

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Pathways Linking Socio-economic Status to Small-for-Gestational Age (SGA) Infants among Primiparae: A Birth Cohort Study in China
AUTHORS	Luo, Xiu; Liu, Lingfei; Gu, Huaiting; Hou, Fang; Xie, Xinyan; Li, Xin; Meng, Heng; Zhang, Jiajia; Xu, Shunqing; Song, Ranran

VERSION 1 – REVIEW

REVIEWER	Dr. Jamie Seabrook Brescia University College, Canada
REVIEW RETURNED	31-Aug-2017

GENERAL COMMENTS	<p>Thank you for the opportunity to review the manuscript, 'Pathways linking socioeconomic status to three birth outcomes among primiparas: A birth cohort study'. While examination of mediators in the SES-birth outcomes relationship is an important and timely topic, the value of this paper is distracted by an unacceptable standard of English writing suitable for publication in BMJ Open. Consequently, all throughout the manuscript, I found myself having to reread sentences to try to decipher what the authors were trying to say. Some sentences may have only been missing a word or two (sentences 34-35,41-42,51-52,57-58,65,78-79,82,84-85,95,101,154,172-173,281,284,290-292); others may have used the wrong word to portray a message (139,140,148,177-178,184,201,210,212,244,245-246,286-287,304-305); and some were just too difficult to understand completely. Some examples of the last point would be this:</p> <p>Lines 96-98: "Results from one study showed comparing normal pre-pregnancy BMI, underweight, overweight and obese women had lower education level. Weight gain during pregnancy was the hotspot related to birth outcomes."</p> <p>Lines 252-253: "In our results, we found that participants of low SES tended to be pre-pregnancy underweight, which then caused to be GWG below IOM."</p> <p>Lines 264-267: "Some of our variables such as micronutrient supplement, physical activity and sleep quality during pregnancy relied self-reported which is a limitation. Although the variables were simple, it was significance that we found them could mediate SES to adverse birth outcomes."</p> <p>Line 316: "The quality of prenatal care during pregnancy is disparities limited by the knowledge as lower education and family income."</p> <p>Lines 322-328: "As SGA, LBW and PTB were relevant public health issues. The results indicated that it had great meanings to publicize</p>
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	<p>to the primiparas especially for low SES reproductive age women. Avoiding pre-pregnancy underweight, keeping normal GWG during pregnancy and good quality of one month before birth and taking multi-vitamins during first trimester pregnancy, physical activity during last trimester of pregnancy positively are practical and feasible measurements.”</p> <p>Introduction Lines 79-80 – Who are “they”? Lines 90-91 – The authors claim that “This review was about two decades before...” Before what? Lines 93-94 – What does “Chinese productive women” mean? Lines 98-99 – The authors indicate that “Weight gain during pregnancy was the hotspot related to birth outcomes.” How much weight gain? Lines 116-118 – Okay, but what are the implications for pregnancy and birth outcomes? Line 119 – should not be the start of a new paragraph. Also, which studies are you referring to? Lines 126-128 – the authors state that this “is the first study to combine SES, maternal characteristics and lifestyles to explore their effect on birth outcomes”. Lines 57-58 says there are “few studies”. So is it the first? In fact, my research team just published a study exploring these precise relationships:</p> <p>Campbell, E. E., Gilliland, J., Dworatzek, P. D., De Vrijer, B., Penava, D., & Seabrook, J. A. (2017). Socioeconomic status and adverse birth outcomes: A population-based Canadian sample. <i>Journal of Biosocial Science</i>, 1-12.</p> <p>Methods Lines 171-173 – I need to know more about how education and occupation were combined into a single SES measure</p> <p>Statistical Analysis Table 1 – How was sleep quality measured? “Bad” vs. “Good” seems quite subjective.</p> <p>Results Table 2 – Which statistical tests were used to compare differences between those of high vs. low SES? There is no indication at the bottom of the table, or in the statistical analysis subsection Table 2 – Since only maternal age used mean +/- SD, it’s clearer to give the actual +/- for that variable in the table. Lines 218-219 – high SES is not a protective factor for SES</p> <p>Discussion Lines 256-258 – What do you mean that the cohort of pregnant women had “certain representativeness to some extent”?</p>
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REVIEWER	Bo Xi Shandong University
REVIEW RETURNED	14-Sep-2017

GENERAL COMMENTS	<p>The authors investigated the direct and indirect effects of socioeconomic status on three birth outcomes in a Chinese Birth cohort study with a very large sample size. The pathway analysis is interesting but this method might be not suitable for the current data as the effects are mainly direct based on their results. I suggest the authors re-analyze the data. The authors can follow one recent publication (<i>JAMA Pediatr.</i> 2017 Aug 1;171(8):781-787.)</p>
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	<p>Further minor revisions:</p> <ol style="list-style-type: none"> 1. B should be corrected as β. 2. Some abbreviations such as GWG and IOM should be noted. 3. SES should be categorized into at least three levels (low, median and high). 4. Some variables such as Pre-BMI and sleep quality should be sufficiently defined. 5. English language should be improved by a native English speaker.
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1:

1. Thank you for the opportunity to review the manuscript, 'Pathways linking socioeconomic status to three birth outcomes among primiparas: A birth cohort study'. While examination of mediators in the SES-birth outcomes relationship is an important and timely topic, the value of this paper is distracted by an unacceptable standard of English writing suitable for publication in BMJ Open. Consequently, all throughout the manuscript, I found myself having to reread sentences to try to decipher what the authors were trying to say. Some sentences may have only been missing a word or two (sentences 34-35, 41-42, 51-52, 57-58, 65, 78-79, 82, 84-85, 95, 101, 154, 172, 173, 281, 284, 290-292); others may have used the wrong word to portray a message (139, 140, 148, 177-178, 184, 201, 210, 212, 244, 245-246, 286-287, 304-305); and some were just too difficult to understand completely.

Some examples of the last point would be this:

Lines 96-98: "Results from one study showed comparing normal pre-pregnancy BMI, underweight, overweight and obese women had lower education level. Weight gain during pregnancy was the hotspot related to birth outcomes."

Lines 252-253: "In our results, we found that participants of low SES tended to be pre-pregnancy underweight, which then caused to be GWG below IOM."

Lines 264-267: "Some of our variables such as micronutrient supplement, physical activity and sleep quality during pregnancy relied self-reported which is a limitation. Although the variables were simple, it was significant that we found them could mediate SES to adverse birth outcomes."

Line 316: “The quality of prenatal care during pregnancy is disparities limited by the knowledge as lower education and family income.”

Lines 322-328: “As SGA, LBW and PTB were relevant public health issues. The results indicated that it had great meanings to publicize to the primiparas especially for low SES reproductive age women. Avoiding pre-pregnancy underweight, keeping normal GWG during pregnancy and good quality of one month before birth and taking multi- vitamins during first trimester pregnancy, physical activity during last trimester of pregnancy positively are practical and feasible measurements.”

Response: Thank you for your comments. We are very sorry for the unacceptable English writing because we are not native English speakers. In our new submission, we have improved our English writing by Proof-Reading-Service. In addition, we had re-analyzed our data set and changed our outcome from three birth outcomes to small-for-gestational age (SGA).

2. Introduction

Lines 79-80 – Who are “they”?

Response : Thank you for your suggestions. In our new submission, we used “researchers” to replace “they” in Line 94.

Lines 90-91 – The authors claim that “This review was about two decades before...” Before what?

Response: In our new submission, we didn't use this review in our introduction.

Lines 93-94 – What does “Chinese productive women” mean?

Response: In our new submission, we used “women of child-bearing age” to replace “Chinese productive women” in Line 308.

Lines 98-99 – The authors indicate that “Weight gain during pregnancy was the hotspot related to birth outcomes.” How much weight gain?

Response: Thank you for your comments. Gestational weight gain (GWG) within the Institute of Medicine (IOM) recommendations were defined as 12.5–18 kg, 11.5–16 kg, 7–11.5 kg and 5–9 kg for underweight, normal weight, overweight, and obese women, respectively. In our opinion, GWG below or above IOM are the risks of the adverse outcomes for not only pregnancy women but also infants. We do not use them in the new submission.

Lines 116-118 – Okay, but what are the implications for pregnancy and birth outcomes?

Response : As the content had changed, we deleted this sentence in our introduction of the new submission.

Line 119 – should not be the start of a new paragraph. Also, which studies are you referring to?

Response: In our introduction of new submission, we have changed our sentence into “However, this review used a bibliographic method to find these evidence and it was hard to reveal mediators without the pathway analysis. Furthermore, the gap between the most and least deprived groups did not narrow for birthweight outcomes over the four decades” in Line 104-107.

Lines 126-128 – the authors state that this “is the first study to combine SES, maternal characteristics and lifestyles to explore their effect on birth outcomes”. Lines 57-58 says there are “few studies”. So is it the first? In fact, my research team just published a study exploring these precise relationships: Campbell, E. E., Gilliland, J., Dworatzek, P. D., De Vrijer, B.,

Penava, D., & Seabrook, J. A. (2017). Socioeconomic status and adverse birth outcomes: A population-based Canadian sample. *Journal of Biosocial Science*, 1-12.

Response: We had changed this sentence into “This is the first study evaluating maternal lifestyles and PIH, which mediate socio-economic status (SES) and SGA among primiparae in China” in Line 66-67.

Methods

Lines 171-173 – I need to know more about how education and occupation were combined into a

single SES measure

Response : SES index was measured by a combination of the education and occupation categories. The scores of education and occupation are listed in Supplementary Table 1 and Supplementary Table 2 of our new submission. SES index was measured based on the formula, $SES = ((0.7 * \text{maternal education}) + (0.4 * \text{maternal occupation}) + (0.7 * \text{paternal education}) + (0.4 * \text{paternal occupation}))/2$. Finally, the

SES index categorization demonstrates that below one third of the study population distribution had low SES and the remainder had high SES. We have introduced the detailed methods about the combination of SES index in Line 156-163.

Statistical Analysis

Table 1 – How was sleep quality measured? “Bad” vs. “Good” seems quite subjective.

Response: We collected our data set from questionnaires. The participants were asked the follow question: “How is your sleep quality one month before the birth?” [response alternatives: (1) excellent, (2) better, (3) general (4) relatively poor, (5) poor]. In our submission, we combined the first three answers as the good sleep quality and the

remainders were defined as bad sleep quality. We acknowledged the measurement of sleep quality was subjective and it was a limitation which we wrote in Line 68-69.

Results

Table 2 – Which statistical tests were used to compare differences between those of high vs. low SES? There is no indication at the bottom of the table, or in the statistical analysis subsection

Response: As SGA was our outcome, differences between SGA and AGA were compared using the Student's t-test for continuous variables and chi-square test for categorical variables. Pearson's correlation was carried out between study variables. Logistic regression models were used to examine the associations between SES and SGA. Secondly, we used the pathway analysis to explore the hypothesized underlying relations between variables of interested. We have mentioned the statistical tests in the statistical analysis subsection in Line 166-171.

Table 2 – Since only maternal age used mean +/- SD, it's clearer to give the actual +/- for that variable in the table.

Response: We had given the actual +/- for maternal age in the Table 2 of our new submission, such as the age of all the participants were 27.70 ± 3.24 years old.

Lines 218-219 – high SES is not a protective factor for SES

Response: In our new submission, we had deleted this sentence since it was a wrong sentence.

Discussion

Lines 256-258 – What do you mean that the cohort of pregnant women had “certain representativeness to some extent”?

Response: Thank you for your comments. In our new submission, we had changed this sentence into “One of the strengths of our study was the large sample size” in Line 230.

Reviewer 2:

1. The pathway analysis is interesting but this method might be not suitable for the current data as the effects are mainly direct based on their results. I suggest the authors re-analyze the data.

Response: Thank you for your suggestions. The indirect effect explained 21.7% (-0.017/-0.078) of the total effect in small-for-gestational age (SGA) in Table 4 of the old submission, which was low in pathway analysis. In our new submission, we had added pregnancy-induced hypertension syndrome (PIH) as a new mediator. Finally, our mediators completely mediated socio-economic status to small-for-gestational Age (SGA). The standardized estimates of direct effect was -0.034 (P=0.299) and indirect was -0.030 (P=0.001) in Table 4 of our new submission.

2. B should be corrected as β .

Response : In our new submission, B and β were expressed as standardized estimate and unstandardized estimates, respectively, in Line 177-178.

3. Some abbreviations such as GWG and IOM should be noted.

Response: GWG and IOM were the abbreviations of gestational weight gain and Institute of Medicine, respectively. All the abbreviations were noted in Line 51-60.

4. SES should be categorized into at least three levels (low, median and high).

Response: We agree with you that SES should be categorized into at least three levels. In our new submission, the SES index categorization demonstrates that below one third of the study population distribution had low SES and the remainder had high SES in Line 155-157. In our study, we combined middle-to-high SES as the high SES group based on the following reasons. Firstly, SES index was a categorical variable. If we categorized it into three levels, the pathway analysis method reported only one coefficient. Secondly, low SES women are more likely to have small-for-gestational age (SGA) and higher blood pressure

compared with higher SES women. In addition, one study from America had also

stratified their analysis by low and middle-to-high SES. (Gavin AR, Morris J. The Association Between Maternal Early Life Forced Sexual Intercourse and Offspring Birth Weight: The Role of Socioeconomic Status. *Journal of women's health* (2002). May 2017;26(5):442-449.)

Given these SES differences, SES was categorized into two levels which were low and middle-to-high in Line 157-163.

5. Some variables such as Pre-BMI and sleep quality should be sufficiently defined.

Response: We calculated pre-pregnancy body mass index (BMI) from the self-reported pre-pregnancy weight in kg divided by height in m^2 . BMI was categorized into four groups based on recommendations by the Working Group on Obesity in China of the Chinese Ministry of Health: underweight ($<18.5 \text{ kg/m}^2$); normal weight ($18.5\text{--}23.9 \text{ kg/m}^2$); overweight ($24\text{--}27.9 \text{ kg/m}^2$); and obese ($\geq 28 \text{ kg/m}^2$). The participants were asked the follow question: "How is your sleep quality one month before the birth?" [response alternatives (1) good, (2) better, (3) general (4) relatively poor, (5) poor]. In our submission, we combined the first three answers as the good sleep quality and the remainder defined as bad sleep quality. More detailed content was found in Line 144-148 and Line 141, respectively.

6. English language should be improved by a native English speaker.

Response: Thank you for your comments. We have improved our English writing by Proof-Reading-Service.

VERSION 2 – REVIEW

REVIEWER	Bo Xi Shandong University
REVIEW RETURNED	20-Jan-2018

GENERAL COMMENTS	I have no further comments.
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REVIEWER	Anne Kjersti Daltveit Department of Global Public Health and Primary Care, University of Bergen, Norway
REVIEW RETURNED	07-Feb-2018

GENERAL COMMENTS	<p>Review Pathways Linking Socio-economic Status to Small-for-gestational-age (SGA) Infants among Primiparae: A Birth Cohort Study.</p> <p>The study is based on 8737 births to primiparae women in China. The authors have used logistic regression and pathway analysis to explore whether the association between maternal socioeconomic status and small for gestational age infant is explained by known risk factors.</p> <p>Overall comments: I have not enough competence to consider the pathway analysis and propose that the statistical part of the paper is reviewed by a statistician.</p> <p>Abstract: In the conclusion you state that “Avoiding PIH, taking a multi-vitamin supplement during early pregnancy, keeping normal pre-pregnancy BMI and gaining reasonable gestation weight may represent important protectors for SGA infants among pregnant women from low SES”. This conclusion, where a change in the factor will represent a change in the outcome, is based on an interpretation where the risk factors are causally related to SGA. Do you think this is true for all of the factors. Or could for example use of multivitamins, which was one of the most important mediators, be a strong indicator of unknown factors causally related to SGA? How does the path analysis take care of such potential relations?</p> <p>Strengths and limitations: Line 64: The meaning of the sentence “This index was more robust when it was compared to education and occupation separately in China” is not clear to me.</p> <p>Introduction: Line 75: Because the prevalence of SGA will highly depend on selected reference population, the sentence about the 27%</p>
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	<p>prevalence of SGA infants in 138 low- and middle income countries, reference population should be mentioned (seems to be 1991 US national reference population).</p> <p>Line 82: “body mass index” could be replaced with “maternal underweight”</p> <p>Methods: Lines 126-133: Gestational age was calculated from LMP or clinical estimate. What was the range? How many had known LMP and how many were clinically estimated? For which gestational weeks were 10 percentiles calculated – from 28 to 42 weeks or other? Were births below a specific gestational week excluded from the analyses? I cannot see that this information is included later on in the paper (Statistical methods or Results).</p> <p>Line 151: Is “Institute of Medicine” a unique name?</p> <p>Lines 157-163: “SES index was measured based on the formula, $SES = ((0.7 * \text{maternal education}) + \dots)$” Is this formula based on reference 20 Zhao et al, and is this formula adequate to this study population?</p> <p>Line 179: As many readers may not be familiar with path analysis, I would prefer a sentence about direct vs. indirect effects when these terms are introduced.</p> <p>Table 1: 11% were coded as low SES and 89% with high SES. Did you consider to stratify into more levels of SES?</p> <p>Discussion and conclusions: The authors should discuss in which populations these results, where multivitamins turn out to be an important factors, will be valid. Are there specific characteristics of the studied population that makes this factor so important?</p>
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REVIEWER	Ritam Chowdhury Tufts Medical Center USA
REVIEW RETURNED	13-Feb-2018

GENERAL COMMENTS	Thank you for the clear and lucid analysis and paper to answer the research question. Please clarify how the models were selected in Table 3. Else please re-run and include sections explaining how model selection was performed.
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VERSION 2 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Bo Xi

Institution and Country: Shandong University

Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

I have no further comments.

Reviewer: 2

Reviewer Name: Anne Kjersti Daltveit

Institution and Country: Department of Global Public Health and Primary Care, University of Bergen, Norway

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

Review Pathways Linking Socio-economic Status to Small-for_gestational-age (SGA) Infants among Primiparae: A Birth Cohort Study.

The study is based on 8737 births to primiparae women in China. The authors have used logistic regression and pathway analysis to explore whether the association between maternal socioeconomic status and small for gestational age infant is explained by known risk factors.

Overall comments:

I have not enough competence to consider the pathway analysis and propose that the statistical part of the paper is reviewed by a statistician.

Abstract:

In the conclusion you state that "Avoiding PIH, taking a multi-vitamin supplement during early pregnancy, keeping normal pre-pregnancy BMI and gaining reasonable gestation weight may represent important protectors for SGA infants among pregnant women from low SES". This conclusion, where a change in the factor will represent a change in the outcome, is based on an interpretation where the risk factors are causally related to SGA. Do you think this is true for all of the factors. Or could for example use of multivitamins, which was one of the most important mediators, be a strong indicator of unknown factors causally related to SGA?

Response: Thank you for the suggestions. It was true that a change in the factor would represent a change in the outcome for all factors in our study. We used four pathways to explain the risk factors related with SGA and added the paragraph below in our discussion part (Page 17, Line 252-265). Besides, we discussed each pathway in detail.

“In the pathway analysis, PIH, taking a multi-vitamin supplement during early pregnancy, keeping normal pre-pregnancy BMI and gaining reasonable gestational weight were all the significant mediators which completely mediated the relationship between SES and SGA. There were four pathways between SES and SGA as following. ① High SES of pregnancy women predicted lower risk of PIH. The risk of SGA was reduced by no-PIH. ② Women from high SES had more chance to take a multi-vitamin supplement during early pregnancy. A multi-vitamin supplement could lead to a lower risk of SGA infants. ③ Women from high SES were more likely to be pre-pregnancy BMI $\geq 18.50\text{kg}/\text{cm}^2$. Furthermore, pre-pregnancy BMI $\geq 18.50\text{kg}/\text{cm}^2$ decreased the risk of SGA infants afterwards. ④ Women from high SES predicted pre-pregnancy BMI $\geq 18.50\text{kg}/\text{cm}^2$. Pregnancy women with pre-pregnancy BMI $\geq 18.50\text{kg}/\text{cm}^2$ could gain adequate gestational weight which was not below IOM recommendations. And the GWG not below IOM recommendations decreased the risk of SGA infants.”

We would like to take a multi-vitamin supplement as an example to explain how the risk factor was causally related to SGA.

Women from high SES tended to be more likely to take a multi-vitamin supplement during early pregnancy ($B = 0.317$). Furthermore, taking a multi-vitamin supplement during early pregnancy was a protector for SGA infants ($B = -0.066$). Thus, SES had a negative indirect effect on SGA via a multi-vitamin supplement during early pregnancy ($B = -0.021$, 95% confidence interval = $-0.037, -0.005$). We explained this mediator in our result section (Page 15, Line 244-248).

As the word limitation of abstract and conclusions in the previous version might be not clearly, we replaced the conclusions with another new paragraph in the revised manuscript as following (Page 3, Line 41-46).

“Women from high SES predicted lower risk of PIH, more chance to take a multi-vitamin supplement during early pregnancy, keeping pre-pregnancy BMI $\geq 18.50\text{kg}/\text{cm}^2$ and gaining adequate gestational weight which was not below IOM recommendations. Furthermore, lower risk of PIH, more chance to take a multi-vitamin supplement, pre-pregnancy BMI $\geq 18.50\text{kg}/\text{cm}^2$ and GWG not below IOM recommendations were associated with a lower risk of SGA infants.”

How does the path analysis take care of such potential relations?

Response: In our pathway analysis, we added covariates in pathway analysis to control potential relations. Covariates, maternal age and passive smoking during pregnancy, were related with SGA according to literatures. Besides, we changed “Covariates were maternal age and passive smoking during pregnancy” into “Covariates (maternal age and passive smoking during pregnancy) were added in pathway analysis to control potential relations” in Line 236-237 of Page 14.

Strengths and limitations:

Line 64: The meaning of the sentence “This index was more robust when it was compared to education and occupation separately in China” is not clear to me.

Response: Thank you for your advice. In our country, we had no standardized measurement tool of SES such as New Zealand Socioeconomic Index (NZSEI-06). Most articles from China used education or occupation to represent SES. Thus, we introduced Green’s two factor indices of SES which combined with education and occupation together. We modified the inappropriate statement in the revised manuscript (Page 3, Line 53-55).

“SES index was combined with parental education and occupation. This index was more representative and reasonable to represent SES compared with using only education or occupation in China.”

Introduction:

Line 75: Because the prevalence of SGA will highly depend on selected reference population, the sentence about the 27% prevalence of SGA infants in 138 low- and middle income countries, reference population should be mentioned (seems to be 1991 US national reference population).

Response: Thank you for the comments. We added the reference population in the revised manuscript as following (Page 4, Line 76-77).

“using the Alexander reference population (US National Center for Health Statistics, 1991; n=3,134,879 livebirths)”

Line 82: “body mass index” could be replaced with “maternal underweight”

Response: Thank you for your suggestions. We replaced “body mass index ($BMI < 18.50 \text{ kg/m}^2$)” with “maternal underweight” in the revised manuscript (Page 5, Line 84).

Methods:

Lines 126-133: Gestational age was calculated from LMP or clinical estimate. What was the range? How many had known LMP and how many were clinically estimated?

Response: Thanks you for your comments. The range of gestational age of our studied people was 28-42 weeks. We added the range of gestational age in our revised manuscript (Page 11, Line 213-214).

