Confirmation of your submission to Malaria Journal - MALJ-D-18-00208

7 messages

Malaria Journal Editorial Office <em@editorialmanager.com> 20 April 2018 at 04:44
Reply-To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>

MALJ-D-18-00208
Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia
Hamzah Hasyim, PhD candidate; Meghnath Dhimal, PhD; Jan Bauer, Dr.med.; Doreen Montag, DPhill; David A. Groneberg, Prof,Dr,PhD; Ulrich Kuch, Dr; Ruth Müller, Dr
Malaria Journal

Dear Mr Hasyim,

Thank you for submitting your manuscript 'Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia' to Malaria Journal.

The submission id is: MALJ-D-18-00208

Please refer to this number in any future correspondence.

During the review process, you can keep track of the status of your manuscript by accessing the journal's website.

Your username is: Hamzah

If you forgot your password, you can click the 'Send Login Details' link on the EM Login page at https://malj.editorialmanager.com/.

Best wishes,

Editorial Office
Malaria Journal
https://malariajournal.biomedcentral.com/

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MALJ-D-18-00208 - Manuscript Sent Back

2 messages

Malaria Journal Editorial Office <em@editorialmanager.com> 20 April 2018 at 17:24
Reply-To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>

MALJ-D-18-00208
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Malaria Journal

Dear Mr Hasyim,

Your submission entitled "Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia" has been received.

Before we can further process it you are kindly requested to make the following corrections to meet the journal's requirements (please also refer to the Submission Guidelines):

http://malariajournal.biomedcentral.com/submission-guidelines

Kindly include all the following section below and put an header "DECLARATION". This section should be include after the list of abbreviations section and before the reference section of your paper.

All manuscripts must contain the following sections under the heading 'Declarations':

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and material
- Competing interests
- Funding
- Authors' contributions
- Acknowledgements
- Authors' information

If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

Please log onto Editorial Manager as an author.

Your username is: Hamzah

If you forgot your password, you can click the 'Send Login Details' link on the EM Login page at https://malj.editorialmanager.com/.

Please go to the menu item 'Submissions Sent Back to Author', and click on 'Edit Submission'. If no changes are to be made in the metadata, please go immediately to the last submission step 'attach files', and replace the appropriate files. Build the PDF, view your submission, and approve the changes.

Thank you for submitting your work to this journal.

With kind regards,

Magesh Murugappan
JEO Assistant

Thank you for approving your submission to Malaria Journal

4 messages

Malaria Journal Editorial Office <em@editorialmanager.com> 20 April 2018 at 23:28
Reply-To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>

Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia
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Malaria Journal

Dear Mr Hasyim,

Thank you for approving the changes and returning your submission entitled 'Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia'.

You will be able to check on the progress of your manuscript during the peer review process by logging on to Editorial Manager as an author.

Your username is: Hamzah

If you forgot your password, you can click the 'Send Login Details' link on the EM Login page at https://malj.editorialmanager.com/.

Thank you for submitting your work to Malaria Journal.

Best wishes,

Editorial Office
Malaria Journal
https://malariajournal.biomedcentral.com/

Malaria Journal Editorial Office <em@editorialmanager.com> 20 April 2018 at 23:28
Reply-To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>
To: Hamzah Hasyim <hamzah.hasyim@stud.uni-frankfurt.de>

[Quoted text hidden]

Hamzah Hasyim <hamzah.hasyim@gmail.com> 20 April 2018 at 23:37
To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>

Dear Dr Magesh Murugappan
JEO Assistant,

Thank you for your information. I have created the manuscript accordingly guidance http://malariajournal.biomedcentral.com/submission-guidelines.

The manuscript has contained already the following sections under the heading 'Declarations'

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and material
- Competing interests

- Funding
- Authors' contributions
- Acknowledgements
- Authors' information

I hope the manuscript will be a reviewed quickly by a reviewer of the journal and the paper succeeded published in the journal like our first paper.

Your assistance in this matter is greatly appreciated. If you require any further information, let me know.

Sincerely,

Hamzah
[Quoted text hidden]

Hamzah Hasyim <hamzah.hasyim@gmail.com> 1 May 2018 at 04:10
To: "Meghnath Dhimal, PhD" <meghdhimal@gmail.com>, "Meghnath Dhimal, PhD" <meghdhimal@nhrc.org.np>

Dear Dr Megnath,

I hope you are doing well. I am delighted to inform you if our paper still under review at the moment. May I ask the editor regarding the progress of the reviewer?

Also, if I want to submit another paper, still concerning malaria issue. Do you have any recommendation the credible journal that more fastly for the review?

Thank you so much for your information. I greatly appreciate the assistance you have provided me.

Sincerely,

Hamzah

---------- Forwarded message ----------
From: **Malaria Journal Editorial Office** <em@editorialmanager.com>
Date: 20 April 2018 at 18:28
Subject: Thank you for approving your submission to Malaria Journal
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>

[Quoted text hidden]

Gmail Hamzah Hasyim <hamzah.hasyim@gmail.com>

MALJ-D-18-00208

1 message

Magesh Murugappan <magesh.murugappan@springer.com> 19 June 2018 at 22:05
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>

Dear Dr. Hasyim,

You may submit your revised paper online upon addressing the reviewer comments.

Thank you very much.

With best regards,

Magesh

Magesh Murugappan (Mr.)

Journals Editorial Office (JEO)

From: Hamzah Hasyim <hamzah.hasyim@gmail.com>
Sent: Tuesday, June 19, 2018 2:54 AM
To: Magesh Murugappan
Subject: Fwd: Your submission to Malaria Journal - MALJ-D-18-00208

Dear Dr **Magesh Murugappan (Mr.)**

Journals Editorial Office (JEO)

I am pleased to inform you if we still doing all the input of reviewer1 and 2. If our feedback finished already, I would send my revised manuscript soon

Respectfully,

Hamzah Hasyim,

Department of Tropical Medicine and Public Health,

Institute of Occupational, Social and Environmental Medicine,

Faculty of Medicine of the Goethe University in Frankfurt am Main

DEUTSCHLAND

http://www.med.uni-frankfurt.de/institut/occupational-medicine/

hamzah.hasyim@stud.uni-frankfurt.de

Phone number: +4915905821418

Occupational Health Safety and Environment Department, Faculty of Public Health, Sriwijaya University,

South Sumatra, Palembang-Prabumulih, KM 32 Inderalaya (Ogan Ilir) 30662

INDONESIA

http://fkm.unsri.ac.id/id/

hamzah@fkm.unsri.ac.id

Phone number: +6281373178328

bit.ly/weM38G

---------- Forwarded message ----------
From: **Malaria Journal Editorial Office** <em@editorialmanager.com>
Date: 12 June 2018 at 18:47
Subject: Your submission to Malaria Journal - MALJ-D-18-00208
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>

MALJ-D-18-00208
Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia
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Malaria Journal

Dear Mr Hasyim,

Your manuscript "Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia" (MALJ-D-18-00208) has been assessed by our reviewers. Although it is of interest, we are unable to consider it for publication in its current form. The reviewers have raised a number of points which we believe would improve the manuscript and may allow a revised version to be published in Malaria Journal. In addition, I feel that you should clearly explain why it may be still be worthwhile to publish 2007 data.

Their reports, together with any other comments, are below. Please also take a moment to check our website at https://malj.editorialmanager.com/ for any additional comments that were saved as attachments.

If you are able to fully address these points, we would encourage you to submit a revised manuscript to Malaria Journal. Once you have made the necessary corrections, please submit online by log onto the journal's website.

Your username is: Hamzah

If you forgot your password, you can click the 'Send Login Details' link on the EM Login page at https://malj.editorialmanager.com/.

Please include a point-by-point response within the 'Response to Reviewers' box in the submission system and highlight (with 'tracked changes'/coloured/underlines/highlighted text) all changes made when revising the manuscript. Please ensure you describe additional experiments that were carried out and include a detailed rebuttal of any criticisms or requested revisions that you disagreed with. Please also ensure that your revised manuscript conforms to the journal style, which can be found in the Submission Guidelines on the journal homepage.

Please note, if your manuscript is accepted you will not be able to make any changes to the authors, or order of authors, of your manuscript once the editor has accepted your manuscript for publication. If you wish to make any changes to authorship before you resubmit your revisions, please reply to this email and ask for a 'Request for change in authorship' form which should be completed by all authors (including those to be removed) and returned to this email address. Please ensure that any changes in authorship fulfil the criteria for authorship as outlined in BioMed Central's editorial policies (http://www.biomedcentral.com/about/editorialpolicies#authorship).

Once you have completed and returned the form, your request will be considered and you will be advised whether the requested changes will be allowed.
By resubmitting your manuscript you confirm that all author details on the revised version are correct, that all authors have agreed to authorship and order of authorship for this manuscript and that all authors have the appropriate permissions and rights to the reported data.

Please be aware that we may investigate, or ask your institute to investigate, any unauthorised attempts to change authorship or discrepancies in authorship between the submitted and revised versions of your manuscript.

The due date for submitting the revised version of your article is 10 Jul 2018.

I look forward to receiving your revised manuscript soon.

Best wishes,

Marcel Hommel, MD, PhD
Malaria Journal
https://malariajournal.biomedcentral.com/

Reviewer reports:

Reviewer #1: in attached file

Reviewer #2: Comments to author for MALJ-D-18-00208 "Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia"

General comment: This work contributes to the literature by providing a large dataset analysis of zooprophylaxis. As the authors state, much of this literature is characterized by studies based on small study populations. The manuscript, while interesting, is difficult to comprehend largely due to language and structure choices. Further, given a lack of detail provided on data collection and methods, the validity of the findings is difficult to assess. Finally, the manuscript would be improved by making clear recommendations based on study findings.

Abstract

1. Line 7 - This sentence suggests that malaria is only transmitted by zoophilic vectors which is misleading. I would suggest rephrasing this.
2. Line 12-14 - The second clause of the second sentence suggests that the findings of the small-to-medium sized surveys are debated. I think that the concept or effectiveness of zooprophylaxis is debated but the study outcomes are not.
3. Line 19 - What is Indonesian basic health research? Is it possible to provide a more specific descriptor here? Is it government-run? What constitutes "basic health research"?
4. Line 46 - Can we say facilitate malaria prevalence? I would suggest something like: our results imply that livestock may contribute to malaria risk (or something to this effect).
5. Line 51 & 58 - Please report statistics in a consistent format. In the first set of parenthesis on like 51, it is not clear what the "1.16%" refers to.
6. Line 5 - Remove "extensive". Let the analysis speak for itself.
7. Line 9-10 - Keeping of pets is mentioned in hte conclusion but there is no evidence for pets role in your results section above except for a control factor in a multivariable analysis. Either remove or explain in the results section of the abstract.

Background

8. Clarify which Plasmodium species this paper focuses on (e.g., P. falciparum vs. other Plasmodium species)
9. Choosing to analyse only rural areas may bias the sample towards zoophilic mosquitoes relative to urban areas. No description is provided regarding the vectors in the locations described.
10. The mechanisms for zooprophylaxis and zoopotentiation are introduced in the discussion section. These should be introduced in the background section.
11. Line 3 - Please add a citation.
12. Line 3 - This sentence is currently presented as a stand-alone paragraph. I would recommend including it in the paragraph that follows.
13. Line 4 - Malaria is spread between humans, the current sentence suggests that it is spread from some other species to humans which it is not unless we're discussing P. knowlesi.
14. Line 4 & - Grammar
15. Line 6 - Please add a reference for this statement.
16. Line 7 - Please clarify who "those people" are and why they are at high risk of contracting malaria.
17. Line 8 - is 2007 the most recent estimate of malaria prevalence in Indonesia? If so, please state this here. If not, it would be helpful to indicate the most recent statistics.
18. Line 8 - please provide a citation.
19. Line 10 - malaria is neither an animal disease nor a zoonotic disease. In the case of Plasmodium falciparum, animals do not contract malaria once bitten by mosquitoes, nor is malaria transmitted from animals to humans. It is a vector-borne disease. Please correct this sentence and update the citation.

20. Line 14 - please clearly categorize livestock in this list. It suggests that cattle are not included in the category of "medium and large ruminants". I would also request that justification (i.e., appropriate examples from the literature) is provided for including pets such as dogs and cats in "livestock".
21. Line 17 - It is not clear what is meant by "sourced". Perhaps "transmitted" would be a better choice of language?
22. Line 17 - This sentence suggests that malaria is only transmitted by zoophilic vectors. This is inaccurate. Species of anopheles vary in their relative zoophily/anthrophily. The article that is referenced here by Franco makes their argument in the context of locations where zoophilic vectors predominate.
23. Line 18 and 19 - the concepts of zooprophylaxis and insecticide treated livestock need to be explained here.
24. Line 20-20 - this paragraph is seemingly intended to summarize the literature on zooprophylaxis, however this section engages with only five articles. The literature in this area is much more robust than indicated. I would recommend a more thorough discussion in this section.
25. Line 29 - the reasons for differences in observed zooprophylactic success have been suggested and should be explained here (see Donnelly et al., 2015).
26. Line 30 - the terms zooprophylaxis and zoopotentiation must be clearly defined.
27. Line 32 - Is it appropriate to say that complex interactions cannot be explored through small or medium sized studies? Please provide adequate evidence from the literature to support this statement or remove it.
28. Line 34 - does "the rural endemic area" refer to a single rural endemic area or rural endemic areas? If the former, the area should be specified.
29. Line 36 - does the percentage in parenthesis reflect the proportion of A. vagus
30. Line 38 - what is meant by constrained? Less abundant? Please clarify.
31. Line 39 - Please define epidemic environments for the purposes of this study.
32. Line 39 - how is "high risk" defined for the purposes of this study.
33. Line 42 - please define "medium livestock" and "big cattle"
34. Line 44 - what is meant by "highest malaria status"?

Methods
35. Overall - the "Riskesdas" is not well described. Who is responsible for data collection? How often dose this occur? What constitutes "basic health data"? An overview should be included in the body of the manuscript while a detailed description could be included as supplemental material.
36. Structure
37. I would suggest that the study area paragraph be followed by the population and sample population. Perhaps retitle the latter as "study population"
38. I might also suggest explaining the data collection/questionnaires prior to describing the research variables as I assume the variables must be based on questionnaire items.
39. Study area - this section does not describe the study area but rather the dataset. This section should describe the geography of the study area/setting
40. Research variables
41. The research variables are not clearly explained. Each variable must be clearly defined with categories where necessary. It may be helpful to refer to Table 1 here where the variables are more clearly defined (See my comments pertaining to Table 1).
42. Line 55 -what is "habit of defecate?"
43. Line 56 - the meaning of the statement within parenthesis is unclear
44. Line 57 - what does "type of container/media" refer to with respect to environmental sanitation? Is it water storage? Toilet or latrine type? Similarly what is meant by "the sewage canal" and the "condition of a chemical sewage canal"?
45. Line 58 - by "existence of livestock/pets" do we mean presence? Or perhaps ownership? Does it refer to a particular location, such as within the compound? This also leads to a broader discussion of how livestock are commonly kept in the areas included in the study. Are they kept communally in common grazing areas or does each family keep their own livestock within a compound? Are they free range, tethered, or penned?
46. Line 58 - what time of cages are referred to here? Poultry would presumably housed differently than cattle but this is not clearly explained. Further, what is meant by medium breeding animals and large breeding animals? These terms have not been defined.

