Reviewer’s report

Title: The association of biomarkers of iron status with peripheral arterial disease in US adults

Version: 1 Date: 22 April 2009

Reviewer: Victor Gordeuk

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Major Compulsory Revisions

1. It would be of important to see the results of the analysis before the extensive exclusions were made as well as after the exclusions. Over one-half of the original sample was excluded for various reasons.

2. The hemoglobin exclusions may have permitted anemic men but not women to remain in the analyzed sample and should be reconsidered. The lower limit of normal of hemoglobin in Caucasian women is usually 12 g/dL, the level used in the study. The lower limit of normal in Caucasian men is usually 13.5 -14 g/dL in men whereas the level used in the study was 13. Using different cutoffs for African Americans is appropriate, as the authors have done.

3. Exclusions or adjustments should include measures of hepatocellular damage. Such damage, which is reflected in elevations in AST and ALT, can profoundly affect serum ferritin concentration and transferrin saturation and may be very common in the population related to such factors as hepatitis C seropositivity (which is often undiagnosed) and heavy alcohol consumption.

4. Inflammation probably does not fit neatly into the categories of CRP < or > 1.0 mg/dL, and revised approaches to accounting for inflammation should be considered. Part of the solution may be to use CRP as a continuous rather than a dichotomous variable. However, the authors should also consider that hepatitis C, heavy alcohol intake and hepatocellular damage in general all lead to a paradoxical decrease rather than an increase in the CRP.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I have served as a consultant and speaker for Novartis, which produces iron chelating pharmaceuticals.