Dietary Patterns Associated with Food Insecurity Predict a Worse Prognosis for U.S. Cancer Survivors: NHANES 1999-2018

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**Abstract**

Purpose

Food insecurity—the lack of unabated access to nutritious foods—is a consequence many cancer survivors face. Food insecurity is associated with adverse health outcomes and lower dietary quality among the general public. In a previous analysis, we extracted dietary patterns in U.S. food insecure cancer survivors using penalized logistic regression, suggesting poor diet quality in this population. This analysis evaluated the association between these patterns and survival after a cancer diagnosis. Comparisons with other dietary patterns analysis techniques were conducted.

Methods

           We implemented two dietary pattern analysis approaches: penalized logistic regression and principal components analysis. Using nationally representative data from the National Health and Nutrition Examination Survey (NHANES) study, we extracted six dietary patterns, two of which (the FI and SNAP patterns) were positively associated with being a food insecure cancer survivor. Additionally, we evaluated the HEI-2015 for comparison. Cox proportional hazards models assessed the relationship between the diet quality indices and survival after a cancer diagnosis.

Results

           There were 981 deaths from all causes and 343 cancer-related deaths. After multivariable adjustment, we found higher risks of all-cause mortality associated with higher adherence to the FI (HR: 1.23; 95% CI: 1.06-1.42) and SNAP (HR: 1.20; 95% CI: 1.03-1.40) patterns among cancer survivors.

Conclusion

           Higher adherence to prevailing dietary patterns specific to the U.S. food insecure cancer survivor population may lead to a worse prognosis.

**Keywords**

nutritional epidemiology; survivorship; dietary patterns; food insecurity; regularization

**Introduction**

A cancer diagnosis can upend several facets of life and well-being. In addition to psychological distress from the diagnosis, financial toxicity and its accompanying distress can emerge for many cancer survivors owing to exorbitant treatment, prescription, and indirect costs (e.g., income loss due to cancer-related job loss or disability) [1]. These phenomena we describe are often magnified for low-income cancer survivors—defined as individuals with a history of cancer—who may lack financial reserves and workplace accommodations while navigating the treatment phases of their cancer [1, 2]. Thus, critical questions arise regarding how these experiences can impact cancer-related outcomes through dietary variables in cancer survivors.

Food insecurity, or the lack of continuous access to healthy and nutritious foods to lead a healthy life, can be a consequence for cancer survivors facing high financial toxicity burdens [3, 4]. A framework of competing demands conceptualizes one manifestation of food insecurity among cancer survivors, involving cancer survivors facing difficult decisions between choosing medical care or nutritious foods [3]. However, a critical public health concern is that food insecurity is associated with adverse health outcomes and lower dietary quality in the general public [5, 6]. Food insecurity may predict a worse prognosis among cancer survivors, though more research is needed to substantiate this conjecture.

Penalized, or regularized, regression emerged as a contemporary method for extracting dietary patterns from dietary intake data collected from food frequency questionnaires or 24-hour recalls [7, 8]. Shrinkage, a property of this class of regression models, is a particularly attractive feature in the setting of collinearity [9]. When using dietary intake data in regression models, collinearity is often encountered given that there tends to be a high correlation among dietary intake variables [10]. In a previous analysis, we characterized dietary patterns describing dietary consumption amongst food insecure cancer survivors using nationally representative data from the National Health and Nutrition Examination Survey (NHANES) [11]. Using penalized logistic regression as a novel supervised learning method for extracting dietary patterns from observed 24-hour recall data, we extracted two major dietary patterns strongly and positively associated with food insecurity among cancer survivors. These patterns emphasized the consumption of added sugars and processed foods and deemphasized fruit and vegetable consumption. Concurrently, we found that a “prudent” dietary pattern emerged that emphasized healthful dietary components such as fruits, vegetables, and whole grains, which was inversely associated with food insecurity in the same population. Whether these dietary patterns affected clinically meaningful outcomes for cancer survivors was left open ended.

Understanding how food insecurity affects different aspects of life, including dietary intake, is a means of delineating at least one potential driving factor behind the health disparities that may arise in cancer survivors experiencing food insecurity. Therefore, the goal of this analysis was to use nationally representative data to examine associations between dietary patterns extracted with penalized logistic regression in the food insecure cancer survivor population and the risk of mortality from various causes. We hypothesized that these dietary patterns describing consumption patterns in the food insecure cancer survivor population would be positively associated with mortality in cancer survivors and food insecure cancer survivors.

**Methods**

*Study Setting and Population*

We employed data from ten consecutive cycles (1999-2018) from the NHANES, a biennial cross-sectional study implemented by the Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics (NCHS), which sampled civilian and non-institutionalized community dwellers in the United States. The study implements a complex multi-stage sampling design that generates a nationally representative sample and aims to characterize the relationships between lifestyle, medical, environmental, and other factors, and health outcomes. It uses surveys that span numerous facets of health and lifestyle and includes a medical examination for a subset of participants.

In Figure 1, we detail the sample flow that arrived at the final analytical sample size of cancer survivors (*n* = 2493), divided into food secure participants (*n* = 2176) and food insecure participants (*n* = 317). We divided the final sample into randomly generated subsets that would be used for training machine learning models and the validation analysis. We discuss this division with greater detail in the coming sections. Food insecurity status was measured using the U.S. Department of Agriculture (USDA) U.S. Food Security Survey Module (U.S. FSSM), which consists of 18 items designed to evaluate the degree of food insecurity experienced by a participant’s household over the preceding year [12]. The survey consists of a series of “yes/no” questions, and responses in the affirmative are used to categorize a household as food insecure (responding in the affirmative to ≥ three items) or food secure (responding in the affirmative to ≤ two items). Cancer history was ascertained via self-reporting using the Medical Conditions Questionnaire (MCQ). Individuals diagnosed with non-melanoma skin cancer and no other cancer were coded as having no history of cancer, given that the prognosis and benign course of this class of malignancies may otherwise bias the sample [13].

Diagram

Description automatically generated

**Figure 1**. Sample flow diagram detailing inclusion and exclusion criteria for arriving at the final sample and the overall analytical plan.

*nfi* = food insecure subset sample size.

*Explanatory Variables: Diet Quality Measures*

NHANES study staff assessed dietary intake through two 24-hour recalls using the USDA Automated Multiple-Pass Method—for cycles between 1999-2002, only a single 24-hour recall was performed [14, 15]. Nutrient intake data were estimated by referencing the Food and Nutrient Database for Dietary Studies (FNDDS). Dietary intake and nutrient intake data were averaged across both 24-hour recalls as previously described [11, 16, 17]. We used the USDA Food Patterns Equivalents Database (FPED) and the MyPyramid Equivalents Database (MPED) to obtain intake equivalents of 37 USDA food pattern components, collapsed further into 26 groups, as previously described [11]. Empirical diet quality measures were extracted from observed dietary data using penalized logistic regression (penalized logit) and principal components analysis (PCA). These 26 food groups were the explanatory variables in these models (see Table 2 for the food groups used in this analysis). In the case of the penalized logit model, food insecurity status (*food insecure*/*food secure*) was regressed on the centered and scaled transformations of the food group variables and total calories—i.e., the latter was included to implement the standard multivariate method for total energy adjustment described by Willett et al. [18]. We trained this model on a random sample (referred to as the “training subsample” here forth) of *n* = 748 subjects (30% of original sample—see Figure 1). PCA for dietary patterns extraction was performed on the food insecure subjects of this training subsample (*n* = 104). The out-of-sample validation analysis (see *Statistical Analysis* section below) was performed on the remaining fraction (*n* = 1745—comprising 70% of the original sample) of subjects (referred to as the “testing subsample” here forth). The supplementary methods file contains additional details about these procedures. For the sake of comparison, we also computed Healthy Eating Index 2015 (HEI-2015) scores and incorporated them into all of the subsequent analyses [19, 20]. The dietary patterns scores generated with PCA and the HEI-2015 scores were energy-adjusted using the residual method [18].

*Response Variables: All-Cause and Cause-Specific Mortalities*

Mortality and time-to-event data were acquired from the NHANES Public-Use Linked Mortality File, which was generated from deterministic and probabilistic linkages of the NHANES survey data (through the 2017-2018 cycle) to the National Death Index, as described elsewhere [21]. We computed time since diagnosis, defined as the difference between the age at the time of the survey and the age at the first cancer diagnosis, and used it as the time scale in our models to minimize potential bias by accounting for left truncation due to delayed study enrollment following diagnosis [22, 23]. Data were right-censored to either the last known date alive or the administrative censoring date on December 31, 2019. We used the International Classification of Diseases, Tenth Revision (ICD-10) codes to classify the causes of death. Survival analyses examined all-cause mortality and cause-specific mortality—deaths due to neoplastic malignancy (ICD-10 codes C00-C97).

*Covariates*

Self-reported demographic and socioeconomic data were obtained during the home interview. Characteristics from the demographic survey (DEMO) included age, sex (*male*/*female*), race and ethnicity (*non-Hispanic White* and *other*), family income-to-poverty ratio (*< 1.3* or *≥ 1.3*), and household size. We obtained health insurance status (*covered by health insurance*/*not covered by health insurance*) from the Health Insurance Questionnaire (HIQ/HID—for 1999-2004). Behavioral characteristics included smoking status (*current smoker*—currently smoking every day or some days—, *former smoker*—not currently smoking but with a lifetime history of ≥ 100 cigarettes— , or *never smoker*—a lifetime history of smoking < 100 cigarettes), drinking status (*heavy drinker*— ≥ 14 g/day for women and ≥ 28 g/day for men—, *moderate drinker*—0.10-13.9 grams/day for women and 0.10-27.9 g/day for men—, and *abstainer*— < 0.10 grams/day), and physical activity (*measured as weekly MET minutes*). These data were obtained from the Smoking Questionnaire (SMQ), 24-hour recalls, and physical activity questionnaires (PAQ and PAQIAF), respectively. Health-related covariates included the Charlson Comorbidity Index score (adapted for NHANES) and body mass index (BMI—kilograms/m2) measured during the physical examination. Physical disability was assessed using the 19-item and validated NHANES Activities of Daily Living (ADL) scale from the Physical Functioning Questionnaire (PFQ), which is described in detail elsewhere [24]. Cancer-related covariates were obtained from the MCQ.

*Statistical Analysis*

We assessed the relationship between diet quality measures and all-cause and cause-specific mortality using Cox Proportional Hazards models. This was an out-of-sample validation analysis performed on the *n* = 1745 subjects not used to extract the dietary patterns (Figure 1). We implemented several model specifications for the conditional log hazard function to assess the robustness of our results (Equations 1-4).

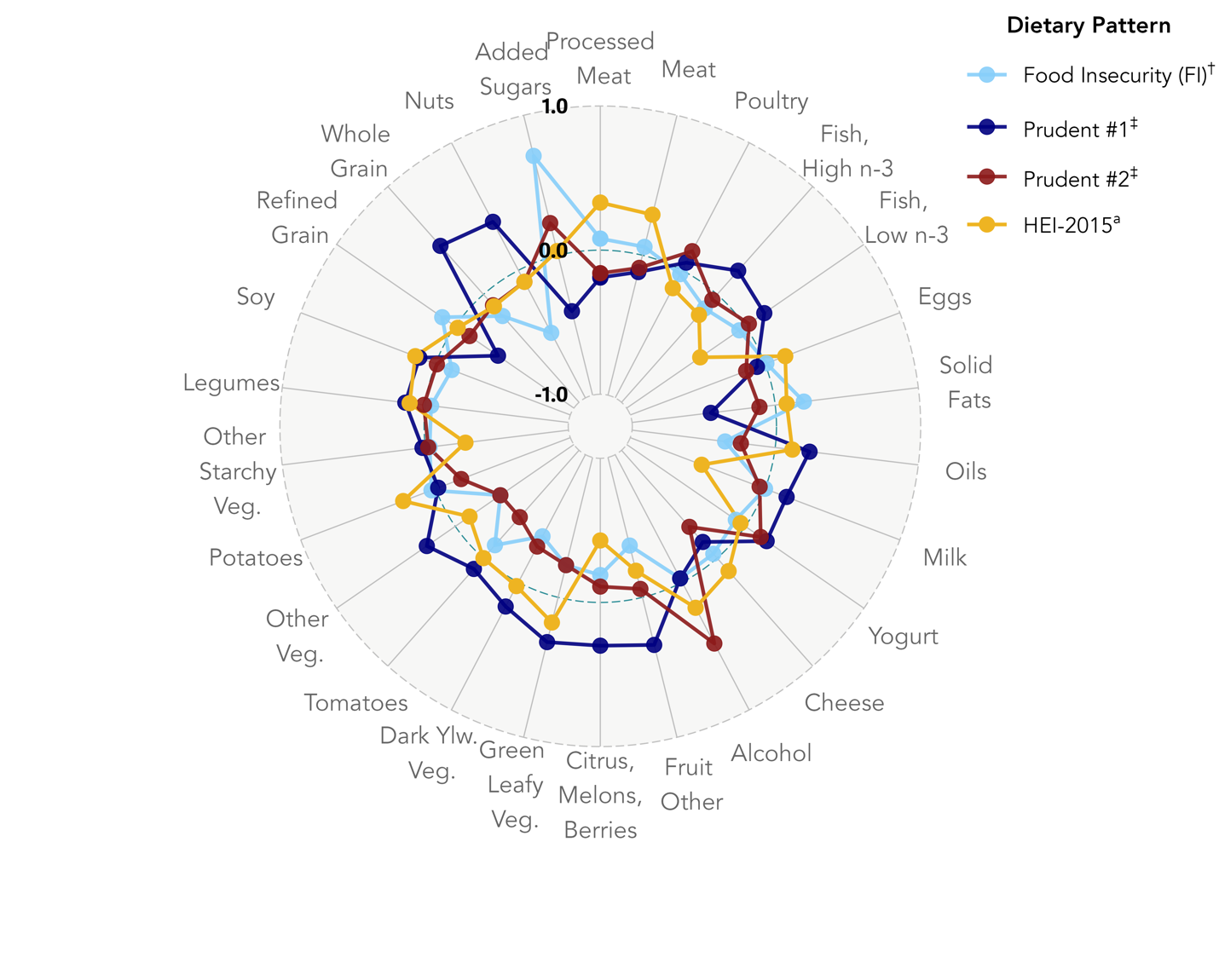
The model in Equation 1 specifies the diet quality index using 1 dummy variables, , which indicates the subject’s membership in one of the quintiles () of the dietary pattern index score. In Equation 2, we conduct a trend test by assigning the subject the median of their respective quintile (where is the set of diet quality index scores for subjects in the quintile) and then modeling it as a continuous variable (). In Equation 3, we specify the diet index as a continuous variable scaled by the standard deviation of the index and in equation 3 we specify the diet index () with a basis expansion of basis functions (see supplementary methods file) for a natural cubic spline. The model fit using Equation 4 used one interior boundary knot (). Given that Model 3 is nested in Model 4, we used the likelihood ratio test to assess for non-linearity [25]. Additionally, all models included parameters () for covariates (). We fit these models to data for the entire sample of cancer survivors in the testing subsample (*n*  = 1745) and separately for food insecure cancer survivors (*n* = 213). Furthermore, we used sequential adjustment within these model specifications. A *Null* model did not adjust for any covariates beyond the dietary pattern index score. A *Basic* model further adjusted for age, sex, and race and ethnicity. A *Full* model further adjusted for BMI, household size, family income-to-poverty ratio, education status, health insurance status, alcohol intake, smoking status, calories, weekly MET minutes, Charlson Comorbidity Index score, food insecurity status, and receipt of SNAP benefits [26, 27]. Covariates were selected *a priori* based on previous literature and working knowledge of potential confounders in the hypothesized pathway. To account for the possibility of downwardly biased survival estimates from the contributions of participants distantly removed from a cancer diagnosis to the risk set, we conducted a sensitivity analysis including only participants with a primary cancer diagnosis within the four years preceding the date of their interview (*n* = 535). We also considered the NHANES ADL score as a covariate, given that food security can be associated with physical disability and functional deficits. However, we did not include it in our primary models, given the significant missingness in this variable. Instead, we conducted a sub-analysis where we further adjusted for physical disability. All analyses accounted for the complex and probability-based sampling methods of the NHANES study by following the analytical guidelines provided by the NCHS and weighting them accordingly. We used = 0.05 as our threshold level for statistical significance and performed all analyses in R v4.2.2 (The R Foundation, Vienna, Austria). The R code and data to reproduce these analyses are publicly accessible at: <https://github.com/cmainov/nhanes-fi-ca-mortality>.

**Results**

The analysis included 603,960 person-months of contribution to the risk set, with 981 deaths from all causes, 343 cancer deaths, and 235 cardiovascular disease-related deaths. The characteristics of the study sample of cancer survivors stratified on food security status are presented in Table 1. On average, food insecure cancer survivors in this sample were younger than food secure survivors, more likely to be female, Non-Hispanic Black, Hispanic, multiracial, have a lower educational status, live under the poverty line, and less likely to be covered by health insurance. Food insecure cancer survivors were also more likely to live in a home with five or more individuals, be physically or functionally impaired, identify as current smokers, have a greater comorbidity burden, and were less likely to be heavy drinkers than their food secure counterparts.

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| **Table 1**. Epidemiologic characteristics of the study sample. | | | | |
| **Characteristic** | **Combined Sample** (*n* = 2493) | **Food insecure** (*n* = 317) | **Food secure** (*n* = 2176) | ***p*** |
| Age | 62.03 (14.85) | 50.4 (16.46) | 63.32 (14.09) | < 0.01 |
| Sex |  |  |  | < 0.01 |
| Male | 1139 (40.9) | 99 (25.1) | 1040 (42.6) |  |
| Female | 1354 (59.1) | 218 (74.9) | 1136 (57.4) |  |
| Race/Ethnicity |  |  |  | < 0.01 |
| Mexican-American | 174 (2.3) | 51 (8.0) | 123 (1.7) |  |
| Other Hispanic | 133 (2.5) | 40 (7.5) | 93 (1.9) |  |
| Non-Hispanic White | 1730 (86.5) | 156 (70.6) | 1574 (88.3) |  |
| Non-Hispanic Black | 376 (6.2) | 56 (9.2) | 320 (5.9) |  |
| Other/Multiracial | 80 (2.4) | 14 (4.6) | 66 (2.1) |  |
| Education Attained |  |  |  | < 0.01 |
| ≤ High School | 1197 (36.5) | 205 (55.5) | 992 (34.4) |  |
| ≥ Some College | 1296 (63.5) | 112 (44.5) | 1184 (65.6) |  |
| Family Income to Poverty Ratio |  |  |  | < 0.01 |
| < 1.3 | 637 (17.3) | 221 (63.5) | 416 (12.2) |  |
| Health Insurance Status |  |  |  | < 0.01 |
| Insured | 2329 (94.1) | 265 (83.7) | 2064 (95.3) |  |
| Household Size |  |  |  | < 0.01 |
| < 5 Persons | 2274 (92.5) | 247 (78.6) | 2027 (94.1) |  |
| ≥ 5 Persons | 219 (7.5) | 70 (21.4) | 149 (5.9) |  |
| NHANES ADL Score | 22.26 (4.56) | 26.1 (7.34) | 21.93 (4.07) | < 0.01 |
| BMI (kg/m2) | 28.92 (6.61) | 29.82 (7.43) | 28.82 (6.51) | 0.08 |
| Weekly MET Minutes | 2249.04 (4387.81) | 5195.27 (8691.45) | 1923.51 (3462.9) | < 0.01 |
| Daily Caloric Intake (kcal) | 1900.17 (679.88) | 1751 (791.25) | 1916.65 (664.54) | 0.02 |
| Charlson Comorbidity Index | 2.98 (1.35) | 3.36 (1.71) | 2.94 (1.3) | < 0.01 |
| SNAP Benefits |  |  |  | < 0.01 |
| Receiving | 347 (11.2) | 158 (55.6) | 189 (6.3) |  |
| Years Since Diagnosis |  |  |  | 0.84 |
| ≤ 4 years | 753 (26.6) | 104 (25.9) | 649 (26.7) |  |
| > 4 years | 1740 (73.4) | 213 (74.1) | 1527 (73.3) |  |
| Smoking Status |  |  |  | < 0.01 |
| Current | 393 (16.9) | 107 (39.2) | 286 (14.4) |  |
| Former | 1021 (39.4) | 79 (21.9) | 942 (41.3) |  |
| Never | 1079 (43.7) | 131 (38.9) | 948 (44.2) |  |
| Alcohol Use |  |  |  | 0.05 |
| Heavy | 268 (13.8) | 23 (4.6) | 245 (14.9) |  |
| Moderate | 381 (15.9) | 32 (16.1) | 349 (15.9) |  |
| None | 1844 (70.3) | 262 (79.3) | 1582 (69.3) |  |
| Cause of Death |  |  |  | 0.42 |
| Cancer | 343 (36.4) | 30 (31.9) | 313 (36.7) |  |
| Cardiovascular Dis. | 235 (25.6) | 11 (20.4) | 224 (25.9) |  |
| Other | 403 (38.0) | 41 (47.7) | 362 (37.4) |  |
| Percentages may not add to 100% given rounding.  *p-*values are from tests for categorical variables and *t*-tests for continuous variables.  Subjects were weighted, and the analysis was performed according to NCHS guidelines. | | | | |

Table 2 and Figure 2 present weighted Pearson correlation coefficients between the extracted dietary patterns and the individual food groups comprising them. The FI pattern was characterized by negative correlations with fruits, vegetables, nuts, and whole grains, a high correlation with added sugars, and a weak-to-moderate positive correlation with solid fats. Prudent #1 was negatively correlated with the consumption of oils, cheese, vegetables, and tomatoes and positively correlated with added sugar consumption and alcohol intake. Prudent #2 was positively correlated with the consumption of processed meats and other meats, alcohol, and potatoes while negatively correlated with milk, seafood, and starchy vegetable consumption. Finally, the HEI-2015 was loaded positively by several fruit and vegetable categories, nuts, whole grains, and high n-3 seafood, and negatively by several meat categories, solid fats, refined grains, and added sugars. HEI-2015 was negatively correlated with all three other patterns but most strongly with the FI pattern. On average, food insecure subjects had significantly higher scores on the FI and Prudent #1 patterns compared to food secure subjects (Table 3). Food insecure survivors also had significantly lower HEI-2015 scores compared to food secure survivors.



**Figure 2.** Radar chart with overlay of select dietary patterns and their correlations to the 26 food groups used in the dietary patterns extraction phase of the analysis.

† Dietary pattern obtained using penalized logistic regression; ‡ Dietary pattern obtained using principal components analysis.

a Healthy Eating Index 2015

Subjects were weighted, and the analysis was performed according to NCHS guidelines.

The correlation analysis was performed on subjects from the testing subsample described in the main text (*n* = 748).

All dietary patterns extraction procedures were performed on the training subsample described in the main text (*n* = 1745).

