Potential Partnerships and Resources

- Collaborative research between academia and community-based treatment facilities
- Collaboration among investigators utilizing multiple methods of data collection and analysis (i.e., quantitative and qualitative methods)
- Collaboration with other community-based organizations or bodies that may provide access to adolescents and young adults (e.g., professional societies, social and/or service organizations, educational/vocational training institutions, faith-based institutions)
- Collaboration with cancer-specific advocacy groups (e.g., Planet Cancer, Ulman Cancer Fund for Young Adults) and professional organizations (e.g., Society of Adolescent Medicine, National Comprehensive Cancer Network) serving AYAs
- Partnership between the National Cancer Institute (NCI) and foundations to create specific funding mechanisms for psychosocial research on AYAs

Concrete Actions in the Next Three Years

- Identify gaps in the literature and evidence-based psychosocial intervention models (e.g., from other disease groups) that may apply to AYAs.
- Identify and secure funding from foundations whose missions may be in concert with psychosocial needs of AYAs.
- Convene psychosocial experts and AYA stakeholders to develop needs assessment tools and other methods.
- Sponsor a consensus conference on assessment of AYA psychosocial needs.

Priority 2

Improve training/education to enhance health care professionals' abilities to deliver developmentally appropriate care and to enhance AYAs' and family members' abilities to be proactive in their health care.

Rationale

Few health care providers possess the requisite knowledge, skill, or comfort levels to address the specific needs and challenges of AYAs. In our fragmented health care system, AYA patients and their families need targeted, tailored, and culturally relevant resources to participate effectively in their health care decision-making.

Implementation Barriers

- Current medical education models do not train health care providers to work with AYAs.
- Clinical education and training are limited in their developmental and cultural relevance and biopsychosocial approach to care.
- AYA families and patients do not routinely have access to developmentally appropriate resources or support agencies.

Potential Partnerships and Resources

- Collaborations among public health, psychology, social work, medicine, and health communication experts
- Health and medical education systems
- Involvement of advocacy groups and stakeholders in developing education and training programs

Concrete Actions in the Next Three Years

- Assess the needs of health care providers (e.g., oncology, primary care, mental health) to enhance AYA psychosocial outcomes.
- Develop Special Interest Groups within the American Society of Clinical Oncology, the American Association for Cancer Research, and other health care professional societies to promote education across the continuum of AYA health care and psychosocial needs.
- Develop multidisciplinary care models and incorporate psychosocial training of AYAs into specialty certification processes.
- Identify factors that promote AYA engagement in their health care and enhance psychosocial outcomes.

Priority 3

Identify, implement, and evaluate innovative peer and family support intervention models throughout the continuum of care (i.e., from diagnosis through treatment, off-treatment survival, and/or end of life).

Rationale

Few evidenced-based peer and family support psychosocial interventions are available for AYAs. Existing peer support models (e.g., AYA support groups, retreats, uses of technology) are being initiated through community-based agencies and some medical centers. These programs have potential for enhancing outcomes (e.g., reducing social isolation, improving psychosocial functioning, promoting successful adjustment) but have yet to be tested empirically. Family-based intervention models from pediatrics (e.g., parent support groups, Impact of Traumatic Stressors Interview Schedule) also may have utility for AYAs.

Implementation Barriers

- Understanding of the most effective types and methods of peer and family support is limited, including types of interventions that are most appropriate for specific subgroups of the AYA population (as defined by age/developmental stage, ethnicity/race, and socioeconomic status).
- Conceptual, nonconventional, and innovative models that may be more effective, appropriate, and culturally relevant for AYAs (e.g., use of media technology for intervention delivery) must be developed and tested; however, this has not been completed to date.
- Limited resources exist to support longitudinal studies to assess the impact and durability of interventions on psychosocial functioning changes over time.

Potential Partnerships and Resources

- Corporate foundations and philanthropic organizations (e.g., Microsoft, Dell, pharmaceutical companies, community service organizations)
- NCI, Lance Armstrong Foundation, American Cancer Society, etc.
- AYA advocacy groups (e.g., Young Survival Coalition, Planet Cancer)

Concrete Actions in the Next Three Years

- Achieve consensus as to key psychosocial outcomes (e.g., reduce social isolation, enhance family communication, increase health promoting behaviors) associated with peer- and family-based intervention participation.
- Develop and evaluate a peer navigator model.
- Develop Requests for Applications/Program Announcements for longitudinal and/or multimethod theory-based approaches to test the efficacy of peer support and family-based psychosocial interventions.
- Evaluate or test existing peer or grassroots interventions.
- Develop a directory of psychosocial care resources.
- Sponsor a consensus conference for psychosocial intervention in AYAs with cancer.
- Develop a network (listserv) of AYA researchers.

Conclusion

AYAs are faced with multiple developmental and psychosocial challenges that can be exacerbated by the experience of cancer. These challenges span several domains, but little is known about the specific psychosocial needs of AYA patients and survivors across these multiple domains. Enhancing the life experiences of AYA cancer patients and survivors requires assessment studies of AYA-specific psychosocial needs, health professional education/training on AYA-specific psychosocial issues, and evidence-based intervention development.

HEALTH-RELATED QUALITY OF LIFE

Co-Chairs

- Ronald Barr
- Carolyn Gotay

Participants

- Daniel Armstrong
- Craig Earle
- David Feeny
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- Beth Virnig
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Background

The rationale for measuring health-related quality of life (HRQL) has been reviewed in detail by Feeny, et al.[1] Purposes for which such measurement can be used include those defined by Guyatt, et al.,[2,3] Lipscomb et al.,[4] and Osoba.[5] These fall into three categories:

- Discrimination – distinguishing the burden of morbidity among groups or individuals at a point in time
- Evaluation – assessing changes in morbidity over time, in longitudinal/prospective studies such as clinical trials
- Prediction – using an HRQL measure to predict the score on another measure or to predict clinical outcome (prognostication)

A plethora of instruments is available for use in adult respondents. Far fewer have been designed for use in children and an even smaller number have been assessed by Eiser and Morse[6] as sound. A limited number of measures have been developed more or less specifically for adolescents,[7] and a few of these have been employed in the assessment of HRQL in young people with cancer.[8,9] Measures of HRQL can be classified as health profiles, which may or may not provide a single summary score, and preference-based measures, which may measure preferences either directly (e.g., by the standard gamble technique) or by the use of multi-attribute health status classification systems and associated preference functions. Health profiles may be specific (applicable to a particular population), generic, or both (modular, e.g., the Peds QL[10]).

HRQL instruments have been designed for self-administration (proxy or self-assessment), including mailed questionnaires, administration by interviews (face-to-face or by telephone), or by computer. Some HRQL instruments have been adapted to multiple cultural/linguistic needs. The challenges posed by HRQL measurement in pre-school age children (e.g., the need for proxy ratings) are well recognized.[11] Such hurdles are less difficult to surmount in adolescents and young adults (AYAs).

Opportunities for research in this area pertinent to adolescent and young adult oncology (AYAO) include the following:

[1] Feeny D, Furlong W, Mulhern RK, Barr RD, Hudson M. A framework for assessing health-related quality of life among children with cancer. *International Journal of Cancer* 1999; Supplement,12:2-9.

[2] Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. *Annals of Internal Medicine* 1993;118:622-629.

[3] Guyatt GH, Jaeschke R, Feeny DH, Patrick DL. Measurements in clinical trials: choosing the right approach. In: Spilker B (ed). Quality of Life and Pharmacoeconomics in Clinical Trials, 2nd edition. Philadelphia, Lippincott-Raven, 1996, pp. 41-48.

[4] Lipscomb J, Gotay CC, Snyder C. Outcomes Assessment in Cancer. Cambridge: Cambridge University Press, 2005.

[5] Osoba DE. Measuring the effects of cancer on health-related quality of life. *PharmacoEconomics* 1995;7:308-319.

[6] Eiser C, Morse R. The measurement of quality of life in children: past and future perspectives. *Developmental and Behavioral Pediatrics* 2001;22:248-256.

[7] Grant J, Cranston A, Horsman J, et al. Health status and health-related quality of life in adolescent survivors of cancer in childhood. *Journal of Adolescent Health* 2006;38:504-510.

[8] Patrick D, Edwards T, Topolski T, et al. Youth quality of life: a new measure incorporating the voices of adolescents. *Quality of Life Newsletter* 2002;28:7-8.

[9] Varni JW, Burwinkle TM, Katz ET, et al. The Peds QL in pediatric cancer: reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales, Multidimensional Fatigue Scale, and Cancer Module. *Cancer* 2002;94:2090-2106.

[10] See note 9.

[11] Nathan PC, Furlong W, Barr RD. Challenges to the measurement of health-related quality of life in children receiving cancer therapy. *Pediatric Blood Cancer* 2004;43:215-223.

- Inclusion of HRQL measures in clinical trials—While this is increasingly common in the adult context and has been essentially mandated by some funding agencies (e.g., the National Cancer Institute of Canada[12]), lamentably few examples involve younger age groups.
- Impact of measurement on treatment decisions and compliance—As yet this opportunity has been addressed largely in theory,[13] but it is especially apposite to the age range encompassed by the AYAO PRG, in which issues of decision-making and adherence/compliance loom large.
- Linkage of HRQL data to a central registry of adolescents and young adults with cancer—So far this registry is a pipe dream, but such a linkage would provide additional grist to the argument for its establishment. A case for quality-adjusted survival has been made[14] and a fledgling example of linking HRQL data to a national registry has been described, in the context of "late effects," with the Canadian Childhood Cancer Surveillance and Control Program.[15]

Priority 1

Identify and/or develop instruments for assessing HRQL appropriate to the AYA population.

Rationale

A paucity of information exists on the HRQL domains that are relevant to the AYA age groups. Appropriate ways to measure these domains also are needed. Important concerns include measurements that: (1) span the survivorship continuum, (2) are developmentally appropriate, (3) include co-morbidity assessment and family well-being, and (4) are appropriate to the patients' literacy level.

Implementation Barriers

- Lack of validated measures that span the developmental trajectory.
- Limited attention to the AYA age groups in HRQL assessments to date.
- Vested interests in available instruments.
- Lack of a conceptual model of HRQL in AYAs.

Potential Partnerships and Resources

- National Cancer Institute (NCI) Cooperative Groups and Cancer Centers
- Professional organizations, e.g., Oncology Nursing Society (ONS), American Society of Clinical Oncology (ASCO), International Society for Quality of Life Research (ISOQOL)
- National Institutes of Health (NIH), NCI
- Military medical organizations that treat AYA cancer patients
- Advocacy organizations, e.g., Lance Armstrong Foundation (LAF)
- Others, e.g., American Cancer Society (ACS)

Concrete Actions in the Next Three Years

- Develop strategies for communication and collaboration among researchers, e.g., an AYA network.
- Explore collaborations with relevant projects, e.g., Patient Reported Outcomes Measurement Information System (PROMIS), Patient Reported Outcomes and Quality of Life Instruments Database (PROQOLID).
- Convene a consensus conference to assess the state of the science and identify future directions for HRQL instrument development relevant to the AYA population, with leadership provided by NCI, LAF, and other stakeholders.

[12] Ganz PA, Moinpour CM, Cella DF et al. Quality-of-life assessment in cancer clinical trials: a status report. *Journal of the National Cancer Institute (USA)* 1992;84:994-995.

[13] Gesundheit B, Greenberg ML, Kapelushnik Y, Koren G. Drug compliance by adolescent cancer patients. In: Bleyer WA, Barr RD (eds). Cancer in Adolescents and Young Adults. Heidelberg, Springer-Verlag (in press).

[14] Barr RD, Sala A. Quality-adjusted survival: a rigorous assessment of cure after cancer during childhood and adolescence. *Pediatric Blood Cancer* 2005;44:201-204.

[15] Pogany L, Barr RD, Shaw A, Speechley KN, Barrera M, Maunsell E. Health status in survivors of cancer in childhood and adolescence. *Quality of Life Research* 2006;15:143-157.

Priority 2

Apply HRQL assessments in clinical care.

Rationale

HRQL assessments have the potential to enhance participation of AYA patients in their own clinical care, including communication, adherence, and decision-making. These assessments also may contribute to improved clinical management by health care providers.

Implementation Barriers

- Lack of solid evidence that HRQL assessments contribute to clinical care.
- A perceived added burden to consumers and providers.
- Perceptions that patients are unable to make autonomous decisions.
- Insufficient information about how to interpret HRQL assessments in clinical care.
- Limited marketing to clinicians by the HRQL community so that potential contributions of the assessments are unrealized.

Potential Partnerships and Resources

- Advocacy organizations
- ASCO
- Cancer centers and children's hospitals
- Department of Defense (DoD), given the age distribution of military personnel
- Health Maintenance Organization (HMO) research networks, e.g., Cancer Research Network
- HRQL professional organizations, e.g., ISOQOL

Concrete Actions in the Next Three Years

- Funding agencies should develop a Request for Applications to support this effort, which could include conducting focus groups with patients and providers.
- Form partnerships with organizations with relevant interests to pilot test promising models. Interventions utilizing new technologies, e.g., linkage with electronic medical records, touch screens, Personal Digital Assistants (PDAs), and devices such as iPods, are particularly ripe for development.

Priority 3

Use HRQL as a primary outcome in research applications.

Rationale

HRQL measures can be used to identify previously unknown, under-appreciated, and under-reported morbidity and prognostic factors. Examples include clinical trials, health services research focused on investigating models of care, prospective studies of late effects, and palliative and end of life care.

Implementation Barriers

- Low priority for funding.
- Need for additional infrastructure for HRQL questionnaire administration and analysis.
- Lack of clear evidence for clinically meaningful differences in HRQL scores.
- Limited training opportunities for physicians and other health care providers in HRQL measurement and application.

Potential Partnerships and Resources

- NCI, Surveillance, Epidemiology, and End Results Program; NCI QOL Intergroup
- ASCO, American Association for Cancer Research
- Cancer centers
- Pharmaceutical companies
- Cooperative groups
- Advocacy organizations
- Academic institutions (e.g., medical schools)
- DoD

Concrete Actions in the Next Three Years

- Include HRQL assessments in studies of survivorship care plans.
- Develop criteria for successful implementation of HRQL assessments in protocols applicable to AYA populations. It is recommended that this action be completed by NCI.

- Convene a consensus conference to assess the state of the science and future directions for work in this area.

Conclusion

HRQL for the AYA population needs to be defined and measured, and the results applied. This will require developing appropriate instruments and identifying uses for them in both clinical treatment and clinical trials. Numerous barriers must be overcome before this goal can be attained. Collaborative relationships involving government agencies, advocacy and professional organizations, academic institutions, cancer centers, cooperative groups, HMO research networks, pharmaceutical companies, and established partnerships (e.g., the NCI QOL Intergroup) will greatly facilitate the achievement of this goal. The strategies for communication and collaboration among researchers, development of appropriate assessment tools, and other priorities outlined in this report offer significant opportunities for increasing understanding of HRQL in the AYA population.

LONG-TERM EFFECTS

Co-Chairs

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Background

An understanding of the long-term health outcomes associated with adolescent and young adult (AYA) cancer and cancer therapy is essential for providing anticipatory risk-based care for survivors. Furthermore, an appreciation of the long-term morbidity and mortality associated with specific therapies is important when developing or refining new cancer treatment strategies. Though the body of knowledge is growing regarding long-term health outcomes in survivors of adolescent cancer and some young adult cancers (e.g., testicular cancer), many significant knowledge gaps impede the care of this high-risk population.

Terminology

The National Cancer Institute (NCI) defines long-term effects as those conditions that develop during therapy and persist after the completion of therapy.[1] Late effects refers to conditions that develop after the completion of therapy. Though some late effects may occur within months after therapy ends, many will not become evident for 10 to 20 years. Ascertaining whether a condition is a long-term or late effect can be difficult, so some researchers group all outcomes together and refer to them as late effects. It also is important, though sometimes difficult, to ascertain whether a late effect is related to previous cancer therapy or is simply due to the normal aging process and the genetic/lifestyle predispositions of the individual. Thus, it is important methodologically to determine the excess risks attributable to various cancer treatment exposures. For the purposes of this report, the term "late effects" is intended to include both long-term and late effects.

Mechanisms of Late Effects in AYA Cancer Survivors

When considering the nature and likelihood of late effects, a first step is to identify the mechanisms leading to such outcomes. Effects due to treatment can be caused either individually or in combination by surgery (e.g., small bowel obstruction, oophorectomy), radiation therapy (e.g., damage to bones, second cancers), chemotherapy, other adjuvant therapies (e.g., secondary leukemia, cardiac damage), and underlying genetic propensity. In addition, growing evidence suggests that the age of cancer onset, or the age at which an individual receives treatment, may differentially affect the likelihood of experiencing an adverse long-term outcome. This latter observation is particularly important because it raises questions about the applicability of knowledge gained from studies of one age group (e.g., the Childhood Cancer Survivor Study–CCSS) to people in other age groups (the AYA population). For example, the cognitive damage seen in children may not occur in adults treated with similar chemotherapies, perhaps due to differences in development-related sensitivity of the brain. Finally, some late effects may reflect the cancer experience rather than any particular treatment. Frequent reports of depression, post-traumatic stress disorder, and risk-taking behavior among survivors are examples of such manifestations.

[1] Aziz NM, Rowland JH. Trends and advances in cancer survivorship research: challenge and opportunity. *Seminars in Radiation Oncology* 2003;13(3):248-266.

Increased Risk of Late Mortality and Morbidity

Compared with age- and sex-specific mortality rates in the general U.S. population, long-term survivors of adolescent cancer face an increased risk of death beyond 5 years from their cancer diagnosis.[2,3] Though less well studied, similar effects have been reported in young adult cancer survivors. The excess mortality is due to late recurrences of the original cancer, second cancers, and heart and lung disease as a consequence of the therapy of the original cancer.[4]

The long-term morbidity associated with AYA cancer therapy likely varies by cancer exposure and age at treatment. Serious effects include second cancers, infertility, gonadal dysfunction and premature gonadal failure, cardiovascular disease, and psychological problems. Depending upon treatment exposure, all organ systems can be affected.

Much of what is known about late mortality and morbidity has been learned from studies focusing on pediatric cancer survivors, including adolescent cancer survivors treated in pediatric settings. The CCSS, an NCI-supported 26-institution cohort study that is tracking the health outcomes of over 14,000 long-term pediatric cancer survivors diagnosed 1970-1986, has been a major contributor to understanding the long-term health outcomes of survivors.[5] We expect that some of this information is applicable to survivors of young adult cancers with similar treatment exposures, such as survivors of Hodgkin's disease, soft tissue sarcoma, and bone tumors. However, further study is needed to determine the differential effect of various treatment exposures based on age at therapy. Moreover, large gaps exist in the understanding of morbidity in survivors of young adult cancers.

[2] Mertens AC, Yasui Y, Neglia JP, et al. Late mortality experience in five-year survivors of childhood and adolescent cancer: the Childhood Cancer Survivor Study. *Journal of Clinical Oncology* 2001;19(13):3163-3172.

[3] Moller TR, Garwicz S, Barlow L, et al. Decreasing late mortality among five-year survivors of cancer in childhood and adolescence: a population-based study in the Nordic countries. *Journal of Clinical Oncology* 2001;19(13):3173-3181.

[4] Fossa SD, Aass N, Harvei S, Tretli S. Increased mortality rates in young and middle-aged patients with malignant germ cell tumours. *British Journal of Cancer* 2004;90(3):607-612.

[5] Robison LL, Mertens AC, Boice JD, et al. Study design and cohort characteristics of the Childhood Cancer Survivor Study: a multi-institutional collaborative project. *Medical and Pediatric Oncology* 2002;38(4):229-239.

Health Care of AYA Cancer Survivors

Recognizing the long-term risks of cancer survivors, NCI[6] and the Institute of Medicine (IOM)[7,8] recommend lifelong follow-up care for all cancer survivors. Adolescent cancer survivors treated in the pediatric oncology setting usually are followed in pediatric-based long-term follow-up (LTFU) programs. These programs provide risk-based health care that is anticipatory and proactive and that includes a systematic plan of prevention and surveillance based on risks associated with the cancer therapy, genetic predispositions, lifestyle behaviors, and co-morbid health conditions.[9] Recommendations for surveillance are based on the Children's Oncology Group (COG) evidence-based guidelines.[10] The greatest challenge in these programs is transitioning the adolescent cancer survivor to adult-based providers in their young adult years.

In the last 5 years, several programs have been developed for survivors of young adult cancer. These are either cancer-specific (e.g., testicular cancer survivor program), treatment modality-specific (e.g., stem cell transplant survivor program), or more comprehensive, including all age groups of cancer survivors. The American Society of Clinical Oncology (ASCO) recently has undertaken an extensive effort to develop evidence-based guidelines for the long-term care of adult survivors, including AYA survivors. However, most AYA survivors are not followed in a survivor-type program, but by primary care physicians who often are unfamiliar with the risks associated with AYA cancer therapy.[11]

[6] Rowland JH, Aziz N, Tesauro G, et al. The changing face of cancer survivorship. *Seminars in Oncology Nursing* 2001;17:236-240.

[7] Hewitt M, Weiner SL, Simone JV (eds). Childhood Cancer Survivorship: Improving Care and Quality of Life. Washington, DC, National Academies Press, 2003.

[8] Hewitt M, Greenfield S, Stovall E. (eds). From Cancer Patient to Cancer Survivor: Lost in Transition. Washington, DC, National Academies Press, 2006.

[9] Aziz NM, Oeffinger KC, Brooks S, Turoff AJ. Comprehensive long-term follow-up programs (LTFU) for pediatric cancer survivors. *Cancer,* in press, 2006.

[10] Landier W, Bhatia S, Eshelman DA, et al. Development of risk-based guidelines for childhood cancer survivors: the Children's Oncology Group Long-Term Follow-Up Guidelines. *Journal of Clinical Oncology* 2004;22:4979-4990; at: www.survivorshipguidelines.org

[11] Oeffinger KC, McCabe MS. Models for delivering survivorship care. *Journal of Clinical Oncology*, in press, 2006.

Challenges in AYA Survivorship Research

Four broad types of studies are needed to fill the gaps in our understanding of AYA survivors:

- Observational epidemiologic studies to identify risk factors for long-term health outcomes and potential modifying factors
- Biologic studies to assess the influence of the gene environment on late effects
- Intervention studies aimed at preventing late effects, reducing morbidity and mortality, and enhancing quality of life
- Studies to compare different methods of caring for AYA survivors

Perhaps the most significant challenge in AYA survivorship research is identifying a population of survivors that is of adequate size to conduct hypothesis-driven studies while minimizing selection and participation biases. Several potential populations for AYA survivorship studies exist, each with different strengths and limitations. The Surveillance, Epidemiology, and End Results (SEER) program registries and state-based cancer registries are well suited for second cancer and late mortality studies but are limited by a lack of treatment exposure data including chemotherapy agent and dose. In addition, the SEER data cannot be used to study long-term morbidity associated with cancer care. Linking SEER with Medicaid databases may increase their usability for some AYA studies. The NCI Cooperative Groups (e.g., COG, Southwest Oncology Group [SWOG], Cancer and Leukemia Group B [CALGB]) provide large and diverse populations, including minorities, an existing infrastructure for research, and readily available detailed treatment exposure data. However, most AYAO patients are not enrolled in cooperative group protocols, survivor studies are a lower priority, and the loss to follow-up rate is high. The CCSS provides a unique opportunity to study survivors of adolescent cancer (diagnosed at 15 to 20 years of age) but does not include any young adults. Finally, populations at single institutions are sometimes of adequate size to conduct AYA survivorship studies. Importantly, none of these population databases are ideal in their current state to be used for AYA survivorship studies. An additional challenge to this area of study is identifying an appropriate control group for comparison.

