Reviewer’s report

Title: Long-term Exposure to Particulate Air Pollution and Brachial Artery Flow-Mediated Dilation in the Old Order Amish

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Reviewer: Marc Claeys

Reviewer's report:

The present study evaluates the effect of longterm exposure to particulate matter (PM2.5 and PM10) on endothelial function (as assessed by FMD) in 615 healthy Amish participants from the Heredity and Phenotype Intervention (HAPI) Heart Study. The authors found an inverse relationship between air pollution (average over 12 month) and FMD.

This finding, though not completely new, remains interesting particularly as the study is carried out in a rural area with very low pollution level (eg PM10 below the stringent WHO criteria). Following issues remain to be clarified and solved in order to increase the scientific attractivity of the study

1. FMD measurements: the paper should document more into detail the conditions of the measurements (time of the day, instructions about food/beverage intake) as well as about the machines used for the measurements (is there an automatic detection of the maximal dilatation?). In addition, the authors should provide data on the intra-observer variability of the measurements.

2. As FMD is very sensitive to short term variations in the environment, authors should correct for acute effect of air pollution on FMD. They should determine the association between FMD and the level of PM in the days before the FMD measurement and include this information in the multivariate analysis for assessing the longterm effect of airpollution exposure on FMD.

3. The finding that the association was more prominent in male than in female is intriguing, which might suggest a protective effect of oestrogen on this relationship. Could you do a subgroup analysis focusing only on healthy people below 50 y in order to exclude menopausal women. The interactive effect could become significant in this subgroup.

4. Do we have information on other pollutants (nitrogen dioxide, sulfur dioxide, carbon monoxide)
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An article of importance in its field

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Acceptable

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