Author's response to reviews

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

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Author's response to reviews: see over
To the attention of Dr. Diana Marshall  
Editor-in-Chief, BMC Infectious Diseases

Submission of a research article

Tempe, Dec 26, 2011

Dear Dr. Diana Marshall

Please find enclosed a manuscript, “Impact of antiviral treatment and hospital admission delay on severity of 2009 A/H1N1 pandemic influenza in Mexico, April-December 2009”, by Gerardo Chowell, Cécile Viboud, Lone Simonsen, Mark A. Miller, Margot González-León, Santiago Echevarría-Zuno, and Víctor H. Borja Aburto, which we wish to submit for publication in BMC Infectious Diseases as a research article.

In Mexico, the 2009 A/H1N1 influenza pandemic was characterized by a three-wave pattern occurring in the spring, summer, and fall of 2009 with substantial geographical heterogeneity (Chowell et al., Plos Med 2011). A recent study suggests that Mexico experienced high excess mortality burden during the 2009 A/H1N1 influenza pandemic relative to other countries (Charu et al., Clin. Inf. Dis. 2011). However, an assessment of potential factors that contributed to the relatively high pandemic death toll in Mexico are lacking. Here, we fill this gap by analyzing a large series of laboratory-confirmed A/H1N1 influenza cases, hospitalization, and deaths monitored by the Mexican Social Security medical system during April 1 through December 31, 2009 in Mexico. We estimated the case fatality rate, which measures the probability of death given infection, and carried out multivariate logistic regression analyses to quantify the adjusted effect of admission delays, antiviral treatment, age, gender, pandemic wave, and geography on the risk of death among A/H1N1 inpatients. Approximately 50% of all A/H1N1 influenza cases (outpatients and inpatients) received antiviral medications during the first two pandemic waves.
while only 9% of confirmed A/H1N1 cases received antiviral medications during the fall pandemic wave (Chi-square test, P<0.0001). We found that the case fatality rate was significantly lower during the period of high antiviral use (April-July, CFRflu=1.1%) than during the period of low antiviral use in the fall (August-December, CFRflu=2.4%, Chi-square test, P<0.0001). After adjusting for age, gender, pandemic wave and geography we found that antiviral treatment significantly reduced the risk of death (OR=0.52 (95% CI: 0.30, 0.90)) while hospital admission delays >2 days after disease onset increased the risk of death by 2.8-fold (95% CI: 2.25, 3.41). Our results suggest that decreasing admission delays and increasing antiviral treatment rates in the inpatient setting could lead to substantial reductions in mortality burden in future influenza pandemics.

Our manuscript is not currently under consideration elsewhere. All authors have contributed to, seen, and approved the final, submitted version of the manuscript.

Yours sincerely,

Gerardo Chowell, Cécile Viboud, Lone Simonsen, Mark A. Miller, Margot González-León, Santiago Echevarría-Zuno, and Víctor H. Borja Aburto

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