PEER REVIEW HISTORY

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Risk of adverse pregnancy outcomes associated with short and long birth intervals in Bangladesh: evidence from six Bangladesh Demographic and Health Surveys, 1996-2014
AUTHORS	Nisha, Monjura Khatun; Alam, Ashraful; Islam, Mohammad Tajul; Huda, Tanvir; Raynes-Greenow, Camille

VERSION 1 – REVIEW

REVIEWER	Erik de Jonge MD MPH, graduate student Dept. of Public Health Erasmus University Medical Center the Netherlands
REVIEW RETURNED	01-Jul-2018

GENERAL COMMENTS	Review "Disparities in adverse pregnancy outcomes for short and long 1 birth intervals in Bangladesh: evidence from six Bangladesh Demographic and Health Surveys, 1996- 2014" by Monjura Khatun Nisha et al. submitted to BMJ Open Erik de Jonge, July 2nd. Summary: a This paper answers the question: does a short (<36 months) or long (>59 months) birth interval increase first day neonatal death, early neonatal death and small size at birth? This question is studied in a singleton non-first live births from six consecutive DHS surveys from Bangladesh (1996-2014). Women participating in the DHS were asked about their deliveries in five years previous tot the interview. The authors descrive their study population (table 1), present the results of a multivariable model for each outcome, with "birth interval <36, 36-59 and >59" as exposure and a series of confounders (maternal age at childbirth, birth order, maternal education, maternal wealth index, maternal employment status, area of residence, maternal BMI, maternal desire of pregnancy, ever use of contraceptive method, number of ANC visits, ANC by SBA, history of any previous pregnancy loss, sex of infant and region). Evaluation

	This is a straight forward cross sectional analysis of birth intervals that basically repeats the analysis of Rutstein, 2005, on more recent DHS data from Bangladesh only. The authors claim that their study is the first in Bangladesh which analysed the effect of birth intervals and other risk factors for first-day neonatal mortality. This might be the case but they don't explain what looking at first day neonatal mortality adds to looking e.g. the usual first 28 day neonatal mortality or early neonatal mortality. If the paper is improved it might be suitable for an specialised academic audience of epidemiologists, biostatisticians and public health practitioners interested in determinants of perinatal outcomes in LMIC countries.
	
	Title
	
	The word disparities in the title suggests the paper discusses health inequalities, which is not the case. Consider rephrasing.
	
	Methods:
	
	- Statistical note: The authors don't describe how they arrive at their list of confounders, but given the number of events (there are only 115 events for first day mortality and 274 events for perinatal mortality) the number of covariates is quite large.
	Results
	
	- I think the results section can be more concise
	  o Is it necessary to describe the covariates for all outcomes. They can be found in table 2 and are not the exposure-outcome relationship of interest.
	Discussion
	
	- The discussion section needs strengthening
	  o The first paragraph needs focus: what are the key findings. Only in the fourth sentence the authors gets to the point.
	  o The discussions would benefit from being divided in alinea's starting with a key message. Now sentence 278-342 are one block of rather lengthy text.
	  o Setence 343 onwards feels like a repetition of results. Feels a bit unnecessary.
	- Really nice to see a discussions of the causal pathways underlying the association between short and long birth interval and adverse pregnancy outcomes (sentence 303 onwards). In the discussion the authors may want to discuss the interesting contributions to the study of birth intervals from econometrics using dynamic panel data models. Using these models economitricians calculated the effect on mortality of state effects (like scarring / replacement) vs. the effect of unobserved confounders that have an effect on consecutive pregnancies. Van Soest and Saha published interesting work using longitudinal data from Matlab, Bangladesh.

	Table 2: - the title doesn't describe what's in the table. The results of the multivariable regression are presented. - Is it necessary to mention which factors the analysis was adjusted for under the table using *? Table 3. - The title doesn't describe what's in the table.

REVIEWER	Shaonong Dang Xi'an Jiaotong University, School of Public Health
REVIEW RETURNED	12-Jul-2018

GENERAL COMMENTS	It is said that the optimal birth interval should be suggested as between 36 and 59 months or at least 24 months, but there still are unclear about association of pregnancy spacing and birth outcome. Pregnancy spacing has been reported to be associated with an increased risk of adverse birth outcomes such as birth weight in different population, but the interval seems different. It is necessary to investigate further this topic among broader populations. This study provides some evidence from Bangladesh women. 1. In the part of methods, authors seems not to present how to deal with the variable of six BDHSs in statistical process. How to pool these data from different survey? Due to larger time spanning, the background of survey may change much. Pls address it issue. 2. Because of many confounders, some explanation about selection of covariates should be presented. In the part of data analysis, authors mentioned "weighted analysis", it is unclear what indicators was calculated by weighted values and not any presentation in the following tables, maybe just for incidence of mortality? 3. In this study, authors use an indicator of small birth size instead of birth weight, which is form mother's perception. This indicator might be a global index reflecting newborn's health rather than birth weight only. So it's association with birth interval seems more complicated. I highly suggest addressing this indicator more in the discussion. 4. table 2\3, the variable of survey time is controlled or not? Or how to deal with this variable? 5. It is unclear about status of birth interval in Bangladesh women of this study. it is better if presented in the results.

REVIEWER	Kulanthayan KC Mani Universiti Putra Malaysia, MALAYSIA nil
REVIEW RETURNED	21-Aug-2018

GENERAL COMMENTS	1. Good paper with minimal comments 2. Agree the main strength of the paper is the large secondary data and also the topic scope looks new focusing on birth intervals. 3. In pg 8, approval obtained from who actually? The body mentioned not clear – Monitoring and Evaluation of which organisation? 4. Ethical approval obtained in both Bangladesh and Australia (representing research team members)? If yes, do report.

	5. Was the outcome of mother mortality during delivery was monitored for cases of first-day neonatal mortality? Is there any link between them which could have effected either way? Any risk to mother?

VERSION 1 – AUTHOR RESPONSE

Reviewer 1:

Reviewer's name: Erik de Jonge

Comment 1: Title- The word disparities in the title suggests the paper discusses health inequalities, which is not the case. Consider rephrasing.

Response: Thank you for your suggestion. We have revised our title to "Risk of adverse pregnancy outcomes associated with short and long birth intervals in Bangladesh: evidence from six Bangladesh Demographic and Health Surveys, 1996-2014". Please see highlighted section, page 1, lines 1-3.

Comment 2: Methods- Statistical note: The authors don't describe how they arrive at their list of confounders, but given the number of events (there are only 115 events for first day mortality and 274 events for perinatal mortality) the number of covariates is quite large.

Response: As per your suggestion, we have added a few lines to explain the selection of covariates in our analysis. Please see below and highlighted section, page 8, lines 170-176.

All covariates associated with each of outcomes at the p value ≤0.25 in unadjusted analysis were included in the final model of multivariable logistic regression. Also, some other covariates (maternal education, maternal wealth status, maternal area of residence, maternal desire of pregnancy, number of ANC and ANC by SBA) were included in the final model regardless of their significant levels because of being known risk factors of adverse pregnancy outcomes based on several previous literature.[1-4] We also checked the variables for multicollinearity.

Comment 3: Results- I think the results section can be more concise, is it necessary to describe the covariates for all outcomes? They can be found in table 2 and are not the exposure-outcome relationship of interest.

Response: As per your suggestion, we have made the results section more concise. Please see page 11.

Comment 4: Discussion- The first paragraph needs focus: what are the key findings. Only in the fourth sentence the authors gets to the point.

Response: We have revised the first two sentences of first paragraph according to your suggestion. Please see below and highlighted section, page 12, lines 269-272.

This study suggests that both short and long birth intervals were associated with the increased odds of adverse pregnancy outcomes. Over the six surveys, a major proportion of infants who died on the first-day, or in the first week or with a small birth size were born before the recommended optimal period of birth interval (36–59 months).

Comment 5: The discussion would benefit from being divided in alinea's starting with a key message. Now sentence 278-342 are one block of rather lengthy text.

Response: We have made changes as per your suggestion. We have now divided the long paragraph into four paragraphs where each of the paragraph starts with a key message. Please see pages 12-15, lines 277-341.

Comment 6: Sentence 343 onwards feels like a repetition of results. Feels a bit unnecessary.

Response: We have omitted sentences between line no. 343 and 349 as per your suggestion. Please see page 15.

Comment 7: Really nice to see a discussions of the causal pathways underlying the association between short and long birth interval and adverse pregnancy outcomes (sentence 303 onwards).

Response: Thank you.

Comment 8: In the discussion the authors may want to discuss the interesting contributions to the study of birth intervals from econometrics using dynamic panel data models. Using these models econometricians calculated the effect on mortality of state effects (like scarring/replacement) vs. the

effect of unobserved confounders that have an effect on consecutive pregnancies. Van Soest and Saha published interesting work using longitudinal data from Matlab, Bangladesh.

Response: It is an interesting work, however as we do not have the information about history of immediate previous pregnancy loss in BDHS data, we were unable to include these effects (scarring/replacement) in our analysis. However, in the 'limitation' section we have added a few sentences (see below) to discuss this. Please see highlighted section, pages 15-16, line 361-368.

A previous investigation conducted in Bangladesh using dynamic panel data models, reported that a previous adverse birth outcome may be subject to 'scarring effect' which leads to a short birth interval (replacement) and thus increases the risk of mortality of the subsequent infant (nutritional depletion); as a mother with a previous pregnancy loss may rush into a pregnancy without properly recovering from the pregnancy loss.[5] In our analysis, we were unable to consider the role of 'scarring effect' related to a previous adverse pregnancy outcome which has an influence on birth interval.

Comment 9: Table 2- the title doesn't describe what's in the table. The results of the multivariable regression are presented.

Response: We have changed the title of table 2 to "Results of multivariable analysis for the association between preceding birth intervals and adverse pregnancy outcomes in Bangladesh: BDHS 1996-2014" as per your suggestion. Please see highlighted section in the attached manuscript on page 22.

Comment 10: Is it necessary to mention which factors the analysis was adjusted for under the table using *?

Response: In our field this is good practice to put the factors adjusted for the multivariable analysis under the table to give the readers an idea of the covariates.

Comment 11: Table 3- The title doesn't describe what's in the table.

Response: We have changed the title of table 2 to "Results of multivariable analysis for the association between preceding birth intervals and adverse pregnancy outcomes by history of any previous pregnancy loss: BDHS 1996-2014" as per your suggestion. Please see highlighted section in the attached manuscript on page 25.

Reviewer 2:

Reviewer's name: Shaonong Dang

Comment 1: In the part of methods, authors seem not to present how to deal with the variable of six BDHSs in statistical process. How to pool these data from different survey? Due to larger time spanning, the background of survey may change much. Please address this issue.

Response: As per your suggestion we have added lines in the end of the methods (please see below and lines 115-122, pages 5-6) about the pooling of datasets from the six survey-years.

We pooled the data files from six surveys into a dataset and analysed the live births occurring during the five years preceding the surveys. Demographic and Health Survey program employs standardised data collection procedures using standard model questionnaires to ensure consistent content over time and across countries allowing comparability across populations cross-sectionally and over time.[6] We selected six surveys in this pooled analysis based on the similarities in sampling design, comparability of survey questionnaires for focus variables of this analysis, and availability of data for the pooled analysis.

Also, we have added a sentence in the limitation about the possibility of changes in the background characteristics of the population over 18 years. Please see below and page 15, line 357-359.

Fifth, as we pooled six BDHS datasets over 18 years, there may be a possibility of changes in the background characteristics of the population over 18 years.

Comment 2: Because of many confounders, some explanation about selection of covariates should be presented.

Response: As per your suggestion, we have added few lines to explain the selection of covariates. Please see below and page 8, lines 170-176.

All covariates associated with each of outcomes at the p value ≤0.25 in unadjusted analysis were included in the final model of multivariable logistic regression. Also, some other covariates (maternal education, maternal wealth status, maternal area of residence, maternal desire of pregnancy, number of ANC and ANC by SBA) were included in the final model regardless of their significant levels

because of being known risk factors of adverse pregnancy outcomes based on several previous literature.[1-4] We also checked the variables for multicollinearity.

Comment 3: In the part of data analysis, authors mentioned "weighted analysis", it is unclear what indicators were calculated by weighted values and not any presentation in the following tables, maybe just for incidence of mortality?

Response: All our findings presented in this paper were adjusted for sampling weights. We have revised the text pertaining to the weighting process in the 'data analysis' section to make it clearer as per your suggestion. Please see below and page 8, lines 185-187.

We used the 'svy' command in all our analyses to calculate the weighted values in order to adjust for the clustering effect and sample stratification.

Comment 4: In this study, authors use an indicator of small birth size instead of birth weight, which is form mother's perception. This indicator might be a global index reflecting newborn's health rather than birth weight only. So its association with birth interval seems more complicated. I highly suggest addressing this indicator more in the discussion.

Response: Birthweight measurement is not collected in BDHS. This is one of the limitations of our study. We mentioned this issue in our discussion (page 13, lines 297-299). However, as per your suggestion, we also have added a sentence in 'strength and limitations' section regarding this issue. Please see below and page 15, lines 354-357.

Fourth, we acknowledge a limitation of using maternal perception on birth size instead of birthweight in our analysis due to unavailability of actual estimates of birthweight in BDHS, which may reflect newborn's overall health status rather than birthweight only.

Comment 5: Table 2\3, the variable of survey time is controlled or not? Or how to deal with this variable?

Response: We compared the results of the models with or without including the 'survey year' variable (results not shown), however the results remained the same. In the unadjusted analysis the p-value of the association between 'survey year' and each of the outcome variables was more than 0.25. Therefore, we did not include the 'survey year' in the final model in the manuscript. In addition,

Demographic and Health Survey employs standardised data collection procedures using standard model questionnaires to ensure consistent content over time (and across countries), allowing comparability across populations cross-sectionally and over time.[6]

Comment 6: It is unclear about status of birth interval in Bangladesh women of this study. It is better if presented in the results.

Response: The current status of birth interval in Bangladesh is in the background based on BDHS report (Pages 4-5, line 93-97). Our objective was to assess the association between birth interval (short or long) and adverse pregnancy outcomes. Hence, we have presented the status of birth interval by adverse pregnancy outcomes (please see figure 3 and table 1).

Reviewer 3:

Reviewer's name: Kulanthayan KC Mani

Comment 1: In page 8, approval obtained from who actually? The body mentioned not clear – Monitoring and Evaluation of which organisation?

Response: Monitoring and Evaluation to Assess and Use Results Demographic and Health Surveys (MEASURE DHS) is an ongoing collaboration between the United States Agency for International Development and country-specific agencies to conduct nationally representative household sample surveys with coverage of a range of population health indicators in low- and middle-income countries (LMICs).[6] As the data were publicly available online, we had to register with the website to request dataset access. Then we downloaded the data from the website; www.measuredhs.com (mentioned in data source, page 5, lines 112-113). No further ethics approval was necessary since the study was based on anonymous public use data with no identifiable information on survey respondents.

Comment 2: Ethical approval obtained in both Bangladesh and Australia (representing research team members)? If yes, do report.

Response: The Demographic Health Survey data were publicly available with no identifiable information on survey respondents. Hence, the ethics approval was not required for our study.

Comment 3: Was the outcome of mother mortality during delivery was monitored for cases of first-day neonatal mortality? Is there any link between them which could have effected either way? Any risk to mother?

Response: This was beyond our scope as the Bangladesh Demographic Health Survey is a cross-sectional survey and data were already collected.

References:

1. Abir T, Agho KE, Page AN, et al. Risk factors for under-5 mortality: evidence from Bangladesh Demographic and Health Survey, 2004–2011. *BMJ Open* 2015;5(8) doi: 10.1136/bmjopen-2014-006722
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3. Ghimire PR, Agho KE, Renzaho A, et al. Socio-economic predictors of stillbirths in Nepal (2001-2011). *PLOS ONE* 2017;12(7):e0181332. doi: 10.1371/journal.pone.0181332
4. Rutstein SO. Effects of preceding birth intervals on neonatal, infant and under-five years mortality and nutritional status in developing countries: evidence from the demographic and health surveys. *International Journal of Gynecology & Obstetrics* 2005;89:S7-S24. doi: 10.1016/j.ijgo.2004.11.012
5. Saha UR, van Soest A. Infant death clustering in families: Magnitude, causes, and the influence of better health services, Bangladesh 1982–2005. *Population Studies* 2011;65(3):273-87. doi: 10.1080/00324728.2011.602100
6. Corsi DJ, Neuman M, Finlay JE, et al. Demographic and health surveys: a profile. *International Journal of Epidemiology* 2012;41(6):1602-13. doi: 10.1093/ije/dys184

VERSION 2 – REVIEW

REVIEWER	Shaonong Dang School of Public Health, Xi'an Jiaotong University, PR China.
REVIEW RETURNED	03-Oct-2018

GENERAL COMMENTS	The authors have addressed most of my comments. And also made some revision. The manuscript have been improved much. However, about comment 5, I suggest that some statement on adjustment of survey year should be added in the methods because this is pooled analysis.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name: Shaonong Dang

Institution and Country: School of Public Health, Xi'an Jiaotong University, PR China.

Comment: The authors have addressed most of my comments. And also made some revision. The manuscript have been improved much. However, about comment 5, I suggest that some statement on adjustment of survey year should be added in the methods because this is pooled analysis.

Response: According to your suggestion, we have added a few lines regarding the reasons of not including 'year of survey' in our final model. Please see below and highlighted section, page 8, lines 174-178.

"The 'year of survey' was not included in our final model as the p-value between 'year of survey' and each of the outcome variables was more than 0.25 in the unadjusted analysis. However, to test the effect of 'year of survey' we repeated the model and included 'year of survey'. This made no difference to the findings (results not shown), and hence, we kept the original model.