

## **Health-related late mortality among aging five-year survivors of childhood cancer: a report from the Childhood Cancer Survivor Study**

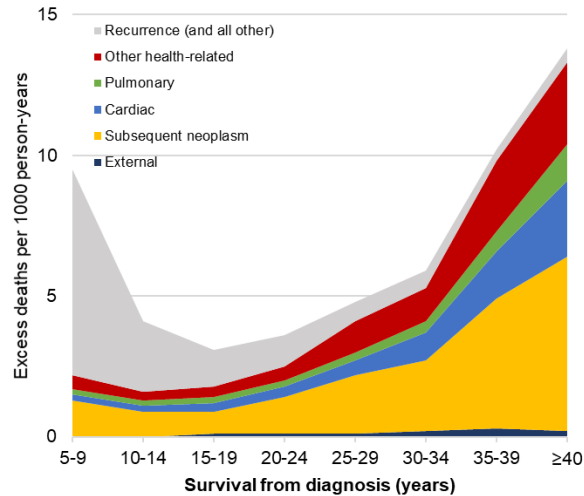
**Aim/Background:** Five-year survival fails to describe the full cancer survival experience. Excess deaths >5 years from diagnosis provides additional information, yet specific causes of excess deaths and impact of modifiable risk factors have not been defined.

**Methods:** All-cause and health-related late mortality (HRM; excludes death from primary cancer and external causes) were evaluated in five-year survivors using the National Death Index. Modifiable lifestyle (smoking status, alcohol use, physical activity, BMI; combined to create categories [unhealthy, moderate, healthy]) and CVRFs (hypertension, diabetes, dyslipidemia) were assessed as time-varying covariates. Standardized mortality ratios (SMRs), and absolute excess risk of death per 1000 person-years (AER/1000py) with 95% confidence intervals (CIs) were estimated.

**Results:** Among 34,230 survivors (median 29.1 years from diagnosis, range 5.0-48.0), 5,916 deaths were observed with 51.2% attributable to health-related causes. Compared to the general population, survivors  $\geq 40$  years from diagnosis continued to experience an over 4-fold increased risk of HRM (SMR 4.4, 95% CI 3.9-5.0). Survivors were at increased risk of many leading non-cancer causes of death in the general population (SMR, 95% CI; heart disease: 4.3, 3.9-4.7; stroke: 5.1, 4.2-6.2; sepsis: 8.1, 6.3-10.1; kidney failure: 6.8, 5.0-9.0). By  $\geq 40$  years from diagnosis we estimated 13.8 excess deaths/1000 person-years driven by 13.1 excess deaths from health-related causes (Figure).

Among 20,051 adult survivors in modifiable risk analyses, 29% reported healthy lifestyle and 19%  $\geq 1$  CVRF. Excess risk of HRM was lowest in those with healthy lifestyle across survival time (e.g. AER/1000py [95% CI]  $\geq 40$  years from diagnosis: healthy 3.9 [0.6-8.8], moderate 16.0 [11.6-21.3], unhealthy 20.0 [15.1-25.9]) with similar trends when stratified by number of CVRFs.

**Conclusions:** Aging survivors have a persistent increased risk of HRM compared to the general population. However, survivors with a healthy lifestyle or no CVRFs experience fewer excess deaths. Interventions targeting modifiable lifestyle and CVRFs may reduce risk.



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