Author's response to reviews

Title: Atherosclerosis Profile and Incidence of Cardiovascular Events: A Population-based Survey

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Author's response to reviews: see over
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Rikki Graham, PhD
Senior Assistant Editor
BioMed Central: Cardiovascular Disorders

Re: MS 9093501292826470 – Atherosclerosis Profile and Incidence of Cardiovascular Events: A Population-based Survey

Dear Dr. Graham:

It is with pleasure that we submit a revised manuscript which addresses the comments from the reviewers. We are pleased that the journal reviewers found the manuscript to be of interest and we found the reviewers’ comments helpful in clarifying the description of our original research.

A point-by-point response to each of the reviewers’ comments is provided below. We look forward to hearing from you regarding the revised manuscript.

**Editor’s comments:**

1. In the background of your abstract, could you please include the rationale and background for your study as well as the aims.

   Response: The rationale/background has been added to the abstract (page 2).

2. Please also let us know if you would like the SHIELD study group to be listed as an author in your manuscript.

   Response: Yes, we would like the SHIELD Study Group as an author in the manuscript. We have included the study group in the ‘authors details’ section of the submission system.
Reviewer #1:

1. The main concern is that the study group is not representative for the general population, or that self-report underestimates the occurrence of subclinical atherosclerosis. Indeed, the prevalence of subclinical atherosclerosis in this study group (2.8%) is much lower than expected on the basis of mean age. In the Multi-ethnic Study of Atherosclerosis cohort (aged 45-84; mean age: 59, compared to 66 for patients who reported sub-clinical atherosclerosis) the prevalence of subclinical atherosclerosis was 34% based on plaque occurrence in carotid arteries with at least 25% stenosis, and even 42% on the basis of a positive Agatston calcium score.

Response: We have added a paragraph to the Discussion section (page 12) addressing the under-estimate of the prevalence of atherosclerosis from self-report compared with cardiac imaging technology. Additionally, the low prevalence rate was already included in the study limitations (page 13).

2. Another concern is that participants did not have to report medication.

Response: We are not clear on what concerns the reviewer on this point. Respondents were asked to write down each of their prescription medications and refer to their pill bottles when completing this portion of the survey. However, the authors felt that medication utilization was not relevant to this analysis of the prevalence of atherosclerosis and predictors of incident CVD events, especially since the definition of atherosclerosis was restricted to self-report of being told by your doctor or health professional that you have narrow or blocked arteries/carotid artery disease. Use of cardiovascular medication was not part of the atherosclerosis definition.

3. To determine the value of self-reported subclinical atherosclerosis for predicting incident CVD, the regression model should contain all respondents with incident CVD, and subclinical atherosclerosis, age, gender, geographic region, dyslipidemia, circulation problems, diabetes, hypertension, and smoking.

Response: We apologize for the lack of clarity on the description of the regression model for predictors of incident CVD events. The description has been clarified in the Methods section (page 8). All respondents with incident CVD events and subclinical atherosclerosis were included in the model. Geographic region was not
included in the incident CVD event model because region was not significantly different as shown in Table 3. Additionally, information on a second regression model was added to the Methods and the Results (page 11) sections. The second model included all respondents with incident CVD events regardless of their atherosclerosis status (with and without atherosclerosis); this model tested the predictive value of atherosclerosis while controlling for other covariates.

4. It is of interest to know which factors predicted incident CVD in respondents without self-reported subclinical atherosclerosis.

Response: A second logistic regression was computed and the results added to the Results section (page 11). This regression model included all respondents with and without atherosclerosis and age, gender, dyslipidemia, circulation problems, diabetes, hypertension and smoking to determine predictors of incident CVD events.

5. As discussed above, one should know how sub-clinical atherosclerosis was diagnosed.

Response: The survey question that was used to identify respondents with atherosclerosis has been added to the Methods section (page 6). Respondents were asked if a doctor or health professional ever told them that they had narrow or blocked arteries/carotid artery disease. We had already addressed the limitation of not having angiographic studies to assess atherosclerosis in the study limitations paragraph (page 13).

6. Was dyslipidemia equal to hypercholesterolemia, or did respondents also report low HDL cholesterol and/or high triglycerides?

Response: The survey question that was used to identify respondents with dyslipidemia has been added to the Methods section (page 7). Respondents were asked if a doctor or health professional ever told them that they had cholesterol problems. Since the survey question did not specify high LDL-C versus low HDL-C or high triglycerides, we categorized the cholesterol problems as dyslipidemia to be encompassing of the different lipid disorders.

7. How were “circulation problems” defined on the questionnaire?
Response: The survey question that was used to identify respondents with circulation problems has been added to the Methods section (page 7). Respondents were asked if a doctor or health professional ever told them that they had circulation problems of any kind. The survey question did not define circulation problems so we did not place any judgment on the responses and categorized it as circulation problems.

8. Did family members report fatal CVD events?

Response: There was no protocol for reporting fatal CVD events. The lack of fatal CVD event ascertainment is already listed in the study limitations (page 13).

Reviewer #2:

The study could be improved by further statistical analysis (that could be reported only in text as “data not shown”): the authors may perform further regression analysis (as shown in Figure 1) in subgroups of subjects with subclinical atherosclerosis and diabetes, dyslipidemia, hypertension, obesity or with current smoking habit. It could be of interest to assess whether the relative risks shown in Figure 1 may vary in subgroups of subjects. Due to the large cohort of subjects included in the study, this may be worth of analysis.

Response: We agree with the reviewer that it would be of interest to understand the relative risk of incident CVD events in subgroups of respondents. However, this is a different research question than the study objectives of determining predictors of incident CVD events. Numerous studies have shown that individuals with diabetes, dyslipidemia, obesity or hypertension have an increased risk of CVD events. Additionally, although the SHIELD study has a large cohort of respondents, there are too few incident CVD events to further stratify the population into subgroups. The estimated relative risks based on the few incident CVD events within the subgroups would be unstable; a larger cohort and longer length of follow-up is required to accumulate sufficient incident events to perform the subgroup analyses.