

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of maternal age on obstetric and neonatal outcome with emphasis on primiparous adolescents and older women-a Swedish Medical Birth Register Study.
AUTHORS	Blomberg, Marie; Birch Tyrberg, Rasmus; Kjolhede, Preben

VERSION 1 - REVIEW

REVIEWER	Jennifer Hollowell National Perinatal Epidemiology Unit, University of Oxford, UK
REVIEW RETURNED	24-Jun-2014

GENERAL COMMENTS	<p>Additional notes</p> <p>2. See below for suggested changes to abstracts 4. Adjustment variables inadequately described 6. Some minor clarifications required (shoulder dystocia, normal vaginal birth) 8. See comments below. 10 Results are understandable but presentation is poor. 11. Discussion of limitations lacks depth. 13 Missing data inadequately described.</p> <p>The stated objective of the study is to evaluate the association between maternal age and a range of maternal and perinatal/neonatal outcomes in primiparous women.</p> <p>There is certainly value in documenting outcomes by age in a large unselected national sample of births and an understanding of age related variations in outcomes may well be useful to a number of audiences. What is less clear is the purpose and intended interpretation of their adjusted analyses. Why is it important to know how outcomes vary with maternal age after adjusting for BMI, smoking and year of birth? Why did the authors choose these variables and not others? Younger and older mothers may differ in other ways that might affect outcomes (prevalence of co-morbidities such as hypertension and diabetes, use of fertility treatment, etc) so there are still many known potential confounders that may explain the age-related patterns of outcome. They also need to explain why they have adjusted the analyses of caesarean section and preeclampsia for gestational age? The authors need to explain their rationale for their adjusted analyses, to justify their selection of adjustment variables.</p> <p>In the methods section the authors need to provide more details of their adjustment variables. For example, was BMI modelled as a continuous or categorical variable. If the former they need to justify this since the relationship between BMI and some of their outcomes</p>
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	<p>in non-linear.</p> <p>The presentation of findings does not follow a standard reporting format. The paper needs a conventional 'table 1' which describes the study population in a bit more detail e.g. distribution of BMI. If the authors have other information to better characterise their study population (ethnicity, socio-economic status, etc), they should include this in table 1. The outcome data should be presented in separate tables.</p> <p>The outcome data are currently presented as percentages in tables 1 -2 and adjusted odds ratios in tables 3-4. This means that it is difficult to see the effect of adjustment. Could the authors consider including unadjusted ORs alongside the adjusted ORs? This could be put in an online supplement if there is too much information to include in the main paper.</p> <p>The tables are extremely dense and might benefit from either broken-up into separate tables or having some subheadings eg 'Labour and delivery', 'Gestational age', 'maternal complications'. Alternatively, they might consider having a separate table for outcomes only assessed in women who delivered vaginally.</p> <p>The authors could also consider being a bit more selective about the outcomes that they report. For example, they could focus on birth outcomes (including mode of delivery) but perhaps excluding epidural analgesia.</p> <p>The authors need to explain their rationale for evaluation some outcomes only in women who delivered vaginally. Clearly some of these outcomes only occur in women who deliver vaginally but calculated in this way the risk of instrumental delivery (for example) is affected by the risk of caesarean delivery. Ideally this would have been mentioned in the methods rather than appearing as a footnote to the tables.</p> <p>The authors provide very limited information about missing data. If the level of missing outcome data is low they need to state this, otherwise they need to provide more information about missing data (as per STROBE guideline).</p> <p>In their discussion of their key findings, the authors need to ensure that they refer to the relevant literature. I was surprised, for example, to find no reference to an earlier Swedish study by Clausson et al which examined SGA in the same Swedish data source (and also did not find an increased risk of SGA in adolescents); and there are certainly more recent and possibly more relevant papers on maternal age and uterine function than the 1981 Morris paper cited.</p> <p>The discussion of study limitations, and in particular of the possible failure to adjust for some potential confounders, lacks depth. They would potentially have been able to adjust for other variables, including some co-morbidities and possibly 'migration status' (ie Nordic/non-Nordic).</p> <p>The conclusion seems rather weak and primarily focuses on providing information about age related risks. If they believe that there is a case for surveillance programmes could they explain this? Perhaps they could also identify some unanswered questions and/or research recommendations?</p>
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	<p>The abstract uses the term 'risks' when referring to odds. The conclusion could be amended as suggested above.</p> <p>Clausson, Britt, Sven Cnattingius, and Ove Axelsson. "Preterm and term births of small for gestational age infants: a population-based study of risk factors among nulliparous women." <i>BJOG: An International Journal of Obstetrics & Gynaecology</i> 105.9 (1998): 1011-1017.</p> <p>Minor comments The title needs to mention that this is a study of primiparous women. P4, Line 28 – please clarify – maternal age at birth? P4, Lines 16 and 18. Use terms 'high-income, 'low-income' etc in preference to 'developed' and 'developing' countries. P6, Lines 33-34. This sentence is not well expressed. This is the largest group so reasonable to use as the reference group whether or not the mean age of a primiparous women is in this range. There is a reference to figure 1 in line 35 which appears to be incorrect since there is only one figure and this is referred to later as 'figure 2'. P6, Line 59. Although the authors state that 'shoulder dystocia' was an outcome, it would be helpful if they could clarify whether they are truly reporting the occurrence of shoulder dystocia or whether they are reporting adverse neonatal outcomes resulting from shoulder dystocia (eg brachial plexus injury) Tables. Define 'normal vaginal delivery' P16, lines 32/33. Rewrite the sentence containing the phrase "exclusively associated with". .Perhaps this could be better expressed as: 'There was a significantly increased risk of stillbirth.... only in women aged 30 years and over'? It is generally preferable to use the term 'birth' instead of 'delivery'.</p>
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REVIEWER	Alon Shrim Hillel Yaffe Medical Center, Israel
REVIEW RETURNED	28-Jun-2014

GENERAL COMMENTS	<p>Re: bmjopen-2014-005840 - Impact of maternal age on obstetric and neonatal outcome with emphasis on adolescents and older women-a Swedish Medical Birth Register Study</p> <p>This is an interesting manuscript on an old and well studied issue of Ob complications in the extremes of maternal age. It doesn't carry new information but the large number of patients included in this large scale registry is a great advantage and I believe that this justifies publication.</p> <p>Major revisions are needed though, in order to accept the manuscript to publication:</p> <ol style="list-style-type: none"> 1. Numbering lines may help in reviewing and commenting 2. All along the text there are typo errors such as missing space between words (carecustomized in conclusions of the abstract, womenaged in the discussion....and many other places) 3. Grammatical errors are spread along the manuscript. Examples are the 1st statement of the introduction and others. I suggest editing by English speaking person. 4. Abstract: The conclusion says "counselling young mothers"... should be "women" or "pregnant women"...as the manuscript talks
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	<p>about primiparous women (who are not mothers...)</p> <p>5. In introduction – lower rate of Ob complications are not "a benefit" of pregnancy of advanced maternal age...</p> <p>6. In the introduction, the part on the lower rate of teen age pregnancies in Sweden is interesting but not relevant to the study (that aims at examining this population...).</p> <p>7. At the end of the introduction and in other places, the word "the" should be inserted ("as well as in [the] socio-demographic..."). This returns in other places in the manuscript, please edit.</p> <p>8. By what definition was "foetal distress" defined? Non reassuring monitoring?...needs to clarify</p> <p>9. "Aspiration of meconium" was it really meconium aspiration syndrome or meconium stained amniotic fluid? If aspiration – by what definition?...</p> <p>10. "Infants" in results – should be newborns...</p> <p>11. Better define the reference age group as the "reference group" or Control group....better than reporting it repeatedly as "the group between 25-29 years..."</p> <p>12. This group 25-29 years old, was selected as such because it is "the average primiparous woman"...by what calculation or previous report?...please clarify.</p> <p>13. "Perineal damage" at the end of results... is actually "perineal lacerations" in methods... needs to be consistent.</p> <p>14. Reporting strengths and limitations occupies almost full page. It should be located to the end of the discussion and be shorter.</p> <p>In summary - the potential and methods of the manuscript are good, however, in order to be published serious editing should take place including English edition, grammatical changes, changing the structure so it is more fluent...according to the comments above.</p> <p>The potential and methods of the manuscript are good. however, in order to be published, editing should take place including English edition, grammatical changes, changing the structure so it is more fluent...according to the comments above.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer Name Jennifer Hollowell

Institution and Country National Perinatal Epidemiology Unit, University of Oxford, UK

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

Additional notes

Is the abstract accurate, balanced and complete? See below for suggested changes to abstracts Are the methods described sufficiently to allow the study to be repeated? Adjustment variables inadequately described Are the outcomes clearly defined? Some minor clarifications required (shoulder dystocia, normal vaginal birth) Are the references up-to-date and appropriate? See comments below.

Are the results presented clearly? Results are understandable but presentation is poor.

Are the discussion and conclusions justified by the results? Discussion of limitations lacks depth.

Is the supplementary reporting complete (e.g. trial registration; funding details; CONSORT, STROBE or PRISMA checklist)? Missing data inadequately described.

The stated objective of the study is to evaluate the association between maternal age and a range of

maternal and perinatal/neonatal outcomes in primiparous women.

There is certainly value in documenting outcomes by age in a large unselected national sample of births and an understanding of age related variations in outcomes may well be useful to a number of audiences. What is less clear is the purpose and intended interpretation of their adjusted analyses. Why is it important to know how outcomes vary with maternal age after adjusting for BMI, smoking and year of birth? Why did the authors choose these variables and not others? Younger and older mothers may differ in other ways that might affect outcomes (prevalence of co-morbidities such as hypertension and diabetes, use of fertility treatment, etc) so there are still many known potential confounders that may explain the age-related patterns of outcome. They also need to explain why they have adjusted the analyses of caesarean section and preeclampsia for gestational age? The authors need to explain their rationale for their adjusted analyses, to justify their selection of adjustment variables.

- We have added text to the introduction to clarify the purpose and intention of the study. Our effort was to evaluate obstetric and neonatal outcome in different maternal age groups compared with women aged 25-29 overall. The only stratifications made were for year of birth, maternal BMI and smoking in early pregnancy. The data on year of birth show that there is variability in the existence of obstetric and neonatal diagnoses during the observation period. This may be due to true changes but may also be a result of changes in recording, including the expanding use of computerized medical records. It was therefore necessary to adjust for year of birth. Maternal BMI affects obstetric and neonatal outcome, well known from many studies (Cedergren MI. Maternal morbid obesity and the risk of adverse pregnancy outcome. *Obstet Gynecol* 2004;103:219-24) To demonstrate a possible causality between the different outcomes evaluated in the analyses and maternal age a great number of putative intermediaries could have been considered such as the use of fertility treatment, fetal size, oxytocin infusion etc. but that was not the purpose of this study. A true confounder affects both the exposure and the outcome. Exposure in this study was maternal age. The variables suggested could be looked upon as intermediaries. There may be other variables (which are not intermediaries) but we have not been able to identify them. If we take maternal disease as an example, it could be of interest but as the higher risk of for instance hypertension is a consequence of maternal age, it is not a true confounder but an intermediary, a way in which high maternal age can affect obstetric and neonatal pathology.

Our approach may be an advantage for clinicians interpreting data when dealing with young and aged mothers.

In the methods section the authors need to provide more details of their adjustment variables. For example, was BMI modelled as a continuous or categorical variable. If the former they need to justify this since the relationship between BMI and some of their outcomes is non-linear.

- Concerning the possible non-linear associations between a continuous BMI scale and some of the outcomes it seems more to be a theoretical than a real problem since the sample size in this study is substantial. We use the continuous value of the BMI all over in our adjusted calculations. Based on the reviewer's considerations we have recalculated the analyses and adjusted with the BMI categories in two selected groups i.e. the age groups < 17 years and 20-24 years of age and found no changes in statistically significant results and practically no differences in ORs. The OR's with adjustment of the BMI as categorical in the youngest age group (i.e. the smallest group) were 0.01 – 0.02 lower in the vast majority of ORs and 0.02-0.03 higher in a very few compared with the OR's when using the continuous value of the BMI for adjustment. For the age group 20-24 years of age only five of the 28 outcome measures had OR's that deviated (0.01) from that of the OR's when adjusting for continuous BMI. In the remaining 23 outcome measures the ORs were even. We therefore do not find it necessary to recalculate all outcome measures for all age groups.

