PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Neonatal outcomes of term live-born singletons in vertex presentation born to mothers with diabetes during pregnancy by mode of birth: A NSW population-based retrospective cohort study
AUTHORS	Zeki, Reem; Wang, Yueping Alex; Lui, Kei; Li, Zhuoyang; Oats, Jeremy; Homer, Caroline; Sullivan, Elizabeth

VERSION 1 - REVIEW

REVIEWER	Verhaeghe, Johan KU Leuven, Belgium Competing interests: None
REVIEW RETURNED	30-Oct-2017

GENERAL COMMENTS	This is a paper that brings new information into the field, and is therefore suitable for publication. In fact, I have been telling students and fellows for years (from personal experience) that instrumental delivery is generally not a good option in diabetic patients. Here is some valuable evidence that may affect clinical practice. Comments: - The authors mention some limitations of the study (p 13). However, for some reason, they exluded a mere 276 pregnancies because of "birth defects". Clearly, the rate of congenital malformations must be higher than 0.4%, particularly in a condition such as maternal diabetes. We therefore need more information on these birth defects (severe, life-threatening defects, eg cardiopulmonary?). If not, I can see no reason for excluding this small number of pregnancies. - A further limitation is the absence on umbilical artery pH or lactate levels. Is this not standard in NSW? - Instrumental deliveries: is this mainly forceps or vacuum? Any figures on this available? - Tables 1 and 2. Clearly, many practicioners in NSW are not following guidelines regarding GA at delivery; a large percentage of mothers with pre-existing diabetes delivered at 39 or >39 weeks GA, and a significant percentage of mothers with GDM delivered at >40 weeks GA. Do the authors see an effect of GA in their analyses? - Table 3. The comparator group (planned vaginal birth) should be presented first. - Table 4 and Discussion. Many adjusted odds ratios are <2 or around 2, ie a moderate increase. What can be extrapolated from these moderate risk increases in terms of long-term encephalopathy (eg, CP)?

	- Table 4 and Discussion. Admission to NICU is only partly driven by clinical necessity but can also be the result of established practice patterns, eg some maternities will routinely admit babies of diabetic mothers with a birthweight >4 kg because of concerns for hypoglyemia. Again, the lack of "hard endpoints" (pH, lactate) is a limitation. - There is a shift going on from primary to secondary cesarean sections in diabetic patients, eg see evidence in Finland (Teramo et al). More and more women with diabetes resent being seen as "pathologic cases" and strongly desire "a natural childbirth, like everybody else". Do the authors have any comments on this change in practice pattern in view of their findings?

REVIEWER	Cooper, Staphanie University of Calgary, Canada Competing interests: nil
REVIEW RETURNED	13-Nov-2017

GENERAL COMMENTS	I believe the data obtained in this study is important and should be published. However, I find the study question unclear. If the primary question is association between mode of birth and neonatal adverse outcomes in maternal diabetes (as suggested in the intervention section), then that should be clarified, with secondary objective of comparison of outcomes in macrosomic vs nonmacrosomic infants. Consequently, the results are difficult to follow and to interpret. The additional analysis of GDM vs pre-existing DM adds a new variable that was not addressed in the primary objective and makes this quite confusing to read. Of note, fetal macrosomia can only be predicted, not diagnosed. Therefore, to make a conclusion that 'Pregnant women with diabetes, particularly those with fetal macrosomia...' cannot be made. This is especially true given the inaccuracy sonographically determined estimated fetal weight. The authors should also address why shoulder dystocia was not addressed, as this is a major clinical concern amongst infants born of diabetic mothers

REVIEWER	Hilliam, Rachel Mary The Open University UK Competing interests: None
REVIEW RETURNED	20-Nov-2017

GENERAL COMMENTS	This is a well written paper in an interesting area. The statistics and explanations are on the whole correct, however see the comments below. As a general comment it is usual to write your odds ratio followed by the CI enclosed in a bracket. Eg AOR 2.1 with 95% CI (1.8,2.5). This is true both for the tables and the text. In the Results section of the abstract an incorrect result has been copied. For TSV to mothers with GDM, intrapartum SC was associated with increased odd of high levels of resuscitation compared to non-instrumental vaginal birth in non-macrosomic TSV (AOR 2.5; 95%CI; 2.2 to 2.9) - this should in fact be AOR 2.3 wiht CI(2.1,2.7). In the 'Study population' section it would be clearer to state in the

	second paragraph that the 276 were excluded from the multivariate logistic regression - and not from the multivariate analysis. This is because multivariate analysis in its true sense has not been undertaken on this data. And again in the final sentence of that paragraph state that 44148 were included in the multivariate logistic regression - not in the multivariate analysis. In the statistical analysis section I think it would help the reader to clearly state why the two types of analysis have been performed. I'm guessing the first which combines all the non pre-planned CS was done first to really get a feel for the data and then the analysis which treats each of the four categories done to gain more information, but it isn't clear to me. If there was some higher level reason for the two analyses (which are essentially the same but with aggregated data) then this should be spelt out, otherwise it looks as if you are over testing equivalent data and therefore increasing the chance of significant outcomes (this is the same as doing multiple t-tests on the same data). Other than these points the results are well argued from the data and the methodology sound.

REVIEWER	Wood, Stephen University of Calgary. Canada Competing interests: None
REVIEW RETURNED	22-Nov-2017

GENERAL COMMENTS	While it presents some interesting data it is not particularly novel and does not really provide information that would improve management of gestational and pre-gestational diabetes in pregnancy. I think that overall the authors need to consider what their primary study question was or did they just wish to describe outcomes. I think more focus on what the important study questions are would lead to needed changes in the analysis and could improve the paper. Specific Comments 1. If they had any intrapartum stillbirths these should have been included. I think they should also state how many antepartum stillbirths occurred and were excluded. If they were unable to distinguish between intrapartum and antepartum stillbirth and this is why they restricted the analysis to live birth this should be stated. Admittedly, intrapartum SB is rare but they have a pretty big population. I think their adverse outcomes should include neonatal death and that the numbers should be explicitly provided. 2. The number of previous cesarean sections should have been provided in table 1 and 2. It would give an idea of how many of the prelabor CS were repeat CS. 3. Type of labor in the non prelabor CS groups would be useful information. 4. I think the second analysis needs a major rethink or at least more considerations of what it means. I think it is very good that the authors have presented an analysis comparing prelabor CS with trial of vaginal birth. This is appropriate as it compares two choices that are available to patients and physicians. The second analysis, (table 4)comparison by eventual route of delivery, does not. Comparing instrumental vaginal deliveries with all intrapartum CS and spontaneous vaginal deliveries does not,as if labor arrests at 6cm or significant fetal distress occurs then there is no option to choose another mode of delivery. However, a comparison between

	instrumental vaginal delivery and intrapartum CS in the second stage, may be more meaningful but is still not perfect unless the authors had data on station at delivery. 5. The authors seem very interested in macrosomia but themanner in which the analysis is presented makes it very unclear if it is associated with an adverse outcome. Macrosomia is not entered into the model itself the results of the adjusted analysis are presented separately for macrosomic and non-macrosomic fetuses……looking at the rates in the tables it really looks like adverse oucomes are not increased in macrosomic fetuses. A term for macrosomia should be entered as a variable in the adjusted analysis. 6. The authors also need to consider how clinically important macrosomia is given that there is absolutely no data suggesting it can be accurately diagnosed prior to delivery. Therefore, even if macrosomia is associated with adverse outcome it is severely limited as a clinically useful marker(1). 7. I think they need more references to support their definition of adverse neonatal outcome. Their definition of “high level resuscitation” includes intermittent PPV by mask which itself does not really indicate a clear neonatal morbidity. Use of intubation for resuscitation or chest compressions is more likely to reflect a hypoxic state at delivery. Using such a mild and common (5-10% had high level resuscitation) may have made detecting differences in true adverse events more difficult. 8. The high rates of NICU/SCN admission in the whole population requires some comment in the discussion. Most of these were likely reflex admissions due to a protocol to admit all of these at some centers. I think they need to describe if there was significant variability by center. 9. I think the analysis should be done separately by GDM and pre-existing DM or these should be variables entered in the model. 1. Anonymous. Practice Bulletin No. 173: Fetal Macrosomia. Obstetrics & Gynecology. 2016;128(5):e195-e209.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

This is a paper that brings new information into the field, and is therefore suitable for publication. In fact, I have been telling students and fellows for years (from personal experience) that instrumental delivery is generally not a good option in diabetic patients. Here is some valuable evidence that may affect clinical practice.

Authors: We thank the reviewer for these comments.

