Reviewer's report

Title: Association between Paraoxonase gene and stroke in the Han Chinese Population

Version: 5 Date: 12 September 2012

Reviewer: Tom Trikalinos

Reviewer's report:

Many thanks to the authors for their revisions. I hate to be a stickler, but I believe that the authors have not responded to my lingering comment on their decision to perform adjusted analyses. The explanation/reply given is not satisfactory. In brief, my comment is that for heritable traits, the total genetic effect is obtained from an unadjusted model. If anything, in genetic epi we have a clearer notion of what the DAG should look like; there is nothing on the left of the Genetic factor.

/*Major Compulsory revisions*/

1. It is clear that the authors and I are not on the same page on this matter. Thus I would urge the authors to add a sentence along the lines of: "It is unclear to us whether adjusted or unadjusted analyses are preferable in this particular application. In other settings, authorities have discouraged the use of adjustments when obtaining the total genetic effect. [ref 1]"

2. Thanks for clarifying the haplotype analyses. I think that a preferable analysis would be an ANOVA in which the factors are the haplotypes. This can be done also in a regression context, where all haplotypes are considered jointly. The analyses you have performed take a haplotype (I presume present either as one copy or as two copies (a diplotype) versus being absent. However, all these analyses are non-independent and are best performed jointly as per my suggestion above. Again, I leave this to the editor to decide how to handle (demand a re-analysis, as I am inclined to suggest, or allow the current analysis with a mention in the discussion that it is a suboptimal approach, as per my comment above.)

3. Finally, please seek the help of an editor. Some additions in the abstract and the text read awkwardly.

My best
TA Trikalinos

References
1: Genotype-guided tamoxifen therapy: time to pause for reflection?
Lash TL, Lien EA, Sørensen HT, Hamilton-Dutoit S.

**Level of interest:** An article whose findings are important to those with closely related research interests

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

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

**Declaration of competing interests:**

I declare that I have no competing interests