

Author Response: Human infections with avian influenza A(H7N9) in China: preliminary assessments of the age and sex distribution

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We thank Dr Viroj Wiwanitkit for his comments on our preliminary assessment of the age and sex distribution of the human cases with avian influenza A(H7N9) virus infection. To clarify, we posed three scenarios which could possibly explain the preponderance of cases among elderly men reported through China's surveillance system: (1) differential exposure due to gender-associated practices and norms, e.g. more high risk behaviours among elderly men; (2) differential clinical course post-exposure/infection, e.g. given similar exposures, elderly men having a more severe outcome relative to other age-gender groups; and (3) differential health care-seeking/access behaviour favouring selection of elderly men, e.g., elderly men accessing health care more than other age-gender groups.¹ There may be more than one of these possibilities in operation, and this initial assessment was intended to pose the question to public health practitioners and researchers and to encourage further study into the causes for the distribution observed for this apparently emerging disease.² Our statement that it appeared unlikely that elderly men were being overly selected was addressing this third possibility.

While we agree with the four possibilities listed by Dr Wiwanitkit "that determine vulnerability to infection," we also believe that vulnerability to severe outcomes (i.e. scenario 2, differential outcomes given an infection) is important when assessing surveillance information given that reported surveillance data are often a function of severity. For example, during the 2009 H1N1 pandemic, while infection rates were lower in the elderly (attributed to likely cross-protection from previous H1N1 infection among the elderly survivors) relative to seasonal

influenza, once infected, the elderly were still at higher risk of serious complications.³

We agree with Dr Wiwanitkit's statement that "the virus can attack any age group." As we reported (age range 4–87 years) and as reported later in August 2013, China's routine influenza-like illness surveillance detected from outpatient visits six avian influenza A(H7N9) cases that skewed towards a younger profile.⁴ Of these, four had complications and were hospitalized. Notably, the non-hospitalized cases were aged two and four years while those hospitalized were older. This adds to the biological possibility that, once infected with avian influenza A(H7N9), the elderly may suffer more severe outcomes relative to their younger cohort. While acknowledging the wide age range for infection, the distribution of the avian influenza A(H7N9) cases continues to tend towards the elderly (more than half of cases are 60 years or older as of late September 2013, $n = 135$); this distribution remains strikingly different from that of avian influenza A(H5N1) and requires further investigation. As we noted regarding seasonal influenza infections, the elderly are generally more prone to suffer from severe clinical manifestation of influenza virus infection,^{3,5,6} and this may be the case for avian influenza A(H7N9).

Lastly, we appreciate Dr Wiwanitkit's comment regarding the possibility of the absence of immunity to the avian influenza A(H7N9) virus among the elderly, hence the true novel nature of the avian influenza A(H7N9) virus in humans causing infection in all ages rather than a detection and/or reporting artefact. We agree with this statement that is supported through extensive

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phylogenetic and virological analyses,⁷ the absence of pre-existing immunity to avian influenza A(H7N9) among high-risk groups before 2013⁸ and the lack of cross-reactive immunity in tested patients previously vaccinated against seasonal influenza viruses.⁹

As the winter influenza season in the northern hemisphere approaches with the potential for additional cases of avian influenza A(H7N9), it is imperative that investigations continue with regards to the observed skewed age and sex distributions.

Conflicts of interest

None declared.

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