



# ASEAN BIODIASPORA VIRTUAL CENTER



# DENGUE

FOCUS REPORT

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# *Dengue Hemorrhagic Fever*



## Introduction

- Dengue is a mosquito-borne viral infection that can cause a mild or severe illness.
- The most common symptoms of dengue are fever, headache, muscle and joint pain, and rash.
- Severe dengue can cause bleeding, shock, and death.
- There is no specific treatment for dengue, but it can be managed with supportive care.
- There are two main types of dengue vaccines available, but they are not yet widely available.
- The best way to prevent dengue is to avoid mosquito bites.

The WHO estimates that there are 390 million dengue virus infections per year, of which 96 million manifest clinically. The greatest burden of dengue is seen in Asia (75%), followed by Latin America and Africa.

There are a number of challenges to controlling dengue, including the rapid spread of the virus, the lack of effective vaccines, and the difficulty of controlling mosquito populations. However, there are a number of measures that can be taken to reduce the risk of dengue, such as:

- Using insect repellent
- Wearing long sleeves and pants
- Sleeping under mosquito nets
- Eliminating breeding sites for mosquitoes
- Raising awareness of dengue and its prevention

## Vaccine Update

### Dengvaxia

- The World Health Organization (WHO)'s Strategic Advisory Group of Experts (SAGE) has recommended the use of CYD-TDV vaccine with a three-dose series schedule to reduce dengue morbidity by at least 25% and mortality by 50% by 2020 (Palanichamy Kala et al., 2023).
- The vaccine should be administered to individuals aged 9 to 45 years who have tested positive for dengue (Palanichamy Kala et al., 2023).
- Pre-vaccination screening should only be implemented in countries with dengue control programs if the risk for seronegative individuals can be minimized. In areas where pre-vaccination screening is not feasible, vaccination can be considered without screening if the documented seroprevalence rates of dengue are at least 80% by the age of nine (Palanichamy Kala et al., 2023).

- Pregnant or lactating women, immunocompromised individuals, and travelers with confirmed dengue infection or seropositivity should not receive the Dengvaxia vaccine due to insufficient data at present (Palanichamy Kala et al., 2023).
- Overall, the Dengvaxia vaccine is highly effective in children aged 9 years or older who have previously been infected with dengue, as these children are at a high risk of severe disease compared to seronegative children aged 2-5 years (Palanichamy Kala et al., 2023)
- The only licensed dengue vaccine is Sanofi Pasteur's Dengvaxia®, which has now been registered in 20 dengue endemic countries, and more recently by European Union (EU) and United States (US) regulatory authorities (Thomas & Yoon, 2019).

### **Takeda QDENGGA Vaccine**

- TAK-003 is a live-attenuated dengue vaccine that has been shown to be safe and effective in clinical trials (Nascimento et al., 2022). The authors found that TAK-003-induced antibodies were able to activate all three pathways of the complement system: the classical pathway, the alternative pathway, and the lectin pathway.
- The authors also found that TAK-003-induced antibodies were able to opsonize dengue virus-infected cells. This means that the antibodies were able to coat the infected cells, making them more easily recognized and destroyed by the immune system.
- Overall, the findings of this study suggest that TAK-003 may be a promising vaccine for the prevention of dengue. However, further studies are needed to confirm these findings in humans.
- The dengue working group of the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) recently (February 23, 2023) reviewed TAK-003 performance indicating; (1) the vaccine protected seropositive recipients against all dengue and hospitalized dengue caused by infection with any serotype; (2) the vaccine protected seronegative recipients against all and hospitalized dengue due to DENV-1 and -2 infection; (3) the vaccine did not protect seronegative recipients against all dengue and hospitalized dengue due to DENV-3, and (4) the vaccine's performance against DENV-4 infection outcomes in seronegative children could not be conclusively determined due to low event numbers.

### **Country Approval**

Takeda has got authorization from Indonesia, the European Commission, and Brazilian regulators to use their two-dose vaccination (TAK-003) in persons aged 4 and up, independent of baseline dengue immune status

(Thomas, 2023).

### **Butantan Dengue Vaccine**

- The Instituto Butantan, the National Institutes of Health (NIH), and Merck (MSD) published the first results of a phase III trial in Brazil with over 16,000 participants and at least two years of disease surveillance (Thomas, 2023). The vaccine (Butantan-DV) was created with components licensed from the United States. NIH and is similar to the previously tested NIH TV003 formulation.
- • The phase III experiment began in 2016 with individuals ranging in age from 2 to 59 years old who got a single dose of vaccination and were followed for any dengue, of any severity caused by any DENV type (Thomas, 2023). The trial comprised both dengue-immune and non-immune subjects.
- Overall efficacy was 79.6%, with dengue immunes doing better (89.2%) than non- immunes (75.3%) (Thomas, 2023). Due to the low prevalence of DENV-3 and -4 during the experiment, only efficacy statistics for DENV-1 (89.5%) and DENV-2 (69.6%) are available. The trial will be held until 2024.

## **Seroprevalence Among ASEAN Member States**

### **Brunei Darussalam**

196 (78.4%) of the 250 serum samples tested positive for dengue IgM, dengue IgG, and dengue NS1 antigen (Rahman et al., 2013). Dengue IgM was found in 143 (73% of the samples). 89 (45.4%) of the samples tested positive for dengue IgG, while 148 (75.5%) tested positive for dengue NS1 antigen.

### **Cambodia**

Dengue seroprevalence was estimated using indirect IgG ELISA screening and PRNT50 assay  $f > 1:40$  for each of the 4 dengue serotypes (Manning et al., 2021). At baseline in 2018, DENV seroprevalence by indirect IgG ELISA was 37%, but confirmatory DENV neutralization assays decreased it to 22.5%. The study found an 18.9% false positivity

rate by ELISA alone, with 113 false positives and 597 true negatives.

### **Indonesia**

Dengue seroprevalence in Indonesia was studied in 30 sub-districts with children aged 1 to 18 (Tam et al., 2018). By the age of nine, 60% of sub-districts are predicted to have a seroprevalence of 70%, increasing to 83% by the age of eleven. The higher population density was associated with a higher risk of seropositivity.

### **Lao PDR**

Based on the study of Peyerl-Hoffmann et al., (2004) 225 blood samples were collected from primarily feverish patients in the Attapeu district of South Laos during the rainy season of August to

October 2001 to investigate the prevalence of dengue antibodies. One (0.4%) sample tested positive in an IgM capture ELISA, while 177 (79%) tested positive in an indirect IgG ELISA.

### **Malaysia**

In a study of Selvarajoo et al., in 2020, out of 85 respondents in Malaysia, 74.1% were positive for dengue IgG and 7.1% for dengue IgM.

### **Philippines**

Dengue seroprevalence in the Philippines is estimated to be between 80 and 85% (Flasche et al., 2019). But in a prospective cohort based study among children 9-14 years of age, 89.3% were seropositive for a previous dengue virus infection (Lopez et al. 2021).

### **Singapore**

Antibodies to DENV1 and DENV2 are more prevalent (35.8% and 36.4%, respectively, among 16 to 60-year-olds in 2013, compared to 15.4% and 7.7% for DENV3 and DENV4), consistent with these being the more common serotypes circulating in Singapore as determined by decades of virus surveillance (Ho et al., 2023). Actual immunity levels are likely to be lower than anticipated due to the high likelihood of cross-reactive antibodies between serotypes.

### **Thailand**

The indirect ELISA sensitivity and specificity of indirect ELISA were found to be about 85%, with a 74.3% overall DENV IgG positivity in Bangphae district, Ratchaburi, Thailand in 2012 and 79.4% by 2015 (Limkittikul et al., 2022). The study found that over 98% of subjects older than 25 were seropositive. Seroconversion rates were measured in paired bleeds, with rates ranging from 4.8% to 14.7%. The dominant serotype of primary DENV infection cases was identified as DENV-2, according to PRNT results.

### **Vietnam**

A study at two primary schools in Binh Thuan Province, Vietn collected sera from 961 children and tested for dengue virus serum antibodies using an ELISA (Thai et al., 2005). The antibody prevalence was 65.7%, increasing from 53.0 to 88.2% with age. The annual incidence of a first dengue infection was 11.7%. Children with dengue IgG antibodies were significantly higher in those using pit latrines, whose domestic environment contained discarded cans, and pigs.

# *Dengue In the ASEAN Region*





## Burden of Dengue

Dengue has significantly increased in recent decades, now endemic in over 100 countries across Africa, the Americas, the Eastern Mediterranean, Southeast Asia, and the Western Pacific. Asia bears 70% of the global burden of dengue, making it a global health threat (Nguyen, 2023). Dengue is no longer a regional issue but a global concern. The ASEAN dengue day theme for 2023 is "ASEAN's commitment to fight against dengue." Currently, only one dengue vaccine, CYD-TDV, has been licensed for use in 20 countries. Challenges in vaccine development include the virus's four major serotypes and the immune response to the vaccine.

Dengue in Southeast Asia has a significant economic and disease burden, with a DALY burden per million inhabitants, surpassing 17 other conditions like Japanese encephalitis, upper respiratory infections, and hepatitis B (Shepard et al., 2013).

Dengue fever has imposed a significant burden on the region, with an annual cost per capita of about US\$1.65 and 372 disability-adjusted life years per million inhabitants (Wiyono et al., 2021). The burden of dengue and COVID-19 may potentially have an impact on

epidemiological analyses, leading to an underestimation of the number of reported cases. While the situation appears to be dire, there have been some encouraging improvements.

ASEAN countries have experienced high dengue outbreaks for decades, with one of the highest rates globally (Wiyono et al., 2021). These outbreaks continue concurrently with the COVID-19 pandemic, posing significant burdens for infection control and the economy. Increased dengue cases were partly due to disruptions in the pathogen-host-vector relationship and lockdowns. The spread of dengue was exacerbated by social distancing policies, which limited coverage of preventive programs and delayed medical management due to co-infection and misdiagnosis. The population must be aware of both diseases and develop dengue vector control strategies using digitalization and remote surveillance.

Critical triage algorithms and further research are also needed to combat co-infection and misdiagnosis (Wiyono et al., 2021). Controlling the spread of COVID-19 through vaccination is also essential to reduce the pandemic's impact

# Dengue Cases in The ASEAN Region in 2023



Figure 1. Dengue Cases in the ASEAN Region from January-May 2023

As of May 31, 2023, the ASEAN Region has 165,749 reported dengue cases. Among the ASEAN member states, Malaysia, the Philippines, Thailand, and Vietnam has already reported more than 15,000 dengue cases in 2023. While Cambodia, Indonesia, Lao PDR, Myanmar, and Singapore have reported dengue cases between 1,000 to 14,999. Brunei Darussalam has no reported cases of dengue in 2023.

Dengue was a major cause of childhood deaths in the 60's, and has since been found in all ages (Rajiah, et al., 2014; Singla, 2016). A positive correlation between dengue case fatality rate (CFR) and average deprivation index (ADI) of an AMS has been observed, i.e. a high ADI may be a factor causing a high CFR.

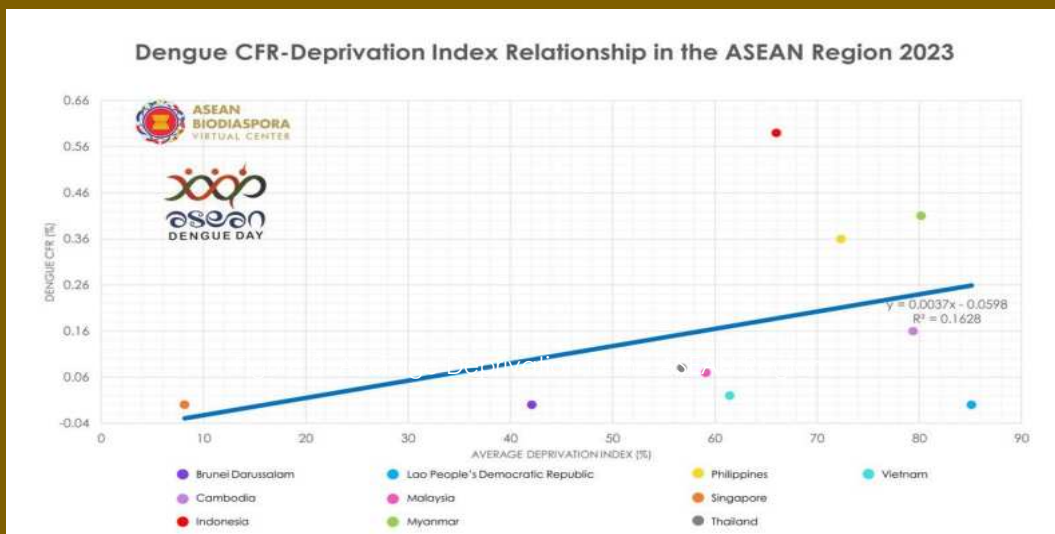


Figure 2. Dengue CFR-Deprivation Index Relationship in the ASEAN Region 2023

COUNTRY	DENGUE CASES 2022	DENGUE CASES 2023	% CHANGE	DEATHS	CASE FATALITY RATE (CFR)	AVERAGE DEPRIVATION INDEX	PREVALENCE PER 100,000 POPULATION
BRUNEI DARUSSALAM	-	-	-	-	-	42.11%(1)	-
CAMBODIA	1,125(2)	3,051(2)	171.20%	5(2)	0.16%	79.39%(1)	18.25
INDONESIA	22,331(1)	4,059(1)	-81.82%	24(1)	0.59%	66.02%(1)	1.48
LAO PDR	669(2)	2,517(2)	276.23%	0(2)	0.00%	85.10%(1)	34.60
MALAYSIA	17,497(2)	46,257(2)	164.37%	31(2)	0.07%	59.14%(1)	142.92
MYANMAR	1,516(1)	1,717(1)	13.26%	7(1)	0.41%	80.18%(1)	3.16
PHILIPPINES	44,653(3)	54,480(3)	22.00%	194(3)	0.36%	72.34%(1)	49.72
SINGAPORE	11,674(2)	3,323(2)	-71.54%	0(2)	0.00%	8.16%(1)	56.80
THAILAND	2,220(4)	16,650(4)	650.00%	14(4)	0.08%	56.78%(1)	23.85
VIETNAM	36,544(2)	33,695(2)	-7.80%	8(2)	0.02%	61.47%(1)	34.62
<b>ASEAN REGION</b>	<b>138,229</b>	<b>165,749</b>	<b>19.91%</b>	<b>283</b>	<b>0.17%</b>	<b>61.07%</b>	<b>24.85</b>

1. BlueDot Developer Portal, accessed June 14, 2023, <https://developer-portal.bluedot.global/>.  
 2. Asian Dengue Voice and Action, "Asian Dengue Dashboard," accessed June 14, 2023, <https://www.adva.asia/asian-dengue-dashboard/>.  
 3. Department of Health of the Philippines, "Statistics," accessed June 14, 2023, <https://doh.gov.ph/statistics>.  
 4. Outbreak News Today, "Thailand: Dengue Cases up in 2023," accessed June 14, 2023, <https://outbreaknewstoday.com/thailand-dengue-cases-up-in-2023/>.



Figure 4. Dengue CFR Deprivation Index Relationship in the ASEAN Region

The average deprivation score for each location, illustrating the concept of multidimensional poverty that extends beyond income. Deprivation is the harmful absence of material benefits that are regarded as essential needs in a community. Index scores vary from 0 to 100, with 0 representing the least deprivation and 100 representing the highest deprivation.

The ASEAN Region has an increase of 19.91% in reported dengue cases in May 2023 compared to the same period in 2022. Cambodia, Lao PDR, Malaysia, the Philippines, and Thailand have shown an increase in dengue cases in 2023 compared to the same period in 2022 and higher than the % change in the region.

Furthermore, Myanmar also has a higher number of dengue cases in 2023 compared to the same period in 2022; however, the % change is lower than that of the region.

On the other hand, Indonesia, Singapore, and Vietnam decreased in dengue cases in 2023 compared to the same period in 2022.

Brunei Darussalam reported 2,025 dengue cases to WHO in 2013 and 436 cases and 2 deaths (CFR: 0.46%) in 2014 (Togami et al., 2023). Reports for previous years were not provided.

The ASEAN Region has also recorded an overall 0.17% case fatality rate (CFR) in 2023. Indonesia, Myanmar, and the Philippines recorded a CFR higher than the region. On the other hand, Cambodia, Malaysia, Thailand, and Vietnam have reported a lower

CFR compared to the region. Furthermore, Lao PDR and Singapore recorded no dengue-related deaths in 2023.

The ASEAN Region has a prevalence proportion of 24.85 dengue cases per 100,000 population. Cambodia, Indonesia, Myanmar, and Thailand recorded a prevalence proportion lower than the overall prevalence in the region.

On the other hand, Lao PDR, Malaysia, the Philippines, Singapore, and Vietnam recorded a high prevalence proportion than the region.

Despite the decrease in dengue cases in Singapore and Vietnam, they still recorded a higher prevalence proportion than the region. This, however, should be interpreted with caution as prevalence may be attributed to the country's testing capacity and reporting.

Malaysia's prevalence proportion is 475% higher than the prevalence in the region and must be interpreted with caution as well.

## ASEAN Dengue Trend 2020-2023

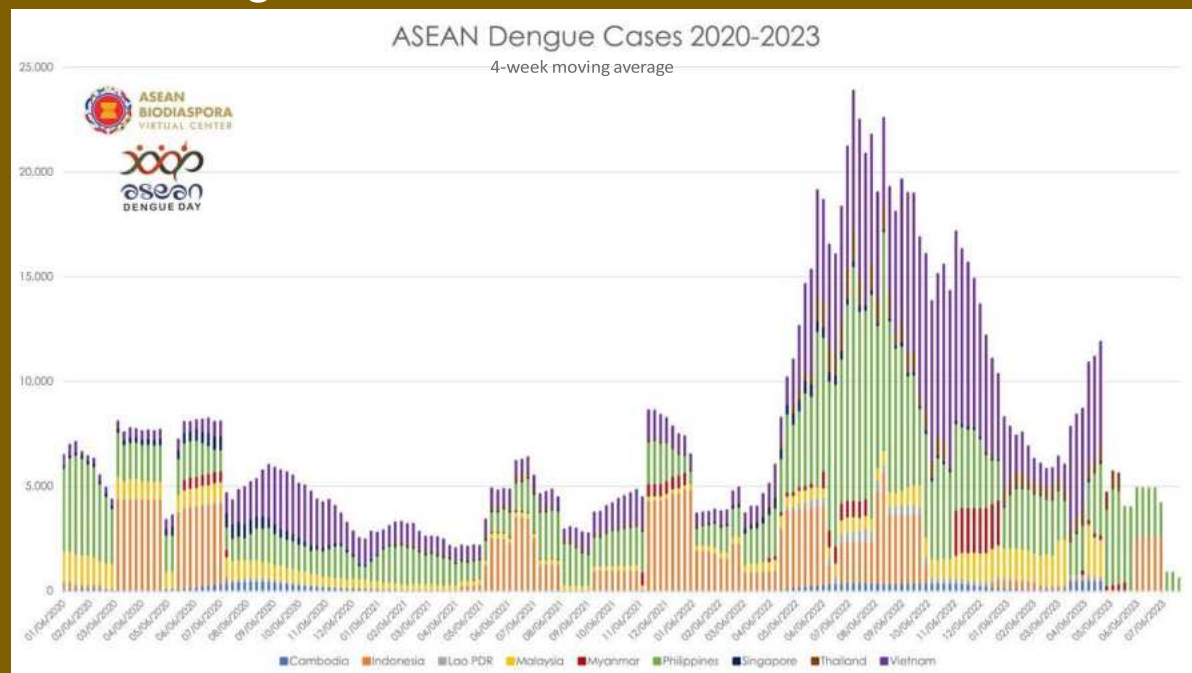


Figure 5. ASEAN Dengue Cases 2020-2023

Since 2020, dengue has been reported in all AMS, except for Brunei, which last reported cases which last reported cases in 2014. It is notable that dengue is seen year round with peaks from July to October coinciding with the rainy season and breeding season of mosquitoes and tapering until December every year (Rajiah, et al., 2014; Singla, 2016). Dengue is hyperendemic in most ASEAN Member States, where all four dengue virus serotypes (DENV-1 to -4) have circulated over different periods.

Epidemic cyclical pattern has been previously reported in Singapore (2-year epidemics during the 2004–2005 and 2013–2014 periods, associated with a switch in the predominant serotype from DENV-2 to DENV-1) (Rajarethinam et al., 2018), Vietnam (1994–2007 characteristic fluctuation in disease incidence related to the sequential replacements of dominant types)

(Recker et al., 2009) and Thailand (predominant serotypes reported were DENV1 in 2004 (56.41%), DENV4 in 2007 (50%), DENV1 in 2008 (57.41%), and DENV3 in 2010 (38.7%), DENV-4 (74%) in 2016 (74%) and DENV-3 (53%) in 2018 (Pongsiri et al., 2012; Nonyong et al., 2021). Each epidemic or fluctuation was associated with a switch in the predominant serotype. Other than switching of predominant serotypes, data from Thailand showed that importation and urbanization increases the risk of dengue outbreaks (Lim et al., 2020; Nonyong et al., 2021).

Looking at the ASEAN dengue trendline 2020-2023, there appears to be a peak of cases in 2022, contributed mostly by the Philippines and Vietnam. But there are no published data on the predominant serotypes during this period. The need for dengue serotype surveillance is emphasized to be able to predict an outbreak.

# *Dengue Cases Among Among ASEAN Member States 2020-2023*



# Brunei Darussalam

Brunei Darussalam reported 2,025 dengue cases to WHO in 2013 and 436 cases and 2 deaths (CFR: 0,46%) in 2014 (Togami et al., 2023). Reports for previous years were not provided.



# Cambodia



# Cambodia

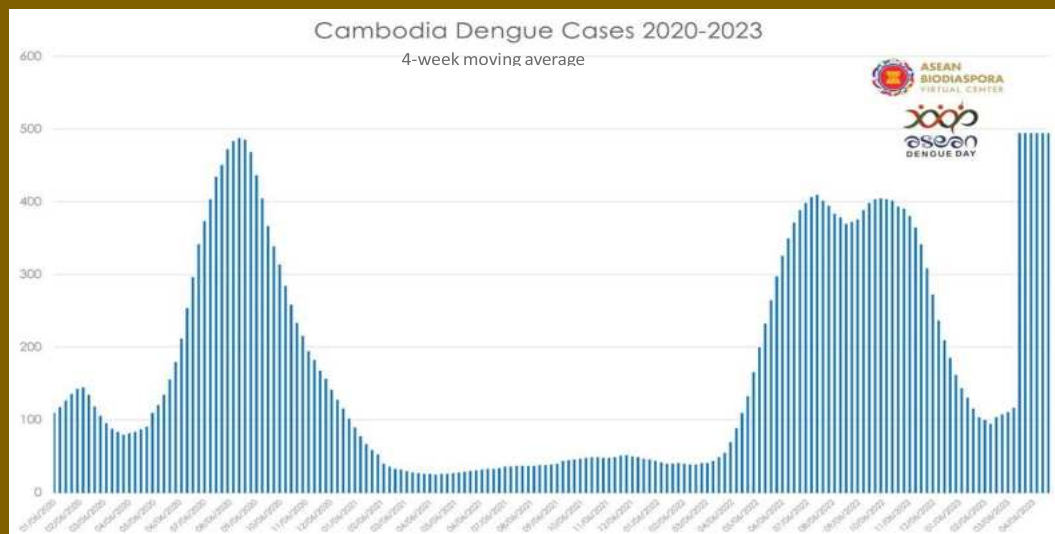


Figure 6. Cambodia Dengue Cases 2020-2023

Over the period of January to May, week 19, 1 death out of 817 cases in Cambodia was recorded in 2022, while in 2023, 4 deaths (Case Fatality Rate (CFR) 0,17%) out of 2,411 cases were reported to the National Dengue Surveillance System.

## Dengue Disease Burden in Cambodia:

Between 2002 and 2020, Cambodia registered 353,270 dengue cases (average age-adjusted incidence 1.75 cases/1,000 persons/year), with a 2.1-fold rise in case incidence between 2002 and 2020 (Yek et al., 2023). The average age of infected people grew from 5.8 years in 2002 to 9.1 years in 2020, whereas case fatality rates fell from 1.77% in 2002 to 0.10% in 2020. National statistics underestimated clinically obvious dengue case incidence by 5.0-fold (95% CI 0.2- 26.5) and overall dengue case incidence (including apparent and inapparent cases) by 33.6-fold (range: 18.7-53.6).

The mean cost per dengue case in Cambodia ranged from US\$36 to US\$75, with patients bearing the highest share of costs (Beauté & Vong, 2010). Dengue costs represent 0.03 to 0.17% of GDP, and health seeking behavior significantly impacts costs.

More accurate estimates will help decision-makers account for dengue costs, particularly among the poor, when introducing a potentially effective dengue vaccine.

## Dengue Prevention in Cambodia:

- Fumigation campaign in the capital and provinces
- Educational campaign
- Get rid of breeding places for mosquitoes • Dispose tires properly

## Surveillance:

Dengue outbreaks occur in Cambodia throughout the rainy season (May-October), but their severity varies. (Cousien et al., 2019) A technique was developed by Cousien et al., 2019 using national surveillance data that can forecast 90% of the variance in peak magnitude by April, when 10% of dengue cases are normally reported. This forecast may assist hospitals in anticipating overcrowding.



# Indonesia



# Indonesia

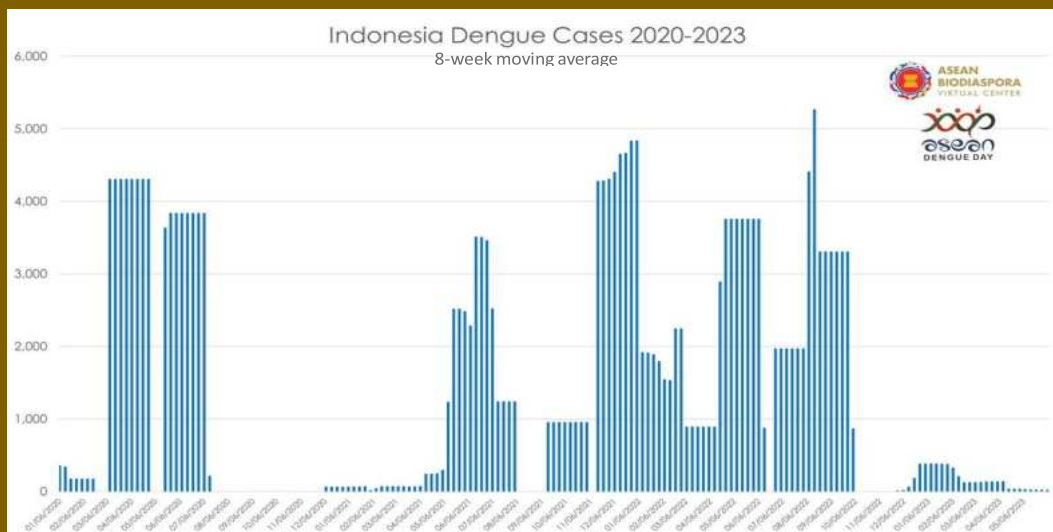


Figure 7. Indonesia Dengue Cases 2020-2023

Reported dengue cases in Indonesia from 2020 to 2023 showed a sporadic distribution.

## Dengue Disease Burden in Indonesia:

Indonesia has one of the highest dengue burdens in the world (Sasmono et al., 2020). In 2016, the national incidence rate (IR) of dengue sickness in Indonesia was 78.9 per 100,000 people, up from 50.8 in 2015. While data on dengue transmission is starting to accumulate in Indonesia, information on CHIKV and ZIKV transmission is scarce. Furthermore, due of their clinical similarities to dengue, their infection rates are frequently underestimated. Misdiagnosis is another typical occurrence. Furthermore, given the huge number of cases with an unknown cause, other infections in circulation may be undiscovered or unreported.

It is estimated that 7.8 million (95% UI 1.8-17.7 million) symptomatic dengue cases occurred in Indonesia in 2015, costing 332,865 (UI 94,175- 754,203) disability-adjusted life years (DALYs) (O'Reilly et al., 2019). The majority of dengue cases did not seek treatment or were difficult to diagnose in outpatient settings, resulting in significant underreporting. The estimated burden was concentrated in a few large cities, with 90% of dengue cases

occurring in 15.3% of the geographical area.

Dengue Prevention in Indonesia:

## Dengue-Free Indonesia with 3M Plus

- Menguras (Draining)
- Menutup (Closing of water containers)
- Mengubur (Burying and reusing used goods that have the potential to become breeding grounds for dengue-transmitting-mosquitoes)

## Surveillance:

Dengue fever has been a notifiable disease in Indonesia since 1968 and is continuously reported into the National Disease Surveillance run by the Directorate General of Disease Prevention and Control of the Indonesian Ministry of Health (Harapan et al., 2019). Reporting DHF to district health authorities by Community Health Centres (Puskesmas) and public or private hospitals is mandatory in Indonesia within 72 hours of diagnosis.

### **Dengue Vaccine in Indonesia**

Recently, Takeda submitted a Biologics License Application (BLA) to the FDA, and it was accepted for priority review (Palanichamy Kala et al., 2023). This decision was based on the recent data from the Tetravalent Immunization against Dengue Efficacy Study (TIDES) phase 3, which consisted of three parts. The study successfully met its primary and secondary endpoints. Currently, the use of TAK-003 is only approved in Indonesia for individuals aged 6 to 45 years.

A two-year update of the study evaluated 19,330 participants (96.3% of the total) to assess the cumulative efficacy of the vaccine (Palanichamy Kala et al., 2023). The evaluation was conducted 27 months after the first dose and 24 months after the second dose. The results showed that the vaccine had a cumulative serotyping-specific efficacy of 72.7% (with a range of 50.4% to 90.8%).

The efficacy rates were 74.8% for individuals who had not been previously infected with dengue, and 67% for those who had been previously infected and hospitalized due to dengue (Palanichamy Kala et al., 2023). Fifteen cases of severe dengue, as defined by the World Health Organization (WHO) or the Dengue Case Severity Adjunction Committee (DCAC), were reported. Overall, the vaccine demonstrated a cumulative efficacy of 81.2% against severe dengue.

Immunogenicity studies revealed a decrease in antibody titers specific to DENV-2 compared to those for DENV-1, DENV-3, and DENV-4 (Palanichamy Kala et al., 2023). This suggests that additional booster doses may be necessary if the data after three years confirms the same trends.

### **Wolbachia Technology in Indonesia**

The World Mosquito Program (WMP) in Indonesia is a global, not-for-profit initiative aimed at protecting local communities from mosquito-borne diseases (Utarini et al,

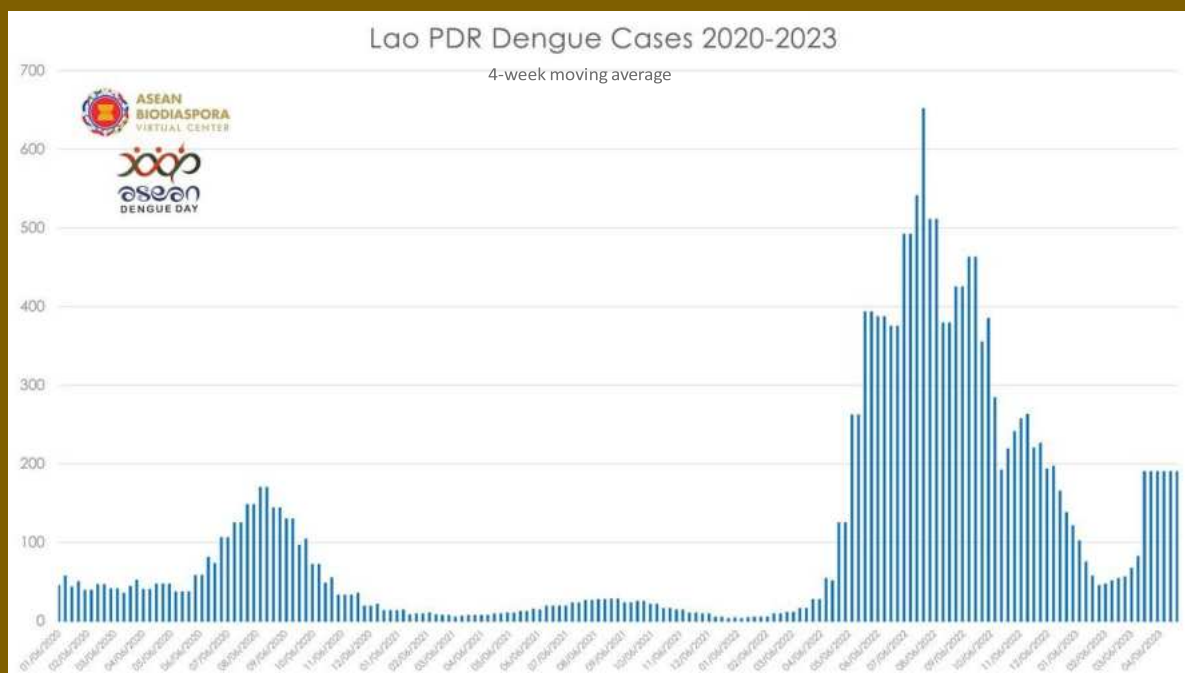
2021). Since 2012, WMP has worked in Indonesia, protecting nearly two million people from dengue and other mosquito-borne diseases. The program has three project sites, reaching 1,760,000 people and covering 539 sq. km. In Yogyakarta and neighboring Sleman and Bantul districts, the project was funded by Yayasan Tahija and implemented in partnership with Universitas Gadjah Mada. The first randomized controlled trial in 2020 showed a 77% reduction in dengue incidence in areas treated with Wolbachia (WMP, 2023a). The program is now evaluating its impact on dengue and other mosquito-borne diseases transmission. In 2023, the program began working in Denpasar and Buleleng, Bali, using Wolbachia technology to "dengue-proof" Bali. The technology has an 88% public acceptance in Yogyakarta, 95% in Sleman District, and 90% in Bantul District.

### **10-year-Trend of Dengue in Indonesia**

Dengue fever is a highly prevalent mosquito-borne viral disease with a high incidence in over 128 countries. Indonesia, a hyperendemic country, has experienced an increase in dengue cases in the last decade (Maula et al., 2018). Indonesia contributed 5.90% to 1,625 dengue-related documents from the SEA region, with the highest publication growth rate in the ASEAN region at 28.87%. The main research topics in the first five years were insect vector and diagnostic method, but in the last five years, other topics like disease outbreak, dengue virus, and dengue vaccine emerged. In the last decade, dengue publications' growth in international journals improved significantly, despite a lower number of publications compared to other SEA countries. Efforts should be made to improve the quantity and quality of publications from Indonesia, and stakeholders and policymakers should develop a roadmap for future dengue research.

# Lao People's Democratic Republic





Lao PDR dengue trend shows year-round distribution with cases starting to peak from June each year from 2020 to 2022, and then tapering down by December. The epidemic in 2022 seen in Lao PDR's dengue trend needs to be correlated with a serotype shift.

#### Dengue Disease Burden in Lao PDR:

Dengue fever is a major public health concern in Lao PDR (Senavong et al., 2021). There have been dengue epidemics in the past: 17,500 cases in 1998 and 2003, 22,890 cases with 46 deaths in

2010, and 44,171 cases with 95 deaths in 2013. The Ministry of Health collaborated with WHO to develop treatment guidelines for dengue patients, provide clinical training at hospitals, and establish laboratory and surveillance systems in five provinces (Champasack, Savannakhet, Laungphrabang, Laun

According to the National Central Laboratory and Epidemiology (NCLE) report, the CFR jumped from 0.18% (nine deaths out of 4,959 cases) in 2013 to 0.98% in the 2018 outbreak. Surveillance:

Veronese et al. (2015) analyzed national dengue surveillance data from 2006 to 2012, finding an annual dengue notification rate of 62-367 cases per 100,000 population. The country has experienced geographical expansion of transmission and co-circulation of all four dengue virus subtypes. The Lao People's Democratic Republic Early Warning Alert and Response Network was introduced in 2008 to provide automated early warning for outbreaks and epidemics. Village outbreaks are primarily notified through event-based surveillance, while the weekly indicator-based system assesses annual epidemic cycles. Dengue case data shows a high and increasing disease burden, and efforts should focus on using available data to prompt more effective outbreak response and guide intervention strategies.

# Malaysia



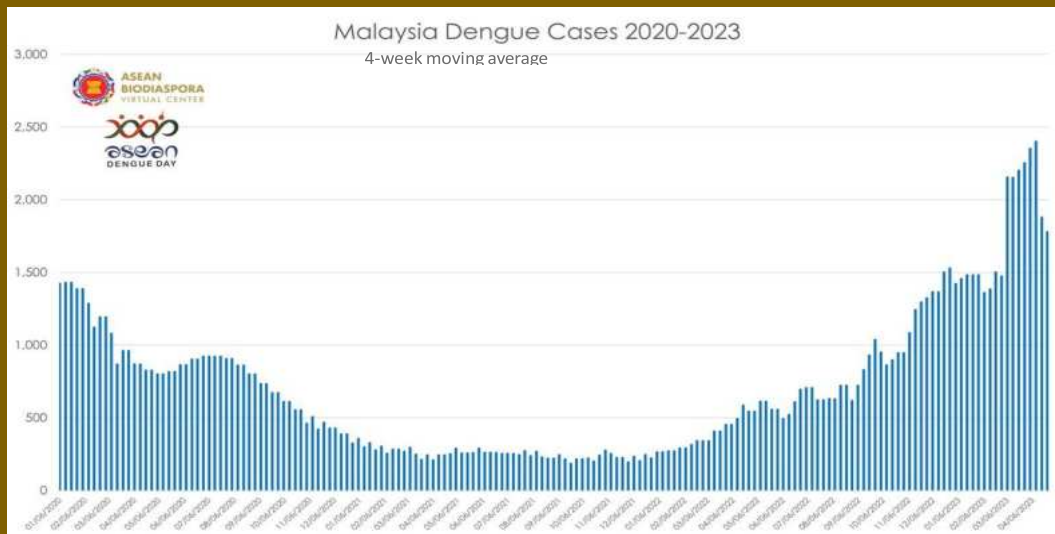


Figure 8. Malaysia Dengue Cases 2020-2023

Malaysia has an increasing trend of dengue cases. The cases in 2023 are higher compared to the same period in 2022. This may be a continuation of the epidemic observed in 2022.

#### Dengue Disease Burden in Malaysia:

Between 2016 and 2019, the regional incidence of dengue fever (DF) was higher than dengue-like fever (DHF), with rates ranging from 13.29-1107.94 and 0-8.99 per 100,000 population, respectively (AbuBakar et al., 2022). The most comprehensive data were reported by Mallhi et al., which found that 667 dengue cases were hospitalized between 2011 and 2013 in Kelantan, Peninsular Malaysia. The mean length of hospital stay was  $4.88 \pm 2.74$  days, with 49.2% of the cases being hospitalized for a prolonged period of >3 days. Among hospitalized patients, 11.1% were diagnosed with DHF and 0.8% met the criteria for dengue shock syndrome.

The total aggregated annual national cost of dengue illness was estimated at \$68.9 million, with the private sector accounting for 45.1% and the public sector 54.9% (AbuBakar et al., 2022). Direct costs represented 33% of the total cost, and indirect costs represented 67%.

Average household days lost due to dengue ranged from 11.2 to 18.7, with the overall household impact being

higher for hospitalized than ambulatory cases (AbuBakar et al., 2022).

#### Dengue Prevention in Malaysia:

Reduce the number of adult mosquitoes in your house (DOSH Malaysia, n.d.). This includes:

- Removing any standing water around your home, such as in buckets, flowerpots, and tires.
- Keeping your gutters clean and free of debris.
- Repairing any holes in screens on windows and doors.

Clean your environment (DOSH Malaysia, n.d.). This includes:

- Sweeping your yard regularly to remove any leaves or other debris that could collect water.
- Keeping your trash cans covered.
- Planting mosquito-repelling plants, such as citronella or lemongrass.

Prevent further mosquito bites (DOSH Malaysia, n.d.). This includes:

- Wearing long sleeves and pants when you are outdoors.
- Using insect repellent that contains DEET or picaridin.
- Applying mosquito nets to your windows and doors.

# Myanmar





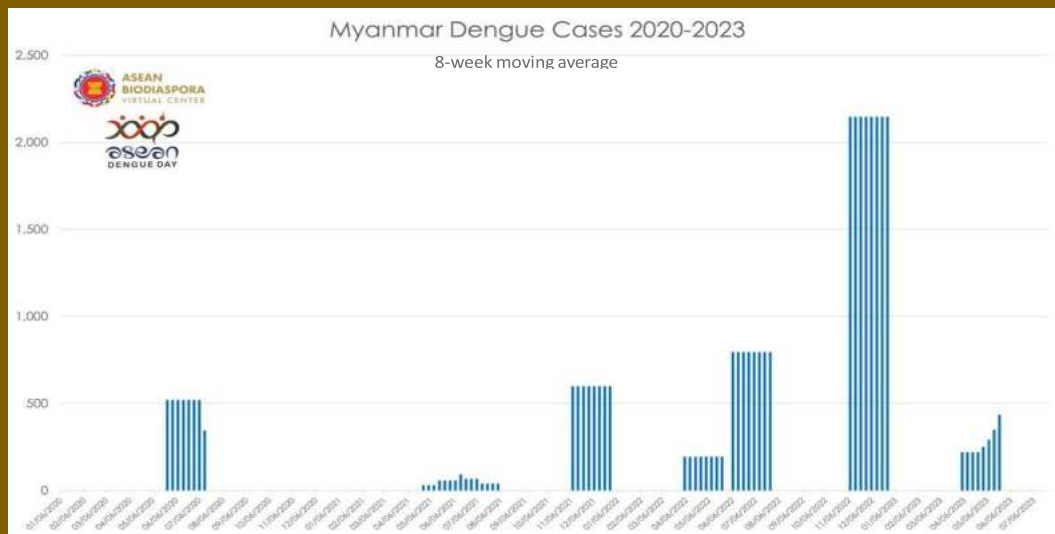


Figure 9. Myanmar Dengue Cases 2020-2023

Myanmar recorded sporadic cases of dengue from 2020-2023. The data should be interpreted with caution.

#### Dengue Disease Burden in Myanmar:

Between 2011 and 2015, Myanmar experienced 89,832 cases and 393 deaths in hospitals, with 97% of cases being in children (Oo et al., 2017). The distribution of dengue deaths mirrored the distribution of cases, with 84% occurring in the wet season and 54% in the delta/lowlands. The highest case fatality rate (CFR) was in 2014 at 7 per 1000 dengue cases, with high CFR per 1000 observed in infants <1 year, adults ≥15 years, those with disease severity grade IV, and those residing in hilly regions. The Myanmar vector-borne diseases control (VBDC) program has collected data on dengue cases, dengue deaths, and vector control measures since 1970 (Oo et al., 2017). However, there is a pressing need to collate, analyze, and interpret this information, particularly to generate location-specific spot maps of the burden of dengue in the country. This study aimed to describe the burden of dengue disease, dengue control measures, and serotype patterns in Myanmar over 5 years between 2011 and 2015. The study aimed to describe public hospital-reported cases of dengue and deaths, dengue vector control measures, and serotype patterns of dengue virus from selected states/regions identified in the National Health Laboratory.

#### Dengue-Prevention Strategy in Myanmar:

The National Dengue Control Strategy aims to reduce dengue and hepatitis B and C incidence rates by implementing effective disease and vector surveillance systems, disease prevention through selective vector control, emergency preparedness, prompt case management, increased community awareness, and improved management and technical support systems (Oo et al., 2017). Measures include larval control using insecticide granules, mosquito control using space spraying, and health education from VBDC teams. The strategy also includes increased awareness of DF/DHF prevention, control, and management through information, education, and communication.

#### Surveillance:

Dengue cases diagnosed by WHO criteria are notified to the health department, which implements dengue source reduction measures (Oo et al., 2017). Data is collected weekly from 90% of public hospitals in Myanmar. During outbreaks, daily reporting occurs, and the data is transferred to the Central VBDC Programme at the Department of Public Health. The Ministry of Health and Sports also reports to WHO SEARO through the WHO Country Office of Myanmar.

# Philippines



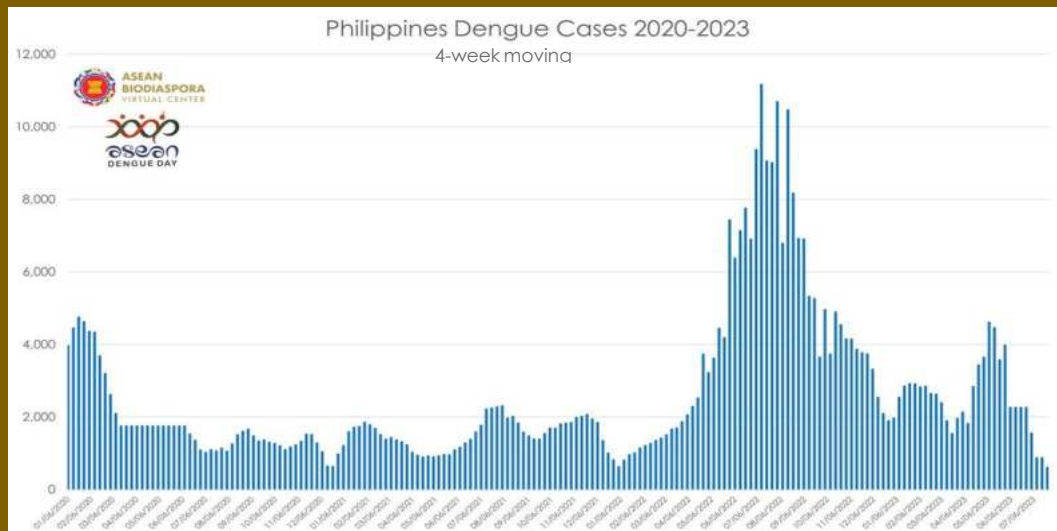


Figure 10. Philippines Dengue Cases 2020-2023

The Philippines recorded an epidemic with the highest cases of dengue in 2022 between May to October. However, the Philippines recorded higher cases in 2023 compared to the same period in 2022.

**Dengue Disease Burden in the Philippines:**

It is estimated 794,255 annual dengue episodes (95% CI: 463,000-2,076,000) and a disease

burden of 535 (95% CI: 380-994) DALYs per million population using age weights and time discounting and 997 (95% CI: 681-1,871) DALYs per million population without age and time adjustments based on surveillance data from the Philippines from 2010 to 2014 (Undurraga et al., 2017).

Dengue fever imposes a significant burden in the Philippines, over ten times the estimated rabies burden, around double the burden of intestinal fluke infections, and roughly 10% of the burden of tuberculosis (Undurraga et al., 2017). The estimations should help policymakers and improve public awareness.

**Dengue Vaccine in the Philippines**

The Philippines was the first country to implement Dengvaxia on a wide scale in high-risk areas, targeting approximately 1 million children aged 9 to 10 (Wilder-Smith et al., 2019). In November 2017, it was reported that there was an increased risk of hospitalization for dengue and severe dengue in vaccinees who had not previously been infected with dengue at the time of vaccination. The Philippine Dengvaxia program was halted following a reanalysis of these results. The WHO

Global Advisory Committee on Vaccine Safety investigated 14 deaths but was unable to determine causality (Thomas & Yoon, 2019).

**Dengue-Prevention Strategy in the Philippines:**

- Enhanced 5S Strategy (DOH Philippines, n.d.)
  - S - eek Early Consultation
  - S - elf Protection Measures
  - S - ay yes to fogging only during outbreaks
- Continuous DOH augmentation of insecticides such as adulticides and larvicides to LGUs for outbreak response (DOH Philippines, n.d.).
- No dengue vaccine is available in the Philippines.

**Surveillance:**

- Case Surveillance through Philippine Integrated Disease Surveillance and Response (PIDSRS)
- Laboratory-based surveillance/ virus surveillance through the Research Institute for Tropical Medicine (RITM) Department of Virology, as a national reference laboratory, and sub-national reference laboratories
- Vector Surveillance through DOH Regional Offices and RITM Department of Entomology

# Singapore



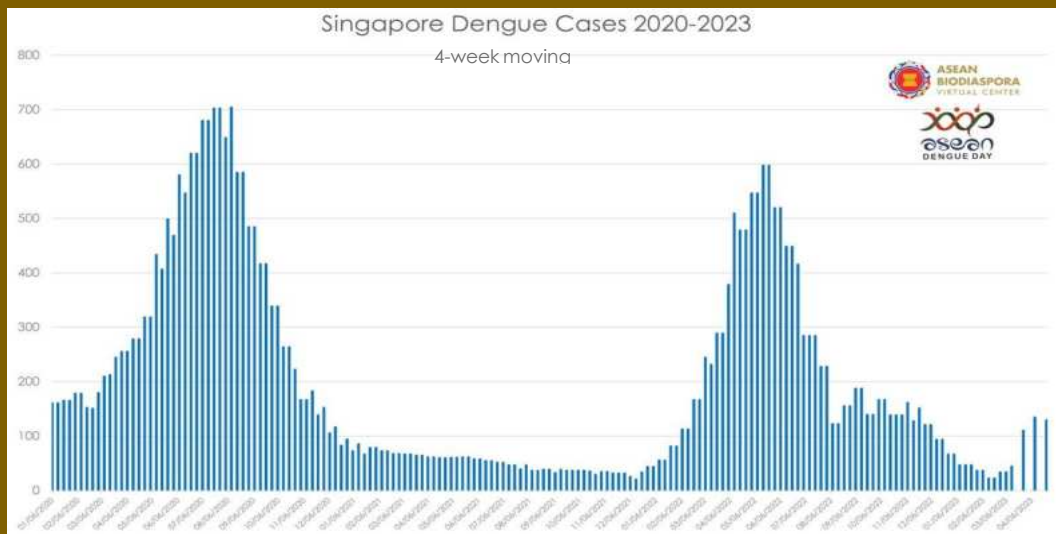


Figure 11. Singapore Dengue Cases 2020-2023

In the week 19 of 2023, there is 65% decreased compared to the same period in 2022 at 100 dengue cases leading to a total of 3,067 cases in Singapore.

#### Dengue Disease Burden in Singapore:

From 2010 to 2020, annual reported dengue case counts increased from 2,767 in 2017 to 35,315 in 2020 (Soh et al., 2021). The largest age group affected the most, with individuals aged 25-34 being the most affected. The burden was lower in children and adolescents, with individuals aged 17 and below comprising around 10% of reported dengue case counts. The total economic cost of dengue from 2010 to 2020 was estimated to be US\$1.014 billion, with higher costs after age-dependent symptomatic rates. The human capital method resulted in significantly higher costs, driven primarily by increased costs of deaths. The indirect costs, such as work productivity loss, also contributed to the costs (Soh et al., 2021). The estimated economic costs from dengue per year closely followed annual reported dengue case counts, with low costs in suppressed years and high costs in elevated years.

#### Dengue Prevention in Singapore:

- Stop dengue with Mozzie Wipeout B-L-O-C-K (NEA Singapore, n.d.)
  - B – reak up hardened soil
  - L – ift and empty flowerpot plates
  - – verturn pails and wipe their rims
  - C – hange water in vases
  - K – eep roof gutter clear and place BTI insecticide
- NEA Produces Wolbachia mosquitoes to prevent females from producing offspring .
- Dengvaxia for use only by Singaporeans aged 12 to 45 who have already been infected with at least one dengue strain (MOH Singapore, 2022). The vaccine is given in three doses over a period of 12 months.

#### Surveillance:

Based on the circulating dengue virus serotypes, EHI has created a dengue epidemic alert system (National Environment Agency, 2023). The viral surveillance system, along with case surveillance (by MOH), vector surveillance (by NEA), and ecological monitoring, form the four pillars of vector-borne illness surveillance in Singapore.

# Thailand



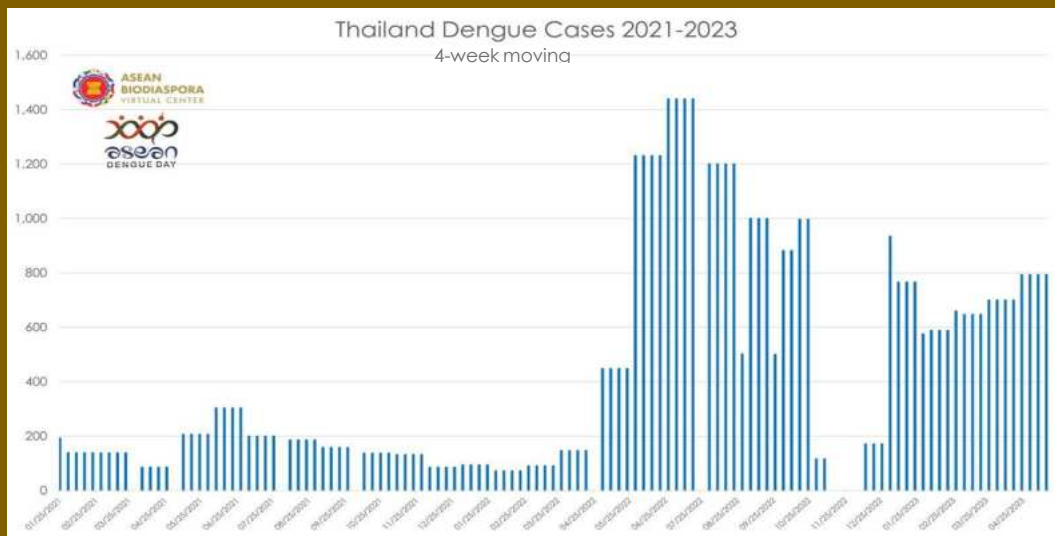


Figure 12. Thailand Dengue Cases 2020-2023

Thailand recorded highest dengue cases in 2022 between June to September. However, Thailand has now recorded higher cases in 2023 compared to the same period in 2022.

### Dengue Disease Burden in Thailand:

Dengue's economic burden in Thailand was assessed at US\$424 million per year in 2013, with a total unit cost of US\$793.6 in 2010. Access to healthcare services varies by demographic and socioeconomic class, which contributes to an underestimating of illness burden.

### Dengue Vaccine:

Dengvaxia has been approved for usage in Thailand since January 2017 and is suggested for children and adults aged 9 to 45 years (Pediatric Infectious Disease Society of Thailand, 2017). Dengvaxia is a safe vaccine with a 65% success rate in protecting against dengue infection. Dengue Prevention in Thailand:

Thailand's Ministry of Public Health has implemented "3 Do's" dengue prevention and control measures:

1. routinely empty or cover water-storage containers
2. appropriately dispose of rubbish
3. keep residences neat and orderly (Department of Disease Control, Ministry of Public Health of Thailand, 2016 as cited in Waewwab et al., 2020).

### Surveillance:

Dengue fever is an illness that must be reported in Thailand (Thisyakorn et al., 2022). Dengue cases, severity, and demographics of detected cases are recorded using a countrywide passive monitoring system with inherent limitations. Active and sentinel surveillance are rarely

# Vietnam





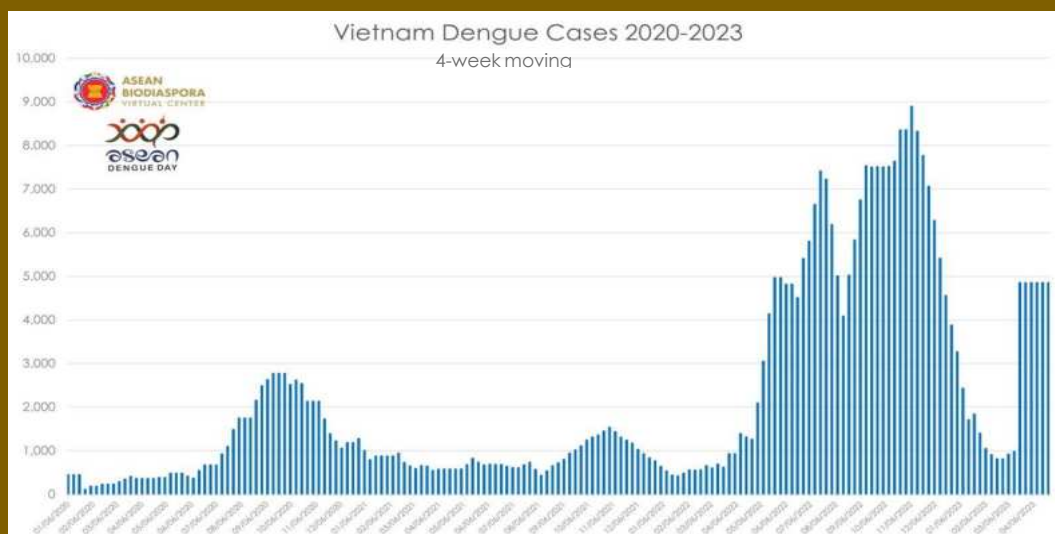


Figure 13. Vietnam Dengue Cases 2020-2023

Vietnam recorded an epidemic in 2022. Dengue cases in 2023 in Vietnam is showing same pattern as the previous year.

#### Dengue Disease Burden in Vietnam:

Dengue fever is expected to represent a significant health and economic burden in Vietnam (Hung et al., 2018). According to the most recent studies, it is responsible for 39,884 disability-adjusted life years (DALYs) every year, reflecting an economic burden of US\$94.87 million per year (in 2016 prices). However, alternate burden estimates are significantly lower. This discrepancy is primarily due to discrepancies in the methods used to estimate the number of symptomatic dengue patients.

#### Dengue Prevention in Vietnam:

HCDC Vietnam (2023) has provided 7 principles in preventing dengue:

- Prevent mosquitoes from contacting water sources by covering containers with materials that mosquitoes cannot fly through.
- Use natural predators of larvae, such as fish or water bugs, to kill larvae.
- Use chemicals to kill larvae under medical guidance.
- Avoid stagnant water in containers by turning them upside down, punching holes, and covering to avoid rainwater.

- Remove scraps and garbage from water containers to prevent mosquito habitats.
- Regularly clean water containers by changing and scrubbing them periodically.
- Use water storage directly from faucets or tanks with tight lids.

Since 2006, the World Mosquito Program (WMP) has been working in Vietnam to introduce *Wolbachia* into *Aedes aegypti* mosquitoes, responsible for transmitting dengue, Zika, and chikungunya (WMP, 2023b). The WMP has released *Wolbachia*-carrying mosquitoes in two locations: Tri Nguyen Island and Vinh Luong. The successful releases have reduced dengue incidence, with cases decreasing by 75% in Tri Nguyen Island. The WMP is expanding the release of *Wolbachia*-carrying mosquitoes to become the dominant strain of *Aedes aegypti* in Vietnam, aiming to protect the population from dengue and other mosquito-borne diseases.

There is no dengue vaccine approved in Vietnam

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