Reviewer’s report

Title: The role of BRCA1 and BRCA2 mutations in prostate, pancreatic and stomach cancers.

Version: 1 Date: 30 March 2015

Reviewer: Elizabeth Bancroft

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Major Compulsory Revisions

1. Does it address an important or timely issue?

   a) This is an issue that has been addressed by others, however it remains an interesting topic because there is still not consensus between studies. However there are several failings in this review. First and foremost the literature reviewed is old, and several notable studies are missing.

   Looking at the reference list, excluding web references out of the 40 references cited, there is one article from 2012, one from 2010 and the majority are much older. For this article to be considered, a thorough review of the literature over the last 5 years should be conducted. Recent notable papers on this very topic are missing. In addition there have been several key publications about the risk of prostate cancer and pancreatic cancer from large international consortia. These should be included.

   b) It is not clear how these cancers were chosen as the focus of this review. In places it sounds like it was to be a review of the risks for men, but this is not the case. The review states that it is also to focus on screening but this has not been included. There is a brief mention of prostate screening but this does not address any of the complexities of this area of debate or include any mention of the IMPACT study which is ongoing and aiming to address this very question.

2. Is it well reasoned?

   a) The authors have not described the methods used to conduct the review, other than stating “the most relevant available literature” – it would be helpful for the reader to understand how the papers reviewed were selected, what the inclusion criteria were, the time frames for the searches and the key words used for the searches. Also an explanation for why these three cancers were chosen out of all the cancers that are associated with these genes? What was the rationale for undertaking this review?

   b) The abstract states the aim was to examine the association of BRCA1/2 germline gene mutations with cancers other than breast or ovarian – this is not the case, it has been limited to three cancers.

   c) The authors have largely considered BRCA1 and BRCA2 to be the same. Better attempts to separate the two genes should be made, particularly in regard to pancreatic and prostate cancer where the evidence for the role of BRCA2 is
much less controversial compared with BRCA1.
d) The review is more of a narrative as written rather than offering a critical viewpoint. Study limitations are rarely drawn on. In particular, in discussing stomach cancer the majority of papers acknowledge that they are using unverified series with self-reported cases of cancers. Stomach cancer is often mistaken for gynaecological cancers and this limitation should be mentioned.
e) A table summarising the key points of all of the papers would be helpful for the reader. This would allow some of the text describing study populations could be taken out of the text.
f) In the prostate cancer survival section – last sentence of para 1 – what does this have to do with the review? Either expand or remove. Likewise the second to last sentence of para 2 – how has the previous sentence informed this statement?
g) Be careful how you review papers that are looking at cohorts of BRCA1/2 carriers vs those looking at disease cohorts and reporting the incidence of mutations, these are not always directly comparable.
h) The last section before the conclusion (impact of BRCA1/2 mutations in other associated cancers). Either this should be fully reviewed and the whole paper changed accordingly or removed as this is not what is stated the review aimed to do.
i) Conclusion – needs to be completely re-written. It is confused and disjointed. State what the review has found, what it adds to the evidence and suggest what implications this has for practice if targeting a clinic journal.

3. Is it relatively balanced, or does it make plain where the author's opinions might not represent the field as a whole?
There is no obvious author bias, but in the absence of a thorough and comprehensive review it is difficult to fully assess.

4. Do the figures appear to be genuine, i.e. without evidence of manipulation?
There are no figures or tables, but as suggested above a summary table would be helpful

5. Is the standard of writing acceptable?
a) The introduction is a little too simplistic for this journals audience and the word count could be cut here. The background to the discovery of BRCA1/2 is not necessary to this audience.
b) Make sure that all statements are appropriately referenced so that it is clear where the data reported has come from.
c) A background to each of the cancers would be beneficial at the start of each cancer section
d) The manuscript is repetitive in places and should be revised to remove repetition
e) Introduction, paragraph 4 – reference 10 does not relate to the Evans et al
f) The manuscript often uses the statement “recent years”, “recent times”, “recently found” when referring to literature dating back over 10 years. This needs to be corrected.

g) In discussing the “founder” mutations the population needs to be defined and explained. Presumably the Ashkenazi Jewish population.

h) Pancreatic cancer – paragraph 4 – too much detail about one study (Axilbund et al) – this should be removed. Paragraph 6 – last sentence is about breast cancer, this should be removed as it is not the focus of this review. Paragraph 8 – last sentence, again this review is not about breast cancer – the evidence for a link of BRCA1/2 with breast cancer is undisputed!

i) Stomach cancer second paragraph - last sentence should be removed.

j) Stomach cancer 5th paragraph last sentence – where is the evidence to support this claim?

**Level of interest:** An article of limited interest

**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.