Author's response to reviews

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

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COVER LETTER

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To: Mr. Jimmar Dizon and Dr. Sarah Damery

Thank you for your consideration of our manuscript, The Health Fair Effect: Bias in Screening for Thyroid Disease. The following lists responses to your comments, and indicates where such changes were incorporated into the revised manuscript.

Regarding Mr Dizon’s letter:

• The ‘Competing interests’ section has been inserted after the Conclusions section and before the ‘Authors’ contributions’ section.

Regarding the Editor’s comments:

• Please see the more detailed description of thyroid disease and what constitutes thyroid dysfunction in the ‘Background’ section.

• Please see the expanded paragraph on health fairs (Background).

• More detail is provided regarding the regression analysis under the Data and Statistical analysis subsection.

• Patients have been separated into those on thyroid medication and those newly diagnosed (not on medication), regarding symptom prevalence. Table 3 shows this information. Comments are included under Results (paragraph six) and Discussion and Conclusions (paragraph 3).
• The sections have been revised to reflect the reviewers’ concerns, and the Discussion and Conclusion section modified to expand the limitations of the study.

Regarding Reviewer KD:

• Why the authors included subjects with known thyroid disease:

We invited all who presented to the health fair to participate in our study by completing the Symptoms Questionnaire. We did not know their medical history at the time they were invited to participate. Information on whether or not the individual had a previous diagnosis of thyroid disease and/or was taking thyroid medication was collected through their completion of the questionnaire. Since our initial project was to determine distinguishing factors between euthyroid and non-euthyroid states, we included everyone and analyzed the groups by biochemical thyroid status according to TSH value. We have separated the participants into those on thyroid medication and those not on thyroid medication as you requested (Please see Table 3 and corresponding text.)

Also, the secondary goal was to look at yield of screening. Interestingly, screening in Colorado (reference #12) identified a large number of people who were on thyroid medication but not biochemically euthyroid. We wanted to see if that finding was reproducible in another population, as this has significant implications for management of patients with thyroid disease.

• Explanation of the term ‘Health Fair Effect’:

Yes, as both reviewers have stated, the population who came to this Health Fair likely had multiple reasons motivating them to seek screening. The “effect” of the health fair was to draw a population more likely to have thyroid disease, for several possible reasons, and thus increase the yield of testing for thyroid disease. Reasons that are likely to motivate participation and likely to increase the probability of thyroid disease include having affected family members, having multiple symptoms associated with thyroid disease, and learning from the media that such symptoms may be associated with thyroid disease, among others.

This health fair focused on only thyroid disease, thus the study population was composed of people who wanted to be tested for reasons that may increase their likelihood of having thyroid disease as compared with the general population. Also, older people and women who are over-represented in this health fair (and health fairs in general) are groups who also have a higher prevalence of thyroid disease.

The reviewer asks what result would be expected if the health fair did not focus
on only thyroid disease. This was the case in The Colorado Thyroid Disease Prevalence Study. The Colorado study gave the same questionnaire to participants in a general health fair that offered screening and information on a broad range of health topics. (Reference #12)

Revisions have been made primarily under the Discussion and Conclusions section to better clarify this term.

• I will defer to the editor and reviewers if they wish to change the title. One suggestion may be Enriched Yield of Thyroid Disease in a Health Fair Population.

• Regarding the funding:

Support for this study included my time and cost of printing the consent forms and the questionnaires, and was provided by my employer at the time (Butterworth Hospital). Additional analyses have been supported by my current employer, the University of Nebraska Medical Center.

The health fair was in place prior to my involvement; it was a joint venture between a health care system in the area (St. Mary’s, not my employer) and Boots Pharmaceuticals. I do not know how much the $5 that each subject paid contributed to the overall costs. While charges for thyroid function testing are higher, the actual cost of running a TSH in batched assays would have been close to $5 at that time.

• Background – ‘our’ is changed to ‘USA’

• I do not have the scripts for TV and radio spots. These did focus, in part, on classical thyroid symptoms, primarily symptoms of hypothyroidism. Absolutely we agree that the promotional process influenced who attended the health fair.

• The Symptoms Questionnaire is attached.

• Insurance information is not known for the participants. It is certainly possible that people with known thyroid disease used this as a way to get their thyroid checked at a low cost.

• Thyroid Awareness sponsors gave the TSH results to all participants. Participants were instructed to provide their results to their primary care providers, regardless of result.

• Bonferroni: Though we planned to correct for multiple comparisons, no symptoms attained statistical significance even at the p = 0.05 level so we did not pursue further with a Bonferroni correction. With over 30 comparisons, the p value would then be 0.001.
• Participation in the study required only providing informed consent and completion of the questionnaire. The thyroid health fair included the TSH blood draw regardless of participation in this study. The consent process took as long as the patient needed to feel comfortable in their decision to participate or not. Most often, this was within ten minutes. The questionnaire takes between five and ten minutes to complete. Phlebotomy was generally completed within 5 – 10 minutes, but I don’t know if some locations were busier than others accounting for any wait time.

• It is possible that weight issues would be a motivation for people to participate in the health fair. Weight was not measured at the health fair.

Regarding Reviewer DM:

• Major (1) - The definition of thyroid dysfunction is clarified in the Background and Methods and Results sections. This level of detail was not included in the Abstract due to space constraints.

• I have elaborated on the terms ‘over-replaced’ and ‘under-replaced’ in the Results section.

• Major (2) - As this was an observational study of a Health Fair, and not a prospectively designed study, we were not able to control for such things as socioeconomic status. Such information was not available to us. Additional treatment of confounders has been added in several areas of the revised manuscript including the Discussion section.

• Major (3) - Regarding single TSH measurement, this is added as a limitation in the Discussion section.

• Regarding co-morbidities, this is reinforced in the Discussion section as directed by the reviewer.

• Major (4) - Demographic data:

The age, gender, family history demographics are provided in Table 1. The breakdown of these by hypothyroidism, hyperthyroidism and euthyroid states are detailed in the Results section. Family history breakdown by disease state is added in the Results section (paragraph five).

• Major (5) - The comment that patients may benefit symptomatically from treatment has been removed.

• Major (6) - The concluding paragraph of the Discussion/Conclusion section has been revised.
Abstract (1) – this has been changed.

Abstract (2) – I have made changes to help clarify. Yes, going back to the referenced article (#13), the symptom prevalence among hypothyroid individuals in the referenced article was higher for some symptoms than reported by hypothyroid individuals in this health fair population. In our study’s health fair population, symptoms did not discriminate because both euthyroid and hypothyroid individuals reported about the same prevalence of symptoms (by lack of statistical significance). It was interesting to us that there was so little difference, when the referenced population study (reference #13) showed some difference in prevalence of reported symptoms between hypo- and eu-thyroid people. Then we saw that what was different in our health fair population was that our euthyroid people reported so many symptoms. The euthyroid population in the referenced study did not report symptoms with such a high prevalence. We concluded that this thyroid health fair attracted people that, for whatever reason, were more likely to have thyroid disease. There are multiple possible explanations for such people to be motivated to attend the health fair. We have expanded this in the Discussion section. That the health fair attracted people with a higher prevalence of disease, we called that the health fair effect.

Abstract (3) – Revised to include more patient demographics and support the high prevalence of symptoms.

Background – added paragraphs with additional information on thyroid disease and health fairs.

Background (1) – revised to clarify that health fairs rarely systematically study what is done and what the outcomes are.

Background (2) – Revised the paragraph to explain why hypothyroid people often go undiagnosed.

Background (3) – I am not clear on this question. Paragraph four did not refer to outside studies and didn’t have a fourth sentence originally. I reviewed the preceding paragraphs, and with the rewrites hope that all the material is sufficiently referenced.

Methods (1) – Data were collected in April 1994.

Methods (2) – The TSH levels were handled by St. Mary’s Health Services who was one of the sponsors of Thyroid Awareness Week. They retained contact information to provide the TSH results to each participant, and requested that all individuals discuss the results with their health care provider regardless of the result. This information has been added to the Methods section.

Data and statistical analysis (1) - Clarification provided.
• Data and statistical analysis (2) – That health fairs can be used to increase yield of screening was not the initial hypothesis, but rather found as a result of our attempt to use symptoms to distinguish between hypothyroid and euthyroid individuals. I have added clarifications to multiple sections of the manuscript.

• Results: The breakdown of hypo- hyper- and eu-thyroid individuals by treatment is presented more clearly in the Results section.

• Results (1): We included the people on thyroid hormone treatment because we wanted to compare people with biochemical thyroid dysfunction with people that were biochemically euthyroid (as measured by TSH). We also included them to point out how many people who are on thyroid hormone replacement are NOT at target biochemically, demonstrating the need for regular monitoring of thyroid function.

• Results (2) – blank

• Results (3) – Revised as follows:

Nor was there a cut point where symptoms became significant. That is, logistic regression showed no statistically significant predictors with TSH >10 µIU/ml. Additionally, we repeated the analysis with TSH level as a continuous variable, and it did not change this finding.

• Table 2 (1) - Yes, as is expected in questionnaire studies, not all participants answered all questions. And definitely, not all participants would be appropriate to answer the menstrual questions.

• Table 2 (2) – This has been corrected, thank you.

• Discussion and conclusions (1) – “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?” Exactly!