Reviewer's report

Title: Survey of childhood empyema in Asia: Implications for detecting the unmeasured burden of culture-negative bacterial disease

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Reviewer: Carrie Byington

Reviewer's report:

1. The major limitation of this paper is the variation in coding methodology for the 4 countries. This limitation cannot be overcome. However, the authors could include further analysis. The differences in proportion of empyema and effusion in China and Taiwan is striking and clearly must be a result of coding. The authors report the bacterial culture results as positive in 20% of patients coded as effusion. I would actually analyze these children as empyema based on culture result. Adding these 211 children could significantly change the Results of the paper. The authors should consider presenting the current analysis and an analysis of empyema based on positive culture results. They could compare the culture positive children to culture negative and might see significant differences.

2. The difference in isolation of pneumococcus between China and Vietnam compared to Taiwan is remarkable. Can the authors provide more information regarding laboratory methods at the different hospitals and information on the referral patterns to the hospitals? Are children more likely to present to the hospital in Taiwan before receiving antibiotics compared to the other hospitals.

3. The literature review is incomplete in the background. Papers from Canada, Spain and the US demonstrating increases in complicated pneumonia and empyema are missing.

4. The authors should comment on whether the incidence of empyema changed statistically over time in any of the countries.

5. The authors need to provide more background regarding the use of pneumococcal vaccine in the countries selected.

6. In other countries, most culture negative empyema has been attributed to S. pneumoniae. Are there any PCR data from any of the countries that could be used to help clarify the etiology of culture negative empyema in these countries?

7. What is the rate of penicillin resistance in S. pneumoniae for the years studied in the various countries?

8. Were data reviewed for blood cultures or only for pleural fluid cultures? Adding blood culture data might improve the results.

9. Can the authors suggest ways to improve methodology in the future, so that prospective surveillance will be reliable in these countries? Is it possible for these
countries to adopt a uniform definition and coding strategy for empyema?

**What next?**: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest**: An article whose findings are important to those with closely related research interests

**Quality of written English**: Acceptable

**Statistical review**: Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests**:

I received grant support from Wyeth to study pneumococcal empyema in 2007-2008.