**Supplemental Digital Content**

**The Contribution of Residential Greenness to Mortality among Men with Prostate Cancer: A Registry-based Cohort Study of Black and White Men**

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**eMethods 1. Supplementary Statistical Appendix**

This appendix provides additional details regarding procedures used for the following analyses conducted in our study:

1. Methods to estimate the impact of hypothetical interventions to increase residential greenness on racial disparities in mortality among men with prostate cancer
2. Sensitivity analyses for competing risks
3. Sensitivity analyses to estimate minimum bounds of bias due unmeasured confounding

**1. Methods to Evaluate Impact of Policy to Increase Residential Greenness on Racial Disparities in Mortality**

We used epidemiologic methods for causal mediation analysis to evaluate whether increasing residential greenness could reduce racial disparities in mortality among men with prostate cancer. Briefly, causal mediation analysis is an analytic approach that allows decomposition of a total effect into a portion that is attributable only to exposure in the absence of a mediator (defined as the *natural direct effect*), and a portion that is attributable to the exposure’s effect on the outcome which flows through the mediator (*natural indirect effect*) (12, 39). In this framework, an effect is defined as the difference in potential outcomes that would be observed in the presence or absence of an exposure.

Causal mediation analysis also allows estimation of the *controlled direct effect*, or the effect of an exposure on an outcome that would occur if the mediator were, possibly contrary to fact, fixed to a specific value (12, 39). Estimating the controlled direct effect is particularly useful when attempting to understand if an intervention that occurs downstream of a particular exposure can reduce the effect of that exposure (59). Estimation of the controlled direct effect requires fewer assumptions than natural direct and indirect effects, namely that (1) the covariate set accounts for confounding of the exposure and outcome (which is implicitly assumed in any observational study), and (2) confounding of the mediator and outcome (12, 39, 59).

Epidemiologists have applied this causal mediation analysis framework to study how policy changes could impact racial and socioeconomic disparities (13-15, 37). In these settings, the type of disparity (for example, the difference in mortality comparing Black and White men) is treated as the “exposure”, and the policy change is treated as the “mediator” (14). Assuming that we have sufficient covariate data to control for confounding of race and our outcome, as well as our policy and our outcome, we can estimate controlled direct effects at different levels of our policy. These controlled direct effects can be interpreted as the disparity that would remain following implementation of the policy under study. Concretely, in our study, controlled direct effects correspond to the residual racial disparities in cause-specific mortality following implementation of hypothetical interventions or policies to fix Normalized Difference Vegetation Index (NDVI) for all men with prostate cancer to specific values.

Since the key focus of this analysis was understanding the extent to which racial disparities could be reduced by increasing residential greenness, we estimated the proportion of racial disparity that would be eliminated by fixing NDVI to the 75th percentile experienced by White men with prostate cancer using the equation below (59):

**Equation 1.**

$Proportion Eliminated= \frac{Racial Disparity-Controlled Direct Effect(NDVI= NDVI at 75th percentile for White Men)}{Racial Disparity}$

We modeled counterfactual 10-year mortality risks for Black and White CaP cases under different levels of NDVI using Cox proportional hazards models. For estimation of the overall racial disparity in mortality, we fit Cox model 1 described in the methods, omitting the NDVI variable. For estimation of controlled direct effects, we fit Cox models using the covariates in model 1, and additionally including a term for continuous NDVI and a term for the interaction between NDVI and race (12, 39). We calculated the survival proportion at each failure time using the Breslow method (60). We then standardized these race-specific counterfactual 10-year mortality risks to the total study population using Robins’ g-formula, a simulation-based procedure. We made three copies of the dataset, one which contained the observed data, one in which the race of all participants was set to White, and one in which the race of all participants was set to Black. Since estimates preserve the distribution of covariates defined above, model estimates correspond to 10-year cause-specific mortality in each racial group, standardized to confounders in the total population (38).

We then computed 10-year mortality risk differences using the standardized 10-year mortality for Black men and White men with CaP, and obtained 95% confidence intervals using 500 bootstrapped samples (38). We repeated this approach separately for each mortality outcome in the total population. We then repeated the analysis separately for high (≥1000 people/mi2) and low (<1000 people/mi2) population density areas because most Black study participants lived in high population density areas. In addition, since NDVI varied between high and low population density areas, thresholds for each policy were set separately by level of population density.

**2. Competing Risks**

When assessing prostate- and CVD-specific mortality, to assess sensitivity to competing risks, we calculated inverse probability of censoring weights for all other causes of death using multiple logistic regression (31). Briefly, the weights simulate experience of a “pseudopopulation” in which death from other causes cannot occur, and so models associations of interest in the absence of those competing risks of death. We compared estimates from these weighted models to our primary analysis to determine whether competing risks would lead to changes in our inference. Since we did not find evidence that competing risks resulted in major changes in inference, we did not apply this approach to our primary analyses.

**3. Unmeasured Confounding**

We computed E-values to estimate bounds of bias due to unmeasured confounding for each hazard ratio point estimate and confidence interval reported in Table 2 (40). The E-value quantifies the minimum strength of the relative association between an unmeasured confounder and either exposure or outcome, conditional on covariates, required to attenuate the observed point estimate to the null value of 1. For confidence intervals, the E-value represents the minimum association needed to shift the confidence interval limit closest to 1 to contain that null value. Larger E-values suggest stronger bias due to unmeasured confounding would be needed to explain the reported association. Smaller E-values provide weaker evidence against unmeasured confounding bias as an explanation for reported findings.

We computed E-values for point estimates and confidence intervals for each of the adjusted hazard ratios estimated for the association between NDVI and cause-specific mortality, under the different sets of confounders in Table 2 of our main manuscript.

**eTable 1. Pearson Correlation Coefficients between census Block Group socioeconomic variables among 128,568 men with Prostate Cancer in Pennsylvania**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Race-Income ICE** | **Median Income** | **% Poverty** | **% Less than high school education** | **Median Home Value** |
| **Race-Income ICE** | 1 | 0.7704 | -0.6378 | -0.5684 | 0.72266 |
|   | <.0001 | <.0001 | <.0001 | <.0001 |
| **Median Income** |   | 1 | -0.5277 | -0.6178 | 0.83861 |
|   |   | <.0001 | <.0001 | <.0001 |
| **% Poverty** |   |   | 1 | 0.50691 | -0.4283 |
|   |   |   | <.0001 | <.0001 |
| **% Less than high school education** |   |   |   | 1 | -0.5267 |
|   |   |   |   | <.0001 |
| **Median Home Value** |   |   |   |   | 1 |
|   |   |   |   |   |

**Abbreviations: ICE = Index Concentration at the Extremes**

**eTable 2. Sensitivity Analysis for Competing Risks: Cox Proportional Hazards Model Estimates of Association between Normalized Difference Vegetation Index (NDVI) at Diagnosis and Prostate-specific Mortality and Cardiovascular Mortality using Inverse Probability of Censoring Weights**

