PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Infant's sex, birth control policy and postpartum well-being: a prospective cohort study in Shanghai, China
AUTHORS	Hua, Jing; Zhu, Liping; Du, Wenchong; Du, Li; Luo, Ting; Wu, Zhuochun

VERSION 1 - REVIEW

REVIEWER	Ling-ling Gao School of Nursing, Sun Yat-sen University, Guangzhou, China
REVIEW RETURNED	02-May-2016

GENERAL COMMENTS	Many thanks for giving me the opportunity to read this interesting paper. This study aimed to explore the association between infant's sex and mother's postpartum well-being, which may be moderated by birth control policy status in China. The paper is well written. However, many references are too old. Further, the authors has not discussed what the clinical implications of this study may have to health care professionals.

REVIEWER	Xiaoqin Liu Aarhus University, Denmark
REVIEW RETURNED	06-May-2016

GENERAL COMMENTS	The study by Hua et al. is based on data from 8 obstetric hospitals. The authors found that the association between infant's sex and mother's postpartum well-being was moderated by birth control policy status in China. This is an interesting study on an important topic. However, I do have some questions, comments and thoughts as below that the authors may wish to address. Major comments: 1. Page 2, abstract: the author mention that they used GWBS to assess maternal well-being at baseline. It is unclear to me when the baseline was measured. Please clarify. 2. Page 3, the strengths and limitations: The authors mention that 29 women refused to take part in the study, but this information is not included in the main text. Also, the description of participants in the main text is contradicted to Figure 1. Suggest revising it accordingly and reporting the participation rate. Moreover, the expression of "227 were missing or excluded" if confusing. Suggest rewording it. I am also curious about whether the finding in this study is generalizable to the entire population in China. Why and why not? 3. The authors include birth control policy settings in the models as a covariate. If the authors' hypothesis that the association between child's sex and maternal postpartum well-being is modified by birth

	control policy holds, we would expect to see different associations among families that fulfil and those do not fulfil two-child policy. Suggest analyzing the data by stratifying on the birth control policy settings instead of adjusting for it in the models. 4. To my knowledge, mothers from the urban and rural area in China may have a different attitude toward child's sex. I would suggest including the household registration in the models if possible. 5. Page 8, line 34-39: It is nice that the authors mention "there were no differences of maternal age, education, vacation…". What about the child's sex? Is the participation rate different between mothers with a male infant and those with a female child? 6. Table 1: The authors categorize birth weight less than 2500g and 4000 g or greater in one group. I question that low birth weight has a similar effect on maternal postpartum well-being as high birth weight. Please clarify. 7. The authors found that sex of the child was significantly associated with maternal depression, positive well-being, and total score in the multiple linear regression models. However, statistical significance does not necessarily mean a clinically relevant observation. What is the clinical significance of 1.5 points difference in total score of GWBS? Suggest treating the measurements as categorical variables instead of continuous ones. 8. Table 4: The authors use the severe distress as the comparison group which comprised 78 women. I would suggest using a different comparison group (the positive well-being women), as the interpretation for readers will be easier. The authors only reported the association with statistical significance in model e. What is the rationality of including several adjusted models and reporting this particular finding? Please clarify. 9. The authors include a 1.5-page conclusion with references and results in the end. Suggest shortening it. The authors mention that "the selection bias induced by non-response and loss to follow-up in a cohort study decline usually to under-estimate the effects." This is an interesting point; however I find it unpersuasive. Can the authors provide evidence such as literature to support their point? Minor comments: 1. Page 5, line 57: "1730 childbearing women eligible for the inclusion and reclusion", I assume here should be "exclusion" 2. Page 8, line 29: "Multiple logistic regression models were also used to analyze the effective…" I assume here the authors mean "…effect…" 3. Page 8, line 31-34: "A value of 0.05 was used for all tests of significance." Should be "A P-value of …" 4. Page 11, line 29: "Our results suggest that the male infant sex was related with less postpartum depression" should be "… related to …" 5. Page 11, line 31: "The result was consistent to the previous…" should be "…consistent with…" 6. Page 11, line 47: "… be more capable to provide financial…" should be "be more capable of providing…" 7. Page 14, line 22: "JH and LZ was responsible…" should be "JH and LZ were responsible…"

REVIEWER	Jing-Bao Nie Bioethics Centre, Division of Health Sciences, University of Otago, New Zealand
REVIEW RETURNED	20-Jun-2016

GENERAL COMMENTS	This is a meaningful study with some original data and innovative discussion. Here are some suggestions to further improve the quality of this paper, in particular spell out its wider implications. A paragraph should be added in the section "Discussion" to examine ethical and social policy dilemmas involved. Particularly, the issue of sexism needs to be specifically addressed. The dilemma or irony is that accommodating the couple's wish for son preference for the sake of their and especially the mother's well-being reinforces the sexist belief and practice in Chinese society at large. But this point has not been clearly made and critically discussed. Also, it would be very helpful if the study could be further contextualized in the broader impact and aftermath of the one-child policy. Does this study further confirm the intended and unintended negative consequences, both immediate and long-term, of the birth control program? Is the one-child policy justifiable from the perspective of well-being? This discussion may be presented in Introduction and especially in Discussion. There are available literature regarding the aforementioned two aspects which the authors need to engage with. The title should specify the city where the study was conducted, that is, Shanghai. So the subtitle can be: "a prospective cohort study in Shanghai, China". It should be mentioned in Abstract and Introduction that the one-child policy was terminated in 2015. The long concluding paragraph may read better if it is broken into three passages, starting a new one at "However, …" and another at "After our study…"

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Ling-ling Gao
Institution and Country: School of Nursing, Sun Yat-sen University, Guangzhou, China
Competing Interests: None declared

Many thanks for giving me the opportunity to read this interesting paper. This study aimed to explore the association between infant's sex and mother's postpartum well-being, which may be moderated by birth control policy status in China. The paper is well written. However, many references are too old. Further, the authors has not discussed what the clinical implications of this study may have to health care professionals.
RESPONSE: Many thanks for the reviewer's suggestion. We have added more references which published in recent time (see the section of reference) and change some "old" references into the

“new” ones (such as reference 10,12). However, we still remain some references if it is necessary for the study (such as reference15,19). Additionally, we added the clinical implications to the section of “Discussion and Conclusions”. (see the fourth and sixth paragraph in the section of discussion, and the first paragraph of the conclusions).

Reviewer: 2
Reviewer Name: Xiaoqin Liu
Institution and Country: Aarhus University, Denmark
Competing Interests: None declared

The study by Hua et al. is based on data from 8 obstetric hospitals. The authors found that the association between infant’s sex and mother’s postpartum well-being was moderated by birth control policy status in China. This is an interesting study on an important topic. However, I do have some questions, comments and thoughts as below that the authors may wish to address.

Major comments:
1. Page 2, abstract: the author mention that they used GWBS to assess maternal well-being at baseline. It is unclear to me when the baseline was measured. Please clarify.
RESPONSE: Many thanks for the reviewer’s comment. We have clarified that when we investigated the GWBS at baseline (see the section of measurement).

2. Page 3, the strengths and limitations: The authors mention that 29 women refused to take part in the study, but this information is not included in the main text. Also, the description of participants in the main text is contradicted to Figure 1. Suggest revising it accordingly and reporting the participation rate. Moreover, the expression of “227 were missing or excluded” if confusing. Suggest rewording it. I am also curious about whether the finding in this study is generalizable to the entire population in China. Why and why not ?
RESPONSE: Many thanks for the reviewer’s comment. We have included the 29 women who refused to take part in the study in the Figure 1. However, we did not include the information in the main text, which may create the confusion. We have added the information of 29 women to the section of population. Additionally, according to the reviewer’s comment, we generalized our results to urban areas of China. We have added the generalization of our results to the section of conclusion.

3. The authors include birth control policy settings in the models as a covariate. If the authors’ hypothesis that the association between child’s sex and maternal postpartum well-being is modified by birth control policy holds, we would expect to see different associations among families that fulfill and those do not fulfill two-child policy. Suggest analyzing the data by stratifying on the birth control policy settings instead of adjusting for it in the models.
RESPONSE: Many thanks for the reviewer’s comment. We think it is good suggestion to explore the associations stratified by one-child family status. However, based on the methods we utilized now(including birth control policy settings in the models as a covariate), we may use another simple way to obtain the associations between child’s sex and maternal postpartum well-being under both one-child and two-child policy status (the code number in our analysis: two-child policy status=1, one-child policy status=0). For instance, in a multiple linear regression model (when the outcome is a continuous variable such as the total scores of GWBS), the coefficient of maternal postpartum were β1, and the coefficient of birth control policy were β2. The association between infant’s sex and maternal postpartum well-being under two-child policy status were ‘β1+β2’, and the association between infant’s sex and maternal postpartum well-being under one-child policy were β1, when the code number of two-child family status was ‘1’, and of the one-child family was 0. When the outcome is a categorical variable (such as the outcome variable in table 4), we use the multiple or binary logistic regression model. If the OR under one-child policy status was exp(β1), and the OR of birth control policy was exp(β2), the association between infant’s sex and maternal postpartum well-being

under two-child family were exp(β1+β2). These methods are based on the literature (see the following books). However, because one of the objects of our study was to examine whether the birth control policy status would moderate the association, we have to include the covariate of birth control policy status to the model, and analyzed the association between infant's sex and maternal well-being if the birth control policy being considered. The method we used is similar to that in other published papers (eg. the reference 5, 6 in the section of reference).
(1)Gurrin LC, Blake KV, Evans SF, Newnham JP. Statistical measures of foetal growth using linear mixed models applied to the foetal origins hypothesis. Statistics in medicine 2001;20(22):3391-409
(2)Kleinbaum DG, Klein M. Logistic Regression A Self-learning Text, Third Edition: Springer, 2010.

4. To my knowledge, mothers from the urban and rural area in China may have a different attitude toward child's sex. I would suggest including the household registration in the models if possible.
RESPONSE: Many thanks for the reviewer's suggestion. Fortunately, we also investigated the resident status (household registration) at the baseline. Therefore, we have included the resident status in the models (see the section of results, table1 and table2).

5. Page 8, line 34-39: It is nice that the authors mention "there were no differences of maternal age, education, vacation…" What about the child's sex? Is the participation rate different between mothers with a male infant and those with a female child?
RESPONSE: So many thanks for the reviewer's comment. We have analyzed retrospectively the differences of maternal age, education, vocation…. between the male and female infants at the baseline. However, one of our inclusion criterion was 'primiparous women', and in this study we aimed to explore the association between infant's sex and mother's postpartum well-being in primiparous women, and examine whether the birth control policy status (if or not the women have the chance to have the second child) moderated the association. Therefore, we could not analyze the difference of infant's sex at the baseline (as they have not delivered their first child at baseline). However, the comment provided us the important clues for our further study (We plan to start our further study from October of this year). We think it is more interesting to analyze the association between the sex of the first child and maternal postpartum welling-being in our further study because China has relaxed its birth control policy and allow all couples to have two children since 2016.

6. Table 1: The authors categorize birth weight less than 2500g and 4000 g or greater in one group. I question that low birth weight has a similar effect on maternal postpartum well-being as high birth weight. Please clarify.
RESPONSE: Many thanks for the reviewer's comment. We divided the birth weight less than 2500g and more than 4000g into two groups (see table 1).

7. The authors found that sex of the child was significantly associated with maternal depression, positive well-being, and total score in the multiple linear regression models. However, statistical significance does not necessarily mean a clinically relevant observation. What is the clinical significance of 1.5 points difference in total score of GWBS? Suggest treating the measurements as categorical variables instead of continuous ones.
RESPONSE: Many thanks for the reviewer's comment. In our study, we firstly explore the association between infant's sex and maternal postpartum well-being using multivariable linear regression models so as to provide the clues for the association between the infant's sex and maternal postpartum well-being. Furthermore, in order to provide more clinical implications, we used the categorical variables which were divided by the proposed cutoffs (60, 72) of the total score of well-being, representing three levels of well-being (positive well-being, moderate distress, and severe distress), and analyzing the association between infant's sex and maternal postpartum well-being (as categorical variables) (see table 4). Unfortunately, the norms or proposed cutoffs of the scores of subscales (Anxiety、Depression、General health、Positive well-being、Self-control、Vitality) are lacking, so we did not divide the scores of subscales into categorical variables.

8. Table 4: The authors use the severe distress as the comparison group which comprised 78 women. I would suggest using a different comparison group (the positive well-being women), as the interpretation for readers will be easier. The authors only reported the association with statistical significance in model e. What is the rationality of including several adjusted models and reporting this particular finding? Please clarify.
RESPONSE: Many thanks for the reviewer's comment. According to your suggestion, we have changed the comparison group of 'severe distress' into 'positive well-being'. Additionally, it can control for numerous confounders (if there is a large enough sample size). Thus logistic regression is a mathematical model that can give an odds ratio which is controlled for multiple confounders. This odds ratio is known as the adjusted odds ratio, because its value has been adjusted for the other covariates (including confounders). The process of accounting for covariates is also called adjustment (similar to logistic regression model) and comparing the results of simple and multiple linear regressions can clarify that how much the confounders in the model distort the relationship between exposure and outcome. In the study, according to the literature and both the obstetric and pediatric professionals' suggestion, we included the socio-demographic characteristic, obstetric characteristic, Infant's health outcome which may be considered as potential confounders or mediators and may distort the association. Therefore, the adjusted coefficient or aOR is necessary to consider (when these factors was controlled) to show the 'real' association between infant's sex and maternal postpartum well-being. Additionally, because one of the objects of our study was to examine whether the birth control policy status would moderate the association, it may be needful to add the covariate of birth control policy status to the model. The method we used in the paper is similar to that of the published papers (see the reference 5, 6 in the section of reference). In our study, our hypothesis is confirmed by the results because the association between infant's sex and maternal postpartum well-being was disappeared (without statistical significance) when birth control policy status was adjusted.

9. The authors include a 1.5-page conclusion with references and results in the end. Suggest shortening it. The authors mention that "the selection bias induced by non-response and loss to follow-up in a cohort study decline usually to under-estimate the effects." This is an interesting point; however I find it unpersuasive. Can the authors provide evidence such as literature to support their point?
RESPONSE: Many thanks for the reviewer's comment. We have shortened somewhat the section of conclusions and broken the conclusion into three passages, according to this reviewer and the third reviewer's suggestions. Additionally, selection bias is the selection of individuals, groups or data for analysis in such a way that proper randomization is not achieved, thereby ensuring that the sample obtained is not representative of the population intended to be analyzed. The prospective cohort studies (we used it in our paper) will have little selection bias as we enroll subjects, because the outcomes are unknown at the beginning of a prospective cohort study. However, the prospective cohort studies may have the differential loss to follow up which is also a type of selection bias. However, we reviewed again the literature (such as the following references) and found that the selection bias may either underestimate or overestimate the association, and may most probably affect the generalizability of the study in an observational study. Therefore, we have revised the description of selection bias in the section of conclusions and added the related references to the section.
Howe CJ, Cole SR, Lau B, Napravnik S, Eron JJ, Jr. Selection Bias Due to Loss to Follow Up in Cohort Studies. Epidemiology 2016;27(1):91-7 doi: 10.1097/EDE.0000000000000409published Online First: Epub Date]|.
Momen-Heravi F. Selection bias. Journal of the American Dental Association 2015;146(7):497-8 doi: 10.1016/j.adaj.2015.05.010published Online First: Epub Date]|.

