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Social determinants of health (SDOH) and late mortality among survivors of childhood cancer: a report from the Childhood Cancer Survivor Study (CCSS)

Background: Neighborhood-level SDOH may increase disparities in adverse cancer-related outcomes. The US CDC-constructed Social Vulnerability Index (SVI) reflects 4 neighborhood-level SDOH domains (socioeconomic status [SES]; household composition; minority status/language; housing/transportation) and captures the vulnerability of underserved communities. Comprehensive investigations of the impact of neighborhood-level SDOH on late mortality among survivors of childhood cancer are needed.

Methods: Analyses included 5-year survivors in the US diagnosed in 1970-1999 participating in the CCSS, a multi-institutional retrospective cohort study. We evaluated geocoded SVI quintiles (Q1 to Q5, from least to most vulnerable) based on residential addresses and personal SES factors including income, education level, and health insurance status collected at CCSS baseline. The impact of SVI and personal-level SES on all-cause and cause-specific mortality rates were evaluated using cumulative incidence and relative rates (RRs) from piecewise exponential regression models adjusted for attained age, sex, age at primary cancer diagnosis, and treatments (any radiation therapy and any chemotherapy). Associations further adjusting for reported life-threatening or disabling chronic health conditions (CHCs with CTCAE grades 3-4, treated as time-varying) were also assessed.

Results: Among 20,261 survivors with geocode data (mean age at cancer diagnosis and baseline evaluation, 7 years and 24 years respectively, with a mean follow up of 17 years), 2,439 survivors died. All-cause late mortality was greater in survivors living in more vulnerable areas (Q5 vs. Q1, at 20y: 14.7% vs. 10.8%, P<0.001). We observed a dose-response relationship between worsening SVI and the all-cause mortality rate (Q5 vs. Q1 RR 1.52, 95% CI 1.32-1.76, P_{trend}<0.001) as well as for mortality rates due to specific health causes (Table). Among the SVI SDOH domains, neighborhood SES (Q5 vs. Q1 RR 1.68, 95% CI 1.45-1.95) showed the strongest association with all-cause mortality followed by household composition (RR 1.43, 95% CI 1.24-1.66). Notably, the associations between SVI and all-cause mortality remained largely consistent after adjusting for personal-level SES as well as in analyses stratified by individual income, education level, and health insurance coverage. The magnitude of these associations also remained unchanged after further adjusting for reported life-threatening or disabling CHCs.

Conclusions: Living in the most socially vulnerable neighborhoods during young adulthood is associated with an approximately 50% increased risk for late mortality among survivors of childhood cancer and is largely unaffected by favorable personal-level SES and persists even after accounting for serious CHCs. Policies and interventions targeting neighborhood-level SDOH during the transition to survivorship care are needed to reduce mortality risk in this population.

Table: Adjusted RRs and 95% confidence intervals for overall and cause-specific mortality

SVI	All cause	Subsequent neoplasm cause	Cardiovascular cause	Other health causes
Q1	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Q2	1.00 (0.88 - 1.14)	0.90 (0.74 - 1.11)	1.09 (0.76 - 1.55)	1.09 (0.85 - 1.39)
Q3	1.16 (1.02 - 1.32)	1.03 (0.84 - 1.27)	1.18 (0.82 - 1.70)	1.24 (0.97 - 1.59)
Q4	1.24 (1.08 - 1.42)	1.12 (0.90 - 1.39)	1.29 (0.88 - 1.90)	1.44 (1.11 - 1.86)
Q5	1.52 (1.32 - 1.76)	1.35 (1.07 - 1.69)	1.54 (1.02 - 2.33)	1.83 (1.38 - 2.42)

SVI Q1 (least vulnerable) is the referent.