

# Special Section: Cancer in Children & Adolescents

## Overview

The news of a cancer diagnosis is never welcome, but may be even more unexpected and difficult when the disease is diagnosed in a child or adolescent. Although cancer is much less common among children compared to older adults, approximately 1 in 285 children in the US will be diagnosed with the disease before the age of 20. While advances in treatment have increased the survival rate for many childhood cancers, the disease is still the second leading cause of death (following accidents) in children ages 5-14.<sup>1</sup>

The types of cancers that develop in children and adolescents differ from those that develop in adults. The predominant types of pediatric cancers (ages 0-19) are leukemia (26%), cancers of the brain and central nervous system (CNS) (18%), and lymphoma (14%). Some of the cancers that develop in children are rarely seen in older individuals, notably those cancers that arise from embryonic cells and originate in developing tissues and organ systems. Embryonal cancers include neuroblastoma (sympathetic peripheral nervous system), Wilms tumor or nephroblastoma (developing kidney), medulloblastomas (brain), rhabdomyosarcomas (muscle), and retinoblastoma (retina of the eye). Some pediatric cancers, particularly those that are more common in adolescents, are more similar to those that arise in adults (e.g., acute myeloid leukemia, Hodgkin lymphoma, thyroid cancer, and melanoma).

Pediatric cancers represent 1% of all new cancers diagnosed in the US. Because these cancers occur in the context of rapid growth and development, most experts strongly recommend that they be treated at medical centers specialized in childhood cancer by multidisciplinary teams including pediatric oncologists, surgeons, radiation oncologists, and other specialists. At pediatric cancer centers, treatment protocols are available for most types of cancer that occur in children and adolescents, and the opportunity to participate in clinical trials is offered to most patients and their families. Clinical trials are generally designed to compare a potential improvement in therapy with therapy that is currently accepted as standard; improvements may result in an increase in cure rates or a reduction in acute or long-term complications. Member institutions of the Children's Oncology

Group (COG), a National Cancer Institute-supported clinical trials group, care for more than 90% of US children and adolescents diagnosed with cancer ([childrensoncologygroup.org](http://childrensoncologygroup.org)). The COG has nearly 100 active clinical trials open at any given time, which include studies to test the efficacy of new treatments for many types of childhood cancers at diagnosis or recurrent diseases, improve understanding of the underlying biology of these diseases, and improve supportive care and survivorship. Children and adolescents diagnosed with types of cancer more commonly seen in adults also benefit from treatment in pediatric cancer centers.

In this special section, we provide an overview of trends in incidence, mortality, and survival for cancers commonly diagnosed in children and adolescents. We also provide more detailed information on risk factors, symptoms, treatment, and important long-term and late effects for these cancers. The major types of cancers included are: leukemias and lymphomas, brain and CNS tumors, embryonal tumors, sarcomas of bone and soft tissue, and gonadal germ cell tumors.

## How Many Cases and Deaths Are Expected to Occur in 2014?

An estimated 10,450 new cases and 1,350 cancer deaths are expected to occur among children (ages 0-14) in 2014. The corresponding figures among adolescents (ages 15-19) are 5,330 new cases and 610 cancer deaths.

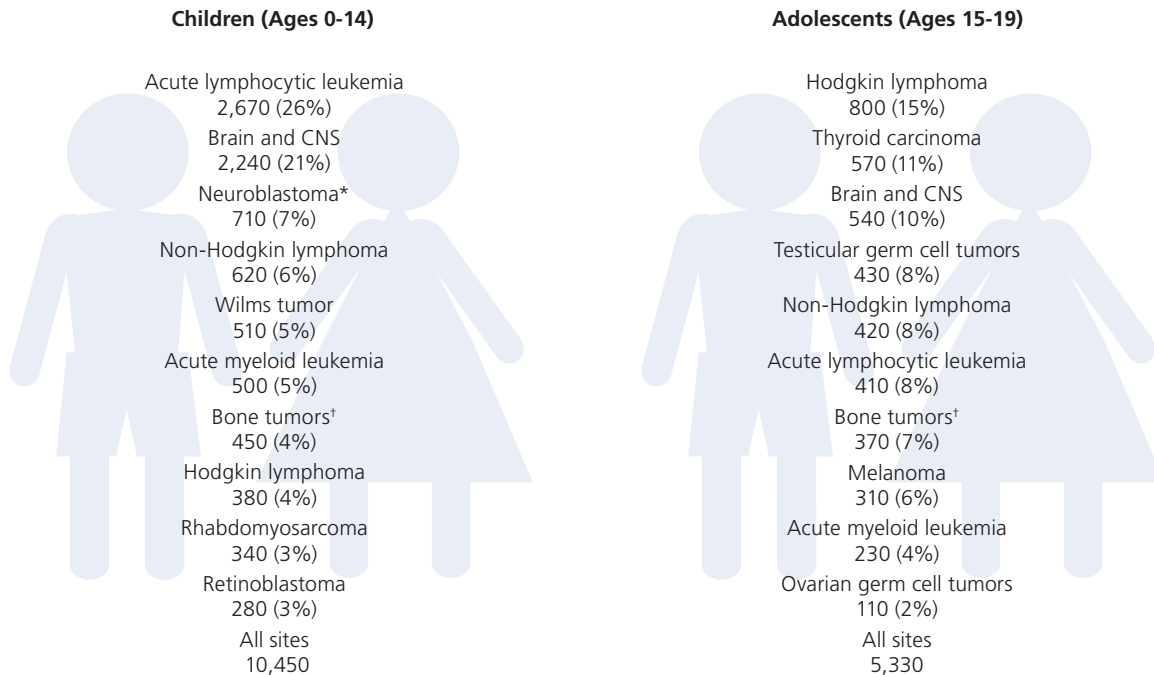
## What Are the Most Common Cancers in Children and Adolescents?

The most common cancers among children and adolescents vary by age and are shown in Figure 1 (page 26).

- Cancers that are most common in children ages 0-14 are acute lymphocytic leukemia (26%), brain and CNS (21%), neuroblastoma (7%), and non-Hodgkin lymphoma (6%).
- The most common cancers among adolescents ages 15-19 are Hodgkin lymphoma (15%), thyroid carcinoma (11%), brain and CNS (10%), and testicular germ cell tumors (8%).

While cancers occurring in adults are classified by the anatomical site of the primary tumor, cancers in children and younger adolescents are classified by histology (tissue type) into 12 major groups using the International Classification of Childhood Cancers (ICCC).<sup>2</sup> Figure 1 (page 26) shows the distribution of the most common cancers in children and adolescents by ICCC group.

**Figure 1. Estimated Cases for Childhood and Adolescent Cancers, US, 2014**



Estimates are for malignant cancers only and are rounded to the nearest 10. In addition, 730 children and 630 adolescents will be diagnosed with benign and borderline brain tumors in 2014.

CNS = central nervous system

\* Includes ganglioneuroblastoma.

† Bone tumors include osteosarcoma and Ewing sarcoma.

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## How Do Childhood and Adolescent Cancers Vary in the US Population?

Table 1 (page 28) summarizes differences in cancer incidence, mortality, and survival rates by sex and race/ethnicity.

### Sex

- In children, incidence and mortality rates are lower in girls than in boys, while survival rates are similar.
- In adolescents, boys and girls have similar incidence rates, while mortality rates are lower and survival is higher for girls. Some of these differences may reflect the different types of cancers that occur in boys compared to girls in this age group.

### Race/Ethnicity

Cancer incidence, mortality, and survival rates show substantial variability by race and ethnicity.

- Non-Hispanic white (white) and Hispanic children have the highest incidence rates for childhood and adolescent cancers.
- Although incidence rates are substantially lower for non-Hispanic black (African American) children and adolescents than for whites and Hispanics, death rates are similar due to lower survival rates in African Americans.

- Incidence and mortality rates for Asian American/Pacific Islander children are lower than those for whites and generally similar to rates in African American children.
- American Indian/Alaska Native children have the lowest cancer incidence and mortality of all racial/ethnic groups.

Reasons for differences in incidence rates of childhood cancers by race and ethnicity in the US are not well understood. Unlike many adult cancers, incidence is not consistently higher among populations with lower socioeconomic status.<sup>3</sup> In general, the incidence of pediatric cancer is higher in industrialized countries than in developing countries, but patterns differ by cancer type.<sup>4, 5</sup>

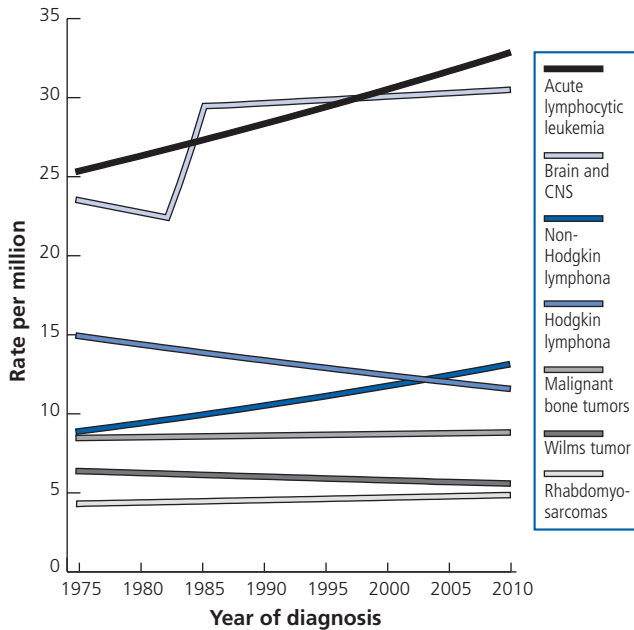
Racial and ethnic disparities in survival for childhood and adolescent cancers have been noted previously.<sup>6, 7</sup> Factors that may be associated with these survival disparities include socioeconomic status, health insurance status, timely diagnosis and quality of treatment and supportive care, and genetic factors.<sup>6</sup>

## How Has the Occurrence of Pediatric Cancers Changed over Time?

### Trends in incidence rates

From 1975 to 2010, the overall incidence of pediatric cancer in the US increased slightly, by an average of 0.6% per year.<sup>8</sup> Specific-

**Figure 2. Trends in Pediatric Cancer Incidence Rates by Site, Ages 0-19, 1975-2010**



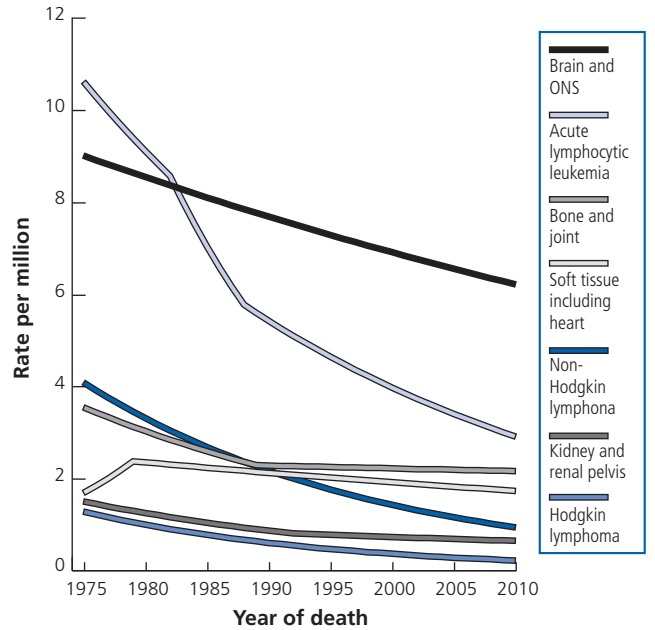
CNS = Central nervous system.

**Note:** lines represent Joinpoint fitted trends. Benign and borderline brain tumors are not included. Malignant bone tumors include osteosarcoma and Ewing sarcoma. Average annual percent change (APC) for cancers with significant trends during most recent period: ALL (0.7), NHL (1.1), and Hodgkin lymphoma (-0.7).

**Source:** Surveillance, Epidemiology, and End Results (SEER) Program, 9 SEER Registries, National Cancer Institute.

American Cancer Society, Surveillance Research, 2014

**Figure 3. Trends in Pediatric Cancer Mortality Rates by Site, Ages 0-19, 1975-2010**



ONS = Other nervous system.

**Note:** Lines are fitted trends based on Joinpoint analyses.

Average annual percent change (APC) for cancers with significant trends during most recent period: ALL (-3.1 during 1988-2010), brain (-1.1 during 1975-2010), NHL (-4.1 during 1975-2010), soft tissue (-1.0 during 1979-2010), kidney (-1.2 during 1992-2010), HL (-4.9 during 1975-2010).

**Source:** National Center for Health Statistics, Centers for Disease Control and Prevention.

American Cancer Society, Surveillance Research, 2014

cally, incidence rates increased for 4 cancer types: acute lymphocytic leukemia, acute myeloid leukemia, non-Hodgkin lymphoma, and testicular germ cell tumors. Incidence rates decreased for Hodgkin lymphoma and remained stable for other cancers (Figure 2). Similar incidence patterns were observed in Europe.<sup>9</sup> Reasons for increases in incidence rates are largely unknown. It is possible that some of this increase may be due to changes in environmental factors. Improved diagnosis and access to medical care over time may also have contributed, as without medical care some children may die of infections or other complications of their cancers without ever being diagnosed.<sup>10</sup> The sharp rise in incidence of CNS tumors that occurred in the 1980s is thought to reflect increased detection of tumors as a result of the introduction of magnetic resonance imaging (MRI) and stereotactic biopsy (biopsy accompanied by computer imaging), leading to more complete reporting (see section on CNS tumors, page 32).<sup>11</sup>

### Trends in mortality rates

Death rates for all childhood and adolescent cancers combined declined steadily from 1975 to 2010 by an average of 2.1% per year resulting in an overall decline of more than 50%. Mortality

declines were observed for all sites in Figure 3 with the steepest declines in Hodgkin lymphoma, non-Hodgkin lymphoma, and acute lymphocytic leukemia. (Please note that the classification of tumors in Figure 3 differs from that used in other tables and figures because deaths are classified according to anatomic site rather than International Classification of Childhood Cancers group.)

### What Is the Probability of Developing a Childhood or Adolescent Cancer?

A child born in the United States has a 0.24% chance of developing cancer before age 15 and a 0.35% chance of developing cancer before age 20.<sup>8</sup> Another way of saying that is 1 in 408 children will be diagnosed with cancer before age 15 and 1 in 285 children will be diagnosed with cancer before age 20.

### How Many Survivors of Pediatric Cancer Are in the US?

An estimated 379,112 survivors of childhood and adolescent cancer (diagnosed at ages 0-19) were alive in the US as of January 1, 2010. The top three cancer types among childhood cancers

**Table 1. Incidence, Mortality, and Survival Rates for Childhood and Adolescent Cancers by Sex and Race/Ethnicity**

Characteristic	Ages 0–14			Ages 15–19		
	Incidence, 2006-2010*	Mortality, 2006-2010*	Observed Survival (%), 2003-2009	Incidence, 2006-2010*	Mortality, 2006-2010*	Observed Survival (%), 2003-2009
<b>Sex</b>						
Boys	178.0	23.3	81.3	237.7	34.5	80.0
Girls	160.1	21.1	82.0	235.5	24.7	85.4
<b>Race/ethnicity</b>						
Non-Hispanic White	178.2	22.4	84.2	259.4	29.0	85.9
Non-Hispanic Black	134.5	21.9	75.3	171.9	30.6	76.8
Hispanic	167.3	22.6	80.3	220.7	32.4	75.8
Asian American/ Pacific Islander	131.9	19.1	78.3	167.8	25.6	80.4
American Indian/ Alaska Native†	117.1	15.8	78.5	200.1	24.0	77.3

\*Rates are per 1,000,000 and age-adjusted to the 2000 US standard population. †Based on data from Indian Health Service Contract Health Service Delivery Areas.

**Note:** Incidence rates include benign and borderline brain tumors.

**Source:** Incidence: North American Association of Central Cancer Registries; Mortality: National Center for Health Statistics, Centers for Disease Control and Prevention; Survival: Surveillance, Epidemiology and End Results (SEER) Program, 18 SEER Registries, National Cancer Institute.

American Cancer Society, Surveillance Research, 2014

survivors are acute lymphocytic leukemia, brain and CNS tumors, and Hodgkin lymphoma (Table 2). Most (70%) survivors of childhood and adolescent cancer are 20 years of age or older. Approximately 1 in 530 adults between the ages of 20 and 39 is a survivor of childhood cancer.

## What Are the Risk Factors for Childhood and Adolescent Cancer?

In contrast to cancers in adults, only a relatively small proportion of childhood cancers have known or preventable causes. Ionizing radiation exposure is a well-recognized risk factor for cancer in children and adolescents based on studies of medical and environmental radiation exposure. The association between low doses of radiation received by an unborn fetus during an x-ray and subsequent risk of leukemia and other childhood cancers was demonstrated in the 1950s.<sup>12</sup> As a result, precautions have been taken to minimize radiation exposure during pregnancy, so this exposure is not likely to be of current concern. Radiation exposure from diagnostic CT scans is higher and more variable than exposures from conventional x-rays, and studies suggest that radiation exposure early in life increases long-term risk of leukemia and brain cancer.<sup>13</sup> Health care providers are encouraged to limit the use of CT scans to situations where there is a definite clinical indication and to optimize scans using the lowest possible radiation dose.<sup>14</sup>

A number of recent studies have found that accelerated fetal growth and higher birth weight are associated with increased

risk for some childhood and adolescent cancers, including acute lymphocytic leukemia, central nervous system (CNS) tumors, Wilms tumor, non-Hodgkin lymphoma, and rhabdomyosarcoma, while lower birth weight has been associated with acute myeloid leukemia and some CNS tumor subtypes.<sup>15-21</sup> Although numerous epidemiologic studies have investigated potential environmental causes of childhood cancers, few strong or consistent associations have been found. The International Agency for Research on Cancer has concluded there is sufficient evidence that parental smoking increases the risk of hepatoblastoma (a type of liver cancer that occurs in young children) and limited evidence for an association with childhood leukemia (particularly ALL).<sup>22</sup> They also found limited evidence that maternal exposure to paint is linked with childhood leukemia.<sup>22</sup> Larger studies with the ability to examine specific histological and/or molecular tumor subtypes may be needed to identify and confirm potential environmental causes of childhood cancer.<sup>23</sup> It is reasonable to suggest that pediatric tumors reflect, at least in part, an inherent risk associated with the complex process of normal development and chance rather than a response to an external exposure. At the same time, it is known that the process of development occurring in immature cells and organisms renders them more vulnerable to toxic exposures than mature cells, and it is therefore important to minimize exposure to environmental agents with potential cancer-causing effects.<sup>24</sup> For more information on precautions to minimize exposures during pregnancy, see sidebar.

