Author's response to reviews

Title: A model-based economic analysis of pre-pandemic vaccination cost-effectiveness

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Author's response to reviews: see over
Dear Editor:

RE: revisions required prior to editorial assessment, 12th Dec 2013

We have revised the submitted manuscripts to include the items omitted as per email request on the 11th Dec 2013. The original cover letter submitted appears on the next page.

The corrections are:

1) A title page has been added as the new page 1, with author details, institution and full postal address of corresponding author.

2) Our study did not involve human subjects or data – the following statement has been added to the manuscript on page 9:

   **Ethics Statement:**
   No human subjects or human data (other than aggregated anonymous statistical data) was used in this study.

3) An acknowledgements section has been added on page 17:

   **Acknowledgements**
   The authors would like to thank Dr Gary Dowse for his help in sourcing pandemic data from Western Australia, for the period 2009-2010. Funding for this study was provided by the Australian National Health and Medical Research Council (grant number 1004415). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.
Cover Letter for “A model-based economic analysis of pre-pandemic vaccination cost-effectiveness”

Dear Editor,

We would be pleased if you would consider our submission “A model-based economic analysis of pre-pandemic vaccination cost-effectiveness” for publication in BMC Infectious Diseases.

The manuscript reports on a cost-effectiveness analysis of two different vaccination-based strategies for mitigating future severe influenza pandemics. In this study we compare a strategy of reactive vaccination, which involves developing a vaccine that is matched to the emerged pandemic influenza strain (the strategy employed in 2009), with a strategy of pre-emptive vaccination, where the population is vaccinated with a pre-pandemic vaccine based on strains of influenza that are thought to present the greatest danger of emerging as a highly pathogenic pandemic strain.

Vaccination represents an ideal response to an influenza pandemic; however the likely scenario, demonstrated in 2009, is that a newly emerged influenza pandemic will have spread throughout the world before a vaccine matched to the pandemic subtype can be produced. The prospect of a pre-pandemic vaccine that can prepare the population prior to a pandemic occurring is therefore attractive.

This modelling study reported in this manuscript compares the relative effectiveness and cost-effectiveness of currently planned reactive vaccination strategies and a potential pre-emptive vaccination strategy. In order to make a meaningful and relevant comparison, both strategies have been made as plausible as possible: the reactive strategy assumes a six month delay to vaccine availability; and the pre-emptive strategy assumes a lower vaccine efficacy and ongoing vaccine renewal costs. All other assumptions that are not related to vaccination have been kept the same for both vaccination policies, including the inclusion of various combinations social distancing and antiviral measures.

Planning for the possibility of a an influenza pandemic due to a novel virus strain or subtype to which humans have little or no immunity is a major public challenge. Although the 2009 H1N1 pandemic turned out to be relatively mild [1], more severe pandemics are certainly possible as evidenced by the 1957, 1968 and especially the 1918 pandemic, which had an estimated case fatality ratio of 0.74% and 1.8% [2-4]. Current concern centers around avian influenza subtypes such as H5N1 and H7N9 that have been detected circulating in domestic bird populations in South-East Asia and China. These subtypes result in high mortality rates in humans who have contracted influenza from infected birds, having an estimated case fatality ratio in patients admitted to hospital of between 30% and 70% [5-10]. This may lead to a major public health disaster if such a virus mutates or reassorts into a form transmissible between humans.

Results from the study give clear guidance as to the expected performance of each strategy and, importantly, how the effectiveness and cost-effectiveness of each depends
upon pandemic severity characteristics, and the characteristics of the contrasted vaccination policies. We believe that our findings are an important contribution to the process of reviewing pandemic preparedness plans in the light of the 2009 pandemic, and inform future research into and development of pre-pandemic vaccination programmes.

Yours Sincerely,
(On behalf of the authors)
Dr Joel Kelso

References