Author’s response to reviews

Title: Human rabies post exposure prophylaxis at the Pasteur Institute of Dakar, Senegal: trends and risk factors

Authors:

Mamadou Korka Diallo (kdiallo@pasteur.sn)
Alpha Oumar Diallo (alphaomar2002@hotmail.com)
Anta Dicko (nadicko@pasteur.sn)
Vincent Richard (virc@hotmail.fr)
Emmanuelle Espié (emmanuelle.espie@gmail.com)

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Review INFD-D-17-01079: Human rabies post exposure prophylaxis at the Pasteur Institute of Dakar, Senegal: trends and risk factors

Editor-in-Chief

Dr. Cecilia Devoto

BMC Infectious Diseases

June 14, 2018

Dear Editor-in-Chief,

Thank you for the consideration you have given to our manuscript “Human rabies post exposure prophylaxis at the Pasteur Institute of Dakar, Senegal: trends and risk factors”.

We would also like to extend our thanks to the reviewers for their comments, which have allowed us to construct a more thorough and complete manuscript. Please find below the attached reviewer comments and our detailed responses, which have been highlighted in red colour.

We look forward to future correspondence regarding our resubmission and are more than happy to provide further information on any questions or comments you may have.

Sincerely,

Emmanuelle Espié, on behalf of the co-authors

Email: emmanuelle.espie@gmail.com

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Technical Comments:

1) Please note that for all research involving human subjects, informed consent to participate in the study should be obtained from participants (or their parent or legal guardian in the case of children under 16). In your "ETHICS APPROVAL AND CONSENT TO PARTICIPATE" declaration, you state that "For children less than 15 years of age, individual written informed consent was obtained from all children’s parents or legal representatives". Were there any children in this study between the ages of 15 and 16? If so, consent to participate should have been obtained for them too.
The sentences regarding the informed consent from children (Lines 147 and 355) have been modified. An informed consent was obtained from parents or representatives of children aged 15 years old and below (i.e. ≤ 15 years old). The ethics committee for research in Senegal considers that the capacity is not related to age or disease and does not depend on the decision itself, but it is a cognitive and affective process of decision-making (http://www.assemblee-nationale.sn/loi-portant-code-d-ethique--pour-la-recherche-en-sante.-l103.xml). Therefore, any child aged between 16 and 18 years, who is sufficiently mature, is able to give his/her agreement.

2) After the references, please add a section called "Figures, tables, additional files".

Figure titles (max 15 words) and legends (max 300 words) should be included in this section, not in the graphic file.

A section called "Figures, tables, additional files" has been inserted in the document.

3) Please clarify where Figure 1 was obtained from.

In order for all figures to be open access, authors must have permission from the rights holder if they wish to include images that have been published elsewhere in non open access journals. Permission should be indicated in the figure legend, and the original source included in the reference list.

The maps used to create the figure 1 are in the public domain. The map of Dakar and neighborhood has been uploaded from https://commons.wikimedia.org/wiki/File:Dakar_departments.png. The map of the 14 regions of Senegal has been uploaded from https://commons.wikimedia.org/wiki/File:Senegal_administrative_divisions--en--monochrome.svg A link to the license (Creative Commons Attribution-Share Alike 3.0 Unported license) was included in the legend.
Reviewer reports:

Navneet Dhand (Reviewer 1): The authors have made many of the suggested changes. The manuscript has substantially improved but I still have a few concerns:

Line 224 and Table 4: The authors say that high distance between patients' house and Pasteur Institute of Dakar (≥ 2 hours) was a risk factor for a partial PEP. However, it is incorrect. Those living at ≥ 2 hours from the institute were LESS likely to get a partial PEP. The results are unintuitive. Please double check and discuss the results in the discussion section.

The authors have double checked and sentences (Lines 224-227) have been adapted accordingly to the results of the univariate analysis.

Line 226: Describe the type of exposure. The table results suggest that those with only scratches or simple contact/licking were LESS likely to get a partial PEP (i.e. were more likely to get a full course of PEP). Again the results are unintuitive. Please double check and discuss the possible reasons.

The authors have double checked the analysis. One of the reasons that might explain that patients with only scratches or simple contact/licking were less likely to get a partial PEP (in the univariate analysis), is probably related to the fact that most of the patients with scratches or licking who received a full schedule of PEP are the ones for whom a rabies exposure was confirmed by lab testing. Thus, among these 79 patients, 30 (38%) were related to the cluster of January 2014.

Line 227: Again the authors mention that immunoglobulins administration at D0 was significant, but actually, if NO immunoglobulin was administered at D0 then the patients were more likely to get a partial PEP. Please reword. However, the line 234 is correct.

Line 230, the sentence has been modified. One of the risk factor for not being compliant with PEP is no administration of immunoglobulins at D0.
Lines 259-260: This is not consistent with the results of the final model.

Surprisingly, the authors did not discuss the results from the regression models. Suggest discuss results from both the univariable and the multivariable models - compare your results with previous findings and discuss their implications.

The authors have added sentences to discuss the results of the regression model in the Discussion section (Lines 265-277).

Ryan M. Wallace (Reviewer 2): The authors have thoroughly addressed the concerns of this reviewer. It is an excellent health-care center study that will provide Senegal and similar countries with essential data to improve rabies control practices. I have only a few more comments to consider to solve some lingering inconsistencies in the manuscript:

LINE 81: Expected, not excepted. Change has been made

LINE 103: specify if a tool was used to determine if PEP was needed or if this is the subjective opinion of the medical provider. The clinical evaluation performed by the physician is based on WHO recommendations and evaluation of the exposure context.

LINE 218: shouldn't the denominator be 847, the number of people who took the D0 doses? The proportion has been calculated among the number of patients who have answered to the questions related to adverse events.

LINE 219: second dose or D7? the first and second doses are both given on D0, are they not? The sentences have been modified to clarify “after the first two doses (administered at D0)” and “after the third dose (administered at D7)”

LINE 250: Line 180 says 4.4% of animals were vaccinated. The sentence has been corrected on line 250: “4.4% instead of 6.5%”
LINE 275 says 2-week but LINE 279 says 10-day. Which is it? The sentence has been corrected on line 275 “2-weeks instead of 3-weeks after exposure”