47. Line 60 - how is malaria status defined? Given that this is the main outcome of interest, it is of utmost importance that this variable is clearly explained.
48. Line 67 - it should be clearly justified why only malaria endemic areas were selected and the limitations section should describe what the possible negative consequences of this choice may be.
49. Line 70-71 - grammar
50. Line 71-73 - this answers, in part, the question in pertaining to line 60. It would be most helpful to specify in a single statement that having malaria was defined as participants who have been diagnosed with malaria by health workers in the last month. Also, what is meant by "diagnosed by a health worker"? Is it based on clinical signs or is the diagnosis confirmed by testing (e.g., blood smear + microscopy, antibody test, antigen test, etc.).
51. Line 76-77 - does this mean that additional data was collected outside of Riskesdas? If so, how was sampling completed? Who administered the questionnaires? Much more detail must be provided.
52. Line 84 - please specify what is meant by "taking into account the complex sampling design".
53. Line 86 - how were explanatory variables identified/selected to be tested?

Results
54. Line 92 - is this a result of this study or is it taken from the literature cited? If it is not based on the results of this investigation, this section should either be deleted or moved to the background section.
55. Line 104-105 - the inconsistency of language around categorizing livestock creates much confusion for the reader. Earlier, definitions included medium- and large-ruminants, then medium- and large- breeding animals. Here we have medium-sized animals and large-sized breeding animals. Please provide definitions early in the manuscript and use them consistently throughout the manuscript.
56. 105-106 - What is the significance of caging? Where would a cage typically be located? Line 118-119 suggests that cages can be inside or outside the house but this is not reflected in Table 1.
57. 127-128 - where is the evidence to show that farmers, fishermen and labourers have a higher odds of contracting malaria because of contact with vectors during their job? It seems that we can only say that there is a higher odds but we cannot state why. Typically, discussion of the potential underlying causes should be limited to the discussion section.
58. Line 131 - remove the statement about the limitation of bivariate analysis for the variable "use of ITNs". This belongs in the discussion section. Also, the analysis does not consider the quality or condition of ITNs which may explain why this variable does not behave in the expected way. This should be further discussed.
59. Lines 136-141 - these statements belong in the methods section rather than results.
60. Lines 145-146 - atypical choice of language around "dominant factors". It is my understanding that in a multivariable logistic regression we are interested in controlling the other factors, e.g., sociodemographics. I would consider rephrasing this statement/providing clarity on what is intended to be communicated here.
61. Line 150 - livestock are not a source of malaria, rather they may potentiate malaria. It is very important that the transmission route of the disease is well understood and explained and that the concepts of zooprophylaxis and zoopotentiation are also well communicated. It is my concern that the findings of the study may easily be misinterpreted by a novice reader of this literature.
62. Lines 154-160 - how does this section relate to the results of this study? It seems that either this section should be removed to the background section or deleted entirely.
63. Line 162 - remove the adjective "strong" allow the data to speak for itself and the reader to draw their own conclusion.
64. Line 164-166 - this is one of the proposed mechanisms for zoopotentiation and belongs in the background section. Here it reads as your own idea. Please provide appropriate references from the literature.
65. Line 168-169 - Yes, absolutely. Again, this belongs in the background section.
66. Line 172-174 - did this analysis measure the abundance of various Anophelines? If

so, it should be clearly explained in the methods section. If not, this sentence should be rephrased to clarify that this is a finding of another study.
67. Lines 175-187 - this literature should be more thoroughly discussed in the background section.
68. Lines 189-192 - Again, the challenge of understanding the meaning of "caged" makes the meaning of this section very unclear.
69. Lines 217-223 - this section should discuss the literature in light of the findings of this study. This analysis revealed that ITNs actually increased odds of having malaria. Some suggestions of why this might be should be presented.

Limitations
70. I would recommend much further discussion of the earlier presented information regarding mosquito vector variability in the study regions. Indonesia, according to the authors, contains 20 Anopheles species - therefore there is likely a wide range in zoophily among vectors. How might this have affected the results of the study and what might have mitigated such effects?
71. By only analysing the provinces/territories where malaria prevalence is high, are we biasing the sample? What other factors could cause this variation in spatial distribution apart from (and including) livestock. This selection is not sufficently justified.

Recommendations
72. Lines 235-241 - my understanding is that one cannot make recommendations that are not supported by the findings of your study. Please limit your comments accordingly. For example, since this analysis does not include ITL it seems inappropriate that the authors make any recommendations regarding ITL. In addition, this study finds that ITNs actually increase malaria risk and therefore I would advise against any recommendations with respect to mosquito nets.
73. Line 238 - It is not recommended to introduce a new concept such as integrated vector management in the concluding sections. Options would include either introducing this concept in the background section or removing this recommendation.

Conclusion
74. Remove "one health" - it's mentioned only briefly in the abstract and conclusion but not discussed in the body of the manuscript. Either introduce in the background section and flesh-out the concept or remove completely.

Table 1
75. Categorical variable descriptions can be shortened as follows
76. Age: 0. Productive age (15-64 years) vs. 1. Not productive age (<15 and >64 years)
77. Education: 0. Completed high school vs. 1. High school not completed vs 2. <10 years of age
78. Question: is there no education in Indonesia for children <10 years? I am concerned that this categorization may be collinear with the Age category.
79. Main occupation: 0. Other occupation vs. 1. Farmer/fisherman/labourer vs. 2. <10 years of age
80. Sleep in mosquito net: 0. Yes vs. 1. No vs. 2. No answer
81. Net insecticide Insecticide treated net: 0. Yes vs. 1. No
82. The habit of defecate Toilet use (or perhaps access?) for defecation: 0. Yes vs. 1. No or no answer
83. Travel time to nearest health facility: 0. <60 minute vs. > 60 minutes
84. Definitions for "health facility" and "community health facility" should be included in the body of the manuscript or the table.
85. All of the environmental sanitation variables require more explanation. For individuals who are not familiar with the rural Indonesian context, it is difficult to imagine what these variables refer to and what effect they may have on malaria transmission. I would encourage a fuller description within the methods section.
86. Existence of livestock/pets Livestock/pet keeping
87. Poultry: 0. No vs. 1. Yes
88. Medium breeding animals: 0. No vs. 1. Yes

89. Large breeding animals: 0. No vs. 1. Yes
90. Pets: 0. No vs. 1. Yes
91. Location of cage - this variable requires clarity. Does this variable ONLY apply to individuals who do keep livestock? If not, then an additional variable e.g., "no poultry" should also be included. Based on the information in supplemental material 1., this variable should actually have 4 categories "cage in the house", "cage outside the house", "inside the house without a cage" and "outdoors without a cage".
92. It does not seem appropriate to group "animals kept outdoors without a cage" with those who do not keep cattle. The risk profile for these two groups would not be the same and should not be considered so. Grouping these categories together has the potential to greatly bias the results. If the participant did not respond to this question, their data should be categorized as missing and dropped from the dataset. Alternatively, data imputation could be used to avoid data loss from missing variables.

Figure 1 - is this data a result of the current study? If so, methods must be included in the methods section. If not, the original source must be referenced.

List of abbreviations - Ristekdikti is not found in the body of the manuscript

Supplemental materials - appendix 1
93. It is my feeling that the reader should not be required to go to the supplemental materials in order to understand the manuscript. The supplemental materials should be reserved for additional materials that may be of interest to a subset of the intended audience but are not critical to the argument. In the case of this manuscript, much of the information provided in the method supplemental materials should be edited and included in the body of the manuscript.
94. Questionnaire items from the Riskesdas could be included as supplemental materials but they are already included in Table 1, and therefore I maintain that this appendix can be removed.
95. Data management -it is explained in the body of the article that Stata is used for data management. I don't believe it is necessary to include the coding approach in the methods section. Additionally, the authors have already provided it Table 1. Users of Stata will be familiar with how the program assigns the reference categories, while those who are not familiar can readily find this information online.
96. Malaria prevalence - much of this information is provided in the body of the manuscript.
97. Characteristics of participants - much of this is included in Table 1.
98. Line 16 - Do we mean sex rather than gender? If participants were asked what gender they identify with, then gender is appropriate, otherwise sex should be used. Given that you are using male/female as categories, it does seem that "sex" is the appropriate variable name.
99. Line 18 - this statement, in addition to the table, suggests that participants less than 1 year of age, or greater than 97 years were removed from the dataset. If this is correct, please state this clearly in the manuscript body.
100. Line 66 - see my previous comment on statistical analysis within the manuscript body.
101. Line 69-77 - describes the codes used but does not explain the structure of the data that makes these choices appropriate. These lines should be replaced with a more specific explanation that pertains to this dataset in particular and included in the body of the manuscript.
102. Line 77-89 - include in the body of the manuscript.

Appendix 2 - results
103. It is my feeling that this information is wasted when included as a supplemental material. I would strongly suggest including these results in the manuscript body. Alternatively, the descriptive data could be published as a stand-alone manuscript. Then, the bi- and multi-variable analysis article would simply refer to the other article. This may solve a number of your length challenges.
104. I would avoid categorizing education as "low" and "high" or "good" and "bad" access to health services. Simply describe the cut off points and avoid value-based language. E.g., "Most participants were able to access health services by traveling for

less than 60 minutes" rather than "The general access to health care was found to be good." Or, "the majority of participants had not completed high school" rather than "there were more participants, who had a low educated level".
105. Lines 17-21 - this type of description of sanitation should be included within the body of the text.
106. Line 89-90 - Here you seem to be comparing people who kept cage pets outside to people who kept poultry indoors. This seems a strange comparison. Should we be comparing pets kept caged outside versus pets kept caged indoors? Then, separately, comparing poultry cages indoors with poultry cages outdoors?
107. Line 92 - regarding "participants who raised poultry either" the meaning is not sufficiently clear.

108. For an interesting discussion on supplemental materials in scientific publications see: Pop M, Salzberg SL. Use and mis-use of supplementary material in science publications. BMC Bioinformatics. 2015;16:237. doi:10.1186/s12859-015-0668-z.

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

Technical Comments from the Editorial Office:

https://malj.editorialmanager.com/l.asp?i=78732&l=0XJDU3TG

If improvements to your figures have been requested or are needed, and you would like professional help, we can recommend our affiliates Peerwith for help with figure editing (https://bmc.peerwith.com/malj/figure-editing). Please note that use of any Peerwith service is neither a requirement nor a guarantee of publication.

Reminder: your revision for Malaria Journal is due soon - MALJ-D-18-00208

12 messages

Malaria Journal Editorial Office <em@editorialmanager.com> 7 July 2018 at 15:15
Reply-To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>

MALJ-D-18-00208
Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia
Hamzah Hasyim, PhD candidate; Meghnath Dhimal, PhD; Jan Bauer, Dr.med.; Doreen Montag, DPhill; David A. Groneberg, Prof,Dr,PhD; Ulrich Kuch, Dr; Ruth Müller, Dr
Malaria Journal

Dear Mr Hasyim,

When checking our records, we noticed that the revised version of your manuscript MALJ-D-18-00208 is due soon on 10 Jul 2018.

If you are ready to submit, please access the manuscript by log onto the journal's website.

Your username is: Hamzah

If you forgot your password, you can click the 'Send Login Details' link on the EM Login page at https://MALJ.editorialmanager.com/.

We are looking forward to receiving your revision.

Best wishes,

Editorial Office
Malaria Journal
https://malariajournal.biomedcentral.com/

Malaria Journal Editorial Office <em@editorialmanager.com> 7 July 2018 at 15:15
Reply-To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>
To: Hamzah Hasyim <hamzah.hasyim@stud.uni-frankfurt.de>

[Quoted text hidden]

Hamzah Hasyim <hamzah.hasyim@gmail.com> 8 July 2018 at 02:46
To: "Dr. Ruth Müller" <Ruth.Mueller@med.uni-frankfurt.de>, "Dr. Ulrich Kuch" <kuch@med.uni-frankfurt.de>

Dear Dr Ruth, and Dr Ulrich,

Gute Nacht from Indonesia.

Kindly see a revised version of our article livestock. Please advise. I am a little bit late send it due to the internet at my home at not stable.

Sincerely yours,

Confirmation of revised submission to Malaria Journal - MALJ-D-18-00208R1

10 messages

Malaria Journal Editorial Office <em@editorialmanager.com> 10 July 2018 at 04:31
Reply-To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>

MALJ-D-18-00208R1
Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia
Hamzah Hasyim, PhD candidate; Meghnath Dhimal, PhD; Jan Bauer, Dr.med.; Doreen Montag, DPhill; David A. Groneberg, Prof,Dr,PhD; Ulrich Kuch, Dr; Ruth Müller, Dr
Malaria Journal

Dear Mr Hasyim,

Thank you for the revised version of your manuscript 'Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia' submitted to Malaria Journal.

You may check the status of your manuscript at any time by accessing the journal's website.

Your username is: Hamzah

If you forgot your password, you can click the 'Send Login Details' link on the EM Login page at https://malj.editorialmanager.com/.

We will inform you of the Editor's decision as soon as possible.

Best wishes,

Editorial Office
Malaria Journal
https://malariajournal.biomedcentral.com/

Malaria Journal Editorial Office <em@editorialmanager.com> 10 July 2018 at 04:31
Reply-To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>
To: Hamzah Hasyim <hamzah.hasyim@stud.uni-frankfurt.de>

[Quoted text hidden]

Hamzah Hasyim <hamzah.hasyim@gmail.com> 10 July 2018 at 05:22
To: Malaria Journal Editorial Office <magesh.murugappan@springer.com>

Dear Dr Magesh,

I obtained a message below. Is it meant our manuscript had been succeeded submit?

Hopefully, the paper will be accepted for publishing in malaria journal. Please let me know if you have any suggestion, and should you have any queries do not hesitate to contact me. Thank you

Sincerely,

Hamzah

Date:	04 Aug 2018
To:	"Hamzah Hasyim" hamzah.hasyim@gmail.com;hamzah.hasyim@stud.uni-frankfurt.de;hamzah@fkm.unsri.ac.id
From:	"Malaria Journal Editorial Office" magesh.murugappan@springer.com
Subject:	Decision has been reached on your submission to Malaria Journal - MALJ-D-18-00208R2

MALJ-D-18-00208R2
Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia
Hamzah Hasyim, PhD candidate; Meghnath Dhimal, PhD; Jan Bauer, Dr.med.; Doreen Montag, DPhill; David A. Groneberg, Prof,Dr,PhD; Ulrich Kuch, Dr; Ruth Müller, Dr
Malaria Journal

Dear Mr Hasyim,

I am pleased to inform you that your manuscript "Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia" (MALJ-D-18-00208R2) has been accepted for publication in Malaria Journal.

Before publication, our production team will check the format of your manuscript to ensure that it conforms to the standards of the journal. They will be in touch shortly to request any necessary changes, or to confirm that none are needed.

Any final comments from our reviewers or editors can be found, below. Please quote your manuscript number, MALJ-D-18-00208R2, when inquiring about this submission.

We look forward to publishing your manuscript and I do hope you will consider Malaria Journal again in the future.

Best wishes,

Marcel Hommel, MD, PhD
Malaria Journal
https://malariajournal.biomedcentral.com/

Comments:

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Proofs for your article in MALARIA JOURNAL (2447) [First Reminder]

9 messages

bmc_corrections@springer.com <bmc_corrections@springer.com> 14 August 2018 at 08:40
To: hamzah.hasyim@stud.uni-frankfurt.de

Dear Author,

The message below was sent to you more than 48 hours ago but we have not yet received your corrections.
Please return your proof as soon as possible so as not to delay the publication of your article.

