Reviewer’s report

Title: Association between HIF-1alpha C1772T/G1790A polymorphisms and cancer susceptibility: An updated systematic review and meta-analysis based on 30 case-control studies

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Reviewer: Sonja Berndt

Reviewer’s report:

This study presents a meta-analysis of two HIF-1 SNPs and cancer risk. Although interesting, in the era of GWAS, the value of this type of analysis is limited. One could obtain the GWAS data (and impute if necessary) for these two SNPs from all cancer studies in dbGAP or other such resource and conduct a meta-analysis with the GWAS data instead of relying on published data, which may be biased toward positive findings.

Major compulsory revisions are as follows:

1) The authors should be consistent and careful in their word choice to reduce confusion. They state that they reviewed 28 articles including 30 studies, but then state that the 28 studies included x cases and x controls in the abstract but 30 studies is stated in the title, making it unclear whether there are 28 or 30 studies were included. Plus, the figure shows 26 studies for 1 snp and 22 studies for the other snp, which makes it more confusing. Also, the authors often use the term pooled analysis, which usually is limited to studies where the raw data is used, instead of the aggregate results, which are used in a meta-analysis.

2) The results section should be condensed. The pheterogeneity values could be provided in the table, instead of the listing them all in the results.

3) The authors should be clear about the genetic model, T vs. C. This appears to be the allelic model (e.g., having T allele vs. having C allele), but the authors refer to it as an additive model, which should refer to the model, where homozygote wildtype is coded a 0, heterozygotes as 1, and homozygote variant as 2 and the term is included as a continuous term in the model. The authors should clarify what they mean by this model.

4) Tables 2 and 3. The authors should include the number of cases and controls for each genotype in the table. It is hard to evaluate the results without knowing the number of cases and controls with each genotype. Also, only two decimal places are needed for the ORs.

Minor essential revisions:

5) The pairwise LD (e.g., r2) information should be provided for the two SNPs.

6) The authors need to provide the precise p-value and not write P=0.000.

7) Figure 4 should be a supplementary figure.
**Level of interest:** An article of limited interest

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

**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.