Reviewer’s report

**Title:** Is the impact of methylmercury and n-3 polyunsaturated long chain fatty acids on myocardial infarction risk modified by genetic polymorphisms in glutathione-related genes? A case-control study.

**Version:** 1 **Date:** 20 December 2010

**Reviewer:** Claudia Gundacker

**Reviewer’s report:**

Engström and colleagues report that genetic polymorphisms in GSH related genes (GSTP1, GCL) have no significant impact on the risk of first ever myocardial infarction (MI) in a Swedish population (N=1027). The issue of genetically determined susceptibility towards disease is very important. This specific gene-environment interaction in relation to MI risk has not been investigated so far. The manuscript is well-written, the methods are appropriate and adequately described. The data are sound and well controlled. Before publication, the manuscript needs some revision (minor essential revisions).

Authors are stating that carriers of the variant alleles, i.e., GCLM-588 TT genotype and joint GSTP1 polymorphisms have lower risk of MI compared to reference genotype. Statistical comparisons show that the observed effects are non-significant. This is explained by the small amount of TT carriers in this sample. Indeed, this may have increased the probability for false-negative results. It would be desirable to provide the number of individuals present in subgroups (Fig. 2 and 3). The reader has to deduce from Table 2 that about 40 study participants are homozygous carriers of the T allele. The distribution among tertiles remains unknown.

It is not explained why authors stratify ORs into tertiles (PUFA- and Ery-Hg-levels, respectively).

Authors state that „the GCLM-588 TT genotype had a lower risk relative to the CC genotype in each P-EPA+DHA or Ery-Hg tertile ...“ This is not true regarding Ery-Hg in tertile 2. Ideally ORs and confidence intervals are presented in a table. It is hard to discern from Fig. 2 and 3 what the exact ORs are. Only the data for GCLM-588 and GSTP1-105/GSTP1-114 genotypes should be divided into tertiles, if at all.

I miss a rationale for evaluating the effects of Hg-related susceptibility genes in relation to PUFA levels. Authors say that in one previous study, the GCLM-588 TT genotype demonstrated the highest levels of Ery-Hg, and that it displayed the lowest risk of MI in each P-EPA+DHA tertile in this study.

It remains unclear whether the GCLM-588 TT genotype has the highest levels of Ery-Hg also in this study (are the study groups the same?). Engström and colleagues are concluding „this suggests that Ery-Hg has a true effect on MI risk..."
and is not only reflecting fish intake“. This statement is not traceable.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**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.