Author's response to reviews

Title: Antenatal screening for Group B Streptococcus: A diagnostic cohort study

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Author's response to reviews: see over
10 May 2005

Dear Dr Dennison

RE: MS 4883792645966636 - Antenatal screening for Group B Streptococcus: A diagnostic cohort study

Thank you for providing us with the opportunity to revise our manuscript. Both assessors acknowledge the contribution that this paper makes to the body of knowledge in this field.

We will respond to the reviewers in turn.

David Isaacs:

1. Sample size.
As with most sample size calculations, there was considerable guesswork involved. The estimates provided in the paper were indeed conservative. In effect we identified a higher prevalence of GBS infection at all time points than we had estimated and the observed differences in sensitivities of over 8% are greater than the hypothesized difference of 6.5% increasing the power above and beyond that which was the basis of our estimates. We did in fact have adequate statistical power to identify all meaningful differences.

A larger sample size would not have changed the need to interpret results that demonstrate advantages and disadvantages with such a strategy. The results of statistical testing, presented in Table 4, indicate that equivocation about interpretation of results is not as a consequence of inadequate power but of trade-offs between different test characteristics. For example, using both a lower vaginal and a perianal swab (vs a lower vaginal swab alone) gives a range of statistically significant results. However some characteristics that you wish to maximize are improved (eg sensitivity and negative predictive value) while other characteristics that you also wish to maximize are significantly reduced in size (eg specificity and positive predictive value). These trade-offs are not apparent in the examination of timing of swabs. A larger sample size would not alter the varying direction of effects noted in the analysis of swab methods. We do not consider therefore that our sample size affects the interpretation of results and thus beg to disagree with the reviewer about the need to make a statement to that effect.

2. We have altered the emphasis throughout the paper from stating that there is “no consensus” to stating that there is a range of possible strategies. Thus we have changed the first paragraph of the abstract and the 3rd paragraph of the background. Elsewhere in the manuscript we have downplayed the variability in practice although not ignored it altogether as even within a relatively small country such as Australia there is variation in
practice. Thus we have removed the word “considerable” (ie “variation in screening” rather than “considerable variation in screening” from the last paragraph in the discussion section but retained mention of the variation in practice within Australia (as described in the 4th paragraph of the background)

3. Abstract: We have reduced the length of the abstract, removing detail from the background and methods.

4 Background: The reviewer is correct. The statement about the US strategy was complete in terms of screening but did not cover the approach to management of preterm births (which is not a screening strategy but a treatment strategy).

5 Results: There was some ambiguity in the way in which we had presented the results without including selective broth. It is 5-7% lower. We have made a correction. As both reviewers expressed interest in these findings we have included a part b. to Table 2 so these results can be presented in detail.

6. Discussion: (See point 5 above). The data on prevalence of colonisation in the absence of selective broth have been moved to results.

Alison Bedford-Russell

1. The paper has been paginated

2. The abstract has been altered to state that the benefit of screening lies in terms of positivity of swabs during labour.

3. References on incidence of GBS infection have been updated including the paper from Heath et al which reports a remarkably similar figure to that available from Australian data. As the focus of the paper is (as pointed out by the reviewer) on colonisation during labour, limited background material is provided on EOGBS among infants as no new data are provided in this paper on this outcome. We retain a preference for using Australian references where possible given the importance of local context noted by the first reviewer.

4. The definition of high risk in this paper is in accord with that in the literature (REF). We did include preterm birth (< 37 weeks) as is standard practice. We did not examine very preterm birth as a separate category as we would not have had the statistical power for such an analysis and it is not specified in most definitions of a high risk group. All infants born pre-term at the Women’s and Children’s Hospital are treated as though they are high risk. The high-risk definition used in this paper included preterm birth (< 37 weeks rather than the <35 weeks noted by the reviewer), GBS bacteruria, prelabour rupture of membranes and/or temperature during labour of greater than or equal to 38 degree Centigrade. This is a more extensive list of risk factors than those used by Heath et al., which included preterm delivery < 37 weeks, prolonged rupture of membranes and/or known genital carriage of GBS during pregnancy. Heath noted that his group did not have access to data on maternal fever in labour (which would otherwise have been included). Our list is consistent with that used in the CDC guidelines.

5. We have included some up-to-date references but wish to include Boyer (from 1983) as it is a key reference in this field. Heath’s finding that the rate of EOGBS is considerably greater among very preterm infants is of interest but does not have an impact on our conclusions. In the clinical environment in which this study was undertaken, in
which screening is universal, the key issue was how to undertake that screening most effectively and in keeping with evidence.

6. We have abbreviated the material on recruitment and patient management without losing detail of value to researchers attempting to replicate this work.

7. We have worked closely with statisticians (Ms Kristyn Willson and Ms Heather McElroy, noted in the acknowledgements) in calculating the sample size and in developing an analysis plan. This level of analysis has not been used before in the presentation of results on antenatal screening for GBS.

8. We have added more data about the colonisaton rates in the absence of selective broth and clarified the ambiguity in the presentation of the data in the original paper. Rates are 5-7% lower rather than 5-7% as highlighted by David Isaacs.

9. Our companion paper was published in “Birth” in 2003. It reports the results of focus groups undertaken with hospital staff and with a subgroup of participants in the quantitative aspects of the study and a number of women who refused to participate in the quantitative component. It would not have been possible to combine results from these companion approaches into a single coherent paper.

Yours sincerely

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cc: Copies to Helen McDonald, Philip Darbyshire, Caroline Crowther