

Issue Overview

Cancer is the leading disease-related cause of death for children and adolescents aged 1-19. While cancer is much rarer in children than in adults, it has an enormous impact because it strikes so early in life. The high rate of late side effects in survivors of pediatric cancer can decrease life expectancy and impact quality of life for decades.¹ The American Cancer Society estimates that in 2026 in the U.S. there will be 9,680 new childhood cancer cases and 1,090 cancer deaths among children (ages 0-14). Among adolescents (ages 15-19), there will be an estimated 5,660 new cancer diagnoses and 730 cancer deaths.² By age 50, 96% of childhood cancer survivors had at least one grade 3-5 (severe, disabling, life-threatening, or fatal) chronic health condition.¹

Despite substantial advances in pediatric cancer research and clinical care over the past decades, important challenges remain. Continued progress will require both the development of more effective therapies and the reduction of short- and long-term adverse effects of existing therapies. Improving outcomes for children with cancer begins by recognizing that cancers that occur in children are not biologically the same as those experienced by adults. Children's bodies are physiologically unique which means that they may respond to treatments in ways that differ from adults. Sometimes these differences may only require altered dosing or formulations of adult drugs, but in most cases, pediatric cancers require unique therapeutic regimens.

While optimization of current therapies can improve outcomes, for many children with cancer, meaningful progress will require new drugs developed specifically for pediatric cancer. It is important to understand current statistics and context surrounding pediatric cancer and examine the research process that underlies the development of new therapies for children. Creating therapies for pediatric cancers involves unique scientific, logistical, economic, and regulatory challenges.³ By understanding these challenges, efforts to create better treatments for children with cancer will have more impact.

Key issues to consider in the pediatric cancer landscape include:

→ **Pediatric cancer statistics:** Although cancer is much rarer in children and adolescents than in adults, the impact of pediatric cancer is substantial because it strikes so early in life. In 2024, cancer deaths in pediatric patients between 0-19 years of age resulted in an estimated 122,600 years of life lost, or a reduced lifespan of an average of about 68 years per death.⁴ Among pediatric patients diagnosed with cancer in 2015–2021, the overall 5-year survival rate was 86%, up from less than 60% in the mid-1970s.⁵ Further, prognoses vary considerably depending on tumor subtype and other factors. For example, while 5-year survival rates among children with low-risk neuroblastoma exceed 95%, children with higher-risk disease need much more intense treatments and have a much lower survival rate of nearly 60%.^{6,7} Among the cancers with the poorest outcomes is diffuse intrinsic pontine glioma (DIPG), with fewer than 10% of children surviving even two years.⁸

- **Biology and preclinical research:** Pediatric cancer is unique biologically, and drugs developed to treat these cancers need to be tailored to the unique physiology of children and adolescents. Because children are still actively growing, treatments can cause side effects that may not occur in adults, or that may be more severe or debilitating in children. Examples of treatment-induced side effects include heart damage, deafness, infertility, or the development of subsequent cancers caused by treatments (e.g. radiation) for the initial cancer.^{9,10} As a result, 96% of survivors will have a severe or life-threatening chronic condition by age 50.¹
- **Clinical research:** Clinical trials are key to determining safety and efficacy of a drug or drug combinations, and often incorporate other treatment modalities such as surgery and radiation therapy. Although children's participation in cancer clinical trials is relatively common compared to adults with cancer, made possible in part through the National Cancer Institute's (NCI's) investment in the Children's Oncology Group network of trial sites, there are nonetheless unique issues when conducting clinical research with children. Trial designs and outcome measures need to be tailored to the specific biology of pediatric cancers and patients, as well as to the small population size of children with cancer.¹¹
- **Research funding and economic forces:** Public policies have created pediatric-specific incentives and requirements to drive more development of drugs for pediatric cancers, yet progress still lags behind that of adult cancers.¹² Research and drug development are expensive and require substantial financial resources to create the final products that result in improved outcomes for children. Private industry, the federal government, and philanthropies all fund cancer research, but they tend to fund different aspects of cancer research. A primary incentive for private investment in drug development is the potential to profit from an approved drug; however, the relatively small number of pediatric cancers means limited incentives for industry investment in treatments for children and adolescents with cancer. With reduced industry funding, federal and philanthropic funding have increased relevance in driving clinical development in pediatric cancer, but these sources cannot fully replace industry funding.
- **Data, data sharing, and artificial intelligence:** While clinical trials are a formalized way to collect data about how a treatment works under very controlled conditions, huge volumes of data are generated every day outside of clinical trials during the normal course of care. Given the relative rarity of pediatric cancer, and the difficulty of running clinical trials, there is great opportunity to leverage a wide array of data to generate research insights. Every patient's medical record has the potential to transform fragmented clinical and research observations into a trustworthy data ecosystem, while maintaining essential patient privacy and data protections. Advances such as those enabled by the Childhood STAR Act, the NCI's investment into the Childhood Cancer Data Initiative (CCDI) and the Advanced Research Agency for Health's investment in the Pediatric Care eXpansion (PCX) program have created a foundation for a data ecosystem.^{12,13,14} Built on that foundation, artificial intelligence (AI) can uncover meaningful patterns, reduce the burden of data-intensive research, test hypotheses, and return knowledge that benefits pediatric cancer patients and their families.
- **Regulatory landscape:** Before a drug can be approved in the U.S., the Food and Drug Administration (FDA) must review evidence submitted by the drug's manufacturer and conclude that the drug is safe and effective, and that its benefits outweigh its risks. While FDA does not conduct clinical trials leading to drug approval, the agency does work closely with drug sponsors, advising them as they design clinical trials so that the evidence collected during clinical trials is the right type, quality, and quantity for FDA to evaluate a drug. Further, FDA enforces regulatory requirements that require some adult cancer drugs to be tested for use as pediatric cancer treatments. These and other regulatory responsibilities are essential, but are time- and labor-intensive, so it is important to provide sufficient resources to researchers and regulators to regularly identify and adopt innovations in evidence generation and evaluation that can ensure that safe and effective therapies can reach pediatric patients in a timely manner.

Understanding the unique aspects of pediatric cancer and the associated research challenges can help guide efforts to overcome these barriers. The collective engagement of children, families, researchers, industry and government can make significant progress possible.

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