Evidence from the Childhood Cancer Survivor Study (CCSS) suggests that changes in childhood cancer treatment and follow-up care have reduced deaths from the late effects of cancer treatment and extended the lives of childhood cancer survivors. St. Jude Children's Research Hospital investigators led the research, which appears today online ahead of print in the *New England Journal of Medicine*.

The study involved 34,033 childhood cancer survivors whose cancers were diagnosed and treated between 1970 and 1999 when they were ages 20 and younger. All lived at least five years after their cancers were discovered and were considered long-term survivors. The analysis showed that the 15-year death rate among these survivors has decreased steadily since 1970 due in part to a reduction in deaths from the late effects of cancer treatment.

The declines coincided with changes in pediatric cancer therapy and follow-up care. The changes included reductions in the use and dose of radiation therapy and chemotherapy drugs called anthracyclines for treatment of acute lymphoblastic leukemia (ALL), Hodgkin lymphoma and Wilms tumor, a cancer of the kidneys. The therapies leave survivors at increased risk for developing second cancers, heart failure and other serious health problems.

"This study is the first to show that younger survivors from more recent
treatment eras are less likely to die from the late effects of cancer treatment and more likely to enjoy longer lives," said the study's first and corresponding author Greg Armstrong, M.D., an associate member of the Department of Epidemiology and Cancer Control and CCSS principal investigator. "The results are a testament to the physicians and scientists who in the past 30 years took a calculated risk of developing new protocols that used less intense therapies that reduced the risk of late effects and maintained excellent five-year survival.

"For CCSS, the next question is what is the quality of life and health that childhood cancer survivors enjoy during their extended life span," he said.

Between 1970-74 and 1990-94, the 15-year death rate for survivors in this study fell from 12.4 percent to 6 percent. During the same period, deaths from the late effects of treatment decreased from 3.5 percent to 2.1 percent due to declining death rates from second cancers, lung or heart problems.

Survivors have benefited from better follow-up care, including risk-based health screening guidelines, Armstrong said. "For survivors at risk of breast cancer due to chest radiation or heart problems because of treatment with anthracyclines, screening tests like mammograms and echocardiograms that result in early detection of late effects of cancer therapy may make a lifesaving difference," Armstrong said.

The biggest beneficiaries of evolving therapy were young patients diagnosed with standard-risk ALL, Hodgkin lymphoma or Wilms tumor as their primary cancer. Together, the cancers account for about 30 percent of the estimated 15,780 cases of pediatric cancers diagnosed annually in the U.S. Five-year survival for pediatric patients with these cancers is now 90 percent or better, according to the American Cancer Society.
Deaths due to heart disease decreased for survivors of ALL, Hodgkin lymphoma and Wilms tumors. Deaths from second cancers declined in survivors of Wilms tumors. These patients were also less likely to be treated with radiation therapy or anthracyclines.

Between the 1970s and the 1990s, the percentage of ALL survivors in this study treated by brain irradiation decreased from 86 percent to 22 percent. In 2009, St. Jude published evidence that pediatric ALL is curable without brain irradiation, and the hospital no longer uses radiation for treatment of ALL. Today, 94 percent of new St. Jude ALL patients are alive five years later.

The percentage of Hodgkin lymphoma and Wilms tumor patients treated with radiation fell from 96 to 77 percent and 77 to 49 percent, respectively. During the same period, the average cumulative anthracycline dose also declined for study participants with those cancers.

Armstrong said treatment late effects continue to take a toll, particularly on survivors of childhood cancers where five-year survival rates have lagged and treatment intensity has increased.

Provided by St. Jude Children's Research Hospital


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