In our dataset, nearly 99 percent of pregnancy women had the date of last menstrual period (LMP) which was recorded on their clinical cases. If the women whose date of LMP couldn’t be obtained from their clinical cases, we estimated gestational age by B-mode ultrasound. To avoid ambiguity, we modified “Gestational age was calculated from the date of the last menstrual period or the clinical estimate of

gestational age based on the clinical case system” into another expression as following (Page 7, Line 127-130).

“Most of the gestational age was calculated from the date of the last menstrual period (LMP) which was recorded on their clinical cases. We estimated gestational age by B-mode ultrasound if the date of LMP couldn’t be obtained.”

For which gestational weeks were 10 percentiles calculated – from 28 to 42 weeks or other? Were births below a specific gestational week excluded from the analyses? I cannot see that this information is included later on in the paper (Statistical methods or Results).

Response: Thanks you for the advice. According to the definition of small-for-gestational age (SGA), it didn’t exclude any gestational age. Thus, we calculated 10 percentiles for the birthweight of all infants. The reference that introduced the definition of SGA listed as below and was cited as number 5 in the manuscript.

(Lee AC, Katz J, Blencowe H, et al. National and regional estimates of term and preterm babies born small for gestational age in 138 low-income and middle-income countries in 2010. *Lancet Glob Health*. 2013;1(1):e26.).

We didn’t exclude any specific gestational week from the analyses and added a sentence in our revised manuscript as following (Page 7, Line 130-131).

“We didn’t exclude any specific gestational weeks from our studied population.”

Line 151: Is “Institute of Medicine” a unique name?

Response: Yes, it is. It is an organization which was founded in 1972 and affiliated with the National Academy of Sciences. The goal of the Institute of Medicine (IOM) is to provide independent medical advice based on scientific facts. The website of IOM is as following: <http://www.iom.edu.np/>. Gestational weight gain (GWG) was categorized according to the recommendations of IOM in our study.

Lines 157-163: “SES index was measured based on the formula, $SES = ((0.7 * \text{maternal education}) + \dots)$ ” Is this formula based on reference 20 Zhao et al and is this formula adequate to this study population?

Response: Thank you for your comments. This method of estimating socio-economic status (SES) index was based on Zhao et al.’s study. This formula was according to another study from China listed as following and we cited this reference as number 22 in our revised manuscript.

(Zhai Y, Sulayiman X, Li WR, Shen C, Zhao WH, Shi XM. The relationship between socioeconomic status and overweight and obesity among elementary school children in China. *Zhonghua yu fang yi xue za zhi* [Chinese journal of preventive medicine]. Oct 2013;47(10):945-948)

The Zhai et al.'s study was a large scale cross-sectional study, which contained a total of 19,934 people from eight provinces in mainland China. This formula was suitable for Chinese population. Our studied population was from Wuhan, Hubei province, which located in central part of China. So we used this formula in our study.

Line 179: As many readers may not be familiar with path analysis, I would prefer a sentence about direct vs. indirect effects when these terms are introduced.

Response: Thanks for the suggestions. We introduced these terms according to the number 24 reference which has been published on International Journal of Epidemiology and added definitions in our revised manuscript as following (Page 10, Line 196-198).

“Indirect effect was defined as the effect of the exposure that acted through a given set of mediators of interest. Direct effect was refer to the effect of the exposure unexplained by those same mediators.”

Table 1: 11% were coded as low SES and 89% with high SES. Did you consider to stratify into more levels of SES?

Response: Thanks for your comments. We classified SES into two levels (low and middle-to-high SES) according to a reference from America. The Gavin AR et al study was added in the revised manuscript listed as number 23.

(Gavin AR, Morris J. The Association Between Maternal Early Life Forced Sexual Intercourse and Offspring Birth Weight: The Role of Socioeconomic Status. *Journal of women's health* (2002). May 2017;26(5):442-449.)

Further, this classification of SES would be better fitted for the pathway analysis and could explain the results clearly. Following your advice, we stratified SES into three levels (low, middle and high) to explore the association between SES and SGA in logistic regression model. The results showed that the ORs of low and high SES were 1.244 (95% CI, 1.055, 1.467) and 0.885 (95% CI, 0.750, 1.044) when compared with middle SES. There was no significant association between high SES and SGA compared with middle SES. Based on above reasons, we thought two levels of SES would be more appropriate in our study.

