Reviewer’s report

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

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Reviewer: Katie Hampson

Reviewer's report:

This manuscript reviews the use of PEP from the Pasteur Institute of Dakar, Senegal and risk factors for not undertaking or completing PEP regimens. This is a useful and timely manuscript given that Gavi, the Vaccine Alliance will consider rabies PEP for the Vaccine Investment Strategy in 2018. The manuscript is generally well written and I only have a few minor suggestions that I think should be considered prior to publication:

The paper is generally well written, but I would suggest review by a native English speaker just to try to correct the minor errors in translation that remain. There are quite a lot and I have only picked up on some in the review (like in the abstract) but not in the main body text.

The paper is somewhat vague in defining a suspect rabies exposure. As far as I can see, the enrolled patients were all due to bites or contact with animals, but insufficient information is reported to know whether they are really suspect animals or not. Indeed later in the paper, it becomes clear that many of these patients were not bitten by suspect animals but were bitten by healthy animals. If the clinical criteria/circumstances of the bite can be used to define risk of rabies amongst these enrolled patients this would be a useful addition to the manuscript.

Once an acronym is introduced it should be used throughout. I would make sure PEP is used consistently after first use on line 59 in the introduction.

The title has a mistake. It should read "Human rabies post-exposure prophylaxis at….."
Abstract:

"…such as sub-Saharan Africa." → "…such as those in sub-Saharan Africa."

The authors should clarify that it is the knowledge, attitude and practices of bite patients that is being studied. i.e. change to "knowledge, attitude and practices of bite patients with respect to rabies and to identify"

"…related to a non-compliant PEP to define recommendations" → "…related to non-compliance with PEP regimens to define recommendations"

"…rabies exposure and sought…" → "…rabies exposure who sought…"

I don't think it is necessary to describe the exclusion criteria in the abstract. However, the abstract should report how many patients were enrolled into the study.

"…compliance of PEP" → "…compliance with PEP"

The wording around exposures needs revision. 87% of exposures were due to bites whereas the remainder were due to scratches or contact.

"….Intramuscular regimens, might be considered…" → "….Intramuscular regimens should be considered…”
Introduction

Line 55: It is not at all evident that the control of stray dogs is a primary concern for rabies control, although is something that should be considered secondarily if mass dog vaccination is in place and surveillance has been improved - which clearly needs to be done in Senegal. I would therefore delete "control of stray dogs".

Line 57: delete "highly"

Line: 59: introduce acronym PEP and continue to use throughout instead of post-exposure prophylaxis.

Line 61: "The WHO-recommended post-exposure treatment consists of" → "The WHO-recommended PEP consists of". Note that PEP includes wound washing and RIG and is not just vaccination. The following sentence (starting "Post-exposure prophylaxis (PEP) should") should therefore be removed because it is redundant.

Line 65: WHO has just recently revised their PEP recommendations: http://apps.who.int/iris/bitstream/10665/259533/1/WER9248.pdf?ua=1

Given these changes and possibly more forthcoming, I would suggest simplifying this sentence to: "Several PEP regimens are current approved including ones administered both intramuscularly and intradermally".

Line 68: "to inhibit viral spread in the interval" → "to provide passive immunity in the interval"

Line 70: replace "have been" with "were"
This paragraph is a bit confusing and does not provide as much background as would be helpful. Quoting the human deaths reported by the Fann University Hospital of Dakar is helpful, but this must only be a small proportion of the total human rabies deaths that actually occur in the country. Saying that the number of deaths is very low, is probably therefore misleading. Reporting of human rabies deaths is likely very low. Many more people are also expected to seek PEP. This whole paragraph needs some revision and clarification.

Furthermore this paragraph states that number of persons seeking PEP has increased in recent years and this is attributed to stray and free-roaming dogs and increased contact. The references for this are from Chad, or are not recent (1980). It is fine to use these references to infer that exposures are likely to be high in urban settings in West Africa but not to infer recent increases in Senegal! I would stick to the evidence here.

Can the authors provide more information about where PEP is available in Senegal. Are there multiple hospitals throughout the country that provide PEP or is it only the Institute Pasteur that provides PEP together with the 2 stated clinics? Is the Institute serving a much wider population than Dakar then? Or only Dakar and then only a proportion because these other 2 hospitals that only started to provide PEP recently?

Methods

Line 92. The dates of the study differ from that reported in Fig 1. These should be made consistent.

Line 93. "All patients with suspected rabid animals" → "All patients reporting contact with suspected rabid animals"

Line 108: "a structured questionnaire collected data" → "a structured questionnaire was used to collect data"
Line 109: what symptoms were recorded? There is no results presented on this.

Line 121. I would suggest replacing "Any PEP" with "no PEP" as this makes more sense. I would make sure this is corrected where relevant in the tables too.

I would also clarify the visits by patients. i.e. if the patients received 2 doses (completed 1 clinic visit) or 3 doses (2 clinic visits) versus all 4 doses (all 3 clinic visits).

Results

Numbers reported in the results (1004) differ from those in Figure 1 (1036). Make this consistent.

It would actually be very interesting to know if during this time period the Institute also received many patients reporting with signs of rabies. Can this additional information also be provided?

Line 168: preliminary treatment at a clinic/health facility or at the Institute Pasteur?

Line 169. I don't understand what "concerned exclusively visitors of the family" means. This text needs clarification.
Discussion

Line 252: I really don't follow the logic in the discussion that the finding could be a result of a lack of infrastructure and rapid immigration of stray dogs! Surely the reason is because rabies is endemic in Senegal, there are apparently no major mass dog vaccination programmes and therefore vaccination coverage is extremely low among the mostly free roaming dog population?

Line 253: Is the pattern being discussed, the observation that most patients originated from Dakar and the surrounding cities?

Line 277: "numbers of stray and free-roaming dogs" → "numbers of unvaccinated free-roaming dogs"

Line 281: I don't understand where the statement that 45.3% of patients were bitten by healthy pet dogs comes from. Can the authors make specific reference to the table/statistic in the results where this is apparent.

Line 285: this last sentence is hard to follow (although I get the point and agree!); it needs revision. I would also suggest that the authors be more proactive and recommend training be conducted to support health workers in better clinical decision-making when administering PEP. There is a nice article by Etheart et al. in Lancet Infectious Diseases where such training was provided, and this kind of approach would ideal for implementation in Senegal based on the findings of this manuscript.

"intra-dermal" → "intradermal"
Conclusions

As mentioned already, I don't think the authors present any evidence that supports their conclusion about needing stray dog control. This should be removed with the focus on the need for dog vaccinations (given the low coverage amongst biting dogs) and improved access to free PEP.

Figures.

I think it would be helpful to include a map of Senegal, with administrative units shown for Dakar and the surrounding cities that are reported in the study, together with the location of the Institute Pasteur.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review? If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

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