Priority 1

Establish a prospective database of AYA cancer patients.

Rationale

Without prospective studies of AYA survivors, the late effects they experience and how these relate to treatment and individual differences will remain unknown. The database would be used in connection with patient-supplied follow-up information to better understand currently recognized late effects and those yet to be identified. Specific treatment and other patient information is best recorded at time of treatment. The database must contain detailed treatment information and include information to permit long-term follow-up so that impact of treatment, common risk factors, and underlying propensity can be linked to the development of late effects including second cancers, cardiovascular problems, musculoskeletal problems, and fertility/gonadal dysfunction.

Implementation Considerations/Barriers

- Sufficient funding will be essential to support the development and maintenance of a national shared database with common data elements. This effort will require a long-term commitment of funds; the time frame for this activity will be longer than the typical grant. Funds are needed for shared infrastructure and to support local data collection efforts.
- Physicians who treat AYA cancer patients, particularly those in community settings, must be willing to enroll patients. Some may cite privacy concerns, others may worry that the quality of care they provide will be critiqued. It is likely that the participation levels of pediatric and adult oncologists will vary. Professional societies (e.g., ASCO) and the NCI Cooperative Groups will be essential for building physician willingness to participate.
- Patients must be willing to allow the recording of initial treatment data and agree to provide information on their long-term health status. Several potential barriers to patient participation exist, as well as an equal number of reasons why

this population might be unusually cooperative. For example, physicians who are unwilling or uncomfortable with participation might do a poorer job of enrolling their patients in the study. Conversely, AYAs' sense of isolation and feeling that they are unique may lead to increased participation as a way to feel that they are part of a community. Advocacy groups, particularly those with an AYA focus, will be important partners as they can encourage both patients and providers to support this effort.

- For this effort to be successful, patients not treated in major cancer centers must be included. While it is easiest to enroll patients of providers who are active research participants and/or oncologists who are active in national organizations such as cancer centers or cooperative groups, late effects need to be assessed in all patients including community providers not involved in research. Reaching those providers (and patients) will take extra effort. Population-based registries such as SEER and state registries will be important resources in this activity.

Concrete Actions in the Next Three Years

- Convene a consensus panel to identify data elements to be included regarding initial treatment—chemotherapy, radiotherapy, surgery, and other treatments. The conference also should identify existing assessments of late effects experienced by AYA survivors.
- Work on strategies to bring patients treated in community settings into this partnership; explore how population-based registries can help identify patients treated by providers who are not active participants in cooperative groups.
- Pilot test the system to assess ease of data collection and feasibility of short- and long-term follow-up.

Priority 2

Improve the long-term health care of AYA cancer survivors.

Rationale

Most AYA cancer survivors are not followed by clinicians familiar with cancer survivors. Risk-based health care for AYA cancer survivors is associated with reduced morbidity and mortality and improved quality of life.

Implementation Considerations/Barriers

- Study design issues for risk-stratified survivor care model development and assessment.
- Lack of consensus on a standard set of outcome measures.
- Issues in integrating innovative technology (e.g., cross-platform electronic health record) into care model development and assessment.
- Relative lack of evidence-based guidelines for survivors of young adult cancers that may lead to premature recommendations.

Concrete Actions in the Next Three Years/Partnerships

- Issue an NCI/Lance Armstrong Foundation (LAF)-sponsored Request for Applications (RFA) for "Best Practice Models for AYA Cancer Survivors" that will fund the testing and comparison of risk-stratified models of survivor care, incorporating methods of formal knowledge transfer from oncology to primary care, and using a common set of measurements across studies. Potential partners include the Robert Wood Johnson Foundation (chronic disease management program), Community Clinical Oncology Programs, and Agency for Healthcare Research and Quality-supported primary care practice-based research networks.
- Develop and disseminate a monograph on AYAO survivorship. Potential partners on this project include ASCO, American Academy of Family Physicians, American Academy of Pediatrics, American College of Physicians, and American College of Obstetricians and Gynecologists.

- Support initiatives to enhance the development and dissemination of survivorship care plans. Existing models include the IOM Implementing Survivorship Care Planning initiative, the Ontario Passport for Health, and LAF LIVE**STRONG**™ notebook.
- Enhance the LIVE**STRONG**™ Web site with dynamic question-and-answer capability and a list of AYA LTFU programs.
- Partner with insurance companies to develop an AYA survivor chronic disease management program.

Priority 3

Conduct studies of AYA cancer survivors to understand the late effects of cancer care experienced by persons who completed cancer treatment.

Rationale

Many gaps remain in our knowledge of the late effects experienced by current cancer survivors. Some gaps are due to the paucity of specific treatment information. For example, SEER does not routinely collect and/or disseminate to the research community detailed treatment information such as chemotherapy agent and dose, radiotherapy dose and target, or surgery. Other gaps are due to incomplete information on treatments received (e.g., indication that radiotherapy was received, but no information about fields and dose) or a lack of focus on the AYA population despite available data. Obtaining knowledge about the late effects experienced by current survivors will inform recommendations for ongoing clinical care for survivors and may lead to changes in primary treatment of newly diagnosed cancer patients.

Implementation Considerations/Barriers

- Recovering sufficient detail about primary (and secondary) treatment may require access to original patient charts. Depending on provider record retention policies, this may not be possible. At best, it will be time consuming and difficult. For this reason, studies that rely on data collection from chart-based resources should be focused and well thought out. Much of the cost of these studies is associated with retrieving the original chart so it is important that data collection be complete and accurate.
- Ideally, these studies will include controls to enable researchers to differentiate between late effects of cancer treatment and the normal aging process. Options for controls include general population controls, siblings or other close relatives as controls, using controls from within the cancer population but treated differently (e.g., received radiotherapy vs. did not) and allowing people to serve as their own controls (e.g., sarcoma within radiation fields vs. outside of radiation fields). Each study type has its own strengths and weaknesses. It is important that these studies be of high quality.
- Although the Health Insurance Portability and Accountability Act (HIPAA) privacy provisions do not necessarily preclude access to medical records for research, HIPAA will increase access barriers and may necessitate obtaining primary consent for access. This access might include both primary treatment information and information on late effects. While most follow-up studies will require patient contact, information on patients who are lost to follow-up will assist with the assessment of bias. Obtaining next-of-kin consent for deceased patients may be difficult, but these patients are of high importance since non-cancer mortality is the most extreme of late effects. Advocacy groups will be an essential partner to help facilitate patient willingness to participate, which is necessary to achieve a high response rate.
- One option for conducting follow-up studies will be to partner with cooperative groups and assess late effects experienced by participants in trials in which the trial contains sufficient numbers of people in the AYA age range. One challenge is the lack of overlap between COG and adult oncology trials. An additional problem is the low participation rate in trials for AYA populations, particularly by racially and economically diverse populations.
- Many existing population-based data sources that are easily accessed by researchers are de-identified (e.g., SEER, American College of Surgeons National Cancer Data Base – NCDB);

these data sources would be more valuable for studies of late effects if they were linked with other data sources that contain information about long-term outcomes. Depending on the source, retrieving identifiable data will require obtaining consent from the entities that contain the identifiers (e.g., individual registries including individual hospitals that contributed to the NCDB).

- AYA survivors tend to be mobile, both switching providers and moving from where they lived while undergoing treatment. Collecting high quality patient identifiers will facilitate follow-up, but loss to follow-up will likely remain a significant problem. The CCSS may provide insight into effective ways to locate those who are lost to follow-up and methods to enhance continued contact. Advocacy groups will be essential to help develop methods for maintaining long-term contact and for helping to leverage existing technology such as the Internet to facilitate data collection and bi-directional information transfer.

Concrete Actions in the Next Three Years

- Issue a focused AYAO RFA for high quality studies of late effects including second cancers, cardiovascular morbidity/mortality, and fertility. These studies will have to balance the need for highly detailed information on treatment with more general treatment information that is population-based.
- Conduct methodologic pilot studies for qualitative research on cancer survivors. Qualitative approaches will give survivors a chance to inform the research/clinical community about the effects they attribute to their cancer treatment. It is likely that many of these will prove to be previously unrecognized or under-reported effects.
- Develop a roster or repository of data sources that can serve as a baseline for follow-up and facilitate the use of common data elements and methodologies while also ensuring that the research effort is spread across the range of issues facing long-term survivors of AYA cancer.

