



## CHAPTER 5. Childhood Cancer

### Workgroup Members

**Dawn Carey, RN, APN, C**  
*The Cancer Institute of New Jersey*

**Doug Cipkala, MD**  
*The Children's Hospital at Saint Peter's University Hospital*

**Alice Ettinger, RN, APN, C (Co-Chair)**  
*The Children's Hospital at Saint Peter's University Hospital*

**David Gordon, MS, LDT-C**  
*Tomorrow's Children Institute  
Hackensack University Medical Center*

**Deborah Halpern, MSW, ACSW**  
*The Leukemia & Lymphoma Society,  
Northern New Jersey Chapter*

**Peri Kamalakar, MD (Co-Chair)**  
*Valerie Fund Children's Center  
Saint Barnabas Health Care System*

**Kim Kinner, MA**  
*American Cancer Society, Eastern Division*

**Libby Klein, MSW, LCSW**  
*Tomorrow's Children Institute  
Hackensack University Medical Center*

**Larissa Labay, PsyD**  
*Tomorrow's Children Institute  
Hackensack University Medical Center*

**Irina Mariano-Brown, MSW, LCSW**  
*The Children's Hospital at Saint Peter's University Hospital*

**Margaret Masterson, MD**  
*The Cancer Institute of New Jersey*

**Barbara Mathis, RN, MSN, FNP, CPON**  
*Children's Hospital of New Jersey at Newark  
Beth Israel Medical Center*

**Beverly Ryan, MD**

**Susan Stephens, LCSW, ACSW**  
*The Cancer Institute of New Jersey*

**Colleen Thornton, MA**  
*The Leukemia & Lymphoma Society, Southern  
New Jersey/Shore Region Chapter*

### Background Research

**Stephanie M. Hill, BS, CTR**  
*New Jersey Department of Health  
and Senior Services  
Office of Cancer Control and Prevention*

**Sharon L. Smith, MPH**  
*New Jersey Department of Health  
and Senior Services  
Office of Cancer Control and Prevention*

### Support Staff

**Margaret L. Knight, RN, MEd**  
*New Jersey Department of Health  
and Senior Services  
Office of Cancer Control and Prevention*

**Susan Sanna, RN, BSN**  
*New Jersey Department of Health  
and Senior Services  
Office of Cancer Control and Prevention*

### External Reviewers

**Barton Kamen, MD, PhD**  
*The Cancer Institute of New Jersey/Robert  
Wood Johnson Medical School*

**Lawrence J. Ettinger, MD**  
*The Children's Hospital at Saint Peter's  
University Hospital  
Drexel University College of Medicine*



## CHILDHOOD CANCER

### IMPORTANCE OF CHILDHOOD CANCER FOR CANCER PREVENTION AND CONTROL

Just as children are not “little adults,” childhood cancer is different in many ways from adult cancer. The most common cancers in adults are breast, cervical, colorectal, lung, and prostate; children almost never contract any of these. Acute leukemia, central nervous system tumors, neuroblastoma, Wilms’ tumor, and non-Hodgkin’s lymphomas (NHL) constitute the top five diagnoses among children under 14 years of age. This is in contrast to Hodgkin’s disease (HD), germ cell tumors, non-Hodgkin’s lymphomas, osteosarcoma, Ewing’s sarcoma, and soft tissue sarcomas, which are more frequent in adolescents and young adults 15 to 19 years of age (Table 1). Contrary to adult cancers, which have identified risk factors and may be preventable, very little is known about the causes and prevention of childhood cancers. Hence, the primary focus of cancer control in childhood cancers is survivorship and the prevention and early detection of long-term effects of treatment.

Today, thanks to advances in cancer treatment, about 80% of children with cancer will be long-term survivors. However, survivorship varies considerably by cancer type, with only 66% of patients with neuroblastoma surviving beyond five years from diagnosis. Regardless of cancer type, childhood cancer survival has shown significant improvement over the last three decades.<sup>1</sup> It has been estimated that by the year 2010, one in every 250 young adults will be a survivor of childhood cancer. Even though cancers among children represent only about 1% of all cancers, their patterns in the population also merit special attention.<sup>2</sup>

As the number of childhood cancer survivors increases, particular attention must be paid to the unique needs of this population. While most adults have completed their education, are employed (or even retired), and often have children before being diagnosed with cancer, many children have not had the opportunity to even begin to realize their life’s goals before they are diagnosed with cancer. Some have not yet started school, and most still have years ahead of them during which they should be achieving physical and mental maturity. Ideally a child who survives cancer would be able to grow and develop normally, complete an education, obtain gainful employment, and eventually have children. However, ongoing aggressive treatment with chemotherapy and, in selected patients, radiation therapy and/or stem cell transplantation that improves the probability of survival can also have profound effects on a child’s physical and psychosocial development and future opportunities. For these reasons the Childhood Cancer Workgroup in contributing to this *Plan* has been challenged to develop solutions for the survivors of childhood cancer in New Jersey.

### CHILDHOOD AND YOUNG ADULT CANCER IN NEW JERSEY AND THE U.S.

In this section we discuss the status of childhood cancer in New Jersey, including incidence, mortality, age patterns, prevalence, survival, and risk factors.