Minor comments:
1. Page 5, line 57: "1730 childbearing women eligible for the inclusion and reclusion", I assume here

should be “exclusion”
2. Page 8, line 29: “Multiple logistic regression models were also used to analyze the effective…” I assume here the authors mean “…effect…”
3. Page 8, line 31-34: “A value of 0.05 was used for all tests of significance.” Should be “A P-value of …”
4. Page 11, line 29: “Our results suggest that the male infant sex was related with less postpartum depression” should be “… related to …”
5. Page 11, line 31: “The result was consistent to the previous…” should be “…consistent with…”
6. Page 11, line 47: “… be more capable to provide financial…” should be “be more capable of providing…”
7. Page 14, line 22: “JH and LZ was responsible…” should be “JH and LZ were responsible…”
RESPONSE: Many thanks for the reviewer’s revisions. We have revised these words in the paper according to the suggestions， and finally invited a native to check the paper.

Reviewer: 3
Reviewer Name: Jing-Bao Nie
Institution and Country: Bioethics Centre, Division of Health Sciences, University of Otago, New Zealand
Competing Interests: None declared.

This is a meaningful study with some original data and innovative discussion.
Here are some suggestions to further improve the quality of this paper, in particular spell out its wider implications.

A paragraph should be added in the section “Discussion” to examine ethical and social policy dilemmas involved. Particularly, the issue of sexism needs to be specifically addressed. The dilemma or irony is that accommodating the couple’s wish for son preference for the sake of their and especially the mother’s well-being reinforces the sexist belief and practice in Chinese society at large. But this point has not been clearly made and critically discussed.
RESPONSE: Many thanks for the reviewer’s comment. We have added a paragraph to discuss the dilemma or irony of son preference in Chinese society in the section of discussion according to the reviewer’s suggestion. (see the fourth paragraph of the discussion) . However, the thesis of sexism may be sensible to Chinese authority, and we have to discuss it with caution.

Also, it would be very helpful if the study could be further contextualized in the broader impact and aftermath of the one-child policy. Does this study further confirm the intended and unintended negative consequences, both immediate and long-term, of the birth control program? Is the one-child policy justifiable from the perspective of well-being? This discussion may be presented in Introduction and especially in Discussion.
RESPONSE: Many thanks for the reviewer’s comment. We have further contextualized the broader impact and aftermath of the one-child policy (see the last paragraph in the section of discussion).

There are available literatures regarding the aforementioned two aspects which the authors need to engage with.
RESPONSE: Many thanks for the reviewer’s comment. We have added the related reference with regard to the aforementioned two aspects according to the suggestion (see the section of reference).

The title should specify the city where the study was conducted, that is, Shanghai. So the subtitle can be: “a prospective cohort study in Shanghai, China”.
RESPONSE: Many thanks for the reviewer’s comment. We have revised the title according to the reviewer’s suggestion.

It should be mentioned in Abstract and Introduction that the one-child policy was terminated in 2015.
RESPONSE: Many thanks for the reviewer's suggestion. We have added the information of termination of one-child policy in 2015 to the section of abstract and introduction.

The long concluding paragraph may read better if it is broken into three passages, starting a new one at "However, …" and another at "After our study…"
RESPONSE: Many thanks for the reviewer's comment. We have broken the conclusion into three passages, according to the reviewer's suggestion.

VERSION 2 – REVIEW

REVIEWER	Jing-Bao Nie Bioethics Centre, University of Otago, New Zealand
REVIEW RETURNED	08-Sep-2016

GENERAL COMMENTS	The revised version has addressed my previous suggestions on critically discussing sexism and the socio-ethical dimensions of the one-child policy as related to infant's sex and women's postpartum well-being. Although the discussion can be more substantial and better, it is by and large adequate.