PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Adverse birth outcomes and childhood overweight at age of 3 to 8 years in a prospective cohort study in Tianjin, China
AUTHORS	Zhang, Rui; Gao, Ming; Li, Weiqin; Liu, Hongyan; Wang, Shuting; Wang, Hui; Li, Ninghua; Li, Jing; Yu, Zhijie; Hu, Gang; Leng, Junhong; Yang, Xilin

VERSION 1 – REVIEW

REVIEWER	Londero, Ambrogio University of Genoa
REVIEW RETURNED	10-Sep-2023

GENERAL COMMENTS	I thought the article to be incredibly intriguing because it included insightful prospective long-time follow-up statistics, which are relatively difficult to come across. I have identified a few minor concerns that need to be addressed in order to improve the document's readability and clarity. 1) Under the "Results" section, when presenting an odds ratio (OR), kindly indicate whether it has been adjusted or not (OR vs. aOR). This change will ensure that it is easily understandable without having to read the entire sentence to which the numbers in brackets correspond. 2) It would be interesting to read a more in-depth examination of the clinical and scientific implications that your data may have in the discussion section of the paper.

REVIEWER	Liu, Jian Brock University
REVIEW RETURNED	24-Oct-2023

GENERAL COMMENTS	Using a prospective cohort study conducted among 1681 woman-child pairs, the authors examined the association of certain adverse pregnancy outcomes with the risk of development of childhood overweight. The results are interesting, but some concepts related issues may need to be clarified to precisely reflect what the research tried to reach. Below are reviewer's comments for authors' consideration: 1. Adverse pregnancy outcomes refer to a range of health complications and unfavorable events, while this study only looked at preterm birth, postterm pregnancy, macrosomia, LGA, SGA, as well as high and low WLR. These are more likely to be birth outcomes related to infants; using "maternal adverse pregnancy outcomes" in the title seemed not to match well with the facts in the study. 2. The introduction and the discussion gave impression that the objective of the study was not clear; it is unclear whether the

authors have tried to examine the risk association between GDM, LGA, and childhood overweight as described in the intro, or actually as the focuses showed in the results and discussion on the risk of LGA and/or WLR on development of childhood overweight. If authors want to explore the LGA and WLR on the development of childhood overweight, they may need to make it clear in the title, objective, and intro. BTW, when describing the inconsistent findings (page 5 line 47 – page 6 line19), one needs to consider the quality of each study design, it is better to describe them from low to high quality in order, ie, cross-sectional, case-control or retrospective, and prospective cohort, or in verse from high to low.

3. A sample size flow chart is recommended, which will help the reader understand the exclusion/inclusion process.

4. Please specify when mean (SD) or median (IQR) will be used. Please specify which variables were described with mean (SD) or median (IQR) in table 1.

5. It is very interesting to observe risk association of LGA at 3-5 years childhood overweight, and high WLR at 6-8 childhood overweight, however, it is not clear what their clinical implications might be. Furthermore, the authors seemed to have ignored the negative risk association between low WLR and childhood overweight at 6-8 years.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

I thought the article to be incredibly intriguing because it included insightful prospective long-time follow-up statistics, which are relatively difficult to come across. I have identified a few minor concerns that need to be addressed in order to improve the document's readability and clarity.

Comment 1: Under the "Results" section, when presenting an odds ratio (OR), kindly indicate whether it has been adjusted or not (OR vs. aOR). This change will ensure that it is easily understandable without having to read the entire sentence to which the numbers in brackets correspond.

Response: Thanks for the comment. We have made the requested revisions as follows:

In the results section:

"After adjusting for confounding factors, the associations of macrosomia, LGA and high WLR at birth with offspring overweight at 3-5 years of age were slightly attenuated but still significant (aOR: 1.89, 1.25-2.85 & 1.86, 1.27-2.72 & 1.67, 1.18-2.37, respectively). The multivariable backward stepwise logistic regression analysis revealed that LGA was independently associated with increased risk of offspring overweight at 3-5 years of age (aOR: 1.86, 1.27-2.72) (Table 3)." (Page 11, Line 225-231)

"In multivariable analysis, the associations of macrosomia, LGA and high WLR at birth with offspring overweight were slightly attenuated but still significant (aOR: 1.92, 1.39-2.65 & 1.99, 1.49-2.67 & 1.82, 1.41-2.34, respectively). On the other hand, low birth weight, SGA and low WLR at birth were still associated with decreased risk of offspring overweight (aOR: 0.41, 0.17-0.98 & 0.53, 0.30-0.95 & 0.52, 0.30-0.90, respectively). The backward stepwise logistic regression in the multivariable analysis revealed that high WLR at birth was independently associated with increased risk of offspring overweight at 6-8 years of age (aOR: 1.82, 1.41-2.34), whereas low WLR at birth was associated with decreased risk of offspring overweight at 6-8 years of age (aOR: 0.52, 0.30-0.90) (Table 3)." (Page 12, Line 242-251)

Comment 2: It would be interesting to read a more in-depth examination of the clinical and scientific implications that your data may have in the discussion section of the paper.

Response: Thanks for your comment. We have made the requested revisions as follows:

In the discussion section:

"This long-term follow-up study supports that LGA and high WLR at birth need to be recognized as risk factors for childhood overweight. On the one hand, our findings highlighted the importance of improving adverse birth outcomes, including LGA and high WLR at birth, for benefits of childhood overweight and possibly well-being in adulthood. Our previous RCT demonstrated that IC for pregnant women with GDM can improve adverse birth outcomes, including LGA14. Therefore, to reduce the incidence of adverse birth outcomes by dietary and physical activity education during pregnancy is one of the possible measures to prevent childhood overweight. On the other hand, special attention should also be given to infants born with LGA and high WLR to help reduce the prevalence of childhood overweight and related chronic disease later in life. Our findings suggest that more efforts should be shifted to early lifestyle interventions for children at high risk of overweight, especially those born to be LGA and high WLR. Indeed, given to the high prevalence of childhood overweight, it is worthwhile to test the effect and cost-effectiveness of healthy lifestyle intervention for prevention of childhood overweight among high-risk children. In addition, our study also indicates that low WLR at birth had a protective effect on childhood overweight at 6-8 years of age. However, it is still unclear its benefits and possibly harms in late childhood and adulthood. Further investigations are needed to evaluate the association of WLR with long-term overweight in the future." (Page 14-15, Line 296-314)

Reviewer 2

Using a prospective cohort study conducted among 1681 woman-child pairs, the authors examined the association of certain adverse pregnancy outcomes with the risk of development of childhood overweight. The results are interesting, but some concepts related issues may need to be clarified to precisely reflect what the research tried to reach. Below are reviewer's comments for authors' consideration:

Comment 1: Adverse pregnancy outcomes refer to a range of health complications and unfavorable events, while this study only looked at preterm birth, postterm pregnancy, macrosomia, LGA, SGA, as well as high and low WLR. These are more likely to be birth outcomes related to infants; using "maternal adverse pregnancy outcomes" in the title seemed not to match well with the facts in the study.

Response: Thanks for your comment. We have revised "maternal adverse pregnancy outcomes" to "adverse birth outcomes" in the whole manuscript as suggested.

Comment 2: The introduction and the discussion gave impression that the objective of the study was not clear; it is unclear whether the authors have tried to examine the risk association between GDM, LGA, and childhood overweight as described in the intro, or actually as the focuses showed in the results and discussion on the risk of LGA and/or WLR on development of childhood overweight. If authors want to explore the LGA and WLR on the development of childhood overweight, they may need to make it clear in the title, objective, and intro. BTW, when describing the inconsistent findings (page 5 line 47 – page 6 line19), one needs to consider the quality of each study design, it is better to describe them from low to high quality in order, ie, cross-sectional, case-control or retrospective, and prospective cohort, or in verse from high to low.

