

Childhood cancer survivors face higher death risk 25 years later, from cancer, circulatory diseases

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Follow-up of a group of British childhood cancer survivors indicates they have an increased risk of death from second primary cancers and cardiac and cerebrovascular causes more than 25 years after their initial cancer diagnosis, according to a study in the July 14 issue of *JAMA*.

"Over recent decades survival from childhood cancer has improved dramatically, yet [mortality rates](#) in [childhood cancer survivors](#) continue to be elevated for many years beyond 5-year survival compared with the general population," the authors write. "Although studies have shown that the risk of death from recurrence decreases with increasing time since 5-year survival, uncertainty about the long-term risks of death from other causes remains. Investigations into long-term cause-specific mortality are important because any excess mortality may be related to long-term complications of treatment." It is also uncertain if increased mortality risks persist beyond 25 years from initial cancer diagnosis.

Raoul C. Reulen, Ph.D., of the University of Birmingham, England, and colleagues examined long-term cause-specific mortality among 17,981 5-year survivors of childhood cancer, who were diagnosed with cancer before age 15 years between 1940 and 1991 in Britain and followed up until the end of 2006.

Overall, there were 3,049 deaths during the study period. Survivors experienced 11 times the number of deaths expected from the general

population (standardized mortality ratio [SMR], 10.7). The SMR declined with follow-up but was still 3-fold higher than expected 45 years from diagnosis.

The absolute excess risk (AER) for deaths from recurrence declined from diagnosis at age 5 to 14 years to beyond 45 years from diagnosis. In contrast, during the same periods of follow-up, the AER for deaths from second primary cancers and circulatory disease (such as from cardiac and cerebrovascular deaths) increased, with survivors after 45 years experiencing 3.6 times the number of deaths expected from the general population for a second primary cancer, and nearly 26 percent of all excess deaths beyond 45 years from diagnosis attributed to circulatory disease. "Beyond 45 years from diagnosis, recurrence accounted for 7 percent of the excess number of deaths observed while second primary cancers and circulatory deaths together accounted for 77 percent," the authors write.

The researchers add that the excess mortality due to second primary cancer and circulatory disease is likely attributable to late complications of treatment. "Second primary cancers are a recognized late complication of childhood cancer, largely due to exposure to radiation during treatment, but specific cytotoxic [toxic to cells] drugs also have been implicated in the development of second primary cancers."

"These findings confirm the importance of very long-term outcome data and that survivors should be able to access health care programs even decades after treatment. Finally, the principal clinical message from these data is straightforward; 77 percent of the excess number of deaths observed among those surviving beyond 45 years from diagnosis of childhood [cancer](#) in Britain are due to second primary cancers and circulatory deaths. Finding ways to successfully intervene to reduce these potentially preventable premature deaths will be complex," the authors conclude.

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