Reviewer's report

**Title:** A randomized controlled trial to assess the clinical and cost effectiveness of a nurse-led Antenatal Asthma Management Service in South Australia (AAMS study)

**Version:** 1  **Date:** 29 July 2013

**Reviewer:** Susan Janson

Reviewer's report:

COMMENTS on the Manuscript: RCT to Assess Clinical and Cost Effectiveness of a Nurse-Led Antenatal Asthma Management Service in South Australia

This manuscript describes a proposed study using a randomized controlled research design. The proposed study is within a topic area that is significant, efficacy of individualized asthma management of pregnant women with asthma on maternal and infant outcomes as well as an assessment of the cost effectiveness of this nurse-led intervention. The findings should be quite useful in promoting asthma control among pregnant women and improving outcomes. The paper is well written but there are some concerns that need to be addressed.

**Major concerns:**

1. Randomization is not explained in detail. Stratified randomization is described variably as by disease severity in the abstract, severity and parity in the manuscript, and no mention of how the two sites are randomized is included.

2. The study design validity may be compromised by two factors: 1. conducting the study at 2 very different sites, and 2: the lack of an attention control strategy for the control group). These two issues should be dealt with before the trial begins. There is no mention of how the two sites may differ in implementation of the intervention or how this potential difference will be assessed, managed, and included in the statistical analysis. The issue of controlling for the large amount of time and attention to be received by the Intervention group with no plan for the control group will create the potential of an alternative explanation for the results.

**Minor concerns:**

1. Abstract: Under trial entry and randomization you specify the sample will be stratified by disease severity only. In the body of the paper you say stratification is by disease severity AND parity. Please reconcile these sentences so they say the same thing.

2. Pg 6 Asthma exacerbations during pregnancy are associated with adverse outcomes: Para 1, Line 2: The definition of an asthma exacerbation as you give it here needs a reference. Please add. Most definitions do not include peak flow rate, exclude or reference.

3. Pg 7 Section: Risk factors for exacerbations. Para 1, Line 1-3. The reference
cited is for one study of 146 women which does not warrant the statement that exacerbations are most likely between 17 – 34 weeks gestation…..unless these findings were confirmed in other studies. Revise to specify the findings are from one study only – generalizability is not yet been shown.

4. Pg 8 section: Existing evidence ….paragraph 1, lines 1-5. What groups are being compared in this nonrandomized study to determine a significant increase in birth weight? Compared to who?

5. Pg 9 paragraph 1, line one: Please clarify the statement that FeNO was associated with a significant reduction in exacerbations rate: was it the FeNO that was associated or was it the increased use of inhaled corticosteroid? If the latter, then insert the words “to titrate the dose of inhaled corticosteroid” after “FeNO in line 1.

6. Pg 11 Recruitment. Paragraph 1 , Line 5: “ventolin or a preventer” Why did you use a brand name for the inhaled beta2 agonist and a colloquial word for the control medication? Was it reliever and preventer? Is the “preventer” assumed to be an inhaled corticosteroid? There are other types of “preventer” asthma medications, such as leukotriene modifiers.

7. Pg 12, paragraph 1, line 12. What is meant by “a purpose designed Asthma Knowledge Quesstionnaire”? Did you create it for this study, and is it not validated? Explain.

8. Pg 12, Paragraph 3: Randomization. Randomization and stratified randomization methods need to be described in detail so that replication is possible. What about the randomization at 2 sites? How does a “telephone randomization service” work? What are number of blocks and how are they filled?

9. Pg 12 Paragraph 4: Standard Care Groups: What exactly happens to women who are randomized to this control group: If you want to just reference Practice Guidelines, you need to reference it so that your method of standard care can be replicated. If some women are being managed by respiratory specialists in the control group, how will you control for contamination? Is this plan meant to follow the intention-to-treat principle? Do you plan to identify and code these women differently for posthoc analyses?

10. Pg 13, paragraph 2, lines 1-4. Intervention Group: Explain how the asthma action plan is “individualized” from the standard template? What variables or patient characteristics are used to “individualize”? How much time is spent by the respiratory nurse with the participants in the Intervention Group? How will you control for all this attention in the Control group?

11. Pg 14: Data Collection: at the data collectors blind to study assignment? Will you have evidence of parity between providers in their level of skill at performing spirometry? Will the same amount of time be spent at the data collection visits in
both groups? Consider spending the same amount of time with participants in both groups by using a different control strategy in the Standard Care group rather than leaving it up to chance. At the least, participants in the Standard Care Group should be seen at 18 weeks same as the Intervention Group – attention control.

12. Pg 15: Primary study outcomes: Clarify that the outcome of incidence of asthma exacerbation is compared between groups, that is you hypothesis is there will be an absolute risk reduction of 20% in the intervention group compared to the control group. This end point is not clear as stated.

13. Pg 16: Sample size: lines 1-3. Isn’t the primary outcome is difference between groups in exacerbation rates, not “change” in exacerbation rate. In this new RCT you are not comparing the reduction rate to the literature (45%). The comparison is between the 2 study groups, so from your hypothesis you are expecting an absolute difference of 20% less exacerbations in the intervention group vs the control. Is this what you mean to say? Also, in the last sentence of this same paragraph you allude to the power to assess the other important outcomes. Were power calculations done for these other outcomes? If so it should be reported for each secondary outcome variable that you plan to analyze. If not, then you cannot make this statement in the last sentence.

14. Pg 16, paragraph 1 Statistical Analysis: What “adjusted” analyses are planned? Adjusted for what? In this paragraph the difference in exacerbation rates is clearly the primary outcome. Use the same language in the previous sections.

15. Pg 16, paragraph 2 lines 6-10. Are these “planned sub-analyses” the same as the adjusted analysis in paragraph 1. Clarify by making lines 6-10 a separate paragraph since these analyses sound like you plan to do this analysis on the primary outcome as well as the secondary ones. Consider using STATA if SPSS is inadequate for the mixed effects models and comparisons you want to make.

16. Pg 17: Cost Effectiveness. A general plan for collecting the data needed to determine costs is described. But it is not clear what statistical approach will be used to determine cost effectiveness of the Antenatal Asthma Management Service intervention. This will be an important outcome of the study as it will affect the generalizability of this intervention.

17. Pg 18 Trial Management: It is not clear whether the data monitoring committee includes the adverse events committee or is separate from the data monitoring committee. All adverse events should be reviewed not just deaths. What do the abbreviations CI and AI mean? Spell out.

18. What is included in the “quality assurance review” conducted by the respiratory specialist every 6 months? What are the credentials of this specialist?

**Level of interest:** An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.