Cancer in children and young adults is relatively rare. An estimated 9,500 new cases are expected to occur among children aged 0–14 in 2006 in the U.S., compared to 1,399,790 adults.<sup>1</sup> In New Jersey, the 2003 childhood cancer incidence rate for children 14 years of age and under was slightly higher compared to U.S. children (15.8 versus 14.4 per 100,000\*\*, respectively). The total childhood cancer

\*\* Rates are per 100,000 and age-adjusted to the 2000 U.S. population standard.



rate for 2003 among boys in New Jersey was higher than that among girls (16.1 versus 15.5 per 100,000\*\* for the 0- to 14-year age group and 22.1 versus 21.4 per 100,000\*\* for the 15- to 19-year age group). U.S. data for 2003 also indicates that childhood cancer rates for 0- to 19-year-olds are higher for boys than for girls (16.6 versus 15.3 per 100,000\*\*, respectively).<sup>3,4</sup> The incidence of cancer among white children and adolescents in New Jersey in 2004 was higher than among black children and adolescents (15.0 versus 13.4 per 100,000\*\* for the 0- to 14-year age group and 25.2 versus 10.4 per 100,000\*\* for the 15- to 19-year age group).<sup>3,4</sup>

Mortality rates for childhood cancer in New Jersey have declined from 1995 to 2003 (from 3.1 to 2.1 per 100,000\*\* for 0- to 14-year-olds and from 4.0 to 2.6 per 100,000\*\* for 15- to 19-year-olds).<sup>5</sup> The largest declines in mortality have occurred for Hodgkin’s lymphoma, soft tissue sarcoma, and leukemia (acute lymphoblastic leukemia, in particular). These trends reflect dramatic successes in the treatment of childhood cancer.<sup>6</sup> An estimated 1,545 deaths from cancer are expected to occur in the U.S. among children aged 0–14 in 2007, about one-third of them from leukemia. Despite its rarity, cancer is the chief cause of death by disease in children between ages 1 and 14.<sup>1</sup>

**Table 1. Incidence rate of most common cancers in 0- to 14-year-old children and 15- to 19-year-old adolescents, New Jersey, 2002–2004\*\***

Cancer Type	<15	15–19
Total childhood cancers	15.8	21.6
Acute lymphoblastic leukemia (ALL)	3.7	1.7
Acute myeloid leukemia (AML)	0.9	0.9
Hodgkin’s disease	0.5	3.5
Non-Hodgkin’s lymphoma	0.8	1.4
Central nervous system tumors	3.5	2.0
Neuroblastoma	1.0	0.0
Wilms’ tumor	0.8	0.2
Germ cell tumor	0.5	2.5
Osteosarcoma	0.4	0.6
Ewing’s sarcoma	0.3	0.5

Source: [New Jersey State Cancer Registry](#)<sup>4</sup>

\*\* Rates are per 100,000 age-adjusted to 2000 U.S. (5-year groups) standard.

**Age patterns.** Incidence patterns for different types of cancer in children vary dramatically by age. For example, the incidence of acute lymphoblastic leukemia increases to a peak before age 5 and declines thereafter, whereas the incidence of acute myeloid (non-lymphoblastic) leukemia is constant throughout childhood. The incidence of Hodgkin’s lymphoma increases throughout childhood and is highest in adolescence. Neuroblastoma, retinoblastoma, and Wilms’ tumor incidence rates are highest between birth and age 1 and decline with increasing age.<sup>6</sup>

\*\*Rates are per 100,000 and age-adjusted to the 2000 U.S. population standard.



**Prevalence.** Childhood cancer prevalence counts (i.e., the number of people alive who have ever been diagnosed with childhood cancer) are not available for New Jersey. However, estimates from the National Cancer Institute indicate that in the United States on January 1, 2003, there were 57,723 survivors of childhood cancer who had been diagnosed within the previous five years. Prevalence counts were slightly higher for males than females (30,378 versus 27,345, respectively). Whites accounted for the highest overall prevalence (48,687), followed by blacks (5,798) and then Asian/Pacific Islanders (1,897). Hispanics accounted for 8,930 of the childhood cancer survivors.<sup>7</sup>

**Survival.** New and improved treatments have been responsible for greatly improving the five-year relative survival rate over the past 30 years from less than 50% before the 1970s to nearly 80% today. For the time period 1996–2002, the five-year survival rate for neuroblastoma is 69%; brain and other nervous system, 74%; bone and joint, 72%; leukemia, 81%; non-Hodgkin’s lymphoma, 86%; Wilms’ tumor, 92%; and Hodgkin’s lymphoma, 95%.<sup>1</sup>

**Risk factors.** Overall, the causes of most childhood cancers remain unknown. Several types of pediatric cancers are related to genetic conditions. However, most pediatric cancers appear to develop spontaneously, with no relationship to carcinogens or inherited syndromes. Considerable research has been conducted to explore the effects of environmental contaminants associated with childhood cancer, although direct causation has not been proven.<sup>8–10</sup>



## GOALS, OBJECTIVES, AND STRATEGIES

The recommendations of the Childhood Cancer Workgroup are summarized below for the following focal areas:

- Adolescent and young adult treatment
- Health-related consequences of childhood cancer and its treatment
- Pain and palliative care
- Family support
- Education

### OVERALL GOAL

To enhance the quality of life of the child, adolescent, and/or young adult patient with cancer from diagnosis through treatment to survivorship across the life span.

