Author's response to reviews

Title: Characterisation of acute respiratory infections at a United Kingdom paediatric teaching hospital (Observational study assessing the impact of influenza A (2009 pdmH1N1) on predominant viral pathogens)

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Author's response to reviews: see over
Dear Editor in Chief,

Please find attached the revisions to our manuscript: *Characterisation of acute respiratory infections at a United Kingdom paediatric teaching hospital (Observational study assessing the impact of influenza A (2009 pdmH1N1) on predominant viral pathogens)*, by Lees et al., which we would like to submit as an original study to BMC Infectious Diseases. We received detailed feedback from the reviewers which we feel has enabled us to improve our manuscript.

I have addressed the major revisions suggested by each reviewer in numerical order:

**Reviewer 1:**

1) The study did receive IRB approval from the study hospital and I have added a statement to reflect this.

2) All reviewers commented on the method of testing samples, which it seems was not made very clear in the original manuscript. Samples from patients with symptoms suggestive of bronchiolitis underwent rapid RSV testing, but all samples were then sent for formal respiratory virus PCR, regardless of whether they were positive or negative for RSV.

3) The opening statement of the discussion was felt to be too strong, so this has been reworded to reflect the spectrum of disease caused by H1N1.

4) A paragraph on limitations of the study has been added to the discussion

5) ‘H1N1’ has been replaced throughout the manuscript with 2009 pdmH1N1 to avoid confusion.

**Reviewer 2:**

1) Cases were selected based on the clinical diagnosis of ARI by admitting doctor and the confirmation of this on coding of notes at discharge. These cases included all types of ARI, not just LRTI.
2) See above statement on method of pathogen testing.

3) The aetiology of cases has been re-described by sample, rather than by patient. There were 653 samples sent for 645 patients, in only 8 cases were additional pathogens picked up on a separate sample – all other co-infections were noted on the original sample sent. Figure 3 has been re-worked to display severity of infection by pathogen in individuals with single infections only, rather than severity of infection by sample.

4) Limitations of the study have been discussed in more detail and the reviewer’s suggestions of limitations taken into account.

Reviewer 3:

1) See above comment on diagnosis of ARI by admitting doctor.

2) See above statement on method of pathogen testing. Details for Binax have been condensed as suggested as the assay is a commercial one.

3) The CDC method for Flu A/B testing has been referenced and the quality control measures introduced prior to transferral of Flu A testing to the study site have been detailed.

4) The results have been improved to give median, IQR and range for all appropriate categories. People with ARI following surgery have been highlighted as a group, as it was felt that they might display different characteristics to those admitted with ARI as primary diagnosis – e.g. more mild disease that wouldn’t necessarily require hospitalisation.

5) Figure 2 has been modified to provide absolute numbers of patients with each type of comorbidity.

6) Numbers of patients having duplicate sampling have been highlighted, and the statements on number of samples that were sent within 24/48 hours have been clarified.

7) Absolute numbers of patients with co-infection are given in table 1, and throughout the results segment of the text, numbers of patients as well as percentages have been added.

8) There was a high mortality rate for H1N1 but there were also numerous patients with H1N1 who had mild disease. These statements are not necessarily contradictory as H1N1 caused a spectrum of severity of illness. Discussion has been altered to try and express this more clearly. Limitations have been added such as lack of bacterial
culture results, which may explain apparently high levels of severe disease in those with hRV which may have been carried asymptomatically.

Reviewer 4:

1) The fact that bacterial culture results were not a part of the study has been highlighted as a limitation, but we feel that the study still provides interesting data on aetiology of circulating respiratory viruses in addition to H1N1.

2) The statement on pathogen detection has been improved to clarify how samples were tested. Samples from patients with symptoms of bronchiolitis were sent for rapid RSV testing to enable cohorting/optimal cubicle use at admission. Regardless of RSV result, all samples were sent for formal PCR testing at the time of admission, which has provided the data on circulating viruses. The study was a retrospective review of case notes and virology results over the period from April 2010-March 2011.

We confirm that the manuscript has not been published elsewhere and is not under consideration by another journal. All authors have approved the manuscript and agree with its submission to BMC Infectious Diseases.

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We look forwards to hearing from you at your earliest convenience.

Yours Sincerely,

Emily Lees

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