Reviewer's report

Title: The Health Fair Effect: Bias in Screening for Thyroid Disease

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Reviewer: Deborah McCahon

Reviewer's report:

Reviewer's general comments

This paper reports the findings from analysis of data obtained from a thyroid screening health fair. The aim of the study was to explore and characteristics and symptoms which increase likelihood of a diagnosis of Overt Thyroid Dysfunction (OTD) and to determine the prevalence of OTD in a health fair population. In addition, the prevalence of OTD in the health fair population was compared with the prevalence data obtained in a large epidemiological study conducted in the UK. The prevalence of self reported symptoms traditionally associated with overt hypothyroidism in euthyroid individuals attending the health fair was compared with euthyroid individuals who participated in a case-control study. This is an interesting topic, however, this paper would benefit from major revision with simplification in some areas and further clarification in others, before being further considered for publication.

Major compulsory revisions

1) I think that throughout the paper, prior knowledge of clinical and subclinical thyroid dysfunction is required to aid interpretation. The definition of thyroid dysfunction is not provided in the abstract or the background sections and the TSH reference criteria used to categorize thyroid function as hypothyroid, euthyroid or hyperthyroid are not provided in the methods section. Furthermore, terms such as ‘over’ and ‘under-replaced’ are used in the results section (paragraph 3 sentence 3) but are not adequately explained.

2) In addition, I am concerned that bias (predominantly selection bias and reporting bias) and confounding (due to factors such as co morbidity, concomitant medication, previous diagnosis of OTD, socioeconomic status and frequency of consultation in the past 12 months) may have not been adequately considered in the study design/methodology or controlled for in the analysis and are not sufficiently addressed in the discussion section of the manuscript.

3) With respect to the prevalence of OTD, there is no comment upon the diagnostic value of a single serum TSH measurement and the possibility of transient alterations in TSH due to non-thyroidal illness and/or concomitant medication. Similarly, with respect to the prevalence of symptoms, no overlap in presentation of symptoms due to co-morbidity is considered.

4) Despite the stated aim being ‘to identify characteristics which increase the
likelihood of hypothyroidism’, demographic data are not presented by thyroid function category and the distribution in these variables (age, gender, use of concomitant medication and family history) is not compared across the 3 thyroid function groups.

5) Discussion and conclusions section, paragraph 6, last sentence, states that ‘screening identifies people who would otherwise go undiagnosed and thus untreated, and who may benefit from treatment because of their symptom load’. This statement, however, is not supported by the findings which suggest that individuals with and without hypothyroidism have a similar symptom burden. It is possible, therefore, that symptoms are likely related to co-morbidity and this being the case, treatment for thyroid dysfunction is unlikely to resolve these symptoms.

6) The concluding paragraph of the Discussion and conclusion section states that ‘greater age, greater proportion of women participants, family history of thyroid dysfunction and high proportion of suspect symptoms may contribute to the ‘health care effect’. Again, the findings presented in the results section fail to support this. Findings from comparisons between the study population and the general population with respect to demography, presence of co-morbidity or concomitant medication have not been presented in the current study.

Other minor essential revisions
Abstract
The abstract is limited and I do not think that it accurately reflects what is presented in the paper. In places it is confusing and can be easily misinterpreted. Specifically;

Abstract, Results
1) Use of the term ‘newly diagnosed thyroid disease’. I would be tempted to use the term ‘previously unknown thyroid dysfunction’ as per the main body of the manuscript.

2) With respect to symptom prevalence you state that ‘hypothyroid and euthyroid participants reported each symptom with a similar prevalence, a prevalence which was high, and in fact higher than in a previously published study of the general population.’ The second part of this sentence is true (underlined) with respect to prevalence of symptoms reported by those with euthyroid function. However, the prevalence of symptoms reported by those with hypothyroidism in the study to which you are referring is similar (or greater if you look at the prevalence of the symptoms hoarser voice, drier skin or deeper voice for example) than the prevalence reported by hypothyroid individuals attending the health fair. The abstract (and discussion section of the main body of the manuscript) should be amended to reflect.

3) There are very few results presented in Abstract, Results. I would be tempted to report data to support the term ‘high’ prevalence of symptoms. Furthermore, since your study hypothesis is that ‘certain patient characteristics enhance the
yield of testing’ I think that it would be appropriate to report and compare demographic data for the euthyroid and hypothyroid health fair groups.

Background
I think, in general that prior knowledge of both health fairs and thyroid dysfunction is assumed by the authors and required by the reader to aid interpretation of the introduction. This section is very short and would benefit from further detail and explanation of the following;
1) Statement, paragraph 2, last sentence - “Rarely, data is collected prospectively to analyse outcomes of the fair” I am not sure I fully understand what is meant by this and would like further explanation.
2) Similarly why do ‘many people with hypothyroidism go undiagnosed’ – paragraph 3, sentence 2.
3) Further clarification of the study or studies to which you are referring in paragraph 4, sentence 4 is also required.

Methods
Elements of the methods section require further clarification, specifically;
1) Paragraph 1- when was thyroid awareness week/ when were these data collected?
2) I would also have liked to know more about when and how the test results were communicated to the patient and what advice was given with respect to follow-up of results that were outside of the TSH reference criteria.

Data and statistical analysis
1) Whilst an attempt has been made to justify the use of the 10uIU/L cut off, further clarification of what is meant by the last sentence of this section is required, i.e. ‘the latter (10uIU/L cut off) was used to test the hypothesis that symptoms become useful only in more severe disease’.
2) This appears to be a ‘new’ hypothesis which has not been previously described. If this hypothesis is being tested within the current study, this should be specified earlier in the paper.

Results
In general, the results are confusing and difficult to interpret. I would like be able to easily identify the number of hypothyroid, euthyroid and hyperthyroid individual's not receiving treatment for OTD and without known OTD, identified at the health fair. This is not currently possible. A flow diagram would enable this and will further aid interpretation of data presented in paragraphs 1 and 2 and in table 1.
1) In terms of the aims/objectives of this study, I am unsure of the relevance or the value of findings presented for the group receiving treatment for thyroid dysfunction. Further justification for inclusion of these data or exclusion of those
receiving treatment is required.

2) Results logistic regression - paragraph 5, sentence 4, the statement ‘nor was there a cut off where symptoms became significant’ requires further clarification.

Table 2

1) The denominator for each of group responding to each item of the questionnaire is not reported and I am unable to calculate this from the data presented. The denominator for symptoms 1-15 is unlikely to be the same as for symptoms 16 and 17. Presumably, there are a number of male hypothyroid postmenopausal hypothyroid women participants who have not completed these questionnaire items? Reporting of 95% confidence intervals around the prevalence estimates would also be very useful.

2) There is a discrepancy between the text and table 2 in the number of symptoms being recorded. In the text ‘Health fair participants reported a wide range of symptoms, from absolutely no symptoms to all 30 symptoms listed on the questionnaire’. Table 2, however, lists 33 symptoms.

Discussion and conclusions

1) Paragraph 3, sentence 3, can you suggest possible explanations for the high prevalence of symptoms reported by the health fair population? Is it possible that prior knowledge of symptoms traditionally associated with OTD lead to greater self reporting of symptoms in both the euthyroid and hypothyroid health fair groups?

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests' below.