Author's response to reviews

Title: Diarrhoeal diseases among adult population in an agricultural community Hanam province, Vietnam, with high wastewater and excreta re-use

Authors:

Phuc Pham-Duc (phucnihe@gmail.com)
Hung Nguyen-Viet (hung.nguyen@unibas.ch)
Jan Hattendorf (jan.hattendort@unibas.ch)
Phung Dac Cam (cam@fpt.vn)
Christian Zurbrügg (christian.zurbrugg@eawag.ch)
Jakob Zinsstag (jakob.zinsstag@unibas.ch)
Peter Odermatt (peter.odermatt@unibas.ch)

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Author's response to reviews:

Ref.: Revision R1 of manuscript entitled “Diarrhoeal diseases among adult population in an agricultural community Hanam province, Vietnam, with high wastewater and excreta re-use”

Dear Editor

Thank you very much for your email with the feedback pertaining to our manuscript submission and the observations and suggestions of the two reviewers. We are very pleased that our manuscript received rather favorable reviews and grateful to the constructive suggestions. Please, find below our point-by-point response to the reviewers’ comments, clearly indicating how and where the manuscript changes have been made. Attached we send a manuscript with track-changes. In addition we send a clean revised version (without track-changes).

Reviewer #1

The reviewed article has a well-defined question relating risk factors to diarrheal incidence in rural Vietnam. The methods used are appropriate and for the most part are well described, with a couple of important exceptions related to the asset index used to assign socioeconomic status and description of the study area. The data collected are reasonable and sound. The manuscript partly adheres to relevant standards of reporting and data deposition, especially in reporting univariate and multivariate regression models. However, I suggest significant changes to presentation of summary statistics of variables used in the regression models.

Answer: Thank you for the rather positive overall assessment of our work. We are most happy about that. We have improved in the result section (please see revised manuscript, various places).
Limitations of the work were addressed in regards to low diarrheal incidence found during the study. I pose a couple of additional questions to help clarify this discussion. Otherwise, I suggest additional opportunities for addressing limitations in other parts of the discussion. Authors do clearly acknowledge work in which they are building, often in the same agricultural context in Vietnam and other locations. I suggest additional discussion of these studies to better integrate and contextualize the authors’ findings with the studies they cite.

Answer: Many thanks. We have improved in regards to low diarrhoeal incidence in the discussion section (please see revised manuscript, lines 400-402 and lines 409-414).

For most of the manuscript, the writing is acceptable, provided some minor grammatical corrections. However, the discussion section is scattered and the authors do not synthesize their work with references. At times, the authors focus more on secondary points of their research and stray from the central findings, complicated by a number of confusing sentences. The title and abstract are suitable, with one suggestion for the closing statement in the abstract.

Answer: Many thanks. We have improved in the discussion section (please see revised manuscript, various places).

Discretionary Revisions

Suggested citations for the authors to address in their discussion:
1. Seasonality discussion (lines 338-348)

Answer: Many thanks. We have added in the discussion section (please see revised manuscript, lines: 416-420 and lines: 422-424).

2. Background and Introduction

Answer: Many thanks. We have added and improved in the Introduction section as suggested (please see revised manuscript, introduction lines: 3-8)

Minor Essential Revisions
1) Abstract – The last sentence of the abstract is too general. Be more explicit about the main suggested public health measures that are suggested by this study.

Answer: Many thanks. We have improved the last sentence of the abstract as suggested (please see revised manuscript, summary).

Methods section
2) A description of seasons should include rainfall and temperature averages and the actual rainfall and temperature throughout the study period should be reported if seasonality is to be discussed in relation to diarrheal incidence. Authors should also include the months included in the description of the season and if possible, provide a reference.

Answer: Many thanks. We have described information of the average rainfall, temperature and humidity of the study area as suggested (please see revised manuscript, lines 44-50).

3) An additional descriptive table is needed that explains the categorization or essential information in defining variables such as SES, definitions of agricultural work, definitions of latrines, use versus handling of excreta, and protective measures. Some of these show up in Table 2, but they would be more useful in one table that explains variable formation.

Answer: Many thanks. We have described the variables were used to assess household’s economic status; definitions of agricultural work, latrines, use versus handling of excreta, and protective measures in the Method section (please see revised manuscript, lines 87-100).

