Author's response to reviews

Title: Risk-adjusted operative delivery rates and maternal-neonatal outcomes as measures of quality assessment in obstetric care. A multicenter prospective study.

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EDITORIAL REQUESTS

CHANGE IN TITLE

CHANGES IN AUTHORSHIP
Gianpaolo Maso, Lorenzo Monasta, Monica Piccoli, Luca Ronfani, Marcella Montico, Francesco De Seta, Sara Parolin, Caterina Businelli, Laura Travan and Salvatore Alberico on behalf of The Multicenter Study Group on Mode of Delivery in Friuli Venezia Giulia.

CHANGES IN THE MANUSCRIPT
Funding-The funding information has been included within the Acknowledgements.
Ethics- Lines 464 and 465 has been removed from the manuscript as the relevant information is already included in the methods section.
Figures- The figures have been removed from the main body of the manuscript.
Tables- The separate descriptions of the tables have been removed from the manuscript.

REPLIES TO REVIEWER 1: JENNIFER LUTOMSKI
Major Revisions

Comment 1: I think the methods could be expanded in this manuscript. Better description of the prediction model would help clarify this work to the reader. I do not feel that it immediately comes across to the reader that adjustments are being made for obstetric volume and that is a critical point.

Our reply: We do agree with the Reviewer. In this regard we considered the obstetric volume into the risk adjustment evaluation of outcomes (new text, lines 214-218), and tried to better explain the methods in general.

Comment 2: I find some of the comparisons in the mode of delivery to be less than ideal. I think the authors should state the tearing is a condition of a vaginal birth and bladder injuries are largely a result of caesarean delivery. In this regard, the authors should state that if a condition is inherent of a mode of delivery, then no comparative analyses were performed.

Our reply: According to the Reviewer’s suggestion, the following sentences has been added into the final text (new text, lines 243-246): “Outcomes varied substantially by mode of delivery and some of them were obviously associated with only one mode of delivery (i.e. III-IV degree perineal tears). If a condition was inherent of a mode of delivery, then no comparative analyses were performed.”

Comment 3: Are the authors able to distinguish emergency versus elective caesarean deliveries? I think this would warrant an important sub-analysis. In this context, I would also recommend an analysis inclusive and exclusive of twin births. Although the numbers are likely small, I think twin births are a residual bias in the analysis.

Our reply: we considered the suggestion of the Reviewer. Instead of including other two sub-analyses, we decided to maintain the number of fetuses and to include the degree of urgency for intervention considering the acknowledged high risk of complications related to the delivery in the presence of impeding maternal and fetal compromise (new text, lines 193-196, 214).

Comment 4: I think there is an over-reliance on p-values throughout this paper. Although the authors remark that this is a relatively small birth cohort (which is true in regards to other obstetric studies), statistically, this number is quite large. For instance, in Table 2, the minor PPH rate varies between 2.32 to 2.48 and this shown to be a significant difference. However, clinically-speaking this is not a large difference – and this is a slippery slope when attempting to distinguish quality of care between units (which in essence what the authors are trying to convey). I think all the p-values should be removed from Table 2. In this regard, I think it would be clearer if the authors could include funnel plots (perhaps just of the composite rates) for the hospitals.

Our reply: We agree with the Reviewer. We removed all p-values from former table 2 and 3, and inserted 95% confidence intervals instead. We also added forest plots for the composite rates.
Comment 5: Perhaps I have missed this in the paper, but I also have a query regarding directionality in the case of neonatal outcomes. Could it be the hospitals with better/more advanced NICU services are the units with above-expected caesarean rates? I recognise that adjustments were made for neonatal complications; still, wouldn’t it be expected, for example, that infants delivered via caesarean have lower Apgar scores and higher admission rates to NICU? Infants at higher risk are more likely to be delivered via caesarean, and I don’t understand how this is a marker of quality of care. Residual confounding is potentially still an issue could obscure this association. Reassessment of neonatal conditions with justification of inclusion would be helpful. This point could also be explored in greater depth in the Discussion. I think this is an important point since the goal is for other obstetric units to monitor deliveries using methods applied by the authors.

Our reply: We thank the Reviewer for this comment. Considering her suggestion we considered the presence or absence of Neonatal Intensive Care Unit into the risk adjustment evaluation of outcomes (lines 217-218). Moreover the differences observed in neonatal outcomes according to mode of delivery and outlier status for assisted vaginal and caesarean deliveries were explored in the discussion (new text, lines 315-324, 353-361)

Comment 6: Given that this is a cohort study, converting the ORs to RRs is methodologically robust. However, there are methods superior to the Zhang conversion. Did the authors attempt a log-binomial regression or a Poisson regression with robust variance? There may be an issue with convergence, however these methods are preferable.