Conclusion

Many late effects of cancer and cancer treatment experienced by AYA survivors have not been characterized and are not well understood. Mechanisms for follow-up care and education of survivors with respect to late effects are not well established. The first and third priorities recommended earlier are designed to create means for identifying late effects and better understanding their causative mechanisms. The second priority addresses strategies for incorporating knowledge of late effects into follow-up care of AYA cancer survivors. These strategies include raising awareness of late effects among survivors and caregivers, maintaining survivors' treatment records, and developing and evaluating evidence-based standards for survivor health care.

APPENDIX C
CHARGE TO THE AYAO PRG

Background

The National Cancer Institute (NCI) supports basic, clinical, and population-based research to study the causes, biology, prevention, early detection, diagnosis, prognosis, control, survivorship, outcomes, and treatment of cancer. NCI's vision for the oncology community is "a nation free from the suffering and death due to cancer by 2015 and dramatic reductions in cancer incidence." NCI's mission is to "reduce the burden and eliminate the adverse outcomes of cancer by leading an integrated effort to advance fundamental knowledge about cancer across a dynamic continuum of discovery, development, and delivery." In an unprecedented partnership, NCI is collaborating with the Lance Armstrong Foundation (LAF) to review the state of research on cancers that primarily affect adolescents and young adults. LAF's mission is to inspire and empower people affected by cancer.

The NCI, in collaboration with LAF, has established the Adolescent and Young Adult Oncology Progress Review Group (AYAO PRG), composed of prominent members of the scientific, medical, and advocacy communities, to develop a national agenda for adolescent/young adult oncology. In developing this agenda, the AYAO PRG will solicit input from the research, clinical, and advocacy communities.

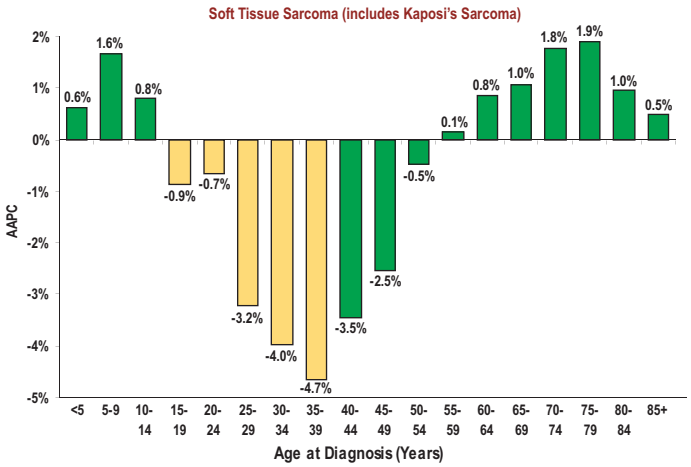
A written report describing the group's findings and recommendations will be presented to the Advisory Committee to the Director. The PRG report will be widely disseminated, and the PRG will meet with oncology community leaders to discuss a plan of action that will ensure that the priority areas of the PRG are well addressed.

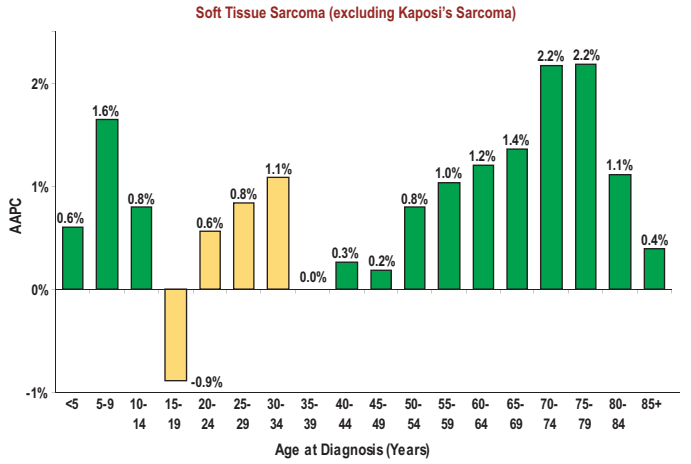
Charge

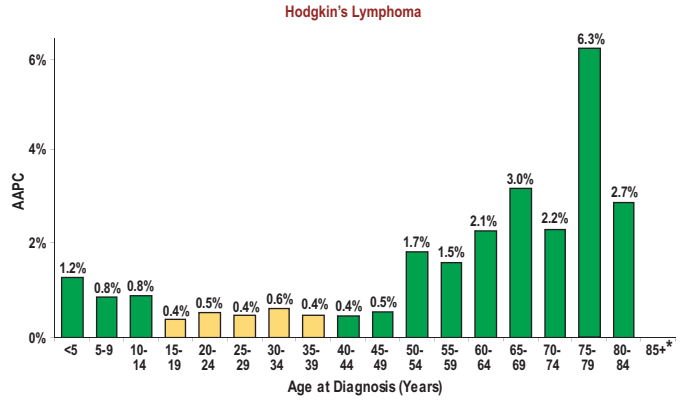
- Assess the state of research in adolescent and young adult oncology. The primary focus will be on prevention, diagnosis, and treatment of cancer in young adults and includes second cancers in pediatric cancer survivors and survivorship issues related to treatment.
  - Comprehensively define and describe issues facing adolescents and young adults with cancer.
  - Identify areas of strength, gaps, and opportunities.
- Define and prioritize investment areas; compare and contrast these priorities with the NCI research portfolio.
- Prepare a written report that describes findings and recommendations for meeting unmet opportunities and needs within the construct of discovery, development, and delivery.
- Discuss a plan of action with NCI leaders and key stakeholders and funders to ensure that the priority areas are well addressed.
- Identify and act on collaborative strategic implementation initiatives.

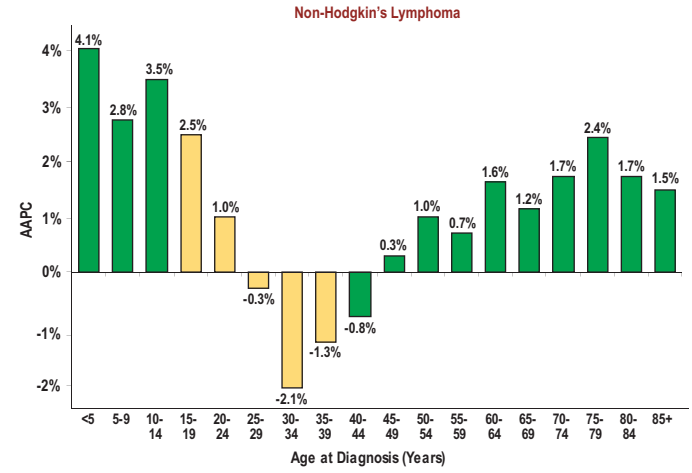
APPENDIX D

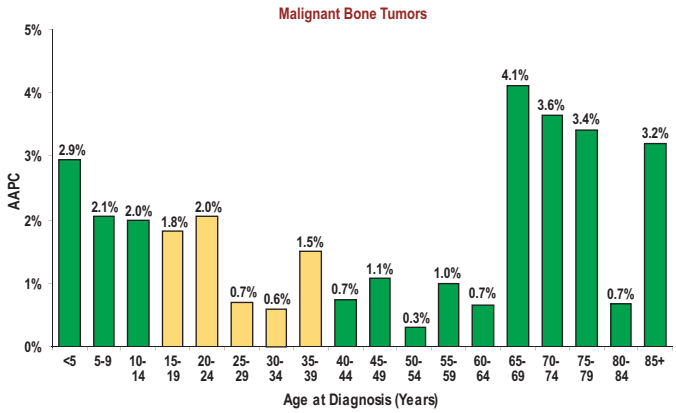
AVERAGE ANNUAL PERCENTAGE CHANGE IN 5-YEAR RELATIVE SURVIVAL OF PATIENTS DIAGNOSED WITH CANCER DURING 1975-1997, SELECTED DISEASES, U.S. SEER

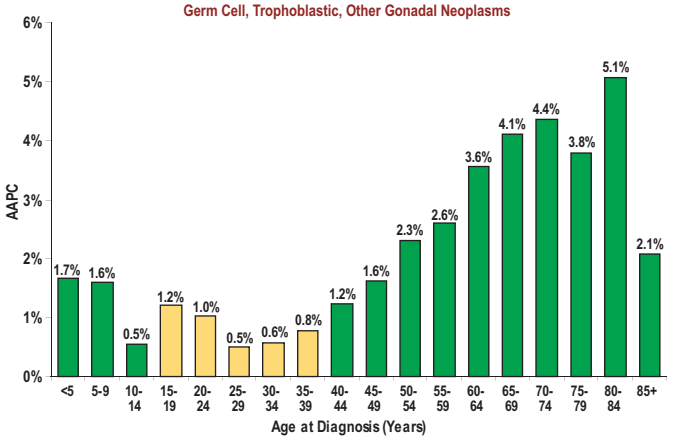


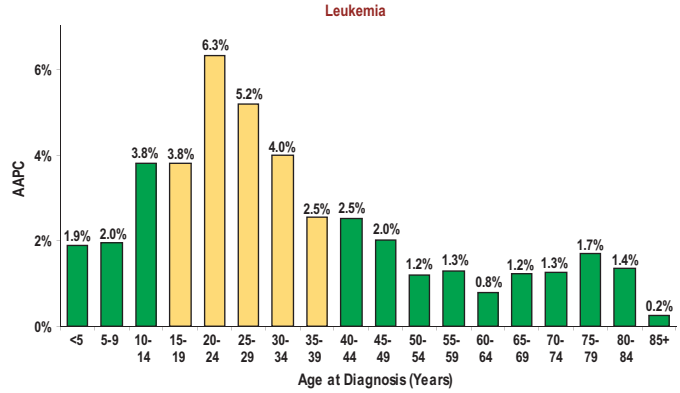


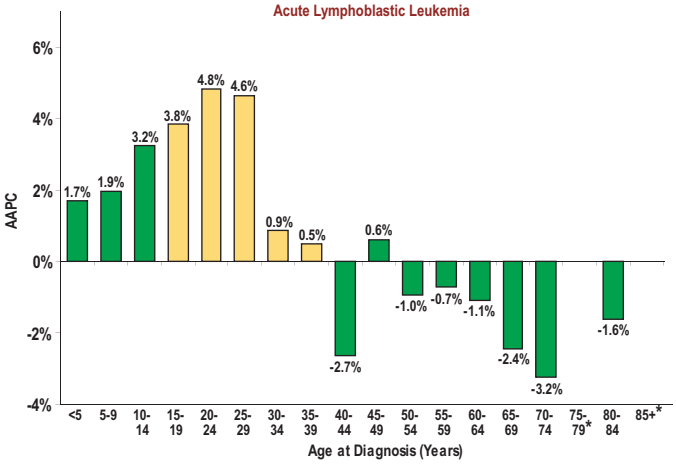












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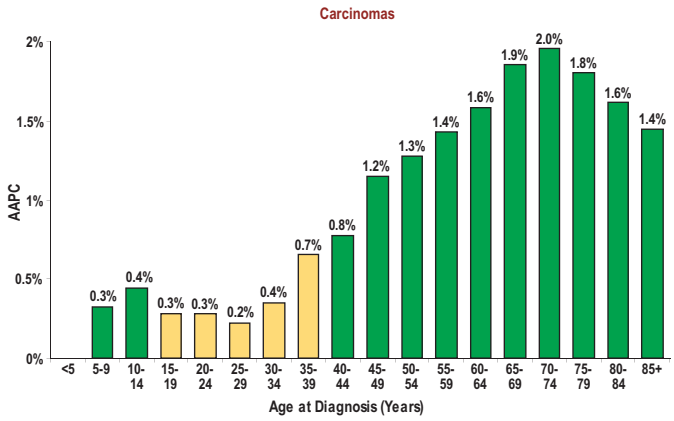

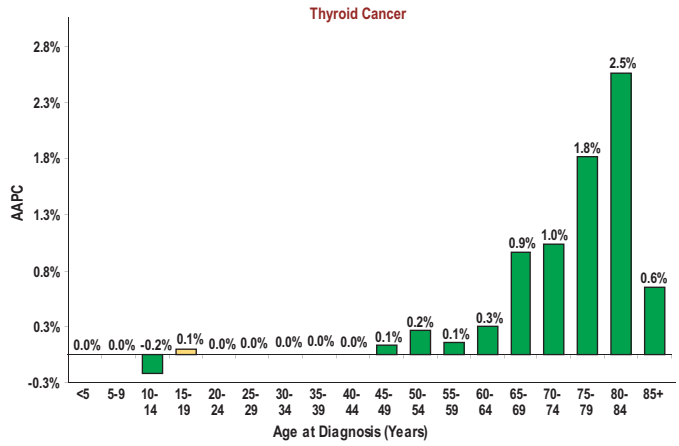

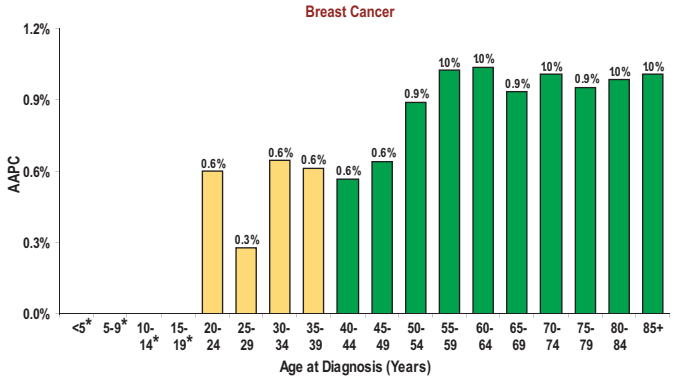

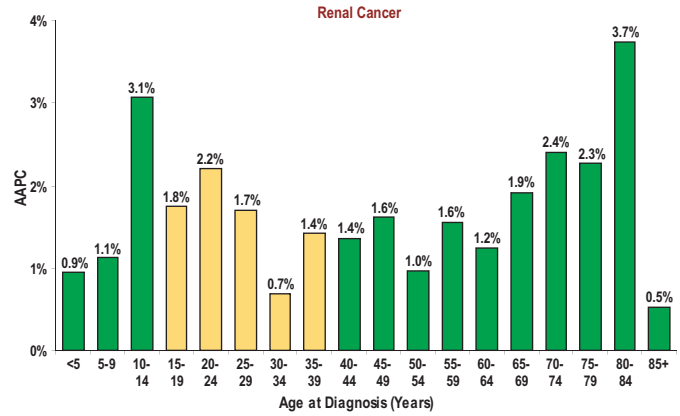

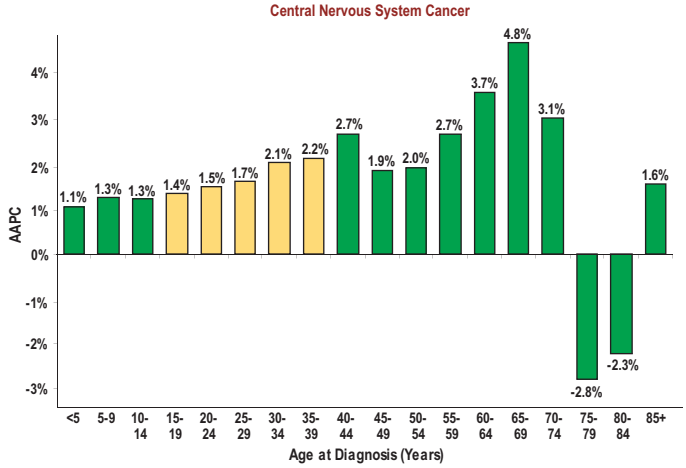

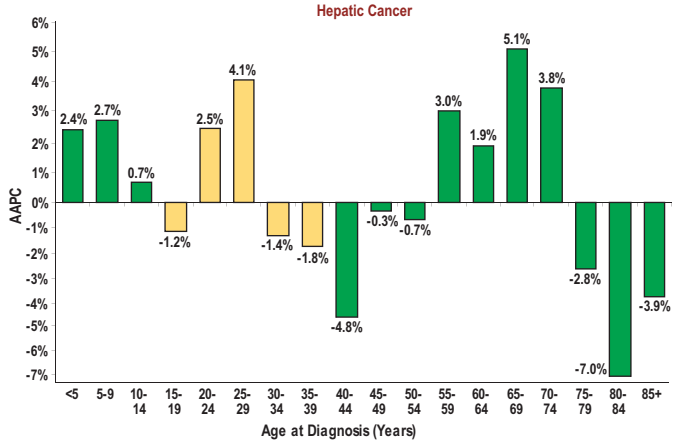

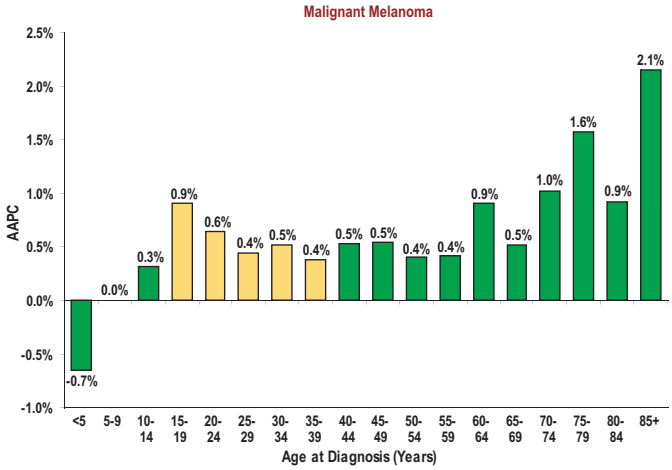

* Incomplete data.

APPENDIX E

GLOSSARY OF TERMS AND ACRONYMS

AACR	American Association for Cancer Research
AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
AAPC	Average annual percent change
ACCC	Association of Community Cancer Centers
ACGME	Accreditation Council for Graduate Medical Education
ACOG	American College of Obstetricians and Gynecologists
ACoS	American College of Surgeons
ACOSW	Association of Clinical Oncology Social Workers
ACP	American College of Physicians
ACS	American Cancer Society
"aging out"	When a dependent child reaches a designated age and is no longer eligible for coverage under his/her parents' health insurance policy.
AHIP	America's Health Insurance Plans
AHRQ	Agency for Healthcare Research and Quality (HHS)
AI/AN	American Indian/Alaska Native
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
API	Asian/Pacific Islander
ASCO	American Society of Clinical Oncology
Avascular Necrosis/ Osteonecrosis	Cellular death of the components of bone, including bone marrow, due to impaired blood supply.
AYA	Adolescents and young adults; individuals 15 through 39 years of age
AYAO	Adolescent and young adult oncology
Behavioral Research	Research into what motivates people to act as they do. The results of such research can be used, for example, to help persuade people to adopt healthy lifestyles and to follow screening and treatment guidelines.
Biomarker	A substance sometimes found in the blood, other body fluids, or tissues. A high level of a biomarker may indicate the presence of a certain type of cancer.
Biospecimen Annotation	Clinical data related to the specimen and patient necessary to optimize the usefulness of the specimen for research purposes.
Blast Cells	Immature cells that normally comprise 5 percent of the bone marrow.

Bolus Infusion	A dose of medication injected at one time rather than spread out in smaller doses over a period of time.
CALGB	Cancer and Leukemia Group B
Cancer Advocacy Community	Organizations and individuals dedicated to or with an interest in communicating and stimulating activities and fiscal support to benefit individuals with cancer or at risk for cancer.
Cancer Burden	The sum of the tangible and intangible costs of cancer borne by individuals, families, a specific population or group, or the nation.
Cancer Care Continuum	The medical and nonmedical services associated with cancer prevention, detection, diagnosis, treatment, survivorship, and end of life care.
Cancer Health Disparities	Differences in the incidence, prevalence, mortality, and burden of cancer and related adverse health conditions that exist among specific population groups in the United States. These population groups may be characterized by gender, age, ethnicity, education, income, social class, disability, geographic location, or sexual orientation.
Carcinoma	Cancer that begins in tissues that line or cover internal organs or in the skin.
Cardiotoxicity	Cardiovascular damage or dysfunction that may occur as a side effect of some chemotherapy drugs.
Caregiver	A family member, significant other, or other lay person who provides care and assistance to a person with cancer.
CCC	(NCI-designated) Comprehensive Cancer Center
CCCG	Coalition of Cancer cooperative groups
CCOP	Community Clinical Oncology Program (NCI)
CCSG	Cancer Center Support Grant
CCSS	Childhood Cancer Survivor Study
CDC	Centers for Disease Control and Prevention (HHS)
Cervical Dysplasia	Precancerous changes of the cervix. Also called cervical intraepithelial neoplasia (CIN).
Chemoprevention	Use of a drug or agent to prevent a disease or medical condition.
Chemoprotectant	Medications administered to patients prior to or in conjunction with chemotherapy to reduce the risk of adverse side effects from anti-cancer drugs.
CHTN	Cooperative Human Tissue Network
CIS	Cancer Information Service (NCI)
CMS	Centers for Medicare and Medicaid Services (HHS)
CNP	Community Network Program (NCI)
COBRA	Consolidated Omnibus Budget Reconciliation Act
COG	Children's Oncology Group
Consensus Panel/ Conference	A group of medical or technical experts convened to clarify issues involving the application of medical technology or research findings to clinical practice.
Co-morbidities	Other medical or psychosocial conditions experienced by a person with cancer.
Cooperative Groups	Networks of academic biomedical institutions and physicians funded by NCI to conduct clinical research.

Copayment	Portion of the cost of a health service for which the patient is liable; may be a fixed dollar amount or a percentage of the total cost.
Creditable Coverage	Generally includes periods of coverage under an individual or group health plan not followed by a break in coverage of 63 or more days.
CTEP	Cancer Therapy Evaluation Program (NCI)
CTWG	Clinical Trials Working Group (NCI)
Cultural and Linguistic Appropriateness	Respect for and responsiveness to cultural and linguistic needs. “Culture” refers to integrated patterns of human behavior that include the language, thoughts, communications, actions, customs, beliefs, values, and institutions of racial, ethnic, religious, or social groups.
Cytogenetics	The study of chromosomes and chromosomal abnormalities.
DoD	Department of Defense
EBV	Epstein-Barr virus
Embryonal Tumor	A mass of rapidly growing cells that begins in embryonic (fetal) tissue. Embryonal tumors may be benign or malignant and include neuroblastomas and Wilms’ tumors.
Empirical Research	Research that uses direct or indirect observation as its test of reality.
Epigenetics	The study of changes in gene silencing that occur without changes in the genes themselves. Many genes in the body are permanently turned off as part of normal development. But sometimes that process goes awry, turning off genes that should otherwise remain active. This field of study and its associated therapies aims to switch these genes back on as a new approach to the treatment of aging, inherited diseases, and cancer.
Etiology	The cause or origin of disease.
FDA	U.S. Food and Drug Administration (HHS)
Genetic Predisposition or Susceptibility	Having one or more altered genes that increase the likelihood of developing a particular medical condition.
Genotype	The genetic makeup, as distinguished from the physical appearance, of an organism or a group of organisms.
Glucose Intolerance	Several distinct disorders, of which diabetes mellitus is the most common.
Gonadal Failure	Inadequate functioning of the testes or ovaries as manifested by deficiencies in the production of sperm or eggs or the secretion of gonadal hormones.
HBCU	Historically Black Colleges and Universities
Health Services Research	A multidisciplinary field of inquiry, both basic and applied, that examines the use, costs, quality, accessibility, delivery, organization, financing, and outcomes of health care services to increase knowledge and understand the structure, processes, and effects of health services for individuals and populations.
Heterogeneity (population)	A group of individuals having similarities that are strong enough to consider them a discrete population, but also having distinct, important differences among individuals within the population.
HHS	Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HPV	Human papillomavirus

