

Dengue Disease Modelling and Forecasting: Utility and Limitations

Shirin Kalimuddin, ¹*MBBS, MRCP*, Jenny GH Low, ¹*MBBS, MRCP*, Eng Eong Ooi, ²*BMBS, PhD, FRCPath*

In a joint statement issued earlier this year, the National Environment Agency (NEA) and Ministry of Health (MOH) announced that dengue cases this year would be expected to exceed 30,000—higher than the record of 22,170 experienced in the 2013 dengue epidemic.¹ This forecast was based on retrospective data analyses collected within the past 10 years on *Aedes* mosquito surveillance, serotype surveillance and weather conditions, as well as statistical modelling based on past incidence of dengue cases. Although the weekly dengue cases showed a rising trend in the first few weeks of 2016, it declined soon after the forecast was announced.² Is forecasting therefore accurate or even useful?

Dengue disease forecasting utilises mathematical models, which often integrate multiple parameters, including population susceptibility, duration of infectiousness, transmissibility of the pathogen, geographical, climatic and even pathogen evolutionary factors. Primarily, such efforts are directed at understanding the relative contribution of the various parameters on past disease trends, which are useful to generate hypotheses for further studies. For instance, models have suggested that delaying infection in a population can paradoxically alter the rate of symptomatic infection to cause increased incidence without increases in vector population density.³ It can also enable us to understand the dynamics of spatio-temporal spread of dengue virus that radiates from urban centres,⁴ which would otherwise be impossible to demonstrate through surveillance data alone. Such insights enable policymakers to focus resources on the hub of the problem.⁵ Perhaps more importantly, such models have enabled us to calculate the proportion of the population that needs to be vaccinated to achieve herd immunity. This was the basis in which the smallpox eradication programme operated successfully⁶ and is now used to determine the population size that needs to be vaccinated against dengue to prevent outbreaks.⁴ Mathematical models have thus

contributed much to public health and our understanding of disease epidemiology.

As a forecasting tool, however, the usefulness of mathematical models remains to be demonstrated. History has shown that epidemic outbreak forecasts often fall far short of the mark, as we have witnessed with the recent Ebola outbreak.⁷ We propose 2 possible reasons. Firstly, the warning raised by the forecast led to scaled-up disease control efforts. While this is plausible, we are skeptical that this is a major contributory factor to the actual observed disease trend as surge capacity in response to outbreak assumes a pool of readily available trained human resource in disease surveillance and control could be activated at short notice. Secondly, mathematical models necessarily make assumptions on various factors where no data is available. Errors within these assumptions likely limit the predictive ability of models.

Inaccuracies in dengue forecasting have the potential to lead to undue alarm, unnecessary expenditure and resource wastage. A classic example of this was dengue forecasting in the Brazilian 2014 FIFA World Cup. Prior to the event, there was much concern among football fans and public health authorities with regards to the risk of dengue acquisition among travellers to Brazil. The source of this concern was several dengue forecast analyses, which predicted that tourists travelling to match sites would be at high risk of acquiring dengue, with the highest risk predicted in the cities of Fortaleza, Natal, Salvador and Recife.⁸⁻¹⁰ Eventually, only 3 cases of dengue affecting tourists were confirmed¹¹—all occurring in Belo Horizonte, which interestingly was never regarded as high risk in the forecast. Two other sites, Sao Paulo and Brasilia, also experienced a high incidence of dengue in June 2014, yet were “missed” in the original forecasts.¹² In Singapore, dengue forecasting could, in theory, allow for the timely

¹Department of Infectious Diseases, Singapore General Hospital, Singapore

²Emerging Infectious Diseases Programme, Duke-NUS Medical School, Singapore

Address for Correspondence: Prof Ooi Eng Eong, Duke-NUS Medical School, 8 College Road, Singapore 169857.

Email: engeong.ooi@duke-nus.edu.sg

prediction of future outbreaks, giving policymakers sufficient lead-time to implement strategies which could help mitigate dengue transmission, as well as to put in place pre-emptive infrastructural support to allow the country to best cope with a surge in cases. In infectious diseases such as influenza, epidemic forecasting allows governments time to ensure a sufficient stockpile of antivirals and vaccines. The situation is rather different with dengue, which has no vaccine licensed for use in Singapore (Dengvaxia® being approved in only a limited number of countries), or effective antivirals.^{13,14} In 2005, Singapore experienced an explosive outbreak with a record number of more than 14,000 dengue cases after many years of low incidence.¹⁵ During that outbreak, dengue admissions overwhelmed the healthcare infrastructure.¹⁶ Since then, every restructured hospital has established dengue protocols for the clinical management of acute dengue. Similarly, the national dengue guideline has continuously undergone update to better inform clinicians on admission criteria based on latest evidence-based practice. These measures have greatly reduced the number of patients requiring hospitalisation for the sole purpose of observation. Furthermore, there are limited number of hospital beds and healthcare workers, with the health system already operating at the limits of capacity constantly. There is thus a limitation to any extra implementation our health agencies can put in place in the face of an impending surge in dengue cases.

Forecasting alone without the capabilities for a swift and robust response can be likened to a body without limbs. The recent Ebola epidemic holds many lessons for how we should prepare for and deal with future outbreaks. This was eloquently articulated in a recent article by Dr Jeremy Farrar, Director of the Wellcome Trust, and Dr Trevor Mundel, President of the Global Health Division at the Bill and Melinda Gates Foundation.¹⁷ Besides having good local health infrastructure in place, there needs to be international coordination to execute effective responses, as well as a transformed approach to research and development of vaccines, drugs or other disease control tools even before an outbreak occurs. Only then can the true potential and utility of forecasting be realised.

REFERENCES

1. National Environment Agency. News release—Dengue cases may exceed 30,000 in 2016. Available at: www.nea.gov.sg/corporate-functions/newsroom/news-releases/dengue-cases-may-exceed-30000-in-2016. Accessed on 28 March 2016.
2. National Environment Agency. Latest dengue data. Available at: www.dengue.gov.sg/subject.asp?id=73. Accessed on 28 March 2016.
3. Nagao Y, Koelle K. Decreases in dengue transmission may act to increase the incidence of dengue hemorrhagic fever. *Proc Natl Acad Sci U S A* 2008;105:2238-43.
4. Salje H, Lessler J, Endy TP, Curriero FC, Gibbons RV, Nisalak A, et al. Revealing the microscale spatial signature of dengue transmission and immunity in an urban population. *Proc Natl Acad Sci USA* 2012;109:9535-8.
5. Wilder-Smith A, Renhorn KE, Tissera H, Abu Bakar S, Alphey L, Kittayapong P, et al. DengueTools: innovative tools and strategies for the surveillance and control of dengue. *Glob Health Action* 2012;5.
6. World Health Organization: Expert Committee on Smallpox. Technical Report Series No.283. Geneva, 1964.
7. Butler D. Models overestimate Ebola cases. *Nature* 2014;515:18.
8. Hay S. Football fever could be a dose of dengue. *Nature* 2013;503:439.
9. Massad E, Burattini MN, Ximenes R, Amaku M, Wilder-Smith A. Dengue outlook for the World Cup in Brazil. *Lancet Infect Dis* 2014;14:552-3.
10. Lowe R, Barcellos C, Coelho CA, Bailey TC, Coelho GE, Graham R, et al. Dengue outlook for the World Cup in Brazil: an early warning model framework driven by real-time seasonal climate forecasts. *Lancet Infect Dis* 2014;14:619-26.
11. Aguiar M, Coelho GE, Rocha F, Mateus L, Pessanha JE, Stollenwerk N. Dengue transmission during the 2014 FIFA World Cup in Brazil. *Lancet Infect Dis* 2015;15:765-6.
12. Lowe R, Coelho CA, Barcellos C, Carvalho MS, Catão Rde C, Coelho GE, et al. Evaluating probabilistic dengue risk forecasts from a prototype early warning system for Brazil. *Elife* 2016;5.
13. Guy B, Saville M, Lang J. Development of Sanofi Pasteur tetravalent dengue vaccine. *Hum Vaccin* 2010;6(9).
14. Wilder-Smith A, Yoon IK. Edging closer towards the goal of a dengue vaccine. *Expert Rev Vaccines* 2016;15:433-5.
15. Koh BK, Ng LC, Kita Y, Tang CS, Ang LW, Wong KY, et al. The 2005 dengue epidemic in Singapore: epidemiology, prevention and control. *Ann Acad Med Singapore* 2008;37:538-45.
16. Ministry of Health, Singapore (2005). Report of the expert panel on dengue. Available at: https://www.moh.gov.sg/content/dam/moh_web/Diseases%20and%20Conditions/D/Dengue/Final_Report-dengue_7_Oct_05.pdf. Accessed on 29 March 2016.
17. Farrar J MT. A global defence system to fight virus threats is urgently needed 2016. Available at: <http://www.theguardian.com/global-development/2016/feb/27/global-defence-against-virus-zika-ebola-needed>. Accessed on 1 April 2016.