Yours sincerely,
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PS: This is an auto reminder generated 48 hours after you have received proofs for corrections. Keeping in mind the global time difference, you may receive reminders even after you have sent in your corrections. If you already have sent us the necessary corrections, kindly ignore this email.

DOES LIVESTOCK PROTECT FROM MALARIA OR FACILITATE MALARIA PREVALENCE? A CROSS-SECTIONAL STUDY IN ENDEMIC RURAL AREAS OF INDONESIA
Article DOI: 10.1186/s12936-018-2447-6

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We are pleased to inform you that your paper is nearing publication. Your article proofs are available at:

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Thank you very much.

Sincerely yours,

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Hamzah Hasyim <hamzah.hasyim@gmail.com> 14 August 2018 at 15:17
To: "Dr. Ruth Müller" <Ruth.Mueller@med.uni-frankfurt.de>, "Dr. Ulrich Kuch" <kuch@med.uni-frankfurt.de>

Dear Dr Ruth, and Dr Ulrich.

Kindly see the message below.

For your information, I cannot access the link which given by Springer Corrections Team and revises the script use my smartphone currently.

Would you please giving proof for our article. I would like to thank you very much for your efforts.

Sincerely,

Hamzah

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From: <bmc_corrections@springer.com>
Date: Tue, Aug 14, 2018, 04:41
Subject: Proofs for your article in MALARIA JOURNAL (2447) [First Reminder]
To: <hamzah.hasyim@stud.uni-frankfurt.de>

Dear Author,

The message below was sent to you more than 48 hours ago, but we have not yet received your corrections.
Please return your proof as soon as possible so as not to delay the publication of your article.

Yours sincerely,
Springer Corrections Team

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DOES LIVESTOCK PROTECT FROM MALARIA OR FACILITATE MALARIA PREVALENCE? A CROSS-SECTIONAL STUDY IN ENDEMIC RURAL AREAS OF INDONESIA
Article DOI: 10.1186/s12936-018-2447-6

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Sincerely yours,

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[Quoted text hidden]

Hamzah Hasyim <hamzah.hasyim@gmail.com> 15 August 2018 at 16:11
To: "Dr. Ruth Müller" <Ruth.Mueller@med.uni-frankfurt.de>, "Dr. Ulrich Kuch" <kuch@med.uni-frankfurt.de>

Dear Dr Ruth, and Dr Ulrich.

Kindly see attached both the script accepted, which I have downloaded from our account at malaria journal and the last file edition before taken.

Please see my feedback for proofs of our manuscript. However, I cannot edit the file at the link which given by Springer Correction Team use my smartphone; please advise.

Dear Springer Correction Team.

Thank you for the excellent feedback for improving our paper.

1. This is correct already. The Goethe Uni is the Affiliation no. 1, and Corresponding author
E-mails: hamzah.hasyim@stud.uni-frankfurt.de, hamzah@fkm.unsri.ac.id

2. In the paper accepted version, we use only 43 references. It is meant that reference number from 44 to 49 as quoted in manuscript previously not used anymore.

Participatory community eco-health approaches might be best suited to work with local people and communities to develop a lasting
intervention together, since a vertical policy, might not be successful [41-43].

Note: For your information the ref number 41-49 at manuscript previously proposed by Dr Dooren.

3. Article structure is correct already.

4. Table 2 is fine

5. Thank you for your correction. Yes, you are correct. The reference number 4 as same as with reference number 6, and the reference number 10 as same as with reference number 14. We should delete duplicate of the reference.

Note: Unfortunately, I cannot edit the sequence of references automatically, because I did not bring my laptop that has the "Endnote" application.
Would you please change the sequence number of references manually. Thank you.

6. Author contribution is appropriate already.

7. Additional file in manuscript previously only for describe of table and graph, since we do not use another file like material and method.

8. Additional file is not needed in the current paper anymore, because the file table and graph have included in the main body text.

9. Reference no. 25
Hanandita W, Tampubolon G. Geography and social distribution of malaria in Indonesian Papua: a cross-sectional study. International journal of health geographics. 2016 Dec;15 (1):13.

Line 45. Spatial variation in malaria prevalence has to be taken into account in Indonesia [25].

Please advise. Once again thank you very much for your great support.

Respectfully,

Hamzah Hasyim,
[Quoted text hidden]

2 attachments

MALJ-D-18-00208_R2.pdf
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539K

Dr. Ruth Müller <ruth.mueller@med.uni-frankfurt.de> 15 August 2018 at 21:58
Reply-To: ruth.mueller@med.uni-frankfurt.de
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>, "Dr. Ulrich Kuch" <kuch@med.uni-frankfurt.de>

Dear Hamzah,

I currently make the proof.

Kindly check and confirm the inserted volume number and page range for trhis reference is appropriate.

Hubungan keberadaan ternak dan lokasi pemeliharaan ternak terhadap kasus malaria di Provinsi NTT (analisis lanjut data Riskesdas 2007). Vektora Jurnal Vektor dan Reservoir Penyakit. 2013;5:73–7.

This is the final request. Than I can submit the proof.

Thanks,

Ruth
[Quoted text hidden]

Hamzah Hasyim <hamzah.hasyim@gmail.com> 16 August 2018 at 02:34
To: "Dr. Ruth Müller" <Ruth.Mueller@med.uni-frankfurt.de>
Cc: "Dr. Ulrich Kuch" <kuch@med.uni-frankfurt.de>

Dear Dr Ruth,

Yes, it is correct, based on scholar google.

Hubungan keberadaan ternak dan lokasi pemeliharaan ternak terhadap kasus malaria di Provinsi NTT (analisis lanjut data Riskesdas 2007).
Vektora: Jurnal Vektor dan Reservoir Penyakit. 2013;5:71–4.

I would like thank you very much for taking the time and effort writing the proof.

Yours sincerely,

Hamzah
[Quoted text hidden]
[Quoted text hidden]

Dr. Ruth Müller <ruth.mueller@med.uni-frankfurt.de> 16 August 2018 at 03:43
Reply-To: ruth.mueller@med.uni-frankfurt.de
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>
Cc: "Dr. Ulrich Kuch" <kuch@med.uni-frankfurt.de>

Dear Hamzah,

please find attached the submitted proof.

Best, Ruth

[Quoted text hidden]

e.Proofing.pdf
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Hamzah Hasyim <hamzah.hasyim@gmail.com> 16 August 2018 at 07:06
To: "Dr. Ruth Müller" <Ruth.Mueller@med.uni-frankfurt.de>
Cc: "Dr. Ulrich Kuch" <kuch@med.uni-frankfurt.de>

Dear Dr Ruth,

Thanks a lot!

May I add my feedback that some of the text may don't need appearing in the current manuscript are

For a more detailed description of the scope of research variables, please refer to additional file 1.

for a more
detailed description of statistical procedure please refer to additional file 1).

for more details see additional file 2
Additional files

Additional file 1: Appendix S1. Detailed description of scope of variables and
statistical procedure.

Additional file 2: Appendix S2. Detailed description of descriptive analysis and
bivariate analysis.

Please refers suggestion from Springer Correction Team 7th and 8th isn't it?

However, if we still need additional file 1 and 2, the file should be attached in our manuscript.

In addition,

42. Agyepong IA, Manderson L. Mosquito avoidance and bed net use in the
Greater Accra Region, Ghana. J Biosoc Sci. 1999;31:79–92.
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Please see the current paper and please refers suggestion from Springer Correction Team 2nd, isn't it?

The current manuscript only consist of 41 references. It is meant that reference number from 42 to 47 as quoted in manuscript previously not used anymore.

Yours sincerely,

Hamzah
[Quoted text hidden]

Hamzah Hasyim <hamzah.hasyim@gmail.com> 16 August 2018 at 11:00
To: dwiummahmaharani@gmail.com
Cc: Yunita Dwi Turissiana <yunita.2061979@gmail.com>

Dear Dr Ruth,

Since we changed the reference number 4 as same as with reference number 6, and the reference number 10 as same as with reference number 14.
After the same reference deleted, so, sequence of reference at current paper changed automatically. Isnt it?

Unfortunately, I cannot edit the sequence of references automatically, using the "Endnote" application that have installed at my laptop.

The sequence of reference as follow : at
the previous script, before proof are

.....the economy [1, 2]. ...Plasmodium parasite [3, 4]. .....Plasmodium falciparum [5]. ..... in Asia [6]. .....was 2.85% in 2007 and 6.0% in 2013 [7, 8]. .....Papua, 18.4%) [7].
to humans [9]. .....reduce malaria transmission [9]. .....known as zoopotentiation [10]. .....survival of mosquitoes [9]. ..... insecticide treatment of livestock (ITL) [11]. ..... developing insecticide resistance [12]. ..... a zooprophylactic effect [13]. ..... where livestock was kept [14]. ..... protective effect [15], ... on the animals [11]. ..... spread of malaria [16, 17]. ..... be a risk factor for the spread of malaria [11]. ..... under debate [11]. .....for different zoophilic vectors [11, 14]. ..... species prefer human hosts [18].
.....Anopheles species [19]. ..... in Maluku) [20]. ..... 26.14% of Indonesia's population [7]. ..... The practice of [7], ... 12.5% raise other [7]. ..... The Indonesian regions [7]. ..... Abundant livestock can [21]. ..... While the larvae of some [20], ... other studies have reported [21]. .....The hypothesis of the present [7]. professionals [7]. ....Thus the respondent [7]..... Further, an independent [22]..... univariate and bivariate [23].....Livestock kept in close proximity [24].....Spatial variation in malaria [25].

And so on....

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19. Elyazar IR, Hay SI, Baird JK. Malaria distribution, prevalence, drug resistance and control in Indonesia. Adv Parasitol. 2011;74:41-175.
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36. World Health Organization: Malaria entomology and vector control. Guide for participants. Geneva: WHO; 2013.

In another hand, at the current script, after proof are

the reference number 9 as same as with reference number 13

.....the economy [1, 2]. ...Plasmodium parasite [3, 4]. .....Plasmodium falciparum [5]. ..... in Asia [6 changed to 4]. .....was 2.85% in 2007 and 6.0% in 2013 [7, 8 changed to 6, 7]. .....Papua, 18.4%) [7 changed to 6]. to humans [9 changed to 8]. .....reduce malaria transmission [9 changed to 8]. .....known as zoopotentiation [10 changed to 9]. .....survival of mosquitoes [9 changed to 8]. ..... insecticide treatment of livestock (ITL) [11changed to 10]. ..... developing insecticide resistance [12 changed to 11]. ..... a zooprophylactic effect [13 changed to 12]. ..... where livestock was kept [14 changed to 13]. ..... protective effect [15 changed to 14], ... on the animals [11changed to10]. ..... spread of malaria [16, 17changed to15.16]. ..... be a risk factor for the spread of malaria [11changed to 10]. ..... under debate [11changed to 10].....for different zoophilic vectors [11, 14 changed to 10.13]. .....species prefer human hosts [18 changed to 17].

....Anopheles species [19 changed to 18] ..... in Maluku) [20changed to 19]... 26.14% of Indonesia's population [7 changed to 8]..... The practice of [7 changed to 6], ... 12.5% raise other [7 changed to 6]. ..... The Indonesian regions [7 changed to 6]. ..... Abundant livestock can [21changed to 20]. ..... While the larvae of some [20 changed to 19], ... other studies have reported [21changed to 20]. .....The hypothesis of the present [7 changed to 6]. professionals [7 changed to 6]. ....Thus the respondent [7 changed to 6]..... Further, an independent [22 changed to 21]..... univariate and bivariate [23 changed to 22].....Livestock kept in close proximity [24 change to 23].....Spatial variation in malaria [25 changed to 24].

And so on....

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Dr. Ruth Müller <ruth.mueller@med.uni-frankfurt.de> 16 August 2018 at 14:18
Reply-To: ruth.mueller@med.uni-frankfurt.de
To: Hamzah Hasyim <hamzah.hasyim@gmail.com>
Cc: "Dr. Ulrich Kuch" <kuch@med.uni-frankfurt.de>

Deart Hamzah,

the proof is lready sumitted and no changes can be made.

The appendices are very important, so I included them again (already during review process).

I deleted references 42-47 because they didn´t appear in the text.

All the best,

Ruth
[Quoted text hidden]

Author's Response To Reviewer Comments

Close

Dear editor,

thank you for helping us to further improve our manuscript.

Please find attached our responses to each point the reviewer addressed.

Sincerely,

Hamzah Hasym (on behalf of all authors)

Close

Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia

Hamzah Hasyim[1,2,*,] Meghnath Dhimal[1,3], Jan Bauer[1], Doreen Montag[4], David A. Groneberg[1], Ulrich Kuch[1,#], Ruth Müller[1,#]

[1]Institute for Occupational Medicine, Social Medicine and Environmental Medicine, Faculty of Medicine, Goethe University, Theodor-Stern-Kai 7, Haus 9b, 60590 Frankfurt am Main, Germany

[2]Faculty of Public Health, Sriwijaya University, Indralaya, South Sumatra, Indonesia

[3]Nepal Health Research Council, Ramshah Path, Kathmandu, Nepal

[4] Barts and the London School of Medicine, Centre for Primary Care and Public Health, Queen Mary University of London, London, UK

#These authors act as equivalent co-senior authors.

[*]Corresponding author

E-mails: hamzah.hasyim@stud.uni-frankfurt.de, hamzah@fkm.unsri.ac.id

Tel. +49 (0) 69 6301 6650

Abstract

Background

Since zoophilic vectors have been transmitting malaria, zooprophylaxis has been used to prevent malaria. At the same time zoopotentiation has been present. The existence of livestock has been widely accepted as an important variable for malaria risk prevalence. The concept of effectiveness of zooprophylaxis is still highly debated. This study aims to critically appraise the effects of the presence of livestock on malaria prevalence using a large dataset from Indonesian basic health research.

Methods

This study made use of a large dataset, based on a cross-sectional survey of the Indonesia basic health research in 2007, called Riskesdas which is organised by National Institute of Health Research and Development, Ministry of Health, Indonesia. Here, the subset included 259,885 study participants who reside in the rural area at 176 regencies of 15 provinces with malaria prevalence higher than the national average. The variable "existence of livestock" and other independent demographic, social and behavioural variables were tested as potential determinants for malaria prevalence by multivariate logistic regressions.

Results

Our results [PLEASE NOTE THAT MALARIA JOURNAL DOES NOT USE FIRST PERSON FORMAT; ADJUST ALL SENTENCES ACCORDINGLY] imply that livestock may contribute to malaria risk rather than to act as a prophylactic tool. We note that most participants were able to access health services by travelling for more than 60 minutes with odds ratio (OR) = 1.633, 95% CI : 1.251-2.131, $P < 0.001$, have open condition of sewage canal (OR = 1.250, 95% CI : 1.095-1.427, $P = 0.001$), and raising medium-sized breeding animals at the house (OR = 2.980; 95% CI : 2.348-3.782, $P < 0.001$), then who keep the animals outside at the house (OR = 1.713; 95% CI : 1.515-1.937, $P < 0.001$) were found to be significant predictors of malaria prevalence. In particular, after adjusting for

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~~sex~~gender, age, community health facility, the condition of a sewage canal, use of mosquito nets, and insecticide-treated bed net, the participants who raised medium-size breeding animal inside at home were 2.8 times more likely to have malaria than respondents who were not raising the kind of livestock with adjusted odds ratio (AOR) = 2.809; 95% CI: 2.207-3.575; $P < 0.001$.

