Reviewer's report

Title: Interplay between heritability of smoking and environmental conditions? A comparison of two birth cohorts

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Reviewer: Jason J.D. Boardman

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BMC: Interplay between heritability of smoking and environmental conditions

This is an interesting paper that builds on a body of work examining cohort variation in biometric estimates for smoking onset. The extension to this cohort is new and the use of data from the Netherlands is also important. It is a fairly basic set of analyses and they find comparable heritability estimates for both cohorts. Based on this evidence they suggest that the genetic influences on smoking are not susceptible to changes in the smoking environments for the two cohorts and thus, this environmental factor may not be relevant to the GxE research on smoking.

I have two main issues:

1. They need to be very clear that this is not a replication of Boardman, Kendler, or Heath, per se. These are two very different cohorts in very different social contexts. Moreover, it would be useful to provide some tentative speculation about why they might not have seen the same results.

2. Very little is made of the theoretical reasons for why they would expect gender differences for this cohort in this context. This is potentially very interesting but it gets lost as a modeling exercise rather than a scientific question. The environmental terms for women are very different from those of men. This needs to be discussed.

3. There is not enough information provided about the models. Typically researchers provide model fit statistics (AIC/BIC/-2LL, etc.) for the different models (A, AE, ADE, etc.). This is simply one univariate model and based on the confidence intervals, I would imagine that they could drop the C estimate for the latter cohort. If my back of the envelope estimates are correct, most of this .06 (for men) would go to the A term and you’d have evidence for a higher heritability in the most recent cohort. Given that this is such a short window of time compared to the other studies, this change is reasonable and it is in line with Boardman but not Kendler. This is worth investigating more thoroughly.

4. Much more information needs to be provided about the design of the study.

5. Some have made a case that regular smoking only makes sense as an outcome when you consider that people have to try it first. There are comparable multinomial models that can be assessed in which never, tried but stopped, tried and progressed to smoking can be assessed. There are different genetic factors
that are linked to initiation (novelty seeking, etc.) versus dependence (nicotine metabolism, etc.). More could be made of this fairly simple dependent variable.

**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.