

Risk of second malignant neoplasms (SMN) 20 years after childhood cancer: The updated experience of the Childhood Cancer Survivor Study (CCSS).

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Background: Survivors of childhood and adolescent malignancies are at increased risk for SMN but there are limited data regarding risks 20+ years following diagnosis. **Objectives:** To determine the incidence and risk factors for SMNs in a well-defined cohort of childhood cancer survivors. **Methods:** Among the CCSS cohort of 20,720 5-yr survivors (diagnosed 1970-86), SMNs are ascertained and verified by pathology reports. Age- and sex-standardized incidence ratios (SIR) were calculated using US Surveillance, Epidemiology and End Results (SEER) data. **Results:** As of June 2003, there were 914 verified SMNs among 14,352 survivors with 198,277 person years of follow-up (including 404 cases of non-melanoma skin cancer (NMSC, 4.3% 20-yr cumulative incidence). Excluding NMSC from the analyses, the overall SIR is 3.9 (95% CI 3.5, 4.2) with a 20-yr cumulative incidence of 5.2%. The 20-yr cumulative incidence of SMN, by original diagnosis: Hodgkin disease (13.9%), Bone tumor (6.6%), Soft tissue sarcoma (5.8%), CNS tumor (3.1%), Leukemia (2.5%), Wilms tumor (2.8%), non-Hodgkin lymphoma (4.0%) and Neuroblastoma (2.7%). Five-year survivors are at significantly increased risk (SIR; 95% CI) for CNS tumors (9.2; 6.9, 12.1), breast cancer (12.7; 10.6, 15.2), bone tumor (14.2; 10.2, 19.9), thyroid cancer (10.5; 8.3, 13.2), soft tissue sarcoma (8.0; 6.1, 10.4), leukemia (6.5, 4.6, 9.1) and melanoma (2.2, 1.5, 3.4). Analyses according to yrs from diagnosis of original cancer demonstrates that risk of SMN remains elevated over time for all survivors, with risks highest for those exposed to radiation therapy. **Conclusions:** Survivors of childhood cancer are at increased risk for second malignancies for >20 yrs from diagnosis. Further study is warranted to better define risk factors, develop effective surveillance and preventive strategies and determine lifetime excess risk.

Yrs from diagnosis	5 – 9	10 – 14	15 – 19	20+
Person Years SIR (95% CI)				
Overall	69235 4.5 (3.8,5.4)	62054 3.8 (3.2,4.4)	41357 3.7 (3.1,4.5)	25631 4.2 (3.6,5.0)
Radiation	40531 5.9 (5.9,7.2)	36458 4.7 (3.9,5.7)	25738 4.1 (3.4,5.0)	16900 5.3 (4.4,6.4)
No Radiation	19548 2.1 (1.3,3.5)	17702 2.2 (1.5,3.3)	10438 1.2 (0.6,2.1)	5598 2.6 (1.6,4.0)