

TEMPORAL CHANGES IN TREATMENT EXPOSURES IN THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background: Well-designed epidemiologic investigations of pediatric cancer survivors inform clinical practice guidelines and future clinical trials. Expansion of the CCSS cohort to include survivors diagnosed across three decades (1970-99) affords the opportunity to evaluate associations between key temporal changes in survivor treatment characteristics and risk for adverse health outcomes.

Methods: We summarized changes in cancer and treatment characteristics of 24,000 CCSS participants. Treatment exposures were abstracted from medical records. Trends across 5 year intervals were evaluated using logistic regression models with weights to account for sampling probabilities.

Results: Within the expanded CCSS, use of chemotherapy significantly increased overall (Table, T1-T6) and for each diagnosis except leukemia which was always 100%. Exposure to radiation (RT) decreased overall and for each diagnosis except soft tissue sarcoma. Overall, chest RT exposure was reduced and notably, exposures of ≥ 30 Gy declined from 85% to 6% (T1 to T6) for Hodgkin lymphoma. Use of anthracyclines (ANT) increased significantly, predominantly for doses lower than 250 mg/m².

| | % With Exposure | | | | | |
|-------------------------------|-----------------|---------------|---------------|---------------|---------------|---------------|
| | T1 1970-74 | T2 1975-79 | T3 1980-84 | T4 1985-89 | T5 1990-94 | T6 1995-99 |
| Any RT* | 79 | 75 | 64 | 50 | 40 | 34 |
| RT to brain* | 30 | 36 | 32 | 24 | 18 | 16 |
| RT to abdomen* | 28 | 22 | 19 | 12 | 8 | 9 |
| RT to chest ≥ 30 Gy* | 21 | 13 | 8 | 4 | 1 | 1 |
| Any Chemotherapy* | 75 | 81 | 81 | 85 | 86 | 87 |
| ANT 1-250 mg/m ² * | 3 | 12 | 18 | 34 | 45 | 52 |
| ANT >250 mg/m ² * | 11 | 24 | 24 | 23 | 17 | 14 |
| Any epipodophyllotoxins* | 1 | 4 | 9 | 25 | 34 | 36 |

*Trend p-value <0.0001

Conclusions: The expansion of the CCSS cohort provides a unique resource to evaluate the impact of historical changes in primary cancer therapy, including reduction of therapeutic intensity for low- and standard-risk populations as well as intensification of specific therapies for high-risk populations, on health and psychosocial outcomes.