PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Benefits of not smoking during pregnancy for Australian Aboriginal and Torres Strait Islander women and their babies: a retrospective cohort study using linked data
AUTHORS	McInerney, Carol; Ibiebele, Ibinabo; Ford, Jane B; Randall, Deborah; Morris, Jonathan M; Meharg, David; Mitchell, Jo; Milat, Andrew; Torvaldsen, Siranda

VERSION 1 – REVIEW

REVIEWER	David Tappin University of Glasgow
REVIEW RETURNED	16-Jul-2019

GENERAL COMMENTS	This is an interesting paper. I would like to draw the author's attention to a paragraph in 'Epidemiology in Medicine' Charles Hennekens and Julie Buring: 'In general, the relative risk is the measure used most commonly by those examining possible determinants of disease because it represents the magnitude of the association and provides information that can be used in making judgements about causality. In contrast, once causality is assumed, from the perspective of public health administration and policy, measures of association based on absolute differences in risk between exposed and nonexposed individuals assume far greater importance. These absolute rates express either the actual incidence of a disease that is attibutable to an exposure (attibutable risk) or the number of cases of disease in the total population that could be elininated by removal of the harmful exposure (population attibutable risk).' I think we have moved on from causation being in question for most of the outcomes in this study. For public health policy makers weighing up the distribution of funding, they want to know how many fewer stillbirths and small for dates babies will occur if smoking cessation during pregnancy interventions are implemented and they succeed to a lesser or greater extent. They want to know what they can expect will be achieved by spending extra public money. This paper can easily give them this information for the outcomes presented. Apologies that I was one of the authors, but please see: Lawder R, Whyte B, Wood R, Fischbacher C, Tappin DM. Impact of maternal smoking on early childhood health: a retrospective cohort linked dataset analysis of 697 003 children born in Scotland 1997–2009. BMJ Open 2019;0:e023213. doi:10.1136/ bmjopen-2018-023213

REVIEWER	Michiyo Yamakawa
	Gifu University Graduate School of Medicine, Japan
REVIEW RETURNED	29-Jul-2019

GENERAL COMMENTS	Although the authors acknowledge that associations of maternal smoking during pregnancy with maternal and child health outcomes are well-known, the findings are not special and this study seems to just provide local information. However, evidence for the associations among Aboriginal mothers, whose smoking rate is surprising high despite pregnancy, is sparse, thus we agree that studies targeting the population are needed. Indeed, the findings from this study are consistent with past studies, but there are some issues to be addressed, e.g., important confounders including environmental tobacco smoke (smoking cohabitants) and maternal lifestyle and dietary factors are not simultaneously controlled for.
	Major comments
	Introduction
	1. Page 4, lines 22 to 27: At a first glance, it seems that this study aims to evaluate the present smoking cessation campaigns targeting pregnant Aboriginal mothers. The sentences would be misleading and please re-write the sentences. Similarly, the second sentence of "What is already known on this topic" should be amended.
	Methods
	2. Exposure: risks of maternal smoking during pregnancy with adverse health outcomes of children may differ by the timing of smoking cessation in terms of pregnancy trimester. If pregnant women smoked, the sooner they quit smoking, the greater the benefits would be. The authors are aiming to develop educational materials among the targeted study population, therefore, if possible, re-organizing the exposure category using the timing of smoking cessation would be more informative.
	3. Outcomes: why did you choose breastfeeding as an outcome, as the other outcomes were related to adverse health events? It is confusing because direct pathway from smoking status during pregnancy to breastfeeding may be unlikely. It would be plausible that breastfeeding is a surrogate factor on the possible pathway.
	4. Covariates: please explain about a clear rationale why these variables were selected as potential confounders. Environmental tobacco smoke (cohabitants' smoking), maternal lifestyle and dietary factors (e.g., smoking status before pregnancy, alcohol drinking and obesity) and individual SES (e.g., educational attainment and income), not area-based SES, should be considered.
	5. In addition, I am wondering if remoteness area and hospital level would be confounders for the associations of maternal smoking during pregnancy with maternal and child health outcomes.
	6. Statistical analyses: considering correlation within data (some mothers had more than one baby during the study period), the authors conducted the analyses using modified Poisson regression. Please report the results from the analyses restricting to mothers' first childbirth during the study period, i.e., the study participants should be included once in the analyses.
	Results

7. Page 8, lines 18 to 25 and lines 40 to 43: data are not found in the tables; however, the information, i.e., change in smoking status during pregnancy among the study participants, would be important, thus please evaluate it as an exposure.