### ADOLESCENT AND YOUNG ADULT TREATMENT

Cancer survival in children under 14 is a great success story of the 20<sup>th</sup> century. Before the 1970s, the five-year survival rate for a child diagnosed with cancer was less than 50%. By the 1990s this had risen to almost 80%.<sup>1</sup>

From 1975 to 2002 there have been substantial gains in survival in the 15- to 19-year age group. However, this gain lagged behind the significant improvements seen in the younger age group. For the period 1975–1977, the older group had a survival rate of 68% versus 58% for children 0–14 years of age. For the period 1996–2002, this increased to 80% and 79% for the respective groups, showing relatively greater improvement in the younger age group (Table 2).<sup>7</sup>

This may be attributable to the greater proportion of children under age 15 being treated at pediatric cancer centers, with over 60% participating in national clinical trials. Comparatively, fewer than 35% of 15- to 21-year-olds are entered into clinical trials.<sup>11</sup>

**Table 2. U.S. five-year survival rates in 0- to 14-year-old children with selected diagnoses**

Time Period	1975–1977 (%)	1996–2002 (%)
Acute lymphoblastic leukemia (ALL)	57.6	87.0
Leukemia	50.3	81.0
Hodgkin's lymphoma	80.5	95.3
Non-Hodgkin's lymphoma (NHL)	42.6	86.0
Bone and joint	51.3	71.6
Brain and other nervous system	56.9	74.1

Source: [National Cancer Institute](#). *SEER Cancer Statistics Review, 1975–2003*<sup>7</sup>



However, survival for the older group may improve through their increased participation in national clinical trials. Many advances in childhood cancer treatment are the result of participation in clinical trials. Perhaps the greatest success has been seen in the treatment of acute lymphoblastic leukemia (ALL), for which survival rates have risen from 15% to 80% in the last 40 years, largely due to the high number of patients participating in clinical trials. It is hoped that, through further clinical research, the same success can be achieved for all childhood cancers, including those in the 15–19 age group.<sup>12</sup> The Children’s Oncology Group (a national organization), as well as National Cancer Institute (NCI)-designated cancer centers such as the Cancer Institute of New Jersey, offer many childhood cancer clinical research trials, characterized by close oversight and a high standard of care.

To investigate the differences between childhood cancer in ages 0–14 and childhood cancer in ages 15–19 and to further the successful treatment of all pediatric malignancies, the Childhood Cancer Workgroup suggests that more clinical research should be directed toward patients with cancer through the age of 21. Physicians, patients, and families need to be made aware of the importance of participation in clinical trials. Pediatric patients treated at pediatric cancer centers are nearly twice as likely to be enrolled in clinical trials as patients treated at non-pediatric centers.<sup>11</sup> As there has been a direct correlation between participation in national protocols and being treated at pediatric cancer centers, the Childhood Cancer Workgroup also recommends that physicians be educated about the importance of referring patients to pediatric cancer centers.

**GOAL CC-1** To improve care for adolescents and young adults diagnosed with cancer through encouraging participation in clinical trials.

### Objective CC-1.1

To educate healthcare providers about the availability of existing clinical research protocols and the referral of young adults through the age of 21 to pediatric oncology centers.

### Strategy

**CC-1.1.1** Collaborate with other organizations to develop and distribute educational materials about the availability and importance of existing clinical research protocols and the need to refer young adults through the age of 21 to pediatric oncology centers.

## HEALTH-RELATED CONSEQUENCES OF CHILDHOOD CANCER AND ITS TREATMENT

Many of the treatments that have been instrumental in reducing mortality from childhood cancer can, themselves, have serious health consequences for the survivor. The late effects of childhood cancer treatment include organ malfunction, secondary cancers, and cognitive disorders.<sup>1,13,14</sup> Two-thirds of childhood cancer survivors experience at least one late effect, while one-fourth experience severe or life-threatening late effects.<sup>14</sup> Adult survivors of childhood cancer have a higher mortality rate than the general population.<sup>15</sup> In fact, a recent study found that adult survivors of childhood cancer are 14 times more likely to develop a secondary malignancy than their siblings; 15 times more likely to



develop congestive heart failure; 10 times more likely to have severe cognitive dysfunction; and greater than 50 times more likely to have major joint replacement.<sup>13</sup>

Survivors of childhood cancer represent a growing population. This pool is expanding because of the increase in survival and cure rates. It is estimated that 1 in 640 individuals between 20 and 39 years of age are survivors of childhood cancer.<sup>14</sup> This number is projected to reach 1 in 250 young to mid-aged adults by 2010.<sup>2,16</sup> This population will challenge their healthcare providers to address the medical, emotional, and societal sequelae of cure. Healthcare professionals dealing with this special population must be diligent in surveillance for late effects. The Institute of Medicine's National Research Council recently made the following recommendations regarding childhood cancer late effects:

1. *Develop evidence-based clinical practice guidelines for the care of survivors of childhood cancer.*
2. *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.*
3. *Improve awareness of late effects and their implications to long-term health among childhood cancer survivors and their families.*
4. *Improve professional education and training regarding late effects of childhood cancer and their management for both specialty and primary care providers.*
5. *The Health Resources and Services Administration's Maternal and Child Health Bureau and its partners should be fully supported in implementing the Healthy People 2010 goals for Children with Special Health Care Needs. These efforts include a national communication strategy, efforts at capacity building, setting standards, and establishing accountability. Meeting these goals will benefit survivors of childhood cancer and other children with special health care needs.*
6. *Federal, state, and private efforts are needed to optimize childhood cancer survivors' access to appropriate resources and delivery systems through both health insurance reforms and support of safety net programs such as the Health Resources and Services Administration's Community and Migrant Health Centers.*
7. *Public and private research organizations (e.g., NCI, National Institute of Nursing Research, American Cancer Society) should increase support for research to prevent or ameliorate the long-term consequences of childhood cancer. Priority areas of research include assessing the prevalence and etiology of late effects; testing methods that may reduce late effects during treatment; developing interventions to prevent or reduce late effects after treatment; and furthering improvements in quality of care to ameliorate the consequences of late effects on individuals and families.<sup>14</sup>*

