Author's response to reviews

Title: A comparison of inpatient with outpatient balloon catheter cervical ripening: a pilot randomized controlled trial.

Authors:

   Chris S Wilkinson (chrisswilkinson@mac.com)
   Pamela Adelson (pamela.adelson@adelaide.edu.au)
   Deborah A Turnbull (deborah.turnbull@adelaide.edu.au)

Version: 4  Date: 27 February 2015

Author's response to reviews: see over
Author responses to BioMed Central Pregnancy and Childbirth re
submitted paper “A comparison of inpatient with outpatient balloon
catheter cervical ripening: a pilot randomized controlled trial” MS:
1065760536138784

Chris Wilkinson
Pamela Adelson
Deborah Turnbull

Reply to editors comment

Please include name of the Institutional Review Board that approved the study
and confirm if it was written informed patient consent that was obtained.

Response - This research was approved by the CYWHS Human
Research Ethics Committee (equivalent to institutional review board) as
approval REC2453/3/15. This is documented on line 103 of the paper.
Written informed patient consent was obtained and is archived by the
researchers. This is documented on line 105 of the paper.
Reply to reviewer 1 (Therese Dowswell) report

1. Is the question posed by the authors well defined?
In many settings world-wide induction of labour is common, with approximately a quarter of pregnant women undergoing induction in the study setting. Induction of labour can lead to potentially life-threatening complications for women and babies. Induction of labour can be expensive both because of the cost of induction agents and the need for women to remain as inpatients. The pilot study described in the paper therefore addresses a very important topic: the use of balloon catheters for pre-induction cervical ripening in inpatient versus outpatient settings. The background section sets out the problem and the question addressed by the trial is well defined.

Response – No response required

2. Are the methods appropriate and well described?
Yes, the manuscript describes a pilot study for an RCT. I would have liked some more information on some of the issues raised.
I was not clear when randomisation took place. In the background it sounded as though randomisation took place BEFORE the catheter was inserted (“just prior to the intervention”) but in the results it was stated three women were not randomised because there were problems with catheter insertion. Would the authors please clarify? Post-randomisation exclusion is potentially a problem.
If women were randomised before the catheter was inserted did this in any way affect the waiting time for catheter insertion, the setting for insertion (clinic or inpatient setting) or insertion technique?
This was a feasibility study; it would be useful to have some further information on why approximately a quarter of eligible women refused to participate.

Response – We thank the reviewer for drawing this inconsistency to our attention, and have corrected it. (line 106 – “Randomisation was delayed until just prior to the intervention”, to “Randomisation was delayed until just after the catheter was inserted”) Randomisation could not take place until after a vaginal assessment was done, to confirm that cervical ripening would be needed. There were no post randomisation exclusions, and this study was analysed by intention to treat. It was felt
to be inappropriate to do a vaginal examination to determine if a catheter was necessary, then randomise, and then repeat a vaginal examination to insert the catheter, as this would unnecessarily increase the number of vaginal examinations (an uncomfortable process for most women). All women were thus randomised after the cervical catheter was successfully inserted, with only one vaginal examination being necessary for both assessment and catheter insertion. We do not think that this affects the generalisability of the study, as planned discharge of women with catheter cervical ripening would only occur if the catheter was successfully inserted, and outpatient care would not be used if cervical prostaglandins were necessary. Since women were not randomised prior to catheter insertion, this did not affect waiting times. Information on patient flow is given in figure 1 (consort diagram). We do not know why a quarter of eligible women refused to participate. In our recently published outpatient cervical ripening trial with prostaglandins (Wilkinson et al. BJOG, 2014;DOI:10.1111/1471-0528.12846), of 1,084 potentially eligible women approached, 827 women were consented (76%), a remarkably consistent figure consent rate compared to our findings in this pilot. In the previous trial, safety concerns were most commonly cited when women declined to participate, but the reasons were not documented for this trial.

3. Are the data sound?
Yes, the data appear sound although (as the authors note) the pilot was under-powered to demonstrate differences between groups for most clinical outcomes. The authors draw attention to a 24% difference in oxytocin group. Other fairly large differences between groups were not mentioned. It seemed more likely that the catheter would be expelled at home – if this is a real difference, what would account for it? The finding re oxytocin – the study was not blinded – although blinding this sort of intervention is not possible, lack of blinding may nevertheless affect clinician behaviour and introduce bias; it would be good if the authors mentioned this. It is possible that interventions in the inpatient group are increased simply because they may receive more monitoring.

Response – We drew attention to the 24% difference in oxytocin group as this difference is statistically significant (-23.6% [-43.8 to -3.5]). The other differences, even though as the reviewer points out, are fairly large, are not statistically significant. We have thus been deliberately cautious, and intentionally not overemphasized the differences, as the study was obviously underpowered, and, even though statistically significant, this difference in oxytocin use may be a type 1 error, but we do feel that drawing attention to the difference is not unreasonable. We do however, point out the homogeneity of the direction of effect of all of the other outcomes in favour of the experimental (outpatient) group, and point out that, as a pilot study, this result is encouraging and provides supportive evidence that may warrant an adequately powered study.
We agree that bias may be introduced in an unblinded study, but of course, blinding was not possible because of the nature of this
intervention. This is reflected in the inserted statement as suggested by the reviewer (lines 392 to 394)

4. Do the figures appear to be genuine, i.e. without evidence of manipulation?  
Yes. The data neonatal outcomes appears to be repeated in tables 2 and 3. Economic data were not reported here; it would be good to see that for the main trial.

Response – Thank you - the inadvertently duplicated data has been removed from table 2.  
As the reviewer has correctly presumed, a full economic evaluation and discrete choice experiment is planned for the main trial.

5. Does the manuscript adhere to the relevant standards for reporting and data deposition?  
Yes,

Response – Not required
6. Are the discussion and conclusions well balanced and adequately supported by the data?  
Yes, see above, more discussion of possible bias would improve the paper.

Response – This has been attended to (see authors response to section 3 - Are the data sound?)

7. Are limitations of the work clearly stated?  
See above.

Response – Not required

8. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?  
Yes.

Response – Not required

9. Do the title and abstract accurately convey what has been found?  
Yes.

Response – Not required

10. Is the writing acceptable?  
Yes.

Response – Not required

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare that I have no competing interests.
Author responses to BioMed Central Pregnancy and Childbirth submitted paper “A comparison of inpatient with outpatient balloon catheter cervical ripening: a pilot randomized controlled trial” MS: 1065760536138784

Chris Wilkinson
Pamela Adelson
Deborah Turnbull

Reply to reviewer 2 (Zvi Vaknin) report

Reviewer's report:

Comments to Author:
This small pilot randomized controlled trails, compares the inpatient with outpatient balloon catheter cervical ripening. Its strength is in the logical background and clinical need, for the use of the balloon catheter cervical ripening in an outpatient low risk pregnant women, and in the questions, ideas and parameters it explores. These factors can be used by a future, larger, randomized controlled study powered to give a statistical significance. Its major weakness is in the small population recruited, and as stated "..not powered for statistically significant differences..". The study is well written and it is a small pilot study, which can give some ideas of what to be expected in a larger and powered study. I recommend the publication of this paper, with some revisions.

Response: Not required

Abstract:
Well written and there are no comments.

Response: Not required

Background:
1. Line 65 - GTC – should be stated as Cardiotocography in the text and not in the end.

Response: Amended has been made as suggested by the reviewer.

Methods:
Well written and there are no comments.

Response: Not required

Results:
1. Line 181, unfortunately, I did not get the Figure-1, that is mentioned, so I cannot give comments regarding this Figure.
Response: We were ambivalent whether to include this figure or not in the paper (the consort flow diagram). It has now been included for the reviewers opinion.

2. Table 1 – WAS - Abbreviation ???

Response: The term “Womens Assessment Service” has replaced the abbreviation “WAS”

3. Table 2 –
-ARM - Abbreviation ???

Response: The term “artificial rupture of membranes” has replaced “ARM”

-Rupture of membranes - in the Outpatient column 4+ 30 = 34, while there were only 33 outpatients.

Response: Thank you – this apparent contradiction is due to 1 woman having a diagnosis of spontaneous rupture of membranes recorded, but later documented as having artificial rupture of membranes performed (see footnote “b”). It may have been a misdiagnosis of spontaneous rupture of membranes, or it may have been that there were residual forewaters that later needed to be ruptured artificially by the clinician. Since we could not be sure which scenario was correct, we reported both, with the explanatory footnote. We apologise for the confusion that results, but are obliged to report accurately. We hope that footnote “b” will be satisfactory explanation.

4. Table 3 –
- There is no mention in the text as for the data in Table-3, it should be pointed at line 199.

Response: Thank you – this has been done at line 203.

- Some of the data given in Table 3 overlaps the data in Table 2, such as the “Apgar <7”, and the “Special care nursery “.

Response: Thank you – this has been corrected.

5. The authors should think to replace Table 3 in a new one regarding the data regarding the acceptability of the catheter to women and clinicians.

Response: We have considered the reviewers suggestion, but the consensus of the authors is that the neonatal outcomes would be of greater interest and be seen as more important by the clinicians reading the paper and concerned regarding the safety of outpatient cervical priming. Although we make no pretense that our study numbers are adequate to prove safety, the authors felt that the reassuring neonatal outcomes should be more comprehensively reported, as a higher
priority than catheter acceptability, as is described in the body of the paper. (lines 262 to 284)

Discussion & conclusion:

1. Well written, in line 342 – ".. with the.." is repeated twice.

Response: Thank you very much - This has been corrected.

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'