|  |  |
| --- | --- |
| **Prostate-specific Mortality** | **Cardiovascular-specific Mortality** |
|  | **Cases/Person-Yearsa** | **aHR (95% CI)** |  | **Cases/Person-Yearsa** | **aHR (95% CI)** |
| *Population Density* |  |  | *Race* |  |  |
| *Low* | 6,742/700,116 |  | *White* | 10,472/881,646 |  |
|  Linear (per 0.14 units) |  | 0.94 (0.89, 1.00) |  Linear (per 0.14 units) |  | 0.90 (0.86, 0.94) |
|  Q1 | 615/49,334 | Ref |  Q1 | 2,063/129,441 | Ref |
|  Q2 | 1,259/124,658 | 0.98 (0.85, 1.11) |  Q2 | 2,287/174,725 | 0.94 (0.86, 1.02) |
|  Q3 | 1,518/156,210 | 0.95 (0.83, 1.08) |  Q3 | 2,223/185,991 | 0.89 (0.81, 0.97) |
|  Q4 | 1,495/174,455 | 0.88 (0.77, 1.01) |  Q4 | 2,053/191,172 | 0.84 (0.76, 0.92) |
|  Q5 | 1,587/195,459 | 0.93 (0.81, 1.06) |  Q5 | 1,849/200,318 | 0.82 (0.75, 0.91) |
|   *Ptrend* |  | 0.10 |  *Ptrend* |  | <.0001 |
| *High* | 3,446/301,159 |  | *Black* | 1,289/104,019 |  |
|  Linear (per 0.14 units) |  | 0.89 (0.83, 0.94) |  Linear (per 0.14 units) |  | 0.98 (0.89, 1.08) |
|  Q1 | 1,951/146,463 | Ref |  Q1 | 827/62,223 | Ref |
|  Q2 | 738/71,551 | 0.90 (0.80, 1.02) |  Q2 | 239/18,538 | 1.06 (0.87, 1.29) |
|  Q3 | 433/43,202 | 0.90 (0.77, 1.04) |  Q3 | 101/10,297 | 0.96 (0.72, 1.28) |
|  Q4 | 238/27,660 | 0.78 (0.64, 0.94) |  Q4 | 91/7,722 | 1.21 (0.91, 1.61) |
|  Q5 | 88/12,284 | 0.75 (0.57, 0.99) |  Q5 | 32/5,239 | 0.69 (0.43, 1.1) |
|   *Ptrend* |  | 0.0028 |   *Ptrend* |  | 0.9446 |
|  *Phet* (quintiles) |  | 0.61 |  *Phet* (quintiles) |  | 0.094 |
|  *Phet* (linear) |  | 0.11 |  *Phet* (linear) |  | 0.064 |

aEstimates from pseudopopulation generated using inverse probability of censoring weights. This model simulates the experience of a population that can only exit the cohort through death from the specified cause.

**eTable 3. E-values for Robustness to Unmeasured Confounding for Cox Model Hazard Ratio Estimates of the Association between Normalized Difference Vegetation Index (NDVI) at Diagnosis and Rate of Cause-specific Mortality among men with prostate cancer**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Full** | **+ Stage/Grade** | **+ Marital Statusa** |
|  | **aHR (Lower Bound)** | **aHR (Lower Bound)** | **aHR (Lower Bound)** |
| *All-cause mortality* |  |  |  |
|  Linear (per 0.14 units) | 1.26 (1.20) | 1.24 (1.18) | 1.21 (1.15) |
|  Q1 | Ref | Ref | Ref |
|  Q2 | 1.26 (1.14) | 1.23 (1.09) | 1.19 (1.00) |
|  Q3 | 1.27 (1.15) | 1.23 (1.09) | 1.19 (1.00) |
|  Q4 | 1.38 (1.27) | 1.32 (1.20) | 1.26 (1.13) |
|  Q5 | 1.41 (1.31) | 1.37 (1.26) | 1.32 (1.20) |
| *Prostate-specific Mortality* |  |  |  |
|  Linear (per 0.14 units) | 1.35 (1.19) | 1.28 (1.06) | 1.23 (1.00) |
|  Q1 | Ref | Ref | Ref |
|  Q2 | 1.49 (1.21) | 1.35 (1.00) | 1.31 (1.00) |
|  Q3 | 1.53 (1.24) | 1.39 (1.00) | 1.34 (1.00) |
|  Q4 | 1.69 (1.41) | 1.40 (1.00) | 1.34 (1.00) |
|  Q5 | 1.52 (1.19) | 1.36 (1.00) | 1.27 (1.00) |
| *Cardiovascular Mortality* |  |  |  |
|  Linear (per 0.14 units) | 1.45 (1.32) | 1.45 (1.32) | 1.41 (1.27) |
|  Q1 | Ref | Ref | Ref |
|  Q2 | 1.29 (1.00) | 1.29 (1.00) | 1.24 (1.00) |
|  Q3 | 1.52 (1.26) | 1.52 (1.26) | 1.47 (1.19) |
|  Q4 | 1.61 (1.35) | 1.61 (1.34) | 1.53 (1.25) |
|  Q5 | 1.75 (1.47) | 1.75 (1.47) | 1.67 (1.39) |

Models adjusted for age (deciles), diagnosis year, race, census block group socioeconomic status (% poverty, median income, median home value, % 25 and older with less than high school education, joint race-income index concentration at extremes (quintiles)), site at diagnosis (University of Pennsylvania Medical Center, University of Pittsburgh Medical Center, Fox Chase, Jefferson Health), network distance to closest cancer facility (minutes), population density

aMarital Status estimated using multiple imputation

**eTable 4.** **Cox Proportional Hazards Models for Association between Cumulative Updated Average NDVI over follow-up and Cause-specific Mortality among Pennsylvania Prostate Cancer Patients Diagnosed between 2000 and 2015**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Full** | **+ Stage/Grade** | **+ Marital Statusa** |
|  | **Cases/Person-Years** | **aHR (95% CI)** | **aHR (95% CI)** | **aHR (95% CI)** |
| *All-cause mortality* | 29,978/916,590 |  |  |  |
|  Linear (per 0.14 units) |  | 1.03 (1.01, 1.05) | 1.02 (1.00, 1.05) | 1.04 (1.02, 1.06) |
|  Q1 | 6,966/176,384 | Ref | Ref | Ref |
|  Q2 | 6,431/179,028 | 0.97 (0.93, 1.01) | 0.97 (0.93, 1.01) | 0.98 (0.94, 1.02) |
|  Q3 | 5,606/187,427 | 0.87 (0.83, 0.91) | 0.89 (0.85, 0.93) | 0.91 (0.87, 0.95) |
|  Q4 | 5,253/190,346 | 0.86 (0.82, 0.90) | 0.88 (0.84, 0.92) | 0.89 (0.85, 0.94) |
|  Q5 | 5,722/183,404 | 1.11 (1.06, 1.17) | 1.11 (1.06, 1.16) | 1.13 (1.08, 1.19) |
|  *Ptrend* |  | 0.007 | 0.033 | 0.002 |
| *Prostate-specific Mortality* | 6,515/916,590 |  |  |  |
|  Linear (per 0.14 units) |  | 1.04 (1.00, 1.09) | 1.03 (0.99, 1.07) | 1.04 (1.00, 1.08) |
|  Q1 | 1,612/176,384 | Ref | Ref | Ref |
|  Q2 | 1,394/179,028 | 0.98 (0.90, 1.06) | 0.97 (0.89, 1.05) | 0.97 (0.90, 1.06) |
|  Q3 | 1,140/187,427 | 0.83 (0.76, 0.91) | 0.90 (0.82, 0.98) | 0.91 (0.83, 1.00) |
|  Q4 | 1,019/190,346 | 0.78 (0.71, 0.86) | 0.81 (0.74, 0.90) | 0.83 (0.75, 0.92) |
|  Q5 | 1,350/183,404 | 1.22 (1.10, 1.35) | 1.19 (1.07, 1.31) | 1.21 (1.09, 1.34) |
|  *Ptrend* |  | 0.021 | 0.24 | 0.0948 |
| *Cardiovascular Mortality* | 7,677/916,590 |  |  |  |
|  Linear (per 0.14 units) |  | 0.97 (0.94, 1.01) | 0.97 (0.94, 1.01) | 0.99 (0.95, 1.02) |
|  Q1 | 1,854/176,384 | Ref | Ref | Ref |
|  Q2 | 1,692/179,028 | 0.93 (0.86, 1.00) | 0.92 (0.86, 1.00) | 0.94 (0.87, 1.01) |
|  Q3 | 1,400/187,427 | 0.79 (0.72, 0.86) | 0.79 (0.72, 0.86) | 0.81 (0.74, 0.88) |
|  Q4 | 1,381/190,346 | 0.83 (0.76, 0.90) | 0.83 (0.76, 0.90) | 0.85 (0.78, 0.93) |
|  Q5 | 1,350/183,404 | 0.96 (0.87, 1.05) | 0.96 (0.87, 1.05) | 0.98 (0.89, 1.08) |
|  *Ptrend* |  | 0.33 | 0.30 | 0.61 |

Models adjusted for age (deciles), diagnosis year, race, census block group socioeconomic status (% poverty, median income, median home value, % 25 and older with less than high school education, joint race-income index concentration at extremes (quintiles)), site at diagnosis (University of Pennsylvania Medical Center, University of Pittsburgh Medical Center, Fox Chase, Jefferson Health), network distance to closest cancer facility (minutes), population density

aMissing values for marital status were obtained using multiple imputation