4) 41 : Address with map and additional description (see Figure 1 revision above)

Answer: Many thanks. We have given more details in the text in the Method section (please see revised manuscript, lines 55-57 and in the Figure 1).

5) 57 – 58 : Clarify this statement, perhaps saying “duration that each respondent was under observation”

Answer: Many thanks. We have adapted as suggested (please see revised manuscript, lines 73-74).

6) Paragraph 2 under study design 61 – 66: Clarify usage of assets to compute the asset index and categories for socioeconomic status (SES). If the authors used a similar set of assets as another study or in other surveys (e.g. Demographic and Health Surveys or Multiple Indicator Cluster Surveys), then references to these should be given. If not, authors should disclose the assets they used for developing socioeconomic status as an additional table or supplement. This is important and relevant to their findings that SES was not significant in regression results.

Answer: Many thanks. We have improved description in the method section (please see revised manuscript, lines 82-91).

7) 87 – 90 : Move this description into paragraph 2 in study design (61 – 66)

Answer: Many thanks. We have moved the description into paragraph 2 as suggested (please see revised manuscript, lines 82-86).

8) 91 - 92 : Change wording to “by recording weekly morbidity” instead of “through a weekly morbidity recorded.”

Answer: Many thanks. We have changed wording to “by recording weekly
morbidity” instead of “through a weekly morbidity recorded” (please see revised manuscript, lines 125-126).

9) 109 – 110 : This statement might be better served at the end of the Data management and analysis section.
Answer: Many thanks. We have moved the statement to the end of the Data management and analysis section (please see revised manuscript, lines 171-172).

10) 122 : A reference or discussion for why variables with p < 0.2 were included in the multivariate model. Also use a lower case p for p-value.
Answer: Many thanks. The thresholds between p < 0.2 and p < 0.3 on the univariate analysis are the mostly used criteria’s to include a variable in the multi-variable analysis. There is not specific reference available for this practice but can be seen in all analysis of large cross-sectional studies exploring relevant risk factors. Variable associated with a p-value of less than 0.3 in the uni-variable analysis are thought to be linked with the outcome.

11) 128 : Put equation on its own line and indent with Equation 1 label.
Answer: Many thanks. We have put the equation on its own line and indent with Equation 1 label (please see revised manuscript, line 162 and line 164).

12) 133 : Explain or provide reference as to why 3 levels of SES were used instead of wealth quintiles. Do three levels better represent this population?
Answer: Thank you for this observation. Given the fact that we had a large number of potential risk factor to be tested we intended to keep the levels in each variable as low as possible in order in order not to lose to much power for the multivariable analysis in which each level of the variable is considered separately. In addition we do feel that the 3 levels of the wealth indicator describe nicely our study population.

13) 163 : Hundred and forty-two should read “One hundred and forty-two”
Answer: Many thanks. We have adapted as suggested (please see revised manuscript, lines 200-201).

Results section
14) 162 – 167 : These results should be included in a case-control flow chart. Inclusion of a case-control flow chart will greatly reduce text and help the reader better understand the study design.
Answer: Many thanks. We have created a case-control flow chart as proposed (please see revised manuscript, Figure 2).

15) 184 – 187: Sentence starting with “Only very few persons…” should be addressed in discussion section.
Answer: Many thanks. We have improved the sentence and moved to the discussion (please see revised manuscript, lines 222-224).
16) 201: “statistically significant associated” does not make sense.
Answer: Thank you for the observation. We have changed to “statistically significantly associated” (please see revised manuscript, line 242).

17) 211 – 213: The term “no risk change” is confusing here and in other places throughout the results section. Why is an odds ratio of 1.9 in the univariate mode and OR of 1.0 in the multivariate model represent “no risk change”? A more accurate description would be a change in the odds ratio or change in risk as represented by OR between the univariate and multivariate models. In this case, it seems that the risk associated with irrigating with Nhue River water is not a significant risk factor as direct contact with Nhue River water in multivariate analyses. Are these two categories different in reality or as observed or asked in surveys? In other words, can irrigation with river water occur without direct contact with river water? Or are there circumstances where these two can occur independently of one another?
Answer: Many thanks. We have improved the sentences in text (please see revised manuscript, lines 252-253)

18) 214: Use of risk change is again confusing, change to different OR in univariate as compared to multivariate models.
Answer: Many thanks. We have improved the sentence in text (please see revised manuscript, lines 255-256)

Discussion section

19) 250: “Our results was…” should read “Our results are…”
Answer: Many thanks. We have corrected as proposed (please see revised manuscript, line 292).