Discussion
8. Page 6, lines 3 to 5: the sensitivity of 58.5% is very low. Does it mean half of smoking mothers cannot be identified as smokers by hospital records? If this is correct, impacts on the associations from the low sensitivity should be discussed.
9. Page 9, lines 16 to 19: please discuss in-depth about why not smoking during pregnancy was not significantly associated with lower risk of severe maternal morbidity. As mentioned above, a possibility of confounding due to those unmeasured factors other than smoking status before pregnancy and alcohol drinking should be discussed.
10. Page 9, lines 32 to 34: please rephrase the sentence "Some commonly included variables such as preterm birth or growth restrictions were not adjusted for as particular care was taken to avoid adjusting for variables on the causal pathway" as it is not clear what it meant.

Minor comments
11. Page 7, lines 32 to 33: Error message appears, "Error! Reference source not found". Please check it and insert the correct reference number.
12. Page 8, lines 45 to 48: please check whether the percentages would be correct (7.3% and 7.0% should replace each other?)

REVIEWER	Mikael Ekblad Human Development and Family Studies, Purdue University, USA and Department of General Practice, University of Turku, Finland
REVIEW RETURNED	02-Aug-2019

| GENERAL COMMENTS | This is a somewhat interesting study on the benefits of not smoking during pregnancy for Australian Aboriginal and Torres Strait Islander women. The results are not new regarding the association between smoking during pregnancy and maternal/ child outcomes. However, the writers justify well the reason for this study (i.e. significantly high prevalence of smoking during pregnancy in this population). In general, the manuscript is well written and includes proper statistical analyses of the outcomes. I have couple of minor comments:

1. Introduction, 3 paragraph. Writers could shortly speculate if the association between smoking during pregnancy and the outcomes could be different among Aboriginal women compared to general population. Is there in general different effect of smoking during pregnancy depending race?

2. Methods, page 5 last paragraph of chapter 'ERA'. I would suggest adding a citation into the last sentence (-- described in more detail elsewhere.).

3. Page 7. I think it was good that the writers included explanation why they framed the manuscript in the positive way.

4. Page 7, third paragraph. Some error code. |

	5. Page 7, last paragraph. The end of the sentence is moved to the next page.
	6. Page 7-8. I think the content of the first paragraph on page 8 would suite better to the methods.
	7. Page 8, last paragraph. In my opinion, the relative risks for specific outcomes should be moved to the respective sentence earlier in the methods section, e.g. '-–compared to 1.8% in smoking mothers (RR=0.58 95% CI 0.44-0.76)'.
	8. Page 9, first paragraph. If women were transferred to another hospital during the birth admission, could this also mean that their deliveries might have been complicated? This could be also mentioned in the paragraph.
	9. Page 10, second paragraph. Further efforts should include also preventing the initial starting of smoking among teenagers (future parents) for this population. This could be added to the paragraph.
	10. Tables: I would suggest presenting the percentages with one decimal in all of the variables throughout the tables (if the author instructions does not tell otherwise).
	11. Table 3. I didn't notice at first the mention of "rate per 1000 total births". I would add the N and per 1000 in the respective columns where N and % are. I understand that perinatal death results are per 1000 total birth and the other one per 1000 live births. This specification could be included underneath the table.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: David Tappin
Institution and Country: University of Glasgow
This is an interesting paper.
I would like to draw the author's attention to a paragraph in 'Epidemiology in Medicine' Charles Hennekens and Julie Buring:
'In general, the relative risk is the measure used most commonly by those examining possible determinants of disease because it represents the magnitude of the association and provides information that can be used in making judgements about causality. In contrast, once causality is assumed, from the perspective of public health administration and policy, measures of association based on absolute differences in risk between exposed and nonexposed individuals assume far greater importance. These absolute rates express either the actual incidence of a disease that is attributable to an exposure (attributable risk) or the number of cases of disease in the total population that could be elininated by removal of the harmful exposure (population attributable risk).'
I think we have moved on from causation being in question for most of the outcomes in this study. For public health policy makers weighing up the distribution of funding, they want to know how many fewer stillbirths and small for dates babies will occur if smoking cessation during pregnancy interventions are implemented and they succeed to a lesser or greater extent. They want to know what they can expect will be achieved by spending extra public money. This paper can easily give them this information for the outcomes presented.
Apologies that I was one of the authors, but please see:
Lawder R, Whyte B, Wood R, Fischbacher C, Tappin DM. Impact of maternal smoking on early

We are incredibly grateful to Reviewer 1 for his review and agree with him entirely, especially given that our purpose in undertaking this study was to be able to provide relevant information which can be used to ultimately reduce smoking rates during pregnancy among Aboriginal women. After consideration and reading the paper above (Lawder et al), we decided to use the same measure, PAF, as that paper. We have had to think carefully about the wording as our study is about the benefits of NOT smoking, rather than the risks of smoking, but obviously the risks of adverse outcomes are attributable to smoking. Hence we have had to use the RRs for smokers, not the RRs presented in the Table 3, which is for non-smokers. We explain this in the methods, pasted below under methods.

The associations between smoking and inter-hospital transfer or severe maternal morbidity are not established causal associations, so we calculated PAFs only for the perinatal outcomes. We moved the maternal outcome results to the end of the results paragraph in the abstract.

We have added the following text to the abstract:

Main outcome measures

Population attributable fractions (PAFs) were calculated using adjusted relative risks.

Results

PAFs (%) were 27% for perinatal death, 26% for preterm birth and 48% for small-for-gestational-age.

Conclusion

The final sentence was changed from: These results highlight why effective smoking cessation programs are urgently required for this population.

To:

These results quantify the proportion of adverse perinatal outcomes due to smoking and highlight why effective smoking cessation programs are so urgently required for this population.

These additions to the abstract meant that we had to delete a few words in order to keep within the 300 word limit.

In the main paper we have added the following:

Methods, Statistical analyses:

In view of the established causal relationship between smoking and adverse perinatal outcomes, we quantified the proportion and number of adverse perinatal outcomes that would not have occurred in this population if all the mothers had been non-smokers during pregnancy. We used the formula: $PAF = [P_s (RR_s-1)]/RR_s$, where P_s is the proportion of babies with the outcome whose mothers smoked and RR_s is the adjusted RR for smokers. The RR_s is the inverse of the RR for non-smokers.

Results:

As indicated by the PAFs (%) in Table 3, more than a quarter of the perinatal deaths and preterm births were attributable to smoking and almost half the small for gestational age births. Among this

cohort of babies, this equates to 68 perinatal deaths, 540 preterm births and 1,131 small for gestational age (<10th percentile) babies attributable to smoking.

Discussion:

The high PAFs for these outcomes highlights the enormous potential for health improvements in this population. Over a quarter of the perinatal deaths and preterm births were attributable to smoking. Being born small for gestational age is associated with short and long-term health sequelae, and these risks are even greater for babies born lower than the third percentile for gestational age and sex. The PAF(%) was highest (57%) for being born less than the third percentile. Almost half (48%) the babies born small for gestational age (<10th percentile) could have had a normal birthweight (≥10th percentile) in the absence of smoking.

In addition to the useful suggestion by Reviewer 1 to include a measure of attributable risk, we also found his paper interesting and relevant to the discussion of our results. In view of this, we have added the following to our discussion:

Our results are consistent with a recent study of a cohort of 697,003 children born in Scotland from 1997–2009 (32). In addition to the adverse perinatal outcomes attributable to smoking, this study followed children until five years of age and found that maternal smoking during pregnancy also increased the risk of the child being hospitalized with acute respiratory infections, bronchiolitis, asthma and bacterial meningitis (32).

Reviewer: 2
Reviewer Name: Michiyo Yamakawa
Institution and Country: Gifu University Graduate School of Medicine, Japan

Although the authors acknowledge that associations of maternal smoking during pregnancy with maternal and child health outcomes are well-known, the findings are not special and this study seems to just provide local information. However, evidence for the associations among Aboriginal mothers, whose smoking rate is surprising high despite pregnancy, is sparse, thus we agree that studies targeting the population are needed. Indeed, the findings from this study are consistent with past studies, but there are some issues to be addressed, e.g., important confounders including environmental tobacco smoke (smoking cohabitants) and maternal lifestyle and dietary factors are not simultaneously controlled for.

Thank you for your comments. We agree that there are important confounders for which we were unable to control. Unfortunately no information on these confounders is collected in the population data. In the limitation section of the discussion, we have added exposure to environmental tobacco smoke to the list of potential confounders about which we had no information.

Please find responses to individual comments below.

Major comments
Introduction
1. Page 4, lines 22 to 27: At a first glance, it seems that this study aims to evaluate the present smoking cessation campaigns targeting pregnant Aboriginal mothers. The sentences would be misleading and please re-write the sentences. Similarly, the second sentence of "What is already known on this topic" should be amended.

In order to provide context for our aim, which is *not* to evaluate smoking cessation campaigns, we have added the following sentence after the sentences about smoking cessation:

Although the benefits of not smoking during pregnancy are unlikely to be any different for Aboriginal mothers from the general population, quantifying the benefits of not smoking among Aboriginal mothers may be regarded as more relevant by this population and thus have the potential to influence smoking cessation.

This now leads more directly into the next sentence so we have removed the paragraph break.

The "What is already known on this topic" section has already been deleted, in response to the Editorial request.

Methods
2. Exposure: risks of maternal smoking during pregnancy with adverse health outcomes of children may differ by the timing of smoking cessation in terms of pregnancy trimester. If pregnant women smoked, the sooner they quit smoking, the greater the benefits would be. The authors are aiming to develop educational materials among the targeted study population, therefore, if possible, re-organizing the exposure category using the timing of smoking cessation would be more informative.

We agree entirely with this comment but we are limited by what is recorded in the population datasets. Unfortunately, no information on smoking cessation was recorded. However, as we point out in our limitations:

'new data around quitting in pregnancy is available from 2016 onward so there is potential for future work to examine this phenomenon further'.

3. Outcomes: why did you choose breastfeeding as an outcome, as the other outcomes were related to adverse health events? It is confusing because direct pathway from smoking status during pregnancy to breastfeeding may be unlikely. It would be plausible that breastfeeding is a surrogate factor on the possible pathway.

Thank you for this comment and we agree entirely that a direct pathway from smoking to breastfeeding is unlikely. We had not appreciated the confusion this may cause until reading this comment. We have now removed breastfeeding as an outcome and deleted all mentions of breastfeeding: in the methods, results, discussion and Table 2.

4. Covariates: please explain about a clear rationale why these variables were selected as potential confounders. Environmental tobacco smoke (cohabitants' smoking), maternal lifestyle and dietary factors (e.g., smoking status before pregnancy, alcohol drinking and obesity) and individual SES (e.g., educational attainment and income), not area-based SES, should be considered.

Our covariate selection was based on known confounding variables but limited by what variables were available. We agree that there are important confounders such as exposure to environmental tobacco smoke and maternal lifestyle factors for which we were unable to control. Unfortunately, no information on these confounders is collected in the population data. In the limitation section, we have added exposure to environmental tobacco smoke to the list of potential confounders about which we had no information. We have also added no data on passive smoking to the limitations in the Article Summary box. The lack of data on alcohol consumption is already mentioned in the limitation section and in the Article Summary box. We agree that individual SES data would be far preferable, but this is not collected and the best proxy available to us is the Socio-Economic Index for Areas (SEIFA) Index of Relative Socio-Economic Disadvantage (IRSD), which is based on the Statistical Local Area of residence. We have added the lack of individual level socioeconomic status as a limitation in the strengths and limitation section.

5. In addition, I am wondering if remoteness area and hospital level would be confounders for the associations of maternal smoking during pregnancy with maternal and child health outcomes.

Remoteness area and the Socio-Economic Index for Areas (SEIFA) Index are very strongly correlated with each other so it was not appropriate to include both variables in the models. We included the SEIFA index in preference to remoteness area for all outcomes except inter-hospital transfer, where remoteness area has a stronger association than SEIFA. Hospital level and remoteness area are also very strongly correlated with each other, hence it was not appropriate to also include hospital level.

6. Statistical analyses: considering correlation within data (some mothers had more than one baby during the study period), the authors conducted the analyses using modified Poisson regression. Please report the results from the analyses restricting to mothers' first childbirth during the study period, i.e., the study participants should be included once in the analyses.

The majority (70%) of mothers had only one baby during the study period. However, in order to account for the correlation within the data for the 30% of mothers who had more than one baby during the period, we conducted the perinatal outcomes analyses using an extension to the modified Poisson regression with an unstructured correlation matrix. Restricting the perinatal outcome analyses to the first childbirth excludes 30% of the babies and offers no advantage so long as the correlation is accounted for in the analyses, which it was in our analyses.

Results
7. Page 8, lines 18 to 25 and lines 40 to 43: data are not found in the tables; however, the information, i.e., change in smoking status during pregnancy among the study participants, would be important, thus please evaluate it as an exposure.

The change in smoking status that we describe in the text of the results is **between** pregnancies, not **during** pregnancy. We state 'For 564 (4%) mothers, their smoking status changed between births…'. To clarify to readers throughout the paragraph that we are describing changes in smoking status **between** pregnancies and **not during** pregnancy we have changed the following sentence: 'For the mothers whose smoking status changed, 47%…', to 'For the mothers whose smoking status changed between pregnancies, 47%…'.

Discussion
8. Page 6, lines 3 to 5: the sensitivity of 58.5% is very low. Does it mean half of smoking mothers cannot be identified as smokers by hospital records? If this is correct, impacts on the associations from the low sensitivity should be discussed.

Yes, the sensitivity of 58.5% **in the most recent separation** in the hospital data is very low and that is why we used the birth data **and all** the hospital records that were available for the mother. It is possible there is still some under-ascertainment and we have added the following statement to the end of the limitations: 'Under-ascertainment of smoking status would similarly bias toward the null.'

9. Page 9, lines 16 to 19: please discuss in-depth about why not smoking during pregnancy was not significantly associated with lower risk of severe maternal morbidity. As mentioned above, a possibility of confounding due to those unmeasured factors other than smoking status before pregnancy and alcohol drinking should be discussed.

The overall rate of severe maternal morbidity was low (<3%) and there are many risk factors for this. Non-smoking mothers did have a lower risk of severe maternal morbidity but if this lower risk is real, a larger population size would be required to detect a statistically significant difference. Interestingly, we

have undertaken similar analyses (not yet published) of non-Aboriginal women in NSW (n=449,590 vs n=18,154 for Aboriginal mothers in this study) and found a similar result, but the result is statistically significant (RR 0.87, 95%CI 0.81–0.93). We have added a sentence to the results about the rate of severe maternal morbidity being low (<3%). We have also added a sentence to the discussion saying that other risk factors may be more strongly associated with severe maternal morbidity than smoking. We have added a paragraph break to separate the maternal and perinatal outcome discussions.

10. Page 9, lines 32 to 34: please rephrase the sentence "Some commonly included variables such as preterm birth or growth restrictions were not adjusted for as particular care was taken to avoid adjusting for variables on the causal pathway" as it is not clear what it meant.

We have deleted this sentence as it is unnecessary and may cause confusion.

Minor comments
11. Page 7, lines 32 to 33: Error message appears, "Error! Reference source not found". Please check it and insert the correct reference number.

We have corrected this and it now reads Table 1, and is no longer linked text.

12. Page 8, lines 45 to 48: please check whether the percentages would be correct (7.3% and 7.0% should replace each other?)
Thank you for picking up this error, we have now corrected it.

Reviewer: 3
Reviewer Name: Mikael Ekblad
Institution and Country: Human Development and Family Studies, Purdue University, USA and Department of General Practice, University of Turku, Finland
This is a somewhat interesting study on the benefits of not smoking during pregnancy for Australian Aboriginal and Torres Strait Islander women. The results are not new regarding the association between smoking during pregnancy and maternal/ child outcomes. However, the writers justify well the reason for this study (i.e. significantly high prevalence of smoking during pregnancy in this population). In general, the manuscript is well written and includes proper statistical analyses of the outcomes. I have couple of minor comments:

1. Introduction, 3 paragraph. Writers could shortly speculate if the association between smoking during pregnancy and the outcomes could be different among Aboriginal women compared to general population. Is there in general different effect of smoking during pregnancy depending race?

