Author’s response to reviews

Title: Association between lifestyle and thyroid dysfunction: a cross-sectional epidemiologic study in the She ethnic minority group of Fujian Province in China

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Author’s response to reviews:

Dear Prof Byrne,

On behalf of my co-authors, I would like to thank you for giving us an opportunity to revise our manuscript. We appreciate the positive and constructive comments and suggestions from the editors and reviewers regarding our manuscript "Association between lifestyle and thyroid dysfunction: a cross-sectional epidemiologic study in the She ethnic minority group of Fujian Province in China.

We have studied the editor and reviewer’s comments carefully and tried our best to revise our manuscript to address the questions and concerns. We have highlighted the changes with red text in our manuscript, which we would like to submit for your kind consideration. The following is our response to the Reviewers’ comments. Should you have any questions, please contact us without hesitation. We look forward to hearing from you.
Thank you and best regards.

Yours sincerely,

Yanling Huang

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Response to the editor:

1) In the section “Ethics approval and consent to participate” in the Declarations, please give the reference numbers for the ethical approval.

We have given the reference number for the ethical approval in reference 12

2) Do not report p values of 0.000, use <0.001 or similar.

Thanks for the reminder. We have changed all the p values of 0.000 to <0.001.

Response to the reviewer1:

1) Sample size should be justified.

The data of this research came from an epidemic survey of diabetes in the She ethnic minority group of Fujian Province in China, carried out from July 2007 to September 2009. The details of the study have been published previously. Among the participants of the study, 5154 subjects were tested for TSH and TPOAb levels, presenting a unique opportunity for investigating potential associations between several lifestyle factors and the incidence of thyroid dysfunction. Initial investigation found that the prevalence of thyroid dysfunction is about 20% (Including hypothyroidism, hypothyroidism and the positive of tpoab or tgb) projecting the minimal sample size needed to be 1536. The number of subjects with thyroid dysfunction-related data available for our study is 5154, exceeding the minimal required sample size for the survey.

2) The details of model building including selection algorithm and the assessment of the appropriate scale for continuous predictors such as BMJ should be described.

We agree and have added relevant descriptions in the manuscript (Page6, Line40-57)
3) The results should be interpreted in light of the effect sizes with 95% confidence intervals as well as P-values.

Thanks for the suggestion. Indeed, some of the effect sizes were very weak, thus it is very important to add the 95% confidence intervals to more precisely represent the results. We have added this part according to the reviewer’s suggestion.

4) Please don’t dichotomize P-values (at 5% level) in the text and abstract.

We have changed the expression in the text and abstract accordingly.

5) P. 7, L. 1: Relative risks can not be estimated in cross-sectional studies.

Thanks to the reviewer’s for pointing out the error. We have made the correction accordingly (Page 6, Line 51-57)

6) Table 4: The intercept row and logistic regression equations are redundant and should be omitted.

We have omitted the intercept row and logistic regression equations as suggested by the reviewer (page 12).

Response to the reviewer 2:

1. The authors showed associations between positive TPOAb and alcohol consumption, smoking, daily staple amount and weight watch. TPOAb is genetic factor. Why does the genetic factor affect these lifestyles? The authors should mention this point.

We agree that additional discussion is needed in the manuscript to clarify the findings. TPOAb is a marker of the thyroid autoimmune disease. What we found was an association between positive TPOAb and certain lifestyles. An association is usually insufficient for inferring causal relationships. We wish to clarify that we did not make any claim that TPOAb affects lifestyles, or vice versa. We were simply reporting the observation of association. Genetic factors often contribute to the development of thyroid peroxidase antibodies (TPOAb), i.e. people with certain genetic background might be predisposed to produce antibodies against thyroid peroxidase. However, environmental and lifestyle factors may also influence epigenetic mechanisms, such as by altering DNA methylation and chromatin modifications, thereby modulating gene expression. We have thanked the reviewer for bringing up this point and have added additional discussion to the text (page 3).
2. Did the authors exclude the syndrome of resistance to thyroid hormone (RTH)?

We thank the reviewer for pointing out this limitation. In this study we only checked TSH level, thus unable to exclude the syndrome of resistance to thyroid hormone (RTH), although the incidence of RTH is very small. We have included discussion of this limitation (page 16).

"3. Hyperthyroidism" defined by the authors included Graves' disease and Hashimoto thyroiditis. The authors should divide into these two groups about lifestyle differences.

We completely agree with the reviewer that it would be more informative to distinguish between Graves' disease and Hashimoto thyroiditis. Unfortunately, the data came from part of an epidemic survey of the diabetes, which was not particularly designed for studying thyroid diseases. Only TSH and TPOAb level was tested in this survey. There is not enough information to help divided patients into groups of Graves' disease and Hashimoto thyroiditis. We nevertheless appreciate the reviewer’s suggestion and hope to conduct additional studies in the future to better understand the influences of lifestyle on the two distinctive diseases.

4. There are many miss-representations.

We are aware of potential inaccuracy in the use of language due to the fact that we are not native speaker of English. We have involved a native speaker to help edit the article in an effort to improve linguistic accuracy. We hope the problem had been addressed in this revision. However, please do not hesitate to point out specific places of mis-representations that might still remains if you found them.