- The authors mention some limitations of the study (p 13). However, for some reason, they exluded a mere 276 pregnancies because of "birth defects". Clearly, the rate of congenital malformations must be higher than 0.4%, particularly in a condition such as maternal diabetes. We therefore need more information on these birth defects (severe, life-threatening defects, eg cardiopulmonary?). If not, I can see no reason for excluding this small number of pregnancies.

Authors: The rate of congenital malformations among the whole population was not captured in our database. The rate presented in the method section (0.4%) is the rate of Live-born term singleton in vertex presentation who admitted to NICU/SCN due to birth defects which can explain the lower rate than the known rate among women with diabetes during pregnancy. Type of birth defect was not captured in our database for this reason we cannot provide more information about type of birth defects. We excluded admission to NICU/SCN due to birth defect from the analysis to reduce the confounding effect of congenital malformations on the neonatal outcomes.

- A further limitation is the absence on umbilical artery pH or lactate levels. Is this not standard in NSW?

Authors: This information was not captured in NSW PDC. This limitation was added to the limitation section which has been updated as detailed below

"The limitation of the study is the lack of information on reasons for NICU/SCN admissions, maternal body mass index and on umbilical artery pH and lactate levels. To remove the confounding related to birth defects, we excluded TSV admitted to NICU/SCN because of birth defects from our multivariable logistic regression. However, we are unable to adjust for maternal body mass index, an independent risk factor for adverse pregnancy outcomes such as low Apgar score and a higher rate of admission to NICU…."

- Instrumental deliveries: is this mainly forceps or vacuum? Any figures on this available?

Authors: Yes, Instrumental vaginal births include forceps or vacuum. Please see below percentages of forceps and vacuum birth among women who had instrumental vaginal birth

	Forceps n (%)	**Vacuum n (%)**	**Total instrumental n (%)**
Pre-existing diabetes	145 (36.5)	252 (63.5)	397 (100.0)
GDM	1726 (34.4)	3291 (65.6)	5017 (100.0)

- Tables 1 and 2. Clearly, many practicioners in NSW are not following guidelines regarding GA at delivery; a large percentage of mothers with pre-existing diabetes

delivered at 39 or >39 weeks GA, and a significant percentage of mothers with GDM delivered at >40 weeks GA. Do the authors see an effect of GA in their analyses?

Authors: A secondary objective of the study was to describe whether the clinical practice varied from the guidelines for pre-existing diabetes and GDM. We agree that our results show that clinical practice is varied from the guidelines, however, Our study is a pre-guideline study NICE guideline was publish in 2015, it will be interesting to know if the practice changed after 2015. Our study focus was on term live-born singleton in vertex presentation. Therefore. We did not stratify the data by gestational age. The text for the discussion section has been updated as detailed below

"Our study provides population-level evidence on the association between mode of birth and neonatal outcomes of TSV bor to mothers with diabetes during pregnancy in NSW. Our study also provides information about clinical practice for mothers with diabetes during pregnancy"

Reference

National Institute for Health and Clinical Excellence (NICE). Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period: National Institute for Health and Clinical Excellence, 2015.

- Table 3. The comparator group (planned vaginal birth) should be presented first.

Authors: Table 3 was revised and planned vaginal birth was presented first

- Table 4 and Discussion. Many adjusted odds ratios are <2 or around 2, ie a moderate increase. What can be extrapolated from these moderate risk increases in terms of long-term encephalopathy (eg, CP)?

Authors: Cerebral palsy is out of our study focus and we acknowledge it as an area for future research

- Table 4 and Discussion. Admission to NICU is only partly driven by clinical necessity but can also be the result of established practice patterns, eg some maternities will routinely admit babies of diabetic mothers with a birthweight >4 kg because of concerns for hypoglyemia. Again, the lack of "hard endpoints" (pH, lactate) is a limitation.

Authors: We **a**gree with the reviewer comment, the text of the limitation section has been revised to clarify that macrosomic babies my routinely admitted to NICU/SCN because of concerns for hypoglycaemia as detailed below

"The limitation of the study is the lack of information on reasons for NICU/SCN admissions as number of macrosomic TSV are routinely admitted to NICU/SCN for expected hypoglycaemia without clinical necessity which increases the rate of admission to NICU/SCN. Some services do have a routine policy of admitting babies born to mothers with diabetes to a NICU/SCN hence the numbers could be higher. Another limitation is the lack of information on maternal body mass index"

- There is a shift going on from primary to secondary cesarean sections in diabetic patients, eg see evidence in Finland (Teramo et al). More and more women with diabetes resent being seen as "pathologic cases" and strongly desire "a natural childbirth, like everybody else". Do the authors have any comments on this change in practice pattern in view of their findings?

Authors: Unfortunately, our dataset does not contain any information on women experiences and satisfaction with their care pathway. However it is true among our study population both pre-labour and intrapartum caesarean section have increased. The increase is in line with the increase in the overall caesarean section among Australian general population (Laws PJ & Sullivan EA 2004; Hilder et al. 2014). Our study provides data to the mothers to help them participate in the decision making around method of birth.

References

Laws PJ & Sullivan EA. Australia's mothers and babies 2002. Perinatal Statistics Series No. 15. Cat. No. PER 28.Sydney: AIHW National Perinatal Statistics Unit, 2004

Hilder L, Zhichao Z, Parker M, Jahan S, Chambers GM. Australia's mothers and babies 2012. Perinatal statistics series no. 30. Cat. no. PER 69. Canberra: AIHW, 2014

Reviewer: 2

I believe the data obtained in this study is important and should be published. However, I find the study question unclear. If the primary question is association between mode of birth and neonatal adverse outcomes in maternal diabetes (as suggested in the intervention section), then that should be clarified, with secondary objective of comparison of outcomes in macrosomic vs nonmacrosomic infants. Consequently, the results are difficult to follow and to interpret. The additional analysis of GDM vs pre-existing DM adds a new variable that was not addressed in the primary objective and makes this quite confusing to read.

Authors: We thank the Reviewer for these comments.

The aim of the study is to compare neonatal outcomes for live-born term singletons in vertex presentation born to women with diabetes during pregnancy by method of birth. The analysis was stratified by diabetes status (pre-existing diabetes, GDM) as pre-existing diabetes and GDM are different in their effect on pregnancy outcomes, with pre-gestational diabetes being associated with more complicated outcomes. (Abouzeid et al. 2014, Shand et al. 2008). In addition, guidelines have different recommendations for the two conditions (NICE 2015).Further classification was done by birthweight (i.e. macrosomic & non-macrosomic) because macrosomia is the main concern in the decision around mode of birth and guidelines recommend different management in case of

suspected macrosomia (ADPIS 2005)(NICE 2015). The text that stated the aim of the study in the introduction section has been revised to clarify the aim of the study as detailed below

“Our study aimed to compare adverse neonatal outcomes for live-born term singletons in vertex presentation (TSV) born to mothers with diabetes during pregnancy (pre-existing diabetes and GDM) by mode of birth stratified macrosomia (macrosomic and non-macrosomic TSV).”

References:

Abouzeid M, Versace VL, Janus ED, Davey M-A, Philpot B, Oats J*, et al.* A population-based observational study of diabetes during pregnancy in Victoria, Australia, 1999–2008. *BMJ Open* 2014;4(11):e005394.

Shand AW, Bell JC, McElduff A,et al. Outcomes of pregnancies in women with pre-gestational diabetes mellitus and gestational diabetes mellitus; a population-based study in New South Wales, Australia, 1998–2002. *Diabet Med* 2008;25(6):708-715.

National Institute for Health and Clinical Excellence (NICE). Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period: National Institute for Health and Clinical Excellence, 2015.

Australasian Diabetes in Pregnancy Society (ADIPS).'The Australasian Diabetes in Pregnancy Society consensus guidelines for the management of type 1 and type 2 diabetes in relation to pregnancy', *Med J Aust* 2005:183(7): pp. 373-7.

Of note, fetal macrosomia can only be predicted, not diagnosed. Therefore, to make a conclusion that 'Pregnant women with diabetes, particularly those with fetal macrosomia...' cannot be made. This is especially true given the inaccuracy sonographically determined estimated fetal weight.

Authors: We agree with the reviewer that fetal macrosomia can only be predicted, the text for the conclusion has been revised as detailed below

“Pregnant women with diabetes, particularly those with suspected fetal macrosomia, need to be aware of the increased likelihood of adverse neonatal outcomes following instrumental vaginal birth and intrapartum CS when planning mode of birth”

The authors should also address why shoulder dystocia was not addressed, as this is a major clinical concern amongst infants born of diabetic mothers

Authors: We agree with the reviewer that shoulder dystocia is a major clinical concern amongst infants born of diabetic mothers. Shoulder dystocia was not captured in NSW PDC. This limitation has been added to the limitation section. The text in the limitation section has been revised as detailed below

"….We used stratification by estimated fetal macrosomia using birthweight to limit the impact of maternal body mass index on the mode of birth and neonatal outcomes. We are also unable to adjust for shoulder dystocia as it was not captured in NSW PDC."

Reviewer: 3

This is a well written paper in an interesting area. The statistics and explanations are on the whole correct, however see the comments below. As a general comment it is usual to write your odds ratio followed by the CI enclosed in a bracket. Eg AOR 2.1 with 95% CI (1.8,2.5). This is true both for the tables and the text.

Authors: We thank the Reviewer for these comments. The text has been revised to write the odds ratio followed by the CI enclosed in a bracket.

In the Results section of the abstract an incorrect result has been copied. For TSV to mothers with GDM, intrapartum SC was associated with increased odd of high levels of resuscitation compared to non-instrumental vaginal birth in non-macrosomic TSV (AOR 2.5; 95%CI; 2.2 to 2.9) - this should in fact be AOR 2.3 wiht CI(2.1,2.7).

Authors: We than the reviewer for indicating this error, the text for the results section in the abstract has been corrected as detailed below

"For TSV to mothers with GDM, intrapartum CS was associated with increased odds of high-levels of resuscitation compared to non-instrumental vaginal birth in non-macrosomic TSV (AOR 2.3; 95% CI(2.1 to 2.7))."

In the 'Study population' section it would be clearer to state in the second paragraph that the 276 were excluded from the multivariate logistic regression - and not from the multivariate analysis. This is because multivariate analysis in its true sense has not been undertaken on this data. And again in the final sentence of that paragraph state that 44148 were included in the multivariate logistic regression - not in the multivariate analysis.

Authors: The text in the 'Study population' section has been revised as detailed below

"Of our study population, 276 (0.4%) TSV were excluded from the multivariate logistic regression due to admision to neonatal intensive care unit (NICU) or special care nursery (SCN) with one or more diagnosed birth defects, and 71 (0.1%) were excluded because of missing data (mode of birth, birthweight, and admission to NICU or SCN due to birth defect). A total of 4 458 live-born TSV born to mothers with pre-existing diabetes and 44 148 born to mothers with GDM were included in the multivariate logistic regression."

In the statistical analysis section I think it would help the reader to clearly state why the two types of analysis have been performed. I'm guessing the first which combines all the non pre-planned CS was done first to really get a feel for the data and then the analysis which treats each of the four categories done to gain more information, but it isn't clear to me. If there was some higher level reason for the two analyses (which are essentially the same but with aggregated data) then this should be spelt out, otherwise it looks as if you are over testing equivalent data and therefore increasing the chance of significant outcomes (this is the same as doing multiple t-tests on the same data).

Authors: The first analysis was to compare neonatal outcomes between live-born TSV born after pre-labour caesarean section and all other mode of birth to inform the decision of performing pre-labour caesarean section or proceed to planned vaginal birth. The second analysis was performed to help inform the decision in the situation were vaginal birth is planned (i.e. to compare non-instrumental vaginal birth to all other mode of births). The text for the statistical analysis section has been revised add further clarification as detailed below

"Multivariate logistic regression was used to investigate the likelihood of adverse neonatal outcomes by mode of birth. Two analyses were conducted; the first compared TSV born by pre-labour CS with TSV born by all other modes of birth combined as planned vaginal births. This first analysis was performed to inform the decision of performing pre-labour caesarean section or proceed to planned vaginal birth. The second compared TSV born by non-instrumental vaginal birth, TSV who were planned as vaginal births but for whom resorting to instrumental birth and intrapartum CS, and TSV born by pre-labour CS. The second analysis was performed to help inform the decision in the situation were vaginal birth is planned"

Reviewer: 4

While it presents some interesting data it is not particularly novel and does not really provide information that would improve management of gestational and pre-gestational diabetes in pregnancy. I think that overall the authors need to consider what their primary study question was or did they just wish to describe outcomes. I think more focus on what the important study questions are would lead to needed changes in the analysis and could improve the paper.

Authors: We thank the reviewer for these comments.

1. If they had any intrapartum stillbirths these should have been included. I think they should also state how many antepartum stillbirths occurred and were excluded. If they were unable to distinguish between intrapartum and antepartum stillbirth and this is why they restricted the analysis to live birth this should be stated. Admittedly, intrapartum SB is rare but they have a pretty big population. I think their adverse outcomes should include neonatal death and that the numbers should be explicitly provided.

Authors: we agree with the reviewer that intrapartum stillbirths are important. We were unable to identify times of stillbirth (antepartum or intrapartum) in our data. Therefore the analysis produced on live-births only. There were 18 (0.4%) stillborn term singletons in vertex presentation born to women with pre-existing diabetes and 83 (0.2%) born to women with GDM. Number of neonatal death was 17 among our population of these two (0.4 per 1000 live-born TSV) born to women with pre-existing diabetes and 15 (0.3per 1000 live-born TSV) born to women with GDM. The study population section in method has been revised to include number and proportion of still birth and the results sections has been revised to include number and rate of neonatal deaths as detailed below

Study population

"There were 48 983 TSV born during the study period of these 101 stillbirth (18 (0.4%) born to mothers with pre-existing diabetes and 83 (0.2%) born to mothers with GDM). Due to our inability to identify times of stillbirth (antepartum or intrapartum), these stillbirths were excluded from the study. The study includes all live-born TSV (n=48 882) born in NSW to mothers with diabetes during pregnancy between 1st January 2002 and 31st December 2012. Of these, 4501 (9.2%) were born to mothers with pre-existing diabetes and 44 381 (90.8%) were born to mothers with GDM."

Results section

Authors: At the end of the first paragraph of the result section, the text has been revised to include neonatal deaths as detailed below

"There were 17 neonatal deaths of these two (0.4 per 1000 live-born TSV) born to women with pre-existing diabetes and 15 (0.3 per 1000 live-born TSV) born to women with GDM."

2. The number of previous cesarean sections should have been provided in table 1 and 2. It would give an idea of how many of the prelabor CS were repeat CS.

Authors: Tables 1 and 2 have been updated to include number of previous caesarean sections.

3. Type of labor in the non prelabor CS groups would be useful information.

Authors: This information is included in the supplementary files (figures S1 & S2)

4. I think the second analysis needs a major rethink or at least more considerations of what it means. I think it is very good that the authors have presented an analysis comparing prelabor CS with trial of vaginal birth. This is appropriate as it compares two choices that are available to patients and physicians. The second analysis, (table 4)comparison by eventual route of delivery, does not. Comparing instrumental vaginal deliveries with all intrapartum CS and spontaneous vaginal deliveries does not,as if labor arrests at 6cm or significant fetal distress occurs then there is no option to choose another mode of delivery. However, a comparison between instrumental vaginal delivery and intrapartum CS in the second stage, may be more meaningful but is still not perfect unless the authors had data on station at delivery.

Authors: Our results from the second analysis showed that compared to non-instrumental vaginal birth, instrumental vaginal birth is associated with the worse neonatal outcomes, this is an important finding from population data which will help in decision making for mode of birth for women with diabetes. We do not have data on second stage CS to compare with instrumental delivery. We added this limitation to the limitation section which has been updated as detailed below

"We used stratification by estimated fetal macrosomia using birthweight to limit the impact of maternal body mass index on the mode of birth and neonatal outcomes. We also lack information on second stage CS which did not allow us to compare between intrapartum CS and instrumental vaginal birth"

5. The authors seem very interested in macrosomia but themanner in which the analysis is presented makes it very unclear if it is associated with an adverse outcome. Macrosomia is not entered into the model itself the results of the adjusted analysis are presented separately for macrosomic and non-macrosomic fetuses……looking at the rates in the tables it really looks like adverse oucomes are not increased in macrosomic fetuses. A term for macrosomia should be entered as a variable in the adjusted analysis.

Authors: Fetal macrosomia is one of the main concerns in management of women with diabetes and macrosomic babies are at greatest risk for perinatal morbidity and mortality Fetal (Maso et al 2014). Clinical practice guidelines suggested different management for women with suspected fetal macrosomia (ADPIS 2005; NICE 2015). Our results show that 25% of women who went into

labour and gave birth to macrosomic TSV, had intrapartum CS and 20% of women who went into labour and gave birth to non-macrosomic TSV had instrumental vaginal birth. which indicates the choice of preforming instrumental vaginal birth or intrapartum cs was influence by suspected fetal macrosomia. For this reason, we decided to stratify the analysis by macrosomia status to look at the results for macrosomic and non- macrosomic TSV separately. For this reason we stratified by macrosomia and not adjusted for it in the model.

References:

National Institute for Health and Clinical Excellence (NICE). Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period: National Institute for Health and Clinical Excellence, 2015.

Australasian Diabetes in Pregnancy Society (ADIPS).'The Australasian Diabetes in Pregnancy Society consensus guidelines for the management of type 1 and type 2 diabetes in relation to pregnancy', *Med J Aust* 2005:183(7): pp. 373-7.

Maso G, Piccoli M, Parolin S, Restaino S, Alberico S. Diabetes in pregnancy: timing and mode of delivery. *Curr Diab Rep*. 2014;14:506.

6. The authors also need to consider how clinically important macrosomia is given that there is absolutely no data suggesting it can be accurately diagnosed prior to delivery. Therefore, even if macrosomia is associated with adverse outcome it is severely limited as a clinically useful marker(1).

Authors: We agree with the reviewer that detecting macrosomia before delivery is imprecise. However, suspected macrosomia remain an important part of the outcome assessment, Clinical practice guidelines suggested different management for women with suspected fetal macrosomia (ADPIS 2005; NICE 2015). This is a retrospective study with macrosomia diagnosed post-delivery. We used birthweight 4000g as a definition for macrosomia. This definition adopted by the International Association of Diabetes in Pregnancy Study Group of birthweight (IDPSG 2015).

Reference:

National Institute for Health and Clinical Excellence (NICE). Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period: National Institute for Health and Clinical Excellence, 2015.

Australasian Diabetes in Pregnancy Society (ADIPS).'The Australasian Diabetes in Pregnancy Society consensus guidelines for the management of type 1 and type 2 diabetes in relation to pregnancy', *Med J Aust* 2005:183(7): pp. 373-7.

The International Association of Diabetes in Pregnancy Study Group Working Group on Outcome Definitions, Feig DS, Corcoy R, et al. Diabetes in pregnancy outcomes: A systematic review and proposed codification of definitions. *Diabetes Metab Res Rev* 2015;31(7):680-90. doi: 10.1002/dmrr.2640

7. I think they need more references to support their definition of adverse neonatal outcome. Their definition of "high level resuscitation" includes intermittent PPV by mask which itself does not really indicate a clear neonatal morbidity. Use of intubation for resuscitation or chest compressions is more likely to reflect a hypoxic state at delivery. Using such a mild and common (5-10% had high level

resuscitation) may have made detecting differences in true adverse events more difficult.

Authors: We agree with the reviewer that intermittent PPV by mask is not advanced resuscitation. According The Royal Australian and New Zealand College of Obstetricians and Gynaecologists guideline (RANZCOG 2015) ventilation via face mask is a basic neonatal resuscitation, therefore, it does not indicate neonatal morbidity. The text and the tables have been revised and "High-level resuscitation" has been change to the "need for resuscitation".

8. The high rates of NICU/SCN admission in the whole population requires some comment in the discussion. Most of these were likely reflex admissions due to a protocol to admit all of these at some centers. I think they need to describe if there was significant variability by center.

Authors: We agree with the reviewer that admission to NICU/SCN may vary by centre, however, we are unable to identify this variation from our data. The limitation section in the discussion has been revised as detailed below

"The limitation of the study is the lack of information on reasons for NICU/SCN admissions as number of macrosomic TSV are routinely admitted to NICU/SCN for expected hypoglycaemia without clinical necessity which increases the rate of admission to NICU/SCN. Some services do have a routine policy of admitting babies born to mothers with diabetes to a NICU/SCN hence the numbers could be higher…."

9. I think the analysis should be done separately by GDM and pre-existing DM or these should be variables entered in the model.

Authors: The current analysis was done separately by GDM and pre-existing diabetes.

VERSION 2 – REVIEW

REVIEWER	Hilliam, Rachel Mary The Open University UK Competing interests: None
REVIEW RETURNED	19-Dec-2017

GENERAL COMMENTS	Thank you for resubmitting this paper and your response to my comments and questions. This is much improved and the analysis is clearer.

REVIEWER	Verhaeghe, Johan KU Leuven, Belgium Competing interests: None

REVIEW RETURNED	26-Dec-2017

GENERAL COMMENTS	No further comments. Acceptable revision. Interesting findings.