# Childhood Cancer in South Carolina 25-YEAR TRENDS IN INCIDENCE, SURVIVAL, AND MORTALITY

South Carolina Childhood Cancer Taskforce South Carolina Central Cancer Registry











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Photos of children impacted by cancer in South Carolina during cancer treatment.

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### **Executive Summary**

**Introduction:** Cancer is a broad category, comprised of many types of cancer that impact both adults and children. The types of cancers, treatments, and prognosis are different among children with cancer as compared to adults and require unique evaluation. South Carolina's inaugural childhood cancer report focuses specifically on cancers impacting those 19 years of age and younger in the state. Childhood cancer is a condition which has impacted every county in South Carolina with 4,457 children diagnosed with cancer and 716 cancer deaths statewide over the past 25 years. The report that follows details the past and present landscape of childhood cancer in South Carolina and lays a foundation for future childhood cancer research, advocacy, and intervention in South Carolina.

**Report Methods:** Population-based childhood cancer data is provided by South Carolina's Central Cancer Registry (under the South Carolina Department of Public Health). The report details trends and current metrics for childhood cancer incidence, survival, and mortality in South Carolina from 1996 through 2020. We describe South Carolina's growing population of childhood cancer survivors. Lastly, the report explores differences in cancer measures by race/ethnicity and rurality in the state.

#### **Overview of Findings**

**Childhood Cancer Incidence:** While the incidence rate in South Carolina (16 cases per 100,000) remained lower than the South Atlantic region (18.1 per 100,000) and United States (18.4 per 100,000), the incidence of childhood cancer in South Carolina had risen 11% between the years 2001 and 2020. Over the same time period the incidence of childhood cancer had risen 13% regionally and 8% nationally. White children and males had a higher incidence of childhood cancer in South Carolina, trends that were also reflected in the nation as a whole. We identified a persistent and worsening racial disparity in childhood cancer incidence among White children as compared to Black children. The highest incidence rates were among children 0-4 years and adolescents 15-19 years. Not all types of childhood cancer were rising in the state. Among the most common cancers, the incidence of leukemias and lymphomas had increased 5% and 47% respectively, while the incidence of brain/CNS (central nervous system) tumors had decreased 7%.

**Childhood Cancer Survival:** For all cancers combined from 2012-2016, the 5-year relative survival was 84%. This marks an 11% increase in survival for childhood cancer in South Carolina between 1996 and 2016. Cancer survival has improved in eight of eleven major cancer types. Survival has improved for both sexes (12% for males and 10% for females). Between 2012 and 2016, the 5-year relative survival was highest for White children with cancer (86%), followed by Hispanic children (83%), and Black children (80%). The survival gap has narrowed among White and Black children (declining 9% to 6%) and slightly among White and Hispanic children (declining 4% to 3%).

**Childhood Cancer Mortality:** Between 2016 and 2020 the childhood cancer mortality rate in South Carolina was 2.3 deaths per 100,000. This represents a 21% decline in cancer mortality over 25 years (1996-2020), consistent with declines in the region and United States. The cancer mortality rate has declined and converged among White children (declining 29%) and Black children (declining 4%). The cancer mortality rate has declined 31% for males and was unchanged among females. Most cancer deaths occurred among adolescents 15-19 years of age. The leading causes of childhood cancer deaths in the state were brain/CNS tumors and leukemias.

**Childhood Cancer Survivors:** South Carolina has a growing population of childhood cancer survivors (diagnosed 1996 through 2015). Among 2,962 childhood cancer survivors in the state, 2,812 were still alive, while 150 had subsequently died. Childhood cancer survivors resided throughout South Carolina, including 15% from rural areas. A relatively higher proportion of Black survivors subsequently died. Children who were older at cancer diagnosis (5 years or greater) and those with brain/CNS tumors comprised a relatively greater proportion of deaths among survivors.

**Racial and Ethnic Disparities in Childhood Cancer:** In previous sections, we identified disparities in cancer incidence, outcomes, and survivorship which are highlighted here. White children had persistently higher cancer incidence than Black children across time periods and the incidence gap between White and Black children increased over time. Hispanic children and Black children with cancer in South Carolina experienced lower 5-year relative survival (83% and 80% survival) as compared to White children (86%). Though Black children had the lowest 5-year relative survival, they experienced the greatest improvement over time (15% increase in survival between 1996 and 2016) compared to White and Hispanic children (10% increase). Although Black children had lower cancer incidence compared with White children, comprising only 27% of new cancer cases statewide, they comprised 34% of cancer deaths. The survival disparity for Black children also extended into cancer survivorship.

**Rurality and Childhood Cancer:** From 1996 to 2020 the incidence rate of childhood cancer is was consistently higher in urban areas. Between 2016 and 2020 the incidence of childhood cancer was 16.2 cases per 100,000 in urban areas compared to 14.9 per 100,000 in rural areas. Between 2012 and 2016 the 5-year relative survival for both urban and rural children is was 84%. The 5-year relative survival has improved 12% among those from urban areas and 7% among those from rural areas. Between 2016 and 2020 the childhood cancer mortality rate was slightly higher in rural areas (2.6 deaths per 100,000) than urban areas (2.3 deaths per 100,000). The mortality rate has also declined less for rural (13%) than urban areas (21%) over time.

**Report Summary:** South Carolina has made tremendous progress in the fight against childhood cancer. This report identifies many favorable trends including rising childhood cancer survival overall and for most cancer types. The cancer mortality rate was consistently trending downward. Those working in childhood cancer across the state should be encouraged by this progress and continue their efforts in caring for and supporting children with cancer and their families. However, the report also demonstrates several priority areas for childhood cancer in South Carolina.

- Although many trends are favorable, the survival for Black and Hispanic children with cancer remained lower than White children with cancer illustrating persistent disparities by race and ethnicity in childhood cancer survival in South Carolina. Racial disparities in survival were also seen among childhood cancer survivors. These persistent survival disparities by race/ethnicity require concentrated attention. Understanding the mechanisms driving these disparities and developing interventions to overcome the causes of the disparities will be key to promote equitable outcomes for all children.
- The incidence of childhood cancer in South Carolina has risen overall including rising incidence trends for leukemia and lymphoma. We identified a persistent and worsening racial disparity with higher cancer incidence among White children as compared to Black children and a widening gap overtime. Further research is needed to better understand these trends both locally and nationally. Because childhood cancer is rare, it is helpful to study incidence changes in the broader context of the rising childhood cancer incidence in the United States.
- With improvements in cancer treatments and survival for children, South Carolina's population of childhood cancer survivors continues to grow. These survivors resided throughout South Carolina and require ongoing specialized medical and preventative health follow up over the lifespan due to the health risks associated with their cancer treatments in childhood. Understanding and addressing the needs of this growing population is a top priority.
- There were differences in childhood cancer metrics by rurality in South Carolina. Though survival has improved among those from rural areas, cancer mortality was slightly higher among children in rural areas as compared to urban areas. The incidence of childhood cancer was consistently higher in urban areas.
- Despite the advancements in treating childhood cancer, not all children are able to be cured. Cancer deaths occurred in all age groups in South Carolina with the highest number of deaths among adolescents. Better understanding the needs of this population, including the unique needs of adolescents, will allow us to promote quality of life and reduce suffering at the end of life.

### A Message from South Carolina Pediatric Oncologists

Childhood cancer remains the most common cause of death by disease among children and adolescents in the United States [1]. Over the last 25 years in South Carolina, 4,457 children have been diagnosed with cancer and 716 children have died from cancer. It is important that we understand the past and present landscape of childhood cancer across the state to ensure we continue to provide the best care for all children with cancer in South Carolina.

We invite you to learn more in the following report, Childhood Cancer in South Carolina, 25-year Trends in Incidence, Survival, and Mortality. This report is possible because of the high-quality cancer surveillance data maintained by the South Carolina Central Cancer Registry under the Department of Public Health. The report that follows is the product of tremendous statewide collaboration between South Carolina's three pediatric cancer hospitals, the South Carolina Cancer Alliance, the South Carolina Central Cancer Registry, and the University of South Carolina's Arnold School of Public Health. This report lays a broad foundation for future childhood cancer research, advocacy, and intervention in South Carolina. Our sincere hope is that by illustrating 25-years of South Carolina data on the incidence, survival, and mortality of childhood cancer we will be taking an important step together in understanding and improving outcomes for children and adolescents with cancer statewide.



**Anna Hoppmann, MD, MPH** South Carolina Childhood Cancer Taskforce Chair

University of South Carolina School of Medicine, Columbia Prisma Health



**Michelle Hudspeth, MD** South Carolina Childhood Cancer Taskforce Member

Division Director, Pediatric Hematology/Oncology Director, Adult and Pediatric Blood and Marrow Transplantation, Medical University of South Carolina



Aniket Saha, MD, MS South Carolina Childhood Cancer Taskforce Member

Medical Director, Division of Pediatric Hematology Oncology Prisma Health University of South Carolina School of Medicine, Greenville



**Stuart Cramer, DO** South Carolina Childhood Cancer Taskforce Member

Aflac Director, Children's Center for Cancer and Blood Disorders Prisma Health University of South Carolina School of Medicine, Columbia

# <u>A Message from Dr. Virginie Daguise</u>

As an epidemiologist and a childhood cancer survivor it is my honor to have been a part of South Carolina's inaugural childhood cancer report. As you will see in the coming pages, South Carolina has made great strides in the fight against childhood cancer. Childhood cancer survival has improved year after year, and we show improved survival for children with cancer from rural areas. Despite this progress, there are still areas that require our attention and renewed efforts moving forward. The key priority areas this report identified for childhood cancer in South Carolina include persistent survival disparities by race/ethnicity, the changing incidence pattern of childhood cancer, and providing care to childhood cancer survivors across the lifespan.

