Author’s response to reviews

Title: Effectiveness of score card-based antenatal risk selection, care pathways, and multidisciplinary consultation (the Healthy Pregnancy 4 All study): study protocol for a cluster randomized controlled trial

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Author’s response to reviews: see over
Dear Editor,

Enclosed please find our manuscript entitled: “Effectiveness of score card-based antenatal risk selection, care pathways, and multidisciplinary consultation (the Healthy Pregnancy 4 All study): study protocol for a cluster randomized controlled trial” and a point –by-point reply to the valuable comments of the reviewers. We believe these suggestions have substantially improved our manuscript.

Yours sincerely, on behalf of all authors,

Amber Vos

Editorial request
Please include an additional file title and legend section after the reference list.
Reply: Sorry for the inconvenience, these were provided in the revised version of the manuscript.

Reviewer’s report
Title: Effectiveness of score card-based antenatal risk selection, care pathways, and multidisciplinary consultation (the Healthy Pregnancy 4 All study): study protocol for a cluster randomized controlled trial. Version:2 Date: 7 November 2014

Reviewer: Audrey Prost
Reviewer’s report:
I commend the authors on this important trial. Minor suggested revisions are outlined below:

1. Will the study design adequately test the hypothesis?
The study design should adequately test the hypothesis that a new antenatal risk screening approach guided by a score card will improve perinatal outcomes in Dutch municipalities.
We agree

2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing?
Considerable detail is provided, but it would be most helpful for the authors to clarify the following:

a. Municipality selection: How were the 14 participating municipalities selected?
In line 120, authors refer us to another publication. However given that this is the main study protocol, it would be helpful to briefly summarise the municipality selection process in line 120.
2a. Reply: Thank you for this suggestion. The following information was added to this paragraph: [page 4, lines 134-140]“The selection of neighborhoods is based on the presence of an elevated incidence of adverse perinatal outcomes (above both the national and municipal average). Municipalities are extracted after a selection process in which zip codes with high adverse perinatal outcome are identified in a thorough analysis. For this analysis, data from all singleton pregnancies in the Netherlands over the period 2000-2008 were obtained with permission from the Dutch Perinatal Registry (PRN).* The detailed selection process of the municipalities and geographical areas are described elsewhere.”

**2b. Intervention feasibility:** Do the authors have data to support the feasibility and acceptability of 28 or more care pathways resulting from the use of the R4U card? This seems like a very complex system. It would be helpful to summarise the results of any prior pilot study for this approach.

**2b Reply:** Thank you for this suggestion. Instruments and prior experiences with this interventions were partly obtained from a ‘the Ready for a baby program’ but also currently being investigated. Also the feasibility of the R4U score card was investigated in this program**.


We have added this information to the manuscript: “The ‘Ready for a baby’ program provided the framework for this national study. It was within this program that scorecard-based risk screening and corresponding care pathways were developed and piloted. Within the context of this program, the Rotterdam area served as a testing ground for a number of experiments, including the development and piloting of the R4U (Rotterdam Reproductive Risk Reduction) scorecard for antenatal risk screening. These former experiences were used to further improve and implement these tools in other municipalities with high perinatal mortality and morbidity in the Healthy Pregnancy 4 All study. The Healthy Pregnancy 4 All study has been launched in 2011 by the Erasmus University Medical Centre in 14 municipalities in the Netherlands. It focuses on preconception care and broadened risk selection during pregnancy.” [page 4, lines 98-105]

**c. Implementation in control areas:** on line 168, the authors suggest that they will implement the intervention in previous control municipality two thirds of the way through the study. In the subsequent sentence, the authors discuss implementing the intervention in all control clusters at the end of the study. This raises two questions:

(i) Which approach is actually being taken? Is this a stepped-wedge trial with phased implementation, or is it a parallel trial with implementation in the control group at the end of the study?

**2ci. Reply:** We apologize for the confusion. It is a parallel trial with implementation in the control group after 2/3 in two thirds of the way through the study. The fact that we had made municipalities aware of their perinatal health statistics and allocated them to be ‘a control’ was contradiction to ambitions to intervene as the control status was felt as a negligent attitude by local health authorities. We were lenient to this aspect and offered them the opportunity to cross-over to use of the intervention after they had reached a certain amount of included subjects or in two thirds of the way through the study.

(ii) Why do the authors commit to implementing the intervention in the control area at the end of the study. Surely this simply depends on whether the intervention is successful at improving perinatal outcomes or not?

**2cii. Reply:** Over the last decade, several studies revealed a disadvantaged position of the Netherlands regarding perinatal mortality. In 2004, the Peristat I study revealed that the Netherlands was one of the European countries with the highest perinatal mortality rates. Dutch mortality rates were almost four times as high as the lowest mortality rate in Europe. The Dutch position slightly improved in 2008, but rates remained relatively high compared to other European countries. For the first time, the unique organization of antenatal care in the Netherlands was openly questioned. In response, health care professionals and policy makers were urged to undertake interventions. As mentioned in our response to your previous question, to be ‘a control’ was therefore a contradiction to the ambitions to intervene as the control status was felt as a negligent attitude by local health authorities. To accommodate these municipalities, this solution was introduced.

