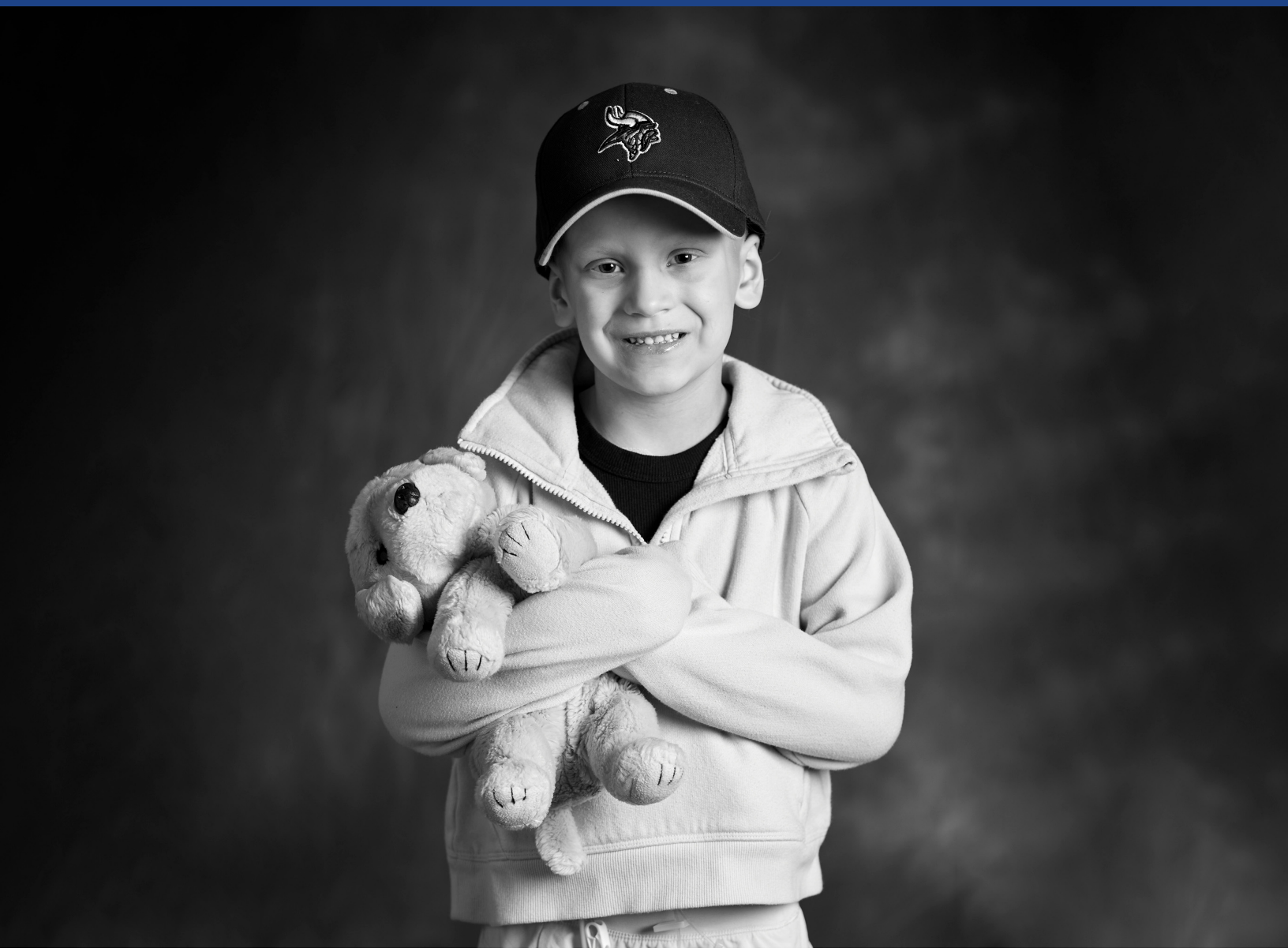
The Childhood Cancer Report

From Diagnosis to Research: Measuring Momentum in the Search for Cures



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Alex's Lemonade Stand
Foundation for Childhood Cancer™

The Childhood Cancer Report 2026

Acknowledgments

Lead Author
Trish Adkins

Scientific Contributor
Justin Ingram, PhD

Copyeditor
Millie Reeve

Fact Checker
Katherine Greene

Editorial Team
Adam Paris, Jay Scott, Liz Scott, Lisa Towry

Research Reviewers
John Maris, MD, Children's Hospital of Philadelphia; Dan Wechsler, MD, PhD, Emory University School of Medicine; Ryan Roberts, MD, PhD, Dana-Farber Cancer Institute; Jesse Berry, MD, Children's Hospital Los Angeles; Jennifer Kalish, MD, PhD, University of Pennsylvania; Stephen Mack, PhD, St. Jude Children's Research Hospital; Eirini Papapetrou, MD, PhD, Icahn School of Medicine at Mount Sinai; Steven DuBois, MD, MS, Dana-Farber Cancer Institute; Zachary Reitman, MD, PhD, Duke University School of Medicine; Kelsey Bertrand, MD, MSc, MBBS, FAAP, St. Jude Children's Research Hospital

Design and Production Team
Melissa Ruiz, Graphic Design
Craig Richetti, Web Design & Development
Clever Name Here, Web Design

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Introduction: The Childhood Cancer Report

In 1970, an oncologist named Donald Pinkel announced that the most common type of childhood leukemia was no longer incurable. He said that 50% of children with acute lymphoblastic leukemia (ALL) could be cured. This was a landmark proclamation—until this point, leukemia killed nearly every child who was diagnosed since the disease was first described in 1827.

But the reality was more complicated than that. Dr. Pinkel later went on to clarify and to ensure no one misinterpreted his words. Yes, at least half the children with ALL could be cured, but only if they have access to optimal care. He wrote, "worldwide the vast majority of children do not receive optimal treatment so that the worldwide apparent cure rate is much lower."[1]

Childhood cancer—its data, diagnosis, treatments, research, and cures—is always complicated and easily misinterpreted. Social media feeds are filled with inconsistent diagnosis counts, outdated information about drug approvals, and general misunderstandings about what childhood cancer is and isn't. At diagnosis, families are instantly transported to a terrifying world where the language is mired in jargon, test results, and unpronounceable drug names, all while trying to save their child's life. During this difficult time, they just want to understand what is happening to their child.

The Childhood Cancer Report is the first comprehensive review written for non-scientific readers. This report is an attempt to strip away the jargon, illuminate the trustworthy data sources, provide an overview of historical milestones, and open the door to discussion. The content inside centers on the data that helps advocates, policymakers, families, and others invested in finding cures for childhood cancer understand the full scope of progress as well as the gaps and barriers that still exist for kids facing cancer.

The information was compiled via interviews, data review, research, and discussion over the period of nearly one year. It is fully referenced to allow readers with more options for further reading. Access dates are included for all references to ensure transparency and accuracy. The data and information is largely based on the United States population, but it does include some overview of the global burden and inequities of childhood cancer.

Dr. Pinkel proclaimed that research worked. He also proclaimed that it didn't work for everyone, yet. This report is written with the firm belief that while we cannot yet control the incidence of childhood cancer, we can indeed count on more cures.

The Data

In 2019, a team of researchers collaborated on a study that modeled the global burden of childhood cancer in disability adjusted life-years (DALYs).[2] DALYs are a way to measure the overall burden of disease—not just the deaths and survival rates. They are a way to measure the potential years lost when a person dies in childhood and also to measure the potential years of life impacted by disease. The study's findings were profound—in the sample year (2017), 11.5 million healthy years were lost to childhood cancer. It is a number too big to fathom—over one hundred centuries of potential gone in just one year.

Yet, by the annual diagnosis numbers, childhood cancer is rare. In any given year, approximately 2 million Americans are diagnosed with cancer[3] and less than 15,000 of those diagnosed are children.[4] Globally, approximately 400,000 children develop cancer each year, but that number is most likely a low estimate—there isn't a global way of counting childhood cancer diagnoses and many low- to middle-income countries lack a centralized registry.

The disparity between the healthy years of life lost and the total cases of childhood cancer are why tracking and analyzing childhood cancer data is so critical. The numbers tell a story of persistent challenges, continued progress, and the urgent need for more research. This section presents the most current data on incidence, survival, and outcomes for children with cancer, primarily in the United States. It also contains some explanations of how this data is collected—and where more data is needed.

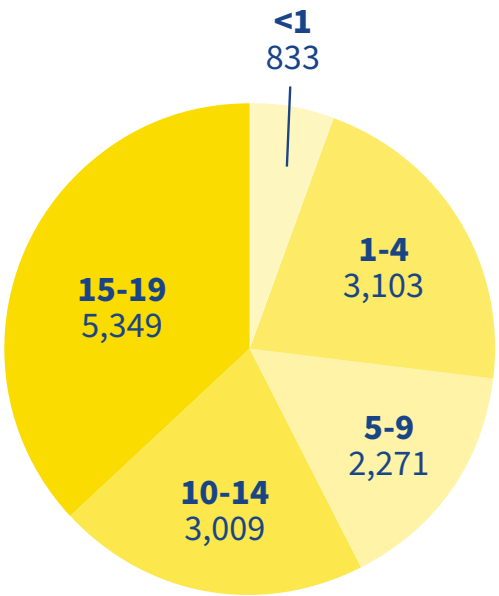
The Burden of Childhood Cancer in the United States

Childhood cancer is a group of diseases in which abnormal cells grow out of control in children and adolescents ages 0-19. It is not just one disease, but dozens of different types. While many tumors are malignant, some tumors in children may be non-malignant but still require oncology treatment. The data in this section shows a holistic overview of childhood cancer. Further ahead, read more about the data around individual disease types (leukemia, neuroblastoma, brain tumors, etc.), as well as the key milestones in research and treatments in Section 2 of this report.

Key Facts:[5]

- Approximately 15,000 children are diagnosed with cancer each year in the United States.
- About 1 in 274 children will be diagnosed with childhood cancer by age 20.
- Childhood cancer is the leading cause of death by disease in the United States.
- While incidence rates of childhood cancer are increasing, less children are dying of cancer.
- There are over 500,000 survivors of childhood cancer in the United States.[6]

Cases of Childhood Cancer in the United States by age, 2023[7]



The average age at diagnosis for childhood cancer is 8 years old. For adult cancers, that age is 67.[8]

Demographics of Childhood Cancer

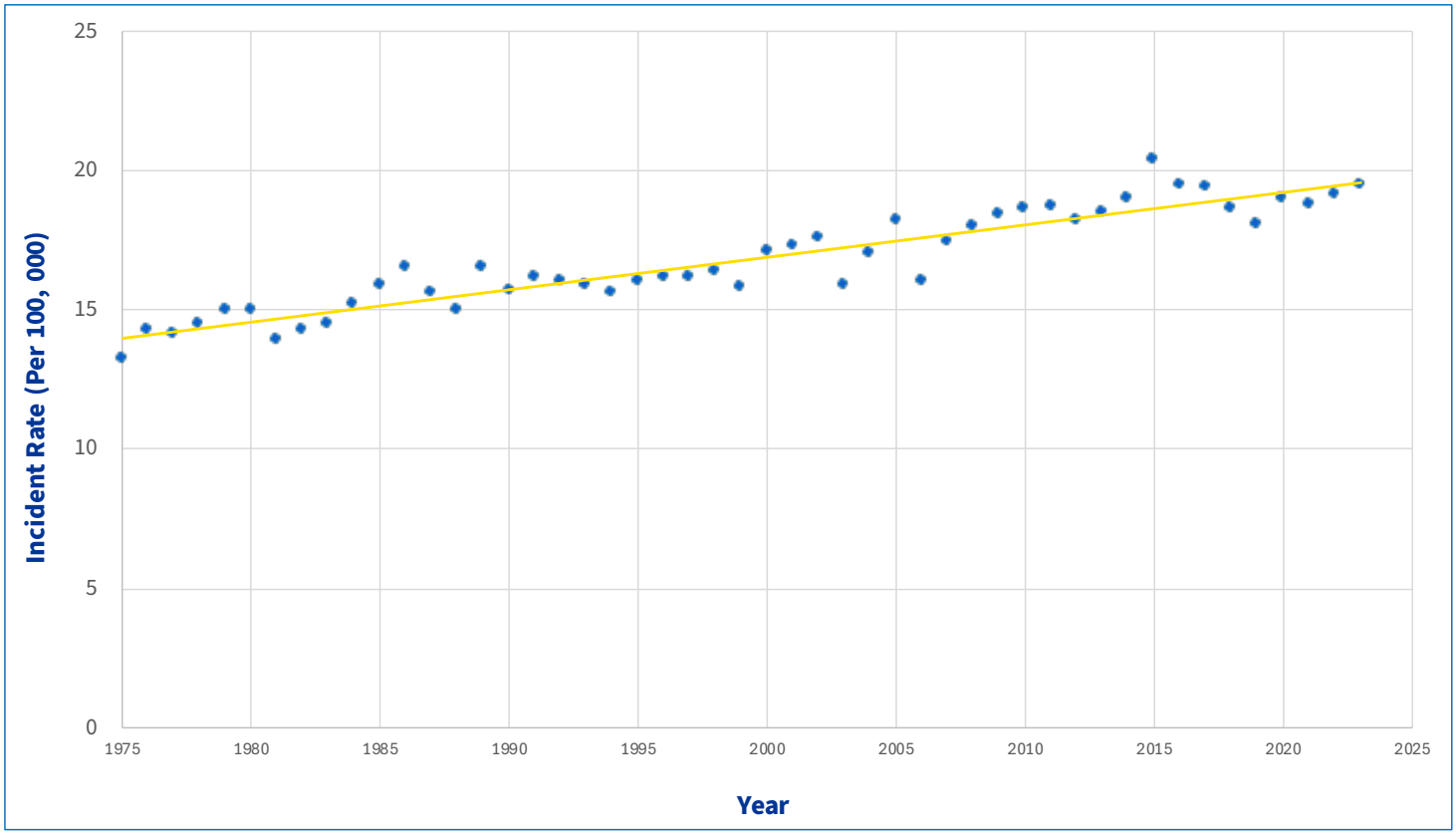
Childhood cancer registrars who maintain and review reported cases of childhood cancer track more than just the diagnosis. They track age, ethnicity, geographic location, and first primary treatment. This data gives valuable insights to oncology researchers as they try to understand the complexities of cancer, and also to researchers who are tracking treatment disparities, cancer clusters (areas with an increased number of cases), and other demographic indicators. For a more in-depth discussion on the demographics of childhood cancer, see Section 3.

Age-Adjusted Incidence Rates[9]

Age-adjusted incidence rates help us understand the risk of cancer in a population by taking age differences into account. For example, a location with more children might appear to have higher rates of childhood cancer because there are more kids, not necessarily because the disease is more common there.

By adjusting for age, experts can make more accurate comparisons between different places or time periods and see whether the actual risk of cancer is truly going up or staying the same.

Age-Adjusted Incidence Rates 1975-2023, United States



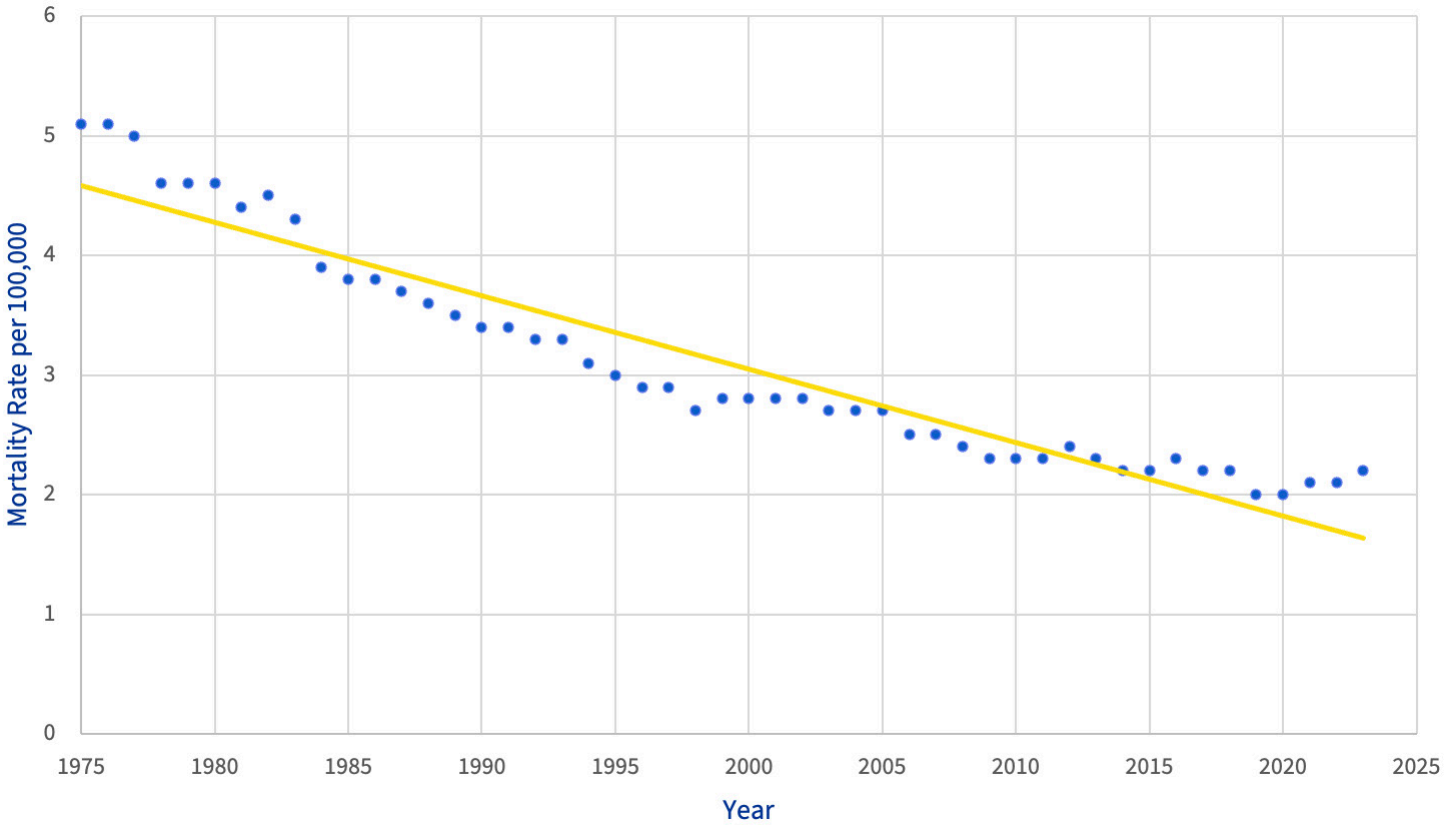
Incident rates have been increasing since 1975. Jump ahead to Incidence and Causation (page 10) for more information.

Mortality Rates

The graph below shows the decline in mortality rates since 1975, thanks to better treatments. In 2024, the most recent year for which mortality data is available, 1,801 children died from cancer.[10]

In the United States, mortality rates are tracked by the National Vital Statistics System, which captures information about every death from all cause from every county in the United States. Mortality data is shared with SEER and reviewed on a different cycle than the incidence data, which is reviewed and collated by cancer registrars. As a result, the timeline for reporting varies due to different agencies managing the data.

Mortality Rates 1975-2024, United States[11]



Cancer mortality rates, which had been steadily declining for decades, showed a slight increase around 2020–2021 for both children and adults. While no single cause has been definitively established, researchers largely attribute this shift to the direct and indirect effects of the COVID-19 pandemic. These included disruptions to healthcare services, delays in cancer screening and diagnosis, interruptions in treatment, and increased vulnerability among patients with cancer. Together, these factors may have contributed to worse outcomes during this period.[12]

Childhood Cancer: A Group of Diseases

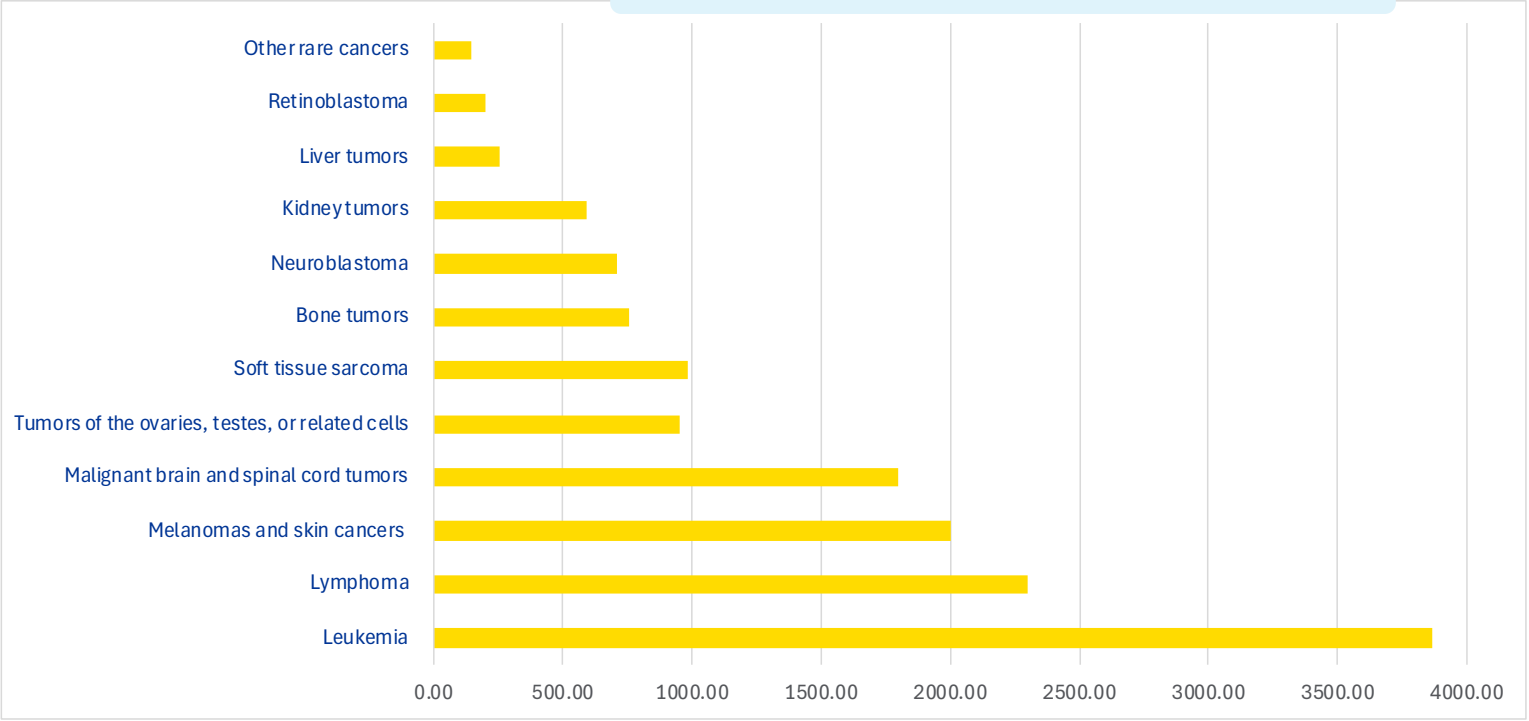
"Childhood cancer" is an umbrella term for many different types of malignancies—diseases in which abnormal cells grow uncontrollably and can spread throughout the body of a child or teen between the ages of 0 and 19. Like normal cells that carry out specific tasks, such as making blood or building bone, cancer cells are also specialized. They have unique biological and genetic features that drive how they grow and behave.

Childhood cancers can arise anywhere in the body:

- **Leukemia** and **Lymphoma** start in the blood and immune system.
- **Sarcoma** develops in bones and soft connective tissues.
- **Brain and spinal cord tumors** can be malignant or benign, but their location in the central nervous system makes them equally serious.
- **Retinoblastoma** attacks the eye, usually in very young children, threatening both sight and life.
- **Neuroblastoma** arises from immature nerve cells, often in the adrenal glands but sometimes in the neck, chest, or spine.
- **Hepatoblastoma** is a childhood liver cancer, and **Wilms tumor** is a kidney cancer.

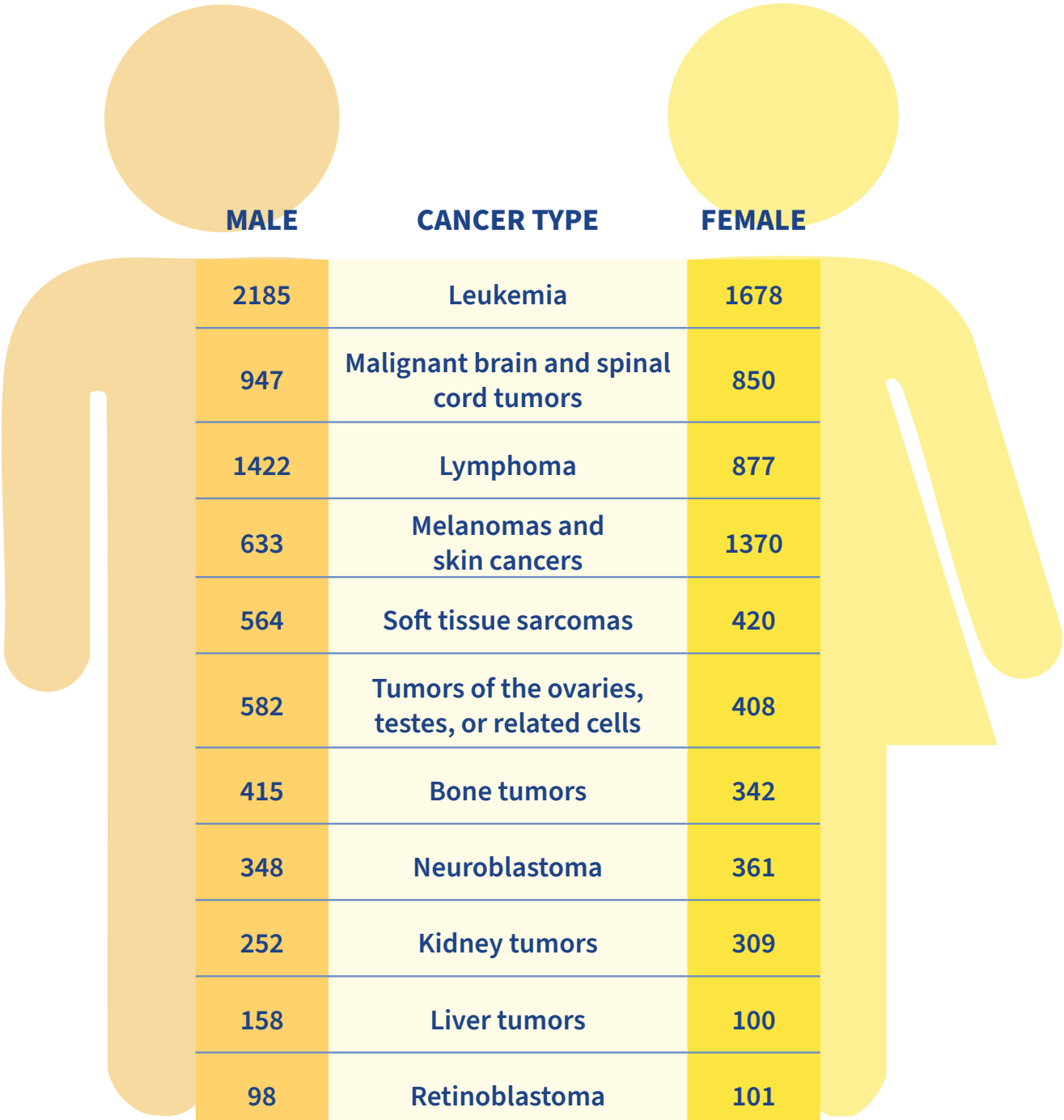
Within each of these types there are many distinct subtypes; for example, there are multiple forms of leukemia, brain tumors, and sarcomas—each with their own cellular and genetic characteristics. Some, like Wilms tumor and acute lymphoblastic leukemia (ALL), now have excellent cure rates. Others, such as diffuse intrinsic pontine glioma (DIPG), a brain tumor, and osteosarcoma, a bone cancer, remain stubbornly difficult to cure.

Cases of Childhood Cancer in the United States by type, 2023[13]



*The counts presented here only include malignant brain tumors, consistent with CDC reporting. When nonmalignant tumors are included the total number of pediatric brain tumor diagnoses is higher.

Cases of Childhood Cancer in the United States by type and sex, 2023[14]

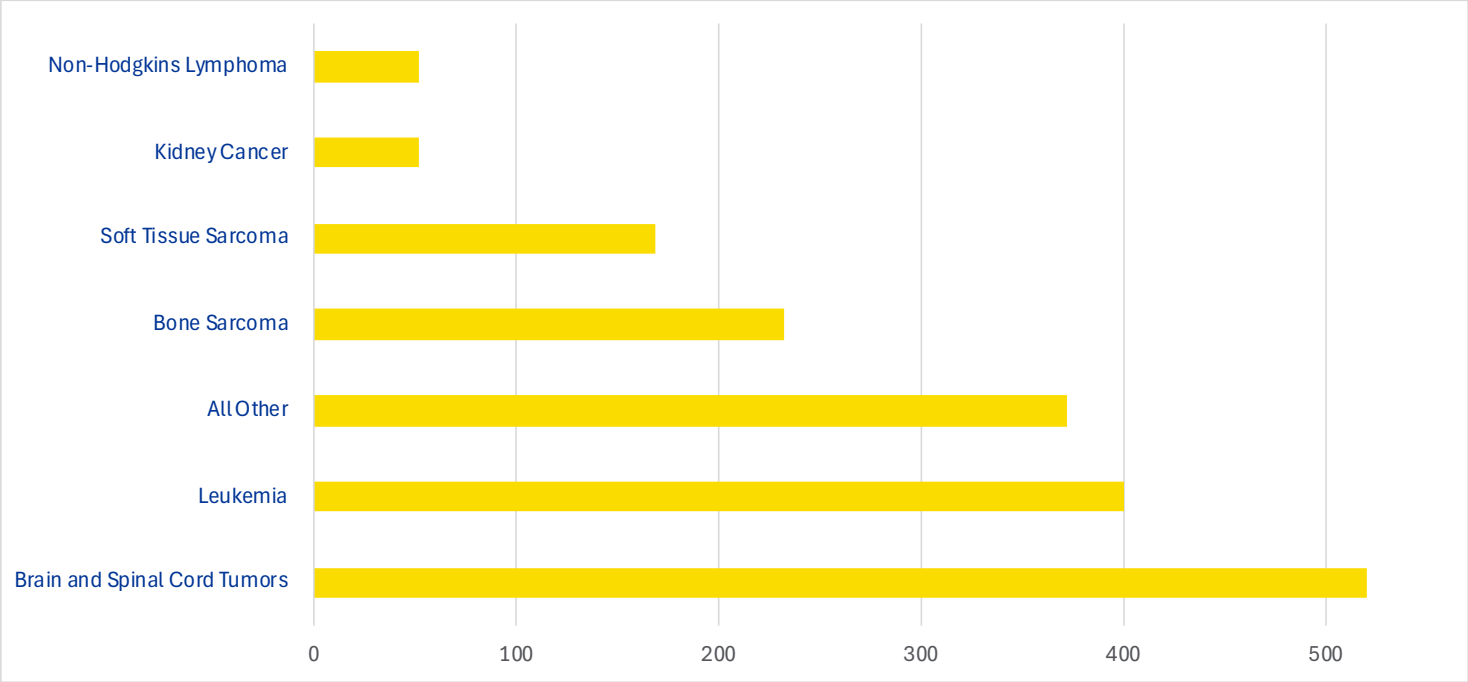


MALE	CANCER TYPE	FEMALE
2185	Leukemia	1678
947	Malignant brain and spinal cord tumors	850
1422	Lymphoma	877
633	Melanomas and skin cancers	1370
564	Soft tissue sarcomas	420
582	Tumors of the ovaries, testes, or related cells	408
415	Bone tumors	342
348	Neuroblastoma	361
252	Kidney tumors	309
158	Liver tumors	100
98	Retinoblastoma	101
56	Other rare cancers	79

In 2023, males were diagnosed with childhood cancer approximately 11% more than females. There is no clear, definitive known reason; however, researchers think it's a mix of biology and genetics. Boys and girls differ in hormones, immune system function, and even how certain genes are expressed (including genes on the X chromosome), which can influence cancer risk. Understanding these differences in diagnosis and sex can help researchers understand the drivers of cancer.

U.S. Childhood Cancer Deaths: A Snapshot of 2024[15]

Childhood cancers are not uniformly deadly. Brain and spinal cord tumors account for the most deaths—a spot once occupied by leukemia.



U.S. 5-Year Relative Survival Rates by Type:[16]

The chart below shows the 5-year relative survival rates of childhood cancer by type. Relative survival is different than overall survival because it compares the survival of children with cancer to children without. Survival is tracked from date of diagnosis through cancer registrars in each state. Relapse and survival is not tracked in the same way but is sometimes tracked in clinical trials and other studies. Relative survival rates are not a prediction for individual children but instead serve as an overall population measure.

By tracking how many children in both groups are still alive after 5 years, researchers can have a realistic sense of prognosis for a disease that is not skewed by unrelated causes of death. For more on survivorship, see page 11.

Cancer Type	5-Year Relative Survival (%)
All Types Combined	87.0%
Leukemia	87.3%
Lymphoma	95.2%
Brain and Spinal Cord Tumors	76.9%
Neuroblastoma	84.9%
Retinoblastoma	97.3%
Kidney Tumors	91.2%
Liver Tumors	76.8%
Bone Sarcomas	71.7%
Soft Tissue Sarcomas	75.0%

Within each of these major types of childhood cancer, there are dozens of subtypes that vary in severity and survivability.

Key Facts

The most common type of childhood cancer is leukemia.

The deadliest childhood cancers are brain tumors, which killed 520 kids in 2024.[17]

Bone cancers like osteosarcoma and Ewing sarcoma tend to metastasize to the lungs, and when this happens, 5-year survival rates drop from around 70% to 30%.

Section 2 explores the treatment and research milestones by specific cancer type.

Incidence and Causation

The steady increase in the incidence of childhood cancer since 1975 gives rise to the question: What causes childhood cancer? But before delving into this question, it is important to clarify what incidence rates explain. In the United States, the childhood cancer incidence rate has increased over the past several decades, from approximately 13–14 per 100,000 children in the late 1970s to about 19 per 100,000 children in recent years (including 2022), representing a roughly one-third increase over time based on SEER registry data. [18]

However, this does not mean that the actual cases of childhood cancer increased by 40%. Incidence rates are population based, which gives scientists more information about what is happening in a population of people (in this case children in the United States) versus raw numbers.

Understanding why the incidence rate is rising is important as scientists study cancer; however, the cause of a vast majority of childhood cancers remains unknown. Here is what is known:

Why incidence rates matter

A group can have more cases just because it has more people. Rates show the chance of getting a disease.

Example:

- **Group A: 10 kids out of 100 are diagnosed with cancer (10%)**
- **Group B: 5 out of 10 are diagnosed with cancer (50%)**

Even though Group A has more cases, Group B has a much higher risk.

Counts show how many. Rates show how likely.

1. **Childhood cancer is distinctly different from adult cancer.** It has unique molecular and biological characteristics. How does this relate to causation? Well, this simply means the things that can cause adult cancer don't necessarily cause childhood cancer.
2. **Tracking and classifying cancer rates continues to improve** and really did not begin in earnest until 1973[19] with the launch of Surveillance, Epidemiology, and End Results (SEER) Program. Before SEER, childhood cancer data were fragmented and largely based on hospital records and mortality statistics, making long-term incidence comparisons less precise.
3. **Classification systems have grown and shifted to identify more tumors as malignancies.** Specifically, previously "benign" brain tumors started to be classified as malignant in the mid-1980s. The World Health Organization also continues to classify and define more subtypes of childhood cancer. This does not mean there is more cancer; it simply means more diseases are considered cancer.[20]
4. **The causes of childhood cancer remain largely unknown.** Most cases arise from random genetic mutations that occur during development or in early childhood.
5. **Current studies indicate that 10-18% of all cancers are caused by cancer predisposition,** including some types of retinoblastoma (see Section 2, page 33). These can be spontaneous syndromes or inherited, like Li-Fraumeni (see Section 2, page 35), which increases a child's lifetime risk of cancer by 90% (females) and 70% (males).[21]
6. **Environmental exposures are suspected contributors to childhood cancer increases,** but there are not widespread conclusive studies. Exposure to radiation could play a role in the development of secondary cancers, as could environmental toxins like pesticides. Several studies on cancer clusters—geographic areas with high childhood cancer incidence rates—point to some correlation between exposure and cancer risk.[22]

Survivorship

In 1989, researchers interviewed 1,928 adult survivors of childhood cancer. The cohort had been diagnosed between 1945 and 1974. Nearly 20% of the survivors didn't know what type of cancer they had, and even more surprising: 14% of the people interviewed said they never had cancer in the first place. The study's authors concluded that "physicians should be aware that a substantial proportion of long-term survivors of childhood cancer may not reveal their past history of cancer and its treatment, and possible clues to the cause of the presenting condition may thus be missed."[23]

Survivorship seemed to be a mystery, even to the survivors themselves.

But the long-term impacts of childhood cancer treatment had long been an interest to scientists. One of the earliest indications that treatments could kill cancer while also harming growing bodies was in 1952, when M. H. Wittenborg, a radiologist, discovered that radiation to the spine would result in scoliosis.[24] In the 1960s, the international Late Effects Study Group was established, which then inspired more efforts.[25]

In 1975, the landmark and much-cited perspective piece "Pediatric Cancer in Perspective: Cure Is Not Enough" was published in the journal *Cancer.*[26] Authored by Dr. Giulio J. D'Angio, this piece fueled the continued belief that survivorship needed to be studied, treatments needed to come without costs, and childhood cancer survivors needed to be able to access long-term care.

Side Effects of Childhood Cancer

At diagnosis, children typically are experiencing symptoms from their cancer. Treatment can reduce those symptoms but can also cause a bevy of short-term, immediate side effects. When those side effects don't go away, they become long-term. But children treated for childhood cancer can also experience late-term side effects—new health conditions that emerge years after diagnosis and treatment.

Both long- and late-term side effects impact quality of life for childhood cancer survivors. There are the physical impacts, which are detailed below and organized by treatment type. There are also long-term impacts on cognitive, psychological, social, and even financial health. Cancer survivors ages 18-64 were more likely to report high out-of-pocket health related expenses, and one-fourth reported having long-term financial hardship.[27]

500,000
childhood cancer survivors in the United States[28]

85%
overall childhood cancer survival rate in the U.S.

At least 60%
of childhood cancer survivors develop one or more chronic health conditions[29]

20%+ of survivors experience severe or life-threatening complications in adulthood

Long- and Late-Term Side Effects from Treatment[30]

Listed below are possible long- and late-term side effects from common childhood cancer treatments. As new treatments, like immunotherapies or targeted drugs, become more widely used, researchers will continue to track and monitor the health of survivors. Read more about these treatments in **Section 4.** The severity and existence of these side effects is dependent upon the dose and frequency of treatment, the area of the body impacted by treatment or surgery, the age at diagnosis and treatment, and many other factors.

- **Chemotherapy**
  Cardiomyopathy (heart muscle damage), lung damage, thyroid problems, growth hormone deficiency, delayed puberty, infertility, early menopause, memory and concentration issues ("chemo brain"), learning problems, nerve damage (neuropathy), hearing loss, vision issues (cataracts, glaucoma), osteoporosis (weak bones), dental abnormalities (short roots, missing teeth), growth issues, kidney and liver dysfunction, increased risk of developing new cancers later in life, depression, anxiety, and PTSD.
- **Radiation**
  Learning disabilities, memory issues, seizure disorders, balance problems, growth hormone deficiency, thyroid issues (hypo/hyperthyroidism), puberty problems (early or delayed), adrenal issues, dental problems (dry mouth, tooth decay, shape/enamel issues), vision/hearing loss (cataracts, glaucoma), jaw stiffness, facial asymmetry, permanent hair loss, short stature, scoliosis (curvature), bone thinning, fractures, reduced muscle growth, joint problems, osteonecrosis (bone death), increased risk of heart conditions, chronic pain (fibrosis), infertility, metabolic issues (obesity, syndrome X), chronic pain, secondary cancers.
- **Stem Cell Transplant**
  Growth hormone deficiency, thyroid issues, delayed puberty, infertility, osteoporosis (bone loss), attention deficits, memory problems, organizational challenges, slower processing speed, poor handwriting, increased risk of heart problems earlier in life, restrictive lung disease, liver scarring, iron overload, kidney toxicity from medications, high blood pressure, Chronic Graft-Versus-Host Disease (cGVHD can affect skin, eyes, mouth, lungs, gut, liver, muscles, and joints and appear months to years post-transplant), cataracts, dry eyes, dental problems, anxiety, depression, sleep disturbances, and social challenges.
- **Surgery**
  Varies greatly per cancer type for brain tumors and surgical resection can cause permanent neurological side effects impacting speech, movement, balance, and vision; it can also head to hydrocephalus, a condition caused by excess cerebrospinal fluid. Because of the dangerous pressure hydrocephalus causes within the brain, a shunt placement is required to drain the excess fluid. Bone tumor resection can lead to limb loss or bone weakening. Surgery to remove tumors on organs can impact those organs' functions.
- **Immunotherapy**
  Since immunotherapies work by boosting the immune system, this can sometimes lead to it attacking the body's own healthy tissues, causing autoimmune-like conditions (like type 1 diabetes) or chronic inflammation.
- **Newer treatments**
  As new treatments are developed and FDA-approved, scientists are working to understand the potential long- and late-term side effects.

Long-Term Follow Up Guidelines

For childhood cancer survivors, long-term follow up at a specialized oncology survivors clinic is critical. The Children's Oncology Group (COG)[31] established survivorship guidelines for childhood cancer survivors. Updated in 2023, the guidelines give clinicians a roadmap for long-term follow up care, including transitioning to adult care (See **Section 3**). While most COG institutions have a dedicated survivor clinic, less than 75% of eligible patients are accessing those services.[32] A survivorship care plan should include:[33]

1. **Exams and imaging to check for recurrance or secondary cancers**
2. **Supportive care for long- or late-term side effects**
3. **Mental health support**
4. **Referrals for legal and financial support**
5. **Referrals to specialists such as cardiologists, neuropsychologists, physical therapists, and others, as needed**
6. **Nutrition and health and wellness planning**
7. **Transition to adult care**

Beyond the **COG Survivorship Guidelines**, the ***Childhood Cancer Survivors* guide** offers practical and personal guidance.

Childhood Cancer Survivor Study

In 1994, a landmark multi-institutional collaborative study, operated by St. Jude Children's Research Hospital, was funded by the National Cancer Institute. The Childhood Cancer Survivor Study (CCSS)[34] first tracked survivors diagnosed between 1970-1986 (and later expanded to 1999). The initial cohort included 14,054 subjects who had survived a variety of cancers: leukemia, brain tumors, neuroblastoma, bone and soft-tissue sarcomas, and kidney tumors.[35] Study leads reviewed medical records and survivors completed a 24-page baseline questionnaire. Siblings of survivors were also included as a comparison control group. The CCSS was and remains the largest and most extensive cohort of childhood cancer survivors. The CCSS data have resulted in over 500 publications, includes 31 collaborating institutions, and has expanded to gather and track data from 38,000 childhood cancer survivors and their siblings. Beyond publications the CCSS also developed "risk calculators," which are tools clinicians can use to judge the risk of secondary malignancies, cardiomyopathy, and other late-term side effects.

Global Childhood Cancer: The Great Divide

In Kenya, there are only a few primary hospitals with specialized pediatric oncology units. Of the estimated 3,200 Kenyan children diagnosed with cancer each year, only 20-30% survive.

In the United States, 85% of children diagnosed with cancer are alive five years later.

Kenya and the United States are just two examples of the great divide that exists for kids with cancer. Low- and middle-income countries have systemic and chronic infrastructure issues, long travel distances to clinics, lack of access to medications and specialized treatments, high out-of-pocket medical costs, and delays in diagnosis, which all contribute to the high mortality rates among childhood cancer types that have low mortality rates in the United States.[36]

Childhood cancer represents a substantial and inequitable global health burden and remains one of the leading causes of death in children worldwide. No one knows the true burden of childhood cancer because there is not a comprehensive global childhood cancer registry. However, estimates suggest around 275,000-400,000 new cases of cancer develop annually in children and that there are more than 100,000 deaths each year.[37]

And while this report primarily focuses on childhood cancer in the United States, the movement to cure childhood cancer is for all children, no matter where they live. Here are some key global childhood cancer facts:

- **Only 29% of low-income countries report that common, widely-used and researched medications are available to their populations compared to 96% of high-income countries.[38]**
- **In some low-middle income countries the 5-year survival rates are 10%.[39]**
- **Population-based incidence rates seem to be steadily increasing globally, as they have been in the United States (see Section 1). This is partly due to improved diagnosis.[40]**
- **The lowest 3-year survival rates are in Africa, followed by South America, parts of Southeast Asia, and the Middle East.[41]**
- **The Global Initiative for Childhood Cancer, launched in 2018 by the World Health Organization and other global partners, aims to increase survival rates to at least 60% by 2030.[42]**

Addressing these disparities is critical, as every child, regardless of where they are born, deserves access to timely diagnosis, effective treatment, and the hope of survival. Global efforts, like the WHO's initiative, highlight that progress is possible when resources, policies, and partnerships align to fight childhood cancer worldwide.

Cancer Registries

Cancer is a reportable disease worldwide, which means when it is diagnosed the law mandates that it must be reported to public health officials.

Tracking cancer had a slow start—in 1929 Yale-New Haven Hospital in Connecticut established the first hospital registry. It was 1956 when the American College of Surgeons required a cancer registry for approved cancer treatment programs. In 1973[43] the Surveillance, Epidemiology, and End Results (SEER) Program launched at the National Cancer Institute, and it started tracking a representative portion of the population. The National Cancer Registrars Association was established a year later as an effort to create consistency and professional training in the field. And then in 1992 the United States Congress passed the Cancer Registries Amendment Act, establishing a registry program within the Centers for Disease Control and Prevention. Congress encouraged states to establish their own registries, and by 2001, the registry, known as the National Program of Cancer Registries (NPCR), was collecting data from all 50 states (who had mandated cancer reporting from hospitals).[44]

The state registries track a wide range of data-demographic, primary treatment type, specific diagnosis, geography, residence, age, patient status, and deaths. All of this critical information can help support public health and oncology researchers as they look for trends in long-term survival (a key indicator treatments are working), in incidence rates (by age, location, and cancer type), and other demographic factors. It can influence state public health programs and funding for childhood cancer and the allocation of community resources.[45]

This is how tracking cases of childhood cancer works:[46]

STEP 1

At diagnosis and before the end of the first cycle of treatment, the hospital registrar enters information about the patient, their diagnosis, and their treatment into their database. That information is then sent to the central cancer registry in the hospital's state.

STEP 2

The state registry verifies the information from the hospital and if the patient happens to be a resident of another state, the registrar will send that information to the state of residence.[47]

STEP 3

Once a year, the central state registries send information on the cancers diagnosed in their state to the Centers for Disease Control and Prevention. There, it is collated and used to produce the U.S. Cancer Statistics (USCS), the official federal source.

STEP 4

In the USCS, central state registry data is combined with data surrounding cancer deaths from offices of Vital Statistics.

The process takes time as registrars work to verify, code, and ensure information is accurate. The data on childhood cancer incidence is 3-4 years behind the current year—so for 2026, the most recent data available is from 2023. Death and mortality data is just 2-3 years behind current time.

SEER also tracks and analyzes cancer rates but uses the data from approximately 18 core registries that represent 48% of the U.S. population. Both USCS and SEER are complementary, not competing, and allow for trend tracking, data comparisons, and modeling of future trends. For example, the American Cancer Society uses SEER and USCS data on an annual basis to model and forecast current rates for the year.[48]

Glossary of Terms

Age-Adjusted
A way of comparing data between different populations by taking into account differences in age distribution. This makes it easier to see true trends, not just the effects of having more younger or older people in one group.

Cancer Registry
A database that collects and stores information about cancer cases, such as diagnosis, type, treatment, and outcomes. Cancer registries help researchers and public health experts track trends and improve care. In the United States, each state office of public health has a cancer registry which reports data to the national registry. Not every country has a robust or comprehensive system of cancer registries.

Case Count
The actual number of children diagnosed with cancer in a certain group or area during a specific period.

Childhood Cancer
Cancers that are diagnosed in children, adolescents, and young adults under the age of 19. These cancers often differ from those seen in adults—they tend to start in developing cells and tissues and are not usually linked to lifestyle or environmental factors.

Incidence Rate
The number of new cases of a disease, such as cancer, diagnosed in a specific group of people during a certain time period—usually expressed as the number of cases per 100,000 children each year.

Malignancy
A term for cancerous tumors or diseases that can grow uncontrollably and spread to other parts of the body.

Mortality Rate
The number of deaths from a disease in a specific group of people during a certain time—usually shown as the number of deaths per 100,000 children each year.

Overall Survival Rate
The percentage of people who are still alive after a certain amount of time (often 5 years) after being diagnosed with cancer, no matter the cause of death.

Population-Based
Data or studies that include all people in a defined population (such as all children in the United States).

Prevalence
The total number of people who are living with cancer or who have ever been diagnosed with it at a given time. Depending on context, this may refer to current prevalence (people currently living with cancer) or lifetime prevalence (all people ever diagnosed, regardless of current status).

Primary Site
The part of the body where the cancer first started to grow, before it spread elsewhere.

Progression-Free Survival
The length of time during and after treatment that the cancer does not get worse. It is often used in studies to see how well a new treatment stops the disease from progressing.

Refractory
Describes cancer that does not respond to treatment or stops responding after an initial response. A refractory cancer keeps growing or does not go away despite therapy.

Relative Survival Rate
A measure that compares how long people with cancer live, on average, after diagnosis compared to people of the same age and sex who do not have cancer. It helps show how well treatments are improving survival. This can also be represented on a specific disease basis.

SEER (Surveillance, Epidemiology, and End Results Program)
A long-running program of the U.S. National Cancer Institute that collects detailed information on cancer cases across many regions of the country. SEER data are used to track trends in cancer incidence, survival, and mortality.

Standard of Care
The best-known and most widely accepted treatment for a disease, based on evidence and expert consensus. It represents what doctors generally agree is the most effective and safest option.

SECTION 2

Childhood Cancer Research Milestones

Childhood Cancer Research Milestones

Just two decades ago, pediatric cancer reached a major milestone: the first ever FDA-approval of a drug specifically to treat cancer in children.[49] The chemotherapy drug, clofarabine, was given accelerated approval for the treatment of some types of relapsed pediatric leukemia. This "first in kids" approval was a rarity; every single other pediatric cancer drug was either first or simultaneously approved for the treatment of adult cancers.

Since 1950, just over 60 drugs have been approved by the FDA for children with cancer. That's the same number the FDA typically approves for adults in a single year.[50]

Despite limited approvals, scientific discoveries in childhood cancer have continuously led the way for all types of cancer research. In the 1940s, Sidney Farber, the father of modern chemotherapy, showed how folic acid antagonist drugs could be used to achieve remission in kids with leukemia. These drugs, which later came to include the foundational chemotherapy methotrexate, are a type of cellular poison that work to block the fuel that cancer cells need to divide and replicate. Later, in the 1950s, this research would lead to the successful treatment of Wilms tumor, a rare pediatric variant of kidney cancer.[51]

Progress in leukemia treatment continues to be the standard to which all cancer treatments aspire to. In 2016, 5-year survival rates for pediatric leukemia as a whole reached 89%[52]—a substantial improvement from the survival rates of less than 10% when Sidney Farber made his early discoveries.* The past several decades have shown what is possible for kids, but the progress has not been uniform across childhood cancer types nor has it been whole or complete within types.

This section details research and progress milestones by childhood cancer type, offering insights on the characteristics of these unique diseases. Included are the current standard treatments—the frontline treatments that children typically receive, but that will vary by patient age, cancer stage, and doctor recommendations. It also provides some historical context to the search for cures (see **Section 4** for more information). Also included are comprehensive reviews of the progress in the treatment of a handful of childhood cancer types (leukemia, lymphoma, brain tumors, spinal cord tumors, retinoblastoma, neuroblastoma, and sarcomas). This list is not exhaustive—there are several more types including hepatoblastoma (liver cancer); Wilms tumor (mentioned above); pediatric cases of ovarian, testicular, pancreatic, and skin cancers; and rare tumors that have been diagnosed and documented in literature only a handful of times.

In addition, this section contains a focus on childhood cancer predisposition factors and syndromes. Scientists estimate that between 10-18% of all cancers are driven by predisposition.[53] While predisposition itself is not a specific cancer type, it is a critical area of research interest. RB1, the gene that drives some types of the childhood cancer retinoblastoma, was discovered in 1985, opening the door to the study of predisposition in both adult and childhood cancers.

Taken together, these milestones show both the remarkable progress and the persistent gaps in childhood cancer research. Understanding the history of these advances provides a critical foundation for charting the path forward.

* This includes all types of leukemia diagnosed in children ages 0-19. Some leukemia types still have poor survival rates for children.

Leukemias and Lymphomas

Leukemia, a cancer of the blood-forming cells in bone marrow, is the most common type of childhood cancer. Over the course of several decades, incredible progress has been made in improving survival rates—from a low of less than 10% in the 1960s to the close to 90% cure rate for children diagnosed with acute lymphoblastic leukemia (ALL) today. This success has happened in high-income countries. In low-income countries, a diagnosis with ALL can still bring a precarious prognosis due to a lack of access to treatments.

Lymphoma, a cancer of the lymphatic system (lymph nodes and related tissues), is grouped with leukemia because both are blood cancers that affect similar immune cells and often behave as systemic diseases requiring similar treatments.

Among childhood cancers in the United States, leukemia stands apart: It has the most FDA-approved treatments and is the only childhood cancer with an FDA-approved CAR T-cell therapy.[54]

While many leukemias and lymphomas are considered cancer therapy success stories, several subtypes continue to be associated with a poor prognosis. For example, acute myeloid leukemia (AML) accounted for 35% of all pediatric leukemia deaths in 2023[55] but only for 8% of all cases in the United States.[56]

Leukemia

Age at Diagnosis	Five-year survival rate[57]
Ages < 1	68.9%
Ages 1-4	93.3%
Ages 5-9	91.4%
Ages 10-14	83.5%
Ages 15-19	79.3%

Lymphoma

Age at Diagnosis	Five-year survival rate[58]
Ages > 1	95.1%
Ages 1-4	95.2%
Ages 5-9	95.7%
Ages 10-14	95.3%
Ages 15-19	95.1%

Leukemias and Lymphomas, by the Numbers in the U.S.

Leukemia

3,863 new cases
in 2023[59]

400 deaths
in 2024[60]

Lymphoma

2,299 new cases
in 2023[61]

52 deaths
in 2024[62]

Standard Treatments

- Chemotherapy
- Stem Cell Transplants
- Radiation[63]

Understanding Drug Names

Before a drug is approved and commercially available, its generic name is created through rules set by the United States Adopted Names Council (USAN) and the World Health Organization (WHO). Drug names can be thought of in two parts: The start or prefix is a unique name, and the end or suffix denotes how the drug works. While there are all sorts of rules around drug naming and approval, here are a few of the commonly used suffixes in pediatric cancer drugs:[64]

- cin: chemotherapy
- taxel: chemotherapy
- nib: small-molecule kinase inhibitors (targeted therapy)
- mab: antibody drug conjugates

Breakthroughs and Research Milestones:

1. **Chemotherapy (1960s-present):**

   The discovery and FDA approval of chemotherapy was a game changer for kids facing leukemia. Years of collaborative research through the Children's Oncology Group (COG)—an organization made up of childhood cancer experts at more than 220 children's hospitals, universities, and cancer centers—and its predecessors, the Pediatric Oncology Group (POG) and Children's Cancer Group (CCG), have defined specific subtypes of leukemia and drug dosing, resulting in improved survival rates. However, chemotherapy brings acute and long-term side effects that can cause cardiac dysfunction, immune system suppression, infertility, hearing loss, and cognitive impairment. Research continues to focus on combination therapies that can protect children from side effects and strategies for lowering the doses of chemotherapy drugs children receive.[65]

2. **Stem cell transplants (1960-present):**

   Stem cell transplantations are typically performed after treatment with high doses of chemotherapy that deplete both healthy and diseased stem cells, followed by an infusion of healthy stem cells from a donor to replenish the depleted cells.[66]

3. **Targeted therapies (2013-present):**

   Targeted therapies provide hope for the treatment of rare leukemias:

   - Tyrosine Kinase Inhibitors (TKIs) such as imatinib, dasatinib, nilotinib, and bosutinib. Imatinib is used primarily in the treatment of chronic myeloid leukemia and Ph+ ALL and was FDA approved for the treatment of Ph+ ALL in 2013.[67,68]

Types of Leukemia

Leukemias are named based on two characteristics: the speed of progression and the type of blood cell affected. Acute leukemia grows quickly. Chronic leukemias, which are rare in children, grow slowly. Lymphoblastic leukemias arise from types of white blood cells called lymphocytes. Myeloid leukemias affect the cells that become monocytes, neutrophils, red blood cells, and platelets.[69]

- **Acute Lymphoblastic Leukemia (ALL)**
- **Acute Myeloid Leukemia (AML)**
- **Juvenile Myelomonocytic Leukemia (JMML)**
- **Chronic Lymphocytic Leukemia (CLL, very rare in children)**
- **Chronic Myeloid Leukemia (CML, very rare in children)**

Types of Lymphomas

Lymphomas are cancers that stem from the overproduction of white blood cells. There are two main types of lymphomas: Hodgkin and non-Hodgkin lymphoma. The subtypes are characterized by the production of cells called Reed-Sternberg cells, with Hodgkin lymphoma having these cells.[70]

- **Hodgkin Lymphoma (HL)**
- **Non-Hodgkin Lymphoma (NHL)**

- Menin inhibitors, such as revumenib, are showing promise for treating certain leukemias. These drugs work by blocking the protein menin from interacting with KMT2A, a gene that normally helps control how blood cells develop but can drive leukemia when it is altered, helping shut down cancer-driving signals that leukemia cells need to grow and survive.[71, 72]

4. **CAR T-cell Therapy (2017 - Present):**

   The "CAR" in "CAR T-cell" stands for chimeric antigen receptor. The word "chimeric" comes from the Chimera, a strange mixed-up beast from Greek mythology made up of a lion, a goat, and a serpent. In the case of CAR T-cell, the "chimeric" represents a protein (the CAR) made in the lab by stitching parts from different proteins that is then placed on a T-cell, allowing it to see and kill cancer in the body (read more about CAR T-cell in Section 3). In 2017, the approval of the CAR T-cell therapy, tisagenlecleucel (brand name Kymriah), provided kids with relapsed ALL a promising new option with potentially less side effects than chemotherapy.[73]

5. **Immunotherapy (2018-present)**

   Beyond CAR T-cell therapy, other types of immunotherapy show promise. **Blinatumomab**, approved for B-ALL, works to connect T-cells from the patient's immune system with cancerous B-cells. The drug helps T-cells recognize malignant B-cells and harnesses their power to slow or stop cancer cell growth.[74] **Pembrolizumab**, a PD-1 inhibitor, has also been approved in the treatment of relapsed and refractory Hodgkin Lymphoma. **Rituximab** is a monoclonal antibody that targets a protein specific to B-cells, CD20, and is FDA-approved in numerous B-cell malignancies. Upon binding to CD20, the B-cells bound by rituximab recruit a host of immune cells, such as NK cells and T-cells, which lead to an immune cell–driven killing of the bound cells.[75] Rituximab was approved by the FDA for treating autoimmune diseases in 1997, and it was approved for pediatric leukemia in 2021.[76,77]

From experimental treatment for relapse to frontline therapy

Blinatumomab is considered a success story in ALL treatment, especially for children with relapsed leukemia. The drug was then tested as a frontline treatment in children newly diagnosed with high-risk B-ALL, alongside standard therapy. These studies showed fewer relapses compared to standard treatment alone. Because of these strong results, blinatumomab is now expected to become part of frontline treatment for many children with high-risk B-ALL.[78,79]

FDA Approvals: Childhood Leukemias and Lymphomas

2021-2026
- **Chemotherapy** (Treosulfan, Azacitidine, Rylaze, Vyxeos)
- **Immunotherapy** (Blincyto, Besponsa, Adcetris, Rituxan)
- **Targeted therapy** (Revuforj, Bosulif, Xalkori, Nivolumab)

2013-2020
- **Chemotherapy** (Asparlas)
- **Immunotherapy** (Keytruda, Mylotarg, Blincyto)
- **CAR T-cell therapy** (Kymriah)
- **Targeted therapy** (Sprycel, Tasigna, Imatinib)

2000-2006
- Chemotherapies (Oncaspar, Arranon, Clolar, Busulfex, Trisenox)

1994-1995
- Chemotherapies (Vesanoid, Oncaspar)

1976-1979
- **Chemotherapy** (Daunorubicin Hydrochloride, Elspar, Gleostine)

1969
- **Chemotherapy** (Matulane, Cytarabine)

6. **Antibody-Drug Conjugates (2020-present)**

Antibody-Drug Conjugates (ADCs) are drugs that allow for selective killing of cancer cells. ADCs bind to cancer cells, carrying a small amount of toxin that is delivered directly to the cancer cell. Because it only sticks to cancer cells, healthy cells remain undamaged.

There are three ADCs that are approved by the FDA for children:

- Gemtuzumab ozogamicin is used to treat AML.[80]
- Inotuzumab ozogamicin has been approved for treating pediatric leukemia, specifically ALL.
- Brentuximab vedotin has been approved in the treatment of classic Hodgkin lymphoma and subtypes of non-Hodgkin lymphoma.[81]

FDA Approvals: Childhood Leukemias and Lymphomas (Continued)

1994-1995
- Tretinoin [Vesanoid]
- Pegaspargase [Oncaspar]

1976-1979
- Daunorubicin Hydrochloride
- Asparaginase [Elspar]
- Lomustine [Gleostine]

1969
- Procarbazine Hydrochloride [Matulane]
- Cytarabine

Brain and Spinal Cord Tumors

Brain and spinal cord tumors, collectively known as central nervous system tumors, are the most common solid tumors in children—and the most common cause of cancer deaths in children. Brain tumors claimed this top spot in 2016, surpassing leukemia. It wasn't that brain tumors had suddenly became more lethal; it was that research had improved outcomes in pediatric leukemia.[82]

There are several things that make brain tumors so deadly. The location within the critical structures of growing brains not only causes the tumors to jeopardize normal function but also makes treatment risky. Mainstays of treatment, like tumor resection (surgery), radiation, and chemotherapy, all come with high risks. And those high risks are important to consider as other less risky treatments, such as immunotherapy, emerge.[83]

Age at Diagnosis	Five-year survival rates[84]
Age <1	63.1%
Ages 1-4	78.2%
Ages 5-9	74.0%
Ages 10-14	79.3%
Ages 15-19	79.9%

Why Brain Tumor Counts Vary

Brain tumor counts can vary depending on what is included. Data from the Centers for Disease Control and Prevention (CDC), which this report uses, focus on malignant tumors, while the Central Brain Tumor Registry of the United States (CBTRUS) includes both malignant and non-malignant tumors. As a result, CBTRUS reports higher totals. For example, an estimated 4,860 children and adolescents will be diagnosed with a primary brain or other CNS tumor in 2025. Although this report uses CDC data for consistency, non-malignant tumors remain an important part of the overall burden because they can still be serious and require intensive treatment and research for kids to be cured.

Brain and Spinal Cord Tumors, by the Numbers in the U.S.

1,797 new cases
(malignant) in 2023

520 deaths
in 2024[85]

Standard Treatments

- Surgery
- Proton or Photon Radiation
- Chemotherapy[86]

Difficulties of Treatment: DIPG

A diagnosis with diffuse intrinsic pontine glioma comes with the poorest prognosis. There simply isn't a 5-year survival rate because almost no children have ever lived that long. The tumor's name says it all. It is diffuse, meaning cancer cells spread and mix among healthy cells within the pons, the part of the brainstem that controls critical bodily functions. As a result, it is inoperable, and treatments can cause dangerous inflammation. However, CAR T-cell therapy combined with a novel drug delivery system have shown promise for a future immunotherapy option.

Breakthroughs and Research Milestones:

1. **Proton radiation for pediatrics (2007-present)**

   In 2007, proton radiation became available in the U.S. as a treatment for pediatric brain tumors. The benefit of this treatment: no exit dose of radiation which minimizes damage to surrounding brain tissue (see more on proton radiation in Section 3).[87]

2. **Innovative drug delivery systems (2010-present):**

   The blood-brain barrier, which is a natural protective system that keeps toxins and other bad things out of the brain, can also keep cancer drugs out. Researchers are developing new ways to deliver treatments and bypass this natural defense. New drug delivery technologies being studied include:

   - Nanoparticles: Tiny particles used to package drugs so they can slip through the blood-brain barrier.[88]
   - Convection-enhanced delivery: Surgical placement of small tubes (catheters) into the brain to allow for drug delivery.[89]
   - Focused ultrasound: The use of sound waves to produce microbubbles that temporarily disrupt the blood-brain barrier, allowing for drugs to bypass this protective layer and enter brain tissue.[90]
   - Intranasal delivery: Drugs that are made into particles that can be sprayed into the nose and enter the brain through nasal tissues.

3. **Approval of targeted therapies (2010-present)**

   The search for targeted, tumor-specific treatments began in the mid-20th century, but the approvals for pediatric brain tumors only began in 2010. These types of therapies bring the promise of being targeted killers: They attack cancer cells and leave healthy cells alone. For children with developing brains and bodies, this is particularly critical. A few examples of novel targeted therapies for brain tumors are:

   - **Everolimus**
     Targets mTOR, a pathway essential for tumor cell growth and survival.
     Approved for: astrocytoma in 2010[91,92]
   - **Dabrafenib and trametinib**
     Targets BRAF, which is essential for tumor cell survival.
     Approved for: certain types of low-grade gliomas in 2023[93]
   - **Vorasidenib**
     Targets a protein called IDH, which is responsible for tumor growth through the regulation of cellular metabolism.[94]
     Approved for: oligodendrogliomas and astrocytomas[95]

Types of Brain and Spinal Cord Tumors

The names of brain tumors all have origins in the names of the normal brain cells, which undergo abnormal DNA changes, leading to the development of a tumor. The most recent classification from the World Health Organization in 2021 categorizes brain tumors as low-grade and high-grade, while also incorporating tissue type (histology) and molecular characteristics. Examples of pediatric brain tumor types include:

- **Medulloblastoma**
- **High-gradee glioma**
- **Low-grade glioma**
- **Diffuse midline glioma (DMG)**
- **Diffuse intrinsic pontine glioma (DIPG)**
- **Glioblastoma**
- **Ependymoma**
- **Atypical teratoid/ rhabdoid tumor**
- **Choroid plexus papilloma**
- **Pineal tumors**
- **Optic nerve tumors**

45-60% of malignant pediatric brain tumors are found in the posterior fossa[96]—the back chamber of the brain where the brain stem and cerebellum are located.

- **Tovorafenib**
  Targets BRAF fusion or rearrangement or BRAF V600 mutation.[97,98]
  Approved for: patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (LGG) in 2024
- **Larotrectinib, Entrectinib, and Repotrectinib**
  Targets the NTRK fusion protein that is present in rare cases in gliomas.[99]
  Approved for: NTRK fusion solid tumors, including CNS in 2018, 2023, and 2024 respectively
- **ONC201[100]**
  Targets a protein-coupled receptor called DRD2, leading to tumor cell death.[101]
  Approved for: diffuse midline glioma in 2025[102]

4. **Medulloblastoma reclassification (2016)[103]**

   Advances in medulloblastoma research led to the 2016 classification of four molecular subtypes based on genetic and molecular features, allowing clinicians to better tailor treatment and improve outcomes. These include WNT-activated (~10% of cases, best prognosis), SHH-activated (~25–30%), Group 3 (~20–25%, generally poorest prognosis), and Group 4 (~35–40%).[104,105]

5. **Immunotherapies (2017-present):** Immunotherapy—a type of treatment that harnesses the body's immune system to fight cancer cells—has shown promise in brain tumor treatment. A few examples of immunotherapies include:
   - Immune stimulating agents, such as PD-1 or CTLA-4 inhibitors, have shown success in treating adult cancers and are currently being explored in clinical trials for pediatric brain tumors, such as high-grade gliomas.[106]
   - CAR T-cell therapy, which trains a patient's own immune cells to attack cancer cells, is being explored across many pediatric cancer indications. Some current studies are focusing on a tumor-specific protein called GD2 as the target agent for these CAR T-cells in DMG and DIPG.[107]
   - Cancer vaccines are currently being tested against pediatric brain tumors, with ongoing clinical trials for the treatment of medulloblastoma, high-grade glioma, ependymoma, and DIPG. These vaccines are designed to train the immune system to recognize and attack tumor cells.[108]
   - Oncolytic viruses, which are re-engineered human viruses that can effectively deliver cancer treatments to tumors, have shown promising results in clinical trials against pediatric CNS tumors.[109]

FDA Approvals: Childhood Brain and Spinal Cord Tumors

2025
- Targeted Therapy (Dordaviprone)

2024
- Targeted Therapy (Voranigo, Ojemda)

2023
- Targeted Therapy (Tafinlar, Mekinist)

2010
- Targeted Therapy (Afinitor)

1976
- Chemotherapy (Gleostine)

Neuroblastoma

Neuroblastoma, which arises from the developing sympathetic nervous system, is the most common type of solid tumor in childhood outside of the brain and spine. The sympathetic nervous system is the part of the body's nervous system that manages the reaction to stress or danger—the flight or fight response. It begins as immature nerve cells called neuroblasts. These neuroblasts are supposed to mature into regular nerve cells, but sometimes they stop changing into normal cells and continue to proliferate, forming tumors. Neuroblastoma tumors are most commonly found in the adrenal glands on the top of the kidneys or in the nerve tissue along the spine in the neck, chest, abdomen, or pelvis.

Treatment for neuroblastoma has evolved significantly over the last two decades, with the 5-year survival rates for low- and intermediate-risk neuroblastoma now above 95%.[110] This has been achieved by more precise molecular "risk assessment" at the time of diagnosis, which allows clinicians to design treatment plans that reduce or eliminate chemotherapy and radiation therapy, thus reducing the toxic side effects affiliated with those treatments.

Children with high-risk neuroblastoma have long-term survival rates of about 60% despite an increase in the amount of treatment given as part of standard of care in the past two decades.[111] Advances in other treatments, such as MIBG (meta-iodobenzylguanidine) radiotherapy, immunotherapies, and targeted therapies, have inspired hope that progress can continue to be made in this devastating disease.

Age at Diagnosis	Five-year survival rates[112]
Ages > 1	93.5%
Ages 1-4	80.3%
Ages 5-9	81.6%
Ages 10-14	83.3%
Ages 15-19	84.4%

Neuroblastoma, by the Numbers in the U.S.

709 new cases
in 2023[113]

233 deaths
in 2023[114]

Standard Treatments

- Surgery
- Proton or Photon Radiation
- Chemotherapy
- High-dose chemotherapy with stem cell rescue (Stem cell transplant)
- Immunotherapy

Types of Neuroblastoma

When diagnosing neuroblastoma, oncologists use a staging system to determine a child's risk of relapse. When determined at diagnosis, this can help guide treatment decisions, reduce exposure to unnecessary toxic treatments, and provide the opportunity for more aggressive treatment when indicated. Each risk group has it's own 5-year survival rate.

Five-year survival rates by risk:[115]

Low-risk group: Higher than 95%

Intermediate-risk group: 95%

High-risk group: 60%

Breakthroughs and Research Milestones:

1. **MIBG radiotherapy (1980s)**

   MIBG is a medicine that can be absorbed by nerve cells, including neuroblastoma cells. When combined with radioactive iodine, it delivers radiation directly into those cancer cells. Because only the cells that absorb MIBG receive radiation, this treatment is less harmful to the rest of the body.[116] Despite MIBG being used in neuroblastoma for over 40 years, no company has commercialized this drug. As a result, patient access is a problem around the world.

2. **Small molecule inhibitors (2000-present)**

   Small molecule inhibitors are drugs that can enter cancer cells to block a specific target. Some notable breakthroughs in this drug class include:

   - In 2009, the Children's Oncology Group Phase 1 trial of crizotinib opened primarily for neuroblastoma and also included other cancers driven by the ALK mutation (see sidebar). The ALK diseases with gene fusions were much more sensitive to crizotinib than neuroblastomas, leading to FDA approvals for ALK+ anaplastic large cell lymphoma and ALK+ unresectable/relapsed inflammatory myofibroblastic tumors.
   - Another ALK-inhibitor, lorlatinib was tested in a clinical trial beginning in 2017. The trial showed that lorlatinib was generally well tolerated, shrank tumors in many patients on its own, and may work even better when combined with chemotherapy, especially in patients with high-risk tumors driven by ALK mutations and MYCN amplification.[117]
   - Eflornithine (DFMO) is a small molecule inhibitor that blocks the formation of essential polyamines, which are small molecules that help neuroblastoma cells grow. This drug was approved by the FDA in 2023 as a continuation treatment option for patients with high-risk neuroblastoma.[118] This FDA approval was based on a comparison of patients who received DFMO more recently to those who did not over a decade ago, and despite the FDA approval, many pediatric oncologist do not prescribe it because they are not convinced by the data.
   - Retinoids are a class of drugs made from vitamin A. One retinoid called isotretinoin has been a standard treatment for children with the high-risk neuroblastoma since the early 2000s.[119]

3. **Proton therapy (2010)**

   The expansion of proton radiation centers in the United States has allowed for this newer form of radiation therapy to be expanded to neuroblastoma with the goal of reducing radiation-induced side effects (see more in **Section 3, page 46**).[120]

An Inherited Cancer

In rare cases, neuroblastoma can be the result of a genetically inherited anaplastic lymphose kinase (ALK) mutation that is present in all cells of the body. This is different from the previously mentioned ALK mutations that are present just in the cells of a tumor. For children with the hereditary form of neuroblastoma, an ALK inhibitor called crizotinib, first approved for the treatment of lung cancer in adults, has been effective as a treatment option.[121]

Types of Neuroblastoma

Neuroblastoma is classified by risk (low-risk, intermediate-risk, high-risk) and also by molecular features, such as:

- **MYCN amplification indicates high-risk, aggressive disease**
- **ALK mutations also indicate aggressive disease and may be treated with targeted therapy**
- **Chromosome 1p or 11q deletions indicate aggressive disease and higher risk of progression[122]**

4. **Immunotherapy (2010-present):**

   Immunotherapy harnesses the body's immune system, activating it to kill cancer cells. Neuroblastoma is the only pediatric solid tumor with FDA-approved immunotherapies—antibodies targeting GD2. This therapy is painful and quite toxic because GD2 is also found on nerves/pain fibers. Combining these antibodies with lower dose chemotherapy can be very effective for relapsed disease but is generally not curative. Many centers are now testing GD2 directed immunotherapies for newly diagnosed patients.

   - Dinutuximab was the first FDA approved immunotherapy for neuroblastoma. The initial trial with this drug that was given after standard upfront therapy showed 61% of patients that received this drug were cancer free after five years.[123]
   - Naxitamab is an additional GD2 targeting monoclonal antibody that has received FDA approval and demonstrated success in neuroblastoma clinical trials.[124]
   - CAR T-cell therapies that are currently FDA-approved for leukemias show promise for neuroblastoma, as do other CAR T-cell therapies being developed.
   - Antibody-drug conjugates are a hybrid of targeted therapies and immunotherapy. ADCs could be available to relapsed high-risk neuroblastoma patients in the coming years.

FDA Approvals: Childhood Neuroblastoma

2026
- Targeted Therapy (daretabart)*

2023
- Targeted Therapy (Iwilfin)

2020
- Immunotherapy (Danyelza)

2015
- Immunotherapies (Unituxin, Qarziba)

*Given Fast Track Designation by the FDA. This designation is designed to speed up the development and review of new drugs. It is strictly reserved for therapies that treat serious or life-threatening conditions and fill an unmet medical need.[125]

Sarcomas

Sarcomas are cancers that form in the connective tissues of the body—the bone, cartilage, fat, muscle, and other supporting tissues.[126] There are more than 70 different types of sarcomas.[127] Osteosarcoma and Ewing sarcoma are two common types that arise from bone cells.[128] Soft tissue sarcomas, like rhabdomyosarcoma, form in the muscles and other connective tissue in the body. Bone sarcomas tend to spread to the lungs, and when they do, the chances of survival drop to 30% or lower.[129]

Encouragingly, some investigations into the genetic causes of specific types of sarcomas have led to breakthroughs, identifying clear disease drivers that can be targeted using FDA-approved treatments.

Childhood Bone Sarcomas

Age at Diagnosis	Five-year survival rates[130]
Ages 1-4	70%
Ages 5-9	75.8%
Ages 10-14	72.9%
Ages 15-19	68.8%

*Bone sarcoma cases among children under 1 are extremely rare and the sample size is too small to produce a reliable survival estimate.

Childhood Soft Tissue Sarcomas

Age at Diagnosis	Five-year survival rates[131]
Ages 1-4	79.5%
Ages 5-9	76.1%
Ages 10-14	73.6%
Ages 15-19	73.8%

Sarcomas, by the Numbers in the U.S.

Childhood Bone Sarcomas

757 new cases
in 2023[132]

232 deaths
in 2024[133]

Childhood Soft Tissue Sarcomas

984 new cases
in 2023[134]

232 deaths
in 2024[135]

Standard Treatments

- Surgery
- Chemotherapy
- Proton or Photon Radiation

Breakthroughs and Research Milestones:

1. **Surgical Breakthroughs (1970s-present)**

   Amputation used to be more prevalent, but recent technologies have improved the ability of surgeons to preserve limb function. Such examples include expandable implants using a magnetic coil and even 3D printing techniques.[136]

2. **Proton therapy (2010)**

   As with neuroblastoma and brain tumors, proton therapy is commonly used to treat pediatric sarcoma patients, with a goal of reducing toxicities associated with radiation.[137]

3. **Immunotherapy (2017-present)**

   Immune checkpoint inhibitors, such as atezolizumab, nivolumab, and pembrolizumab, are undergoing testing for various types of pediatric sarcomas, with atezolizumab approved by the FDA for children and adults with alveolar soft part sarcoma. An additional type of immunotherapy called CAR T-cell therapy is currently being explored as a potential treatment option in sarcomas. Cancer vaccines are also being tested in treating pediatric sarcomas, in combination with targeted therapies or other immunotherapy agents, such as immune checkpoint inhibitors.[138]

4. **Targeted therapy (2018-present)**

   Targeted therapy agents that can help treat sarcomas:

   - Larotrectinib is effective against sarcomas with a type of alteration in the NTRK gene called a fusion. This includes infantile fibrosarcoma, for which larotrectinib is now a standard treatment, often making surgery and chemotherapy unnecessary. Relative to chemotherapy, this drug has very few side effects, even in small infants.
   - Tazemetostat works by blocking EZH2, an enzyme that regulates the machinery controlling patterns of gene expression within cells. Tazemetostat has been FDA-approved in patients 16 and older with epithelioid sarcoma, and studies are ongoing to assess this drug in younger patients.[139]
   - Cabozantinib works by blocking processes that are essential for tumor cell growth and survival. Cabonzantinib is currently used in the treatment of osteosarcoma and Ewing sarcoma.[140] Anlotinib, regorafenib, and pazopanib, like cabozantinib, simultaneously target multiple pathways that promote tumor growth. Each of these drugs exerts anti-tumor activity in ways that are complex, diverse, and not yet well-understood. However, their proven clinical activity has fueled widespread use in patients with high-risk sarcomas.[141,142]

Examples of Types of Sarcomas

Bone Sarcomas

- Osteosarcoma
- Ewing sarcoma

Soft Tissue Sarcomas

- Rhabdomyosarcoma
- Infantile fibrosarcoma
- Desmoplastic small round cell tumor (DSRCT)
- Alveolar soft part sarcoma
- Desmoid tumors
- Inflammatory myofibroblastic tumor
- NTRK-rearranged spindle cell sarcomas

- Entrectinib and Repotrectinib are tyrosine kinase inhibitors that block fusion proteins containing ROS1 or NTRK domains—mutations that drive cancer. Numerous types of sarcomas have these fusion proteins and the FDA has approved these drugs for the treatment of NTRK fusion sarcomas.[143,144]
- Crizotinib is an ALK inhibitor that has been FDA-approved for the treatment of children with a rare sarcoma called an inflammatory myofibroblastic tumor.

FDA Approvals: Pediatric Sarcomas[145]

2024
- Targeted therapy

2023
- Targeted therapy

2022
- Immunotherapy
- Targeted therapy

2020
- Targeted therapy

2018
- Targeted therapy

1964
- Chemotherapy

1953
- Chemotherapy

Retinoblastoma

Retinoblastoma is a pediatric cancer that occurs in the developing retina and often results in removal of the impacted eye. More than 98% of retinoblastoma tumors form due to a genetic mutation in the tumor in a gene called RB1. Early groundbreaking studies found that 45% of retinoblastoma was inherited, meaning that families carried a gene that causes eye cancer. For kids with the inherited type of retinoblastoma, the disease was most frequently present in both eyes. These early studies were the first time cancer was ever linked to an inherited gene, opening the door to understanding inherited cancer risks for all human cancers.[146,147]

Retinoblastoma tumors begin in the retina of the eye, with the potential to spread outside the eye to the optic nerve, brain, and throughout the lymph nodes, liver, bones, and lungs if not treated.[148]

Pediatricians, parents, and other caregivers most frequently notice a glow in the eye, which is medically referred to as leukocoria. Recognizing leukocoria facilitates early detection, and treatment can save both sight and lives.

Age at Diagnosis	Five-year survival rates[149]
Ages > 1	98.4%
Ages 1-4	96.2%
Ages 5-9	100%

Retinoblastoma cases among children ages 10-19 are extremely rare and the sample size is too small to produce a reliable survival estimate.

The Promise of Liquid Biopsies

Pediatric oncologists often wrestle with a core dilemma: how to treat cancer aggressively without causing lasting harm. In retinoblastoma, removing the eye can cure the disease, but the child will lose their eye and vision.

Traditional biopsies aren't possible in the retina, but researchers have pioneered a new approach: liquid biopsy. By analyzing a tiny sample of aqueous humor (the fluid in the front of the eye) doctors can gauge tumor aggressiveness, track disease, and tailor treatment. The result: a better chance of saving not just the child's life but also their vision.

The use of liquid biopsy can also help with diagnosis in unusual cases and can even help detect recurrences before they can be seen visually by the doctor.

Retinoblastoma, by the Numbers in the U.S.

199 new cases
in 2023[150]

Standard Treatments

- Surgery
- Chemotherapy
- Specialized radiation

Types of Retinoblastoma

Retinoblastoma can occur in one eye (unilaterally) or both (bilaterally). There are two types:

- **Hereditary: 45% (often bilateral)**
- **Nonhereditary: 55% (typically unilateral)[151]**

Breakthroughs and Research Milestones:

1. **Laser Therapy (1960s):**

   A laser beam is directed in the pupil of the patient. The high temperature of the laser is able to kill the tumor cells within the eye.[152]

2. **Cryotherapy (1960s):**

   A metal probe is cooled to very low temperatures and placed on the surface of the eyeball near the tumor. The very low temperatures of the probe is able to kill the surrounding tumor cells on the surface of the eye. This is still used today, but in a very limited capacity.[153]

3. **External beam radiotherapy (1980s):** Radiotherapy to help kill cancer cells.[154]

4. **Chemotherapy (1990-present):**

   The most common chemotherapy agents used for treating retinoblastoma are vincristine, etoposide, and carboplatin.[155] One method of delivering these chemotherapy agents is through a technique called intra-arterial chemotherapy, which delivers chemotherapy agents directly to the ophthalmic artery, which is the primary blood supply source to the eye.[156]

5. **Plaque brachytherapy (1993-present):**

   A radioactive plaque that is made of metal and radioactive material, such as Iodine-125 or Ruthenium-106, is surgically stitched to the surface of the eye, allowing for a continuous low dose of radiation to be administered directly to the eye.[157]

Predisposition

At diagnosis, the burning question parents often have is "What caused my child's cancer?" Not only is childhood cancer rare, but children simply haven't lived long enough to have collected the risk factors that come with environmental and lifestyle exposures. While researchers do not have a full answer to that question, they do know that up to 18%[158] of childhood cancers are driven by predisposition.

Predisposition means that an individual has a genetic mutation that makes them more likely to develop cancer. These mutations can be inherited from a parent but can also form spontaneously without a familial link. Mutations can exist on their own, like in the case of RB1 and retinoblastoma, or be linked to a syndrome, which can come with both cancer predisposition and additional symptoms in the body.

18% of all childhood cancers are driven by predisposition[159]

Common Predisposition Types:

1. **Neurofibromatosis-driven cancers:[160]**

   Neurofibromatosis type 1 (NF1) is a condition caused by a mutation in the NF1 gene that leads to the development of tumors that are mostly benign but also have the potential to become malignant.[161] NF1 primarily leads to the formation of malignant peripheral nerve sheath tumor (MPNST), but also leads to the increased risk of other tumors, such as gliomas, juvenile myelomonocytic leukemia, or other malignancies.[162] Neurofibromatosis type 2 (NF2) is similar to NF1; however, malignant tumor formation is less common than what is observed in NF1. The most common type of tumors developed in NF2 are tumors of the brain and spine, such as ependymoma.

   ***Neurofibromatosis-driven cancers milestones:** Mirdametinib is a small molecule that inhibits an enzyme called MEK, which helps to reduce the size of the tumors formed in NF1. This drug has been approved by the FDA for treating patients with NF1 in 2025.[163] Selumetinib, like mirdametinib, is a small molecule inhibitor of MEK that is also used to treat patients with NF1. This drug received FDA approval in 2020 for the treatment of NF1.

2. **Li-Fraumeni Syndrome:**

   Li-Fraumeni Syndrome (LFS) is a cancer predisposition syndrome caused by a mutation in a tumor suppressor gene called TP53. When TP53 is mutated, a large variety of different cancers may form, and patients with this syndrome undergo frequent cancer prevention screening tests.[164] LFS is rare, occurring in 1 in 5,000 to 1

Types of Predisposition

- Ataxia-telangiectasia
- Beckwith-Wiedemann syndrome
- DICER1 syndrome
- Familial adenomatous polyposis
- Hereditary neuroblastoma
- Hereditary paraganglioma-pheochromocytoma syndrome
- Juvenile polyposis syndrome
- Li-Fraumeni syndrome
- Multiple endocrine neoplasia type 1 (MEN 1)
- Multiple endocrine neoplasia type 2 (MEN 2)
- Neurofibromatosis type 1
- Neurofibromatosis type 2
- Nevoid basal cell carcinoma syndrome
- Noonan syndrome
- Peutz-Jeghers syndrome (PJS)
- PTEN hamartoma tumor syndrome
- Retinoblastoma
- Rhabdoid tumor predisposition syndrome
- RUNX-1
- Von Hippel-Lindau (VHL) syndrome
- WT1-related Wilms tumor (WT) syndromes
- X-linked lymphoproliferative syndrome

in 20,000 people worldwide.[165] The types of pediatric cancers that LFS patients are more likely to develop are soft-tissue sarcomas, osteosarcomas, brain tumors, and acute leukemias.[166] There are no direct treatment options for patients with LFS, rather enhanced cancer screening protocols are used, along with treatment of the cancer that may have formed from this condition.[167]

3. **Beckwith-Wiedemann Syndrome:**

   Beckwith-Wiedemann Syndrome (BWS) is a cancer predisposition syndrome that is caused by a mutation in a gene called CDKN1C that leads to the overgrowth of cells and organs and subsequent predisposition to certain types of pediatric cancer, namely Wilms tumor and hepatoblastoma.[168,169] BWS, like LFS, does not have any direct treatment options to treat the syndrome, but rather requires enhanced surveillance to help find and treat associated diseases.[170]

FDA Approvals: Pediatric Predispositions

2020
- Targeted Therapy (Selumetinib)

2025
- Targeted Therapy (Mirdametinib)

SECTION 3

Critical Gaps: Challenges in Funding, Treatment, and Access

Critical Gaps: Challenges in Funding, Treatment, and Access

Overall, more children are surviving cancer than ever before thanks to advances in technology, geographic growth in specialized cancer centers that offer therapies like proton radiation and CAR T-cell therapy, increased private funding, and decades of research.

This is particularly true in the United States, Canada, and Europe, where over 80% of the children diagnosed with cancer will be alive five years after their initial diagnosis—a massive increase from five-year relative survival rates of 58% in the 1970s. Low- and middle-income countries without comprehensive public health infrastructures still lag decades behind in survivorship rates (see **Section 1** for more information).

For some childhood cancers, survival rates remain extremely low, no matter where a child lives. Developing new drugs for kids—creating, testing, and getting FDA approval—remains a major challenge. Since the 1950s, many more cancer drugs have been developed and approved for adults than for pediatric cancers, with most pediatric oncology approvals occurring in the past two decades. Even for survivors, cancer is a lifelong condition, often requiring management of long-term and late effects of treatment.[171]

The section ahead details how geography can impact survival rates, explores the hidden costs of cancer care to families, examines the current climate of research funding and legislation, discusses the challenges in research and drug development, and shines a light on some of the solutions on the horizon.

How Geography Determines Survival

Even in high income countries, like the United States, geography plays an enormous role in access to treatment. In rural and medically underserved areas, access to pediatric oncologists, specialty care centers, and research hospitals is often limited. Travel, even just an hour by car, can present time and financial burdens. And for children with harder to treat cancers, clinical trial access might not even be available in a child's state, let alone in their zip code.

When families live greater than an hour from a treatment center, they are 30% more likely to require an ambulance for a medical emergency.[172] And while all families experience missed work (an average of 16 days during the first month of diagnosis),[173] families in rural areas with a more than two-hour commute to a treatment center missed an average of eight more days in that first month.[174]

When families are experiencing pre-existing financial barriers, the impact of geography is compounded—placing more children at risk for poor outcomes.

The maps ahead examine the childhood cancer incidence and death rates by state, as well as the locations of Children's Oncology Group hospitals and centers for proton radiation and CAR T-cell therapy.

The other 90%

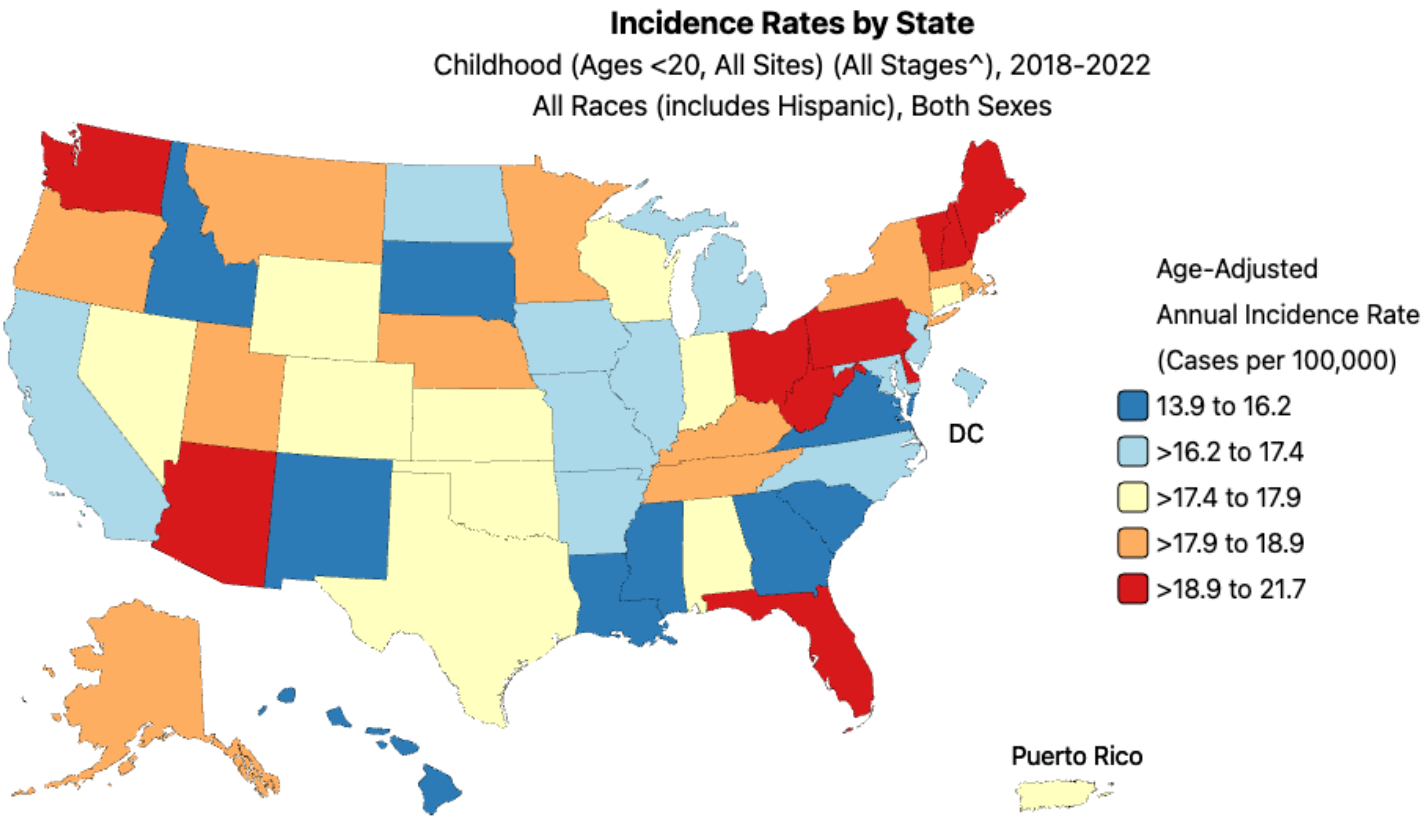
90% of the world's population resides in a low- and middle-income countries. In these countries, without robust scientific and public health infrastructure, survival rate data for children with cancer is grim: only 20-30% of those children will be alive five years after a diagnosis. These children lack access to timely diagnoses, essential medicines and surgeries, trained specialists, and curative treatment options.

Childhood Cancer by State

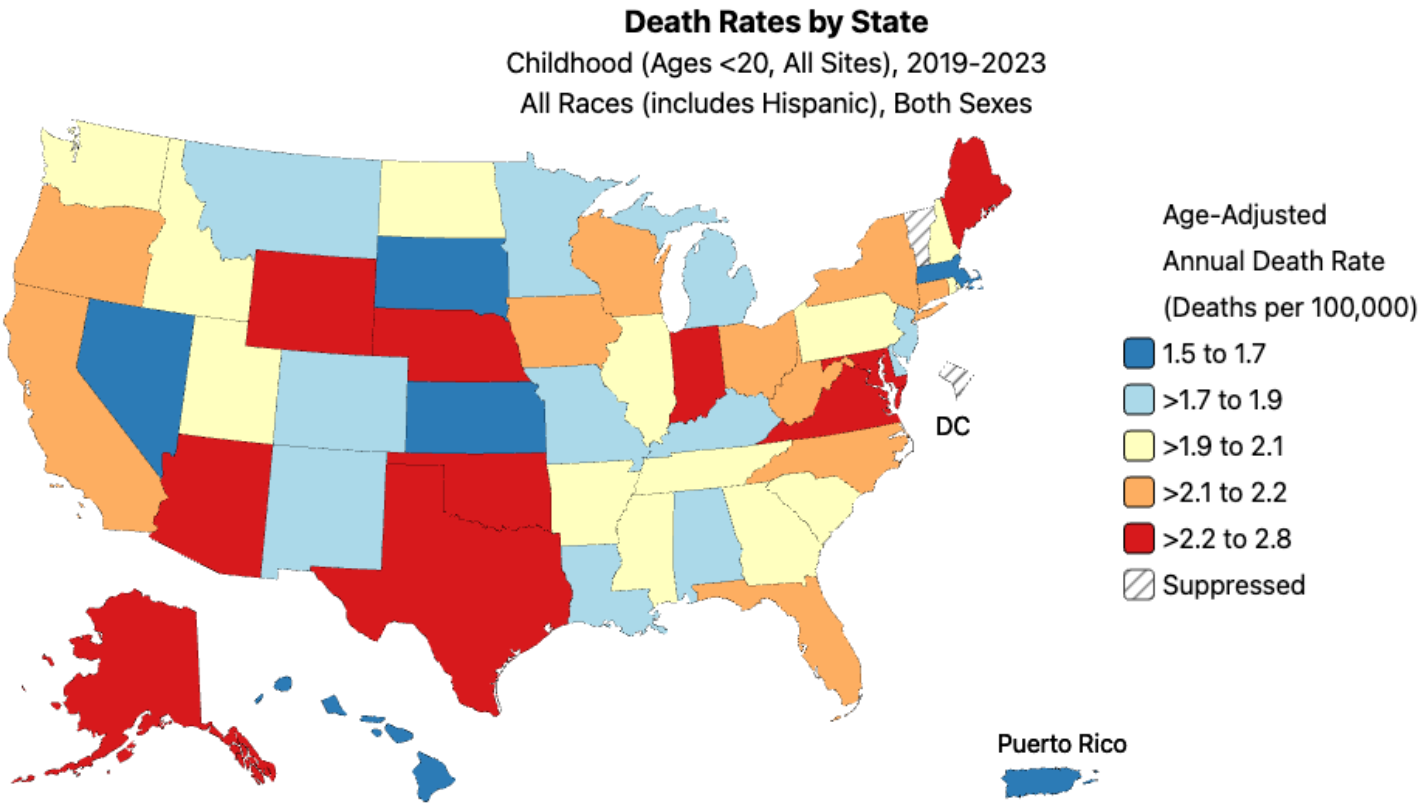
Incidence rates by state are age-adjusted to allow fair comparisons between populations that have different age structures. For example, in Utah about 30% of the population is under 20, compared to Maine with one of the smallest proportions of children (just 20%). By adjusting incident rates for the age of the population, scientists can have a clear understanding of the prevalence of childhood cancer.

Death rates, tracked by the National Vital Statistics System, are also age adjusted. By comparing incidence rates and death rates, researchers can start to hypothesize what leads to specific outcomes.

Childhood Cancer Incident Rates by State, 2017-2022[175]



Childhood Cancer Deaths by State, 2018-2023[176]



The Reach—and Limits—of the COG Network

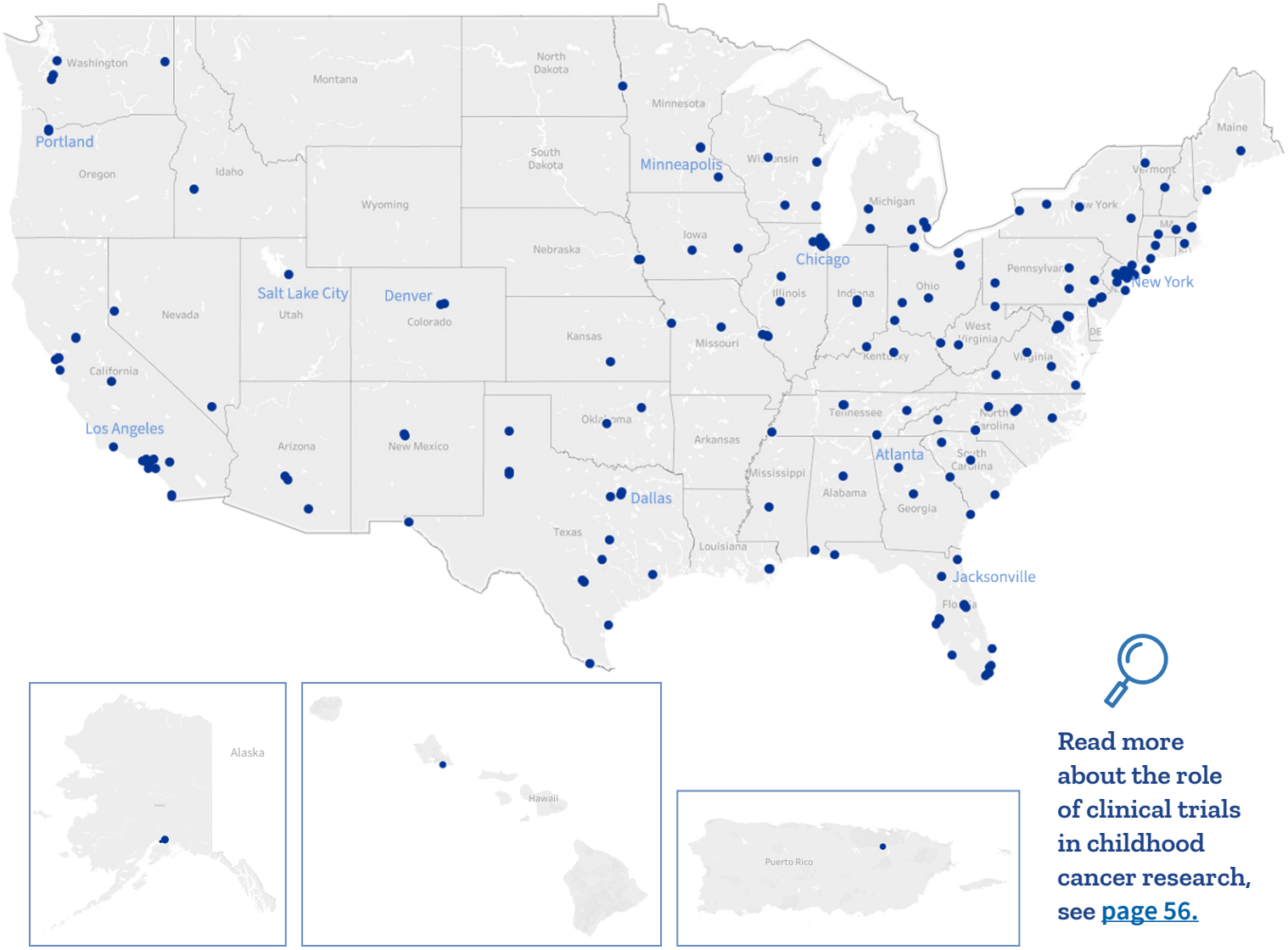
The Children's Oncology Group (COG) brings together more than 220 hospitals and cancer centers around the world. It is the largest childhood cancer research network, and most children with cancer in the United States—more than 80% according to COG—are treated at member institutions.[177] These hospitals collaborate on research, communicate on rare cases, and launch multisite clinical trials. By working together on clinical trials, these hospitals can offer children with cancer more treatment options, while helping researchers learn faster by studying new therapies across a larger group of patients.

But, geography still plays a role in access, with children in rural areas lacking access to a COG institution.

COG estimates that approximately 12,000 children enroll in one of the 100 COG trials each year.[178] Beyond COG, pediatric researchers collaborate on research and clinical trials through private grant funding programs, the National Institutes of Health, and National Cancer Institute. One collaborative trial group called the Pediatric Brain Tumor Consortium lost its funding during the federal budget reallocation process in 2025.

Globally, researchers are continuing to push forward with improving access to treatment and trials. One project called Global HOPE (hematology-oncology pediatric excellence) has worked to deliver care to children in Africa through capacity building, training, and collaboration. [179]

Children's Oncology Group Centers in the United States



Read more about the role of clinical trials in childhood cancer research, see page 56.

Where Proton Radiation Is (and Isn't)

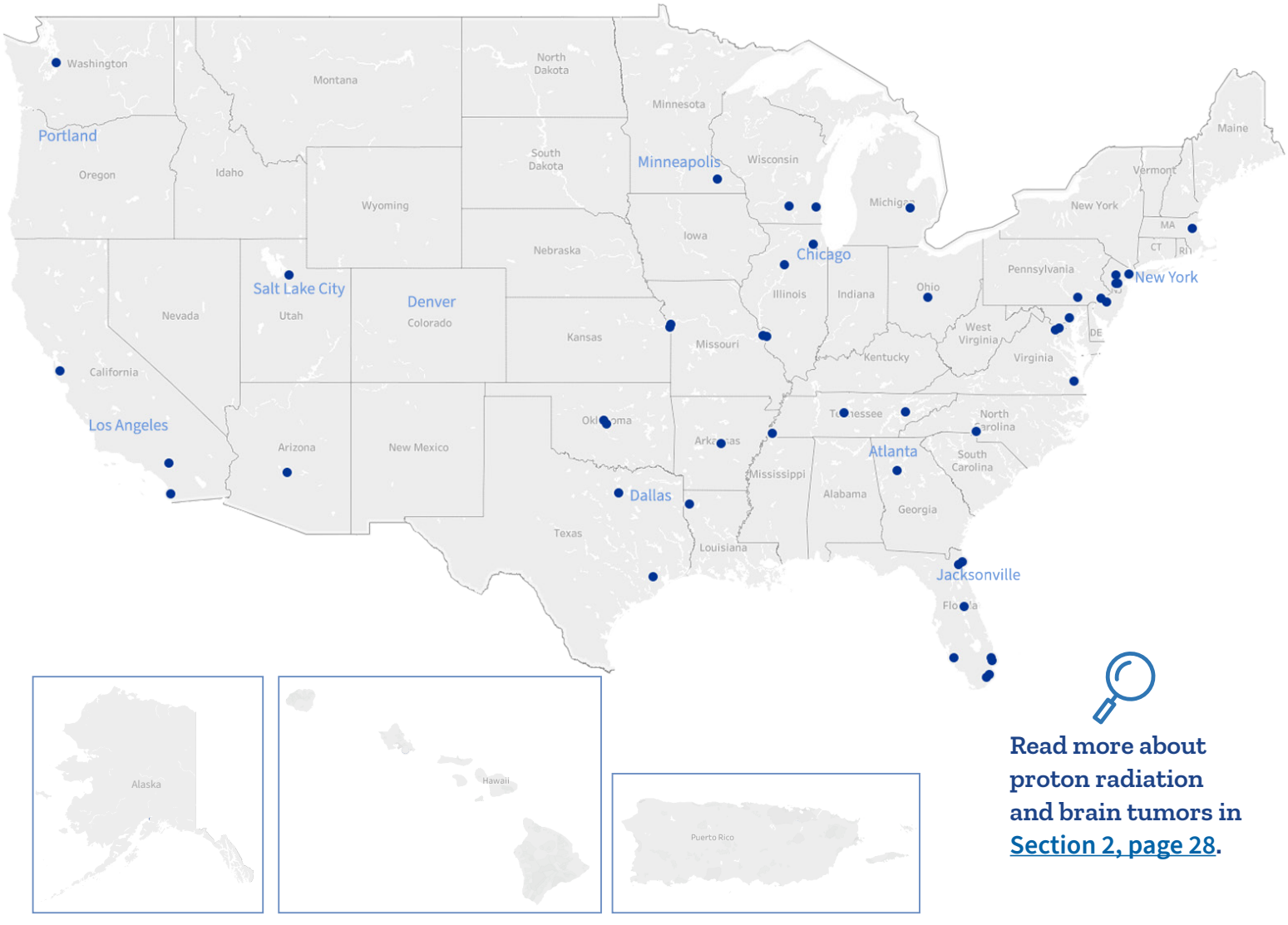
Proton radiation, a type of targeted radiation, was first approved by the FDA in 1988. It was not until 2007 that it was integrated into the care of children with brain tumors.[180] Today, it is used for additional types of pediatric cancer—neuroblastoma, sarcoma, and other solid cell tumors. The therapy is as effective as the more common photon radiation but comes with less side effects, thanks to highly precise beams that minimize damage to healthy tissue.

However, proton radiation is still out of reach for many children in the United States. Over 70% of the population lives more than 100 miles away from the nearest proton center.[181] Those living in rural areas face the longest drive times and hurdles to access.

In 2007, there were three proton radiation centers in the United States providing care to children with brain tumors. In 2026, the number of proton radiation centers in the United States has increased to 48, with 8 more in development. Most of these centers provide therapy to children, but specific eligibility for treatment depends on age, diagnosis, the need for sedation, and other factors.[182] The National Association for Proton Therapy[183] maintains a database of proton centers in the United States as well as other resources.

Globally, there are just 100 proton centers, with access concentrated to high-income countries. The United States is the only country in North or South America with proton radiation therapy.

Proton Radiation Centers in the United States



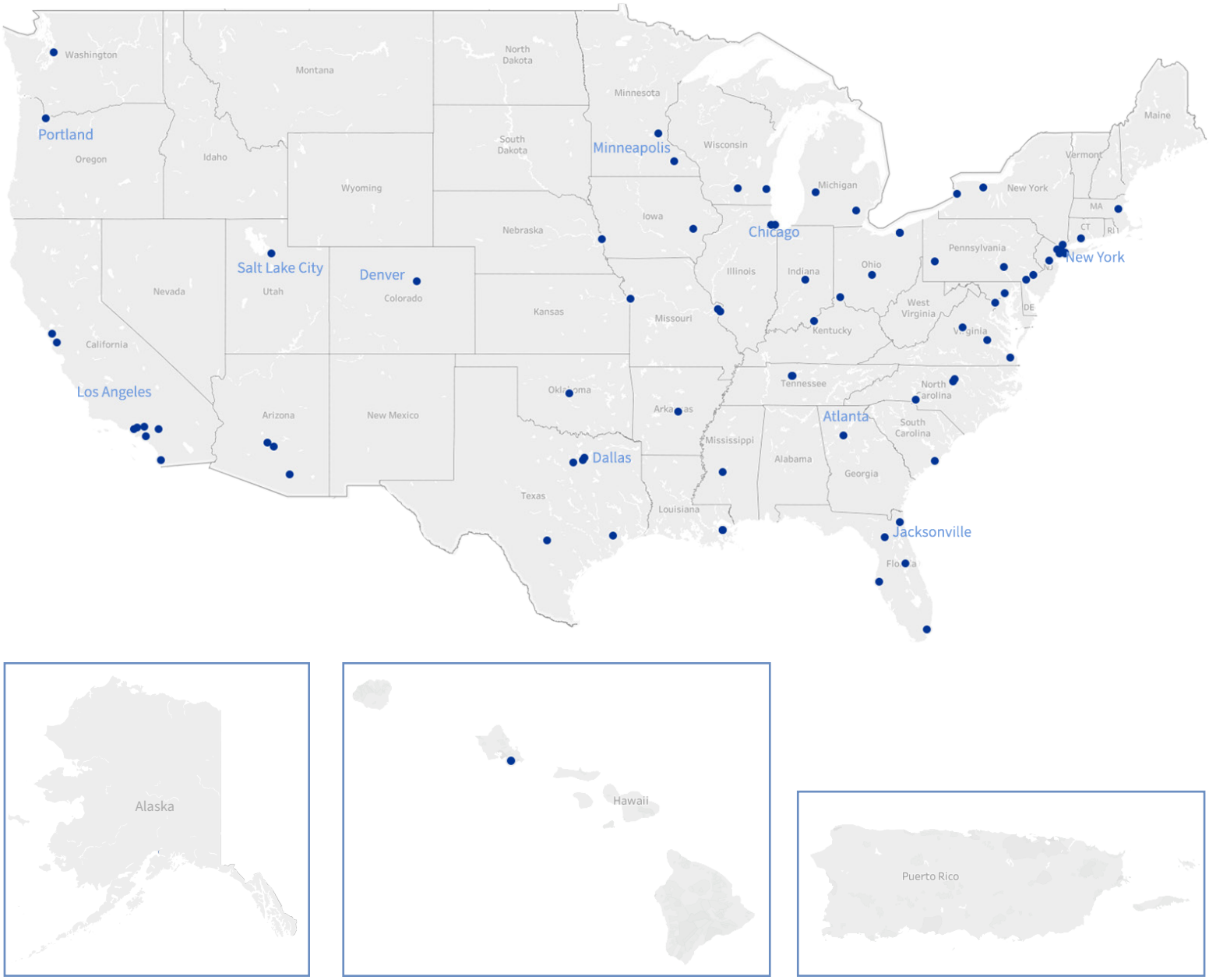
Read more about proton radiation and brain tumors in Section 2, page 28.

CAR T-cell Therapy

Chimeric Antigen Receptor T-cell (CAR T-cell) therapy was approved by the FDA as a treatment for certain types of leukemia in 2017. It shows extraordinary promise in the treatment of blood cancers with ongoing studies for solid cell tumors. The treatment is customized for each child. A child's T cells are harvested, then the T cells are genetically altered by adding a special protein that is programmed to kill cancer cells, and then the altered T cells are returned. They get to work and kill cancer.

While this is a promising new technology for the treatment of childhood cancer, access remains a critical issue. Only centers authorized to offer cellular therapy have CAR T-cell therapy available.[184] In addition, because each of the treatments are personalized, patients must travel to treatment centers, often multiple times over the course of several months, creating additional barriers to access.[185]

CAR T-cell Therapy Centers in the United States



Demographics of Childhood Cancer: Racial and Ethnic Disparities

Racial and Ethnic Disparities

In the United States, Black and Hispanic children are less likely to be diagnosed early, are more likely to experience treatment delays, and have lower survival rates than their white peers, even when diagnosed with the same cancer type. A study of Hispanic children with ALL showed that those children were 5-10% less likely to survive versus their non-Hispanic peers.[186]

Treatment differences can be attributed to a range of factors:

- Language barriers and lack of culturally competent care
- Structural racism within healthcare systems
- Lack of access to high-quality care and clinical trials

As researchers work to understand existing disparities, treatment centers are also looking at ways to increase access by making clinical trials available at other campuses away from the hospital center.

Implicit Bias

Implicit bias refers to the unconscious attitudes, stereotypes, or assumptions that healthcare providers may hold about certain groups of people. These biases operate automatically, without intentional awareness, and can subtly influence clinical decisions, communication, and the quality of care.

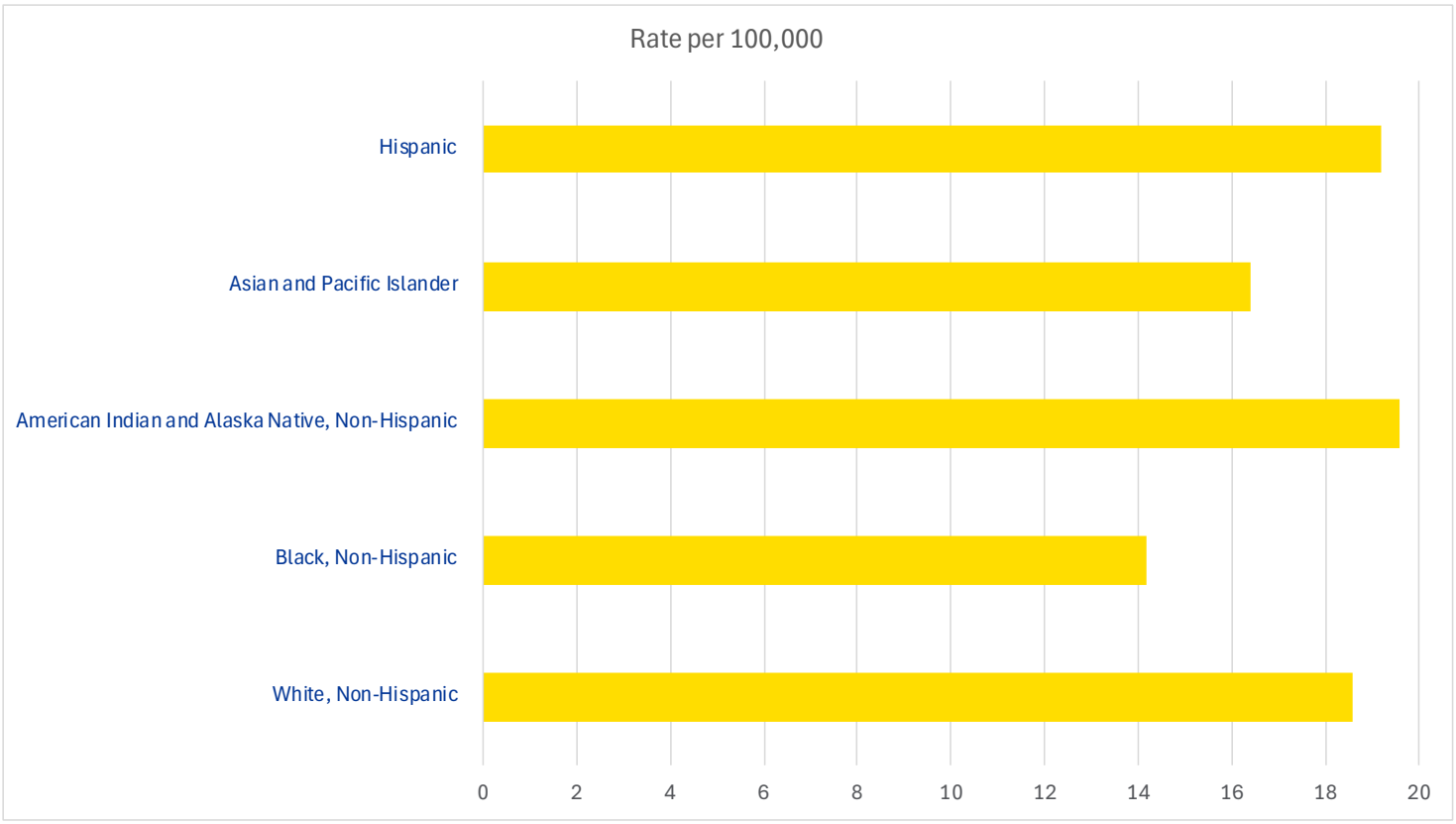
Incidence versus Survival

Survival rates have improved significantly for children with cancer. However, disparities exist. The charts on the next page show the incidence and mortality rates of childhood cancer by race. For example, non-Hispanic Black children have a lower incidence rate of childhood cancer overall but a higher mortality rate.

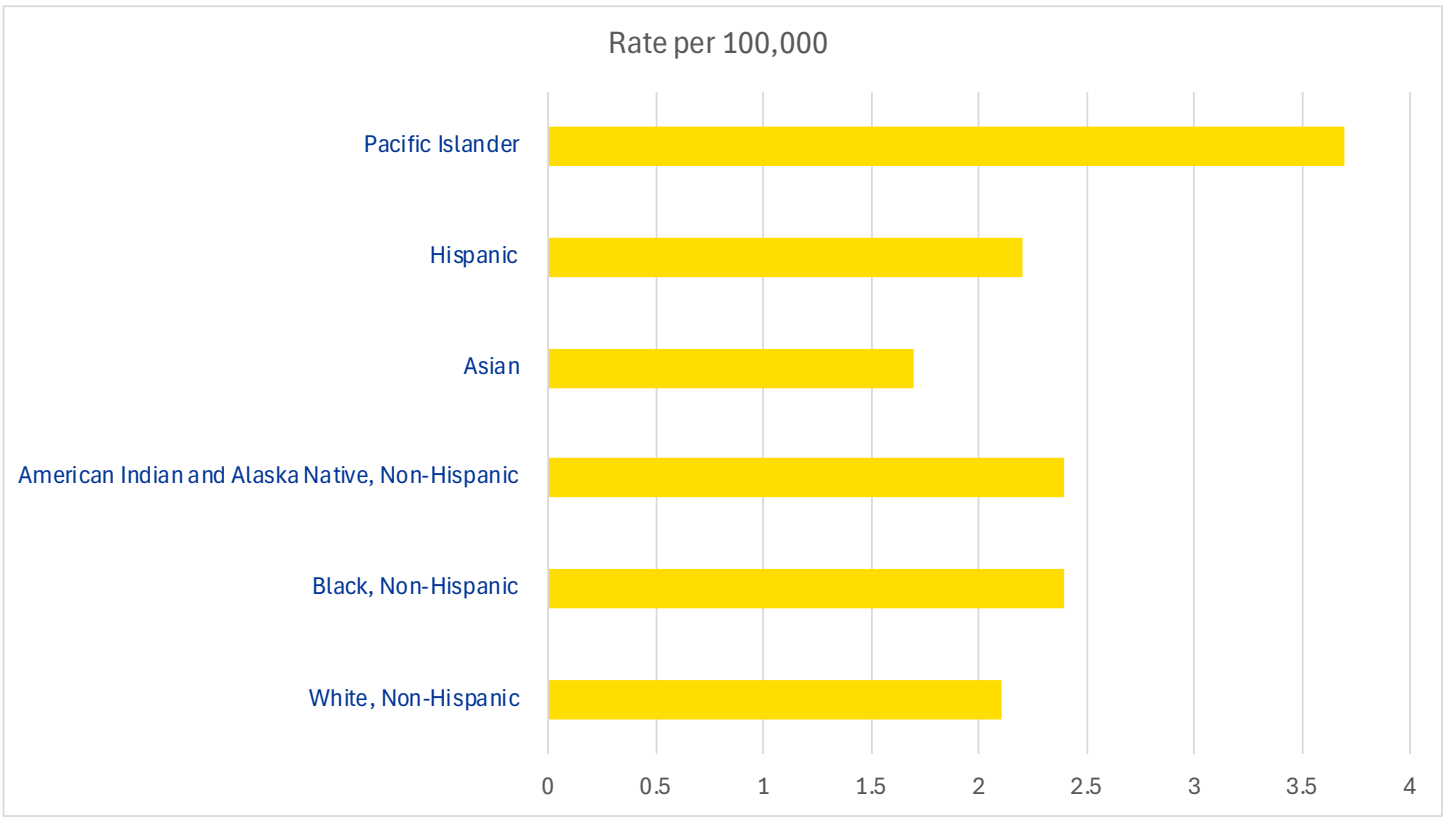
Race and Clinical Trials

One study found that Hispanic children have a significantly higher incidence rate of leukemia and lymphoma but a poorer 5-year survival rate versus their non-Hispanic white counter parts. This in part might be attributable to lower clinical trial enrollment rates. Another study showed that only 2% of 10,000 clinical trial enrollees were minorities.[187,188]

Childhood Cancer Incidence by Race, United States, 2019-2023[189]



Childhood Cancer Mortality by Race, United States, 2020-2024[190]



Socioeconomic Barriers

The social determinants of health (race, ethnicity, insurance, employment, income, education, and place of residence) can be barriers to cancer treatment, survival, and long-term follow-up care.

Families with limited financial resources face challenges affording gas and parking for treatment, taking unpaid leave, managing insurance gaps, using Medicaid across state lines, and securing food and housing during care. While public and private insurance typically cover childhood cancer treatment (and clinical trial costs are covered by the trial), co-pays for repeated clinic and care visits add up. These costs can be devastating to families, even those who begin the cancer journey in a financially secure position.

These costs can also influence treatment decisions and long-term care of survivors (see **Section 1**), especially because geographic access to pediatric oncology care isn't equal and some types of treatment centers are concentrated along the east and west coasts of the United States (**See Maps of COG, Proton, and CAR T-cell therapy centers**).

Although not an exhaustive list, the section ahead pulls out some of the hidden costs of childhood cancer treatment and offers some suggestions on future directions in improving care.

There are **only about 200 cancer centers** in the United States that offer access to hematopoietic stem cell transplantation (HSCT), a critical and curative intervention for certain types of childhood cancer.[198] Patients with low- and middle-class socioeconomic status are nearly 25% less likely to undergo HSCT, according to one retrospective study.[199]

Insurance and Healthcare Costs

It's no surprise that insurance coverage can influence access to cancer care. Insurance coverage often requires providers and facilities be "in-network." Children who are covered by Medicaid (nearly 37.3 million as of April 2025) can experience difficulties getting treatment across state lines. While the federal government offers guidance on Medicaid coverage for medically complex children,[191] how that coverage works varies from state to state and largely depends on prior authorization, the availability of specialists, and whether the providers participate in Medicaid. This can add hurdles for families as well as oncology clinics, who are managing treatment plans and working towards cures.

As the cost of living rises nationwide, the number of people on Medicaid has also risen—there were 14% more Americans on public health insurance in 2025 versus 2024.[192] Among the childhood cancer patient population, 1 in 3 children receive health insurance through Medicaid.[193]

Private insurance can offer similar network treatment difficulties as well as put financial strain on families. Annual employer-sponsored premiums have risen 7% for American families from 2023 to 2024.[194] The average specialist co-pay in the United States is $43.71.[195] For children who have frequent clinic and other healthcare provider visits (physical therapy, occupational therapy, speech therapy, etc.), these costs can add up. During active treatment, outpatient appointments could be daily and even include multiple providers per day. After cancer treatment, the required medical care continues on. One study estimated that childhood cancer survivors visit a medical practitioner an average of 11.4 times per year.[196] Drug costs are also a significant out-of-pocket expense for families, and coverage can vary greatly depending on insurance plans and providers.[197]

Travel Costs

Medical costs are just one piece of the financial burden that impacts families dealing with childhood cancer. Traveling to a clinic—whether just a few miles or several hours or several states away—significantly adds to the financial strain for families. One study estimated that for rural families the cost of each clinic visit was $138 due to additional travel costs.[200] Another study estimated that every additional travel minute added $9.14 of travel costs and each additional mile added $8.85.[201]

Hidden Costs: Time Away from Regular Lives

Beyond the medical and travel costs, socioeconomic barriers generate additional hidden costs. Children with cancer in remote areas miss more days of school and remain at risk for repeating grades. Parents miss more days of work—and those without vacation or sick leave lose much needed income. Time away from siblings produces more than just a financial impact on families.[202, 203]

Travel Costs[210,211] in the United States:

Average per-night cost of a hotel room in the U.S.:

$162.72

Average parking fees at cancer centers in the U.S. per 24 hour period:

$7.79

Challenges in Drug Development

The key to curing pediatric cancer without lasting side effects is having a comprehensive library of effective drugs with minimal side effects. Between 2020 and 2025, the FDA approved 322 drugs for oncology indications[204]—only 53 of those drugs are approved for children.[205] Children do benefit from adult approvals, as those approved therapies can be used, as appropriate, in pediatric studies without the need for researchers to develop a new drug. However, a significant gap still exists. Children wait 6.5 years longer for new cancer drugs than adults.[206] A survey of the oncology clinical trials open in the United States shows the disparity in research options for kids: Only 17% of the 26,000 recruiting clinical trials are for children.[207, 208]

Without research, drugs cannot be studied, developed, and approved.

Money, both the small portion of the federal research budget (see Section 3, page 50) and the lack of pharmaceutical investment in pediatric cancer, is the main driver of the gap. The rarity of childhood cancer also creates small sample population sizes which further hinders data collection and clinical trial accruals. And other barriers exist for children. For example, the format of the study drug can limit access for younger children and babies, as they cannot swallow a pill and a liquid formulation of the drug may not be available. Language and cultural barriers can limit trial enrollment. And, of course, geography and access to pediatric oncology research centers can present a barrier.

However, oncology researchers are working to optimize clinical trial designs in a variety of ways to accelerate drug development. At the federal level, one piece of key legislation called the Research to Accelerate Cures and Equity (RACE) for Children Act (passed in 2017) mandates pediatric cancer drug testing for new adult cancer drugs that also have pediatric targets and has made a small difference in drug development (see Section 3). Between 2017 and 2024, the FDA approved 61 adult cancer drugs relevant to children, and while most pre-2020 drugs were tested in kids only after approval, post-2020 drugs under the RACE Act were more often tested before approval and included formal pediatric testing requirements.[209]

From Early Stage Research to FDA Approval

Having a drug go from early stage research to clinical trials and eventual FDA approval takes a significant amount of time and study on behalf of the researchers and the clinicians. When the FDA considers approving a drug, it usually looks at three main things:

- **The condition and current treatments:** They review the disease the drug is meant to treat and compare it to existing treatments to understand the potential benefits and risks.
- **Evidence from clinical trials:** They examine the data from studies to see how well the drug works and whether it could help patients faster.
- **Managing risks:** They check the known risks of the drug and how steps can be taken to reduce or manage those risks.

