Reviewer's report

Title: Influenza-attributable deaths in south-eastern France (1999 to 2010): mortality predictions were undependable.

Version: 2 Date: 2 March 2015

Reviewer: Barbara Rath

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The authors aim to show that influenza-attributable deaths caused by the A(H1N1)2009 pandemic in the South-East of France were much lower than expected.

To this end, they used a methodology previously established by Redlberger-Frity et al. applying it to an Austrian cohort. It is therefore not surprising that their results seem to follow the Redlberger-Frity et al. hypothesis; the authors support the idea that influenza A(H1N1)2009 had a much smaller impact than initially predicted.

Major Compulsory Revisions

1. Abstract, Background
The authors need to clearly state the objective/hypothesis of the study, which is not 100% transparent to the reader.

A statement of purpose should be included at the end of the Introduction Section similar to a sentence in the beginning of the Abstract, but to be completed to state the actual hypothesis:

Abstract L29: “we aimed to estimate the influenza-attributable deaths during the periods form 1999 to 2010.. in order to corroborate the hypothesis that…”

The sentence should continue with one (or both) of the following:

a)… influenza-attributable deaths caused by influenza A(H1N1)2009 viruses were much lower than initially expected (then specify expectation including reference or citation!)

b) …. in South-Eastern France primarily affected young people

2. Methods

Is there a specific reason why the authors did not calculate the number of life years lost? This calculation would be very insightful to be presented and discussed. Calculation of life years lost would provide additional detail regarding the overall effect of Influenza A(H1N1)2009 disease on a population level. Due to the fact that the age groups affected during the pandemic differed from previous seasons/ epidemics, the effect on the population of losing the young versus losing elderly people are different (long term losses versus short term losses).

This calculation would also provide stronger evidence for the final point in the
discussion regarding the overall number of deaths during the 2009-2010 season compared to previous ones (see comments L.225-226).

3. Conclusion
The fact that the age group most affected by the Influenza H1N1pdm(2009) viruses included children and young adults, does not mean that the virus was not serious. It seems that older adults and the elderly were more likely to be vaccinated and/or protected naturally.

Infants and children however, were quite significantly infected (incl. number of deaths). It may also be noted (and considered in the analysis) that infants and children were most likely to be un(der) diagnosed, due to the mere number of affected cases and the many competing viral causes of ILI in this age group.

Among those not immunized against the new strain, the death rate increased in all the 3 age groups incl. those younger than 55 years of age, (from an average of -0,035 to 0,28; an average of 0 to 0,58; and an average of 0,31 to 0,62). A simple estimate of the increase in number of deaths in each age group should give a rough estimate of the pandemic strength adjusted by age.

4. Conclusion (2)
A statement should be added to the effect that vaccination past exposure to antigenetically related viruses are both important when estimating/modeling the disease impact of a new viral threat. The A(H1N1)2009 pandemic could have had serious consequences, had the age group of the elderly not been partially immune to the virus. Using an effective vaccine in the children on the other hand, could have major impact on preventing spread of pandemic viruses – including to other risk groups, such as the elderly.

Discretionary Revisions

5. Methods
Even though the authors use the same procedure and statistical approach derived from a previously published study, the statistical methods used should be explained in more detail. This would allow the reader to follow the reasoning without having to have the initial paper by Redlberger-Frity et al. at hand (incl. readership in low-resource settings). Basic information which statistical package was used and how excess death rates were calculated, should be included.

Minor Essential Revisions

L 47. The authors should specify what is meant by the term “global”. After reading it seems to become clear that the “total n” in the study is the population in the PACA region of South-East France (which is represented in the study given their sampling design).

L49. “same approach of an Austrian study”. suggest: “same approach as in a previously published study using an Austrian population sample”.

L49, please specify the term “excess respiratory mortality (as opposed to “excess
mortality”). What is the baseline rate of “respiratory mortality” in South-East France? How is this data gathered? Does this include all age groups and respiratory disease or specific ones? Are there statistical data (publications or public health figures) which could be referenced?

L50. Thus, (comma)
L51 As direct result, (comma)
L52. saved
L51-53. The sentence goes back and forth. Rephrase so that there is some order in the sentence
L133- “where as” is “whereas”
L157-159. How were the groups divided? Please explain this somewhere.
L187. We considered it interesting to analyze the excess…
L192. Prevented
L190-192. The meaning of this sentence is unclear. Rephrasing this sentence would be advisable, for example: “Pre-existing exposure to closely related viruses prior to 1957 may have provided cross-reactive immunity during the A(H1N1)2009 outbreak in the same way influenza vaccination may reduce the incidence of influenza-related complications”.
L.199. The sentence is not complete, please specify which mortality rate(s) the “lower mortality” is compared to.
L215. Suggested citation. INSERM CepiDc?
L217. “none could forecast” or “none could have forecasted”
L219. “Was” suggest replacing by “had been”
L219.” In the global population” should be “for the general population”
L224. -The authors seem to overuse the term “global”. recommend to substituting by specific terms or “general” or “total” as applicable.
“The global assessment of the situation” is an overly generalist phrase. Its coverage should be substantially reduced. Example: “The assessment of this study “ is … “according to our observations”…. Or directly “The 2009 influenza pandemic….”
L.225. “has corresponded” is misused. Should be substituted by “has resulted in a reduction of the …. “.
L.225-226. This sentence repeats what was already stated in 224-225. It may be deleted. If the authors want to go into more detail, they should mention that the reduction in deathrates during the pandemic season occurred exclusively in the elderly population. As this age group accounts for the biggest share of deaths in the population studied, the overall number of deaths caused by the A(H1N1)2009 pandemic in the PACA population resulted in a smaller death toll compared to seasonal/epidemic years (see previous comments in Methods, second paragraph).
L.230. Consistency in headings: Colon in/out?
L.242. References style is different from all the previous heading styles

Figure 1. Y axis: Excess mortality per 100,000 inhabitants

Figure 1. X axis tags. Should not cover the figure itself. Tags should be under the bars.

References:

Ref 1,4: The references for online resources are incomplete and need to be revised to include author names, access dates and titles etc.

Ref. 4. Should be cited following the newspapers citation format.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests