Temporal trends in chronic disease among survivors of childhood cancer diagnosed across three decades: A report from the Childhood Cancer Survivor Study (CCSS).

Background: Modifications in childhood cancer treatments in recent decades have contributed to reductions in late mortality among 5-year survivors. We use the recently expanded CCSS cohort to investigate whether these changes have also reduced the incidence of chronic disease.

Methods: We evaluated the incidence of severe, disabling/life-threatening, or fatal chronic health conditions (CTCAE grades 3-5) among 5-year survivors diagnosed prior to age 21 years from 1970 through 1999. We calculated the 15-year cumulative incidence of chronic health conditions by decade of cancer diagnosis and compared risk across decades using Cox regression to estimate hazard ratios (HR) and 95% confidence intervals (CI).

Results: Among 23,601 survivors, median age 28 years (range 5-63), 21 years from diagnosis (5-43), the 15-year cumulative incidence of grade 3-5 conditions decreased from 12.7% in survivors diagnosed in the 1970s to 10.1% and 8.8% in those diagnosed in the 1980s and 1990s (per 10 years, HR 0.84 [95% CI=0.80-0.89]). The association with diagnosis decade was attenuated (HR 0.92 [0.85-1.00]) when detailed treatment data were included in the model, indicating that treatment changes/reductions mediated risk. Adjusted for sex and attained age, significant reduction in risk over time was found among survivors of acute lymphoblastic leukemia (HR=0.86 [0.76-0.98]), astrocytomas (HR=0.77 [0.64-0.92]), Hodgkin lymphoma (HR=0.75 [0.65-0.85]), non-Hodgkin lymphoma (HR=0.79 [0.63-0.99]), and Wilms tumor (HR=0.57 [0.46-0.70]). Decreases were largely driven by a reduced incidence of endocrine conditions (1970s: 4.0% v. 1990s:1.6%; HR 0.66 [0.59-0.73]) and subsequent malignant neoplasms (1970s: 2.4% v. 1990s: 1.6%; HR 0.85 [0.76-0.96]). Significant reductions were also found for gastrointestinal (HR 0.80 [0.66-0.97]) and neurological conditions (HR 0.77 [0.65-0.91]), but not cardiac or pulmonary conditions.

Conclusion: Changes in childhood cancer treatment protocols have not only extended lifespan for many survivors, but have also reduced the incidence of serious chronic morbidity in this population.