

REPLY TO AUTHORS

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We appreciate the correspondence from Collignon et al. [1], as it allows us to clarify the findings of our study on trivalent inactivated influenza vaccine (TIV) and the implications for vaccination policy.

We provided complete information on adverse events following vaccination in the primary reports of our trial [2,3] which are both open access articles and should now be linked on ClinicalTrials.gov. No serious adverse reactions were observed, while myalgia and local reactions at the injection site were reported more frequently in TIV than placebo recipients. The trial protocol specified a follow-up period of 1 year for the small pilot study [2] and 1 year for the subsequent larger trial in 2009-10 [3]. Subsequently we took advantage of the assembled cohort by extending the latter study to a second and third year thus permitting further observations on annual risks of influenza in children and their household contacts.

Collignon et al. claimed that only 4 influenza B infections were prevented by TIV in our trial, but in fact the incidence rate of virologically-confirmed influenza B virus infections over the first year of follow-up was 3% in the 479 children randomized to TIV versus 8% in the 317 children randomized to placebo [3], i.e. a 5% absolute risk reduction (24 prevented virologically-confirmed infections in the 479 TIV recipients). Furthermore, not all influenza infections were virologically confirmed in this study, as in other similar studies, because of asymptomatic infections and underreporting of symptomatic infections.

We agree with Collignon and colleagues that the significant increase in acute respiratory illnesses in year 2 of follow-up in TIV recipients [4] deserves further investigation, but has not been reported in other studies. The 1-year Australian study cited by Collignon et al. has now been updated with 5 years of data and no evidence of an increased risk of non-influenza viruses in vaccinated children [5].

Many randomized controlled trials have demonstrated that vaccination is efficacious in protecting against influenza virus infections [6], yet we also know that immunity following natural infection can be stronger, broader, and can last for longer than vaccine-induced immunity. It is possible to hypothesize that vaccinated persons could face a slightly greater risk of influenza virus infections 2-3 years following vaccination, when vaccine-induced immunity has waned and circulating strains have drifted. For this reason in part, annual vaccination is recommended.

We agree with Collignon et al. that more prospective studies of TIV in school-age children would be welcome. This would however require substantial, sustained investment of human and financial resources that have time and again proved a step too far for overstretched funding bodies with limited foresight.

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