Reviewer’s report

Title: Increased Breast Cancer Risk in Women with Neurofibromatosis Type 1: A Meta-analysis and Systematic Review of the Literature

Version: 0 Date: 29 Jan 2019

Reviewer: D Gareth Evans

Reviewer's report:

The authors have undertaken a meta-analysis of studies assessing breast cancer incidence pathology and survival. They have identified only 4 studies that fulfilled their preset criteria. The study is well executed and provides a useful overview. It is a shame that their timeline has missed the important large Finnish population based study -Uusitalo et al. Why is it so long since the timeline?

1. Comparisons were made with the general population using the SEER database. This needs to be at least controlled for year at diagnosis. It should also be acknowledged that survival in SEER is better than in some countries of origin of cases such as the UK

2. 'A recently published study not included in the meta-analysis of this manuscript was conducted by Uusitalo et al. to evaluate the cancer incidence and mortality in a population-based cohort of 1,404 (737 women) Finnish patients with NF1.' -it is a shame this study was not included we are now over 3 years after the end date of their PubMed search. This is quite a long time to get a meta-analysis conducted and reviewed for publication. The Uusitalo study is clearly important and would boost he numbers substantially

3. '..The NF1 gene and (BRAC1) gene are both on chromosome 17,' Misspelling of BRCA1

4. 'However, pathogenic variants in the NF1 gene were not associated with increased risks of breast cancer. [91]' -Please see recent review of panel testing (https://www.ncbi.nlm.nih.gov/pubmed/30510771) it is highly likely that NF1 is selected out of testing due to known diagnosis or other factors.

5. 'Furthermore additional studies are required to assess the influence of NF1 pathogenic variants identified in patients undergoing clinical genetic testing on breast cancer risk in individuals without clinical evidence of NF1.' -The authors may have also missed this recent publication on genotype-phenotype -https://www.ncbi.nlm.nih.gov/pubmed/30530636

Level of interest
Please indicate how interesting you found the manuscript:

An article of importance in its field
Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

None

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal