PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Possible relationship between general and pregnancy-related anxiety during the first half of pregnancy and the birth process: a prospective cohort study
AUTHORS	Koelewijn, Johanna; Sluijs, Anne; Vrijkotte, Tanja

VERSION 1 - REVIEW

REVIEWER	Marleen van Gelder Assistant professor Radboud university medical center The Netherlands
REVIEW RETURNED	04-Aug-2016

GENERAL COMMENTS	In this study, the authors evaluated associations between general and pregnancy-related anxiety and several indicators of the birth process. The results suggest that high general anxiety and pregnancy-related anxiety are associated with a number of outcomes, but not all outcomes, with some differences between primiparae and multiparae. I think some major adjustments have to be made before this paper is potentially suitable for publication in BMJ Open. Major comments: 1. The authors state that this is the first study measuring anxiety in the first trimester of pregnancy. However, the questionnaire was administered at an average gestational age of 16 weeks (IQR 14-18 weeks; page 6). Therefore, the overwhelming majority of participants completed the questionnaire in the second trimester. 2. In the Introduction, it was outlined that specific types of anxiety may have different effects on the birth process. Although three aspects are distinguished in the PRAQ (page 7), the authors chose only to analyze the total score. I think it would be more informative to report on the subscales as well, with the exception of 'fear of labor' as argued in the Discussion section (or only separate for primiparae and multiparae). 3. Concerning the analyses / outcome parameters: what is the underlying (etiologic) model? Some of the confounders, including gestational hypertension, gestational diabetes, gestational age at delivery, and (estimated) birth weight are likely to be intermediates as they are indications for induction of labor (and sometimes for primary CS as well). More information about the indication for induction would benefit the analyses, especially since in some cases, induction might have been at the request of the woman. 4. For a substantial part of the study population (19.5%), outcome data are unavailable. Do these women differ in STAI/PRAQ scores compared with the women with complete information? 5. Table 2 is very large, splitting it into 2 separate tables, for

	example one for general anxiety and one for pregnancy-related anxiety, would benefit the reader. In general, due to all subgroup analyses and the focus on interaction effects, the Results section is at some points relatively hard to read. 6. The authors argue that the results promote an intervention to reduce anxiety, in particular pregnancy-related anxiety. However, in the absence of data on the course of anxiety throughout pregnancy (page 20), I think this recommendation is not completely supported by the data available. 7. In multiparous women, could reverse causation (bias) play a role? With other words, is it possible that women with complications during an earlier delivery are more often anxious in the index pregnancy (because of experience) and at an increased risk of complications because of their obstetric history? Minor comments: 1. The most recent literature reference is from 2014, are there any updates available? 2. It is generally acknowledged that the prevalences of gestational hypertension and gestational diabetes are underestimated in the PRN. Could this have any influence on the results? 3. The proportion of women with high general anxiety (31.0% according to the Results section, 30.9% according to the Abstract) seems very high. How does this compare to other studies? 4. Table 1: the median score in high pregnancy-related anxiety among multiparae is not between the min-max given. 5. Page 10: The authors compare the PRAQ scores between nulliparous and multiparous women, but in the Methods section they argued that the scores cannot be compared due to a different number of items. 6. Page 15: I think multivariate should be multivariable. 7. Distinguish between significance and statistical significance. 8. Some hypotheses in the Discussion section are not supported by data or references (e.g., “The increased risk for induction […] will be successful in multiparae” (page 22)).

REVIEWER	Isabel Ramos and Chris Dunkel Schetter UCLA Health Psychology, USA
REVIEW RETURNED	11-Sep-2016

GENERAL COMMENTS	Manuscript ID bmjopen-2016-013413 Brief Overview of Study This prospective study explored whether maternal anxiety in the first trimester (both general and pregnancy-specific) were related to interventions required during labor in a large multi-ethnic cohort in the Netherlands. Results indicate that both general and pregnancy-related anxiety were associated with pain relief and/or sedation. Results differed by parity. Key Strengths • Study considers the effects of both general and pregnancy-specific anxiety on intervention during labor • Study examines the relationship between anxiety on interventions during labor and the progression of labor, both important outcomes. • Possible ethnic differences of these relationships are explored within the Dutch population sampled. • Close attention was paid to nulliparous and multiparous expecting mothers in all steps of the analyses

