Reviewer's report

Title: The INSIG2 rs7566605 polymorphism is not associated with body mass index and breast cancer risk

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Reviewer: Niloufar (Neely) Kazerouni

Reviewer's report:

The study by Campa et al. attempts to explore the association between the single nucleotide polymorphism rs7566605 and BMI and BC risk, respectively. The study design is a nested case-control study within the very large EPIC cohort. The majority of women and BC cases included in the study are post-menopausal women, which needs to be highlighted in the article.

The BC analysis was also conducted by menopausal status. Did the sample size among pre-menopausal women yield an adequate power to explore any associations between BC risk and the polymorphism? Was a stratified analysis by menopausal status also done for the BMI association?

There is no mention of the family history of BC in the study. I am wondering whether the inclusion of such variable in the BC risk logistic regression model would make any differences in the estimate of associations.

In the calculation of OR for the association of BC risk and the polymorphism in Table 2 is the CC genotype the common allele and the referent group? If so, this should be mentioned in the footnote of the Table. Also, it should be clarified that the OR in the table is the OR for BC risk. As for the BMI analysis in Table 2, it seems that you have reported the results from the unconditional regression analysis and not from the logistic regression. This needs to be clarified in the Table. It would be more informative to report the results from the logistic regression analysis for the BMI in the same table or in a separate table as well with clarifications regarding the comparison groups (different BMI categories) and the referent allele group.

In the text for results and discussion section, 3rd paragraph, by dominant, codominant, and recessive models do you mean GG genotype for dominant, GC genotype for codominant, and CC for the recessive model? If so, I would add these genotypes in parentheses. Also, I would separate the results and discussion sections according to the instructions to authors: http://www.biomedcentral.com/bmccancer/ifora/. The discussion could start from the second page of this section starting with the paragraph “in this report we explored....” Also, under this section, 5th paragraph, the reference for Walley, 2009 needs to be mentioned under the references section.

In Table 1, with the use of an asterisk, it should be noted in the footnote that the 2,194 controls include 52 duplicate controls. Also, under the “selection of case
and control subjects” section, it is mentioned that the 123 cases and 125 controls had genotyping failure, while in Table 1 and in the text under statistical analysis, these incomplete matched sets are included in the counts for subjects with genotypes. This needs to be clarified.

Under the key words, insulin should be spelled as insulin.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.