**Table 2. US Childhood and Adolescent Cancer Survivors by Cancer Site, as of January 1, 2010**

**Complete Prevalence Counts  
by Age at Prevalence**

Site	Ages 0–19	Ages 20+	All Ages
All Sites	113,782	265,330	379,112
Acute lymphocytic leukemia	30,171	30,318	60,489
Acute myeloid leukemia	4,045	4,222	8,267
Hodgkin lymphoma	4,514	30,739	35,253
Non-Hodgkin lymphoma	6,442	16,301	22,743
Brain and CNS	20,430	38,653	59,083
Neuroblastoma	9,704	9,748	19,452
Wilms tumor	7,831	15,707	23,538
Bone tumors	3,766	9,366	13,132
Soft tissue sarcomas	6,849	24,599	31,448
Testicular germ cell tumors	2,755	17,890	20,645
Ovarian germ cell tumors	2,464	14,628	17,092

CNS= central nervous system.

**Note:** Does not include benign and borderline brain tumors.

**Source:** Howlader, et al, 2013.<sup>8</sup>

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Some pediatric cancers, such as Wilms tumor and retinoblastoma, are associated with recognized genetic factors. Potential environmental and genetic risk factors for pediatric cancers will be discussed in relation to specific cancer types.

## What Are Signs and Symptoms for Pediatric Cancers?

Early diagnosis of cancer in children is often difficult because of the similarity of symptoms to more common diseases of childhood.<sup>27</sup> Parents should ensure that children have regular medical checkups and be alert to any unusual signs or persistent symptoms. Some common symptoms of childhood cancer that should alert parents and health care providers include an unusual mass or swelling; unexplained paleness or loss of energy; a sudden tendency to bruise; a persistent, localized pain or limping; a prolonged, unexplained fever or illness; frequent headaches, often with vomiting; sudden eye or vision changes; and excessive, rapid weight loss. Information on symptoms for specific cancer types is discussed in the next section.

## Major Cancer Types

### Leukemia and lymphoma

Leukemia is a cancer of blood-forming cells arising in the bone marrow. Lymphomas are cancers of a certain type of white blood cell (lymphocyte) that can arise anywhere lymphocytes can be found, including bone marrow, lymph nodes, the spleen, the intestines, and other areas of the lymphatic system. Leuke-

## Precautions to Minimize Exposures during Pregnancy

Some of the changes in cells that lead to the development of childhood cancer may take place during pregnancy. Radiation exposures, both in utero and during early life, have been found to increase cancer risk. It is also possible that environmental exposures to either parent prior to the child's conception may influence childhood cancer risk. Research studies have not identified strong and consistent preventable causes of childhood cancer (other than exposure to ionizing radiation). However, since the developing fetus is more sensitive to some exposures than adults, women are advised to take precautions to minimize exposures during pregnancy. With respect to environmental exposures, the Office of Women's Health, Department of Health and Human Services recommends that during pregnancy, women should avoid exposure to:<sup>25</sup>

- Lead – Found in some water and paints, mainly in homes built before 1978
- Mercury – The harmful form is found mainly in large, predatory fish.
- Arsenic – High levels can be found in some well water.
- Pesticides – Both household products and agricultural pesticides
- Solvents – Such as degreasers and paint strippers and thinners
- Cigarette smoke

Additional precautions include:

- Clean in only well-ventilated spaces. Open the windows or turn on a fan.
- Check product labels for warnings for pregnant women and follow instructions for safe use.
- Do not clean the inside of an oven while pregnant.
- Leave the house if paint is being used, and don't return until the fumes are gone.

The National Institute for Occupational Safety and Health provides additional recommendations for women who are employed in occupations with potential toxic exposures.<sup>26</sup>

mias and lymphomas are classified according to the type of cell that is exhibiting uncontrolled growth.

The two most common types of leukemia in children and adolescents are acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML). Chronic leukemias are very rare in children and adolescents. ALL accounts for about 80% of leukemia cases in children and 56% of leukemia cases in adolescents. Acute myeloid leukemia (AML) is less common in children than ALL, comprising about 15% of leukemia cases in children and 31% in adolescents. There are two types of lymphoma: Hodgkin



lymphoma (HL) and non-Hodgkin lymphoma (NHL). HL accounts for about 38% of lymphomas in children and about 65% in adolescents, while NHL accounts for 62% of lymphomas in children and 35% of lymphomas in adolescents.

### Acute lymphocytic leukemia (ALL)

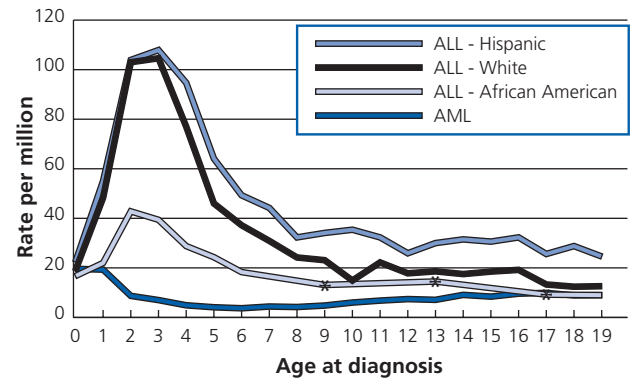
An estimated 2,670 children and 410 adolescents will be diagnosed with ALL in 2014 (Figure 1, page 26). ALL is the most common cancer in children, accounting for 26% of cancers diagnosed in ages 0-14. Similar to lymphomas, ALL is a cancer of lymphocytes. Most often ALL in children involves B lymphocytes, the type of lymphocyte that makes antibodies to infections, but it can also involve T lymphocytes, which help the body fight disease in other ways.

ALL occurs in children throughout the world, but it is more common in industrialized countries than in developing countries. In the US, ALL is more common in boys than in girls and in Hispanic and white children than in African American children (Table 3). In industrialized countries, there is a sharp peak in ALL incidence rates at ages 2-4, which is not apparent among children in developing countries.<sup>10</sup> The characteristic age peak for ALL in the US is striking for white and Hispanic children, but less so for African American children (Figure 4).

There is evidence that some cases of ALL arise in utero, including a frequent concordance of ALL in identical twins.<sup>28</sup> Inherited risk factors associated with ALL include trisomy 21 (Down syndrome), which confers a 10- to 20-fold increased risk, certain genetic syndromes (Bloom syndrome, Fanconi anemia, and Nijmegen breakage syndrome) and congenital immunodeficiency diseases.<sup>28</sup> Although many epidemiologic studies have sought to find the causes of ALL, few environmental agents are definitively linked with this disease. According to the International Agency for Research on Cancer, there is limited evidence that parental smoking and maternal exposure to paint increase the risk for childhood leukemia (particularly ALL).<sup>22</sup> Higher birth weight has also been associated with higher ALL risk in a number of studies.<sup>23, 29</sup> Recent studies suggest that early exposure to infections (such as occurs in infant day care settings) may be protective for childhood ALL.<sup>30, 31</sup>

Improved treatment for ALL in childhood has increased the 5-year survival rate from 57% in 1975-1979 to 90% in 2003-2009 (Table 4, page 35). Treatment is generally in three phases, and consists of 4-6 weeks of induction chemotherapy (chemotherapy given to induce remission) administered in the hospital, followed by several months of consolidation chemotherapy and 2-3 years of maintenance chemotherapy.<sup>28</sup> The central nervous system (CNS) is a common site for relapse, so children receive specific treatment to prevent this (CNS prophylaxis). Bone marrow transplantation is recommended for some children whose leukemia has high-risk characteristics at diagnosis and for children who relapse after remission.<sup>28</sup> It may also be used if the

**Figure 4. Age-specific Incidence Rates of Acute Lymphocytic Leukemia (ALL) by Race/ethnicity and Acute Myeloid Leukemia (AML) All Races Combined, 2001-2010**



**Note:** Data not shown for ages with fewer than 25 cases. Data for whites and African Americans exclude Hispanic ethnicity. Due to sparse data for ALL in African Americans for some ages, data are shown for combined age groups: 7-10, 11-14, 15-19 marked by asterisks.

**Source:** Surveillance, Epidemiology, and End Results (SEER) Program, 18 SEER Registries, National Cancer Institute.

American Cancer Society, Surveillance Research, 2014

leukemia does not go into remission after a successive course of induction chemotherapy. Successful treatment of ALL requires multidisciplinary teams to provide supportive care and careful monitoring for infection and adequate nutrition.

Disparities in survival between white and African American children treated for ALL have been documented in a number of studies.<sup>4, 5, 32</sup> Notably, this disparity has diminished in recent years, from a 21% difference in 5-year survival during 1980-84 (68% vs. 47%, in whites and African Americans, respectively) to a 6% difference in 2003-2009 (90% vs. 84%, respectively).<sup>33</sup>

Long-term adverse health effects among children treated for ALL can include neurocognitive defects, growth deficiency, and increased risk of second cancers, including AML and CNS tumors.<sup>34</sup> Early forms of CNS prophylaxis that combined high doses of radiation and intrathecal (injected into the fluid surrounding the brain and spinal cord) chemotherapy had a high risk of damage to brain tissue resulting in neurocognitive defects; less toxic therapies that avoid the use of radiation have reduced, but not eliminated these risks. Radiation therapy is now used in only a small fraction of ALL patients at high risk of CNS relapse. Children treated with anthracyclines are at risk for late cardiac effects.<sup>28</sup>

### Acute myeloid leukemia

An estimated 500 children and 230 adolescents will be diagnosed with AML in 2014. AML arises from blood-forming cells, most often those that would turn into white blood cells (except

lymphocytes). The incidence of AML is highest in the first two years of life (Figure 4). Incidence rates for AML are slightly higher in Hispanic children compared to other racial/ethnic groups (Table 3).

Radiation exposure is an established risk factor for childhood leukemia, and some studies have found associations of childhood leukemia with specific chemicals, such as benzene, and drugs used to treat cancer, such as alkylating agents and topoisomerase II inhibitors; these are more strongly associated with AML than ALL.<sup>35</sup>

Children with AML and high white blood cell counts may develop symptoms due to impaired transit of cancer cells (blasts) through small blood vessels.<sup>36</sup> Many AML patients are prone to excessive bleeding and other blood clotting disorders. Death occurs during the first 2 weeks after diagnosis in 2-4% of children with AML.<sup>36</sup> Treatment for AML consists of induction chemotherapy, CNS prophylaxis, and post-remission therapy. Stem cell transplant has been investigated in clinical trials and has been shown to improve survival rates for some children with

AML.<sup>36</sup> Treatment toxicity and long-term effects for AML are similar to those for ALL; however, AML less often requires treatment or prophylaxis of the CNS, so side effects related to radiation of the brain are not as common.<sup>36</sup> The 5-year survival rate for AML for children diagnosed in 2003-2009 was 64% (Table 4, page 35). Survival rates for AML have improved in recent decades, but remain lower than for ALL.

### Hodgkin lymphoma

An estimated 380 children and 800 adolescents will be diagnosed with HL in 2014. HL is a cancer of lymphocytes that often starts in the lymph nodes in the chest, neck, or abdomen. There are two major types of HL: classic, which is the most common and is characterized by the presence of multinucleated giant cells called Reed-Sternberg cells, and nodular lymphocyte predominant, which is characterized by so called “popcorn cells.” This type is rare and tends to be slower growing than the classic form.<sup>37</sup>

HL is rare among children younger than age 5; incidence rates increase slightly up to about age 10 and then rise rapidly through

**Table 3. Pediatric Cancer Incidence Rates\* by Sex and Race/Ethnicity, Ages 0-19, US, 2006-2010**

	All Races		Non-Hispanic White	Non-Hispanic Black	Hispanic	Asian American/ Pacific Islander
	Boys	Girls				
All ICCC sites	196.7	182.3	201.7	146.1	184.2	140.8
Leukemia	52.0	43.1	46.9	29.9	59.6	39.4
Acute lymphocytic leukemia	38.4	30.2	34.2	18.3	44.9	28.7
Acute myeloid leukemia	7.9	8.0	7.7	7.1	8.7	8.0
Lymphomas and reticuloendothelial neoplasms	29.8	20.7	27.4	22.2	21.6	18.3
Hodgkin lymphoma	12.9	11.8	13.9	10.3	10.2	7.5
Non-Hodgkin lymphoma	15.1	7.7	11.9	11.4	9.5	10.0
Brain and CNS	45.5	45.9	50.9	36.1	38.7	28.6
Ependymoma	3.2	2.4	3.0	2.1	2.7	2.6
Astrocytoma	16.5	15.5	18.8	12.3	12.0	9.1
Medulloblastomas	5.1	3.3	4.8	2.7	3.7	3.3
Neuroblastoma and ganglioneuroblastoma	8.5	7.6	9.7	6.8	5.2	5.9
Retinoblastoma	2.9	3.3	2.7	3.4	3.4	3.1
Wilms tumor	5.3	6.3	6.2	6.7	4.5	2.9
Hepatic tumors	2.8	1.8	2.2	1.7	2.5	3.0
Bone tumors	9.8	7.7	9.2	7.2	8.9	6.7
Osteosarcoma	5.5	4.5	4.6	5.7	5.4	3.9
Ewing sarcoma	3.3	2.4	3.7	0.5	2.5	2.0
Rhabdomyosarcoma	5.4	4.2	4.8	5.5	4.5	2.9
Testicular germ cell tumors	9.9	---	10.9	1.4	13.6	6.1
Ovarian germ cell tumors	---	4.4	3.4	5.3	6.1	4.7
Thyroid carcinoma	3.0	12.6	9.1	2.8	7.2	6.9
Melanoma	3.7	5.8	7.1	0.5	1.4	†

ICCC=International classification of childhood cancers. CNS=Central nervous system.

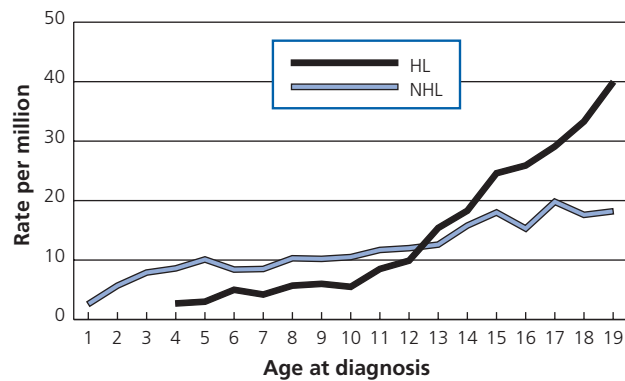
\*Rates are per 1,000,000 and age-adjusted to the 2000 US standard population. †Statistic not displayed if based on fewer than 25 cases.

Note: Rates include benign and borderline brain tumors.

Source: North American Association of Central Cancer Registries. Data are included from all US states and the District of Columbia except Arkansas, Minnesota, Nevada, Ohio, and Virginia. Rates by Hispanic ethnicity also exclude data from Massachusetts.

American Cancer Society, Surveillance Research 2014

**Figure 5. Age-specific Incidence Rates of Non-Hodgkin Lymphoma (NHL) and Hodgkin Lymphoma (HL), 2001-2010**



Note: Data not shown for ages with fewer than 25 cases.

Source: Surveillance, Epidemiology, and End Results (SEER) Program, 18 SEER Registries, National Cancer Institute.

American Cancer Society, Surveillance Research, 2014

adolescence (Figure 5). HL is the most common cancer in adolescents, accounting for about 15% of cancers diagnosed between ages 15 and 19 (Figure 1, page 26). Incidence rates for HL are about 30% higher among white children compared to African American and Hispanic children (Table 3, page 31). Asian American/Pacific Islanders have the lowest incidence rate for HL. Risk factors for HL include Epstein Barr virus (EBV) or a having a personal history of mononucleosis and human immunodeficiency virus (HIV) infection.

Survival rates for HL increased from 87% in 1975-1979 to 97% in 2003-2009 (Table 4, page 35). HL is highly sensitive to radiation, and cure can be achieved in some patients by radiation therapy alone, although this is seldom the preferred treatment in children and adolescents. The high dose of radiation used to treat HL in past decades was found to be damaging to organs such as the lungs and heart, so current therapies usually combine lower doses of chemotherapy and radiation to achieve a high cure rate with less toxicity.<sup>37</sup> Long-term and late effects of treatment may include pulmonary and cardiac diseases, thyroid abnormalities, infertility, and second cancers. Girls age 10 and older and young women treated with radiation to the chest for HL have an exceptionally high relative and absolute risk of developing breast cancer.<sup>38, 39</sup> The American Cancer Society recommends annual MRI in addition to mammographic screening for women were treated for HL.<sup>40</sup>

### Non-Hodgkin lymphoma

An estimated 620 children and 420 adolescents will be diagnosed with NHL in 2014. The most common subtypes among children and adolescents in the US are Burkitt lymphoma (BL) (19%), diffuse large B-cell lymphoma (DLBCL) (22%), lympho-

blastic lymphoma (20%), and anaplastic large cell lymphoma (10%).<sup>41</sup> Both the incidence and distribution of NHL subtypes vary throughout the world. For example, in equatorial Africa, lymphomas account for nearly one-half of childhood cancers, reflecting the very high incidence of BL.<sup>10</sup> The high incidence of BL in equatorial Africa is associated with high rates of co-infection with EBV and malaria.<sup>10</sup> BL in Africa, also known as endemic BL, is much more common in boys than in girls and often arises in the jaw or around the eyes. In the US, the incidence of BL is also much higher in boys than in girls, but occurs most frequently in the abdomen and is less common in African American than in white children (Table 3, page 31).

EBV infection is also associated with many other types of NHL, although not as strongly as for BL in Africa. Immunosuppression from a variety of causes increases the risk of NHL, including inherited immunodeficiency disorders, HIV infection, and post-transplantation immune suppression.<sup>42</sup> Multiagent chemotherapy is the main form of treatment for most types of NHL. The dramatic improvement in survival rates for adults with DLBCL when rituximab (a monoclonal antibody) is administered with multiagent chemotherapy has stimulated clinical trials to evaluate the role of monoclonal antibodies in treatment of pediatric DLBCL.<sup>42</sup> Survival rates for NHL in children and adolescents have increased dramatically in recent decades: from 47% in 1975-1979 to 85% in 2003-2009 (Table 4, page 35). Long-term and late effects of NHL include heart damage, cognitive effects, infertility, and low bone density.

### Brain and central nervous system tumors (CNS tumors)

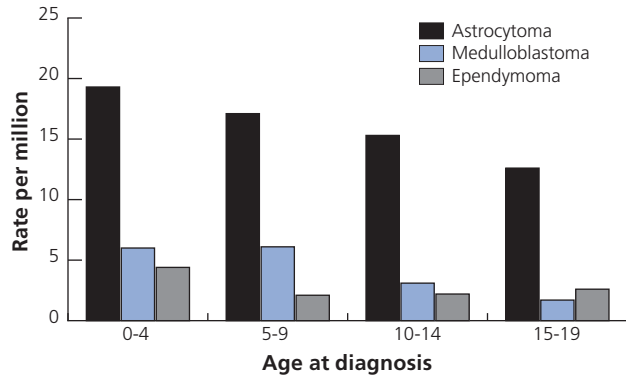
An estimated 2,240 children and 540 adolescents will be diagnosed with malignant CNS tumors in 2014. CNS tumors are the second most common cancer in children, accounting for 21% of cases, and the third most common cancer type in adolescents, accounting for 10% of cases. CNS tumors are classified by the cells and tissues in which they originate and their location and grade, ranging from I (low) to IV (high). Symptoms of benign tumors and side effects of treatment can be quite severe; therefore since 2004, cancer registries have been collecting data for benign as well as malignant CNS tumors. Statistics with benign and malignant tumors combined are used in this report when available. In 2014, an estimated 730 children and 630 adolescents will be diagnosed with benign and borderline malignant brain tumors.

Figure 5 provides age-specific incidence rates for three common categories of CNS tumors in children and adolescents:

- Astrocytoma, the most common type of CNS tumor, accounts for 35% of CNS tumors in ages 0-19. These tumors arise from brain cells called astrocytes. Astrocytomas range from low grade to high grade. Pilocytic astrocytoma, the most common type of astrocytoma in children, is a low-grade tumor



**Figure 6. Age-specific Incidence Rates for CNS Tumors, US, 2006-2010**



CNS=Central nervous system.

**Source:** North American Association of Central Cancer Registries. Data are included from all US states and the District of Columbia except Arkansas, Minnesota, Nevada, Ohio, and Virginia.

American Cancer Society, Surveillance Research, 2014

that typically arises in the cerebellum. Fibrillary astrocytoma, another common type of astrocytoma in children, is usually found in the mid-brain, has less well-defined borders and can spread throughout both sides of the brain.<sup>43</sup>

- Medulloblastoma most commonly diagnosed in children younger than 10 (Figure 6). It is a highly invasive embryonal tumor that arises in the cerebellum and has a tendency to spread throughout the central nervous system early in its course.<sup>44</sup>
- Ependymoma is a tumor that begins in the ependymal lining of the ventricular system (fluid-filled cavities in the brain) or the central canal of the spinal cord. Ependymomas range from low to high grade.<sup>43</sup>

The symptoms of brain tumors are varied, as is the time course over which symptoms develop and increase in severity. Signs and symptoms of brain cancer depend on the tumor location, the developmental stage and communication ability of the child or young person, and whether intracranial pressure is raised.

Trends in CNS tumors have been of interest because of a sharp increase in overall incidence in the mid-1980s (Figure 2, page 27), with significant increases in incidence rates for pilocytic astrocytoma, primitive neuroectodermal tumor (PNET)/medulloblastoma, and mixed glioma.<sup>11,43,45</sup> Many experts believe that this short-term increase in incidence resulted from the introduction of MRI for evaluating children with neurologic conditions and increased use of computer image-guided biopsies to document tumors that could not otherwise be biopsied. Furthermore, the rate of increase in pilocytic astrocytoma was similar to the rate of decrease for astrocytomas NOS (not otherwise specified), suggesting an improvement in classification.<sup>46</sup> After the increase in the mid-1980s, the incidence rate of CNS tumors stabilized (Figure 2, page 27).

The cause of brain tumors in childhood is unclear.<sup>47</sup> Children with certain genetic syndromes (e.g., Turcot syndrome, Li-Fraumeni syndrome, neurofibromatosis type 1, and neurofibromatosis type 2) have increased risk of brain and CNS tumors.<sup>43</sup> High-dose therapeutic radiation is a recognized cause of brain tumors, and children who receive cranial irradiation for ALL or other cancers have an excess risk of brain and CNS tumors. A number of studies have also found associations between consumption of cured meats during pregnancy and childhood brain tumors.<sup>48-51</sup>

Treatment of brain and other CNS tumors depends on the cancer type, grade, location, size, and other prognostic factors. Whenever possible, surgery is performed to remove as much of the tumor as possible while avoiding damage to healthy tissue. Optimal therapy, which may include chemotherapy and/or radiation, requires coordinated efforts of pediatric cancer specialists in fields such as neurosurgery, neuropathology, radiation oncology, and pediatric oncology. Late effects can include impaired growth and neurologic development following radiation therapy, especially in younger children. For this reason, children under age 3 usually receive chemotherapy first with delayed and/or reduced radiation. Radiation is not always needed for low-grade tumors.<sup>43</sup>

Survival rates vary depending on tumor type, location, and grade. Trends in survival rates over time are available for malignant brain tumors only (Table 4, page 35). While there has been progress in survival for CNS tumors overall, there has been little progress for some subtypes, such as DIPG (diffuse intrinsic pontine glioma), for which the median survival time after diagnosis remains less than one year.<sup>51</sup>

## Embryonal tumors

Embryonal tumors arise from cells in developing tissues and organ systems of a fetus. These tumors are usually diagnosed in children before age 5. Age-specific incidence rates for three common types of embryonal tumors in children (neuroblastoma, Wilms tumor, and retinoblastoma) are presented in Figure 7 (page 34). Other embryonal tumors, including medulloblastoma and rhabdomyosarcoma, are discussed in other sections of this report.

### Neuroblastoma

An estimated 710 cases of neuroblastoma will be diagnosed among children (ages 0-14) in 2014. It is the third most common childhood cancer and represents 7% of the total cases in this age group. Neuroblastoma develops from certain types of very primitive nerve cells in the embryo and is the most common cancer diagnosed during the first year of life; it is very uncommon after age 10. The incidence of neuroblastoma is slightly higher in boys than girls and substantially higher in whites than children of other races/ethnicities (Table 3, page 31). Although epidemiologic studies have investigated environmental factors that may

be associated with neuroblastoma, no strong or consistent risk factors have been identified. A family history of neuroblastoma is present in 1% to 2% of cases. Children who have siblings with neuroblastoma are nearly 10 times more likely to be diagnosed with the disease than children without a family history.<sup>52</sup>

Neuroblastoma can spread through the lymph system and blood, and over half of children have regional or distant stage disease at diagnosis.<sup>53</sup> A rare form of neuroblastoma (stage 4S) occurs in infants with a specific pattern of metastatic disease and often regresses with little or no treatment.<sup>54</sup> Depending on stage and other prognostic factors, children with neuroblastoma are most commonly treated with surgery and/or chemotherapy and radiation therapy; patients with high-risk disease may receive high-dose chemotherapy followed by stem cell transplant.<sup>53</sup> Overall survival rates for neuroblastoma have increased from 54% in 1975-1979 to 79% in 2003-09 (Table 4). However, survival remains poor for children with high-risk disease. Children treated for high-risk disease also have the greatest risk of treatment-related complications, including severe hearing loss, infertility, cardiac toxicity, and second cancers related to the use of high-dose chemotherapy.<sup>53</sup>

### Wilms Tumor

An estimated 510 cases of Wilms tumor will be diagnosed among children in 2014. Also called nephroblastoma, Wilms tumor is an embryonal tumor of the kidney that usually occurs in children under age 5 (Figure 7). The vast majority (92%) of kidney tumors in this age group are Wilms tumor.<sup>41</sup> The incidence rate of Wilms tumor is slightly higher in girls than boys and in African American children compared to children of other races/ethnicities (Table 3, page 31). Wilms tumor is bilateral (occurring in both kidneys) in about 5-10% of cases.<sup>55</sup> About 10% of cases are associated with a birth defect such as urogenital tract abnormalities.<sup>56</sup> Epidemiologic studies have not identified strong or consistent environmental risk factors for Wilms tumor.

