Reviewer's report

Title: Differing clinical characteristics between influenza strains among young adults in the tropics

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Reviewer: Benjamin Cowling

Reviewer's report:

This manuscript describes an evaluation of the etiology of acute URTIs among young adults in Singapore, and specifically a comparison of the clinical presentation of cases confirmed with influenza A/H1N1-2009, A/H3N2 and B.

A major concern with the study is the analytic sensitivity of the Resplex II assay. Do authors have data on the proportion of flu infections confirmed by flu-specific PCR that would be identified by the Resplex II assay or are there any relevant data in the literature? If not, authors may need to retest a subset of the original specimens by PCR to confirm the sensitivity of the Resplex II assay. This is important because the Resplex II assay may have low sensitivity in specimens with lower viral loads which could also have milder clinical presentation.

Please provide a figure of the timing of the confirmed cases through the study period. Did the subtypes co-circulate or did for example pH1N1 circulate in mid 2009 and sH3N2 circulate in mid 2010? If healthcare-seeking behavior also changed through the study period, with milder infections more likely to seek care during the height of the pandemic in mid 2009, this would have a serious impact on the comparison between subtypes.

Minor comments

Abstract background, and introduction section -- determining the presentation of influenza is important for epidemiological and clinical reasons -- could authors elucidate the clinical reasons? How are acute URTIs managed in Singapore and would it be affected by whether or not influenza etiology was suspected, without laboratory confirmation? In many countries URTIs are treated empirically and the underlying etiology is not particularly important?

I am slightly confused by the analysis in Table 1. Why would various symptoms act as confounders and how should the adjusted odds ratios be interpreted? Usually a confounder is a variable which is implicitly upstream (i.e. preceding) the outcome of interest, but the various symptoms and signs in this table would be consequent to the specific viral infection?

Regarding Figure 2, it is not common to use p-values as measures of the degree of association between two binary variables; why not use a direct measure of correlation such as the kappa coefficient or the newer measures such as the AC1 statistic?
Authors' bibliography suggests that studies of the clinical presentation of done outside of Singapore over the past 50 years, particularly in the US and UK, were not relevant for comparison? One obvious exclusion is the well-known JAMA paper "does this patient have influenza?" and there are many others.

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I have no competing interests.