Reviewer's report

Title: Influence of advanced age of maternal grandmothers on Down syndrome

Version: 1 Date: 1 March 2005

Reviewer: Mathias Forrester

Reviewer's report:

General

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

Abstract:

1. The first three sentences of the Results section of the Abstract are confusing and may not be important considering the primary topic of the manuscript. They should either be deleted from the Abstract or revised.

2. The first sentence of the Conclusions section of the Abstract contains information that should be in the Results section, namely comparison of the percent of maternal grandmothers of advanced age among cases and controls.

Background:

3. In the first sentence of the last paragraph, why is the number of individuals with Down syndrome likely to increase? Because of the increased life expectancy of individuals with Down syndrome, as suggested by the reference cited? However, studies in Europe and North America have found that the number of individuals born with Down syndrome is lower than expected based on maternal age distribution and is perhaps decreasing due to the use of prenatal diagnosis of the Down syndrome and elective termination of the affected fetuses. Admittedly, such may not be the situation in other parts of the world that do not practice prenatal diagnosis and/or elective termination to the degree that Europe and North America do. Perhaps it would be better if the authors state that until trisomy 21 conceptions can be prevented, fetuses will continue to be conceived and infants continue to be born with Down syndrome.

Methods:

4. How were the controls selected? From hospitals? Were the controls the 200 families or 200 infants or children or individuals?

Results:

5. In the first paragraph, all except the last two sentences belong in the Background section and include references.

6. Table 1 and the accompanying text describe the number of children (I am assuming children prior to the proband or prior to and including the proband) born to parents of different ages at delivery of the proband. This information does not appear to be of importance to the primary objective of the
manuscript, which is the influence of maternal age of the grandmother at birth of the daughter on the risk of Down syndrome among the daughter’s offspring. The authors need to either state the importance of information on the number of children or delete it from the manuscript.

7. It would be useful if the authors compared the maternal age distribution of the cases and controls in order to demonstrate that the two have a similar distribution. This would eliminate one potential confounding factor for the analysis. This information is currently included in Table 1 but could be presented in a more clear fashion.

8. Some of the information in the last part of the first new paragraph on page 7 should probably be moved to the Discussion section.

9. It is not clear what the information included in Figures 1 and 2 and the accompanying text contribute to the topic beyond what was provided in Tables 2 and 3 and the accompanying text. The authors need to either describe the importance of this information or exclude it from the manuscript.

Discussion:

10. In the first new paragraph on page 9, the authors need to compare the maternal grandmother age of cases and controls, not just present the maternal grandmother age, in order to support their conclusion.

11. In the third sentence of the second new paragraph on page 10, should it be that the findings can or cannot be applied?

Conclusion:

12. It appears that the first sentence should state that the age of the grandmothers is significantly more likely to be advanced.

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

13. Throughout the manuscript the cut-off point of maternal age groups does not appear to be consistent. In some places, it appears to be less than 29 years. In other places it appears to be less than 30 years. The age ranges need to be clarified.

14. It would be useful if Table 3 included percentages.

Discretionary Revisions (which the author can choose to ignore)

Background:

15. Is there and reference for the statement made in the first sentence of the first paragraph?

Methods:

16. Is Mysore city in South India? The authors may want to clarify this for those readers unfamiliar with the geography of India. It also might be better if the description of the cases was moved to before the description of the controls.
17. The first two paragraphs might be better placed in the Background section.

**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:** Not suitable for publication unless extensively edited

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.