Use of Prediction Models for Risk Analysis and Decision-Making in Public Health—The Catch-22 Conundrum

Dear Editor,

Shirin Kalimuddin and colleagues presented a paper on "Dengue disease modelling and forecasting: utility and limitations" in the April 2016 edition of Annals. Referencing the joint media release by the National Environment Agency (NEA) and Ministry of Health (MOH) on 18 February 2016,[1] Kalimuddin et al discussed the limitations of models and forecasting as useful tools for eliciting a response to an impending outbreak. We believe the paper misrepresents some aspects of how dengue is controlled and managed in Singapore.

We agree that, as with many scientific methods, mathematical modelling has its limitations, and we welcome the authors particularly highlighting studies such as the Ebola models. However, readers would be wrong to conclude that mathematical modelling outputs should be dismissed. In particular, the authors did not mention the many successful modelling studies that have facilitated public health policies, such as the robust regression analysis method—least absolute shrinkage and selection operator (LASSO)—behind the Singapore dengue forecast.[2] As discussed in the published paper, because LASSO is built to optimise the accuracy of prediction by the forecast model, using separate sub-models for each forecast week shows little degradation in the quality of its long-term predictions. In fact, in the past years, we have accurately predicted the large dengue outbreaks of both 2013 and 2014, and the lull year of 2015. This was enabled by a good knowledge of the overall epidemiology of dengue in Singapore, to which modelling contributes. Yap and colleagues have described the comprehensive risk analysis, in addition to the model, performed by NEA that supported the prediction of a higher number of cases in 2016, in the media release.[3]

Based on NEA's surveillance and risk analysis programme, factors such as warmer temperature, increase in mosquito population and switch in serotype of circulating virus were taken into consideration together with output from the dengue model to arrive at the dengue forecast, as elaborated below. Briefly, the 2015 El Niño phenomenon is expected to drive up the dengue incidence on both the global and regional scale. The unusually high dengue incidence observed at the beginning of 2016 was likely due to the increase in temperature caused by this weather condition. Correlation analysis of the previous peak El Niño 3.4 sea surface temperature (SST) in 1997 showed a two-tiered delayed effect on dengue cases. The dengue incidence increased 1 to 2 months after the peak of El Niño 3.4 SST, and again 7 to 8 months later—leading to the well-known 1998 dengue pandemic that affected many countries globally. This was further supported by a collaborative study where researchers analysing dengue epidemics in Southeast Asia saw a synchronised increase in dengue incidence in this region in 1998, 1 year after the 1997 El Niño simultaneously heated up this large area.[4] The 2015 El Niño 3.4 SST peaked in December and has appeared to be just as strong as that observed in 1997, thus suggesting a poor dengue outlook in 2016.

At the same time, the *Aedes aegypti* mosquito population, from NEA's Gravitrap surveillance system, showed a persistent increase from the end of 2015 to the beginning of 2016. Compared to the same period in January 2015, 50% more *Aedes aegypti* mosquitoes were caught in Gravitraps deployed islandwide. The number of *Aedes aegypti* breeding in homes found during NEA's regular inspections in early 2016 was also 50% more than in the same period in January 2015. Furthermore, NEA's and MOH's virus surveillance had detected a switch in the predominant dengue serotype (from dengue virus type 1 [DENV-1] to dengue virus type 2 [DENV-2]) towards the end of 2015. In the last 10 years, it has been observed that a change in predominant dengue virus serotype has been followed by a spike in dengue cases.[5]

NEA's studies on blood donor samples from Singapore residents, in collaboration with the Health Sciences Authority of Singapore (HSA), have shown consistently low dengue herd immunity in our resident population. Dengue seroprevalence in young adults (16 to 30 years old) was low, with serotype-specific immunity of 13.4% for DENV-1 and 16.3% for DENV-2 in 2013. Thus, the Singapore resident population remains highly susceptible to dengue.

The warmer temperatures, increase in mosquito population and change in main circulating virus serotype, juxtaposed with low dengue herd immunity of Singaporeans, support the statistical projection of dengue cases in 2016. This model has been a useful tool to support decision-making for NEA and has been continuously finetuned to incorporate more data as they become available.

Readers may erroneously assume that a pre-emptive response to a dengue outbreak involves only a surge capacity contributed by a "pool of readily available trained human resource in disease surveillance and control (that) could be activated at short notice". It is noteworthy to highlight that an effective dengue control programme involves the collective and coordinated effort of many stakeholders, including the community.[6] The article "Dengue is a community battle" in the media demonstrates such understanding, even in the lay community.[7] Besides public education and mobilisation, NEA leads an Inter-Agency Dengue Task Force (IADTF) comprising 25 stakeholders from the public, private and people (3P) sectors, to coordinate nationwide dengue control efforts. Temporal risk stratification through forecasting has allowed NEA and MOH to make a timely call for action among stakeholders through national campaigns and internal coordination.

A case in point is the media release "Dengue cases may exceed 30,000 in 2016" referenced by the authors.[6] In view of the potential risk of a severe dengue outbreak in 2016, the release was put out as a public risk communication, designed to disseminate this alert to stakeholders and the community, and advise the public on what they could do to suppress the mosquito population, such as taking appropriate precautions to prevent mosquito breeding. Risk communication is an integral part of any public health programme and it is not done lightly. It is a fundamental part of the Singapore dengue control programme which strongly focuses on interepidemic surveillance and control, risk-based prevention and intervention, and coordinated intersectoral cooperation.[6]

Internally, NEA has stepped up its outbreak response to the heightened threat alert. This includes enhanced vector surveillance with the assistance of additional temporary officers to augment the regular vector control workforce. Since then, over 350,000 home inspections have been performed, with over 3000 *Aedes* breeding sites containing approximately 100,000 larvae, removed. Islandwide Gravitrap surveillance, where 30,000 traps across 5000 Housing and Development Board (HDB) blocks have been deployed, has also removed over 20,000 adult *Aedes* mosquitoes. The risk analysis prompted NEA's earlier outbreak preparation, including stockpiling of diagnostic kits, insect repellent and insecticides.

The recent decline in dengue cases noted by Kalimuddin et al is of course highly encouraging. Though climatological drivers could have contributed to this fall, the combined impact of participation in source reduction from the community and stakeholders must be given due credit. After all, the low dengue seroprevalence of the local population and low endemicity testifies to the positive impact of such integrated vector management practice in Singapore.[8] The low seroprevalence rate among Singapore residents[9] puts Singapore in the unusual situation of being a low transmission area with a low force of infection,[10] despite being a location that is highly suited to high *Aedes* endemicity. Nevertheless, Singapore cannot rest on its laurels. The typical dengue season is approaching and a high number of cases prior to the season could serve as a launching pad that quickly drives dengue cases to epidemic levels.

As the statistician, Dr George EP Box, wisely said: "Essentially, all models are wrong, but some are useful". The use of prediction models for risk analysis and decision-making in public health is a catch-22 situation. If the outbreak occurs as predicted, it may be perceived that intervention measures were insufficient or ineffective, as they failed to mitigate the heralded outbreak, but if the actual case count is lower or higher than predicted, it is natural to infer that the model itself was inaccurate. It is clearly not feasible to observe what would happen in the absence of control efforts and validate predictions of large epidemics that require a strong response; this is one reason why no forecaster would ever claim absolute certainty, especially when pertaining to complex biological, ecological, meteorological and environmental systems, such as those governing dengue transmission. Modelling output, as much as other signs of an impending outbreak such as mosquito numbers or meteorological data, has a role to play in guiding—but not dictating—policy, and public health authorities and policy makers should not be deterred from using prediction models to guide risk communications, outbreak preparation and response.

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