Peer Review File

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Review Comments

In this study, authors determined the association between dietary sodium, potassium intake and lung cancer risk based on the prostate, lung, colorectal and ovarian cancer screening trial and the Women's Health Initiative (WHI). And, authors suggested that appropriate consumption of potassium has a protective effect against lung cancer and high consumption of sodium is related to an increased risk of lung cancer, along with the presence of a dose-response relationship despite the modest magnitude of estimate. The research method for deriving the results is reasonable and reliable. Hypotheses and experimental designs are sufficient to support the results. However, I have some comments to be addressed.

Major comments:

Comment 1: *Correlation coefficients between dietary mineral intake and their dietary food sources.*

Reply 1: Thank you for the suggestion. We have added the correlation coefficients between dietary mineral intake and food sources in the revised **Supplementary Table 3.**

Changes in the text: We added the description of correlation coefficients in the Results Section. (*See page 6, lines 136-137*).

Comment 2: *The FFQ, although practical for large epidemiology studies, has been associated with measurement errors. Accuracy of intake of the wide range of nutrients is always a concern.*

Reply 2: Thank you for this important comment. We agree that the measurement error is an important issue in large scale epidemiology studies.

Previous studies showed that a few dietary components unbiased measurements of short-term intake, such as 24-hour recalls, could be used as the reference measurements in regression calibration in order to reduce the bias due to measurement errors (1).

As for the WHI cohort, we estimated the calibrated intake with the "calibration" equations (2) and performed the Cox proportional hazards regression based on the calibrated intake. As shown in **Table A** below, the consistent dose-response relationship was observed for the calibrated intake, although the width of the 2.5th and 97.5th percentile intervals was more than that for the original intake. The PLCO trial does not collect the 24h recalls data, which make it almost impossible to perform regression calibrations. Besides, we also noticed that previous publications on PLCO also relied on FFQ intake directly (3,4).

However, we do agree that we should notice the potential bias due to the measurement error. Therefore, we considered it as a limitation in this manuscript.

Changes in the text: We have added our text as advised in the Methods Section *(See page 5, lines 110-113)* and Result Section *(See page 8, lines 178-180)*, which states *"In order to reduce the bias due to measurement errors, we applied the "calibration" equations, details of the study have been described in* (2)*, to FFQ data to estimate calibrated intake and performed the same Cox proportional hazards regression as another sensitivity analysis for the WHI cohort.",* and *"In the sensitivity analysis using calibrated potassium and sodium intake, consistent dose-response relationship were observed in the WHI cohort (data not shown)."* And modified the Strengths and limitations Section of the manuscript accordingly, which states *"Nevertheless, several limitations needed to be noted, including only description of the dietary baseline information, possible residual confounding or confounding by unmeasured factors, and the accuracy of dietary intake measurement." (See page 11, lines 256-259)*.

Table A. Hazard ratios and 95% confidence intervals of lung cancer based on calibrated potassium and sodium intake in the WHI

	Calibrated potassium				Calibrated sodium			
	case	Person-years	HR [a]	95% CI	case	Person-years	HR [a]	95% CI
Continuous	1522	1050612	0.98	0.88,1.09	1522	1050612	1.01	0.78,1.29
Quintile 1	321	179163	Ref	-	440	202285	Ref	-
Quintile 2	368	196605	1.04	0.90,1.21	344	211626	0.95	0.82,1.11
Quintile 3	348	211818	1.05	0.90,1.23	297	214943	1.01	0.84,1.21
Quintile 4	264	222803	0.88	0.74,1.06	279	214386	1.22	0.98,1.51
Quintile 5	221	240222	0.91	0.73,1.12	162	207372	1.11	0.82,1.50

[a] Cox proportional hazard models were used to adjust age, body mass index (kg/m2), energy intake (kcal/day), educational level (3 categories), alcohol consumption (g/day), smoking status (never smokers, former smokers <20 pack-years, former smokers ⩾ 20 pack-years, current smokers <20 pack-years, current smokers ⩾20 pack-years), history of diabetes (yes or no), and family history of cancer (yes or no).

Comment 3: *Classification of lung cancer (for example, small cell carcinoma, etc.).*

Reply 3: Thanks for this suggestion. Per this suggestion, we have added the analyses for different type of lung cancer (non-small cell lung cancer and small cell lung cancer) in the revised **Supplementary Table 8 & 9.** The results for NSCLC were basically consistent with the main findings, while no significant results for SCLC due to the lack of cancer patients.

Changes in the text: We have added our text as advised in the Methods Section *(See page 5, lines 117-118)* and the Results Section, which states *"Besides, we observed that stratified analyses by smoking status or cancer type showed consistent results with the main analysis, although the association is not significant for SCLC patients due to limited sample size (Supplementary Table 6-9)." (See page 8, lines 180-183)*.

Comment 4: *Impact of participant location and race differences on outcome.*

Reply 4: Thank you, we appreciate these suggestions. We have added a sensitivity analysis for race in the revised **Supplementary Table 5.**

Changes in the text: We have added our text as advised in the Methods Section *(See page 5, lines 108-110)* and the Results from the Sensitivity Analysis

Section *(See page 8, lines 177-178)*.

References:

1. Keogh RH, Shaw PA, Gustafson P, et al. STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: Part 1-Basic theory and simple methods of adjustment. STAT MED 2020;39:2197-231.
2. Huang Y, Van Horn L, Tinker LF, et al. Measurement error corrected sodium and potassium intake estimation using 24-hour urinary excretion. HYPERTENSION 2014;63:238-44.
3. Peters U, Chatterjee N, McGlynn KA, et al. Calcium intake and colorectal adenoma in a US colorectal cancer early detection program. AM J CLIN NUTR 2004;80:1358-65.
4. Zhao J, Giri A, Zhu X, et al. Calcium: magnesium intake ratio and colorectal carcinogenesis, results from the prostate, lung, colorectal, and ovarian cancer screening trial. Br J Cancer 2019;121:796-804.