Author’s response to reviews

Title: A cluster-randomized field trial to reduce cesarean section rates with a multifaceted intervention in Shanghai, China

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Dear Editor,

Thank you and the reviewers for the useful comments. Our responses are as follows:

Reviewer #2 Barry S Schifrin, M.D.: REVIEW

Comment 1: The authors offer the statement that vaginal delivery (presumably if successful) is associated with fewer complications than is cesarean section (for all deliveries). This may be true, but the statement camouflages the understanding that if you are only going to have one child and the child's outcome is the primary concern, that an elective cesarean section at term is more likely to realize that objective than a attempted vaginal delivery - including operative vaginal delivery. That would seem to be a notion that has not been lost on patients with previously restricted reproductive options that have only very recently been removed.

Response 1: We agree with the reviewer in that some women are willing to take any health risk in order for the baby to avoid any possible risk. While this is understandable, the hazard that a CS may exert, despite small, is real particularly at low level, rural hospitals.

Comment 2: I offer these comments (derived from Wikipedia and from the authors) to suggest that the situation with regard to obstetrical care and the route of delivery is likely in considerable flux in China (as well as other countries) given the incentives to reduce their very high national cesarean section rate in the face of the very recent abandonment of the one-child restriction. I believe that more attention should be given in this paper to these issues.

Response 2: Thank you for your suggestion. We agree with the caution that it may not be realistic to rapidly reduce the overall CS rate in a short run because the high prevalence of scarred uterus has resulted in an elevated rate of repeat CS. We have added the following sentence in the Discussion (Line 354-355, page 16): “It should be noted that the considerable flux of declining primary CS and increasing repeat CS may hamper a substantial decline in the overall CS rate in the near future.”

Comment 3: The authors set out to implement a multifaceted (3-tier) intervention program to reduce the frequency of cesarean section including more targeted prenatal health education improved hospital policy and training of doulas and midwives. They found that this approach implemented over a rather large population did not significantly reduce the cesarean section rate, at least over the short term, in the subject hospitals in Shanghai, China. It is difficult to fault the design of the study in terms of the baseline survey conducted prior to the intervention. This baseline survey involving well over 10,000 deliveries represented about one-sixth of the total births in Shanghai in the 1st half of 2016.

Response 3: Thank you.

Comment 4: An intention-to-treat analysis used generalized estimating equations (GEE) to assess the effects of these multifaceted interventions on cesarean section rates. The authors further evaluated the intervention effect in each group according to the classification of the timing and urgency of cesarean section. In this respect, the authors do not mention the use of operative vaginal delivery - statistics
which should be included if one is to make sense of the outcomes.

Response 4: Thank you for the suggestion. We agree that operative vaginal delivery can also be an important outcome. Unfortunately, the incidence of this delivery mode was uncommon (about 2%, Table 1), making it statistically underpowered to be used as a separate outcome. Thus, our study focused on CS rate as the primary outcome. Nonetheless, we examined this issue in Table 5, which showed that the intervention had a suggestive but statistically non-significant effect \( \text{OR}=0.61 (0.31, 1.21) \) (Table 5). We are now highlighting this finding in the Results section (Line 286-288, page 13).

Comment 5: There are several features of this study that would seem to have preordained the outcome of the study. Most obvious would appear to be the notion that it is the impact of the cesarean section rate, across-the-board, that is being assessed, irrespective of the fact that certain indications for cesarean section, with marginal room for reduction, contribute only minimally to the overall cesarean section rate. Assessing the impact of interventions on the total cesarean section rate is not likely to be as helpful as a more focused assessment according to the indication for intervention. Thus, success rates of initiatives to lower the cesarean section rate will likely differ according to indication. Attempting to reduce intervention for dysfunctional labor or fetal distress will likely prove more effective than for indications of fetal malposition, compound presentation or catastrophic event. Concentrating on the overall cesarean section rate only camouflages subsets of indication for cesarean section where progress has indeed been made. Indeed, in the study, the authors found a reduction in the use of cesarean section in patients in labor, but an increase in the use of repeat cesarean section. To me, the reduction in intrapartum cesarean section represents progress and is an area that should be explored and offered as a provisional benefit of the study rather than the conclusion that there was no change in the (overall) cesarean section rate. The increase in the cesarean section rate for repeat cesarean sections likely requires a different initiative and a changed demographic. This is likely happening at the present time with the simultaneous introduction of initiatives and the removal of the one-child policy.

