Reviewer's report

Title: Tumour spectrum in non-BRCA hereditary breast cancer families in Sweden

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Reviewer: Thilo Dork

Reviewer's report:

Wendt and colleagues report that endometrial cancer is overrepresented in Swedish non BRCA families, compared to the general population. Their study supports a previous study from Wachenfeldt et al. and extends the observation to families without BRCA1 and BRCA2 mutations. The present results also indicate an excess of ovarian, pancreatic and prostate cancer in such families. The data are interesting and seem to base on solid grounds in regard that most cancer diagnoses were verified from cancer registry or medical records.

The statistical procedure may be better judged by other experts but it is a bit unclear what the authors mean with "indirect standardization" and why a cancer diagnosis was regarded as overrepresented in the relatives of the breast cancer patients if the confidence interval was above both population reference values (shouldn’t the latter have confidence limits themselves?). Although the authors state in the abstract that the observed differences were significant, the level of significance is not clear.

Some minor suggestions to further improve this manuscript:

1. The introductory part from “Major advances…” to “…still remains unclear” is unnecessarily long and verbous, this should be condensed since known breast cancer susceptibility genes have been covered by several reviews.

2. In the Discussion part, the authors may wish to be more cautious with their statement that “there is no association with breast cancer” in Lynch Syndrome. While this view is supported by Reference 44, others have provided evidence for some role of mismatch repair gene mutations in breast cancer.

3. The authors propose that PALB2 could partly explain the excess risk for prostate, ovarian and pancreatic cancer. However, PALB2 mutations are quite rare and it would be worthwhile to test whether their population frequency and penetrance are sufficiently high to result in the excess of these cancers.

4. Gene symbols should be in italics and should follow consensus nomenclature, e.g. “BRCA2” instead of “BRCA 2”. Typo in Table 1: Thyroid.

Level of interest: An article of importance in its field

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

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests