

INSTITUTE OF MEDICINE

Shaping the Future for Health

CHILDHOOD CANCER SURVIVORSHIP: IMPROVING CARE AND QUALITY OF LIFE

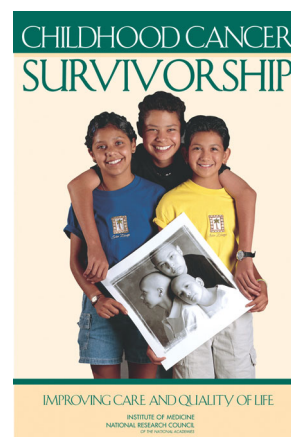
The treatment of childhood cancer is one of oncology's great success stories. Most children and young adults under 20 years of age had little hope of cure prior to 1970. Since then, cure rates, as measured in five year survivals, have increased to 78 percent, largely as the result of the development of intensive multimodal treatments. Treatment improvements have depended heavily on entrance of most children (about 60 percent) in clinical trials at specialized cancer centers where about half, or slightly more, of childhood cancer is initially treated. Children are usually exposed to combinations of two or three of the mainstays of cancer treatment: chemotherapy, radiation therapy, and surgery.

The impressive gains in survival have been achieved at a price, however. Only more recently has it been realized that the intense effort to care for and cure a child with cancer does not end with survival. Continued surveillance and a variety of interventions may, in many cases, be needed to identify and care for consequences of treatment that can appear early or only after several decades and impair survivors' health and quality of life. Models of health care delivery, surveillance, and research are beginning to take shape, but, to date, there has been no systematic review of the policy implications of this relatively new era of childhood cancer survivorship. The National Cancer Policy Board in its report, *Childhood Cancer Survivorship: Improving Care and Quality of Life*, has undertaken that systematic review.

CHILDHOOD CANCER—INCIDENCE AND TYPES

An estimated 12,400 children and adolescents under age 20 were diagnosed with cancer in 2000. New cases develop among children at a rate of 15.3 per 100,000 per year, and the risk of any individual child developing cancer between birth and 20 years of age is about 1 in 300. About 2,300 children died of cancer in 2000, representing around 8 percent of childhood deaths, making cancer the third leading cause of death in children 1 to 4, and the second leading cause of death in the 5 to 14 year age group. So, cancer in children, while rare, is a significant contributor to child mortality, and the emotional and social impact of the death of any child on families and society is disproportionate to the numbers.

Figure 1 illustrates the distribution of childhood cancers. The majority of these are leukemias, central nervous system cancers, and lymphomas. Remarkable progress has been made in the most common form of leukemia—almost an 80 percent 5 year survival. Less dramatic results are achieved with central nervous system cancers—about two thirds of children survive 5 years. Hodgkin's disease survivals have risen to 92 percent and non-Hodgkin's lymphoma to 73 percent. With rare exceptions (for exam-

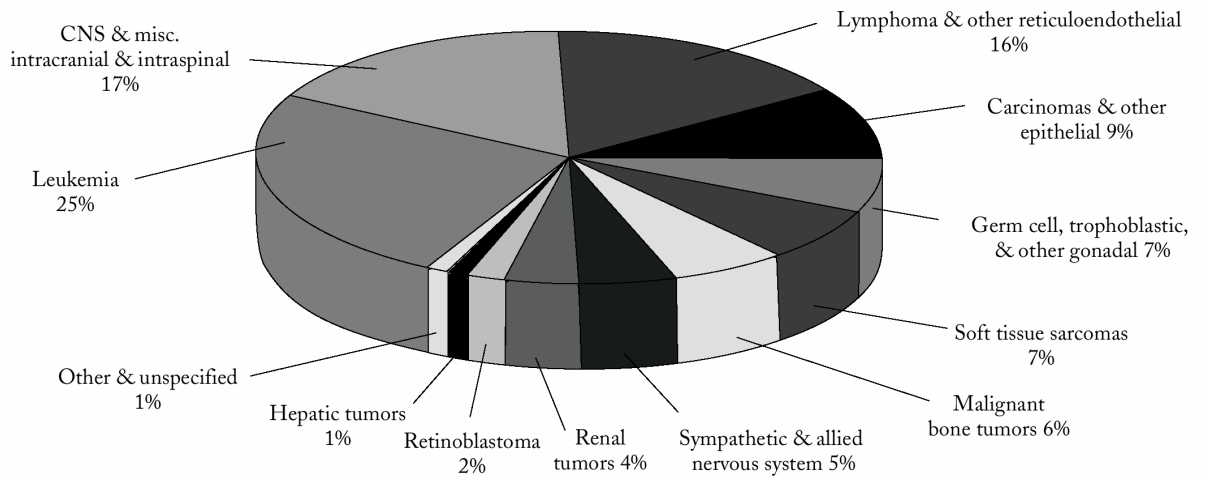


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ple, acute myeloid leukemia), all of the cancers identified in the figure have survival rates over 50 percent, and several are over 90 percent. Improvements in most categories have been substantial since before 1970, although some, such as soft tissue sarcomas, have been more resistant to progress. The 78 percent overall survival rate for children compares favorably with the 62 percent overall adult survival rate.

