Author’s response to reviews

Title: Hepatitis B virus vaccination booster does not provide additional protection in adolescents: A cross-sectional school-based study

Authors:

Yung-Chieh Chang (tonyijane@hotmail.com)
Jen-Hung Wang (paulwang@tzuchi.com.tw)
Yu-Sheng Chen (lister3813401@yahoo.com.tw)
Jun-Song Lin (8887241@ms21.url.com.tw)
Ching-Feng Cheng (chengcf@mail.tcu.edu.tw)
Chia-Hsiang Chu (chuchia@ms6.hinet.net)

Version: 6 Date: 2 September 2014

Author’s response to reviews: see over
Dear Editor:

We thank the reviewers for their insightful and helpful comments. We have revised our manuscript, responding in detail to all comments raised by the reviewers and sent it for professional language editing. We hope this revised manuscript answers all questions asked by the reviewers and will be acceptable for publication. Point-by-point replies to the reviewers’ comments are attached in the following pages.

Best Regards,

Yung-Chieh Chang, M.D.
Fellow of Pediatric Gastroenterology
Department of Pediatrics
Hualien Tzu-Chi Medical Center, Taiwan
Authors’ response to reviewers

Title: Hepatitis B virus vaccination booster does not provide additional protection in adolescents: A cross-sectional school-based study

Authors:
Yung-Chieh Chang (tonyijane@hotmail.com)
Jen-Hung Wang (paulwang@tzuchi.com.tw)
Yu-Sheng Chen (lister3813401@yahoo.com.tw)
Jun-Song Lin (8887241@ms21.url.com.tw)
Ching-Feng Cheng (chengcf@mail.tcu.edu.tw)
Chia-Hsiang Chu (chuchia@ms6.hinet.net)
Reviewer’s report

Title: Hepatitis B virus vaccination booster does not provide additional protection in adolescents: A cross-sectional school-based study

Version: 5 Date: 5 August 2014

Reviewer: Thomas Peto

Reviewer’s report:

The authors have addressed all of my comments and I have no further suggestions to make. This is a nice paper.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics

Declaration of competing interests:
I declare that I have no competing interests
Reviewer’s report

Title: Hepatitis B virus vaccination booster does not provide additional protection in adolescents: A cross-sectional school-based study

Version: 5 Date: 21 August 2014

Reviewer: Noele Nelson

Reviewer’s report:

Major Compulsory Revisions
- None

Minor Essential Revisions
- Methods, 3. Epidemiology study, B. Explain equation

There was only one equation in our paper, which was presented in Method, 4. Subgroup analysis, B. Booster effects for double seronegative subjects of hepatitis B markers at 15 years of age. Therefore, we explained the calculation of this equation in the following way:

This equation was modified from the formula by Wu et al (reference 13 in our paper). In their study, the overall anti-HBs seropositive rate, designated as PR_T, after a booster dose of HB vaccine, was approximated by the following formula:

\[ PR_T = PR_1 + (1-PR_1) \times PR_2 \]

PR_1 is the anti-HBs seropositive rate before the booster
PR_2 is the response rate in the booster recipients

In our equation:
Post-booster seropositive rate = pre-booster seropositive rate + (pre-booster seronegative rate) × (booster rate) × (response rate)

“Post-booster seropositive rate” has also been changed to “Post-booster anti-HBs seropositive rate” so as not to be confused
with “booster response rate.” “Post-booster anti-HBs seropositive rate” also indicates the immunogenicity response after booster.

All of the seronegative subjects had received a booster dose in the Wu et al study [13]. Therefore, no booster rate was needed in their formula. In our study, the booster rate was defined as the percentage of seronegative subjects receiving one booster dose. The response rate was defined as the proportion of those booster recipients whose post-booster anti-HBs titer was $\geq 10$ mIU/mL.

Example from Table 3 of our study:
The data from year 2007 [birth cohort 1992] showed 84.6% (66/78) of subjects with double seronegativity (negative HBsAg and anti-HBs) had received one booster dose of HBV vaccine. The booster rate was therefore 84.6%.
Among these 66 booster recipients, 83.3% (55/66) regained anti-HBs seropositivity. Therefore, the booster response rate was 83.3%.
Thus:

$$\text{Post-booster anti-HBs seropositive rate} = 53.6\% + 46.4\% \times 84.6\% \times 83.3\% = 86.3\%$$ (as in Table 3)

Discretionary Revisions
- Result, part 2: subgroup analysis, 2. Immunogenicity response…, line 218, clarify that booster response refers to a post-booster titer $\geq 10$ mIU/mL

  Thank you for the suggestion. We have clarified that the booster response indeed refers to a post-booster titer of $\geq 10$ mIU/mL (line 233 in the new edition).

- Conclusion, last sentence: restate the current Taiwan ACIP booster strategy

  Thank you. This has now been included in our concluding sentence (line 418 in the new edition).

Minor issues not for publication
- Background, line 64, change “demonstrates” to “demonstrate”

  It has been corrected according to your suggestion (line 70 in the new edition). Thank you.
- Methods, 3. Epidemiology study, line 113, leave out “Ab” since it’s redundant. Anti-HBs means hepatitis B surface antibody
  “Ab” was deleted in our sentence (line 119 in the new edition). Thank you for your correction.

- Methods, 3. Epidemiology study, B. –insert a title for C, like for A and C.
  “Booster effects” or other appropriate title.
  “Immunogenicity response in booster recipients in the 15-year age group” is used as the title (line 142 in the new edition).

- Methods, 3. Epidemiology study, B. Change “clinic about average 6 weeks” to “clinic an average of 6 weeks”
  Thank you for the suggestion, we have corrected it (line 147 in the new edition).

- Methods, Subgroup Analysis, A and in the Discussion “Ricombivax” should be spelled “Recombivax”
  Thank you for the correction. “Ricombivax” has been changed to “Recombivax” (line 134 and 314 in the new edition).

- Results, part 2: subgroup analysis, 3. Longitudinal study, insert a title.
  “Longitudinal study”
  “Longitudinal study” has been inserted as the title in this part (line 239 in the new edition). Thank you.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published.

**Statistical review:** Yes, and I have assessed the statistics in my report

**Declaration of competing interests:**
I declare that I have no competing interests