**Organ malfunction.** Many common childhood cancer treatments, such as chemotherapy and radiation, can result in severe and permanent damage to vital organs, including the brain, heart, lungs, kidneys, and endocrine systems.<sup>15</sup>

Cognitive disorders as a result of cancer treatments are perhaps the most severe late effect of childhood cancer and are discussed in detail later in this chapter under a separate heading.



Certain childhood cancer treatments are known to have toxic effects on cardiac tissue. Survivors who have undergone these treatments should be screened for early onset of cardiovascular disease and counseled on the particular importance of practicing heart-healthy behaviors, including eating a diet low in fats and avoiding tobacco use.<sup>13,15</sup>

The impact of childhood cancer treatment on endocrine system function can result in abnormal physical development (i.e., delayed or accelerated onset of puberty), obesity, and reproductive failure.<sup>13,15,17</sup>

Childhood cancer survivors should be counseled on the potential long-term effects of treatment and monitored not only for these outcomes, but also for the psychosocial effects of organ malfunction.

**Secondary cancers.** Second malignant neoplasms (SMN) are rare events, but they exact a considerable emotional toll on young adult survivors and their families. Recent studies have estimated the cumulative risk of developing an SMN to be approximately 12% within 25 years of initial diagnosis.<sup>15</sup>

These findings emphasize the need for surveillance to detect and intervene early in the occurrence of SMN. All primary care physicians who treat survivors of childhood cancer should have an increased index of suspicion for an SMN based upon the survivor's individual risk profile. With identification of specific high-risk factors among the survivors, surveillance is more focused, providing an opportunity for early prevention and treatment. The list of high-index suspicion subsets should be inclusive to single out those survivors needing special consideration for increased surveillance by primary care providers.<sup>18</sup>

**Cognitive disorders.** Healthcare professionals are increasingly accepting the need for psychological assessment and care for childhood cancer survivors. Recent research has shown that survivors of childhood cancer often develop psychological distress, thought to be related to diminished social functioning as a result of cancer or treatment. Distress may be manifested as anxiety, posttraumatic stress, depression, and suicidal ideation.<sup>19</sup> Less severe, but no less deserving of attention, are symptoms of lowered self-esteem and body image and other concerns over the long-term effects of cancer treatment.<sup>20-22</sup> Prolonged illness and treatment may result in isolation from peers and overdependence on caregivers during the adolescent years when children usually strive for independence. This contradiction often leads to unrecognized and unmanaged feelings of frustration, anger, depression, and rebelliousness in the survivor.<sup>23</sup> The incidence and severity of psychological symptoms and suicidal ideation may increase with age due to an increasing burden of responsibility and the demands of adulthood.<sup>20,21,24</sup>



**GOAL CC-2** To reduce incidence and impact of late effects of childhood cancer and its treatment.

### Objective CC-2.1

To identify guidelines for screening of individuals who have been diagnosed with childhood cancer.

### Strategies

- CC-2.1.1** Conduct a literature review and interview experts in order to compile guidelines for screening of childhood cancer survivors.
- CC-2.1.2** Convene a consensus conference and produce a report that will contain a consensus statement and the development of screening guidelines for childhood cancer survivors where needed.
- CC-2.1.3** Disseminate screening guidelines for childhood cancer survivors through the development of a publication to be distributed to all healthcare providers and patients.

### Objective CC-2.2

To disseminate healthy lifestyle information to childhood cancer survivors to reduce factors contributing to late effects.

### Strategy

- CC-2.2.1** Develop a media campaign and brochures to educate childhood cancer survivors on risk factors for late effects.

## PAIN AND PALLIATIVE CARE

The World Health Organization affirms that palliative care should be incorporated into the care of all children with cancer utilizing a multidisciplinary approach.<sup>25</sup> There has been some confusion, however, over the term *palliative care*, since this term is often associated with terminal illness where there is no hope for survival and where the treatment shifts from curative intent to providing comfort for the last few weeks of life. However, palliative care has in recent years undergone a paradigm shift (see Chapter 3 Palliation). As recently as 1987, when palliative care was first recognized as a medical specialty, the focus was on patients whose prognosis was poor and was limited to maximizing quality of life at the end of life. A more global approach was suggested by the World Health Organization in 1990:



“... control of pain, of other symptoms, and of psychological, social and spiritual problems is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families. Many aspects of palliative care are also applicable earlier in the course of the illness in conjunction with anticancer treatment.” More recently, in 2001, a white paper produced by the Children’s International Project on Palliative/Hospice Services stated: “Palliative care is the science and art of lessening physical, psychosocial, emotional, and existential suffering. Palliative care can benefit patients and families whether the overall goals of care are to cure, prolong life, maximize the quality of life that remains or ease the pain of bereavement. Thus, palliative care may be provided concurrently with, or as an alternative to life sustaining medical intervention ... A palliative care knowledge base exists that can substantially improve the experience of children living with life threatening conditions. However, because this knowledge is not widely taught in health professors’ training programs, and in part because it is care that is currently unpaid, pediatric palliative care is not widely available.”<sup>26</sup> Concurring with these positions, the Childhood Cancer Workgroup recommends that healthcare professionals be made aware of the importance of incorporating palliative care into the treatment of all children with cancer, beginning at the time of diagnosis.

Beyond addressing the emotional impact of the cancer diagnosis, implicit in this broader concept of palliative care is the intent to deal with multiple complications related to both the underlying disease and the treatment of the cancer. These symptoms include diarrhea and constipation, nausea and vomiting, fatigue, anorexia, dyspnea, and pain.<sup>27</sup>

Pain continues to be of paramount importance in that it is very often the prevalent symptom from the time of diagnosis and throughout treatment. Pain is multi-factorial; it can be related to the cancer itself, the invasive procedures used to diagnose or treat the cancer, or the therapies used such as surgery, chemotherapy, or radiation. It is also very often the most important issue for the child dying of cancer. Studies have shown that a significant number of childhood cancer patients experience pain from the time of diagnosis, and this pain is insufficiently managed.<sup>27,28</sup>

**GOAL CC-3**

To promote awareness of palliative care strategies for the child with cancer among healthcare professionals, patients, and families. Pain management can be used as an example of how these strategies can be implemented successfully.

**Objective CC-3.1**

To educate healthcare professionals, childhood cancer patients, and families about palliative care strategies in the management of cancer-related symptoms including pain.

**Strategy**

**CC-3.1.1** Partner with providers, childhood cancer patients, and family members to promote a statewide educational forum that will include palliative care and pain management strategies.



## FAMILY SUPPORT

Every pediatric oncology medical treatment program in New Jersey should provide emotional support services to a patient's siblings and parents as well as to the patient.

The literature documents the negative impact on siblings and parents when a child is diagnosed with cancer. Much of the literature has focused on posttraumatic stress in relation to the family after a childhood cancer diagnosis, with an indication of parental symptoms consistent with Post-Traumatic Stress Disorder (PTSD) (e.g., avoidance, intrusive thoughts, hypervigilance, etc.). Kazak et al. completed a study comparing symptoms of anxiety and posttraumatic stress in parents of children and adolescents diagnosed with cancer with a control group of parents whose children and adolescents were not diagnosed with a chronic illness.<sup>29</sup> The study, involving 130 cancer survivors and their parents with a comparison group of 155 children and their parents, included five measures of anxiety and stress, with two of the measures involving family functioning and social support. The results of the study revealed significantly higher levels of posttraumatic stress symptoms in parents of children diagnosed with cancer as compared to those parents whose children have not been diagnosed with a chronic illness. Moreover, study findings linked parents' perceived higher levels of social support to fewer posttraumatic stress symptoms. This confirms the notion that quality of life of survivors, siblings, and parents can be improved by addressing impact at time of treatment and subsequently through psychosocial support at treatment centers.

The services of the child life/creative arts specialist are essential to meeting the goals of providing emotional support, age-appropriate explanations of the diagnosis and treatment, preparation for procedures, and the modalities with which the child may express his or her anxieties, frustrations, and anger over interruption of "normal" life. These modalities include the use of art, music, dance, and play, with which the therapist seeks to engage the child in counseling and comfort consistent with their developmental age. The effects of such interventions are often beneficial to the family's coping, to siblings' well-being and interactions, and allow for more time- and cost-efficient delivery of healthcare.

The Academy of Pediatrics has recognized the importance of child-life services and recommended that such services should not be withheld because of financial constraints. Child-life services represent an important foundation for providing a better quality of life for the youngster during treatment and help ensure that child survivors meet the emotional and social milestones of their peers.

Literature supports the nature and severity of stressors, reactions, and coping strategies that point toward possible interventions. Stuber and Kazak<sup>30</sup> found that clinical interventions during treatment reduced not only the family's immediate stress levels, but also continue to provide emotional benefits after acute care. In keeping with current research, Stuber and Kazak recommended reducing family stress levels by assisting the family in "developing a realistic but hopeful understanding of life threat and reducing the perception of treatment intensity."<sup>30</sup> In addition, the study recommended "adequate and developmentally appropriate explanations and preparations for procedures and treatment, and careful control of pain and nausea." Interventions can be specific in terms of types of professionals used (psychologists, social workers, creative life therapists) and ratio of patients to professionals recommended/required. Delivery of services can also be measured in terms of groups/programs offered at a given institution. Studies document the poor quality of life related to sibling/parent anxiety, grief (losses, not only death), and perseverance over problems lasting over time. The literature also compares parent populations only by child's disease severity or prognoses, not by geography, ethnicity, etc.



**GOAL CC-4** To foster the psychosocial health of the child with cancer and the family.

### Objective CC-4.1

To maximize the quality of life of the child with cancer and the family.

#### Strategies

- CC-4.1.1** Conduct a statewide survey to identify existing psychosocial support mechanisms at each pediatric oncology treatment center.
- CC-4.1.2** Identify community resources for psychosocial support for children with cancer and their families in conjunction with a capacity and needs assessment.

### Objective CC-4.2

To assess the psychosocial mechanisms utilized in treatment centers and the community.

