

Healthy lifestyle associated with reduced mortality risk in childhood cancer survivors

April 6 2023



(L to R) Co-author Yutaka Yasui, Ph.D., and senior author Greg Armstrong, M.D., M.S.C.E., both of St. Jude Department of Epidemiology and Cancer Control, and first and corresponding author Stephanie Dixon, M.D., M.D., MPH, St. Jude Department of Oncology. Credit: St. Jude Children's Research Hospital

A report from the Childhood Cancer Survivor Study (CCSS) provides

strong evidence of the importance of a healthy lifestyle for adults who were treated for cancer as children. The study is the first to find that the specific primary causes of death in long term survivors are many of the same leading causes of death in the U.S. population, often occurring at younger than expected ages. It also found that adult survivors of childhood cancer experience four times the risk of late mortality as the general population, even 40 years after diagnosis. However, the study contains reason for hope: survivors without certain modifiable lifestyle and cardiovascular risk factors had a lower risk of death, suggesting survivors may be able to improve their odds. For example, survivors maintaining a healthy lifestyle had a 20% lower risk of mortality than those following an unhealthy lifestyle. The findings were published today in *The Lancet*.

Empowering survivors with the numbers

Despite the finding of excess [mortality](#) in survivors, the investigators found that patients' health behaviors had an impact on their risk. Maintaining a [healthy lifestyle](#) (defined as having a healthy weight, not drinking more than moderate amount of alcohol, not smoking and exercising at or above the intensity recommended by the Centers for Disease Control guidelines) was associated with a 20% reduction in the risk of mortality, compared to those who did not.

"These findings provide important evidence that the high-risk for mortality that this population faces may be able to be reduced through changes in their health behaviors," said senior author Greg Armstrong, M.D., M.S.C.E., St. Jude Department of Epidemiology and Cancer Control chair. "This is important because our goal is to extend the lifespan of survivors and to improve their healthspan as well."

In addition to lifestyle, several major risk factors for [heart disease](#) and related issues were associated with mortality risk. Survivors with

hypertension or diabetes had a significantly higher mortality rate than survivors without those conditions. However, these conditions are modifiable—patients can improve or prevent them, and physicians can provide treatments effective against these diseases.

"Much research has demonstrated that survivors are vulnerable to early onset of chronic disease and mortality," said co-author Melissa Hudson, M.D., St. Jude Cancer Survivorship Division director. "The study highlights the importance of encouraging survivors to practice healthy behaviors and maintain good control of cardiovascular disease risk factors to improve their healthspan and lifespan."

Excess mortality and cause of death in survivors

In addition to the importance of potentially modifiable risk factors, this report is the first to detail that the specific primary causes of death in long term survivors are similar to the leading causes of death in the U.S. population, occurring earlier in survivors.

"We identified that long-term survivors of childhood [cancer](#) are experiencing a large number of deaths in excess of what would be expected for the general, aging population," said the first and corresponding author Stephanie Dixon, M.D., MPH, St. Jude Department of Oncology. "We were the first to find that decades after treatment, these excess deaths are predominantly due to the same leading causes of death as in the [general population](#), including second cancers, heart disease, cerebrovascular disease/stroke, chronic liver and kidney disease and infectious causes of death, experienced at a younger age and higher rate, in childhood cancer survivors," Dixon said.

Treatments for childhood cancers have improved to the point where over 85% of U.S. patients are effectively cured of their primary tumor after frontline treatment. As more patients survive their childhood cancer,

there is a growing population of adult survivors. By comparing the CCSS cohort to the public, the researchers found that decades after treatment survivors still experience four times the expected risk of death.

The largest cancer survivor cohort feeds discovery

The researchers were able to understand the problems affecting survivors using detailed health data from thousands of CCSS participants. The CCSS is the largest cohort of cancer survivors in North America, representing an estimated 20% of all childhood cancer survivors in that region. The scientists were able to take this vast swath of data to statistically isolate variables affecting [survivor](#) mortality. The group showed that even when common confounders, such as sociodemographic features, were controlled for, the gap in mortality between survivors and the general public persisted, but so did the protective effects of a healthy life.

"What was most exciting to see was that, independent of prior treatment exposures and sociodemographic factors, a healthy lifestyle and absence of hypertension or diabetes were each associated with a reduced risk of health-related mortality," Dixon said. "This suggests that while continued efforts to reduce treatment intensity while maintaining (or improving) 5-year survival are needed, future research should also focus on interventions for modifiable lifestyle and [cardiovascular risk factors](#) which may need to be specifically tailored to survivors with the goal of reducing chronic disease development and extending the lifespan of survivors of childhood cancer."

Intensive treatments continue to tax childhood cancer survivors

Patients treated with more intensive therapies continued to experience higher mortality than other survivors. Much research has focused on

minimizing the harms of therapy, but many survivors in the CCSS were treated before improved techniques were widely available. This study showed that physicians and researchers need to consider interventions that can decrease risk for the vulnerable population of survivors that were treated with aggressive therapies in their youth.

"The Childhood Cancer Survivors Study continues to provide important insights into the long-term outcomes of the growing number of children successfully treated for cancer," said co-author Leslie Robison, emeritus St. Jude Department of Epidemiology and Cancer Control chair. "The findings from the current analysis further emphasize the need to expand our efforts to reduce acute, chronic and late-onset toxicities of treatment, particularly those toxicities that can directly or indirectly result in premature mortality."

The study's other authors are Matthew Ehrhardt, Kirsten Ness, Kevin Krull, and Yutaka Yasui, of St. Jude; Qi Liu, University of Alberta; Eric Chow, and Wendy Leisenring, Fred Hutchinson Cancer Research Center; Kevin Oeffinger, Duke University; Paul Nathan, The Hospital for Sick Children, University of Toronto; and Rebecca Howell, The University of Texas at MD Anderson Cancer Center and Ann C. Mertens, Emory University School of Medicine.

More information: Stephanie B Dixon et al, Specific causes of excess late mortality and association with modifiable risk factors among survivors of childhood cancer: a report from the Childhood Cancer Survivor Study cohort, *The Lancet* (2023). [DOI: 10.1016/S0140-6736\(22\)02471-0](https://doi.org/10.1016/S0140-6736(22)02471-0)

Provided by St. Jude Children's Research Hospital

Citation: Healthy lifestyle associated with reduced mortality risk in childhood cancer survivors (2023, April 6) retrieved 21 November 2023 from <https://medicalxpress.com/news/2023-04-healthy-lifestyle-mortality-childhood-cancer.html>

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