Author's response to reviews

Title: Adverse birth outcomes among native-born and foreign-born mothers in Taiwan: A population-based birth cohort study

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Author's response to reviews: see over
Dear Editor,

Thank you very much for giving us a second opportunity to revise our manuscript entitled "Adverse birth outcomes among native-born and foreign-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 analyses 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 by a professional editor.

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,
Tung-liang Chiang

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Point-to-point response to reviewers’ concerns

Reviewer: 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.
   Your response is satisfied. Be sure to write the relevant response but short text in the revised manuscript.

Thank you for pointing out the lack of description on this issue in the text of the article. The representativeness of the sample is now added to discussion of the revised manuscript as follows,

“TBCS is a nationally representative sample drawn from a single birth cohort (all live births from Taiwan Birth Reporting Database, 2005). It applied two-stage stratified sampling method, with the target sample size set at 25,000 (sampling rate 12%). Chi-square goodness-of-fit test used to determine TBCS sample representativeness showed that the TBCS sample was consistent with the population. The distribution 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 ($x^2=1.20, p=0.5488$) were not significantly different between the TBCS sample and the population, except for birthing setting ($x^2=14.29, p=0.0007$). This may due to large sample size and more hospital births in the TBCS sample (0.68% in sample, and 0.67% in population). Therefore, we conclude that the results in the present study may be generalized to the population.” (p. 15-16, para.3)

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.
   Your response is not satisfied. You need to tell the rationale of having two foreign-born mothers (China-born mothers and Southeast Asia-born mothers) in the introduction and summarize the difference in the discussion.

In the revised manuscript, we have two immigrant groups, China-born and Southeast Asia-born mothers, for the description of the similarity and the difference of family and maternal characteristics between the two groups. However, the two birth outcomes were
not statistically significant after Bonferroni correction (Table 2). In pairwise comparisons, no significant difference was shown in birth outcomes between China-born and Southeast Asia-born mothers (Table 2). Moreover, there is no statistically difference in odds for low birth weight and preterm birth between China-born and Southeast Asia-born mothers in multiple logistic regression. Therefore, two immigrant groups were combined into one for assessing the interaction between income and nativity in multivariate analysis. The rationale of having two groups of immigrant mothers for better description of mother and family characteristics is in method of the text as follows,

“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 capture the heterogeneity of immigrant groups [18]. In Taiwan, mothers who emigrated from China share the same language and similar cultures as Taiwanese mothers, whereas other Southeast Asian women do not. These social and cultural factors have an important role in cultural assimilation that may influence future birth outcomes. Therefore, mothers were categorized into the following three groups according to their self-reported country of origin: Taiwan, China, and Southeast Asia for univariate analysis.” (p.7, para.1)

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.

Other than gestational diabetes mellitus, conditions during pregnancy may be lower in Taiwan Birth Reporting Database. I would like to see a paragraph about the difference in conditions during pregnancy in Taiwan Birth Reporting Database and your data.

The rates for pregnancy complications in Taiwan Birth Cohort Study (TBCS), Taiwan Birth Reporting Database, and clinical data are shown below.

<table>
<thead>
<tr>
<th></th>
<th>Taiwan Birth Cohort Study (TBCS)</th>
<th>Taiwan Birth Reporting Database</th>
<th>Clinical report(^1) or National Health Insurance Database(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>gestational diabetes</td>
<td>2.2</td>
<td>0.6</td>
<td>2.2(^1), 3.6(^2)</td>
</tr>
</tbody>
</table>
pregnancy-induced hypertension 2.2 0.6 0.5
pre-eclampsia 0.7 0.5 0.7
placenta previa 1.8 0.9 1.7
placental abruption 0.4 0.4 0.2

Other than pregnancy-induced hypertension, the rates of other pregnancy complications in TBCS are similar to those in clinical reports. The rates of pregnancy complications in Taiwan Birth Reporting Database are mostly lower compared to those in the other two data sources. The rates of pregnancy complications in TBCS may be under- or over-reported due to recall bias, whereas rates of the same complication may subject to underreporting or miscoding in Taiwan Birth Reporting Database since the rates are low among most pregnancy complications relative to clinical data.

Information on gestational age and birth weight of the infants in TBCS was directly retrieved from Taiwan Birth Reporting Database. Therefore, the rates of low birth weight and preterm in the present study are similar to the literature using the data from Taiwan Birth Reporting Database. This is addressed in the article on p. 16, last paragraph of the discussion:

“The rates of maternal complications in TBCS are higher than the rates of same complications in Taiwan Birth Reporting Database. This difference may due to recall bias in TBCS, or underreporting in Taiwan Birth Reporting Database. Higher rates of maternal complications in clinical reports [28, 29] suggest the underreporting in Taiwan Birth Database may be the case.”

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

Your response is satisfied. Be sure to write the relevant response but short text as a limitation in the revised manuscript.

