Further available immunization option to prevent pneumococcal disease [version 1; peer review: 2 approved]

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Abstract
In their recent review, Charles Feldman and Ronald Anderson provide an overview of various clinical aspects of pneumococcal infections. We would like to complete this report by providing some additional information on a widely-used immunization option, which was not originally mentioned in the article. The protein D pneumococcal conjugate vaccine (PHiD-CV) has been pre-approved by WHO and its impact is supported by real-life data from the regions of its use.

Keywords
PHiD-CV, efficacy, post-marketing surveillance

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Competing interests: IV and BH are employed by GSK group of companies. BH owns stock in GSK group of companies.

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Correspondence

We write in response to the report by Charles Feldman and Ronald Anderson about the recent advances in the understanding of Streptococcus pneumoniae infections.

While this article provided an informative and complete review of the current burden of the disease, pathogenesis and therapeutic options, we have noted a significant omission in the chapter dealing with available immunization strategies, which did not mention the WHO prequalified Pneumococcal Nontypeable Haemophilus influenzae Protein D Conjugate Vaccine (PHID-CV; GSK Vaccines, Belgium). This vaccine is currently licensed in more than 125 countries with more than 200 million doses distributed as of August 2014 and is used in vaccination programmes in more than 40 countries or regions.

We feel it is important that health care professionals are made aware of the available evidence supporting the use of this vaccine in order that they are able to make an informed choice about the best care for their patients, and therefore we provide additional information to supplement the review article. It is the only modern pneumococcal conjugate vaccine with impact on invasive pneumococcal disease, pneumonia and acute otitis media that has been proven in two pivotal randomized controlled efficacy trials performed in Finland and Latin America. Thanks to its world-wide use, there is also a plethora of post-marketing and epidemiology data spanning five continents, recently reviewed by Plosker, that proves its impact on the pneumococcal disease and makes it a worth-while alternative to the pneumococcal conjugate vaccine PCV13 which the health care community should be made aware of. We have summarized the main effectiveness and impact data in Table 1.

### Table 1. Summary of the main effectiveness and impact data of PHID-CV. IPD: Invasive Pneumococcal disease; VE: vaccine efficacy; RR: relative rate reduction.

<table>
<thead>
<tr>
<th>Region</th>
<th>Indication</th>
<th>Invasive Pneumococcal Disease</th>
<th>Acute Otitis Media</th>
<th>Consolidated pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Finland</strong></td>
<td>Vaccine serotype - 3+1</td>
<td><strong>VE=100%</strong> (95% CI: 83, 100)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Vaccine serotype - 2+1</td>
<td><strong>VE=92%</strong> (95% CI: 58, 100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any Serotype - 3+1/2+2+1</td>
<td><strong>VE=93%</strong> (95% CI: 75, 99)</td>
<td>X</td>
<td><strong>VE=44%</strong> (95% CI: 24, 59)</td>
</tr>
<tr>
<td><strong>Latin America</strong></td>
<td>Vaccine serotype - 3+1</td>
<td><strong>VE=100%</strong> (95% CI: 77, 100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vaccine serotype - 19A</td>
<td><strong>VE=70%</strong> (95% CI: 30, 87)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any Serotype - 3+1</td>
<td><strong>VE=67%</strong> (95% CI: 22, 86)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clinical Diagnosed</td>
<td><strong>VE=19%</strong> (95% CI: 4, 31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>VE=26%</strong> (95% CI: 8, 40)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Impact and surveillance data on Invasive Pneumococcal Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quebec (case-controlled study)</td>
</tr>
<tr>
<td>Vaccine-type (+6A)</td>
</tr>
<tr>
<td>19A IPD</td>
</tr>
<tr>
<td>All IPD</td>
</tr>
<tr>
<td>Brazil (case-controlled study)</td>
</tr>
<tr>
<td>Vaccine type</td>
</tr>
<tr>
<td>19A</td>
</tr>
<tr>
<td>Finland (time series analysis)</td>
</tr>
<tr>
<td>Vaccine type</td>
</tr>
<tr>
<td>19A</td>
</tr>
<tr>
<td>All IPD</td>
</tr>
</tbody>
</table>
Author contributions
IV wrote the abstract and the main body of the article. BH supervised the process. Both authors critically edited the correspondence and agreed to the final content.

Competing interests
IV and BH are employed by GSK group of companies. BH owns stock in GSK group of companies.

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References
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The correspondence article “Further available immunization option to prevent pneumococcal disease” from Vojtek & Hoet provides relevant information regarding one of the currently available pneumococcal conjugate vaccines. This information was missing in the review article (Recent advances in our understanding of Streptococcus pneumoniae infection) written by Feldman & Anderson.

The correspondence article is well written and should be considered for indexing.

I have only minor comments:

○ In the second paragraph, when mentioning that the PHID-CV vaccine is currently licensed in more than 125 countries, the authors should make clear that the vaccine is licensed for active immunization against invasive disease, pneumonia, and acute otitis media (AOM) caused by S. pneumoniae in infants and young children up to 5 years of age.

○ In the third paragraph, when mentioning that the PHID-CV vaccine is a worth-while alternative to the pneumococcal conjugate vaccine PCV13, the authors should add: ... in children younger than 5 years of age.

○ In Table 1, when showing the different study results observed with the PHID-CV vaccine, the authors should specify which results are vaccine efficacy data and which are vaccine effectiveness data.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
I read with great interest the letter of Vojtek and Hoet. Well done and necessary. I have some remarks and suggestions:

- In the abstract the term “pre-approved” is not clear to all the readers. The exact date of approval would be useful because it could inform the readers that PHiD-CV has a long and great history.

- Page 2: “prequalified” is not clear (see above)

- Page 2, second column, third line. I would add “evidence based” before “informed choice” in order to stress the big amount of available rigorous data.

- Page 2, 11th line: I would say “proves its beneficial impact…”

- It should be underlined that PHiD-CV is approved for use in children younger than 5 years of age (that could be one the reason why it was not quoted in the paper of Feldam which focuses mostly on adult/elderly patients)

- In the table I would add “schedule” before “3+1” or “2+1”. In the current version one may read “minus 3 plus 1” and may misunderstand.

**Competing Interests:** No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
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