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| **Table 2**. Pearson correlation coefficients showing the contributions of each food group to the extracted dietary patterns. Correlations amongst the dietary patterns themselves are included at the bottom of the table in the lower triangular matrix form. | | | | | |
| **Pattern** | | **Food Insecurity (FI) †** | **Prudent**  **#1 ‡** | **Prudent #2 ‡** | **HEI-2015**a |
| **Food Groups** | |
| Processed Meats | | 0.080 | -0.16 | **0.33** | -0.19 |
| Meats | | 0.060 | -0.090 | **0.29** | -0.12 |
| Poultry | | -0.030 | 0.15 | -0.14 | 0.060 |
| Seafood—High n-3 | | -0.13 | -0.050 | -0.19 | **0.22** |
| Seafood—Low n-3 | | -0.050 | 0.030 | **-0.38** | 0.16 |
| Eggs | | 0.010 | -0.14 | 0.15 | -0.060 |
| Solid Fats | | **0.20** | -0.11 | 0.080 | **-0.45** |
| Oils | | **-0.35** | **-0.24** | 0.12 | **0.24** |
| Milk | | 0.00 | -0.040 | **-0.47** | 0.16 |
| Yogurt | | -0.080 | 0.13 | -0.040 | 0.18 |
| Cheese | | -0.040 | **-0.29** | 0.12 | -0.15 |
| Alcohol | | -0.030 | **0.48** | **0.20** | -0.030 |
| Fruit—Other | | **-0.37** | -0.060 | -0.19 | **0.34** |
| Fruit—Citrus, melons, and berries | | -0.19 | -0.11 | **-0.43** | **0.30** |
| Tomatoes | | -0.12 | **-0.38** | 0.00 | 0.10 |
| Dark-Green Vegetables | | **-0.23** | **-0.23** | 0.18 | **0.32** |
| Dark-Yellow Vegetables | | **-0.36** | **-0.28** | 0.030 | 0.19 |
| Other Vegetables | | **-0.38** | **-0.38** | -0.12 | **0.24** |
| Potatoes | | 0.030 | -0.19 | **0.24** | -0.020 |
| Other Starchy Vegetables | | -0.030 | -0.020 | **-0.28** | 0.020 |
| Legumes | | -0.040 | 0.010 | 0.11 | 0.14 |
| Soy | | -0.12 | -0.010 | 0.15 | 0.12 |
| Refined Grains | | 0.11 | -0.12 | -0.020 | **-0.36** |
| Whole Grains | | **-0.20** | -0.10 | -0.11 | **0.45** |
| Nuts | | **-0.49** | -0.090 | -0.090 | **0.38** |
| Added Sugars | | **0.71** | **0.23** | 0.030 | **-0.40** |
| Food Insecurity (FI)† | | -- |  |  |  |
| Prudent #1‡ | | **0.40** | -- |  |  |
| Prudent #2‡ | | 0.090 | -0.080 | -- |  |
| HEI-2015a | | **-0.64** | -0.19 | **-0.25** | -- |
| † Dietary pattern obtained using penalized logistic regression; ‡ Dietary pattern obtained using principal components analysis.  a Healthy Eating Index 2015  Correlation coefficients (*r*) ≥ |0.20| are bolded to ease the identification of notable food groups characterizing the different patterns.  This correlation analysis was performed on the testing sample described in the main text (*n* = 1745).  Subjects were weighted, and the analysis was performed according to NCHS guidelines. All dietary patterns extraction procedures were performed on the training subsample described in the main text (*n* = 748). | | | | | |
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| **Table 3**. Means and standard deviations of the extracted dietary patterns across levels of food security status. | | | | | |
| **Dietary Pattern** | **Combined Sample**  (*n* = 1745) | **Food-insecure** (*n* = 213) | **Food-secure** (*n* = 1532) | **Cohen’s *d*** | ***p*** |
| Food Insecurity Pattern†  Mean (SD) | -0.02 (0.17) | 0.07 (0.2) | -0.03 (0.16) | 0.23 | < 0.01 |
| Prudent Pattern #1‡  Mean (SD) | -0.03 (0.63) | 0.10 (0.52) | -0.04 (0.64) | 0.18 | < 0.01 |
| Prudent Pattern #2‡  Mean (SD) | 0.13 (0.91) | 0.23 (0.88) | 0.12 (0.92) | 0.12 | 0.10 |
| HEI-2015a  Mean (SD) | 55.13 (14.3) | 50.84 (12.44) | 55.61 (14.42) | -1.30 | < 0.01 |
| *p-*values are for survey-weighted t-tests comparing food-secure and insecure survivors from the testing subsample described in the main text (*n* = 1745).  † Dietary pattern obtained using penalized logistic regression; ‡ Dietary pattern obtained using principal components analysis.  Subjects were weighted, and the analysis was performed according to NCHS guidelines. All dietary patterns extraction procedures were performed on the training subsample described in the main text (*n* = 748).  a Healthy Eating Index 2015 | | | | | |

In our primary analysis, and after multivariable adjustment, we found significant associations between the extracted dietary patterns and mortality (Table 4 and Supplementary Table 1). Among the testing sample of all cancer survivors (*n*  = 1745), the highest quintile of the FI pattern had a 1.53-fold greater risk of all-cause mortality than the lowest quintile and a standard deviation increase in the index score was associated with a 25% increased risk of all-cause mortality (in the *Full* model—Table 4). There was a similar positive association between Prudent #1 and all-cause mortality, but unlike the FI pattern the relationship did not appear to follow a linear or dose-dependent pattern (*p*non-linear < 0.01; Figure 3). We found an inverse dose-dependent relationship between the HEI-2015 and all-cause mortality, where a standard deviation increase in the HEI-2015 score was associated with a 12% reduced risk of all-cause mortality (Table 4; Figure 3). Among food insecure cancer survivors only (*n*  = 213), there was a 47% reduced risk of all-cause mortality for every standard deviation increase in the HEI-2015 score (Supplementary Table 1). The hazard ratio for the FI pattern was similar to the analysis involving all cancer survivors, although it was nonsignificant and had a higher variance (Supplementary Table 1).

