Study Title: Association of Individual and Neighborhood characteristics and adverse outcomes in childhood cancer survivors

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1. Background and Rationale

Approximately 83% of children diagnosed with a pediatric cancer survive at least 5 years.¹ However, cure does not come without subsequent risk for adverse late effects as these survivors age, including the development of chronic conditions such as cardiovascular disease², cardiometabolic abnormalities³, and second cancers.⁴ Multiple factors contribute to the development of chronic conditions in childhood cancer survivors, including late effects of treatment⁵, aging⁶, modifiable risk factors² and health behaviors.⁷ However, social and built environment factors influence health outcomes across the cancer continuum⁸, and are an important area for further research.

Current evidence links neighborhood of residence and individual socioeconomic status to poor health outcomes⁹ and mortality¹⁰ in the general population. Recently, Keegan et al.¹¹ examined whether the incidence of medical conditions (e.g., circulatory, respiratory, endocrine, liver and chronic kidney diseases) differed by neighborhood SES (nSES) status in adolescent and young adult survivors of Hodgkin lymphoma who had survived ≥ 2 years from diagnosis. Survivors who lived in low SES neighborhoods had higher 10-year cumulative incidences of circulatory, respiratory, chronic kidney and endocrine diseases. In time to event models adjusted for sex, race/ethnicity, treatment, age at diagnosis, and health insurance status, survivors in low SES neighborhoods had a higher likelihood of onset of respiratory and endocrine medical conditions. Further, recently published work from our group utilizing the SJLIFE cohort, indicates that the neighborhood environment (e.g., low nSES, rurality) is associated with increases in obesity¹², a risk factor for subsequent morbidity. Differences in chronic condition prevalence in survivors by neighborhood environment may be due, in part, to access to

healthcare. In general, rural residents have higher cancer death rates¹³, lower access to oncologists¹⁴, and spend a significant amount of time traveling to see a cancer provider.¹⁵ Rural childhood cancer survivors report concerns about lack of risk-based follow up care¹⁶ and report difficulties getting to appointments along with greater travel costs.¹⁷ Additionally, population-level SES is a predictor of low access to follow-up care in childhood cancer survivors, even after adjusting for individual-level SES and self-reported health behaviors.¹⁸ In fact, Liu et al. demonstrated that differences in overall mortality rates by race in the CCSS were largely attributed to lower SES.¹⁹

The effects of treatment on subsequent morbidities in childhood cancer survivors have been well characterized in the literature. However, investigations that have examined how individual socioeconomic status and neighborhood factors (both social and physical) contribute to chronic condition incidence and prevalence are scarce. We conceptualize this relationship as presented in Figure 1 below. As outlined in the dotted box, it is likely that treatment intensity influences poorer individual level SES, which then leads to survivors living in neighborhoods associated with lower SES and that are rural (and therefore, less healthcare access/utilization) but also suboptimal health behaviors, perhaps as a way of coping. The interplay between suboptimal health behaviors and suboptimal neighborhood characteristics has been well described in the general population^{20,21}, as well as the interplay between these factors and increased mortality and morbidities. However, this has not been globally examined in the childhood cancer survivor population to date. The efforts on this project will provide a new set of data, garnered through geospatial methods, that describe the social-environmental influences on chronic conditions. This includes the geocoding of the entire CCSS cohort at baseline and last known follow-up as well as the linkage of census and other public data. This will allow for future proposals within the CCSS to utilize these data to further understand how contextual factors, such as a neighborhood where a survivor resides, influence late effects of cancer treatment.

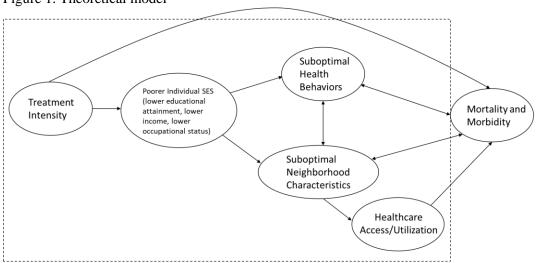


Figure 1. Theoretical model

2. Specific Aims

- 2.1. Aim 1a: <u>Using geospatial methodology and publicly-available geospatial health and</u> <u>social data</u>, describe the association between treatment exposures and neighborhood characteristics (e.g., rurality, area-level health-related indicators such as healthcare availability, health outcomes, and health behaviors, small-area socioeconomic indicators) of survivors at baseline and at last follow-up in the CCSS cohort.
 - 2.1.1. Aim 1b: Compare the individual-level and neighborhood-level characteristics of survivors to their sibling counterparts at baseline and last follow-up.
- 2.2. Aim 2: Examine the direct and indirect effects of the combination of individual-level and neighborhood-level characteristics (e.g., rurality, area-level health-related indicators such as healthcare availability, health outcomes, and health behaviors, small-area socioeconomic indicators) at follow-up on chronic health condition prevalence, considering the mediating effects of healthcare access and healthcare utilization.
- 2.3. Aim 3: Assess the association between the individual-level and neighborhood-level characteristics at the baseline survey and subsequent incidence rates of chronic health conditions (including subsequent neoplasms) and late mortality.

3. <u>Hypotheses</u>

- 3.1. We hypothesize that siblings will be more likely to live in neighborhoods with higher SES, better neighborhood-level health outcomes and higher levels of positive health behaviors than survivors.
- 3.2. We hypothesize that survivors with poor individual SES (e.g., lower educational attainment, lower income) and those who live in adverse neighborhoods (lower SES, rural census tracts, poor area level health outcomes and poor area level health behaviors) at follow-up will have a higher prevalence of chronic conditions. This relationship will be mediated, in part, by healthcare access and healthcare utilization.
- 3.3. We hypothesize that survivors who live in neighborhoods with poor individual SES (e.g., lower educational attainment, lower income) and those who live in adverse neighborhoods (lower SES, rural census tracts, poor area level health outcomes and poor area level health behaviors) at baseline will have higher incidence of chornic conditions and mortality after the baseline.

4. Methods

- 4.1. **Study Population**: The study population will include survivors and siblings in both the original and expansion CCSS cohorts who have geocoded addresses at baseline recruitment. We will use chronic condition data from follow-up 5 (or follow-up 6 if data is available at time of analysis) for the analysis examining new chronic health condition onset. Analyses regarding treatment variables will be restricted to survivors who have signed medical record releases and have treatment exposure data abstracted by CCSS institutions.
- 4.2. **Outcome Variables:** The following variables collected via CCSS surveys at baseline and through FU5 (or FU6 if available) and the US National Death Index (NDI). Relevant information for analysis (e.g., date of onset) will also be utilized.
 - 4.2.1. Chronic health conditions: Chronic health conditions scored using the severity of each condition using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, will be used in the analysis as done in prior CCSS studies

(ref). Conditions are separated by organ/system (i.e., SMN, cardiovascular, endocrine, respiratory, neurological, renal) and graded as mild (grade 1), moderate (grade 2), severe (grade 3), life-threatening or disabling (grade 4) or fatal (grade 5). Results will be described based on chronic conditions as a binary outcome (grade 3-4 vs. grade 0-2 conditions, overall and by individual organ system) and as a continuous variable based on the duration (years) the condition was present (as done in Hayek et al²²).

4.2.2. Mortality: Vital status (alive/dead) and date of death will be used to examine if neighborhood-level characteristics influence mortality outcomes. CCSS data extracted from the most recent NDI search will be used for vital status. Underlying cause of death has been determined from death certificates and will be examined based on categories used by Armstrong et al²³: 1) recurrence or progression of primary cancer; 2) external causes (accidents, suicides, poisonings, and other external causes) and 3) health-related causes including subsequent neoplasms, cardiac, pulmonary and all other causes. cause-specific deaths will also be examined if numbers permit grouped into three causes: cardiac related, diabetes related, and cancer related.

4.3. Predictor variables

- 4.3.1. <u>Individual-level SES</u>: Household income, educational attainment, employment status, occupation code, current residential status. For modeling that combines individual SES with neighborhood factors, we will distill these variables into an index following a similar methodology to Diex Roux et al.²⁴
- 4.3.2. Neighborhood-level
 - 4.3.2.1. Geocoding of the CCSS cohort
 - 4.3.2.1.1. Baseline address used at recruitment.
 - 4.3.2.1.1.1. Approximately n=23,000 survivors and n=1500 sibilings have addresses at time of recruitment to send for geocoding. Note we will look to see if this is a biased sample by comparing those with address at recruitment vs those without before proceeding with analysis.
 - 4.3.2.1.2. Last follow up known address at date of most recent follow up
 - 4.3.2.1.2.1. Approximately n=21,000 survivors and n=1300 sibilings have addresses at at least one follow-up timepoint.
 - 4.3.2.1.3. Yields X,Y coordinates that can then be used to link a survivor to a geographical unit (e.g., county, census tract, block group). Area data are then merged by geographical unit to describe the characteristics of the location where a participant resides. A CCSS protocol led by Carrie Howell is currently being amended to allow for an outside company called Geocodio to complete the geocoding.
 - 4.3.2.2. Neighborhood SES (nSES)²⁵⁻³⁰ census tract level
 - 4.3.2.2.1. Developed by Yost²⁷ (sometimes referred to as the Yost SES index). Utilizes 7 components from the census that cover categories of: education, income and home values, and employment status. Once connected to our data by census tract of residence, principal component

analysis is used to develop a weighted linear combination of the census variables to create a value for each census tract. Data are then divided into quintiles for analysis. Will need to align census data wth survey years.

- 4.3.2.3. Rurality census tract level. Defined using RUCA codes (Rural-Urban Commuting Area Codes) utilized by the USDA. Codes range from 1-10, will group into four categories: Metropolitan area, Micropolitan area, Small town, Rural.
- 4.3.2.4. Additional neighborhood-level data
 - 4.3.2.4.1. County Health Rankings: Includes indicators of health outcomes, health behaviors, clinical care, social and economic factors, and environment. We will take care to link specific releases of area level data to match the closest date of survey when characterizing a survivor's residence. See attached Appendix that explains types of data, various data sources and additional focus area measures that are included in these broader groupings. As with individual SES, and to deal with multicollinearity among variables in the broad groupings, we will distill the variables into an index variable for each grouping to include in modeling.

4.4. Mediators

- 4.4.1. Health Care Access US Department of Health and Human Services Health Resources and Services Administration Data Warehouse Primary Care Service Area Data. Provides count of primary-care physicians in tract. The Division of Policy and Shortage Designation in the Health Resources and Services Administration Bureau of Health Workforce provides the following categories:
 - 4.4.1.1.1. Health Professional Shortage Areas (HPSAs) shortage of primary medical care or mental health providers in an urban or rural area, population groups, or medical or other public facilities.
 - 4.4.1.1.2. Medically Underserved Areas (MUAs) define underserved areas based on health care shortages.
 - 4.4.1.1.3. Medically Underserved Populations (MUPs) define specific groups living in a geographic area with a shortage of primary care health services who often barriers to health care
- 4.4.2. Health care utilization captured in the follow-up surveys in the section titled "Medical Care". Questions B1-B6 on the follow-up 5 survey.

4.5. Covariates / Additional variables for descriptive purposes:

- 4.5.1. Gender, race/ethnicity, age at diagnosis, age at assessment, insurance status
- 4.5.2. Health behaviors: smoking, physical activity, risky/heavy drinking
- 4.5.3. Chemotherapy, radiation, surgery: treatment exposure data including doses

5. <u>Statistical Approach</u>

5.1. For Aim 1, descriptive statistics will be used to characterize the neighborhoods (using neighborhood-level data) where survivors and siblings reside and compared between the two groups using chi-square or two sample t-tests. The associations of neighborhood characteristics with treatment exposures and other childhood cancer characteristics will be examined by multivariable linear and logistic regression analyses.

- 5.2. For Aim 2, we will first construct multi-level logistic regression models with random effects (small-area of residence as a random intercept) to assess prevalence of each type of chronic health condition with both neighborhood- and individual-level characteristics, following the theoretical model in Figure 1 above, adjusting for demographic and clinical factors including treatment exposures. We will perform this analysis for each chronic health condition group (overall, cardiac, second malignancies, neurological, endocrine, renal, and respiratory) as well as mortality in survivors. Inference on the associations with neighborhood-level characteristics and those with individual-level characteristics will be performed in a unified manner using the multi-level analysis framework. We will then utilize the mediation analysis strategy of Baron and Kenny and three stages of regression models will be constructed. We will repeat this method looking at the mediating effects of healthcare utilization.
- 5.3. The purpose of Aim 3 is to supplement/confirm the associations observed in the prevalence analysis in Aim 2 with an incidence analysis, addressing the issue of reverse-causality. We will use multi-level piecewise exponential models with random effects to explore the associations between neighborhood-level characteristics and individual-level variables at the CCSS baseline survey and subsequent incidence rates of chronic conditions. As in Aim 2, we will estimate associations for each chronic condition group as well as mortality in survivors.

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Appendix 1. County health rankings data

| FOCUS AREA | MEASURE | SOURCE | | |
|----------------------|---|---|--|--|
| HEALTH OUTCOM | ÆS | | | |
| Mortality | Premature death —Years of potential life lost before age 75 (YPLL-75) rate | Vital Statistics, National Center for Health Statistics (NCHS | | |
| Morbidity | Self-reported health—Percent of adults reporting fair or poor health | Behavioral Risk Factor Surveillance System (BRFSS) | | |
| | Mean physically unhealthy days/month for adults | BRFSS | | |
| | Mean mentally unhealthy days/month for adults | BRFSS | | |
| | Percent of live births with low birthweight (< 2500 grams) | Vital Statistics, NCHS | | |
| HEALTH FACTOR | RS: HEALTH BEHAVIORS | | | |
| Tobacco Use | Percent of adults that report currently smoking | BRFSS | | |
| Diet and Exercise | Percent of adults that report a BMI ≥ 30 | Centers for Disease Control and Prevention | | |
| Alcohol Use | MV deaths per 100K population (crude rate) | Vital Statistics, NCHS | | |
| | Percent of adults that report binge drinking in the past 30 days | BRFSS | | |
| Sexual Behavior | Chlamydia rate per100K population | Centers for Disease Control and Prevention | | |
| | Teen birth rate per 1,000 female population, ages 15–19 | Vital Statistics, NCHS | | |
| HEALTH FACTOR | RS: CLINICAL CARE | | | |
| Access to Care | Percent of population < age 65 without health insurance | Small Area Health Insurance Estimates (SAHIE), Census | | |
| | Primary care provider rate per 100K | Health Resources and Services Administration, Area | | |
| | | Resource File (ARF) | | |
| Quality of Care | Hospitalization rate for ambulatory-care sensitive conditions | Medicare claims/Dartmouth Atlas | | |
| | Percent of diabetic Medicare enrollees that receive HbA1c screening | Medicare claims/Dartmouth Atlas | | |
| | Percent of chronically ill Medicare enrollees in hospice care last 6 months of life | Medicare claims/Dartmouth Atlas | | |
| HEALTH FACTOR | S: SOCIAL & ECONOMIC FACTORS | | | |
| Education | Averaged freshman graduation rate—Percent of ninth grade cohort that graduates | National Center for Education Statistics | | |
| | in 4 years | | | |
| | Percent of population age 25+ with 4-year college degree or higher | American Community Survey (ACS) | | |
| Employment | Percent of population age 16+ unemployed but seeking work | Local Area Unemployment Statistics, Bureau of Labor | | |
| | | Statistics | | |
| Income | Percent of children in poverty | Census/CPS—Small Area Income and Poverty Estimates | | |
| | | (SAIPE) | | |
| | Gini coefficient of income inequality | Decennial Census | | |
| Family and Social | Percent of adults without social/emotional support | BRFSS | | |
| Support | Percent of all households that are single-parent households | American Community Survey (ACS) | | |
| Community Safety | Violent crime rate per 100K population | Uniform Crime Reporting, Federal Bureau of Investigation | | |
| | Homicide death rate per 100K population (age-adjusted) | Vital Statistics, NCHS | | |
| HEALTH FACTOR | S: ENVIRONMENT | | | |
| Environmental | Annual number of unhealthy air quality days due to ozone | CDC-Environmental Protection Agency (EPA) | | |
| Quality | Annual number of unhealthy air quality days due to fine particulate matter | Collaboration | | |
| Built Environment | Percent of zip codes in county with healthy food outlets | Census Zip Code Business Patterns | | |
| | Liquor store density | Census County Business Patterns | | |

| | Survivors (N=XXXXX) | Siblings (N=XXXXX) | p-value |
|---------------------------------|------------------------|-----------------------|---------|
| Demographics | | | |
| Sex | | | |
| Male | | | |
| Female | | | |
| Age at Baseline | | | |
| 18-29 years | | | |
| 30-39 years | | | |
| 40-49 years | | | |
| \geq 50 years | | | |
| Race | | | |
| NHW | | | |
| NHB | | | |
| Hispanic | | | |
| Other | | | |
| Household income | | | |
| <\$40,000 | | | |
| ≥\$40,000 | | | |
| Not reported | | | |
| Educational attainment | | | |
| Less than high school | | | |
| High school graduate | | | |
| College graduate | | | |
| Post graduate | | | |
| Not specified | | | |
| Employment status | | | |
| Employed | | | |
| Unemployed, or looking for jobs | | | |
| Student or retired | | | |
| Not specified | | | |
| Health Insurance | | | |
| Yes | | | |
| No | | | |
| Health Behaviors | | | |
| Smoking | | | |
| Never | | | |
| Current | | | |
| Former | | | |
| Not reported | | | |
| Physical Activity | | | |
| <150 minutes / week | | | |
| ≥150 minutes/week | | | |
| Heavy drinking | | | |
| No, N (%) | | | |
| Yes, N (%) | | | |
| Chronic Conditions | | | |
| | | | 1 |

 Table 1. Demographic and chronic condition characteristics of survivors and siblings

| Grade 3-4 chronic condition, N (%) | | |
|--|--|--|
| Duration (years) | | |
| Mean (SD) | | |
| Median | | |
| Range [Min–max] | | |
| Endocrine condition grade 3-4, N (%) | | |
| Duration (years) | | |
| Mean (SD) | | |
| Median | | |
| | | |
| Range [Min-max] | | |
| Respiratory condition grade 3-4, N (%) | | |
| Duration (years) | | |
| Mean (SD) | | |
| Median | | |
| Range [Min–max] | | |
| Cardiac condition grade 3-4, N (%) | | |
| Duration (years) | | |
| Mean (SD) | | |
| Median | | |
| Range [Min–max] | | |
| Renal condition grade 3-4, N (%) | | |
| Duration (years) | | |
| Mean (SD) | | |
| Median | | |
| Range [Min–max] | | |
| SMN grade 3-4 , N (%) | | |
| Duration (years) | | |
| Mean (SD) | | |
| Median | | |
| Range [Min–max] | | |
| Neurologic condition grade 3-4 , N (%) | | |
| Duration (years) | | |
| Mean (SD) | | |
| Median | | |
| Range [Min–max] | | |
| Musculoskeletal condition grade 3-4, N (%) | | |
| Duration (years) | | |
| | | |
| Mean (SD) | | |
| Median | | |
| Range [Min-max] | | |
| All other grade 3-4 conditions, N (%) | | |
| Duration (years) | | |
| Mean (SD) | | |
| Median | | |
| Range [Min–max] | | |

| | | Baseline | Follow-up | | | |
|--|-----------|-----------|------------------|-----------|-----------|---------|
| Neighborhood Characteristic | Survivors | Siblings | Siblings p-value | | Siblings | p-value |
| nSES ^a | N (%) | N (%) | | N (%) | N (%) | |
| Quintile 1 | | | | | | |
| Quintile 2 | | | | | | |
| Quintile 3 | | | | | | |
| Quintile 4 | | | | | | |
| Quintile 5 | | | | | | |
| Rurality ^b | N (%) | N (%) | | N (%) | N (%) | |
| Metropolitan area | | | | | | |
| Micropolitan area | | | | | | |
| Small town | | | | | | |
| Rural | | | | | | |
| Area level health outcomes | Mean (SD) | Mean (SD) | | Mean (SD) | Mean (SD) | |
| Mortality | | | | | | |
| YPLL Rate | | | | | | |
| Morbidity | | | | | | |
| Percent with poor/fair health | | | | | | |
| Physically unhealthy days/month | | | | | | |
| Mentally unhealthy days/month | | | | | | |
| Percent low birth weight births | | | | | | |
| Area level health behaviors | Mean (SD) | Mean (SD) | | Mean (SD) | Mean (SD) | |
| Smoking | | | | | | |
| Percent adult current smokers | | | | | | |
| Obesity | | | | | | |
| Percent adults BMI \ge 30kg/m ² | | | | | | |
| Alcohol use | | | | | | |
| Percent of adult binge drinking | | | | | | |
| <u>Area level clinical care</u> | Mean (SD) | Mean (SD) | | Mean (SD) | Mean (SD) | |
| Access to care | | | | | | |

Table 2. Neighborhood characteristics at baseline and follow-up for survivors and siblings

| Percent adults without health insurance | | | | | |
|---|-----------|-----------|-----------|-----------|--|
| Quality of care | | | | | |
| Primary care provider rate per 100k | | | | | |
| Preventable hospital stay rate | | | | | |
| Percent receive diabetes screening | | | | | |
| Percent admitted to hospice | | | | | |
| Area level social and economic factors | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | |
| Education | | | | | |
| Averaged freshman graduation rate | | | | | |
| Percent with 4yr college degree or higher | | | | | |
| Employment | | | | | |
| Percent unemployed | | | | | |
| Income | | | | | |
| Percent of children in poverty | | | | | |
| GINI coefficient of income inequality | | | | | |
| Family and social support | | | | | |
| Percent adults without social/emotional | | | | | |
| support | | | | | |
| Percent single parent households | | | | | |
| Community safety | | | | | |
| Violent crime rate | | | | | |
| Age adjusted homicide rate | | | | | |
| Area level physical environment | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | |
| Environmental quality | | | | | |
| Number of days unhealthy air quality | | | | | |
| Built environment | | | | | |
| Percent with access to healthy foods | | | | | |
| Liquor store rate | | | | | |

a: Developed using seven census variables that are combined to create a weighted linear combination. Higher quintiles indicate poorer socio-economic status in the survivor's place of residence.

b: Defined using the USDA's Rural-Urban Commuting Code classifications.

| Baseline | Chemotherapy | Radiation | Surgery | Followup | Chemotherapy | Radiation | Surgery |
|-------------------|--------------|-----------|---------|------------------|--------------|-----------|---------|
| Neighborhood | | | | Neighborhood | | | |
| Characteristic | | | | Characteristic | | | |
| | β or OR | β or OR | β or OR | | β or OR | β or OR | β or OR |
| <u>nSES</u> | | | | <u>nSES</u> | | | |
| Quintile 1 | | | | Quintile 1 | | | |
| Quintile 2 | | | | Quintile 2 | | | |
| Quintile 3 | | | | Quintile 3 | | | |
| Quintile 4 | | | | Quintile 4 | | | |
| Quintile 5 | | | | Quintile 5 | | | |
| Rurality | | | | Rurality | | | |
| Metropolitan area | | | | Metropolitan | | | |
| | | | | area | | | |
| Micropolitan area | | | | Micropolitan | | | |
| | | | | area | | | |
| Small town | | | | Small town | | | |
| Rural | | | | Rural | | | |
| Area level health | | | | Area level | | | |
| <u>outcomes</u> | | | | <u>health</u> | | | |
| | | | | outcomes | | | |
| Mortality | | | | Mortality | | | |
| YPLL Rate | | | | YPLL Rate | | | |
| Morbidity | | | | Morbidity | | | |
| Percent with | | | | Percent with | | | |
| poor/fair health | | | | poor/fair health | | | |
| Physically | | | | Physically | | | |
| unhealthy | | | | unhealthy | | | |
| days/month | | | | days/month | | | |