The presentation of findings does not follow a standard reporting format. The paper needs a conventional 'table 1' which describes the study population in a bit more detail e.g. distribution of BMI.

If the authors have other information to better characterise their study population (ethnicity, socio-economic status, etc), they should include this in table 1. The outcome data should be presented in separate tables.

- A conventional Table 1 is now added. Unfortunately we do not have data on ethnicity and socio economic status (discussed upon in the Discussion section as a limitation). The Swedish Medical Birth Registry does not contain these data.

The outcome data are currently presented as percentages in tables 1 -2 and adjusted odds ratios in tables 3-4. This means that it is difficult to see the effect of adjustment. Could the authors consider including unadjusted ORs alongside the adjusted ORs? This could be put in an online supplement if there is too much information to include in the main paper.

- Unadjusted data is now added in table 3 and 4 as suggested

The tables are extremely dense and might benefit from either broken-up into separate tables or having some subheadings eg 'Labour and delivery', 'Gestational age', 'maternal complications'. Alternatively, they might consider having a separate table for outcomes only assessed in women who delivered vaginally.

- Thank you for the excellent advice. The tables now include subheadings.

The authors could also consider being a bit more selective about the outcomes that they report. For example, they could focus on birth outcomes (including mode of delivery) but perhaps excluding epidural analgesia.

- Actually the outcomes have been selected. The variables are all clinically relevant from an obstetric point of view. The use of epidural is on ongoing debate and we think it is of interest to present this over the maternal age strata.

The authors need to explain their rationale for evaluation some outcomes only in women who delivered vaginally. Clearly some of these outcomes only occur in women who deliver vaginally but calculated in this way the risk of instrumental delivery (for example) is affected by the risk of caesarean delivery. Ideally this would have been mentioned in the methods rather than appearing as a footnote to the tables.

- The OR for instrumental vaginal delivery was calculated among women with vaginal births only in order to exclude women with an instrumental attempt to deliver followed by an emergency CS. The ORs of perineal lacerations were for obvious reasons also estimated among women with vaginal births only. The information concerning use of epidural analgesia was also restricted to vaginal births only. Epidural is an analgesic method that has been widely used in the delivery wards for vaginal births during the entire time period. In contrast the use of epidural analgesia in CS has varied substantially over the time period and has almost exclusively been used in elective CS. Our purpose was to evaluate the odds ratio for epidural use over the maternal age strata and consequently we selected the mode of delivery that exhibited the least variation in the use of the analgesic method over the time period, i.e. vaginal births. This is now described in the Methods section.

- The possibility to differentiate between elective and acute CS was only available in a subsection of the cohort. This information is now added in the Methods section.

The authors provide very limited information about missing data. If the level of missing outcome data is low they need to state this, otherwise they need to provide more information about missing data (as per STROBE guideline).

- The information on missing data is now included in the new Table 1 concerning the maternal characteristics. The validation including information about missing data of the MBR are thoroughly described and discussed in reference 25 (Källén B, Källén K, Olausson PO. The Swedish Medical Birth Register: a summary of content and quality. Research Report, Article no: 2003-112-3. Centre for Epidemiology, National Board of Health and Welfare Stockholm 2003. Available from:

<http://www.socialstyrelsen.se/publikationer2003/2003-112-3> (Accessed May 2014.)) We don't find it practical or necessary to copy-paste the information from this source to the manuscript. The interested reader should be able to easily find this information.

In their discussion of their key findings, the authors need to ensure that they refer to the relevant literature. I was surprised, for example, to find no reference to an earlier Swedish study by Clausson et al which examined SGA in the same Swedish data source (and also did not find an increased risk of SGA in adolescents); and there are certainly more recent and possibly more relevant papers on maternal age and uterine function than the 1981 Morris paper cited.

- There are numerous publications based on data from the Swedish Medical Birth Register concerning different maternal and neonatal outcomes. The particular reference (Clausson et al) that the referee advocates deals with the same study group but from 1992 and 1993 only. Besides being an old material it is also significantly smaller than our 19 years material. Comparisons with other data sources are in our opinion more relevant so we prefer not to add this reference.
- The references concerning ageing and uterine function are updated.

The discussion of study limitations, and in particular of the possible failure to adjust for some potential confounders, lacks depth. They would potentially have been able to adjust for other variables, including some co-morbidities and possibly 'migration status' (ie Nordic/non-Nordic).

- The discussion of study strengths and limitations has been edited as suggested.

The conclusion seems rather weak and primarily focuses on providing information about age related risks. If they believe that there is a case for surveillance programmes could they explain this? Perhaps they could also identify some unanswered questions and/or research recommendations?

- The conclusion is now edited and putative surveillance programs for older women are specified. Further research recommendations are added.

The abstract uses the term 'risks' when referring to odds. The conclusion could be amended as suggested above.

- We would prefer to keep the term risk. The conclusion has been re-evaluated and consequently changed

Clausson, Britt, Sven Cnattingius, and Ove Axelsson. "Preterm and term births of small for gestational age newborns: a population-based study of risk factors among nulliparous women." *BJOG: An International Journal of Obstetrics & Gynaecology* 105.9 (1998): 1011-1017.

Minor comments

The title needs to mention that this is a study of primiparous women.

- We agree and has added primiparous to the title.

P4, Line 28 – please clarify – maternal age at birth?

- Has been done.

P4, Lines 16 and 18. Use terms 'high-income, 'low-income' etc in preference to 'developed' and 'developing' countries.

- Has been changed accordingly

P6, Lines 33-34. This sentence is not well expressed. This is the largest group so reasonable to use as the reference group whether or not the mean age of a primiparous women is in this range.

- We have deleted the sentence about the reason for using the group as reference groups. This group is further mentioned as the reference group.

There is a reference to figure 1 in line 35 which appears to be incorrect since there is only one figure and this is referred to later as 'figure 2'.

- Thank you! Apologize for this careless error.

P6, Line 59. Although the authors state that 'shoulder dystocia' was an outcome, it would be helpful if they could clarify whether they are truly reporting the occurrence of shoulder dystocia or whether they are reporting adverse neonatal outcomes resulting from shoulder dystocia (eg brachial plexus injury) Tables. Define 'normal vaginal delivery'

- Shoulder dystocia is equivalent to the obstetric event coded as ICD 10 O66.0, this information is now added under the section Methods. Definition of normal vaginal birth has been added in the section Methods.

P16, lines 32/33. Rewrite the sentence containing the phrase "exclusively associated with". .Perhaps this could be better expressed as: 'There was a significantly increased risk of stillbirth.... only in women aged 30 years and over'?

- Thanks. Has been reworded accordingly.

It is generally preferable to use the term 'birth' instead of 'delivery'.

- "delivery" is now replaced by "birth", except for mode of delivery, we hope that is acceptable.

Reviewer Name Alon Shrim

Institution and Country Hillel Yaffe Medical Center, Israel

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

This is an interesting manuscript on an old and well studied issue of Ob complications in the extremes of maternal age.

It doesn't carry new information but the large number of patients included in this large scale registry is a great advantage and I believe that this justifies publication.

Major revisions are needed though, in order to accept the manuscript to publication:

1. Numbering lines may help in reviewing and commenting

- In our pdf file from the submission the numbering lines were shown. It is very interesting that the version the referee received from the Journal did not contain the numbering. It seems to be a problem in the electronic handling of the manuscript and transferring to the referee. We have now added line numbering in the Word version!

2. All along the text there are typo errors such as missing space between words (carecustomized in conclusions of the abstract, womenaged in the discussion....and many other places)

- We are sorry, but we could not find all those typos (the submission PDF has also been scrutinized).

