



Dengue Alliance

**Accelerating development of dengue treatment through
an endemic country-led collaboration**

**ANRS|MIE Scientific Days in Vietnam
Towards ending epidemics
15-16 Nov 2023
Hải Phòng, Vietnam**

Vanessa Daniel, Alliance and Operation Lead, DNDi

DNDi
Best Science
for the Most Neglected **20** years

Content

- About DNDi
- Dengue: Burden, impact & management
- The Dengue Alliance: A South-South collaboration



FACTS



3.9 Bn
people at risk
of being infected



About
390 M
infections per year



This disease
is endemic in
129
countries

20
YEARS
12

TREATMENTS
Saving millions of lives



DNDi
Best Science
for the Most Neglected
20 years

DNDi ORIGINS

BORN ON THE FRONTLINES OF MEDICAL ACTION



DNDi was created in response to the frustration of clinicians and the desperation of patients faced with medicines that were ineffective, unsafe, unavailable, unaffordable, or that had never been developed at all.

The root of the problem?

The prevailing profit-oriented model for medical research and development (R&D) leaves little incentive to develop drugs for the poorest and most vulnerable communities.

WHY DNDi?

For neglected diseases, a fatal imbalance remains

1975- 1999



1.1% of the 1,393 new drugs were for neglected diseases that represent **12%** of the global disease burden*



> 1 IN 5 PEOPLE worldwide are affected by diseases you may never have heard of

* SOURCE: MSF & the DND Working Group, 2001. *Fatal Imbalance: The Crisis in R&D for Neglected Diseases*. Médecins Sans Frontières.



A patient needs-focused, globally networked R&D organization

Treatments delivered

12 

field-adapted and affordable treatments for 6 deadly diseases

R&D pipeline replenished



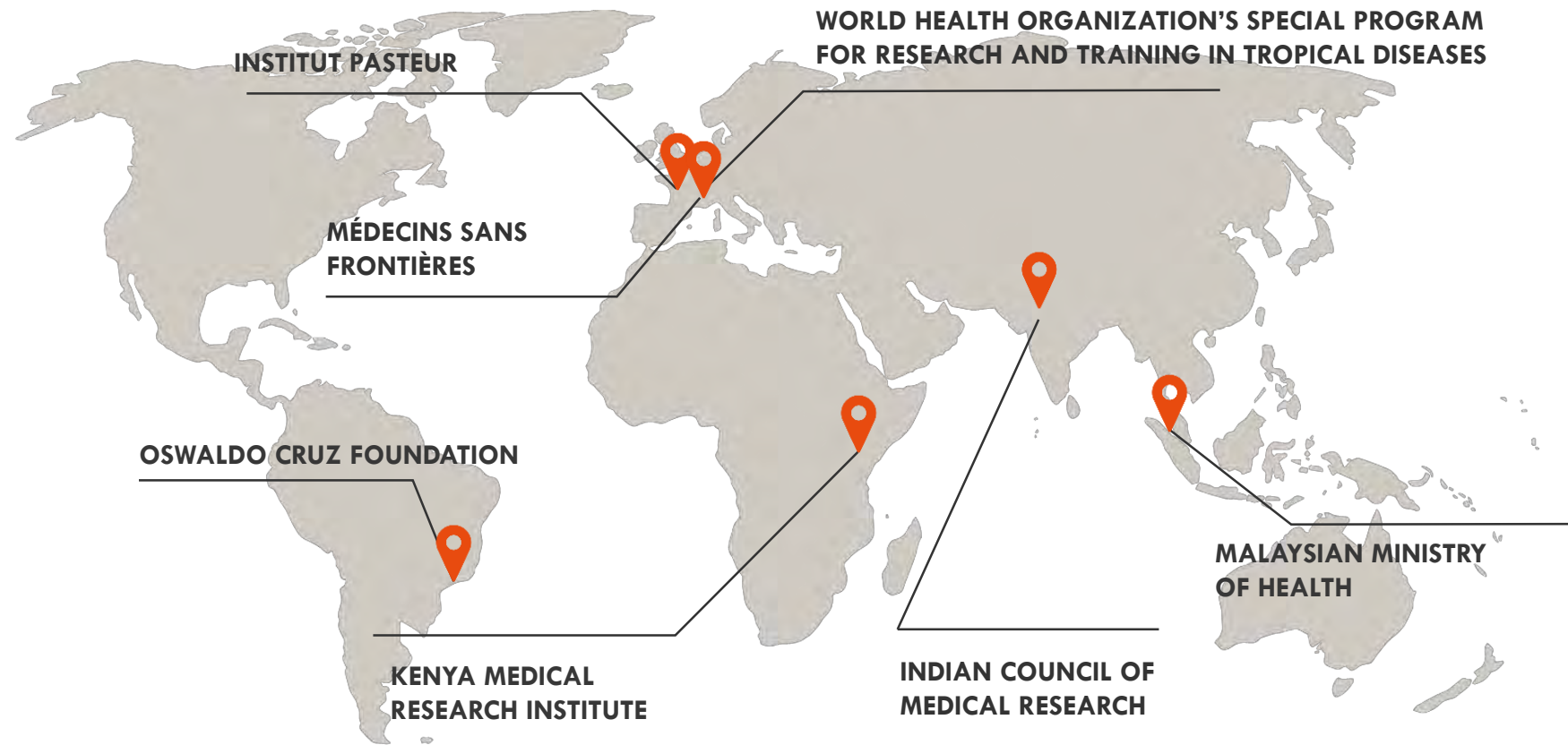
- 19 projects to discover & develop NCEs
- 4 million+ compounds screened
- 9 projects in Phase III and registration

A healthy pipeline of drug candidates for 9 deadly diseases

Clinical trials conducted



An average of 20 active clinical studies per year





Deliver 15 - 18 treatments from 2021 - 2028*
for a total of 25 treatments in our first 25 years