But before the FDA even considers an approval, the drug is thoroughly studied and tested in both the lab and in patients in clinical trials:

1. **Lab experiments:** Early research on cells in a lab (not in animals or people) to see if a potential drug can affect cancer cells by slowing their growth or killing them.
2. **Model Development:** New lab models are created for pediatric cancers to better predict how drugs might work in animals and humans.[212]
3. **Drug and Target Matching:** Scientists screen for molecules or therapies (like small molecules, antibodies, or new technologies) that can affect the target.
4. **More Lab Experiments:** Promising compounds are tested in the lab to make sure they specifically and effectively hit the target, and chemists work on improving potency and making the drug safe for animals.
5. **Animal Models:** The compound is tested in animals to check if it reduces tumor growth, reaches the tumor, and is safe.
6. **Phase I clinical trial:** If animal results are good, the drug moves to humans, starting with a small trial to find the safest and most effective dose.
7. **Phase II/III clinical trials:** If Phase I is successful, larger trials test how well the drug works at slowing tumor growth in more patients.
8. **FDA approval:** If trials show the drug is safe and effective, it can be approved for use in that cancer type.

Research Funding and Legislation

Childhood cancer research in the United States is primarily funded through four different mechanisms:

1. **Federal funding** through the National Cancer Institute (NCI), the National Institutes of Health, the Department of Defense, the Centers for Disease Control and Prevention, and key legislative and executive actions.
2. **Private/nonprofit funding** via foundations, charities, and family-led organizations.
3. **Institutional funding** from hospitals, academic medical centers, and universities.
4. **Industry funding** via commercial pharmaceutical and biotech companies.

While this range of funding sources may suggest an abundance of opportunities, the reality is stark. In the United States, childhood cancer research is vastly underfunded by the federal government as compared to adult and overall cancer research. Often the statistic of "less than 4%" is shared and used to describe the portion of the federal budget dedicated to childhood cancer research.[213] This number is often cited as representing the estimated share of the National Cancer Institute budget directed toward childhood cancer research. However, it is not a formal earmark and is based on analyses of funded grants, which can vary over time depending on methodology. In addition, all cancer research—whether specifically for adults or kids—could have a meaningful impact in the scientific community's understanding of childhood cancer and could benefit from more funding from the Department of Defense and other legislation like the STAR Act.[214]

Regardless of how this all adds up, childhood cancer research is underfunded and kids, who have many, many years of life ahead of them, are left without sufficient research funding.

RACE Act

Before the RACE Act, drug companies could skip pediatric studies for new cancer drugs, even if those drugs targeted the same molecular pathways or mutations in both adult and pediatric cancers. The RACE act now requires drug companies to study drugs if there is an indication for pediatrics, opening the door for more clinical trials and faster access for kids.

NCI Budget Deep Dive, 2025[215]

Total NCI Budget: $7.2 Billion

Allocation to Research: $3.1 Billion (43% of total budget)

Allocation to kids (based on 4% average): $124 Million

Specific Allocations:

The Childhood Cancer Data Initiative (CCDI): $50 million[216]

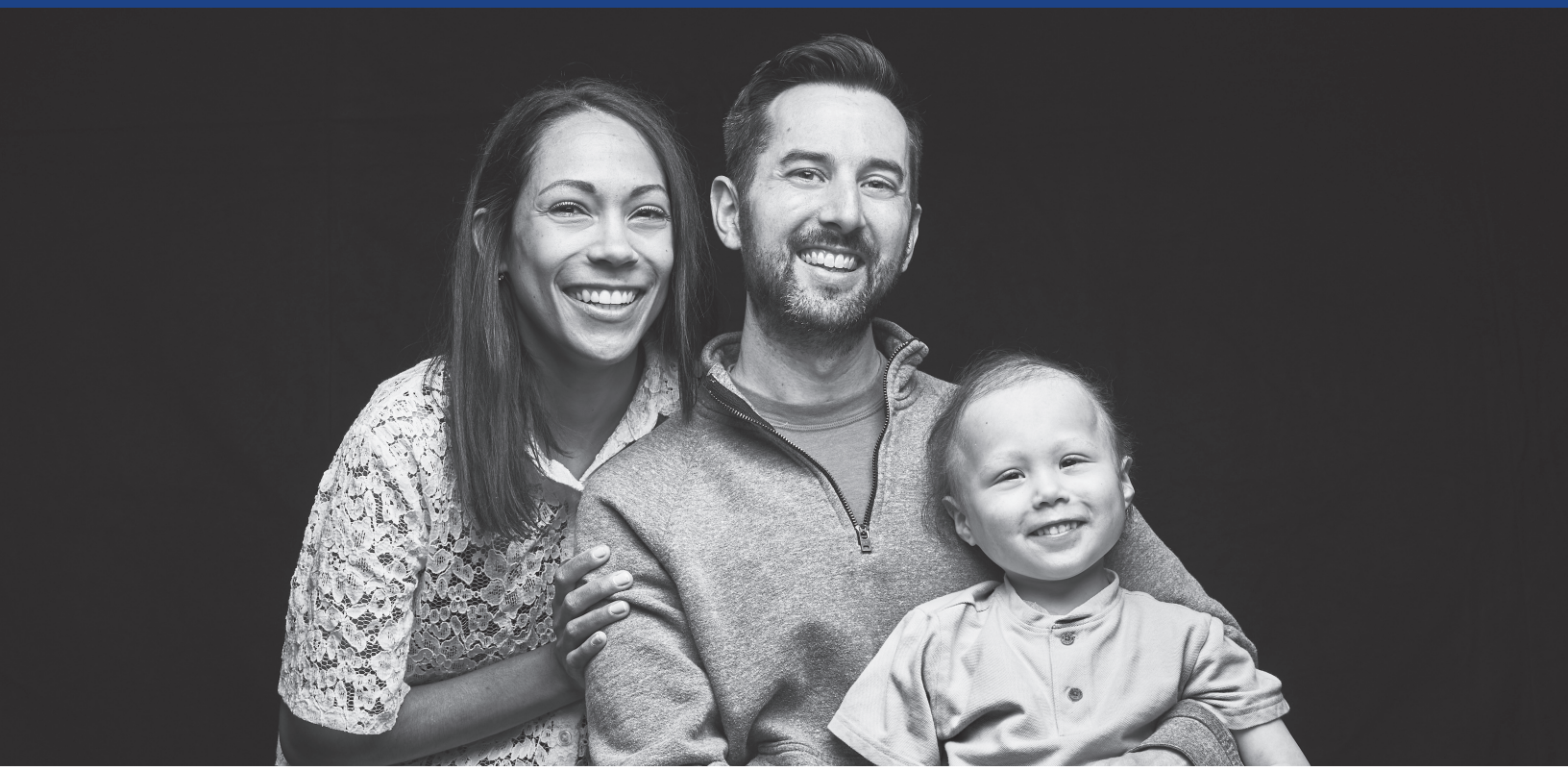
STAR Act: $28 million

Key U.S. Childhood Cancer Legislation

- **Gabriella Miller Kids First Research Act (2014)[217]**
- **Research to Accelerate Cures and Equity for Children (RACE) Act (2017)[218]**
- **Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act (2018, Reauthorized 2023)**
- **Unlocking Cures for Pediatric Cancer with Artificial Intelligence Executive Order (2025)**
- **Mikaela Naylon Give Kids a Chance Act (2025-2026)**
- **Gabriella Miller Kids First Research Act 2.0 (2025)**

SECTION 4

Toward the Future



Toward the Future

When a child was diagnosed with Wilms tumor in the early 20th century, the treatment protocol was high-risk surgery and care to ensure what was then called an "easeful death," the 1890s version of palliative care. Five-year survival rates did not exist until pediatric surgeon Dr. William E. Ladd pioneered new techniques in the operating room, removing surgery risk and ensuring successful removal of kidney tumors. Combined with radiation, this treatment protocol elevated cure rates to 25% in the 1940s and then to 47% in the 1950s. Later, Dr. Sidney Farber would introduce chemotherapy to the mix, and in doing so, children with Wilms tumor received a treatment plan instead of a death sentence.[219]

Today, thanks to continued innovation and research, a child diagnosed with Wilms tumor has a five-year survival rate of nearly 90%.[220]

Similar stories can be told for other types of childhood cancer (**see Section 2 for examples**). Research works. Scientists of all disciplines, from chemistry to genetics to data to the pioneering frontier of AI, continue to advance toward breakthrough treatments. Their inspiration comes from the foundational successes of researchers like Dr. Ladd and Dr. Farber and from the stories of real children who have cures today that did not exist just five years ago.

The section ahead reviews some of the research and treatment trends that are emerging—a novel frontier where the foundational knowledge is being matched with treatments for children with cancer.

Drug Development and Emerging Technologies

Researchers are continuing to discover new cancer proteins, which are molecules in the cells that drive the growth of cancer cells. These proteins represent potential targets for drugs. There are thousands of these proteins,[221] with the most infamous being TP53, a mutation in the p53 suppressor gene. This mutation is responsible for the development of many human cancers and is the main driver of Li-Fraumeni syndrome.[222] But the challenge remains: How can these cancer proteins be targeted so that more children are cured?

One way of increasing treatment options for patients is by expanding technologies that can "drug the undruggable," which consists of finding new ways to change the behavior of molecular targets that have a known link to driving cancers but are difficult to target with existing technologies. New technologies, like **molecular degraders**, can attach to these targets and break them down directly. This approach opens the door to targeting things that researchers couldn't before, including certain "master control" proteins in cells called transcription factors.[223] Early research shows promise, and most ongoing studies are looking at blood cancers, like lymphoma, and breast cancer in adults. In the future, these treatments may also be adapted for children with cancer.

Future directions will be potentially expanding existing molecular degraders into pediatric cancer indications and developing molecular degraders that can specifically target pediatric cancer driving factors.

Additional New Classes of Drugs

Antibody-drug conjugates (ADCs)

These are an additional class of drugs that can expand treatment options for pediatric cancer patients. There are three approved ADCs for the treatment of pediatric leukemia, and further efforts are ongoing to test ADCs outside of leukemia as potential treatment options. There has been progress made in developing ADCs to treat neuroblastoma and sarcomas, with the goal of launching clinical trials soon.[224,225]

CAR T-cell therapy

Although only one CAR T-cell therapy has been approved for use in pediatric cancer patients (see Section 3), significant progress has been made in advancing CAR T-cell therapies in both blood cancers and solid tumors. There have been many clinical trials focused on CAR T-cell therapy in pediatric and young adult cancer patients, with most focusing on leukemia; however, significant progress has been made in solid tumors as well, with clinical trials ongoing for brain tumors, sarcomas, and neuroblastoma.[226] Future CAR T-cell therapy trials can greatly expand treatment options in pediatric cancer patients going forward.

Other immunotherapy

In addition to CAR T-cell therapies, ongoing clinical trials are exploring additional immune cell populations that can potentially be used to target cancer cells. Two such examples are Natural Killer (NK) cells and macrophages. CAR-NK and CAR-Macrophage studies are ongoing to determine if either immune cell population may be beneficial in slowing down the growth of pediatric cancers. While early, these studies are showing promise, both preclinically and in early clinical trials.[227]

Precision medicine

Technologies such as next-generation sequencing give clinicians the ability to identify mutations driving tumor formation and the possibility of creating highly individualized treatment plans, especially if there is a current approval therapy for the mutation. This type of approach is called precision medicine and is rapidly evolving as more sequencing technologies and anticancer therapies are made available to patients.[228] Precision medicine approaches are especially valuable to patients that have very rare tumors without a standard treatment approach and to patients with relapsed or refractory cancers.[229]

Surgery and Diagnostics

In parallel to treatment options, there are emerging ways to diagnose and to potentially remove tumors in pediatric cancer patients.

- **Advancements in surgical techniques** for treating pediatric cancer patients will continue to progress into the future to provide better treatment options for pediatric cancer patients. These include minimally invasive surgical techniques and the enhanced use of robotics.[230] Laparoscopy, a surgery performed with a tiny camera inserted through a small incision, is an increasingly safe and effective tool for diagnostics and biopsies.[231]
- **Liquid biopsies** and circulating tumor DNA (ctDNA) offer even less invasive methods to diagnose cancer in patients and to monitor how well treatments are working. Liquid biopsies consist of analyzing the blood and other fluids of a patient, looking for tumor specific markers as a mechanism of detection.[232] ctDNA is an example of a tumor specific marker that can be observed in liquid biopsies. ctDNA can be beneficial to monitor both in initial diagnosis and during treatment to observe the presence of a tumor and how well a tumor is responding to treatment, based on the levels of ctDNA that is present in the blood of a patient.[233]
- **Next generation sequencing** can also detect potential cancer-driving mutations before cancer develops. This type of approach is called predisposition detection where patients can undergo enhanced cancer surveillance to catch cancer early in high-risk patients.[234]

Clinical Trial Design

Clinical trials are a critical step in the research process, and for those kids for whom approved drugs have failed, they are a critical step towards survival. Despite their importance, design and access to clinical trials has presented a challenge because of the rarity of childhood cancer types and subtypes (see Section 3). As researchers study new drugs and interventions, they are also turning their attention to designing clinical trials that accelerate science and provide more access to children both upfront and with relapsed disease. Unlike adult cancer research which has heavy investment from the private sector and pharmaceutical companies, pediatric cancer trials are often led by academic labs.[235] As research evolves and federal legislation like the RACE act (see Section 3, page 50) demand more industry involvement in childhood cancer research, the academic-industry partnership will also evolve.

Some other trends in clinical trial design include:

- Using master protocol trials to test many treatments under one big trial[236]
- Leveraging data from adult trials and using a flexible statistical technique called Bayesian to make trials smaller and faster but still reliable[237]
- Continuing to focus on tumor mutations versus where the tumor started in the body to guide trial eligibility[238]
- Designing trials that are more flexible, and adapting those trials as the data comes in[239]

Artificial Intelligence

The September 2025 U.S. Presidential Executive Order "Unlocking Cures for Pediatric Cancer with Artificial Intelligence" significantly increased federal funding of the Childhood Cancer Data Initiative.[240] This government investment opens the door for the study of how AI might support children with cancer through early detection, diagnosis, treatment, and beyond. Using AI has the potential to speed up discovery and allow for more precise medicine approaches to treatment. Because childhood cancers are rare and varied, diagnosing and studying them is challenging, which makes new approaches like AI especially promising. In the future, AI can be used to quickly review tumor data and match that data with potential molecules that could someday become treatments for kids with cancer. [241]

Focus on Survivorship

There are over 500,000 childhood cancer survivors in the United States. As more children survive cancer and as more new treatments are being added to the standard of care, a focus on survivorship becomes critical as these children navigate life after treatment (**see Section 1**). Federal funding of grants studying cancer survivorship (for both adults and pediatrics) has more than doubled in the past ten years.[242] The Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act, passed in 2018, has a special focus on enhancing resources for survivors and their families (**see Section 3**).[243] Of special interest is survivorship among the adolescent and young adult population. Some key areas of survivorship focus include barriers to follow-up care, impact of socioeconomic status on survivor outcomes, risk factors and predictors of long-term side effects, and newer treatments' imapct on physical health.

Endnote

In 1997, Alex Scott was wheeled out of the operating room following her first surgery to remove a neuroblastoma tumor that was precariously positioned around her kidneys and spine. It was her very first birthday. Alex would only get seven more—but in her 8 years, Alex, although just a child, held firm to a vision that everyone could make a difference.

Her story would include more surgeries, experimental treatments, several hospitals, not enough first days of school, three brothers, and lemonade stands. Alex was 4 when she first asked her parents if she could host a lemonade stand to raise money for her doctors.

Little did they know that Alex would be one of the many incredible visionaries who would shape and change the trajectory of research for childhood cancer.

Nearly 30 years later, children diagnosed with cancer in the United States have an 85% chance of long-term survival. Still, 15% of children in the United States will die from cancer. And most children are still receiving treatments that, while effective, leave lasting, irreversible side effects.

And then there is the great global divide created by disparities in financial resources and public health infrastructure that leaves 90% of the world's childhood cancer population with only slivers of hope for cures. These children, who are diagnosed with cancers that are treatable and curable in countries like the United States, have limited treatment options and may not even be able to access the earliest, most inexpensive chemotherapies. These are the children who might not ever be diagnosed and instead will succumb to an unnamed disease, while their families navigate impossible to quantify grief.

As we look toward the future, we know research holds the key to unlocking cures. But we also know that bridging barriers in access will take much more than scientific breakthroughs. It will take more funding, more legislative change, and more collaboration across oceans and political borders.

A reporter once asked little Alex Scott if her goal of raising $1 million was possible and Alex said: "I think if we all work together, we can do it."

The progress made in finding cures for children with cancer has been challenging, but it has happened thanks to collaboration—collaboration that will continue to grow and spread so that someday all children have cures.

References

1 "Study of Leukemia Biology Needed to Improve Treatment, Pinkel Says," *The Cancer Letter* 4, no. 14 (1978): 6, https://cancerletter.com/issues/19780407/.

2 GBD 2017 Childhood Cancer Collaborators, "The Global Burden of Childhood and Adolescent Cancer In 2017: An Analysis of the Global Burden of Disease Study 2017," *The Lancet Oncology* 20, no. 9 (2019), https://pubmed.ncbi.nlm.nih.gov/31371206/.

3 "Cancer Stat Facts," National Cancer Institute, accessed April 10, 2026, https://seer.cancer.gov/statfacts/.

4 "Childhood Cancers by International Classification of Childhood Cancer (ICCC)," U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://gis.cdc.gov/Cancer/USCS/#/special-topic/childhood-cancer-iccc?cancer=87&indicator=value&timeperiod=1&sexes=1&races=1&tab=1&view=chart&xaxis=ages.

5 "Childhood Cancers by International Classification of Childhood Cancer (ICCC)," U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://gis.cdc.gov/Cancer/USCS/#/special-topic/childhood-cancer-iccc?cancer=87&indicator=value&timeperiod=1&sexes=1&races=1&tab=1&view=chart&xaxis=ages.

6 "People Diagnosed Before Age 20 and Alive (U.S. Prevalence) on January 1, 2022," NCCR*Explorer, National Cancer Institute, accessed October 14, 2025, https://nccrexplorer.ccdi.cancer.gov/application.html?site=1&data_type=5&graph_type=11&compareBy=sex&chk_sex_1=1&series=9&age_at_prev=1&advopt_precision=1#resultsRegion1.

7 "Childhood Cancers by International Classification of Childhood Cancer (ICCC)," U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://gis.cdc.gov/Cancer/USCS/#/special-topic/childhood-cancer-iccc?cancer=87&indicator=value&timeperiod=1&sexes=1&races=1&tab=2&view=table&xaxis=ages.

8 "Age and Cancer Risk," National Cancer Institute, accessed September 18, 2025, https://www.cancer.gov/about-cancer/causes-prevention/risk/age.

9 "All Cancer Sites Combined Recent Trends in SEER Age-Adjusted Incidence Rates, 1975-2023," Cancer Statistics Explorer Network SEER* Explorer, National Cancer Institute, accessed June 15, 2026, https://seer.cancer.gov/statistics-network/explorer/application.html?site=1&data_type=1&graph_type=2&compareBy=sex&chk_sex_1=1&rate_type=2&race=1&age_range=15&hdn_stage=101&advopt_precision=1&advopt_show_ci=on.

10 "Rate of Cancer Deaths in the United States, 2024," Cancer Statistics: Mortality All Cancer Sites Combined, United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://gis.cdc.gov/cancer/USCS/#/special-topic/childhood-cancer-primary-site?datatype=2&cancer=1&indicator=value&timeperiod=26&sexes=1&races=1&ages=21&tab=1&view=chart.

11 "All Cancer Sites Combined: Recent Trends in U.S. Age-Adjusted Mortality Rates, 2000-2024," Cancer Statistics Explorer Network SEER* Explorer, National Cancer Institute, accessed June 15, 2026, https://seer.cancer.gov/statistics-network/explorer/application.html?site=1&data_type=1&graph_type=2&compareBy=age_range&chk_age_range_15=15&rate_type=2&sex=1&race=1&hdn_stage=101&advopt_precision=1&advopt_show_ci=on.

12 Joachim Worthington et al., "Covid-Related Disruptions to Colorectal Cancer Screening, Diagnosis, and Treatment Could Increase Cancer Burden in Australia and Canada: A Modelling Study," PLOS ONE 19, no. 4 (2024): e0296945, https://doi.org/10.1371/journal.pone.0296945.

13 "Childhood Cancers by International Classification of Childhood Cancer (ICCC)," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://gis.cdc.gov/cancer/USCS/#/special-topic/childhood-cancer-iccc?cancer=87&indicator=count&timeperiod=1&sexes=1&races=1&tab=1&view=chart&xaxis=ages.

14 "United States Cancer Cases and Death Statistics at a Glance," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://gis.cdc.gov/cancer/USCS/#/special-topic/childhood-cancer-iccc?cancer=87&indicator=count&timeperiod=1&sexes=3&races=1&tab=1&view=chart&xaxis=ages.

15 "United States Cancer Cases and Death Statistics at a Glance," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

16 "Cancer Site Comparison 5-Year Relative Survival Rates, 2015-2021," NCCR*Explorer, National Cancer Institute; Accessed October 14, 2025 https://nccrexplorer.ccdi.cancer.gov/application.html?site=1&data_type=4&graph_type=5&compareBy=sex&chk_sex_3=3&chk_sex_2=2&series=9&race=1&age_range=1&advopt_precision=1&advopt_show_ci=on.

17 "Rate of Cancer Deaths in the United States, 2023," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessedJune 15, 2026, https://www.cdc.gov/cancer/dataviz.

18 "Long-Term Trends in SEER Age-Adjusted Incidence Rates, 1975-2023," Cancer Statistics Explorer Network SEER*Explorer, National Cancer Institute, accessed March 6, 2026, https://seer.cancer.gov/statistics-network/explorer/application.html?site=1&data_type=1&graph_type=1&compareBy=age_range&chk_age_range_15=15&rate_type=2&sex=1&race=1&advopt_precision=1&advopt_show_ci=on.

19 Steve Friedman and Serban Negoita, "History of the Surveillance, Epidemiology, and End Results (SEER) Program," *J Natl Cancer Inst Monogr.* 65 (2024): 105-109, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11300016/.

20 "Facts and Figures," Congressional Childhood Cancer Caucus, accessed December 11, 2025, https://childhoodcancer-mccaul.house.gov/facts-and-figures.

21 Katherine Schneider et al., "Li-Fraumeni syndrome," in *GeneReviews* (University of Washington, 1999), https://www.ncbi.nlm.nih.gov/books/NBK1311.

22 Jared Marsh, "Danger: Pesticides Raise Death Risk 60% for Kids with Leukemia," *University of California San Francisco*, September 17, 2025, https://www.ucsf.edu/news/2025/09/430731/danger-pesticides-raise-death-risk-60-kids-leukemia.

23 Julianne Byrne et al., "Childhood Cancer Survivors' Knowledge of Their Diagnosis and Treatment," *Annals of Internal Medicine* 110, no. 5 (1989): 400–403, https://doi.org/10.7326/0003-4819-110-5-400.

24 E. B. D. Neuhauser et al., "Irradiation Effects of Roentgen Therapy on the Growing Spine," *Radiology* 59, no. 5 (1952): 637–643, https://doi.org/10.1148/59.5.637.

25 Jeanne Harvey et al., "Providing Quality Care in Childhood Cancer Survivorship: Learning from the Past, Looking to the Future," *Journal of Pediatric Oncology Nursing* 16, no. 3 (1999): 117-125, https://doi.org/10.1016/S1043-4542(99)90009-7.

26 G. J. D'Angio, "Pediatric Cancer in Perspective: Cure Is Not Enough," *Cancer* 35, no. 3 (1975): 866–870, https://doi.org/10.1002/1097-0142(197503)35:3+<866::AID-CNCR2820350703>3.0.CO;2-F.

27 Donatus U. Ekwueme et al., "Annual Out-of-Pocket Expenditures and Financial Hardship Among Cancer Survivors Aged 18–64 Years—United States, 2011–2016," *Weekly* 68, no. 22 (2019): 494–499, https://doi.org/10.15585/mmwr.mm6822a2.

28 "Childhood Cancer Survivor Study: An Overview," National Cancer Institute, accessed December 11, 2025, https://www.cancer.gov/types/childhood-cancers/ccss.

29 Jelena Roganovic, "Late Effects of the Treatment of Childhood Cancer," *World Journal of Clinical Cases* 13, no. 7 (2025), https://doi.org/10.12998/wjcc.v13.i7.98000.

30 "Late Effects of Treatment for Childhood Cancer (PDQ®)–Patient Version," National Cancer Institute, accessed December 11, 2025, https://www.cancer.gov/types/childhood-cancers/late-effects-pdq.

31 "Survivorship Guidelines: Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers," Children's Oncology Group, accessed December 11, 2025, https://childrensoncologygroup.org/survivorshipguidelines.

32 K. E. Effinger et al., "Current Pediatric Cancer Survivorship Practices: A Report from the Children's Oncology Group," *Journal of Cancer Survivorship* 17 (2022): 1139–1148, https://doi.org/10.1007/s11764-021-01157-w.

33 "Care for Childhood Cancer Survivors," National Cancer Institute, accessed December 11, 2025, https://www.cancer.gov/about-cancer/coping/survivorship/child-care.