No, there is no evidence that the effect of smoking varies by race. As mentioned in our response to Reviewer 2, comment 1, we have added the following sentence to the introduction:

Although the benefits of not smoking during pregnancy are unlikely to be any different for Aboriginal mothers from the general population, quantifying the benefits of not smoking among Aboriginal mothers may be seen as more relevant by this population and thus have the potential to influence smoking cessation.

2. Methods, page 5 last paragraph of chapter 'ERA'. I would suggest adding a citation into the last sentence (-- described in more detail elsewhere.).

We have added a citation to a study that we undertook at the same time as this one. Its aim was to examine any differences between women recorded as Aboriginal and those assigned an Aboriginal

status, and to assess the effects of different algorithms to estimate within group comparisons for Aboriginal people. This citation is (23) and does not show up in tracked changes (EndNote updates do not appear as tracked changes). We did not include the citation in the original submission as the manuscript was still under review. It has now been accepted for publication so can be included.

3. Page 7. I think it was good that the writers included explanation why they framed the manuscript in the positive way.

Thank you. This has also been commented on by audiences to whom we have presented the findings. Aboriginal audience members have particularly had very positive comments.

4. Page 7, third paragraph. Some error code.

As per the response to Reviewer 2, comment 11, this has been corrected.

5. Page 7, last paragraph. The end of the sentence is moved to the next page.

We don't know why this formatting error occurred. The sentence is no longer broken and we will check the final version to ensure it has not happened again.

6. Page 7-8. I think the content of the first paragraph on page 8 would suite better to the methods.

In the methods we already state: 'To increase ascertainment, birth data and mother's hospital birth record(s) were used to assign smoking status.' We agree it is unnecessary to repeat it in the results, so we have deleted the first part of this sentence, which says: 'Ascertainment of smoking information was increased by using both the birth and hospital data…'

7. Page 8, last paragraph. In my opinion, the relative risks for specific outcomes should be moved to the respective sentence earlier in the methods section, e.g. '—compared to 1.8% in smoking mothers (RR=0.58 95% CI 0.44-0.76)'.

We were unsure what the intention of this comment was, but have moved the final results paragraph, which reports on specific outcomes, so that it continues on from the previous paragraph, which reports on perinatal deaths and includes the sentence mentioned in the comment (–compared to 1.8% in smoking mothers)

8. Page 9, first paragraph. If women were transferred to another hospital during the birth admission, could this also mean that their deliveries might have been complicated? This could be also mentioned in the paragraph.

We have added the sentence:

Inter-hospital transfers may be due to complications arising before, during or after the birth.

9. Page 10, second paragraph. Further efforts should include also preventing the initial starting of smoking among teenagers (future parents) for this population. This could be added to the paragraph.

We have added the following sentence to the end of the paragraph:

Investment to discourage women, especially young women, from taking up smoking and encouraging and appropriately supporting smokers to quit need to remain priorities.

10. Tables: I would suggest presenting the percentages with one decimal in all of the variables throughout the tables (if the author instructions does not tell otherwise).

We have presented all the percentages as two significant digits. We believe that percentages in tables are much easier to read when presented as whole numbers and for larger numbers the additional decimal place does not add any useful information. Presenting percentages to two significant digits means that percentages <10 are to one decimal place. However, we can change all percentages to one decimal place if directed to do so by the Editor.

11. Table 3. I didn't notice at first the mention of "rate per 1000 total births". I would add the N and per 1000 in the respective columns where N and % are. I understand that perinatal death results are per 1000 total birth and the other one per 1000 live births. This specification could be included underneath the table.

Within the table, we have added ** to direct readers to the footnote underneath the table which states Rate per 1,000 total births, and ^^ for Rate per 1,000 live births.

VERSION 2 – REVIEW

REVIEWER	David Tappin University of Glasgow
REVIEW RETURNED	11-Sep-2019

GENERAL COMMENTS	Please clarify in the text if non-smoking women of Aboriginal descent have similar birth outcomes to NON-SMOKING non-Aboriginal women or ALL non-Aboriginal women.

REVIEWER	Michiyo Yamakawa Gifu University Graduate School of Medicine, Japan
REVIEW RETURNED	14-Sep-2019

GENERAL COMMENTS	Statistical analyses: as the authors commented, restricting the perinatal outcome analyses to the first childbirth excludes 30% of the babies and thus might provide less advantage so long as the correlation is accounted for in the analyses. However, ex-smoking mothers (categorized as no smoking mothers in this study), who smoked in their first childbirth but quitted smoking thereafter, may have a higher relative risk of having worse maternal and perinatal outcomes, compared with never smoking mothers. Specifically, smoking mothers could change their habits in case such worse outcomes occurred in their first childbirth. Therefore, I think the restricted analyses seem to be worth addressing, although only 4% of mothers in this study changed smoking status between the births.

REVIEWER	Mikael Ekblad Human Development and Family Studies, Purdue University, USA and Department of General Practice, University of Turku, Finland
REVIEW RETURNED	10-Sep-2019

GENERAL COMMENTS	I have no additional comments.

Reviewer: 1

Reviewer Name: David Tappin
Institution and Country: University of Glasgow

Please clarify in the text if non-smoking women of Aboriginal descent have similar birth outcomes to NON-SMOKING non-Aboriginal women or ALL non-Aboriginal women.

The general NSW population includes both smoking and non-smoking mothers and Aboriginal and non-Aboriginal mothers. To clarify this, in the second paragraph of the discussion, we have changed '…the general NSW population' to:

> '…the overall NSW population of mothers giving birth in 2014, of whom 9.3% reported smoking and 3.9% were recorded as Aboriginal.'

Reviewer: 2
Reviewer Name: Michiyo Yamakawa
Institution and Country: Gifu University Graduate School of Medicine, Japan

Statistical analyses: as the authors commented, restricting the perinatal outcome analyses to the first childbirth excludes 30% of the babies and thus might provide less advantage so long as the correlation is accounted for in the analyses.
However, ex-smoking mothers (categorized as no smoking mothers in this study), who smoked in their first childbirth but quitted smoking thereafter, may have a higher relative risk of having worse maternal and perinatal outcomes, compared with never smoking mothers.
Specifically, smoking mothers could change their habits in case such worse outcomes occurred in their first childbirth.
Therefore, I think the restricted analyses seem to be worth addressing, although only 4% of mothers in this study changed smoking status between the births.

Thank you. We have given this a lot of consideration and made some changes to the manuscript but have not excluded these mothers for the reasons outlined below. We hope our changes clarify the issue.

As noted, only 4% of mothers changed their smoking status between the births in this study period. The percentage who smoked in one pregnancy and then not in the subsequent one is less than half of this. We have added the numbers to the text to clarify this, and the last sentence of the third paragraph of the results now reads:

> Of the 564 mothers whose smoking status changed between pregnancies, 266 (47%) changed from smoking to non-smoking, 271 (48%) changed from non-smoking to smoking in all subsequent pregnancies and 27 (5%) moved between smoker and non-smoker status.

If, as suggested by Reviewer 2, the mothers who smoked in one pregnancy and not in a subsequent pregnancy, and who are classified as non-smokers in the subsequent pregnancy, are more likely to have worse outcomes in the subsequent pregnancy compared with never smoking mothers, this would lead to an under-estimation of the effect of smoking, ie it would bias towards the null. However, any effect would be negligible due to the very low numbers (<2% of the study population). In response to Reviewer 2's comment we have also added the following three sentences to the end of the strengths and limitation section of the discussion:

Mothers who smoked in one pregnancy but not in a subsequent pregnancy were classified as non-smokers in the subsequent pregnancy. If these mothers were more likely to have worse outcomes in the subsequent pregnancy compared with never smoking mothers, this would also bias towards the null. However, any effect would be negligible due to the very low numbers (<2% of the study population).

Even if we did exclude the mothers who smoked during the first pregnancy in our study period and then not in a subsequent pregnancy, we do not have smoking information about pregnancies prior to the study period. This means that mothers who smoked in a pregnancy (or pregnancies) prior to 2010 but did not smoke in pregnancies between 2010–2014 (our study period) would still be included. This would be a less consistent method than the one we have chosen.

In addition to the reasons listed above, our purpose in undertaking this study was to be able to provide relevant information which can be used to ultimately reduce smoking rates during pregnancy among Aboriginal women. We are hoping the results will encourage mothers who smoked during their pregnancy to quit prior to or during their next pregnancy. About one quarter of babies born to mothers who smoked had an adverse outcome. Reviewer 2 comments that mothers who had an adverse outcome in one birth may be more influenced by our findings. Whilst this is certainly possible, these are the mothers we would like to influence the most. If they are excluded from this study then Aboriginal mothers who smoked and had a previous adverse outcome may feel that these results are not applicable to them. Excluding them also risks sending the message that if you smoked during one pregnancy, there is no point in quitting for subsequent pregnancies. It is well established that this is not the case.

Reviewer: 3
Reviewer Name: Mikael Ekblad
Institution and Country: Human Development and Family Studies, Purdue University, USA and Department of General Practice, University of Turku, Finland

I have no additional comments

VERSION 3 – REVIEW

REVIEWER	David Tappin Glasgow University Scotland UK
REVIEW RETURNED	08-Oct-2019

| GENERAL COMMENTS | Please look at the
'Encouragingly, despite some rates being marginally higher, overall very little difference exists between the rates of adverse perinatal outcomes among the non-smoking Aboriginal mothers in this study and the overall NSW population of mothers giving birth in 2014, of whom 9.3% reported smoking and 3.9% were recorded as Aboriginal.(14)'
I am not a statistician, but I understand from my colleague who undertook the statistical analysis of a recent paper we published: DOI 10.1186/s13063-016-1552-5; that it is not correct to include Aboriginal mothers in both sides of this comparison. It should be Aboriginal mothers versus the rest, rather than Aboriginal mothers versus the whole population (including Aboriginal mothers). |

REVIEWER	Michiyo Yamakawa
	Gifu University Graduate School of Medicine, Japan
REVIEW RETURNED	15-Oct-2019

GENERAL COMMENTS	I have no additional comments.

VERSION 3 – AUTHOR RESPONSE

Response to Reviewer 1's Comment:
Reviewer Name: David Tappin
Institution and Country: University of Glasgow

Please look at the 'Encouragingly, despite some rates being marginally higher, overall very little difference exists between the rates of adverse perinatal outcomes among the non-smoking Aboriginal mothers in this study and the overall NSW population of mothers giving birth in 2014, of whom 9.3% reported smoking and 3.9% were recorded as Aboriginal.(14)'

I am not a statistician, but I understand from my colleague who undertook the statistical analysis of a recent paper we published: DOI 10.1186/s13063-016-1552-5; that it is not correct to include Aboriginal mothers in both sides of this comparison. It should be Aboriginal mothers versus the rest, rather than Aboriginal mothers versus the whole population (including Aboriginal mothers).

Thank you and yes, we agree that if we had undertaken statistical analyses for this comparison it should be Aboriginal mothers versus the rest (ie non-Aboriginal mothers only). However, we did not undertake any analyses of comparisons between non-smoking Aboriginal women and the general population. The sentence referred to by Reviewer 1 is in the discussion, not the results section of our manuscript, and we reference the publication which has the whole population data. However, the population data do form a column in Table 3 and the heading 'NSW population' is not referenced. We apologise for this and have corrected it which should make it clearer to readers that these are not our data. There are no published data available on outcomes among the non-Aboriginal population of NSW. Although we would have these data in our dataset, we do not have ethics approval to conduct this analysis. We only had approval to undertake analyses within the Aboriginal population.

We think it is worthwhile to include the published population outcome data to provide some context and hence we would like to keep the sentence in the discussion and the column in Table 3. Given that only 3.9% of the population are Aboriginal, the population outcomes will mostly reflect the non-Aboriginal population. Leaving this reference in the manuscript provides evidence to readers that most of the adverse perinatal outcomes in babies born to Aboriginal mothers is likely to be due to smoking during pregnancy and thus preventable. As we clarified to readers in our last revisions '…the overall NSW population of mothers giving birth in 2014, of whom 9.3% reported smoking and 3.9% were recorded as Aboriginal.' Hence readers can draw their own conclusions. If Reviewer 1 and/or the Editors still feel strongly that no reference should be made to the NSW published population data, we can remove the sentence from the discussion and the column from Table 3.

VERSION 4 – REVIEW

REVIEWER	David Tappin University of Glasgow
REVIEW RETURNED	23-Oct-2019

GENERAL COMMENTS	I am happy with explanation and to leave manuscript as it is.