Author's response to reviews

**Title:** Treatment of pelvic girdle pain with acupuncture: adverse effects of standard treatment, acupuncture and stabilising exercises on the pregnancy, mother, delivery and the fetus/neonate.

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**Author's response to reviews:**

“Response to reviewers”

Reviewer: Adrian White
Reviewer's report:

Review

This is a well presented report of the assessments of adverse events occurring in a trial of acupuncture for pregnancy girdle pain already published. It is an important addition to the literature on the safety of acupuncture.

Major compulsory revision:

The study methods are not clear in one important area:

Page 8: all adverse events of treatment were recorded. Does this represent just the practitioners observations? or was the patient actually asked whether she identified an side effect? If so, was she presented with a list of possible side effects, or asked a general question on whether she had experienced any adverse effects? How was the terminology expressed so that it was comprehensible to everyone? These factors may influence the successful collection of data on safety.

We agree that this information has to be clarified. No, the reported adverse events of treatment do not reflect just the practitioner’s observations. Additional information of recording of adverse events is now added in the method section, page 8-10.

Discretionary revision

I believe the claims made for the value of this study are on the border of being
excessive and could with benefit be toned down. Only 125 women were treated with acupuncture, compared with over 400 in Smith's study. Smith also collected data on congenital abnormalities, which was not done in this study. Although I accept that the cardiotocograh data are novel and reassuring, and the blood pH data are innovative, I wonder about their overall relevance.

There is a longstanding problem with the nomenclature in this area, concerning attribution of an adverse event to the effect of acupuncture. There is some logic in regarding the study as collecting data on adverse events not adverse effects for example, the incidence of induction of labour has been measured and this is an adverse event in the wider meaning of the term, but not an adverse event that can be attributed to acupuncture. This discussion is rather semantic and the authors may not want to be involved. They are lucky that no event occurred which required them to evaluate whether acupuncture had a role in causing it.

We agree that the value of the study could be further toned down and that it is important not to over interpret the results and also that there certainly is a need for additional studies concerning safety of acupuncture for PGP in pregnant women. The following information has been added in the discussion section, page 13, paragraph 2. "It is not easy to find safety data of acupuncture given to women in the second and third trimester of pregnancy because these women are seldom offered acupuncture due to the fact that pregnancy sometimes is regarded as a relative contraindication to acupuncture (because of an old Chinese proposal of an increased risk of uterine contractions leading to abortion or pre-term delivery. There are only four other studies published (171 women in total) of acupuncture for PGP and/or LBP [10-12, 14]. Two of them (n=71) registered Apgar score and infant weight. However these studies used weaker stimulation than in our study. Kvorning et al. [11] started treatment with only two segmental points, stimulated to achieve de-qi twice during the session which only lasted for about three minutes. The needles were then withdrawn and the patient was allowed to rest for ten minutes [45] . Guerreiro da Silva et al [12] used 8 to 12 sessions with 12 needles for 25 minutes". In addition, Smith et al. [17].who treated 583 pregnant women with acupuncture for hyperemesis during the first trimester [17] reported no influences on the pregnancy outcome. But as in our study the sample size in that study was only able to detect large differences in pregnancy outcomes. These authors declared that a sample size of 19,476 women would have been required to detect an increased from 6 to 7 % in spontaneous abortions.

Also, we did not select the variables from the women’s records for our study we simply decided to use the same antenatal, intrapartum, neonatal and infant data that is registered on all births in Sweden in the Swedish Medical Birth register. This data has been complied on all births in Sweden by the Swedish Medical
Birth register since 1973. It offers a unique possibility to obtain reliable prevalence figures regarding obstetric and neonatal outcome. Unfortunately this register has no data of frequency of acupuncture during the antenatal period. If that had been possible it would have been easy to collect data from all pregnant women in Sweden that had got acupuncture for PGP and/or LBP. Information about selection of variables have been added in the method section, page 9, paragraph 4 and it is further discussed in the discussion section, page 14, paragraph 3 and page 15, paragraph 1.

Minor editorial recommendations:
Abstract Methods: Adverse effects were recorded of adverse effects
This sentence has been changed to: Adverse effects were recorded during treatment and throughout the pregnancy.

Results: but women rated acupuncture favourably even though this
Information about this have been shortened in the abstract as suggested. result is given prominence, the methods section does not describe it.

The following sentence is now added in the method section in the abstract: “After treatment, the women rated their overall experience of the treatment and listed adverse events if any in a questionnaire”.

Results: severe not servere (also in Table 4)
This has been corrected in the result section as well as in Table 4.

Page 4 bottom: have concluded (not has)
This has been corrected.

Page 5, line 3, close bracket missing-
This has been corrected.

Page 5, Cardiotocography.
This has been corrected.

Page 6, line 4 should be comma not full stop.
This has been corrected.

Page 8. Patients rated their opinions: what options were offered to them? these should be briefly summarised here, though presented in full in the Table.

These questions have been used in a previous study of acupuncture and physiotherapy for back pain during pregnancy (Wedenberg et al.). We have now added the following sentences in the method section, Page 9, paragraph 3: The women were also asked to indicate their overall experience of the treatments. The options were: no help, some help, good help and very good help.

All references to Table and Figure should be capitalised.
This has been corrected.

Page 9, 2nd line: completing would be better than fulfilling.
We agree, this has been corrected.

Page 10 middle: withdrew, not withdraw.
This has been corrected.

64 minor adverse events occurred do the data allow the authors to state in how many patients these events were recorded? Some women may be more susceptible than others.

Yes, we agree and it is true. 64 minor adverse events were experienced of 43 women in the acupuncture group; 22 in the stabilising exercise group experienced minor adverse events while eight women experienced minor adverse events in the group receiving standard treatment alone. This result has been commented in the discussion sections (page 12, paragraph 2) as well as in Table 4.

Page 11, middle: has resulted or may have resulted, not have resulted.
This has been corrected.

Page 12, 6 lines from bottom, missing SD.
This has been corrected.

Page 13. Should explore the power of the study a little more and give the reader some indication, even if only qualitatively. It seems probable that a very large study would be required to identify a change of premature birth rate from 5% to 6%, and that the sample size of this study could only identify a difference very much larger than that. That is not to diminish the importance of this study, but to indicate the difficulty of this area of research.

We agree and as described earlier we have added information about this subject in the discussion section, page 13, paragraph 2.

Pave 14 line 1. Delete â##thatâ##.

????

Item 1, Data emerged from a relatively large trialâ## should be linked more closely with item 5, insufficient size. The relevant point is that an efficacy RCT is not an appropriate design to provide evidence of safety, even if it is large (in RCT terms). Studies of 30,000 or more have been used in the past.

We agree and have now added the following information: The data emerged from a relatively large randomised trial, but we are aware that an efficacy randomised
controlled trial is not an appropriate design to provide evidence of safety. Studies of more than 97 000 participants' have been used in the past [26]. The reference to Melchart et al's safety study published in 2004 is given.

Table 2, Use of oxytocin
This has been corrected.

Table 7. infiltration of what? Local anaesthetic?
Yes, this information has been added in Table 7.

Figure 1. Nickel allergy not nicel.
This has been corrected.

What next?: Accept after minor essential revisions
Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I receive a fee from the British Medical Acupuncture Society for editing the journal Acupuncture in Medicine

Reviewer's report
Title: Treatment of pelvic girdle pain with acupuncture: adverse effects during pregnancy and delivery.
Version: 2 Date: 22 February 2008
Reviewer: isabella Neri
Reviewer's report:
Minor essential revision.
The question posed is well designed and the methods are appropriate.
The results are clearly reported even if the efficacy on pain relief is not well explained (VAS scale was not used in the study)
Discussion and conclusion are balanced. In the paragraph "CTG readings" at page 12 the first sentence "This is the first study..." is not true (see the reference Neri et al "Non-stress test changes during acupuncture plus moxibustion on BL67 point in breech presentation" J Soc Gynecol Investig; 2002, 9:157-162).