*4 delivered so far



10 - 12 new treatments from
current mature portfolio (2021-24)



5 - 7 new treatments from earlier-stage
NCEs and portfolio expansion (2025-28)

FOCUS ON 5 CROSS-CUTTING STRATEGIC IMPERATIVES



1 Deliver new treatments and expand access for neglected patients by addressing R&D gaps for NTDs and viral diseases, including pandemic-prone and climate-sensitive diseases



2 Join with public health leaders and R&D actors in low- and middle-income countries to advance sustainable innovation ecosystems that address neglected patients' needs



3 Contribute to building a proactive agenda for maternal and child health and gender-responsive R&D



4 Champion open science and transparency



5 Leverage new technologies to accelerate R&D and access

▶ DRIVE IMPACT ACROSS THE 3 PILLARS OF OUR MISSION



INNOVATE TO SAVE LIVES

- Deliver **15-18 new treatments**
- Identify **8-10 new drug candidates** from discovery efforts
- Conduct at least **6 new studies on indications for paediatric use**
- Develop strategies tailored to target diseases and countries' specific needs to ensure **equitable and affordable access and delivery of new treatments**



FOSTER INCLUSIVE & SUSTAINABLE SOLUTIONS

- Grow partnerships for **'end-to-end' R&D** in LMICs
- **Proactively collaborate** with LMIC pharmaceutical and other partners
- Conduct **half of first-in-human Phase I studies** in LMICs
- Train **600 to 1,000 frontline clinicians and researchers** every year



ADVOCATE FOR CHANGE

- **Secure concrete policy changes** to make the innovation system more needs-driven, collaborative, equitable, open and transparent, inclusive, and sustainable
- **Engage with 50+ strategic advocacy partners** to build stronger coalitions and networks of influence
- **Document and share key lessons** from DNDi's model

Asia Pacific

Bangladesh grapples with record deadly outbreak of dengue fever

By Ruma Paul

August 5, 2023 12:43 PM GMT+5:30 · Updated a month ago



nature

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NEWS | 27 July 2023

Dengue is breaking records in the Americas – what’s behind the surge?

Increasing temperatures contribute to longer dengue seasons, and could drive the geographical expansion of the disease.

Mosquito-borne dengue grows deadlier in South Asia as planet warms



Mosabber Hossain, Aadesh Subedi

Published: September 08, 2023

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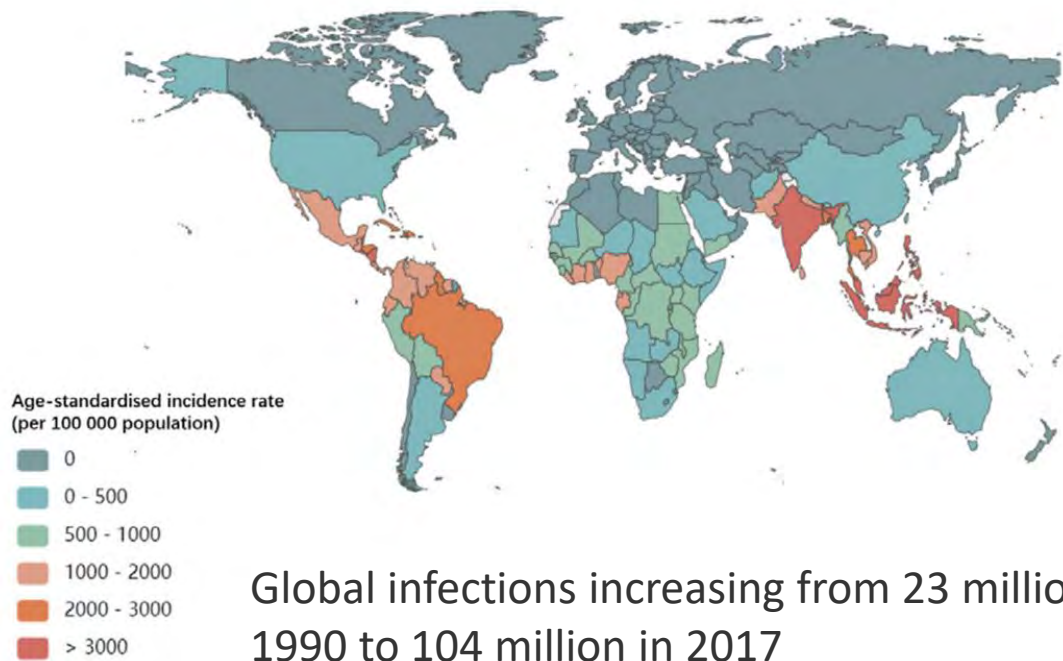
The Daily Star

Sports Business Entertainment Life & Living Youth Tech & Startup

Dengue Outbreak: 2023 already the deadliest year

Global, regional, and national dengue burden from 1990 to 2017: A systematic analysis based on the global burden of disease study 2017

