Reviewer's report

Title: Heritability of Cardiovascular Risk Factors in a Brazilian Population: Baependi Heart Study

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Reviewer: Harold Snieder

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De Oliveira et al. Heritability of Cardiovascular Risk Factors in a Brazilian Population: Baependi Heart Study

This study reports on heritabilities of risk factors for CV disease in 1666 individuals of 81 families from a rural population in Brazil. This population will be valuable for future gene mapping efforts. I have the following suggestions.

1) Use of citations does not always seem appropriate and needs to be revised. Particular statements need to be supported with specific references. For example, studies 1-4 seem to be QTL mapping studies, whereas the current study is not. Also, twin studies are mentioned but not referenced as far as I could see. Finally, it is uncommon to cite 24 studies in one go, perhaps cite some key review papers instead?

2) At the end of the introduction the authors state: "Thus, the purpose of this study etc." However, please justify why the pedigrees were recruited from a "highly admixed population of a rural city in Brazil" for the purpose of this study. Furthermore, what do the authors mean by "rural city"? A small city in a rural area?

3) P4: What type of questionnaire was administered, i.e., was it based on standard questionnaires used in other studies? If so, give reference. If not, please state that questionnaire was specifically developed for this study. Was the questionnaire administered by research nurses or assistants or filled out by the participants (self report)? Please provide information on scoring of variables (dichotomous, continuous etc.), especially if reported in the current paper.

4) P5/6: In my opinion, adjustment for medication use is not the right thing to do and may be the cause of the unexpected drop in heritability estimates in Model 3. For the analysis of blood pressure, correction procedures have been suggested for those individuals using antihypertensives. In this way, individuals on medication (that may be most informative for genetic studies) can still be included in the analyses. See e.g.: Palmer, Hypertension, 2003 Feb;41(2):197-8; Kupper et al., Hypertension, 2005 Jan;45(1):80-5. For the analysis of lipids, individuals on lipid lowering medication should probably be excluded, because correction procedures such as those available for BP do not exist for lipids as far as I'm aware. The same is true for the analysis of fasting glucose: please exclude diabetic patients and/or individuals on antidiabetic medication. Please report prevalence of medication use in Table 1 for this cohort. Please describe
clearly which medications are considered (e.g., excluded) for which analyses. Currently, this is not clearly described.

5) Shared (or familial) environmental variance is confounded with genetic factors in the current design. This should at least be mentioned in the discussion as a potential limitation.

6) Please note that the definition of heritability as given on p7 is incorrect! Do the authors mean: â##each of the variance componentsâ##?

7) Please state on which information (give references) cut-off values for dichotomization of traits is based (p7).

8) P8: Why were only 81 out of the total of 119 families analysed? I suspect families with <3 individuals were excluded?

9) P8:â##Hypertension was prevalent among men.â## In fact prevalence is higher in women.

10) P9: Iâ##m not sure the heritability estimates are protected? The authors probably wanted to prevent biased heritability estimates?

11) P10: I donâ##t believe heritability estimates for glucose can be trusted if measurements were conducted in non-fasting samples. Thus, the corresponding estimate of the FHS should be removed from Table 4.

12) P11: Truncal obesity is a dichotomous trait. When reporting the results of the Northern Manhattan Study, do the authors really mean truncal obesity or rather waist circumference (continuous trait)?

13) The discussion on changes in heritability estimates after adjustment for medication needs to be revised based on new analyses as stated under point 4. What do the authors mean by: â##communication between covariates and variance components spacesâ##?

14) The authors may want to elaborate on the value of dichotomous versus quantitative traits for gene mapping effort. Arenâ##t quantitative traits inherently more informative?

15) Variable names in Table 3 should reflect their dichotomous nature: i.e., truncal obesity instead of waist circumference, high glucose, high TRG, low HDL and hypertension. Why are high TC and high LDL not given?

Minor points:

1) Abstract: it is unclear why only 81 families were used out of the total of 119. Please spell out TC.

2) P5: ONROM = OMRON?

3) P6: factures = factors; contributed to variation = contributing to variation

4) P8: equivalent to = similar for

5) P11: in despite of = despite; final estimate for waist circumference, SBP and BMI = final estimate for waist circumference, SBP, DBP and BMI

6) Table 4: Please be consistent in providing either 1 or no decimal.
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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: No, the manuscript does not need to be seen by a statistician.

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