

SECOND MALIGNANT NEOPLASMS IN FIVE-YEAR SURVIVORS OF CHILDHOOD CANCER: AN UPDATE FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: With improved survival rates among childhood cancer patients, second malignancies (SMNs) are of growing concern.

Objectives: To determine the incidence and risk factors for SMNs in a well-defined cohort of childhood cancer survivors.

Methods: Among the CCSS cohort, SMNs are ascertained and verified by pathology reports. Age- and sex-standardized incidence ratios were calculated using US Surveillance, Epidemiology and End Results (SEER) data.

Results: As of June 2003, there were 1095 verified SMNs among 14,352 five-year survivors (including 404 cases of non-melanoma skin cancer (NMSC), 4.3% cumulative incidence at 20 years). Excluding the NMSC, the SIR is 4.30 (95% CI 3.94,4.70), 20-year cumulative incidence is 5.84% with an absolute excess risk (AER) per 1000 person-years of 2.22. Compared with our previous analysis in 2000, despite higher expected numbers in the general population, risk of SMN remains elevated and 20-year incidence and AER have increased for most primary diagnoses. Similarly, risk of specific SMN subtypes remains elevated above that of the general population.

Primary Diagnosis	SIR (95% CI)	20-yr cumulative Risk (%)	AER / 1,000 person-years of follow-up
All Diagnoses			
2000	6.38 (5.69, 7.13)	3.18%	1.88
2003	4.30(3.94, 4.70)	5.84%	2.22
Hodgkin's Disease			
2000	9.70 (8.05,11.59)	7.63%	5.13
2003	7.13 (6.22, 8.19)	16.19%	7.04
Soft Tissue Sarcoma			
2000	7.03 (4.92, 9.73)	3.98%	2.33
2003	4.57 (3.53,5.92)	5.86%	2.74
Neuroblastoma			
2000	6.59 (3.28,11.79)	1.87%	0.95
2003	5.62 (3.75, 8.41)	2.65%	1.42
Kidney Tumor			
2000	6.03 (3.37, 9.95)	1.62%	1.01
2003	3.75 (2.46, 5.73)	3.04%	1.06
Leukemia			
2000	5.66 (4.37, 7.22)	2.05%	1.20
2003	2.88 (2.34, 3.54)	2.54%	0.97
Bone Tumor			
2000	4.50 (2.96, 6.55)	3.28%	1.79
2003	3.19 (2.38, 4.28)	7.88%	2.27
CNS Tumors			
2000	4.44 (2.88, 6.56)	2.14%	1.13
2003	3.09 (2.22, 4.31)	3.62%	1.30
Non-Hodgkin's Lymphoma			
2000	3.21 (1.76, 5.39)	1.87%	0.89
2003	3.10 (2.16, 4.46)	3.04%	1.06

Second Malignancy	O/E Ratio (95% C.I.)
Leukemia	
2000	6.86 (4.39, 10.21)
2003	6.64 (4.72, 9.35)
CNS Tumors	
2000	9.85 (6.90, 13.63)
2003	9.86 (7.53, 12.90)
Lymphoma	
2000	1.51 (0.80, 2.58)
2003	1.44 (0.90, 2.31)
Thyroid	
2000	11.34 (8.20, 15.27)
2003	11.71 (9.39, 14.68)
Bone Tumors	
2000	19.14 (12.72, 27.67)
2003	14.59 (10.48, 20.33)
Soft Tissue Sarcoma	
2000	6.33 (4.33, 8.94)
2003	8.54 (6.56, 11.13)
Breast Cancer	
2000	16.18 (12.35, 20.83)
2003	15.93 (13.31, 19.08)
Melanoma	
2000	4.04 (2.43, 6.32)
2003	2.61 (1.75, 3.87)
All Other CA	
2000	4.01 (3.05, 5.18)
2003	1.58 (1.31, 1.90)

Conclusions: Survivors of childhood cancer continue to be at increased risk for second malignancies. While this should not overshadow the therapeutic successes in childhood cancer, further study is warranted to better define risk factors and develop effective strategies that involve surveillance for early detection and possible prevention. This will permit selected patients to be appropriately monitored, and will help determine the lifetime excess cancer risk.