Table 3. Unadjusted associations between baseline neighborhood characteristics and treatment exposures among survivors

| Mentally | Mentally | |
|----------------------|----------------------|--|
| unhealthy | unhealthy | |
| days/month | days/month | |
| Percent low birth | Percent low | |
| weight births | birth weight | |
| | births | |
| Area level health | <u>Area level</u> | |
| <u>behaviors</u> | health | |
| | <u>behaviors</u> | |
| Smoking | Smoking | |
| Percent adult | Percent adult | |
| current smokers | current smokers | |
| Obesity | Obesity | |
| Percent adults | Percent adults | |
| $BMI \ge 30 kg/m^2$ | $BMI \ge 30 kg/m^2$ | |
| Alcohol use | Alcohol use | |
| Percent of adult | Percent of adult | |
| binge drinking | binge drinking | |
| <u>Area level</u> | <u>Area level</u> | |
| <u>clinical care</u> | <u>clinical care</u> | |
| Access to care | Access to care | |
| Percent adults | Percent adults | |
| without health | without health | |
| insurance | insurance | |
| Quality of care | Quality of care | |
| Primary care | Primary care | |
| provider rate per | provider rate | |
| 100k | per 100k | |
| Preventable | Preventable | |
| hospital stay rate | hospital stay | |
| | rate | |

| Percent receive | Percent receive | |
|-------------------|------------------|--|
| diabetes | diabetes | |
| screening | screening | |
| Percent admitted | Percent | |
| to hospice | admitted to | |
| r r r | hospice | |
| Area level social | Area level | |
| and economic | social and | |
| factors | economic | |
| | factors | |
| Education | Education | |
| Averaged | Averaged | |
| freshman | freshman | |
| graduation rate | graduation rate | |
| Percent with 4yr | Percent with | |
| college degree or | 4yr college | |
| higher | degree or higher | |
| Employment | Employment | |
| Percent | Percent | |
| unemployed | unemployed | |
| Income | Income | |
| Percent of | Percent of | |
| children in | children in | |
| poverty | poverty | |
| GINI coefficient | GINI | |
| of income | coefficient of | |
| inequality | income | |
| | inequality | |
| Family and | Family and | |
| social support | social support | |
| Percent adults | Percent adults | |
| without | without | |

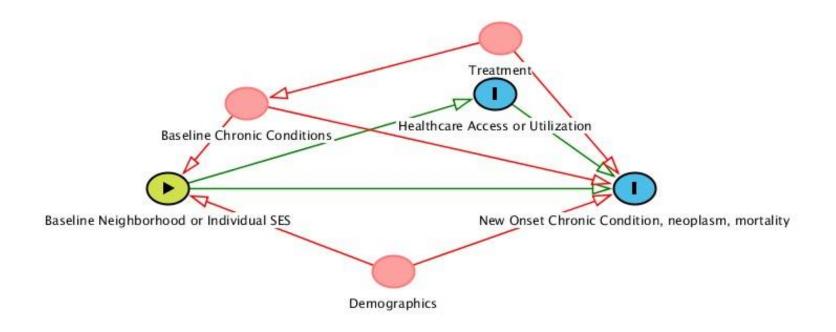
| social/emotional | social/emotiona | |
|--------------------|--------------------|--|
| support | l support | |
| Percent single | Percent single | |
| parent households | parent | |
| | households | |
| Community | Community | |
| safety | safety | |
| Violent crime rate | Violent crime | |
| | rate | |
| Age adjusted | Age adjusted | |
| homicide rate | homicide rate | |
| <u>Area level</u> | <u>Area level</u> | |
| <u>physical</u> | physical | |
| environment | <u>environment</u> | |
| Environmental | Environmental | |
| quality | quality | |
| Number of days | Number of days | |
| unhealthy air | unhealthy air | |
| quality | quality | |
| Built | Built | |
| environment | environment | |
| Percent with | Percent with | |
| access to healthy | access to | |
| foods | healthy foods | |
| Liquor store rate | Liquor store | |
| | rate | |