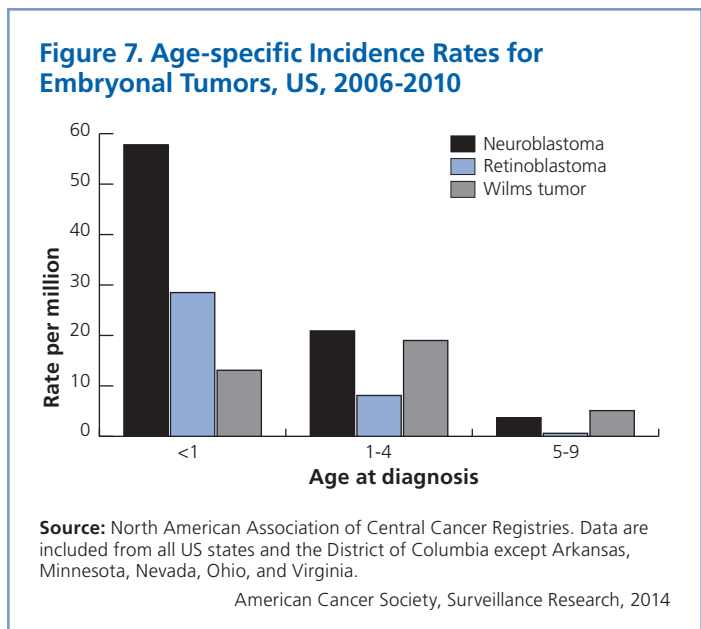
The majority of children with Wilms tumor are diagnosed with an asymptomatic abdominal mass that is incidentally noted while bathing or dressing the child.<sup>57</sup> Wilms tumor may spread locally or through the bloodstream; distant metastases are uncommon at diagnosis. Treatment involves surgery and may include radiation and/or chemotherapy. In addition to stage, histology (how the cancer cells look under the microscope) and age at diagnosis are important prognostic factors.<sup>57</sup> Survival rates for Wilms tumor increased from 75% in 1975-1979 to 90% in 2003-2009 (Table 4). Late effects observed among survivors of Wilms tumor include heart damage, diminished lung and kidney function, reduced fertility and pregnancy complications among girls treated with radiation, and an increased risk of second cancers.<sup>57</sup>

### Retinoblastoma

An estimated 280 children will be diagnosed with retinoblastoma in 2014. Retinoblastoma is a cancer that starts in the retina, the very back part of the eye. Retinoblastoma usually occurs in children under age 5 and accounts for 6% of cancers in this age group (Figure 7). The incidence of retinoblastoma is similar in boys and girls, does not vary substantially by race and ethnicity, and has been stable in the US population since 1975 (Table 3, page 31, Figure 2, page 27). Symptoms of retinoblastoma may include “white pupil,” in which the pupil of the eye appears white instead of red when light shines into it, eye pain or redness, and vision problems.

Most cases of retinoblastoma are due to a mutation in the *RBI* gene. Approximately one-third of retinoblastomas are inherited, meaning that the *RBI* mutation is in all of the body’s cells (i.e., a germline mutation).<sup>58</sup> Genetic counseling should be an integral part of the therapy for the family of a patient with retinoblastoma.<sup>58</sup> Patients who carry a germline *RBI* mutation have an increased risk of second cancers, especially if they receive radiation therapy.<sup>59</sup>

The type of treatment required for retinoblastoma depends largely on the extent of the disease within the eye and whether the disease has spread beyond the eye. Treatment options consider both cure and preservation of sight. Small tumors may sometimes be treated with cryotherapy (freezing), laser therapy, or thermotherapy (heat laser). Patients with more advanced disease, but that only involves one eye without spread to nearby tissues, are often treated with surgery to remove the eye (enucleation), which may be the only treatment needed.<sup>58</sup> Children with bilateral (both eyes are affected) disease, and some children with unilateral disease, may be treated with chemotherapy to shrink tumors to a size where local treatment is effective.



**Table 4. Pediatric Cancer Five-year Observed Survival Rates for Two Time Periods, Ages 0-19**

	Year of Diagnosis	
	1975-79 %	2003-09* %
All ICCC sites	63	83
Leukemia	48	84
Acute lymphocytic leukemia	57	90
Acute myeloid leukemia	21	64
Lymphomas and reticuloendothelial neoplasms	72	91
Hodgkin lymphoma	87	97
Non-Hodgkin lymphoma	47	85
Brain and CNS	59	75
Ependymoma	37	81
Astrocytoma	69	85
Medulloblastoma	47	70
Neuroblastoma and ganglioneuroblastoma	54	79
Retinoblastoma	92	99
Wilms tumor	75	90
Hepatic tumors	25	74
Bone tumors	49	73
Osteosarcoma	45	71
Ewing sarcoma	42	72
Rhabdomyosarcoma	49	64
Testicular germ cell tumors	74	96
Ovarian germ cell tumors	75	94
Thyroid carcinoma	99	98
Melanoma	83	95

ICCC=International classification of childhood cancers.

CNS=Central nervous system.

\*Cases were followed through 2010.

Note: Does not include benign and borderline brain tumors.

Source: Surveillance, Epidemiology, and End Results (SEER) program, 9 SEER registries, National Cancer Institute.

American Cancer Society, Surveillance Research, 2014

Patients with more advanced disease are treated with chemotherapy and sometimes surgery and/or radiation.<sup>59</sup> Recent studies have investigated the efficacy of intra-arterial chemotherapy with promising results.<sup>60</sup> Five-year survival rates for retinoblastoma have increased from 92% in 1975-1979 to 99% in 2003-2009 (Table 4). Late effects of retinoblastoma include visual impairment and increased risks of second cancers, including bone and soft tissue sarcomas and melanoma.<sup>61</sup>

### Bone tumors and soft tissue sarcomas

Sarcomas are tumors that develop from connective tissues in the body, such as muscles, fat, bones, membranes that line the joints, or blood vessels. An estimated 450 children and 370 adolescents will be diagnosed with bone tumors in 2014. The two most common types of bone tumors in children and adolescents are osteosarcoma and Ewing sarcoma. The most common type of soft tissue sarcoma is rhabdomyosarcoma, which will be diagnosed in an estimated 340 children in 2014. Age-specific

incidence rates for these three types of sarcoma are presented in Figure 8, page 36. Another type of soft tissue sarcoma, Kaposi sarcoma, while extremely rare among children in the US, is very common in children in Africa due in part to the high prevalence of HIV infection.<sup>4, 5</sup>

### Osteosarcoma

Osteosarcoma is the most common type of bone cancer in children and adolescents. The incidence of osteosarcoma increases with age throughout childhood and adolescence; it is very rare among children under age 5 (Figure 8, page 36). The incidence of osteosarcoma is slightly higher in boys than girls and also higher in African American and Hispanic children than in white and Asian American/Pacific Islander children (Table 3, page 31). Osteosarcoma arises from primitive bone-forming stem cells and usually develops in areas where the bone is growing rapidly, such as near the ends of the long bones around the knee. Osteosarcoma commonly appears as sporadic pain in the affected bone that may worsen at night or with activity, with progression to local swelling.<sup>62</sup>

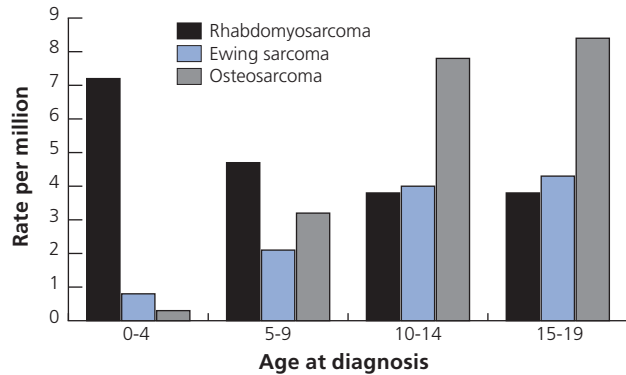
Prior radiation treatment for another tumor increases the risk of osteosarcoma. Radiation-associated osteosarcomas usually occur 7 to 15 years after treatment of the primary tumor. Some studies have found that taller children are at greater risk of osteosarcoma, while others have not.<sup>63</sup> The incidence of osteosarcoma is increased among individuals with the hereditary form of retinoblastoma and Li-Fraumeni syndrome, as well as several other genetic syndromes.<sup>62</sup>

About 20% of patients have detectable metastases (distant spread) at diagnosis, most commonly in the lung.<sup>64</sup> Nearly all patients receive systemic therapy (chemotherapy given through the blood stream to reach cancer cells throughout the body) due to the high risk of metastases. Current standard therapy consists of neoadjuvant chemotherapy to shrink the tumor, followed by surgery and adjuvant chemotherapy.<sup>62</sup> Amputation is rarely needed. The 5-year survival rate for osteosarcoma was 71% in 2003-09, up from 45% in 1975-79 (Table 4). Therapy-related late effects can include heart damage, hearing loss, kidney dysfunction, second cancers, and infertility. Patients treated for osteosarcoma may also have physical limitations resulting from surgery.<sup>62</sup>

### Ewing sarcoma

Ewing sarcoma is the second most common malignant bone tumor in children and adolescents. It is more common among older children and adolescents than young children (Figure 8, page 36). Notably, incidence rates of Ewing sarcoma in whites are nearly 7.5 times higher than in African Americans, and moderately higher than in Hispanics and Asian American/Pacific Islanders (Table 3, page 31). Similar differences in incidence are observed globally.<sup>10</sup> Ewing sarcoma is a highly aggressive cancer, and it is characterized by a mutation in the *EWSR1* gene.<sup>65</sup>

**Figure 8. Age-specific Incidence Rates for Bone and Soft Tissue Sarcomas, US, 2006-2010**



**Source:** North American Association of Central Cancer Registries. Data are included from all US states and the District of Columbia except Arkansas, Minnesota, Nevada, Ohio, and Virginia.  
American Cancer Society, Surveillance Research, 2014

Ewing sarcomas arise about equally in bones of the extremities and those in other parts of the body, and may also arise in soft tissues.<sup>66</sup> The first symptom is usually pain at the tumor site, sometimes along with a mass or swelling. Metastases are present in about 25% of patients at diagnosis; the most common metastatic sites are the lungs, bone, and bone marrow.<sup>67</sup> Treatment for Ewing sarcoma typically involves induction chemotherapy followed by local therapy (surgery and/or radiation) and adjuvant chemotherapy. There is continuing uncertainty about whether surgery or radiation therapy is preferred for local control, and sometimes radiation therapy is used both before and after surgery.<sup>68</sup> Survival rates for Ewing sarcoma have increased from 42% in 1975-1979 to 72% in 2003-09 (Table 4, page 35). Ewing sarcoma survivors are at increased risk for developing a second cancer, heart and lung conditions, infertility, and musculoskeletal problems.<sup>68</sup>

### Rhabdomyosarcoma

Rhabdomyosarcoma is a cancer made up of cells that normally develop into skeletal muscles. This cancer accounts for 3% of childhood cancers and 2% of adolescent cancers. There are two major subtypes of rhabdomyosarcoma: embryonal rhabdomyosarcoma (about 75% of cases), which is most common in children under age 5, and alveolar rhabdomyosarcoma (about 16% of cases), for which incidence does not vary by age in children and adolescents.<sup>69</sup> Embryonal rhabdomyosarcoma most commonly occurs in the head and neck, whereas alveolar rhabdomyosarcoma is most common in the trunk and extremities. The first symptoms often include pain and/or a mass or swelling at the site of origin. Rhabdomyosarcoma is associated with a number of genetic syndromes, including Li-Fraumeni syndrome and neurofibromatosis type 1.

All patients with rhabdomyosarcoma receive several types of treatment, including chemotherapy in conjunction with surgery, radiation, or a combination thereof.<sup>70</sup> Although survival for rhabdomyosarcoma has improved (from 49% in 1975-1979 to 64% in 2003-09), it remains lower than many other pediatric cancers (Table 4, page 35). Treatments for patients with intermediate and high-risk disease continue to be studied in clinical trials in hopes of achieving better outcomes.<sup>71</sup> Late effects of treatment for rhabdomyosarcoma depend on whether radiation therapy was given and the specific chemotherapy agents received, which have varied over time.

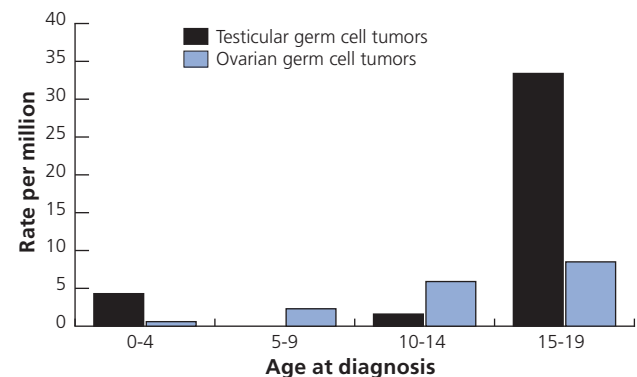
### Gonadal germ cell tumors

Gonadal germ cell tumors are a diverse group of tumors that arise from either the ovaries in girls or the testicles in boys. These tumors are more common in adolescents than in young children and occur more frequently in boys than girls (Figure 9). Incidence rates vary by race/ethnicity, with Hispanic children having the highest rates and African American children having the lowest (Table 3, page 31).

### Ovarian germ cell tumors

An estimated 110 adolescent girls will be diagnosed with ovarian germ cell tumors in 2014. Ovarian germ cell tumors are more common in older girls (ages 10-14) and adolescents than in younger girls (Figure 9). The risk of ovarian tumors is increased among individuals with several genetic syndromes involving sex chromosomes, including Turner syndrome and Swyer syndrome.<sup>72</sup> Ovarian germ cell tumors often cause abdominal pain, swelling, and weight gain.<sup>73</sup> Surgery is the primary treatment; removal of only the affected ovary and fallopian tube is an option for most patients who wish to preserve fertility. Patients with early stage disease may be monitored after surgery, while those

**Figure 9. Age-specific Incidence Rates for Gonadal Germ Cell Tumors, US, 2006-2010**



Rates are not shown when based on fewer than 25 cases.  
**Source:** North American Association of Central Cancer Registries. Data are included from all US states and the District of Columbia except Arkansas, Minnesota, Nevada, Ohio, and Virginia.  
American Cancer Society, Surveillance Research, 2014



with more advanced disease receive chemotherapy. The 5-year survival rate is 94% (Table 4, page 35). The chemotherapy regimens most commonly used for ovarian germ cell tumors may cause hearing loss and kidney damage.<sup>74</sup>

### Testicular germ cell tumors

An estimated 430 testicular germ cell tumors (TGCT) will be diagnosed in boys ages 15-19 in 2014, making it the fourth most common cancer in this age group. Some TGCT also occur in boys under the age of 4 (Figure 9). The incidence of TGCT is higher among whites and Hispanics than among African Americans (Table 3, page 31). There are two major types of TGCT: non-seminomas (accounting for the majority of TGCT in adolescents) and seminomas.<sup>75</sup> A lump on the testicle is usually the first sign and often leads to diagnosis at an early stage. Risk factors for TGCT include a history of an undescended testicle and a family history of testicular cancer.<sup>74</sup> Removal of the affected testicle is the primary treatment for all TGCT; subsequent treatment varies by stage. Early stage cancers (stages I and II) may be observed closely after surgery, while those with continued elevation of serum markers should undergo radiation therapy. Later-stage cancer requires chemotherapy. Survival rates for testicular cancer have improved substantially since the mid-1970s (from 74% to 96% in 2003-2009), and most patients have a good prognosis (Table 4, page 35).

### Side Effects and Support during Cancer Therapy

Children with cancer may suffer from pain and other symptoms due to the cancer itself, pain and anxiety related to medical procedures and hospitalizations, physical side effects of treatment, separation anxiety, and psychological distress.<sup>76,77</sup> Pediatric nurse oncologists and other members of the health care team play important supportive roles in assessing and managing pain, distress, and other symptoms that may arise in children

and adolescents undergoing cancer treatment. Optimal care for children with cancer may also involve consultation with specialists, such as psychologists and social workers, who are trained and experienced in methods to reduce pain and suffering for pediatric cancer patients and to provide psychosocial and other support to patients, siblings, parents, and other caregivers.<sup>76, 78</sup> Major pediatric centers that treat cancer in children also have palliative care teams that specialize in managing pain and other distressing symptoms. Palliative care, also called supportive care, should be provided throughout the course of pediatric cancer treatment and continued as needed to minimize pain and suffering, improve patient and family quality of life, facilitate decision making, and assist in care coordination between clinicians and across sites of care.<sup>78, 79</sup>

Caring for a child who is undergoing cancer treatment is difficult for many families. Psychosocial support for parents and other family members is an important component of care.<sup>81</sup> Oncology social workers, psychologists, child life specialists, and other staff at pediatric cancer centers provide psychosocial support to families, as well as help to address practical issues such as insurance and opportunities for the child to continue their education while under treatment. To further advance health care provider and health system efforts to deliver optimal care that integrates psychosocial and palliative care alongside disease-directed treatment, several patient quality of life-focused public policy initiatives are now under way involving a coalition of patient advocacy and professional organizations. For more information, see the Advocacy section on page 38.

Despite advances in treatment and survival for some cancers, some children with cancer will not survive the disease. Although patients, families, and health care providers often find it difficult to discuss issues concerning prognosis, goals of care, and transitions to end-of-life care, it is important that health care providers are available, attentive, and sensitive to these concerns.<sup>80,82</sup> Pediatric oncology centers often partner with the

#### Common side effects of cancer treatment<sup>80</sup>

- Low red blood cell counts (anemia) can result in pallor, dizziness, weakness, lack of energy, headache, and irritability. Low platelet counts (thrombocytopenia) can result in easy bleeding and bruising. Low white blood cell counts (including low neutrophil counts or neutropenia) reduce the body's ability to fight infection. Low blood cell counts can be treated by transfusions or hematopoietic growth factors, and risk of infection may be reduced by prophylactic antibiotics.
- Gastrointestinal side effects are common among children receiving chemotherapy or radiation therapy, and can include oral mucositis (irritation and/or sores in the mouth), diarrhea or constipation, nausea, vomiting, and retching. Gastrointestinal side effects can result in poor nutritional intake, leading to weight loss and delayed growth. Medications, such as antiemetics given before chemotherapy, are available to reduce some of these side effects, and nutritional advice is available to help children and parents with these issues. Nutritional support, such as tube feedings, intravenous feedings, or appetite stimulants, may be recommended.
- Pain may arise from the tumor as it presses on bone, nerves, or body organs; it can also result from procedures, including surgeries and needle sticks. Pain can also be a side effect of some cancer treatment, such as neuropathic pain from some chemotherapy drugs. Pain is often treatable by medication and other integrative non-medicine therapies. Children whose pain cannot be well-controlled by available interventions should be seen by a specialist in pediatric pain management.

family's pediatrician and hospice professionals to provide care to terminally ill children to manage pain and other symptoms, help families to make informed decisions about the child's care, and support them through bereavement.<sup>83,84</sup> The loss of a child to cancer is an incredibly difficult experience. A variety of resources (see page 39) are available for helping people through their grieving process, including assistance in obtaining referrals for counseling and community-based support services.

## Transition from Active Treatment to Survivorship Care

Children treated for cancer often maintain their relationship with their primary care pediatrician.<sup>85</sup> Following cancer treatment, children and adolescents may be monitored by their pediatric oncologist for 3 or more years, depending on the disease, age of the patient, and other factors. Follow-up care by pediatric oncologists focuses on checking for recurrence; more extensive follow-up may be offered by the treating oncologist or by referral to a comprehensive clinic. When the time comes for discontinuing visits to the pediatric oncologist for initial follow-up care, long-term follow-up care is still needed. Such follow-up care includes assessment of short- and long-term complications and late effects of cancer therapies; detection of recurrent and secondary cancers; counseling about behaviors such as smoking, diet, and physical activity; assessment of psychosocial adjustment and quality of life; and treatment for any identified late effects.

Many of the late effects of childhood and adolescent cancer may not become apparent until adulthood. Therefore, it is important that young adults who are transitioning from pediatric to adult primary care receive information regarding their cancer experience, including diagnosis and treatment, as well as follow-up recommendations, especially if they are not participating in specialized survivorship care programs.<sup>85</sup> The Children's Oncology Group (COG) has developed long-term follow-up guidelines for survivors of childhood cancers.<sup>86</sup> These guidelines help health care providers and patients know what to watch for, what type of screening tests should be done to look for problems, and how late effects can be treated. For more information on these guidelines, visit the COG Web site at [survivorshipguidelines.org](http://survivorshipguidelines.org).

## Global Burden of Childhood Cancer

An estimated 175,000 cases of cancer are diagnosed annually in children younger than 15 years of age worldwide, and fewer than 40% of patients (mostly in high-income countries) are adequately diagnosed and treated.<sup>87</sup> A child's probability of surviving cancer is poor in less developed countries, and extreme discomfort is likely in the absence of palliative care. Many childhood cancers are highly curable if diagnosed at an early stage, and some treatment regimens are relatively simple, inexpensive, and well-established.<sup>88</sup> For example, about 50% of African BL can be

cured with a 28-day course of low-dose cyclophosphamide and prednisone and four intrathecal injections costing less than \$50.<sup>89</sup> A number of organizations have drawn attention to the survival disparity for retinoblastoma between high- and low-income countries, and to the possibility that interventions such as public awareness campaigns, physician education, hospital partnerships, and donation of equipment could improve early detection and treatment in low-income countries.<sup>90</sup>

## What Is the American Cancer Society Doing about Cancer in Children and Adolescents?

### Advocacy

The Society's nonprofit, nonpartisan advocacy affiliate, the American Cancer Society Cancer Action Network<sup>SM</sup> (ACS CAN), supports laws and policies that increase funding for cancer research, improve the quality of life of all adults and children with cancer and their families, and broaden access to quality care.

A top and ongoing priority for ACS CAN is protecting and increasing federal funding for cancer research at the National Institutes of Health and the National Cancer Institute (NCI). NCI funds about \$200 million a year in research specific to childhood cancer. For more information, visit [acscan.org/research](http://acscan.org/research) and [ovaonline.org](http://ovaonline.org).

ACS CAN has worked with the Society to develop a menu of new public policy proposals focused on increasing quality of life (QOL) and scientific research on survivorship, boosting the health care workforce, and improving access to quality health care. In partnership with diverse stakeholders, ACS CAN is currently advancing federal and state legislation to promote pain and symptom management and other aspects of palliative care integrated with disease-directed treatment. These initiatives include specific emphasis on addressing the quality-of-life needs of children and adolescents who are facing cancer or other serious illness. For more information about this QOL campaign, visit [acscan.org/qualityoflife](http://acscan.org/qualityoflife).

Moreover, for more than a decade, ACS CAN has worked on a variety of childhood cancer public policies and legislative initiatives. Specifically, ACS CAN endorsed a number of bills, which became law in 2012, that focus on pediatric cancer, including the Reauthorization of the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA). In addition, ACS CAN has endorsed the pediatric cancer community's legislative priorities for the 113th Congress, including the Childhood Cancer Survivors' Quality of Life Act, and reauthorization and appropriations for the Caroline Pryce Walker Conquer Childhood Cancer Act.

ACS CAN is also an active participant in the Alliance for Childhood Cancer — a coalition of more than 25 member organizations dedicated to advancing childhood cancer issues.

More information about the Alliance can be found at [allianceforchildhoodcancer.org/about](http://allianceforchildhoodcancer.org/about).

ACS CAN has successfully advocated for the inclusion of the following and other patient protections in the Affordable Care Act that are vitally important to childhood and adolescent cancer patients and survivors:

- Protecting children and others from being dropped from health insurance plans when they get sick
- Banning lifetime dollar caps on coverage and annual dollar limits so that those with cancer get access to needed care
- Allowing families with children with life-threatening illnesses to enroll their children in hospice that is provided concurrently with disease-directed treatment
- Enabling dependent children to remain on their parents' health insurance policy up to age 26

## Research

The American Cancer Society, through its Extramural Grants program, funds individual investigators engaged in cancer research or training at medical schools, universities, research institutes, and hospitals throughout the US. As of September 2013, this program is funding approximately \$29 million in research specifically related to childhood and adolescent cancer through 56 research grants. Additionally, the Society is funding about \$16 million in brain cancer research, \$28 million in leukemia research, and \$15 million in lymphoma research covering both childhood and adult disease.

Following are some examples of ongoing Society-funded childhood and adolescent cancer research projects:

- Researchers at the University of Texas, Southwestern Medical Center are focused on what causes rhabdomyosarcoma. They have discovered that many cases are associated with a fusion of two genes. The team is currently conducting studies to understand the consequences of this gene fusion, with the goal of creating new therapies for this difficult-to-treat cancer.
- Investigators from the University of Kansas Medical Center are attempting to better understand metastasis in osteosarcoma. The investigators have discovered that a particular regulatory protein, MTBP, can interfere with the primary growth of osteosarcoma and its ability to metastasize to distant sites. A better understanding of the molecular events that promote metastases will provide the framework for improved prevention and treatment.
- A research team at the Children's Hospital of Los Angeles is focused on trying to improve treatment of medulloblastoma. Recent studies have shown that radiation treatment, when added to surgery and chemotherapy, may not be necessary for some children. The researchers are trying to develop a prognostic tool that would identify those children who might be

cured without use of radiation to spare them the additional side effects associated with radiation.

- Researchers at Yale University are comparing two survivorship models for children with cancer to improve long-term outcomes and quality of life in these patients. Specifically, the researchers are comparing the effectiveness of "survivorship clinics" to care provided by primary care physicians with training in survivorship care.

## Resources for clinicians and parents

A detailed guide with additional information and resources on cancer in children is available on the Society Web site: [cancer.org/cancer/cancerinchildren](http://cancer.org/cancer/cancerinchildren). This guide includes a listing of additional Society publications that may be downloaded or ordered by calling our toll-free number, 1-800-227-2345.

Other national organizations and Web sites that provide information and support:

- American Childhood Cancer Organization: [acco.org](http://acco.org)
- Children's Oncology Group (COG): [childrensoncologygroup.org](http://childrensoncologygroup.org)
- CureSearch for Children's Cancer: [curesearch.org](http://curesearch.org)
- National Cancer Institute resources for childhood cancer: [cancer.gov/cancertopics/types/childhoodcancers](http://cancer.gov/cancertopics/types/childhoodcancers)
- National Children's Cancer Society, Inc: [thencs.org](http://thencs.org)

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