ANRS|MIE Scientific Days in Vietnam

Towards ending epidemics

15th to 16th of November, 2023

Dengue control: Status quo, challenges and Prospects

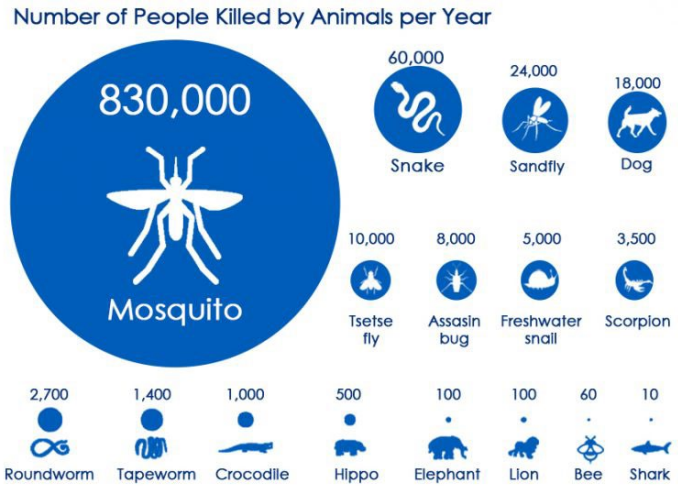
DO Kien Quoc, MPH

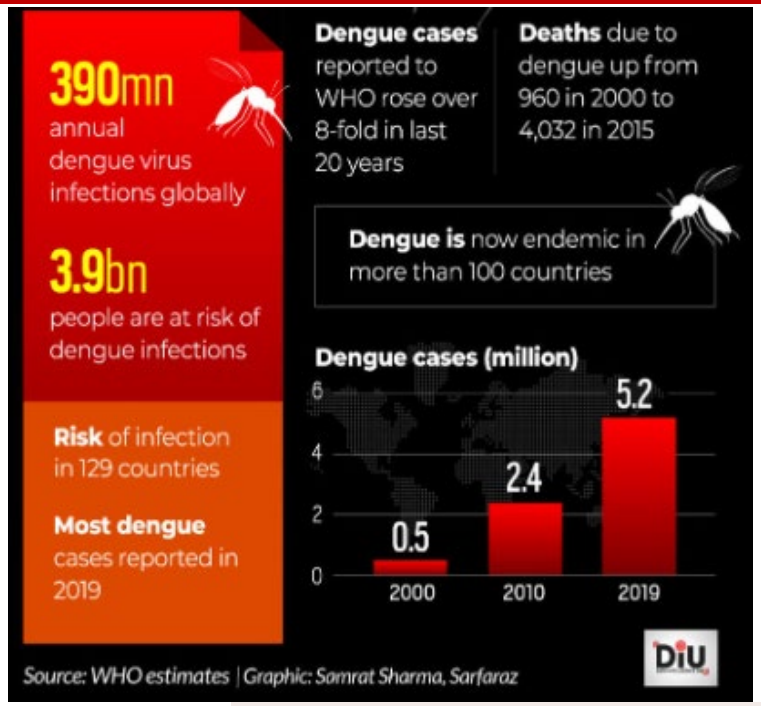
Institute Pasteur in Ho Chi Minh City, Vietnam

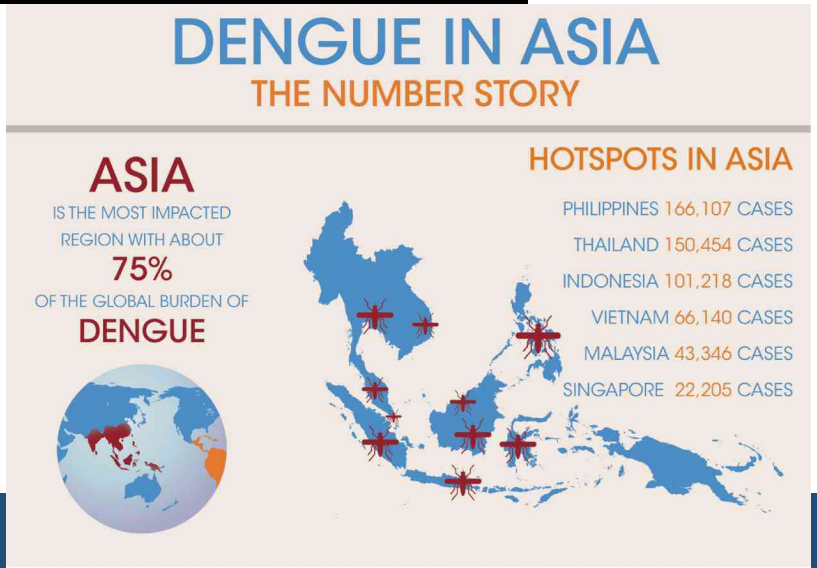
Contents

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

Dengue burden

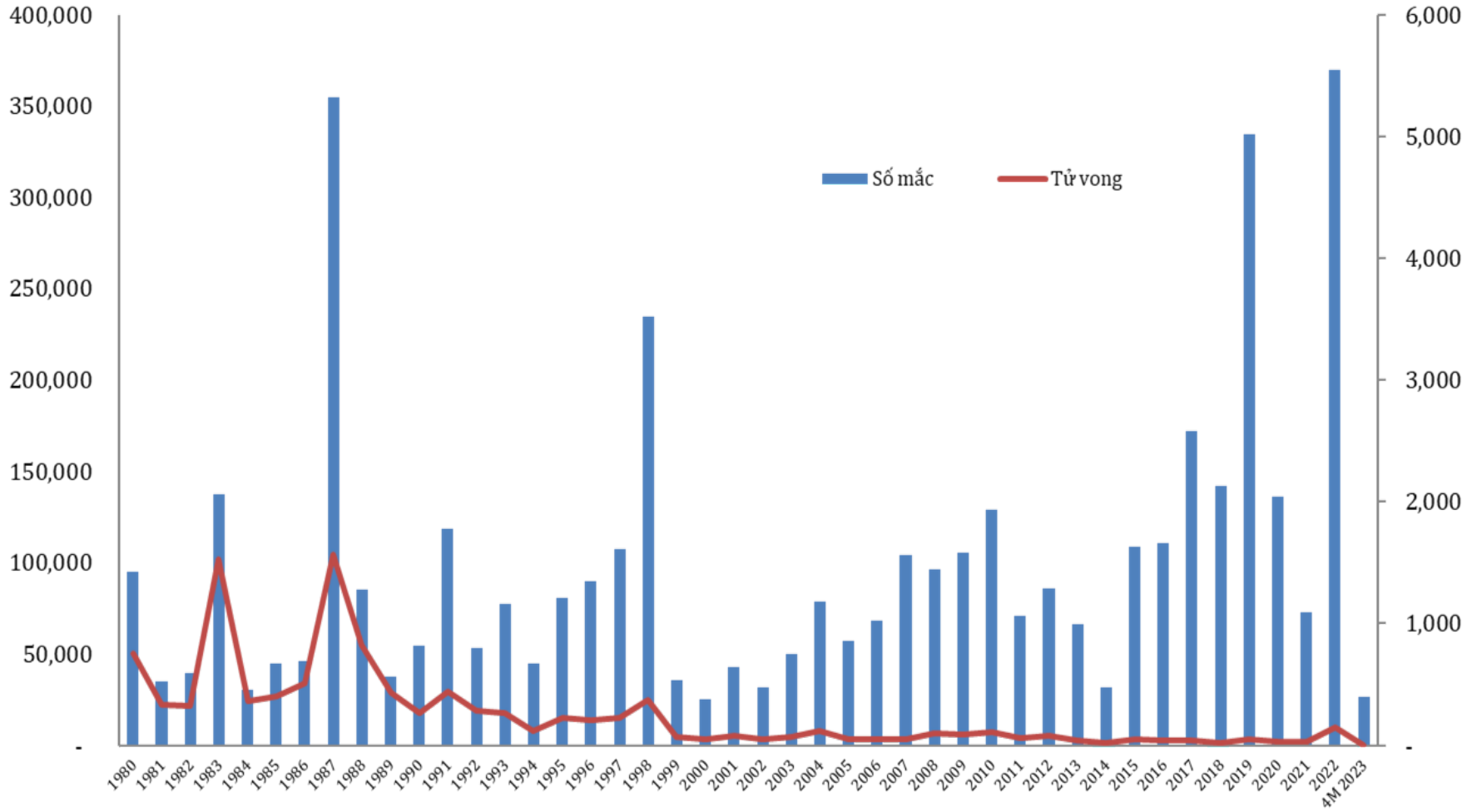






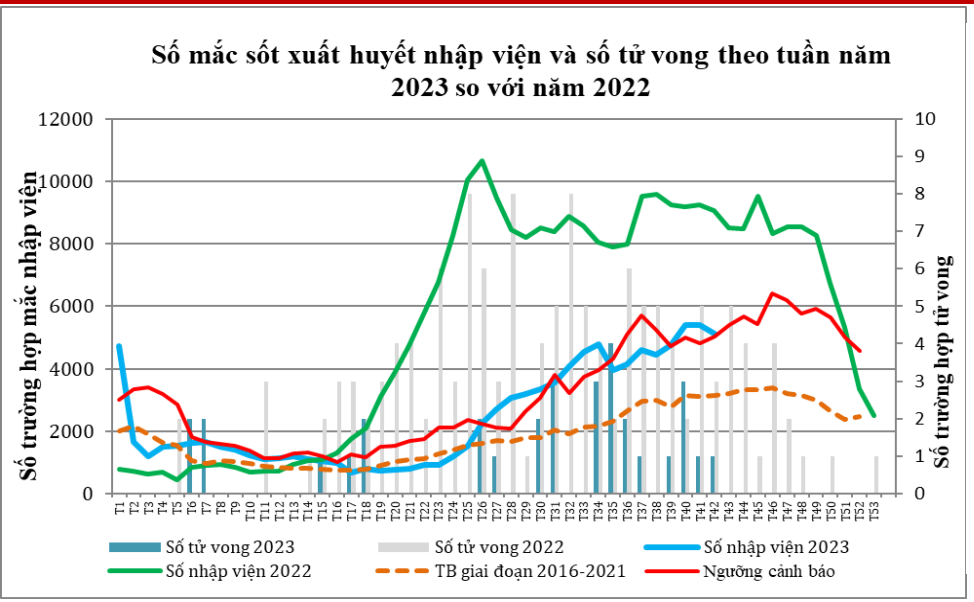
Dengue burden

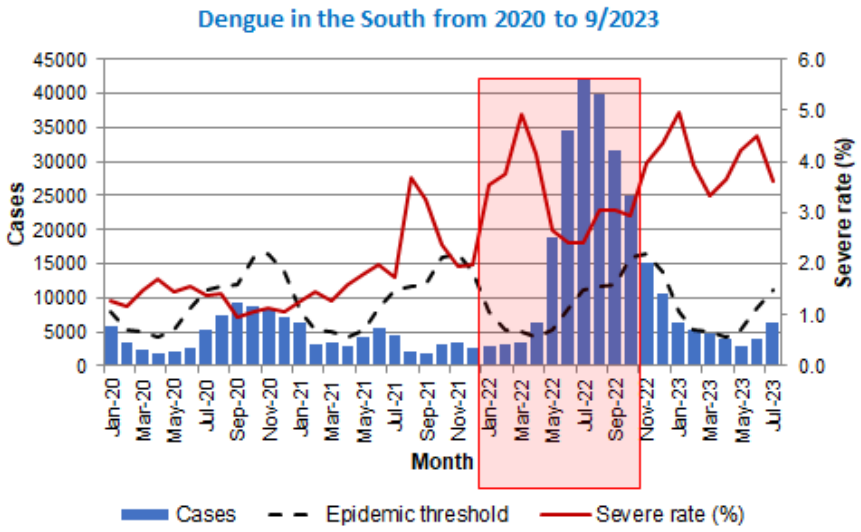
Dengue infection and fatality in Vietnam during 1980 - 2023



Source: General Department of Preventive Medicine – Ministry of Health

Dengue burden





Regions	Cumulative to W42/2023		Cumulative to W42/2022	Cases discrepancy (%)
	Cases	Cases / 100,000 person		
North	37306	90.0	17669	111.1
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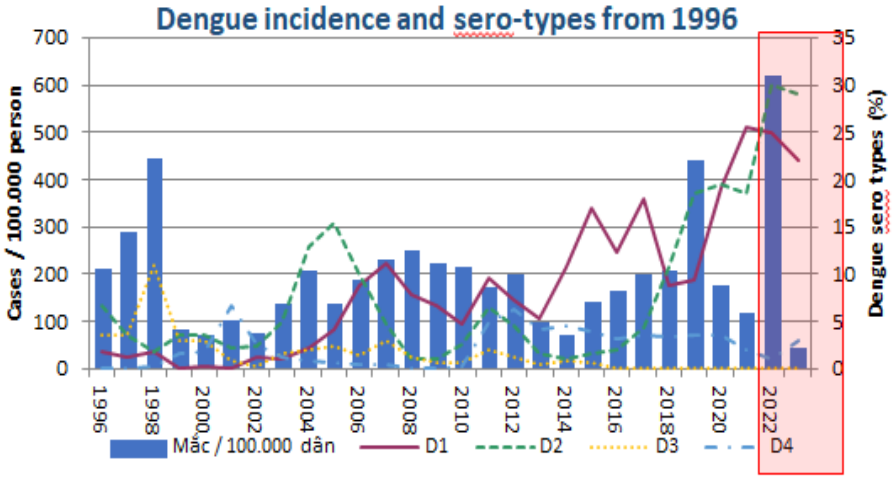
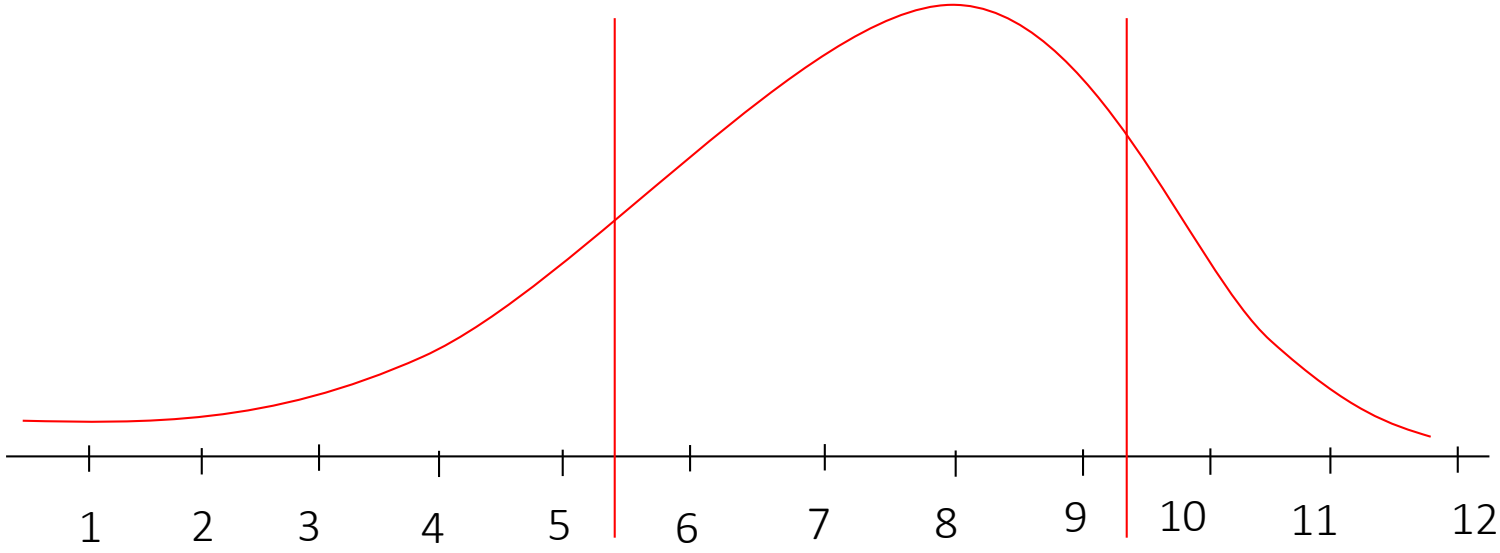


Source: Pasteur Institute in Ho Chi Minh City, Vietnam

Response



Continuously prevention

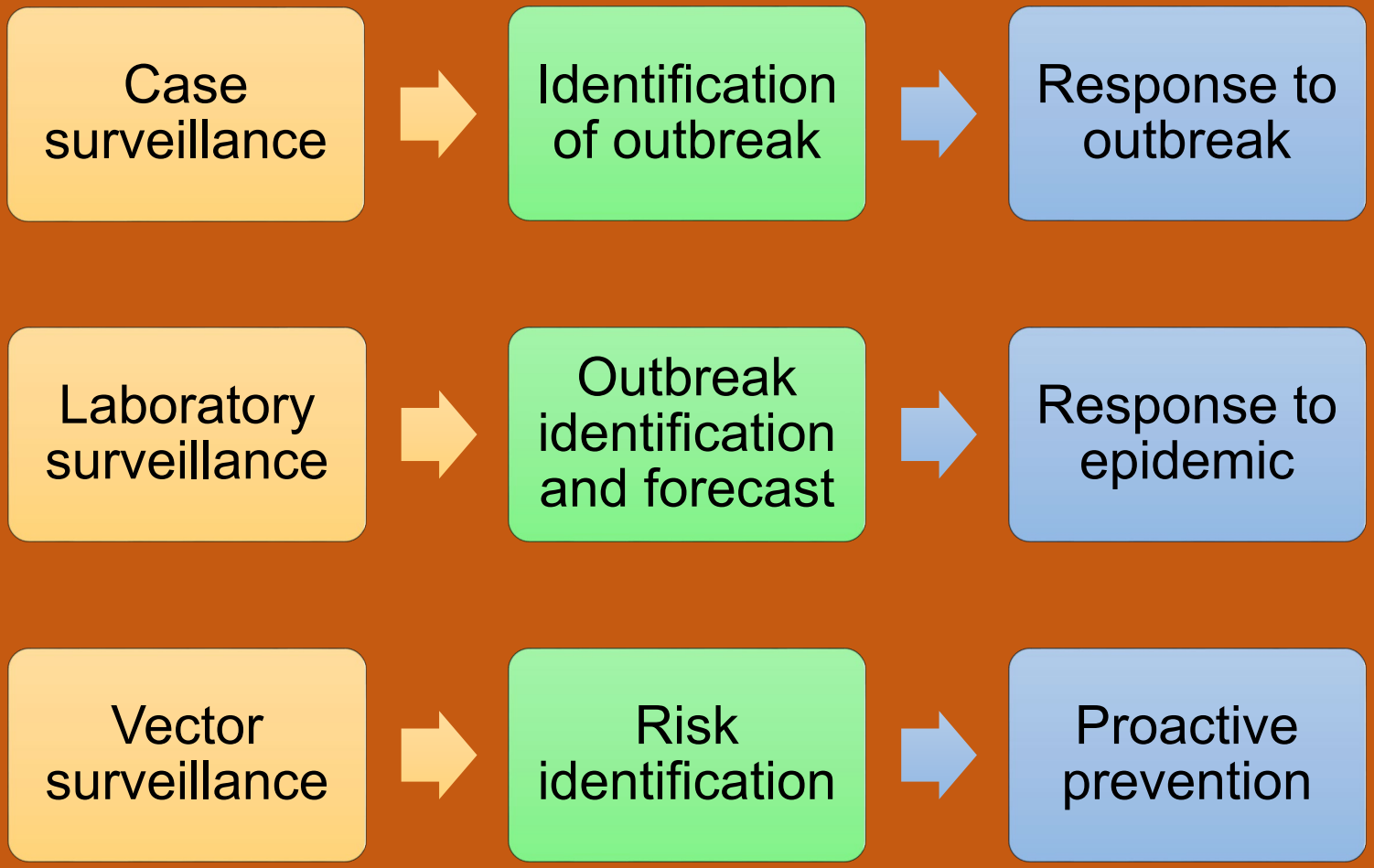
Outbreak intervention

Source reduction campaign

Epidemic intervention

Response

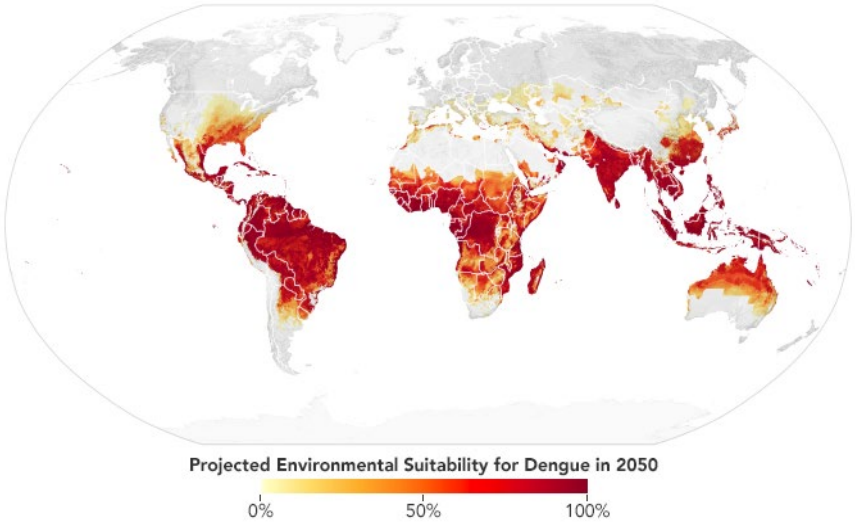
"Surveillance for action"



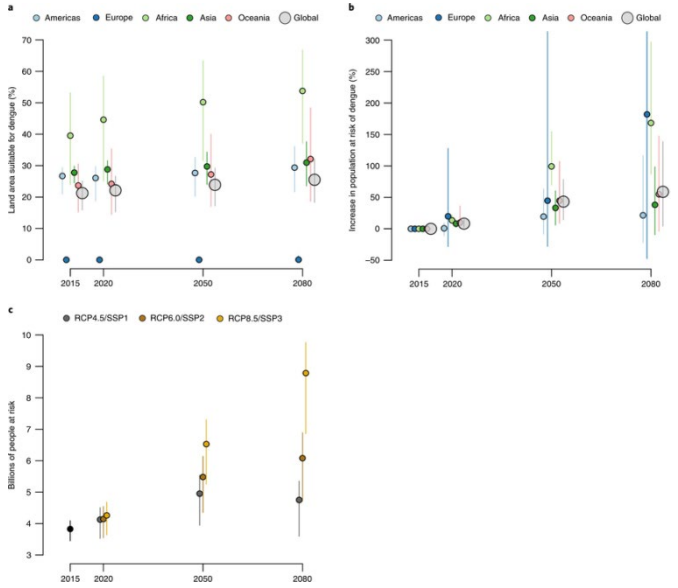
Challenges


2. Exploding demand for mobility/ New Normal
1. Global climate change
3. Lack of control for urbanization
Dengue outbreak
6. Human factor and unstable investment
4. Diverse and complicated habitats of vector
5. Late and inadequate response

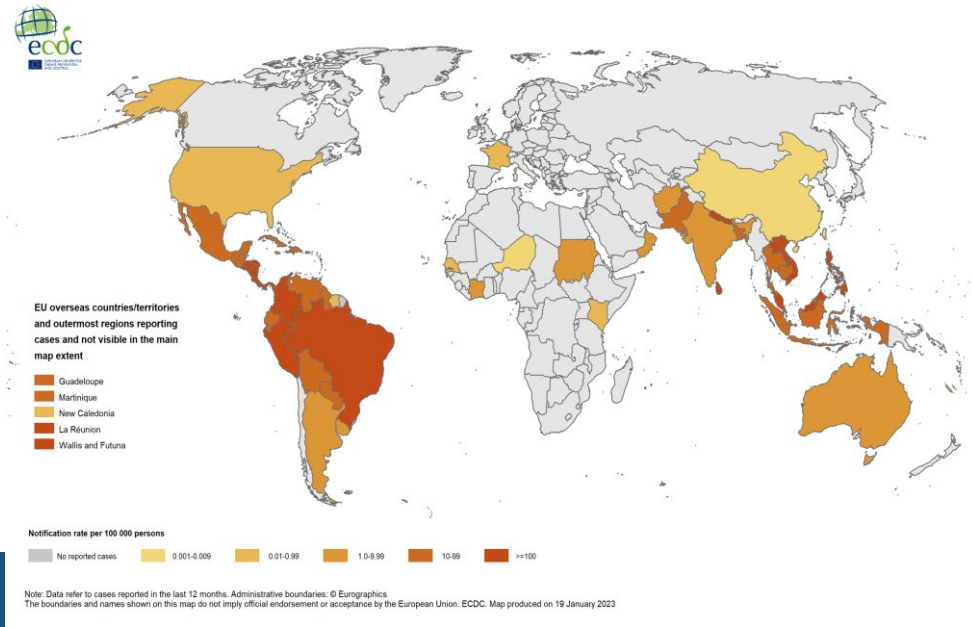
Challenges



Source: NASA, Of Mosquitoes and Models: Tracking Disease by Satellite, Of Mosquitoes and Models: Tracking Disease by Satellite (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



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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
11/7/2023 9:15:15 AM

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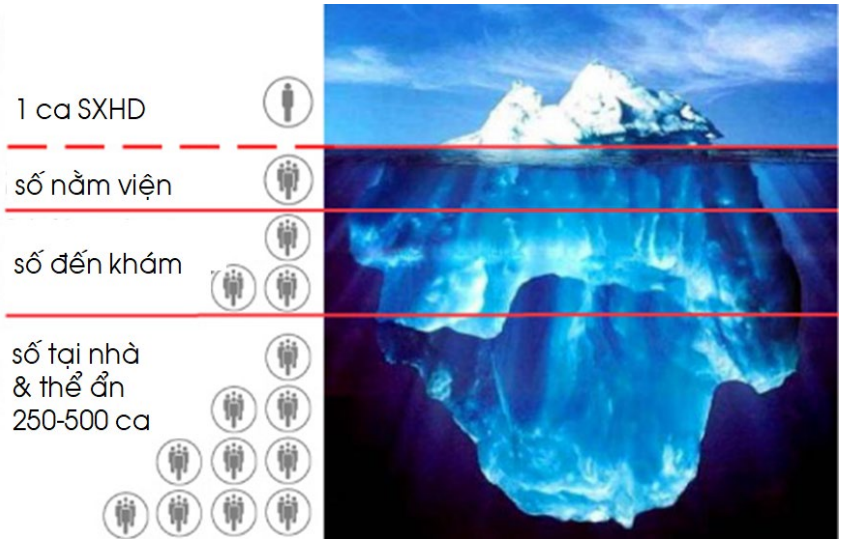
(MENAFN- IANS) London, Nov 7 (IANS) Increasing climate change is expected to drive dengue, a mosquito-borne disease that kills thousands of people every year, to newer areas like the US and Europe, warned a scientist at the World Health Organization (WHO) calling health authorities to start preparing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

Challenges

Source: *https://kinhtemoitruong.vn/*

Challenges



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[1*], S. GOYET[1], S. LY[1], C. NGAN[2], R. HUY[2], V. DUONG[1], O. WICHMANN[3], G. W. LETSON[3], H. S. MARGOLIS[3] AND P. BUCHY[1]

[1] *Institut Pasteur in Cambodia, Réseau International des Instituts Pasteur, Phnom Penh, Cambodia*
[2] *National Dengue Control Programme, Ministry of Health, Phnom Penh, Cambodia*
[3] *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.

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

A prospective study of dengue infections in Bangkok.

Burke DS[1], Nisalak A, Johnson DE, Scott RM.

Abstract

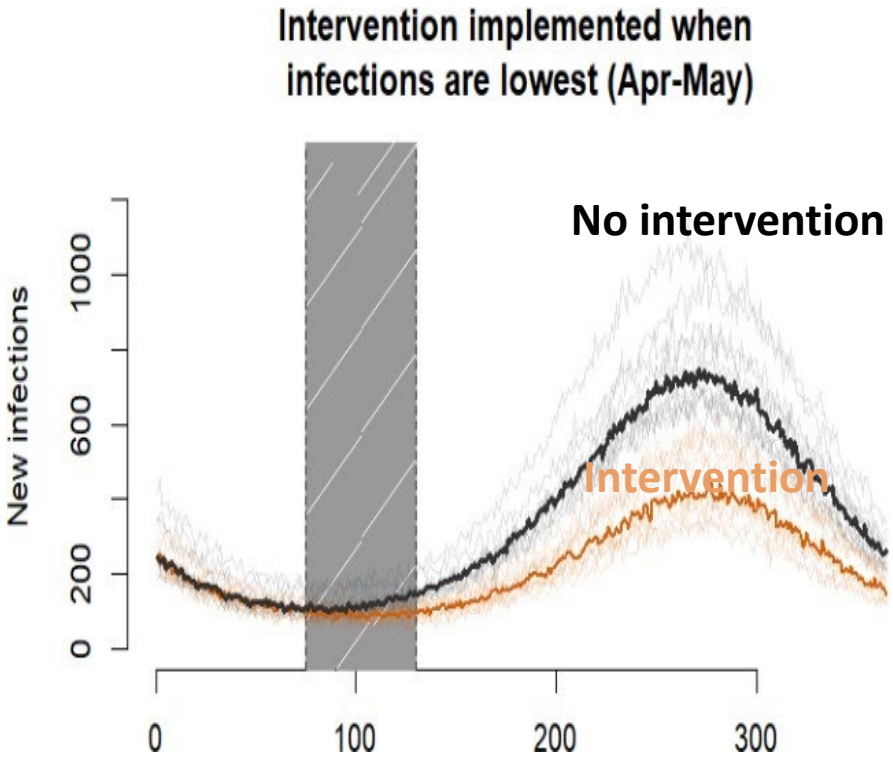
Dengue infections were prospectively studied among 4- to 16-year-old students at a Bangkok school. Blood samples were obtained from 1,757 students in June 1980, before the dengue season, and in January 1981, after the season, and tested for dengue antibodies by the hemagglutination inhibition method. 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.

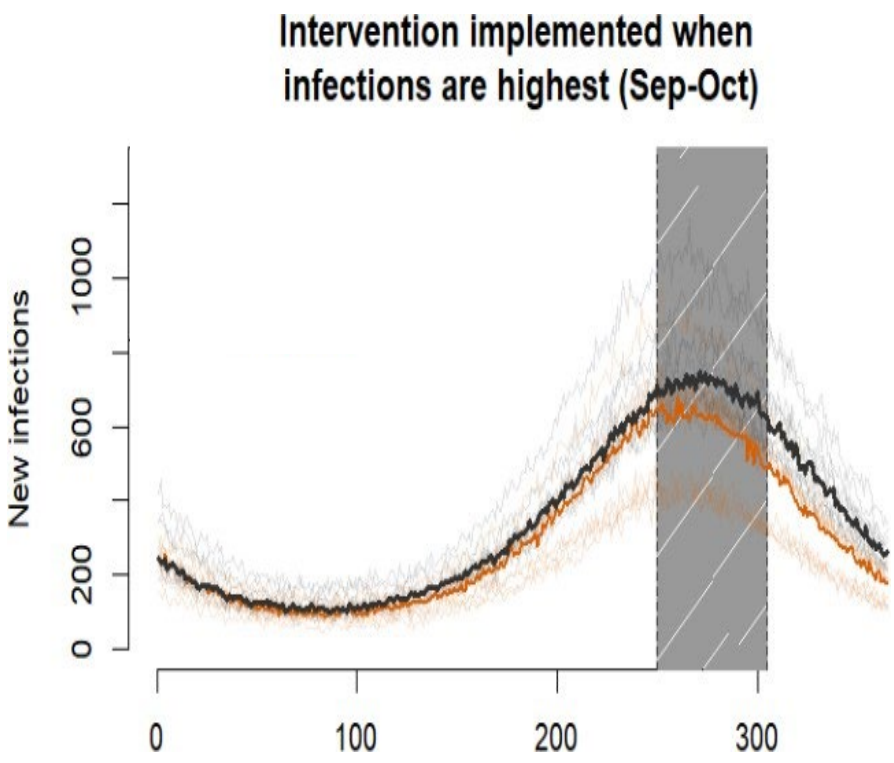
Asymptomatic humans transmit dengue virus to mosquitoes

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

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

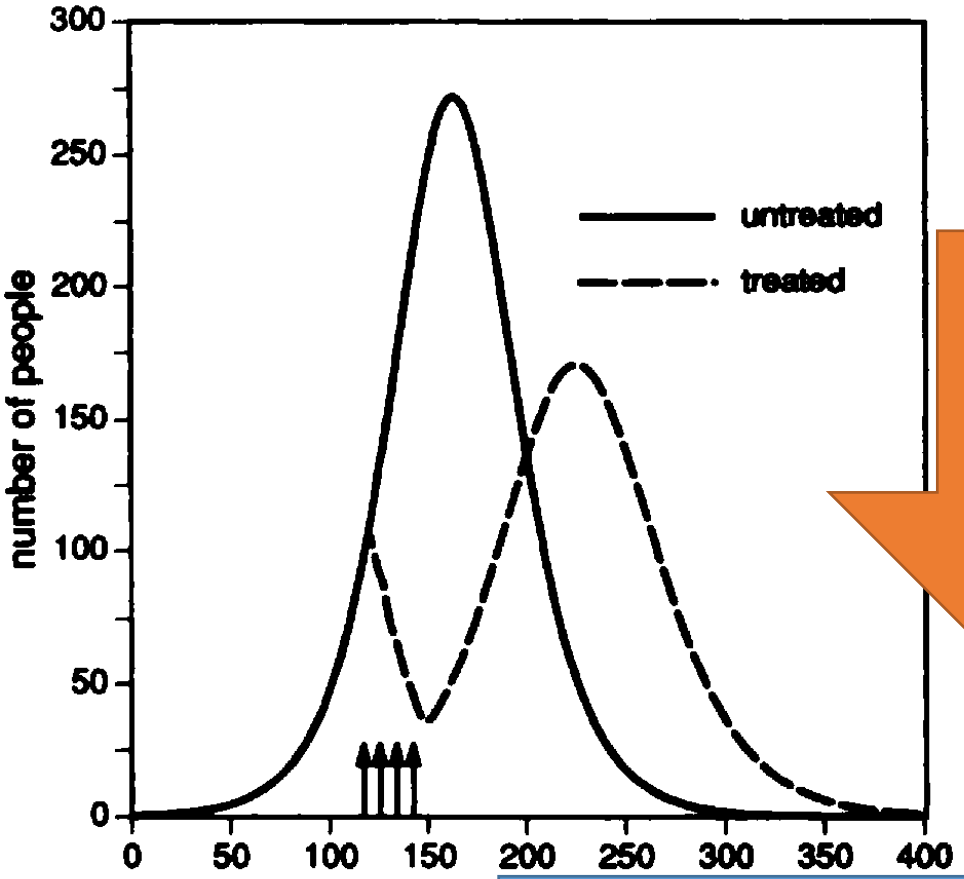
Challenges





Unpulished data by US.CDC, Dengue unit, Puerto Rico

Challenges

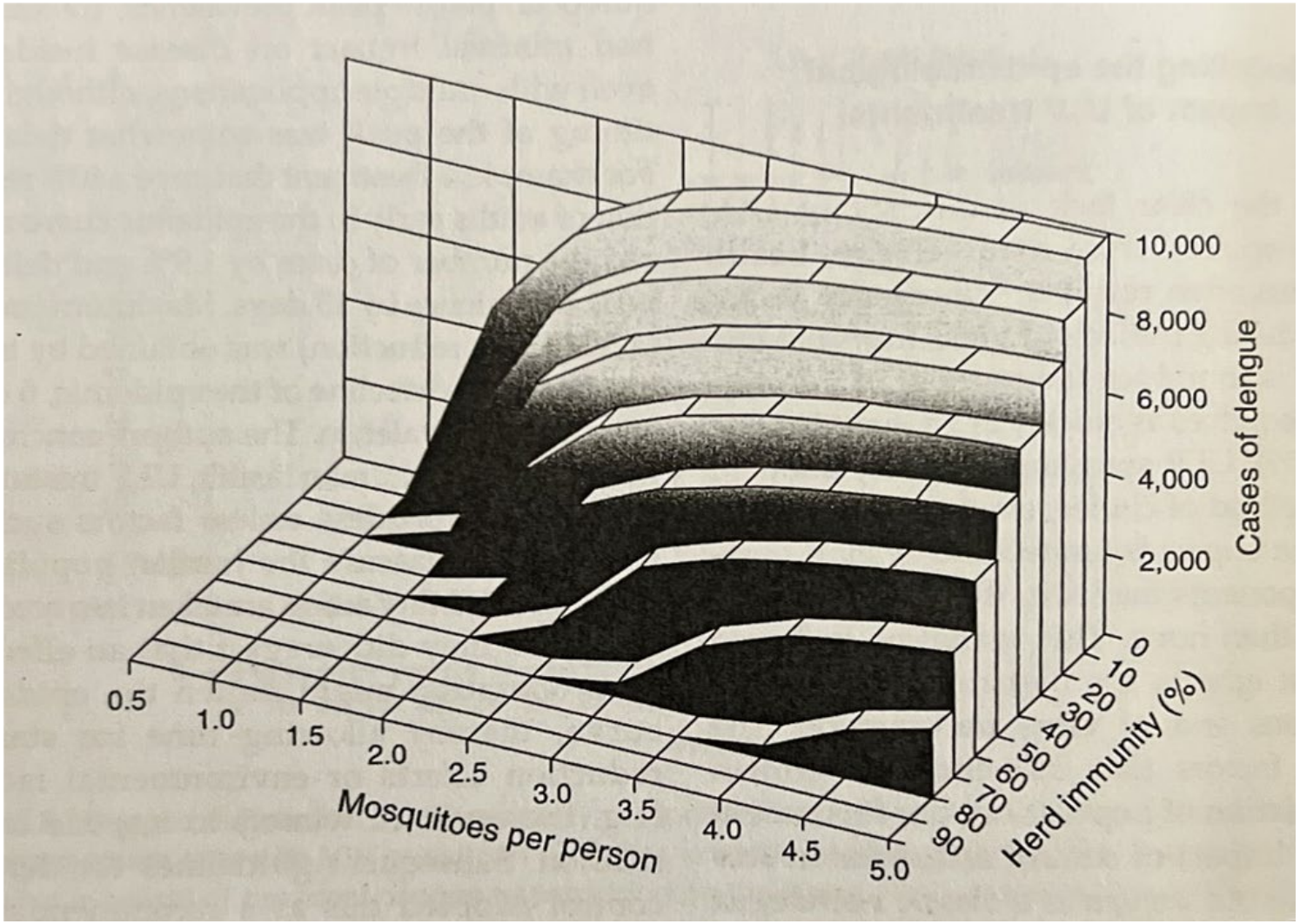


1,6% of cases

Postpone the epidemic peak by 15 days

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

Prospects



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

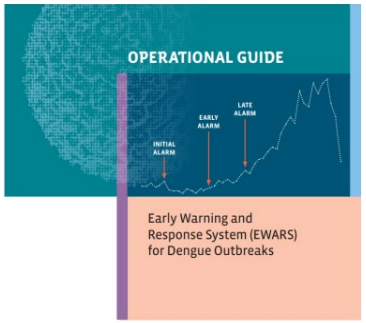
Prospects

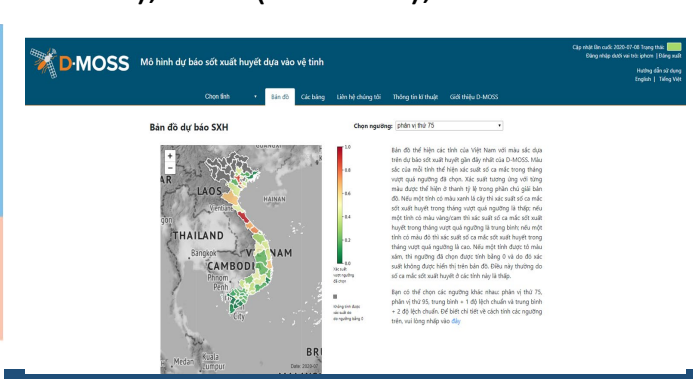
- **Models**
  - **EWARDS (WHO-TDR):** logistics regression
  - **D-MOSS (UK) & E-DENGUE (Australia)**: synthesis of many mathematical models (Mathematical ensembles)

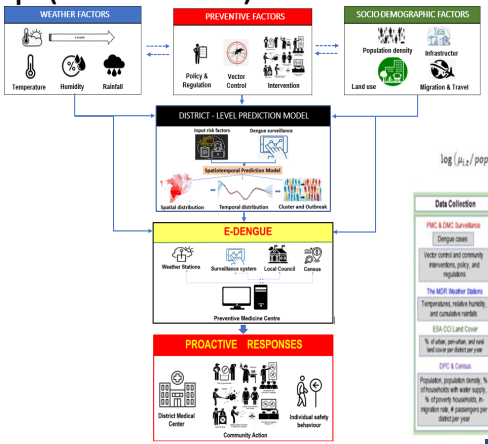
- **Input parameters:**
  - EWARDS: monthly cases, hydrometeorology
  - D-MOSS: monthly disease cases and hydro-meteorological forecast
  - E-DENGUE: monthly cases, hydrometeorology, socio-economics and intervention activities

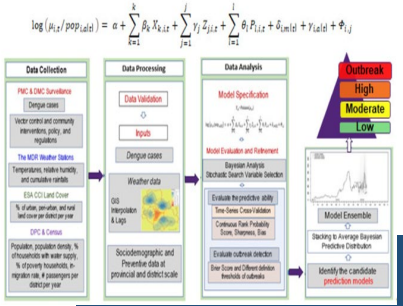
- **Predictability:**
  - Forecast time window: from 1 week to 6 months (D-MOSS: 6 months in advance, E-DENGUE: 2 months in advance, EWARDS: 1 to 12 weeks in advance)
  - Forecast level: depends on the tool (D-MOSS to province, E-DENGUE to districts and possibly communes)

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



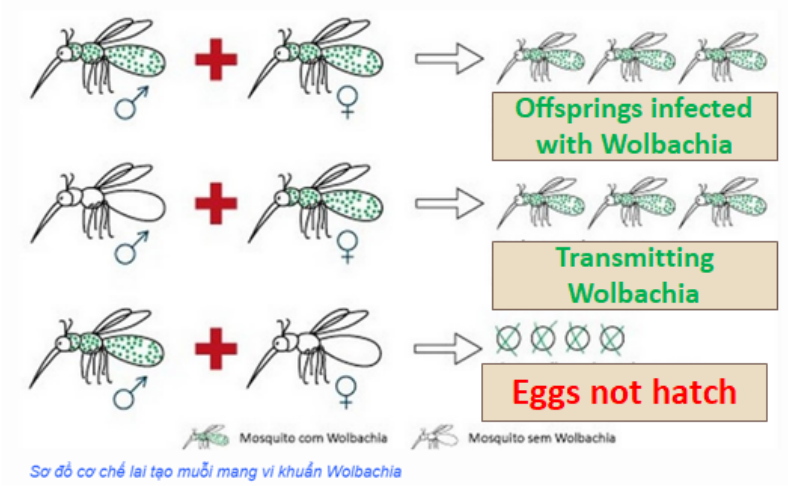




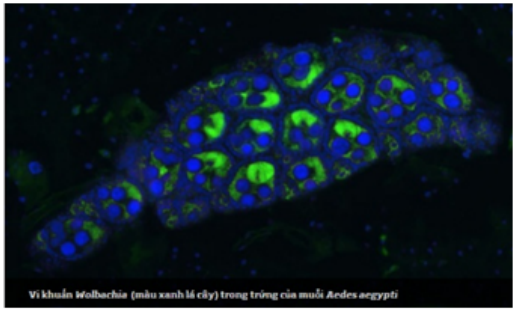


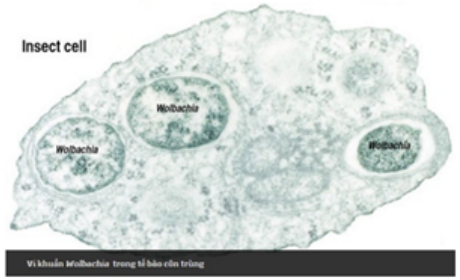
Prospects

- 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)



Sơ đồ cơ chế lai tạo muỗi mang vi khuẩn Wolbachia





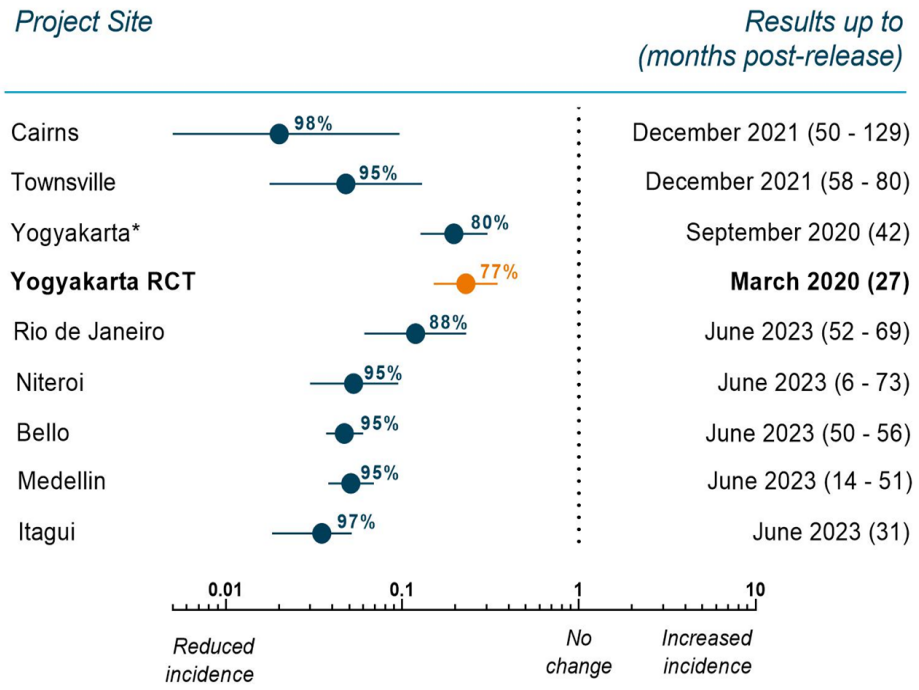
Source: World Mosquito Program-WMP

Prospects

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

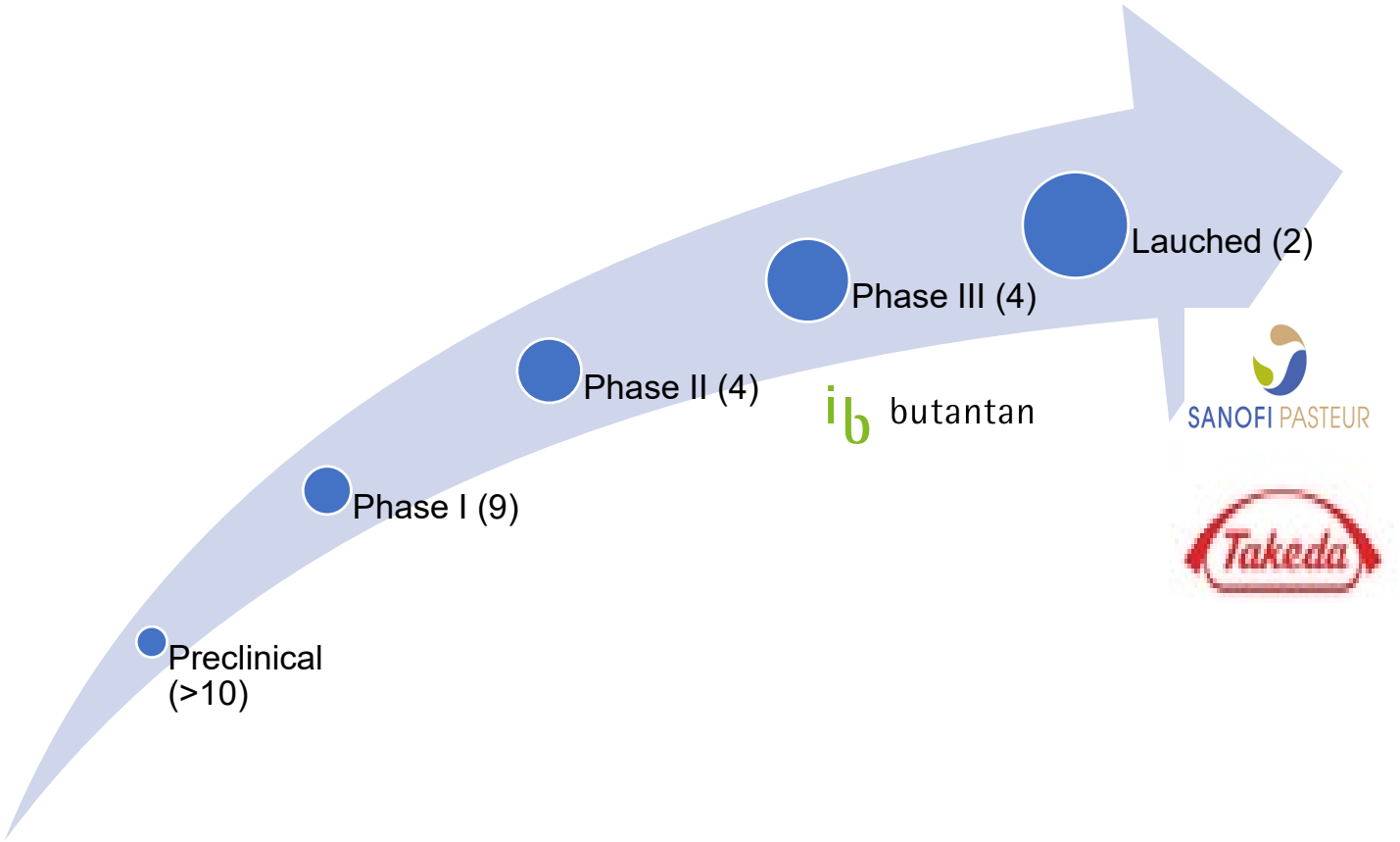
Estimates of the effect of WMP's *Wolbachia* method on dengue incidence



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

Prospects

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



*Based on current vaccine landscape (02/2023)

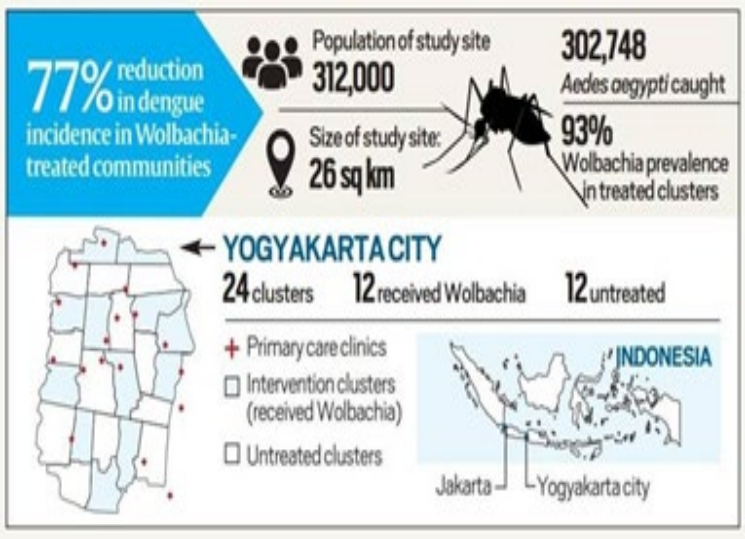
Prospects

	CYD-TDV	TAK-003
Ages	9-45 years old *(Required serological testing before vaccination)*	≥ 4 years old *(non-required serological testing before vaccination)*
Dose	3 doses (0, 6, 12 month)	2 doses (0, 3 month)
VE against VCD (virologically confirmed dengue)	65,6% (60,7-69,9)	62% (56,6-66,7)
VE against hospitalization VCD	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!

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Phòng chống sốt xuất huyết: Thực trạng, thách thức và Triển vọng

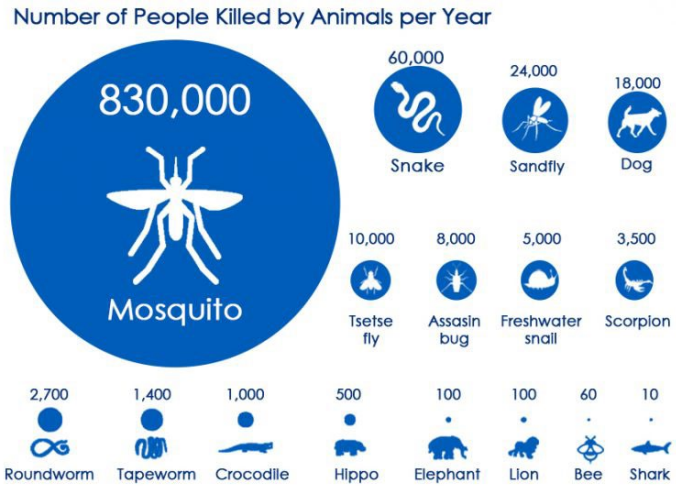
DO Kien Quoc, MPH

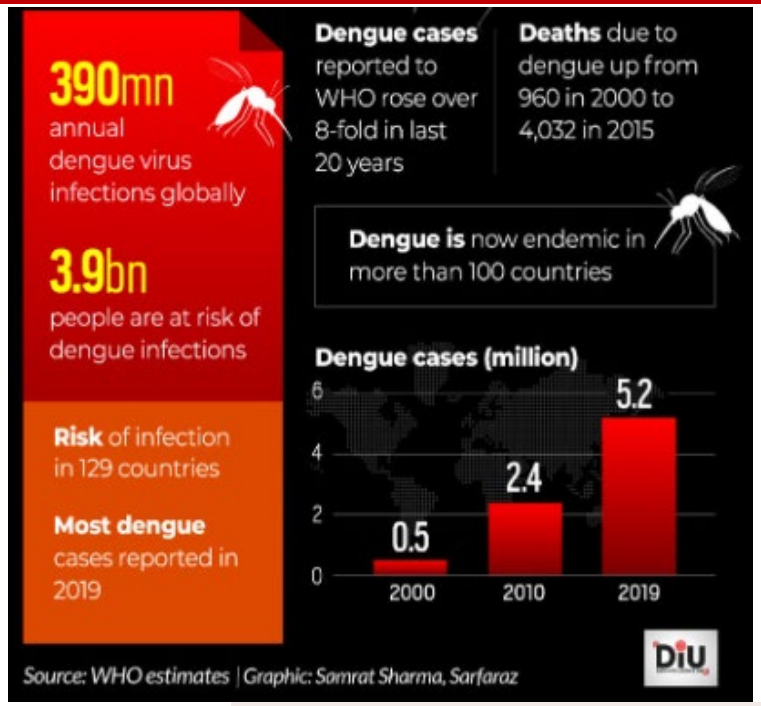
Institute Pasteur in Ho Chi Minh City, Vietnam

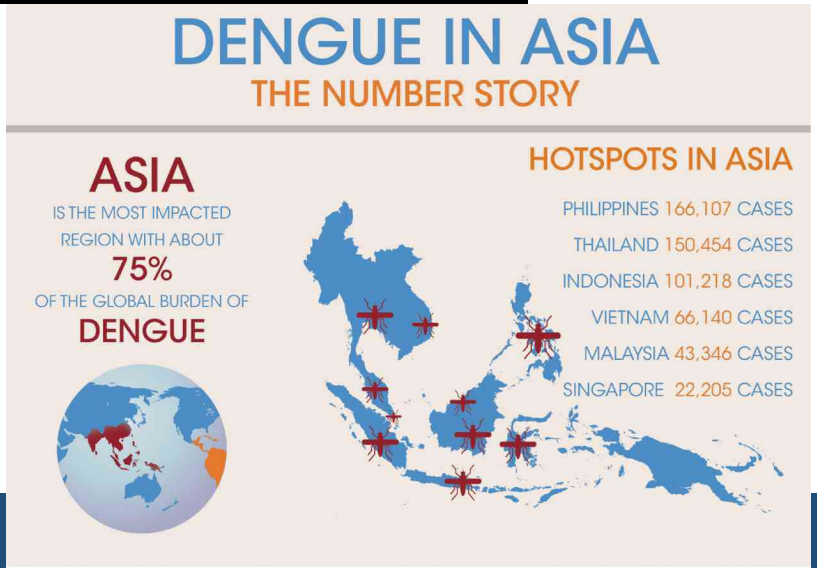
Nội dung

- Gánh nặng của sốt xuất huyết
- Ứng phó với sốt xuất huyết
- Thách thức
- Tương lai
- Các giải pháp

Gánh nặng của sốt xuất huyết

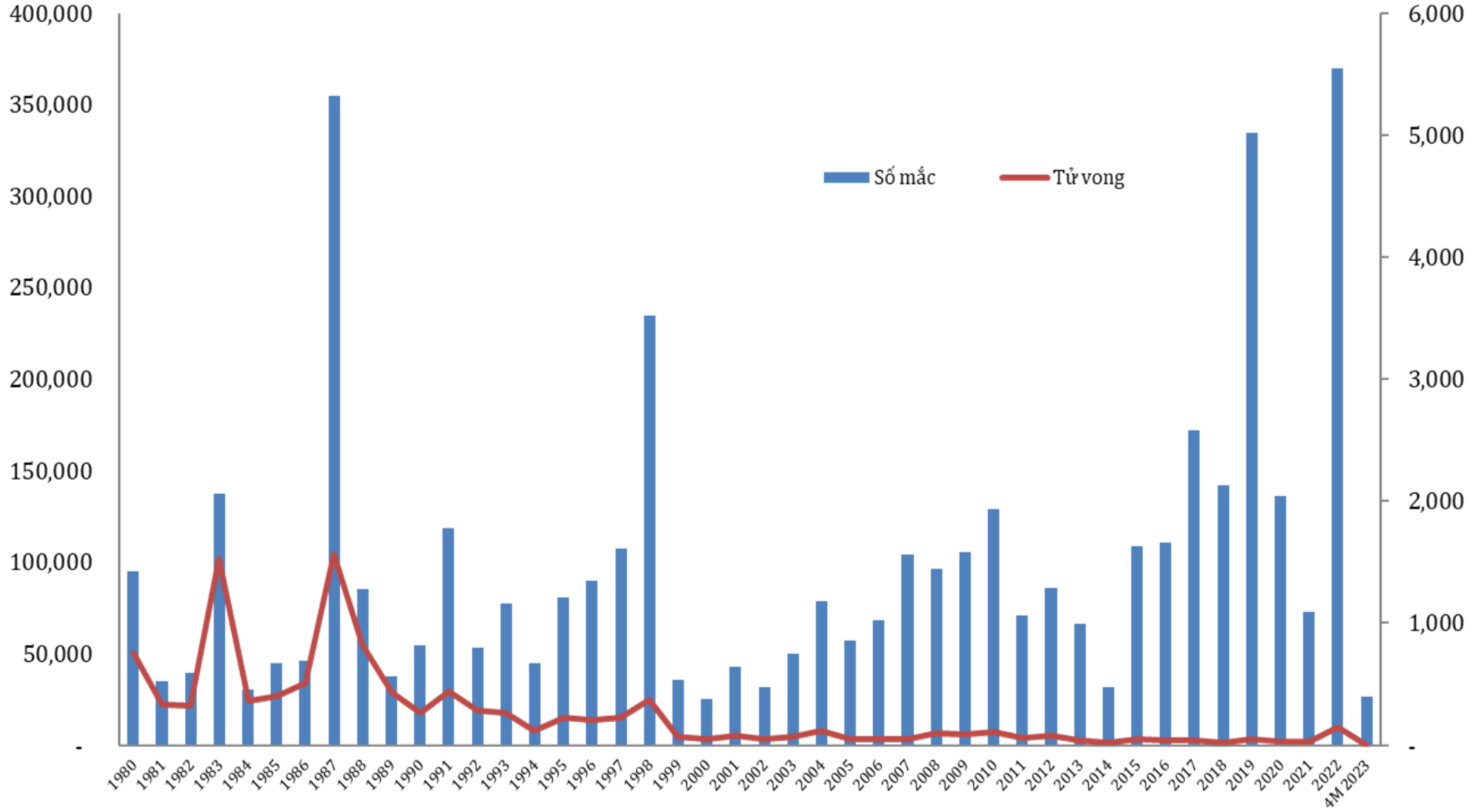






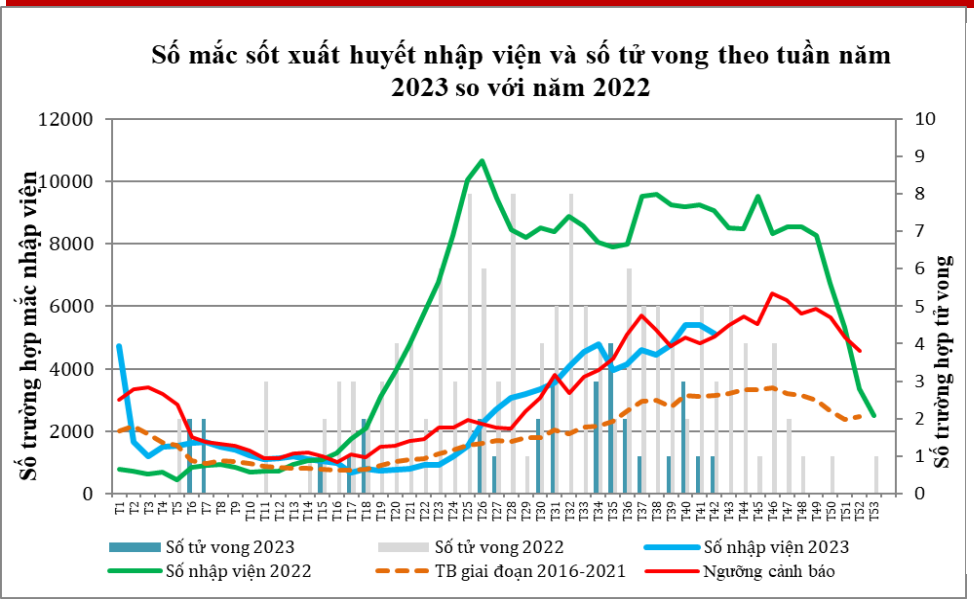
Gánh nặng của sốt xuất huyết

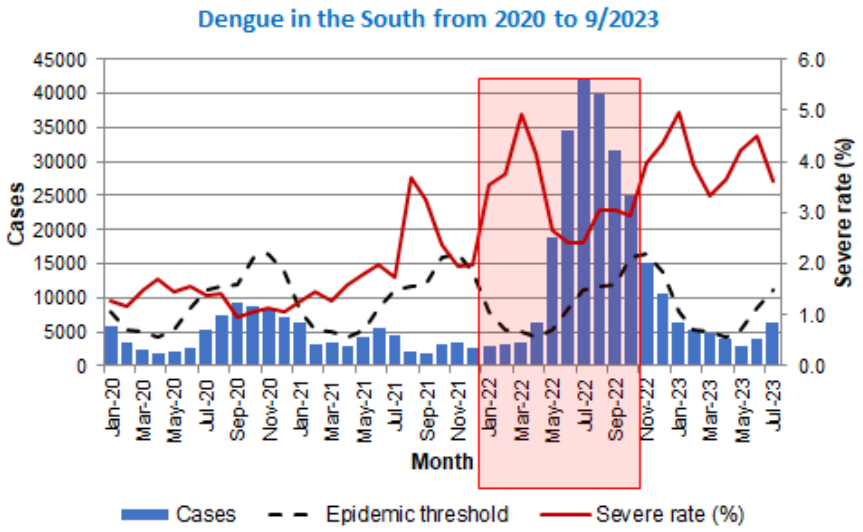
Số cac sốt xuất huyết và tử vong ở Việt Nam trong giai đoạn 1980 - 2023



Nguồn: Cục Y tế dự phòng – Bộ Y tế

Gánh nặng của sốt xuất huyết





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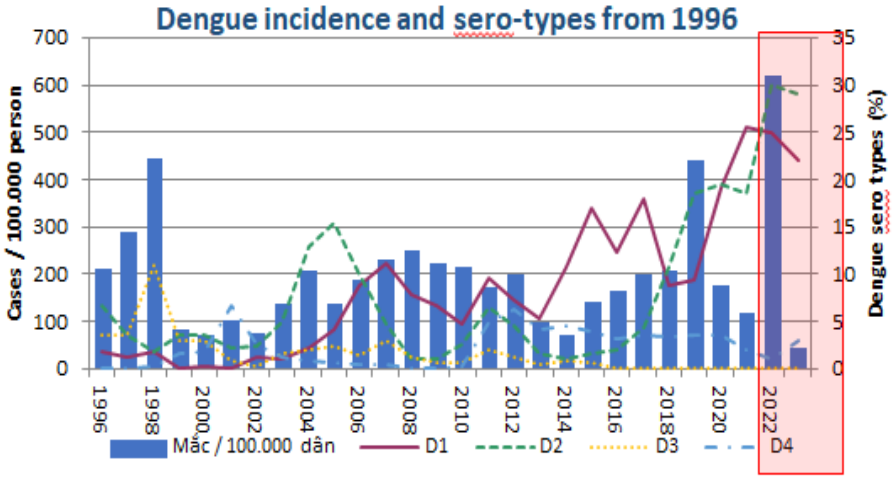

Source: Pasteur Institute in Ho Chi Minh City, Vietnam

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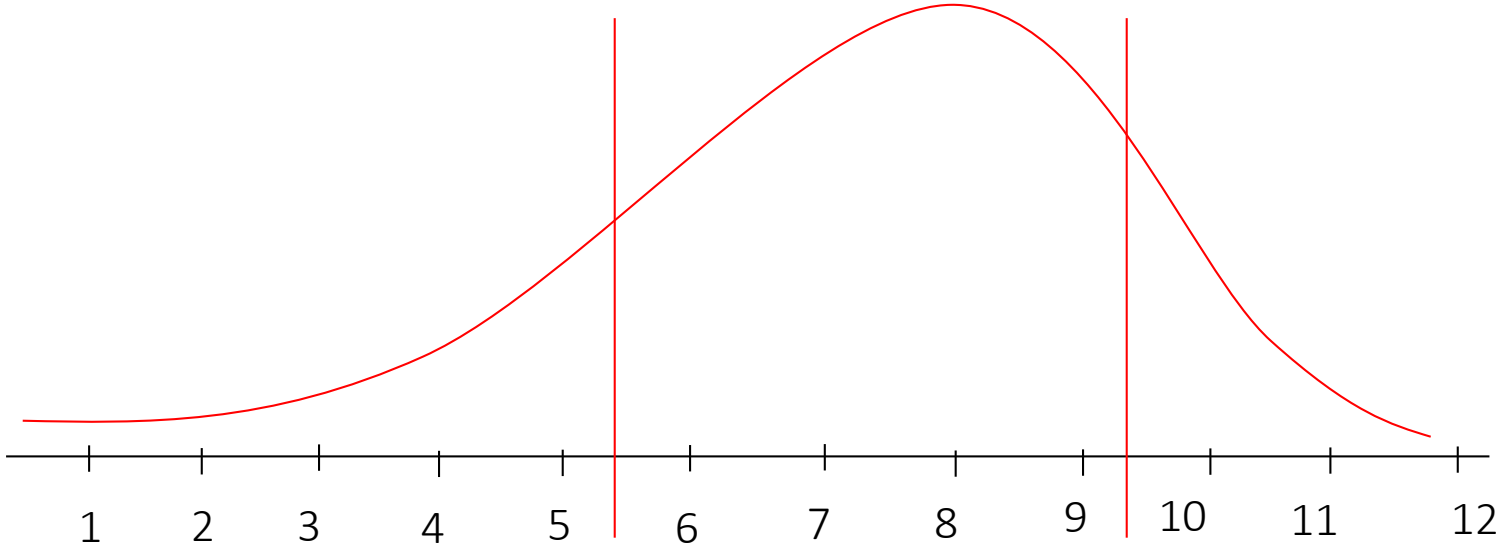


Phòng ngừa liên tục

Can thiệp vào ổ dịch

Giảm nguồn lây nhiễm

Can thiệp dịch bệnh

Ứng phó

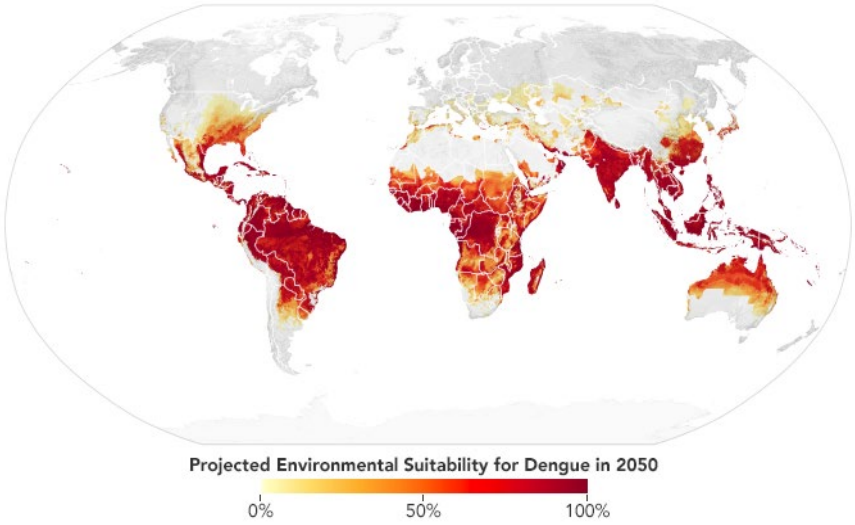
"Giám sát để hành động"

Giám sát ca bệnh	Xác định ổ dịch	Ứng phó với ổ dịch
Giám sát phòng thí nghiệm	Xác định và dự báo ổ dịch	Ứng phó với dịch bệnh
Giám sát véc tơ	Xác định nguy cơ	Chủ động phòng ngừa

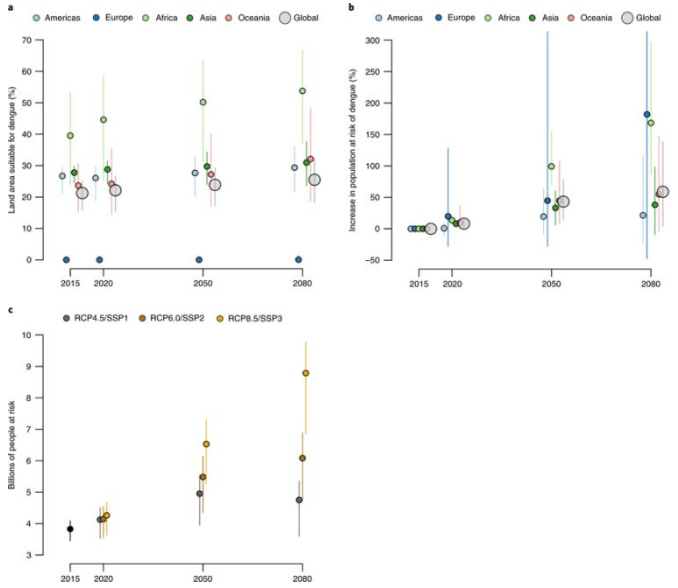
Thách thức


2. Bùng nổ nhu cầu dịch chuyển/ Trạng thái bình thường mới
1. Biến đổi khí hậu toàn cầu
3. Thiếu kiểm soát tình trạng đô thị hoá
Ổ dịch sốt xuất huyết
6, Yéu tố con người và đầu đầu tư thiếu ổn định
4. Môi trương sống đa dnagj và phức tạp của véc tớ truyền bệnh
5. Phản hồi muộn và thiếu đầy đủ

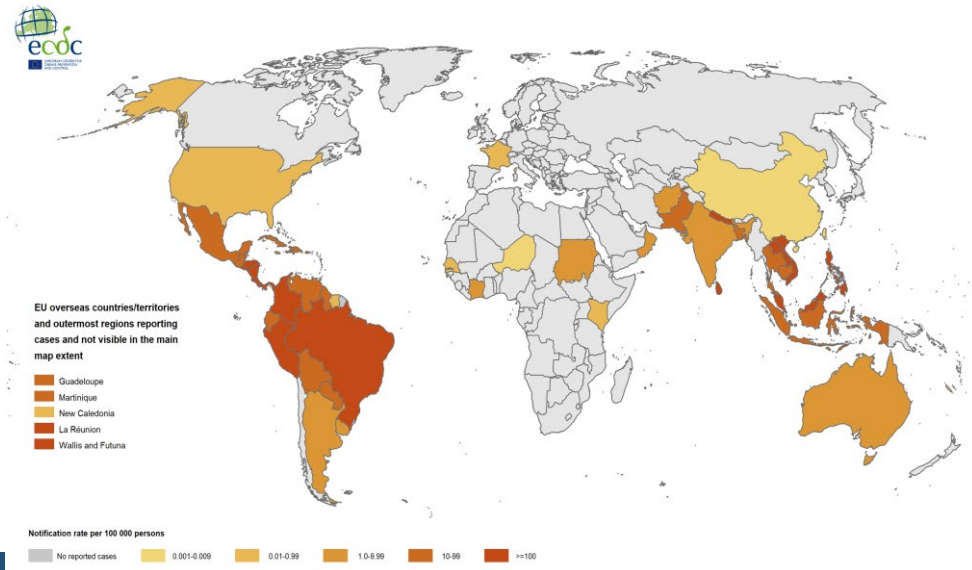
Thách thức



Source: NASA, Of Mosquitoes and Models: Tracking Disease by Satellite, Of Mosquitoes and Models: Tracking Disease by Satellite (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



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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
11/7/2023 9:15:15 AM

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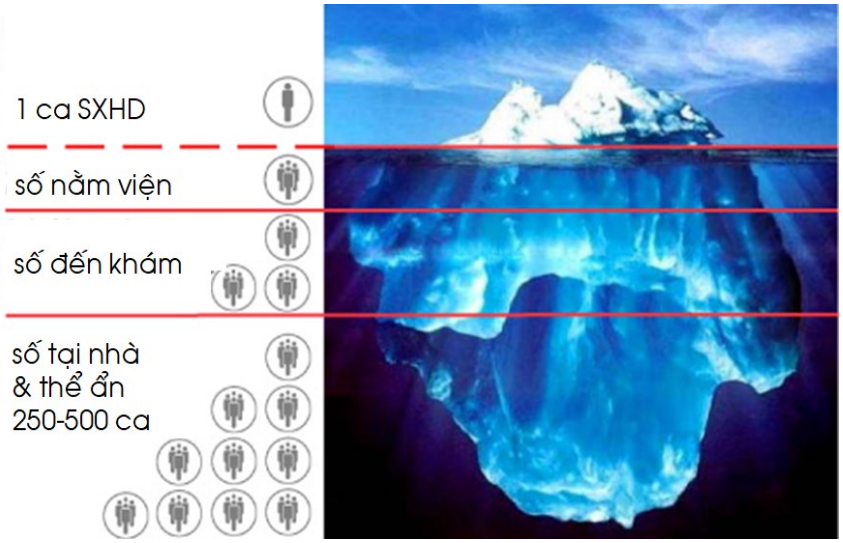
(MENAFN- IANS) London, Nov 7 (IANS) Increasing climate change is expected to drive dengue, a mosquito-borne disease that kills thousands of people every year, to newer areas like the US and Europe, warned a scientist at the World Health Organization (WHO) calling health authorities to start preparing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

Thách thức

Source: *https://kinhtemoitruong.vn/*

Thách thức



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[1*], S. GOYET[1], S. LY[1], C. NGAN[2], R. HUY[2], V. DUONG[1], O. WICHMANN[3], G. W. LETSON[3], H. S. MARGOLIS[3] AND P. BUCHY[1]

[1] *Institut Pasteur in Cambodia, Réseau International des Instituts Pasteur, Phnom Penh, Cambodia*
[2] *National Dengue Control Programme, Ministry of Health, Phnom Penh, Cambodia*
[3] *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.

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

A prospective study of dengue infections in Bangkok.

Burke DS[1], Nisalak A, Johnson DE, Scott RM.

Abstract

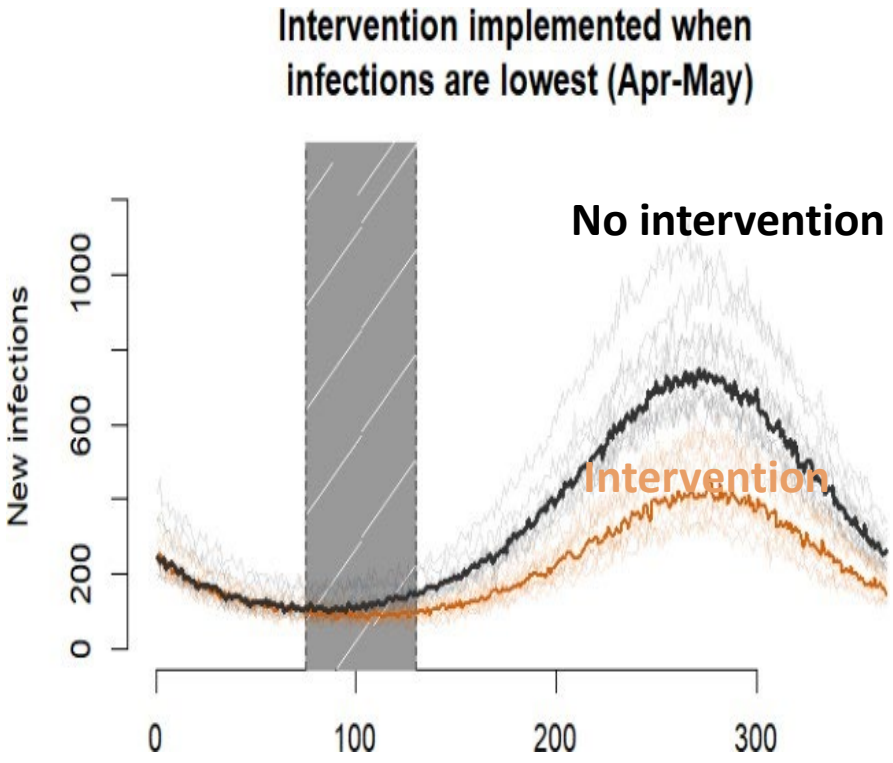
Dengue infections were prospectively studied among 4- to 16-year-old students at a Bangkok school. Blood samples were obtained from 1,757 students in June 1980, before the dengue season, and in January 1981, after the season, and tested for dengue antibodies by the hemagglutination inhibition method. 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.

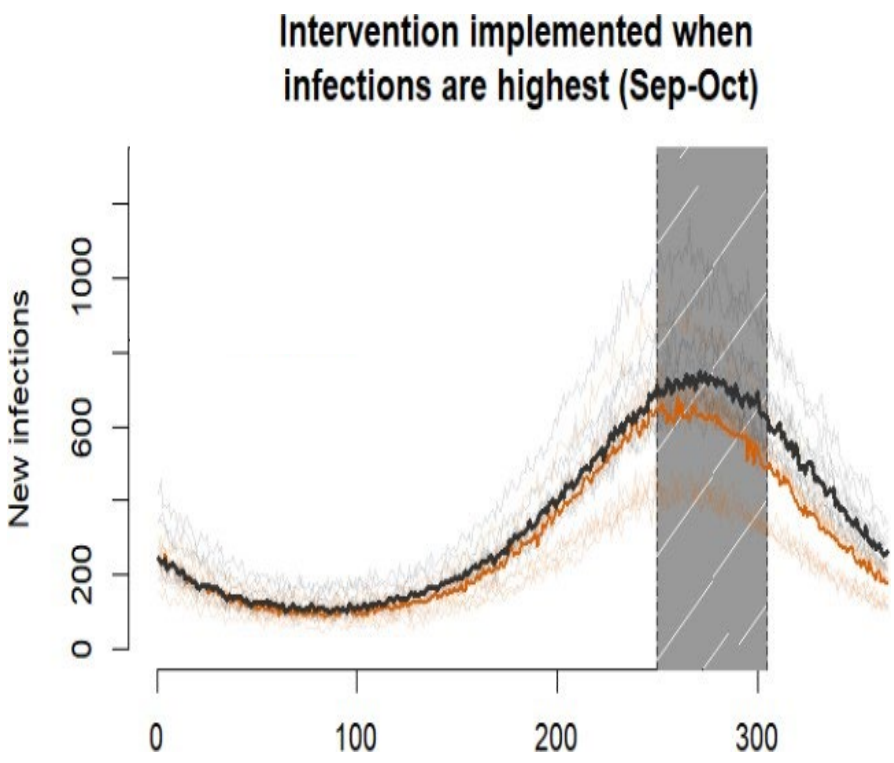
Asymptomatic humans transmit dengue virus to mosquitoes

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

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

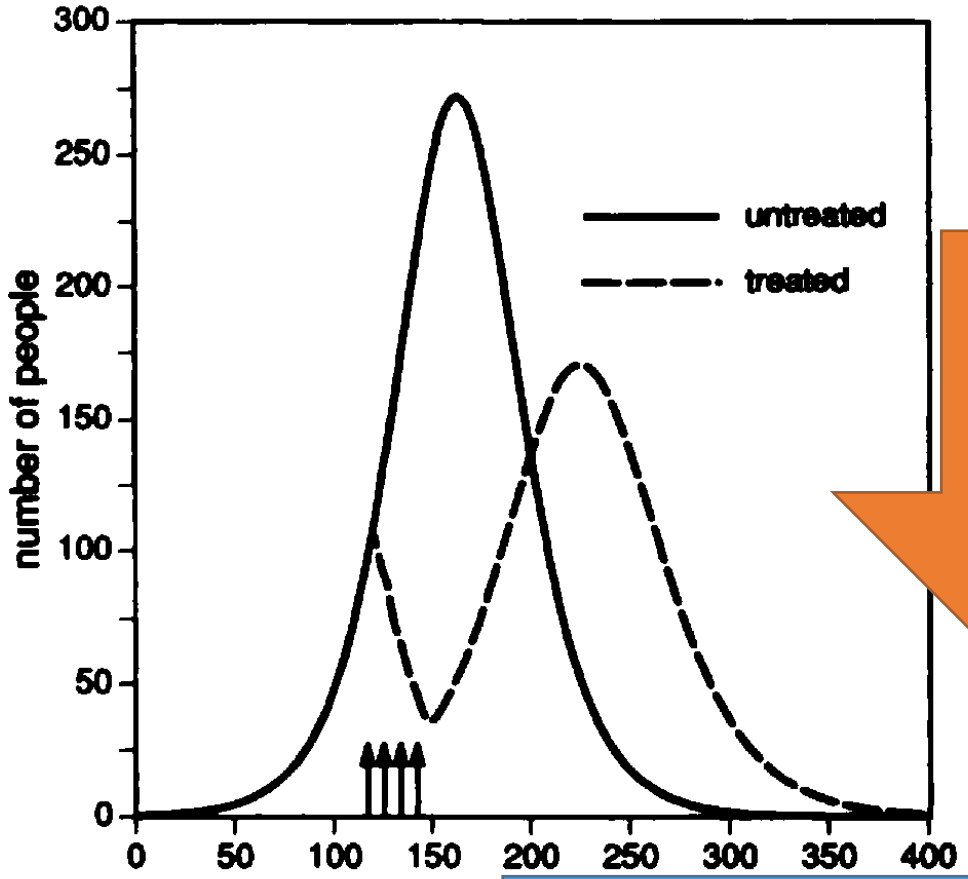
Thách thức





Dữ liệu chưa được công bố của US.CDC, đơn vị sốt xuất huyết, Puerto Rico

Thách thức

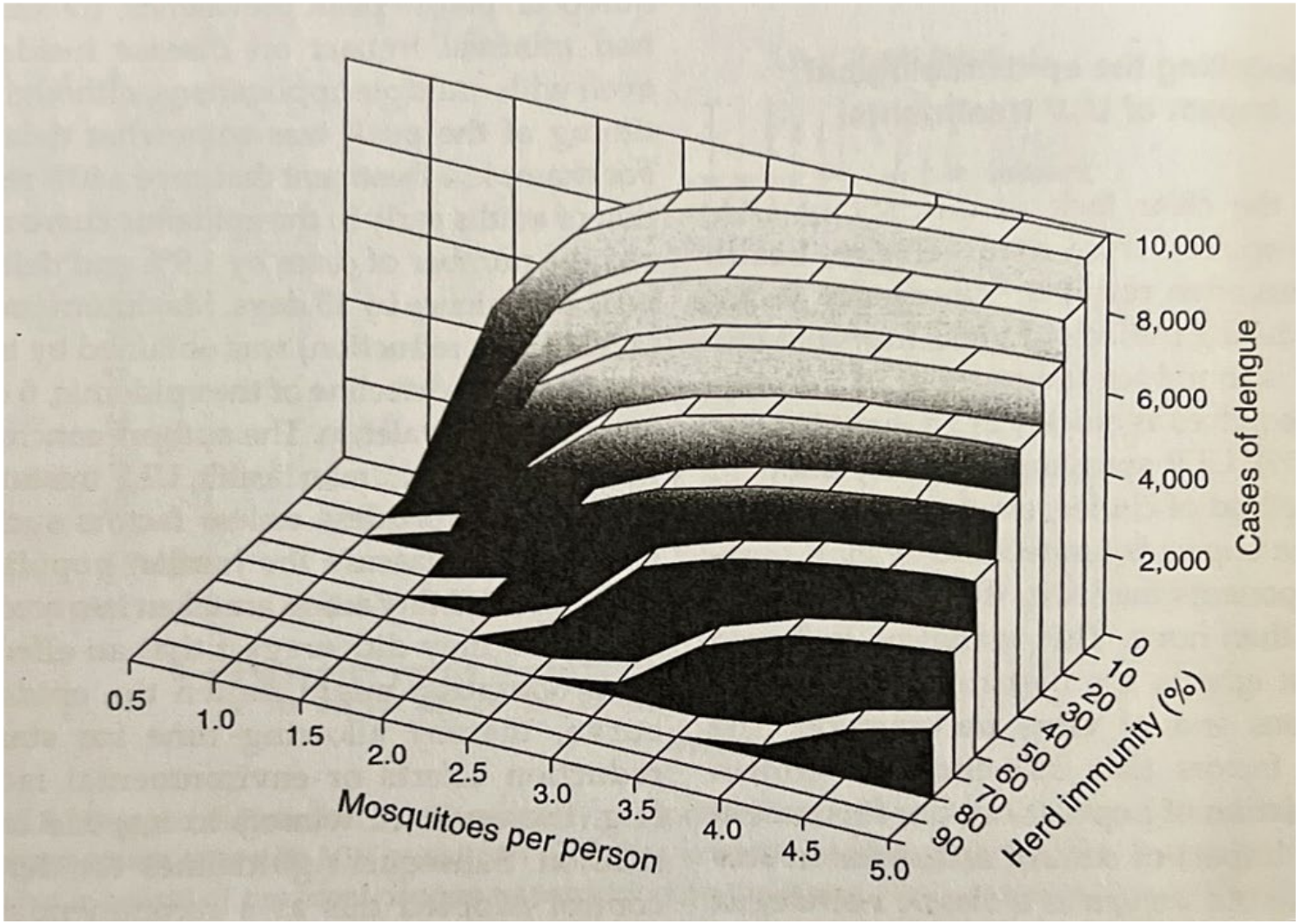


Giảm 1,6% số ca nhiễm

Trì hoãn đỉnh dịch trong 15 ngày

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

Triển vọng



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

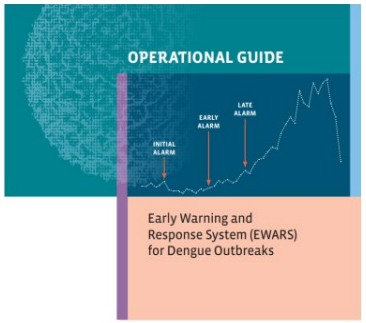
Triển vọng

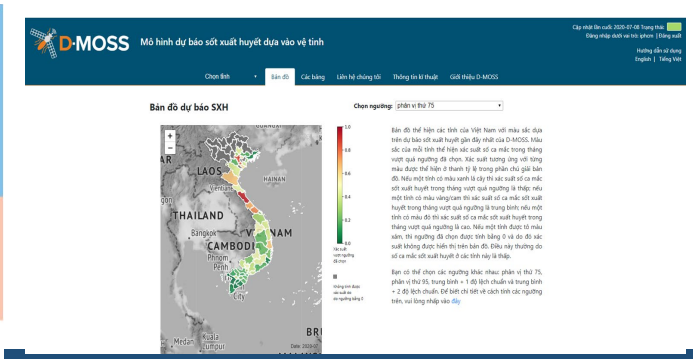
- **Mô hình**
  - **EWARDS (WHO-TDR):** logistics regression
  - **D-MOSS (UK) & E-DENGUE (Australia)**: tổng hợp nhiều mô hình toán học (Mathematical ensembles)

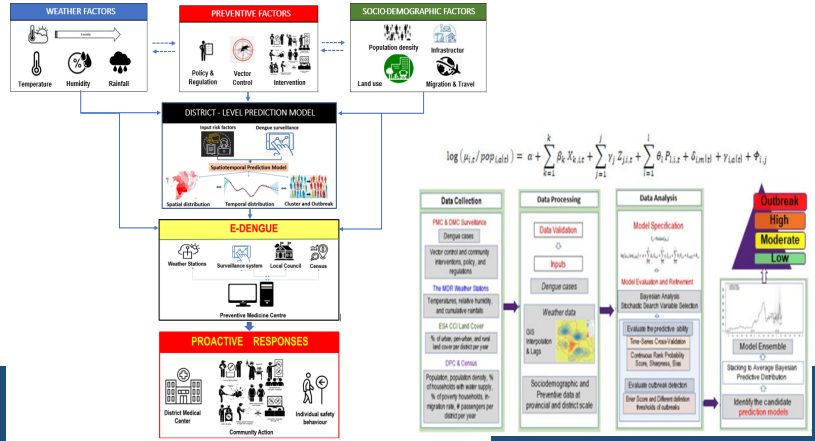
- **Thông số đầu vào:**
  - EWARDS: các ca hàng tháng, khí tượng thuỷ văn
  - D-MOSS: các ca bệnh hàng tháng và dự báo khí tượng thuỷ văn
  - E-DENGUE: các ca bệnh hàng tháng, khí tượng thuỷ văn, kinh tế - xã hội và các hoạt động can thiệp

- **Khả năng dự đoán:**
  - Khoảng thời gian dự báo: từ 1 tuần đến 6 tháng (D-MOSS: trước 6 tháng, E-DENGUEtrước 2 tháng, EWARDS: trước 1 đến 12 tuần)
  - Mức độ dự báo: tuỳ theo công cụ (D-MOSS cho tỉnh, E-DENGUE cho quận/ huyện và có thể cả xã)

- **Tiện ích:** kit (EWARDS), web (D-MOSS), web + ứng dụng trên điện thoại (E-DENGUE)

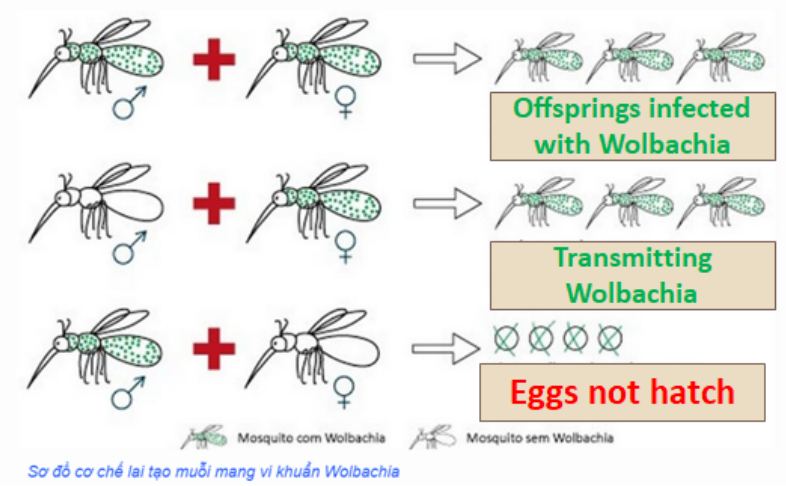




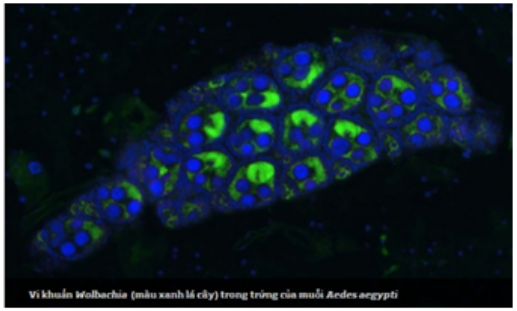


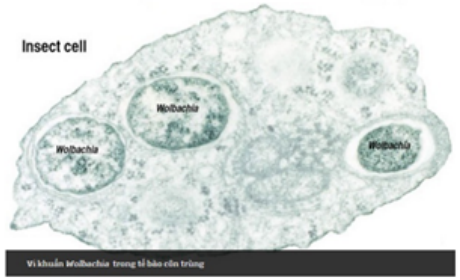
Triển vọng

- 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)



Sơ đồ cơ chế lai tạo muỗi mang vi khuẩn Wolbachia



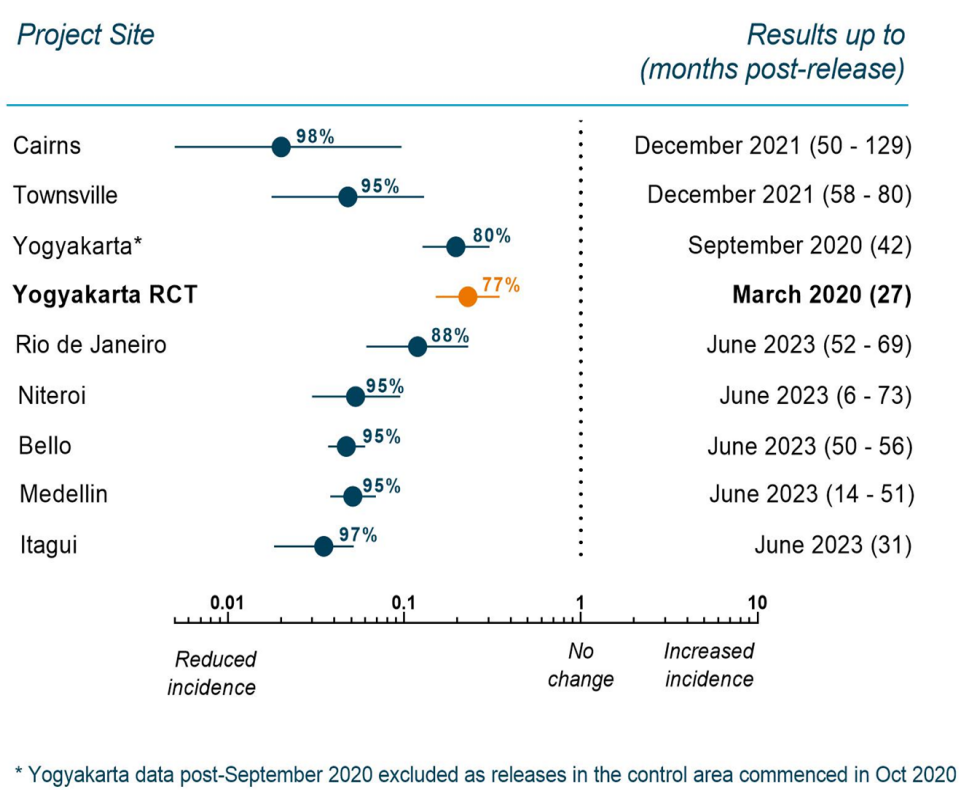


Source: World Mosquito Program-WMP

Triển vọng

Có bằng chứng ở mức độ toàn cầu về việc giảm tỷ lệ mắc bệnh sốt xuất huyết sau khi thực hiện thả muỗi mang wMel

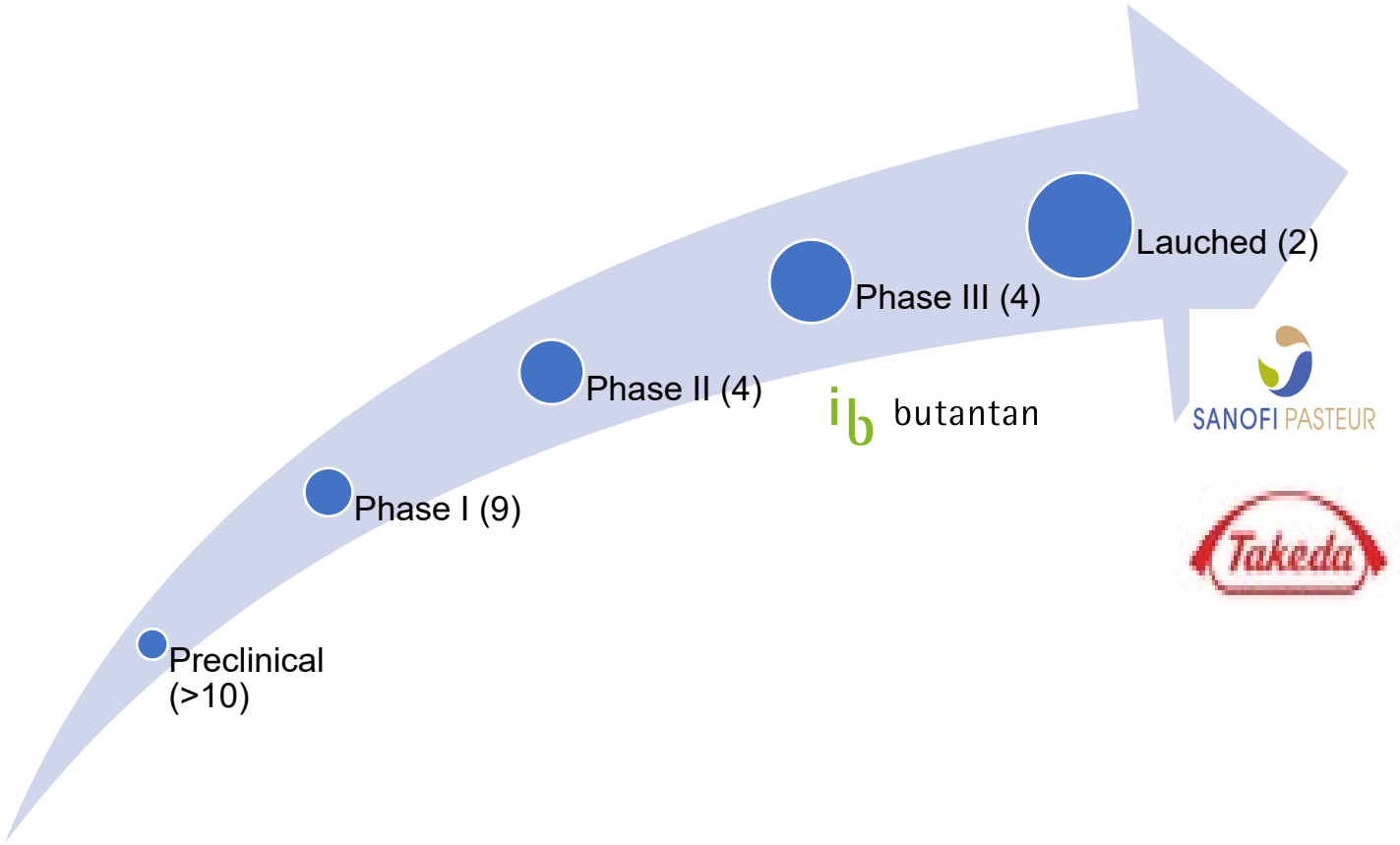
Source: World Mosquito Program-WMP



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

Triển vọng

Có nhiều loại vắc xin phòng bệnh sốt xuất huyết đang được nghiên cứu và phát triển



*Based on current vaccine landscape (02/2023)

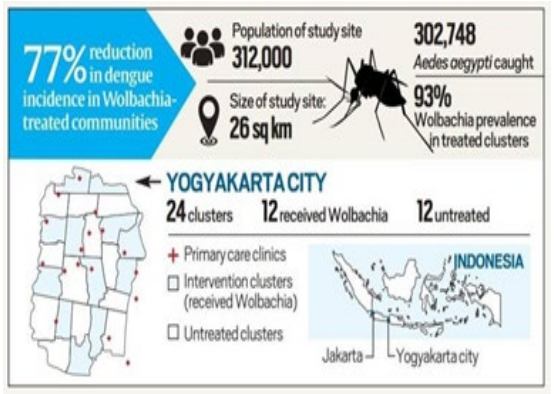
Triển vọng

	CYD-TDV	TAK-003
Tuổi	9-45 tuổi *(Cần xét nghiệm huyết thanh học trước khi tiêm chủng)*	≥ 4 tuổi *(không bắt buộc xét nghiệm huyết thanh học trước khi tiêm)*
Số liều	3 liều (0, 6, 12 month)	2 liều (0, 3 month)
VE against VCD (xác nhận sự có mặt của vi rút Dengue)	65,6% (60,7-69,9)	62% (56,6-66,7)
VE against hospitalization VCD	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

Giải pháp

- Hướng tới tương lai bằng công cụ phòng ngừa mới hiệu quả hơn
  - Vắc xin
  - Kiểm soát véc tơ truyền bệnh:
    - Muỗi mang *Wolbachia*
    - Muỗi biến đôi gen



Thank you!