Author's response to reviews

Title: First-year results of the Global Influenza Hospital Surveillance Network: 2012-2013 Northern hemisphere influenza season

Authors:

Joan Puig-Barberà (puig_joa@gva.es)
Anita Tormos (tormos_ani@gva.es)
Anna Sominina (anna@influenza.spb.ru)
Elena Burtseva (elena-burtseva@yandex.ru)
Odile Launay (odile.launay@cch.aphp.fr)
Meral Ciblak (ciblakm@yahoo.com)
Angels Natividad Sancho (angels.natividad@hotmail.co.uk)
Amparo Buigues Vila (buigues_marvil@gva.es)
Sergio Martinez-Úbeda (sergi.mtz@gmail.com)
Cédric Mahé (cedric.mahe@sanofipasteur.com)

Version: 3
Date: 7 May 2014

Author's response to reviews: see over
Dear Editor,

Thank you for your recent comments on our manuscript, “First-year results of the Global Influenza Hospital Surveillance Network: 2012-2013 Northern hemisphere influenza season” (MS 2312452061257091). We were informed by Ms. Dalumpines that you would like us to a point-by-point response to the following comments:

The statement about vaccination on page 12 that "...this study confirmed that vaccination uptake is low in many European countries..." is too strong. The study design cannot confirm vaccination uptake. The study includes patients hospitalised with an influenza infection. If the vaccine is at all effective, then the incidence of vaccination among influenza-infected patients will be lower than the general population. The effectiveness of the vaccine was probably variable according to the various strains circulating in each country, so no firm conclusions can be drawn. I think the vaccination status should be reported as a measured characteristic, for example, in Table 5.

The statement "...the coverage rate in France was highest at 47.0%..." should be changed. You have not measured a coverage rate of the population. You have measured the proportion of the hospitalised patients with influenza infection in your study that had been vaccinated. This is a very different thing. The high proportion deserves comment.

Why was such a large proportion of vaccinated patients becoming infected? Please refer to some literature on influenza vaccine effectiveness.

Point-by-point response to the comments

We would first like to clarify that vaccination status was a measured characteristic for patients in the study, regardless of their influenza status. Therefore, we can report the proportion of hospitalized patients in our study that had been vaccinated irrespective of their influenza status. Not including this in previous versions of Table 5 was an oversight. The information on the vaccination status of hospitalized patients in our study who were positive for influenza has now been added to Table 5 and is shown below:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Valencia, Spain</th>
<th>St. Petersburg, Russia</th>
<th>Moscow, Russia</th>
<th>Turkey</th>
<th>France</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated 2012-2013</td>
<td>N=236</td>
<td>N=652</td>
<td>N=471</td>
<td>N=36</td>
<td>N=150</td>
</tr>
<tr>
<td>Yes</td>
<td>82 (34.8)</td>
<td>11 (1.7)</td>
<td>6 (1.3)</td>
<td>5 (13.9)</td>
<td>50 (33.3)</td>
</tr>
<tr>
<td>No</td>
<td>154 (65.3)</td>
<td>641 (98.3)</td>
<td>465 (98.7)</td>
<td>31 (86.1)</td>
<td>100 (66.7)</td>
</tr>
</tbody>
</table>

All values are number of subjects with percent in brackets.

We agree with the comment that the results are not representative of the overall population and that no firm conclusions can be drawn. We have revised the text accordingly.

The high proportion of vaccinated patients becoming infected could have been due to the fact that the influenza vaccines administered had only a moderate protecting effect (Osterholm et al. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. Lancet 2012;12(1):36-
44) and the possibility of incomplete matching between vaccine and circulating strains of influenza virus.

We have modified the discussion as follows (new text underlined):

> Although the patients included in this study were not necessarily representative of the overall population (i.e. subset of hospitalized patients with a diagnosis possibly associated with influenza), vaccination rates in these patients were lower than recommended by the WHO for European countries [24]. The French patients in this study had the highest vaccination rate at 47.0%, which was similar to the overall rate for France reported in 2010-2011 (50.4%) [25]. However, it is not unusual to observe some influenza cases in vaccinated individuals because seasonal influenza vaccines have only a moderate protecting effect, especially in elderly adults [26]. The lowest vaccination rates for these patients were in the Russian Federation, where fewer than 2% reported being vaccinated for seasonal influenza. This may have been due to the peculiarity of the groups enrolled (e.g. mostly pregnant women in Moscow and mostly children in St. Petersburg), poor uptake, the ability of the vaccine to prevent hospitalization, or a combination of these factors, although these influences remain to be assessed over the coming years.

Thank you for the opportunity to publish our manuscript in *BMC Public Health*. We look forward to hearing from you.

Sincerely,

Joan Puig-Barberà
FISABIO-Salud Pública