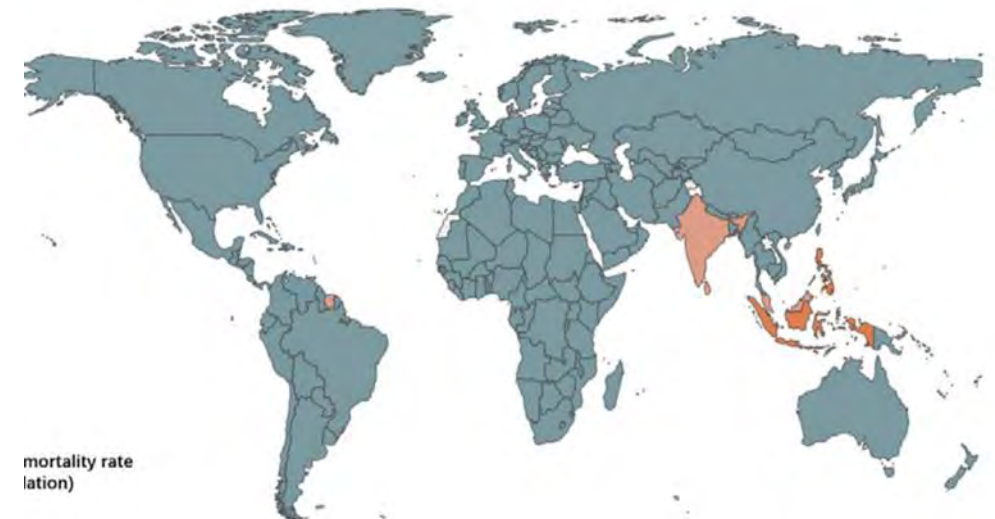
Zhilin Zeng ¹ • Juan Zhan ¹ • Liyuan Chen • Huilong Chen   • Sheng Cheng • [Show footnotes](#)



Global infections increasing from 23 million in 1990 to 104 million in 2017

WHO named dengue as one of the top ten threats to global health in 2019

70% of burden in Asia



Although the incidence of dengue is similar in Latin America and Asia, the mortality rates are higher in Asia

DENGUE BURDEN

Why is there a sudden surge of dengue in 2022/2023?

- It is not sudden!
- WHO named dengue as one of the top ten threats to global health in 2019
- Reasons for gradual increase in dengue
 - Increase temperatures
 - Erratic rains
 - Urbanization
 - Overcrowding and population expansion

Pakistan floods: Dengue cases soaring after record monsoon

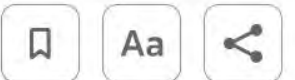
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El Nino rains intensify record dengue outbreak in Peru

By Marco Aquino

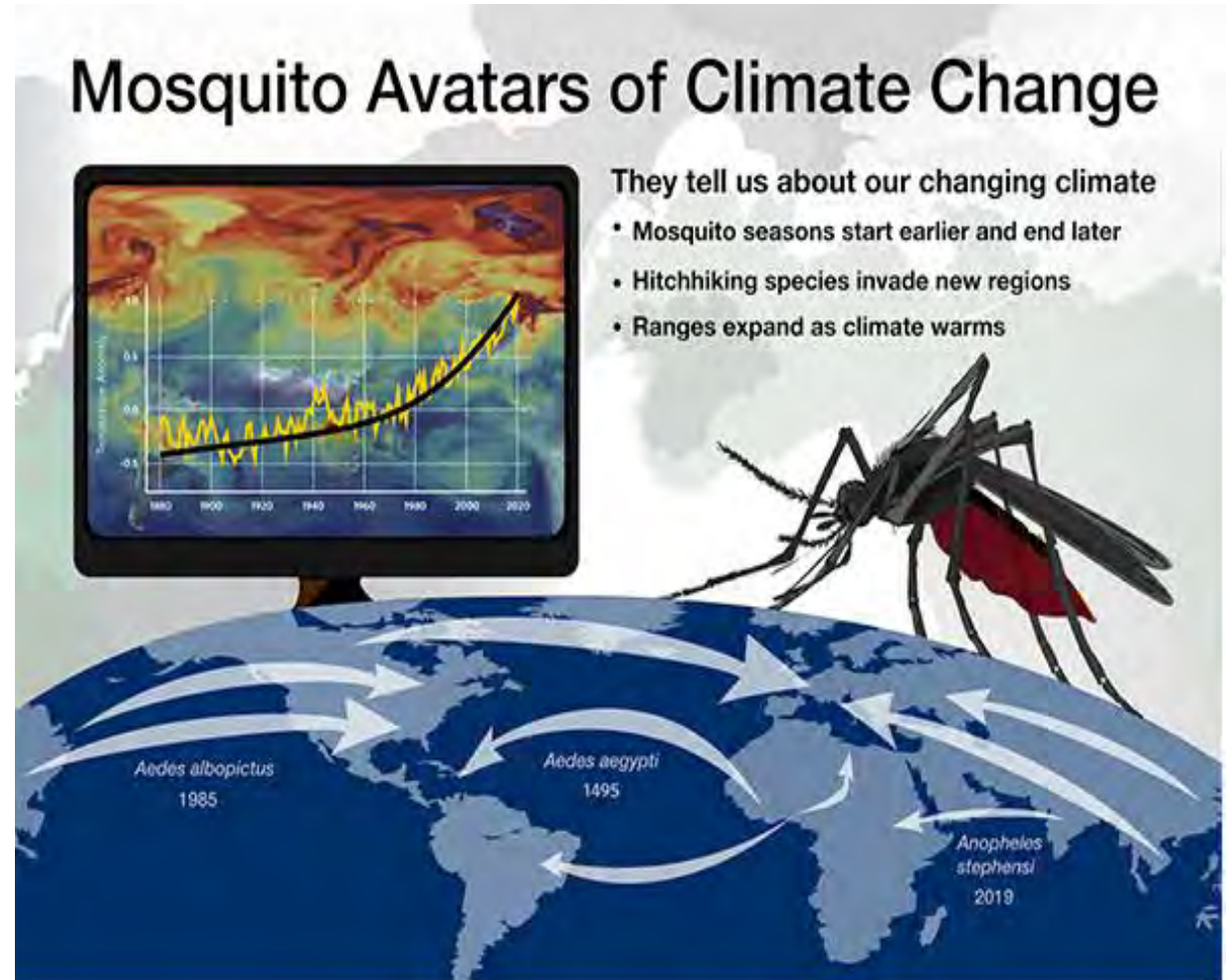
June 9, 2023 2:35 AM GMT+5:30 · Updated 20 days ago



How does climate change affect *Aedes* mosquitoes?

Increase in temperature:

1. Stimulates egg hatching and accelerates growth of larva. Development of *Aedes* from egg to adult was:
 - 7.2 days at 35 °C
 - 39.7 days at 15°C
2. The mosquito gonadotropic cycle shortens:
 - more time for the female mosquito to be in contact with host (longer duration of the ability to infect)
3. At higher temperatures, the mosquitoes bite more frequently
4. Increased virus replication within the mosquito at higher temperatures



Change in the epidemiology of dengue and implications



Dengue infections in pregnancy



- Dengue increases maternal death by 3 times and DHF increases maternal death by 450 times, compared to pregnant women without dengue (Paixao et al,2018).
- Pregnant women were more likely to require ICU admission, ventilatory support and multiorgan failure (Brar et al, 2021)
- Foetal complications: still birth, low birth weight, preterm delivery, foetal distress, miscarriages (Martin et al, 2023).

Comorbidities Associated with Severe Dengue

Diabetes, cardiac disorders and asthma as risk factors for severe organ involvement among adult dengue patients: A matched case-control study

Junxiong Pang^{1,2}, Jung Pu Hsu¹, Tsin Wen Yeo^{1,3}, Yee Sin Leo^{1,2,4} & David C. Lye^{1,3,4}

SCIENTIFIC REPORTS | 7:39872 | DOI: 10.1038/srep39872

The association between diabetes and obesity with Dengue infections

S. D. Sekaran^{1*}, Z. M. Liew², H. C. Yam² and C. S. Raju³

Sekaran *et al.*
Diabetology & Metabolic Syndrome (2022) 14:101

Is Diabetes a Risk Factor for a Severe Clinical Presentation of Dengue? - Review and Meta-analysis

Nan Shwe Nwe Htun^{1,2}, Peter Odermatt^{1,2}, Ikenna C. Eze^{1,2}, Noémie Boillat-Blanco^{1,2,3}, Valérie D'Acremont^{1,2,4}, Nicole Probst-Hensch^{1,2*}

Original Article

Diabetic patients suffering dengue are at risk for development of dengue shock syndrome/ severe dengue: Emphasizing the impacts of co-existing comorbidity(ies) and glycemic control on dengue severity

Ing-Kit Lee^{a,b}, Ching-Jung Hsieh^{c,§}, Chien-Te Lee^{b,d}, Jien-Wei Liu^{a,b,*}

Journal of Microbiology, Immunology and Infection (2020) 53, 69–78

Diabetes with Hypertension as Risk Factors for Adult Dengue Hemorrhagic Fever in a Predominantly Dengue Serotype 2 Epidemic: A Case Control Study

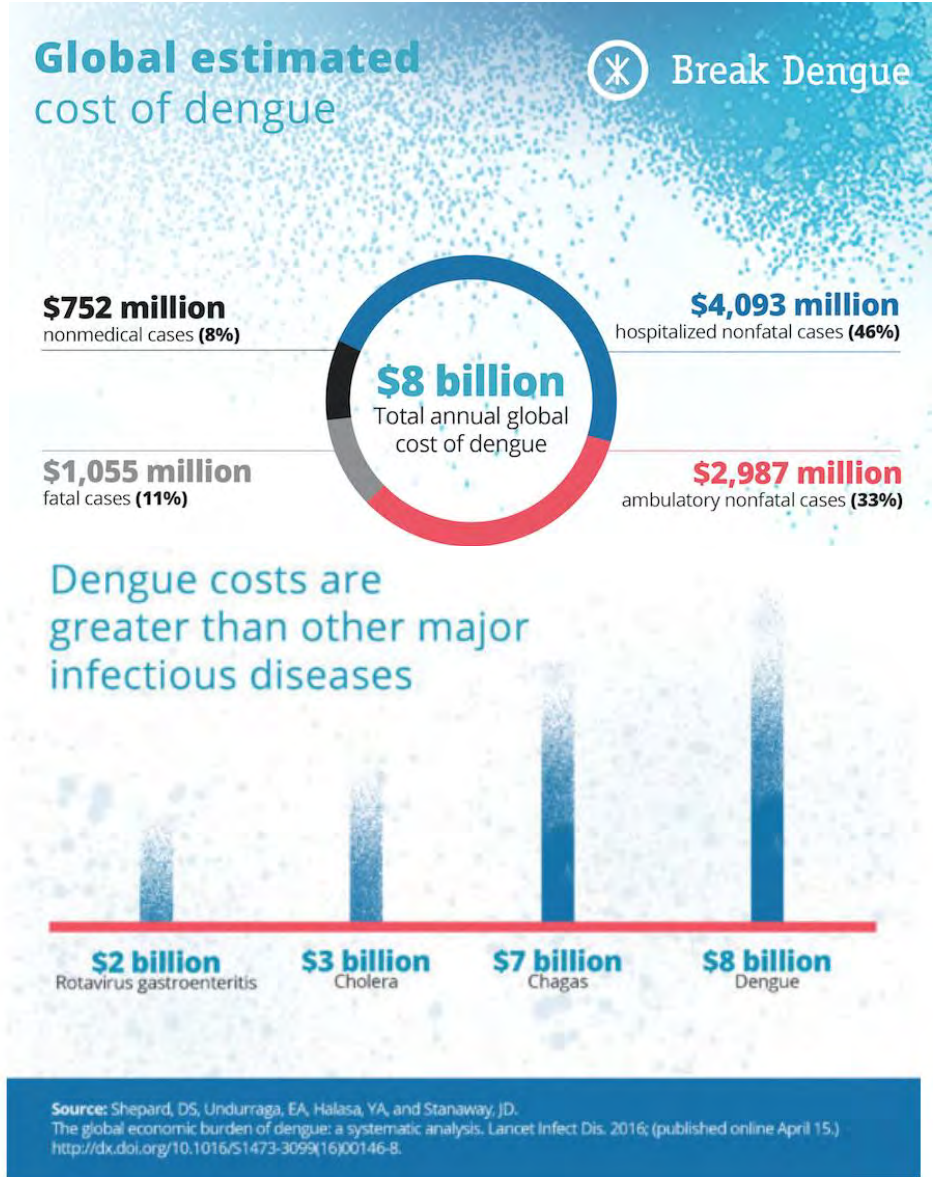
Junxiong Pang^{1,2*}, Agus Salim², Vernon J. Lee^{2,3}, Martin L. Hibberd^{1,2}, Kee Seng Chia², Yee Sin Leo^{4,5}, David C. Lye^{4,5}