Response 5: This is an excellent point. While the primary outcome of the trial was the overall CS, we had planned to examine CS rates in the Robson 10 subgroups (Table 3). We have now made this point clearer in the Abstract (Line 56-58, page 2) and Methods sections (Line 189-190, page 8). Unfortunately, almost all the subgroup analyses turned out to be statistically non-significant, making our conclusions difficult to draw. To be conservative, we decided to conclude with a statement of null overall effect.

Comment 6: I am disturbed by the authors' use of the term "unnecessary cesarean section," a term that is not defined and indeed is probably undefinable. One really cannot speak of "unnecessary" cesarean sections in an environment where the indications are so diverse and the mother is entitled to make decisions for cesarean section on an elective basis. For example, it seems contradictory, to refer to cesarean section for "fetal distress" or one of its euphemisms as "unnecessary" unless the pH of the umbilical artery is less than 7.0. Such an assessment places more value on the "diagnosis" than on the outcome. A better term is required; perhaps "justifiable/not justified," "defensible / not defensible," or "reasonable / not reasonable". Similarly, a requirement for a "second-opinion" introduces political considerations and cannot be relied upon during an emergency situation. True peer review of both the clinical details along with an authoritative review of the fetal monitor tracing and affirmative feedback to the practitioner will probably provide a more effective teaching (remedial) experience.

Response 6: We would agree with the reviewer in that “unnecessary CS” is often ill-defined, subjective and included a variety of causes. Unfortunately, an optimal term without suffering from the same deficiencies seems hard to find. We, therefore, turned to the literature on this issue. In our references, 8
publications, including a WHO Statement and a paper in the Lancet, used the term “unnecessary CS” (references 6, 16, 20, 21, 23, 27, 38, 44). Thus, we are inclined to keep this term, to be consistent with the literature. But we are still open to suggestions.

Comment 7: To have a material effect on the cesarean section rate which varies so widely by physician, by practice type, by insurance, by patient desires, will ultimately require a cultural change along with more directed initiatives. The authors do not provide an assessment of the variations in practice among the different hospitals. Perhaps, requiring the surgeon to complete a detailed (pre-formatted) reporting form that uncovers the indications (and intentions - behavior) of the surgeon would better inform the approach remedial policies should take. In this respect, an understanding of what created the emergency (excessive contractions, pushing strategy, timely assessment of progress in labor, evolution of the CTG) will better inform the decision to intervene. A program dedicated to the marked reduction of the rate of "emergency" cesarean section during a trial of labor is a measure of the quality of obstetrical care whose understanding and amelioration would likely make labors safer and ultimately reduce the overall cesarean section rate. A measure of urgency should be added to the Robson criteria.

Response 7: Thank you for this suggestion for future studies. Unfortunately, our study did not conduct such a survey among the obstetricians. We have now added this point to the Discussion (Line 379-388, page 17-18): “We also knew that physicians play a critical role in CS decision making, prelabor and intrapartum. But the “physician factor” is also complicated by multiple forces. The shortage of medical staff to handle the large volume of delivery, financial incentives, and constrained doctor-patient relationship all likely draw the decision leaning towards CS. Physicians’ practice pattern is often unclear. Our trial did not attempt to address the physician factor directly, which may be an important determinant in the success of an intervention trial on reducing CS rate. For future studies, an assessment of practice pattern among physicians may provide useful insights. For example, asking the surgeon to complete a detailed reporting form that uncovers the indications as well as intentions and actions of the surgeon may help to identify potential targets for intervention. Given its importance, the physician factor could be a focus for future research.”

Comment 8: It seems reasonable to view the article, with its considerable effort and large number of patients as an anchor point for subsequent studies on the impact of the various initiatives as the population moves away from the generation-long restriction imposed on reproductive activities by the one-child policy. The authors are encouraged to pursue their efforts over time - the objective of safely reducing the cesarean section rate is a worthy one.

Response 8: Thank you. We will do that.

Reviewer #3 Manuel C Vallejo, MD, DMD: BMED-D-19-01548

Comment 9: Page 7, line 132 - what were the components of the baseline survey? What questions were asked?

Response 9: Medical records of mothers and newborns were retrieved and information on maternal demographic characteristics, reproductive history, as well as maternal and neonatal conditions were abstracted by specially trained research staff for both the baseline and evaluation surveys (Methods section, line 155-158, page 7).

Comment 10: Page 7, line 144 - what specifically was the previous research?
Response 10: Relevant references have been added (Methods section, line 160, page 7).

Comment 11: Discussion - since you had a non-effect with your intervention(s), what would you do or recommend for future studies? You imply the government intervention is needed to effect meaningful change; would you elicit government intervention in the future to decrease the cesarean section rate? Would you target Obstetricians in the future?

Response 11: Yes, we would recommend to work with government and also conduct interventions targeting obstetricians. In the Discussion, we have now added the following paragraph on Discussion section (Line 379-388, page 17-18): “We also knew that physicians play a critical role in CS decision making, prelabor and intrapartum. But the “physician factor” is also complicated by multiple forces. The shortage of medical staff to handle the large volume of delivery, financial incentives, and constrained doctor-patient relationship all likely draw the decision leaning towards CS. Physicians’ practice pattern is often unclear. Our trial did not attempt to address the physician factor directly, which may be an important determinant in the success of an intervention trial on reducing CS rate. For future studies, an assessment of practice pattern among physicians may provide useful insights. For example, asking the surgeon to complete a detailed reporting form that uncovers the indications as well as intentions and actions of the surgeon may help to identify potential targets for intervention. Given its importance, the physician factor could be a focus for future research.” And in the Discussion, we concluded on Page 18 (Line 388-389): “But the government health policy that can address some of the above issues may be more effective.”

Comment 12: Table 5 - please discuss why artificial rupture of the membranes is significant in the results section?

Response 12: Thank you for pointing this out. After a second thought, we agree with the reviewer that AROM is probably not so important an outcome. Therefore, we delete this item in narrative and Table 5.

Reviewer #4 Anna Locatelli: The paper reports the effect of a multifaceted intervention intended to reduce CS in Shanghai with negative results. After this strong effort we hoped to see different results.

Comment 13: Methodological observations: The type of assistance proposed to the women should be clearly expressed: i.e. the % of doula was different in the two groups but with such a low rate of doula and epidural how many women had a midwife in one-to-one relationship?

Response 13: There appeared to have had some difference in the rate of doula use but it did not reach statistical significance. In public hospitals in China, there is hardly any one-to-one midwife service because of the high volume of delivery. All our participating hospitals were public hospitals.

Comment 14: The intervention continued during the period of post-intervention group? Did the author could evaluate a possible temporal trend in some categories?

Response 14: We were no longer making conscious efforts during the post-intervention period because the operation of the interventions did cost money to run. The project had to be closed due to the funding limitation. Thus, data afterwards may not be reliable for a possible temporal trend.
Comment 15: The Robson classification should be reported as in WHO document, with the same use of the 10 classes proposed (i.e. breech are separated from transverse lie..)

Response 15: All breech and transverse lie combined accounted for less than 5% of the deliveries. We did not have sufficient statistical power to test the difference between the intervention and control groups in a meaningful way. More importantly, these groups had such a high CS rate (e.g., 100% in transverse lie) that they contributed little useful information for the purpose of our study. Thus, we combined these three categories into “non-cephalic presentation group”. We have made a note in Table 3.

Comment 16: The results should be more detailed in the text because only reading the tables we can understand some main results, like the rate of CS in the main categories of Robson

Response 16: Thank you for the suggestion. We have added more narratives in the Results on Page 12.

Comment 17: Table 2 and 5: report also statistical comparisons between pre and post intervention

Response 17: We have added the statistical comparisons between pre and post intervention in Table 2 and Table 5.

Comment 18: Table 5: row on operative delivery in patients with previous CS are useless, they are episodic cases

Response 18: Yes, the incidence of assisted vaginal delivery was small. But Reviewer 2 thought that it is important to present this outcome. Thus, we are inclined to keep them in the table but not to highlight this finding.

Comment 19: Regarding the interpretation of the data the main problem in Shanghai seems to be the culture of delivery because the high rate of prelabor cesarean section in nulliparous, pluriparous and previous CS limit the effect of the intervention proposed and probably the effect could not be seen in such a short interval of time. If this culture is deep-rooted in the women and in the doctors only a longer time could demonstrate a beneficial effect of the intervention proposed. We should also emphasize that the interventions were mostly educational and education needs time.

