Reviewer’s report

Title: Commonly-used Approaches to Estimating Long-term Exposure to Fine Particulate Matter (PM2.5) Components and Prevalence of Subclinical Atherosclerosis in the Multi-Ethnic Study of Atherosclerosis

Version: 1 Date: 14 February 2013

Reviewer: Bart Ostro

Reviewer’s report:

This manuscript reports the results from a cross-sectional analysis of the association between PM2.5 and several of its constituents with two markers of subclinical atherosclerosis, carotid intima-media thickness (CIMT) and coronary artery calcium (CAC). It also examines the relative impact of three different exposure metrics. The manuscript is an important contribution to the literature given: (1) the importance of studies linking PM2.5 to cardiovascular mortality (2) the increased interest in determining the relative toxicity of PM2.5 constituents and (3) the mixed results of previous studies of particulate matter and CIMT and CAC. The MESA cohort is well recognized for the quality of the data and the study team is experienced and known for its thoughtful analytical approaches. Nevertheless, there are several issues that should be considered prior to acceptance.

Major Compulsory Revisions

1. The exposure strategy was not entirely clear. In each of the MESA sites, the authors co-located one of their own monitors next the EPA chemical speciation monitor (CSN). Presumably this was to make full use of that data. However, in the Discussion, it is stated that only the MESA monitors were used in the study. It seems like more species, over a longer exposure period, could be used from the CSN. Was there any comparisons made between your monitor and the CSN species monitor? Also, you could assign 2000-2002 (or longer) readings from the CSN to a subset of study participants located close to the monitor. In addition, it is indicated that two-week samples of PM2.5 and its constituents were collected, but the equipment was deployed for over a year. It’s not clear if the monitors provided data for every two-week period for the 50-week average used in the study and whether there were extra requirements placed on data completeness for each two-week period.

2. A major concern is the cross-sectional nature of the study. As you indicate, the fact that the associations became null when MESA site was added to the regression model suggests that cross-site differences in CIMT is driving the results. Were there any repeated measures that could be matched with CSN readings so that the full benefit of the longitudinal cohort could be utilized? It seems that within-city differences could be investigated for the species, especially for Los Angeles, where there should be sufficient exposure contrasts. I
am not clear about the statement in the Discussion “While we put most interpretive weight on models that did not control for metropolitan area, it may have been preferable to place more weight on findings from models with control for metropolitan area if the data had permitted it.” You did, in fact, control for metropolitan area. Maybe you should include regional and neighborhood variables from the Census to provide additional controls.

3. Give some previous findings of associations between cardiovascular outcomes and silicon, the low concentrations found in these study sites should be mentioned in the discussion. Silicon was the only species which showed a decrease over time in several of the MESA areas. Also, correlation coefficients for Figure 3 should be provided.

4. There should be some discussion of the biological plausibility (or lack of knowledge) for an association with CIMT but not CAC.

Discretionary Revisions

1. Given that statins will alter CIMT and may impact CAC, it may be useful to stratify by statin use since it may mask the impact of PM2.5. It would be of interest to see the interactive effect of PM2.5 and species on non-statin users. In addition, some analysis of other potential effect modifiers would be of interest.

Minor Essential Revisions

In Table1, there is a double asterisk for Lipid lowering medication and it is not clear what that signifies.

I declare that I have no competing interests.

**Level of interest:** An article of importance in its field

**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.