

**To all Reviewers:**

We thank the reviewers for their thoughtful commentary, and we believe that with their comments and suggestions, we are submitting a significantly stronger revision. We made some substantial changes to the analysis at the request of both reviewers and we would like to summarize those large changes here before discussing them in greater detail in the responses below:

1. We split the original final sample into *training* and *testing* subsamples that were used for the two phases of the analysis (training dietary patterns extraction models and testing the dietary patterns using survival analysis)—suggestion by reviewer 1
2. We added sequential adjustment. We now have three sets of covariates that we adjust for including an unadjusted model—suggestion by reviewer 1
3. We removed some dietary patterns from the analysis (i.e., the additional dietary patterns extracted using penalized logit that appeared to have significant overlap with the FI pattern). We only extract one dietary pattern with penalized logit—suggestion by reviewer 2
4. We added a propensity score matching sensitivity analysis to further assess the potential for confounding and test the robustness of the results
5. We renamed all the extracted dietary patterns— suggestion by reviewer 2

Given these requests and changes to the analysis, the results section was significantly updated.

**Note:** The version we are submitting has tracked changes so that the changes made to the manuscript are easier to identify.

**Reviewer 1**

This study investigated the association of various dietary patterns with mortality among cancer survivors from NHANES between 1999-2018. Dietary patterns associated with food insecurity and several other factors were extracted from the 2,493 cancer survivors in the study from 24-hour dietary recalls and then used in the same population to determine their association with mortality.

**Comment:** Ideally, the analyses with mortality should be done in a separate population as using the same population is likely to bias the results. A discussion of this and the potential implications of using the same study population should be included in the manuscript.

**Response:** We thank the reviewer for the thoughtful suggestion. We agree with the reviewer and originally, we would have liked to perform analysis on separate subsets (one subset for training the models and generating the dietary patterns and a separate subset for performing the survival analysis). We decided to not go along with the idea originally given that the sample size of cancer survivors is quite small in the NHANES dataset. Nevertheless, given the suggestion by this reviewer, we amended the analysis and did as we just described and pursued this out-of-sample validation analysis. We

split the original sample into 30%-70% subsets and performed the training models and testing models separately on those subsets, respectively. Please note that this changed the results and, thus, the results section has been significantly modified. However, the major conclusions have not changed. In the methods we have indicated this change in the analysis in lines 173-177, 213-214, 294-295, 315-315. We also changed Figure 1 to make it clearer to readers how the subsets are divided and used for each analysis. We also note that because of the change in the methods resulting in a smaller testing sample size, we ran into significant issues with optimizer convergence when fitting models for cardiovascular disease mortality given the small counts of observed deaths from CVD. Thus, we removed all analyses involving deaths from CVD from the analysis given that we were no longer able to analyze those data comprehensively as with all-cause and cancer-specific mortality.

**Comment:** The food-insecure cancer survivors had higher levels of numerous characteristics known to affect health including being non-white, living under the poverty level, being current smokers, and having more comorbidities. While all these factors were adjusted for in the statistical models, the possibility of confounding by these and related factors that were not controlled for remains. Factors such as the type of cancer and stage at diagnosis, for which information may not be available, could also confound the results. The authors should make efforts to address the potential of residual confounding and show unadjusted and adjusted results. That some potential confounders could not be adjusted for should be noted as a limitation.

**Response:** We thank the reviewer for this suggestion. We remind the reviewer that we adjusted for as many potential confounders as we could and there was a great deal of thought that went into the selection of the covariates to adjust for, using our team's combined expertise on nutrition, food insecurity, and the social determinants of health. This is clearly indicated in the methods and results sections. We cannot adjust for unmeasured confounders since they are unobserved. We also remind the reviewer that clinical staging data are not available in the NHANES dataset. At the suggestion of this reviewer, we have changed our analysis so that results for two other models (one that is unadjusted for any other confounders, which we call the *null model*, and a second that adjusted for a basic set of confounders—namely age, sex, and race, that we call the *basic model*) are now included. The methods section (Statistical Analysis section—lines 315-335) has been updated to account for this and the results the reviewer requests are now presented in the updated Table 4 and Supplementary Table 1. We also remind the reviewer that our manuscript already makes mention of residual or unmeasured confounding as a limitation of the analysis: lines 811-813. We have also added two sentences talking about the clinical staging and tumor site data specifically and how that may have confounded the results (lines 813-816). We also added a line about residual confounding due to smoking (lines 826-829). In addition, given the concerns for confounding expressed by both reviewers, we added a new sensitivity analysis that involved propensity score matching; a well-documented approach for addressing confounding from observed data. Details about this procedure have been added to the methods section of the manuscript and the supplementary methods file. The results are presented in Supplementary Tables 4 and 5.

**Comment:** The authors conclude that their findings that food insecurity may be associated with higher mortality in cancer survivors should motivate efforts to address this in cancer clinics. However, there is no evidence that the influence of food insecurity on mortality is any different in cancer survivors than for people who have never had cancer. This would require including the latter group in the analyses. The discussion of the potential policy implications of the findings should be tempered and the absence of a cancer survivor – cancer-free comparison acknowledged.

**Response:** We thank the reviewer for these suggestions. We remind the reviewer that our conclusion reads as such:

*“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.”*

As stated, the conclusion was *not* that food insecurity is associated with mortality, but rather that the major dietary patterns of the food insecure cancer survivor population are themselves associated with mortality among cancer survivors. We extracted dietary patterns of the food insecure cancer survivors in the NHANES data and tested whether those dietary patterns are associated with mortality. Indeed, we found that a few of those dietary patterns were positively associated with all-cause and cancer-specific mortality among all cancer survivors and among food insecure cancer survivors. Thus, because we are not looking at the relationship between food insecurity and mortality, there is no need to do a comparison analysis with those without cancer. We are simply just restricting our analysis to cancer survivors. Our results suggest that the dietary patterns of food insecure cancer survivors may not be meeting the guidelines recommended by large research and policy-setting organizations (AICR, FDA, etc.). This finding itself, we believe, warrants more careful attention to food insecurity in cancer clinics. Our analysis also suggests that these dietary patterns may, themselves, be associated with a higher risk of mortality from various causes, thus increasing the urgency of making this an important policy issue given that 11% of the general population faces food insecurity and that food insecurity may be even more prevalent among cancer survivors that face extraordinary financial burdens from the cancer treatment process. If cancer survivors are screened for food insecurity, they can be referred to the appropriate services (e.g., food pantries, dieticians, community organizations, etc.) that may help with food access and bolstering diet quality. We have removed statements from the policy section in the Discussion that do not completely align with what we just detailed here in our response and condensed the policy recommendations section at the request of this reviewer (lines 767-781). If there are any additional aspects of the policy recommendations that this reviewer would like us to reconsider or remove, we are open to more detailed suggestions.

**Comment:** Given all the issues discussed above, the title of the manuscript should be revised to reflect more of the nature of the study rather than a declaration of the

conclusion as it is now. In addition, “prognosis” should be replaced by “mortality” because that was the only outcome investigated.

**Response:** We thank the reviewer for these suggestions. We agree with the reviewer and have changed the title accordingly to reflect the nature of the study rather than the conclusion. We have also changed all instances of “prognosis” to “mortality” or “survival”.

## **Reviewer 2**

Thank you for the opportunity to conduct a peer review of this manuscript. This manuscript builds on a prior study that identified dietary patterns among cancer survivors with food insecurity using NHANES data, to examine the associations between the previously identified dietary patterns and cancer survival outcomes. The prior study used penalized logistic regression and principal component analysis and found that of the 6 dietary patterns, the ‘FI pattern’ and ‘SNAP pattern’ were the two patterns that were positively associated with being a food insecure cancer survivor. The current study used cox proportional hazard models to find that these two patterns were associated with higher risk of all-cause mortality among cancer survivors.

**Comment:** As a standalone paper, I found it a bit cumbersome to follow. The Introduction appears to need further description of the major dietary patterns that were associated with food insecurity among cancer survivors, particularly in the FI pattern, SNAP pattern, and the prudent pattern. These are not intuitively understood, and even referring to the prior paper, it is a bit hard to follow.

**Response:** We thank the reviewer for this suggestion. We agree that the repeated referral to the previous paper may cause confusion. To address this, we have changed the language and removed several references to the previous paper so that the current manuscript stands alone. The changes made throughout the paper assume that the reader does not need to have read the previous paper and that the analysis of the current manuscript is one that involves characterizing the dietary patterns of food insecure cancer survivors, using several methods, and validating them in a survival analysis. We also remove emphasis on the tool of penalized regression and make the focus of the paper the dietary patterns themselves. We believe that paring down the focus of the paper makes it easier to follow. We have also added more detail to Figure 1 to make the analysis easier to understand (especially for visual learners) and less cumbersome to follow. However, we are open to any more specific and further recommendations from the reviewer for making the manuscript less cumbersome to follow.

**Comment:** Furthermore, there is not a clear description in the manuscript in terms of the qualitative difference between the FI pattern and the SNAP pattern. While two different patterns may have emerged from the prior analysis using penalized logistic regression and PCA, it is unclear why the readers should care about these two patterns

as they seem very similar to one another, and is acknowledged as such in the Discussion.

**Response:** We thank the reviewer for this consideration. We agree with the reviewer that there is significant overlap between the FI and SNAP patterns in the previous version of the manuscript. Moreover, there was also significant overlap among all the dietary extracted using patterns penalized logit. Unlike PCA, which generates orthogonal components, penalized logit does not generate orthogonal sets of coefficients, leading to highly correlated dietary patterns. Thus, given this reality and the suggestion by the reviewer, we made a decision to only use food insecurity status as an outcome in the penalized logit model so that we only have one dietary pattern from that procedure. We only investigate relationships between four dietary patterns and survival in the new version of the manuscript (as opposed to seven in the previous version). We also believe that doing so makes the manuscript less cumbersome to follow, which also addresses another comment this reviewer made earlier.

**Comment:** The manuscript would benefit from a conceptual model or framework that can delineate how dietary patterns, food insecurity, socioeconomic status, and cancer mortality are associated with one another. In the first paragraph of the Introduction, I found the last sentence that read “thus, critical questions arise regarding how these experiences can impact cancer-related outcomes through dietary variables in cancer survivors” to be a stretch for the reader, because there is no discussion of diet preceding it, other than low-income.

**Response:** We agree with the reviewer about the last sentence of the first paragraph of the introduction section and we have removed it since it does feel out of place. Concerning the point about the conceptual framework: we did use a conceptual framework described by Seligman and Shillinger (DOI: 10.1056/NEJMp1000072), who describe the relationship between food insecurity and adverse health outcomes with diet quality as a mediating factor. We have made this more clear by making a direct reference to it in the first sentence of the second paragraph of the introduction. This allows the readers to visit that original publication to learn more about the framework we used to guide our analysis.

**Comment:** Furthermore, while smoking is included as a covariate and the findings in Table 1 show much higher rates of smoking among food-insecure vs. food-secure cancer survivors, this is not discussed or acknowledged as a factor that may contribute to mortality.

**Response:** We thank the reviewer for this consideration. The reviewer is correct that even though we adjusted for smoking status in all our analyses, there may be residual confounding related to smoking behaviors. Previously, our limitations section acknowledged this by stating that residual or unmeasured confounding is entirely possible and that there should be no causal interpretation to the results. Given the suggestion by this reviewer, we have added a sentence specifically mentioning the potential residual confounding by smoking status (lines 826-829). In addition, given the

concerns for confounding expressed by both reviewers, we added a new sensitivity analysis that involved propensity score matching; a well-documented approach for addressing confounding from observed data. Details about this procedure have been added to the methods section of the manuscript and the supplementary methods file. The results are presented in Supplementary Tables 4 and 5.

**Comment:** Much of the Methods section (and the methods section of the abstract) seems to describe the previous study rather than the current study. This makes it a bit unclear which findings are from the current study vs. the previous study. For instance, a sentence in the Results section reads “The Food Insecurity (FI) and Food Assistance (SNAP) patterns suggested ‘unhealthy’ dietary intake behavior” but those results seem to have been previously reported.

**Response:** We agree with the reviewer that this makes the passage hard to follow. We have updated the methods so that they describe only the methods used in this analysis. We have also removed the sentence that the reviewer refers to. Overall, we have also removed mention of the previous study throughout the manuscript so that this paper stands alone.

**Comment:** Clarity on the wording throughout the manuscript would be helpful. I found the wording throughout is confusing because ‘food insecurity’ (or food insecure) refers to both categorical measure of food insecurity per the USDA measure, as in Table 1, and it also refers to the food insecurity pattern that was previously found, as in Table 2 and Table 4.

**Response:** We thank the reviewer for this thoughtful suggestion and agree that the naming conventions we adopted for identifying the dietary patterns may present some confusion. To address this, we have renamed all extracted dietary patterns in a uniform and objective manner (“Patterns #1-3) and also in a qualitative way (“Patterns #1-3 are also referred to as the “High Fat & Sugar, Low Vegetable”, the “High Alcohol & Added Sugar”, and the Meat & Potatoes patterns, respectively, periodically throughout the tables, figures, and text).

Minor points

**Comment:** Introduction: rephrase from ‘...magnified for low-income cancer survivors – defined as individuals with a history of cancer – who may lack financial reserves’ to ‘...magnified for cancer survivors – defined as individuals with a history of cancer – with low income who may lack financial reserves’

**Response:** We thank the reviewer for catching this error and we have changed the sentence structure with the reviewer’s suggestion.

**Comment:** In the statistical analysis section, it states that ‘food security can be

associated with physical disability and functional deficits'. It should be worded as food insecurity.

**Response:** We thank the reviewer for catching this. We have updated it to read "food insecurity" and ensured consistency throughout the rest of the manuscript.

**Comment:** Referring to groups as "non-White" is problematic.

**Response:** We agree with the reviewer and apologize for not catching this error before the initial submission. We have made the necessary changes and ensured that the entirety of the manuscript adheres to the NIH guidelines for reporting race and ethnicity.