We apologize for this error and have now added information about Neri et al's study in the discussion section, page 14, paragraph 2. "Our results of no signs of fetal distress in connection with acupuncture is supported by Neri et al [34] who found no signs of fetal distress or changes in short-or long-term variability on
computerized CTG before, during and after minimal and true acupuncture plus moxibustion for breech presentation in 15 pregnant women”.

What next?: Accept after minor essential revisions
Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:
I declare that i have no competing interests'

Reviewer’s report
Title: Treatment of pelvic girdle pain with acupuncture: adverse effects during pregnancy and delivery.
Version: 2 Date: 25 March 2008
Reviewer: Irene Lund
Reviewer’s report:
1. Perhaps the title should be corrected in order to more thoroughly reflect the content of the report such that even stabilizing exercises and standard treatment beside acupuncture was evaluated and furthermore that the status of the fetus was studied.

We agree and have accordingly changed the title to: “Treatments of pelvic girdle pain in pregnant women: adverse effects of standard treatment, acupuncture and stabilising exercises on the pregnancy, mother, delivery and the fetus/ neonate”.

2. The content of the background section could perhaps be condensed by for instance moving the sentences regarding the CTG technique to the method section?

We agree, and we have moved the sentence regarding the CTG technique to the method section, page 8, paragraph 2 and page 9, paragraph 1.

3. Please clarify the aim of the study regarding for instance the types of interventions that were delivered.
The aims with the interventions as well as more details of the interventions are now described in the method section page 7-8.

4. Please clarify what is meant by segmental and extrasegmental acupuncture points. Furthermore, is it possible to comment the rational of the numbers of used segmental and extrasegmental points (10 segmental and 7 extrasegmental)?
Description of what is meant by segmental and extrasegmental acupuncture points are given as follows in the method section page 7, paragraph 2. Ten classical acupuncture points were selected individually in the same segments as the location of PGP after diagnostic palpation to identify sensitive spots (Table 1). Two acupuncture points on the medial side of the leg and foot were selected in the same segment as the PGP and extra-segmental points to the lumbosacral area were used to strengthen and lengthen the effect of the central control systems.

The number and selection of acupuncture points was based on clinical experience and expert knowledge of acupuncture in pregnant women with PGP. This information has been added in the method section, page 7, paragraph 2.

5. If possible, explain the differences between the exercises instructed in the treatment strategy and those meant to be stabilizing exercises since in the present text they are both described as exerting low load on pelvic structures.

To clarify the difference between the exercises given in the standard treatment group and the stabilising exercises, more details of the interventions are now described in the method section page 7-8.

6. Is it possible to more specific about what is meant by adverse events in the method section?

Additional information regarding adverse events has been added in the method section, see earlier comments to dr Adrian White.

7. Please clarify what is meant by stating that means and SD of the data was calculated when possible.

We meant when appropriate but have now omitted this information from the text as we think that this information is unnecessary.

8. Table 2. In the text this table is referred to being baseline data. Could it however, be a mix between baseline data and outcome deliveries? If so omit the information of mean maternal age and frequency of primipara from the table and report this in the text. The p-values of these two variables should not be reported since they were not stated to be tested. The function of the randomization procedure is to arrange that there will be no differences between the groups. Perhaps also the information of non significant results could be omitted from the table and just reported very shortly in the text.

The information about mean maternal age, frequencies of primipara have been omitted from the table and are reported in the method section page 6, paragraph 2. We believe that the information about delivery, use of analgesia during labor
and infant data are important descriptive data even if no statistical significant differences was found between the treatment groups, therefore we have decided not to omit these tables. But the columns for the p-values have been omitted in tables showing no statistical significant differences between groups.

9. Please give the rational why only the acupuncture treated women and their fetuses were evaluated with CTG.

The reason that we only performed computerized CTG in women receiving acupuncture was that we did not expect to find fetal distress during either standard treatment or stabilising exercises i.e. low force physiotherapy exercises. Low force exercises have been used in pregnant women with LBP and/or PGP for a long time. To date there are numerous published studies without showing serious adverse events after physiotherapy for PGP and/or LBP in pregnant women (see discussion, subsection: physiotherapy/ Stabilising exercises, page 14 paragraph 1. As described in this section no association between exercise performed after 18 weeks of gestation and risk of miscarriage was seen in a prospective epidemiological study of 92 671 pregnant women. Although, we did not expect fetal distress of acupuncture, we decided to apply computerized CTG to assure well-being of the fetus during acupuncture because of the fact that many pregnant women with PGP do not get acupuncture because pregnancy sometimes is regarded as a relative contraindication to acupuncture. This is due to an old Chinese proposal of an increased risk of uterine contractions leading to abortion or pre-term delivery. Also, when planning the study there was no previous published study on this subject.

10. The differences between the groups shown in table 5 is very interesting but is the testing between the groups associated with the aim of the study and does? Yes, a secondary aim with the study was to evaluate participant’s opinions of the treatment.

As described before these questions have been used in a former study (Wedenberg et al. Acta Obstet Gyn Scand: 2000) of acupuncture and physiotherapy for back pain during pregnancy.

Furthermore, are the mothers experience associated with the outcome of the adverse events of the different treatments?

We do not understand this question, experience of what? We have presented reported adverse events of the women at each visit, immediate adverse events registered in the hospital records connected to acupuncture as fainting, adverse events/ disadvantages/ help of treatment reported of the women at follow-up after end of treatment and, data of pregnancy outcomes. In addition, pregnancy complications reported by other caregivers have been collected from the women’s hospital records.

Significantly fewer women in the stabilising group reported harm of treatment compared to the acupuncture group ACU-SE p <0.001. This finding is in line with
the reporting 22 minor adverse events in the stabilising exercise group compared to the reported 64 minor adverse events in the acupuncture group presented in Table 4. Significantly more women in the stabilising group and the acupuncture group compared to the standard group would use the same treatment again ACU-SE p <0.001, S-ACU p <0.001 which is in line with the earlier published report in 2005 of efficacy of the treatments.

11. Table 7 and 8. See earlier recommendation of just shortly reporting of non significant and significant results and in the text i.e. omit the columns of p-value.

Please, read earlier comments about the importance of descriptive data.

12. Please summarize the results of the three different treatment strategies more condensed in the initial part of the discussion section.

We have added the following sentence in the initial part of the discussion section, page 11, paragraph 4: “As, expected, no serious adverse events were found after standard treatment and stabilising exercises.”

13. The section of the ctg recordings could be comprised by omitting the comments of possible mechanism of needle stimulation of the autonomic nervous system function since the recordings that are referred to were performed on non pregnant women.

We don’t agree, The study by Zeisler et al was performed on pregnant women. They measured the mean S/D ratios of the uterine artery and fetal heart rate before and after acupuncture.

14. In the clinical comments please: omit the first and the last sentence, also comment the results of the other interventions beside acupuncture as well.

We don’t agree, we think that data emerged from a relatively large randomised trial even if a much larger study is appropriate when safety is evaluated. However we have added the following sentence: “The data emerged from a relatively large randomised trial, but we are aware that an efficacy randomised controlled trial is not an appropriate design to provide evidence of safety. Studies of 97 000 participants’ or more have been used in the past”. Also we have given reference to Melchart et als safety study published in 2004 in the text.

In addition we think that it is important to point out the loss of power of the study to exclude negative effects of the treatments on preterm delivery, perinatal morbidity and mortality as well as to detect fetal distress of acupuncture on CTG. As written in the discussion section a very big sample size is required to detect an increased frequency in uncommonly complications in normal pregnancies. Also, we have omitted acupuncture from the following sentence: 2. A substantial number of women started acupuncture treatment already during the second trimester of pregnancy because it was the case for the women in the standard group and stabilising exercise group to. We have commented the results of the other interventions to. Now, it is only paragraph number 2 that include
information of solely acupuncture.

15. Conclusions – based on earlier comments, should not the other treatment strategies be mentioned at all?

Results of standard treatment and stabilising exercises are now added in the conclusion.