Author’s response to reviews

Title: Using Hashimoto thyroiditis as gold standard to determine the upper limit value of thyroid stimulating hormone in a Chinese cohort

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Author’s response to reviews:

Dear Editor,

Thank you for your letter concerning our manuscript (BEND-D-16-00046R2) entitled “Using Hashimoto thyroiditis as gold standard to determine the upper limit value of thyroid stimulating hormone in a Chinese cohort”. We are truly grateful to yours and other reviewers’ critical comments and thoughtful suggestions. Based on these comments and suggestions, we have made careful modifications on to the original manuscript. We hope the new manuscript will meet your journal’s standards. Attached, you will find our point-by-point responses to the reviewers’ comments.

Sincerely,

Jin-Kui Yang, MD, PHD

Reviewer #3: General Comments
This paper estimates the upper limit of normal TSH values using two different methods. In general I am satisfied with the statistical analyses, but I do have some comments.

Major Compulsory Revisions

1. Figure of joinpoint regression. I did not find a figure with this analysis. Given it is one of your methods of estimating a TSH cutoff, it is essential to include it. It appears to me that Figure 2 is simply deciles of TSH.

RE: According to the reviewer’s comment, we added the flowchart about the algorithm of joinpoint regression in the supplementary file of the paper. Please see the following figure. The detailed algorithm description was seen from the reference: Czajkowski, M., Gill, R. and Rempala, G. (2008). Model selection in logistic joinpoint regression with applications to analyzing cohort mortality patterns. Statistics in Medicine 27, 1508-1526.

Specially, we added the joinpoint regression analysis result in Figure 2. Accordingly, Figure 2 was modified as following:

Where Figure 2B showed only one joinpoint was found, and this joinpoint presented in the ninth decile group. Therefore, the lower limit value of this group of 2.89 was taken as the cutoff.

Minor Essential Revisions

1. Abstract, line 37 and throughout the paper, jointpoint regression. I believe the authors mean joinpoint regression. In the Methods, please cite a statistical reference along with the ljr package [ > citation ( 'ljr' ) ].

RE: According to the reviewer’s suggestion, we have added the corresponding reference in the revised text (page5, line108).
2. Results, lines 118 and 125 and throughout paper, percentages. Is 0.1% or 0.01% all that important? I believe all percentages, including area under the curve, can be rounded to the nearest integer.

RE: According to the reviewer’s comment, all percentages have been rounded to the nearest integer.

3. Results, line 139. Please report the actual P value rather than just P > 0.05.

RE: The actual P value has been shown in the text as a substitution for “P > 0.05”.

4. Results, lines 142-143. Axle should be axis.

RE: The word “axle” has been replaced by “axis”.

5. Results, lines 152-158. The ROC curve depends on the cutoff used. Therefore, the sentence that mentions a cutoff of 2.6 should come before the sentence that describes the area under the ROC curve.

RE: As suggested by the reviewer, the sequence of the words has been adjusted.

6. Discussion, lines 200-201. Does 4.6% overall [5% overall] refer to the entire distribution of TSH values (from minimum to maximum) or to the distribution of TSH values below the cutoff of 2.6?

RE: 4.6% refers to the distribution of TSH values below the cutoff of 2.9, which means the number of HT below this point divided by the number of population below it. Therefore, it’s more reasonable to delete the word “overall” as you suggested.

7. Discussion, lines 228-229. Elder should be older.

RE: “Elder” has been replaced by “older”.

8. Table 1, reporting of SD. The +/- sign is not needed for SD. The preferred format to report SD is 35.9 (SD 9.15). P values cannot truly be 0. P < 0.001 is sufficient. Please round P values to 2 decimal places if greater than 0.01.

RE: Revisions have been made as the reviewer suggested.

9. Figure 1. Please mention how the distributions of TSH were smoothed.

RE: The way of how it was smoothed has been mentioned in Figure 1.

10. Figure 3. Please include the cutoff value of TSH in the figure legend.

RE: It has been described in the Figure 3 and Figure 3 legend according to the reviewer’s comment. See the followings:

Figure 3. ROC curve describing the cutoff value of TSH in detecting participants with HT. When maximizing the sensitivity and specificity, the cutoff value of TSH equaled to 2.6 mU/L, with the sensitivity of 52% and the specificity of 77%.