www.plosntds.org

May 2012 | Volume 6 | Issue 5 | e1641

With the rise in diabetes, obesity and metabolic disease in our countries, we are likely to see more people developing severe dengue

Economic burden of dengue



Economic burden of dengue illness in India from 2013 to 2016: A systematic analysis

Dhwani Hariharan^a, Manoja Kumar Das^b, Donald S. Shepard^a, Narendra Kumar Arora^b.

^a *Heller School for Social Policy and Management, Brandeis University, Waltham, MA, USA*

^b *The INCLIN Trust International, New Delhi, India*

Global costs of USD 8 billion in 2014 is a gross under estimation, when the costs in India alone in 2018 was **USD 5.71 billion**

Productivity costs from a dengue episode in Asia: a systematic literature review

A review of 31 studies

- Outpatient: USD 3.8 to 1332
- Hospitalized: USD 6.7 to 1445.9
- Fatal dengue: USD 12.035 to 1,453,237

Loss of workdays (Thailand)

Dengue fever: 8.4

Dengue hemorrhagic fever: 9.7

Shock: 12.3

How can we face these challenges?

Healthcare & Pharmaceuticals | Public Health

Bangladesh fears record high death toll from dengue outbreak



Dengue fever crisis forces Peru minister to resign

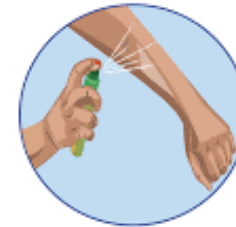
🕒 16 June



Vector Control



Use insect repellent

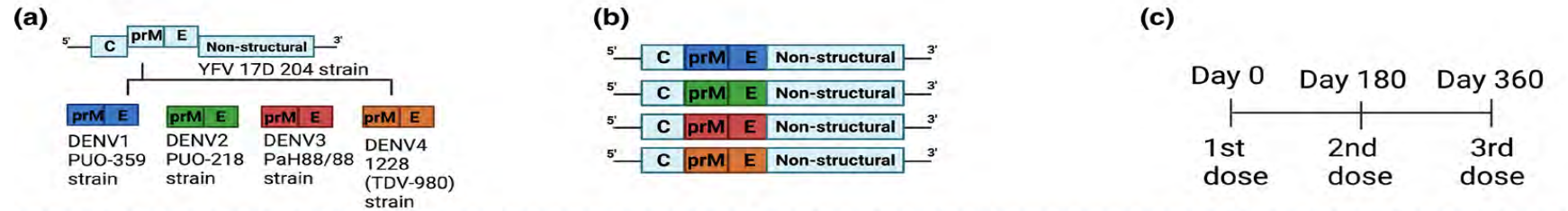


Cover skin

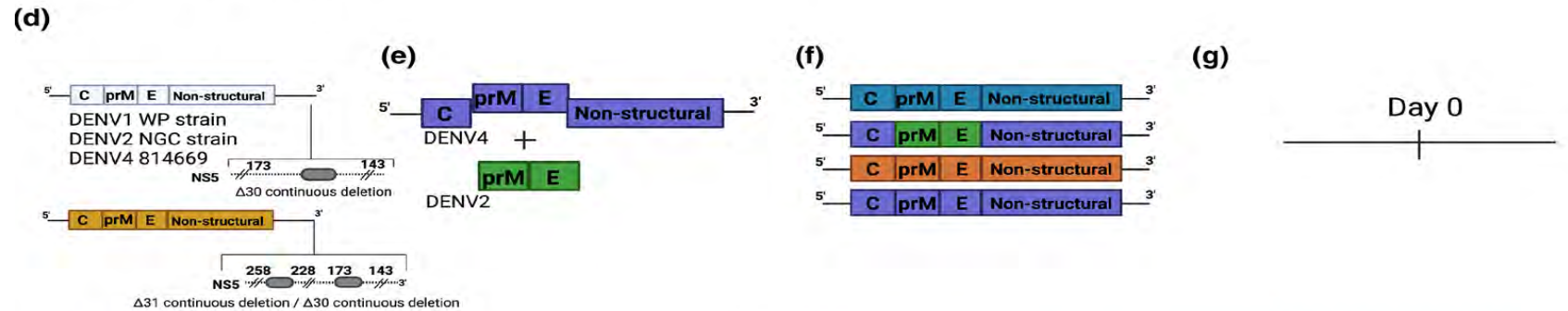


Dengue vaccines currently in Phase 3 trials or approved

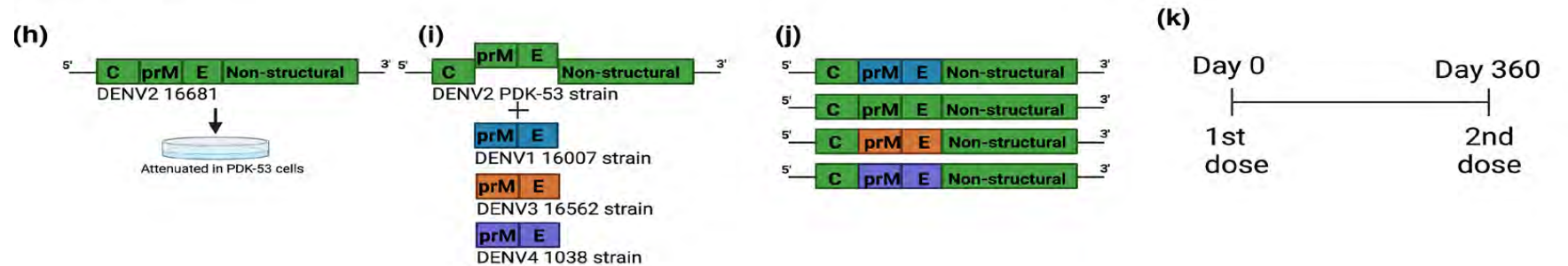
Dengvaxia®




NIAID LATV TV003

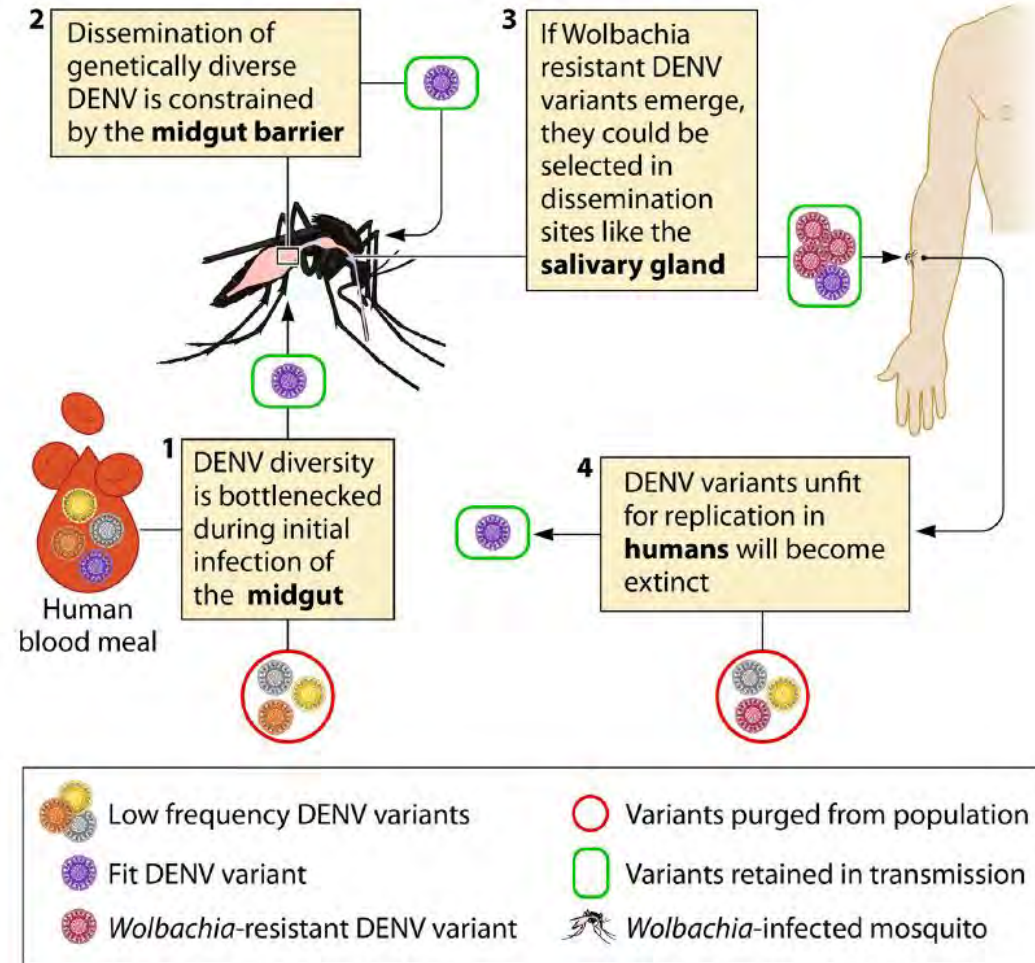


TAK-003



Using *Wolbachia* to Eliminate Dengue: Will the Virus Fight Back?

Kathryn M. Edenborough,^a Heather A. Flores,^a Cameron P. Simmons,^{b,c,d}  Johanna E. Fraser^{a,e}

