Reviewer’s report

Title: Do intrauterine or genetic influences explain the foetal origins of chronic disease? A novel experimental method for disentangling effects.

Version: 1 Date: 11 March 2007

Reviewer: Dawn Misra

Reviewer’s report:

General

This is an interesting paper on an intriguing topic. The paper did not accomplish the aims put forth. The level of sophistication and information promised was not delivered. There were a number of areas that were found lacking.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1) The authors give short shrift to the concept of gene-environment interactions. Rather genetics and environment are emphasized as separately contributing to the outcomes. This is an important omission given recent research in these areas.

2) The authors focus on separating the influence of the maternal genome from the intrauterine environment. However, the maternal and fetal genome are obviously correlated and the fetal genome may also influence the intrauterine environment. While the example on smoking mentions how the mother and child share genes, the discussion is superficial. This example is also a bit of a stretch in believability as the authors are speculating that the genes that lead a woman to smoke might be the same genes that cause ADHD? The various scenarios described in the paper (e.g. sperm donation, egg donation) could be discussed in more depth with regard to what they could tell us about separating maternal, paternal, and fetal/infant genes and not just maternal genetic and environmental factors.

3) The authors hint at providing information on what data can be feasibly obtained from this proposed approach but gloss over the details with regard to the groups where the woman who delivers the fetus is a surrogate. It will likely be very difficult to obtain comprehensive pregnancy data from these groups and yet these are the groups that are quite important in the proposed design to disentangle effects. There is likely more bias as well as less complete data for these groups. The willingness of a surrogate mother to participate at all, let alone truthfully report her health behaviors after the birth is a major issue in such a design. Table 3 combined data across all groups so we could not even begin to assess these issues. Nor do the authors focus on these issues. This issue is briefly commented on in the conclusions but should be considered much more carefully.

4. Maternal and paternal imprinting, as well as maternal transmission through mitochondrial DNA, are also important topics to examine within the purported focus of this paper but are not discussed by the authors.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

None.

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Discretionary Revisions (which the author can choose to ignore)

None.

Which journal?: Not appropriate for BMC Medicine: an article whose findings are important to those with
closely related interests and more suited to BMC Medical Research Methodology

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.