Author's response to reviews

Title: Obesity and Male Breast Cancer: Provocative Parallels?

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Version: 4 Date: 19 May 2015

Author's response to reviews: see over
Reviewer – Prof. Louise Brinton

We would like to thank Prof Brinton for her second iteration of comments.

Reviewer's report:
The authors have responded reasonably well to most of my review comments, although I still believe that they should emphasize more the possibility that increases in the incidence of male breast cancer primarily reflect increased disease detection rather than a true increase in incidence. I still remain concerned about the relevance of the section on treatment, as this information is not incorporated into either the abstract or the article summary. The article summary also brings up notions regarding effects on risk of dietary intakes and environmental estrogens, which are not previously discussed (nor are the links well established for female breast cancers). On a more minor editorial note, the section on survival rates and treatment for MBC has several incomplete reference citations.

Quality of written English: Needs some language corrections before being published

Point 1. “…they should emphasize more the possibility that increases in the incidence of male breast cancer primarily reflect increased disease detection rather than a true increase in incidence”

We have included the following text on page 3 in the “Increasing incidence of male breast cancer” section to firm up the point made in the “Obesity and cancer” section on page 4 and sentence three in the “summary” The new text reads;

“It is possible that perceived increases in MBC incidence may simply reflect increased disease detection. Men are generally more health conscious than in previous generations, perhaps aided by increased awareness of breast cancer in general, and public education in male breast cancer specifically, for example through the John W Nick Foundation [24]; part of their mission statement is “to educate the world about the risk of breast cancer in men”. Such campaigns may encourage men to present to a physician with breast-related symptoms, potentially increasing detection rates. Age, the single biggest risk factor for breast cancer, should also be considered; as an ageing population, increased male breast cancer may well parallel increased longevity. However increase in MBC is also reflected in age-standardised rates [15] , which probably negates this argument.”
Point 2. “...the relevance of the section on treatment, as this information is not incorporated into either the abstract or the article summary”.

We have added to sentence 5 in the abstract. The sentence now includes the following text;

“...including how this may impact treatment.” Page 1.

Additionally we have included the following text into the “Summary” section. The text included reads:

“When considering treatment, a contextual perspective should be adopted with the atypical microenvironment, created and exacerbated by obesity, taken into account.” Page 7.

Point 3. “The article summary also brings up notions regarding effects on risk of dietary intakes and environmental estrogens, which are not previously discussed (nor are the links well established for female breast cancers)”.

The addition of environmental estrogens argument was included to address a point made by Prof Brinton in the first response. We refer to peer review document from Referee 3 which stated; “The article brings up many analogies with female breast cancers, but does not discuss the extensive attention that has focused on purported reasons for observed increases in the incidence of female breast cancers, which are much more likely to result from changes in reproductive practices and use of exogenous hormones than from changing anthropometric measures.”

We would be happy to amend this sentence should Prof Brinton wish to have it removed. Additionally, we do offer a caveat along with this statement by ending with “there are no substantive data to support this”

Point 4. “On a more minor editorial note, the section on survival rates and treatment for MBC has several incomplete reference citations”.

Thank you for this observation. Our appologies. We have imported references from the reference manager program EndNote and due to a formatting error some references were incorrectly displayed. We have scrutinised the references within this section and have found that the “Shaaban AMB, G. R. Brannan, R. .... “ Should have read “Shaaban AM, Ball, G. R. Brannan, R. ....”. Please find the corrected reference [34] on page 11.
Point 5. Quality of written English: Needs some language corrections before being published.

This issue was not raised previously by reviewer 1, 2 or 3. The initial response was “Quality of written English: Acceptable”. In addition comments by reviewer 1 stated “This is a generally well-written and cogently argued paper.” Without specific direction we are unaware of the language requiring correction.

Editorial Review Comments

Regarding the figures, it will now be necessary to include some information about the sources in the legend. I have detailed the information required below:

Figures 1-2: Thank you for confirming that these figures were made exclusively for this manuscript using data from SEER. Please add a statement to the figure legend to say these figures were made for this manuscript using the data.

The legend in figures 1-2 now includes the sentence “Data obtained and graphs generated from SEER using the Fast Stats registry”

2. Figure 3: Please could you clarify whether the figure was generated using data from CRUK, or whether the figure itself is from CRUK, and include an explanatory statement in the legend?

The data was generated by analysing raw data from the CRUK website. Included in the legend new text reads “Figure generated from raw date taken from CRUK”

3. Figure 4: Please confirm whether you have permission from the copyright holder to adapt this image and publish it in an open access journal (under a creative commons license), and include a statement about this in the figure legend. This would read ”Image adapted from [25] with permission from Elsevier”.

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now reads. “Increase in the global prevalence of obesity in males and females ≥20 years old from 1980–2013. Image created from data from [25].

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Lee
4. Figure 5: Please provide the source of this figure, and include a statement about copyright permissions.

This diagram was drawn by the author. Information assembled from several sources and publications. The legend included new text which reads: “Image was compiled by the author by drawing on information from (Tchernof, A. et al. J Steroid Biochem Mol Biol. 2015 Mar;147C:56-6; Blouin K et al Mol Cell Endocrinol. 2009 Mar 25;301(1-2):97-103 and Tomlinson JW and Stewart PM. Horm Metab Res. 2002 Nov-Dec;34(11-12):746-51)

In addition to a conversation with Clare Barnard regarding referencing publications in figure legends I wish to point out that the figures and legends have been submitted in a separate document from the main manuscript which may affect the accuracy of citation. Additionally the references drawn upon to create figure 5 do not appear in the main manuscript and as such do not appear in the reference list and have no citation number associated with them to quote in the legend. Consequently I have written the papers in the legend.