Our reply: We agree. We used a log-binomial regression to recalculate all RRs.

Comment 7: In the discussion, the authors explain that the impact obstetric volume differed relative to other studies. I think there should be shown in the results section. This would be the added benefit of the funnels plots for readers; they would be able to quickly and easily assess the impact of obstetric volume. Moreover, it is easier to visualize inter-unit variation.

Our reply: We agree. We used a log-binomial regression to recalculate all RRs. In regard to the obstetric volume, this variable has been included into the risk adjustment evaluation of outcomes and, stated in the discussion, differences in outcomes still remain among institutions (new text, lines 376-380: “This might not be the case of our study, because inter institutional variations in operative delivery rates and frequencies of adverse outcomes remained either between centers with less than 1000 deliveries/year and institutions with more than 1000 deliveries/year, despite the inclusion of obstetric volume, of type of neonatal organization (NICU availability) and delivery grade of urgency (emergency – no emergency) into the adjusted model.”).

Minor Revisions
1. Introduction, Line 82: I find the phrase “reflect efficient and appropriate care” misleading – I think I would prefer reflect “evidence-based intervention”.
Our reply: We modified the text according to Reviewer’s suggestion (new text, lines 78: “...with the implicit assumption that low rates may reflect evidence-based intervention”).

2. I believe it should be very clear in the introduction if adjusted rates in other studies are solely adjusting for obstetric volume, maternal risk factors or both. Our reply: The limitations of these studies are considered in depth in the discussion (new text, lines 325-343).

3. Introduction, Line 110: Instead of “our Region” the north-eastern region of Italy would be clearer for readers. Our reply: We modified the text according to Reviewer’s suggestion (new text, line 107).

4. Methods, Line 115: 18-month (singular); Also, I am not clear when the study was carried out. Would you please add the start and end date? Our reply: We modified the text according to reviewer’s suggestion (new text, lines 113-114: “We prospectively collected data on all deliveries occurring in the 11 hospitals of Friuli Venezia Giulia in a period of 18 months between July 2006 and December 2007.”)

5. Methods: Would the authors please specify if nearly all births are captured for the region? It appears so, but it would be interesting to know, for example, the home birth rate or if there are midwifery-led centers in the region. I think it would be also useful to clearly state that these are all hospitalised deliveries (or at least that is what I presume since they were all classified as Level I or Level III units). Our reply: We specified this point in the following sentence: “Virtually all births of the region were included in the study, given the very low rate of home births and the absence of birthing centers in area” (new text, lines 116-118).


7. Methods, Line 180: When is maternal BMI taken? This could have a impact on BMI figures. Typically, if recording pre-pregnancy BMI, <25kg/m2 or less is healthy weight and 25 to <30 is overweight and >=30kg/m2 is obese. BMI thresholds are slightly different in this paper, so a citation would be helpful Our reply: There was an error. We considered the pre-pregnancy maternal BMI as stated in the World Health Organization (2000) Obesity: preventing and managing the global epidemic. Report of the WHO consultation. WHO Technical Report Series. Geneva: World Health Organization (reference 16 has been added).
8. Methods: What infants were included in this analysis, i.e. what are the gestational age and/or birthweight thresholds? What viability cut-off is used for this study? It seems that there was only a gestational age/birth weight restriction for admission to NICU. I do not understand why this was the case and think this restriction warrants further explanation in the methods.

Our reply: Only deliveries with infants weighting more than 500 grams and/or after 24 weeks’ gestation were included into the analysis. The following sentence has been added in new text-lines 166-169: “Pregnancies complicated by antepartum stillbirths and/or life-threatening fetal congenital anomalies and deliveries with infants weighting less than 500 grams and/or below 24 weeks’ gestation were excluded, to avoid potential bias in the evaluation of the outcomes.”

9. Methods, Lines 210-213: Weren’t the data also adjusted for gestational age?
Our reply: this was already specified in the manuscript - new text, lines 177-178 “gestational age at delivery (reference 37-41 weeks, <30 weeks, 30-36 weeks, >41 week)”

10. Results: There is too much information on Table 1, impeding readability. I would suggest splitting the table into two separate tables. Table 1 would be the incidence rates and Table 2 would be the risk ratios. Moreover, the p-values should be removed from the table and replaced with the 95% CIs. The p-values are essentially meaningless, and better interpretation of the data can be yielded with the CIs.
Our reply: Table 1 was split as suggested. p-values were removed and replaced with 95% CIs.

11. Results, Line 242: It would be helpful if the authors would more clearly state how the bivariate and multivariate analyses differed. Across what specific components?
Our reply: We decided to delete the sentence on the differences existing between bivariate and multivariate analyses. Of course, as expected, there are many differences, because, as expected, multivariate analyses took into account several well know confounders in the relation between delivery mode and maternal and neonatal outcomes. However, this is not exactly the focus of this study, and we thought this might end up “confounding” the readers.

12. The CI-ranges can be added to Figure 1.
Our reply: The CI-ranges have been added.

13. Methods, Lines 182-183: The sentence structure switches which makes it a bit confusing. To keep the flow, it would be better to say parity (reference multiparous, nulliparous), gestations (reference singleton, twin).
Our reply: We modified the text according to the Reviewer’s suggestion (new text, lines 179-180)
REPLIES TO REVIEWER 2: JEREMY OATS

Comment 1: In the Methodology the antenatal clinical risk factors that were used must be detailed.

Our reply: Antenatal risk factors have been described in the text according with Reviewer’s suggestion (new text, lines 183-192). We used the scheme adopted by Bailit et al. in their manuscript Bailit JL, Love TE, Dawson NV: Quality of obstetric care and risk-adjusted primary caesarean delivery rates. Am J Obstet Gynecol 2006, 194:402-7.

Comment 2: A very important determinant of perinatal and obstetric outcome is socio-economic status and this needs to be considered and adjusted for in the data analysis.

Our reply: We thank the reviewer for this comment. As indicated in the discussion this point was a limitation of our study as specified in new text-lines 389-395: “Second, we did not include other variables, such as race/ethnicity or socio-economic status or habits (i.e. smoking), in the risk adjustment. However, the former was not assessed because of the very low prevalence of non-Caucasians in our region and considering this variable should not have a relevant role in the prediction of operative delivery [32]; the latter was not considered because the collected data included all the clinical adverse conditions that are associated with “bad” habits (i.e. intrauterine growth restriction, preterm delivery).”

Comment 3: Was cigarette smoking data collected and analysed?

Our reply: See previous reply.

Comment 4: The classification of “minor” maternal adverse outcomes is unusual eg admission to adult ICU. In most analyses of severe maternal morbidity, this is used as the primary determinant.

Our reply: We decided not to consider this parameter as a variable of severe morbidity because semi-intensive care is not available in the units of our region and the intensive care unit is commonly used in cases needing a strict post-partum follow up (e.g. pre-eclamptic mother soon after delivery). Anyway we used similar criteria as those proposed by McMahon MJ, Luther ER, Bowes WA, Olshan AF: Comparison of a trial of labor with an elective second caesarean section. N Engl J Med 1996;335:689-95 (reference 10 added)

Comment 5: Likewise severe neonatal hypoxia as indicated by a cord pH <7.0 and base deficit >12 mmol/l, admission to NICU > 24 hours are not considered by many as being "minor".

Our reply: We did not consider this parameter as a variable of severe morbidity, because it does not imply the inevitable onset of neonatal severe complications. Nonetheless we considered the possible sequelae of severe acidosis, such as perinatal mortality, including intrapartum death, and abnormal neurological
outcome. In this regard the reference Fong KW, Ohlsson A, Hannah ME, Grisaru S, Kingdom J, Cohen H, Ryan M, Windrim R, Foster G, Amankwah K: Prediction of perinatal outcome in fetuses suspected to have intrauterine growth restriction: Doppler US study of fetal cerebral, renal, and umbilical arteries. Radiology 1999;213:681-9, has been added [12]. Anyway we replaced the terms major and minor adverse outcomes with life threatening and non-life threatening complications, respectively, according to Editor’s suggestion.

Comment 6: What was the definition of severe intrauterine growth factor?
Our reply: There is no agreement on the definition of IUGR. As stated in new text-lines 189-190, we adopted the following definition, “…fetal abdominal circumference or estimated fetal weight less than the 10th centile.”

Comment 7: It is not clear if intrapartum fetal deaths were included or excluded and again many would consider these to be major perinatal adverse events. This needs to be clarified.
Our reply: We thank the reviewer for this comment. As stated in new text-lines 166-169: “Pregnancies complicated by antepartum stillbirths and/or life-threatening fetal congenital anomalies and deliveries with infants weighting less than 500 grams and/or below 24 weeks’ gestation were excluded to avoid potential bias in the evaluation of the outcomes”.