Correspondence


The 2007 dengue outbreak in Singapore

To the Editor

We read with disappointment the work by Massad and others entitled ‘A hypothesis for the 2007 dengue outbreak in Singapore’ [1]. The authors blamed the haze that resulted from forest fires in Sumatra in 2006 for the mismatch between the observed dengue incidence in Singapore and that predicted by their model [2]. They postulated that the 2007 dengue outbreak in Singapore would have happened in 2006 as their model had predicted if not for the haze that reduced the mosquitoes’ lifespan and hence transmission intensity. There are a number of inaccuracies and flaws in their paper that need to be addressed.

First, the authors failed to conduct a thorough review of the epidemiology of dengue in Singapore. Had they done so, they would have found that in late 1997 to early 1998, a haze blanketed much of Southeast Asia, including Singapore. The pollution standard index (PSI) in 1997 was in the moderate and unhealthy ranges for 48 and 3 days, respectively, while the PSI in 1998 was in the moderate range for 30 days [3]. The incidence of dengue in 1997 and 1998 were the highest in Singapore in the 1990s, which represented the peak of a 6- to 7-yearly cycle of dengue epidemic observed in Singapore [4]. High incidence of dengue in 1997 and 1998 were the highest in Singapore in the 1990s, which represented the peak of a 6- to 7-yearly cycle of dengue epidemic observed in Singapore [4]. High incidence of dengue was also observed in many Southeast Asian countries in 1997–1998, many of which were also affected by the haze that resulted from forest fires [5]. In contrast, the PSI in 2006 was in the moderate and unhealthy ranges for 14 days and 1 day, respectively. There is thus little basis to support the hypothesis that the haze shortened the lifespan of *Aedes aegypti*, and hence reduced the observed incidence of dengue compared to that predicted by their model [2].

Second, the authors failed to take into account the growing population of Singapore through immigration. Their model had factored only birth rate as a contributor to the susceptible population [1]. Data from the Department of Statistics [6], Singapore indicates that the annual birth rate has declined from 51,142 in 1990 to 39,490 in 2007. Conversely, the Singapore population has continued to expand (Fig. 1) due to the attractive economy and infrastructure. A seroprevalence study to determine the proportion of the immigrant population that is immunologically naive to dengue and hence adds to the susceptible population growth would be useful. Nonetheless, the use of birth rate alone probably underestimates the growth rate of the susceptible population.

Third, the model assumes that all dengue viruses result in a similar likelihood of symptomatic disease upon infection. This too, cannot be supported by epidemiological observations. The positive-stranded RNA genome of dengue virus mutates randomly upon replication in humans and mosquitoes [7], which could result in virus strains emerging, which have greater epidemic potential. Recent molecular epidemiological studies have indicated that in the Pacific (1970s), Puerto Rico (1980s), Sri Lanka (1990s), the Americas (1990s) and elsewhere, dengue epidemics have resulted from the emergence of new clades or subtypes of viruses that were associated with increased frequency of severe disease outcomes and epidemic potential [8–11]. It is likely that different genotypes of the dengue virus interact differently with host factors and these then give rise to different disease manifestations and epidemiological outcomes [12].

Mathematical models remain a powerful tool for epidemiological analyses and are likely to play a prominent role in the study of epidemic dengue. However, multiple intrinsic host factors, both human and vector, as well as extrinsic environmental factors, such as temperature, rainfall and humidity, affect epidemic dengue virus transmission [13] and theoretical analysis of a single factor would thus be misleading. Mathematical models of dengue must
take these into consideration and be based on well-validated field and laboratory observations. We encourage mathematical modellers to work closely with epidemiologists and clinicians to ensure quality and thus utilize the full power of modelling in the development and implementation of prevention and control strategies for dengue and other infectious diseases.

Declaration of Interest
None.

References

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The authors reply:
The above letter by Ooi et al. entitled ‘The 2007 dengue outbreak in Singapore’ heavily criticizes our paper ‘A hypothesis for the 2007 dengue outbreak’ [1].

Ooi et al. suggest that our explanation for the mismatch between the observed dengue incidence in Singapore and that predicted by our earlier model is unfounded. They argue that a previous (1997–1998) outbreak of dengue in Singapore coincided with the worst and most prolonged haze in recent history. However, this claim is based on the assumption that haze would be the sole or the most important factor influencing dengue incidence, a statement that we never made. The authors did not consider that 1997 and 1998 had the highest annual average temperatures in a 15-year period, reaching 28.3°C, which is almost 2°C above the annual average for 1989 (see Fig. 2) Therefore, the 1997–1998 period was atypical in at least two factors. However, as far as we know, the 2003–2007 period that we analysed had only one atypical factor, namely, haze.
Those 2 °C above the annual average for 1989 temperature would perhaps offset the potential effect of haze in the biennial of 1997–1998 by increasing the number of mosquitoes. Perhaps, without this increase in the temperature the number of cases would be much less than that observed. Therefore, the 1997–1998 outbreak by itself does not invalidate our hypothesis. We agree with Ooi et al. that any hypothesis needed to explain the low number of cases in 2006 should be supported by experimental evidences that unfortunately we are not competent to carry out.

There were three major criticisms raised by Ooi et al.:

(1) ‘Authors failed to conduct a thorough review of the epidemiology of dengue in Singapore. Had they done so, they would have found that in late 1997 to early 1998, a haze blanketed much of Southeast Asia, including Singapore.’

We made reference to the 1997 episode in our paper. We also provided a correlation between the total number of dengue cases in Singapore and number of days with PSI > moderate (see Fig. 1 of original paper).

(2) ‘Authors failed to take into account the growing population of Singapore through immigration.’

In a model involving only derivatives and with no mention of age, the parameter $r_H$ includes birth rate (zero-aged people) and immigration rate. However, the authors rightly pointed out our oversight in calling this parameter only birth rate. We apologize for this mistake.

(3) ‘Model assumes that all dengue viruses result in a similar likelihood of symptomatic disease upon infection.’

This is a fair point. However, the fit provided by our model to the data was a reasonably good one. It is not clear how the incorporation of greater complexity into the model would improve the explanatory power of our model.

We are sorry that our paper caused such distress to Ooi et al. On the other hand we are glad that the authors recognize that there is a very interesting phenomena to be explained, namely, why is it that there was no sizable outbreak in 2006? Our paper is just a hypothesis to explain this occurrence. It may be false, but alternative hypotheses should be proposed before dismissing it. We are disappointed that the authors do not bring any new alternative hypotheses but we are sure that their criticisms may induce others to carry out experiments (the influence of haze on the mortality of mosquitoes, temperature effects on dengue transmission, etc.) that we are not competent to do.

In summary, in our view our paper presents a hypothesis to explain an unexpected observed fact. We
agree that further analysis to include other climatic, environmental, and intervention variables should be the next step.

References


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