Reviewer's report

Title: Risk Factors for Mycobacterium ulcerans Infection (Buruli Ulcer) in Togo — A Case-Control Study in Zio and Yoto Districts of the Maritime Region

Version: 0 Date: 17 Sep 2017

Reviewer: Lance A. Waller

Reviewer's report:

Comments for authors regarding BMC Infectious Disease manuscript INFD.D.17.01146 "Risk Factors for Mycobacterium ulcerans Infection (Buruli ulcer) in Togo - A Case-Control study in Zio and Yoto Districts of the Maritime Region".

General Comments:

1. Thank you to the authors for an interesting study. I found the results interesting, but I do have many suggestions for making the language more precise. I do feel it is important to qualify associations by their statistical significance, especially because the study did not quite attain the desired sample sizes to achieve the desired statistical power.

2. More specifically, on page 9, the authors' sample size calculations require 100 cases and 200 controls, but the study ended with 83 cases and 128 controls. Does this mean the study is underpowered? The potential consequences of not meeting the sample size required for the desired power and should be addressed in the Results on page 10 and in the Discussion. I am particularly concerned about the small proportion of controls in the under 10 age group which may be driving results (see General Comment 4 below).

3. The paper needs to be carefully edited for wording. In multiple places the authors claim high risk or no risk but these should be expressed as statistically significant increases or decreases in risk and the comparison group needs to be carefully defined. Many specific instances are mentioned below, but I also suggest careful proofreading to see if any other corrections are necessary.

4. Comparing Tables 4 and 6, there is a large change in the odds ratio associated with receiving an insect bite near a river between the univariate model (OR = 2.16) and the multivariate model (OR = 10.76, adjusting for age and bathing in an open borehole). I believe this may be due to the limited number of controls in the under 10 year age category (11.7% of controls compared to 47% of cases). This discrepancy in the number of controls under age 10 years, should be discussed and I suggest presenting some cross tabulations of the insect bite and bathing variables...
by age group to help interpret any potential age confounding or effect modification in the multivariate model in Table 6.

Specific Comments: (note, line numbers refer to actual lines of text, not the line numbers in the margins (which don't correspond to lines of text)

1. Abstract, paragraph 1, line 6. "cases was" to "cases were".

2. Abstract, paragraph 1, line 9. "matched by the sex" to "matched by sex".

3. Abstract, paragraph 1, line 10. "and be conditional logistic" and "and conditional logistic".

4. Abstract, paragraph 2, line 1. Are the percentages necessary in this sentence?

5. Abstract, paragraph 2, line 6. "crossing a water" to "crossing water".

6. Abstract, paragraph 2, line 7. "trouser" to "trousers".

7. Page 5, line 7. "of BU have been" to "of BU were".

8. Page 5, line 2. "study on" to "study of", "confirmation of BU" to "confirmed BU", and "proved that prevalence of BU" to "established prevalence of BU".

9. Page 6, line 10. "used the PCR" to "used PCR".

10. Page 6, line 3. "mine careers" to "mining", "to the environmental" to "to environmental", and "and the spreading of" to "and may contribute to the spread of".

11. Page 7, line 6. "place of residence". Is this home, village, etc?

12. Page 7, line 3. "originated from" to "originate".
13. Page 7, line -2. "a population estimated to" to "an estimated population of". Also, "1,767.518" to "1,767,518".

14. Page 8, line 3. Is the "depression of Lama" indicated on the map?

15. Page 8, line 4. Move "(Figure 1)" to line 6, after "lac Togo".

16. Page 8, line 7. "seasonal variations" to "seasonal variations in participation"?

17. Page 9, line 9. "was set at 2. Hence, we calculated a sample size" to "was wet at 2, yielding a sample size...". Also see General Comment 1 above.

18. Page 10, line 2. "as dependent variable" to "as the dependent variable".

19. Page 10, line 3. "The exact Fisher test" to "Fisher's exact test". Also, it is not clear to me why Fisher's exact test is used to compare mean or median age...this should be a t test or a non-parametric comparison of medians, shouldn't it?

20. Page 10, line 4. "significant level was set" to "with significance level set".

21. Page 11, lines 6-7. "The median age was significantly different between cases and controls (p=0.001)" Please describe the difference (which group has a higher medial age?).

22. Page 11, lines 7-8. "women (60%) were more frequently affected than men (40%) (p=0.01)." This seems to be different than the p-value reported in Table 3. Also, the p-value is associated with a test comparing the percentage of women between cases and controls, not comparing 60% to 40%. This should be clarified.

23. Page 11, line -10. "pump (p=0.49) was not" to "pump (p=0.49) were not".

24. Page 11, line -9. "open borehole was a high risk" to "open borehole was associated with higher risk".
25. Page 11, line -7. "did not provide any protection against BU" to "was not associated with reduced risk of BU".

26. Page 11, line -4. "mud was not associated with the risk" to "mud did not significantly increase risk".

27. Page 11, line -2. "in a river was" to "in a river were".

28. Page 12, line 6. "compared to other parts of the body". Can we tell from the data whether the body location of the insect bites correspond to the body location of the ulcers?

29. Page 12, line 6. "at home was" to "at home were".

30. Page 12, line 14. "did not provide any protection against BU" to "did not provide any significant reduction in risk of BU". Also, I suggest starting a new paragraph with "Farming occupation".

31. Page 12, line 13. "Wearing frequently trousers" to "Frequently wearing trousers".

32. Page 12, line 14. "provided additional protection during farming activities" to "during farming activities provided significant reduction in risk".

33. Page 12, line -6. "that living (p" to "that living with (p"

34. Page 12, line -5. "did not represent a risk" to "did not represent a significant increase in risk"

35. Page 12, line -5. "In addition, receiving bites or scratch of" to "Neither did receiving bites or scratches from". And delete "was not at risk of BU disease."

36. Page 12, line -3. "was not associated with an infection" to "was not significantly associated with increased risk of infection"

37. Page 13, line 3. "ensured to know" to "were familiar with"?
38. Page 13, line 4. "Regarding the treatment behavior" to "Regarding treatment behaviors".


40. Page 13, line 7. "though" to "thought", and "surrounding could be at risk" to "surroundings could increase risk".

41. Page 13, line -2. "children under 15 years of age were at high risk". Should this be "higher risk"? Is this in comparison to adults? This needs to be specified.

42. Page 14, line 2. "would" to "could".

43. Page 14, line 4. "was a high risk" to "was associated with higher risk"

44. Page 14, line 6. "bathing were" to "bathing was".

45. Page 14, line 8. "a high risk" to "an increased risk". Also on lines 8 and 9 there are two references to reference 38 but they seem to come to opposite conclusions? This needs to be carefully revised.

46. Page 14, line -12. "provided from the commercial" to "provided from commercial".

47. Page 14, line -9. "The same results" to "Similar results".

48. Page 14, line -7. "This would explain the location of wounds…” Does "wounds" refer to insect bites, ulcers, or both?

49. Page 14, line -1. "provide protection against Buruli ulcer" to "provide significant reduction in Buruli ulcer risk."

50. Page 15, line 2. "pants or hats provide protection from the mycobacterial" to "pants or hats are associated with reduction in risk of mycobacterial".
51. Page 15, line 11. "may cause BU disease" to "may increase risk of BU disease".

52. Page 15, line 12. "we observed…of contracting BU." to "we did not observe significant increase in risk associated with contact to domestic animals."

53. Page 15, line 15. "any difference" to "any significant difference".

54. Page 15, line 16. "lack the impact of the BCG" to "lack a significant association with BCG".

55. Page 15, line -6. "any association" to "any significant association".

56. Page 15, line -1. "the situation in five years ago" to "the situation five years ago" and provide a reference.

57. Page 16, line 4. "The personal poor" to "Personal poor".

58. Page 16, line 5. "surrounding has been recognized" to "surrounding were recognized".

59. Page 16, line 5. "potential risk of contracting BU" to "potential risk factor for participants".

60. Table 1. I suggest adding "%" after 51.9 and 70.5 to make the table to read quickly. Similarly for Table 2.

61. Table 3. The p-value reported for sex is 0.32, which is different than the p-value reported in the text, see Specific Comment 22 above.

62. Table 4. Should the HIV positive case be excluded?
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?
If not, please explain in your comments to the authors.

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

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal