Reviewer’s report

Title: Prospective hospital-based case-control study to assess the effectiveness of pandemic influenza A(H1N1) vaccination and risk factors for hospitalization in 2009-2010 using matched hospital and test-negative controls

Version: 1 Date: 23 November 2011

Reviewer: michiel van boven

Reviewer’s report:

Summary

In this manuscript the authors present a prospective case-control study to evaluate the effectiveness of vaccination against pandemic influenza A(H1N1) preventing hospitalisation, and to identify risk factors for hospitalisation with pH1N1 and ARI. The authors conclude that pH1N1 positive cases in the hospital were 1) more likely to be unvaccinated than hospital controls, 2) more likely to have exposure to children in the household than hospital controls, and 3) less likely to have had a recent hospitalisation than controls. Furthermore, the analyses show that exposure to children was positively associated with ARI en a comparison of ARI cases with matched controls, while having had pH1N1 vaccination was negatively associated with ARI.

Evaluation

The manuscript by Hellenbrand and colleagues provides valuable information on the effectiveness of pH1N1 vaccination that deserves to become available in the public domain. I would like to commend the authors for their honesty, clearly stating that their study may be somewhat underpowered. I do have couple of suggestions that may help improving the manuscript. First, I would like to encourage the authors to perform an analysis of the characteristics of persons with ARI that did not participate to rule out that ARI cases included in the study are a non-random sample of all ARI cases. Second, I find Table 2 overly complex, and would like to suggest moving the table to online material. I would then present three (possibly two, see the next point) simpler tables in which only the significant factors in each of the analyses are included. Third, the analyses of pH1N1 cases with test-negative controls contains little interesting information, other than the finding that pH1N1 cases tend to be younger than pH1N1 negative cases. Therefore, I would suggest to drastically shorten the relevant sections on p12-13 and p16-17, to remove the formal analyses by simply stating that these analyses yielded no significant results, and possibly also to remove the relevant parts of Table 2 (blue), as in the present manuscript it distracts attention from the main findings.

Below are the answers to the editorial questions:

1. Is the question posed by the authors well defined? Yes
2. Are the methods appropriate and well described? Yes
3. Are the data sound? Yes, as far as I can judge.
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? I would have liked the authors to make the raw (anonymised) data publicly available. Other than that I got a good feel for the data.
5. Are the discussion and conclusions well balanced and adequately supported by the data? Yes.
6. Are limitations of the work clearly stated? Yes, very clearly.
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes, as far as I can judge.
8. Do the title and abstract accurately convey what has been found? Yes.
9. Is the writing acceptable? Yes.

Recommendation
Based on the above positive evaluation I recommend the manuscript by Hellenbrand and colleagues to be accepted for publication BMC Infectious Diseases after a minor revision that addresses the above points of concern, and that corrects a number of typos as detailed below.

Minor comments
p5: first instance of mentioning ARI. Please spell out.
p9: Bracket missing in equation for VE.
p10: ‘24 pH1N1 positive cases was PH1N1-vaccinated’ -> ‘24 pH1N1 positive cases were PH1N1-vaccinated’.
p11: ‘and >= 1 hospitalization in the past year’. Mention that this is a negative association.
p13: ‘equivalent to’ -> ‘yielding’.
p14: ‘In a register-based cohort study in Scotland … VE was 1005 (95%CI: -infinity-100%)’. If this is really was this study found then it adds nothing, and should be removed from the discussion and references.
p14: ‘were be included’. Remove typo.
p14: ‘In addition, vaccination …’. Clumsy second part of the sentence. Please rephrase.

---