

# Conquering Childhood Cancer

by **Andrea Northup, Kunal Kothari, and David B. Kendall**

The war on cancer has failed our children. Since President Nixon's famous 1971 declaration of a national effort against all forms of cancer, the number of childhood cases diagnosed each year has risen steadily. Despite substantial advances in treatment, cancer remains the leading cause of death by disease among children. More children are being diagnosed with deadly cancers with each passing year, while cancer rates for adults have declined since their peak in 1992.<sup>1</sup>

Childhood cancer incidence overall has risen by 33 percent since Nixon's declaration; brain and other nervous-system cancers in young children have increased by over 50 percent; and the incidence of non-Hodgkin's lymphoma in teenagers has more than doubled.<sup>2</sup>

The prospects for the future are not good either. Scientists only began to take note of these trends in the late 1990s, and a decade later, researchers are stumped as to what is causing these sustained increases in childhood cancer incidence rates.<sup>3</sup> The disease is difficult to study because its causes are generally unknown and the possibilities present a complex puzzle.

The rising cancer rates are just one indicator of broader trends affecting children's

health. Autism rates in this decade are tenfold more than in previous decades,<sup>4</sup> and childhood obesity rates have tripled since the 1970s.<sup>5</sup> Many other child health problems are also worsening, including low birth weight, asthma, allergies, diabetes, and mental health disorders.<sup>6</sup>

While doctors have been increasingly successful in treating many childhood cancers, we lack a clear understanding of what lies at the root of these increases in disease rates. The causes are widely unknown because we are studying disease late in its course, in an uncoordinated fashion, and using surveillance that is incomplete or non-existent.

The nation needs a systematic effort to stop the rise in childhood diseases. A strategy

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focusing on childhood cancer could provide a template for fighting other diseases. Cancer's relatively high mortality rate, its rising incidence rates, and its scientific complexity make it an ideal candidate for such an initiative. The model used to uncover truths about the rises in childhood cancer incidence may illuminate approaches to other comparably serious diseases in children and adults.

The Progressive Policy Institute proposes that Congress adopt a strategy for conquering childhood diseases based on the following policies:

***1. Create a national health information network to provide accurate, real-time cancer data.***

The nation's premier cancer database covers only one-fourth of the population.<sup>7</sup> Personal electronic health-record accounts would enable monitoring of disease incidence in real time across the entire population. Each American should have a secure and private electronic record for all of his or her medical information. Patients or their parents could authorize scientists to conduct approved studies and public-health surveillance programs to view their records without divulging their identity or releasing their records to a government database. Independent Health Record Trusts would issue and maintain such accounts, as Reps. Dennis Moore (D-Kan.) and Paul Ryan (R-Wisc.) have proposed.<sup>8</sup>

***2. Fund the National Children's Study and the International Children's Cancer Cohort Consortium.***

These studies would carefully follow the health of thousands of individuals from before birth to age 21. They will help identify the

causes of childhood health problems. The Bush administration has opposed funding for the study and tried to end it before it got underway. Fortunately, Congress started funding the study last year, but funding is at risk again this year due to White House opposition.

***3. Create an American Center for Cures within the National Institutes of Health (NIH) that would develop a national strategy for cures; coordinate and accelerate breakthrough research; and speed adoption of new treatment protocols.***

Congress can and should apply this same strategy to other major childhood diseases such as autism and immune-related disorders such Type 1 diabetes, asthma, and food allergies. A joint effort would draw support from the hundreds of thousands of families struggling with these debilitating and life-threatening diseases.

## **Children's Health is Declining**

Health indices demonstrate that pediatric cancer incidence (the number of children diagnosed with cancer each given year) is on the rise. In 1975, 11.5 childhood cancer cases were diagnosed per 100,000 U.S. children, and the count rose to 14.6 per 100,000 in 2002.<sup>9</sup> Scientists determined that children are contracting these serious diseases at higher rates than ever before, but do not know why.

The deeper one looks into the childhood cancer statistics, the more confusing they become. Children contract cancers at different rates depending on the type of cancer, and on the child's age, gender, race/ethnicity, geographic location, and socioeconomic status.<sup>10</sup> For example, a

recent British study showed that wealthier children and those living in rural areas are more likely to develop cancer than their counterparts in more crowded urban areas.<sup>11</sup>

Each of these patterns may reflect a complex set of possible factors in the causes of childhood cancer.<sup>12</sup> For example, the British study raises a question about the source of cancer: Do rural and wealthier children develop cancer from local environmental circumstances because they are not exposed to hazards that bolster immunity, or do they develop it from viruses that migrate to rural populations from urban populations that have built up resistance to the virus?<sup>13</sup>

Faced with the variations in cancer incidence rates, scientists realize that different types of cancer can be caused by a number of complex factors. Familial and genetic factors have been implicated in 5 percent to 15 percent of childhood cancers.<sup>14</sup> Chromosomal mutations such as Down syndrome and certain viral infections such as HIV/AIDS have been shown to elevate a child's risk. There is a growing list of potentially carcinogenic environmental factors, which are studied repeatedly but without definitive outcomes. These include air pollution, radiation, maternal smoking, parental occupational exposures, diet, and many others. Most likely, a combination of all of these factors (and other unknown risks) is causing cancer incidence rates to rise among kids. If we want to stop the rises in cancer incidence, we must get at the root of the problem.

### **Children Get Better Treatments, But Prevention Falls Short**

We have won a few battles in the war on cancer. Both children and adults benefit from advancements in life-prolonging cancer treatments. Survival rates in children have increased by 20 percent in boys and 13

percent in girls since the late 1970s.<sup>15</sup> As a nation, we spend an estimated \$72.1 billion on cures, surgical techniques, chemotherapy treatments, and radiation therapies that will continue to prolong the lives of cancer patients.<sup>16</sup>

Yet while we devote a great amount of resources to extending lives, our nation's youth are contracting serious cancers and other childhood diseases at astonishing rates. Although it is natural and right to respond to the suffering of a child who has developed cancer, we must do more to understand the causes and develop strategies to prevent cancers' occurrence in children in the first place. We have had some success in developing cures. Now we need equally monumental gains in defining cancer's causes and reducing incidence rates.

Uncovering the environmental, social, and cultural factors that trigger the disease would reduce the number of children who suffer from cancer—and from its grueling treatments, which bring devastating side effects such as severe nausea, vomiting, anemia, and infections. Children who survive these treatments have other health problems to worry about as a result. They are at higher risk for developing heart disease, secondary cancers, cognitive defects, and other chronic conditions, and little is known about the long-term treatment effects. Treatments, of course, do not stop children from acquiring the disease in the first place. We must stop cancer before it starts by looking at its causes.

### **Focusing on Childhood Cancers**

The resilience of these children—and of their families—is profoundly inspiring. Their struggles represent the most compelling incentive for stepping up the fight against cancer and other diseases that are increasingly affecting the lives of our children. Yet there are other sound reasons why investigating childhood disease trends must become a national priority.

When compared to adults, children may be disproportionately affected by adverse environmental conditions that cause disease.<sup>17</sup> Children grow, metabolize, and develop rapidly, putting their organ systems at risk of damage. Therefore they are at higher risk for developing cancer and other diseases associated with environmental exposures than adults. We must not continue to treat them as “little adults”; rather, we must systematically devote more resources to understanding children’s increased sensitivity to cancer and other diseases connected to the environment.

Adults are not immune to the rise in cancer incidence. Cancer death rates for adults are almost uniformly on the decline, but the occurrence of a few serious cancers has increased over the past 20 years.<sup>18</sup> Lung cancer in females, non-Hodgkin’s lymphoma, and melanoma are all on the rise.<sup>19</sup> We know little about what causes these trends in adults. While the types of cancers rising among adults are not necessarily the same as those affecting children, redefining our cancer research strategy can have implications for more productive study of cancers for all age groups and populations. Developing an integrated childhood cancer research strategy could lay the groundwork for effective study of other serious diseases affecting both children and adults.

