Author's response to reviews

Title: Lifestyle behaviors, obesity, and perceived health among men with and without a diagnosis of prostate cancer: a population-based, cross-sectional study

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Author's response to reviews: see over
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BMC Public Health
Editorial office

Dear Editor,

Please note the enclosed revised manuscript entitled “Lifestyle behaviors, obesity, and perceived health among men with and without a diagnosis of prostate cancer: a population-based, cross-sectional study” being submitted for possible publication by BMC Public Health as an original research article. As mentioned in the original cover letter, all authors have read and approved the manuscript. The manuscript represents results of original work that have not been published elsewhere. This manuscript has not and will not be submitted for publication elsewhere until a decision is made regarding its acceptability for publication in BMC Public Health. If accepted for publication, it will not be published elsewhere. The authors do not have any potential conflict of interest related to this manuscript.

The authors appreciate the opportunity to revise and resubmit the manuscript. The following provides a point-by-point description of our changes and/or response to the reviewers in bold type:

General (not in response to a specific reviewer comment):

Minor typographical errors have been corrected and the literature review has been updated to include relevant citations published since the original submission.

“As such, the current investigation represents a novel contribution to the literature; the question posed by the authors is well defined. According to my judgment, the manuscript adheres to the relevant standards for data reporting. The title is appropriate and the abstract accurately conveys the main study finding. The manuscript is well written. The major strengths of the current report are its large sample size with 2,524 cases of prostate cancer, and its broad generalizability. One limitation of the current study is its cross-sectional design, which precludes an evaluation of whether observed lifestyle differences preceded or were the result of being diagnosed with prostate cancer. The authors appropriately acknowledge this shortcoming in the discussion section of the manuscript.”

The authors appreciate the reviewer’s accurate assessment of the manuscripts strengths and limitations.
“The abstract overstates the inverse association of obesity in the subgroup of men older than 65 years because the 95% confidence interval of that risk estimate includes the null value of 1.0 and is therefore not statistically significant.”

This has been removed from the abstract and the 1\textsuperscript{st} paragraph of the discussion has been changed to remove overstating the association.

“In table 3, please show the numbers of cases in each cell. This would enable an evaluation of whether statistically non-significant results are due to a true lack of an association or small numbers of cases.”

The authors acknowledge the usefulness of this suggestion and had considered including number of cases prior to the original submission. However, we experienced several difficulties. Because of the weighting required due to the cluster sampling, the unweighted numbers would not be a true reflection of the analyzed value and the weighted prevalence numbers would be too large to express the sample size differences. Furthermore, additional numbers reduced the readability of the table and detracted from the primary purpose of the table.

“It would be nice to see whether apparent differences across strata are statistically significant based on formal tests for heterogeneity.”

Data analyses with interaction terms have been added to test if the differences in odds ratios across strata are statistically significant (methods/data analysis/3\textsuperscript{rd} paragraph, results/last paragraph, conclusions, and table 3). This procedure was chosen by the authors in an effort to achieve the primary goal of both this reviewer comment and the one by the second reviewer below related to effect modification.

“The assessments of exposures and endpoints were based on self-reports and there appears to be no available data regarding the validity and reproducibility of these assessments. This limitation and its implications regarding the results could have been made clearer in the discussion section. Specifically, what are the consequences of an imperfect specificity or sensitivity of the case ascertainment method in the current study?”

A citation supporting the reliability and validity of the BRFSS survey is included in the methods, 1\textsuperscript{st} paragraph (i.e., Nelson DE, Holtzman D, Bolen J, Stanwyck CA, Mack KA. Reliability and validity of measures from the Behavioral Risk Factor Surveillance System (BRFSS). Social and Preventive Medicine, 2001;46Suppl 1:S03-S42). Additional comments concerning the limitations of using self-report to determine a diagnosis of prostate cancer has been added to the discussion, 5\textsuperscript{th} paragraph.

“The discussion section would benefit from a brief mention of the possibility that multiple comparisons in table 3 may have resulted in statistically significant associations by chance in some instances.”

This has been added to the discussion, 5\textsuperscript{th} paragraph.

“It would have been interesting to investigate whether differences in lifestyle factors between men with and without prostate cancer varied according to time since prostate cancer diagnosis and primary prostate cancer treatment. Is such information available in the BRFSS data?”
This information is not available in the BRFSS data and has been clarified in the discussion, 3rd paragraph.

“The methods employed are adequately described. However, the statistical analyses involved multivariate adjustment for only a small number of variables: race, age, education, and urbanicity. No adjustments were made for smoking, alcohol use, sedentary behavior, or body mass, factors that could conceivably have confounded the associations observed. For example, the main study finding of a positive relation of fruit and vegetable intake to prostate cancer diagnosis could likely have been over-estimated due to confounding by smoking. Please re-run the main analyses to rule out the possibility of confounding by smoking, alcohol use, sedentary behavior, and body mass.”

The authors originally considered other potential confounding variables. Specifically, we ran the regression models adjusting for race, age, education, urbanicity, health status, whether or not the respondent had a personal doctor, whether or not the respondent had health insurance, geographic region in the U.S. (i.e., west, northeast, south, midwest), and body mass index. Because it is difficult to adjust for all possible confounders in a nonrandomized, observational study using public domain data with predetermined variables and data collection procedures, we felt that these variables were adequate for acting as surrogate markers for other health-related factors. Because the odds ratios did not differ when adjusted for all variables compared with adjusting for race, age, education, and urbanicity alone, we chose to report the odds ratios adjusted for these four variables only. This has been added to the methods/data analysis/2nd paragraph and discussion/5th paragraph.

“Likewise, the results from the stratified analyses shown in table 3 could have been affected by residual confounding. For example, the analyses of lifestyle factors according to men aged <=65 years and >65 years are not adjusted for age within the two strata defined by age.”

The authors agree that residual confounding is frequently a risk in epidemiologic studies and attempted to assess the potential confounding by surrogate markers of other health-related factors that might have been overlooked or not measured (see note above). Nevertheless, the authors considered adjustment for age as suggested but were concerned about maintaining consistency across the analyses presented in table 3. Specifically, adjustment for age across the dichotomized strata was not done because similar adjustment for the other three variables in table 3 (i.e., race, education, and urbanicity) was not possible because the three variables were not continuous. For example, if urbanicity is dichotomized for the analysis then all individuals will have the same value when the sample is stratified into rural versus urban for table 3 precluding adjustment for degree of urbanicity. The authors felt this would be a reasonable approach since confounding due to age would be expected to be similar in both groups, thus, not influencing the comparison of differences across strata which is needed for achieving the second study aim. A possible limitation of residual confounding has been added to the discussion/5th paragraph.

“Page 8, paragraph 2 – The authors should match on age using a 4:1 control:survivor ratio since there is more than a 15 year age difference in survivors and controls and adjustment for age would not appear to be sufficient to overcome this substantial difference.”

The authors appreciate the reviewer bringing this to our attention and acknowledge that the odds ratios calculated may not be as precise when there is a significant imbalance in a potential covariate between the two groups compared. Nevertheless, the BRFSS
data collection uses cluster sampling so that over sampling occurs in certain geographic areas. Because of this, the analyses must weight the data to obtain estimates for the U.S. population as a whole. Matching the controls will require choosing from different clusters and potentially altering the effectiveness of the weighting procedures. Therefore, the authors are hesitant to proceed with this request and have noted this risk of lower precision in the discussion. Because this manuscript is primarily hypotheses generating for future studies, we hope the reviewer will find this approach satisfactory.

“Page 8, paragraph 2 – The authors should categorize race/ethnicity more finely than black/non-black.”

Although this approach was originally considered by the authors, dichotomization of race/ethnicity was done due to relatively small stratum specific sample sizes and the need to limit the number of comparisons to minimize noting differences based on chance (see reviewer comment above).

“Page 9, paragraph 2 – The authors should assess confounding by other risk factors rather than just adjusting based on the literature.”

Please see note above describing other potential confounder factors analyzed.

“Page 9, paragraph 3 – The authors should assess effect modification and present p-values for interaction by age, race, education and urbanicity and provide justification for the possibility of biological differences for each of these variables.”

As mentioned in the response to the first reviewer, this had been done. Only the significant p values have been added to Table 3 to simplify presentation of the data. Justification for the expected differences based on demographics has been added to the introduction, 3rd paragraph. Additional 2-way, 3-way, and 4-way interactions were not tested because this would have significantly increased the number of comparisons tested. For example, to test all possible 2-way interactions, over 40 interaction terms would have to be tested for each column. Therefore, the authors chose to focus on only those interactions specifically relevant to the stated study aims.

“Page 11, paragraph 1 – The authors should not comment on changes between unadjusted and adjusted odds ratios since this just proves adjustment was necessary to control confounding.”

This change has been made as recommended.

“Page 12, paragraph 2 – The authors should mention a real limitation of the study, the inclusion of men with other cancers.”

This has been added to the discussion, 5th paragraph.

“Page 13, paragraph 2 – The authors provide no justification for why measurement error should be similar in survivors and controls, since an illness generally results in recall bias.”

This has been added to the discussion, 5th paragraph.

“Table 1 – The authors should include a column of p-values.”
A column with p-values has been added to Table 1.

‘Page 5, paragraph 1 – The authors should reword “…poorer treatment response and survival in cancers other than prostate.” As “…poorer treatment response and survival in head and neck cancer, and lung cancer.” Since these cancers are clearly associated with smoking.”

Lung and head/neck cancer have been specified.

“Page 5, paragraph 1 – The authors should reword “…higher alcohol intake has been associated with reduced survival in cancer other than prostate.” As “…higher alcohol intake has been associated with reduced survival in breast cancer.” Since both papers refer to breast cancer.”

Breast cancer has been specified.

Thank you for your consideration of this revised manuscript.

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Sincerely,

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