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**Health-Related Unemployment Trends Among Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS).**

**Background:** The impact of treatment era and chronic health conditions on health-related unemployment among childhood cancer survivors has not been studied.

**Methods:** Childhood cancer survivors (age  $\geq 25$  years) enrolled in the CCSS (3,420 diagnosed in the 1970s, 3,564 in the 1980s, and 2,853 in the 1990s) were matched 1:5 on sex, race/ethnicity, census bureau division, age, and year of survey to the Behavioral Risk Factor Surveillance System (BRFSS), a nationally representative population. Among survivors, health-related unemployment was defined as self-reported unemployment due to illness/disability and for BRFSS participants as self-reported inability to work. To standardize follow-up, health-related unemployment was assessed either in 2002-05 or 2014-16 for both cohorts. Sex stratified standardized prevalence ratio (SPR) and relative SPR (rSPR) with 95% confidence intervals (CI) for health-related unemployment were estimated using multivariable generalized linear models, with BRFSS background rates to assess the impact of treatment era and moderate to severe health conditions (per the Common Terminology Criteria for Adverse Events).

**Results:** Prevalence of health-related unemployment in survivors (median age 9 years [range 0-20] at diagnosis and 33 years [25-54] at follow-up) was significantly higher compared to BRFSS participants (females: 11.3% vs 3.7%; SPR 3.0, 95% CI 2.7-3.3; males: 10.5% vs 3.0%; SPR 3.5, 95% CI 3.1-3.9). Health-related unemployment risks declined among survivors in more recent decades ( $p_{\text{trend}} < 0.001$ ) for females: 1970s SPR 3.8, 95% CI 3.2-4.5, 1980s SPR 2.9, 95% CI 2.5-3.5, 1990s SPR 2.5, 95% CI 2.1-3.0; and males: 1970s SPR 3.6, 95% CI 2.9-4.4, 1980s SPR 3.8, 95% CI 3.1-4.7, 1990s SPR 3.0, 95% CI 2.5-3.7. Among survivors, multivariable models identified associations between presence of specific health conditions and elevated health-related unemployment (Table) adjusting for all statistically significant health conditions, race/ethnicity, treatment era, age at survey, and diagnosis. Among females, rSPR for endocrine conditions differed between 1970s and 1990s (interaction  $p = 0.04$ ); fewer significant health conditions remained in the final model for males.

**Conclusions:** While prevalence for health-related unemployment has declined over time, childhood cancer survivors remain at higher risk compared to the general population. These elevated risks are associated with chronic health conditions and affect female survivors more than male survivors.

Health Conditions	Female: rSPR of health-related unemployment	95% CI	Male: rSPR of health-related unemployment	95% CI
Hearing	1.8	1.5, 2.3	1.6	1.3, 2.0
Vision	1.9	1.5, 2.4	1.9	1.4, 2.5
Endocrine, 1970s	1.0	0.7, 1.4	-	-
1980s	1.2	0.9, 1.6	-	-
1990s	1.7	1.2, 2.5	-	-
Respiratory	1.6	1.1, 2.5	-	-
Cardiac	2.2	1.8, 2.7	1.7	1.3, 2.2
Musculoskeletal	2.3	1.7, 3.0	1.8	1.3, 2.5
Neurologic	3.9	3.2, 4.8	4.6	3.6, 5.9