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| **Table 4**. Adjusted hazard ratios (HRs) and 95% confidence intervals from the *Null*e, *Basic*f, and *Full*g models for the risks of all-cause and cause-specific mortalities, in relation to the dietary patterns, in the testing subsample (*n* = 1745). | | | | | | | | | |
| **Dietary Pattern** | **Model** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | ***p***a**trend** | **HR**b**continuous** | ***p***c**non-linear** |
| *All-Cause Mortality* | | | | | | | | | |
| Food Insecurity (FI)**†** | *Null* | 1.00 | 0.79 (0.50-1.24) | 1.13 (0.77-1.66) | 1.34 (0.91-1.97) | 1.28 (0.80-2.03) | 0.08 | 1.14 (1.01-1.29)\* | 0.09 |
|  | *Basic* | 1.00 | 0.88 (0.54-1.42) | 1.23 (0.84-1.82) | 1.45 (1.01-2.07)\* | 1.97 (1.24-3.13)\*\* | < 0.01\*\* | 1.36 (1.17-1.59)\*\* | 0.63 |
|  | *Full* | 1.00 | 0.75 (0.44-1.25) | 1.08 (0.72-1.62) | 1.23 (0.82-1.85) | 1.53 (1.00-2.35)\* | 0.02\* | 1.25 (1.09-1.43)\*\* | 0.49 |
| Prudent #1**‡** | *Null* | 1.00 | 1.49 (0.98-2.26) | 1.78 (1.12-2.82)\* | 1.49 (0.94-2.37) | 1.82 (1.16-2.85)\*\* | 0.01\* | 1.14 (1.02-1.27)\* | 0.02\* |
|  | *Basic* | 1.00 | 1.84 (1.20-2.82)\*\* | 2.10 (1.35-3.27)\*\* | 2.01 (1.26-3.21)\*\* | 2.11 (1.29-3.43)\*\* | < 0.01\*\* | 1.20 (1.06-1.35)\*\* | < 0.01\*\* |
|  | *Full* | 1.00 | 1.84 (1.17-2.91)\*\* | 2.06 (1.27-3.34)\*\* | 2.03 (1.21-3.41)\*\* | 1.98 (1.17-3.35)\* | < 0.01\*\* | 1.15 (1.01-1.31)\* | < 0.01\*\* |
| Prudent #2**‡** | *Null* | 1.00 | 0.91 (0.63-1.32) | 0.69 (0.47-1.01) | 0.63 (0.37-1.05) | 0.71 (0.46-1.07) | 0.04\* | 0.83 (0.71-0.97)\* | 0.41 |
|  | *Basic* | 1.00 | 0.94 (0.67-1.32) | 0.77 (0.52-1.14) | 0.91 (0.56-1.48) | 0.86 (0.56-1.31) | 0.43 | 0.91 (0.78-1.07) | 0.30 |
|  | *Full* | 1.00 | 0.98 (0.68-1.42) | 0.72 (0.47-1.10) | 0.83 (0.53-1.32) | 0.80 (0.52-1.22) | 0.22 | 0.88 (0.75-1.02) | 0.38 |
| HEI-2015d | *Null* | 1.00 | 1.15 (0.71-1.86) | 0.88 (0.57-1.37) | 1.02 (0.64-1.63) | 0.74 (0.45-1.21) | 0.14 | 0.93 (0.83-1.05) | 0.13 |
|  | *Basic* | 1.00 | 0.89 (0.56-1.42) | 0.77 (0.51-1.16) | 0.74 (0.49-1.11) | 0.49 (0.30-0.79)\*\* | < 0.01\*\* | 0.81 (0.72-0.92)\*\* | 0.34 |
|  | *Full* | 1.00 | 0.98 (0.64-1.51) | 0.87 (0.60-1.26) | 0.88 (0.62-1.27) | 0.62 (0.39-0.97)\* | 0.02\* | 0.88 (0.78-0.99)\* | 0.48 |
| *Cancer-Specific Mortality* | | | | | | | | | |
| Food Insecurity (FI)**†** | *Null* | 1.00 | 0.87 (0.44-1.72) | 0.82 (0.46-1.46) | 1.30 (0.67-2.54) | 1.93 (0.92-4.05) | 0.08 | 1.27 (1.03-1.57)\* | 0.58 |
|  | *Basic* | 1.00 | 0.98 (0.49-1.99) | 0.93 (0.51-1.67) | 1.38 (0.70-2.71) | 2.77 (1.33-5.80)\*\* | 0.02\* | 1.50 (1.15-1.95)\*\* | 0.88 |
|  | *Full* | 1.00 | 0.88 (0.43-1.80) | 0.92 (0.51-1.68) | 1.35 (0.67-2.73) | 2.23 (1.31-3.78)\*\* | < 0.01\*\* | 1.36 (1.13-1.63)\*\* | 0.88 |
| Prudent #1**‡** | *Null* | 1.00 | 0.99 (0.54-1.84) | 1.78 (0.97-3.29) | 1.39 (0.70-2.78) | 2.70 (1.36-5.37)\*\* | < 0.01\*\* | 1.24 (1.07-1.44)\*\* | 0.10 |
|  | *Basic* | 1.00 | 1.27 (0.65-2.46) | 2.08 (1.10-3.94)\* | 1.84 (0.87-3.89) | 2.95 (1.40-6.22)\*\* | < 0.01\*\* | 1.26 (1.09-1.46)\*\* | 0.04\* |
|  | *Full* | 1.00 | 1.21 (0.62-2.36) | 2.12 (1.07-4.20)\* | 1.72 (0.81-3.65) | 2.23 (1.15-4.35)\* | 0.01\* | 1.16 (1.00-1.34)\* | 0.08 |
| Prudent #2**‡** | *Null* | 1.00 | 0.64 (0.39-1.06) | 0.53 (0.30-0.92)\* | 0.74 (0.31-1.80) | 0.78 (0.45-1.37) | 0.58 | 0.95 (0.70-1.29) | 0.04\* |
|  | *Basic* | 1.00 | 0.70 (0.43-1.13) | 0.60 (0.33-1.12) | 1.04 (0.45-2.44) | 0.91 (0.54-1.54) | 0.95 | 1.02 (0.78-1.34) | 0.06 |
|  | *Full* | 1.00 | 0.73 (0.44-1.21) | 0.63 (0.33-1.20) | 0.84 (0.50-1.41) | 0.84 (0.50-1.40) | 0.59 | 0.96 (0.76-1.22) | 0.12 |
| HEI-2015d | *Null* | 1.00 | 0.88 (0.33-2.37) | 0.48 (0.22-1.05) | 0.88 (0.39-1.98) | 0.50 (0.22-1.17) | 0.15 | 0.88 (0.71-1.08) | 0.42 |
|  | *Basic* | 1.00 | 0.71 (0.27-1.85) | 0.43 (0.20-0.92)\* | 0.69 (0.33-1.44) | 0.37 (0.17-0.83)\* | 0.02\* | 0.79 (0.65-0.97)\* | 0.69 |
|  | *Full* | 1.00 | 0.81 (0.38-1.74) | 0.52 (0.30-0.89)\* | 0.84 (0.53-1.35) | 0.44 (0.25-0.77)\*\* | < 0.01\*\* | 0.83 (0.70-0.97)\* | 0.75 |
| \*\* *p* < 0.01; \* *p* < 0.05  a Test for trend across the quintiles of the dietary exposure. See Equation 2 in the main text.  b Hazard ratio for a standard deviation increase in the dietary exposure. See Equation 3 in the main text.  c Likelihood ratio test *p*-value for a natural cubic spline model (Equation 4 in the main text) compared to specifying the model with the scaled dietary exposure (Equation 3).  d Healthy Eating Index 2015  e Includes the dietary pattern score variable with no additional covariates that were adjusted for.  f Further adjusts for age, sex, and race.  g Further adjusts for BMI, household size, family income-to-poverty ratio, education status, health insurance status, receipt of SNAP benefits, food insecurity status, alcohol intake, smoking status, total caloric intake, weekly MET minutes, and the Charlson Comorbidity Index score  **†** Dietary pattern obtained using penalized logistic regression; **‡** Dietary pattern obtained using principal components analysis (PCA).  Subjects were weighted, and the analysis was performed according to NCHS guidelines.  This survival analysis was performed on the testing subsample described in the main text (*n* = 1745). All dietary patterns extraction procedures were performed on the training subsample described in the main text (*n* = 748). | | | | | | | | | |