The response is added as a limitation in the manuscript (p.16, last paragraph of the discussion). “Data on syphilis, a predisposing maternal factor for adverse birth outcomes were not collected in TBCS. In previous studies [17, 30], immigrant mothers in Taiwan (including native Chinese and Southeast Asian) were more likely to have syphilis than native Taiwanese mothers. Although syphilis had an effect on birth weight
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. I do not agree with suppression is a reason why preterm births of Southeast Asia-born mothers was insignificance in Model 2a and became significant in Model 2b (Table 4). Based on the result in Table 3, interaction between income and maternal nativity may be a cause. Did you check interaction part? Interaction between SES and maternal nativity is needed for logistic regression (Table 4) based on the result in Table 3.

Thank you for the suggestion on the matter of interaction between maternal nativity and income. Interaction term is added to the analysis in this revised manuscript. The results of the analysis are shown in Table 3 and Table 4 (p.25-26), described in detail on p.11-12. There is interaction between income and maternal nativity, to low birth weight and preterm birth.

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. Your response is satisfied.

Title should be more specific: how about change birth outcomes to LBW and preterm birth? Your response is satisfied.

New. Multiple comparison is needed for Table 1, 2 to show how three groups are different.

Thank you for the suggestion on multiple comparison. Bonferroni correction was used to examine the difference among three groups (Table 1 and Table2, p.22-24).

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).

You still need reference on “however, only a few have shown the birth outcomes of foreign-born women in the Asia-Pacific region.”(p.4, para 3, last sentence)

The sentence is rephrased and referenced as, “however, few studies have shown the birth outcomes of immigrant women in the Asia-Pacific region [14-17].” (p.4, para.3)

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).
Your response is satisfied.

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. odd 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”.
Your response is satisfied.

New Minor essential revisions:

1. Incorrect citation: reference 16 did consider predisposing maternal factors to preterm birth (p.5, para 1, line 8). Reference 14, 17 did have maternal age, pregnancy complication.

Thank you for pointing out the mistake in citing references. The citation is revised as follows,

“Other studies using either county- or country-level birth report data also confirmed better birth outcomes among immigrant mothers in Taiwan [14, 16, 17]. Some predisposing maternal factors to birth outcomes, such as maternal age and pregnancy complications, have been considered in previous studies; however, other important factors, such as the timing and number of prenatal visits, were not considered [16, 17].” (p.4-5).

2. Specify the written language used for the Chinese reference.
Non-English references are now specified (p.17-21, ref. 1, 4, 8, 9, 19).

3. Punctuation: ‘.’ Missing in p. 12, para 2, line 10. “4,82” should be “4.82” in Table 3

Both para.2, line 10 and Table 3 were completely revised.

4. Strange logic: How Table 1 show “foreign-born mothers may experience discrimination and stress before and during pregnancy, but the exposure may not be sufficient enough to cause adverse birth outcomes due to their short stay in Taiwan” (p.14, para 1, line 4-7).

Table 1 shows the average length of stay of Chinese mothers (3.3 years) and Southeast Asian mothers (3.5 years) in Taiwan. According to Geronimus’s weathering hypothesis, “the effect of social inequality on health status may compound with age, leading to growing gaps in health status through young and middle adulthood that can affect fetal health.” The immigrant mothers may experience social inequality and discrimination in Taiwan, however, due to their short length of stay after entering Taiwan, the exposure may not be strong enough to reflect as adverse birth outcomes among their children. (p.14, para.2)

5. English editing is needed.

This manuscript has been proof-read by a professional editor.

6. Table 1: title should add “maternal and family characteristics”

The title of Table 1 is now “Maternal and family characteristics of infants by maternal nativity: Taiwan Birth Cohort Study, 2005.” (p.22)
Reviewer: Nathalie Auger

Major revisions:

1. I received the revised version of the manuscript, and continue to have some concerns regarding the scientific content, including several interpretations related to the “epidemiologic paradox” that are put forth. What the authors need to be clearer about is that they are evaluating the relationship between a variable measuring immigrant status and a birth outcome. There is an extensive literature on the healthy immigrant effect that the authors need to be aware of, including several major reviews on this issue. See for example,


   The epidemiologic paradox, however, is a separate issue. The authors in fact found no evidence of an epidemiologic paradox in Taiwan. Had an epidemiologic paradox been present, they would have observed, for instance, that odds of preterm birth were lower for China-born but not SE Asia-born cases (relative to native-born), despite the lower socioeconomic status of both groups. This is clearly not the case – all the foreign-born groups in Table 4 were less likely to have adverse birth outcomes relative to the native-born population (which is merely an indication of the healthy immigrant effect). The discussion as it currently stands is not supported by the results.

   Thank you for providing us the two references listed above. We have read them and others in order to clarify the “epidemiological paradox” and the “healthy migrant” effect. We have revised our analyses by adding interaction term for maternal nativity and income.

