Author’s response to reviews

Title: Streptococcus pneumoniae colonisation in children and adolescents with asthma: impact of the heptavalent pneumococcal conjugate vaccine and evaluation of potential effect of thirteen-valent pneumococcal conjugate vaccine

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Version: 1 Date: 17 Oct 2015

Author’s response to reviews:

Editor
BMC Infectious Diseases

Milan, 18 October 2015
Dear Editor,

Thank you for considering our manuscript #INFD-D-15-00037 “Streptococcus pneumoniae colonisation in children and adolescents with asthma: impact of the heptavalent pneumococcal conjugate vaccine and evaluation of potential effect of thirteen-valent pneumococcal conjugate vaccine”, which we submit for publication in BMC Infectious Diseases.

Please find attached the revised manuscript and our replies to reviewer’s comments and recommendations. The authors, all of whom contributed significantly to the manuscript and declare that they have no potential conflict of interest, have seen and approved the final version of the manuscript.

We declare that the text has been reviewed by a native English speaker with appropriate knowledge of the subject matter. We hope that you will now find the paper suitable for publication in BMC Infectious Diseases.

Yours faithfully,

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Reviewer 2

Thank you very much for your comments. We have modified the paper in accordance with your suggestions.

1. We have added that a limitation of this study is represented by the absence of a control group of healthy children. However, advanced methods were used for pneumococcal detection and our findings are important because these high rates of pneumococcal colonization rise concerns on IPD risk in these patients (pp. 15-16, lines 358-375).

2. It has been clarified that in a recent study, it was shown that oropharyngeal sampling appeared significantly more effective than nasopharyngeal sampling in identifying and characterizing pneumococcal carrier status in adolescents (p. 11, lines 236-239).

3. It has been explained that the reduced circulation of these serotypes has positive effects also in unvaccinated subjects who are significantly less colonized than in the period before vaccine use (p. 5, lines 88-90).
4. References have been added as recommended (p. 11, lines 236-248).

5. The sentence on the study of Bisgaard et al. has been clarified (pp. 11-12, lines 249-264).

6. The word has been corrected as suggested (p. 13, line 318).

7. The study published by Le Polain de Waroux et al. has been discussed in details (pp. 13-14, lines 311-339).

8. We have clarified that booster doses have to be administered in order to avoid the risk or recolonization (p. 14, lines 354-355).

Reviewer 3

Thank you very much for the appreciation of our manuscript. The text has been revised according to the suggestions.

1. The Title has been modified as suggested (p. 1, lines 1-4).

2. The Short title has been modified as recommended (p. 2, line 28).

3. In the Abstract, “PCV13” has replaced “13-valent PCV” (p. 3, line 56).

4. Age groups have been defined in the Methods (p. 8, line 175) and are discussed in the Results (p. 9, lines 185-188). Male gender was not associated to pneumococcal carriage in this analysis (p=0.97, see Tables 1 and 2).

5. We better specified the results and the % in the Results section (pp. 9-10, lines 202-208).

6. Table 4 has been revised as requested.

7. The word has been corrected as suggested (p. 13, line 318).

8. This analysis is already included in Table 3.

Reviewer 4

Thank you very much for your suggestions. We have modified the paper accordingly.

1. Details on asthma classification used in the enrolled population have been presented at the beginning of the Methods section (p. 6, lines 114 and 117-119).

2. In Table 2, we better clarified the multivariate models that were applied and we added a column to provide unadjusted results, as suggested.
3. In Table 3, we added a column to provide unadjusted results, as suggested.

4. In Table 4, we added a column to provide unadjusted results, as suggested.

5. The differences are not significant and the limited number of studied patients with severe asthma cannot permit to draw conclusions. We have added that further studies are needed on this issue (p. 13, lines 302-304).

6. Thank you for the useful comment. We changed the reference category to "Intermittent asthma" and calculated the new ORs.