#### Strategies

- CC-4.2.1** Conduct a literature review to investigate psychosocial standards of care.
- CC-4.2.2** Collaborate on a consensus statement for psychosocial standards of care with key stakeholders.

### Objective CC-4.3

To ensure that appropriate and continuous psychosocial support is provided for every child with cancer and the child's family.

#### Strategies

- CC-4.3.1** Through a legislative initiative, require the assignment of a professional caseworker to provide *ongoing* psychosocial assessment and intervention of every child and his/her family as per standard of care.



- CC-4.3.2** Research existing reimbursement policies and mechanisms to evaluate current trends in non-reimbursement for psychosocial services.
- CC-4.3.3** Partner with the insurance industry to further reimbursement of psychosocial services on an *ongoing* outpatient basis.

## EDUCATION

According to estimates in the U.S. college-age population, in the year 2010, approximately 67,000 individuals between the ages of 18 and 21 will be childhood cancer survivors. Some reports suggest that up to 50% of survivors are likely to have late effects of their cancer therapy, which may lead to significant disabilities that alter quality of life. This brings to light the need to screen childhood cancer survivors for late effects of their past treatment.

Many survivors see their pediatric oncologists, either regularly or on an occasional basis, after completing treatment for the underlying malignancy, so that they can be monitored and screened for late effects of their therapy. Their primary medical care is managed by pediatricians, family practitioners, internists, and nurses. It is extremely important for these caretakers to be aware of the consequences of survivors' previous treatments for normal tissues and organ systems. A medical passport that includes a short summary of medical history and treatment can be a useful tool for monitoring late effects.

The available literature has well documented late effects of treatment for survivors of childhood cancer, whether surgically, chemotherapy-, or radiation-induced. Adverse effects have been shown on many organ systems, such as the central nervous system, neuroendocrine, ocular, dental, musculoskeletal, cardiovascular, pulmonary, gastrointestinal, hormonal function, fertility, and risks of secondary malignancies.

**Central nervous system.** Neurocognitive deficit (difficulty reading, language, verbal and non-verbal memory, arithmetic, receptive and expressive language, decreased speed of mental processing, attention deficit, decreased IQ, behavior problems, poor school attendance, poor hand-eye coordination); leukoencephalopathy (seizures, neurologic impairment); focal necrosis (headaches, nausea, seizures, papilledema, hemiparesis, speech, learning and memory deficits); stroke; blindness; ototoxicity (abnormal speech development, hearing loss); myelitis (paresis, spasticity, altered sensation, loss of sphincter control); peripheral neuropathy (generalized weakness, localized weakness, lack of coordination, tingling and numbness).

**Neuroendocrine.** Growth hormone deficiency (poor growth/growth retardation); adrenocorticotrophic hormone (ACTH) deficiency (muscular weakness, anorexia, nausea, weight loss, dehydration, hypotension, abdominal pain, increased pigmentation); thyrotropin-releasing hormone (TRH) deficiency (hoarseness, fatigue, weight gain, dry skin, cold intolerance, dry brittle hair, alopecia, constipation, lethargy, poor linear growth, menstrual irregularities, pubertal delay, bradycardia, hypotension); precocious puberty (early growth spurt, false catch-up, premature sexual maturation); gonadotropin deficiency (delayed or absent pubertal development, testicular atrophy, infertility, abnormal menses, estrogen deficiency); hyperprolactinemia (abnormal menses, infertility, galactorrhea, osteopenia, loss of libido, hot flashes, impotency).

**Ocular system.** Dry, red eyes; tearing; ulcerations; tortuous vessels; pain; decreased visual acuity; cataracts.



**Head and neck/dental.** Decreased saliva, dental decay, thrush, ulcerations, chronic rhinitis, facial pain, headache, hearing impairment, chronic ear infections, hair loss.

**Musculoskeletal.** Muscular hypoplasia, spinal abnormalities (scoliosis, kyphosis, etc.), limb length discrepancy, pathological fracture, osteoporosis, osteonecrosis, osteo-cartilaginous exostoses, slipped capito-femoral epiphysis.

**Cardiovascular.** Cardiomyopathy, valvular damage, pericardial damage, coronary artery disease.

**Pulmonary.** Pulmonary fibrosis.

**Gastrointestinal.** Enteritis, adhesions, esophageal strictures, fibrosis of small and large intestines, hepatic fibrosis/liver failure.

**Thyroid dysfunction.** Hypothyroidism, thyroid nodules, hyperthyroidism.

**Infertility.** Ovarian failure, premature menopause, decreased or absent sperm production, testicular atrophy.<sup>31,32</sup>

With the longer life span and increasing numbers of survivors of childhood cancer, it is important to help educate primary care physicians, pediatricians, family practitioners, internists, and nurses on these late effects, the need for screening, and treatment/referral recommendations.<sup>31-33</sup>

**GOAL CC-5** To increase awareness by healthcare providers of late effects in childhood cancer.

### Objective CC-5.1

To identify guidelines for screening and management of late effects of childhood cancer.

### Strategies

- CC-5.1.1** Collate and condense guidelines for referral and/or management recommendations of childhood cancer survivors for primary care physicians including a summary of medical care.
- CC-5.1.2** Disseminate condensed guidelines for management of childhood cancer survivors through the New Jersey Department of Health and Senior Services, Office of Cancer Control and Prevention website and/or printed updates for all practitioners. Update as new information becomes available.



