Reviewer’s report

Title: Assessment of two complementary influenza surveillance systems: Sentinel primary care Influenza-like Illness versus severe hospitalized laboratory-confirmed influenza using the moving epidemic method

Version: 2 Date: 27 Mar 2019

Reviewer: Joan Puig-Barbera

Reviewer's report:

Dear Editor,

Thank you for the opportunity to review the Assessment of two parallel influenza surveillance systems: Sentinel primary care Influenza-like Infection versus severe hospitalised laboratory-confirmed influenza manuscript.

This study is based on surveillance data of ILI incidence rates from primary care sentinel surveillance, virology results from sampling by sentinel primary care physicians and severe laboratory-confirmed influenza (SHLCI) that required hospital admission during seven influenza epidemic seasons, from 2010 to 2017, in Catalonia. The authors assess the parallelism of community primary care activity and severe hospitalisations related to influenza during seven influenza seasons using the Moving Epidemic Method (MEM). MEM has been recently (2011-2013) endorsed by ECDC and WHO Europe and is actually in the focus of the public health community [1-5]. The integration of ILI/ARI data with virological information should improve and validate MEM usefulness and has been covered recently and is an actual ongoing field of study [2,4,6,7].

The manuscript should, therefore, be of interest to BMC Public Health audience, but, in its current format, it needs a major revision before being accepted for publication. English use, wording (Mobile is to be named Moving), underpinning conceptual framework presentation, a more concise and ordered discussion and recent MEM references should be included and discussed.

Paper goal
The authors compare two surveillance systems in their capacity to describe epidemic intensity levels.
1. Sentinel primary care Physicians / (ILI) and ILI with laboratory-confirmed influenza
2. Reporting hospitals: / (SHLCI) severe hospitalised with laboratory-confirmed influenza cases.

And conclude that:
1. Influenza sentinel surveillance system combining primary care and hospital data provides a timely and accurate syndromic and virological assessment of influenza epidemic intensity.
2. The implementation of a third hospital warning system based on data from emergency department records for laboratory-confirmed influenza would be desirable.

Title
Actual:
"Assessment of two complementary influenza surveillance systems: Sentinel primary care Influenza-like Infection versus severe hospitalised laboratory-confirmed influenza."
Is Sentinel primary care a proxy for Primary care Sentinel Surveillance System?
Its Sentinel primary care "Influenza-like Infection"? Or "Influenza-like illness"?
Please clarify both.
The sentence "using the moving epidemic method" should be added at the end of the title.
All this would convey a more explicit message to readers.
Abstract
Page 2
Line 13: Suggest: "...epidemiological study carried out during seven influenza seasons (2010-2017) in Catalonia, with data from..."
Line 13, where it says: "data from influenza sentinel surveillance of primary care physicians."
What is reported by primary care physicians? If it is ILI
Suggest: data from sentinel surveillance of primary care physicians reporting influenza-like illness (ILI)
Line 15, can be misread, do hospitals provide data on outpatients?
Suggest:
and 12 hospitals that provided data on severe hospitalised cases with laboratory-confirmed influenza (SHLCI).
Line 18 and 19, it says:
"Epidemic thresholds for incidence rates were assessed by the Mobile Epidemics Method."
All the literature refers to the "Moving Epidemic Method" (see [1-5,8]). This is a significant drawback. If the term Mobile is used, it will prevent retrieval as this is not the widely accepted (ECDC, Who Europe, see references) of how the method should be named.
Were it says:
"Epidemic thresholds for incidence rates were assessed by the Mobile Epidemics Method "
It should say
"Epidemic thresholds for ILI incidence rates and (which SHLCI metric was used, % Of positives by week? Admissions with Influenza lab confirmed population rates?) were assessed by the Moving Epidemic Method (MEM) "
Swap "Mobile" by "Moving" all over the text.
Line 25 and Line 31 PIDIRAC. FLU, ILI, FLUA and FLUB are unexplained acronyms. There is extreme use of non-standard abbreviations.
Considering influenza A and influenza B, plus influenza overall adds a layer of complexity that is not adequately covered in the Abstract background or Methods. Moreover, subtype analysis would be the proper approach given the differences between A(H3N2) and A(H1N1)pdm09, even between B/Yamagata and B/Victoria lineages, and it should be discussed if this is robust approach given the small number of training seasons to implement MEM.
Was, therefore, and study goal to further differentiate by influenza virus type? If this were the case, this should be included in the Abstract Background or Methods, in the appropriate same manuscript sections.
This conclusion cannot be implied from the data presented and would be more adequately argued in the Discussion's last paragraph. I do not see, however, that the results presented and what is already published support adding this new layer on top of reported admissions with severe hospitalised laboratory-confirmed influenza cases (SHLCI). So the authors should offer reasoning or fact supported evidence to justify that statement.

Background
Page 3

Line 58, "Random" or "systematic sampling"? A sampling method can be either systematic or random, but not both. Review that also in Methods.

Page 4

Line 7. Is this the case in Catalonia or are it and overall characteristic in those systems?, please, provide evidence (i.e. Reference(s))

Line 18, the first appearance of an acronym in the text should be anteceded by its explanation, please, include it here.

Lines 29-37
How do severe cases reach the hospital and are admitted? This paragraph is a bit confusing, are not the majority of severe cases admitted to the hospital after discharge to admission from the Emergency Department? Please make this clear. Moreover, Reference 6, is the Catalan health care system similar to Australia's... are included hospital third level care hospitals?

Which rates (parameters) are considered when including SLCIH? Population rates by n/time? Percentage of positives by week? Explain.

Line 38, When was the Primary Care Sentinel Surveillance System was implemented? Please, explain.

Methods,
Data sources
Page 4,
line 59
Omit the bullet points, and introduce your "Data sources" subsection in the Methods section as such, in a single heading.
Subheadings for the Primary Care based ILI Surveillance System and Severe Admissions with lab-confirmed influenza can be included if needed. But, a describing paragraph for each one should suffice.

Page 5,
Line 4, omit "random", "systematic sampling of the first 2 patients"... is perfectly adequate
Lines 10 and 11, other respiratory viruses are not of interest here, but how the samples are treated is of relevance. RT-PCR? Subtyping? Reporting consistency (timeliness)? When dealing with hospital cases, we are told that positives were subtyped. If primary care lab-confirmed influenza (LCI) cases were or not subtyped. Is this primary care information included in Figure 1? As sampling was performed in the first two cases each week, could you explain which rates and how they were estimated for primary LCI influenza cases (PIDIRAC-FLUA and FLUB)? Please, add in the discussion how it could impact the comparison with the thresholds obtained from hospital LCI cases.

Line 20. Clarify the meaning of incidence rates here, (denominator, per 100,000 inhabitants? per week?) that will facilitate the interpretation of the information reported thereon.

Line 29, "Mobile" -> "Moving" "Epidemics" -> "Epidemic"

Lines 29 to 36 should move to the Statistical analysis section, preceding Page 6, line 24.

See also my comment below for Table 1.

Page 6.

Line 9 and 13 both mention rates. Before in the text, we have been told that no population denominators were available and that (because) some (all?) hospitals were reference hospitals (level of care?) Please clarify, which rates do you refer to in lines 9 and 13?

Do not duplicate rates description for SLCIH.

Line 11, in MEM thresholds, are estimated to predict the beginning of the epidemic season and to describe levels of intensity. I would counsel to omit the word activity in the text. It is used with different meanings in different parts of the manuscript, and that use as a proxy of different situations is in detriment of exposition clarity.

Line 13 to 19, should under the Statistical analysis section, following the paragraph (lines 23-29, Page 5) that should open the Statistical analysis Methods subsection.

Statistical analysis

Line 22

MEM is part of the Statistical analysis and should be referred here as the first paragraph of Statistical analysis subsection in methods, explaining here that it was used to estimate statistics (enumerate and describe) for both Primary Care and Hospital derived data, as requested above.

Overall, the paragraph in lines

Line 31, "activity" -> intensity, the activity is here redundant, delete, or say intensity levels.

Lines 38 to 45, review those two incomplete "sentences or depended on clauses" as one presents the problem and the second tells how it will be solved, but instead of being connected as a logical flow, they are separated by a period and presented as two different things. I suggest the authors transform both into a single sentence, with a problem and its solution.

Line 40, "activity"-> epidemic
Line 42, "Level" -> "estimated epidemic threshold".

All in all, the sentences contained in lines 30 to 45 are critical to understanding how the authors will compare the different systems. The analysis is, however, presented first by comparing intensity levels and their thresholds estimated for the surveillance systems considered followed by the ability to predict the epidemic onset. Notice that this is not a logical order, as first, we expect an epidemic to begin to know afterwards about its intensity. This contrarian presentation of issues does not help reading and understanding. Please, consider.

Could you add the predicted epidemic onset in the figures?
Results
Page 6, Line 53.
The first sentence refers to Table 1, note that in the submission Table1 is positioned after Table 2.
Please, order the tables consecutively, first 1, then 2.
In the text, we are told that epidemic levels are presented there, but the title in Table 1 refers to "threshold levels."
In fact, the table reports (?) "threshold levels" such as epidemic and intensity, but not activity threshold levels, according to the results usually obtained (and named) when applying the MEM approach.

Accordingly, I suggest:

a. I would recommend that this is made clear beforehand in the text by the authors, describing in Methods, Statistical Analysis, MEM, the definition and meaning of threshold level(s), epidemic and intensity levels. I would suggest that this is also made clear in the text and that the Table caption and column headings are both consistent with the main text and table contents.

b. The table caption should be following the text and explicitly mention that what is presented in the Table is the threshold value for epidemic onset and for intensity levels.

c. The first column heading. This column will show Data Sources. Not rates for the surveillance systems described.

d. Second column title should be Epidemic threshold, notice that baseline and threshold levels are not the same estimate (see Vega et al., 2013).

e. Rest of column heading are thresholds for intensity (activity) levels: low, medium, high. Please make this clear with an umbrella heading with levels as subheadings.

f. Footnote, specify rates of what/per how many/time.

Page 7, Line 38, severity or intensity?
Line 55-56, epidemic activity weeks, which is the difference between "epidemic weeks"? The word "activity" is redundant, see my comment above.
Table 2 does not report rates whatsoever, why duplicate the footnotes in Table 1 in which rates are actually reported.

Discussion
Page 8.
First paragraph, lines11 to 35 is out of place, it probably would fit in the Introduction, where the definition of the context and background of the main manuscript theme is being explained.
This paragraph, however, does not fit the manuscript content as the logical conclusion of the ideas exposed would be that an annual influenza vaccine effectiveness monitoring system is needed. The goal of the manuscript goes about predicting the beginning of the influenza season and levels of intensity and peeks by two different reporting systems, primary care ILI and hospital virological data and additionally primary care and hospital virological information.
The next page paragraph, lines 38 to 51, is definitely a first paragraph for the Discussion of results and methods.

Line 49 What do you mean here by "activity", season onset? Peak? Intensity?
I would suggest a carriage return in line 51, to make a clear distinction between what has been observed versus the proper discussion of what is the interpretation of the observed results and its limitations. "Case definition…" should be the beginning of a new paragraph.

Lines 55 to 60. While interference among respiratory viruses has been previously described, regarding the surveillance of influenza epidemics the interference or variability of MEM sensitivity and specificity due to the circulation of other viruses has been observed in ARI based surveillance systems. Can the authors discuss this?

Page 9,
Lines 9 to 20, could the authors review and compare their arguments here with Murray et al. findings in the UK (Murray JLK, Marques DFP, Cameron RL, et al. Moving epidemic method (MEM) applied to virology data as a novel real time tool to predict peak in seasonal influenza healthcare utilisation. The Scottish experience of the 2017/18 season to date. Eurosurveillance 2018; 23. Available at: http://www.ncbi.nlm.nih.gov/pubmed/29560854 )?

Line 22. The authors introduce the "strengths and limitations" discussion, but this section does not follow a step by step reasoning thread.

Lines 27 and 29.
MEM is intended to trigger harm reduction activities due to its sensitivity and specificity in predicting season onset and peak. In addition of intensity, accordingly "intensity and severity" are outplaced, as is the preeminent influenza epidemic in itself, independently of intensity and severity, that will trigger those measures justified by an over the baseline circulation of influenza, for instance, the crossing of the therapeutic threshold for the use of antivirals, public communication, resources allocation… non-pharmacological measures and so on. Please, review that phrase.

Line 40 to line 3 on page 10. The authors introduce here a discussion on intensity and severity appreciation that is not related to the proper strengths and limitations of this particular study. They then discuss alternative surveillance systems, some of them no longer active (Google flu trends, for instance), all in all, this alternative source description is misplaced here.

Lines 53-54, please, provide evidence (reference reporting empirical observation) supporting the assertion that "Case definitions with a lower relative specificity for influenza, such as ILI can decrease the specificity of the model to detect an influenza season."

Page 10.
Lines 4 to 13 to
Can the author consider moving this whole paragraph and the discussion on alternative surveillance systems that begins in line 58 of page 9, at the end of the discussion of the limitations, just before conclusions, that is to line 46 in age 10.

References


Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I am able to assess the statistics

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