Response 19: This is a good point. Thank you. More discussion has been added (Discussion section, line 363-366, page 17).

Comment 20: The increase (induction) or absence of reduction (episiotomy) of the medical intervention should be discussed and justified.

Response 20: The induction rate increased slightly in the post-intervention period because the two-child policy has encouraged some women to want to have a vaginal birth. In these women, when the gestational age is close to 41 weeks, for example, obstetricians would recommend an induction now rather than an outright CS. The gradual decline in episiotomy is a general trend. Our intervention did not include that component. We appreciate the suggestions by the reviewer, but felt that these two points are not directly related to the main issue of the trial. And the Discussion is already becoming lengthy. Thus, we decided not to include another paragraph to discuss the above issues. Should this be deemed necessary, however, we would be glad to add that to the Discussion.
Comment 21: The authors report that in China rise in CS is related to reasons that could not be corrected in 6 months.

Response 21: We have placed additional discussion (Discussion section, line 363-366, page 17).

Comment 22: Regarding the present study in particular:
Fear of labor pain, concerns about complications such as urinary incontinence and lower quality of sex life after vaginal delivery: we see a low rate of doula and epidural and high rate of episiotomy not changed during the study, this result should be deeply discussed.

The shortage of nurses/midwives and the large volume of deliveries often lead to more convenient and scheduled CS: in this field education should be for politicians!

The constrained doctor-patient relationship and insufficient training in vaginal delivery also exacerbated the situation: this problem regards academia

Higher financial incentives for CS versus vaginal delivery may lead to the preferred choice of CS: idem see previous points

I appreciate the effort of the authors but I think that their results should not dishearten clinicians that in other situation could benefit of this kind of interventions. The conclusion of the study should be different: that a multifaceted educational intervention affirmed but not performed in his essence (i.e. not transformed in a change of assistance) could not change the rate of CS where the high rate is mostly due to prelabor cesarean section

Response 22: We appreciate the reviewer’s thoughtful comments and suggestions. We have now added substantial amount of discussion as follows: “CS issue is extremely complex and deeply-rooted. Despite our recognition of their importance, some measures were beyond what our study could do while other measures were difficult to implement. For example, we knew that fear of pain could be effectively addressed by providing epidural analgesia, but some hospitals were constrained by anesthesia resources. Only 8 hospitals in our study provided epidural analgesia, resulting in still low epidural analgesia use (20-30% of women who attempted labor). Doula is effective in reducing CS use and increasing women’s satisfaction. But the overwhelming volume of deliveries in Chinese public hospitals hampers one-to-one doula or midwife support. In our study, only one-third of parturients had doula. And a doula is often shared by more than one laboring woman.

We also knew that physicians play a critical role in CS decision making, prelabor and intrapartum. But the “physician factor” is also complicated by multiple forces. The shortage of medical staff to handle the large volume of delivery, financial incentives, and constrained doctor-patient relationship all likely draw the decision leaning towards CS. Physicians' practice pattern is often unclear. Our trial did not attempt to address the physician factor directly, which may be an important determinant in the success of an intervention trial on reducing CS rate. For future studies, an assessment of practice pattern among physicians may provide useful insights. For example, asking the surgeon to complete a detailed reporting form that uncovers the indications as well as intentions and actions of the surgeon may help to identify potential targets for intervention. Given its importance, the physician factor could be a focus for future research. But the government health policy that can address some of the above issues may be more effective.” (Discussion section, line 370-389, page 17-18).

Editorial comments:
Comment 23: Please rename supplementary files as ‘Additional file X’, and cite explicitly by additional file name in the manuscript e.g. ‘Additional file 1: Fig. S1’. Please ensure that if you have more than one additional file that they are cited in ascending order within the main body of text.

The abstract should be formatted as Background/Methods/Results/Conclusions, and be no more than 350 words.

Response 23: Thank you. We have shortened the abstract within 350 words. The supplementary files have also been renamed correctly and cited explicitly.

We hope that these revisions have met with your requirement. Thank you very much for your time.

Sincerely,

Jun Zhang