Reviewer’s report

Title: Lack of association of two common polymorphisms on 9p21 with risk of coronary heart disease and myocardial infarction

Version: 3 Date: 5 June 2008

Reviewer: Benjamin D Horne

Reviewer’s report:

The authors have revised the manuscript well, but have failed to respond adequately to two previous comments.

Major Compulsory Revisions

1. The previous studies of the 9p21 locus examined either MI (fatal or nonfatal) or CHD (MI or revascularization). The phenotypes included in the aggregate clinical endpoint in this paper are much more broad than those that have been previously studied, thus this cannot be called a replication study. If the authors wish to label their study a replication attempt of previous findings, they should limit their phenotype (at least for their primary analysis) to the previously-evaluated phenotype. Otherwise this is just an attempt to apply the 9p21 locus to associations with a broad cardiovascular phenotype and is a first association attempt for that phenotype. Phenotype in genetic association studies is crucial and must be consistently defined in order to make a study comparable to previous work.

2. Without full follow-up of all controls to the end of life ... it cannot be assumed that the controls are all actually controls. As the authors mention, those in this study are more likely to have coronary disease since they are older, thus it is also reasonable to assume that more controls have disease that is-- as yet-- undiagnosed, but that is present. This lack of clarity in the control group should be explained in a limitations paragraph.

Which journal?: Appropriate or potentially appropriate for BMC Medicine: an article of importance in its field

What next?: Accept for publication in BMC Medicine after minor essential revisions

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.