

**Late cause-specific mortality in long-term survivors of childhood and adolescent cancer:
An update from the Childhood Cancer Survivor Study (CCSS).**

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Background: The CCSS is a retrospective cohort study designed to determine late effects in children and adolescents diagnosed with cancer.

Methods: Eligibility criteria for entry into this cohort are: subjects diagnosed between 1970-1986 at one of 25 consortium centers, before 21 years of age, and survived at least five years after diagnosis. This analysis investigates the mortality rates and the specific cause of death in cohort members. Standardized mortality ratios (SMR) were calculated using age- and sex-specific rates from U.S. Mortality Statistics, National Center for Health Statistics for all causes of death. Information on the underlying cause of death was obtained from death certificates on cases who resided in the United States and had died before Dec 31, 2002. Deaths were categorized as death due to: recurrent disease, treatment sequelae of cancer treatment, or other causes.

Results: In this cohort of 20,505 five-year survivors, 2878 (14.0%) subjects died. The highest percentage of deaths was seen in CNS tumor (19.8%) and Hodgkin's disease (19.2%), with a relatively low proportion of deaths among five-year survivors of Wilms tumor (5.8%) and neuroblastoma (6.7%). Subjects accrued a total of 342,657 person years (PY) of follow-up. The annual absolute all-cause mortality rate for five-year survivors was 8.4 per 1000 PY. The overall SMR for this cohort was 8.3 (95% CI=8.0, 8.6). SMR were higher in females (13.2, 95% CI=12.5,14.0) than males (6.6, 95% CI=6.3,7.0). SMR differed by type of cancer received, with the highest seen with combination chemotherapy, radiation and surgery (10.1, 95% CI=9.5,10.8). Recurrence of cancer was the leading cause of death in survivors of childhood cancer, with 58% having died from their original cancer diagnosis. Risk of death was also high for treatment sequelae: second neoplasm (14.8%), cardiac-related (7.0%), respiratory disease (1.8%), and other sequelae (16.7%).

Conclusion: While recurrent cancer represents a major cause of late mortality, long-term treatment-related complications account for a sizable proportion of deaths.