HRQL	Health-related quality of life
ICMJE	International Committee of Medical Journal Editors
Incidence	Number of new cases of a disease that occur in a population over a period of time.
Insurance Rating	The setting of premium price classes to which an insurance company assigns individuals or groups based on its assessment of the risk of insuring them.
IOM	Institute of Medicine
ISOQOL	International Society for Quality of Life Research
LAF	Lance Armstrong Foundation
Late Effects	Conditions that develop after the completion of cancer therapy.
Late Mortality	The total number of deaths in the late stages of an ongoing treatment, or a significant length of time after treatment of an acute condition.
Long-term Effects	Conditions that develop during therapy and persist after the completion of therapy.
LTFU	Long-term follow-up
Medicaid	A program that uses Federal and state funds to pay for medical services for low-income individuals (Centers for Medicare and Medicaid Services, HHS).
MI	Minority-serving institutions
Microsatellite Instability	A change that occurs in the DNA of certain cells (such as tumor cells) in which the number of repeats of microsatellites (short, repeated sequences of DNA) is different than the number of repeats that was in the DNA when it was inherited. The cause of microsatellite instability may be a defect in the ability to repair mistakes made when DNA is copied in the cell.
NAIC	National Association of Insurance Commissioners
NCCN	National Cancer Comprehensive Network
NCCS	National Coalition for Cancer Survivorship
NCDB	National Cancer Data Base
NCI	National Cancer Institute (NIH)
Neuropathy	Functional disturbances or pathologic changes in the peripheral nervous system.
NHLBI	National Heart, Lung, and Blood Institute (NIH)
NIA	National Institute on Aging (NIH)
NIH	National Institutes of Health
Observational Research /Study	A type of study in which individuals are observed or certain outcomes are measured. No attempt is made to affect the outcome (for example, no treatment is given).
ONS	Oncology Nursing Society
Oophorectomy	Surgical removal of one or both ovaries.
Osteonecrosis	See: *Avascular Necrosis*
Ototoxicity	Damage to auditory function that may occur as a side effect of some chemotherapy agents.
Outcome	Referring to the medical, psychosocial, socioeconomic, or other result of cancer or cancer treatment.

PA/PAR	Program Announcement
Palliative Care	Care that does not have curative intent, but is focused on symptom control and patient quality of life.
Pathogenesis	The development of disease; specifically the cellular events, reactions, and mechanisms occurring in the development of disease.
Patient-centered Care	A system and philosophy of care that includes: (1) respect for patients' values, preferences, and expressed needs; (2) coordination and integration of care; (3) information, communication, and education; (4) physical comfort; (5) emotional support—relieving fear and anxiety; and (6) involvement of family and friends.
Patient Navigator/Coach	A trained individual, often a cancer survivor or other layperson, who assists newly diagnosed patients and their caregivers. This assistance generally begins at the point of an abnormal finding and continues throughout diagnosis and the treatment process. Navigators assist patients in finding needed information, making and keeping appointments, arranging supportive services, and facilitating patient communication with the treatment team, among other duties.
Peer Review	A system for evaluating research applications that uses reviewers who are the professional equals of the applicant.
Pharmacogenetics	The convergence of pharmacology and genetics dealing with genetically determined responses to drugs.
Pharmacokinetics	The activity of drugs in the body over a period of time, including the processes by which drugs are absorbed, distributed in the body, localized in the tissues, and excreted.
Prevalence	The number of all new and old cases of a disease in a defined population at a particular point in time.
Prevention, primary	Interventions aimed at blocking the initial onset of disease.
Prevention, secondary	Interventions aimed at detecting disease in its earliest stages of development.
Prevention, tertiary	Interventions targeting the post-diagnosis period.
PRG	Progress Review Group
PROMIS	Patient Reported Outcomes Measurement Information System
PROQOLID	Patient Reported Outcomes and Quality of Life Instruments Database
Psychodevelopmental Stage	Time in life at which individuals are concerned primarily with personality, social knowledge and skills, and emotions.
PTSD	Post-traumatic stress disorder
Quality of Life	The overall enjoyment of life. Many clinical trials assess the effects of cancer and its treatment on the quality of life. These studies measure aspects of an individual's sense of well-being and ability to carry out various tasks.
Randomized Controlled Trial	A prospective study in which participants are randomly assigned to one or more groups exposed to an experimental intervention and a control group that is not exposed to the experimental intervention.
RFA	Request for Applications
RWJF	Robert Wood Johnson Foundation
SARC	Sarcoma Alliance for Research through Collaboration
SCHIP	State Child Health Insurance Program (Medicaid)

Second Cancer	A second primary tumor occurring in an individual that may or may not be related to previous cancer therapy; not a metastasis (spread) of the original tumor.
SEER	Surveillance, Epidemiology, and End Results Program (NCI)
Sequelae	Undesirable physical or psychosocial after-effects of disease or disease treatment.
SES	Socioeconomic status. A measure of access to social and economic resources, most commonly indicated by income, level of education, or type of occupation. Similar: socioeconomic position.
Sociocultural	Referring to a highly variable complex of factors including but not limited to values, beliefs, customs, language, communications, institutions, socioeconomic status, and education.
Stakeholder	An organization, agency, individual, or group of individuals having an interest in a particular issue, disease, or other matter.
Standard of Care	Treatment that experts agree is appropriate, accepted, and widely used. Health care providers are obligated to provide patients with the standard of care. May also be called standard therapy or best practice.
Supportive Care	Any of a broad range of medical, psychosocial, and practical interventions provided to a cancer patient/survivor. The goal of supportive care is to prevent or treat as early as possible the symptoms of the disease, side effects caused by treatment of the disease, and psychological, social, and spiritual issues related to the disease or its treatment. Also called palliative care, comfort care, and symptom management. Caregivers also may receive supportive services, such as counseling.
Surveillance	Monitoring of disease incidence, prevalence, survival, mortality, and trends. Also, monitoring of an individual after cancer treatment for late or long-term effects, including second cancers.
Survival	The period of time from cancer diagnosis until death.
Survival, disease-free/ event-free	The period of time following cancer treatment during which there is no evidence of recurrence or residual disease.
Survival, overall	The percentage of people in a study, a treatment group, or a defined population who are alive for a defined period of time, usually 5 years. Usually reported as time since diagnosis or treatment. Individuals may still have evidence of active disease or may be disease free. Also called the survival rate.
Survival, relative	A specific measurement of survival. For cancer, the rate is calculated by adjusting the survival rate to remove all causes of death except cancer. The rate is determined at specific time intervals, such as 2 years and 5 years after diagnosis.
Survivorship	In cancer, survivorship covers the physical, psychosocial, and economic issues of cancer, from diagnosis until the end of life. It includes issues related to the ability to get health care and follow-up treatment, late effects of treatment, second cancers, and quality of life. It also may include financial and legal issues.
SWOG	Southwest Oncology Group
TCGA	The Cancer Genome Atlas
Toxicity-related Death	Mortality due to toxic effects of chemotherapy or other cancer treatment.
Translational Research	Research that advances findings from basic research studies into interventions or technologies intended for use in clinical practice.

Tumor Microenvironment	The cells surrounding a tumor, also called the stroma, that influence the growth of the tumor and its ability to progress and metastasize. The stroma also can limit the ability of therapeutics to reach the tumor, alter drug metabolism, and contribute to the development of drug resistance. Manipulating human/host-tumor interactions may be important in preventing or reversing the conversion of a normal cell to a malignant one and in re-establishing normal control mechanisms.
Underwriting	The process of evaluating applications for insurance based on an established set of guidelines. Underwriting determines the risk associated with an applicant and either assigns the applicant to a rating class or declines to offer a policy.

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NIH Publication No. 06-6067
Printed August 2006