Combining both questions, the following information was added to this section:

“As mentioned in our introduction, several studies revealed a disadvantaged position of the Netherlands regarding perinatal mortality. For the first time, the unique organization of antenatal
care in the Netherlands was openly questioned. In response, health care professionals and policy makers were urged to undertake interventions. The fact that we made municipalities aware of their perinatal health statistics and allocated them to be ‘a control’ was contradiction to ambitions to intervene as the control status was felt as a negligent attitude by local health authorities. We are lenient to this aspect and offer them the opportunity to start with the intervention after they had reached a certain amount of included subjects or in two thirds of the way through the study. Therefore, we aim to implement and facilitate this new approach in all 14 municipalities at the end of the study period. This implies that the study design remains a parallel trial in which only pregnancy outcomes from regular antenatal healthcare in control municipalities will be analysed. Pregnancy outcomes of women enrolled after the ‘cross-over’ in control municipalities (i.e. women in control municipalities that were exposed the intervention) will not be analysed for this purpose.

3. Is the planned statistical analysis appropriate?
More details could be provided on statistical analyses for the two primary perinatal outcomes (logistic regression with random effects)?
3. Reply: We plan to use multilevel logistic regression with random effect model. We have changed this part of the manuscript into the following:
“Data will be analyzed according to the intention to treat principle. The effectiveness of the R4U score card, corresponding care pathways and multidisciplinary consultation versus conventional antenatal healthcare (measured as the difference in SGA and preterm birth between both groups) will be assessed by using multilevel logistic regression with random effects. Results will be presented as effect estimates with a measure of precision (95% confidence interval). Data will be analysed anonymously on two levels: maternal and municipal level. To guarantee anonymity, we will not analyse the data on community practice or hospital level. Study participants, municipalities, and community and hospitals practices will not be traceable. Other analyses related to our intervention are based on differences in the use of referrals facilities between community midwives and gynaecologists, adequacy in risk assessment (e.g. detection of growth restriction in the antenatal phase), and the contribution of non-medical risk factors to adverse birth outcomes between the intervention and control group. These outcomes will be assessed with univariate and multivariate regression analysis with 95% confidence intervals.” [page 12, lines 309-320]

4. Do the figures appear to be genuine, i.e. without evidence of manipulation?
Yes, the figures appear to be genuine.
Thank you

5. Is the writing acceptable?
It would be helpful to carefully edit the manuscript for grammar and syntax, perhaps with the help of a native speaker.

5. Reply: Thank you for this suggestion. We edited the manuscript for grammar and syntax errors accordingly. Especially the sentences below were modified according to the reviewers’ suggestions.

Some phrases could be misinterpreted, for example:

Line 68: “immigrants who are poorly integrated in society’ has slightly pejorative connotations.
Reply: This was changed into: "Poor outcomes were especially observed in deprived districts and are often associated with socio-economic and ethnicity related risk factors such as low education, low-income and poor integration into society.” [page 3, line 67]

Line 87: “These risk factors remain highly underexposed in the current risk selection.” I would suggest ‘these factors are usually not considered in current risk screening practices’.
Reply: This was changed according to the reviewers’ suggestion. [page 4, line 88-90]
Appendix: Randomisation procedure

25 januari, 2012

CL

Randomizing municipalities

This is a description of the randomization procedure for assigning 10 municipalities to intervention or control group. It was thought cautious to match municipalities on size, as to prohibit all small municipalities to be in one arm. Therefor the municipalities were numbered according to the expected number at risk.

The principal researcher then was asked to choose an integer number from 50 provided to her, in order to _x the seed for the random number generator. The whole procedure was performed in R and the result listed at the end of this message.

Five random numbers were drawn from the uniform distribution between zero and one. If the number was below 0.5 the rst of the pair would be assigned to the intervention, otherwise to the control group.

The result is that numbers 1, 4, 6, 7 and 9 became the intervention group, the others the control

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statistician

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> matrix(round(runif(50,1,1000)),nrow=5)
[1,] 356 758 823 18 902 394 563 881 272 468
[2,] 805 542 890 332 687 192 907 215 587 510
[3,] 234 469 587 502 557 741 894 472 859 123
[4,] 729 898 232 922 206 949 63 435 994 957
[5,] 753 330 504 33 984 592 161 241 324 915
> rm(list=ls(all=TRUE)) # clear the memory
> options(digits=4) # options for number of significant digits > options(width=158)
>
> set.seed(949)
>
> nr <- 1:10
> paar <- rep(1:5,each=2)
> cbind(nr,paar)
   nr paar
[1,] 1  1
[2,] 2  1
[3,] 3  2
[4,] 4  2
[5,] 5  3
[6,] 6  3
[7,] 7  4
ran01 <- runif(5)
> ran01
[1] 0.46505 0.77163 0.95071 0.45522 0.01422
> ran01>0.5
[1] FALSE TRUE TRUE FALSE FALSE
> 1+ifelse(ran01>0.5,1,0)+(0:4)*2
[1] 1 4 6 7 9
> interv <- rep(FALSE,10)
> interv[1+ifelse(ran01>0.5,1,0)+(0:4)*2] <- TRUE
> cbind(nr,paar,interv)
nr paar interv
[1,] 1 1 1
[2,] 2 1 0
[3,] 3 2 0
[4,] 4 2 1
[5,] 5 3 0
[6,] 6 3 1
[7,] 7 4 1
[8,] 8 4 0
[9,] 9 5 1
[10,] 10 5 0
2