Reply to Sullivan and Kelly and Skowronski et al

TO THE EDITOR—We appreciate the insightful comments of Sullivan and Kelly and Skowronski et al concerning our article on influenza vaccine effectiveness in households during the 2010–2011 season. The comments of Sullivan and Kelly overall confirm, in another setting and influenza season (2012), that past vaccination may have a negative effect on current season vaccine effectiveness (VE). They also bring to light important issues of what might be the appropriate comparison groups for determination of VE when considering prior year vaccination. In doing the initial exploratory analyses to explain the low effectiveness observed in our study, we identified that there was significant interaction between current and prior year vaccination. For this reason, current year VE could not be estimated without taking this into account, which we did in a standard stratified analysis. We realized that, from a biologic basis, there were 4 groups to consider: vaccinated both years, vaccinated in the current year and not the previous year, vaccinated in the previous year but not the current year, and not vaccinated in either year. Instead of running another model, similar to Sullivan and Kelly’s model B, we opted, in our final table, to present risk of influenza infection, divided by these 4 groups. Examination of risk was the chosen option because we also had to deal with the unusual issue of previous vaccination with the pandemic vaccine, which was also available in the prior year. This approach also allowed making comparisons without having to choose a single or combined referent group. Given the limitation of small numbers, it is still possible to order the risks from the lowest to highest in those ≥9 years of age, where the need for 2 vaccinations for protection is not recommended [1]. For past receipt of seasonal vaccine, the lowest risk was seen in persons vaccinated in the current year and not the prior year, and the highest in those vaccinated in both years; risk was intermediate for those unvaccinated in both years. It is impossible to draw definitive conclusions from these data, in light of the small numbers, but it does suggest that the effect of repeated annual vaccination needs further examination.

This is the overall conclusion drawn by Sullivan and Kelly as well.

Skowronski and colleagues, citing observations from their network in Canada in 2010–2011, raise another explanation for the low VE against influenza A (H3N2) demonstrated in our study, namely, antigenic drift of the circulating strains away from the vaccine strains [2]. The World Health Organization (WHO) strain selection process of updating the virus composition in the vaccine is based on antigenic similarities and differences, informed by amino acid sequences. Based on strains circulating in 2010–2011, the WHO recommendation for the 2011–2012 vaccine did not result in a change in the influenza A(H3N2) virus strain selected; this decision was based on lack of significant differences in antigenicity in representative strains analyzed [3]. The amino acid substitutions pointed out by Skowronski et al were known at the time, and as she acknowledges, did not result in changes in antigenicity. It should be noted that this year (2012–2013), we have a somewhat similar situation, relatively low VE against influenza A(H3N2) in preliminary estimates from the US Influenza Vaccine Effectiveness Network [4], but little evidence of antigenic changes in the circulating viruses as an explanation [5]. In final analyses of these network data, the effect of past vaccination will be examined, but that is not possible at this time.

Overall, these questions raised by current examinations of VE indicate the value of such studies, but also indicate the need to understand better the biologic mechanisms that bring about lower than expected VE.

Notes

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