Review of: "Thermal Stress and Dengue Fever: Exploring the Correlation between Elevated Temperatures and Heat Waves in Disease Dynamics"

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Potential competing interests: No potential competing interests to declare.

Thank you for giving me the opportunity to read your review paper. The topic is interesting and important, but I have to agree with many of the previous reviewers that it lacks depth. When I finished reading your pre-print, I didn't feel like I learned anything new - this might be because I already know a lot about this topic. However, I do believe that going into more detail, comparing and contrasting specific studies in different regions would be more useful, even for a review article. I also agree with many of the previous reviewers' comments that focusing on temperature and heatwaves alone might be misguided, as climate change has many other impacts, which you yourself talk about. I would also like you to define and differentiate heatwaves from just increased average temperatures. Apart from italicizing the species names of the mosquitoes involved, I would also suggest not capitalizing the name of the virus (using dengue instead of Dengue).

You make two statements that are puzzling to me. First, in the “High Temperatures and Aedes Mosquito Vectors” section, you state that “Mosquitoes with shorter lifespans may become infected with the Dengue virus sooner after hatching, making them more likely to transmit the virus during their relatively brief lives." You cite the paper by Harrington, but reading through the relevant portion of the paper, I couldn't see the source of this citation. How would this even work? Mosquito larvae do develop faster in warmer conditions, but how would that make their infectious period longer?

The other statement, in the section titled “High Temperatures and Dengue Virus”, which is also referenced to the same paper by Laura Harrington, says “The shortened survival time forces the virus to infect new hosts more rapidly, contributing to an elevated transmission rate during periods of high temperature”. Again, I found no evidence for this in the paper you cited. How would this work again? Are you suggesting that the virus evolved to be more infectious? But then once it evolved to be more infectious, then it evolves back to be less infectious when it's less hot? Why would it do that, when it still benefits against other variants by being more infectious? Overall, I'm not convinced by your argument that the reduced lifespan of the mosquitoes due to higher temperatures would be compensated by higher viral replication rates, infectivity, or a longer infectious period. I do think that there are temperatures that are too hot for both the mosquito and the virus to transmit, and that there would be a unimodal distribution of the force of infection of dengue with respect to temperature. Now, the higher threshold might be beyond optimal or habitable conditions for humans as well, that I don't know.

The last sentence of this same section reads like it belongs to the next section on Human Behaviour.

In the section on “Human Behavior and Heatwaves,” it would be useful to talk about the daily activity profile of Aedes mosquitoes and how shifts in human behavior due to the heatwaves (e.g., being more indoors or outdoors at different parts of the day) may create more exposure to the mosquitoes when they are active. I'm also dubious that people in poor areas can afford to travel to cooler places, as they can't afford that. I'm wondering if heatwaves, in fact, cause people to travel less because it is too hot.

In the section “Epidemiological Studies and Observations,” you talk about a study. What study do you mean? Do you mean the meta-analysis by Damtew et al.? The other paper you cite by Frentiu is simply an editorial on the same paper, but you cite it as a separate paper. The meta-analysis does provide actual information and is very useful. I do wonder, then, what your review provides that goes beyond this meta-analysis, apart from putting it in the context of other parts of the literature. I also wonder why all of this information and the mention of the meta-analysis is not integrated throughout the manuscript. This is the first section where you mention the EIP, even though you talk about viral replication before. I was also confused by the sentence that says “This explains why the relative risk associated with minimum and mean temperatures was higher than that for maximum temperature.” Do you mean that the “relative risk associated with increases in the minimum and mean temperatures was higher than that for the increase in maximum temperature.”? I was also confused by the next sentence on the time resolution, or monthly analysis showing a higher relative risk.

The next two pages have a bunch of subsections that are only a single paragraph. Do you really need them as separate subsections? They are awfully small. Perhaps you could combine some of them.

In your section on “Vector Control Strategies,” you mention the release of genetically modified or Wolbachia-infected mosquitoes to reduce the Aedes population. While it is true that you can do that, the main purpose of releasing Wolbachia-infected mosquitoes is to spread Wolbachia into the wild population of mosquitoes, making them refractory and less able to transmit the dengue virus.

In the Climate change mitigation and Dengue fever section, you argue that reducing greenhouse gas emissions will help mitigate the increased risk of dengue transmission. How would this work? Indirectly? How would mitigation actions directly reduce dengue transmission risk? In a related note, you state that “Investment in clean energy and transportation options aids…limiting the spread of dengue to new regions.” How would that work? Some clean energy options actually create potential breeding sites.

In your last section on “Recent Advances”, you state that new climate models offer “more accurate predictions of extreme weather events and Dengue outbreaks". Then you cite a paper on climate models, but one that has nothing to do with dengue. Can you cite a paper where they actually predicted dengue outbreaks using input from climate models, or observations, and validated those predictions?

In the same section, you talk about vaccine development. While vaccine development is important, I fail to see the connection between vaccines for dengue and the topic of the paper, which is the effect of higher temperatures and heatwaves on dengue transmission. Sure, if there's more dengue, we have a greater need for vaccines, but vaccine development and deployment won't affect the relationship between temperature and dengue. If you only included a

mention of vaccines to cover your bases, I'd suggest removing it.

Unfortunately, I agree with a previous reviewer that this review is not a substantial contribution to the literature on dengue, and given the statements unsupported by evidence, it would need to be revised before it would be ready for publication.