Reviewer’s report

Title: Association of an INSIG2 obesity allele with cardiovascular phenotypes is gender and age dependent

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Reviewer: Paul Nyquist

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In its present form the manuscript addressed the question of the influence of the INSIG2 obesity allele gene variant on CAD phenotypes. This is a candidate gene study that uses a mixed population of African American and Caucasian American participants. It uses a retrospective analysis of a prospectively gathered database. The methods are well described and the authors have taken adequately tested and verified that the population is in Hardy Weinberg equilibrium.

The data are not based on a population-based study allowing for the unidentifiable influence of different selection biases on the analysis. This is a weakness of the study. That said, the approach appears to have selected a population in hardy Weinberg equilibrium for the desired genes with a well described phenotype. In addition, the authors have completed a logistic regression analysis in which the odds ration confidence interval crosses unity and the p value is less than that required by the Bonfiorri adjustment controlling for most significant confounders. All data is gathered from a registered controlled trial and is adequately reported.

In response to my review the authors have rewritten the manuscript using a more succinct writing style. They have completed a more concise discussion that is greatly improved and more directly addresses the limitation of the study. However, issues such as the limitation of a non-population based study are not mentioned. The authors need to replicate the findings in larger population based study or database to verify the significance of their findings.

The manuscript in its present form appears to be acceptable for publication.