3. Grammatical errors are spread along the manuscript. Examples are the 1st statement of the introduction and others. I suggest editing by English speaking person.

- The manuscript has been edited by an English speaking person (a native US-citizen, who is professor emeritus at Rochester University) as declared in the cover letter. Of course we could search for someone else to perform a second opinion if the Editor demands that.

4. Abstract: The conclusion says "counselling young mothers"... should be "women" or "pregnant women"...as the manuscript talks about primiparous women (who are not mothers...)

- Has been changed according to the preference of the referee. However, concerning the MBR all included women are mothers!

5. In introduction – lower rate of Ob complications are not "a benefit" of pregnancy of advanced maternal age...

- We have reworded the sentence, hopefully more correct.

6. In the introduction, the part on the lower rate of teen age pregnancies in Sweden is interesting but not relevant to the study (that aims at examining this population...).

- This part has been withdrawn.

7. At the end of the introduction and in other places, the word "the" should be inserted ("as well as in [the] socio-demographic..."). This returns in other places in the manuscript, please edit.

- Has been edited. See also point 3.

8. By what definition was "foetal distress" defined? Non reassuring monitoring?...needs to clarify

- This is now clarified in the Methods section.

9. "Aspiration of meconium" was it really meconium aspiration syndrome or meconium stained amniotic fluid? If aspiration – by what definition?...

- This is now clarified in the Methods section.

10. "Infants" in results – should be newborns...

- "Infants" is replaced by "newborns".

11. Better define the reference age group as the "reference group" or Control group....better than reporting it repeatedly as "the group between 25-29 years..."

- Has been done throughout the manuscript.

12. This group 25-29 years old, was selected as such because it is "the average primiparous woman"...by what calculation or previous report?...please clarify.

- Please, see comment from referee 1 and our response to her request/suggestion.

13. "Perineal damage" at the end of results... is actually "perineal lacerations" in methods... needs to be consistent.

- Thanks, now consistent.

14. Reporting strengths and limitations occupies almost full page. It should be located to the end of the discussion and be shorter.

- Strengths and limitations section is now moved to the end of the discussion but not shortened due to referee one's suggestions.

In summary - the potential and methods of the manuscript are good, however, in order to be published serious editing should take place including English edition, grammatical changes, changing the structure so it is more fluent...according to the comments above.

VERSION 2 – REVIEW

REVIEWER	Jennifer Hollowell University of Oxford
REVIEW RETURNED	20-Aug-2014

GENERAL COMMENTS	The authors have made some substantial improvements to this paper. In particular the presentation of results is much clearer, and they have provided some information on missing data (as per the STROBE guideline). However, they have not addressed several
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	<p>important issues raised in my previous review.</p> <p>There are many existing studies evaluating outcomes by maternal age in various populations. This study has the obvious strength that it covers a large, unselected population and is able to describe the relationship between maternal age and a wide range of outcomes, but many of these relationships are well documented in the existing literature (as they note in their discussion). Despite the changes made by the authors, the rationale for the design of the study (particularly the selection of adjustment variables) is still unclear and the conclusions, although reasonable, do not appear to specifically relate to any new findings in this study.</p> <p>The authors provide a reasonable explanation for not adjusting for variables that may be on the causal path but they do not (as requested in my previous review) provide a clear justification for the variables that they have included (they do not explain why they adjust some analyses for gestational age; and surely BMI and smoking might also be considered to be on the causal path?) As I commented in my previous review it remains unclear what interpretation can be put on their findings. It is a minor point, but the definition that they provide of a confounder in the discussion is incorrect.</p> <p>As an example of an issue relating to adjustment. The authors devote a paragraph of their discussion to their finding of an absence of increased risk of SGA in adolescent and younger women. This is a potentially interesting finding but their discussion leaves the reader unclear as to whether they consider there is a real difference between their findings and those of other studies, and I think this example well illustrates the reasons for justifying and explaining their adjustment variables. From table 4 it appears that the excess risk (crudeOR 1.32, 95% CI 1.07 – 1.63 in their youngest group) disappears after they adjust for year, smoking and BMI. Should one interpret this as suggesting that adolescents do indeed have an increased risk of SGA that is potentially explained by smoking and BMI? Given that the stated purpose of the study was to reveal risk groups that may need more attention antenatally, I feel that their interpretation lacks depth.</p> <p>The authors' response to the question regarding their statistical methods is somewhat unsatisfactory. It is clear from table 3 that adjustment appears to have a relatively small effect on the estimated odds for younger age groups and a much more substantial effect on the estimated odds in older age groups. In justifying their decision to adjust for BMI as a continuous variable it is therefore unhelpful that they provide the results of their 'sensitivity analyses' only for the younger age groups. Information on their methods should also be included in the manuscript itself not just in the response to the journal. They also could helpfully comment on the possible effects of missing data on their adjustment since the level of missing data on BMI and smoking is not negligible in the youngest age groups.</p> <p>With regard to the use of the term 'risks', I accept that it has a colloquial usage but when reporting results such as "...a 4-fold increased risk for caesarean section" I consider that scientific accuracy requires that they refer to odds and not risks. Their response that they "prefer to keep the term risk" is not adequate.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer Name Jennifer Hollowell

Institution and Country University of Oxford

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

The authors have made some substantial improvements to this paper. In particular the presentation of results is much clearer, and they have provided some information on missing data (as per the STROBE guideline). However, they have not addressed several important issues raised in my previous review.

There are many existing studies evaluating outcomes by maternal age in various populations. This study has the obvious strength that it covers a large, unselected population and is able to describe the relationship between maternal age and a wide range of outcomes, but many of these relationships are well documented in the existing literature (as they note in their discussion). Despite the changes made by the authors, the rationale for the design of the study (particularly the selection of adjustment variables) is still unclear and the conclusions, although reasonable, do not appear to specifically relate to any new findings in this study.

- The description of the rationale for the design of the study and the methods used are further expanded both in the Methods and the Discussion section.

The authors provide a reasonable explanation for not adjusting for variables that may be on the causal path but they do not (as requested in my previous review) provide a clear justification for the variables that they have included (they do not explain why they adjust some analyses for gestational age; and surely BMI and smoking might also be considered to be on the causal path?) As I commented in my previous review it remains unclear what interpretation can be put on their findings. It is a minor point, but the definition that they provide of a confounder in the discussion is incorrect. As an example of an issue relating to adjustment. The authors devote a paragraph of their discussion to their finding of an absence of increased risk of SGA in adolescent and younger women. This is a potentially interesting finding but their discussion leaves the reader unclear as to whether they consider there is a real difference between their findings and those of other studies, and I think this example well illustrates the reasons for justifying and explaining their adjustment variables. From table 4 it appears that the excess risk (crudeOR 1.32, 95% CI 1.07 – 1.63 in their youngest group) disappears after they adjust for year, smoking and BMI. Should one interpret this as suggesting that adolescents do indeed have an increased risk of SGA that is potentially explained by smoking and BMI? Given that the stated purpose of the study was to reveal risk groups that may need more attention antenatally, I feel that their interpretation lacks depth.

- This part is now expanded and deepened. We cannot see that the definition of a confounder is incorrect, even if it might be a little bit short.

The authors' response to the question regarding their statistical methods is somewhat unsatisfactory. It is clear from table 3 that adjustment appears to have a relatively small effect on the estimated odds for younger age groups and a much more substantial effect on the estimated odds in older age groups. In justifying their decision to adjust for BMI as a continuous variable it is therefore unhelpful that they provide the results of their 'sensitivity analyses' only for the younger age groups. Information on their methods should also be included in the manuscript itself not just in the response to the journal. They also could helpfully comment on the possible effects of missing data on their adjustment since the level of missing data on BMI and smoking is not negligible in the youngest age groups.

- Information on the methods is included in the manuscript and the putative effects of missing data are commented upon.

With regard to the use of the term 'risks', I accept that it has a colloquial usage but when reporting results such as "...a 4-fold increased risk for caesarean section" I consider that scientific accuracy

requires that they refer to odds and not risks. Their response that they “prefer to keep the term risk” is not adequate.

- Done