Response: Thanks for your comment. This study aimed to explore the association of adverse birth outcomes with childhood overweight among Chinese women and the findings indicated that LGA and high WLR at birth were associated with increased risk of offspring overweight, while low WLR at birth was associated with decreased risk of offspring overweight. As your suggestion, we have made the requested revisions as follows:

In the introduction section:

"Childhood overweight is a complex, multifactorial condition stemming from interactions between genetic and non-genetic factors, including unhealthy dietary patterns, inadequate physical activities, shortened sleep duration, increased sedentary time and excessive psychological stress3 4. It has also been reported that the intrauterine and early postnatal conditions can have a significant impact on increased risk of developing overweight in later life5 6. Therefore, the exploration for risk factors of childhood overweight could be extended to infant adverse birth outcomes." (Page 5, Line 88-91)

In addition, we have also revised the discussion of inconsistent findings in the introduction section as your suggestion.

"For example, a cross-sectional analysis from Australia found that low birth weight was associated with decreased risk of overweight among girls at 4-5 years of age11. However, a retrospective study in Tianjin, China observed that low birth weight was not associated with overweight among children aged 3-6 years12. On the other hand, a retrospective study in Xiamen, China failed to find a significant association between infants with LGA of women with GDM and later overweight at 1-6 years of age13. However, a large cohort study from Canada found that children born with LGA of mothers with GDM were 2.79 times more likely to be overweight at 4-6 years of age compared to children born with appropriate for gestational age (AGA) of mothers without diabetes14." (Page 5-6, Line 93-102)

Comment 3: A sample size flow chart is recommended, which will help the reader understand the exclusion/inclusion process.

Response: Thanks for your comment. We have added a sample size flow chart in figure 1 per your comment.

Comment 4: Please specify when mean (SD) or median (IQR) will be used. Please specify which variables were described with mean (SD) or median (IQR) in table 1.

Response: Thanks for your comment. We have made the requested revisions as suggested in table 1 and table 2.

Comment 5: It is very interesting to observe risk association of LGA at 3-5 years childhood overweight, and high WLR at 6-8 childhood overweight, however, it is not clear what their clinical implications might be. Furthermore, the authors seemed to have ignored the negative risk association between low WLR and childhood overweight at 6-8 years.

Response: Thanks for your comment. We have made the requested revisions as follows:

In the discussion section:

"This long-term follow-up study supports that LGA and high WLR at birth need to be recognized as risk factors for childhood overweight. On the one hand, our findings highlighted the importance of improving adverse birth outcomes, including LGA and high WLR at birth, for benefits of childhood overweight and possibly well-being in adulthood. Our previous RCT demonstrated that IC for pregnant women with GDM can improve adverse birth outcomes, including LGA14. Therefore, to reduce the incidence of adverse birth outcomes by dietary and physical activity education during pregnancy is one of the possible measures to prevent childhood overweight. On the other hand, special attention should also be given to infants born with LGA and high WLR to help reduce the prevalence of childhood overweight and related chronic disease later in life. Our findings suggest that more efforts should be shifted to early lifestyle interventions for children at high risk of overweight, especially those born to be LGA and high WLR. Indeed, given to the high prevalence of childhood overweight, it is worthwhile to test the effect and cost-effectiveness of healthy lifestyle intervention for prevention of childhood overweight among high-risk children. In addition, our study also indicates that low WLR at birth had a protective effect on childhood overweight at 6-8 years of age. However, it is still unclear its benefits and possibly harms in late childhood and adulthood. Further investigations are needed to evaluate the association of WLR with long-term overweight in the future." (Page 14-15, Line 296-314)

VERSION 2 – REVIEW

REVIEWER	Liu, Jian Brock University
REVIEW RETURNED	29-Nov-2023

GENERAL COMMENTS	I'm satisfied the revisions with minor change suggestions: a) the title maybe changed as "Adverse birth outcomes and childhood overweight at 3 to 8 years in a prospective cohort study, China Tianjin"; b) remove "among Chinese women" from the objective in the abstract.

VERSION 2 – AUTHOR RESPONSE

Reviewers' comments:

Reviewer 2

Comment 1: The title maybe changed as "Adverse birth outcomes and childhood overweight at 3 to 8 years in a prospective cohort study, China Tianjin.

Response: Thanks for your comment. We have revised the title per your comment.

Comment 2: Remove "among Chinese women" from the objective in the abstract.

Response: Thanks for your comment. As your suggestion, we have made the requested revision as follows:

In the abstract section:

"To explore associations between adverse birth outcomes and childhood overweight at 3-8 years of age." (Page 3, Line 35-36)