Reviewer's report

Title: Cost-effectiveness of Introducing a Rotavirus Vaccine in Developing Countries: the Case of Mexico

Version: 1 Date: 10 January 2008

Reviewer: David Bishai

Reviewer's report:

General Comments

This could be an important paper for policymakers weighing the merits of adopting rotavirus. The paper offers a limited description of the policy context for current rotavirus vaccine decisions, so its overall importance is somewhat unclear. The results are time sensitive, so I hope the need to improve the paper doesn’t stand in the way of getting the results out soon. The most important (compulsory) improvements are providing more clarity in describing how a child’s age by month was treated in the model and how the onset of vaccine benefits midway through infancy are handled by the model. Second, and of equal (compulsory) importance are the need to check the robustness of results to alternative distributional assumptions and the need to actually present uncertainty intervals for costs and effects as well as the CE ratio. Other revisions are discretionary.

Other than these and a few minor points, the paper is technically sound and could make a good contribution

Specific Comments

Page 4 What is the current policy in Mexico regarding the rotavirus vaccine? CE results are one item in an adoption decision. What other concerns besides cost-effectiveness should policymakers bear in mind in deciding to adopt?

Page 5 estimate the expected number by month and age [in what units?]

Page 6 according to the month of the year and the age [in what units?]

Page 8 top line also ambiguous whether national data on diarrhoea incidence was by age in months for the first year of life or was stratified into mortality by age under 12 and age over 12 months

Need to clarify. It is great that the model accounts for seasonal effects by month, but it is unclear whether the model accounts for child age in months or in years. Table 1 only shows age effects by year raising suspicion that age related changes in mortality are modeled year by year. However, for the first year of life, the model will be sensitive to age effects by month. This is because
the earliest the vaccination schedule can be completed is 14 weeks. In fact the cost model assumes the vaccination schedule will parallel DPT schedule so children won’t derive full protection until 6 months of age. Espinoza et al(1997) find that greater than 50% of Nicaraguan children show evidence of prior infection by age 2 months before a rotavirus vaccine could have become effective. (Mexican case may not be so severe, but are there corresponding Mexican data?) Thus the model may overestimate the mortality reduction by assuming that 12 months of mortality exposure is reduced by the vaccine, when the child only derives 6-9 months of reduced mortality exposure.

Page 8. Assumption of no antigenic shift though plausible is optimistic. Evidence on this will need 5-10 years.

Page 10. Are the PRV efficacy estimates different for children of different ages. Efficacy is presumably 0 for children below 2 months?

Given the history of the Glaxo vaccine, paper should state and support the assumption that vaccine related morbidity and mortality are negligible.

Page 10. correspond to the first year starting 14 days Give more detail so readers can ascertain whether mortality reductions in the first year of life were pro-rated by the proportion of the first year spent unprotected.

Page 11. Equation formatting and choice of notation could be made more attractive using subscripts like Epp and NPP etc.

Page 13. Paper should flag the assumption that infants who die of rotavirus would have otherwise lived lives of normal length. Some might hold the belief that children who die of rotavirus may be more likely to suffer from other chronic diseases that shorten life expectancy. Indeed, many vaccine programs used to be built around the assumption that those at high risk of complications can be targeted ex ante and the vaccine could be targeted. Authors may want to address the ability of their model to address the cost effectiveness of a rotavirus vaccine targeting program.

Page 16. Describe the upper and lower bounds of what emerged for deaths averted, life years saved and costs from the probabilistic sensitivity analysis. Not enough to present just Figure 4 and be done with tell readers all they need to know.

Conclusion: Since the premise of the paper is that other countries can learn from a model for Mexico, paper should give guidance regarding the limits of extrapolation of CE estimates. What should be similar about another country’s diarrhea prevalence, overall child health, and medical costs before the Mexican results would be relevant? What differences would be most important in making an extrapolation.

Table 3 needs to display the units for any epidemiological rates, (e.g. events per 100,000 infants age xx) or (Percent) or (Pesos in 2007)
Table 4. It is unconventional to model the distributions for probabilities as being uniformly distributed or as truncated normal. (Briggs, 2000). These are typically taken to be beta distributions with medians set as per table 3 and 5th and 95th percentiles as per table 3. Exponential distribution for hospital day costs is correct. It would be important to test conclusions from current distributional assumptions against better assumptions. If results are very robust to alternative distributional assumptions AND authors can somehow defend current distributional assumptions then unconventionality would be tolerable. Sources of these distributional assumptions may not be available, so they need to be justified based on Bayesian priors for what best reflects the world’s state of knowledge.

Table 5. Since @risk was used. Table 5 can and should present the uncertainty interval (5th and 95th percentile) emerging from the 100,000 iterations studied. Intervals should be presented for both the numerator (costs) and denominator (effects).

Figure 4 is oddly normal. Cost effectiveness ratios aren’t always distributed normally especially when the denominator has a significant density over zero. Given that the CE ratio is normal, it can be fully summarized by mean and SD and the histogram is unnecessary. That is the beauty of normal distributions. So can eliminate Figure 4.


What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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