Reviewer's report

Title: Thyroid function and Age-related Macular Degeneration: a prospective population-based cohort study - The Rotterdam Study

Version: 1

Date: 8 February 2015

Reviewer: Carrie E Huisingh

Reviewer's report:

The authors examine the relationship between thyroid function and incident AMD using the Rotterdam Study cohort. AMD diagnosis was based on color fundus photos and graded according to the Wisconsin AMD Grading system. Thyroid function was defined based on thyroid-stimulating hormone (TSH) and free thyroxine (FT4). In addition, the association was examined using Retinal Pigment Alterations (RPA) as the outcome. Finally, genetic variants were examined to see whether they were associated with AMD or thyroid function. Models were stratified by age, sex, and presence/absence of genetic variation to examine differential risks. TSH levels were not associated with AMD incidence, whereas higher FT4 values were associated with a higher risk of AMD and incident RPA. Overall, the article is well-written, the topic is relevant and the statistical analysis is appropriate. The conclusions are indicative and important. Below are a few minor comments and suggestions.

Minor essential revisions

1. The abstract did not describe the genetic analysis in the methods or the results. Suggest adding a sentence in the methods to at least indicate that there was a genetic component to the analysis.
2. Page 8, line 187 change “drusenarea” to “drusen area”
3. Table 1 and Supplemental Table 1a should state “sex” instead of “sexe”
4. In Supplemental Table 1a, there are two columns labeled with “model 2”. Please check labels.
5. In Supplemental Table 1a and 1b, the footnote indicates that model 1 is adjusted for sex. For the models stratified by sex, why were they adjusted for sex? Similar comment for age-stratified models and adjustment for age. Was age as a continuous variable included in these models? Perhaps clarify the footnotes.

Discretionary Revisions

1. What was the rationale for using the middle quintile as the reference group for TSH and FT4? Authors may want to consider providing a rationale in the methods section.
2. The methods suggested there were plots made in R, but I did not see any figures in the submission. Would it be possible to include a figure in the manuscript, perhaps from the analysis with FT4 quintiles and AMD incidence?
Quality of written English: Acceptable

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

Declaration of competing interests:
I declare that I have no competing interests.