34 "About CCSS," Childhood Cancer Survivor Study, St. Jude Children's Research Hospital, accessed December 11, 2025, https://ccss.stjude.org/about-the-study.html.

35 Leslie L. Robison et al., "Study Design and Cohort Characteristics of the Childhood Cancer Survivor Study: A Multi-Institutional Collaborative Project," Medical and Pediatric Oncology 38, no. 4 (2002): 229–239, https://doi.org/10.1002/mpo.1316.

36 "Big 5 Challenges Kenya Faces in Fighting Childhood Cancer," Kenyatta University Teaching, Referral, and Research Hospital, accessed December 2025, https://www.kutrrh.go.ke/big-5-challenges-kenya-faces-in-fighting-childhood-cancer/.

37 "Childhood Cancer," International Agency for Research on Cancer, World Health Organization, accessed December 2025, https://www.iarc.who.int/cancer-type/childhood-cancer/.

38 "Childhood Cancer," World Health Organization, accessed December 11, 2025, https://www.who.int/news-room/fact-sheets/detail/cancer-in-children.

39 "Childhood Cancer," World Health Organization, accessed December 11, 2025, https:// www.who.int/news-room/fact-sheets/detail/cancer-in-children.

40 "Global Initiative for Childhood Cancer," Union for International Cancer Control, accessed December 2025, https://www.uicc.org/what-we-do/advocacy/working-together/global-initiative-childhood-cancer.

41 "The Burden: Childhood Cancer," The Cancer Atlas, accessed December 11, 2025, https://canceratlas.cancer.org/burden-of-cancer/childhood-cancer/.

42 "The Burden: Childhood Cancer," The Cancer Atlas, accessed December 11, 2025, https://canceratlas.cancer.org/burden-of-cancer/childhood-cancer/.

43 "S.3312 - 102nd Congress (1991-1992): Cancer Registries Amendment Act," Congress.gov, accessed December 11, 2025, https://www.congress.gov/bill/102nd-congress/senate-bill/3312.

44 "NPCR Timeline," National Program of Cancer Registries, Centers for Disease Control and Prevention, accessed December 11, 2025, https://www.cdc.gov/national-program-cancer-registries/about/npcr-timeline.html.

45 "S.3312 - 102nd Congress (1991-1992): Cancer Registries Amendment Act," Congress.gov, accessed December 11, 2025, https://www.congress.gov/bill/102nd-congress/senate-bill/3312.

46 "How Cancer Registries Work," National Program of Cancer Registries, Centers for Disease Control and Prevention, accessed December 11, 2025, https://www.cdc.gov/national-program-cancer-registries/about/how-cancer-registries-work.html.

47 Stephanie Hill, NAACCR, Personal Communication/Phone Interview, June 18, 2025.

48 "Cancer Surveillance Programs and Data Tracking," American Cancer Society, accessed December 11, 2025,https://www.cancer.org/cancer/preparing-for-treatment/cancer-surveillance-programs-and-data-tracking.html.

49 "Pediatric Oncology Drug Approvals," U.S. Food and Drug Administration Oncology Center of Excellence, accessed October 29, 2025, https://www.fda.gov/about-fda/oncology-center-excellence/pediatric-oncology-drug-approvals.

50 "Oncology (Cancer)/Hematologic Malignancies Approval Notifications," U.S. Food and Drug Administration, accessed October 29, 2025, https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancerhematologic-malignancies-approval-notifications.

51 Siddhartha Mukherjee, *The Emperor of All Maladies: A Biography of Cancer* (Scribner, 2010), Part Two: "An Impatient War."

52 "All Cancer Sites Combined: Recent Trends in SEER Age-Adjusted Incidence Rates, 2000-2023," Cancer Statistics Explorer Network SEER*Explorer, National Cancer Institute; accessed October 29, 2025, https://seer.cancer.gov/statistics-network/explorer/application.html.l

53 Christian P. Kratz, "Re-Envisioning Genetic Predisposition to Childhood and Adolescent Cancers," *Nature Reviews Cancer* 25 (2025): 109-128, https://www.nature.com/articles/s41568-024-00775-7.

54 Kinga Panuciak et al. "Insights into Modern Therapeutic Approaches in Pediatric Acute Leukemias," Cells 11, no. 1(2022): 139, https://pmc.ncbi.nlm.nih.gov/articles/PMC8749975/.

55 "Cancer Site Comparison: Recent Trends in U.S. Age-Adjusted Mortality Rates, 2000-2024," Cancer Statistics Explorer Network SEER*Explorer, National Cancer Institute, accessed December 5, 2025, https://seer.cancer.gov/statistics-network/explorer/application.html?site=96&data_type=2&graph_type=2&compareBy=site&chk_site_20=20&chk_site_47=47&chk_site_40=40&sex=1&race=1&age_range=15&advopt_precision=1&advopt_show_ci=on&advopt_show_count=on#resultsRegion0.

56 "Acute Myeloid Leukemia (AML): Recent Trends in SEER Age-Adjusted Incidence Rates, 2000-2023," Cancer Statistics Explorer Network SEER*Explorer, National Cancer Institute, accessed December 5, 2025, https://seer.cancer.gov/statistics-network/explorer/application.html?site=96&data_type=1&graph_type=2&compareBy=age_range&chk_age_range_15=15&rate_type=2&sex=1&race=1&hdn_stage=101&advopt_precision=1&advopt_show_ci=on&advopt_show_count=on#resultsRegion0.

57 "I. Leukemias: 5-Year Relative Survival Rates, 2015-2021," NCCR*Explorer, National Cancer Institute, accessed December 5, 2025, https://nccrexplorer.ccdi.cancer.gov/application.html?site=100&data_type=4&graph_type=5&compareBy=age_range&chk_age_range_2=2&chk_age_range_3=3&chk_age_range_4=4&chk_age_range_5=5&chk_age_range_6=6&series=9&sex=1&race=1&advopt_precision=1&advopt_show_ci=on.

58 "II. Lymphomas: 5-Year Relative Survival Rates, 2015-2021," NCCR*Explorer, National Cancer Institute, accessed December 5, 2025, https://nccrexplorer.ccdi.cancer.gov/application.html?site=200&data_type=4&graph_type=5&compareBy=age_range&chk_age_range_2=2&chk_age_range_3=3&chk_age_range_4=4&chk_age_range_5=5&chk_age_range_6=6&series=9&sex=1&race=1&advopt_precision=1&advopt_show_ci=on#resultsRegion1.

59 "United States Cancer Cases and Death Statistics At a Glance," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

60 "United States Cancer Cases and Death Statistics At a Glance," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

61 "Childhood Cancers by International Classification of Childhood Cancer (ICCC)," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

62 "United States Cancer Cases and Death Statistics At a Glance," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

63 "Treating Childhood Leukemia," American Cancer Society, accessed December 5, 2025, https://www.cancer.org/cancer/types/leukemia-in-children/treating.html#:~:text=How%20is%20childhood%20leukemia%20treated,with%20Acute%20Promyelocytic%20Leukemia%20(APL).

64 "USAN Council," American Medical Association, accessed December 5, 2025, https://www.ama-assn.org/about/united-states-adopted-names-usan/usan-council.

65 "Chemotherapy for Childhood Leukemia," American Cancer Society, accessed December 5, 2025, https://www.cancer.org/cancer/types/leukemia-in-children/treating/chemotherapy.html.l.

66 "Stem Cell Transplantation for Leukemia in Children," NYU Langone Health, accessed December 5, 2025, https://nyulangone.org/conditions/leukemia-in-children/treatments/stem-cell-transplantation-for-leukemia-in-children.

67 Maria Moschovi and Charikleia Kelaidi, "Chronic Myeloid Leukemia in Children and Adolescents: The Achilles Heel of Oncogenesis and Tyrosine Kinase Inhibitors," International Journal of Molecular Sciences 22, no. 15 (2021): 7806, https://pmc.ncbi.nlm.nih.gov/articles/PMC8345932/#:~:text=Overall%2C%20in%20terms%20of%20overall,time%20point%20of%2012%20months.

68 "Pediatric Oncology Drug Approvals," U.S. Food and Drug Administration, accessed December 5, 2025, https://www.fda.gov/about-fda/oncology-center-excellence/pediatric-oncology-drug-approvals.

69 Devon Carter, "Chronic versus Acute Leukemia: Different Diagnoses, Different Treatments," The University of Texas MD Anderson Cancer Center, accessed December 5, 2025, https://www.mdanderson.org/cancerwise/what-is-the-difference-between-chronic-and-acute-leukemia--different-diagnoses--different-treatments.h00-159461634.html.

70 "Pediatric Lymphomas," Memorial Sloan Kettering Cancer Center, accessed December 5, 2025, https://www.mskcc.org/pediatrics/cancer-care/types/pediatric-lymphomas.

71 "Targeted Therapy Drugs for Childhood Leukemia," American Cancer Society, accessed December 5, 2025, https://www.cancer.org/cancer/types/leukemia-in-children/treating/targeted-therapy.html.

72 Hannah J Uckelmann et al., "Therapeutic Targeting of Preleukemia Cells in a Mouse Model of NPM1 Mutant Acute Myeloid Leukemia," Science 367, no. 6477 (2020): 586-590, https://pmc.ncbi.nlm.nih.gov/articles/PMC7754791/.

73 Zhang, W. et al. "Advances in CAR-T Therapy for Pediatric Leukemia." Frontiers in Oncology, 9 (2020), https://gis.cdc.gov/Cancer/USCS/#/explore/mortality?cancer=1&datatype=2&dataset=standard&indicator=value&area=1&timeperiod=26&sexes=1&races=1&ages=23&tab=1&view=map&xaxis=sexes&shownational=true/.

74 "BLINCYTO® Is a BiTE® Therapy That Binds CD3 and CD19," Amgen, accessed December 5, 2025, https://www.blincytohcp.com/about-blincyto/mechanism-of-action.

75 Timothy M. Pierpoint et al., "Past, Present, and Future of Rituximab—The World's First Oncology Monoclonal Antibody Therapy," *Frontier Oncology* 8 (2018), https://doi.org/10.3389/fonc.2018.00163.

76 "Immunotherapy for Childhood Leukemia," American Cancer Society, accessed December 5, 2025, https://www.cancer.org/cancer/types/leukemia-in-children/treating/immunotherapy.html.

77 Nazma Hanif and Faiz Anwer, "Rituximab," StatPearls [Internet], National Library of Medicine, accessed December 5, 2025, https://www.ncbi.nlm.nih.gov/books/NBK564374/#:~:text=Rituximab%20is%20an%20anti%2DCD20,for%20use%20in%20several%20conditions.&text=As%20a%20single%20agent%20in%20low%2Dgrade%20non%2Dprogressive/,and%20Prednisolone%20(CVP)%20chemotherapy.

78 Anurekha G. Hall and Rachel E. Rau, "Blinatumomab Use in Pediatric B-ALL: Where Are We Now?" *Blood Advances* 9, no. 15 (2025): 3946–3954, https://ashpublications.org/bloodadvances/article/9/15/3946/537699/Blinatumomab-use-in-pediatric-B-ALL-where-are-we.

79 Carmen Phillips, "Blinatumomab Boosts Chemotherapy as Initial Treatment for Some Kids with ALL," National Cancer Institute, published on February 13, 2025, https://www.cancer.gov/news-events/cancer-currents-blog/2025/childhood-leukemia-blincyto-first-treatment.

80 Michele Gottardi et al., "Therapeutic Targeting of Acute Myeloid Leukemia by Gemtuzumab Ozogamicin," Cancers 13, no. 18 (2021): 4566, https://pmc.ncbi.nlm.nih.gov/articles/PMC8469571/#:~:text=It%20(%20Gemtuzumab%20Ozogamicin%20)%20targets%20leukemic,chemotherapy%20during%20induction%20regimens%2C%20pre%2D%20and%20post%2Dtransplantation.

81 Edward Winstead, "Brentuximab Approved for High-Risk Hodgkin Lymphoma in Children and Adolescents," National Cancer Institute, published December 15, 2022, https://www.cancer.gov/news-events/cancer-currents-blog/2022/fda-brentuximab-children-hodgkin-lymphoma.

82 Quinn T. Ostrom et al. "CBTRUS Statistical Report: Pediatric Brain Tumor Foundation Childhood and Adolescent Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2014–2018," *Neuro-Oncology* 24, no. Supplement_3 (2022), https://academic.oup.com/neuro-oncology/article/24/Supplement_3/iii1/6692860.

83 "Pediatric Brain Tumors," Mayo Clinic, accessed October 29, 2025, https://www.mayoclinic.org/diseases-conditions/pediatric-brain-tumor/diagnosis-treatment/drc-20361706.

84 "III. Central Nervous System Neoplasms (Malignant): 5-Year Relative Survival Rates, 2015-2021," NCCR*Explorer, National Cancer Institute, accessed October 29, 2025, https://nccrexplorer.ccdi.cancer.gov/application.html?site=300&data_type=4&graph_type=5&compareBy=sex&chk_sex_1=1&series=9&race=1&age_range=1&advopt_precision=1&adopt_show_ci=on#resultsRegion0.

85 "United States Cancer Cases and Death Statistics At a Glance," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

86 "PBTF Childhood and Adolescent Brain Tumor Facts," *Neuro-Oncology* 27, no. Supplement_1, (2025), https://doi.org/10.1093/neuonc/noaf214.

87 "Proton Therapy for Brain Tumors," Johns Hopkins Medicine, accessed October 29, 2025, https://www.hopkinsmedicine.org/health/conditions-and-diseases/brain-tumor/proton-therapy.

88 Clara Guido et al., "Nanoparticles for Diagnosis and Target Therapy in Pediatric Brain Cancers," *Diagnostics* 12, no. 1: 173, https://doi.org/10.3390/diagnostics12010173.

89 Mark M. Souweidane et al., "Convection-Enhanced Delivery for Diffuse Intrinsic Pontine Glioma: A Single-Centre, Dose-Escalation, Phase 1 Trial," *The Lancet Oncology* 19, no. 8 (2018): 1040–1050, https://doi.org/10.1016/S1470-2045(18)30322-X.

90 Kelsi M. Chesney et al., "The Role of Focused Ultrasound for Pediatric Brain Tumors: Current Insights and Future Implications on Treatment Strategies," Child's Nervous System 40 (2024): 2333–2344, https://doi.org/10.1007/s00381-024-06413-9.

91 Darcy A. Krueger et al., "Everolimus for Subependymal Giant-Cell Astrocytomas in Tuberous Sclerosis," The New England Journal of Medicine 363, no. 19 (2010): 1801-1811, https://www.nejm.org/doi/full/10.1056/NEJMoa1001671.

92 David N. Franz et al., “Everolimus for Subependymal Giant Cell Astrocytoma: 5-Year Final Analysis,” *Ann Neurol* 78, no. 6 (2015): 929-938, https://pmc.ncbi.nlm.nih.gov/articles/PMC5063160/.

93 Edward Winstead, “Dabrafenib–Trametinib Combination Approved for Solid Tumors with BRAF Mutations,” National Cancer Institute, accessed October 29, 2025, https://www.cancer.gov/news-events/cancer-currents-blog/2022/fda-dabrafenib-trametinib-braf-solid-tumors.

94 Thomas Pfefer et al, “Immunometabolites and Cancer: The Role of 2-Hydroxyglutarate, Succinate, Fumarate and Itaconate in Tumour Development and Anti-Tumour Immunity,” *Immunology Letters* 279 (2026), https://doi.org/10.1016/j.imlet.2026.107153.

95 “FDA Approves Vorasidenib for Grade 2 Astrocytoma or Oligodendroglioma with a susceptible IDH1 or IDH2 Mutation,” U.S. Food and Drug Administration, accessed October 29, 2025, https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-vorasidenib-grade-2-astrocytoma-or-oligodendroglioma-susceptible-idh1-or-idh2-mutation.

96 Cleiton Formentin et al., “Posterior fossa tumors in children: current insights,” *European Journal of Pediatrics* 182 (2023): 4833–4850, https://doi.org/10.1007/s00431-023-05189-5.

97 Lindsay B. Kilburn et al., “The Type II RAF Inhibitor Tovorafenib in Relapsed/Refractory Pediatric Low-Grade Glioma: The Phase 2 Firefly-1 Trial,” Nature Medicine 30 (2024): 207-217, https://www.nature.com/articles/s41591-023-02668-y.

98 Kilburn LB. “FDA Approval Summary: Tovorafenib for Relapsed or Refractory BRAFAltered Pediatric LowGrade Glioma.” Clinical Cancer Research 31(8) (2025). https://aacrjournals.org/clincancerres/article-abstract/31/8/1383/754518/FDA-Approval-Summary-Tovorafenib-for-Relapsed-or?redirectedFrom=fulltext.

99 Xiaonan Zhao et al., “NTRK Fusions Identified in Pediatric Tumors: The Frequency, Fusion Partners, and Clinical Outcome,” *JCO Precision Oncology* 5 (2021): 204-214, https://ascopubs.org/doi/10.1200/PO.20.00250.

100 “Pediatric Oncology Drug Approvals,” U.S. Food and Drug Administration, accessed October 29, 2025, https://www.fda.gov/about-fda/oncology-center-excellence/pediatric-oncology-drug-approvals.

101 Mark N. Stein et al., “First-in-Human Clinical Trial of Oral ONC201 in Patients with Refractory Solid Tumors,” *Clinical Cancer Research* 23, no. 15 (2017): 4163–4169, https://aacrjournals.org/clincancerres/article/23/15/4163/257537/First-in-HumanClinical-Trial-of-Oral-ONC201-in.

102 Chi, Anthony S., et al. “Dordaviprone in diffuse midline glioma: early results.” The New England Journal of Medicine (2025). https://pubmed.ncbi.nlm.nih.gov/37679511/.

103 Northcott, Paul A, “The whole-genome landscape of medulloblastoma subtypes,” Nature, 2017 Jul 20, https://pmc.ncbi.nlm.nih.gov/articles/PMC5905700/.

104 Brent A. Orr, “Pathology, diagnostics, and classification of medulloblastoma,” Brain Pathology 30, no. 3 (2020): 664-678, https://pmc.ncbi.nlm.nih.gov/articles/PMC7317787/.

105 “Medulloblastoma: Diagnosis and Treatment,” National Cancer Institute, accessed October 29, 2025, https://www.cancer.gov/rare-brain-spine-tumor/tumors/medulloblastoma.

106 Edwin S. Kulubya et al., “Advances in the Treatment of Pediatric Brain Tumors,” *Children* (Basel) 10, no. 1 (2022): 62, https://pmc.ncbi.nlm.nih.gov/articles/PMC9856380/.

107 Linda Wang, “Experimental CAR T-Cell Therapy Shrinks Tumors in Children with Deadly Brain Cancer,” *National Cancer Institute*, accessed October 29, 2025, https://www.cancer.gov/news-events/cancer-currents-blog/2025/car-t-cell-therapy-gd2-diffuse-midline-gliomas.

108 Edwin S. Kulubya et al., “Advances in the Treatment of Pediatric Brain Tumors,” *Children (Basel)* 10, no. 1 (2022): 62, https://pmc.ncbi.nlm.nih.gov/articles/PMC9856380/.

109 Gregory K. Friedman et al., “Oncolytic HSV-1 G207 Immunovirotherapy for Pediatric High-Grade Gliomas,” *The New England Journal of Medicine* 384, no. 17 (2021): 1613-1622, DOI: 10.1056/NEJMoa2024947.

110 “Neuroblastoma,” Cleveland Clinic, accessed October 30, 2025, https://my.clevelandclinic.org/health/diseases/14390-neuroblastoma.

111 “Survival Rates by Risk Group for Neuroblastoma,” American Cancer Society, accessed October 11, 2025, https://www.cancer.org/cancer/types/neuroblastoma/detection-diagnosis-staging/survival-rates.html.

112 National Childhood Cancer Registry Explorer (NCCR*Explorer), National Childhood Cancer Registry & National Cancer Institute, accessed December 4, 2025, https://nccrexplorer.ccdi.cancer.gov/application.html?site=400&data_type=4&graph_type=5&compareBy=age_range&chk_age_range_2=2&chk_age_range_3=3&chk_age_range_4=4&chk_age_range_5=5&chk_age_range_6=6&series=9&sex=1&race=1&advopt_precision=1&advopt_show_ci=on#resultsRegion1.

113 "United States Cancer Cases and Death Statistics At a Glance," United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

114 Sidharth Mahapatra and Kishore B. Challagundla, "Neuroblastoma," StatPearls [Internet], National Library of Medicine, accessed December 4, 2025, https://www.ncbi.nlm.nih.gov/books/NBK448111/.

115 "Survival Rates by Risk Group for Neuroblastoma," American Cancer Society, accessed December 4, 2025, https://www.cancer.org/cancer/types/neuroblastoma/detection-diagnosis-staging/survival-rates.html.

116 "MIBG Treatment," Texas Children's Hospital, accessed December 4, 2025, https://www.texaschildrens.org/content/conditions/mibg-treatment#:~:text=What%20is%20MIBG%20therapy?,better%20tolerated%20than%20other%20therapies. Texas Children's.

117 "Researchers Show Lorlatinib is Safe, Effective for Patients with High-Risk Neuroblastoma," Children's Hospital of Philadelphia, accessed December 4, 2025, https://www.chop.edu/news/researchers-show-lorlatinib-safe-effective-patients-high-risk-neuroblastoma.

118 Jianxiong Jiang and Ying Yu, "Eflornithine for Treatment of High-Risk Neuroblastoma," *Trends in Pharmacological Sciences* 45, no. 6 (2024): 577-578, https://pmc.ncbi.nlm.nih.gov/articles/PMC11162306/.

119 Atsushi Makimoto et al., "Retinoid Therapy for Neuroblastoma: Historical Overview, Regulatory Challenges, and Prospects," *Cancers (Basel)* 16, no. 3 (2024): 544, https://pmc.ncbi.nlm.nih.gov/articles/PMC10854948/.

120 James Stallard, "Reduced Radiation for Neuroblastoma Could Lessen Children's Side Effects Later," Memorial Sloan Kettering Cancer Center, accessed December 4, 2025, https://www.mskcc.org/news/reduced-radiation-dose-neuroblastoma-could-spare-children-complications-later.

121 Yaël P. Mossé et al., "Anaplastic Lymphoma Kinase Inhibition Therapy for Hereditary Neuroblastoma," *JCO Precision Oncology* 9 (2025), https://doi.org/10.1200/PO-24-00886.

122 Junko Takita, "Molecular Basis and Clinical Features of Neuroblastoma." *JMA Journal* 4, no. 4 (2021): 321-331, https://pmc.ncbi.nlm.nih.gov/articles/PMC8580727/.

123 "FDA Approves First Therapy for High-Risk Neuroblastoma," National Cancer Institute, accessed December 4, 2025, https://www.cancer.gov/news-events/cancer-currents-blog/2015/dinutuximab-neuroblastoma.

124 Rosa Nguyen and Carol J Thiele, "Immunotherapy Approaches Targeting Neuroblastoma," *Current Opinion in Pediatrics* 33, no. 1 (2021): 19-25, https://pmc.ncbi.nlm.nih.gov/articles/PMC8818321/.

125 Renaissance Pharma Limited, an Essential Pharma Company, Secures FDA Fast Track Designation and IND Clearance for Daretabart (hu1418K322A) in High-Risk Neuroblastoma," Yahoo! Finance, April 14, 2026, https://sg.finance.yahoo.com/news/renaissance-pharma-limited-essential-pharma-060000802.html?guccounter=1.

126 "Childhood Soft Tissue Sarcoma Treatment (PDQ®)–Patient Version," National Cancer Institute, accessed October 30, 2025, https://www.cancer.gov/types/soft-tissue-sarcoma/patient/child-soft-tissue-treatment-pdq.

127 Vanessa Eulo et al., "Secondary Sarcomas: Biology, Presentation, and Clinical Care," *American Society of Clinical Oncology Educational Book* 40 (2020): 463-474, https://ascopubs.org/doi/10.1200/EDBK_280985.

128 Regan F. Williams et al., "Pediatric Sarcomas," *Surgical Clinics of North America* 96, no. 5 (2016): 1107-1125, https://pubmed.ncbi.nlm.nih.gov/27542645/.

129 Audra J. Reiter, "Survival Outcomes in Pediatric Patients with Metastatic Ewing Sarcoma Who Achieve a Rapid Complete Response of Pulmonary Metastases," *Pediatric Blood & Cancer* 71, no. 7 (2024), https://pmc.ncbi.nlm.nih.gov/articles/PMC11116042/.

130 "VIII. Bone Tumors: 5-Year Relative Survival Rates, 2015-2021," NCCR*Explorer, National Cancer Institute, accessed October 30, 2025, https://nccrexplorer.ccdi.cancer.gov/application.html?site=800&data_type=4&graph_type=5&compareBy=sex&chk_sex_1=1&series=9&race=1&age_range=2&advopt_precision=1&advopt_show_ci=on#resultsRegion0.

131 “IX. Soft Tissue Tumors: 5-Year Relative Survival Rates, 2015-2021,” NCCR*Explorer, National Cancer Institute, accessed October 30, 2025, https://nccrexplorer.ccdi.cancer.gov/application.html?site=900&data_type=4&graph_type=5&compareBy=age_range&chk_age_range_2=2&chk_age_range_3=3&chk_age_range_4=4&chk_age_range_5=5&chk_age_range_6=6&series=9&sex=1&race=1&advopt_precision=1&advopt_show_ci=on#resultsRegion1.

132 “Childhood Cancers by International Classification of Childhood Cancer (ICCC),” United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

133 “United States Cancer Cases and Death Statistics At a Glance,” United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

134 “United States Cancer Cases and Death Statistics At a Glance,” United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, Accessed June 15, 2026 https://www.cdc.gov/cancer/dataviz.

135 “United States Cancer Cases and Death Statistics At a Glance,” United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

136 “The Latest in Limb-Sparing Techniques for Pediatric Patients with Sarcoma,” Cleveland Clinic, Consult QD, accessed October 30, 2025, https://consultqd.clevelandclinic.org/the-latest-in-limb-sparing-techniques-for-pediatric-patients-with-sarcoma.

137 Matthew M. Ladra and Torunn I. Yock, “Clinical Implications of Long-Term Survivorship in Soft Tissue Sarcomas,” *Cancers (Basel)* 6, no. 1 (2014): 112-127, https://pmc.ncbi.nlm.nih.gov/articles/PMC3980591/.

138 Pampina Pilavaki et al., “Exploring the Landscape of Immunotherapy Approaches in Sarcomas,” *Frontiers in Oncology* 12 (2022), https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2022.1069963/full.

139 “Tazemetostat,” ScienceDirect, accessed October 30, 2025, https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/tazemetostat.

140 Anthony B. El-Khoueiry et al., “Cabozantinib: An Evolving Therapy for Hepatocellular Carcinoma,” *Cancer Treatment Reviews* 98, no. 102221 (2021), https://doi.org/10.1016/j.ctrv.2021.102221.

141 Guoshuang Shen et al., “Anlotinib: A Novel Multi-Targeting Tyrosine Kinase Inhibitor in Clinical Development,” *Journal of Hematology & Oncology* 11, no. 120 (2018), https://jhoonline.biomedcentral.com/articles/10.1186/s13045-018-0664-7.

142 Suying Lu, “Safety and Feasibility of Anlotinib in Children with High Risk, Recurrent or Refractory Sarcomas: An Open-Label, Single-Centre, Single-Arm, Phase Ia/Ib Trial,” *eClinicalMedicine* 84, no. 103258 (2025), https://pmc.ncbi.nlm.nih.gov/articles/PMC12151220/.

143 Michael Barbato et al., “FDA Approval Summary: Repotrectinib for Locally Advanced or Metastatic ROS1-Positive Non-Small Cell Lung Cancer,” *Clinical Cancer Research* 30, no. 16 (2024): 3364-3370, https://pmc.ncbi.nlm.nih.gov/articles/PMC11326972/.

144 Qinghua Jiang et al., “Entrectinib, a New Multi-Target Inhibitor for Cancer Therapy,” *Biomedicine & Pharmacotherapy* 150 (2022), https://www.sciencedirect.com/science/article/pii/S0753332222003638#:~:text=Entrectinib%20is%20a%20selective%2C%20oral.

145 “Pediatric Oncology Drug Approvals,” U.S. Food & Drug Administration, accessed October 30, 2025, https://www.fda.gov/about-fda/oncology-center-excellence/pediatric-oncology-drug-approvals.

146 W. Du and J. Pogoriler, “Retinoblastoma Family Genes,” *Oncogene* 25 (2006): 5190–5200, https://www.nature.com/articles/1209651.

147 Junne Kamihara et al., “Update on Retinoblastoma Predisposition and Surveillance Recommendations for Children,” Clinical Cancer Research 31, no. 9 (2025): 1573-1579, https://aacrjournals.org/clincancerres/article/31/9/1573/761249/Update-on-Retinoblastoma-Predisposition-and.

148 Kirandeep Kaur and Bhupendra C. Patel, “Retinoblastoma,” StatPearls [Internet], National Library of Medicine, accessed December 5, 2025, https://www.ncbi.nlm.nih.gov/books/NBK545276/.

149 “V. Retinoblastoma: 5-Year Relative Survival Rates, 2015-2021,” NCCR*Explorer, National Cancer Institute, accessed December 5, 2025, https://nccrexplorer.ccdi.cancer.gov/application.html?site=500&data_type=4&graph_type=5&compareBy=age_range&chk_age_range_2=2&chk_age_range_3=3&chk_age_range_4=4&chk_age_range_5=5&chk_age_range_6=6&series=9&sex=1&race=1&advopt_precision=1&advopt_show_ci=on#resultsRegion1.

150 “United States Cancer Cases and Death Statistics At a Glance,” United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

151 Retinoblastoma,” StatPearls [Internet], National Library of Medicine, accessed March 5, 2026, https://www.ncbi.nlm.nih.gov/books/NBK545276/.

152 “Treatments for Intraocular Retinoblastoma,” Canadian Cancer Society, last medical review September 2025, https://cancer.ca/en/cancer-information/cancer-types/retinoblastoma/treatment/intraocular-retinoblastoma.

153 Chemotherapy for Retinoblastoma,” American Cancer Society, Date Accessed March 5, 2026, https://www.cancer.org/cancer/types/retinoblastoma/treating/chemotherapy.html.

154 “External Beam Radiation Therapy for Cancer,” National Cancer Institute, accessed December 5, 2025, https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy/external-beam#:~:text=It%20is%20a%20local%20treatment%2C%20which%20means,used%20to%20treat%20many%20types%20of%20cancer.

155 “Children’s Retinoblastoma Eye Cancer Treatment,” Memorial Sloan Kettering Cancer Center, accessed December 5, 2025, https://www.mskcc.org/pediatrics/cancer-care/types/retinoblastoma/treatment.

156 “Intra Arterial Chemotherapy for Retinoblastoma,” Children’s Hospital of Philadelphia, accessed December 5, 2025, https://www.chop.edu/treatments/intra-arterial-chemotherapy-iac-retinoblastoma#:~:text=What%20is%20intra%2Darterial%20chemotherapy,removal%20of%20the%20affected%20eye.

157 “Radioactive Plaque (Brachytherapy),” World Eye Cancer Hope, accessed December 5, 2025, https://wechope.org/retinoblastoma/care/treatment/radiation-therapy/radioactive-plaque/#:~:text=A%20radioactive%20plaque%20looks%20a,cells%20so%20they%20cannot%20divide.

158 “AACR Pediatric Cancer Progress Report,” American Association for Cancer Research, accessed March 5, 2026, https://cancerprogressreport.aacr.org/pediatric/pcpr25-contents/pcpr25-executive-summary/.

159 AACR Pediatric Cancer Progress Report,” American Association for Cancer Research, Accessed March 5, 2026, https://cancerprogressreport.aacr.org/pediatric/pcpr25-contents/pcpr25-executive-summary/.

160 “Neurofibromatosis Type 1 (NF1),” American Cancer Society, accessed December 5, 2025, https://www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes/neurofibromatosis-type-1.html.

161 “NF1 Associated with More Cancer Types Than Previously Known,” National Cancer Institute, accessed December 5, 2025, https://www.cancer.gov/news-events/cancer-currents-blog/2021/nf1-associated-with-more-cancer-types.

162 “Neurofibromatosis Type 2 (NF2),” Johns Hopkins Medicine, accessed December 5, 2025, https://www.hopkinsmedicine.org/health/conditions-and-diseases/neurofibromatosis/neurofibromatosis-type-2.

163 M.A. Akbarzadeh et al., “Mirdametinib Approval for Neurofibromatosis Type 1 with Inoperable Plexiform Neurofibromas: The Journey of Mek Inhibitors,” *ESMO Rare Cancers* 3 (2025), https://doi.org/10.1016/j.esmorc.2025.100015.

164 “Li-Fraumeni Syndrome (LFS),” American Cancer Society, accessed December 5, 2025, https://www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes/li-fraumeni-syndrome.html.

165 “Li-Fraumeni Syndrome,” MedlinePlus, accessed March 5, 2026, https://medlineplus.gov/genetics/condition/li-fraumeni-syndrome/.

166 “Li-Fraumeni Syndrome,” Children’s Hospital of Philadelphia, accessed December 5, 2025, https://www.chop.edu/conditions-diseases/li-fraumeni-syndrome#:~:text=References-,What%20is%20Li%2DFraumeni%20syndrome?,which%20tend%20to%20progress%20rapidly.

167 “Li-Fraumeni Syndrome,” Cleveland Clinic, accessed December 5, 2025, https://my.clevelandclinic.org/health/diseases/22073-li-fraumeni-syndrome.

168 “Beckwith–Wiedemann Syndrome (BWS),” American Cancer Society, accessed December 5, 2025, https://www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes/beckwith-wiedemann-syndrome.html.

169 Suzanne P MacFarland et al., “Diagnosis of Beckwith-Wiedemann Syndrome in Children Presenting with Wilms Tumor,” *Pediatric Blood Cancer* 65, no. 10 (2018), https://pmc.ncbi.nlm.nih.gov/articles/PMC6107414/.

170 “Beckwith–Wiedemann Syndrome,” Cleveland Clinic, accessed December 5, 2025, https://my.clevelandclinic.org/health/diseases/21993-beckwith-wiedemann-syndrome.

171 “Pediatric Oncology Drug Approvals,” U.S. Food and Drug Administration, accessed March 6, 2026, https://www.fda.gov/about-fda/oncology-center-excellence/pediatric-oncology-drug-approvals.

172 Mark N. Fluchel et al., “Geography and the Burden of Care in Pediatric Cancers,” Pediatric Blood & Cancer 61, no. 11 (2014): 1918–1924, https://doi.org/10.1002/pbc.25170.

173 “Survival at All Costs,” Family Reach, published August 2016, https://familyreach.org/wp-content/uploads/2016/08/16-FamilyReach-Survival-at-all-costs.pdf#:~:text=Rural%20parents%20required%20to%20travel%20more%20than,of%20 missed%20work%20in%20the%20first%20month.

174 Naveen Premnath et al., “Park the Parking,” JCO Oncology Practice 16, no. 5 (2020): 215–217, https://doi. org/10.1200/OP.20.00065.

175 “Incident Rates by State, Childhood,” State Cancer Profiles, accessed June 15, 2026, https://statecancerprofiles.cancer.gov/map/index.php?statefips=00&areatype=state&datagroup=1&statistic=515&datatype=01&race=00&sex=0&year=0#results.

176 “Death Rates by State, Childhood,” State Cancer Profiles, accessed June 15, 2026, https://statecancerprofiles.cancer.gov/map/index.php?statefips=00&areatype=state&datagroup=1&statistic=515&datatype=02&race=00&sex=0&year=0#results.

177 “COG Institution Locations,” Children’s Oncology Group, accessed September 4, 2025, https://www.childrensoncologygroup.org/apps/instmap/default.aspx.

178 “About Us,” Children’s Oncology Group, Accessed February 2026, https://childrensoncologygroup.org/about.

179 “History of Texas Children’s Global HOPE Program,” Texas Children’s, accessed September 8, 2025, https://www.texaschildrens.org/texas-childrens-global-health/programs/global-hope.

180 Arnold dela Cruz Paulino, MD, PhD, (Section Chief of Pediatric Radiation Oncology, University of Texas MD Anderson), Interview, June 2025.

181 Todd Burus et al., “Travel-Time Disparities in Access to Proton Beam Therapy for Cancer Treatment,” *JAMA Network Open* 7, no. 5 (2024), https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2818955.

182 Jennifer Maggiore (Executive Director, National Association of Proton Centers), Interview, July 2025.

183 “Find a Proton Therapy Center Near You,” The National Association for Proton Therapy, accessed September 9, 2025, https://proton-therapy.org/findacenter/.

184 Rebecca Gardner, MD, (St. Jude Children’s Research Hospital), Interview, June 26, 2025.

185 “Find a KYMRIAH Treatment Center,” Kymriah, accessed July 2025, https://us.kymriah.com/treatment-center-locator.

186 Justine M. Kahn et al., “An Investigation of Toxicities and Survival in Hispanic Children and Adolescents with ALL: Results From The Dana-Farber Cancer Institute ALL Consortium Protocol 05-001,” *Pediatric Blood Cancer* 65, no. 3 (2018), https://pubmed.ncbi.nlm.nih.gov/29090520/.

187 Paula Aristizabal, “Diverse Populations and Enrollment in Pediatric Cancer Clinical Trials: Challenges and Opportunities,” *Pediatric Blood Cancer* 67, no. 11 (2020), doi: 10.1002/pbc.28296.

188 Nadine J. Barrett et al., “Factors Associated with Biomedical Research Participation within Community-Based Samples Across 3 National Cancer Institute–Designated Cancer Centers,” *Cancer* 126, no. 5 (2020): 1077-1089, https://doi.org/10.1002/cncr.32487.

189 United States Cancer Cases and Death Statistics At a Glance,” United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

190 United States Cancer Cases and Death Statistics At a Glance,” United States Cancer Statistics: Data Visualizations, U.S. Centers for Disease Control and Prevention, accessed June 15, 2026, https://www.cdc.gov/cancer/dataviz.

191 “Guidance on Coordinating Care Provided by Out-Of-State Providers for Children with Medically Complex Conditions,” Medicaid.gov, published October 20, 2021, https://www.medicaid.gov/federal-policy-guidance/2021-10-20/126981.

192 "Medicaid and CHIP Eligibility Operations and Enrollment Snapshot," Medicaid.gov, accessed July 2025, https://www.medicaid.gov/resources-for-states/downloads/eligib-oper-and-enrol-snap-aprl2025.pdf.

193 Xu Ji et al., "Narrowing Insurance Disparities Among Children and Adolescents with Cancer Following the Affordable Care Act," *JNCI Cancer Spectrum* 6, no. 1 (2022), doi: 10.1093/jncics/pkac006.

194 "2024 Employer Health Benefits Survey," KFF, published October 9, 2024, https://www.kff.org/health-costs/2024-employer-health-benefits-survey/.

195 "Table I.F.19 Average Copayment (in dollars) for an Office Visit to a Specialist Physician per Employee Enrolled in a Health Insurance Plan That Had a Specialist Copayment at Private-Sector Establishments by Firm Size and Selected Characteristics: United States, 2019," Agency for Healthcare Research and Quality, https://meps.ahrq.gov/data_stats/summ_tables/insr/national/series_1/2019/tif19.htm.

196 James S. Miser et al., "The Health Care Utilization and Medical Costs in Long-Term Follow-Up of Children Diagnosed With Leukemia, Solid Tumor, or Brain Tumor: Population-Based Study Using the National Health Insurance Claims Data," JMIR Public Health and Surveillance 9 (2023), https://pmc.ncbi.nlm.nih.gov/articles/PMC10020904/.

197 Nicolas Iragorri et al., "The Out-of-Pocket Cost Burden of Cancer Care—A Systematic Literature Review," Current Oncology 28, no. 2 (2021): 1216-1248, doi: 10.3390/curroncol28020117.

198 Nancy Cruz Sitner, "How Socioeconomic Status Affects Diagnosis and Referral Pathways to HSCT," Oncology Nursing Society, published June 18, 2024, https://www.ons.org/publications-research/voice/news-views/06-2024/how-socioeconomic-status-affects-diagnosis-and.

199 Stergios Intzes et al., "Socioeconomic Status Is Globally a Prognostic Factor for Overall Survival of Multiple Myeloma Patients; Synthesis of Studies and Review of the Literature," *Mediterranean Journal of Hematology and Infectious Diseases* 13, no. 1 (2021), https://doi.org/10.4084/MJHID.2021.006.

200 Mark N. Fluchel et al., "Geography and the Burden of Care in Pediatric Cancers," *Pediatric Blood Cancer* 61, no. 11 (2014): 1918–1924, doi: 10.1002/pbc.25170.

201 Mallory F. Happ et al., "The Impact of Distance to Care on Unmet Nonmedical Costs Among Families of Children with Cancer," *Authorea* (2025), doi: 10.22541/au.175562133.30864810/v1.

202 Mark N. Fluchel et al., "Geography and the Burden of Care in Pediatric Cancers," *Pediatric Blood & Cancer* 61 (2014): 1918–1924, https://doi.org/10.1002/pbc.25170.

203 Jamie A. Weiner and Lisa K. Woodley, "An Integrative Review of Sibling Responses to Childhood Cancer," Journal of Child and Adolescent Psychiatric Nursing 31 (2018):109-119, doi: 10.1111/jcap.12219.

204 "Oncology (Cancer) / Hematologic Malignancies Approval Notifications," U.S. Food and Drug Administration, accessed December 10, 2025, https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancerhematologic-malignancies-approval-notifications.

205 "Pediatric Oncology Drug Approvals," U.S. Food and Drug Administration, accessed December 10, 2025, https://www.fda.gov/about-fda/oncology-center-excellence/pediatric-oncology-drug-approvals.

206 Dylan Neel et al., "Timing of First-in-Child Trials Of FDA-Approved Oncology Drugs," *European Journal of Cancer* 112 (2019): 49–56, https://doi.org/10.1016/j.ejca.2019.02.011.

207 Search results for older-adult studies recruiting in the United States, ClinicalTrials.gov, National Library of Medicine, accessed December 10, 2025, https://clinicaltrials.gov/search?aggFilters=ages:adult%20older,status:rec&locStr=United%20States&country=US.

208 Search results for child-age, recruiting studies in the United States, ClinicalTrails.gov, National Library of Medicine, accessed December 10, 2025, https://clinicaltrials.gov/search?aggFilters=ages:child,status:rec&locStr=United%20States&country=US.

209 Ian T. T. Liu and Aaron S. Kesselheim, "The RACE Act and Pediatric Trials of Adult Cancer Drugs," *Pediatrics* 154, no. 4 (2024), https://doi.org/10.1542/peds.2024-066920.

210 Anna Lee et al., "Nickel and Dimed: Parking Fees at NCI-Designated Cancer Centers," *Journal of Clinical Oncology* 38, no. 15_suppl (2020), https://doi.org/10.1200/JCO.2020.38.15_suppl.2029.

211 Anna Lee et al., “Nickel and Dimed: Parking Fees at NCI-Designated Cancer Centers,” *Journal of Clinical Oncology* 38, no. 15_suppl (2020), https://doi.org/10.1200/JCO.2020.38.15_suppl.2029.

212 D. Isabel Petrescu et al., “Preclinical Models for the Study of Pediatric Solid Tumors: Focus on Bone Sarcomas,” *Frontiers in Oncology* 14 (2024), https://doi.org/10.3389/fonc.2024.1388484.

213 “An Analysis of the National Cancer Institute’s Investment in Pediatric Cancer Research,” National Cancer Institute, published September 2013, https://www.cancer.gov/types/childhood-cancers/research/pediatric-analysis.pdf.

214 “NCI Budget Fact Book,” National Cancer Institute, accessed June 15, 2026, https://www.cancer.gov/about-nci/budget/fact-book.

215 “NCI Budget Fact Book,” National Cancer Institute, accessed June 15, 2026, https://www.cancer.gov/about-nci/budget/fact-book.

216 “Unlocking Cures for Pediatric Cancer with Artificial Intelligence [Executive order],” The White House, accessed December 10, 2025, https://www.whitehouse.gov/presidential-actions/2025/09/unlocking-cures-for-pediatric-cancer-with-artificial-intelligence/.

217 “H.R.3391 - Gabriella Miller Kids First Research Act 2.0,” Congress.gov, accessed December 10, 2025, https://www.congress.gov/bill/118th-congress/house-bill/3391.

218 “Pediatric Cancer Studies: Early Results of the Research to Accelerate Cures and Equity for Children Act,” U.S. Government Accountability Office, accessed December 10, 2025, https://www.gao.gov/products/gao-23-105947.

219 John Raffensperger, “Max Wilms and His Tumor,” *Journal of Pediatric Surgery* 50, no. 2 (2015): 356-359, https://pubmed.ncbi.nlm.nih.gov/25638637/.

220 “Wilms Tumor and Other Childhood Kidney Tumors Treatment (PDQ®) – Health Professional Version,” National Cancer Institute, accessed December 5, 2025, https://www.cancer.gov/types/kidney/hp/wilms-treatment-pdq#_551_toc.

221 Julia Evangelou Strait, “Scientists Reveal How Proteins Drive Growth of Multiple Cancer Types,” Washington University School of Medicine, accessed December 5, 2025, https://medicine.washu.edu/news/scientists-reveal-how-proteins-drive-growth-of-multiple-cancer-types/.

222 Magali Olivier et al., “TP53 Mutations in Human Cancers: Origins, Consequences, and Clinical Use,” *Cold Spring Harbor Perspectives in Biology* 2, no. 1 (2010), doi: 10.1101/cshperspect.a001008.

223 Xingui Liu and Alessio Ciulli, “Proximity-Based Modalities for Biology and Medicine,” *ACS Central Science* 9, no. 7 (2023): 1269–1284, https://doi.org/10.1021/acscentsci.3c00395.

224 Jihane Balla et al. “Antibody Conjugates in Neuroblastoma: A Step Forward in Precision Medicine,” *Frontiers in Oncology* 15 (2025), https://doi.org/10.3389/fonc.2025.1548524.

225 Pooja Hingorani et al., “Trastuzumab Deruxtecan, Antibody-Drug Conjugate Targeting HER2, Is Effective in Pediatric Malignancies: A Report by the Pediatric Preclinical Testing Consortium,” Molecular Cancer Therapeutics 21, no. 8 (2022): 1318-1325, doi: 10.1158/1535-7163.MCT-21-0758.

226 David A. Martínez-Gamboa et al, “CAR T-Cell Therapy Landscape in Pediatric, Adolescent and Young Adult Oncology – A Comprehensive Analysis of Clinical Trials,” *Critical Reviews in Oncology/Hematology* 209 (2025), https://doi.org/10.1016/j.critrevonc.2025.104648.

227 Pan, K., et al. CAR race to cancer immunotherapy: from CAR T, CAR NK to CAR macrophage therapy. J Exp Clin Cancer Res 41, 119 (2022). https://doi.org/10.1186/s13046-022-02327-z.

228 Loretta M. S. Lau et al., “Precision-Guided Treatment in High-Risk Pediatric Cancers,” *Nature Medicine* 30 (2024): 1913–1922, https://doi.org/10.1038/s41591-024-03044-0.

229 “Center for Precision Medicine for High-Risk Pediatric Cancer,” Children’s Hospital of Philadelphia, https://www.chop.edu/centers-programs/center-precision-medicine-high-risk-pediatric-cancer.

230 Marc W. H. Wijnen and Andrew M. Davidoff, “Minimally Invasive Techniques in Pediatric Surgical Oncology,” Surgical Oncology Clinics of North America 30, no. 2 (2021): 417–430, doi: 10.1016/j.soc.2020.11.008.

231 William W. Spurbeck et al., "Minimally Invasive Surgery in Pediatric Cancer Patients," *Annals of Surgical Oncology* 11 (2004): 340–343, https://doi.org/10.1245/aso.2004.04.021.

232 "Breakthroughs in Pediatric Oncology: Recent Advances in 2024," TFS HealthScience, accessed December 5, 2025, https://tfscro.com/resources/breakthroughs-in-pediatric-oncology-recent-advances-in-2024/#:~:text=Recent%20advances%20in%20pediatric%20oncology%20include%20the%20development%20of%20liquid,%2Dpass%20whole%2Dgenome%20sequencing.

233 Feifei Cheng et al., "Circulating Tumor DNA: A Promising Biomarker in the Liquid Biopsy of Cancer," *Oncotarget* 19, no. 7 (2016): 48832–48841, doi: 10.18632/oncotarget.9453.

234 "Breakthroughs in Pediatric Oncology: Recent Advances in 2024," TFS HealthScience, accessed December 5, 2025, https://tfscro.com/resources/breakthroughs-in-pediatric-oncology-recent-advances-in-2024/#:~:text=Recent%20advances%20in%20pediatric%20oncology%20include%20the%20development%20of%20liquid,%2Dpass%20whole%2Dgenome%20sequencing.

235 Bram De Wilde et al., "The Critical Role of Academic Clinical Trials in Pediatric Cancer Drug Approvals: Design, Conduct, and Fit for Purpose Data for Positive Regulatory Decisions," *Journal of Clinical Oncology* 40, no. 29 (2022), doi: 10.1200/JCO.22.00033.

236 Yimei Li et al., "Unlocking the Potential: A Systematic Review of Master Protocol in Pediatrics," *Therapeutic Innovation & Regulatory Science* 58, no. 4 (2024): 634–644, doi: 10.1007/s43441-024-00656-z.

237 Jingjing Ye et al., "A Bayesian Approach in Design and Analysis of Pediatric Cancer Clinical Trials," *Pharmaceutical Statistics* 19, no. 6 (2020): 814-826, doi: 10.1002/pst.2039.

238 Howard (Jack) West, "Novel Precision Medicine Trial Designs: Umbrellas and Baskets," *JAMA Oncology* 3, no. 3 (2017): 423, doi:10.1001/jamaoncol.2016.5299.

239 Bram De Wilde et al., "The Critical Role of Academic Clinical Trials in Pediatric Cancer Drug Approvals: Design, Conduct, and Fit for Purpose Data for Positive Regulatory Decisions," *Journal of Clinical Oncology* 40, no. 29 (2022), doi: 10.1200/JCO.22.00033.

240 "Unlocking Cures for Pediatric Cancer with Artificial Intelligence," The White House, accessed December 5, 2025, https://www.whitehouse.gov/presidential-actions/2025/09/unlocking-cures-for-pediatric-cancer-with-artificial-intelligence/.

241 "The Potential Role of Artificial Intelligence in Transforming Childhood Cancer Care," *eClinicalMedicine* 72 (2024), https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(24)00284-0/fulltext.

242 "Trends in Survivorship Grant Funding," National Cancer Institute, accessed December 5, 2025, https://cancercontrol.cancer.gov/ocs/funding/trends-survivorship-grant-funding.

243 "Childhood Cancer STAR (Survivorship, Treatment, Access, Research) Act (Public Law No. 115180) & STAR Reauthorization Act (Public Law No. 117350)," National Cancer Institute, accessed December 5, 2025, https://www.cancer.gov/about-nci/legislative/recent-public-laws/star-act.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