Title: Age, mode of conception, health service use and pregnancy health: A prospective, cohort study of Australian women

Authors:

Jane Fisher (jane.fisher@monash.edu)
Karen Wynter (karen.wynter@monash.edu)
Karin Hammarberg (karin.hammarberg@monash.edu)
John McBain (john.mcbaie@mivf.com.au)
Frances Gibson (frances.gibson@mq.edu.au)
Jacky Boivin (boivin@cardiff.ac.uk)
Catherine McMahon (cathy.mcmahon@mq.edu.au)

Version: 2 Date: 23 November 2012

Author's response to reviews: see over
23 November 2012

Dear Editors,

Re: Age, mode of conception, health service use and pregnancy health: A prospective, cohort study of Australian women (Manuscript ID 1589971991683860)

Thank you for the careful reviews and editorial considerations of this paper and the valuable suggestions to strengthen it. We have made the following revisions to the paper in line with these recommendations.

**Reviewer 1 Dr K Joseph**

**Major Compulsory Revisions**

1. Maternal age should not be modelled as a continuous variable. The results of modelling with indicator variables should be presented unless the linearity assumption can be shown to be appropriate.

   *We agree with KJ’s suggestion that maternal age be modeled using indicator variables, and have implemented this change in all three models.*

2. Modeling ‘self rated general health’ and ‘feeling unsupported’ as continuous variable is also questionable.

   *We agree with KJ that these variables are not continuous, and have recoded both to be binary variables. Self-rated general health is coded as Excellent (reference category) versus all other responses. Needing, but not having support has been recoded to Never (reference category) versus all other responses.*

3. The issue of adjusting for variables for instance twin pregnancy and Physical Component Summary score in the causal pathway is particularly important. It may be helpful to have 4 models i.e., an additional one that adjusts for all determinants in the current model 3 except those potentially in the causal pathway.

   *We agree with KJ that the models include variables that are in the causal pathway. As these factors are predictors for the outcome, we believe that it is important to retain them. However, we have restructured the hierarchical steps of the models to indicate: 1. Variables of primary interest (maternal age and mode of conception) 2. Variables potentially in the causal pathway and 3. Socio-demographic and reproductive variables being adjusted for in the models. Thus the reader has a clear idea of the contribution of each of these groups of variables to the model.*

4. There were differences noted between age groups and between mode of conception groups in terms of pregnancy complications. Although the authors state the mean gestational age of the entire study population they do not provide the mean gestational age for each of the contrasted categories. Did the compared groups differ in terms of gestational age and if so should this have been accounted for in the analysis?

   *This is an important observation. We have now reported on these group comparisons (Additional Document 1). Weeks of gestation at the time of assessment did not differ significantly between mode of conception groups, but did differ significantly between the middle and older age groups. We have therefore controlled for weeks of gestation when modeling Physical Component Summary scores.*
Minor Essential Revisions

5. The Introduction may benefit from being shorted with a focus on studies examining issues most similar to what the authors studied i.e., self rated health, not physician diagnosed outcomes. Similarly extraneous details in the Method section can be deleted (e.g., all data were entered into password protected computer files). The Discussion section could benefit from reorganization. Typically the first paragraph of the Discussion section should provide an overview of the study findings, the next couple of paragraphs situate the findings with regard to the main objectives against the literature, one paragraph talks about the study’s strengths, another about the study’s limitations and the final paragraph summarizes the study.

We have reduced the Introduction by 273 words. We have referred to papers which addressed the conditions which were assessed in this study. Extraneous details have been removed from the Methods. We are accustomed to the tradition in public health in which the reader is informed of the strengths and limitations of the study in order to be able to judge the authors’ interpretation of the data against these and would therefore prefer to retain the structure of the Discussion as submitted. We have added sub-headings to provide a clearer structure to the Discussion.

6. Tables 2 to 4 may benefit from judicious editing. For instance, the standardized differences could be labeled ‘Mean difference’ i.e., if the standardized coefficient for maternal age is 0.011 in the second model (Table 2), this represents the mean difference in the Physical Component Summary Score for unit increase in maternal age. Steps 1, 2 and 3 could be labeled models 1, 2 and 3, etc.

We have shortened Tables 2 to 4. We have referred to “steps” rather than models to avoid confusion between hierarchical structure of each model (steps) and the three models with outcomes PCS score, MCS score and hospital admissions respectively. We prefer to retain the descriptor ‘standardized coefficients’ as we believe that it is more widely understood.

7. It would be preferable to use a consistent scheme for creating all indicators variables (e.g., Yes=1 and No=0). Currently Yes=1 for some indicators such as ‘Twin pregnancy’ and Yes=0 for others such as ‘English spoken at home’.

To aid interpretation, we have coded all categorical variables with the reference category reflecting the more optimal state and assigned a value of 0.

Reviewer 2 Dr Reija Klemetti

It is not entirely clear from Dr Klemetti’s review which are compulsory and which are discretionary revisions. We have responded to her comments and suggestions for change in the following way:

1. Abstract: reflects the content of the article but some corrections are needed. Main outcome measures: SF 12 PCS, SF 12 MCS and health service use are clearly presented in the method section. How about health behaviours mentioned in the purpose of the study? They are not mentioned in results, methods and conclusions. If they are important, they can be added while shortening the other parts.

Limited words are permitted for the abstract. We describe all data that were collected and those that remained as significant predictors of the outcomes in multivariable models. We believe that this is an appropriate way of summarizing the study succinctly. Health behaviours did not remain in the model and so have not been described separately.

2. Background could be shortened to point out clearer the most important aspects. The article is well written but quite long and it could be useful to shorten/condense it. Introduction: is very detailed and therefore quite long.

The introduction has been shortened by 273 words.
3. Result section includes some interpretation of results these can be transferred into discussion section. Please, refer to tables when you reporting the results.

These changes have been made.

4. The moment version needs re-writing and editing as well as discussion comparing previous results and results received in this study. I would prefer a structured discussion: 1) short summary of the results, 2) strengths and limitations of the study (well described in the present version with the exception of small numbers), 3) interpretation of results and comparison with earlier findings (much information can be reached from “Introduction” or “Background”) and then 4) conclusions.

As outlined in our response to KJ’s review, the Discussion has been structured and we have made the links to prior research more distinct.

5. My main concerns relate to small numbers and including twin pregnancies in the models. After stratifying by age and especially furthermore by health insurance status, number of women per each group was quite small (and this might be one reason that no associations could be found). This could be added into the limitations of the study as well as into conclusions.

We have added a statement acknowledging the limitation of cell numbers less than 40.

6. Somehow it is strange that multiple gestation is in the models because it is a key element in ART – one reason which cause problems. I would consider leaving out multiples from the analysis (or analyze them separately which might not be possible because they are so few). As well as that the model includes twin pregnancies – I think it is not a confounder or background variable but an outcome and therefore I think singletons and multiples should be studied separately.

We have changed the wording so that variables potentially in the causal pathway are not referred to as confounders or background variables. The revised models also reflect the contributions of variables which are causal and other variables which may be confounders separately.

We do not believe that it is appropriate to leave twin pregnancies out of the models because multiple gestation is a risk to pregnancy health and is more common among ARTC women. Our data have revealed that it is not assisted conception per se that is associated with antenatal hospital admissions, rather it is multiple gestation. This is very important evidence to support the practice of single embryo transfer and we prefer to retain it.

7. It was also a little bit confusing that so many measurements were included. Are all of them important to include in this study?

We have removed several self-reported symptoms from the list reported in Additional Document 1, and now include only 3 previously-reported symptoms for which the evidence is as yet inconclusive. We have also removed some of the self-reported health behaviours (Additional Document 1) and categories of health practitioners consulted (Additional Document 2) so that the tables are shorter.

8. Results: A flow diagram could describe more clearly the number of eligible and participated women than the long text at the beginning of the result section.

We have included a flow diagram rather than text, as suggested.

9. Tables: were informative. If the health behaviours are important, one of the main outcomes (mentioned in the purpose of the study), at least one table of health behaviours would be useful to include in main tables not only as an additional table.

The health behaviors are in the tables in the Additional Documents because the journal requires tables in landscape format to be submitted as Additional Documents.
10. I would suggest using ART instead of ARTC – even “C” is referring to conception.

We believe that it is a more accurate descriptor of the participants in this study to classify them as having conceived with assisted reproductive technologies (ARTC) or spontaneously (SC) and therefore prefer to retain the acronyms that have been used.

11. Why the authors used untypical classification by age (up to 30, 31-36 and 37+)? Could you please explain this?

We have justified our classification further in the Participants & Recruitment section and included two references to support it.

12. In Table 4 95%CI is enough – please do not repeat Adj OR.

We have deleted the repeated text.

We look forward to hearing from you about whether the paper is now suitable for publication in BMC Pregnancy and Childbirth.

Yours sincerely

Professor Jane Fisher on behalf of all authors