Reviewer's report

Title: Effectiveness of the trivalent influenza vaccine in Navarre, Spain, 2010-2011: a population-based test-negative case-control study

Version: 2 Date: 10 October 2012

Reviewer: Joan Puig-Barberà

Reviewer's report:

I have reviewed the comments made by Prof. Heath Kelly and also the one I made to the first version of the manuscript. I've read carefully the answer of the authors and the changes they have made in their manuscript.

The author's have included in their resubmitted version most of both reviewers comments.

However, given their results on the null effect of the pandemic vaccine, on the absence of interaction between past and current vaccine, and, finally, the strong correlation with previous and current vaccination, authors (and readers) should be suspicious of the 20 points improvement on influenza vaccine effectiveness when both, current and previous vaccine, are considered as one unique exposure. This is surely due to bias due to background and unknown population characteristics.

In fact the population included is a mix of low risk, high-risk and no risk at all; of targeted for influenza subjects and people that were vaccinated because they choose to. This unequal study base is clearly shown in the age distribution of cases and controls, the majority in the 15 to 44 age group, a group at extremely low risk for mild or severe influenza, and the mix of outpatient and hospitalized patients, with disproportionate different numbers. I would advise against presenting a biased result as relevant as is done in table 3 of the manuscript. Nevertheless, this is a decision up to the authors.

The authors have modulated their discussion and their conclusions, and I would advise potential readers to opt for the caution in interpretation comments in the discussion.