Association between Neighborhood-Level Social Vulnerability and the Incidence of Subsequent Malignant Neoplasms: A Report from the Childhood Cancer Survivor Study

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Background: It is unknown whether neighborhood-level social vulnerability impacts subsequent malignant neoplasm (SMN) risk among survivors of childhood cancer. We evaluated associations between neighborhood-level social vulnerability and SMN incidence among participants in the Childhood Cancer Survivor Study.

Methods: This analysis included five-year survivors of childhood cancer diagnosed between 1970-1999 in the US with residential addresses from CCSS baseline that have been geocoded. Using the US Centers for Disease Control and Prevention's Social Vulnerability Index (SVI), we evaluated the quartiles (Q1 to Q4 = most to least vulnerable) of overall SVI and subdomains (socioeconomic status, household composition, minority status and language, and housing and transportation). All SMNs that developed > 5 years after the initial diagnosis, including breast, colorectal, and thyroid, were self-reported, confirmed by pathology review, and included. Relative rates (RRs) were adjusted for attained age, sex, age at primary cancer diagnosis, and treatment exposures specific to each outcome (breast, colorectal, and thyroid SMNs).

Results: Among 20,739 survivors with baseline SVI data (median age at baseline: 25 years, IQR = 19-30 years), the 25-year cumulative incidence of SMNs was 13% (95% CI 13-14%). 1369 survivors developed an SMN, including 358 breast, 95 colorectal, and 272 thyroid SMNs. For all SMNs, there was a significant association observed between residence in a less socially vulnerable neighborhood and higher rates of SMNs (overall SVI, reference Q1 [most vulnerable]: Q4 RR 1.43, 95% CI 1.2-1.71; Q3 RR 1.23, 95% CI 1.02-1.48; Q2 RR 1.25, 95% CI 1.03-1.51; *p-trend* = < 0.001). Additionally, a significant association between lower

vulnerability and a higher rate of SMNs was observed for the SVI socioeconomic subdomain (Q4 vs Q1 RR 1.25, 95% CI 1.05-1.49, *p-trend* = 0.0098) and household composition subdomain (Q4 vs Q1 RR 1.27, 95% CI 1.07-1.5, *p-trend* = 0.004). No statistically significant association was observed with neighborhood-level social vulnerability in either overall or subdomain SVI for subsequent breast or colorectal cancer (breast overall SVI Q4 vs Q1 RR 1.38; 95% CI 0.95-2.0 and colorectal overall SVI Q4 vs. Q1 RR 0.74; 95% CI 0.38-1.44). However, for thyroid SMNs, residing in lower neighborhood-level social vulnerability communities was significantly associated with an increased SMN rate (overall SVI Q4 vs. Q1 RR 1.61; 95% CI 1.08-2.41; *p-trend* = 0.04), but no individual SVI subdomains were significantly associated.

Conclusions: Among survivors of childhood cancer, residing in less socially vulnerable neighborhoods was associated with higher rates of SMNs overall, driven largely by thyroid SMNs. Given that rising incidence of some cancer types (e.g., primary thyroid cancers) may be attributed to increased detection related to advances in imaging, these findings raise the possibility that the relationship between neighborhood-level social determinants of health and SMN incidence may reflect improved diagnosis, detection bias, or some combination of the two. Future studies should evaluate the extent to which healthcare access and detection practices contribute to SMN burden, especially thyroid SMNs, among survivors.