Author's response to reviews

Title: Adverse birth outcomes among native-born, China-born, and Southeast Asia-born mothers in Taiwan: A population-based birth cohort study

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Author's response to reviews: see over
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The Editor, BMC Pregnancy and Childbirth

Dear Editor,

Thank you very much for giving us an opportunity to revise our manuscript entitled "Adverse birth outcomes among native-born, China-born and Southeast Asia-born mothers in Taiwan: A population-based birth cohort study" (originally entitled "Birth outcomes among native-born, China-born and Southeast Asia-born mothers in Taiwan: A population-based birth cohort study") by Shiao and Chiang for publication in BMC Pregnancy and Childbirth. We are thankful to the reviewers and the Editor for pointing out some important modifications needed in the manuscript. We have taken these comments into account in the revision. The explanation of what we have changed and why in response to the reviewers’ concerns is given point by point in the following pages.

We think the comments have been highly constructive and very useful to the revision of our manuscript. We believe that the added descriptions and stratified analysis of birth outcomes included in the revised article really improved the quality of the manuscript and made it more persuasive. The written English of this manuscript has been proofread.

We hope that all these changes fulfill the requirements to make the manuscript acceptable for publication in BMC Pregnancy and Childbirth.

Thank you for your time and consideration. We are looking forward to hearing from you soon.

Sincerely yours,
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Point-to-point response to reviewers’ concerns

Reviewer 1: Lai-Chu See

Major Compulsory Revisions:

1. Representative of the sample: please discuss or analyze the difference between the sample (Taiwan Birth Cohort Study) and the population.

The detailed sampling procedure and the test for representativeness of the sample are as follows. TBCS is based on a nationally representative sample drawn from a single birth cohort, all live births in 2005 from the birth report database. The target sample size was set at 25,000, with a sampling rate approximating 12%. TBCS applied two-stage stratified sampling method. The primary sampling unit (PSU) was township, and all 369 townships in Taiwan were organized into 12 stratifications by administrative unit and total fertility rate. The sampling rate was determined proportionate to its number of births in 2002. In the first-stage sampling, 89 townships (85 PSUs) were selected by using systematic random method. The next stage involved selecting individual births by random sampling within each selected PSU. The latter procedure was conducted from January to December 2005 on a monthly basis when a list of babies ranked by date of birth was made available. The final target sample came to 24,200 live births in the whole year.

The population of the study is all live births in 2005 from the birth reporting database (N=206,205). We used Chi-square goodness-of-fit test to determine whether the Taiwan Birth Cohort Study sample data were consistent with the population. The distribution of infant sex, multiple births, birth weight, gestational age, and birthing setting between the sample and the population were tested. Only the distribution of birthing setting between
the TBSC sample and the population ($x^2=14.29$, $p=0.0007$) showed inconsistency, as it may due to large sample size and more hospital births in the sample (0.68% in sample, and 0.67% in population). The Chi-square statistics of infant sex ($x^2=0.74$, $p=0.3896$), multiple births ($x^2=0.37$, $p=0.8311$), birth weight ($x^2=1.79$, $p=0.4086$), and gestational age ($x^2=1.20$, $p=0.5488$) showed that the TBCS sample was consistent with the population.

2. **The rationale of having two foreign-born mothers (China-born mothers and Southeast Asia-born mothers):** I do not see any discussion about the maternal characteristics and birth outcomes between these two groups.

One important limitation identified in the literature on birth outcomes of immigrant women is the use of broad ethnic or racial categories, which fails to take the heterogeneity of immigrant groups into account [1]. The broad categorizations limit examination of potential social and cultural explanations of underlying effects on birth outcomes of immigrant women. In our study, China-born mothers share the same language and similar cultures to Taiwanese, whereas South-east Asian women do not. These social and cultural factors play an important role in their adaptation to life in Taiwan, which may later have some influence on their birth outcomes.

The maternal characteristics of China-born and Southeast Asia-born mothers are described in results on p.8-11. In general, China-born mothers were more likely to be older, have higher family income, receive longer formal education, and have a partner with longer formal education than Southeast Asia-born mothers. Southeast Asia-born mothers were more likely to be younger and first-time mother. China-born mothers also
had higher rates in pregnancy complications and later entry of prenatal care, but more prenatal visits than Southeast Asia-born mothers (Table1). As for birth outcomes, infants of China-born mothers had the highest mean birthweight among three groups, while infants of Southeast Asia-born mothers had the lowest (Table2).

3. Comparison of maternal characteristics and birth outcomes between this submitted article and literature: I found that LBW rate and preterm birth rate in this submitted article are similar to the literature but the maternal characteristics of this submitted article are very different from the literature. I would like to see some discussion on this issue.

Although the rates of maternal risk factors, such as pregnancy complications in the study were higher than the rates in the literature using Taiwan Birth Reporting Database data [2, 3], the rates of maternal factors were similar to clinical reports in Taiwan. The incidence rate of gestational diabetes mellitus reported in Taiwan is 2.03% [4], and the rate in our study is 2.23%.

4. Syphilis, a predisposing maternal factors, is not available: some discussion of this aspect is needed.

Thank you very much for raising the question on the unavailability of syphilis data in this study. Unfortunately, data on syphilis were not collected in TBCS. In previous studies [2, 3], foreign-born mothers in Taiwan (including both China-born and Southeast Asia-born) were more likely to have syphilis than Taiwan-born mothers. According to
those studies, although syphilis had an effect on birth weight [2], it was not significantly associated with preterm birth in Taiwan [3].

5. Strange result about insignificance in preterm birth of southeast Asia-born mothers in model 1 but became significance in model 2 (Table 4): I suggest the authors look at this problem comprehensively. Stratification, interaction, or restriction may be cues.

Thank you very much for the suggestion. We think the result of insignificance in preterm births of Southeast Asia-born mothers in Model 2a that then became significant in Model 2b (Table 4) was due to suppression. By inclusion of the suppressor variables—socioeconomic factors in the model, the relation between maternal nativity and preterm increased. (p.24)

In order to clarify this relationship, a stratified analysis of two adverse birth outcomes by maternal nativity in different family income strata was conducted (p.8, para 1) The result showed that “Both low birthweight and preterm birth were more frequent among Taiwan-born mothers with lower family income (Table 3), however, among mothers with family income over NT$70,000, adverse birth outcomes were more frequent among Southeast Asia-born mothers. Only the association in income group under NT$30,000 reached a significant level (p=0.03). This showed that with disadvantaged family income, China-born and Southeast Asia-born mothers had lower rates of adverse birth outcomes.” (p.10)

6. Results of Chi-square and t tests which compare the bivariate relationships
between maternal nativity, risk factors and birth outcomes (p.9, para 2, line 4-6) is not seen.

Thank you very much for pointing out this mistake. The results of Chi-square and t-tests were added to the text (p.9-10), and Tables 1 and 2 (p.20-22). The revised paragraph is as follows, "except for infant sex (p=0.99), the distributions of birth order, maternal age, place of residence, smoking during pregnancy, pregnancy complications, and prenatal care use were significantly different (p<0.05) by maternal nativity."

7. Title should be more specific: how about change birth outcomes to LBW and preterm birth?

Thank you very much for the suggestion on the title. In consideration of the suggestion to be more specific, we changed the title to “Adverse birth outcomes among native-born, China-born, and Southeast Asia-born mothers in Taiwan: A population-based birth cohort study." (p.1)

Minor essential revisions:

1. “very limited studies have shown the birth outcomes of foreign-born women in the Asia-pacific region (p. 5, para 2, last sentence)” should be deleted as this statement is not true (see reference 14-17).

Thank you very much for reminding us of the number of existing studies. The statement “very limited studies have shown the birth outcomes of foreign-born women in
the Asia-Pacific region” was deleted from the manuscript. Instead, the description on previous study in Taiwan is now as follows, “however, only a few have shown the birth outcomes of foreign-born women in the Asia-Pacific region.” (p.4, para 3, last sentence)

2. Wrong number of education grouping: the correct number should be three (0-9, 10-12, 13+), not 4 (p. 9, para 1, line 1) and 5 (p.9, para 1, line 3).

Thank you very much for pointing out the mistakes in education groupings. The education groupings were revised to three. The correct text is as follows, “maternal education was measured as years of formal education received, and categorized into three groups as 0-9, 10-12, and 13+ years. Parental education was also categorized into three groups as 0-9, 10-12, and 13+ years of formal education.” (p.7, para 2)

3. Incorrect text “when family socioeconomic factors such as family income and maternal education were adjusted, the difference in risk of LBW and preterm birth was reduced (p.14, para 3, last 3 sentences)” should be increased (e.g. odds ratio (OR) of preterm birth: 0.67 (model 1)#0.57 (model 2) for the China-born mothers, etc.) because the magnitude of OR depends on how OR away from “1”.

We appreciate the suggestion of correcting the description of logistic regression results in discussion. We have taken the suggestion and revised it to “when family socioeconomic factors such as family income and maternal education were adjusted, the odds ratio of low birthweight and preterm birth for China-born and Southeast Asia-born
mothers was reduced, and with even higher statistical significance (Model 1b, Model 2b in Table 4).” (p.12, para 2)

Reviewer 2: Nathalie Auger

Abstract

1. Methods need to be more clearly described. At present the description of study outcomes is unclear, and the statistical analysis is not provided.

Explanations on the study outcomes and the statistical analysis were added to the method section of the abstract. It has been revised as the following, “health outcome variables examined included two adverse birth outcomes: low birthweight and preterm birth. Multiple logistic regression was used to examine the contribution of socioeconomic factors to birth outcomes among three groups.” (p.2)

Background

1. My main comment is related to the study objective. The authors state that the aim was to “examine disparities in low birthweight and preterm birth across nativity groups, and how socioeconomic status mediates the disparities (page 6). Though the background was sufficient to support the objective of examining disparities, I did not feel the background was sufficient to explain why a mediation analysis was necessary.

We have revised the aim of the study to “examine the contribution of socioeconomic factors to disparities in low birthweight and preterm birth across China-born, Southeast
Asia-born, and Taiwan-born mothers.” (p.5) We did not intend to do a mediation analysis in the current study, however, we appreciate the point that the reviewer raised, and it will be well taken into account for our future study.

**Methods**

1. **Specify that the units of education was years (page 9)**

   The unit of education is added to the text on page 7 (originally page 9). The revised description on education is as follows, “Maternal education was measured as years of formal education received, and categorized into three groups as 0-9, 10-12, and 13+ years.”

2. **“All unknown answers were excluded from the regression model (p. 9)” What unknown answers, and how frequently did this occur?**

   To clarify the description on missing data, the statement “All unknown answers were excluded from the regression model” was deleted (p.7). More detailed descriptions of missing data were added to the manuscript. “We excluded births with either parent deceased (n=627), and missing information on birth order (n=17), paternal education (n=175), maternal education (n=38), family monthly income (n=73), smoking during pregnancy (n=25), first-time prenatal care (n=43), and number of prenatal visits (n=213). Only infants with Taiwanese fathers, with either Taiwan-born, China-born or Southeast Asia-born mothers were included in the present study, leaving a final sample of 20,090 births (94.6%), which consisted of 17,441 Taiwan-born (86.8%), 917 China-born
(4.6%), and 1,732 Southeast Asia-born mothers (8.6%).” (p.6, para 2).

3. “I do not understand the statement that begins: “Parental education was categorized into five groups as maternal education.... (p. 9)”

Thank you very much for pointing out the confusing descriptions. This sentence is rephrased with “Parental education was also categorized into three groups as 0-9, 10-12 and 13+ years. Since family income and paternal education were highly correlated (r=0.44), only family income and maternal education were taken as proxies of the family socioeconomic position.” (p.7)

4. This sentence does not make sense: “Logistic regression was used to examine dependent variables such as birth outcomes associated with family socioeconomic factors across three maternal nativities”. Exactly what was the analysis that was performed?

The sentence has been rephrased to “multiple logistic regression was used to examine the contribution of socioeconomic factors to low birth weight and preterm birth among China-born, Southeast Asia-born, and Taiwan-born mothers.” (p.8)

5. The study objective states that mediation by socioeconomic status was evaluated. Please describe how this was done. For examples, see: Gray R Bonellie SR, et al. Contribution of smoking during pregnancy to inequalities in stillbirth and infant death in Scotland 1994-2003. BMJ 2009;339:b3754 and
Mortensen LH, Diderichsen F, et al. The social gradient in birthweight at term: quantification of the mediating role of maternal smoking and body index. Human reproduction 2009;24:2629-2635. If the intention was not to examine mediation (and only to adjust for socioeconomic status), then this aspect of the study should not be a study objective.

Thank you very much for the great suggestion on the point of mediation by socioeconomic status. We have revised the objective to “to examine the contribution of socioeconomic factors to disparities in low birthweight and preterm birth across China-born, Southeast Asia-born and Taiwan-born mothers.” (p.5). We did not intend to examine mediation with a sophisticated analysis in this study, but to demonstrate the effect of socioeconomic status on the disparities in birth outcomes among three nativity groups.

6. How was gestational age collected?

The data on gestational age was from the national birth reporting database, from which the sample of Taiwan Birth Cohort Study is drawn. In Taiwan, birthing facilities are obligated to report each birth to Bureau of Health Promotion to form the Taiwan Birth Reporting Database. Gestational age is calculated from the first day of the last menstrual period (LMP) to the date of birth. In addition, obstetric ultrasonography is also often used to assist the determination of gestational age by measuring the size of the fetus in Taiwan.

Results
1. The term odds is more appropriate than risks, since odds ratios (and not relative risks were estimated). This issue applies to the entire manuscript.

The term risk used throughout the manuscript was changed to odds.

2. Provide the results for the mediation objective (or drop this objective).

We decided to drop the objective for testing mediation. The objective now is to “examine the contribution of socioeconomic factors to disparities in low birthweight and preterm birth across China-born, Southeast Asia-born, and Taiwan-born mothers.” (p.5)

3. A table showing the proportions of preterm birth and low birth weight according to the study covariates is needed.

Thank you very much for the suggestion on adding one more table. We have added Table 3 to address the proportion of low birthweight and preterm birth by maternal nativity according to family income. (p.23)

4. Why are tables 1 and table 2 separated? They show the same type of data, and should preferably be combined.

Table 1 and 2 are now merged into one table. (Table 1, p.20-21)

5. Very low birth weight was an outcome Please provide the results.
Very low birthweight was for describing the distribution of birthweight. Since it was not a study outcome, it has been removed from both the text and table in the manuscript.

Discussion

1. Page 15 “Our findings lend support to the literature on “epidemiologic paradox”...” The epidemiologic paradox is a term originally used to describe the unexpectedly favourable health status of Hispanic populations that are socioeconomically disadvantaged. To evaluate the epidemiologic paradox, one therefore has to at least assess effect modification, ie modifying effects of nativity status on the relation between socioeconomic status and the outcome (or vice versa). This can be done by testing a nativity-by-socioeconomic status interaction term, or by running separate models for each strata of socioeconomic status. By simply adjusting the association between nativity and birth outcome for socioeconomic status, the authors assess the overall influence of nativity on birth outcomes (or the healthy immigrant effect). It has been a while since I have looked at the literature on the epidemiologic paradox; however, I do not why the study performed here supports this paradox. Can the authors either revise this conclusion, or explain in greater detail why they believe their analysis supports this conclusion. This applies to the study conclusion as well. The results do, however, support the healthy immigrant effect.

Thank you very much for the insightful suggestion on epidemiological paradox. We
have taken the suggestion into account, and assessed epidemiological paradox with simple stratified analysis to test nativity-by-socioeconomic status interaction. Stratification of two adverse birth outcomes by maternal nativity in different family income strata was conducted. We found that “both low birthweight and preterm birth were more frequent among Taiwan-born mothers with lower family income (Table 3), however, among mothers with family income over NT$70,000, adverse birth outcomes were more frequent among Southeast Asia-born mothers. Only the association in income group under NT$30,000 reached a significant level (p=0.03). This showed that with disadvantaged family income, China-born and Southeast Asia-born mothers had lower rates of adverse birth outcomes.” (p.10) The preliminary result of the stratified analysis lent support to an “epidemiological paradox” of birth outcomes in Taiwan.

2. Page 17. This sentence is unclear “The strength of this study lies in factors”.

The sentence was now replaced with “The strength of this study is as follows.” (p.14)

3. Discuss the mediation objective.

The mediation objective was dropped in the study.

4. Some researchers argue that low birth weight is merely a marker for preterm birth (and hence that analyzing both outcomes does not provide added information). This appears to be the case in Table 4, as the results for low birth weight and preterm birth were nearly identical. Please address.
Birthweight is determined by both duration of gestation and the rate of fetal growth. Low birthweight can occur when an infant is born either too early (preterm birth) or small for the gestational age. Thus, low birthweight is not a marker only for preterm birth, but the net result of either or both adverse situations. The determinants and the consequences of preterm birth and small for gestational age are also different [5]. Moreover, low birthweight and preterm birth have been well used as indicators in comparison of early child health. Although the results of both outcomes were similar in this study, the difference in significance between low birthweight and preterm birth before and after adjusting family socioeconomic status showed that the contribution of socioeconomic factors to either result may be different. (p.24, Table 4)

5. Please address study limitations (not only study strengths).

Thank you very much for the suggestion on providing limitations of the study. It is now added to p.15 of the manuscript as follows, “A limitation of our study is that the data was collected with a self-report procedure. The self-report results may be subject to mistakes, exaggeration or underreporting due to recall or social desirability bias.”

Table

1. Table 4. Provide the unadjusted model results.

Results of unadjusted model were added to Table 4 on p.24. The description of the analysis was added to the text on p.10, “Table 4 compares the results of multiple logistic regression analysis of risk factors for low birthweight and preterm birth in three models,
unadjusted, before and after adjusting for socioeconomic characteristics in three maternal nativity groups”.

Minor:

1. Use placental abruption instead of placenta abrupt.

   The term “placenta abrupt” was replaced with “placental abruption” throughout the manuscript.

2. What does NT$ correspond to in terms of US dollars?

   The currency rate of NT$ corresponding to US dollars was added to the text and the table. “One US dollar equals 32.167 New Taiwan dollars” (p.7, 21, 23)
References:


