Author’s response to reviews

Title: Associations between XRCC3 Thr241Met polymorphisms and breast cancer risk: Systematic-review and meta-analysis of 55 case-control studies

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Response to comments

Reviewer reports:

Teguh Haryo Sasongko (Reviewer 1): This is a well-written systematic review by the authors Dashti et al that assessed the association of XRCC3 Thr241Met with breast cancer. There are a few minor editing that would improve clarity:

1. Conclusion shown in the abstract should tally with that shown in the conclusion section of the text.

Response: Conclusion shown in the abstract was matched with that shown in the conclusion section of the text and was highlighted.

2. Is there publication time restriction on searching?

Response: Yes, there is. We mentioned it in manuscript. (1990/01/01:2018/03/31)

3. How were the classification determined? NOS is using star scoring system (e.g. how many stars for good, fair and poor?). This can then be mentioned in Tables 1 and 2 if a study is considered good or fair or poor.

Response: We mentioned it in manuscript. (Quality of studies based on NOS star scoring system: 1-2 stars: poor, 3-5 stars: fair and 6-10 stars: good)
4. In the methodology section, information on publication bias analysis should be in a separate sub-section.

Response: It was done.

5. It should be "grey literature", not "gray literature".

Response: It was done.

6. The term used is usually "study or studies", not "research or researches" to refer to the articles included/excluded.

Response: It was done.

7. PRISMA Flowchart: There are 3731 records remained after duplicates removed. How were these screened to come down to 287? How, then, 187 records were removed? Title/Abstract screening?

Response: That was mentioned in figure 1.

The duplicates were removed By EndNote™ X8 then 187 records were removed by Title/Abstract screening.

Sumantra Chatterjee, PhD (Reviewer 2): The study by Dashti et al is a meta analysis of 30966 sporadic and 1174 familial multi ethnic breast cancer cases with 32890 controls to find association between a specific polymorphism in the gene XRCC3 and breast cancer. The authors report association with the SNP in Arab populations in a recessive model and in a dominant model in Asian population.

This is a standard meta analyses and doesn't provide any new insight in to the role of this polymorphism in breast cancer. Furthermore breast cancer is extremely heterogeneous disorder. The authors should try to separate the cases into ER positive, ER negative and triple negative breast cancer and re do the Meta analyses. This might even show that the concerned SNP is indeed significantly associated with a particular subtype of breast cancer in all or particular ethnicity.

This will make the analyses more useful to the community.

Response: We appreciate for your valuable comment and we completely agree with you but there are some limitations in the primary studies and we did not find any genotyping data according to
breast cancer subtypes. We found just 3 studies with triple negative breast cancer genotyping data and due to few number of primary studies, the result of meta-analysis is not reliable.