

# Dengue numbers may swell again, so urgent mitigation efforts needed

The 2022 situation in Singapore bears a striking resemblance to the 2020 dengue surge, which offers actionable insights

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While the world focused on beating back the Covid-19 pandemic over the past two years, another insidious but endemic disease has spread quietly through countries like Singapore.

More than 30,000 cases of dengue have been reported in Singapore in 2022 thus far, a sixfold increase from 2021.

Although infections peaked at 1,568 weekly cases in May and seem to be on the decline at 200 to 300 a week, these numbers remain far higher than the 2021 figures.

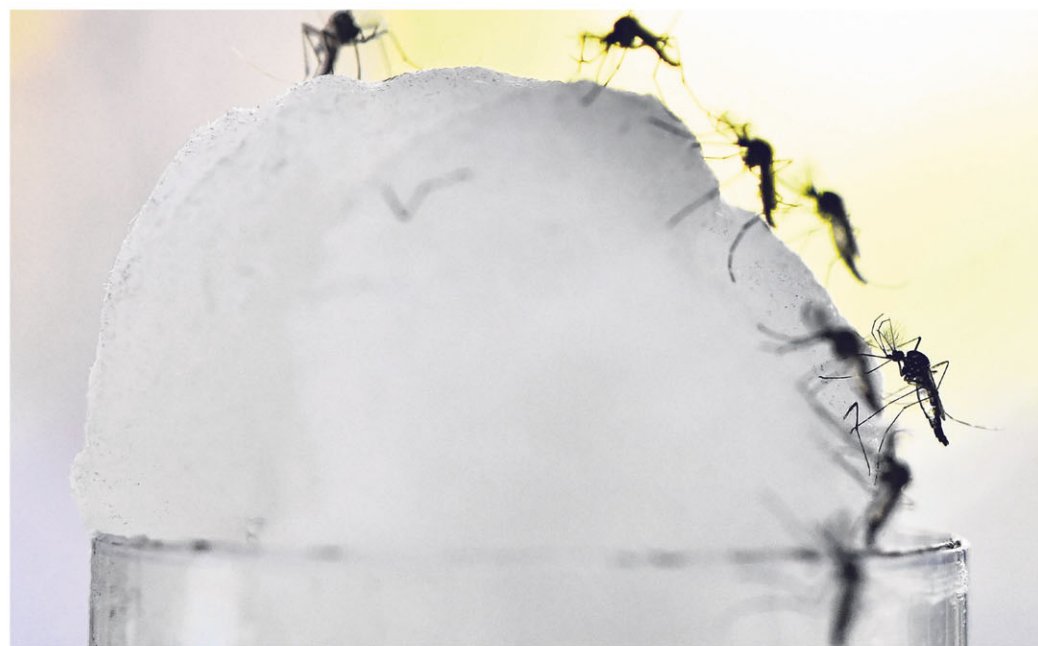
## SIMILARITIES TO THE DENGUE WAVE IN 2020

This 2022 peak bears striking similarities to a wave seen in 2020, when cases surged to 1,792 weekly infections in July, according to the National Environment Agency (NEA). This was just after the circuit breaker curbs were lifted and more Singaporeans moved around and commuted for work, leisure and other activities. In both cases, the warm mid-year weather conducive to mosquito breeding and the greater movement of people created the perfect storm.

Virological studies confirm that a distinctive version of the dengue virus known as DenV-3, a less commonly found serotype in Singapore's dengue history for which the population has low herd immunity, caused the 2020 spread. Similarly, more than 86 per cent of cases thus far in 2022 were caused by this new, more transmissible and infectious DenV-3, according to the NEA.

The dengue virus exists as four distinct serotypes. Infection with one confers protection against only the infecting serotype and not the other three. Moreover, a second infection with a different serotype can increase the risk of severe dengue symptoms.

But the 2022 spike also throws into doubt the 2020 theory that more people caught dengue because they spent more time at home during the day. If anything, the larger numbers of people returning to workplaces as Covid-19 restrictions were eased



Despite extensive measures to stem the spread of *Aedes* mosquitoes, Singapore's high population density, lowered herd immunity and an ageing population continue to place the Republic at risk of serious dengue outbreaks. ST FILE PHOTO

in Singapore and travelling overseas as border rules were relaxed might account for the heightened threat.

This is consistent with Duke-NUS Medical School's Professor Ooi Eng Eong's ground-breaking 2006 study, which proved that dengue transmission largely occurred away from homes. His research found that schools, construction sites and factories had more mosquito breeding sites than residential areas inspected and that people, especially school-age children, were more likely to contract dengue if they spent more time outside of the home.

The drop in cases in 2021 may be a blip as the surge in Covid-19 infections – which cause symptoms similar to those of dengue, such as fever, muscle aches, nausea and fatigue – may have led to dengue cases going undetected and under-reported.

## TACKLING DENGUE WITH NEW ANTIVIRALS AND VACCINES

Dengue is a major public health threat. Dubbed one of the top 10 threats to global health by the World Health Organisation just before the onset of Covid-19, the disease infects almost 400 million worldwide each year and kills about 40,000.

Based on the United States Centres for Disease Control and Prevention, approximately one in 20 patients infected with dengue can get life-threatening haemorrhagic fever, which can lead to severe bleeding and organ failure, even though most patients do not present symptoms or have

only mild symptoms. The very young, the elderly, the immunocompromised and those who are reinfected are the most vulnerable to severe dengue.

But countries have learnt from the history of medicine as well as from our collective Covid-19 experience that vaccination against endemic diseases is the most cost-effective strategy to reduce the burden of disease, and have moved swiftly to employ this strategy in tackling the scourge of dengue.

Although the currently licensed dengue vaccine in Singapore, Dengvaxia, is less effective for those with no prior exposure, the other leading vaccine, Qdenga, developed by Japanese pharmaceutical company Takeda and which uses the attenuated DenV-2 serotype as its genetic backbone, was recently approved for use by the European Union and is undergoing a fast-tracked review by the US Food and Drug Administration.

Another dengue vaccine, Butantan-DV, which uses inactivated forms of the four serotypes, has also shown promising outcomes in a recent study performed in Brazil. These vaccines should help reduce the severity and spread of dengue worldwide if clinical trials show strong efficacy and if they are eventually approved by the authorities for use.

A second lesson learnt from Covid-19 is that antiviral therapeutics can be a valuable addition to our toolbox in helping vulnerable patients manage disease symptoms. Currently, there are no licensed therapeutics

that directly target the dengue virus.

But recent phase one clinical trials carried out by Johnson & Johnson found an antiviral compound, which blocks virus replication, to be safe and effective when administered in a prophylactic setting in animals. More studies will be needed to assess the efficacy of the drug in larger population cohorts and in human beings. The authorities will also need to ensure that we get the right vaccines and antiviral therapeutics that offer protection from specific emerging dengue virus variants in Singapore.

## MAINTAIN PUBLIC VIGILANCE

Even as we keep an eye on the dengue situation and the development of useful drugs to arrest and treat the disease, Singapore should continue to be vigilant in its stringent vector control measures to stem the spread of *Aedes* mosquitoes.

Intense insecticidal treatment and site inspections of residences and commercial workplaces, complemented by persistent community education, where Singaporeans in schools and in community events are taught to perform the Mozzie Wipeout "B-L-O-C-K" steps to reduce the mosquito population by reducing breeding sites, have stemmed the spread.

However, despite these extensive measures, the high population density, lowered herd immunity due to reduced dengue transmission during the 1970s to 1980s, and an ageing population

continue to place Singapore at risk of serious dengue outbreaks.

Innovative measures to contain dengue, like Project Wolbachia, which releases male mosquitoes carrying the Wolbachia bacteria in high-risk areas to reduce the mosquito population over time, have huge potential in reducing dengue caseloads in Singapore, but will take time to play out.

Preliminary studies have shown promising results, with significant suppression of the mosquito population and dengue cases seen within one year of Project Wolbachia mosquito releases in Tampines and Yishun. Targeted releases in parts of Choa Chu Kang, Keat Hong, Hong Kah North and Bukit Gombak have also dramatically reduced the mosquito population within the vicinity of where the releases took place.

These results are consistent with studies in Brazil and Indonesia, where dengue incidences were substantially reduced following the release of modified mosquitoes. However, more research is needed to determine if the effectiveness of using Wolbachia to curb the dengue situation in Singapore can be sustained over the long term. Research should focus on examining whether the dengue virus can evolve to confer resistance against Wolbachia, or if mosquitoes in the wild can develop mechanisms to evade invasion of modified Wolbachia mosquitoes.

## MID-YEAR SWELL OF DENGUE INFECTIONS EXPECTED

Since the implementation of the vector control programme in 1973, the mosquito population in Singapore has been lowered to around two mosquito larvae found per 100 evaluated sites. Achieving complete mosquito elimination is impossible, as natural breeding habitats are created as quickly as they are removed.

With Project Wolbachia taking off, other factors such as herd immunity, increased movement and the introduction of new dengue strains and serotypes will contribute more significantly to any future spikes in the disease. Strains that are more transmissible are more likely to be dominant.

Will we see more peaks, or will dengue cases slowly taper off? Surveillance will remain important in predicting dengue outbreaks, as intensive research to pinpoint the virus' genetic sequences associated with the increased outbreaks is under way.

We may be experiencing a lull in dengue cases during the cooler year-end season before infections surge again during the warmer months of May to July – the prime season for mosquito breeding and biting activities.

But if the virus population can be successfully contained within the insect and human hosts, we may see dengue reach its endemic phase – as the numbers fluctuate at around 200 to 300 a week – until the introduction of a new DenV strain or serotype that can displace this current circulating strain.

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