Author's response to reviews

Title: Motivators and barriers of tamoxifen use as risk-reducing medication amongst women at increased breast cancer risk: A systematic literature review

Authors:

Bettina Meiser (b.meiser@unsw.edu.au)

W.K. Tim Wong (tim.wong@unsw.edu.au)

Michelle Peate (michelle.peate@unimelb.edu.au)

Claire Julian-Reynier (claire.julian-reynier@inserm.fr)

Judy Kirk (judy.kirk@sydney.edu.au)

Gillian Mitchell (gillian.mitchell@petermac.org)

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Author’s response to reviews:

1 August 2017

Professor Jan Lubinski
Editor-in-Chief
Hereditary Cancer in Clinical Practice

Dear Professor Lubinski,

Re: Re-submission of revised review article entitled: ‘Motivators and barriers of tamoxifen use as risk-reducing medication amongst women at increased breast cancer risk: A systematic literature review’

Please find attached the revised review entitled ‘Motivators and barriers of tamoxifen use as risk-reducing medication amongst women at increased breast cancer risk: A systematic literature review’, which we would like to re-submit to Hereditary Cancer in Clinical Practice.

We are very grateful for the many helpful suggestions of the reviewers, each of which we have addressed, as detailed below.

Reviewer #1: It has been observed that tamoxifen use can reduce the risk of breast cancer in women. This is especially important for patients with a high risk breast cancer. Authors reviewed
the literature on this issue, focusing on patient motives and barriers to use tamoxifen to reduce cancer risk. The work is written systematically. It refers to most problems. However, the authors do not refer to the time duration of the intervention needed to achieve the effect. Due to the risk of side effects, the shortest intervention potentially is safer and of course, more comfortable. Recently, Gronwald et al. observed that the annual use of tamoxifen was sufficient to achieve a reduction in the risk of breast cancer. The issue of the duration of the intervention as well as its potential impact on the decision should be incorporated into the discussion.

In response, the following paragraph was included in the discussion on page 11:

“Women should also be provided with information on the time duration to achieve the effect. The recommended duration of tamoxifen (five years) for risk reduction is based on data on contralateral breast cancers among women who were treated for primary breast cancer. However, the optimum duration of tamoxifen for treatment of breast cancer and for risk reduction are not necessarily the same. Due to the risk of side-effects, the shortest intervention is preferable. In a case-control study, Gronwald et al. observed that 1-year of tamoxifen use was sufficient to achieve a reduction in the risk of breast cancer. These authors suggest that a randomized controlled trial of 1-year of tamoxifen versus placebo in BRCA1 and BRCA2 mutation carriers is warranted.”

Reviewer #2: In general very nice work. My main comment is that Result section and Discussion section may benefit from being differentiated more clearly from one another, and Results section would benefit from being structured somewhat different.

The results and discussion sections were edited extensively to differentiate them more clearly from one another.

Results - The list of motivators and barriers should follow in the same order, makes it easier to follow. Make sure you don’t revisit same argument/result in different sections. I.e. Regarding barrier: "side-effect" make sure you don’t have several head-lines for the same topic, i.e. "access to information on side-effects" p 7, line 48, and "Side-effects" p 8 line 54 could be combined?

In order to avoid any repetition the results section was completely restructured. In the submitted version the results section was divided into “motivators” and “barriers”. The revised version of the manuscript no longer divides the results section into separate sections on motivators and barriers; instead each factor is described in turn”.

I also the believe the last section "Side-effects" also lists what may be described as "beliefs/opinions on taking medication" rather than side-effects per se.

The heading was reworded as “Concerns about side-effects” (page 7)
p 8  line 23 starting with "however.... " I believe is better placed in Discussion. The same goes for the paragraph starting with "Since publication..." line 43- 51.

Both sentences were deleted from the results section and replaced with the following sentence in the discussion on page 12:

“Many of the studies included in the review were published some time ago, and more data have become available since to support the efficacy of tamoxifen [39]. It is possible that women’s preferences have changed as a result of recent evidence, and the replication of studies such as the one by Metcalfe et al. [2] would be of interest.”

Thank you very much for your consideration of this manuscript.

Yours sincerely,

Bettina Meiser

Professor
University of New South Wales