Figure 1. Distribution of Childhood Cancers (Age 0-19) by ICCC Category, 1975-1995



SOURCE: Data from the Surveillance, Epidemiology, and End Results Program (SEER), Division of Cancer Control and Population Sciences, National Cancer Institute.

TREATMENT OF CHILDHOOD CANCER AND THE RESULT—SURVIVORS

The treatment of childhood cancer is complex. It involves consideration of many factors, including cancer type, site, stage, and microscopic appearance and the child’s age, symptoms, and general health. Most children are treated with a combination of chemotherapy, radiation therapy, and surgery, and about 44 percent receive all three. Although there are exceptions, childhood cancers tend to respond well to chemotherapy because they involve fast-growing cells, the target of most forms of chemotherapy. Many of the gains in childhood cancer survival have come through the development of combination chemotherapies using multiple agents and multimodality therapy using different types of treatment. Children participate in clinical trials much more frequently than adults and have therefore benefited from ongoing variation in treatment, new combinations of agents, different dosages of drugs or radiation, alternate modes of administration, or entirely new approaches like immunotherapy. Some improvements in therapy have been the result of information about late effects that has led to modifications that minimize those effects. Introduction of more aggressive treatments in the 1980s has, however, exposed children to increased risk of late effects.

Advances in treatment have contributed to a growing number of survivors of childhood cancer. This report has adopted the National Cancer Institute (NCI) Office of Cancer Survivorship definition of survivorship: “an individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life. Family members, friends, and

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caregivers are also impacted by the survivorship experience and are therefore included in this definition.” As of 1997, there were 270,000 survivors of childhood cancer of all ages in the United States. This translates to about 1 in 640 adults between ages 20 to 39 years or about 1 in 1,000 total U.S. population, and, as more and more of the children benefiting from improving treatment grow into adulthood, a larger group of long-term survivors can be expected. Greater attention, better information, and more effective interventions will be needed to properly care for this important population.

KINDS OF LATE EFFECTS: CAUSES AND CONSEQUENCES

Late effects of childhood cancer include complications, disabilities, or adverse outcomes that are the result of the disease process, the treatment, or both. Patterns of late effects have emerged among groups of childhood cancer survivors that have contributed to an appreciation of cancer as a chronic disease with implications for continuing care. As many as two-thirds of childhood cancer survivors are likely to experience at least one late effect, with perhaps one-fourth experiencing a late effect that is severe or life threatening. The seriousness of late effects is illustrated by the recent finding of a 10.8-fold increase in mortality in survivors from 1970-1986. While most of these deaths were due to recurrence of the primary cancer, 21.3 percent were caused by treatment-related secondary cancers, heart toxicity, and lung complications, among others.

The emergence of late effects depends on many factors including age at diagnosis and treatment, dosages and parts of the body exposed to chemotherapy and radiation, and the severity of the initial disease. Complicating the management of late effects is their variable nature. Some late effects are identified early in follow-up—during childhood and adolescence—and resolve without consequence. Others may persist or develop in adulthood to become chronic problems or influence the progression of other diseases. Understanding late effects is hindered by the constant evolution of treatments. Groups of patients, representing different treatment eras, may experience unique sets of effects.

Selected late effects are listed in Table 1. One of the most debilitating of these is cognitive impairment among children whose cancer or its treatment involved the central nervous system, in particular children with brain tumors and those with leukemia or lymphoma who receive radiation to the head or chemotherapy reaching the brain after injection into the spinal canal. Learning impairments, social difficulties, behavioral adjustment problems, and long-term education and vocational handicaps may be experienced.

Since leukemias and lymphomas account for about 40 percent of childhood cancer and tumors of the central nervous system account for nearly 20 percent, a total of almost 60 percent of children are at risk for neurocognitive damage, especially children who are of young age when treated or who receive particularly intense or prolonged treatment. Impairment may become apparent over time and include loss of as many as 50 IQ points, deficits in short-term memory, processing speed, visual motor integration, attention, and concentration, among others. Among other important late effects are psychosocial limitations, like poor adjustment, depression, and diminished functioning in the area of social contacts and friendships.

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Table 1. Selected Physical Late Effects Associated with Childhood Cancer

Cancer	Potential Late Effects	
Leukemias	<ul style="list-style-type: none"> ▪ Cognitive effects (e.g., learning disabilities) ▪ Abnormal growth and maturation ▪ Heart problems ▪ Second cancers ▪ Hepatitis C (effects of blood transfusion) 	<ul style="list-style-type: none"> ▪ Weakness, fatigue ▪ Obesity ▪ Osteoporosis ▪ Avascular necrosis of bone ▪ Dental problems
Brain cancer	<ul style="list-style-type: none"> ▪ Neurologic and cognitive effects (e.g., learning disabilities) ▪ Abnormal growth and maturation ▪ Hearing loss ▪ Kidney damage 	<ul style="list-style-type: none"> ▪ Hepatitis C ▪ Infertility ▪ Vision problems ▪ Second cancers
Hodgkin’s disease	<ul style="list-style-type: none"> ▪ Adhesions and intestinal obstruction (if spleen removed) ▪ Decreased resistance to infection (potential for life-threatening sepsis) ▪ Abnormal growth and maturation ▪ Hypothyroidism (effect of neck radiation) ▪ Salivary gland malfunctioning (effect of jawbone irradiation) 	<ul style="list-style-type: none"> ▪ Lung damage ▪ Heart problems ▪ Infertility ▪ Hepatitis C ▪ Second cancers (e.g., breast cancer in females)
Non-Hodgkin’s lymphoma	<ul style="list-style-type: none"> ▪ Heart problems ▪ Hepatitis C ▪ Cognitive effects 	<ul style="list-style-type: none"> ▪ Infertility ▪ Osteopenia/osteoporosis
Bone tumor	<ul style="list-style-type: none"> ▪ Amputation/disfigurement ▪ Functional, activity limitations ▪ Damage to soft tissues and underlying bones (radiation may cause scarring, swelling, or inhibit growth) ▪ Heart problems 	<ul style="list-style-type: none"> ▪ Hearing loss ▪ Kidney damage ▪ Second cancers ▪ Hepatitis C ▪ Fertility problems
Wilm’s tumor	<ul style="list-style-type: none"> ▪ Heart problems ▪ Kidney damage ▪ Damage to soft tissues and underlying bones (radiation may cause scarring, swelling, or inhibit growth) 	<ul style="list-style-type: none"> ▪ Second cancers ▪ Fertility problems ▪ Scoliosis
Neuroblastoma	<ul style="list-style-type: none"> ▪ Heart problems ▪ Damage to soft tissues and underlying bones (radiation may cause scarring, swelling, or inhibit growth) ▪ Neurocognitive effects 	<ul style="list-style-type: none"> ▪ Hearing loss ▪ Hepatitis C ▪ Second cancers ▪ Kidney damage
Soft tissue sarcoma	<ul style="list-style-type: none"> ▪ Amputation/disfigurement ▪ Functional, activity limitations ▪ Heart problems ▪ Damage to soft tissues and underlying bones (radiation may cause scarring, swelling, or inhibit growth) 	<ul style="list-style-type: none"> ▪ Second cancers ▪ Hepatitis C ▪ Kidney damage ▪ Cataracts ▪ Infertility ▪ Neurocognitive effects

Some kinds of chemotherapy damage the heart, as does radiation. Children who have had these exposures particularly at high cumulative doses, rates of administration, or receipt of both chemotherapy and radiation, are at increased risk for congestive heart failure as time passes. Other kinds of chemotherapy, alone or combined with radiation, can cause debilitating scarring of the lungs. Radiation to the chest of young girls, for example, for Hodgkin's disease, can cause striking increases in breast cancer with a cumulative incidence of 35 percent 20-25 years later. Radiation therapy has been associated with development of thyroid, skin, breast, brain, bone, and other cancers, and chemotherapy is also carcinogenic. The cumulative risk of second malignancies in childhood cancer survivors after 20 years varies between 3 and 10 percent, and is five to 20 times greater than that of the general population. Other late effects include growth retardation, endocrine abnormalities and decreased fertility, obesity, and damage to various organs (liver, kidney, bladder, gastrointestinal, immune system, for example).

WHAT IS TO BE DONE?

There is general agreement that survivors of childhood cancer should be systematically followed-up, but there is no consensus regarding where such care should take place, who should provide it, and what its components should be. In short, an organized system of care and a method of care for childhood cancer survivors need to be devised. Table 2 identifies the functions of an ideal system.

Because of the uncertainty about the best care, the report recommends as its highest priority, that the NCI convene an expert group to review available clinical practice guidelines and to: *Develop evidence-based clinical practice guidelines for the care of survivors of childhood cancer.* The optimal periodicity of follow-up contact, the value of specific screening/monitoring tests, and the effectiveness of interventions to ameliorate some late effects are not well understood. Protocols are available, but they have generally been developed by individual institutions and vary in their recommendations. The lack of clarity regarding the effectiveness of interventions contributes to problems with health insurance.

The report next recommends: *Define a minimum set of standards for systems of comprehensive, multidisciplinary follow-up care that link specialty and primary care providers, ensure the presence of such a system within institutions treating children with cancer, and evaluate alternate models of delivery of survivorship care.* An expert group to do this should be convened by the NCI, the results should be endorsed by relevant bodies such as the Children's Oncology Group, and the oncology and pediatric specialty societies, and these and other groups, such as states, the Health Resources and Services Administration (HRSA), and others should take appropriate follow-up action. Four supportive care components are especially important in follow-up programs: services to address the psychological implications of cancer for survivors and their families; educational support through school transition programs; personnel to assist with insurance and employment problems; and a plan to facilitate the transition of grown survivors of childhood cancer into adult systems of care.

Other recommendations aimed at the overall objective of developing and improving ways to deliver services and better care for childhood cancer survivors include steps to:

- *Improve awareness of late effects and their implications for long-term health among childhood cancer survivors and their families.* Clinicians delivering pediatric cancer care should provide survivors and their families written information re-

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garding the specific nature of their cancer and its treatment, the risks of late effects, and a plan for follow-up;

- *Improve professional education and training regarding late effects and their management for providers.* Professional societies, primary care training programs, the NCI, oncology training programs, oncology boards, and professional meetings should all focus on further information and education about late effects and care of survivors in curricula, continuing medical education, websites, publications, and the like;
- *Support the Children with Special Health Care Needs programs.* HRSA and its Bureau of Maternal and Child Health, in partnership with state and local governments, have launched a program to ensure that the needs of children with special health care needs are met; these have the potential to extend supportive services to survivors of childhood cancer and to provide links between highly specialized care and primary care and should be supported;
- *Optimize childhood cancer survivors' access to appropriate resources and delivery systems through health insurance reforms and support of safety net programs.* State and federal governments need to consider innovative ways to help childhood cancer survivors through Medicaid, S-CHIP, state high-risk insurance pools, safety net providers, and other programs; and
- *Increase support for research in survivorship from institutions like the NCI, the National Institute for Nursing Research, and the American Cancer Society.* Only systematic follow-up of large cohorts of survivors can reveal the full extent of late effects. Amelioration of these effects will require investments in intervention and clinical research to find targeted therapies that maximize survival and minimize late effects. Ways of delivering clinical and supportive care services need to be improved through research and demonstration.

Table 2. Functions of an Ideal Follow-up System for Survivors of Childhood Cancer

Provide services

- Identify late effects (or the risk of late effects)
- Review prior disease history and treatments
- Conduct clinical examinations and tests
- Evaluate symptoms
- Develop plan for long-term surveillance
- Coordinate specialists involved in diagnosis and treatment of late effects (e.g., cardiologists, neurologists)
- Ameliorate late effects through rehabilitation services (e.g., physical therapy, occupational therapy)
- Provide psychosocial support
- Counsel regarding educational and occupational issues
- Counsel regarding disease prevention, health promotion
- Refer to clinical trials or other research initiatives
- Provide care coordination/case management (including the transition from pediatric to adult care)
- Provide family-based care and education and outreach to survivors and their families in the community

Table 2 Continued. Functions of an Ideal Follow-up System for Survivors of Childhood Cancer

Educate and train professionals

- Consult with primary care providers
- Consult with schools and educators
- Provide long-term perspective to oncology care providers
- Alert providers and researchers to new late effects
- Train primary care and oncology care providers

Conduct research

- Measure prevalence of late effects
- Identify etiology of late effects
- Evaluate effectiveness of interventions to ameliorate late effects
- Evaluate and modify treatment approaches to minimize late effects
- Develop standards of follow-up care

For More Information...

Copies of *Childhood Cancer Survivorship: Improving Care and Quality of Life* are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, <http://www.nap.edu>. The full text of this report will be available at <http://www.nap.edu>

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