Discussion and conclusions: The authors should discuss in which populations these results, where multivitamins turn out to be an important factors, will be valid. Are there specific characteristics of the studied population that makes this factor so important?

Response: Thank you for the suggestions. We discussed in which population multi-vitamins turn out to be an important factor in our revised manuscript as following (Page 20, Line 329-333).

“As our large-scale studied population came from the city of Wuhan, the results of our study could extend to pregnancy women in Hubei province, which included 12 cities. However, extrapolation of our findings to Chinese women should be cautious. Multicenter cohort studies from different cities of China will be needed in further studies.”

We didn't think there were any specific characteristics of our studied population. This research was a large cohort study in Wuhan and participants were selected when they planned to deliver babies in the Women and Children Medical and Health-care Centre of Wuhan. We added a statement about the important of taking multi-vitamins in our revised manuscript as following (Page 20, Line 319-328).

“In China, most people believe that they should obtain vitamins from daily diet, i.e. fresh vegetables and fruits, which is a natural way instead of taking multi-vitamin supplements every day. Pregnant women are recommended to take multi-vitamin supplements, since they are unable to obtain an adequate nutrient status from their diet alone. Most pregnant women take folic acid, because the government provides folic acid free of charge. For the multi-vitamin supplements, pregnant women decide to take them or not depending on their own opinions. The different dietary habits and customs might explain part of why taking multi-vitamin supplements is significant. Our results showed that high SES was significantly related to a daily supplement of multi-vitamin.”

Reviewer: 3

Reviewer Name: Ritam Chowdhury

Institution and Country: Tufts Medical Center, USA

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

Thank you for the clear and lucid analysis and paper to answer the research question. Please clarify how the models were selected in Table 3.

Response: Thanks for your positive comments. Model 1 was univariate logistic regression analysis and model 2-3 were multivariate logistic regressions. Table 2 was shown the differences distribution of the characteristics among SGA and AGA.

In model 1, we aimed to assess the risk of having a SGA newborn among primiparae from low SES.

In model 2, we evaluated the risk of giving birth to a SGA newborn from low SES after adjustment for potential confounders. We selected the list of potential confounders according to two reasons as following. Firstly, variables, such as maternal age, pre-pregnancy BMI, gestational weight gain (GWG) and a multi-vitamin supplement during the first trimester of pregnancy, were significant different between two groups in Table 2. Secondly, other confounders (sleep quality in the month before the birth, physical activity during last trimester and passive smoking during pregnancy) were all the lifestyles of pregnancy

women. As these lifestyles associated with infants' birth weight were repeatedly reported by literatures, we added them in model 2 although they were not significant in Table 2.

Basing on model 2, we brought in PIH as another confounder in model 3. PIH was an obvious risk factor according to the literature review where women with PIH had twice the risk of having a SGA, compared with women having no PIH.

Else please re-run and include sections explaining how model selection was performed.

Response: Thanks for your advice.

We re-ran our dataset and had got the same results in Table 3.

We included sections explaining how models selection was performed in our revised manuscript as following (Page 9-10, Line 173-187).

“Univariate logistic regression analysis was used to assess the risk of having a SGA newborn among primiparae from low SES. Multivariate logistic regressions were used to explore the risk after adjustment for potential confounders. We selected the list of potential confounders according to two reasons as following. Firstly, variables, such as maternal age, pre-pregnancy BMI, gestational weight gain (GWG) and a multi-vitamin supplement during the first trimester of pregnancy, were significant different between two groups in Table 2. Secondly, other confounders (sleep quality in the month before the birth, physical activity during last trimester and passive smoking during pregnancy) were all the lifestyles of pregnancy women. As these lifestyles associated with infants' birth weight were repeatedly reported by literatures, we added them in model 2 although they were not significant in Table 2. Basing on model 2, we brought in PIH as another confounder in model 3. PIH was an obvious risk factor according to the literature review where women with PIH had twice the risk of having a SGA, compared with women having no PIH.”