



## ANRS | MIE Scientific Days in Vietnam

*Towards ending epidemics*

15<sup>th</sup> to 16<sup>th</sup> of November, 2023

# Dengue control: Status quo, challenges and Prospects

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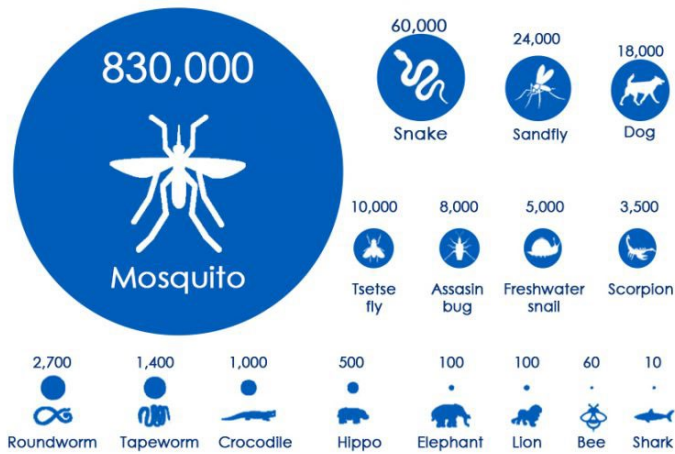


- Dengue burden
- Dengue response
- Challenges
- Prospects
- Solutions

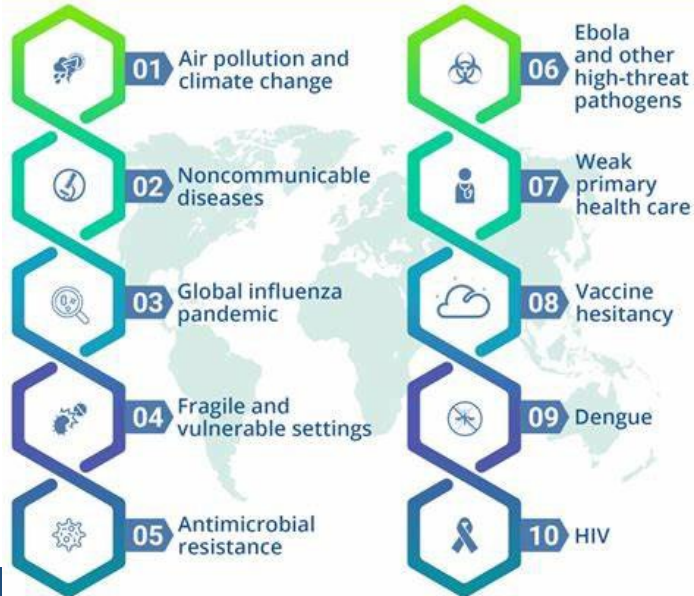
# Dengue burden



Number of People Killed by Animals per Year



## Ten Threats to Global Health in 2019



**390mn**  
annual dengue virus infections globally



**3.9bn**  
people are at risk of dengue infections

**Risk of infection**  
in 129 countries

**Most dengue cases reported in 2019**

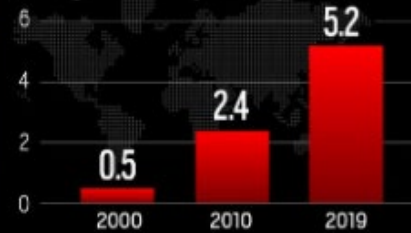
**Dengue cases** reported to WHO rose over 8-fold in last 20 years

**Deaths** due to dengue up from 960 in 2000 to 4,032 in 2015

**Dengue is now endemic** in more than 100 countries



**Dengue cases (million)**



Source: WHO estimates | Graphic: Somrat Sharma, Sarfaraz



## DENGUE IN ASIA THE NUMBER STORY

**ASIA**  
IS THE MOST IMPACTED REGION WITH ABOUT **75%** OF THE GLOBAL BURDEN OF **DENGUE**



### HOTSPOTS IN ASIA

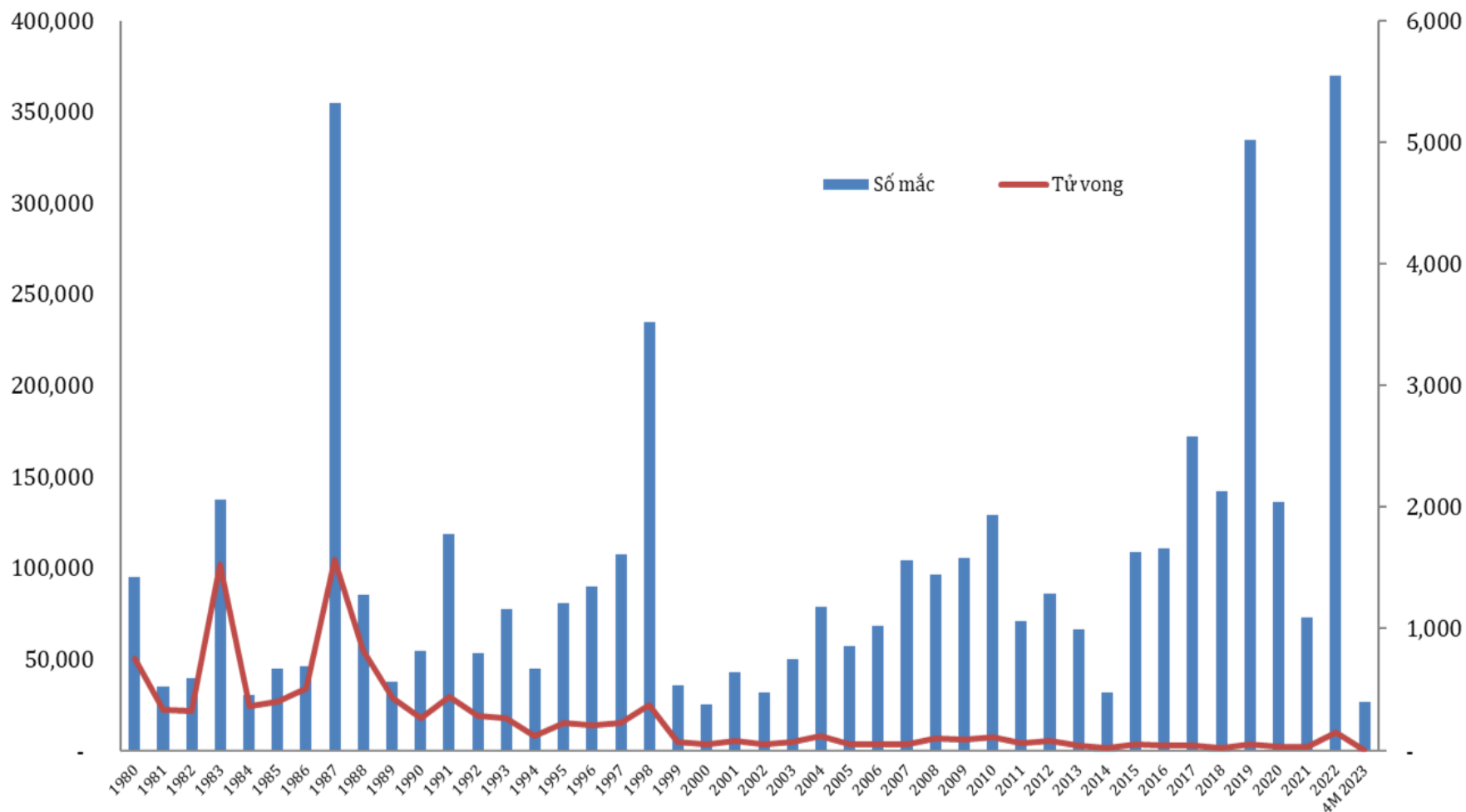
PHILIPPINES 166,107 CASES  
THAILAND 150,454 CASES  
INDONESIA 101,218 CASES  
VIETNAM 66,140 CASES  
MALAYSIA 43,346 CASES  
SINGAPORE 22,205 CASES



# Dengue burden



## Dengue infection and fatality in Vietnam during 1980 - 2023

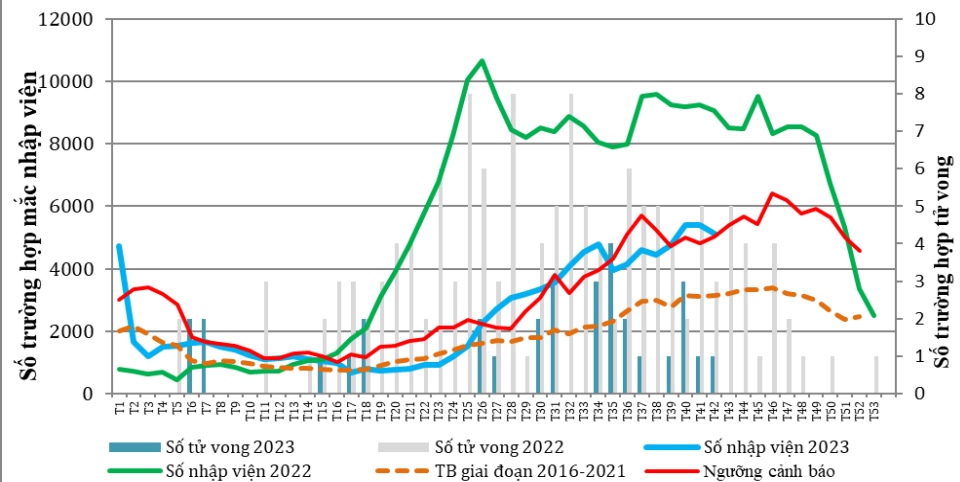


Source: General Department of Preventive Medicine – Ministry of Health

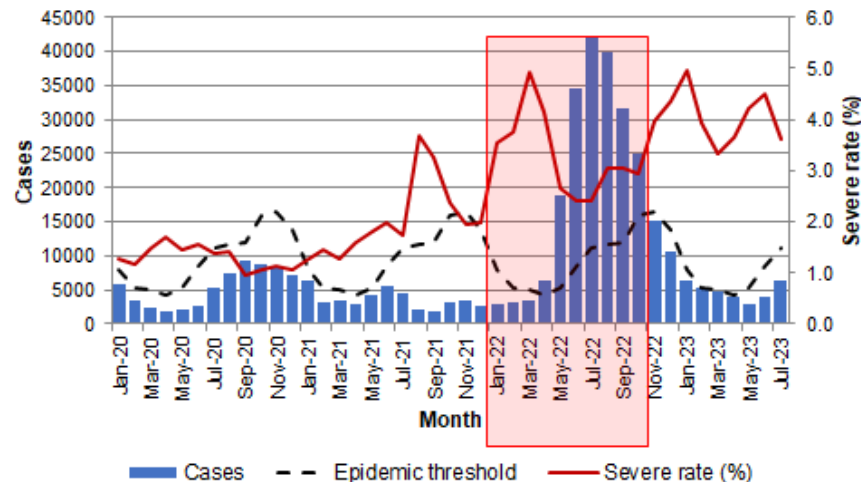
# Dengue burden



Số mắc sốt xuất huyết nhập viện và số tử vong theo tuần năm 2023 so với năm 2022

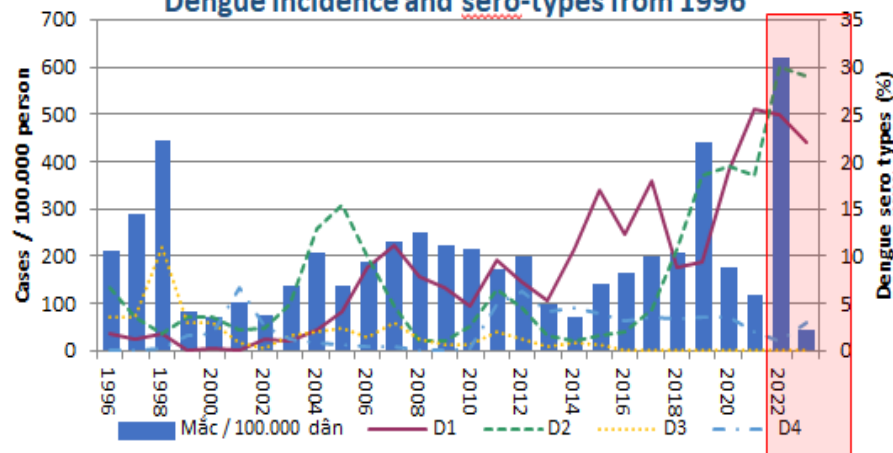


Dengue in the South from 2020 to 9/2023



