

**Chronic Health Conditions and Premature Mortality in Long-term Survivors of Cancer Diagnosed Between the Ages of 15 and 20 years: A Report from the Childhood Cancer Survivor Study**

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**Introduction:** The incidence and severity of chronic health conditions (CHCs) and the risk for late mortality among survivors of cancer diagnosed during adolescence and early young adulthood have not been well defined.

**Methods:** We compared 2,491 five-year survivors of cancer diagnosed between 15-20 years of age enrolled in the Childhood Cancer Survivor Study (CCSS) with 2,931 age-matched siblings. We assessed the frequency, severity, and cumulative incidence of self-reported CHCs classified using the Common Terminology Criteria for Adverse Events 4.0. Hazard ratios (HR) with 95% Confidence Intervals (CI) compared CHCs between survivors and siblings. Vital status and cause of death were determined from the National Death Index. Survival probabilities and standardized mortality ratios (SMRs) were calculated for overall and cause-specific deaths.

**Results:** The distribution of cancer diagnoses included: Hodgkin lymphoma (37.5%), bone cancers (19.5%), leukemias (13.1%), soft tissue sarcomas (11.3%), non-Hodgkin lymphoma (9.1%), brain cancers (8.7%), and other (0.9%). Among survivors, 71.9% (1790/2491) had at least one CHC. Over half (51%; 914/1790) of these individuals with a CHC developed a severe/life-threatening/fatal condition (Grade 3-5). Compared to siblings, survivors were at higher risk for developing grade 3-5 CHCs (HR=4.6, 95% CI=4.0-5.3), subsequent malignant neoplasms (SMN; HR=8.4, 95% CI=6.1-11.6) and cardiovascular events (HR=6.7, 95% CI=5.0-9.1). Overall cumulative mortality was 24% (95% CI=23%-26%) at 30 years from diagnosis. Compared to age- and sex-specific US population rates, survivors had a SMR=6.4 (95% CI=6.0-6.9).

Nonrecurrence/nonexternal causes contributed to 46% of deaths followed by recurrence/progression of primary disease (42%), unknown (6%), and external causes (5%). Elevated cause-specific SMRs included deaths due to SMN (SMR=9.0, 95% CI=7.7-10.4), cardiac events (SMR=5.4, 95% CI=4.4-6.8), and pulmonary complications (SMR=8.4, 95% CI=5.9-12.0).

**Conclusion/Implications:** Cancer survivors diagnosed during adolescence and early young adulthood are at increased risk for CHCs and premature death. These findings underscore the importance of appropriate lifelong surveillance.

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