Conclusions

Based on our data analysis we recommend that livestock-based interventions should play a significant role in malaria control programmes. Livestock-based interventions should focus on households with a high proportion of medium-sized breeding animals in rural areas. We firmly recommend the implementation of an overall "One Health" strategy to eliminate malaria in Indonesia by 2030.

Keywords Malaria, rural area, livestock, zooprophylaxis, zoopotentation.

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Background

Malaria is a life-threatening disease with widespread and long-term impact on quality of life and the economy [1, 2]. ~~Plasmodium as a one-celled parasite causing malaria through~~Infection is caused by the bite~~s~~ of a female *Anopheles* mosquito, vector ~~that has been infected by~~of the *Plasmodium* parasite [3, 4]. In Indonesia, malaria is mostly caused by *Plasmodium vivax*~~,~~ and *Plasmodium falciparum* ~~is the most common source of human malaria~~ [5]. Malaria threatens almost half of the world's inhabitants, around 2.3 billion people who are living in Asia [6]. ~~Those people who had been diagnosed with malaria by health workers professional in health services and who are mainly at high risk of contracting malaria.~~ Based on the Riskesdas, the national average malaria prevalence in Indonesia was 2.85% in 2007, and in 2013 was 6.0 % [7, 8]. Livestock contributes significantly to the livelihoods of hundreds of millions around the world. Animals can ~~be~~ play a role in diverting mosquitoes from feeding on and transmitting the ~~disease~~ parasite to humans [9]. The percentage of people that keep livestock varies in Indonesia. ~~The proportion of households who raise livestock in urban areas is lower than in rural areas.~~ The areas with a high percentage of families involved in raising livestock in Indonesia showed ~~in parallel~~also the highest prevalence of clinical malaria (East Nusa Tenggara, 12.0%; Papua, 18.4%) [7].

The diversion of disease-carrying insects from humans to animals may reduce transmission of malaria, understood as zooprophylaxis [9]. ~~Zooprophylaxis is believed playing a significant role in the malaria elimination following an increase in livestock keeping.~~ This strategy, which uses ~~of~~ alternative host species to distract malaria vectors away from people, has long been ~~avowed~~ recommended as a potential environmental strategy for the decrement of malaria transmission (reference). Nevertheless, increasing the opportunity of alternative hosts, such as livestock, could alternatively intensify human malaria exposure, as zoopotentiation [10]. ~~The opposite of~~

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~~zooprophylaxis is zoopotentiation.~~ Increased numbers of animals who live close to mosquito breeding sites, improved availability of blood meals may increase mosquito survival and behaviour of mosquito, ~~tends~~ leading to zoopotentiation. In this situation, the zooprophylaxis may be ineffective because the improved availability of blood meals may increase mosquito survival, thereby countering the impact of diverting feeds [9]. However, use of animals as bait to attract mosquitoes to insecticide is predicted to be a promising strategy. Where zoophilic vectors transmit malaria., two types of malaria control approaches using livestock have been suggested; zooprophylaxis and insecticide treatment of livestock (ITL) to prevent malaria infection [11]. Zooprophylaxis indicates control of vector-borne diseases by withdrawing vectors to livestock in which the pathogen cannot substantiate. The combined use of insecticide spray and zooprophylaxis in some situations, be controlled without mosquitoes developing insecticide resistance [12]. Increases in blood feeding in cattle can reduce the likelihood of vector infection, zooprophylactic effect [13]. A prophylactic effect of livestock for malaria risk has also been observed in Papua New Guinea and Sri Lanka [11]. In Kenya and Zambia, malaria prevalence became significantly reduced in areas where livestock was kept [14]. Also donkeys, rabbits and pigs show a significant protective effect [15], possibly because vector breeding sites are nearby to livestock enclosures rather than to houses, and then the mosquitoes might prefer to feed on the animal, and in particular if the behaviour of the *Anopheles* species tends to be endophagic and exophilic [11]. In accordance, the presence of cattle could be used as a barrier to the occurrence of malaria [16, 17]. However, research studies in Pakistan, Philippines and Ethiopia show that the presence of cattle ~~turned out~~can also ~~to~~ be a risk factor for the incidence of malaria [11]. The value of zooprophylaxis and reasons for differing zooprophylactic success remain under debate [11]. Zooprophylaxis takes place in areas where livestock is kept at a spacing from human sleeping quarters at night, and where nets or other protective measures are used. Instead, zoopotentiation occurs where livestock is housed within or nearby human sleeping quarters at night and where mosquito species prefer

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human hosts [18]. The controversy about zooprophylaxis *versus* zoopotentation for malaria prevalence may account for the variety of studied livestock species and animal keeping practices and an associated varying attractiveness for different zoophilic vectors [11, 14].

Indonesia has been chosen as the geographical centre for this research because:

1.) in Indonesia, there is a high vector diversity as indicated by the presence of 20 *Anopheles* species [19]. The most abundant malaria vector throughout Indonesia is *Anopheles vagus* (46% at 349 sites), whereas *Anopheles* ~~*An.*~~ *bancroftii* was the most constrained (1%; 7 locations in Papua, 1 in Maluku) [20].

2.) 26.14% of Indonesia's population lives in malaria epidemic environments. Most of the areas at high risk for malaria are rural and located in Eastern Indonesia [7].

3.) The keeping of livestock is widely distributed in the Indonesian population. At the national level, 39.4% of households raise poultry, 11.6% raise medium livestock to refer to goats, sheep, pigs, 9.0% raise large-sized breeding animals refer to cattle, horses, buffaloes [7], and 12.5% raise other animals such as dogs, cats or rabbits [7].

4.) The Indonesian areas with a high proportion of households involved in raising livestock presented the highest malaria prevalence [7]. Abundant livestock can enhance the survival and abundance of mosquitoes, and in this situation, zooprophylaxis may become ineffective. Similarly, malaria prevalence was higher amongst families that kept cattle than those that did not [21]. *Anopheles*~~*An.*~~ *farauti s.l.* larvae were found in temporary man- and animal-made habitats, such as borrow pits, pig-gardens, and pools along river and stream margins [20]. On the contrary, the formation of a barrier between the anopheline breeding sites and human residential places through an active deployment of pigs and cows has been reported [21]. However, the linking of this zooprophylaxis is controversially discussed, most probably due to complex vector-host

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relationships. Our hypothesis in this study is that there is a relationship between the presence of livestock kept and malaria prevalence in rural endemic areas in Indonesia.

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Methods

This study made use of a large dataset, based on a cross-sectional survey of the Indonesia basic health research in 2007, (Indonesia acronym: Riskesdas), in 2007, which is ~~organised~~ organized by Balitbangkes with a sample framework conducted by the Central Bureau of Statistics (Indonesia acronym: BPS). Riskesdas is a nationwide community-based ~~Health~~ health ~~Research~~ research to district/city level that is held every five to six years that the duration is considered an appropriate interval to assess the development of public health status, risk factors, and the progress of health development efforts.

Study area

The Riskesdas dataset was filtered for participants residing in the rural area in 15 highly malaria-endemic (above the national average) out of 33 Indonesian provinces (~~Figure~~ Fig. 1). The 15 provinces with malaria prevalence above the national average were West Papua, Papua, East Nusa Tenggara, Central Sulawesi, North Maluku, Bengkulu, Bangka Belitung, Maluku, West Nusa Tenggara, Nanggroe Aceh Darussalam, Central Kalimantan, West Kalimantan, Jambi, Gorontalo and North Sumatera. Moreover, the provinces of Maluku, North Maluku, West Papua, Papua, and East Nusa Tenggara were highly endemic areas.

Research variables

The independent variables, such ~~us~~ as characteristics of participants (gender, age, education, ~~and~~ principal occupation), ~~the~~ behaviour of participants (sleep ~~in~~ under a mosquito net, use a net insecticide, ~~and the habit of~~ ~~defecate~~defecating habits), and ~~the~~ accessibility and ~~utilisation~~ utilization of health service (participants were able to access health services by travelling), environmental sanitation (type of container/media, ~~the~~ sewage canal, ~~and the~~ condition of a sewage canal), and ~~the~~ location of cages (medium breeding animals and large breeding animals) were tested for a potential relationship with the response variable malaria using the binary category "yes" and "no". In this study, malaria status are those having the disease.

The respondent reported having been diagnosed as malaria-positive by a health professional with malaria during the past month. The variable was defined as participants who have ever been diagnosed with malaria by health workers. In the questionnaire (code B07)~~,~~ : ~~I~~in the last one month, has [name] ever been diagnosed to suffer from malaria, which was confirmed by blood ~~checking~~ test taken by health professionals. Generally, the diagnosis was confirmed ~~can be~~ by ~~testing~~ use of rapid diagnostic tests (RDTs) and microscopy in health services. ~~However, m~~Malaria infection was not ~~tested anymore~~checked by interviewer [7]. The outcome variable, malaria status, is coded as a binary variable whose value equals to one if participant within the past month has ever been diagnosed as malaria-positive by health professionals [7]. Further, an independent data collection was taken from an individual and household questionnaire. All the measurements on each person are made at one point in time [22].

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Study population

Participants of all ages representative for the entire Republic of Indonesia were interviewed with questions related to malaria. Household samples and household members in Riskesdas 2007 are

designed to be identical to households and households member list in the National Socioeconomic Survey (Indonesia acronym: Susenas) 2007 [7]. Regions designated as rural were used as survey subsample by the location data retrieval used in the Riskesdas survey 2007 [7]. The analyses in the present research are based on a massive dataset with 259,885 out of 973,657 Riskesdas participants who represent a total population size of 30,152,651 Indonesians.

Questionnaires

A set of questionnaires was used as an instrument for data collection. The data collection for Riskesdas was done in two stages, the first stage was begun in August 2007 and continued until January 2008 in 28 provinces, the second stage was in August - September 2008 in 5 provinces (NTT, Maluku, North Maluku, Papua and West Papua). Riskesdas had ~~mobilised~~ mobilized 5,619 enumerators, all (502) researchers from National Institute of Health Research, and 86 lectures from health technical schools, Local Governments in Province Regions and district/city, Provincials' labs, Hospitals, and Universities were also involved. The process of editing, entry, and data cleaning of Riskesdas data was started in early January 2008, while there was a process of discussing work plans and strategy of analysis. Various questions related to Indonesian health policy were operated to be research questions and finally developed to be variables collected by using several approaches. In Riskesdas 2007, there are around 900 variables spread out in 6 (six) kinds of questionnaires. The questionnaire covered malaria and included 20 explanatory variables. Regarding raising livestock, data were collected by asking all heads of households whether they were keeping poultry, medium-sized livestock (goats, sheep, and pigs), large sized livestock (cows, buffaloes, and horses) or pets such as dogs, cats, and rabbits. If livestock was kept, then it was noticed whether the livestock was kept inside the house or outdoors [7].

Statistical analyses

Data were analysed using statistical data processing applications by Stata, taking into account the complex sampling design. Sampling design in Susenas 2007 was (using two-stage sampling). By using Stata complex sample in processing and analysing Riskesdas data, in complex samples, the validity of analysis result can be optimisedoptimized. This application makes it possible to utilise use a two-stage sampling design as implemented in Susenas 2007. Both univariate and bivariate analysis was carried out using chi-square tests. In the next stage of multivariable analysis, a series of binary logistic regressions were run. Explanatory variables that may have predictive value for the response variable were selected for the multiple regression models (Wald test, $P < 0.25$) [23].

analysis Analysis of multivariable logistic regression was carried out to specify the relationship amongst multiple independent variables with the dependent variable malaria prevalence. The final model includes seven explanatory variables as follows: characteristics of participants (sexgender, age, education, and job), the behaviour of participants (using insecticide-treated mosquito nets), and the existence of livestock (keeping of medium-sized breeding animals). In table Table 2, the adjusted odds ratio (AOR), as a result of parsimonious logistic models, is shown for independent variables affecting the prevalence of malaria in rural endemic areas of 15 high malaria-endemic provinces of Indonesia.

Results

Malaria prevalence

Prevalence of malaria in Indonesia in 2007, shown in figure Fig. 1, revealed that malaria prevalence was 3.5% (95% CI: 0.033 - 0.037) in 15 provinces with malaria prevalence higher than

the national average (2.85% in 2007) [7]. The study area map uses the World Geodetic System (WGS84) as its reference coordinate system. The mapping of malaria prevalence based on Riskesdas data was performed using the software Aeronautical Reconnaissance Coverage Geographic Information System (ArcGIS 10). The highest malaria prevalence found was 41.0% at South Sorong (marked as a black area in Fig~~.ure~~ 1), a regency located in West Papua province of Indonesia with an area of 3,946.94 km^2 and a population of 37,900 (2010 census).

The existence of livestock

Based on the Riskesdas questionnaire, the animal domestic ~~categorised~~ categorized are livestock, pets and poultry. The term livestock includes ~~here~~ large-sized breeding animals (cattle, horses, buffaloes), and medium-sized breeding animals (goats, sheep, pigs). Additionally, poultry, such as chicken and ducks, and pets, such as dogs, cats and rabbits, are included in the term ~~of~~ *pets*. A majority of participants raises chicken, ducks, and birds was 53.7%, followed by pets (dogs, cats, and rabbits; 25.2%), medium-sized breeding animals (goats, sheep, and pigs; 22.2%), and large-sized breeding animals (cows, buffaloes, and horses; 10.2%) (Fig. 2). ~~Particular for this study,~~ ~~w~~We further analysed the raising of livestock both large-sized breeding animals (cattle, horses, buffaloes), and medium-sized breeding animals (goats, sheep, pigs) connected with malaria prevalence. We note 0.52% (95% CI: 0.004-0.007) participants keep large-sized breeding animals, and 1.63% (95% CI: 0.014-0.019), participants keep medium-sized breeding animals inside at the house besides. We found 9.64% (95% CI: 0.091-0.102) participants keep large-sized breeding animals, and 20.59% (95% CI: 0.197-0.215) participants keep medium-sized breeding animals outside at the house. Livestock kept in nearby proximity to humans can support the higher transmission by attracting mosquitoes into areas where they will encounter and feed on human hosts opportunistically (zoopotentiation) [24].

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Univariate and bivariate analysis

Table 1 ~~summarises~~ summarizes the percentage of participants having or not having diagnosed positive for malaria for each of the explanatory variables and bivariate analysis. In brief, we observe the participants who keep large-sized breeding animals inside the house (0.52%, 95% CI: 0.004-0.007), and the participants who keep the animals outside the house (9.64%, 95% CI: 0.091-0.102). Besides, participants who keep medium-sized breeding animals inside the house (1.63%, 95% CI: 0.014-0.019), and the participants who keep the animals outside the house (20.59%, 95% CI: 0.197-0.215). Further, in ~~table~~ Table 2 connected with malaria prevalence, we note the participants who keep medium-sized breeding animals inside at the house (OR = 2.980; 95% CI: 2.348-3.782, $P < 0.001$), and the participants who keep the animals outside the house (OR = 1.713; 95% CI: 1.515-1.937, $P < 0.001$) more contracting malaria than those who have not such animals. On the contrary, the keeping of large-sized breeding animals does not considerably increase malaria prevalence. Besides, we note that males are more likely to have malaria than females (OR = 0.849, 95% CI: 0.811-0.888, $P < 0.001$). The participant who has productive age in 15-64 years (OR = 0.861, 95% CI: 0.812-0.912, $P < 0.001$) more contracting malaria than who have not in productive age. In addition, we observed most participants were able to access health services by travelling for more than 60 minutes (OR = 1.633, 95% CI: 1.251-2.131, $P < 0.001$) more having malaria than another.(what does this mean ?) The majority of participants who have others or open condition of sewage canal are at higher odds of contracting the disease (OR = 1.250, 95% CI: 1.095-1.427, $P = 0.001$). Additionally, we found both participants who were using mosquito nets ~~(nets)~~ and insecticide-treated bed net (ITNs), as a protection factor for malaria prevalence than who not use such the protection with OR < 1. (this sentence is un-clear, please rewrite)Besides, there was a negative correlation between the use of ITNs with the prevalence of malaria (r = -0.023, $P < 0.001$). This statistic implies for participants who increasingly used ITNs, the prevalence of malaria decreased.

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Multivariable regression logistic

The estimated AOR of malaria for participants who kept medium-sized breeding animals (goats, sheep, pigs) inside at home signifies a 2.81 times higher risk to contract malaria adjusted other variables (AOR = 2.809; 95% CI: 2.207-3.575; $P < 0.001$) in rural endemic areas of 15 highly malaria-endemic provinces of Indonesia. Other six controlling factors for malaria prevalence relate to sociodemographic, socioeconomics and behaviour.

Discussion

In the present study, the presence of medium-sized livestock increased the likelihood to contract malaria by 2.81. Our results imply that this certain livestock may potentiate malaria. Other principal factors affecting the prevalence of malaria are the demographic factors, ~~sex~~gender, age, health facility, environmental health, and the behaviour of participants for protection malaria to use mosquito nets and ITNs.

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Spatial heterogeneity of malaria prevalence.

Spatial variation in malaria prevalence has to be taken into account in Indonesia [25]. The highest malaria prevalence found at South Sorong a regency located in West Papua province of Indonesia. Likewise, reporting of Riskesdas that the area is malaria endemic province. Similarly, a gradient of malaria prevalence from rural (58.9%) to urban areas (33.9%) is likewise known from Bata district in Equatorial Guinea (EG) [26]. The situation is consistent with the identified high-risk in the rural context that found in West Papua, Papua [25] and East Nusa Tenggara [7, 27]. A similar variation of spatial malaria distribution was observed in a cross-sectional study in rural areas in Haiti (4 to 41%) and demographic data indicated some focal disease transmission [28].

Keeping medium-sized breeding animals as a significant determinant for malaria prevalence

Our data provide evidence for a positive relationship between kept medium-sized breeding animals inside at home (AOR = 2.809; 95% CI: 2.207-3.575; $P < 0.001$) and the malaria prevalence in the human population living in rural, highly endemic areas of Indonesia. An explanation for the fact that livestock facilitates malaria in our study could be the increased abundance of vectors for *Plasmodium* species in the presence of livestock. Increasing the availability of selection hosts, such as livestock, could otherwise gain human malaria exposure bring cause zoopotentiation, which happens if the heat and odour cues emitted by animals attract a higher number of vectors to households in or near where they are kept (please rewrite, unclear). Also, zoopotentiation could occur if the physical disturbances created by animals (e.g., puddles, hoof prints, watering sites) increase~~s~~ larval habitat and thus adult vector density near households. Similarly, in this study, the participants who have an open sewage canal are at higher odds of contracting malaria than others. The splitting of people and livestock dwellings on this scale shows to be sufficiently large to dodge a zoopotentiation effect [10]. An increasing abundance of goats or sheep has been demonstrated to increase the abundance of *Anopheles* mosquitoes within a radius of 20 m around the household in Kenya [13]. By our evidence for zoopotentation, there are positive correlations between donkeys, pigs, and also humans, and the abundance of malaria-transmitting mosquitoes [13, 29]. For example, the probability that humans are bitten by the zoophilic *Anopheles~~An.~~ stephensi* may increase if sleeping close to a cow or a goat in the evenings. In contrast, the ~~anthropophilic~~ anthropophily of *Anopheles cuficifacies* is only slightly influenced by the presence of livestock.

In Kenya, each additional goat or sheep increased the abundance of the local malaria vector [13], and one may assume there a higher human-biting rate as well. At least, participants who kept pigs and sheep in Mozambique have significantly increased odds of malaria infection, although to a lesser extent in case of sheep [29]. For the zoophilic *An. stephensi* the nightly man-biting has been

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shown to increase by 38% in the existence of a cow and by 50% in the availability of two goats [21]. An integrative vector control strategy including ITNs and indoor residual spraying reduction (IRS) combined with ITL may improve the zooprophylactic effectiveness [30].

Keep livestock at a distance

In particular, participants who were raising medium-sized breeding animals inside their home were more likely to have malaria (OR = 2.980; 95% CI: 2.348-3.782; $P < 0.001$), and participants who were raising medium-sized breeding animals outside their home were more ~~probable~~ likely to have malaria (OR = 1.713; 95% CI: 1.515-1.937; $P < 0.001$) than those who did not raise the livestock. In contrast to our outcome, livestock may indeed have a prophylactic effect in the case that only zoophilic vectors are present and livestock is placed in a way to act as a protective barrier for anopheline mosquitoes [11]. Otherwise, zoopotentation takes often place when livestock is kept indoors or near the household and if mosquito vectors are mainly anthropophilic [18]. A parallel approach of insecticide-treated livestock (ITL) and arranging the livestock located as far from man as possible is sufficient to reduce malaria [11, 21]. Likewise, in the Macha area in the Southern Province of Zambia, farm animals revealed a dramatically declining risk of *P. falciparum* infection at the house level with increasing distance between livestock (cattle, goats, dogs, cats) and dwelling structures.

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Demographic and social determinants for malaria status

Participants in the age range 15-64 years and especially male participants contracted malaria significantly more than others. Malaria prevalence also differs by gender, with men ~~are~~ more likely to be parasitaemic than older women in the Democratic Republic of Congo [31]. Similarly, in a larger scaled survey of households in Ethiopia, the frequency of suspected malaria in men was significantly higher than in women; however, the prevalence of malaria was not significant

between gender [32]. In contrast, women in the adult population of an endemic area in Kenya are by 50% more likely to become infected with malaria parasites than ~~males~~ men [33].

Behavioural determinants for malaria status

Protective behaviour (mosquito nets and ITNs) can reduce malaria risk. In rural highly malaria endemic areas of Indonesia, the risk of contracting malaria significantly decreased if ITNs were used. Similarly, ITNs are the most protruding prevention of malaria in highly endemic areas in Malaysia [34], and other community-based preventive measures, such as bed nets benefit [35]. Furthermore, ITNs and long-lasting insecticidal nets (LLINs) were combined with indoor residual spraying to accelerate success in malaria control in tropical Africa [36]. Seemingly using of ITNs in 2007 is not more effective for as protection for malaria with ($r = -0.023$, $P < 0.001$), due to the number of ITNs distributed at the time, the number of people protected is low, and lack behaviour of the community use of ITNs in the research area [19, 37]. Furthermore, the malaria program has been used ~~long~~ long-lasting insecticidal net (LLIN), which are more effective than ITNs. LLINs have significantly been used as an effective alternative to ITNs for over a decade [38].

Limitations of research

A weakness of the cross-sectional design is that it cannot decide how the chances of getting malaria for participants who were before and after exposure to covariate variables. However, the benefits of a large-scale cross-sectional design are the gain of information about preliminary phenomena which allows subsequently to design studies with particular foci [39]. There are other factors also proven to determine malaria prevalence, such as bionomics of different *Anopheles* species [40]. Understanding the kind of *Anopheles* species, and behaviour of *Anopheles* mosquitoes can help conceive how malaria is transmitted and ~~it~~ can assist in designing appropriate control strategies. Unfortunately, in the Riskesdas 2007, these factors were not monitored.

Recommendations

Participants who are raising medium-sized breeding animals inside their home have higher malaria prevalence in 15 provinces throughout the rural endemic area, so we recommend placing livestock outside the house. However, an anthropological study needs to be undertaken to understand why people are holding livestock the way they do in the first place. Secondly, a participatory community eco-health approach might be best suited to work with local people and communities to develop lasting intervention together, as a horizontal policy might not be successful [41-43]. Besides, participants in a productive age in 15-64 years should be provided with ~~tools~~ the means for protection from *Anopheles* biting during their working in the rural endemic area, ~~. Such actions~~ includ~~e~~ing personal protection, behaviour modification and environmental modification. Personal protection using insecticides and repellent, use of long-sleeved clothing and trousers. Environmental modification is aimed at reducing mosquito habitat, remove the shrubs around, cover a leaky roof, and others. Also, there is a need for improving sanitation by enclosing the sewage canal to reduce the breeding places of *Anopheles* mosquitoes. Seemingly using of ITNs in 2007 is not more effective for as protection for malaria with ($r = -0.023$, $P < 0.001$). So we, recommend the distribution of ~~Long Lasting Insecticidal Net (~~LLINs~~)~~ distributed to and used by all people in rural endemic areas followed by community-based interventions with the improvement of knowledge, attitude and practice use and maintenance LLINs of the indigenous community for malaria prevention. (please rewrite, unclear) Again, later point needs to be best accompanied through anthropological and community-based work to understand the current situation of no use-or limited use. Any potential intervention could make use of existing anthropological literature from different areas across the world [44-49]. Based on our extensive data analysis, we recommend that livestock-based interventions should focus on rural endemic areas and households with a high proportion of medium-sized breeding animals.

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Conclusion

The presence of only certain ownership livestock is the major (meaning ?)risk factor for contracting malaria in rural endemic Indonesia. Other factors such as sociodemography and behaviour are also important for having a high risk of malaria infection. Livestock-based interventions should focus on endemic rural areas on households with a high proportion of medium-sized breeding animals. Further, we recommend eco-health community approach research that encompasses understanding local perceptions of malaria, malaria transmission and livestock and bed nets and ~~than~~ an adequate development of an integrative prevention strategy to protect from *Anopheles* biting.

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List of abbreviations

AOR	:	Adjusted odds ratio
API	:	Annual parasite incidence
ArcGIS	:	Aeronautical Reconnaissance Coverage Geographic Information System
IDHS	:	the Indonesian Demographic and Health Survey
IRS	:	Indoor residual spraying reduction
ITL	:	Insecticide-treated livestock
ITNs	:	Insecticide-treated mosquito nets
IVM	:	Integrated vector management
LLINs	:	Long Lasting Insecticidal Net
MHD	:	Man-hour density
MOH	:	Ministry of Health
NIHRD	:	National Institute of Health Research and Development
NTT	:	East Nusa Tenggara (Indonesia acronym: NTT)
OR	:	Odds ratio
PHCs	:	Primary health centres
RDTs	:	Rapid diagnostic tests
Riskesdas	:	Indonesia basic health research (Indonesia: Riset kesehatan Dasar)
Ristekdikti	:	Ministry of Research, Technology and Higher Education (Indonesia acronym: Ristekdikti)
Susenas	:	the National Socioeconomic Survey (Indonesia acronym: Susenas)
USAID	:	the US Agency for International Development
VBDs	:	Vector-borne diseases
WGS84	:	the World Geodetic System 1984

Declarations

Ethics approval and consent to participate

The ethical clearance for primary data has been obtained from the National Institute for Health Research and Development, Ministry of Health, Republic of Indonesia. The ethical clearance for secondary data used in our paper is not required to be obtained. Since the paper uses secondary data, also the consent to participate is not applicable to the present study.

Consent for publication

Not applicable.

Availability of data and materials

The raw dataset of Indonesia Basic Health Research 2007 has been generated at the National Institute of Health Research and Development (NIHRD), Ministry of Health (Indonesia). Derived secondary data and analysis/findings of this study are available from the corresponding author (HH) on request.

Competing interests

The authors declare that they have no competing interests. RM is currently active as a consultant for the non-profit company PoloGGB, Italy, which aims to develop and assess new genetic vector control tools for malaria vectors in Africa. The present study is however not related to PoloGGB activities.

Funding

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Authors' contributions

HH obtained the Riskesdas sub-dataset. The study was conceived and designed by HH, DAG, UK and RM. The data was analysed by HH, MD, JB, UK, DM and RM.

RM, DAG, MD, DM and UK drafted the manuscript with subsequent contributions and revisions. All authors read and confessional the final manuscript.

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Table legends

Table 1: Description of variables research [%] within the categorical variable: malaria prevalence, characteristics of participants, the accessibility and utilisation of health service, environmental sanitation, the behaviour of participants, and the location of cages of livestock.

Table 2: The logistic regression analysis associated with the prevalence of malaria in rural highly malaria-endemic endemic areas in 15 provinces of Indonesia, with n = 259.885

Figure legends

Fig. 1: The proportion of malaria in regencies and cities within rural areas of Indonesian provinces with malaria prevalence above the national average.

Fig. 2. The proportion of rural population (n = 259,885 household members) raising livestock [%] and the location of cages [%] in highly malaria-endemic endemic areas in 15 provinces of Indonesia. The category of poultry includes chicken, ducks and birds. The category of pets includes dogs, cats and rabbits. The category of medium-sized breeding animals includes goats, sheep and pigs. The category of large-sized breeding animals includes cows, buffaloes and horses.

Review of “Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia”

This is an analysis of a massive dataset. I think the analysis is worth publishing, but two serious weaknesses should be acknowledged and addressed.

First, on page 3, the definition of ‘malaria’ in Riskesdas 2007 is inaccurately described. Not only was malaria not diagnosed during the the riskesdas, but the question as to whether a health worker had diagnosed malaria, or whether the respondent had malaria symptoms, was addressed to the respondent. Neither health records nor health workers were consulted; the classification of ‘malaria’ or ‘not malaria’ was based upon the interview only. The phrase “has ever been diagnosed as malaria-positive by health professionals” is misleading in this regard. A more accurate sentence would be “the respondent reported having been diagnosed as malaria-positive by health professional, or reported having symptoms consistent with malaria during the past month”. The English in the paper should accurately reflect the Indonesian description of the method of diagnosing malaria in the original survey report.

The language from Riskesdas 2007 is as follows:

Kepada responden yang menyatakan “tidak pernah didiagnosis malaria oleh tenaga kesehatan” dalam satu bulan terakhir ditanyakan apakah pernah menderita panas tinggi disertai menggigil (perasaan dingin), panas naik turun secara berkala, berkeringat, sakit kepala atau tanpa gejala malaria tetapi sudah minum obat antimalaria. Untuk responden yang menyatakan “pernah didiagnosis malaria oleh tenaga kesehatan” ditanyakan apakah mendapat pengobatan dengan obat program dalam 24 jam pertama menderita panas.

In 2007, especially in eastern Indonesia, clinical diagnosis was the norm in most districts. The methodology described – clinical diagnosis by retrospective interview -- is likely is associated with an overdiagnosis of malaria, which may bias the results of this analysis. This should be discussed.

Second, as the authors note but do not adequately address, this massive analysis utterly fails to capture important small scale ecological interactions among humans, their livestock, and mosquito fauna across this most diverse of archipelagos. These smaller scale interactions are, in my mind, likely more relevant than a large scale and hard to understand broad correlation with medium (why medium?) sized animals. The mosquito fauna and cultural norms of Papua are radically different from those in Bengkulu. Why should the same general pattern occur in both areas? Indeed, was any effort made to stratify the analysis by different areas with different mosquito fauna (Asian vs. Australian/Papuan, for instance), or by major island (Java, Sumatra and Kalimantan might group nicely; Wallacea (Sulawesi and the Malukus could form another group); Papua and West Papua, a third island group. I would suggest that some analytical effort be made to address this crucial issue, rather and merely extracting data from rural, higher prevalence areas.

Malaria Journal

Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia

--Manuscript Draft--

Manuscript Number:	MALJ-D-18-00208R2
Full Title:	Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia
Article Type:	Research
Funding Information:	
Abstract:	Background Ever since it was discovered that zoophilic vectors can transmit malaria, zooprophylaxis has been used to prevent the disease. However, zoopotentiation has also been observed. Thus, the presence of livestock has been widely accepted as an important variable for the prevalence and risk of malaria, but the effectiveness of zooprophylaxis remained subject to debate. This study aims to critically analyse the effects of the presence of livestock on malaria prevalence using a large dataset from Indonesia. Methods This study is based on data from the Indonesia Basic Health Research ("Riskesdas") cross-sectional survey of 2007 organized by the National Institute of Health Research and Development of Indonesia's Ministry of Health. The subset of data used in the present study included 259,885 research participants who reside in the rural areas of 176 regencies throughout the 15 provinces of Indonesia where the prevalence of malaria is higher than the national average. The variable "existence of livestock" and other independent demographic, social and behavioural variables were tested as potential determinants for malaria prevalence by multivariate logistic regressions. Results Most participants were able to access health services by travelling for more than 60 minutes, with an odds ratio (OR) = 1.633, 95% CI : 1.251-2.131, P < 0.001 for those who are openly exposed to sewage canals (OR = 1.250, 95% CI : 1.095-1.427, P = 0.001), Raising medium-sized animals in the house was a significant predictor of malaria prevalence (OR = 2.980; 95% CI : 2.348-3.782, P < 0.001) when compared to keeping such animals outside of the house (OR = 1.713; 95% CI : 1.515-1.937, P < 0.001). After adjusting for gender, age, access to community health facility, sewage canal condition, use of mosquito nets and insecticide-treated bed nets, the participants who raised medium-sized animals inside their homes were 2.8 times more likely to contract malaria than respondents who did not (adjusted odds ratio = 2.809; 95% CI: 2.207-3.575; P < 0.001). Conclusions The results of this study highlight the importance of livestock for malaria transmission, suggesting that keeping livestock in the house contributes to malaria risk rather than prophylaxis in Indonesia. Livestock-based interventions should therefore play a significant role in the implementation of malaria control programmes, and focus on households with a high proportion of medium-sized animals in rural areas. The implementation of a "One Health" strategy to eliminate malaria in Indonesia by 2030 is strongly recommended.
Corresponding Author:	Hamzah Hasyim, PhD candidate Goethe-Universitat Frankfurt am Main Fachbereich 16 Medizin Frankfurt am Main, Hessen GERMANY
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	Goethe-Universitat Frankfurt am Main Fachbereich 16 Medizin
Corresponding Author's Secondary Institution:	
First Author:	Hamzah Hasyim, PhD candidate

First Author Secondary Information:	
Order of Authors:	Hamzah Hasyim, PhD candidate
	Meghnath Dhimal, PhD
	Jan Bauer, Dr.med.
	Doreen Montag, DPhill
	David A. Groneberg, Prof,Dr,PhD
	Ulrich Kuch, Dr
	Ruth Müller, Dr
Order of Authors Secondary Information:	
Response to Reviewers:	Dear editor, thank you for helping us to further improve our manuscript. Please find attached our responses to each point the reviewer addressed. Sincerely, Hamzah Hasym (on behalf of all authors)
Additional Information:	
Question	**Response**
Is this study a clinical trial?<hr>A clinical trial is defined by the Word Health Organisation as 'any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes'.	No

Does livestock protect from malaria or facilitate malaria prevalence? A cross-sectional study in endemic rural areas of Indonesia

Hamzah Hasyim[1,2,*], Meghnath Dhimal[1,3], Jan Bauer[1], Doreen Montag[4], David A. Groneberg[1], Ulrich Kuch[1,#], Ruth Müller[1,#]

[1]Institute of Occupational Medicine, Social Medicine and Environmental Medicine, Faculty of Medicine, Goethe University, Theodor-Stern-Kai 7 60590 Frankfurt am Main, Germany

[2]Faculty of Public Health, Sriwijaya University, Indralaya, South Sumatra, Indonesia

[3]Nepal Health Research Council, Ramshah Path, Kathmandu, Nepal

[4]Barts and the London School of Medicine, Centre for Primary Care and Public Health, Queen Mary University of London, London, UK

#These authors act as equivalent co-senior authors.

[*]Corresponding author

E-mails: hamzah.hasyim@stud.uni-frankfurt.de, hamzah@fkm.unsri.ac.id

Tel. +49 (0) 69 6301 6650

Fax +49 (0) 69 6301 7053

Abstract

Background

Ever since it was discovered that zoophilic vectors can transmit malaria, zooprophylaxis has been used to prevent the disease. However, zoopotentiation has also been observed. Thus, the presence of livestock has been widely accepted as an important variable for the prevalence and risk of malaria, but the effectiveness of zooprophylaxis remained subject to debate. This study aims to critically analyse the effects of the presence of livestock on malaria prevalence using a large dataset from Indonesia.

Methods

This study is based on data from the Indonesia Basic Health Research ("Riskesdas") cross-sectional survey of 2007 organized by the National Institute of Health Research and Development of Indonesia's Ministry of Health. The subset of data used in the present study included 259,885 research participants who reside in the rural areas of 176 regencies throughout the 15 provinces of Indonesia where the prevalence of malaria is higher than the national average. The variable "existence of livestock" and other independent demographic, social and behavioural variables were tested as potential determinants for malaria prevalence by multivariate logistic regressions.

Results

Most participants were able to access health services by travelling for more than 60 minutes, with an odds ratio (OR) = 1.633, 95% CI : 1.251-2.131, $P < 0.001$ for those who are openly exposed to sewage canals (OR = 1.250, 95% CI : 1.095-1.427, $P = 0.001$), Raising medium-sized animals in the house was a significant predictor of malaria prevalence (OR = 2.980; 95% CI : 2.348-3.782, $P < 0.001$) when compared to keeping such animals outside of the house (OR = 1.713; 95% CI : 1.515-1.937, $P < 0.001$). After adjusting for gender, age, access to community health facility, sewage canal condition, use of mosquito nets and insecticide-treated bed nets, the

participants who raised medium-sized animals inside their homes were 2.8 times more likely to contract malaria than respondents who did not (adjusted odds ratio = 2.809; 95% CI: 2.207-3.575; $P < 0.001$).

Conclusions

The results of this study highlight the importance of livestock for malaria transmission, suggesting that keeping livestock in the house contributes to malaria risk rather than prophylaxis in Indonesia. Livestock-based interventions should therefore play a significant role in the implementation of malaria control programmes, and focus on households with a high proportion of medium-sized animals in rural areas. The implementation of a "One Health" strategy to eliminate malaria in Indonesia by 2030 is strongly recommended.

Keywords Malaria, rural area, livestock, zooprophylaxis, zoopotentation.

Background

Malaria is a life-threatening disease with a widespread and long-term impact on the quality of life and the economy [1, 2]. Infection is caused by the bite of a female *Anopheles* mosquito which is a vector for the *Plasmodium* parasite [3, 4]. In Indonesia, malaria is mostly caused by *Plasmodium vivax* and *Plasmodium falciparum* [5]. Malaria threatens almost half of the world's inhabitants, around 2.3 billion of which live in Asia [6]. In Indonesia, the national average of malaria prevalence was 2.85% in 2007 and 6.0% in 2013 [7, 8]. Livestock contributes significantly to the livelihoods of hundreds of millions around the world. In Indonesia the percentage of people who keep livestock varies geographically and culturally. Regions of Indonesia where a high percentage of families is involved in raising livestock also had the highest prevalences of clinical malaria in the country (East Nusa Tenggara, 12.0%; Papua, 18.4%) [7].

In the context of malaria, animals can play a role in diverting mosquitoes from feeding on humans, thereby preventing transmission of the parasite to humans [9]. Using alternative host species to distract malaria vectors away from people, a concept known as zooprophylaxis, has long been recommended as a potential environmental strategy to reduce malaria transmission [9]. However, increasing opportunities to feed on alternative hosts such as livestock could also increase human exposure to malaria: An increase in the number of animals living close to mosquito breeding sites, resulting in improved availability of blood meals, could alternatively attract more mosquitoes, increase their survival and the risk of disease transmission to humans, a phenomenon known as zoopotentiation [10]. In such a situation, zooprophylaxis may be ineffective because the effect of diverting blood meal seeking mosquitoes to non-human prey may be countered by higher numbers and longer survival of mosquitoes [9]. Nevertheless, the

use of animals as bait to attract mosquitoes has been propagated as a promising alternative to insecticide use. For areas where zoophilic vectors transmit malaria, two types of malaria control approaches using livestock have been suggested; zooprophylaxis and insecticide treatment of livestock (ITL) [11]. As understood in this context, zooprophylaxis is supposed to control vector-borne diseases by withdrawing vectors to livestock species within which the pathogen in question cannot spread. By combining the use of insecticide spray with zooprophylaxis, vector populations in some situations may be controlled without mosquitoes developing insecticide resistance [12]. Increased blood feeding on cattle can reduce the likelihood of human infections in the sense of a zooprophylactic effect [13]. A prophylactic effect of livestock on malaria risk has also been observed in Papua New Guinea and Sri Lanka [11]. In Kenya and Zambia, malaria prevalence became significantly reduced in areas where livestock was kept [14]. Donkeys, rabbits and pigs also showed a significant protective effect [15], possibly because vector breeding sites were closer to livestock enclosures than to houses, and especially endophagic and exophilic *Anopheles* species might prefer to feed on the animals [11]. Accordingly, the presence of cattle could be used as a barrier to the spread of malaria [16, 17]. However, research conducted in Pakistan, the Philippines and Ethiopia showed that the presence of cattle can also be a risk factor for the spread of malaria [11]. The practical value of zooprophylaxis and the reasons for observed zooprophylactic success have therefore remained under debate [11]. Part of the controversy about zooprophylaxis *versus* zoopotentation for malaria prevalence may be accounted for by the variety of analysed livestock species and animal keeping practices, and the associated variable attractiveness for different zoophilic vectors [11, 14]. For example, zooprophylaxis may more likely take place in areas where livestock is kept at a distance from human sleeping quarters at night, and where nets or other protective measures are used, whereas zoopotentiation may be more likely in places where livestock is housed within or near human sleeping quarters at night and where mosquito species prefer human hosts [18].

The present study addresses the relationship between livestock keeping and malaria prevalence in rural endemic areas of Indonesia. The country has been chosen as the geographical centre for this research because:

1) there is high vector diversity as indicated by the presence of 20 *Anopheles* species [19]. The most abundant malaria vector throughout Indonesia is *Anopheles vagus* (46% at 349 sites), whereas *Anopheles bancroftii* was the geographically most constrained one (1%; 7 locations in Papua, 1 in Maluku) [20].

2) 26.14% of Indonesia's population live in malaria epidemic environments. Most of the areas at high risk for malaria are rural and located in eastern Indonesia [7].

3) The practice of keeping livestock is widely distributed throughout the Indonesian population. At the national level, 39.4% of households raise poultry, 11.6% raise medium-sized livestock, i.e., goats, sheep, and pigs, 9.0% raise large-sized animals, i.e., cattle, horses, or buffaloes [7], and 12.5% raise other animals such as dogs, cats or rabbits [7].

4) The Indonesian regions where a high proportion of households is involved in raising livestock also presented the highest prevalence of malaria [7]. Abundant livestock can enhance the survival and abundance of mosquitoes, and in this situation zooprophylaxis may become ineffective. Similarly, malaria prevalence was higher among families who kept cattle compared to those who did not [21]. While the larvae of some malaria vectors in Indonesia, such as *Anopheles farauti sensu lato*, were found in a wide variety of temporary man-made and animal-made habitats, such as borrow pits, pig-gardens, and pools along rivers and streams [20], other studies have reported the formation of a barrier between anopheline breeding sites and human residential areas through an active deployment of pigs and cows [21]. However, this example of zooprophylaxis has been discussed in a controversial manner. The hypothesis of the present

study is that there is indeed a relationship between the presence of livestock and malaria prevalence in rural endemic areas in Indonesia.

Methods

This study made use of a large dataset based on a cross-sectional survey of the Indonesia Basic Health Research (Indonesia acronym: Riskesdas), in 2007, which is organized by Balitbangkes with a sample framework conducted by the Central Bureau of Statistics (Indonesia acronym: BPS). Riskesdas is a nationwide community-based health research project at the district/city level that is conducted every five to six years - a duration that is considered an appropriate interval to assess the development of public health status, risk factors, and the progress of health development efforts.

Study area

The Riskesdas dataset was filtered for participants residing in the rural areas of 15 highly malaria-endemic (above the national average) provinces (Fig. 1). These 15 provinces include West Papua, Papua, East Nusa Tenggara, Central Sulawesi, North Maluku, Bengkulu, Bangka Belitung, Maluku, West Nusa Tenggara, Nanggroe Aceh Darussalam, Central Kalimantan, West Kalimantan, Jambi, Gorontalo and North Sumatera. Moreover, the provinces of Maluku, North Maluku, West Papua, Papua, and East Nusa Tenggara were highly endemic areas.

Research variables

The outcome variable, malaria status, is coded as a binary variable whose value equals one if a participant within the past month was ever diagnosed as being malaria-positive by health

professionals [7]. Thus the respondent reported having been diagnosed as malaria-positive by a health professional during the past month. In the questionnaire (code B07): in the last one month, has [name] ever been diagnosed to suffer from malaria, which was confirmed by a blood test taken by health professionals. Generally, the diagnosis was confirmed by use of rapid diagnostic tests (RDTs) and microscopy in health services. The interviewer did not check for a malaria infection [7]. Further, an independent data collection was taken from an individual and household questionnaire. All the measurements on each person are made at one point in time [22].

The independent variables, such as characteristics of participants (gender, age, education, principal occupation), behaviour of participants (sleep under a mosquito net, use net insecticide, defecating habits), and accessibility and utilization of health services (participants were able to access health services by travelling), environmental sanitation (type of container/media, sewage canal, sewage canal conditions), and location of cages (medium breeding animals and large breeding animals) were tested for a potential relationship with the response variable malaria using the binary category “yes” and “no”. In this study, malaria status include those who have the disease.

Study population

Participants of all ages representative of the entire Republic of Indonesia were interviewed with questions related to malaria. Household samples and household members in Riskesdas 2007 are designed to be identical to households and the household member list in the National Socioeconomic Survey (Indonesia acronym: Susenas) 2007 [7]. Regions designated as rural were used as a survey subsample by the location data retrieval used in the Riskesdas survey 2007 [7].

The analyses in the present research are based on a massive dataset with 259,885 out of 973,657 Riskesdas participants who represent a total population size of 30,152,651 Indonesians.

Questionnaires

A set of questionnaires was used as an instrument for data collection. The data collection for Riskesdas was done in two stages: the first stage was begun in August 2007 and continued until January 2008 in 28 provinces; the second stage was in August - September 2008 in 5 provinces (NTT, Maluku, North Maluku, Papua and West Papua). Riskesdas had mobilized 5,619 enumerators, all (502) researchers from the National Institute of Health Research, and 86 lectures from technical health schools, local governments in provincial regions and districts/cities, provincial labs, hospitals, and universities were also involved. The process of editing, entry, and cleaning Riskesdas data was started in early January 2008, while there was also a process for discussing work plans and strategies of analysis. Various questions related to Indonesian health policy were research questions and were finally developed to become variables collected by using several approaches. In Riskesdas 2007, there are around 900 variables spread out in 6 (six) kinds of questionnaires. The questionnaires covered malaria and included 14 explanatory variables. Regarding raising livestock, data were collected by asking all heads of households whether they were keeping poultry, medium-sized livestock (goats, sheep, and pigs), large-sized livestock (cows, buffaloes, and horses) or pets such as dogs, cats, and rabbits. If livestock was kept, then it was noted whether the livestock was kept inside of the house or outdoors [7].

Statistical analyses

Data were analysed using statistical data processing applications by Stata, taking into account the complex sampling design (using two-stage sampling). By using a Stata complex sample in processing and analysing Riskesdas data, the validity of analysis result can be optimized. Both

univariate and bivariate analyses were carried out using chi-square tests. In the next stage of multivariable analysis, a series of binary logistic regressions were run. Explanatory variables that may have predictive value for the response variable were selected for the multiple regression models (Wald test, $P < 0.25$) [23].

Analysis of multivariable logistic regression was carried out to specify the relationship amongst multiple independent variables with the dependent variable 'malaria prevalence'. The final model includes the following seven explanatory variables: characteristics of participants (gender, age), community health facility, the condition of sewage canal, the behaviour of participants (using mosquito nets, and insecticide-treated mosquito nets), and raising medium-sized breeding animals). In Table 2, the adjusted odds ratio (AOR), as a result of parsimonious logistic models, is shown for independent variables affecting the prevalence of malaria in rural endemic areas of 15 high malaria-endemic provinces of Indonesia.

Results

Malaria prevalence

Prevalence of malaria in Indonesia in 2007, shown in Fig. 1, revealed that malaria prevalence was 3.5% (95% CI: 0.033 - 0.037) in 15 provinces with malaria prevalence higher than the national average (2.85% in 2007) [7]. The study area map uses the World Geodetic System (WGS84) as its reference coordinate system. The mapping of malaria prevalence based on Riskesdas data was performed using the software Aeronautical Reconnaissance Coverage Geographic Information System (ArcGIS 10). The highest malaria prevalence found was 41.0%

at South Sorong (marked as a black area in Fig. 1), a regency located in the West Papua province of Indonesia with an area of 3,946.94 km^2 and a population of 37,900 (2010 census).

The existence of livestock

Based on the Riskesdas questionnaire, the animals are categorized as livestock, pets and poultry. The term livestock includes large-sized breeding animals (cattle, horses, buffaloes), and medium-sized breeding animals (goats, sheep, pigs). Additionally, poultry, such as chicken and ducks, and pets, such as dogs, cats and rabbits, are included in the term *pets*. With 53.7%, the majority of participants raises chickens, ducks, and birds, followed by pets (dogs, cats, and rabbits; 25.2%), medium-sized breeding animals (goats, sheep, and pigs; 22.2%), and large-sized breeding animals (cows, buffaloes, and horses; 10.2%) (Fig. 2). This research further analysed the raising of both large-sized breeding animals (cattle, horses, buffaloes) and medium-sized breeding animals (goats, sheep, pigs) that are connected with malaria prevalence. This research inevitably reveals that 0.52% (95% CI: 0.004-0.007) of participants keep large-sized breeding animals and 1.63% (95% CI: 0.014-0.019) of participants keep medium-sized breeding animals inside the house. This study also found that 9.64% (95% CI: 0.091-0.102) of the participants keep large-sized breeding animals, and 20.59% (95% CI: 0.197-0.215) participants keep medium-sized breeding animals outside of the house. Livestock kept in close proximity to humans can contribute to the higher transmission, as they attract mosquitoes into areas where they will encounter and feed on human hosts opportunistically (zoopotentiation) [24].

Univariate and bivariate analysis

Table 1 summarizes the percentage of participants having or not having been diagnosed positive for malaria for each of the explanatory variables and bivariate analyses. In brief, this survey observes the participants who keep large-sized breeding animals inside of the house (0.52%,

95% CI: 0.004-0.007), and the participants who keep the animals outside of the house (9.64%, 95% CI: 0.091-0.102). It additionally observes, participants who keep medium-sized breeding animals inside of the house (1.63%, 95% CI: 0.014-0.019), and the participants who keep the animals outside the house (20.59%, 95% CI: 0.197-0.215). Furthermore, Table 2 in this investigation, which is connected with malaria prevalence, records the participants who keep medium-sized breeding animals inside of the house (OR = 2.980; 95% CI: 2.348-3.782, $P < 0.001$), and the participants who keep the animals outside of the house (OR = 1.713; 95% CI: 1.515-1.937, $P < 0.001$) and who contract malaria more than those who do not have such animals. On the contrary, keeping large-sized breeding animals does not considerably increase malaria prevalence. Besides, this watchfulness reveals that males are more likely to have malaria than females (OR = 0.849, 95% CI: 0.811-0.888, $P < 0.001$). Participants who are aged 15-64 years (OR = 0.861, 95% CI: 0.812-0.912, $P < 0.001$) contract malaria more than those who have not yet reached that age. In addition, this research found that most participants who were able to access health services by travelling for more than 60 minutes (OR = 1.633, 95% CI: 1.251-2.131, $P < 0.001$) were more susceptible to contract malaria than participants who were able to access health services by travelling less than 60 minutes. The majority of participants who use open sewage systems (domestic wastewater or municipal wastewater) at home and those without a sewage system are at higher odds of contracting the disease (OR = 1.250, 95% CI: 1.095-1.427, $P = 0.001$) than participants who have closed sewage systems. The study additionally found that both participants who were using mosquito nets OR = 0.805 and insecticide-treated bed nets (ITNs) with OR = 0.508 as protective factors against malaria prevalence compared to who do not use such protection. Besides, there was a negative association between the use of insecticide-treated bed nets and the prevalence of malaria (r = - 0.023, $P < 0.001$). This statistic implies for participants who increasingly used ITNs that the prevalence of malaria decreased.

Multivariable logistic regression

The estimated AOR of malaria for participants who kept medium-sized breeding animals (goats, sheep, pigs) inside at home signifies a 2.81 times higher risk of contracting malaria adjusted for other variables (AOR = 2.809; 95% CI: 2.207-3.575; $P < 0.001$) in rural endemic areas of 15 highly malaria-endemic provinces of Indonesia. The other six controlling factors for malaria prevalence relate to sociodemographic, socioeconomics and behaviour.

Discussion

In the present study, the presence of medium-sized livestock increased the likelihood of contracting malaria by 2.81. The results of this study therefore suggest that the presence of certain livestock types may potentiate malaria risk. Other principal factors affecting the prevalence of malaria were demographic factors such as gender, age, access to health facility, environmental health, and the behaviour of participants concerning protection against malaria by means of mosquito nets and ITNs.

Spatial heterogeneity of malaria prevalence

Spatial variation in malaria prevalence has to be taken into account in Indonesia [25]. The highest malaria prevalence was found in South Sorong, a known malaria endemic province [7]. A gradient of malaria prevalence from rural (58.9%) to urban areas (33.9%) has been known in the Bata district of Equatorial Guinea (EG) [26]. This situation is consistent with the identified high-risk in the rural context that was found in West Papua, Papua [25] and East Nusa Tenggara [7, 27]. A similar variation of spatial malaria distribution was observed in a cross-sectional study

in rural areas in Haiti (4 to 41%), and demographic data indicated some focal disease transmission [28].

Keeping medium-sized animals is a significant determinant for malaria prevalence

This investigation provides evidence for a positive relationship between medium-sized animals that are kept inside the house (AOR = 2.809; 95% CI: 2.207-3.575; $P < 0.001$) and the prevalence of malaria in the human population living in rural, highly malaria endemic areas of Indonesia. An explanation for these results could be that the presence of livestock increased the abundance of vectors for *Plasmodium* species. Increasing the availability of selection hosts such as livestock could increase human malaria exposure by means of zoopotentiation if the heat and odour cues emitted by animals attract a higher number of vectors to households in or near the area where they are kept [10]. Zoopotentiation could also occur if the physical disturbances created by animals (e.g., puddles, hoof prints, watering sites) increase the potential for larval habitats and thus adult vector density near households. In this study, the participants who had an open sewage canal were at higher odds of contracting malaria than others, highlighting the importance of potential larval habitats near houses. The splitting of people and livestock dwellings on this scale proves to be too large to dodge a zoopotentiation effect [10]. An increasing abundance of goats or sheep has been demonstrated to increase the abundance of *Anopheles* mosquitoes within a radius of 20 m around the household in Kenya [13]. Other evidence for zoopotentation includes positive correlations between donkeys, pigs, and humans, and the abundance of malaria-transmitting mosquitoes [13, 29]. For example, the probability that humans are bitten by the zoophilic *Anopheles stephensi* may increase if one sleeps close to a cow or a goat in the evenings. In contrast, the anthropophily of *Anopheles culicifacies* was only slightly influenced by the presence of livestock. In Kenya, each additional goat or sheep increased the abundance of the local malaria vector [13], and one may assume that there was a

higher human biting rate as well. At least participants who kept pigs and sheep in Mozambique had significantly increased odds of malaria infection, although to a lesser extent in the case of sheep [29]. For the zoophilic *An. stephensi*, nightly human biting increased by 38% in the presence of a cow and by 50% in the presence of two goats [21]. An integrative vector control strategy including ITNs and indoor residual spraying (IRS) reduction, combined with ITL, may improve zooprophylactic effectiveness [30].

Keep livestock at a distance

In particular, participants who were raising medium-sized breeding animals inside their home were more likely to have malaria (OR = 2.980; 95% CI: 2.348-3.782; $P < 0.001$), and participants who were raising medium-sized breeding animals outside their home were more likely to have malaria (OR = 1.713; 95% CI: 1.515-1.937; $P < 0.001$) than those who did not raise the livestock. In contrast to the outcome of the study, livestock may indeed have a prophylactic effect in cases in which only zoophilic vectors are present and livestock is placed in a way to act as a protective barrier for anopheline mosquitoes [11]. Otherwise, zoopotentation often takes place when livestock is kept indoors or near the household and if mosquito vectors are mainly anthropophilic [18]. A parallel approach of insecticide-treated livestock (ITL) and arranging the livestock as far from man as possible is sufficient to reduce malaria [11, 21]. Likewise, in the Macha area in the southern province of Zambia, farm animals revealed a dramatically declining risk of *P. falciparum* infection at the house level, with an increasing distance between livestock (cattle, goats, dogs, cats) and dwelling structures.

Demographic and social determinants of malaria status

Participants in the age range of 15-64 years, and especially male participants, contracted malaria significantly more than others. Malaria prevalence also differs by gender, with men more likely

to be parasitaemic than older women in the Democratic Republic of Congo [31]. Similarly, in a larger scaled survey of households in Ethiopia, the frequency of suspected malaria in men was significantly higher than in women; however, the prevalence of malaria was not significant between genders [32]. In contrast, women in the adult population of an endemic area in Kenya are 50% more likely to become infected with malaria parasites than men [33].

Behavioural determinants of malaria status

Protective behaviour (mosquito nets and ITNs) can reduce the risk of malaria. In rural, highly malaria endemic areas of Indonesia, the risk of contracting malaria significantly decreased if ITNs were used. Similarly, ITNs are the most protruding prevention of malaria in highly endemic areas in Malaysia [34], along with other community-based preventive measures, such as bed nets [35]. Furthermore, ITNs and long-lasting insecticidal nets (LLINs) were combined with indoor residual spraying to accelerate success in malaria control in tropical Africa [36]. Seemingly using of ITNs in 2007 is not more effective for as protection for malaria with ($r = -0.023$, $P < 0.001$), due to the number of ITNs distributed at the time, the number of people protected is low, and lack behaviour of the community use of ITNs in the research area [19, 37]. Furthermore, the malaria program has been using long-lasting insecticidal nets (LLIN), which are more effective than ITNs. LLINs have been used significantly more as an effective alternative to ITNs for over a decade [38].

Limitations of research

A weakness of our study is that the clinical diagnosis of malaria by retrospective interview of last 4 weeks may underestimate malaria positive respondents. We expect that if we would increase the period for clinical diagnosis, more people would report positive malaria diagnosis. The cross-sectional design cannot decide how the chances of getting malaria for participants

were before and after exposure to covariate variables. However, the benefits of a large-scale cross-sectional design are the increase in information on preliminary phenomena which subsequently allows for designing studies with particular foci [39]. There are other factors also proven to determine malaria prevalence, such as the bionomics of different *Anopheles* species [40]. Understanding the kind of *Anopheles* species, and the behaviour of *Anopheles* mosquitoes can help conceive how malaria is transmitted and can assist in designing appropriate control strategies. Unfortunately, in the Riskesdas 2007, these factors were not monitored.

Recommendations

In this study, participants who raised medium-sized animals inside their homes had a higher malaria prevalence in 15 provinces throughout the rural malaria endemic areas of Indonesia. Hence, the main recommendation from this study is to keep this livestock outside of the house, and to focus livestock-based interventions on households with a high proportion of medium-sized animals in rural malaria endemic areas of Indonesia. In this context, anthropological studies should be undertaken to understand in the first place why people in different parts of Indonesia are keeping livestock the way they do. Participatory community eco-health approaches might be best suited to work with local people and communities in order to develop a lasting intervention together, since a vertical policy might not be successful [41-43].

Besides, participants aged 15-64 years should be provided with the means for protection from *Anopheles* bites while working in rural malaria endemic areas, including personal protection, behaviour modification and environmental modification. Personal protection includes using insecticides and repellent and the use of long-sleeved clothing and trousers. Environmental modification is aimed at reducing mosquito habitats, removing shrubs, covering leaky rooves, among others. There is also a need for improving sanitation by closing sewage canals to reduce

the breeding places of *Anopheles* mosquitoes. Seemingly using of ITNs in 2007 is not more effective for as protection for malaria with (r = - 0.023, $P < 0.001$). This study therefore recommends the distribution of LLINs to all people in rural endemic areas together with community-based interventions to improve the knowledge, attitude and practical use and maintenance of LLINs for malaria prevention.

Conclusion

The presence of medium-sized livestock (goats, sheep, and pigs), is the major risk factor for contracting malaria in rural malaria endemic areas of Indonesia. Sociodemographic and behavioural factors are also important for having a high risk of malaria infection. Thus, livestock-based interventions should be prioritized in Indonesia and focus on households with a high proportion of medium-sized animals in malaria endemic rural areas. 'One Health' community research approaches that encompass understanding local perceptions of malaria, malaria transmission and livestock as well as the use of preventive tools like long-lasting insecticide impregnated bed nets should be strengthened in Indonesia to inform the adequate development of an integrative malaria prevention strategy.