Some scientists argue that the rising rates of cancer in children may not be real. They claim that new diagnostic technologies, changes in disease-reporting requirements, or updated disease definitions may create a false impression that childhood cancers are on the rise. However, the fact remains that most childhood cancers and other serious childhood conditions have been steadily increasing for the past 30 years—and that this increase has occurred among a broad range of nations, age groups, and cancer types. This well-documented phenomenon cannot be attributed to mere speculation.

Many respected medical professionals believe the increase is real, and that we must take steps to reverse it.<sup>20</sup> The fact that cancer studies can be contradictory and empirically weak only fuels the need for a more definitive childhood-cancer strategy.

## The Cancer Challenge

Why is the scientific community not further along in this quest to understand the diseases that are affecting our nation’s youth? Features of childhood cancer make it difficult to study, even by some of the smartest scientists in the most expensive health-care system in the world. These stem from the complexity of the disease, the epidemiological barriers to study, the lack of directed research efforts, and an inadequate cancer-surveillance system.

***Cancer is a disease that is inherently difficult to understand.*** All diseases have their inherent complexities, but childhood cancer is especially challenging. Each cancer type differs with respect to its effects on the body, its target age groups, and its biological characteristics. Each unique feature hints at different combinations of factors that may elevate one’s risk of contracting the disease.

With cancer, researchers must consider how genes can put one at risk, in addition to how one’s social, cultural, behavioral, geographic environments interact to cause cancer. The extent to which each factor contributes to cancer development is widely variable and unknown. There exists the possibility for risk analysis from a number of levels. Scientists can look as wide as the social environment (such the availability of fast food) all the way down to viral interactions that might cause cancerous cells to proliferate. Researchers want to cover all the bases, but

studies that attempt to look at a broad array of possible exposures become large, expensive, complicated, and statistically ineffective.

***Cancer poses epidemiological challenges.*** The primary goal of scientists trying to find out what causes a disease is to determine its risk factors. Risk factors are variables associated with people who have a certain disease; for example, a common risk factor for lung cancer is smoking. Once a variable is said to be “associated with” a disease, scientists must prove that it is actually this variable that causes the disease to occur and not merely a characteristic of those who might get the disease for a different reason.

Two major types of epidemiological studies are used to evaluate the links between an exposure (such as a mother receiving a radiograph during pregnancy) and disease outcome (such as a child developing leukemia). “Cohort” studies follow a population at risk over time in order to detect who contracts the disease of interest and who does not. By contrast, “case-control” studies look at differences in exposures of those who already have the disease (cases) and similar study participants who do not (controls). By comparing the disease rates in the exposed versus the unexposed, scientists can determine which exposures put individuals at increased risk for contracting a disease.

Every major pediatric cancer study conducted over the past few decades has been of the case-control design. This is because while childhood cancers are on the rise, they are quite rare in the population at large. A cohort study would require following millions of children over a number of years to assure enough cancer cases to study with statistical significance.<sup>21</sup> Policymakers and scientists have dismissed this option as expensive and infeasible. Instead, public-health policymakers have created a cycle of

enforcing weak hypotheses with weak scientific evidence from case-control studies.<sup>22</sup>

Case-control studies are not effective in childhood cancer research for a number of reasons:<sup>23</sup>

- ❑ Parents of children with cancer may offer faulty information out of emotional stress, guilt, or efforts to attribute their child’s cancer to something concrete;
- ❑ Cancer latency periods (the time between acquiring a disease and actually seeing symptoms) may extend the duration between an exposure and outcome. It is difficult for parents to remember conditions as they were before their child’s cancer diagnosis;
- ❑ Control populations typically underrepresent ethnic minorities and families of low socioeconomic status because they are less likely to participate in such studies;
- ❑ Scientists looking backward in time cannot collect biological specimens or physical exposure data (e.g., air quality measurements) exactly at the time when they affected the patients; and
- ❑ It is difficult to find control populations that are similar to cancer patients in all other respects besides their disease.

Cohort studies that follow healthy individuals over time to see who develops cancer during childhood are more conclusive. They are not subject to the biases that result from retrospective exposure recall and grouping by disease status. Instead, cohort studies have a broad and diverse participant base, and they collect more accurate exposure data using real-time

measurements supplemented by interviews and questionnaires.

***Cancer researchers focus on narrow specialties instead of collaborating to cover a more effective cross section of research areas.*** With such an inherently complex disease, researchers tend to become specialized to the extent that their findings are incomprehensible to fellow researchers, let alone to the general public. There is little communication across areas of expertise, and this fragmentation hinders progress. This must be remedied if we are to have any chance of stabilizing our nation's escalating childhood cancer incidence rates.

***Cancer surveillance in the United States is incapable of providing real-time, systematic, reliable cancer data.*** The United States lacks the infrastructure for a national insurance system, birth registry, population roster, or health-information database that would provide scientists with the cancer information necessary to effectively study it.<sup>24</sup> The cancer registries that exist provide outdated, unreliable, and incomplete information.<sup>25</sup> Time lags between the occurrence and discovery of childhood cancer trends have complicated research efforts to understand the disease. Developing a more proactive system will depend on real-time surveillance. Our nation's youth (as well as our medical budget) would directly benefit from such a prevention-oriented approach.

### **Solutions: Monitor, Analyze, and Cure**

It is the responsibility of public policymakers across the nation to provide the direction and funding necessary to understand and reverse childhood cancer trends. Efforts must be refocused on surveillance, causes, and cures of childhood cancers as follows:

#### ***1. Create a national health information network to provide accurate, real-time cancer data.***

Scientists could more effectively study the rapid increases in pediatric cancers and other childhood diseases if they knew when and where they were occurring in real time. Opportunities to prevent and cure diseases are not realized, because patients' health-care records are not digitized and available for instant analysis by researchers.

As PPI proposed in the paper entitled "Building a Health Information Network," Congress should set a strategy for health-information networks that would, among other purposes, enable monitoring of the outbreak of disease in real time.<sup>26</sup> Each American should have a secure and private electronic record of all of his or her medical information. Patients could authorize scientists to view their records without divulging their identity or releasing their records to a government database. Independent Health Record Trusts would issue and maintain such accounts, as Reps. Moore and Ryan proposed.<sup>27</sup>

Widespread use of electronic health records would enable researchers to monitor which diseases are on the rise and would equip the federal government to quickly allocate resources to areas deserving immediate attention.<sup>28</sup> The federal government would also have a more accurate picture of the nation's overall health status and could use that information to allocate funds for research, prevention, and cure.<sup>29</sup>

#### ***2. Fund the National Children's Study and the International Children's Cancer Cohort Consortium.***

The multitude of small case-control studies have not been sufficient to discover what

lies beneath the rising trends in childhood cancers. We cannot improve this situation by adding to the mediocre evidence using similar studies of the same design.

We must fund and support larger cohort studies with the capacity to discover what underlies the rises in cancer incidence. The National Children's Study is one such effort. It is the largest and most comprehensive children's cohort study ever, following more than 100,000 participants from across the United States from before birth to age 21. Scientists will investigate the potential impacts of environmental, genetic, and behavioral influences on a variety of childhood conditions such as low birth weight, asthma, obesity, heart disease, and other disorders.

Cancer is not on the list of diseases that the study will examine. Because cancer is such a unique and complex disease, even a study of this magnitude will not be able to detect meaningful causal relationships between potential exposures and cancer outcomes.<sup>30</sup>

This is why coordinators of the National Children's Study established the International Childhood Cancer Cohort Consortium (I4C). The I4C would bring together questionnaire data and biological samples taken from all of the large children's cohort studies in existence and in preparation around the world, of which the National Children's Study is one.<sup>31</sup> The study will be a true international effort to understand the root causes of childhood cancer, including at least 11 studies representing four continents and more than 700,000 children.<sup>32</sup> Investigators will pool the measurements of exposures such as diet, growth rates, chemicals, and parental smoking from across the various cohorts for analysis to determine which exposures cause cancer.

An international cancer cohort would prompt other childhood cohorts to form and join, laying the foundation for the study of other rare but serious diseases. Scientists will have the opportunity to look across

generations, racial and ethnic lines, and genetically and socioeconomically diverse populations in order to understand what causes cancer and other serious childhood diseases.<sup>33</sup>

A notable feature of the I4C is its exclusive focus on childhood leukemia, the most frequently occurring cancer in children. By narrowing the scope of the study to examine a single cancer type, researchers can examine exposures and outcomes specifically and therefore get more targeted and meaningful results. A successful method for determining root causes could then extend to other childhood cancers and diseases. Preliminary research on childhood leukemia suggests certain exposures that may lead to elevated risk for the disease, and a study of this magnitude has the potential to find conclusive results.<sup>34</sup>

Unfortunately, the National Children's Study and its larger I4C cousin are in jeopardy. Last year, Congress appropriated \$111 million to support the study over White House objections. President Bush's 2009 budget again proposes to end all appropriations for the study. At current funding levels, results could be published as early as 2013,<sup>35</sup> but only if Congress again prevails over the president's opposition to the study.

The I4C is dependent on funding from all of its cohorts. The United States is in a unique position to take an international leadership role with respect to both the continued financial and organizational support crucial to the project's success. The White House is missing a critical opportunity to prioritize the I4C as a key step in the fight against childhood cancer.

### ***3. Create an American Center for Cures.***

While we must work toward understanding the root causes of childhood cancer, we must not underemphasize the importance of finding effective cures.

Prevention never works 100 percent of the time, so we must assure that cures are available to effectively treat children with cancer.

The federal government should establish an evidence-based strategy for research and development on cancer treatments based on the causal mechanisms detected through high-quality cancer surveillance systems and well-designed cohort studies. In order to coordinate these efforts, Congress should establish an American Center for Cures within the NIH. Such a center would develop and advance a national strategy for accelerating the discovery, development, and delivery of cures for a range of diseases, including childhood cancer.

Currently, we are not getting enough value for our research dollar. All too frequently, funding for the discovery of cancer treatments is allocated haphazardly to increasingly specialized and uncoordinated researchers. Scientists pursue independent research in highly particularized areas and therefore do not necessarily see the most likely pathways to cures. A national cure center would draw on public and private resources to create multi-disciplinary teams to foster greater collaboration, prevent overlap, and share information across research specialty areas.

The Conquer Childhood Cancer Act, introduced by Sen. Jack Reed (D-R.I.) and Rep. Deborah Pryce (R-Ohio) and enacted in July 2008, recognizes that increased pediatric cancer funding is needed. The act authorizes \$150 million over a five-year period to expand research programs. But in doing so, Congress has simply extended funding toward further fragmented, individual research rather than coordinated efforts toward specific goals. These funds should now be put to better use under the NIH Cure Center where teams of professionals in various disciplines would create strategic plans to develop and deliver cures.

## **Conclusion**

Many Americans do not realize the gravity of the situation playing out in families across the United States. More and more children are being diagnosed with serious illnesses, including cancers, in spite of our advancements in curing these very diseases among children and adults. So far, there has been no actionable explanation for these trends, but with a greater understanding of what causes cancer and other lethal illnesses, we can more effectively develop cures. If we are to win the war on cancer, the time to act is now.

## Endnotes

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