Author's response to reviews

Title: Risk factors for nasopharyngeal carriage of drug-resistant Streptococcus pneumoniae: data from a nation-wide surveillance study in Greece.

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Version: 2 Date: 15 December 2008

Author's response to reviews: see over
Dear Dr Zauner,

Please let me first thank you on behalf of the authors for the fruitful comments on our manuscript from the editing and reviewing team of BMC Infectious Diseases.

Please find attached the revised manuscript entitled “Risk factors for nasopharyngeal carriage of drug-resistant Streptococcus pneumoniae: data from a nation-wide surveillance study in Greece” by I Katsarolis et al, submitted to your peer-reviewed online journal for review.

All incorporated changes and additions according to the reviewers´ comments and suggestions have been highlighted in the abstract text, the core text, references and tables/figures. The manuscript has been formatted according to the online instructions.

I would like to inform you on behalf of the authors´ team that the names of Professor H Giamarellou and Professor K Kanellakopoulou have changed in the authors´ order of names reciprocally.

We would like to address the referees´ comments and suggestions and point the changes made to the manuscript.

Referee #1 (Raquel Sa-Leao)

1. Line 158 (at present manuscript 193): “in total” has been deleted
2. Lines 278-280 (at present 332): the comment about children having a diagnosis of AOM has been added
3. In Table 3 decimal figures have been added
4. Lines 64-65 (at present 83) “mostly only a few” has been added.
5. Line 176 (at present 211) Moxifloxacin and levofloxacin have replaced respiratory fluoroquinolones.
6. In the two final paragraphs of discussion/conclusion, a reference has been added (Fazao et al) for the effect of PCV7 vaccination on antibiotic resistance in a setting of high antibiotic consumption, and in the conclusion it is stressed that multilevel strategies may have an effect on antibiotic resistance.
7. A map has been added (Figure 1) with indication of every geographical region sampled and respective carriage rates and penicillin resistance rates.

Referee #2 (Anne Malfroot)

1. Abstract: The conclusion section has been changed according to suggestions.
2. Background: 2 regional studies have been added in the manuscript (Syrogiannopoulos et al, Souli et al) with comparable methodology to the present study. Also, a recent regional study by Syrogiannopoulos group (Grivea et al) in the post vaccination era became available soon after the submission of the present study to BMC Infectious Diseases. Although regional in its scope, the results are discussed both in the background and the discussion text.
3. Methods. A) Questionnaires were distributed by the local teams of doctors visiting the day-care centres 1-2 days before the sampling visit. Questionnaires were completed by the parents. On the sampling day, questionnaires were reviewed by the doctors’ team. In the section of recent antibiotic use parents were asked to provide commercial names of all the medications received in the last month or trimester if possible, and the appropriate classification was performed by the responsible doctors in the sampling site. Questionnaires were accepted for analysis only if all sections were appropriately filled. That is why in the final analysis we included 2536 questionnaires and accompanying samples out of a total children population of 2595 (97.7%).
   B) In lines 141-145 nasopharyngeal sampling method is stated as suggested by the reviewer.
4. Results: A) Let me apologize to the editing team and the reviewers for the fact that no comments were available for the submitted tables. There must have been an error on the upload of the manuscript and the supporting material. In
the revised manuscript, the already existing comments and legends are available. In support of Table 1 a Figure is also provided.

B) In line 183 in the revised manuscript mean age has been replaced by median age, and numbers have been changed accordingly.

5. Discussion: A) In the discussion section in lines 264-277 an explanation between the differences in carriage rates and resistance rates is attempted. Carriage rates did not affect resistance rates in the present study. Antibiotic use among regions did not differ but per se had a strong effect on the isolation of an antibiotic resistant strain. Resistance rates displayed significant differences among regions (appropriately highlighted in tables 3 and 4). Nevertheless, the fact that serotyping was available only for the resistant population, an accurate association between serotype and resistance pattern was not possible.

B) Grammar changes have been made and highlighted in the text

C) Final conclusion has been tailored to our own study results, as suggested.

6. All tables are appropriately accompanied by comments, explanations and legends in the revised submission.

Referee #3 (Dr Elmer Villanueva)

A new version of table 4 with all OR, 95%CI and $p$ values is provided in the revised manuscript both for the univariate and the multivariate analysis for each of the four outcomes.

Please consider the present revised manuscript for review and publication in your peer-reviewed journal. On behalf of all contributing authors and the study group, we are looking forward to your reply.

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