Reviewer's report

Title: Endothelial nitric oxide synthase gene polymorphisms and risk of diabetic nephropathy: a systematic review and meta-analysis

Version: 1 Date: 12 January 2013

Reviewer: Elias Zintzaras

Reviewer's report:

The analysis performed in the paper is not valid. We cannot compare Diabetics with Nephropathy vs Diabetics without Nephropathy (controls) since the phenotype of the controls in definite (a control may become a case after a period of time). Thus, the paper by Zintzaras et al in Genetics in Medicine is absolutely valid!

The paper can have a venue for publication only if the authors analyse the studies using the Generalized Odds Ratio (ORG), a novel methodology proposed by Zintzaras (Stat Appl Genet Mol Biol 2010 and J Appl Stat 2012). The ORG utilizes the complete genotype distribution and provides an estimate of the magnitude of the association between disease progression and genotype. In general, ORG expresses the probability of a subject being more diseased relative to the probability of being less diseased, given that the subject has a higher mutational load. ORG with values greater than one suggests that disease progression is proportional to increased genetic exposure and inversely proportional for values less than one.

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

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'