Reviewer’s report

**Title:** Impact of antiviral treatment and hospital admission delay on severity of 2009 A/H1N1 pandemic influenza in Mexico, April-December 2009

**Version:** 2  **Date:** 10 February 2012

**Reviewer:** Vernon Lee

**Reviewer’s report:**

This paper is an important contribution to the literature on the association between antiviral treatment and delays in treatment to severe outcomes. The sample size is appropriately large, covering multiple periods of the local epidemic, and across broad geographical areas. The authors have adequately addressed the main hypothesis, and the paper is well written. There are some issues that I hope the authors could clarify.

1. It is interesting to note that the ILI definition is different from other classical definitions of ILI. While it is not an issue among those without PCR-confirmed influenza, is there any literature on the specificity and sensitivity of this definition for influenza.

2. How was the influenza testing done among the different groups of patients. Were more hospitalized and death cases tested, compared to those who only had ILI in the outpatient setting? Were more or less cases tested later in the course of the pandemic. It would be interesting to discuss this as if may have affected the results if anti-viral use was linked to testing.

3. It seems from the methods and results that severity was assessed broadly as outpatient, inpatient, and death. However, hospital admission itself was not an outcome variable unlike the case fatality rate. In which case, should the assessment of severity be more appropriately changed to assessment of mortality? And the title of the paper changed accordingly to impact on case fatality?

4. The authors stratified the admission delay into two groups, but not antiviral treatment into those that receive treatment <=2 and >2 days. Is there an implicit assumption that antiviral treatment is only given immediately upon admission to hospital. I would assume that antiviral treatment could be given before or some time after hospitalization. It would be important to explore the time to antiviral treatment and the relationship to the time to hospital admission, if this data was available.

5. Similarly, the reason for the antivirals administered more frequently to patients with short admission delay could be due to increased treatment in early-onset severity, rather than patients who may be well initially and therefore untreated, and deteriorated subsequently and needed hospital treatment. This possibility should be discussed in the absence of additional data to validate or refute this
hypothesis.

6. Discussion, 1st paragraph, line 8. The analysis does not directly support the effectiveness of antivirals when administered during the early symptomatic phase (<=2 days). At best, this is an indirect extrapolation because the time to treatment data was not available.

**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 had received unrelated research grants from GSK in the past.