Author’s response to reviews

Title: Associations between fruit and vegetable, and antioxidant nutrient intake and age-related macular degeneration by smoking status in elderly Korean men

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Author’s response to reviews:

Response to the Reviewer #1

Thank you for your very valuable comments and helpful suggestions. Please see our detailed responses below. We have revised the inclusion and exclusion criteria and re-conducted statistical analysis. In the revised manuscript, the subjects were categorized as nonsmokers, former smokers, and current smokers. We have also added the estimation of α-carotene, β-cryptozanthin, lutein/zeaxanthin, and lycopene using carotenoids database and analysis for the associations between carotenoid intakes and AMD by smoking status.

Q1: In this study, the author mentioned "former smokers were categorized as nonsmokers, because their general characteristics and did not differ from those of nonsmokers". Whether there is difference in the diet intake is not addressed clearly in the manuscript. What's the proportion of former smokers were also not mentioned. If there is a large proportion of people who were former smokers, it is should be analyzed separately.

- Following your suggestion, we have analyzed former smokers separately and revised manuscript and all tables. (Table 1 – 3)

Q2: Please give a note which population did the author assessed using the models a and b (Table 2).
We have added a note on the description of the population that was assessed in the model 1 and model 2 in Table 2.

Q3: Why did not the author consider the length of the smoking? The average smoking years is 49, it is a long duration.

- Following your suggestion, we have revised model 2 to include duration of the smoking and daily smoking amount in former smokers and current smokers. (Page 8, lines 135 - 137)

Q4: Table 3, please explain why model 2 adjusted for "smoking status"?

- In the revised manuscript, the smoking related covariates used in statistical model differed by the nonsmokers, former smokers, and current smokers, separately. Further, for former smokers, the data on daily smoking amount and duration of smoking was included in model 2. For the current smokers, current daily smoking amount and duration of smoking were adjusted in model 2. (Page 8, lines 135 - 137)

Response to the Reviewer #2

Thank you for your very valuable comments and helpful suggestions. Please see our detailed responses below. We have revised the inclusion and exclusion criteria and re-conducted statistical analysis. In the revised manuscript, the subjects were categorized as nonsmokers, former smokers, and current smokers. We have also added the estimation of α-carotene, β-cryptoxanthin, lutein/zeaxanthin, and lycopene using carotenoids database and analysis for the associations between carotenoid intakes and AMD by smoking status.

Methods: How has AMD been assessed? How was diet assessed? Did the assessment include dietary supplements?

- Following your suggestion, we revised method for assessment of AMD, diet, and dietary supplements in more detail. (Page 6 - 7, lines 77 – 87 and 113 - 118)

Results: It should be mentioned that overall, there was no association between antioxidant nutrient intake and odds of AMD. Hence, I believe that the first statement in the conclusion is slightly misleading.
- Following your suggestion, we revised the result section. (Page 8 – 9, lines 141 – 145 and 155 - 160)

Discussion: l. 159: "unlike in other studies" - which studies? Please add references.

- We have added references [8, 16]. (Page 10, lines 177)

l. 175 ff: Did other studies stratify by smoking status and report inverse associations in smokers only?

- There has been no observational study showing relationships between dietary intake and AMD according to smoking status. However, some experimental studies have shown the protective effects of micronutrients derived from fruits and vegetables, such as vitamin A (particularly β-carotene), vitamin C, vitamin E, folic acid, and phenolic compounds, against smoke-induced toxicity, via prevention of lipid peroxidation. (Page 11, lines 197 - 201)

l. 173f: Why do the authors believe that the effect is not visible in a population with high F&V intake? What is the range of intake in the current and in previous studies (i.e. how does intake differ between participant with high and low intake)?

- The range of intake was 194 g/d (Q1) to 925 g/d (Q2) in our study and 187 g/d (Q1) – 579 (Q4) in a study that consisted of Chinese males. Considering the range, we revised the sentence in the discussion as follow. We presume that in our study, among Korean elderly male nonsmokers other risk factor for AMD will be more effective than intake of fruits and vegetables. (Page 10, lines 191 – 193)

l. 195: The CI cited for study [51] looks odd. Can you check, please?

- We have checked again. But that was originally presented as OR (95% CI) = 0.1 (0.0-0.9).

l. 216ff: The authors state that they only have limited information on dietary supplements. However, the might be able to estimate who much dietary supplements contribute to antioxidant nutrient intake and make a general statement (e.g., in 2010/2011, supplements contributed x% to beta-carotene intake in this population).
We agree this is one of the major limitations and we analyzed intakes of vitamin A and vitamin C from dietary supplements. There was no significant difference for vitamin A and C from dietary supplements according to smoking status (vitamin A: 292.8±161.6 for nonsmokers, 153.2±31.7 for former smokers, and 89.2±41.6 for current smokers; vitamin C: 121.5±32.8 for nonsmokers, 137.2±20.1 for former smokers, and 93.5±29.8 for current smokers). However, we have limited data on nutrient intakes from dietary supplements [515 subjects (36.4%)] and this data was available for years, 2010 and 2011 only not 2012. Also, data for dietary supplement use in Table 1 was for the subjects who had supplementation for more than 2 weeks during the previous year. Therefore, we were unable to estimate nutrient intakes from foods and supplements. We have statements explaining these issues in the limitation. (Page 12, lines 237 – 243)

A further limitation is that the result in smokers is based on a small number of cases and interaction is only significant for beta-carotene. It should also be mentioned that the majority of participants 65+ years old were actually excluded from the analysis. Hence, the authors only looked at a very selective group of the population. It is sometimes not entirely clear, why some participants have been excluded.

Thank you for this comment. We have revised exclusion criteria on the basis of other previous cross-sectional study1) and re-analyzed. We excluded subjects without 24 hour dietary recall data (n = 122); those without fundus photograph data (n = 439); and those lacking smoking status data (n = 56). A total of 1,414 participants were included in the final analysis. (Page 5, lines 69 – 72)