	• Given the findings of the study, recommendations can be made for screening women for general and pregnancy-specific anxiety early in pregnancy in this geographical area. Key Weaknesses • Introduction lacks clarity and organization, and a more thorough literature review of the effects of pregnancy anxiety on labor complications and potential differences by ethnicities and pathways; the problems is that this literature has a long history and the review is slanted toward recent, not historical studies. • Stronger argument should be made for how and why anxiety is related to labor complications; though mechanisms may not be tested, they should be discussed to clarify the theoretical underpinnings. • Authors did not address why measuring anxiety in first trimester (as opposed to second, third, or all) is relevant to labor complications, interventions, progression of labor. Presumably it concerns detecting it earlier rather than later but if it can be measured later, why not? Specific Points Introduction • Might be useful to know what the rate of interventions (i.e. cesarean section) during childbirth is currently (or at least more recently), as opposed to from 1993-2002. And useful to make some reference to rates in other western nations specifically, do they differ? How and why/ • Authors should consider making the argument that maternal anxiety is associated with obstetric complications (page 4, lines 27-34) stronger to convince reader. The way it is written now is overly speculative and not convincing. • May be helpful to expand on the “cultural, social, and organizational characteristics” that are thought to mediate or exacerbate the effect of anxiety on the use of interventions during labor (page 4, lines 46-47). How and why is this important? • Unclear how differences in maternal characteristics influencing the association between anxiety and birth process (page 4, lines 551-54) is different from cultural, social, and organizational characteristics mentioned in lines 46-47 (page 4). The examples given for maternal characteristics seem to overlap with cultural, social, and organizational characteristics. • End of the introduction (page 5, lines 3-20) needs to be restructured to guide readers into understanding the different ways that anxiety may influence intervention during labor. As is, this portion of the introduction lacks direction and clarity, and does not successfully argue that parity, ethnicity, and level of care at the start of labor relate to intervention and anxiety in pregnancy. • In sum the background to this paper is not much advanced over very early work on this mainly in nursing. Updated references to pregnancy anxiety and to C section are available to add. Methods • Page 6, line 13: Authors should consider specifying what “psychosocial conditions” were in the initial pregnancy questionnaire • Page 7 line 46, unclear what “linking our records with the PRB database” means for obtaining the outcome data on the birth processes I do not use acronyms?) Results • Providing associations between anxiety and intervention/labor process according to parity is very useful • Whether all of the interesting interactions are tested is unclear; a

	rationale for those tested perhaps a bit thin. Discussion • Authors might consider differentiating “interventions during labor” and “progression of birth” (page 19, line 13-14) as two distinct outcomes from outset and here • (Page 19, lines 48-53) Authors should consider elaborating on why using both general anxiety and pregnancy-related anxiety is a strength of the study. Why is it useful and worthwhile to assess both? What do these assessments capture differently? • The use of the specific pregnancy anxiety measure needs mention; there are only two older validation papers and apparently it has items that only apply to primips (?) though even multips can have fear of childbirth. Also there are other instruments now in the literature that might be stronger. Why not measure childbirth anxiety specifically for this purpose? Do address that at least. • Page 22 lines 4-6; authors should consider elaborating on how parity is associated with the birth process since this is central to the findings In summary, there is much merit in this work but this manuscript can be improved.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Marleen van Gelder
Institution and Country: Assistant professor Radboud university medical center, The Netherlands
Please state any competing interests: None declared

Please leave your comments for the authors below In this study, the authors evaluated associations between general and pregnancy-related anxiety and several indicators of the birth process. The results suggest that high general anxiety and pregnancy-related anxiety are associated with a number of outcomes, but not all outcomes, with some differences between primiparae and multiparae. I think some major adjustments have to be made before this paper is potentially suitable for publication in BMJ Open.

Major comments:
1.The authors state that this is the first study measuring anxiety in the first trimester of pregnancy. However, the questionnaire was administered at an average gestational age of 16 weeks (IQR 14-18 weeks; page 6). Therefore, the overwhelming majority of participants completed the questionnaire in the second trimester.
Answer: Thank you for your comment. You are right. We have changed this in our manuscript in ‘the first half of pregnancy’.

2.In the Introduction, it was outlined that specific types of anxiety may have different effects on the birth process. Although three aspects are distinguished in the PRAQ (page 7), the authors chose only to analyze the total score. I think it would be more informative to report on the subscales as well, with the exception of ‘fear of labor’ as argued in the Discussion section (or only separate for primiparae and multiparae).
Answer: Our focus was on general anxiety, using a well-validated questionnaire. In addition, we reported pregnancy-related anxiety in general. Reporting the subscales would be informative, but we think this is an overflow of information to insert in the manuscript. Our choice is in agreement with other questionnaires, such as the Wijma Delivery Expectancy Questionnaire (W-DEQ), conceptualized as a uni-dimensional instrument to measure fear of childbirth, as we discussed in our discussion section.

3.Concerning the analyses / outcome parameters: what is the underlying (etiologic) model? Some of the confounders, including gestational hypertension, gestational diabetes, gestational age at delivery, and (estimated) birth weight are likely to be intermediates as they are indications for induction of labor (and sometimes for primary CS as well). More information about the indication for induction would benefit the analyses, especially since in some cases, induction might have been at the request of the woman.
Answer: You are right that gestational hypertension, gestational diabetes, gestational age at delivery and (estimated) birth weight might be intermediates for some of the outcomes and no confounders. For that reason we included these covariates in our multivariate model in the second step. Because there were no significant differences between the model adjusted only for background characteristics and the fully adjusted model, we decided to present only the fully adjusted model. We mentioned this is in paper at page 16. The PRN-data did not provide detailed information about the indication for induction. We performed a separate analysis for 'elective induction'; this resulted in a stronger association with anxiety. We decided not to report this, because the interpretation of 'elective induction' might differ between obstetric care providers; some will code 'elective induction' in case of induction on the request of the woman, but others might also code as 'elective induction' an induction between 41 and 42 weeks of pregnancy to prevent postmaturity.

4.For a substantial part of the study population (19.5%), outcome data are unavailable. Do these women differ in STAI/PRAQ scores compared with the women with complete information?
Answer: The mean score on pregnancy-related anxiety did not differ between the group with and without outcome data (20.9 versus 21.1). The mean STAI-score was significantly higher (39.5 versus 38.2) in the group without outcome data. However, there is no reason to assume that the associations between anxiety and the birth process will be different in the group without outcomde data. We have added this information in the result section (page 11)and referred to women with missing outcome data in the discussion section (page 20).

5.Table 2 is very large, splitting it into 2 separate tables, for example one for general anxiety and one for pregnancy-related anxiety, would benefit the reader. In general, due to all subgroup analyses and the focus on interaction effects, the Results section is at some points relatively hard to read.
Answer: We prefer to present these data in one table, enabling to compare the associations between general and pregnancy-related anxiety. We leave it to the editor to present these data in one table or in two.

6.The authors argue that the results promote an intervention to reduce anxiety, in particular pregnancy-related anxiety. However, in the absence of data on the course of anxiety throughout pregnancy (page 20), I think this recommendation is not completely supported by the data available.
Answer: We changed the text to make clear that in case of early detection of (pregnancy) anxiety there is sufficient time for treatment or therapy. In case of severe or phobic fear of childbirth we could argue that fear will increase during pregnancy, because the event that is feared is unavoidable and slowly coming closer.We added this arguing on page 21. We added information about other serious consequences of anxiety during pregnancy on page 5, and argued that, if maternal anxiety should be associated with complications and interventions during the birth process, there would be all the more reason for screening early in pregnancy,

7.In multiparous women, could reverse causation (bias) play a role? With other words, is it possible that women with complications during an earlier delivery are more often anxious in the index pregnancy (because of experience) and at an increased risk of complications because of their obstetric history?
Answer: Yes, that might be possible. This might have played a role in the higher risk for a primary caesarean section in multiparous women with high pregnancy-related anxiety. We have made this

more clear in our discussion section (page 23).
Unfortunately, it is not possible to investigate this thorougly in our data because this should have become clear from the subscale measuring fear of labour. However, in this subscale the question 'I am scared of labour and birth because I have never experienced this' was not suitable for multiparous women, while no question measured the experience during the foregoing delivery.

Minor comments:
1.The most recent literature reference is from 2014, are there any updates available?
We have added some more recent references (nr 2,22, 50)
2.It is generally acknowledged that the prevalences of gestational hypertension and gestational diabetes are underestimated in the PRN. Could this have any influence on the results?
Answer: hypertension and diabetes were based not only on PRN-data, but also on self-reported data in the questionnaire (about pre-existent diseases) as well as data from the infancy questionnaire, sent three months after birth, in which some questions about hypertension and diabetes during pregnancy were included. (See: De Beer et al. Relation of maternal hypertension with infant growth in a prospective birth cohort: the ABCD study, Journal of Developmental Origins of Health and Disease, Volume 1, Issue 5. October 2010, pp. 347-355) We decided not to mention these details in our manuscript, because our methods are reported in extenso in other articles. However, if the editor thinks it is desirable to mention this details in our article, we can do so.

3.The proportion of women with high general anxiety (31.0% according to the Results section, 30.9% according to the Abstract) seems very high. How does this compare to other studies?
Answer: Yes, this is a large proportion. In the Dutch study of Fontein-Kuipers (2015) 14.4% of the women showed high general anxiety. She used the STAI trait, while we used the STAI state, which might generate a somewhat higher score during pregnancy if pregnancy-related anxiety is also present. In particular, the difference might be explained by our multiethnic population, while in Fontein's study >95% of the women was Dutch. Koelewijn reports a mean STAI trait of 34.0 in a control group of women with a negative screening for erythrocyte antibodies. In this study most women were of Dutch origine. We have referred to these studies in the discussion on page 22.

In the results section we have changed the proportion of 31.0% general anxiety in 30.9% and in the abstract we have changed the 11.0% high PRAQ-score in 11.1%, which are the more accurate percentages.

4.Table 1: the median score in high pregnancy-related anxiety among multiparae is not between the min-max given.
Answer: Thank you for your remark. We have corrected the min-max.

5.Page 10: The authors compare the PRAQ scores between nulliparous and multiparous women, but in the Methods section they argued that the scores cannot be compared due to a different number of items.
Answer: Thank you for your remark. You are right that the scores cannot be compared. We have changed this in the text.

6.Page 15: I think multivariate should be multivariable.
Answer: We agree with you and have changed this in the text.

7.Distinguish between significance and statistical significance.
Answer: we have added 'statisticallly' where this was meant.

8.Some hypotheses in the Discussion section are not supported by data or references (e.g., "The

increased risk for induction […] will be successful in multiparae" (page 22)).
Answer: We have added references about the chance of successfull induction of labour in multiparous women compared to nulliparous.

Reviewer: 2
Reviewer Name: Chris Dunkel Schetter (with input from Isabel Ramos) Institution and Country: UCLA Health Psychology, USA Please state any competing interests: None

Please leave your comments for the authors below Manuscript ID bmjopen-2016-013413 Brief Overview of Study This prospective study explored whether maternal anxiety in the first trimester (both general and pregnancy-specific) were related to interventions required during labor in a large multi-ethnic cohort in the Netherlands. Results indicate that both general and pregnancy-related anxiety were associated with pain relief and/or sedation. Results differed by parity.

Key Strengths
•Study considers the effects of both general and pregnancy-specific anxiety on intervention during labor
•Study examines the relationship between anxiety on interventions during labor and the progression of labor, both important outcomes.
•Possible ethnic differences of these relationships are explored within the Dutch population sampled.
•Close attention was paid to nulliparous and multiparous expecting mothers in all steps of the analyses
•Given the findings of the study, recommendations can be made for screening women for general and pregnancy-specific anxiety early in pregnancy in this geographical area.

Key Weaknesses
•Introduction lacks clarity and organization, and a more thorough literature review of the effects of pregnancy anxiety on labor complications and potential differences by ethnicities and pathways; the problems is that this literature has a long history and the review is slanted toward recent, not historical studies.
•Stronger argument should be made for how and why anxiety is related to labor complications; though mechanisms may not be tested, they should be discussed to clarify the theoretical underpinnings.
•Authors did not address why measuring anxiety in first trimester (as opposed to second, third, or all) is relevant to labor complications, interventions, progression of labor. Presumably it concerns detecting it earlier rather than later but if it can be measured later, why not?
Answer: We have made the points above more clear in our introduction and in the discussion (see the yellow parts in the introduction).
Regarding the second point: the message from our study (supported by the existing literature) is that anxiety is not strongly related with the progress of the birth progress, but more with the interventions made. One explanation is that fear of childbirth of the pregnant woman is influencing the obstetric caregiver, for example in offering medical pain relief, or in performing a Caesarean Section.
Regarding the third point: please see our answer to question 6 of the first reviewer.

Specific Points
Introduction
•Might be useful to know what the rate of interventions (i.e. cesarean section) during childbirth is currently (or at least more recently), as opposed to from 1993-2002. And useful to make some reference to rates in other western nations specifically, do they differ? How and why.
Answer: we have added a reference about the caesarean rate from 2008-2013. We have also mentioned that the caesarean rates are higher in other Western countries, but our focus was on the rise of these rates in all countries.

•Authors should consider making the argument that maternal anxiety is associated with obstetric complications (page 4, lines 27-34) stronger to convince reader. The way it is written now is overly speculative and not convincing.
Answer: We added in the introduction some more evidence about the relationship of anxiety with gestational age and of the higher risk of postpartum mental health problems. Furthermore we have argued that the evidence fort the association between anxiety and birth complications is inconclusive . Our study is meant to find more evidence.

•May be helpful to expand on the "cultural, social, and organizational characteristics" that are thought to mediate or exacerbate the effect of anxiety on the use of interventions during labor (page 4, lines 46-47). How and why is this important?
Answer: We have specified these factors on page 5, such as difference between ethnic groups.
•Unclear how differences in maternal characteristics influencing the association between anxiety and birth process (page 4, lines 551-54) is different from cultural, social, and organizational characteristics mentioned in lines 46-47 (page 4). The examples given for maternal characteristics seem to overlap with cultural, social, and organizational characteristics.
Answer: You are right. We have deleted the sentence about maternal characteristics.

•End of the introduction (page 5, lines 3-20) needs to be restructured to guide readers into understanding the different ways that anxiety may influence intervention during labor. As is, this portion of the introduction lacks direction and clarity, and does not successfully argue that parity, ethnicity, and level of care at the start of labor relate to intervention and anxiety in pregnancy.
Answer: we have tried to make this more clear by additional information about the effects of anxiety on maternal and neonatal health.

•In sum the background to this paper is not much advanced over very early work on this mainly in nursing. Updated references to pregnancy anxiety and to C section are available to add.
Answer: As mentioned above we have added more information about earlier studies. We do not agree that our references are mainly from nursing journals. For example, we refer to obstetric journals like BJOG, Journal of Psychosomatic Obstetrics and Gynecology, Acta Obstet Gynec. Scand. and others

Methods
•Page 6, line 13: Authors should consider specifying what "psychosocial conditions" were in the initial pregnancy questionnaire
Answer: There is no place to report in detail all the psychosocial conditions in the questionnaire. We have added that measurements of general and pregnancy-related anxiety were included. (page 6)

•Page 7 line 46, unclear what "linking our records with the PRB database" means for obtaining the outcome data on the birth processes I do not use acronyms?)
Answer: the acronym PRN (Dutch Perinatal Database) has been explained on page 6. The method of record linking has been described in the paper of (ref 39: Tromp M, van Eijsden M, Ravelli AC, Bonsel GJ. Anonymous non-response analysis in the ABCD cohort study enabled by probabilistic record linkage. Paediatr Perinat Epidemiol. 2009;23:264-72.

Results
•Providing associations between anxiety and intervention/labor process according to parity is very useful
•Whether all of the interesting interactions are tested is unclear; a rationale for those tested perhaps a bit thin.
Answer: we have tested in our models the interaction between parity, ethicity, resp. care at start of

labour with general and pregnancy-related anxiety. This is added on page 10 (statistical analysis). Only significant interactions are reported in the result section.

Discussion
•Authors might consider differentiating “interventions during labor” and “progression of birth” (page 19, line 13-14) as two distinct outcomes from outset and here.
Answer: Thank you for your suggestion. We have made this distinction in the results section. We did not change the order of outcome measures in the tables, because we reported the outcomes in the order of occurrence during labour. Also in the discussion section we made this distinction more clear. On page 23 we added a reflection on the fact that we did not find an association with the duration of labour, and concluded that an association between anxiety with the birth process is unlikely in our population.

•(Page 19, lines 48-53) Authors should consider elaborating on why using both general anxiety and pregnancy-related anxiety is a strength of the study. Why is it useful and worthwhile to assess both? What do these assessments capture differently?
Answer: in most studies only pregnancy-related anxiety is elaborated. So, the strength of our study is to investigate general anxiety. This is the main focus of our study.
Pregnancy related anxiety is more specific about the coming birth and it often exists without general anxiety problems, although state/trait anxiety is correlated with pregnancy anxiety. By examining both we can specifiy which variables are related to general anxiety and which with pregnancy anxiety. We showed, as in other studies, that pregnancy anxiety is more often related to interventions than general anxiety.

•The use of the specific pregnancy anxiety measure needs mention; there are only two older validation papers and apparently it has items that only apply to primips (?) though even multips can have fear of childbirth. Also there are other instruments now in the literature that might be stronger. Why not measure childbirth anxiety specifically for this purpose? Do address that at least.
Answer: we agree with the reviewer that the use of the PRAQ limits the possibility to measure fear of labour in multiparous women. We have mentioned that in our discussion

•Page 22 lines 4-6; authors should consider elaborating on how parity is associated with the birth process since this is central to the findings
Answer We have made this more clear in our discussion.(page 23)

In summary, there is much merit in this work but this manuscript can be improved.

VERSION 2 – REVIEW

REVIEWER	Marleen van Gelder Radboud university medical center, The Netherlands
REVIEW RETURNED	07-Nov-2016

GENERAL COMMENTS	The authors did a great job in revising this manuscript. However, I still have a few comments as outlined below. Major comments: 1. I do not agree with the authors that the focus of the manuscript is on general anxiety. I believe the focus in the results and discussion is approximately equal for general anxiety and pregnancy-related anxiety. Analysis on the subscale of pregnancy-related anxiety could give more insight into the underlying model, which is still only based on hypotheses that are not supported by references to the literature. One of the examples is the arguing that fear of childbirth is

	increasing during pregnancy because the event is coming closer (page 22, line 45). 2. Although correction for the potential intermediate variables (gestational diabetes, hypertensive disorders, gestational age, and (estimated) birth weight) did not yield “significant differences” between the model adjusted for only background characteristics and the fully adjusted model, overadjustment should be avoided (e.g., Schisterman et al., Epidemiology 2009). Minor comments: 1. According to the methods section, data on gestational diabetes and hypertensive disorders originated from the PRN registry, and not from the questionnaire as described in the response. I feel the authors should give a full overview of the methods of data collection to get more insight in the possible degree of measurement error. 2. In Table 2, both overall and results stratified for parity are shown. However, if there is effect modification (as may be the case here for parity), it is questionable whether the overall effects should be presented (and discussed) as these apply to nobody.

VERSION 2 – AUTHOR RESPONSE

We thank the reviewer for carefully reading our manuscript and for the suggestions to improve it. Hereafter, we will answer the comments.

Major comments:
1.I do not agree with the authors that the focus of the manuscript is on general anxiety. I believe the focus in the results and discussion is approximately equal for general anxiety and pregnancy-related anxiety. Analysis on the subscale of pregnancy-related anxiety could give more insight into the underlying model, which is still only based on hypotheses that are not supported by references to the literature. One of the examples is the arguing that fear of childbirth is increasing during pregnancy because the event is coming closer (page 22, line 45).

ANSWER:
We agree with the reviewer, that in the results and discussion the focus is on general anxiety as well as pregnancy-related anxiety. Because of the unusefullness of the subscale for ‘fear or labour’ in multiparous women, and to avoid the presentation of excessive data, we decided not to present the subscale scores. However, we have added the associations between the scores on the subscales ‘fear of labour’ (only for nulliparous women) and ‘fear of getting a handicapped or mentally retardated child’ with the outcome measures as supplemental files (2a, 3a and 4), and reported some results of these analyses in the main manuscript:
On page 8 we have stated that our focus was on the total score on pregnancy-related anxiety. On page 9: We performed additional explorative analyses, using the PRAQ subscales ‘fear of labour’ (only for primiparous women) and ‘fear of child’. Based on the 10th percentile, the cut-offs for ‘fear of labour’ and ‘fear of child’ were 10 and 12, respectively
Pag 17 (analyses according to parity): Analyses with the subscales showed similar trends with one exception: fear of labour was associated with an increased risk for pain relief/sedation in (primiparous) women, which was not the case for high ‘fear of child’.
Page 18 (analyses according to ethnicity): Analyses with the subscales showed similar trends. However, in Dutch women with high ‘fear of labour’ the risk for a first stage of labour longer than 12 hours and for a second stage of labour longer than 1,5 hour was increased. High ‘fear of child’ was not associated with an increased risk for any of the outcome parameters. (Supplemental table 3a).
Page 21 (analyses according to level of care at the start of labour): The subscale analyses showed that fear of labour was associated with pain relief/sedation, which was not the case of high ‘fear of

child'. (Supplemental table 4).
In the discussion we have referred to the subscale analyses:
Page 25: We did not find such an association (with prolonged first stage of labour; JK) with general or pregnancy-related anxiety, except for an association with the PRAQ subscale 'fear of labour' within the subgroup of Dutch women. However, this result from an explorative analysis should be interpreted with caution.
The arguing that fear of childbirth is increasing during pregnancy because the event is coming closer (page 22, line 45), was changed to
in case of fear of childbirth/labour it might be possible that fear will increase during pregnancy (page 23).
2.Although correction for the potential intermediate variables (gestational diabetes, hypertensive disorders, gestational age, and (estimated) birth weight) did not yield "significant differences" between the model adjusted for only background characteristics and the fully adjusted model, over adjustment should be avoided (e.g., Schisterman et al., Epidemiology 2009).

ANSWER:
We have reconsidered the two steps of adjustment, and we agree with the reviewer that there is a risk for over adjustment, since diabetes, hypertensive disorders, gestational age and birth weight might be, at least partially, intermediate variables. Therefore, we have replaced the adjusted ORs by the ORs found after adjustment for background characteristics only. (We also replaced the crude ORs, since some were slightly different; this difference was caused by inclusion of records with missing values on one or more intermediate variables, which were excluded from the model we used before).
We reported before, that the adjusted ORs were only slightly different from the ORs we presented before. However, some associations reached statistical significance, and some other associations were not significant. This concerns:
- page 18 (Table 2): Subgroup analysis (according to parity;JK) showed an increased risk for primary caesarean in highly anxious multiparous women. This association was not significant after the 2nd step of adjustment, but we did find a significant interaction between parity and general anxiety.
- Table 2: The risk for referral during labour in primiparous women with high pregnancy-related anxiety was not significant anymore.
- Table 3: we found a significant decreased risk for primary caesarean in Moroccon women with high general anxiety and an increased risk for instrumental delivery in Moroccon women with high general anxiety.
- Supplemental table 1: The increased risk for pain relief/sedation in multiparous women starting labour in secondary care, was not significantly increased anymore

Minor comments:

1.According to the methods section, data on gestational diabetes and hypertensive disorders originated from the PRN registry, and not from the questionnaire as described in the response. I feel the authors should give a full overview of the methods of data collection to get more insight in the possible degree of measurement error.
ANSWER:
We have added this information in the method section op pag 7:
Three months after birth the women who gave permission for follow-up (n=6854) received a questionnaire concerning, amongst other things, the course of pregnancy and delivery. A total of 5218 mothers filled out this questionnaire.
And on page 10:
Missing data concerning parity, birth weight and gestational age were extracted from the three months questionnaire; hypertension and diabetes were encoded as 'yes' these diseases were reported in the PRN database and/or in the three months questionnaire.

2.In Table 2, both overall and results stratified for parity are shown. However, if there is effect modification (as may be the case here for parity), it is questionable whether the overall effects should be presented (and discussed) as these apply to nobody.
ANSWER:
We agree with the reviewer and have removed the overall effects from table 2.

VERSION 3 – REVIEW

REVIEWER	Marleen van Gelder, PhD Radboud university medical center, The Netherlands
REVIEW RETURNED	14-Feb-2017

GENERAL COMMENTS	The authors did a great job in revising the manuscript. I have no further comments.