

Title: Adverse Health Outcomes among Childhood Cancer Survivors with and without Congenital Anomalies

Authors: Janitz AE, Qiu W, Schraw JM, Mostoufi-Moab S, Mirabello L, Stewart DR, Neglia JP, Turcotte LM, Bhatia S, Yasui Y, Armstrong GT, Lupo PJ

Purpose: We estimated the rate of chronic health conditions (CHCs), subsequent malignant neoplasms (SMNs), and mortality among five-year survivors of childhood cancer with and without congenital anomalies.

Methods: We included childhood cancer survivors with and without self-reported anomalies from the Childhood Cancer Survivor Study (n=22,247). Using Cox regression, we estimated hazard ratios (HR) and 95% confidence intervals (CI) of CHCs per the Common Terminology Criteria for Adverse Events from 1 (mild) to 5 (fatal) and SMNs comparing survivors by anomaly status. We calculated age-sex-calendar year-specific mortality rates and standardized mortality ratios (SMR) for survivors compared to the US population, stratified by the presence of anomalies.

Results: Among survivors, 16.9% (n=3,880) reported an anomaly. Survivors with anomalies had a higher rate of any CHC (grades 1-5 HR: 1.31, 95% CI: 1.23-1.39), severe CHCs (grades 3-5 HR: 1.42, 95% CI 1.28-1.58), and multiple CHCs (≥ 2 any grade HR: 1.36, 95% CI 1.27-1.46; ≥ 3 any grade HR: 1.49, 95% CI 1.37-1.63), compared to survivors without anomalies. Survivors with anomalies had increased rates for adverse outcomes across body systems (all $p < 0.001$), including: hearing/vision/speech (HR: 1.37); urinary (HR: 1.42); hormonal/endocrine (HR: 1.24); heart/circulatory (HR: 1.35); digestive (HR: 1.49); and brain systems (HR: 1.42). Survivors with anomalies had an increased rate of SMNs: bone cancer (HR: 3.29, 95% CI 1.29-8.39); soft-tissue sarcomas (HR: 2.39, 95% CI 1.27-4.49); and melanoma (HR: 2.02, 95% CI 1.00-4.09). We observed no difference in all-cause mortality (SMR: 1.00) of survivors with anomalies relative to the US general population. However, survivors with anomalies had lower mortality due to recurrence or progression of the primary cancer diagnosis compared to those without anomalies (mortality rate: 0.64 vs. 0.90 per 1,000 person-years).

Conclusion: Cancer survivors with congenital anomalies had higher rates of adverse outcomes across body systems and increased risk of certain SMNs. All-cause mortality was not different than in the general U.S. population.

Keywords: childhood cancer survivors, congenital anomalies, chronic health conditions