

## Childhood leukemia survivors struggle with long-term comorbidities

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Survival rates of childhood cancers, especially leukemia, have improved greatly in the past three decades, but survivors of this disease still seem to face many health and lifestyle challenges as young adults. Depending on the extent of their disease and treatment methods, many continue to struggle with one or more life-long medical conditions and decreased quality of life, according to a study prepublished online in *Blood*, the official journal of the American Society of Hematology.

Acute lymphoblastic leukemia (ALL) is the most common childhood leukemia and childhood cancer overall, accounting for about one-fourth of all pediatric cancers. Each year about 3,000 new cases are diagnosed in the U.S., though recently the cure rate has improved and the estimated five-year survival rate is now greater than 80 percent. While therapies for the disease are generally very effective, previous studies have shown that survivors still face challenges with ongoing chronic health conditions and overall quality of life.

The population evaluated in this study was part of the Childhood Cancer Survivor Study (CCSS), a National Cancer Institute (NCI) funded, multi-institutional cohort, the largest comprehensive research cohort of long-term childhood cancer survivors. Of the 5,778 ALL survivors in the cohort, 4,151 (86 percent) completed questionnaires to evaluate rates of comorbidities, multiple chronic conditions, and other health markers, as well as lifestyle factors including marriage, education, employment, and health insurance coverage. For comparison, the study also evaluated the survivors' siblings with similar questionnaires.



In addition to self-reported effects up to 25 years post-diagnosis, the study also assessed the treatment regimens and disease relapse to understand how these factors might have long-term effects on survivors' quality of life. Specifically, the team compared patients who had received radiation therapy (RT) as part of their ALL therapy regimen (62 percent) with those who did not, as well as with those with or without recurrences within the first five years after original diagnosis.

"Children diagnosed with ALL are exposed to significant therapeutic intervention very early in their lives," said Dr. Rajen Mody, of the Department of Pediatrics, University of Michigan, and lead author of the study. "Looking at such a large cohort of long-term survivors, we sought to understand the real latent effects of aggressive cancer treatments and what specific factors could affect various health outcomes and quality of life by adulthood."

The analysis found that for the five-year ALL survivors, the survival at 25 years was 87 percent, and treatment method as well as relapse status seemed to affect survival. Survivors treated with RT had an overall survival of 87 percent compared with 96 percent for those without RT, and overall survival in those who relapsed within the first five years after diagnosis was just 63 percent compared with 93 percent for those who did not relapse early.

With regard to related health conditions, at least half of survivors reported one or more chronic medical conditions (cumulative incidence of 65 percent), compared with only 38 percent of their siblings. Importantly, survivors were 3.7 times more likely to have a severe or life-threatening medical condition and 2.8 times more likely to suffer from multiple chronic conditions than their siblings. These most often included musculoskeletal, cardiac, and neurological conditions. Significantly more survivors experienced poorer health, mental health problems, activity limitations, and functional impairment as compared



with their siblings.

Again, RT and relapse status affected survivors' risk of chronic disease; patients with RT or an early relapse experienced higher rates of chronic or life-threatening conditions than non-RT, non-relapsed survivors. For example, the cumulative incidence of severe, life-threatening chronic conditions was 23 percent for RT survivors, compared with just 13 percent for non-RT survivors.

Survivors' social and economic outcomes, including rates of marriage, college graduation, and health insurance coverage, were also significantly lower than those of their siblings. Both female and male survivors were more likely to be unemployed than their siblings, though only in the females were the differences statistically significant. Most socioeconomic factors were not affected by relapse status, with the exception of male employment rates. However, RT seemed to affect these outcomes, as female RT survivors reported significantly lower rates of marriage, college graduation, and health insurance coverage than non-RT female survivors. Male RT survivors also reported lower rates of education attainment compared with non-RT survivors.

"Our findings suggest that the vast majority of the children with ALL who survive five years from the time of diagnosis are likely to be long-term survivors. Survivors treated without radiation therapy who did not relapse appear to have health outcomes and quality of life similar to the general population. However, survivors who have suffered a relapse of the disease or who have been treated with radiation therapy continue to fight with excess comorbidities and poor socioeconomic outcomes for many years following therapy, and it is important that we educate the patients, families, and their physicians about these long-term issues," said Dr. Mody. "As therapeutic interventions improve and more children beat leukemia, it's important to work toward not only higher survival rates, but also improved overall wellness."



Source: American Society of Hematology

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