## GOAL CC-6

To increase the awareness of neurocognitive and psychosocial deficits in childhood cancer patients.

### Objective CC-6.1

To educate patients and families on neurocognitive deficits in childhood cancer patients post treatment.

### Strategy

**CC-6.1.1** Collaborate with other organizations to maintain a statewide educational forum for educators, childhood cancer survivors, and family members that would address the issue of neurocognitive deficit.

## ADVOCACY

Advocacy for individual childhood cancer patients and their families should begin at the time of diagnosis. Education and advocacy are inextricably intertwined. Parents who are still in shock after being told their child has cancer must suddenly deal with a multitude of problems. They must learn the unfamiliar skills involved in taking care of their sick child, such as administering medications on schedule and taking care of central venous catheters. They must learn how to interact with the school system to ensure their child receives an appropriate education and is not penalized for having to miss school. They must also continue to meet the ongoing, day-to-day needs of the patient's siblings. One parent may need to take a leave of absence from work, or even relinquish a job to devote additional time to their sick child.

Legislation passed in the mid-1990s has given patients and their families some new rights regarding education and health insurance. Parents should learn what Family Medical Leave Act benefits entail in order to obtain a leave of absence from work without penalty.

**Education.** The various legal protections, programs, and designations available to children with cancer and their families are well described in Keene et al.,<sup>33</sup> Weiner et al.,<sup>34</sup> and Monaco et al.<sup>35</sup> For various reasons, some schools and systems are easier to work with than others. Parents may need help in negotiating with an individual school system. Fortunately, the guidelines in these references are reasonably clear and straightforward. A child receiving treatment should be eligible for a number of programs designed to permit continuation of schooling. Because of the late effects of some types of treatment (e.g., cranial irradiation), children may not experience learning difficulties until years after conclusion of treatment. A child who has always managed to do well in grade school by working hard may be unable to handle the additional work required in junior high or high school. Not all child study teams or school psychologists (to say nothing of teachers) are aware of the learning problems children with cancer or survivors of childhood cancer may face.



**Employment.** Keene et al.,<sup>33</sup> Weiner et al.,<sup>34</sup> and Monaco et al.<sup>35</sup> also explain the legal protections and practicalities of employment. The fact is noted, for example, that a potential employer has no right to ask health history questions or to require a physical examination until after a preliminary job offer has been made. The importance of accurate assessment of cancer survivors' abilities and appropriate vocational counseling is also mentioned. It is particularly important that survivors left with neuropsychological problems and/or neurodevelopmental delay be given adequate support, as they are at increased risk of being unable to secure or maintain a job. Unfortunately, many survivors who have had brain tumors or who have required high doses of cranial irradiation are left with such neurological deficits.

**Insurance (during the child's treatment).** Few people are familiar with all the nuances of their health insurance coverage. Such dearth of knowledge is further complicated by the changes frequently made in these plans requiring prior authorization or requiring laboratory tests to be performed at designated facilities. Different insurance companies and health maintenance organizations (HMOs) vary greatly in their procedures and requirements related to the patient's care. Sometimes the procedures required by the insurance companies actually delay a patient's care. One program that many New Jersey residents are unaware of is the New Jersey Department of Human Services Catastrophic Illness in Children Relief Fund. This fund provides financial assistance for children's medical expenses that are not fully covered by insurance, state, federal programs, or other sources and meet the program's income requirements.

**Insurance (for the cancer survivor).** Vann et al.<sup>36</sup> found that young adult survivors of childhood cancer were "more likely to be denied health insurance than their siblings, with an adjusted odds ratio of 15.1" and "had health insurance policies that excluded care for pre-existing medical conditions more often than their siblings (OR = 5.5)." Now the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and the Consolidated Omnibus Budget Reconciliation Act of 1985 (COBRA) have improved the situation for cancer survivors and their families. If a parent of a child diagnosed with cancer or a cancer survivor changes jobs, these laws protect them from losing their health insurance. If a family (or patient) does not have insurance in effect at the time of diagnosis, it can still be extremely difficult to obtain insurance. If a young adult who has survived childhood cancer no longer qualifies for coverage under his parent's insurance, he may find it nearly impossible to obtain health insurance coverage without a substantial waiting period (usually a year) for coverage of pre-existing conditions. Private individual insurance may be prohibitively expensive; an insurer cannot refuse to issue a policy, but the premiums may be very high because of an individual's health history. The guide by Keene et al. advises the cancer survivor not to look for a job in a small company: "The easiest way to get insurance is for you or your spouse to work for a large corporation or government agency that provides a group health insurance policy. The larger the pool of employees, the less likely you are to be rejected from health coverage..."<sup>33</sup>

Despite some progress, cancer survivors have more difficulty obtaining insurance than their peers, and this situation is not likely to improve. The results of several studies of five-year (and more) survivors of childhood cancer have reported the incidence of secondary malignancies in these patients and an increased late mortality experience, e.g., deaths due to late effects of chemotherapy and radiation, not just to relapsed cancer or secondary malignancies.<sup>37</sup> A program to follow survivors of childhood cancer will use the results of these studies to plan for screening for cardiac or pulmonary dysfunction, as well as secondary malignancies.<sup>18</sup> Will insurance pay for these tests? Will an insurer consent to enroll a new client with these documented additional risks?

An increasing number of "cancer genes" have also been identified. Li's exemplary discussion of the dilemmas posed by detecting one of these genes in an individual (and in a family) includes the RB1



retinoblastoma gene.<sup>38</sup> Fortunately, it is very rare: an infant who inherits the RB1 gene has a 90% likelihood of developing retinoblastoma, usually in both eyes. The child who survives hereditary retinoblastoma has an increasing chance of subsequently developing another cancer; a 50% likelihood of developing another cancer by age 50 (compared to a 5% risk of a second cancer in a patient with sporadic retinoblastoma). As each new cancer gene is identified, the dual opportunity appears. The physician can potentially identify a patient who should have earlier and more frequent screening for particular cancers, thereby increasing the probability of early detection (and, hopefully, cure) of cancer. Yet the insurer can also potentially identify a high-risk participant. Although legislation has been developed to protect the privacy of patients, and various attempts have been made to prevent insurance companies from obtaining the results of tests for cancer genes, legal protections need to be developed to allow physicians to order appropriate screening for at-risk individuals without breaking confidentiality requirements.

**Long-term follow-up.** Oeffinger et al. sent a brief questionnaire to the 219 institutional members of the Children’s Cancer Group and Pediatric Oncology Group; 182 members responded.<sup>39,40</sup> Only 80 of the institutions who responded had long-term follow-up clinics. Although 44% had a mechanism for following up adult survivors, only 15% of the programs had established a formal data base for young adults. The institutions were asked which of several factors interfered with long-term cancer-related follow-up for young adults, and responses included patients’ uncertainty about the need for follow-up (76%), patients’ unwillingness to come (66%), and lack of insurance (63%). The same group found that among the 99 patients participating in the long-term follow-up program, 69% had at least one late effect (36% had two or more) and 30% had a CTCv2 Grade 3 or 4 late effect (Common Toxicity Criteria, version 2, of NCI). Sklar reported that of 650 survivors followed in the Long Term Follow-Up Clinic at Memorial Sloan-Kettering Cancer Center, “the most common sequelae are endocrine complications, which are seen in 40% of the patients.”<sup>41</sup> Strickland et al. reported that among those surviving patients transfused between 1961 and March 1992, 66% were found to be infected with Hepatitis C.<sup>42</sup>

With HMOs dropping Medicare populations and then Medicaid populations because of the expense involved in their care, protecting these “predictably expensive” childhood cancer patients and survivors will be a difficult undertaking.

**Conclusions.** The importance of educating cancer survivors cannot be overemphasized. Blacklay et al. describe providing an information booklet to 50 adult survivors of cancer in childhood.<sup>43</sup> The booklet for survivors over the age of 14 included “information about treatment of cancer, general advice about a healthy lifestyle, the rationale for long-term follow-up, and information about employment and life insurance problems.” A small survey was then administered to these patients to evaluate whether the booklet had been effective. Over three-quarters of the patients reported they had learned new information from the booklet and better understood the risks of sunbathing and the importance of follow-up.

Perhaps the simplest solution to the problems of educating patients and families about the complications and possible late effects of the disease, as well as about problems likely to be encountered in education, employment, and insurance, would be to distribute a copy of the book by Keene, Hobbie, and Ruccione.<sup>33</sup> It is remarkably comprehensive, practical, and easy to read. Published in 2000, it includes numerous helpful references and websites, as well as email addresses of two of the authors to assist patients in locating follow-up clinics.



**GOAL CC-7**

To increase advocacy for childhood cancer, especially on issues related to long-term survivorship, education, employment, and insurance coverage.

**Objective CC-7.1**

To educate legislators and key decision-makers about issues in childhood cancer.

**Strategies**

- CC-7.1.1** Collaborate with grassroots childhood survivorship organizations to advocate for childhood cancer issues.
- CC-7.1.2** Develop and obtain funding for an advocacy campaign on childhood cancer concerns targeting legislators.

**Objective CC-7.2**

To educate childhood cancer survivors and families about issues in childhood cancer.

**Strategies**

- CC-7.2.1** Investigate established models for teaching childhood cancer advocacy to the lay community. Host a statewide conference for parents and childhood cancer survivors utilizing the model with demonstrated effectiveness for teaching advocacy.
- CC-7.2.2** Collaborate with multi-disciplinary organizations, e.g., American Cancer Society, Inc., New Jersey Education Association, New Jersey State School Nurses Association, to re-institute educator conferences on childhood cancer survivorship issues.



### Objective CC-7.3

To educate insurance companies about issues in childhood cancer.

#### Strategy

**CC-7.3.1** Utilize the grassroots childhood cancer survivorship organization to educate insurance companies on the cost effectiveness of surveillance.

**GOAL CC-8** To ensure that New Jersey residents and physicians remain up to date on currently available childhood cancer technologies and resources.

### Objective CC-8.1

To continue to monitor and disseminate current advances in childhood cancer diagnosis and treatment.

#### Strategies

**CC-8.1.1** Conduct periodic literature reviews to determine the state of the science in childhood cancer research and to identify potentially promising new technologies.

**CC-8.1.2** Work with stakeholders to disseminate, as they become available, evidence-based advances to healthcare providers through CME offerings.

### Objective CC-8.2

To continue to monitor trends in childhood cancer incidence, mortality, and survival.

#### Strategy

**CC-8.2.1** Request appropriate data, as needed, from the New Jersey State Cancer Registry and other applicable sources.



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