This report identified nearly 3,000 childhood cancer survivors statewide. In survivorship, most childhood cancer survivors have specialized health needs due to their prior treatments. Systematic ongoing follow-up for pediatric cancer survivors is critical to promote early detection of treatment-related complications. We must also acknowledge the psychosocial needs of children who endured such treatments, and the toll it takes on them psychologically. Both the quality and longevity of life for childhood cancer survivors can be positively impacted by specialized medical care post treatment. The Children's Oncology Group is a great resource that provides resources for both medical professionals and childhood cancer survivors. <u>Children's Oncology Group (survivorshipguidelines.org)</u>

From a public health perspective, we must work together as a state to understand and care for this growing population of childhood cancer survivors. It remains critical to continue supporting our cancer registry that provides data to identify trends and patient outcomes. We also must be diligent to ensure we are reaching this vulnerable population with the recommended medical and preventative health services to address behaviors such as tobacco use, diet, exercise, and the need for cancer screenings.

I would like to thank the pediatric oncology community for all their work in this field. We have come a long way yet still have a long way to go. I would also like to recognize the researchers and data scientists who help us identify gaps to address local disparities. This report will be a step in the right direction, by providing a framework for future work in childhood cancer in South Carolina and raising awareness about the unique needs of this population. Lastly, and most importantly, I want to acknowledge the patients as well as the parents and caregivers of children with pediatric cancer, who are the inspiration for this work.

Virginie G. Daguise, PhD, MSPH Director Bureau of Chronic Disease and Injury Prevention South Carolina Department of Public Health

# Introduction to Childhood Cancer

Cancer is a broad group of diseases that impact individuals across the lifespan. Readers may be most familiar with the impact of cancer on adults; however, cancer is also diagnosed in childhood. The cancer epidemiology, treatments, prognosis, and duration of time in survivorship is considerably different for children as compared to adults facing cancer. Childhood cancer requires independent study and interpretation as a unique subset of the overall cancer burden in South Carolina, which prompted the development of South Carolina's Childhood Cancer Taskforce and the state's inaugural childhood cancer report.

Childhood cancer specifically is the term to describe cancer diagnosed in children and adolescents through 19 years of age. Cancer is diagnosed in children of all ages, with most cases occurring in young children (0-4 years) and older adolescents (15-19 years) [2]. There are many different types of childhood cancers. The most common types are leukemia, lymphoma, and brain and central nervous system (CNS) tumors. Among these larger groups, there are various cancer subtypes that are treated differently. For example, some types of leukemia include acute lymphoblastic leukemia and acute myeloid leukemia. Lymphomas are comprised of Hodgkin Lymphomas and Non-Hodgkin's Lymphomas (which includes several subtypes). Different types of solid tumors also occur in children. Examples of these are soft tissue sarcomas, malignant bone tumors, neuroblastoma, renal tumors, germ cell tumors, liver tumors and retinoblastoma[3].

#### Why do children get cancer?

Unlike cancer in adults, childhood cancer is rare. For most cases of childhood cancer, the cause is unknown. Among adults, certain lifestyle factors including smoking tobacco or obesity increase the chance of developing cancer, however childhood cancer is not associated with behavioral or lifestyle factors [4, 5]. There are inherited cancer predisposition syndromes (genetic changes parents pass to offspring) that increase the chance of childhood cancer occurring, though these disorders account for less than 10% of cancers during childhood [6].

Very few environmental exposures have been linked to childhood cancer. Examples of environmental exposures that have been linked to specific childhood cancers include ultraviolet (UV) light (associated with melanoma) and very high doses of ionizing radiation (for example, in atomic bomb or Chernobyl accident survivors) which is associated with thyroid cancer and leukemia [7-9]. Because childhood cancer is rare, studying environmental exposures that may increase the risk of cancer in children is challenging. The relationship between many types of environmental risk factors and their association with childhood cancer remains unclear. The complexity of studying environmental exposures is further complicated by the high likelihood that cancer risk is likely determined by an interaction of environmental exposures with markers of genetic susceptibility.

#### Can you screen for childhood cancer?

Cancer screenings (for example, mammography or colonoscopy) can detect cancers early in adults, but there are no recommended cancer screenings for children. Most childhood cancers develop quickly, and children present to the doctor's office or the emergency room because of progressive unexplained or concerning symptoms.

#### I am a parent. Is there anything I can do to prevent my child from getting cancer?

The cause of most childhood cancers is unknown, and there are no known ways to prevent them. However, there are healthy behaviors parents can start in childhood to reduce the risk of cancer developing over a child's lifetime. These behaviors include practicing sun safety, getting your child vaccinated for HPV, maintaining a healthy diet and weight and active lifestyle, discouraging tobacco use, and preventing secondhand smoke exposure. For more information on how to start protecting your child from cancer over the lifespan visit:

Cancer Prevention Starts in Childhood Feature | CDC

#### How is childhood cancer treated?

Treatments for childhood cancer vary based on the type of cancer and can include chemotherapy, surgery, radiation therapy, bone marrow transplant and immunotherapy. A given child may need one or several types of treatment. In South Carolina, we have three Children's hospitals that care for children and adolescents with cancer (**Figure 1** from North to South: Prisma Health Upstate, Prisma Health Midlands, Medical University of South Carolina). All three Children's hospitals are members of the Children's Oncology Group which is the largest clinical trials and research organization for childhood cancer in the world [10]. Participating in the Children's Oncology Group allows these centers to provide the most up-to-date treatments through clinical trials for children from across South Carolina.

#### Figure 1: South Carolina Children's Oncology Group Treatment Centers



#### What is the prognosis for childhood cancer?

During the last 50 years, the prognosis for childhood cancer has greatly improved due to high enrollment in clinical trials and improved supportive care. In present day, more than 80% of children diagnosed with cancer will survive 5 years from cancer diagnosis and beyond [11]. The survival rates vary significantly by cancer type. For example, among children with acute lymphoblastic leukemia (the most common childhood cancer) the current 5-year survival rate exceeds 90%, compared to a 5-year survival rate of 65% for rhabdomyosarcoma (a soft tissue tumor)[2]. Children with diffuse intrinsic pontine glioma (a rare brain cancer) have a very poor prognosis with only 10% of children surviving 2 years following the diagnosis [12]. Once the original cancer is cured, some children face cancer relapse (the original cancer returning). Other children are at risk for secondary malignant neoplasms (new cancers) caused the by original cancer treatment.

#### What happens when a child's cancer can't be cured?

There are times when a child's cancer can't be cured. When a cancer progresses, a child may face challenging symptoms and benefit from ongoing supportive and medical care. In South Carolina, this care can be provided by the child's oncologist and medical team in the clinic or hospital and/or through a hospice and palliative care team in the child's home. Hands of Hope is the only pediatric hospice and palliative care provider in South Carolina. An individual child may die at home or in the hospital depending on a family's wishes and available resources.

#### What unique challenges do adolescents and young adults with cancer face?

Those diagnosed with cancer between ages 15-39 years of age are termed adolescents and young adults (AYAs). The report that follows includes adolescents and young adults diagnosed with cancer between the ages of 15-19. Individuals in the AYA age group have not seen the same increases in survival that younger children with cancer have seen over time [13]. Because of the age at cancer diagnosis, AYAs also face unique vulnerabilities including issues related to autonomy and health decision making, fertility preservation, and health insurance coverage [14]. In terms of mental health, AYA survivors are at risk for anxiety, depression, and post-traumatic stress [15].

#### What are cancer disparities?

Cancer disparities are differences in cancer measures among groups. For childhood cancer in the United States, Black and Hispanic children have lower survival rates as compared to White children [11]. To improve racial/ethnic survival disparities in childhood cancer, it is important to understand what is driving the differences among groups.

Previous studies have shown that measures of access to healthcare including insurance coverage and socioeconomic status in part explain differences in childhood cancer survival between racial and ethnic groups in the United States [16]. These types of exposures are called social determinants of health and can impact patients and their families at multiple overlapping levels as described below [17].

#### Multi-level examples of modifiable drivers of racial/ethnic survival disparities in childhood cancer

Child level: insurance coverage and continuity
Family level: health literacy, caregiver support systems
Healthcare system level: quality care through delivery of clinical trials and care guidelines, cultural competency
Community level: structural racism, public policy

Adapted from Ji, X, Sohn H, Soumitri, et al, Cancer Epidemiology, Biomarkers and Prevention, 2022

#### What is a childhood cancer survivor?

A childhood cancer survivor is a person who has been cured from their original pediatric cancer and recovered from cancer treatments and is at least 2 years beyond the end of cancer treatment. There are approximately 500,000 childhood cancer survivors in the United States, and the number of survivors continues to grow with improvements in cancer treatment [3, 18]. Unfortunately, the treatments required to cure childhood cancer can have serious side effects over time (termed late effects) and cause health problems over the lifespan [18-20]. Any childhood cancer experience can be associated with anxiety, depression, or financial hardship, while specific types of cancer treatment carry additional risks for neurocognitive impairment, endocrine disorders, heart disease or other late effects (Table 1). Childhood cancer survivors are also at risk for secondary neoplasms [21]. Secondary malignant neoplasms (Table 1) are new and different cancers that survivors develop because of prior cancer treatments.

#### Table 1: Late Effects Associated with Childhood Cancer Treatments

Rody system	Potential late effect	Therapy-related exposures
body system		inclupy-related exposures
	Anxiety, depression,	
Psychosocial	financial hardship	Any cancer experience
	Neurocognitive	Cranial radiation, high dose
CNS	impairment	or intrathecal methotrexate
	Growth hormone	Cranial radiation, total body
	deficiency	irradiation
	Hypothyroidism,	
Endocrine	diabetes	Total body irradiation
	Cardiomyopathy	chest radiation
Cardiac	Cardiovascular disease	Chest radiation
	Basal cell carcinoma	Any radiation
	Thyroid cancer	Head or neck radiation
		Chest radiation,
		anthracycline and alkylating
	Breast cancer	agent chemotherapies
		Abdominal radiation, pelvic
Secondary	Colorectal cancer	radiation, or total body
neoplasms	Glioma/Meningioma	Cranial radiation
Adapted	from Bhatia S. Tonorezos	F and Landier W IAMA 2023

Because of the cancer treatment received in childhood, the majority of childhood cancer survivors have at least one serious or life-threatening health condition by the time they reach middle age [22]. Childhood cancer treatment also impacts life expectancy; children treated for cancer in the 1990s have an average life expectancy of less than 60 years [23]. Compared to the general population, childhood cancer survivors have a 4-fold increased risk of death at 20 years from their cancer diagnosis [20]. Due to these risks, childhood cancer survivors require ongoing specialized medical care over the lifespan to promote a healthy lifestyle and allow for early detection and management of treatment-related complications [24].

#### What medical care do childhood cancer survivors need?

The goal of childhood cancer survivorship care is to promote health and wellbeing in former patients over the lifespan. Most survivors of childhood cancer need survivorship care at least once annually, or more frequently based on an individual patient's needs. Survivorship care can be provided by the same facility that treated the child's cancer, through a specialized Long-Term Follow Up program, or in partnership with local primary care physicians. Childhood cancer survivors can reduce their risk of late health effects by maintaining a healthy lifestyle [20]. The Children's Oncology Group has developed expert Long-term Follow Up Guidelines to help doctors care for survivors over the lifespan and provides recommendations based on prior cancer treatments [24]. Below is an example of a long-term follow up guideline for a childhood cancer survivor.

#### Childhood cancer survivor long-term follow up guideline

Consider a female patient treated for childhood cancer with chest radiation. This patient should begin mammography at age 25 or 8-years following radiation (whichever occurs later) compared to the general population which starts mammography at 40 years of age. This is because the patient faces an increased risk of early occurring breast cancer due to radiation treatment.

### **Report Methods**

South Carolina's inaugural childhood cancer report leverages the high-quality population-based cancer data maintained by the South Carolina Central Cancer Registry (SCCCR) for over 25 years. Cancer is a mandatory reportable condition by law in South Carolina and all new cases are reported and reviewed by the SCCCR [25]. As a result, the childhood cancer data presented in this report accurately represent the burden of childhood cancer in South Carolina. The goal of this report is that the data will be used to direct priorities for childhood cancer efforts across the state. There are several measures that can help us better understand childhood cancer in South Carolina:

#### **Childhood Cancer Measures and Definitions**

**Childhood Cancer Incidence:** Childhood cancer incidence is a measure of the risk of developing childhood cancer. The incidence rate is calculated as the number of new childhood cancer cases seen over a given time over the size of the population for this age group. This rate is age-adjusted and standardized to the general population.

**Childhood Cancer Survival:** Childhood cancer survival describes the proportion of children who are alive following a cancer diagnosis.

**Relative Survival:** A measure comparing the survival of those with a specific disease with those who lack the condition over a certain time period. For example, the proportion of children with cancer alive five years following diagnosis compared with the percentage of the general population of the same age and sex who are also alive at the end of the same period. This measure shows if a disease shortens life expectancy.

**Childhood Cancer Mortality:** The childhood cancer mortality is a measure of the risk of dying from childhood cancer. The mortality rate is calculated as the number of deaths from cancer over a given time over the size of the population for this age group. This rate is age-adjusted and standardized to the general population.

**Examining Differences in Cancer Metrics:** Trends over time are reported as a percent difference. For example, a mortality rate of 5 deaths per 100,000 declining to 2.5 deaths per 100,000 is a 50% reduction in mortality. When examining differences at one point in time between two groups, we will list the exact rates or percentages of each group.

**Patient Inclusion and Data Categorization:** For this report, cancers diagnosed in individuals 19 years of age and younger between 1996-2020 are included. Data on all cancers combined are used to explore state trends in childhood cancer incidence, survival, and mortality. Data for specific types of childhood cancer provide additional information on cancer incidence trends over time and current estimates (2011-2020). Cancers are categorized following the International Classification of Childhood Cancer [26]. To provide consistency across our state cancer reports, we report childhood cancer rates per 100,000 rather than rates per 1 million at risk. Current estimates reflect the most recent 10-year period from 2011-2020 to provide an adequate sample for stable estimates. For estimates of survival, the period of observation ends with cancers diagnosed in 2016 to allow at least 5 years of follow up following diagnosis. Comparisons are made to the United States and South Atlantic Region (including Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia) [27].

The report aims to present as much data as possible. In order to provide stable and reliable estimates across cancer metrics, data are suppressed when there are fewer than 16 cases. This is also a precaution for patient confidentiality. For this reason, we do not show all reported races due to the low number of childhood cancer cases in some groups. When shown, race and ethnicity are categorized as non-Hispanic White, non-Hispanic Black, and Hispanic. When examining metrics by cancer type, not all cancer types are shown due to low numbers in some groups. Urban/rural designations are based on the Rural Urban Continuum Codes (2013) and categorized as urban and nonmetro/rural combined. Supplementary data and additional information on statistical significance is available in the appendix.

**Data Analysis:** Data was analyzed with SEER\*Stat Software from the Surveillance Research Program of the National Cancer Institute [29].

**Data Interpretation:** Trends are presented with overlapping 5-year periods spanning 1996-2020. Estimates of mortality are death caused by cancer (cancer-specific mortality) except for the survivorship section which looks at death from any cause (all-cause mortality). Childhood cancer survivors are defined as those living at least 5 years from cancer diagnosis, regardless of disease or treatment status [28]. Data estimates for Hispanic children should be interpreted with caution. Over time the registry in accordance with national best practices has improved the methods to identify Hispanic individuals. This can cause a shifting cancer portrait overtime because of improved identification of Hispanic patients.

# **Childhood Cancer Incidence in South Carolina**

Each year in South Carolina approximately 200 children are diagnosed with cancer. From 2001-2005 to 2016-2020 the incidence rate of childhood cancer in South Carolina increased 11% following a broader regional and national trend, with peak incidence from 2013-2017 of 16.8 cases per 100,000 population at risk **(Figure 2)**. The childhood cancer incidence rate in South Carolina remained lower than the South Atlantic Region and the United States.

White children had the highest incidence of childhood cancer overall in South Carolina and the United States [3]. In South Carolina from 1996 to 2020 the incidence of childhood cancer increased 18% for White children, 10% for Black children and 33% for Hispanic children (**Figure 3**). There was a persistent and increasing racial disparity in childhood cancer incidence among White and Black children. Between 1996 and 2020 the incidence for White children increased from 15.4 to 18.1 cases per 100,000. For Black children over the same time period, the incidence rate increased from 11.5 to 12.7 cases per 100,000. Differences in cancer incidence were predominantly by race rather than sex (**Figures 4 and Figure 5**). Between 1996 and 2020 White children (males and females) had higher cancer incidence than Black children (males and females, **Figure 4**). For most time periods, males (all races combined) had a slightly higher incidence of childhood cancer than females. From 2016-2020, the incidence among males was 16.8 cases (per 100,000) higher as compared to 15.2 cases (per 100,000) among females (**Figure 5**).

From 1996 to 2020 among the more common childhood cancer types, the incidence of leukemia increased 5% and lymphoma increased 47% (**Figure 6**). Among lymphoma, non-Hodgkin lymphoma was the main driver of the increasing incidence trend in the state. The incidence of childhood leukemia and lymphoma have also risen in the broader United States as a whole [3]. However, not all types of childhood cancers are rising in South Carolina. The incidence of brain/CNS (central nervous system) tumors has decreased 7% over the same time period (**Figure 6**). The report also identified a rising trend of a broad category termed "other and unspecified carcinomas" that requires follow up to better understand.

#### Figure 2: Childhood Cancer Incidence Trends for South Carolina, South Atlantic Region, and United States, 2001-2020\*

5-year age-adjusted rate per 100,000



Percenta	ge Change from 20	01-2020*
US 8% ↑	SA 13% 个	SC 11%↑

Between 2001 and 2020 the incidence of childhood cancer increased 11% in SC, though remains lower than the South Atlantic region and United States.

\*Limited to 2001 based on US data availability.

#### Figure 3: Childhood Cancer Incidence Trends by Race & Ethnicity, South Carolina, 1996-2020

5-year age-adjusted rate per 100,000



Percentage Change from 1996-2020				
White '	18% ↑	Black 10% <b>↑</b>	Hispanic 33% 1	

The incidence of childhood cancer was higher among White children compared to Black children with a widening gap overtime. For Hispanic children the incidence rose through 2005-2009 then declined.

\*There has been improved identification of Hispanic individuals over time which may contribute to the increasing incidence among Hispanic children.

#### Figure 4: Childhood Cancer Incidence Trends by Sex and Race, South Carolina, 1996-2020

5-year age-adjusted rate per 100,000



Childhood cancer incidence increased for Black and White children of both sexes. White children showed a persistently higher cancer incidence and a steeper increase as compared with Black children.

