Reviewer’s report

Title: Elucidating the impact of the pneumococcal conjugate vaccine programme on pneumonia, sepsis and otitis media hospital admissions in England using a composite control

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Reviewer: Anne Von Gottberg

Reviewer's report:

This is a manuscript exploring the impact of the pneumococcal vaccine on clinical endpoints using ICD10 codes for respiratory and sepsis diseases compared to non-pneumococcal conditions.

Abstract

The abstract methods are a little confusing, as the changes compared to trends of other disease used the period from April 2004 through March 2015, while the incidence rate ratios comparisons were done using two periods.

Consider presenting the trend methods first, then the IRR changes - as is done in the main manuscript.

Average should be corrected to "mean". I think figure 3 is meant to show the mean with min-max, but the quality of the figure is difficult to see. Or is it only in table 2 - but then the column heading should state" mean (min-max)"? as stated in the figure title. Was the mean (min-max) only done for the composite control - again this is not clear in the abstract.

Introduction line 54: meningitis and septic arthritis are also considered invasive disease - not just bacteraemia, so just to reword sentence more carefully.

Methods

Identification of cases line 97: were all these ICD10 codes for the primary analysis only used if the first ICD10 code - only for the sensitivity analysis were first 3 and then all codes used? Please make clear from the start.
Some information should be given in line 116, for the risk groups considered. This will also be needed as a footnote for Table 3. The reader cannot just be referred to the supplement; and for table 3, no details are given.

Line 125: financial years (also mentioned earlier) are ok related to the winter seasonal disease in the northern hemisphere? And are almost like the epidemiological years often used (end of June to beginning of July) - it would be good to make the case that using the years in this manner makes sense for this disease (and then just to consider if any summer seasonal diseases were used in the control that may have affected the year-on-year comparisons).

Line 128: related to comment for line 125 above, what I then do not understand is why 1 Sept 2004 to 31 August 2006 is compared to an April March period for post vaccine?

Results

Line 176 - Table S4 - are there supplementary tables S1 to S3?

Line 254 - did you really mean "decreased" in 65+? You refer to Table 3 "once controlling", but table 3 is looking at risk factors vs no risk factors? So in which group are you now presenting your results?

What about in other age groups - what did the sensitivity analysis show in summary.

Table 1 title - the period should be from April 2004 through March 2015, "between" may be considered to leave out the months mentioned

Table 2: I do not understand why the results for pneumococcal pneumonia etc. (<2) are similar to the composite mean (min-max)? I am misunderstanding something, but this needs to be more carefully explained in the methods and for the table heading/title.

Line 182: I cannot find the 47% in Table 1? If percentages are reported to one decimal point in the tables - it may be easier for the reader to do so in the text as well - so consistently throughout.

Figure quality is poor throughout. Layout works, but really difficult to read and see what is going on.
All titles for tables and figures should more accurately reflect time/place/person and allow for interpretation or understanding as a stand-alone result.

Line 274: why are these data know presented from 2007 vs 2015? I may have missed this, but this result has no method in methods?

Discussion

Rather than repeating the methods in the first paragraph of the discussion (and say "first study"), it would be much more useful to highlight the main findings from this study.

Line 333: secular trends in non-vaccine serotypes, not only serotype replacement, may explain changes over time?

Lines 335 to 342: no other studies are referred to, no references are given, just this study's results are given and validated by authors' opinions.

Line 406 - reference the fracture data, or was the same methods used but data not shown?

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.

Yes
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 recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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I have received research grants from Pfizer; and have had speaker travel expenses reimbursed by Pfizer, Sanofi and Novartis.

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