

Impact of cancer predisposing variants on mortality examined in survivors

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Childhood cancer survivors who are carriers of cancer predisposing variants have increased subsequent malignant neoplasm-related late mortality, according to a study published in the October issue of *The Lancet Oncology*.

Cheng Chen, from the Shanghai Jiao Tong University School of

Medicine, and colleagues used data from two retrospective cohort studies—St. Jude Lifetime Cohort (SJLIFE) and the Childhood Cancer Survivor Study (CCSS)—with prospective follow-up of patients alive for at least five years after diagnosis of childhood [cancer](#) with corresponding germline whole genome or whole exome sequencing data. Cancer predisposing variants affecting 60 genes that were linked to autosomal-dominant cancer-predisposition syndromes were characterized.

A total of 12,469 participants were included: 4,402 from SJLIFE and 8,067 from CCSS. The researchers found that 5.1 percent of the participants had cancer predisposing variants (6.7 and 4.3 percent in the SJLIFE and CCSS cohorts, respectively), which were significantly associated with increased severity of subsequent malignant neoplasms. Overall, there were 263 (2.1 percent) and 426 (3.4 percent) subsequent neoplasm-related and other-cause deaths, respectively.

At 10 years after the first biospecimen collection, cumulative subsequent malignant neoplasm-related mortality was 3.7 and 6.9 percent in SJLIFE and CCSS carriers of cancer predisposing variants, respectively, versus 1.5 and 2.1 percent in noncarriers. The risk for subsequent neoplasm-related [mortality](#) was increased in association with carrying a cancer predisposing [variant](#) (subdistribution hazard ratios, 3.40 and 3.58 in SJLIFE and CCSS, respectively).

"These results have crucial implications on the provision of genetic counseling and testing and on informing future clinical recommendations for precision medicine for this growing population," the authors write.

More information: Cheng Chen et al, Cancer germline predisposing variants and late mortality from subsequent malignant neoplasms among long-term childhood cancer survivors: a report from the St Jude Lifetime Cohort and the Childhood Cancer Survivor Study, *The Lancet Oncology* (2023). [DOI: 10.1016/S1470-2045\(23\)00403-5](https://doi.org/10.1016/S1470-2045(23)00403-5)

Cécile M Ronckers et al, Cancer-predisposing germline variants and subsequent cancer risk, *The Lancet Oncology* (2023). [DOI: 10.1016/S1470-2045\(23\)00461-8](https://doi.org/10.1016/S1470-2045(23)00461-8)

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