#### Figure 5: Childhood Cancer Incidence Trends by Sex, South Carolina, 1996-2020

5-year age-adjusted rate per 100,000



For most periods of observation, males had a slightly higher incidence of childhood cancer than females.

#### Figure 6: Childhood Cancer Incidence Trends for Top 3 Cancer Types, South Carolina, 1996-2020\*

5-year age-adjusted rate per 100,000



\*The scale of the y-axis is smaller on Figure 6 to better illustrate the rates of specific cancer types.

Percentage Change from 1996-2020			
Leukemias 5%个	Lymphomas 47% 个	Brain/CNS 7% ↓	

The incidence trend varied by cancer type. The incidence of childhood lymphoma increased 47% from 1996-2000 to 2016-2020, while leukemia incidence increased 5% and the incidence of brain/CNS tumors declined 7%.

### **Current Estimates of Childhood Cancer Incidence**

The general population of South Carolina includes over 1.2 million children (Figure 7 and Table 2). Childhood cancer impacts all ages, though most cases occur among young children (diagnosed 0-4 years of age) and adolescents (15-19 years at diagnosis). Children 0-4 years comprised 23% of the state population (Figure 7) but 30% of new cancer cases (Figure 8). Likewise, adolescents 15-19 years comprised 26% of the state population (Figure 7) but 31% of new cancer cases (Figure 8). These two age groups comprised over 60% of new childhood cancer cases in South Carolina (Figure 8). These age groups had the highest incidence rates of childhood cancer (20.5 cases per 100,000 among those 0-4 years and 19.1 cases per 100,000 among those 15-19 years).

Childhood cancer in South Carolina impacts both sexes and among new cancer diagnoses 51.7% were male while 48.3% were female. Childhood cancers can originate in different parts of the body with leukemias and lymphomas arising from blood cells, while brain and central nervous system tumors start in the brain or spinal cord. Epithelial cancers arise from various locations including the skin and oral cavity. Children in South Carolina were diagnosed with many different types of cancers (**Figure 9**) with leukemias (24.4%), lymphomas (17.3%) and brain/CNS tumors (16.9%) most common in the state. These three cancer types are also most prevalent in the United States [3]. The incidence rate of various cancer types also varied by age (**Table 3**). Though leukemias were most common overall, among adolescents (15-19 years) in South Carolina lymphomas and epithelial cancers/melanomas had the highest incidence rates.

This page illustrates the total population of all children in South Carolina in 2020 (Figure 7 and Table 2). This is to provide a population-level context for the childhood cancer burden and incidence estimates.

# Figure 7: Population statistics for children aged 0-19 years, South Carolina, 2020



#### Table 2: Population statistics for children aged 0-19 years, South Carolina, 2020

Age group	Count	Percent
0 - 4 years	291,296	23%
5 - 9 years	308,821	25%
10 - 14 years	327,318	<b>26</b> %
15 - 19 years	325,272	<b>26</b> %

The distribution of children in South Carolina includes 23% of children ages 0-4 years, 25% of children 0-9 years, 26% of children 10-14 years, and 26% of children 15-19 years.

#### Figure 8: Percentage of childhood cancer cases in South Carolina by age at diagnosis, 2011-2020



Table 3: Number of childhood cancer cases in South Carolina by age at diagnosis, 2011-2020

Age Group	Case Counts	Incidence Rates
0 - 4 years	601	20.5
5 - 9 years	347	11.3
10 - 14 years	430	13.8
15-19 years	610	19.1

\*Age-adjusted rates per 100,000

Children of all ages were diagnosed with cancer with most cases occurring in young children and older adolescents. Between 2011-2020 there were 601 children (ages 0-4y) and 610 adolescents (15-19y) diagnosed with cancer.

#### Figure 9: Percentage of Incident Childhood Cancer Types in South Carolina, 2011-2020



Leukemias (24%), lymphomas and brain tumors (17% each) were the most common types of childhood cancers in South Carolina.

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# Table 4: Top 4 Incident Cancers in Children in South Carolina, Overall and Stratified by AgeGroup, 2011-2020

Total		Stratified by Age Group			
Children age 0-19	Incidence rate*	Children age 0-14	Incidence rate*	Children age 15-19	Incidence rate*
Leukemia	4.0	Leukemia	4.4	Lymphomas and reticuloendothelial neoplasms	4.6
Lymphomas and reticuloendothelial neoplasms	2.8	CNS and miscellaneous intracranial and intraspinal neoplasms	2.9	Other malignant epithelial neoplasms and melanomas	4.4
CNS and miscellaneous intracranial and intraspinal neoplasms	2.7	Lymphomas and reticuloendothelial neoplasms	2.1	Leukemias, myeloproliferative & myelodysplastic diseases	2.8
Other malignant epithelial neoplasms and melanomas	1.7	Neuroblastoma and other peripheral nervous cell tumors	1.1	CNS and miscellaneous intracranial and intraspinal neoplasms	2.3

\*Incidence rates per 100,000 population at risk

Leukemia was the most common type of childhood cancer overall with an incidence rate of 4.0 cases per 100,000 population at risk. Among adolescents the most common diagnoses were lymphoma (4.6 per 100,000 at risk) and epithelial cancers and melanoma (4.4 per 100,000 at risk).

# **Childhood Cancer Survival in South Carolina**

South Carolina has seen tremendous improvement in childhood cancer survival overall and among Black, White and Hispanic children. The 5-year relative survival from childhood cancer in South Carolina has improved 11% between 1996 and 2016.\* Among children diagnosed with cancer in the most recent period, 84% survived 5 years and beyond (**Figure 10**). This significant progress in South Carolina and reflects the positive national trend in childhood cancer survival [3]. Black, White, and Hispanic children with cancer experienced improvements from 1996 to 2016, with the highest survival increase among Black children (15% increase in survival compared to 10% among both White and Hispanic children, **Figure 11**). The survival gap has decreased between Black and White children with cancer from 9% in 1996-2000 to 6% in 2012-2016. For Hispanic children as compared to White children the survival gap was 4% in 1997-2001 followed by 3% among children diagnosed 2012-2016. Though the trends are favorable, the survival for Black and Hispanic children with cancer remained lower than White children with cancer illustrating persistent disparities by race and ethnicity in childhood cancer survival in South Carolina.

Cancer survival improved in both sexes and for most childhood cancer types over the study period. From 1996-2016 the survival for males improved 12% and 10% for females (Figure 12). When comparing the most recent decade to the prior (2007-2016 vs. 1996-2006) survival improved in eight of eleven major cancer types including leukemias, lymphomas, brain/CNS tumors, neuroblastoma, retinoblastoma, renal tumors, hepatic tumors and other malignant epithelial cancers and melanoma (Figure 13). Among these, the greatest improvement in survival was for leukemia, which improved from 70% to 82% survival among those diagnosed between 1996-2006 and 2007-2016, respectively. The field of pediatric oncology has made great strides in understanding and effectively treating childhood leukemias, particularly among the most common type of leukemia, acute lymphoblastic leukemia [30]. In contrast, soft tissue sarcomas and bone tumors are among the cancer types with the lowest 5-year relative survival. For some cancer types in these categories, no new treatments have been developed in decades.

\* Survival estimates end with cancers diagnosed in 2016 to allow for 5 years of follow up. This allows us to determine if a patient diagnosed in 2016 is still alive in 2021, which is the most recent year of vital status data available.

#### Figure 10: Childhood Cancer 5-Year Relative Survival Trend, South Carolina, 1996-2016\*

Relative survival percentage



#### Percentage Change from 1996-2016

All cancers 11% ↑

The 5-year relative survival for children with cancer in South Carolina has improved 11% from 1996-2016.

\*Data unavailable for survival comparison to the region or US. Survival estimates end in 2016 to allow 5 years of follow up.

#### Figure 11: Childhood Cancer 5-Year Relative Survival Trends by Race and Ethnicity, South Carolina, 1996-2016\*

Relative survival percentage



Percentage Change from 1996-2016		
White 10% 个	Black 15% 个	Hispanic 10% 个

From 1996-2016 the 5-year relative survival improved 10% for White and Hispanic Children and 15% for Black Children. The survival gap between Black and White children has narrowed over time.

\*Data unavailable for Hispanic children 1996-2000.

#### Figure 12: Childhood Cancer 5-Year Relative Survival Trends by Sex, South Carolina, 1996-2016

Relative survival percentage



Percentage Change from 1996-2016		
Males 12% <b>Females 10% ↑</b>		
Both males and females with childhood cancer saw improvements in 5-year relative survival. From 1996-2016		

the survival improved 12% for males and 10% for females.

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# Figure 13: 5-year Relative Survival Percentage by Cancer Type and Period of Diagnosis, South Carolina, 1996-2006 and 2007-2016



Comparing the most recent time period (2007-2016) to the prior (1996-2006) the majority (8 out of 11) childhood cancers have shown improvements in survival with the greatest improvement in childhood leukemia. The survival for soft tissue sarcomas and bone tumors had not improved in the recent decade. Along with hepatic tumors these cancers had the lowest 5-year relative survival.

# **Childhood Cancer Mortality in South Carolina**

Considering children diagnosed with cancer from 1996 – 2020 in South Carolina there were a total of 998 deaths, including 716 deaths from cancer (**Table 5**). This section focuses on death from cancer. Childhood cancer mortality has consistently trended downward in South Carolina. From 1996 to 2020 the childhood cancer mortality rate decreased 21% in South Carolina, mirroring the trend of the South Atlantic Region and the United States (**Figure 14**). The mortality rate has declined for both White and Black Children (decreasing 29% and 4% respectively, **Figure 15**). There was a slight increase in the cancer mortality rate among Black children (2016-2020, 2.5 cases per 100,000 from 2.3 cases per 100,000) that should be followed to determine if this marks an unfavorable trend moving forward (**Figure 15**). For males, the mortality rate decreased 31% with no change for females (**Figure 16**).