When we examined cancer-specific mortality, the parameter estimates for all cancer survivors were similar to those for all-cause mortality, particularly for the FI pattern (Table 4). However, no results other than an inverse association involving Prudent pattern #1 were statistically significant at the level of = 0.05. Considering cardiovascular disease mortality, the effect sizes were close to null, and we observed a significant and inverse association between Prudent #1 pattern and risk of cardiovascular disease-related mortality. Further adjustment for the NHANES ADL score did not significantly alter the results (Supplementary Table 2) despite the loss of many participants from the risk set. Finally, in our sensitivity analysis that included only participants with a primary cancer diagnosis within the five years before their study interview (Supplementary Table 3), we found that the association between the FI pattern and all-cause mortality was amplified. The SNAP pattern in this analysis yielded results that were similar to those observed in the primary analysis. Notably, the relationships between the Prudent #1 and #2 patterns and all-cause mortality were attenuated towards the null.

Chart, line chart

Description automatically generated

**Figure3**. *Panel A*: Survival curves detailing the relationships between the dietary patterns and all-cause mortality in the testing subsample (*n* = 1745). Adjusted survival curves were generated from models specified with quintile dummy variables. *Panel B*: Spline curves from expanding the diet quality index using a basis expansion for a natural cubic spline with one interior knot. All models adjusted for age, sex, race, BMI, household size, family income-to-poverty ratio, education status, health insurance status, alcohol intake, smoking status, calories, weekly MET minutes, the Charlson Comorbidity Index score, receipt of SNAP benefits, and food insecurity status*.*

a Healthy Eating Index 2015

Subjects were weighted, and the analysis was performed according to NCHS guidelines.

All dietary patterns extraction procedures were performed on the training subsample described in the main text (*n* = 748).

**Discussion**

Using a nationally representative sample of U.S. cancer survivors, we found that dietary patterns associated with being a food insecure cancer survivor were positively associated with all-cause and cancer-specific mortality after adjusting for several confounders. In a previous analysis, we validated the utility of penalized logistic regression as a novel *a posteriori* method for extracting dietary patterns associated with a particular risk factor or outcome [11]. The results of this follow-up analysis demonstrated the clinical value of these dietary patterns and their relationship with survival. Of the six dietary patterns we extracted from the observed 24-hour recall data (four with penalized logit and two with PCA), two of these patterns—the FI and SNAP patterns, which were both loaded by high consumption of palatable and processed foods and low loadings of fruits, vegetables, and other healthy components—were robustly and positively associated with all-cause and cancer-specific mortalities among cancer survivors and a subset of food insecure cancer survivors. However, unlike PCA, which generates a set of orthogonal eigenvectors and thus orthogonal dietary patterns, the FI and SNAP patterns, generated with penalized logit, overlapped significantly, suggesting that they may have been measuring a similar or the same underlying latent phenomenon (Table 2, Figure 2).

There was also evidence that prudent-style patterns (i.e., those characterized by high consumption of fruits, vegetables, and other healthy components) extracted with PCA, which were inversely correlated with food insecurity status, were also inversely associated with all-cause and cancer-specific mortality. However, the evidence for these patterns was not as strong as that of the others mentioned. Moreover, the results we observed were robust after performing multiple sensitivity analyses. Finally, the validity of all extracted dietary patterns was supported by comparison to the HEI-2015, which indicated lower diet quality in food insecure survivors compared to food secure survivors and which harbored significant correlations to the extracted dietary patterns.

Our findings contribute to evidence highlighting the adverse associations between food insecurity and health outcomes. However, our work is novel in that we focused on cancer survivors, a population that has, overall, received relatively little scrutiny within the broader context of food insecurity despite the fact that this population may have an elevated risk of experiencing food insecurity [3, 28, 29]. Several lines of evidence tie food insecurity to an increased comorbidity burden, including increased risks of hypertension, hyperlipidemia, diabetes, and mental health conditions [5, 30, 31]. Moreover, food insecurity is associated with poor overall health status, and recent analyses using NHANES data demonstrated significant and positive associations between food insecurity status and the risk of all-cause and cardiovascular disease mortality [27, 32–35]. Our analysis complements this body of work by demonstrating that dietary intake may be pertinent to the pathway between food insecurity and increased mortality in cancer survivors.

Across studies, place, population, and time, diet quality is associated with physiological outcomes that may explain the differential propensity for survival, as observed in our analysis. In a longitudinal sample of older adults from the Health and Retirement Study, higher diet quality, as measured by the HEI-2015, was associated with better lipid and C-reactive protein (CRP) profiles and decreased likelihood of depression and functional deficits [36]. In another longitudinal sample from the Health, Eating, Activity, and Lifestyle (HEAL) prospective cohort study, higher postdiagnosis HEI-2015 scores were associated with lower CRP levels in breast cancer survivors [37]. A nested cross-sectional study from the Multiethnic Cohort Study examined relationships between four *a priori* diet quality indices (AHEI-2010, HEI-2010, aMED, and DASH) and several serum carotenoids and biomarkers (leptin, HOMA-IR, glucose, CRP, insulin, and triglycerides) and found that higher diet index scores were positively associated with carotenoid markers and inversely associated with other biomarkers [38]. Finally, in a cross-sectional analysis of newly diagnosed head and neck squamous cell carcinoma patients, higher diet quality, measured by a “whole foods” dietary pattern extracted using PCA from FFQ data, was inversely associated with several pro-inflammatory cytokines [39]. Thus, the link between diet quality and downstream inflammation may explain our observed results, particularly in the context of cancer, where higher inflammatory biomarkers exacerbate disease progression, resulting in a poor prognosis [40–42].

Our findings have important policy implications. As alluded to in our previous analysis, screening for food insecurity is not a clinical best practice widely implemented in cancer clinics, although the National Comprehensive Cancer Network recently incorporated an item dedicated to food insecurity in its Distress Thermometer screener [3, 11, 43]. Alongside calls from those working in this area, we believe our results are grounds for further pushing food insecurity and cancer survivorship to the forefront of discussion within major medical organizations [44]. Identifying food insecure patients in the oncology care setting, early in the cancer care continuum and later as care progresses and financial hardship may be exacerbated, can facilitate prompt referral to additional support resources. These resources could be accessed, for example, through a case manager or social worker that assists the cancer survivors in leveraging personal and community-level resources or providing referrals to federal and local nutrition assistance programs [3, 45]. The establishment of hospital-based food pantries is another avenue that has shown promise for cancer survivors to access nutritious foods that they may otherwise lack access to [49]. Thus, tailoring community- and higher-level initiatives prioritizing food support throughout the treatment phase and the prolonged post-treatment phase may be critical to mitigating the negative health consequences that food insecure cancer survivors may experience secondary to a lack of a steady stream of nutritious foods [47]. Although community-level strategies may yield benefits, particularly in the short term, more comprehensive system-level approaches, such as innovative medical insurance models, are needed for more wide-ranging effects on food insecure survivors [3, 48, 49].

This analysis has several strengths, including the nationally representative sample from the NHANES, the use of a validated food insecurity measurement tool, the quality and quantity of covariate data used to account for potential and known confounders, and the quality of the linked mortality data through the NCHS Linked Mortality Files. Nevertheless, there are limitations to note. First, we used a static measure of dietary intake. However, we know that dietary intake patterns are dynamic and circumstantial, and our analysis could not account for any variation in dietary intake over time despite using time-to-event measures that occurred substantially after the measurement instance. Similarly, it is worth considering that food insecurity can be a transient phenomenon that subjects recover from, which may have occurred for participants in the intervening window between the study visit and the time of the observed event or censoring. An additional consideration concerning the measurement of dietary intake using 24-hour recalls is that it may be subject to systematic measurement errors that we were unable to quantify with the available data. We must also qualify that our findings are based on a set of 24-hour recalls, which are not designed to capture and may not accurately represent long-term dietary intake, unlike other measurement tools such as FFQs. However, we acknowledge that these data are the best we currently have for answering our research questions in the setting of a large epidemiological survey study. Second, with any analysis of observational data outside of a rigid set of assumptions, we must conclude that unmeasured or residual confounding cannot be excluded and that no causal interpretations can be made with these results. Tumor staging data may have confounded the results, but we could not control for this given that these data are not collected in either the NHANES survey or examination. Similarly, we were not able to control for tumor site. Third, although we did not account for stress as a confounding variable, given limitations with measures of psychological stress or allostatic load in the NHANES survey and our sample size, we believe it is appropriate to conclude that measures of food insecurity, such as those captured by the USDA FSSM, are likely to be highly correlated with measures of stress. Indeed, the U.S. Household FSSM includes questions designed to capture concern and stress about food insufficiency, such as:*“(I/We) worried whether (my/our) food would run out before (I/we) got money to buy more”* [50]. Fourth, selection bias may have occurred in the recruitment of cancer survivors into the NHANES study (e.g., survivors with more advanced cancers or with specific cancer types may have exhibited lower response rates), but any bias is conjectural given the lack of clinical or staging data in the NHANES study to make any conclusions on this type of bias and should be front of mind when generating conclusions from our results. Finally, a critical reflection of using the U.S. Household FSSM is that a measure of household food insecurity may not capture the burden of food insecurity exacted on any individual within that household. It is also critical to qualify that the dietary patterns extracted in this analysis reflect population-level means in terms of dietary intake and cannot be appropriately used to make conclusions about dietary intake for an individual cancer survivor experiencing food insecurity.

In summary, we conclude that dietary patterns extracted with penalized logistic regression, used to characterize the overall dietary composition of U.S. food insecure cancer survivors, may deleteriously impact cancer-related outcomes such as all-cause and cause-specific mortality. These patterns, characterized by the consumption of added sugars and processed foods with concomitant low consumption of fruits, vegetables, whole grains, and other healthy diet components, highlight an urgent public health challenge demanding innovative policy and community-level solutions. We identified several avenues for future research in this area. One avenue includes developing and evaluating community- and individual-level interventions for bolstering food security among food insecure cancer survivors throughout the early treatment and cost-prohibitive phases of the cancer care continuum. A second avenue should focus on piloting interventions for medical provider training in screening for food insecurity in oncology settings. A third avenue should implement this analysis on other large survey studies to understand the reproducibility of these dietary patterns within this target population. A final avenue of research should extend our work and continue surveillance of dietary intake patterns amongst U.S. food insecure cancer survivors using nationally representative data. Ultimately, advances in such areas will ideally abate the disparities in health outcomes observed by food insecure cancer survivors that our work and others highlight.

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**Statements and Declarations**

*Competing Interests*

The authors have no relevant financial or non-financial interests to disclose.

*Funding*

CAMV is a scholar in Health Policy Research Scholars, a national leadership program supported by the Robert Wood Johnson Foundation. It supports scholars from diverse disciplines and backgrounds in applying and advocating for policy change that improves health and equity. The project described in this article is supported by the program. The views expressed here do not necessarily reflect the views of the Foundation. [www.healthpolicyresearch-scholars.org](http://www.healthpolicyresearch-scholars.org/).

*Author Contributions*

CAMV—study conception, results interpretation, data management, data analysis, writing of original manuscript

RZ—data analysis, editing of original manuscript

FG—results interpretation, supervision, editing of original manuscript

BDK—results interpretation, supervision, editing of original manuscript

AEA—results interpretation, supervision, editing of original manuscript

All authors reviewed and approved the final version of the manuscript.

*Data Availability*

The datasets generated during and/or analyzed during the current study are available in a public GitHub repository, <https://github.com/cmainov/nhanes-fi-ca-mortality-mirror>.

*Ethics Approval*

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by National Center for Health Statistics Ethics Review Board. Written informed consent was obtained from all subjects/patients. Because this analysis involved de-identified secondary data, it was exempt from Institutional Review Board approval at the University of Illinois Urbana-Champaign.

*Consent to Participate*

Informed consent was obtained from all individual participants included in the study.