Reviewer's report

Title: Investigation of 95 variants identified in a genome-wide study for association with mortality after acute coronary syndrome

Version: 1  Date: 21 January 2011

Reviewer: Aaron Isaacs

Reviewer's report:

Morgan et al. investigate 95 SNPs derived from a genome-wide association study of MI for association with mortality after acute coronary syndrome. Generally, this work was well-conducted and the manuscript is well-written. The authors are careful to detail limitations of their study. There are some concerns, however.

Major Compulsory Revisions:
1. Conformation to Hardy-Weinberg proportions was tested using a chi2 test. A number of genotypes are quite rare, however, and these should be tested with an exact test.
2. Multiple testing corrections are described on page 7. It is unclear, however, if these corrections are ever actually applied. P-values cited in the text appear to be unadjusted. In table 3, a Bonferroni correction would yield no significant results. This issue, in particular, requires some clarification.
3. The authors should supply a table (perhaps supplementary) with the association results for these SNPs from the Myocardial Infarction Genetics Consortium study from which they were selected. Additionally, the authors should consider requesting look-ups for their SNP of interest in the CARDIoGRAM study.

Minor Essential Revisions:
4. Power calculations suggest adequate power to detect SNPs with very high hazard ratios. Given that the HRs typically seen in GWAS are quite small, it would be instructive to see what sort of power they have for a SNP with an HR of 1.15 or 1.2.
5. At the end of the first paragraph on page 9, Table 2 is cited for the deviation from HWE. This should be Table 3.
6. Table 3 is quite cluttered and difficult to read.
7. 95% confidence intervals should be supplied for HRs in the text.
8. In the first paragraph of the discussion (page 10), "confirmed" is a strong word given the statistical evidence supporting this association. Generally, the replication evidence weakens support for an association of this SNP.

Discretionary Revisions:
9. Although the authors are careful not to overstate their findings, they might consider writing it as a truly negative result. The replication weakens their initial (already non-compelling) association.

**Level of interest:** An article of limited interest

**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.