#### Figure 14: Childhood Cancer Mortality Trends for South Carolina, South Atlantic Region, and United States, 1996-2020\*

5-year age-adjusted rate per 100,000



Percentage Change from 1996-2020			
US 21% ↓	SA 21% ↓	SC 21% ↓	

From 1996-2020 the childhood cancer mortality rate decreased 21% in South Carolina. Similar trends were seen in the region and US.

\*The scale of the y-axis is smaller on mortality figures (0-5 cases per 100,000 individuals at risk) to better illustrate the mortality rates.

#### Figure 15: Childhood Cancer Mortality Rate Trends by Race, South Carolina, 1996-2020\*

5-year age-adjusted rate per 100,000



Percentage Change f	rom 1996-2020
White 29% 🗸	Black 4% ↓

From 1996-2020 the childhood cancer mortality rate decreased 29% for White children and 4% for Black children.

\*Data for Hispanic children is suppressed due to low numbers.

#### Figure 16: Childhood Cancer Mortality Rate Trends by Sex, South Carolina, 1996-2020

5-year age-adjusted rate per 100,000



Percentage Change from 1996-2020		
Males 31% 🔸	Females 0%	

From 1996-2020 the childhood cancer mortality rate decreased 34% for males and increased 4% for females.

### <u>Current Estimates of Childhood Cancer Mortality in</u> <u>South Carolina</u>

Between 1996 and 2020 there were a total of 716 deaths from childhood cancer with 261 deaths occurring between 2011 and 2020 (Figure 17 and Table 5). Twenty percent of deaths occurred among children 0-4 years of age, 25% among those 5-9 years, 24% among those 10-14 years and 31% among those 15-19 years (Figure 17). The leading causes of childhood cancer deaths were brain/CNS tumors (32% of deaths) and leukemias (28% of deaths, Figure 18). Other malignant cancers comprised 20% of deaths; this is a broad category listed on the child's death certificate and can include cancers of the liver, lung, kidney, endocrine system, ovary or nasopharynx. Across all age groups, brain/CNS tumors followed by leukemias had the highest cancer mortality rates.

#### Figure 17: Percentage of Childhood Cancer Deaths by Age at Death in South Carolina, 2011-2020



Table 5: Number of Childhood Cancer Deaths by Age at Death in South Carolina, 1996-2020 and 2011-2020\*

Overall 199	2011-2020	
Age Group	Deaths	Deaths
0 - 4 years	157	51
5 - 9 years	165	66
10 - 14 years	169	63
15-19 years	225	81
<b>Total Deaths</b>	716	261

Over the 25-year period 716 children died from cancer. Among those who died, 157 children died at 0-4 years of age, 165 children died at 5-9 years of age, 169 children died at 10-14 years of age and 225 adolescents died at 15-19 years of age.

\*Excludes children who died from cancer >19 years of age

Figure 18: Percentage of Cancer Deaths by Childhood Cancer Types in South Carolina, 2011-2020\*



The leading causes of childhood cancer deaths were brain/CNS tumors (32%) and leukemias (27%).

\*Primary site of other malignant cancers include: liver, lung and bronchus, kidney and renal pelvis, endocrine system, ovary, nasopharynx. Cancer death codes reflect ICD codes and are not as detailed as cancer incidence codes.

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# <u>Childhood Cancer Survivors in South Carolina</u>

Between 1996 and 2020, there were 4,457 children diagnosed with cancer in South Carolina. This section focuses on the 2,962 childhood cancer survivors who lived at least 5 years from cancer diagnosis. Childhood cancer survivors were diagnosed in all regions of South Carolina with 664 children from the Lowcountry, 900 children from the Midlands, 556 children from the Pee Dee Region, and 838 from the Upstate **(Figure 19)**. Fifteen percent (444 children) were diagnosed in rural areas.

Readers may not know that those with a history of childhood cancer remain at elevated risk for serious health problems and death across the lifespan. Death can be from a recurrence of the original cancer or from long-term side effects of cancer treatment including heart disease or secondary cancers. Of the childhood cancer survivors diagnosed in South Carolina, 2,812 were still alive, while 150 had subsequently died (**Figure 20**). These 150 deaths are deaths among patients who had already survived at least 5 years from the original cancer diagnosis. The average age of death was 21 years old. There were no meaningful differences in risk of death among childhood cancer survivors by South Carolina region, sex, or rurality. Black children (**Figure 21**) and those with older age at cancer diagnosis (5 years or greater, **Figure 22**) comprised a relatively higher proportion of deaths. Childhood cancer survivors in the state were diagnosed with a variety of cancer types including leukemias (24%), lymphomas (18%) and brain/CNS tumors (16%, **Figure 23**). Among the top 3 cancer types, childhood cancer survivors with brain/CNS tumors (a relatively larger proportion of deaths (9%) compared to those with a history of leukemia or lymphoma (each 4%, **Figure 24**).

Figure 19: Case Counts of Children with Cancer who Survived at least 5 Years from Diagnosis by Region at Diagnosis, South Carolina, 1996-2020\*



South Carolina's 2,962 childhood cancer survivors were diagnosed across the state with 15% diagnosed in rural areas.

\*The estimated number of childhood cancer survivors in South Carolina does not include survivors diagnosed prior to 1996. This estimate does not account for childhood cancer survivors who moved to South Carolina after cancer diagnosis.

#### Figure 20: Vital Status among Children with Cancer who Survived at least 5 Years from Diagnosis, South Carolina, 1996-2020



Most childhood cancer survivors diagnosed in SC were still alive, while 150 had subsequently died at an average age of 21 years old.

#### Figure 21: Vital Status by Race among Children with Cancer who Survived at least 5 Years from Diagnosis, South Carolina, 1996-2020



A higher proportion of Black childhood cancer survivors subsequently died than White childhood cancer survivors.

#### Figure 22: Vital Status by Age at Diagnosis among Children with Cancer who Survived at least 5 Years from Diagnosis, South Carolina, 1996-2020



Childhood cancer survivors who were diagnosed with cancer at age 5 or greater had a higher proportion of deaths than childhood cancer survivors diagnosed at age 4 years or less.

#### Figure 23: Initial Type of Cancer among Children who Survived at Least 5 years from Diagnosis, South Carolina, 1996-2020



Childhood cancer survivors were diagnosed with a variety of cancer types, predominantly leukemias, lymphomas and brain/CNS tumors.

#### Figure 24: Vital Status for Top 3 Cancers among Children with Cancer who Survived at least 5 Years from Diagnosis, South Carolina, 1996-2020



Among children with leukemia, lymphoma and brain/CNS tumors who survived at least 5 years, approximately 4% those with leukemia/lymphoma and 9% of those with brain/CNS tumors had subsequently died.

# <u>Racial and Ethnic Disparities in Childhood Cancer in</u> <u>South Carolina</u>

The report identified racial/ethnic disparities across childhood cancer metrics in South Carolina which are highlighted in this section. As described in the Childhood Cancer Incidence section (**page 17**), White children consistently had the highest incidence of childhood cancer among all groups and the incidence gap between White and Black children had widened over time (**Figure 25**). In the most recent period, the incidence of childhood cancer was 18.1 per 100,000 among White children, 12.7 per 100,000 among Hispanic children, and 13.4 per 100,000 among Black children (**Table 6**). These incidence disparities by race and ethnicity were also present for the United States as a whole (**Figure 26**).

White children also experienced the highest 5-year relative survival from childhood cancer of all groups (**Table 6**). Black children in contrast, had the lowest incidence of childhood cancer and the lowest 5-year relative survival of all groups (**Figure 3**). The 5-year relative survival among those diagnosed between 2012-2016 was 80% among Black children with cancer compared to 83% among Hispanic children and 86% among White children (**Table 6**). Black children comprised a lower proportion of new cancer cases and a relatively higher proportion of cancer deaths (**Figure 27**).

#### Figure 25: Childhood Cancer Incidence and Mortality Trends by Race, South Carolina, 1996-2020



The incidence of childhood cancer remained consistently higher in White children as compared to Black children with a widening gap overtime. The mortality rates for both groups remains low and were trending downward.

#### Table 6: Childhood Cancer Incidence and Mortality Rates (2016-2020), and Relative Survival (2012-2016) by Race and Ethnicity in South Carolina.

5-year age-adjusted rates per 100,000 and relative survival percentage

Race and Ethnicity	Incidence Rate	5-year Relative survival	Mortality Rate
Non-Hispanic White	18.1	86%	2.2
Non-Hispanic Black	12.7	80%	2.5
Hispanic	13.4	83%	۸

^Data suppressed due to counts <16.

#### Figure 26: Childhood Cancer Incidence and Mortality Trends by Race, United States, 2001-2020



As compared to South Carolina, the United States also had disparities in cancer incidence by race and ethnicity, with White children having the highest incidence rate over time.

\*Limited to 2001 based on US data availability.

#### Figure 27: Relative Percentage of Cancer Incidence and Deaths by Race and Ethnicity, South Carolina, 2011-2020



In South Carolina, Black children comprised a lower proportion of new childhood cancer cases but a relatively higher proportion of cancer deaths in the state. This is due to poorer survival among Black children with cancer compared to White children.

# **Rurality and Childhood Cancer in South Carolina**

Survival had improved for children with cancer from both rural and urban areas with a narrowing gap overtime. In the most recent period (2012-2016) the 5-year relative survival for children with cancer from urban and rural areas was 84% (Figure 28). From 1996-2016 the 5-year relative survival improved 12% for those from urban areas and 7% among those from rural areas. The incidence of childhood cancer had risen in both rural (14%) and urban areas (15%) but remained consistently higher in urban areas (16.2 per 100,000 vs. 14.9 per 100,000 between 2016-2020, Figure 29). In the most recent time period (2016-2020) the cancer mortality rate was slightly higher for children from rural areas as compared to urban areas (2.6 per 100,000 vs. 2.3 per 100,000) which should be followed overtime to determine if this is an unfavorable trend. The childhood cancer mortality rate has declined more in urban (21% decrease) than rural areas (13% decrease) in South Carolina (Figure 29). Children with cancer from rural areas comprised a similar proportion of new cancer cases (14%) and cancer deaths (14%) (Figure 30).

#### Figure 28: Childhood Cancer 5-Year Relative Survival Trends by Rurality, South Carolina, 1996-2016

5-year relative survival





From 1996-2016 the 5-year relative survival improved 12% for those from urban areas and 7% for those from rural areas. In the most recent time period, rural and urban children had 5-year relative survival of 84%.

#### Figure 29: Childhood Cancer Incidence and Mortality Trend by Rurality, South Carolina, 1996-2020

5-year age-adjusted rate per 100,000



Percentage Change in Incidence from 1996-2020				
Urban 15% ↑ Rural 14% ↑				
Percentage Change in Mortality from 1996-2020				
Urban 21% 🗸	Rural 13% ↓			

The incidence of childhood cancer was consistently higher in urban areas. The incidence rate increased for both rural and urban areas. The mortality rate declined 21% in urban areas compared to 13% in rural areas.

#### Figure 30: Relative Percentage of Cancer Incidence by Rurality, South Carolina, 2011-2020

Figure 31: Relative Percentage of Cancer Deaths by Rurality, South Carolina, 2011-2020



Children in rural areas comprised equal proportions of new cancer cases (14%) and cancer deaths (14%).

### **Conclusions**

The preceding scientific report is South Carolina's inaugural state report on childhood cancer. The South Carolina Childhood Cancer Taskforce brought together experts from across South Carolina for the first time in a unified effort to better understand childhood cancer statewide. The robust data maintained by the South Carolina Central Cancer Registry under the South Carolina Department of Public Health allowed us to examine childhood cancer benchmarks, including where metrics have been, where they are presently, and to identify goals for the future. Areas that we identified for future childhood cancer research, advocacy, and intervention in South Carolina are re-summarized below:

#### Priority Areas for Childhood Cancer in South Carolina

- Among children with cancer in South Carolina, there were persistent survival disparities by race and ethnicity that require renewed and concentrated efforts. Racial disparities in survival were also seen among childhood cancer survivors. Understanding the mechanisms driving these disparities and developing interventions to overcome the causes of the disparities will be key to promote equitable outcomes for all children.
- The incidence of childhood cancer in South Carolina was rising overall including rising incidence trends for leukemia and lymphoma. Racial disparities in incidence were worsening over time with White children having persistently higher incidence of childhood cancer than Black children. Further research is needed to understand the changing incidence trend patterns in the broader context of rising childhood cancer incidence and incidence disparities in the United States.
- South Carolina has a growing population of childhood cancer survivors that require ongoing specialized medical care over the lifespan due to the risk of morbidity and premature mortality associated with cancer treatments in childhood. Understanding and addressing the needs of this growing population is a top priority.
- South Carolina had differences in childhood cancer metrics by rurality. The incidence of childhood cancer was consistently higher in urban areas.
- Despite tremendous progress, not all children with cancer are able to be cured. Better understanding the needs of this population, including the unique needs of adolescent and young adult patients, is critical to promote quality of life and reduce suffering at the end of life.

Data alone cannot fully share the impact of childhood cancer. We close the report with the words of children and families impacted by childhood cancer in South Carolina.

Leilani is now 10 years old having successfully been treated for neuroblastoma as a young child. At the time of her cancer diagnosis her little brother was an infant and her father was working nights. Her family reflects on the tremendous community support they received along the way in addition to the support of their doctors and nurses.



Leilani was diagnosed with metastatic neuroblastoma at 21 months of age. She is now 10 years old and has been in remission since August of 2018. At the time of her diagnosis, her mother was 6 months pregnant, and her father had just accepted a new job working the night shift which allowed him to be in the hospital with Lelani during the day. Lelani's treatments lasted for approximately two and a half years including chemotherapy, radiation, surgery and traveling for a vaccine clinical trial in New York.

Her mother reflects upon having a new infant and going back and forth between Leilani's hospital room and the Ronald McDonald House as well as traveling for additional treatments sharing, "It may seem crazy but during her treatment, hospital visits were the best times for our family because this is when we were all together. Even though Lei was getting chemotherapy, we were together as a family."

Leilani's family had many people supporting them throughout their journey including family members and school friends, however the biggest support came from the doctors and nurses at the hospital. She states, "I wouldn't trade anything for the nurses and the doctors that we had during her treatment. There were times when the nurses would even come and grab Leilani's brother and walk with him and love on him because he was essentially raised in the hospital. They really treat you like family which is so comforting and a huge load off. They show up in ways you didn't even know you needed; it's amazing."

Skyla was treated for leukemia and reached a remission though subsequently developed treatment-related acute myeloid leukemia and died at 8 years of age. She was well known to her care team for her adventurous nature and pranks during hospital stays. Her parents founded the Skyla Strong Foundation to support other parents and children facing childhood cancer.



Skyla, well known for her pranks throughout her many hospital stays, was often seen hoverboarding into the pediatric cancer clinic in full protective gear for her appointments. She was treated for leukemia with approximately two and a half years of chemotherapy. After several months of remission, she developed a second type of leukemia, treatment-related acute myeloid leukemia. Despite the best treatments, this leukemia recurred.

Her parents Shannon and Brian reflect upon their conversation with Skyla regarding her cancer returning and the decision to go home with hospice care. They sought to never hold anything back from Skyla. They told her that there was one last treatment Skyla could try but it was very toxic. Brian told Skyla, "If we go home, your 9th birthday is going to be in heaven." He remembers that Skyla stroked her chin and said, "well I was planning on going to Carowinds for my birthday, but they probably have bigger roller coasters in heaven."

Skyla had a private conversation with her doctor and together, they made the "toughest decision anyone should never have to make" to go home with hospice care where they spent 15 weeks as a family making lots of memories. In recounting the night that Skyla passed away, Shannon brought her to the hospital as she "knew she wanted to be back with the people who had started this with us. I just felt so safe with all of them. We were a family. Brian and I both had our hands on her heart, and we felt her heartbeat for the last time and she took her last little breath. And went to heaven."

Her parents started the Skyla Strong Foundation to support other children and families impacted by childhood cancer. Brian states, "Through Skyla Strong, I get to engage with families. I wish the end to my story was different. It's been my healing to be there and help people on their walk that are going through what I've been through."

*Emma remains on treatment for childhood leukemia and is in a remission. Her mother describes the shock of the initial diagnosis and the isolation she has sometimes felt during the treatment journey. She is grateful Emma is feeling more like herself. Treatment for Emma's type of leukemia lasts for approximately 2.5 years.* 



Emma was diagnosed with leukemia at 7 years of age. Her mother remembers having a gut feeling something was wrong when Emma would no longer laugh because laughter caused her physical pain, and her ongoing leg pain caused her to avoid activities she typically loved. Her mom recalls, "I got on my knees and prayed for it to be anything but that - arthritis, a bone infection, anemia, anything - but in the pit of my stomach I knew." The doctors shared that her blood work was concerning for cancer which was confirmed with additional tests.

Her mother shares her thoughts during that first week of cancer treatment remembering, "Our world collapsed on top of us, but we are slowly processing this new world that will be our new life and our new normal for quite some time. I have gone through all 7 stages of grief since and reached acceptance... I am hopeful she will be cured."

Treatment for this type of childhood leukemia is long, lasting approximately two and a half years. Her treatment includes chemotherapy in the hospital and clinic and being sedated for additional chemotherapy being delivered through spinal taps. Her mom describes going through cancer treatment as "isolating at times even when you have a crowd of people in a room supporting you." During these times, she has relied on her faith, her oncology team, and the outpouring of love and support from their friends, family, and community.

Emma is currently in a remission and remains under treatment for her leukemia. Her mother describes her as a "rockstar" bringing joy to all in her presence.

Collin was diagnosed with a brain tumor at age 2, facing multiple relapses over his life and passing away at age 15. Despite his long medical journey, his upbeat attitude was contagious when he would declare his plans to "wake up, kick butt, repeat!" His medical journey spanned more than a decade. His mother wished there was more support along the way for him to be around other children and do activities like art or yoga to help with his anxiety. She continues their fight as a clinical trials research nurse for pediatric cancer.



Collin was diagnosed with an ependymoma at 2 years of age. After being sick off and on for about 6 months, his mother had him admitted to the hospital for evaluation. She was working as a nurse at the time and recalls, "It just hit me. He has a brain tumor. [He was down getting a CT scan but] I already knew." Due to his age and the risks of radiation, Collin had specialized radiation therapy out of state. He returned home and his mother remembers, "I knew all about the cognitive effects [of radiation] and had him enrolled in early intervention and speech therapy. He was really thriving at that point."

When Collin was 7 years old, he relapsed. His mom describes that day, which was 5 years from the end of treatment. "He was supposed to be cancer free. I was six months pregnant at the time and they said it [his tumor] had come back in a different part of his brain, a distant metastasis." Collin underwent additional brain surgery and radiation therapy, and though he did experience some side effects from radiation including high frequency hearing loss, he was still able to do what he loved. His positive attitude was contagious, and he would declare, "I'm gonna wake up, kick cancer's butt and repeat!"

It was a long journey for their family spanning more than a decade. Collin had anxiety from all he had experienced, and his therapist recommended a support group. "Ok – where do I find that?" his mother shares, "We live in a rural area." His mother wished there had been more support along the way, more chances to be around other children facing the same thing. When Collin suffered further relapses a clinical trial gave him two additional good years. He ultimately passed away at 15 years of age after treatments had stopped working. His mother shares, "I told him he could rest, and I would continue to fight." Collin's mother works in childhood cancer clinical trials. Collin would have turned 19 years old this year.

Kaycen was diagnosed with neuroblastoma at age 8 and completed over 2 years of treatment. He is now 11 years old and thriving as a straight A student who loves playing baseball. His mother remembers the challenges of frequent travel to and from the oncology clinic and the long hospital stays made more challenging during the COVID-19 pandemic. She acknowledges her faith and his medical team for getting her family through the scariest time of their lives.



Kaycen was diagnosed with high-risk neuroblastoma at 8 years of age. His mother remembers the day of his cancer diagnosis sharing, "During our diagnosis we were numb. Hearing your child has cancer is one of the worse feelings ever. From that point, our lives changed forever." For his cancer, Kaycen required over 2 years of treatment that included chemotherapy, surgery to remove his tumor, immunotherapy, two stem cell transplants and radiation. It was a challenging time for their family as his mother recalls, "Countless days and nights in the hospital and days without seeing our younger son [Kaycen's brother] and family back home about 73 miles away! We would travel back and forth [to the hospital] sometimes 3-4 times a week to get blood work and to check on Kaycen because chemotherapy would make him so sick." Kaycen underwent treatment during the beginning of the COVID-19 pandemic and the strict visitation policy didn't allow extended family members to visit, however, "The staff quickly became family and they will always hold a special spot in our hearts!"

Kaycen remains in remission and is now 11 years old having completed his treatment. As a childhood cancer survivor, his mom feels he is thriving. He is a straight A student in school and loves playing baseball. She wonders how her family was able to get through such a long and intensive treatment saying, "Sometimes we look back and wonder how did we get through all of it! Faith, prayer, and our love for God is our how! It was one of the scariest times of our lives but we are forever thankful for today's medicine and our oncology family!"

Ellie is a childhood cancer survivor, now 12 years old who was treated for a germ cell tumor at 2 years of age. Her mother remarks how cancer will always be part of their lives and story. Ellie has side effects of her childhood cancer treatments and required a hip replacement as a result. Ellie uses her creative strengths to raise awareness about childhood cancer and plans to be a child life specialist to help other children when she grows up.



Ellie was diagnosed with a germ cell tumor of her mediastinum at 2 years of age. Her initial cancer was cured though she relapsed at 6 years of age requiring additional treatments. In total she received two rounds of chemotherapy as well as radiation and a bone marrow transplant. She is currently 12 years old and in remission.

Ellie speaks about being a childhood cancer survivor. She is most proud of "being able to come back better and stronger as well as still be who I am." Her mother acknowledged that this diagnosis will never disappear completely from their lives sharing, "Yes, Ellie beat cancer, but cancer will unfortunately always be a part of our lives. We wonder if it will come back again. Ellie still deals with the after effects of her treatments including alopecia from her radiation as well as leg length discrepancy [from] when the chemotherapy stunted her growth in her left leg. She had hip reconstruction surgery two years ago for this. I do not think many people are aware of everything that goes into a diagnosis of [childhood] cancer."

Ellie uses her artistic talents to inform others about childhood cancer. Last summer she drew pictures of cartoon characters with gold ribbons beside them (representing childhood cancer awareness month) and sold them around her neighborhood to raise awareness. Due to her experience with childhood cancer, Ellie plans to be a child life specialist when she grows up.

Tori was treated for osteosarcoma at age 16, completing treatment at 21 years of age which included chemotherapy, surgery and two clinical trials. She is now 26 years old and a childhood cancer survivor. She remembers the financial stress of her years in cancer treatment. She was able to endure her long journey by focusing on one day at a time.



Now 26, Tori is a childhood cancer survivor diagnosed at 16 years of age with osteosarcoma, a type of bone tumor. She was an athlete accustomed to pain but when persistent discomfort remained in her arm, a bone scan confirmed the diagnosis of cancer. She completed nine months of treatment and when unsuccessful, she underwent additional surgery and participated in two clinical trials, completing treatment at 21 years of age.

Tori shared that her insurance did not cover medical expenses until there was a diagnosis. That uncertainty added to the financial hardship while undergoing cancer treatments which included outof-pocket costs like parking, travel, lodging and meals – costs that she shared lasted for years.

She stressed the importance of taking the punches as they come because there are no guarantees and every patient's situation is different. During her cancer treatment journey, she checked off the days of her treatment roadmap, which helped her stay focused and endure the long journey.

### **Report Partners**

#### South Carolina Cancer Alliance

Since 2003, the Alliance has been dedicated to the prevention and early detection of cancer as well as improving the treatment and quality of life of those diagnosed with cancer. The Alliance consists of over 800 members who represent the state's medical community, academic institutions, public health professionals, nonprofit organizations, and various community groups. Every five years, the members work together to develop the five-year South Carolina Cancer Plan. This plan serves as the official road map in the fight against cancer in the state. To view the plan, visit sccancer.org. Pediatric Cancer objectives are discussed in section 4.2 of the plan and serve to enhance the quality of life of the child, adolescent, and/or young adult patients with cancer from diagnosis through treatment to survivorship across the life span. To learn more about the work of the South Carolina Cancer Alliance visit <a href="https://www.sccancer.org">https://www.sccancer.org</a>.

#### South Carolina Central Cancer Registry

The South Carolina Central Cancer Registry (SCCCR) is the state's population-based cancer surveillance system that collects, processes, analyzes, interprets, and disseminates cancer incidence (newly diagnosed cases) and cancer mortality (deaths due to cancer) to stakeholders to guide cancer prevention and control efforts, and to researchers in South Carolina and beyond. South Carolina Division of Public Health's Division of Vital Statistics provides information on cancer mortality to the SCCCR. Data from the SCCCR are used to study trends in cancer incidence, mortality, patient survival rates, and disparities across demographics and regions. Funded primarily by the Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR) along with some state funds, SCCCR annually contributes data to NPCR for inclusion in the official cancer statistics publication for the nation, United States Cancer Statistics. The SCCCR has consistently received the CDC Registry of Distinction award for excellence, as well as Gold Certification from NAACCR, which is their highest level of excellence for data timeliness, completeness, and quality.

#### The University of South Carolina's Arnold School of Public Health

Established in 1975, the Arnold School of Public Health at the University of South Carolina is the 19th accredited school of public health in the United States. The Arnold School of Public Health boasts record enrollments and tremendous growth of faculty research funding while offering diverse academic programs and conducting groundbreaking research. The Department of Epidemiology and Biostatistics at the school has a proud tradition of excellence rooted in a deep, abiding commitment to advance the public's health through research. The next generation of epidemiologists and biostatisticians are trained and empowered as they collaborate to work toward the shared goal of generating and analyzing data to advance the public's health. Another part of the school, the Rural and Minority Health Research Center, aims to address health and social inequities in rural and minority populations through policy-relevant research and advocacy.

# <u>Glossary</u>

**Age adjustment:** This process standardizes the estimates based on the distribution of ages in the United States. This makes areas comparable to each other, even with different age compositions.

All cancers: The term used when all types of cancer are analyzed together as one group.

**All-cause mortality:** A death from any cause including cancer, health-related causes, or accidents. This represents the total number of deaths in a group over a designated time.

**Cancer disparities:** Differences in cancer measures between groups (for example by race and ethnicity or geography).

**Cancer incidence:** The number of new cancer cases diagnosed over a given time.

**Cancer survival:** A measure of the proportion of people diagnosed with cancer that are still alive.

**Cancer-specific mortality:** A measure of deaths due to cancer over a certain time period. This measure does not include deaths from other causes (for example, health-related causes).

**Cancer type:** When cancers are broken down into smaller groups. For childhood cancer there are 12 main categories as well as additional smaller categories. The cancer type in addition to other factors determines the treatment and prognosis.

**Childhood Cancer Survivor:** There are variable definitions of cancer survivor. For this report we use the term to describe someone who is alive and in remission at least 5 years following childhood cancer diagnosis.

**Center for Disease Control and Prevention:** The national health agency tasked with ensuring the public's health. Childhood cancer: Cancer diagnosed in children and adolescents. For this report the term identifies cancers in those ≤ 19 years.

**Children's Oncology Group:** A largest clinical trials and research organization for childhood and adolescent cancer. The Children's Oncology Group is supported by the National Cancer Institute.

**Incidence rate:** The number of new cases (e.g. of cancer) in a given population over a standard time, divided by the size of the population at risk. Childhood cancer incidence rates are normally expressed as new cases per 100,000 children and adolescents at risk.

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# <u>Glossary</u>

**International Classification of Childhood Cancer:** The standard guide to classify and categorize childhood cancers based on the cancer's histology, primary site, and behavior.

**Mortality rate:** The number of deaths in each population over a standard time, divided by the size of the population at risk. The mortality rate in childhood cancer is normally expressed as deaths per 100,000 children and adolescents at risk.