20) 254: “where was” should be changed to “who”
Answer: Many thanks. We have revised (please see revised manuscript, lines 295-296).

21) 255: Remove “In” from sentence that starts “In an earlier study…”
Answer: Many thanks. We have removed “In” from sentence (please see revised manuscript, line 297).

22) 259: Last sentence starting with “In addition, farmers did not…” is too brief and not accurate. According to Table 2, some farmers were reported as using protective gear. This should be more central in the discussion as this is an important finding.
Answer: Thank you for the observation. We have improved the sentence and explained the situation (please see revised manuscript, lines 301-306).

23) 280: Add a sentence or two relating this work to the relevant findings of the study in Ethiopia.
Answer: Many thanks. We have added a sentence in the discussion section
24) 287 – 288: The statement about the sludge layer needs to be better explained or reorganized, perhaps by detailing the proposed pathway that chickens and other domesticated animals (289 – 290) defecate on the roof and those potential pathogens may be growing in the rainwater collection system.

Answer: Many thanks. We have reorganized the sentences. (please see revised manuscript, lines 336-346)

25) 293 – 294: If collected, observations of removing water from rainwater storage would be useful to explain contaminated rainwater. There are several studies that discuss how contaminated hands and wide-mouthed storage containers increase risk of fecal contamination of stored water (authors provide one citation). This route of hand-contamination of stored water should be addressed more explicitly in discussion. This could also be discussed in the context of risk due to infrequent hand washing.

Answer: Many thanks. We have improved and added more relevant information. (please see revised manuscript, lines 349-353)

26) 297 – 306: Reorganize paragraph in discussing pathways of contamination from lack of protective gear and infrequent hand washing. Organize to show how contaminants are brought from fields into the home and in contact with others. More specifically, lines 300 – 302 could be expanded to a richer description of this contamination pathway.

Answer: Many thanks. We have improved as suggested (please see revised manuscript, lines 365-369)

27) 310: This sentence needs clarification, the use of the word “omitting” does not make sense as written. Did researchers statistically control for handwashing with soap and observations of absence of proper drainage?

Answer: Many thanks. We have improved the sentence (please see revised manuscript, lines 373-374)

28) 317: Where respondents reheating food to an appropriate temperature to kill pathogens?

Answer: Many thanks. We have improved the sentence (please see revised manuscript, lines 380-381)

29) 319: Change the wording from common belief to a discussion of well supported research from the scientific literature.

Answer: Many thanks. We have improved and added the relevant sentences (please see revised manuscript lines 384-387)

30) 322: Synthesize these studies into a statement of support, specifically what was similar about their findings and those found in this study.

Answer: Many thanks. We have synthesized these studies into a statement of support (please see revised manuscript, lines 390-391)
31) 323 : The finding that SES did not account for differences in diarrheal incidence is important. A deeper explanation and synthesis of the reference provided is needed. Why would low SES not increase risk of diarrheal incidence in this system?

Answer: Many thanks. We have improved as suggested (please see revised manuscript, lines 393-394)

32) 328 – 337 : While it is important that underestimation of incidence may have occurred during this study, it may not be the only factor accounting for lower observed incidence in this population than in other low-income settings. Based on observations during this study and the referenced Hanoi study, what are other differences in this system that could also account for lower detected incidence?

Answer: Many thanks. We have improved in the discussion (please see revised manuscript, lines 400-402 and lines 409-414)

33) 338 - 339 : I do not see data that directly supports this claim. Incidence is not presented by season, nor is season included in any of the analyses. Is this based on Figure 3?? Seasons should be clearly outlined in the description of the study location in the Methods study, including average rainfall and temperature and what months are included in each season.

Answer: Many thanks. We have improved in the discussion (please see revised manuscript, lines 416-420 and lines 422-424)

Figures and Tables

34) Figure 1 – In the second panel, it does not appear that the Nhat Tan communities border the Nhue River. This requires further explanation, adding a map scale, and perhaps a more detailed map that shows how these communities are contacting Nhue River water.

Answer: Many thanks. We have updated the map in Figure 1 (please see revised manuscript, Figure 1).

35) Figure 2 – Add error bars or indication of variance for each group.

Answer: Many thanks. We have added error bars in each group of the Figure 3 (please see revised manuscript, Figure 3).

36) Table 1 – This should be organized in a similar way as Table 2, into groups of variables. Such as Water and Sanitation, Demographic characteristics, and Agricultural practices. Showing all categories of each variable would also help readers understand the full distribution of variables, such as all levels of socio-economic status.

Answer: Many thanks. We have re-organized Table 1 (please see revised manuscript, Table 1).

37) Table 2 – “No use of protective measures” with No and Yes as presented answers is confusing.

Answer: Many thanks. We have revised table 2 as suggested (please see
revised manuscript, Table 2).

38) Tables 2 & 3 – These could be arranged into one Table with Unadjusted (Univariate) and Adjusted (Multivariate) columns, denoting key p values by symbols to save column space. This would help the reader follow the modelling methodology and process used by the authors.

Answer: Thank you for this idea and proposed option. However, we wish to retain the separation of the two tables as we fear that a combined table would be overloaded. There are many variables and several risk reported which could make the table difficult to read.

Reviewer #2:

This paper presents a thorough and rigorous epidemiological study on risk factors for diarrhoeal disease among farmers exposed to wastewater and excreta in Hanam province of northern Vietnam. The brevity of this review should no means be interpreted as a review lacking in thoroughness: I went through the paper with a fine-toothed comb and have concluded that it is an outstanding and useful piece of research. I have no problems at all with experimental design or analysis. Furthermore, I think the paper is very well written. Most important of all though, it provides clear findings on an important question. Below are listed some very minor comments. I believe that this paper is acceptable for publication in BMC Public Health without modification.

Answer: We thank this reviewer for a very positive assessment of our work. Many thanks!

MINOR COMMENTS

Summary section, second line: insert “the” before adult. Likewise, insert “The” before “highest” at the start of the sixth last sentence.

Answer: Many thanks. We have changed as suggested (please see revised manuscript, Summary).

Lines 9–10: There are many reports making statements about the relative rankings of various disease impacts, but they are all secondary sources (including who documents) and many are based on old research. The most recent stats are found in the following paper, and I think it would make sense to cite this original piece of research: Murray et al. (2012) Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380: 2197–223.

Answer: Many thanks. We have updated and added the reference as requested (please see revised manuscript, lines 17-19).

Line 21: adults’: possessive.

Answer: Many thanks. We have revised as requested (please see revised manuscript, line 29).
Lines 57–58. The word “time” is repeated.
Answer: Many thanks. We have adapted as suggested (please see revised manuscript, lines 73-74).

Line 100: To me “questionnaire interview” is bordering on a tautology.
Answer: Many thanks. We have adapted as proposed (please see revised manuscript line 134).

Line 109: Data were (not was)
Answer: Many thanks. We have revised accordingly (see revised manuscript line 171).

Line 185: Rephrase in terms of having a meaningful sample size to test a hypothesis rather than talking about finding differences.
Answer: Many thanks. We have revised as suggested and followed reviewer 1 suggested (please see revised manuscript, lines 222-224).

Line 208: “respectively” is redundant here. Likewise on line 211.
Answer: Many thanks. We have revised it (please see revised manuscript line 249).

Line 253: replace “was” with “were”
Answer: Many thanks and we have replaced it (please see revised manuscript line 295).

Line 254: missing “it” after “where”
Answer: Many thanks. We have revised it (please see revised manuscript line 296).

Answer: Many thanks. We have revised it (please see revised manuscript line 297)

Line 297: Change to “The lack of protective. . . “
Answer: Many thanks. We have revised it (please see revised manuscript line 356)

Line 309: “poses”
Answer: Many thanks. We have revised it (please see revised manuscript line 372)

Line 318: Insert comma after “education”.
Answer: Many thanks. We have revised it (please see revised manuscript line 383)

Line 319: Change “believe” to “belief”
Answer: Many thanks. We have revised it (please see revised manuscript line 383)

Line 347: “spp.” should not be italicised. Figure 3 caption: state what the error bars represent.

Answer: Many thanks. We have revised it (please see revised manuscript line 431); and we have adjusted Figure 4 caption state the error bars represent (please see Figure 4)

In addition to the above change we have also improved the English editing of our manuscript (please see revised manuscript, various places). We hope that with all these modifications and improvements, our manuscript can be accepted for publication in BMC Public Health. We look forward to your reply.

With best regards

Yours sincerely

Phuc Pham Duc