Reviewer's report

Title: The benefits and risks of bacille Calmette-Guerin vaccination among infants at high risk for both tuberculosis and severe combined immunodeficiency: assessment by Markov model

Version: 1 Date: 30 August 2005

Reviewer: Neil Hawkins

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General
General Comments

1) The paper is interesting and clearly presented.

Specific comments

1) Although it is stated that the primary outcome modelled is quality-adjusted life expectancy, the model has a time horizon of 15 years. As it is believed there may be differences in mortality rate between the intervention, it may be more appropriate to have a lifetime horizon for the model, maybe using life-tables to estimate life-expectancy beyond 15 years of age.

2) As the focus of the analysis is decision-analysis I would suggest concentrating on the selection of the option that maximises expected QALE consistent with a risk neutral decision maker (as in the threshold analysis shown in figure 5) rather than the significance tests shown in table 4. For instance, in the abstract it is stated that ‘QALE is not significantly improved by BCG unless SCID incidence is 0’. However is could also be stated that ‘QALE is not significantly approved by withdrawing BCG unless SCID incidence is 23’. To provide an indication of uncertainty it may useful to provide estimates of the probability that BCG is optimal for a range of SCID incidence. Maybe a graph or a table giving the probability that BCG is optimal as a function of SCID incidence for a range of ARI values. This would be analogous to a cost-effectiveness acceptability curve. I think this would make better use of the work done to make the decision-analytic model probabilistic.

3) If significance tests are used I would suggest using phrases such as ‘BCG results in a statistically significant increase in QALE (p=0.05)’ rather than ‘BCG significantly increases QALE’ which might be taken to imply that the magnitude of the change is clinically significant. I would also question the statement in the results section of the abstract: ‘with this ARI (0.1), BCG is contraindicated if SCID incidence exceeds 23 per 100,000’ as figure 5 indicates that expected QALE is reduced by BCG where SCID exceeds 4 per 100,000.

4) It would be useful if we were provided with some values of expected QALYs for the different strategies as a function of SCID and ARI so we have some indication of the magnitude of the differences between the options. This may be useful if decision-makers are not risk neutral. Currently we are given an indication of which is the optimum strategy and some indication of significance but no indication of the magnitude of the differences in the primary modelled outcome.


Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)