Reviewer's report

Title: Effect modification of serum bilirubin and coffee consumption on the association of gamma-glutamyltransferase with glycated hemoglobin in a cross-sectional study of Japanese men and women

Version: 1 Date: 15 August 2012

Reviewer: Vidar Hjellvik

Reviewer's report:

Major Compulsory Revisions
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None

Minor Essential Revisions
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Methods, "Laboratory measurements":
- As I understand, GGT was measured up to one year earlier than HbA1c and bilirubin (and the reports of coffee consumption) for 3924 persons. Could high GGT-measurements for some of these result in life-style changes or medication which affected the levels of HbA1c / bilirubin / coffee consumption at the survey? It would be reassuring if the authors could show that the association between GGT and HbA1c / bilirubin / coffee was the same for those with GGT measurements done at and before the survey.
- How many of the blood samples for HbA1c was fasting and non-fasting, respectively? And what about the GGT measurements from within the past year? Were they fasting or non-fasting?

Methods, alcohol (in sub-sections "Lifestyle questionnaire" and "Statistical analysis"):
- The authors say that "alcohol users were defined as those who had consumed alcoholic beverages at least once per week over a period of one year" (in sub-section "Lifestyle questionnaire"). Further, they classify alcohol consumption as "never, past and current drinking with a consumption < 30, 30-59 or ≥ 60 ml/day" (in sub-section "Statistical analysis"). Was a person who had not consumed alcoholic beverages at least once per week over a period of one year classified as 'never-drinker'? And I assume the limits of 30 and 60 ml/day is pure alcohol? 30 ml/day seems high as a lower limit. Should it be ml/week? As the GGT-level is affected by alcohol consumption I would like to see more detailed information on alcohol consumption in Table 1.

Methods, "Statistical analysis":
- lines 2-4: Were the cut-off points for bilirubin chosen to have "groups as equal a
size as possible" - i.e. the gender-wise medians - or because they "appeared to be a threshold in the relationship with HbA1c levels"?

Results, second paragraph:
- line 6: I suspect the upper limit of 5.13 in the last CI is wrong: 5.06 (95% CI 5.04-5.13) as it makes the CI asymmetric and the corresponding P-value improbable

Results, third paragraph / table 3:
- Even though the p-value for trend in women is < 0.05, the authors should be careful to conclude that there is an association between coffee and Hb1Ac in (and only in) women with low bilirubin. As there are four p-values in table 3, there is 15% chance that at least one of them will be 0.04 or less if there is no association between coffee and Hb1Ac (1 - 0.96^4). This should be mentioned.

Spelling:
- HbA1c is sometimes written with 1c as subscript, sometimes not. In the 5th paragraph of the discussion, line 2, "Hb" is missing.
- Abstract: "Meethods" should be "Methods"
- Abstract, results: Something is missing in the last sentence
- Background, §2, line 4: An "of" is missing in "GGT may be a marker oxidative stress.."
- Background, §2, line 9: "individulas" should be "individuals"

- Discretionary Revisions

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Methods, "Statistical analysis":
- line 5: I suggest categorizing coffee consumption as <1, 1-3 and #4
- line 9: Please specify which association in "Trend of the association was evaluated..."

Results:
I can not find any information about how the variables adjusted for (age, BMI, smoking, alcohol) are related to GGT, HbA1c, bilirubin, and coffee consumption. I suggest that the authors
- include curves of the crude associations in Figure 1 to see the effect of the adjustments.
- include a table similar to table 1, but with the columns representing categories of GGT, HbA1c, bilirubin, and coffee consumption in stead of gender.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests