Gmail **Michelle Evans <mvevans89@gmail.com>**

Decision on your PLOS Neglected Tropical Diseases submission (PNTD-D-17-02116) - [EMID:514afc1a62e9deec]

6 messages

PLOS Neglected Tropical Diseases <em@editorialmanager.com> Wed, Feb 7, 2018 at 3:30 PM
Reply-To: PLOS Neglected Tropical Diseases <plosntds@plos.org>
To: "Michelle V. Evans" <mvevans@uga.edu>

Dear Ms. Evans,

Thank you very much for submitting your manuscript "Carry-over effects of larval microclimate on the transmission potential of a mosquito-borne pathogen" (PNTD-D-17-02116) for review by PLOS Neglected Tropical Diseases. As with all papers submitted to the journal, your manuscript was reviewed by members of the editorial board. The reviewers appreciated the attention to an important topic, but they raised substantial concerns about the paper. Based on the reviews, I regret that we will not be able to accept this manuscript for publication in the journal.

This decision is based principally on the lack of a within-study control, with attribution of carryover effects instead depending on a less-than-ideal comparison based on modeled estimates for vector competence and fecundity at an adult temperature of 27C by Mordecai et al. The fitted estimates remove the variability in the parameter estimates, and data from that study show high variability in the data around 27C, which suggests that results are likely to depend on mosquito and virus strain, among other factors.

The reviews are attached below, and we hope they may help you should you decide to revise the manuscript for submission elsewhere. We are sorry that we cannot be more positive on this occasion, but hope that you appreciate the reasons for this decision and that you will consider PLOS Neglected Tropical Diseases for other submissions in the future.

Thank you again for your interest in and support for PLOS Neglected Tropical Diseases and open-access publishing. Please don't hesitate to get in touch if we can provide any further assistance.

Sincerely,

Christopher M. Barker
Associate Editor
PLOS Neglected Tropical Diseases

Michael Johansson
Deputy Editor
PLOS Neglected Tropical Diseases

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Reviewer #1: The manuscript by Evans et al. entitled "Carry-over effects of larval microclimate on the transmission potential of a mosquito-borne pathogen" reports field experimental results on the effect of microclimates on the vectorial capacity of Aedes albopictus for Dengue virus. To that aim, authors exposed mosquitoes to natural climatic conditions during their larval development. They chose different places according to their proportion of impervious surfaces which are susceptible to produce different microclimatic conditions. Then, they exposed adult mosquitoes to an infectious blood meal and proceeded to their dissection 21 days later to determine the infection status of the salivary glands, the head and the body to assess the susceptibility of the mosquito to the virus. They used some entomological data from the literature and from their study to parameterized epidemiological models to determine if exposition of larvae to different microclimatic conditions can
affect the capacity of the adults to transmit dengue. Authors found that when larval microclimatic parameters are included into the model, it affects substantially the vectorial capacity. However, this result needs to be presented more precisely (see comments below).

The rationale is well steered, statistics sound good and results support conclusions (but see my comment on fecundity). However, the material and method section lacks of precision to make the study reproducible. Some term definitions also need to be provided and a strict choice in terms used should be done and used consistently throughout the manuscript to make the reading easier.

My main concern is about the position of the data loggers which were located 3 feet above the larval trays and not in the water with the larvae. Consequently, microclimatic data do not reflect exactly the ones larvae experienced during their development (please see my comments below). The authors should explain this choice and specify why it is acceptable and/or discuss this drawback.

As I am not qualified to review the part about modeling I did not make any comments on it.

This work is in the vein of other recent papers of interest combining experimental data and modeling to investigate impact of larval environment on both adult vectorial capacity and epidemiological outcomes. Such work is susceptible to interest ecologists, epidemiologists and medical entomologists.

Hereafter are some comments intended to help the authors to improve the manuscript.

Abstract
-Line 12: Please provide precisions about which land and which season present a lower transmission potential.

Introduction
-Line 42: a reference is needed
-Line 54: delete the "a" before "the Aedes albopictus-dengue virus"

Materials & Methods
-Line 59: Microclimates experienced by mosquitoes in the field are diverse. The authors considered a scale of several miles but some microclimates also exist at meter scales and even millimetre if we consider the surfaces on which mosquitoes chose to rest (larval or adult stages). I recommend to the authors to strictly define what scale of microclimate is considered in the study and why.

-Line 59-62: How were the sites chosen? Why the criterion of impervious surface was used and not another one?

-Line 63: What was the size of the plastic trays? This detail is highly important as trays with large surface to volume ratio may suffer from more evaporation which could affect larval interaction/competition and water temperature.

-Line 64: Please provide some information about the leaf infusion (at least the leaf species)

-Lines 68-69: Why data loggers were recording air temperature and humidity? The work focus on larval ecology and aquatic data loggers would have been more appropriate. Indeed, water temperature is known to change more slowly than air temperature. Moreover, larvae were exposed to water temperature and not air temperature at 3 feet high. If aquatic data loggers were not available, aerial data loggers should have been place under the same setup than trays. Indeed, screen mesh and cages with top made of plastic vinyl could impact temperature changes (fewer air movements). As is, the data do not correspond to larval microclimate but environmental or site microclimate. Authors have to provide justifications for the choice of this design.

-Line 72: Please change for "to collect and quantify emerging mosquitoes by tray per day." The part about body size and infection should not appear in the "semi-field experimental design" section.

-Line 81: What was the size of the cages?

-Line 87: Please provide a minimum of information about how was prepared the infectious blood meal and how long were the mosquitoes allowed to feed on the feeders. Did all mosquitoes feed? What has happened to those that did not feed?

-Lines 90-92: Could the authors explain why the infection was assessed in different tissues. It is not obvious for non specialist.

-Lines 91-92: Please provide a minimum of information on salivation procedure.

-Line 98: Up to this stage, no information was provided on the way wings were measured.

-Line 100: Please define "per capita population growth rate" and delete the "per" before "following".

-Line 107: Please define vectorial capacity

-Line 138: "time to female emergence". It is the first time this term/data appears. How data were collected? Please, define it somewhere.

Results

-Lines 152-155: How large were the differences in temperature and humidity between seasons and sites. Please provide some means or magnitudes.

-Line 158: The terms "proportion of female emerging" and "survival" seem to be used interchangeably. If I am correct, please use only one term and use it consistently troughout the manuscript (text, tables and figures). I personally think that the term survival is misused or should be define. If I am wrong please define the two terms and provide some precisions on how data were collected.

-Lines 159-160: These are basic results and should appear at the very beginning of the Results section.

-Line 162: "the mean rate of larval development". This term appears here for the first time, what is it? (see also line 215)

-Line 167: Please provide at least the mean length of wings.

-Lines 167-168: What about urban sites in the interaction? A figure could help.

-Legend of the Figure 1 line 4: Do the authors mean "standard deviation" instead of "standard data"?

-Line 170: "date of emergence"?

-Lines 172-173: The authors wrote that there was no difference in population growth across temperature. However, the factor "temperature" has a P value < 0.001 in the table 2.

-Line 176: "exposed to an infectious blood meal" instead of "assessed for infection status"

-Lines 178-179: Please be more specific in the description of results. Which land class and season increase the probability to be infected?

-Line 182: It should be place in the discussion section.

-Line 188: Do the authors mean "temperature" instead of "microclimate"?

-Is it possible to produce a figure of infection and dissemination rates as a function of temperature?

-Line 194-197: Not convincing. These sentences could be deleted.

Discussion

-Line 205: the reference 22 could be completed with:

-Shapiro 2016 Proceedings of the Royal Society B. Larval food quantity affects the capacity of adult mosquitoes to transmit human malaria.

-Vantaux 2016 Scientific Reports. Larval nutritional stress affects vector life history traits and human malaria transmission.

-Bara 2015 Plos One. Effect of larval competition on extrinsic incubation period and vectorial capacity of Aedes albopictus for Dengue virus

-Lines 209 & 263: I did not see any result about fecundity.

-Line 210: delete "an urban"

-Line 215: "higher survival rate" should be replaced by "higher emerging rate".

-Line 217: "mean larval temperature" should be replaced by "temperature" or "mean site temperature"

Supporting information

-Line 281: Red not black?

-Lines 285 & 287: "across trays" not very appropriate as the data logger was not in the trays

-Fig S3: legend is missing for filled and empty bars

References

-all the species name should be italicized
-please check for the spell of journal names and correct abbreviations (if abbreviations are needed)
-in titles, first letter of words are sometimes capitalized, sometimes not.
-Line 369: "piece" not "peice"

Figures
Fig. 1: Please add letters to sub figures (A to F).
Fig. 2: What is the unit for the vectorial capacity?

End of comments.

Reviewer #2: In this important study, the authors have investigated the impact of larval environment on the ability of Ae. albopictus to transmit dengue virus. This information could make modeling vectorial capacity more accurate. In general, I believe the manuscript is well written, but many of the critical figures are included as supplemental. This gives the impression that the results are less important. I have included detailed comments/suggestions in the attached PDF.

Reviewer #3: General comments

This paper deals with "carry-over" effects of microclimate variation (and specifically temperature) during larval development on DENV transmission by adult Aedes albopictus mosquitoes. The authors attempt to demonstrate the need to incorporate the impact of temperature-driven carry-over effects to predict vectorial capacity. The study relies on a combination of semi-field experiments and mathematical modeling using the empirical data. Quantifying the epidemiological importance of carry-over effects for vectorial capacity is definitely worthy, and the approach chosen is a laudable one. However, several important methodological shortcomings question the validity of the conclusions.

Major comments

The most fundamental issue with this study is that it compares vectorial capacity between two models, with and without carry-over effects, which are not directly comparable. The two models use the same parameter values except for two adult traits, vector competence and lifetime fecundity. For these two traits, the model without carry-over effects incorporates parameter values derived from thermal responses obtained in prior studies, using a fixed adult temperature of 27°C and an unknown (presumably fixed) larval temperature. The model without carry-over effects uses parameter values derived from thermal responses obtained in the current study, in which larval temperature varied following natural fluctuations in the semi-field experimental setting and the adult temperature was fixed at 27°C. This results in two main problems:
(i) the thermal response obtained for the model without carry-over effects is unrealistic because in this model vector competence and lifetime fecundity are considered independent of temperature. This leads to a conceptual paradox in Fig. 2 because vectorial capacity is represented to vary across a range of temperatures, although the two models being compared in the figure only considered an adult temperature of 27°C. In fact, Fig. 2 shows a thermal response for which the temperature gradient refers either to larval temperature or adult temperature, but not both, depending on the parameter.
(ii) the parameter values being compared are estimated in different studies, instead of side by side within the same experiment. There could be several confounding factors, for example the use of different mosquito and/or virus strains among the studies. A more rigorous approach would be to calculate the mean value of the parameter across temperatures from the model with carry-over effects, and use this mean value as a uniform thermal response for this parameter in the model without carry-over effects.

Another significant issue is that the estimate of lifetime fecundity, one of the two parameters included in the comparison of vectorial capacity models with and without carry-over effects, could be wrong. This is because lifetime fecundity was calculated as daily fecundity (inferred from an assumed linear relationship with wing length) divided by the expected lifespan. Although the daily fecundity was actually estimated from wing length measurements in the semi-field experiment and thus accounted for the carry-over effects, the potential carry-over effects on adult lifespan were ignored.

A related limitation of the study is that only two parameters (vector competence and lifetime fecundity) were included in the comparison of vectorial capacity models with and without carry-over effects. Lifespan is arguably one of the most important parameters, however it was ignored the model comparison. Moreover, as mentioned above, this has an indirect effect on lifetime fecundity, which is estimated from wing length (measured) and lifespan (not measured).

Minor comments

It is unclear how the thermal responses were derived from the natural environmental gradient. Given that both the mean and amplitude of daily temperature fluctuations vary in the field, how was the thermal response constructed for a given

trait?

The vector competence parameter used in the vectorial capacity equation is defined the proportion of infectious mosquitoes (proportion of all DENV-exposed mosquitoes with detectable infectious viral particles in their saliva). There seems to be a discrepancy with the infectiousness variable analyzed in Table 2, because in the latter case the denominator seems to be mosquitoes with a disseminated infection. Both should be consistent, or at least clearly defined.

Line 44: What do you mean by "ambiguous"? Please elaborate.

Lines 90-98: Was the same cohort of mosquitoes followed for all infection phenotypes, or were different groups of mosquitoes used for each phenotype? Please clarify.

Lines 90-98: How many mosquitoes were tested per phenotype and per condition?

Line 124: Murdock et al. should read Mordecai et al.

Lines 144-146: The authors addressed collinearity between microclimate variables, but how did they deal with the same issue between class, season and temperature?

In the abstract and throughout the paper, it would be more correct to replace "disease transmission" and "dengue transmission" by "pathogen transmission" and "dengue virus transmission", respectively.

Figure 1 legend: Panels letters are missing from the figure.

carry_over_effects_2018.pdf
1723K

Michelle Evans <mvevans@uga.edu> Mon, Feb 26, 2018 at 8:57 AM
To: "John M. Drake" <jdrake@uga.edu>, Courtney Murdock <cmurdock@uga.edu>

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Michelle Evans
PhD Student, Integrative Conservation and Ecology
University of Georgia, Odum School of Ecology
mvevans@uga.edu | mvevans89.github.io

carry_over_effects_2018.pdf
1723K

Courtney Murdock <cmurdock@uga.edu> Mon, Feb 26, 2018 at 10:31 AM
To: Michelle V Evans <mvevans@uga.edu>, John M Drake <jdrake@uga.edu>

Hi Michelle,

These actually are not that bad. When you finish the YF manuscript, let's meet to discuss. We can decide whether using the model is appropriate for comparing carry-over effects (I do take the point that it would have been nice to have a within experiment control...a constant 27 C treatment - if we could have managed it logistically - we could go back and do this now if we wanted to), if we should just use VC as a measure of pathogen fitness across these environments and discuss carry-over effects throughout the discussion, or if we should take reviewer 3's suggestion on averaging across temperatures - which I think John suggested earlier on prior to this submission (with coming up with a grand mean for each trait across our sites...???).

Anyways, we can discuss later. Thanks for sending.

Courtney

From: Michelle V Evans
Sent: Monday, February 26, 2018 8:57:58 AM
To: John M Drake; Courtney Murdock
Subject: Fwd: Decision on your PLOS Neglected Tropical Diseases submission (PNTD-D-17-02116) - [EMID:514afc1a62e9deec]

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Michelle Evans

mvevans89.github.io

Hi! I'm Michelle. I'm a PhD student in the Integrative Conservation and Ecology program at the University of Georgia, advised by Dr. John Drake and Dr. Courtney Murdock.

Michelle Evans <mvevans@uga.edu> Wed, Mar 14, 2018 at 9:04 AM
To: Courtney Murdock <cmurdock@uga.edu>
Cc: Michelle V Evans <mvevans@uga.edu>, John M Drake <jdrake@uga.edu>

Courtney and John,

I'm beginning to think about how to rework this for resubmission elsewhere. I think how it is done will partly depend on the journal because of length and figure limitations. I think many of the reviewers' comments will be easy to address if we are no longer limited by word count, particularly reviewer one's. Do you have any preference for the journal? Courtney had mentioned Parasites and Vectors, which doesn't have a page limit, which I think is a good idea.

As for the modeling section, I think we should either use the grand mean as a 'control' or simply propagate the effect of temperature through the model to give an idea of vectorial capacity, without comparing to anything (similar to what Courtney did in her PLoS NTD microclimate paper). Given a choice between these, I prefer the first, as it may still allow us to say something about whether carry-over effects are having an effect.

Any thoughts?

Best,
Michelle
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John Drake <john@drakeresearchlab.com> Wed, Mar 14, 2018 at 9:54 AM
To: Michelle V Evans <mvevans@uga.edu>
Cc: Courtney Murdock <cmurdock@uga.edu>, John M Drake <jdrake@uga.edu>

I’m supportive of both journal choice and approach to modeling

--
John M. Drake
University of Georgia

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Courtney Murdock <cmurdock@uga.edu> Wed, Mar 14, 2018 at 11:22 AM
To: John Drake <john@drakeresearchlab.com>, Michelle V Evans <mvevans@uga.edu>
Cc: John M Drake <jdrake@uga.edu>

Ditto.

Court

From: John Drake <john@drakeresearchlab.com>
Sent: Wednesday, March 14, 2018 9:54:20 AM
To: Michelle V Evans
Cc: Courtney Murdock; John M Drake
Subject: Re: Decision on your PLOS Neglected Tropical Diseases submission (PNTD-D-17-02116) - [EMID:514afc1a62e9deec]

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