**Pediatric oncologist:** A doctor with specialized training and certification to diagnosis and treat children with cancer. Prognosis: The anticipated outcome or course related to a disease.

**Relative survival:** A measure comparing the survival of those with a specific disease (cancer) without the condition over a particular time period. For example, the proportion of children with cancer alive five years following diagnosis compared with the percentage of the general population of the same age and sex also alive at the end of the same period. This measure determines if a disease shortens life.

**South Carolina Cancer Alliance:** The state organization responsible for determining and implementing the South Carolina Cancer Plan. The SCCA is divided into workgroups including a Pediatric Cancer Work Group. These workgroups are responsible for developing, implementing, and evaluating specific projects comprised in the South Carolina Cancer Plan.

**South Carolina Cancer Plan:** The Cancer Plan for the state of South Carolina. The Centers for Disease Control and Prevention supports states to prepare plans with data-driven approaches for cancer work in the state.

**South Carolina Central Cancer Registry (SCCCR):** The state cancer surveillance system responsible for maintaining information on new cancer cases in accordance with national standards and reporting population-based cancer statistics for South Carolina. The SCCCR falls under SC Department of Public Health.

**South Carolina Department of Public Health:** The state agency that is responsible for protecting the public's health in South Carolina.

Trend: A measure of how a particular metric changes over time

**Vital Status:** A determination of if a patient is still alive. Deaths were verified by reporting source or via data linkages to state vital records data or National Death Index data. Patients are presumed to be alive in absence of confirmation of death. This method is explained in further detail on the SEER website here: <u>Months Survived Based on Complete Dates - SEER (cancer.gov)</u>

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Anthony Alberg, PhD, MPH University of South Carolina

Stephanie Chiodini, MSPH South Carolina Department of Public Health

Stuart Cramer, DO USC School of Medicine, Columbia, Prisma Health

> Elizabeth Crouch, PhD University of South Carolina

Virginie Daguise, PhD South Carolina Department of Public Health

> Judy Fulmer South Carolina Cancer Alliance

Rahul Ghosal, PhD, MS University of South Carolina

Anna Hoppmann, MD, MPH USC School of Medicine, Columbia, Prisma Health

> Michelle Hudspeth, MD Medical University of South Carolina

Bezawit Kase, PhD South Carolina Department of Public Health

Aniket Saha, MD USC School of Medicine, Greenville, Prisma Health

> Henry Well, Director Former Director, SC Cancer Alliance

Patient narrative collection: Olivia Baumgarten, MD; Karly Dubs, DO; and Sallyann Koontz

An electronic copy of the report is available for download at sccancer.org. For a hard copy please contact us at: South Carolina Cancer Alliance (Alliance) 1800 St. Julian Place, Suite 408, Columbia, SC 29204 | Phone: 803-708-4732

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# <u>Appendix</u>

# Data in the supplementary appendix are provided from the South Carolina Cancer Incidence Data [31] and the Mortality Data for South Carolina Provided by the Office of Vital Statistics [32].

Table S1. Number and percentage of new childhood cancer diagnosis in South Carolina overall and from 2011-2020\*

	1996 - 2020		2011	-2020
	Count	Percent	Count	Percent
All	4,518		1,988	
Age at diagnosis				
0 - 4 years	1,379	30.5%	601	30.2%
5 - 9 years	788	17.4%	347	17.5%
10 - 14 years	957	21.2%	430	21.6%
15-19 years	1,394	30.9%	610	30.7%
Sex				
Male	2,386	52.8%	1,028	51.7%
Female	2,132	47.2%	960	48.3%
Race and ethnicity				
Non-Hispanic White	2,910	64.4%	1,252	63.0%
Non-Hispanic Black	1,246	27.6%	532	26.8%
Hispanic	261	5.8%	151	7.6%
Address at diagnosis				
Urban	3,838	84.9%	1,710	86.0%
Rural	674	14.9%	275	13.8%

	1996 - 2020		2011	-2020
	Count	Percent	Count	Percent
All	4,518		1,988	
Type of cancer				
Leukemias,				
myeloproliferative &				
myelodysplastic diseases	1,147	25.4%	486	24.4%
Lymphomas and				
reticuloendothelial				
neoplasms	728	16.1%	343	17.3%
Brain and central nervous				
system neoplasms	807	17.9%	336	16.9%
Neuroblastoma and other				
peripheral nervous cell				
tumors	229	5.1%	105	5.3%
Retinoblastoma	86	1.9%	38	1.9%
Renal tumors	234	5.2%	109	5.5%
Hepatic tumors	60	1.3%	28	1.4%
Malignant bone tumors	234	5.2%	97	4.9%
Soft tissue and other				
extraosseous sarcomas	301	6.7%	125	6.3%
Germ cell & trophoblastic				
tumors & neoplasms of				
gonads	244	5.4%	112	5.6%
Other malignant epithelial				
neoplasms and				
melanomas	448	9.9%	209	10.5%

\*4,518 cancers were diagnosed in 4.457 children. An individual child may be diagnosed with more than one cancer.

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# <u>Appendix</u>

**Table S2.** Characteristics of childhood cancer deaths in South Carolina by time period\*

	1996 - 2020		2011	-2020
	Count	Percent	Count	Percent
All	716		261	
Age at death				
0 - 4 years	157	21.9%	51	19.5%
5 - 9 years	165	23.0%	66	25.3%
10 - 14 years	169	23.6%	63	24.1%
15-19 years	225	31.4%	81	31.0%
Sex				
Male	397	55.4%	139	53.3%
Female	319	44.6%	122	46.7%
Race and ethnicity				
Non-Hispanic White	412	60.3%	144	57.6%
Non-Hispanic Black	234	34.3%	85	34.0%
Hispanic	37	5.4%	21	8.4%

	1996 - 2020		2011	-2020
	Count	Percent	Count	Percent
Address at diagnosis				
Urban	590	82.4%	225	86.2%
Rural	126	17.6%	36	13.8%
Type of cancer				
Leukemias	232	32.4%	72	27.6%
Lymphomas	42	5.9%	16	6.1%
Brain and Other Central Nervous System	182	25.4%	83	31.8%
Bones and Joints	53	7.4%	18	6.9%
Soft Tissue including Heart	51	7.1%	17	6.5%
Endocrine system	56	7.8%	^	~
Digestive system	26	3.6%	^	^
Urinary system	24	3.4%	^	^

\*Deaths occurring in those >19 years of age are excluded. ^Data suppressed due to counts <16. This table illustrates death from malignant cancer, other causes of death are excluded. There were 998 deaths overall in the cohort from all causes.

# <u>Appendix</u>

Table S3. Childhood cancer survivors with at least 5 years of survival time in South Carolina

	All	Alivea	Deceased <sup>a</sup>	p-values <sup>b</sup>
Total	2962	2812	150	
Sex				
Male	1550 (52.3%)	1468 (94.7%)	82 (5.3%)	0.559
Female	1411 (47.6%)	1343 (95.2%)	68 (4.8%)	
Age at diagnosis (Mean, (SD))	9.6 (6.4)	9.5 (6.4)	11.0 (5.8)	0.006
Age groups at diagnosis				
0 – 4 years	924 (31.2%)	897 (97.1%)	27 (2.9%)	0.005
5 – 9 years	511 (17.2%)	480 (93.9%)	31 (6.1%)	
10 – 14 years	618 (20.9%)	580 (93.9%)	38 (6.1%)	
15 – 19 years	909 (30.7%)	855 (94.1%)	54 (5.9%)	
Current age <sup>c</sup> (Mean, (SD))	23.9 (8.8)	24.0 (8.8)	21.0 (7.5)	<0.0001
Race and Ethnicity				
Non-Hispanic White	1962 (66.3%)	1875 (95.6%)	87 (4.4%)	0.024
Non-Hispanic Black	784 (26.4%)	729 (93.0%)	55 (7.0%)	
Hispanic	154 (5.2%)	Data suppressed	due to counts < 16	
SC Regions				
Lowcountry	664 (22.4%)	629 (94.7%)	35 (5.3%)	0.551
Midlands	900 (30.4%)	860 (95.6%)	40 (4.4%)	
Pee Dee	556 (18.8%)	522 (93.9%)	34 (6.1%)	
Up State	838 (28.3%)	797 (95.1%)	41 (4.9%)	
Address at diagnosis				
Rural	444 (15.0%)	419 (94.4%)	25 (5.6%)	0.56
Urban	2514 (85.0%)	2389 (95.0%)	125 (5.0%)	

	All	Alive <sup>a</sup>	Deceased <sup>a</sup>
Total	2962	2812	150
Cancer type			
Leukemias, myeloproliferative & myelodysplastic diseases	718 (24.2%)	691 (96.2%)	27 (3.8%)
Lymphomas and reticuloendothelial neoplasms	544 (18.4%)	525 (96.5%)	19 (3.5%)
Brain and central nervous system neoplasms	477 (16.1%)	432 (90.6%)	45 (9.4%)
Neuroblastoma and other peripheral nervous cell tumors	146 (4.9%)	۸	^
Retinoblastoma	69 (2.3%)	^	۸
Renal tumors	169 (5.7%)	^	^
Hepatic tumors	29 (1.0%)	^	^
Malignant bone tumors	136 (4.6%)	^	^
Soft tissue and other extraosseous sarcomas	178 (6.0%)	^	^
Germ cell & trophoblastic tumors & neoplasms of gonads	183 (6.2%)	^	۸
Other malignant epithelial neoplasms and melanomas	313 (10.6%)	^	۸

*a* vital status as of end of 2021, b based on chi-square test or t-test, c estimated age as of end of 2021 or by time of death. ^Data suppressed due to counts <16

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