Author's response to reviews

Title: The use of reimbursement data for timely monitoring of vaccination coverage: the example of human papillomavirus vaccine following public concerns about vaccine safety

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Version: 4 Date: 16 September 2015

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

**Re: Timely monitoring of human papillomavirus vaccination coverage using reimbursement data following public concerns about vaccine safety**

We are grateful for your consideration of this manuscript for publication in BMC Public Health. We thank you and the referees for the detailed and constructive comments on our manuscript.

Please find enclosed a revised version of our manuscript that takes into account all the comments and requests for changes. You will find below the point-by-point responses to reviewers’ comments including the description of the changes made.

We hope you will find this new version suitable for publication in BMC Public Health.

Please do not hesitate to contact us if you require further information.

Yours sincerely,

Daniel Levy-Bruhl, on behalf of all the authors.
Responses to reviewers’ comments

Reviewer’s report
Title: The use of reimbursement data for timely monitoring of vaccination coverage: the example of human papillomavirus vaccine following public concerns about vaccine safety
Version: 2
Date: 15 April 2015
Reviewer: Sara Boccalini

Reviewer’s report:
The study analyses a new rapid tool (reimbursement database) for monitor HPV vaccination coverage in female adolescents in France, especially related to negative public concerns about vaccination safety. The paper results well written but not enough detailed. In addition, the data on vaccination coverage by reimbursement database, although limited, are well described. However, the correlation between vaccination coverage and public concerns (objective of the study) is not sufficiently stressed and proved both in result and discussion chapter. Lastly, the use of reimbursement data for monitoring vaccination coverage should be previously evaluated on vaccination coverage routinely monitored (for example, paediatric immunizations).

Major Compulsory revisions:
Are the PSB and the General Health Insurance Scheme representative of all French population? Authors should prove further this aspect. In addition, two other schemes were integrate in the PBS during the period analysis: are they similar to General Health Insurance Scheme and representative? Please, specify further. Could that create possible bias in the analysis of data?

Regarding your remark we are certain of the representativeness of the PSB, we now mentioned:

Line 143: “Beneficiaries are selected totally randomly. Indeed the beneficiaries with a strictly secret value of their National Identity Register (NIR) control key number (going from 1 to 97) are selected and included in the PSB whether they have consumed care or not”.

Line 163: “First, our analysis focused on the beneficiaries of the General Health Insurance Scheme covering only 77% of the population and no data comparing the vaccination attitudes of the population according to their insurance coverage were available until recently. However, since 2011, data from two other schemes, covering an extra 10% of the population, have been progressively integrated in the PSB. Vaccination coverage for one dose among 15 years old girls born in 1998 covered by these schemes, was 18.9% (95% CI [12.9-24.9]) and 18.5% (95% CI [12.6-24.3]), respectively, consistent with our estimation (95% CI (17.8% [16.4-19.2])).”
2) In the study data related to HPV vaccines purchased were extracted since 2007. Why? As a matter of fact, the first girl cohort analysed in the study (1995) was 12 year old in 2007 and that cohort should not be vaccinated.

We added a sentence in the methods part to explain this choice:

Line 97: “We extracted data from the date of the first admission to reimbursement as some girls may have been vaccinated before 14 years of age, the marketing authorization of both vaccines having been granted for girls from 9 years of age.”

3) In the results chapter, authors show simply the coverage data collect with reimbursement database, without no correlation with the specific public concerns arose in French in the same period. If this was the objective of the study, that aspect should be more stressed and discussed. Idem in the discussion part.

We added some information in the Figure1 and we changed the first part of the discussion:

Line 127: “The one dose HPV vaccine coverage dropped after the first publication from 25.6% at the end of 2011 to 19.8% at the beginning of 2012. We did not observe a second drop in vaccination coverage after the 2013 decision of a Regional commission for compensation for medical accidents in favor of the partial responsibility of the HPV vaccine in the development of multiple sclerosis in an adolescent girl. At this time the vaccination coverage was already very low (17.5% for 1 dose) which could explain that it did not decreased further. Unfortunately, in 2011, the positive statement from the High Council for Public Health was not reported in the media and therefore could not impact favorably the HPV vaccination coverage.”

4) The authors did not investigate other possible factors influencing the vaccination coverage. Could that factors be also collected by the reimbursement database?

We added some sentences in the discussion part:

Line 172: “Limited information on factors that could have influenced the vaccine coverage is available in the PSB. However, the proportion of individuals registered in the PSB and benefiting from the Universal Health Care Coverage, which gives full free access to care to the most disadvantaged ones, did not changed during the study period. This indicator can be considered as a proxy of the socio-economic status of the PSB beneficiaries. Furthermore, the vaccination offer did not change during the study period”.

5) If the authors' hypothesis is right (lowering of vaccine coverage by reimbursement database following the articles published in summer 2011), in October 2011 (publication of a statement by High Council for Public Health) we should observe an increase of vaccination coverage and on the contrary in autumn 2013 (decision of
Regional Commission for compensation for medical accident) we should observe a reduction of vaccination coverage. This trend did not happen. Why? How can you explain it? In addition, the vaccination coverage increased between the 16 and 17 years-age cohorts though a limited catch up: the negative impact of public concerns should be evident also in that aspect.

As written in response to comment N°3, we changed the discussion:

Line 127: “The one dose HPV vaccine coverage dropped after the first publication from 25.6% at the end of 2011 to 19.8% at the beginning of 2012. We did not observe a second drop in vaccination coverage after the 2013 decision of a Regional commission for compensation for medical accidents in favor of the partial responsibility of the HPV vaccine in the development of multiple sclerosis in an adolescent girl. At this time the vaccination coverage was already very low (17.5% for 1 dose) which could explain that it did not decreased further. Unfortunately, in 2011, the positive statement from the High Council for Public Health was not reported in the media and therefore could not impact favorably the HPV vaccination coverage.”

6) Lastly, new relevant actions promoting HPV vaccination are in progress in 2015 in France: the impact of this favourable interventions should be also evaluated on the HPV vaccination coverage collected by reimbursement database. In the same way the enlargement of vaccination age (from 11 to 11-14 years) and the reduction of doses number should be result in increase of vaccination coverage during the 1st and the 2nd of half-years in 2014 (not yet available).

We agree with this remark. This is now mentioned in the discussion:

Line 193: “A new vaccine coverage assessment will be made by end-2015 and will allow measuring the impact on the recently implemented countermeasures on HPV vaccine coverage”

7) The references should be improved and also translate in English.

We translated the references when they have an English title. We improved the references.
Reviewer's report

**Title:** The use of reimbursement data for timely monitoring of vaccination coverage: the example of human papillomavirus vaccine following public concerns about vaccine safety

**Version:** 2  **Date:** 16 June 2015

**Reviewer:** Obinna Ikechukwu Ekwunife

**Reviewer's report:**

Minor Revisions

1. Abstract, Background section 2nd paragraph: We explored ... assess impact of signals... I suggest deleting ‘impact of signals’in the sentence as it makes the sentence confusing.

   In order to clarify the sentence we replaced this sentence by:

   Line25: “We explored the relevance of using vaccines reimbursement data to assess the impact of those public concerns on vaccination coverage.”

2. Abstract, Method section 1 – 3rd paragraph: Method section of the abstract is not informative. Asides the reimbursement data used, what else was done in the study?

   We added a sentence to precise the Methods part:

   Line 31: “We estimated HPV vaccination coverage among girls born between 1995 and 1999 at their 15th, 16th and 17th birthday.”

3. Abstract, Result section 1st paragraph: Delete ‘has’ in the sentence

   We deleted “has” in the sentence:

   Line 34: “The coverage for complete vaccination among 16 years old girls decreased from 26.5% in the first semester of 2011 to 18.6% in the first semester of 2014.”

4. Introduction, last sentence – In my opinion, I think that the authors should delete ‘impact of public concerns’ from the sentence. The sentence will read better without it.

   Our objective is to monitor the HPV vaccination coverage to assess the impact of public concern. In order to be clear we wish to maintain these words in the last sentence of the introduction part.
5. Result, 1st sentence – Authors should state actual percentage coverage instead of ‘around 25%’.

We provided actual percentages:

Line 108: “The vaccine coverage for at least one dose at the 15th birthday varied very little from 23.7% (95% confidence interval, CI [20.9-26.5]) to 26.5% (95% CI [24.1-28.9]) between 2010 and 2011.”

6. Result, 2nd paragraph – Authors should provide actual percentage coverage instead of ‘around 27 – 28%’

We provided actual percentages:

Line 113: “The vaccine coverage for the full series on the 16th birthday varied very little from 26.5% (95% CI [23.6-29.4]) to 28.2% (95% CI [25.8-30.6]) until the first half of 2012.”

7. Result: It is not clear what the parenthesis means e.g. 18.6% [16.5 – 20.7]. Authors should specify whether they are standard deviation (SD) or 95% confidence interval (95% CI) e.g. 18.6% [95% CI 16.5% - 20.7%]

We specified in the results part that the parenthesis mean “95% confidence interval”.

8. Reference no 6: Change to ‘available online’ and not ‘on ligne’

We changed it.

9. Table 1. Specify what the values in parenthesis mean.

We specified in the title that the table present also the 95% confidence intervals:

“Table1: HPV vaccination coverage (%) and its 95% confidence interval at 15th, 16th and 17th birthday as of June 30 2014, France”

10. Figure 2 should be consistent with figure 1 - Vaccination coverage (%) and then presents only numeric figures.

We changed the two figures in order to make them consistent.