Reviewer’s report

Title: The burden of rotavirus gastroenteritis and nosocomial rotavirus gastroenteritis among children aged <6 years in Japan: A multi-hospital, retrospective, epidemiological survey

Version: 3 Date: 18 January 2013

Reviewer: Julie A Bettinger

Reviewer’s report:

While the revised manuscript is much improved, and the reviewer appreciated the authors thoughtful response, there are still some major issues with the manuscript that need to be addressed.

Major compulsory revisions:

1. Methods lines 3-5. While the authors may not be able to provide the catchment areas for the hospital they should provide the population of children <6 years of age in the regions where the hospitals are located and that proportion of the entire population of children <6 years of age this represents. Without this information, one cannot judge the representativeness or generalizability of the results.

2. Methods and table 3: The logistic regression models were intended to model the risk of hospital acquired infection. However, with a total N of 13767 the authors did not remove the acute gastroenteritis or the community acquired cases from the logistic regression models. Clearly these children were not at risk for hospital acquired infection and the risk estimates are not correct. In their risk estimates, the authors should control for underlying health status and season, two variables which their descriptive analysis and the literature indicate are important. The authors also should show the number of hospitals with 7 nurses per patient, the number with 10 nurses per patient, the number with < 30 beds, the number with >= 30 beds and the number with and without isolations rooms. The authors need to use a model that will account for the hospital effects in their estimates as they are using individual level variables and hospital level variables.

Without significantly more development (adding important other covariates, adjusting for hospital effects, etc.) the risk estimates are the weakest part of this paper and the authors should remove them. Given the limited variables included (especially without an adjustment for the various types of underlying health conditions) they do not provide much useful information. Moreover, the interpretation of the estimates in the discussion is not correct.

3. The authors still have not provided the mean or median and range for duration of stay for patients with hospital acquired infection. They are only providing their calculation of additional days. The reader still cannot judge how they derived this
number nor the outliers that may be influencing this calculation. This information should be added given its use in the discussion to derive costs estimates. In addition, the authors need to describe the original conditions which caused the admission or the underlying health status of this group in order to understand the characteristics of these HA cases. The authors should also examine whether or not the length of stay for HA infections and the proportion of HA infections differs by the centers in their study.

4. Results page 11 lines 12-16. It is difficult to track the numbers in each group and this section should be rewritten to explain 1) number and % hospitalized with acute GE 2) number % hospitalized with rotavirus and 3) number and % hospitalized with HA rota. Once those numbers have been presented the testing patterns should be explained. The discussion mentions 32% of cases did not have a rapid test. This needs to be explained in the methods and results (see comment 9).

5. Page 14 line 4: This sentence should reflect the % due to rotavirus GE (4.8%) not all GE given the focus of this manuscript is rotavirus and the costs associated with rotavirus infection.

6. Page 15 lines 11-21: The interpretation of the risk estimate is incorrect. If estimates are not significant in the adjusted model then the risk is not higher. If the estimate and CI is above 0 then the risk is increased.

7. Page 17 line 3: please describe in the methods and results the % of patient without a RV rapid test. How was the rotavirus diagnoses determined for these cases? This is different than the information already presented in the methods and results.

8. Table 1 should present the % of underlying health conditions found in each group. And whether the types of conditions differed by group (Acute GD, RVGE and HA RVGE).

Minor revisions:
1. Figure 2: the figure legends should read hospital acquired rather than nosocomial.
2. Page 11 and page 12 lines 21-22: the reference to figure 2 should be removed. These data are not shown in Figure 2.
3. Results page 11-12 lines 22-2. Please clarify whether or not this is a mean or median. By using the word average this implies a mean. Given the range of values and the outliers a median is the appropriate measure to present.
4. Page 12 line 10 the reference to table 1 should be removed. These data are not described in table 1 and the characteristics of HA cases in table 1 have already been referred to on page 11 line 10.
5. Page 13 lines 3-4. The authors cannot say infants in intensive care are more likely (than whom?) to acquire hospital infection based on these data. They have not compared these infants to other groups. Also they have not indicated to which ward these infants were admitted.
6. Page 14 line 8: add hospitalized before RVGE.
7. Page 14 line 16: the proportion of HA RVGE is 0.6% NOT 12.2%. Please change.

8. Page 14 line 20-21: please add in “the incidence of 1.0 per 1,000 hospital days of HA RVGE reported in our study...” and “reported in Europe by Forster..”

9. Page 15 line 1 please change "high standard of care" to "infection control procedures". Japan does not have a higher standard of care than Europe.

10. Page 15 lines 5 and 6: Unless these studies measured transmission dynamics, you cannot determine who is more likely to acquire HA RVGE. Please reword.

11. Page 15 line 9: is 4.7 the average duration of hospitalization or the mean additional days of hospitalization? Please clarify.

12. Page 16 lines 3-4: what is the duration of a single hospitalization from which the $1,888 is derived? Please make this clear.

13. Page 13 line 13: these results cannot be applied to the general population. They may be generalizable to Japanese children < 6 years of age hospitalized for acute GE. Please reword.

14. Table 3: the N in the title is incorrect.

Discretionary revisions:
1. Methods line 7 typo.
3. Table 2: Please reorganize the age group to < 2 years; 2-<5 years and 5-<6 years and total (<6 years).
4. Results page 11 lines 16-17. The data on children < 5 can be presented in the table (with the relevant footnote as to why these data are being presented) but should not be presented in the text. It is confusing to switch back and forth between <5 and <6.
5. Figure 3 is not necessary. The data are nicely summarized in the text.
6. Page 12 lines 14-17: these data can go into table 2.
7. Page 15 line 1 The authors should consider commenting on the difference in infection control procedures practiced at the hospitals in this study compared to hospitals in Europe.

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

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare I have no competing interests.