List of abbreviations

AOR	:	Adjusted odds ratio
API	:	Annual parasite incidence
ArcGIS	:	Aeronautical Reconnaissance Coverage Geographic Information System
IDHS	:	the Indonesian Demographic and Health Survey
IRS	:	Indoor residual spraying reduction
ITL	:	Insecticide-treated livestock
ITNs	:	Insecticide-treated mosquito nets
IVM	:	Integrated vector management
LLINs	:	Long-Lasting Insecticidal Net
MHD	:	Man-hour density
MOH	:	Ministry of Health
NIHRD	:	National Institute of Health Research and Development
NTT	:	East Nusa Tenggara (Indonesia acronym: NTT)
OR	:	Odds ratio
PHCs	:	Primary health centres
RDTs	:	Rapid diagnostic tests
Riskesdas	:	Indonesia basic health research (Indonesia acronym: Riset kesehatan Dasar)
Ristekdikti	:	Ministry of Research, Technology and Higher Education (Indonesia acronym: Ristekdikti)
Susenas	:	the National Socioeconomic Survey (Indonesia acronym: Susenas)
USAID	:	the US Agency for International Development
VBDs	:	Vector-borne diseases
WGS84	:	World Geodetic System 1984

Declarations

Ethics approval and consent to participate

The ethical clearance for primary data has been obtained from the National Institute for Health Research and Development, Ministry of Health, Republic of Indonesia. The ethical clearance for secondary data used in our paper is not required to be obtained. Since the paper uses secondary data, also the consent to participate is not applicable to the present study.

Consent for publication

Not applicable.

Availability of data and materials

The raw dataset of Indonesia Basic Health Research 2007 has been generated at the National Institute of Health Research and Development (NIHRD), Ministry of Health (Indonesia). Derived secondary data and analysis/findings of this study are available from the corresponding author (HH) on request.

Competing interests

The authors declare that they have no competing interests. RM is currently active as a consultant for the non-profit company PoloGGB, Italy, which aims to develop and assess new genetic vector control tools for malaria vectors in Africa. The present study is however not related to PoloGGB activities.

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Authors' contributions

HH obtained the Riskesdas sub-dataset. The study was conceived and designed by HH, DAG, UK and RM. The data was analysed by HH, MD, JB, UK, DM and RM.

RM, DAG, MD, DM and UK drafted the manuscript with subsequent contributions and revisions. All authors read and confessional the final manuscript.

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Table legends

Table 1: Description of variables research [%] within the categorical variable: malaria prevalence, characteristics of participants, the accessibility and utilization of health service, environmental sanitation, the behaviour of participants, and the location of cages of livestock.

Table 2: The logistic regression analysis associated with the prevalence of malaria in rural highly malaria-endemic endemic areas in 15 provinces of Indonesia, with n = 259.885

Figure legends

Fig. 1: The proportion of malaria in regencies and cities within rural areas of Indonesian provinces with malaria prevalence above the national average.

Fig. 2. The proportion of rural population (n = 259,885 household members) raising livestock [%] and the location of cages [%] in highly malaria-endemic endemic areas in 15 provinces of Indonesia. The category of poultry includes chicken, ducks and birds. The category of pets includes dogs, cats and rabbits. The category of medium-sized breeding animals includes goats, sheep and pigs. The category of large-sized breeding animals includes cows, buffaloes and horses.

Table 1: **Description of variables research [%] within the categorical variable: malaria prevalence, characteristics of participants, the accessibility and utilisation of health service, environmental sanitation, the behaviour of participants, and the location of cages of livestock.**

Variable research with n = 259.885	**Proportion**	**95% CI**	
		Lower	Upper
The **dependent** variable			
Malaria prevalence			
0. No	96.53%	0.963	0.967
1. Yes	3.47%	0.033	0.037
The **independent** variables			
Sex			
0. Male	49.29%	0.491	0.495
1. Female	50.71%	0.505	0.509
Age (years)			
0. Productive age (15-64 years)	60.09%	0.598	0.604
1. Not productive age (<15 and >64 years)	39.91%	0.396	0.402
Education			
0. Completed high school	12.42%	0.12	0.128
1. High school not completed	63.98%	0.636	0.644
2. <10 years of age	23.60%	0.234	0.238
Main Occupation			
0. Other occupation	45.43%	0.449	0.46
1. Farmer/fisherman/labourer	30.97%	0.304	0.315
2. <10 years of age	23.60%	0.234	0.238
The time to reach the nearest hospital			
0. <60 minute	93.18%	0.925	0.938
1. > 60 minutes	6.82%	0.062	0.075
The time to reach the nearest community health facilities			
0. <60 minute	95.24%	0.947	0.957
1. > 60 minutes	4.76%	0.043	0.053
The type of container/media used			
0. Closed container	62.57%	0.614	0.637
1. Others	37.43%	0.363	0.386

The sewage canal			
0. Closed container in the yard	5.52%	0.051	0.06
1. Others	94.48%	0.94	0.949
The condition of sewage canal			
0. Closed canal	9.92%	0.094	0.105
1. Others	90.08%	0.895	0.906
Mosquito nets			
0. Yes	43.99%	0.428	0.452
1. No	55.22%	0.54	0.564
2. No answer	0.79%	0.007	0.009
Insecticide-treated bed net			
0. Yes	11.43%	0.107	0.122
1. No	29.01%	0.279	0.301
2. No answer	59.56%	0.584	0.607
The habit of defecate			
0. Yes	44.29%	0.433	0.453
1. No	32.11%	0.312	0.33
2. <10 years of age	23.60%	0.234	0.238
Raising large-sized breeding animals (cows, buffaloes, horses)			
0. No have	89.84%	0.892	0.904
1. Cage inside the house	0.52%	0.004	0.007
2. Cage outside the house	9.64%	0.091	0.102
Raising medium-sized breeding animals (goats, sheep, pigs)			
0. No have	77.78%	0.768	0.788
1. Cage inside the house	1.63%	0.014	0.019
2. Cage outside the house	20.59%	0.197	0.215

Table 2: **The logistic regression analysis associated with the prevalence of malaria in rural highly malaria-endemic endemic areas in 15 provinces of Indonesia, with n = 259.885**

Risk Factor	*P-value*	Unadjusted OR (95% CI)	*P-value*	Adjusted OR (95% CI)
Sex				
(Male versus female)	0.000	0.849 (0.811-0.888)	0.000	0.842 (0.804-0.882)
Age (years)				
(Productive age (15-64 years) versus Not productive age (<15 and >64 years)	0.000	0.861 (0.812-0.912)	0.000	0.837 (0.790-0.887)
Community health facility				
(<60 minutes versus > 60 minutes)	*0.000*	*1.633 (1.251-2.131)*	*0.005*	*1.446 (1.120-1.866)*
The condition of sewage canal				
(Close canal versus others)	*0.001*	*1.250 (1.095-1.427)*	*0.015*	*1.177 (1.033-1.343)*
Mosquito nets				
(Yes versus Not)	0.000	0.805 (0.727-0.890)	0.157*	0.879 (0.736-1.051)
Mosquito nets				
(Yes versus others)	*0.002*	*1.911 (1.273-2.868)*	*0.005*	*1.838 (1.208-2.797)*
Insecticide-treated bed net				
(Yes versus Not)	0.000	0.508 (0.439-0.588)	0.000	0.509 (0.440-0.589)
Insecticide-treated bed net				
(Yes versus others)	0.000	0.527 (0.457-0.608)	0.000	0.590 (0.481-0.725)
Raising medium-sized breeding animals				
(Not have versus Inside)	*0.000*	*2.980 (2.348-3.782)*	*0.000*	*2.809 (2.207-3.575)*
Raising medium-sized breeding animals				
(Not have versus Outside)	*0.000*	*1.713 (1.515-1.937)*	*0.000*	*1.643 (1.460-1.849)*

Risk factors with $P < 0.001$ or $P < 0.05$ and OR > 1 are shown in *italic face*
* $P > 0.05$ a confounding factor.

Figure

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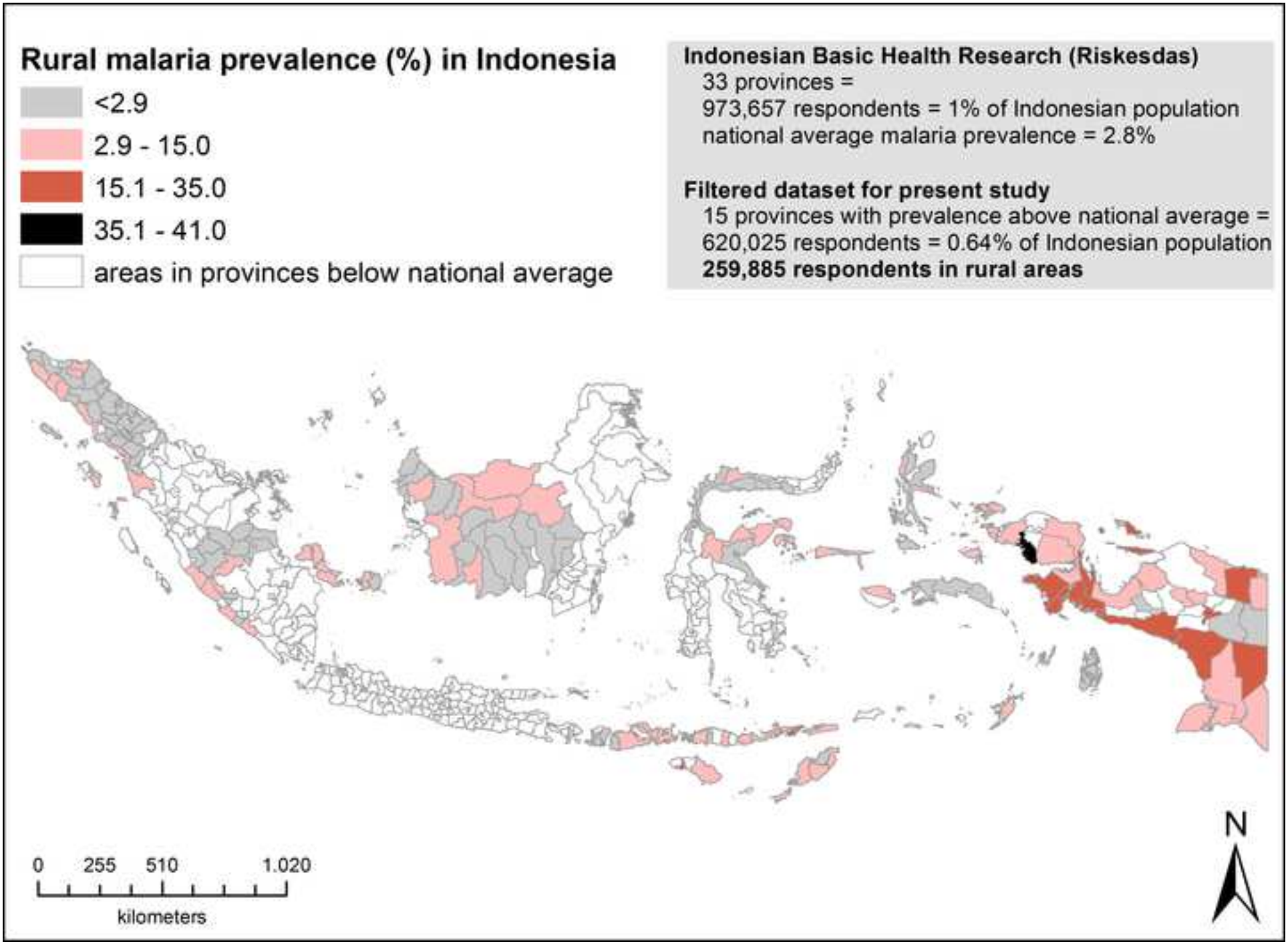

Figure

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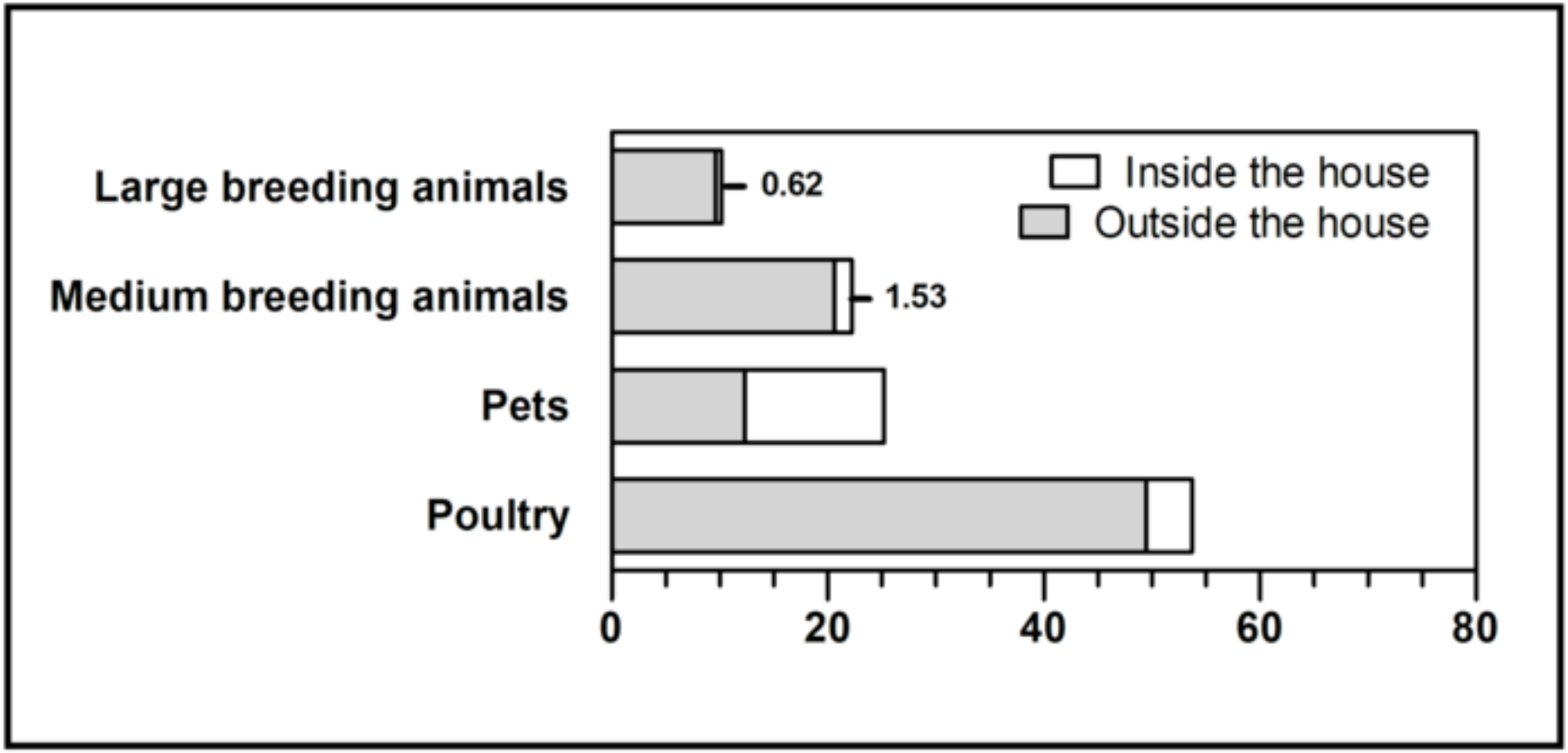

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Submitted by	Hamzah Hasyim (hamzah.hasyim@gmail.com)
Submitted	19 Apr 2018

Invoice address:

Email	hamzah.hasyim@gmail.com
Phone number	+6281373178328
Department	Inst. f. Arbeits,- Sozial- und Umweltmedizin
Organization	Goethe Universit\u00E4t Frankfurt
Address line 1	9b
Address line 2	Theodor-Stern-Kai 7
City	Frankfurt am Main
State/Province	Hessen
Zip/Postcode	60590
Country	Germany

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