

## **Injury-Related Late Mortality Among Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)**

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**Background:** Long-term survivors of childhood cancer have an elevated risk of premature mortality. Research has primarily focused on health-related mortality with considerably less known about external causes of death among survivors.

**Methods:** Injury-related late mortality (>5 years from diagnosis) was examined in survivors (median [min-max] 34.7 [5.6-68.5] years of age; 26.2[5.0-48.0] years from diagnosis) enrolled in CCSS (n=34,223). Using the National Death Index, external causes of death were classified as intentional (suicide) or unintentional (e.g., accidental falls, motor vehicle accidents, accidental poisonings). Standardized mortality ratios were estimated using age-, sex-, and calendar-year matched U.S. population rates. Separate multivariable piecewise exponential models examined associations between diagnosis and treatment (n=23,183), and health-related variables including alcohol use, physical activity, and pain (n=16,084) and mortality. Among survivors who completed the Brief Symptom Inventory-18 (n=15,793), suicidal ideation was examined as a risk factor for injury-related mortality, due to potential for death misclassification and overlapping etiologies of intentional and unintentional injury-related deaths.

**Results:** Survivors had a similar risk for suicide mortality (observed n=99) compared to the general population (SMR=1.05, 95% CI 0.86-1.27). Conversely, higher risk of unintentional injury-related deaths (observed n=296) was observed among survivors (SMR=1.46, 95% CI 1.31-1.62). CNS tumor diagnosis (RR=2.6, 95% CI 1.2-5.7), neuroblastoma diagnosis (RR=3.7, 95% CI 1.3-10.4), cancer-related pain (RR 3.5, 95% CI 1.2-9.9), and depressive symptoms (RR=4.2, 95% CI 1.4-12.6) were associated with increased risk of suicide mortality. Cranial radiation >30Gy was associated with an increased risk of unintentional injury deaths (RR=1.7, 95% CI 1.1-2.6), as was lower household income (RR=2.0, 95% CI 1.0-4.2), risky/heavy drinking (RR=2.2, 95% CI 1.1-4.4), and physical inactivity (RR=2.8, 95% CI 1.3-5.9). Suicidal ideation was associated with an increased risk of suicide mortality (RR=7.7, 95% CI 2.1-27.4) and unintentional injury-related mortality (RR=4.1, 95% CI 1.8-9.0).

**Conclusions:** Survivors of childhood cancer had higher rates of unintentional injury-related deaths compared to the general population. Injury-related mortality was associated with modifiable risk factors including alcohol misuse, physical inactivity, depression, and suicidal ideation. While associations between depression and suicidal ideation with suicide mortality were expected, their associations with unintentional injury-related mortality were not. The potential impact of psychological variables on accidental deaths should be further explored in this population.