

Novel statistical method captures long-term health burden of pediatric cancer cures

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Senior author Leslie Robison, Ph.D., chair of the St. Jude Department of Epidemiology and Cancer Control, with first and corresponding author Nickhill Bhakta, M.D., a St. Jude hematology-oncology fellow. Credit: St. Jude Children's Research Hospital / Seth Dixon

Using a statistical method developed at St. Jude Children's Research



Hospital, investigators found that survivors of pediatric Hodgkin lymphoma not only have more cardiovascular conditions than adults who did not have cancer in childhood, but the problems are more severe. The research, which appears today in the journal *The Lancet Oncology*, should aid efforts to reduce and better manage the late effects of cancer treatment.

Researchers created a measurement called "cumulative burden" to better capture the distribution and magnitude of chronic disease in childhood cancer survivors. The metric showed that by age 50 Hodgkin lymphoma survivors had more than twice as many cardiovascular problems than adults who had not had cancer as children. The survivors were also five times more likely to have severe, life-threatening or fatal heart conditions.

"With cure rates for pediatric cancer at historic highs, the question becomes what is the legacy of that cure? We are doing a better job of keeping patients alive, but are we doing a better job at addressing the chronic diseases that are sometimes the price of that cure," asked first and corresponding author Nickhill Bhakta, M.D., a St. Jude hematology-oncology fellow. "Cumulative burden is a new tool for studying chronic illness in childhood cancer survivors or any patient population with significant morbidity, such as diabetes or HIV/AIDS."

Unlike currently used statistical methods that count health conditions once at diagnosis, cumulative burden tracks individuals' multiple, recurring treatment-related health conditions. Cumulative burden should help researchers refine health screening guidelines for survivors and design clinical trials aimed at maintaining high cure rates while reducing the late effects of treatment. Pediatric Hodgkin lymphoma patients are among the possible beneficiaries. Newly identified Hodgkin lymphoma patients enjoy a cure rate of more than 80 percent, but the chest radiation and chemotherapy drugs called anthracyclines used in the cures



leave the survivors at an increased risk for multiple, life-long cardiovascular problems and premature death.

This study focused on calculating the cumulative burden of cardiovascular disease in 670 pediatric Hodgkin lymphoma survivors based on a detailed health analysis of 348 individuals enrolled in the St. Jude Lifetime Cohort Study (St. Jude LIFE). The survivors were at least 18 years old and had survived at least 10 years beyond their cancer diagnoses. St. Jude LIFE brings survivors back to the hospital for a battery of tests to evaluate health, functioning and other factors with the goal of improving the lives of current and future pediatric cancer survivors.

The St. Jude LIFE participants had been assessed for 22 chronic cardiovascular conditions, including heart attacks, hypertension, arrhythmias and structural heart defects. Researchers used those and other clinical findings to calculate the cumulative burden by tracking the incidence and severity of cardiovascular disease. Investigators also determined the cumulative burden for a comparison group of 272 St. Jude LIFE community volunteers who underwent the same health assessments. The community volunteers were similar in age and gender to the survivors, but had no history of childhood cancer.

The analysis showed that the cumulative burden of cardiovascular disease, including severe and life-threatening conditions, was greater among survivors at 30 and 50 years of age than among the comparison group. In fact, the cumulative burden of the most serious heart problems, including heart attacks, was similar for 30-year-old survivors and 50-year-old community volunteers.

While severe, chronic heart conditions became more common with age in both groups, researchers reported that serious problems accumulated more rapidly in survivors. "Survivors tended to have more severe disease



across the lifespan and likely need an individualized screening and treatment plan," Bhakta said.

The results also highlighted trade-offs to consider in designing future clinical trials, he said. For example, researchers found that reducing the dose of anthracyclines will lower the rate, but not the severity of cardiovascular disease in pediatric and young adult Hodgkin lymphoma survivors. In contrast, lowering the heart radiation dose will not significantly lower the rate of <u>cardiovascular disease</u>, but it will reduce the severity. "Cumulative burden provides us with a global view of tradeoffs between different treatment late effects that must be considered when designing new interventions," Bhakta said.

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