2. There is lack of congruence between the revised study objective and the statistical analyses. The objective states that the study sought to “examine the contributions of socioeconomic factors to disparities in low birth weight and preterm birth across China-born, SE Asia-born and Taiwan-born mothers.
However, the associations between socioeconomic status and these outcomes are not reported for any of the three groups (or for the sample overall). The results only demonstrate that the healthy immigrant effect was not confounded by socioeconomic status (since the association with foreign-born status remained protective against adverse birth outcomes even when adjusting for socioeconomic status). I sense that the confusion in the study objective relates to the need to better grasp the wider literature in terms of the distinction between the epidemiologic paradox and the healthy immigrant effect. As it stands, the study objective should be “To determine the relationship between nativity and adverse birth outcomes accounting for maternal characteristics including socioeconomic status.” This applies to the abstract as well (objective and last line of methods are unclear, page 2). The remainder of the text should also reflect this issue.

Thank you for the suggestion. We have modified the present study in order to meet our study objectives by introducing interaction term between maternal nativity and income to the analyses.

The analyses and the results are both revised to fulfill our study objectives written in method of the abstract “this study sought to determine whether disparities in birth outcomes exist between native and immigrant mothers in Taiwan.” (p. 2) as well as in the main text “this study examined the correlations between socioeconomic factor and disparities in low birth weight and preterm birth among foreign-born and Taiwanese mothers who reside permanently in Taiwan.” (p.5, para.2)

The last line of methods in the abstract is revised to “Multiple logistic regression was used to examine the association between income and immigration status, as well as birth outcomes among both groups. (p.2).” The change also applies to the rest of the article.

Other essential revisions:
3. I found that several of the comments by reviewer # 1 were constructive. Although the authors responded to the comments in a response, they did not address the issues in the manuscript. In particular, the authors should carefully address generalizability in the text.
The issue of generalizability is addressed in discussion of the text as follows, “TBCS is a nationally representative sample drawn from a single birth cohort (all live births from Taiwan Birth Reporting Database, 2005). It applied two-stage stratified sampling method, with the target sample size set at 25,000 (sampling rate 12%). Chi-square goodness-of-fit test used to determine TBCS sample representativeness showed that the TBCS sample was consistent with the population. The distribution 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 \( x^2 = 1.20, p=0.5488 \) were not significantly different between the TBCS sample and the population, except for birthing setting \( x^2 = 14.29, p=0.0007 \). This may due to large sample size and more hospital births in the TBCS sample (0.68% in sample, and 0.67% in population). Therefore, we conclude that the results in the present study may be generalized to the population.” (p.15, para. 2)

4. Source of gestational age – the authors responded to my question, but should provide the information in the manuscript, and address the limitation of using dating based on last menstrual period in the limitations section.

This information is provided in discussion under study limitations as follows, “Using LMP for the determination of gestational age may also lead to miscalculation resulting from recall bias; however, adjusting gestational age with obstetric ultrasonography should minimize the bias.” (p.16, para.2)

5. Background, page 4, last line. Sentence not clear.

This sentence was revised as follows, “However, few studies have shown the birth outcomes of immigrant women in the Asia-Pacific region [14-17].” (p.4, last line in para.3)

6. Methods, page 5 - Delete the sentence “Parental education was also categorized... “. Not clear why it is needed here. Methods, page 8 – the two newly added sentences are unclear, as no results showing ORs for nativity in different income strata are provided, nor are ORs for socioeconomic status in different nativity strata shown. What the authors currently provide are results for the following analysis: “Multiple logistic regression was used to examine the association between nativity and lbw and ptb in unadjusted models, and
models adjusted for (list the covariates here).” Discussion, first paragraph, page 12 – delete point (1) which is redundant (the same information is stated in point (2)).

The sentences “Parental education was also categorized...” in method (p.7, para.3) and point (1) in discussion (p.12, para.2) are deleted from the text of the manuscript.

In this revised manuscript, we provided results showing ORs for nativity in different income strata and ORs for socioeconomic status in different nativity strata. Therefore, in method on p.8, we addressed,

“The association between maternal nativity and birth outcomes in family income strata, and the association between family income and birth outcomes by maternal nativity was assessed. Multiple logistic regression was used to examine the association among nativity, family income, and two birth outcomes in unadjusted models, as well as models adjusted for infant sex, birth order, maternal age, singleton, place of residence, maternal education, smoking during pregnancy, pregnancy complications, first-time prenatal care, and frequency of prenatal visits.”

7. The authors often use the term “reached a significant level”. There is a distinction between something being “statistically significant” as opposed to being “significant”. The authors appear to be referring to statistical significance, and should say so in the text.

The distinction is now made clear between something “significant” and “statistically significant” in the article. The statements referring statistically significant are emphasized with “statistically” significant, otherwise referring something significant.
References