Author's response to reviews

Title: Impact of Patient Characteristics on the Risk of Influenza/ILI-Related Complications

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Dear Ms. King:

Following please find our responses to the reviewers’ helpful comments.

Dr. Mauskopf’s requests:

1. Reporting the percent of total health care costs attributable to influenza/ILI in the 21-day interval of care is not a key outcome and should not be included in the results and conclusions in the abstract. It is fine to include it in the body of the paper, just not in the abstract.
   **We have omitted these from the abstract.**

2. A justification for the 21-day interval should be given in the methods section.
   **We have inserted the justification.**

3. A justification for the 30-day health service use pre-influenza/ILI for complications or manifestations on influenza should be given in the methods section.
   **We have inserted the justification.**

4. A table showing the ICD codes and what they refer to should be given to identify the complications and manifestations of Influenza/ILI - otherwise the reviewer and the reader cannot judge whether these are sensible codes to use to define complications or manifestations.
   **We have listed out all the codes and their meanings in a new Appendix A.**

5. The discussion is too long and repetitive - I suspect that this may be a typographical error in the submission - page 16 and most of page 17 is repeating what has been said before.
   **As Dr. Mauskopf points out, the discussion was literally repetitive as well as figuratively so. We have eliminated duplicate text (apologies, this was a paste without a cut), and we have removed the most obvious statements, such as to say that we have not evaluated costs that were not in our data.**

6. I do not think that it makes sense to include the results of the impact of vaccination on hospitalization or complications since this is clearly a biased population as mentioned by the authors - those getting vaccinated are more likely to be high risk for complications. Thus, the results from this analysis are really not informative (without an analysis that compensated for the biased selection), are potentially misleading (i.e. being vaccinated makes you more likely to get complications), and would be better omitted from the paper.
   **We have not removed the result, but we have greatly strengthened the caution against interpreting this as a causal effect.**
7. The comments made in two or three places in the paper, that the results of the analysis are likely to be an underestimate of the true costs of influenza/ILI should be modified always by including the words "for the population of people that visit the physician for the condition". If one were able to include the majority of people who do not visit the physician with influenza/ILI, then it is more likely that the costs presented would overestimate the average costs of a case of influenza/ILI. **We have been careful to specify that we are talking about health care costs. We have expanded on the limitations in the eighth paragraph of the discussion.**

8. The sentence "The recent marketing of influenza antivirals may have an even greater impact on the predictors of complications and health care related costs of influenza" should be modified. There is some evidence that the new drugs will reduce complication rates - e.g. the Lancet paper on zanamivir demonstrates a reduction in complication rate. I am not aware of published evidence that the total costs per case of influenza/ILI will be lower with the new drugs when the drug costs are included. **We have referred to the Lancet paper with respect to the occurrence of complications and we have removed speculation about the cost impact of oseltamivir and zanamivir.**

9. In table 2, 'ref' should be explained in a footnote. **Corrected.**

10. In table 4, I find the two 'sum' columns confusing. They either need more explanation or should be omitted. **Sum columns have been removed.**

Dr. Fleming’s comments and requests:

1. The authors correctly point out that comparatively few persons aged 65 and over were included and this is a serious limitation. **No response required.**

2. There is an inherent assumption that all influenza related disease is labelled influenza-like illness. From experience of surveillance in the UK it is evident that conditions such as acute bronchitis and acute otitis media are also increased during influenza outbreak periods inferring that influenza is the probable cause. The authors have not examined diagnoses other than those coded as influenza (ICD 9 code 487). **Correct. We have included this limitation in the eight paragraph of the Discussion.**

3. The time period for this examination was the beginning of October to the end of the following April. It would be useful to show the distribution of cases (preferably by week) and for any comments on that distribution especially in the light of available virological data even if not from the same population. They refer to such virological data on page 16 but provide no indication as to the timing of virus circulation. **We have in preparation a manuscript that examines weekly onsets for a much larger and more geographically dispersed set of populations, which we can compare to CDC data. We have not done so here.**

4. It is not possible to generalise from one epidemic experience to others.
Though we disagree with the absolute nature of this assertion (how else could we learn anything at all, ever?), we have not made any claims for generality.

Thanks to you and to the reviewers for your careful attention to our manuscript.

Sincerely,

Alexander M. Walker