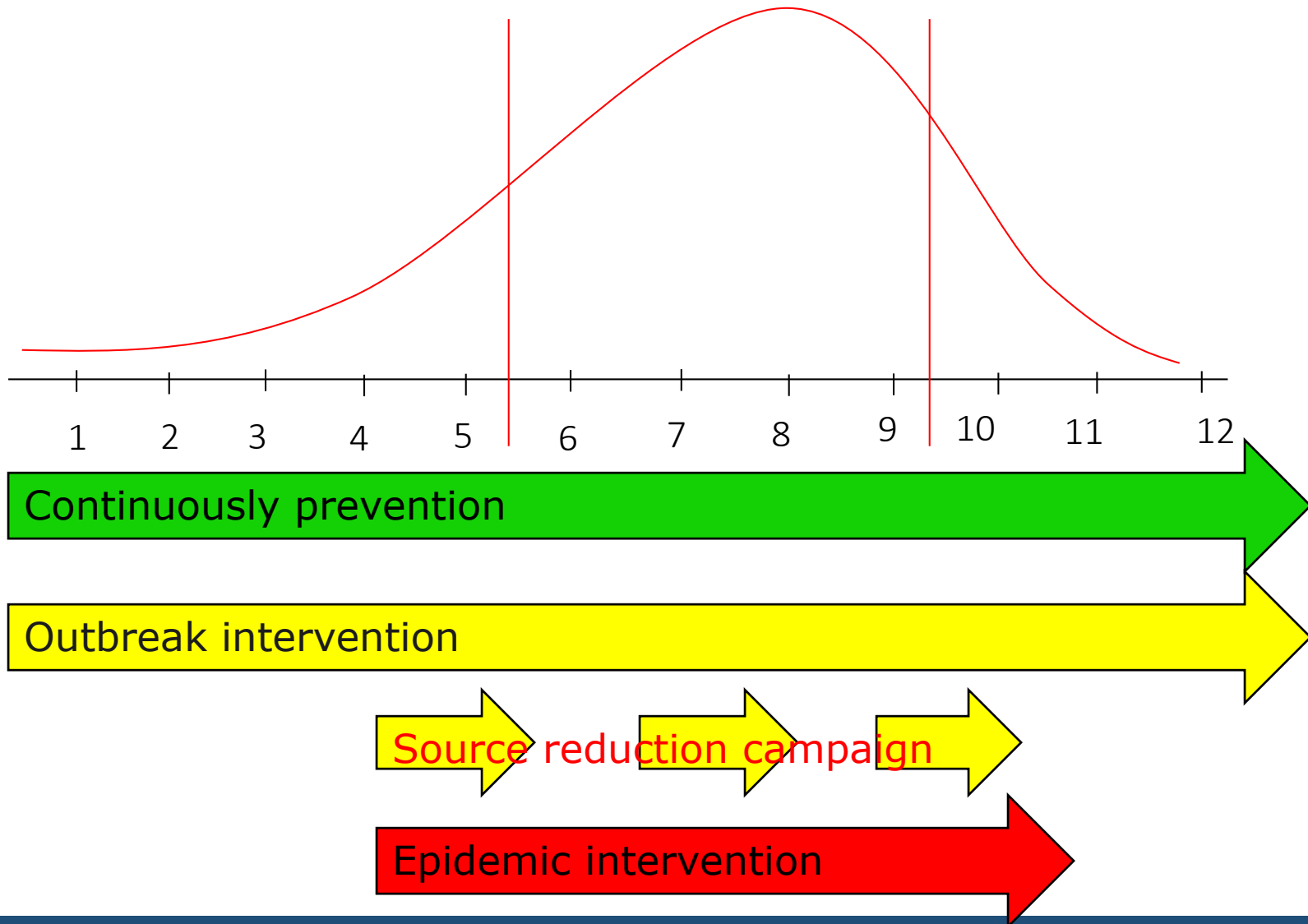
Regions	Cumulative to W42/2023		Cumulative to W42/2022	Cases discrepancy (%)
	Cases	Cases / 100,000 person		
North	37306	90.0	17669	111.1
Centre	18686	152.6	50581	-63.1
Highland	10204	239.5	18895	-46.0
South	55168	127.4	188476	-70.7
Nation	121364	119.9	275621	56

Dengue incidence and sero-types from 1996



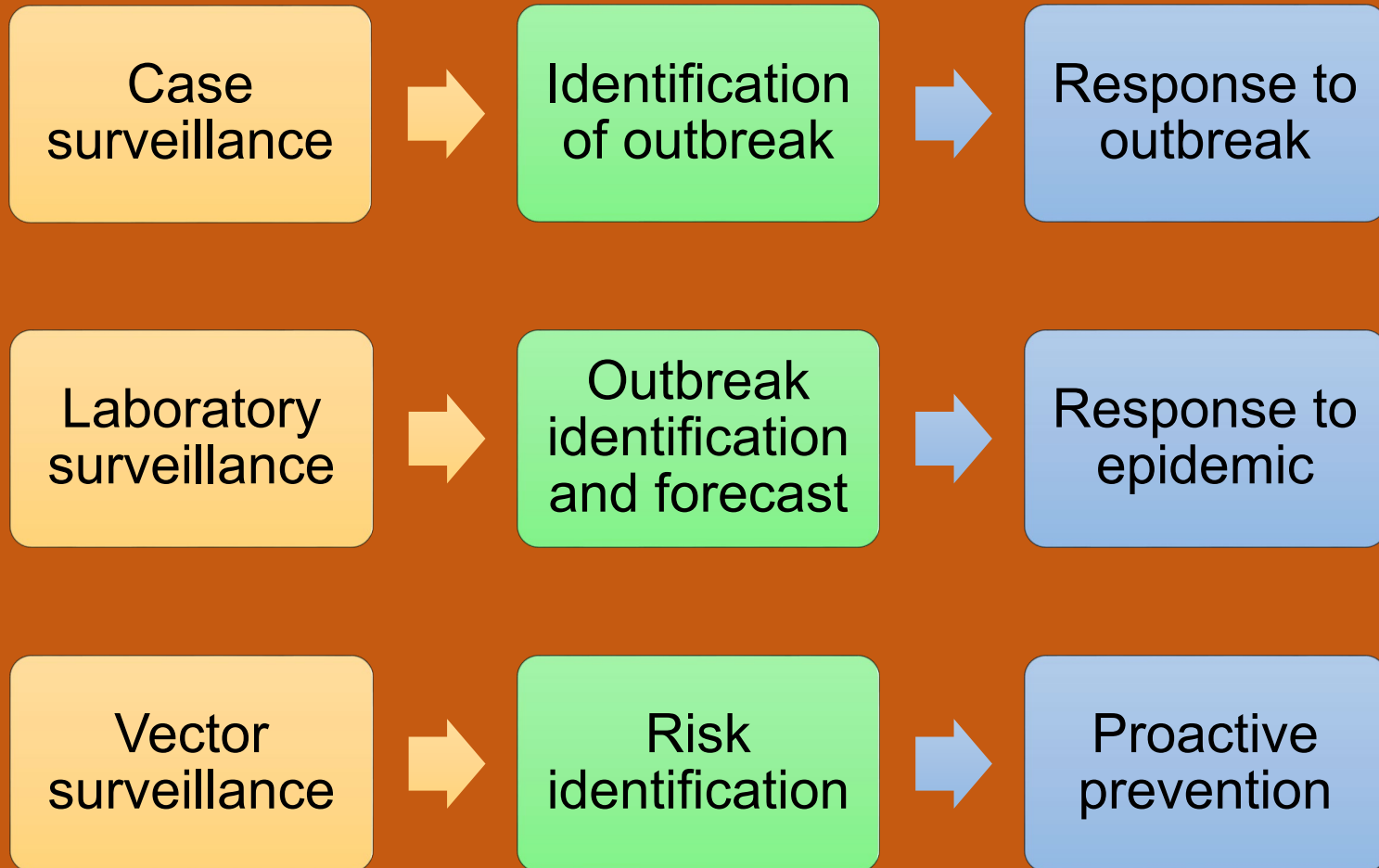
Source: General Department of Preventive Medicine – Ministry of Health

Source: Pasteur Institute in Ho Chi Minh City, Vietnam



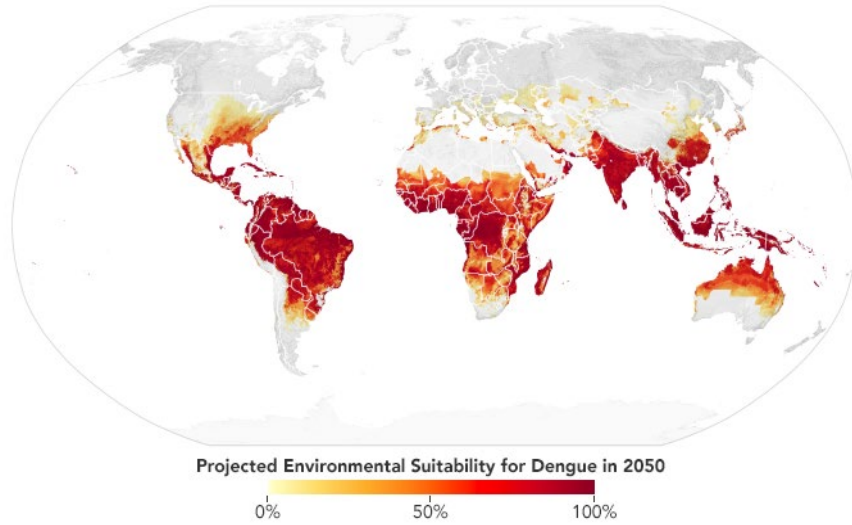


## *“Surveillance for action”*

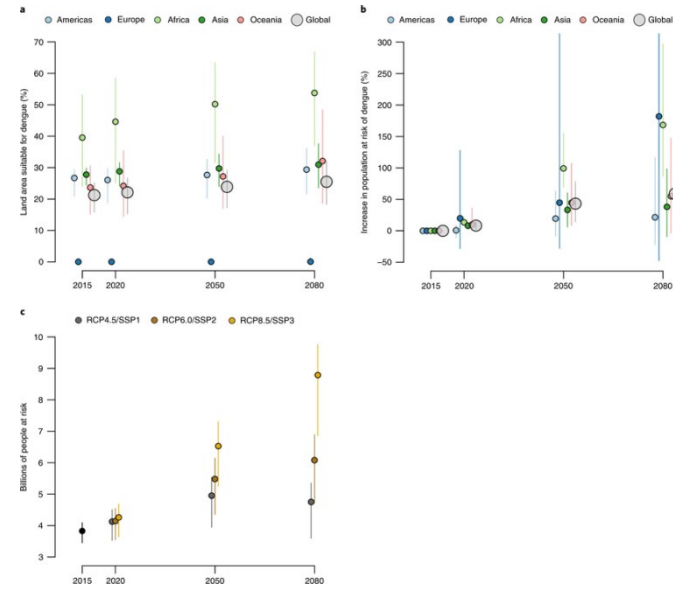




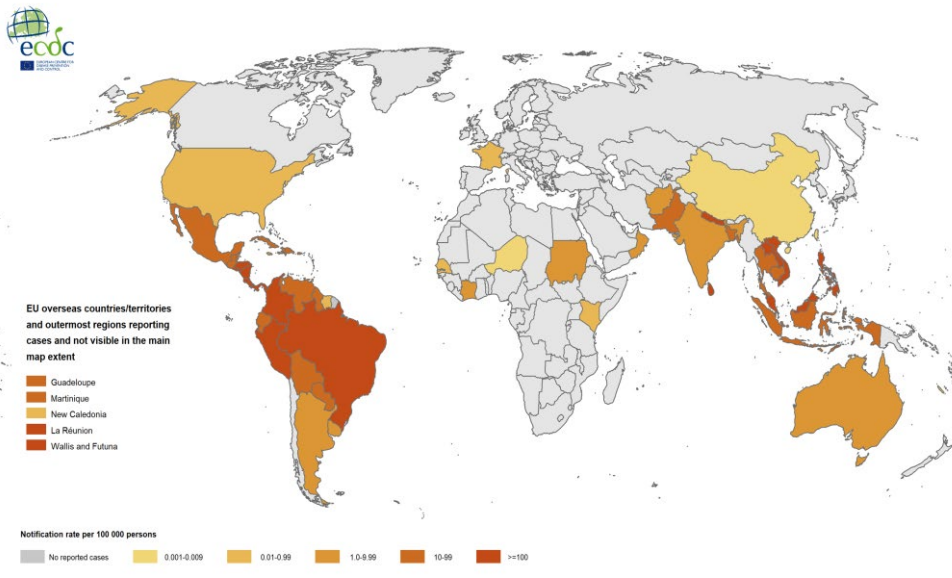
# Challenges



Source: NASA, *Of Mosquitoes and Models: Tracking Disease by Satellite*, *Of Mosquitoes and Models: Tracking Disease by Satellite* ([nasa.gov](https://nasa.gov))



Source: Jane Messina, Oliver J Brady et al, The current and future global distribution and population at risk of dengue, *Nature Microbiology* 4(9):1-8, DOI:[10.1038/s41564-019-0476-8](https://doi.org/10.1038/s41564-019-0476-8)



Note: Data refer to cases reported in the last 12 months. Administrative boundaries: © Eurographics. The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 19 January 2023

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NEWS EXPLAINER | 31 October 2023

## Dengue is spreading in Europe: how worried should we be?

The post-COVID travel boom combined with a warm summer have led to dengue outbreaks in Italy and France.

### Warming Temperatures To Spike Dengue In US, Europe: WHO Scientist

Date: 17/7/2023 9:15:15 AM

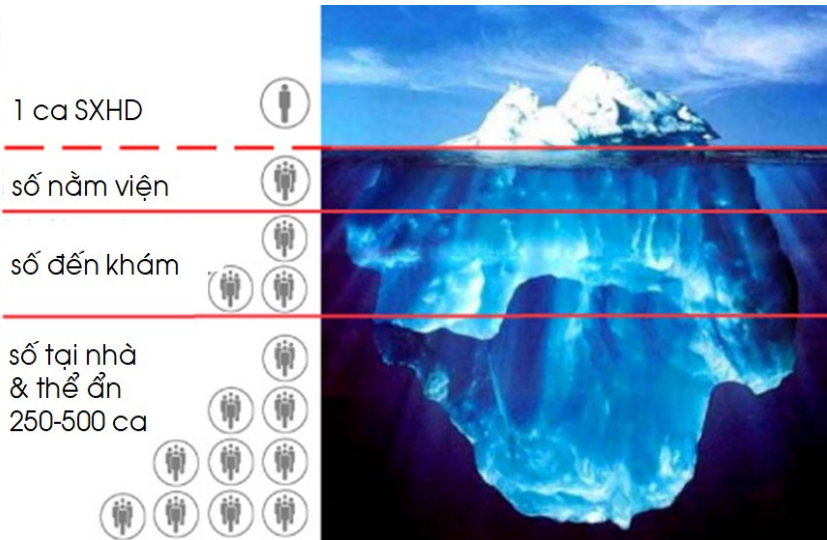
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(MENAFN- IANS) London, Nov 7 (IANS) Increasing climate change is expected to drive dengue, a mosquito-borne disease that kills thousands of people every year, to newer areas like the US and Europe, warned a scientist at the World Health Organization (WHO) calling health authorities to start preparing to combat the disease.

# Challenges



# Challenges



*Am J Trop Med Hyg.* 1988 Jan;38(1):172-80.

## A prospective study of dengue infections in Bangkok.

Burke DS<sup>1</sup>, Nisalak A, Johnson DE, Scott RM.

### Abstract

Dengue infections were prospectively studied among 4- to 16-year-old students at a Bangkok school. Blood samples were obtained from 1,757 students in June 1980, before the dengue season, and in January 1981, after the season, and tested for dengue antibodies by the hemagglutination inhibition method. Classrooms were monitored daily for school absences. Fifty percent of the children had antibodies to, and were presumably immune to, at least 1 dengue serotype by the age of 7 years. **Most (90/103, 87%) students who became infected by dengue viruses during the study period were either asymptomatic or minimally symptomatic (absent only 1 day).** Most (7/13, 53%) of the symptomatic dengue infections (absent with fever for greater than or equal to 2 days) were clinically recognized as cases of dengue hemorrhagic fever which required hospitalization. None of 47 primary dengue infections required hospitalization, whereas 7 of 56 secondary infections did ( $P = 0.012$ ). Preexistent dengue immunity, as detected by conventional serologic techniques, was a significant (odds ratio greater than or equal to 6.5) risk factor for development of dengue hemorrhagic fever.

*Epidemiol. Infect.* (2012), **140**, 491–499. © Cambridge University Press 2011  
doi:10.1017/S0950268811001191

## Under-recognition and reporting of dengue in Cambodia: a capture–recapture analysis of the National Dengue Surveillance System

S. VONG<sup>1\*</sup>, S. GOYET<sup>1</sup>, S. LY<sup>1</sup>, C. NGAN<sup>2</sup>, R. HUY<sup>2</sup>, V. DUONG<sup>1</sup>, O. WICHMANN<sup>3</sup>, G. W. LETSON<sup>3</sup>, H. S. MARGOLIS<sup>3</sup> AND P. BUCHY<sup>1</sup>

<sup>1</sup> Institut Pasteur in Cambodia, Réseau International des Instituts Pasteur, Phnom Penh, Cambodia

<sup>2</sup> National Dengue Control Programme, Ministry of Health, Phnom Penh, Cambodia

<sup>3</sup> Pediatric Dengue Vaccine Initiative, International Vaccine Institute, Seoul, Korea

the annual incidence ranged from 13.4 to 57.8/1000 person-seasons. During the same period, NDSS incidence rates ranged from 1.1/1000 to 5.7/1000, which was 3.9- to 29.0-fold lower than found in the capture–recapture study. **In hospitalized cases, the rate of under-recognition was 1.1- to 2.4-fold.** This study shows the substantial degree of under-recognition/reporting of dengue and that reported hospitalized cases are not a good surrogate for estimating dengue disease burden.

## Asymptomatic humans transmit dengue virus to mosquitoes

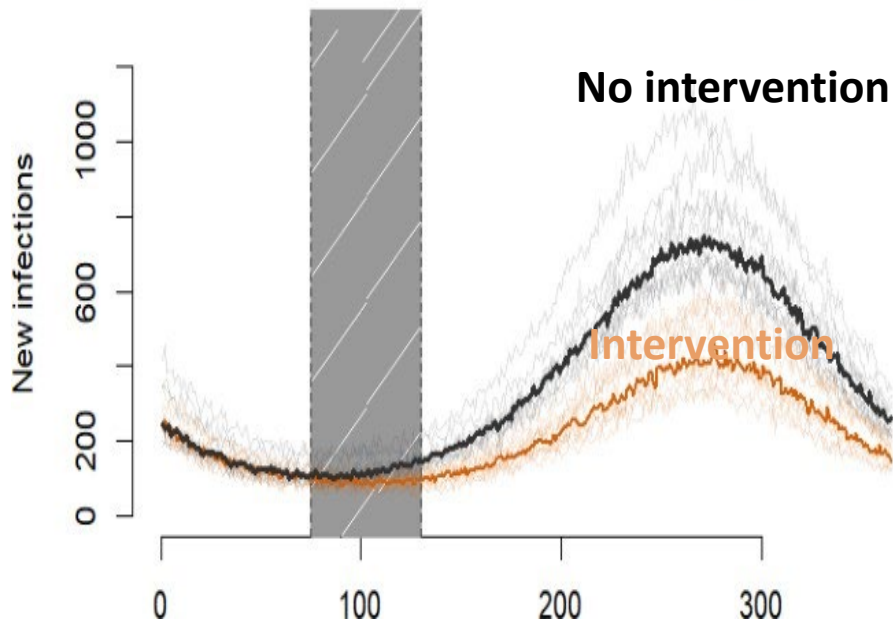
[Veasna Duong](#),<sup>a,1</sup> [Louis Lambrechts](#),<sup>b,c,1</sup> [Richard E. Paul](#),<sup>c,d</sup> [Sowath Ly](#),<sup>e</sup> [Rath Srey Lay](#),<sup>a</sup> [Kanya C. Long](#),<sup>f</sup> [Rekol Huy](#),<sup>g</sup> [Arnaud Tarantola](#),<sup>e</sup> [Thomas W. Scott](#),<sup>f,h</sup> [Anavaj Sakuntabhai](#),<sup>c,d</sup> and [Philippe Buchy](#)<sup>a,i,2</sup>

Moreover, at a given level of viremia, **DENV-infected people with no detectable symptoms or before the onset of symptoms are significantly more infectious to mosquitoes than people with symptomatic infections.** Because DENV viremic people without clinical symptoms may be exposed to more mosquitoes

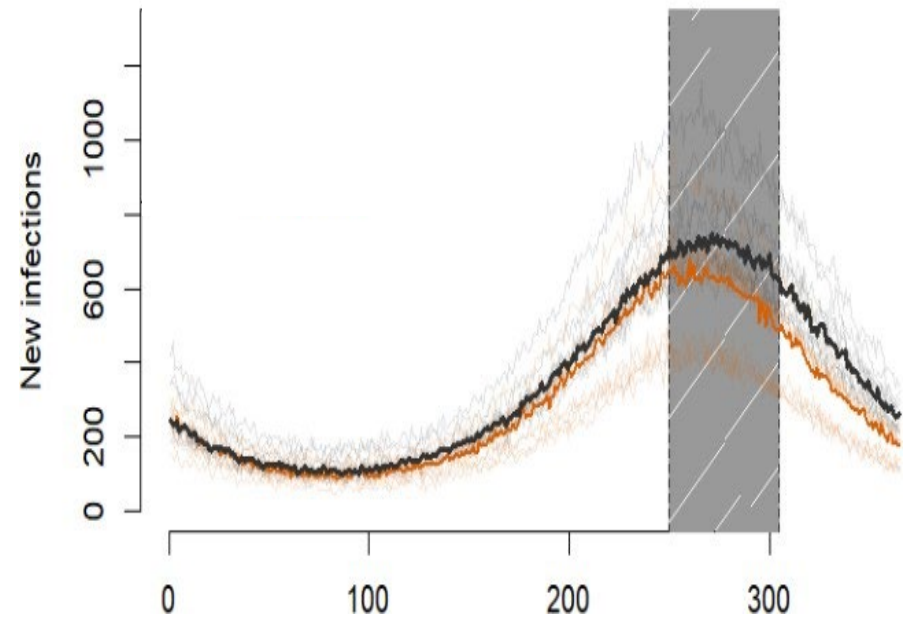
# Challenges



Intervention implemented when infections are lowest (Apr-May)

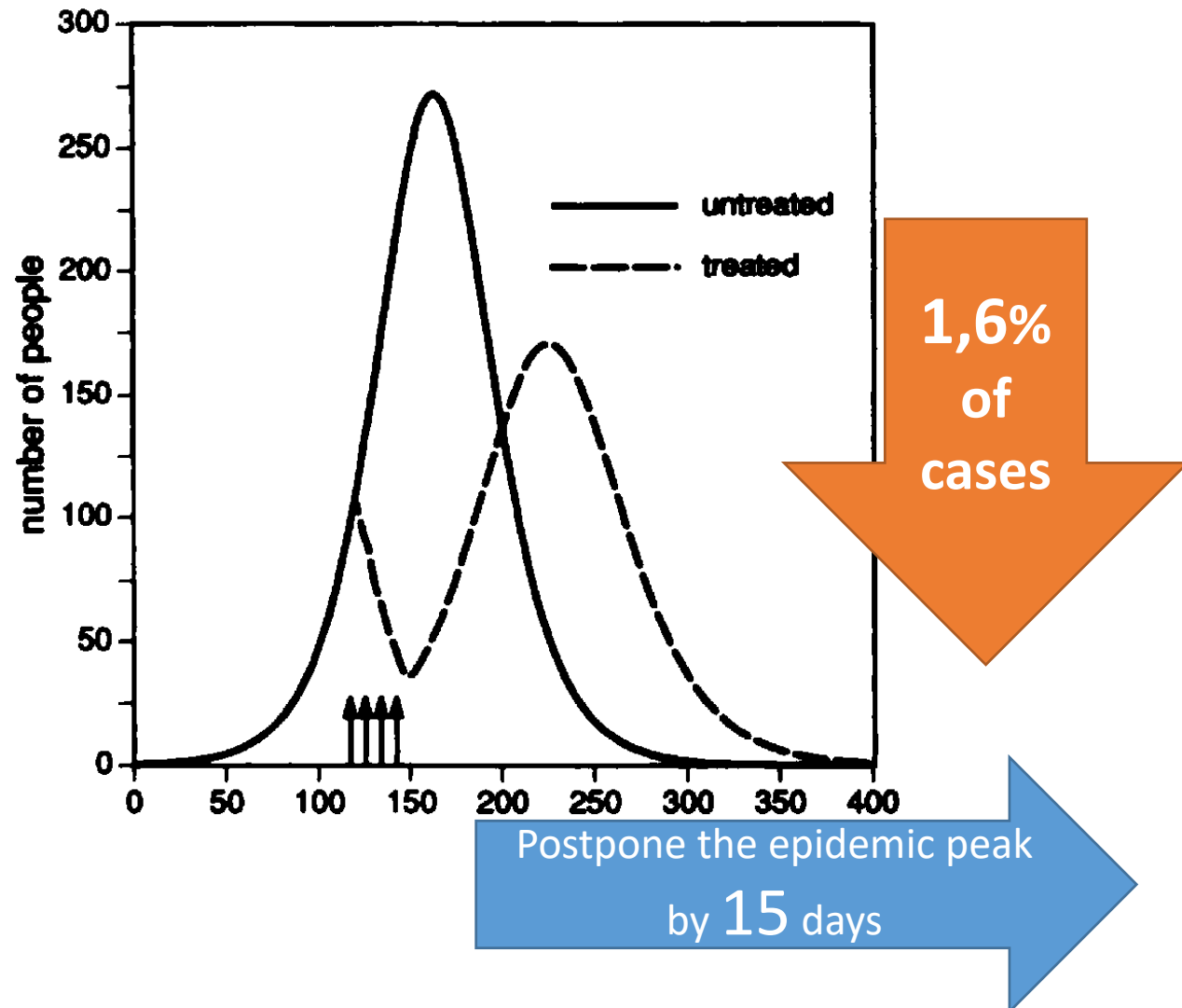


Intervention implemented when infections are highest (Sep-Oct)

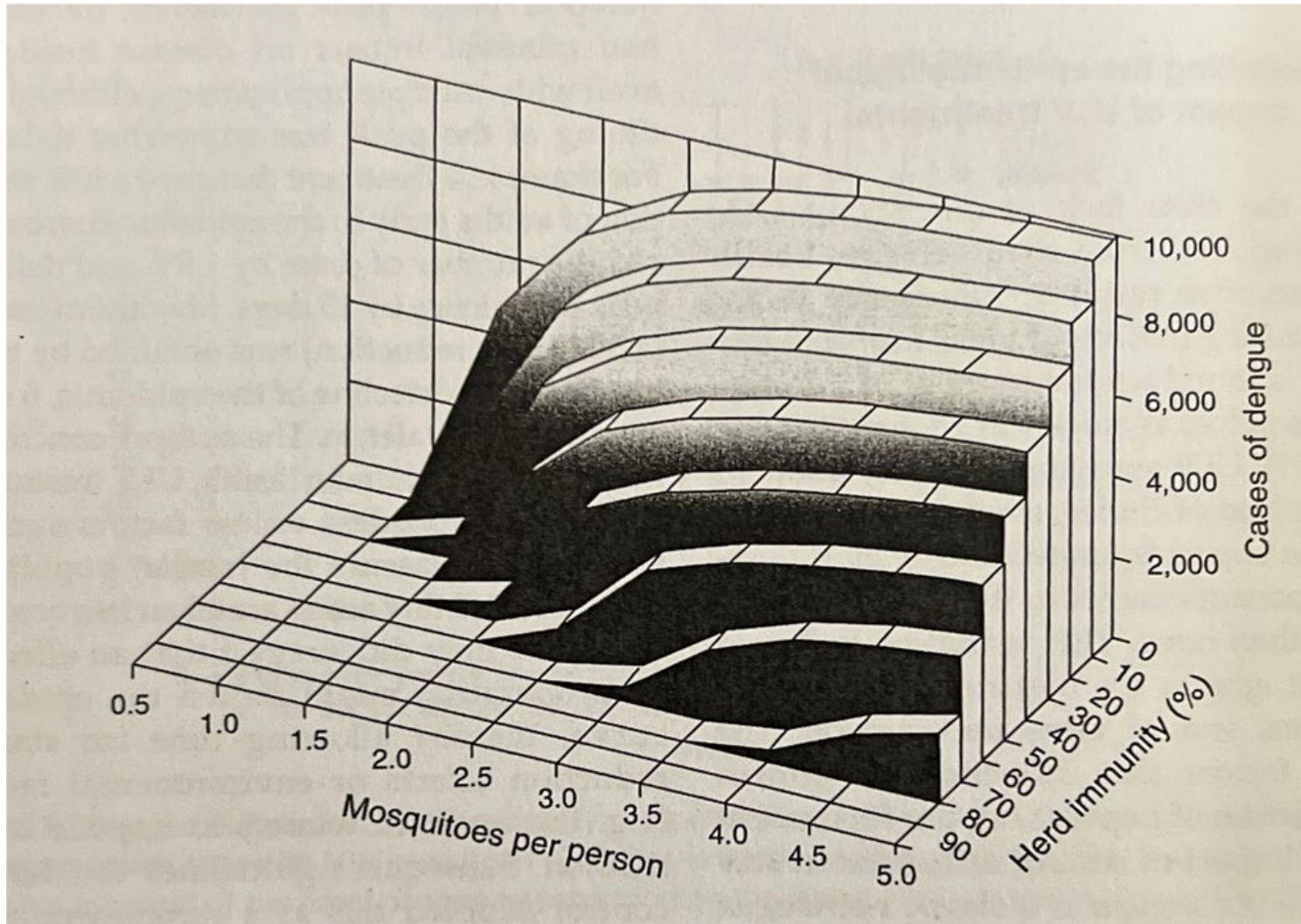


*Unpublished data by US.CDC, Dengue unit, Puerto Rico*

# Challenges



Source: Newton, E. and Reiter, P. (1992), *Am. J. Trop. Med. Hyg.*, 47(6), 1992, pp. 709-720



Source: Reiter, P. and Newton, E. (1992), *Dengue, a Worldwide Problem, a Common Strategy*, MoH, Mexico City



## Models

- EWARDS (WHO-TDR): logistics regression
- D-MOSS (UK) & E-DENGUE (Australia): synthesis of many mathematical models (Mathematical ensembles)

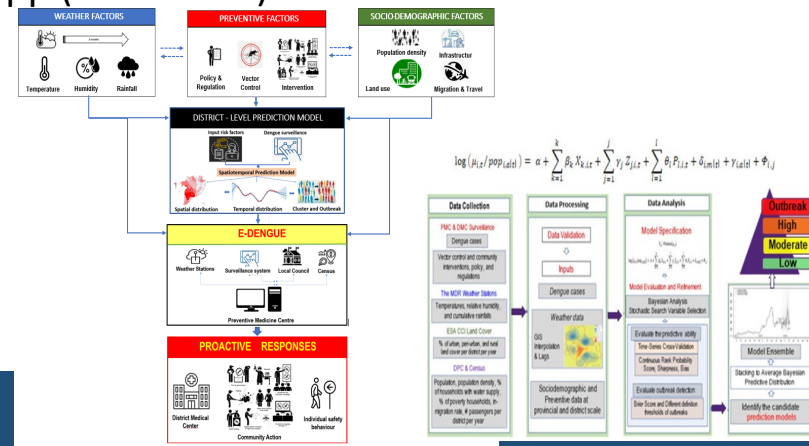
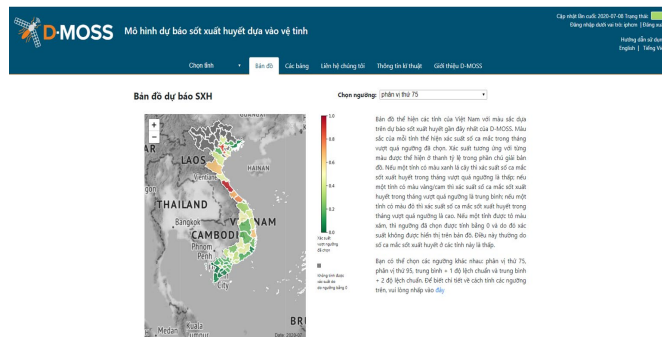
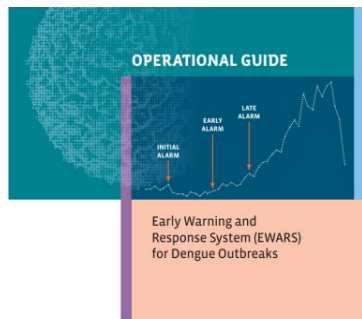
## Input parameters:

- EWARDS: monthly cases, hydrometeorology
- D-MOSS: monthly disease cases and hydro-meteorological forecast
- E-DENGUE: monthly cases, hydrometeorology, socio-economics and intervention activities

## Predictability:

- Forecast time window: from 1 week to 6 months (D-MOSS: 6 months in advance, E-DENGUE: 2 months in advance, EWARDS: 1 to 12 weeks in advance)
- Forecast level: depends on the tool (D-MOSS to province, E-DENGUE to districts and possibly communes)

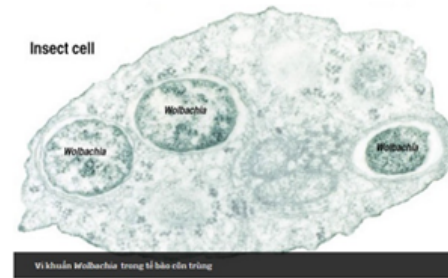
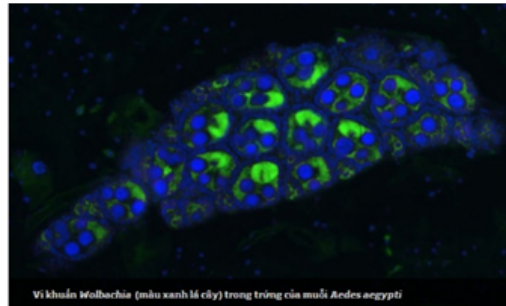
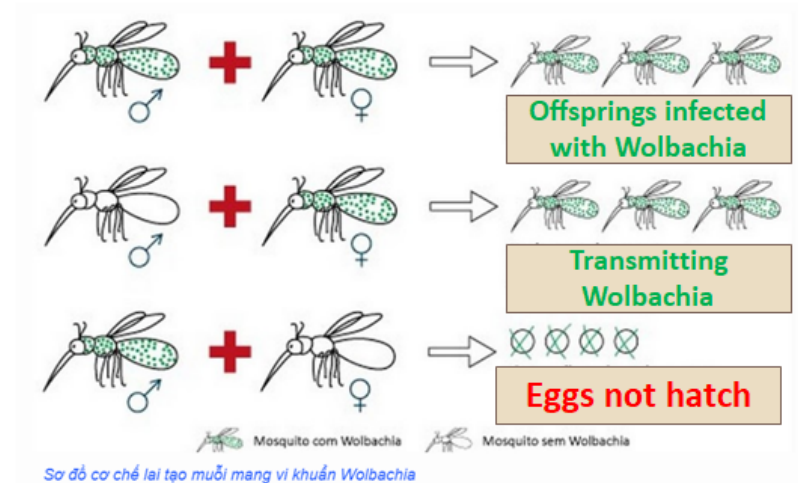
## Utilities: kit (EWARDS), web (D-MOSS), web + mobile app (E-DENGUE)



# Prospects



- Wolbachia is a natural bacteria
- To be transmitted from mosquitoes to their offsprings via eggs
- Safety for human, animals, and environment
- To reduce disease transmission by mosquitoes (Dengue, Zika, Chikungunya)



Source: World Mosquito Program-WMP

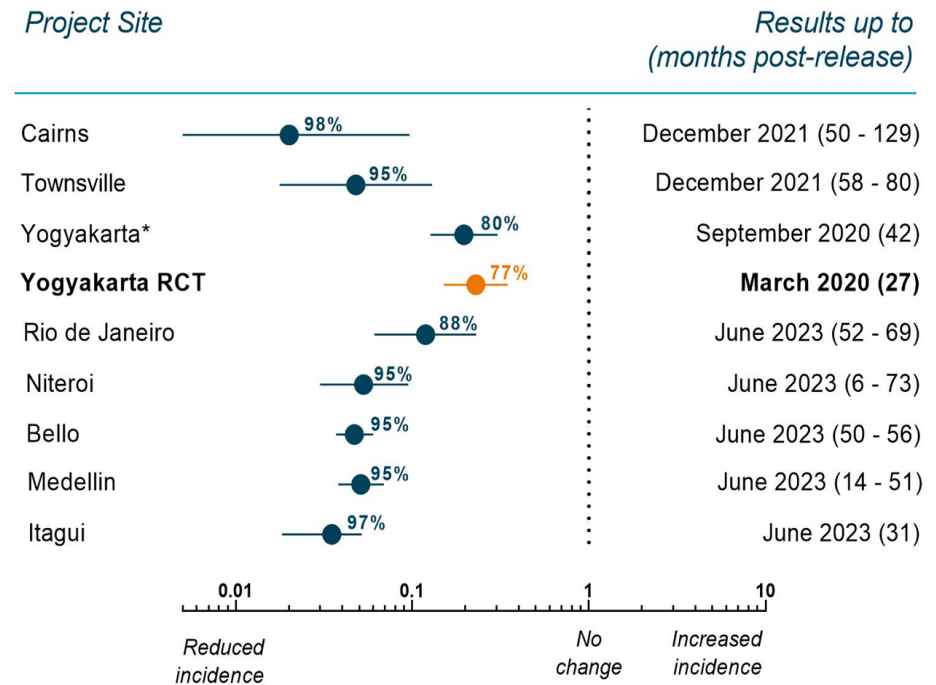


There exists consistent global evidence of a reduction in the incidence of dengue following the implementation of the release of wMel-carrying mosquitoes



Source: World Mosquito Program-WMP

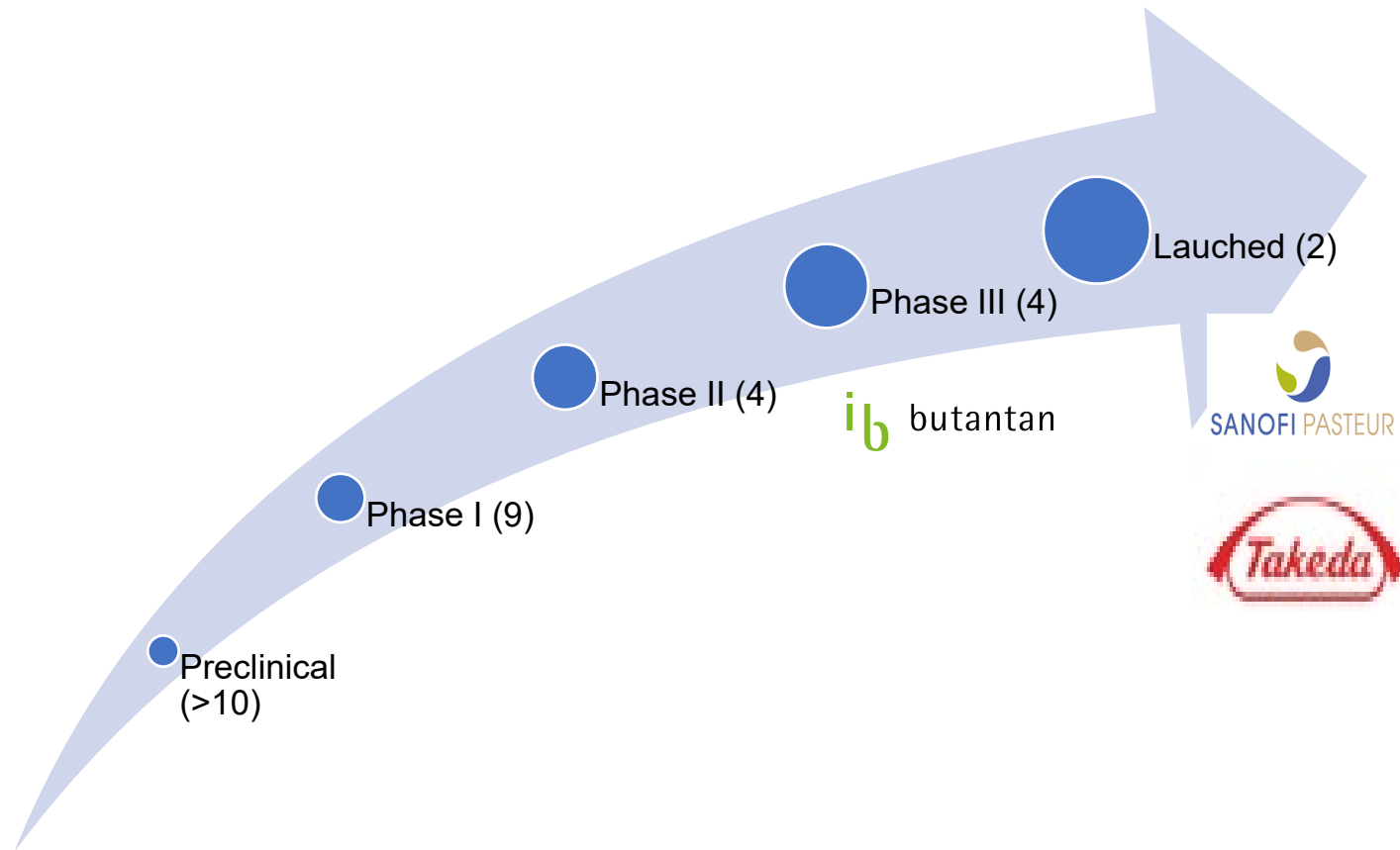
## Estimates of the effect of WMP's *Wolbachia* method on dengue incidence



\* Yogyakarta data post-September 2020 excluded as releases in the control area commenced in Oct 2020



There are many vaccines against dengue that are being researched and developed



\*Based on current vaccine landscape (02/2023)



	<b>CYD-TDV</b>	<b>TAK-003</b>
<b>Ages</b>	9-45 years old <i>(Required serological testing before vaccination)</i>	≥ 4 years old <i>(non-required serological testing before vaccination)</i>
<b>Dose</b>	3 doses (0, 6, 12 month)	2 doses (0, 3 month)
<b>VE against VCD (virologically confirmed dengue)</b>	65,6% (60,7-69,9)	62% (56,6-66,7)
<b>VE against hospitalization VCD</b>	80,8% (70,1-87,7)	83,6% (76,8-88,4)

Source:

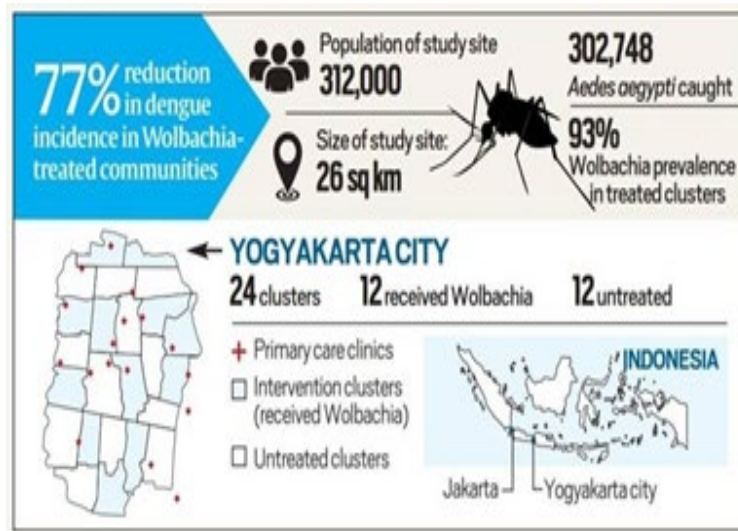
Hadinegoro SR, *N Engl J Med* 2015; 373:1195-1206;

Rivera L, *Clin Infect Dis*, 2022 Aug 24;75(1):107-117

# Solutions



- Toward to the future by new prevention tool with more efficacy
  - Vaccine
  - Vector control:
    - Mosquito carry *Wolbachia*
    - **Genetically** modified mosquito



Thank you!

