Author’s response to reviews

Title: More to Gain: Dietary Energy Density is Related to Smoking Status in US Adults

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Response to Reviewers

Reviewer reports:

Neal David Freedman (Reviewer 1): The authors examine the association of dietary quality, as assessed by dietary energy density, with smoking status using publicly available data from the nationally representative NHANES study.

1. In my opinion, the authors over-interpret previously published data on the potential benefits of micronutrients and antioxidants to disease. For example, in the introduction the authors write that smokers require more antioxidant vitamins, such as Vitamin E, C, beta-carotene, and selenium. In the discussion, the authors argue that low Vitamin C and beta-carotene are risk factors for cardiovascular disease and cancer. In the conclusion, the authors write that their results have important implications for "oxidative stress reduction in an at-risk population." However, most epidemiologic studies have not found associations between micronutrients and antioxidants and cancer or other diseases. Furthermore, the paper fails to mention the adverse effects of supplementation on current smokers that were found in the ATBC and CARET trials. With the results of those trials in hand, substantial caution on the role micro-nutrients in disease is warranted, particularly for smokers.

We agree and acknowledge the trials demonstrating that caution must be used when recommending supplementation of any micronutrient, particularly for smokers. In accordance with critiques from both reviewers, we have removed analyses of micronutrients and limited our discussion of antioxidants as they pertain to energy density. Specifically, these vitamins are often found in fruits and vegetables, which are part of a low-ED diet. As suggested above, we have also made note of prior studies that advocate caution in using supplements to address antioxidant deficiencies in smokers.
We hope that the re-focusing along with the added references addresses concerns about antioxidant analyses raised by both reviewers.

2. The current cross-sectional study indicates that cigarette smokers likely have worse diets than never smokers. This is not a new observation and coincides with prior data that cigarette smoking coincides with other negative health behaviors including a lack of physical exercise, sedentary behavior, alcohol drinking, and a range of other behaviors. It would be helpful for the authors to place their results in the context of this past work.

This reviewer is correct that multiple other studies have reported that poor diet (among other negative health behaviors) is common in smokers. However, very few studies have evaluated dietary patterns that are amenable to intervention and promote consumption of foods that can address nutritional deficiencies characteristic of smokers. No studies have evaluated ED in a US population of smokers. We believe that ED is uniquely suited to advance our understanding of poor diet in smokers and provide inroads to potential interventions. We have added references to show how the present study is a continuation of previous work, see lines ###-###.

3. Nevertheless, as this is a cross-sectional study, the correlation of smoking and dietary patterns does not equal causation and does not necessarily mean that changing diet would benefit smokers. Further care should be taken in the way that the authors present their results.

The reviewer is correct and we apologize for any wording or phrasing that assumes or insinuates causality. We have carefully revised the manuscript to appropriately discuss the study results. We also include as a limitation “Finally, the cross-sectional nature of the NHANES allows for evaluation of correlation, but not causality.” (line ###).

4. In a related point, in the discussion section, the authors write that the inclusion of formers smokers allows them to evaluate associations with dietary change and abstinence. However, the cross-sectional nature of the current study precludes interpretation of cause and effect.

As stated above, we agree and have carefully removed language that could misleading with respect to causality. For example, we have removed all references to a “change” in diet.

5. The authors also write in their conclusion section, that their results "suggest that consumption of a diet low in energy density may be a successful strategy for preventing weight gain following smoking cessation.” However, the cross-sectional results of the current study do not address this question.

We agree and have revised to carefully indicate that correlation is not causation, and have also removed the line that says “these results indicate”, as we agree with the reviewer that it our present study results do not indicate a change in weight.
6. It is not clear why this particular dietary pattern was chosen, as opposed to other ones that could be examined using the NHANES data.

Energy density is a cornerstone of current dietary recommendations in the US, the WHO, and the WCRF/AICR. Dietary energy density has been previously shown to correlate directly to diet quality in epidemiological data (references to support this have been added). The pattern of dietary energy density focuses on the entire diet, and is not food-specific. Diets that are both low- and high- in ED have been previously categorized, specifically with regard to the types of foods that can be found in low- and high-ED diets; more specifics have been added.

7. Introduction and discussion should be shortened. For example, the authors discuss barriers to smoking cessation—however the relevance of this admittedly important topic to the current study is not clear.

We agree that extensive discussion about barriers to smoking cessation may not be appropriate for our cross sectional study. We have removed much of the material relation to barriers to cessation, which has resulted in a shorter and more focused introduction and discussion.

8. "any amount of cigarette consumption" in the abstract and results is misleading, as the authors required participants to smoke 100 cigarettes per day to be considered a smoker.

We respectfully correct the reviewer that the NHANES categorization for former smokers is individuals who have smoked greater than 100/cigarettes per lifetime but do not currently smoke. Any individual who is considered a smoker is one who reports that they currently smoke either every day or on some, but not all days. We have revised the statement to read “any amount of current cigarette consumption”, as this supports our results that both non-daily and daily smokers have worse diets than non-smokers (both former and never). To avoid confusion we have now explicitly refer to never smokers and former smokers and have removed the term “non-smokers” in our analysis.

9. Participants who smoked less than 100 cig/day should be classified as never smokers not non-smokers. Non-smokers could either be never and former smokers.

We respectfully correct the reviewer that the NHANES categorization for former smokers is individuals who have smoked greater than 100/cigarettes per lifetime but do not currently smoke. All individuals who report that they do not currently smoke, nor have they smoked 100 cigarettes / lifetime are considered never-smokers. We have changed this as suggested, and clarified this in the manuscript.

Doug Manuel (Reviewer 2): More to Gain: Dietary Energy Density is Related to Smoking Status in US Adults
Overall

This paper examines evaluate the correlation of smoking and diet quality in relation to other risk factors, using NHANES.

The population importance of this paper is large. Smoking cessation is the most important health intervention for smokers. Weight gain during and following smoking cessation is an relevant issue.

Major comments

1) Much of the paper is about antioxidant vitamins, rather than energy density. It seems there are two options:

   a. Focus the paper on energy density.
   b. Change to title and objectives to include an objective on antioxidant vitamins.

We agree and have revised to focus the paper on energy density, as suggested. As stated in our response to reviewer 1, we have eliminated the analysis of antioxidant vitamins and limited our discussion of these vitamins as they relate to dietary ED.

It could be argued, as the authors do, that antioxidants are also important context for energy density and smoking. However, seems off focus given the title and stated objectives. The argument for antioxidant focus could be more clearly presented with more supporting references.

We agree and have revised to focus the paper on energy density, as previously suggested. We mention antioxidant intake as it relates to the types of foods consumed in a low-ED diet (fruits and vegetables).

In terms of sub-group analyses a more important objective, rather than antioxidants, is type of energy dense food. Which foods and drinks, if any, contribute to the findings?

In our revision of the paper, we have added specific details about the types of foods consumed in the low- and high-ED diets. (See lines 57-63)

2) The role of antioxidants and smoking was well referenced. There is controversy regarding the role of antioxidants and lung/other cancers.

Although we have reduced the focus on antioxidants, we acknowledge some of the mixed findings with respect to antioxidants and disease (see lines 158-165, ref 35, 36).

   a. Are there not many negative studies of antioxidants and cancer, including negative/harmful RCTs? What do the systematic reviews indicate?
In our revision of the paper, we have added references to the harmful effects of antioxidant supplementation and cancer. Our goal with the discussion of antioxidant vitamins is to demonstrate the importance of the vitamins and minerals obtained through the diet alone, where there is little risk of toxicity. (See lines 163-165)

b. Are there not more important food/nutrients that are related to cancer, such as fruit and vegetable consumption?

In our revision of the paper, we have added specific details about the types of foods consumed in the low- and high-ED diets. These foods include fruits & vegetables. (See lines 57-63). We have added references to specifically mention fruits and vegetables and cancer.

3) Study reproducibility. There was not a fulsome description of the study methods.

a. Can the authors confirm that a research can follow the steps outlined and reproduce the findings?

In our revision of the paper, we have clarified details about methods. Yes, we can confirm that a researcher can follow the steps outlined and reproduce the findings – the specific method to calculate energy density in the NHANES has been published; we direct the reviewer the methods section statement “Complete details of this method of calculating energy density in a nationally representative sample have been previously described [34].”

b. Was there any additional data cleaning, adjustment for measurement error, etc? See minor comments #5, 6, 9, 20 and others.

All data cleaning was mentioned on lines 95-97. No additional cleaning was done.

c. Does the study meet STROBE criteria and/or other relevant reporting guidelines?

We believe that we have met STROBE criteria. If this reviewer would like more specifics on how we met each criterion we would be happy to provide additional information.

4) There is the notion of diet quality being defined solely through "energy density" as diet quality represents a much more complex interplay of foods and nutrients, their amount, frequency and the proportion by which they are consumed. Energy density may still be of value, but consideration can be given to reflect focus the objective, methods and results on energy density, rather than the broader definition of "diet pattern".

Energy density is highly correlated with diet quality (see refs 27-30), as the energy density of the diet depends on all factors you list above (food types, proportion of food). As previously suggested, we have re-focused the paper on energy density.
Minor comments:

1) Lines 4-6: "Diet quality in relation to risk factors associated with poor health" - this is unnecessary, can just say energy density (ED)

Corrected as suggested.

2) Line 45: change 'and' to 'an'

Corrected as suggested.

3) Line 79: See Major comment #4. Although there is a high correlation between the two concepts, there are higher calorie components in an overall dietary pattern that are known indicators of diet quality (e.g., olive oil in Mediterranean diet, whole grains for CVD prevention, etc.)

As energy density relates to calories per gram of food, we are not suggesting that a low-ED diet must also be low in calories. Instead, we are suggesting incorporating more low-ED foods (fruits, vegetables, pasta, rice – all consistent with Med diet, DASH, etc.) into the diet as a strategy for lowering overall dietary energy and potentially reducing post-cessation weight gain as opposed to following “typical” recommendations of eating less (which, may potentially be smaller portions of higher ED foods) in order to prevent weight gain. As stated in the manuscript “The difference in energy density indicates that on average, current daily smokers consume approximately 200 calories more per day than non-smokers, despite eating significantly smaller portions of food.” – we are seeking to demonstrate that smokers consumer fewer grams of food (smaller portions) but still end up eating more kcal – this dietary behavior will likely be linked to weight gain, and by adding more low-ED foods, individuals can eat larger portions for either the same or fewer kcals.

4) Line 99: General statements regarding "disease risk" could be more specified.

Corrected as suggested.

5) Line 137-139: Confusing. Also how did you consider carbonated drinks ED? And in line 150: If they were a covariate, did you include tea, coffee and water for example? What is the rationale for adjusting one energy density for the other?

As stated in line 177 ED is calculated “excluding all beverages”. We provide the citation

We provide the citation for the exact method in which ED was calculated (REF #28). As stated in line 177 ED is calculated “excluding all beverages”. Beverages, including caloric carbonated beverage (we assume the reviewer refers to caloric carbonated beverages, such as regular soda)
disproportionately lowers the ED of the diet, despite their contribution to total calorie intake. By adjusting for beverage ED, we are accounting for both the calories consumed from beverages and the amount of additional grams consumed during the day. This method of ED calculation and beverage adjustment is widely accepted for use in these types of studies (Refs 22,24,28,29,46)

6) Line 140: Is this analysis focused on day 1 of diet recall only?

Yes; revised to clarify this point.

7) Line 141: n=5535 in parentheses

Revised as suggested.

8) Lines 154-161: Helpful to include P-values for all comparisons.

All p-values are included; we eliminated the line about “significance is determined at…”

9) Table 2: No adjustment for energy/day is done and hence values are confounded by total energy intake.

We have eliminated Table 2 in our effort to focus the paper on ED.

10) Lines 165-168: too strong a conclusion (also wrong place for interpretation of results). It can only be said that being a current smoker is associated with higher ED vs. non-smoking. Authors also say any amount of smoking is associated with poor diet when in the next sentence; former smokers have comparable diet to non-smokers who are assumed to have better diet?

Revised as suggested.

11) Line 168: remove mention of diet quality and better diets… change to ED

Revised as suggested.


Revised as suggested, with estimate +/- SE of former smokers added.
13) Lines 169-171: explain how this result was derived, no supporting analyses are presented

Energy density is a property of food; kcal/gram. If you have 1000 grams of food, an ED of 1.79 would be equivalent to ~1800kcal, and an ED of 2.02 would be equivalent to ~2020kcal for the same portion of food.

14) Line 174: P-value for vitamin A = 0.0003, but stated as P<0.0001 in Table 2.

Table 2 has been eliminated; it is possible that the previously reported numbers were from the initially presented poster before the final statistical model was selected.

15) Line 175: P-value for b-carotene does not match Table 2.

Table 2 has been eliminated.

16) Line 182: confusing to state it as “inverse” relationship (what is the inverse of smoking status? It is not a binary variable)

Excellent point. Revised to read “the results of the present highlight a similar negative correlation between smoking status and diet quality, as measured by energy density.”

17) Line 209: how accurate is ED a marker of overall diet, if authors' reference 31 reported association between smoking and overall diet but not smoking and ED? Important throughout paper not to conflate ED with overall diet quality as nutrition science literature does not always support this notion as noted above

ED is an established marker for overall diet quality; we again direct the reviewer to references 17-19, which specifically demonstrate the association between diet quality and energy density.

18) Line 217: change maker to marker

Revised as suggested.

19) Line 225: unclear

Revised.

20) Line 229-231: no mention in methods of how usual intake was estimated. Were two recalls averaged? if yes then not a good estimation of usual dietary intake.
We respectfully disagree with this comment, as the manuscript specifically states “The unique survey design of the NHANES allows for estimation of mean of the population’s distribution of usual dietary intake, strengthening confidence in the results presented (REF #43)”. Quite simply, the nature of the NHANES allows for one day of 24HR to be used to determine the mean of the population’s distribution of usual intake. We do not claim to determine usual intake, in any other manner, as we did not employ both days of recall nor did we use the NCI or other methods for quantifying usual intake.

21)  Line 234-238: would need SE of former smokers to say this

Mean +/- SE has been added to the text.

22)  Table 1: statistical significance is for which comparisons?

Comparisons are done with never-smokers as the referent category. Table 1 is revised to include this.