Authors' reply: Benefit and risks of trivalent 2010 seasonal influenza vaccine in Australian children

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To the editor: Dr Lopert from Australia's regulatory body for therapeutic goods, the Therapeutics Goods Administration (TGA), raises a number of issues about our quantification of the risk-benefit ratio for seasonal trivalent influenza vaccines administered to children aged six months to four years in Australia in 2010 [1]. While we continue to believe the current data support vaccination of healthy children, it is important to conduct robust post-marketing surveillance, support an open scientific discussion of the observations, and ensure a rapid, comprehensive response to any potential adverse events following immunisation (AEFI).

The authors of the Cochrane review of influenza vaccine effectiveness in children have commented on the relative paucity in the public domain of good quality safety data on influenza vaccines for children aged less than five years [2]. Risk-benefit estimations, such as the approach we have explored, are also uncommon. However, one should not dismiss febrile convulsions as an adverse event. Febrile convulsions would be expected only rarely as demonstrated in a recent large population-based safety study which reported no significantly elevated risk for adverse events (including seizures in children) following administration of more than one million doses of trivalent influenza vaccine to children under the age of 18 years between 2005 and 2008 in the United States [3].

Our rapid communication to *Eurosurveillance* aimed to explore a method to quantify both risk and benefit [4] and was prompted by the TGA status report of 1 July 2010 that describes the investigation of an observed increase in febrile convulsions in young children following receipt of seasonal influenza vaccine in Australia [5] and contains a detailed analysis of risk by the vaccine manufacturer CSL Biotherapies. We did this after governments in New Zealand and Australia had recommended against using the CSL vaccines in children aged less than five years [4] and after the CSL vaccines had been licensed for use in the United States only for children nine years or older [6]. Our results support this decision. Moreover we indicated that our estimate of an unfavourable risk-benefit ratio

applied only to one vaccine manufacturer in one year. Generalisation to wider vaccine programmes would have been inappropriate.

Three of the four authors of our article are involved in the Western Australian programme aimed at assessing the public health impact of providing seasonal influenza vaccines to children aged less than five years. We believe that our involvement in promoting a vaccination programme to protect children from influenza, while being prepared to examine both the risks and the benefits of this programme, does not constitute a conflict of interest.

We chose to examine hospital admission for a febrile convulsion within 24 hours of receipt of seasonal influenza vaccine because hospital admission (or prolongation of hospital admission) is one of the four *serious* AEFI identified by the World Health Organization. The other three are death, permanent disability and any event that is life-threatening [7]. We acknowledge that hospital admission for febrile convulsion may be of shorter duration than hospital admission for influenza and that associated morbidity may be different, but suggest it is important not to underestimate the impact of either cause of hospital admission. It is also important to compare outcomes in the current context

Since 2008, for reasons we outlined in our rapid communication, Western Australia has conducted a population-wide vaccination programme aimed at assessing the public health benefits of providing greater access to influenza vaccines for children under five years of age [8,9]. This is not a clinical trial, but a programme using influenza vaccines licensed for use pre-school aged children, evaluated by observational studies. It is consistent with recommendations in the Australian Immunisation Handbook which states: '*Annual influenza vaccination is recommended for any person > 6 months of age who wishes to reduce the likelihood of becoming ill with influenza*' [10]. Universal vaccination of healthy children in this age cohort has been recommended by the Advisory Committee on Immunization Practices in the United States since 2006 [11].

Moreover a study from South Australia supports the need to evaluate a policy of providing influenza vaccine to healthy children, as well as those with known underlying conditions. The study demonstrated that 81% of children aged less than five years admitted to hospital with influenza between 1996 and 2006 had no documented risk factor that increased their risk of a serious outcome following infection [12].

We believe assessing risk and benefit will ultimately improve confidence in vaccine programmes.

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