| Neighborhood | Any | Cardiac | SMN | Neurological | Musculoskeletal | Endocrine | Renal | Respiratory | Mortality |
|------------------------|----------------------|------------|------------|--------------|-----------------|------------|------------|-------------|------------|
| Characteristic | chronic condition | conditions | conditions | conditions | conditions | conditions | conditions | conditions | |
| | PR (95%CI) | PR (95%CI) | PR (95%CI) | PR (95%CI) | PR (95%CI) | PR (95%CI) | PR (95%CI) | PR (95%CI) | PR (95%CI) |
| Model One ^b | | | | | | | | | |
| Individual SES | | | | | | | | | |
| Index | | | | | | | | | |
| Neighborhood | | | | | | | | | |
| Level SES Index | | | | | | | | | |
| Rural vs Urban | | | | | | | | | |
| | | | | | | | | | |
| Model Two ^c | | | | | | | | | |
| Individual SES | | | | | | | | | |
| Index | | | | | | | | | |
| Rural vs Urban | | | | | | | | | |
| Area level health | | | | | | | | | |
| outcomes index | | | | | | | | | |
| Area level health | | | | | | | | | |
| behaviors index | | | | | | | | | |
| Area level clinical | | | | | | | | | |
| care index | | | | | | | | | |
| Area level social | | | | | | | | | |
| and economic | | | | | | | | | |
| factors index | | | | | | | | | |
| Area level | | | | | | | | | |
| physical | | | | | | | | | |
| environment | | | | | | | | | |
| index | | | | | | | | | |

Table 4. Associations between follow-up neighborhood characteristics and chronic condition prevalence among survivors^a

PR: Prevalence rate ratio; a: adjusted for demographic and clinical factors, including treatment exposures; b: Model 1 will include neighborhood SES described using the Yost SES index and derived through census tract indicators; c: Model 2 will include additional area level data but without the Yost SES Index

Figure 2. Directed acyclic graph that will guide the mediation analysis



| Neighborhood | Any | Cardiac | SMN | Neurological | Musculoskeletal | Endocrine | Renal | Respiratory | Mortality |
|------------------------|----------------------|------------|------------|-----------------|-----------------|------------|------------|------------------------|---------------|
| Characteristic | chronic condition | conditions | conditions | conditions | conditions | conditions | conditions | conditions | |
| | β (SE) | β (SE) | β (SE) | β (SE) | β (SE) | β (SE) | β (SE) | β (SE) | β (SE) |
| Model One ^b | p (3E) | p (5E) | μ (SE) | р (<u>БЕ</u>) | p (BE) | p (BE) | p (BE) | p (3E) | р (ВЕ) |
| Individual SES | | | | | | | | | |
| Index | | | | | | | | | |
| Neighborhood | | | | | | | | | |
| Level SES Index | | | | | | | | | |
| Rural vs Urban | | | | | | | | | |
| | | | | | | | | | |
| Model Two ^c | | | | | | | | | |
| Individual SES | | | | | | | | | |
| Index | | | | | | | | | |
| Rural vs Urban | | | | | | | | | |
| Area level health | | | | | | | | | |
| outcomes index | | | | | | | | | |
| Area level health | | | | | | | | | |
| behaviors index | | | | | | | | | |
| Area level clinical | | | | | | | | | |
| care index | | | | | | | | | |
| Area level social | | | | | | | | | |
| and economic | | | | | | | | | |
| factors index | | | | | | | | | |
| Area level | | | | | | | | | |
| physical | | | | | | | | | |
| environment | | | | | | | | | |
| index | | | | | | | | | |

Table 5. Associations between baseline neighborhood characteristics and duration of new onset chronic conditions among survivors^a

PR: Prevalence rate ratio; a: adjusted for demographic and clinical factors, including treatment exposures; b: Model 1 will include neighborhood SES described using the Yost SES index and derived through census tract indicators; c: Model 2 will include additional area level data but without the Yost SES Index