Reviewer's report

Title: Early BCG vaccine to low-birth-weight infants and the effects on growth in the first year of life: A randomised controlled trial

Version: 1 Date: 27 October 2014

Reviewer: Hazel Dockrell

Reviewer's report:

This study reports the effects of BCG vaccine on growth when given to low birth weight infants at birth rather than delayed to the time when other vaccines are given at around 6 weeks of age. The results as interpreted indicate that Guinea Bissau could move to giving BCG to such low birth weight (LBW) children without any adverse effects on growth, and that it might have a positive effect on growth in girls.

These effects can be complicated and I am not qualified to review the statistical analyses. However there are a few points in the ms that deserve further discussion or clarification.

Major Compulsory Reviews

1. This study is complicated by the fact that 1717 of the infants, a rather high proportion of those recruited, were additionally randomised to receive Vitamin A with Vitamin E, or Vitamin E alone. The text on page 8 suggests that as early analysis had not identified an interaction between BCG and Vitamin A supplementation (VAS), the VAS status was disregarded in the analysis here; there is certainly no mention of VAS in the Results. However the second sentence of the Results section of the Abstract states that BCG had beneficial effects when given with, but not given without, VAS. Either there is an effect of VAS which must be taken into consideration, or not and this must be clarified.

2. The LBW children randomised to receive BCG early received it either at birth or at the first contact with a health centre after birth. Information should be included to clarify the spread of age at vaccination in both the early and late BCG groups.

3. One potential flaw in the design of the study is that it seems that the early BCG group received BCG Danish while the late BCG group were vaccinated at local health centres. Which BCG vaccine or vaccines did the late BCG group receive? If this was a different strain of vaccine there should be some discussion about whether this might have affected the results.

4. When the purpose of the paper is to compare the effects of the early BCG and late BCG vaccination, it is unclear why in Figure 2 only a single line is plotted for both groups together?

5. In Figure 3, it does appear that there are significant negative effects of early BCG on some growth parameters for boys, but these are not considered further?
6. It might help readers to know whether Guinea-Bissau is unusual in delaying giving BCG to LBW infants or if this is common in other countries?

Minor essential reviews
Page 3, Background line 3, suggest rewording to “vaccine given to low…”
Page 3, Conclusion, line 1, suggest rewording to “recommended to be given to LBW…”
Page 5, Study design, line 2, delete “the frames”.
Page 5, Study design, line 10, suggest rewording to “consent was given, ….”
Page 6, 3 lines from bottom, suggest rewording to “If children were briefly absent at the time of the home visit, an attempt was made to revisit them shortly afterwards.”
Page 9, Results, line 7, suggest rewording to “examined were travelling..”
Page 13, line 6, suggest rewording to “The weight-stratified analysis lends some support to the latter interpretation.”

Discretionary Revisions.
1. If would be useful to note that similar proportions of both the early and late BCG groups received oral polio, as this information is only included in the supplementary files.

**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 have been participating in the OptImmunize group led by Dr Benn. However I declare that I have no competing interests relating to this study.