Reviewer's report

Title: Serum Thyroid-Stimulating Hormone Levels are not Associated with Exercise Capacity and Lung Function Parameters in two Population-Based Studies

Version: 3 Date: 1 July 2014

Reviewer: Stephanie MacNeill

Reviewer's report:

The authors have duly taken on board many of the comments I raised in my initial review of this manuscript. My feedback is noted below addressing each of the original comments

MAJOR

1. Initial comment: The researchers have not described any of the demographic characteristics of the patients with high/low TSH.

Comment based on revised manuscript: The changes made to the text (Results section) were minor and not consistent. For example, the authors state that "in the pooled population measurements of spirometry and CPET were lower in individuals with low TSH compared to individuals with serum TSH in the reference range while these measurements did not differ substantially between individuals with low TSH and individuals with TSH in the reference range". Please be specific and consistent.

2. Initial comment: The authors rightfully identify in the Discussion that their analyses are based on a population based sample with few subjects with clinically relevant hyperthyroidism.

Comment based on revised manuscript: While the authors did not perform the sample size calculation requested, it is clear that they have considered the issue. I would suggest, however, that they include in the manuscript some statistics on the number of individuals in their study that they consider to have clinically relevant hyper/hypothyroidism.

MINOR

1. Original comment: Please indicate whether the lack of consistency in how the blood samples were taken might have influenced the interpretation of TSH levels.

Comment on revised manuscript: The authors addressed this issue in their letter to the editor. It would be helpful, however, for the exact results presented in this letter to be included in the manuscript as well.

2. Original comment: The participation rate of CPET and spirometry is low. It would be helpful to have some details of how participants differed from non-participants.
Comment on the revised manuscript: The authors did a good job of addressing this issue through the use of inverse probability weighting. It would be helpful, however, if the direction of the bias (initially) were described in the text. For example, was the BMI higher or lower in non-participants? This should also be discussed in the Discussion section.

3. Original comment: The authors used median regression for their analyses.
Comment on the revised manuscript: The justification for this was satisfactory.

4. Original comment: Table 1 provides details of the age distribution of participants in both studies. Please quote the minimum and maximum as well as inter-quartile ranges.
Comment on the revised manuscript: This was addressed satisfactorily.

5. Original comment: It would be helpful to report what proportion of the cohort were currently taking treatments for hypo/hyperthyroidism and incorporate this into the analysis.
Comment on the revised manuscript: This was addressed satisfactorily.

6. Original comment: The presentation of results in table 2 is unclear.
Comment on the revised manuscript: This was addressed satisfactorily.

7. Original comment: In the discussion the authors state that their data "provides evidence that serum TSH levels are not associated with spirometry and exercise capacity." It would be prudent to rephrase this as not having found evidence of an association.
Comment on the revised manuscript: This was addressed satisfactorily although the conclusion (page 10, lines 11-12) could be re-worded to "Our results suggest that there is no evidence of an association between thyroid dysfunction and lung function and CPET in the general population."

ADDITIONAL MINOR COMMENTS:

1. The authors state that "FEV1, FVC and FEV1/FVC values did not differ significantly across TSH quintiles (table 30)" (page 7, lines 8-9). This statement does not accurately reflect the analysis that was performed. The analysis compared quintile of TSH with the median quintile.

2. The authors conducted a sensitivity analysis excluding individuals taking thyroid medication (page 7, last 2 lines). It would be helpful to have had such results in an online appendix.

3. In the first sentence of the discussion the authors state that "In two independent large population-based studies from Northeast-Germany..") (page 8, lines 2-3). The authors would be better to state "In data pooled from two independent large population-based studies from Northeast-Germany..")

4. Throughout the discussion the authors suggest that no significant associations
were found, yet later state that those results that were statistically significant were likely due to chance (page 9, lines 21-23). It would be sensible to acknowledge such significant findings earlier then describe that such associations may be due to chance.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no competing interests in relation to this paper.