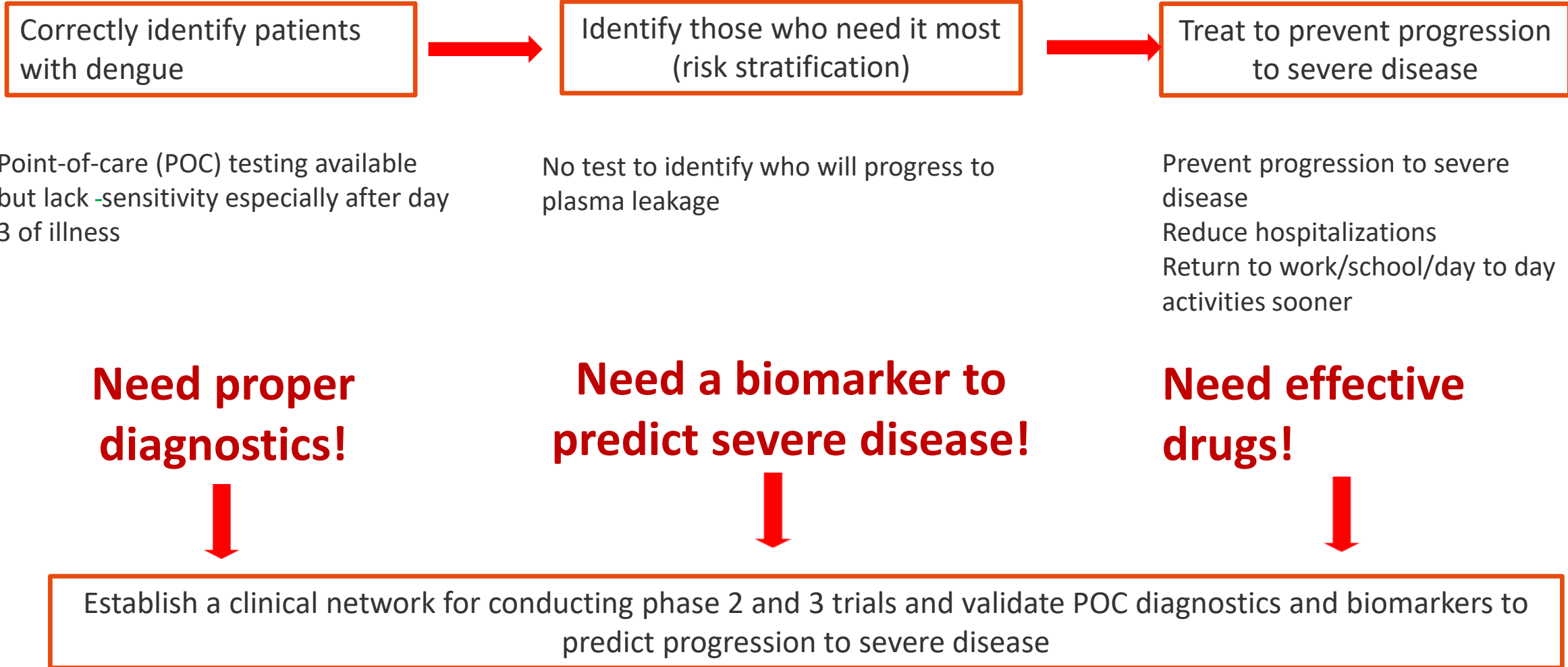


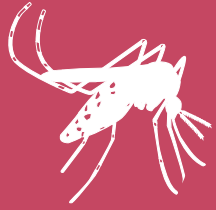
CONCLUDING REMARKS

With a body of evidence now demonstrating that *Wolbachia*-*Ae. aegypti* introgression methods can substantially reduce the burden of dengue in areas of endemicity, it is expected that application of this technology will undergo a major expansion in coming years (17, 19, 24, 26). The intention is that this will lead to long-term control or local elimination of human-pathogenic arboviruses. Achieving long-term suppression in the field would be dependent upon the evolutionary stability of the *Wolbachia*, *Ae. aegypti*, and DENV tripartite interaction. *Wolbachia* and *Ae. aegypti* evolve slowly compared to DENV, and *Wolbachia*-carrying mosquitoes collected years after release have so far retained their antiviral profile. Yet the rapid mutation rate of RNA viruses suggests it is inevitable that viruses like DENV will eventually adapt to *Wolbachia*'s selective pressure and become resistant to the intervention. The question is, how long will this take?

ABSTRACT Recent field trials have demonstrated that dengue incidence can be substantially reduced by introgressing strains of the endosymbiotic bacterium *Wolbachia* into *Aedes aegypti* mosquito populations. This strategy relies on *Wolbachia* reducing the susceptibility of *Ae. aegypti* to disseminated infection by positive-sense RNA viruses like dengue. However, RNA viruses are well known to adapt to antiviral pressures. Here, we review the viral infection stages where selection for *Wolbachia*-resistant virus variants could occur. We also consider the genetic constraints imposed on viruses that alternate between vertebrate and invertebrate hosts, and the likely selection pressures to which dengue virus might adapt in order to be effectively transmitted by *Ae. aegypti* that carry *Wolbachia*. While there are hurdles to dengue viruses developing resistance to *Wolbachia*, we suggest that long-term surveillance for resistant viruses should be an integral component of *Wolbachia*-introgression biocontrol programs.

Dengue Strategy: An Oral Treatment for Patients of All Ages, with Acute Dengue Infection to Prevent progression to Severe Disease





DENGUE

FORGING GLOBAL PARTNERSHIPS TO TACKLE A RAPIDLY SPREADING CLIMATE-SENSITIVE DISEASE

FACTS

3.9 billion
people at risk

About
390 million
infections per
year

Endemic in
129
countries
around the
world

CHALLENGES

- **Most prevalent** mosquito-borne viral disease
- **Climate sensitive:** rising burden of disease
- **No existing treatments for uncomplicated dengue fever** to prevent progression to severe disease and complications

OPPORTUNITIES

- **Window of opportunity** to meet growing medical need
- **Well-defined populations** for clinical trials and endpoints to define success
- **Opportunities in small-molecule drugs and/or biologicals**
- **COVID-19 learnings** and opportunities for cross-fertilization

OUR GOALS

2021- 2028: Advance treatment solutions that can prevent progression to severe disease and reduce burden on public health systems

- Together with leaders in endemic countries, coordinate **public-private partnerships for dengue R&D**
- Accelerate evaluation of **candidate repurposing agents** as well as **novel treatments**, in monotherapy and in combination
- **Antiviral + host-directed therapy combination**, to be deployed with rapid diagnostic tests at point of care
- **Affordable, sustainable, and adapted** for use in resource-limited settings, suitable for children/adults/elderly



MAIN PARTNERS: Ministry of Health Malaysia, Mahidol University (Faculty of Medicine Siriraj Hospital) - Thailand, Oswaldo Cruz Foundation (Fiocruz) - Brazil, Translational Health Science and Technology Institute - India

Dengue Alliance and Supporting Ecosystem



THSTI, India

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- 2. Dr Dinesh Mahajan
- 3. Dr Sweety Samal
- 4. Dr Supratik Das
- 5. Dr Shailendra Asthana

FIOCRUZ, Brazil

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- 2. Prof Thiago Moreno L. Souza

Siriraj Hospital, Mahidol University

- 1. Prof Panisadee Avirutnan
- 2. Prof Prasert Auewarakul
- 3. Dr Sansanee Noisakran

UFMG, Brazil

- 1. Prof. Mauro Teixeira
- 2. Prof Vivian Vasconcelos Costa



Duke-NUS, Singapore

Prof. Ashley St. John

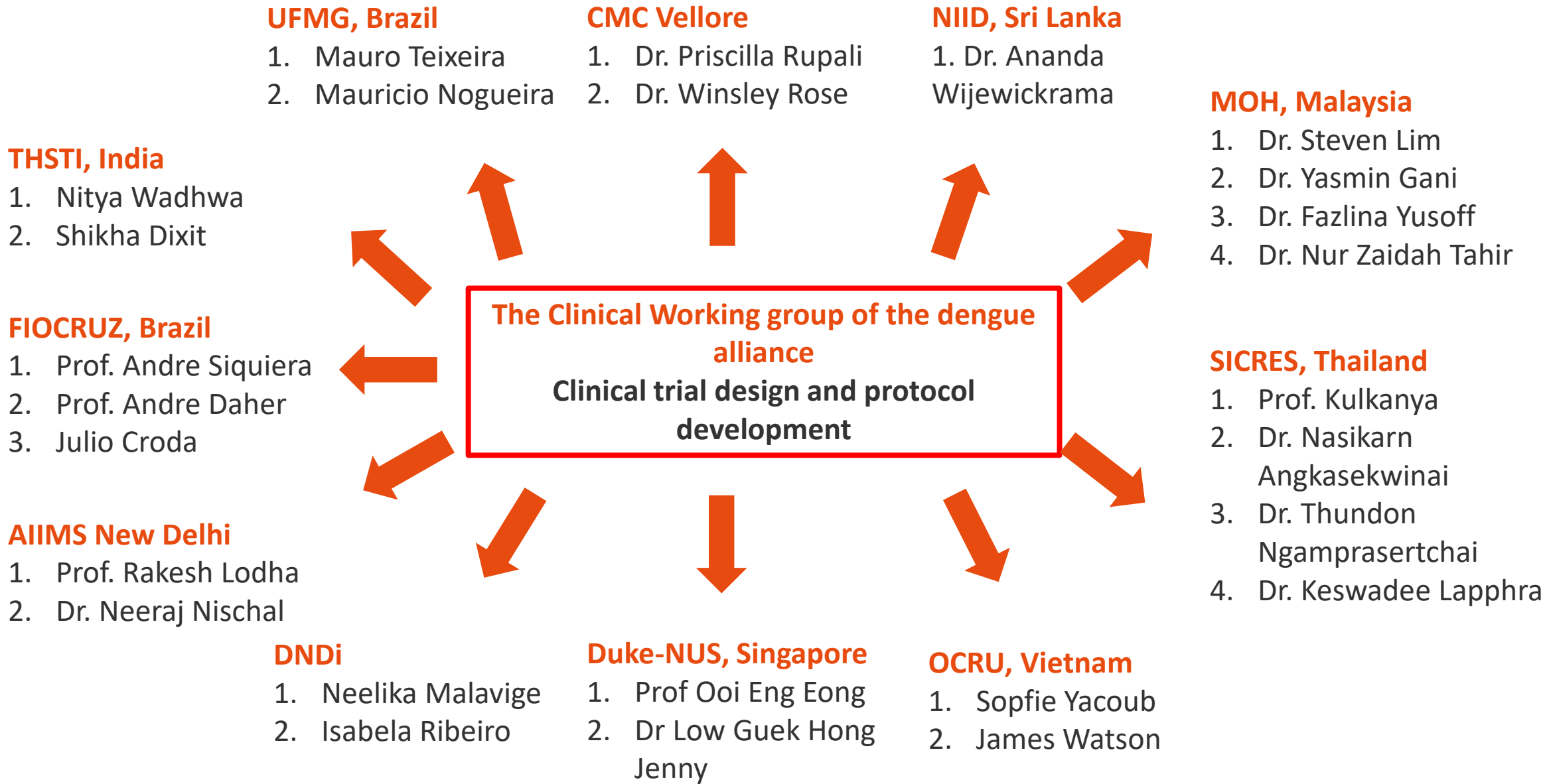
IMR, Malaysia

- 1. Dr Ami Fazlin BT. Syed Mohamed
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- 4. Dr Murizal B Zainol
- 5. Dr Ravindran Thayan
- 6. Dr Rozainanee Mohd Zain
- 7. Dr Tahir Bin Aris
- 8. Mr Terence Tan Yew Chin
- 9. Dr Jeevanathan Kalyanasundram
- 10. Ms. E. Kavithambigai Ellan

DNDi

- 1. Dr. Peter Sjo
- 2. Dr. Graeme Bilbe
- 3. Prof. Neelika Malavige
- 4. Dr. Isabela Ribeiro

Nomination of candidates expected soon.



Clinical trial protocol almost finalized at this stage.

An Endemic Country-Led Collaboration to Accelerate Development of Dengue Treatment

Treatments for dengue: a Global Dengue Alliance to address unmet needs



Dengue is currently the most rapidly spreading mosquito-borne viral infection in the world, with half of the world's population at risk of becoming infected.¹ As a result of climate change, rapid urbanisation, and widespread international travel, the incidence of dengue is rapidly increasing, overwhelming health-care systems in many lower-income countries. Climate change has increased the burden of dengue in endemic countries and has also led to expansion of this infection to new territories in Europe and North America.²

in India; the Oswaldo Cruz Foundation in Brazil; and the Federal University of Minas Gerais in Brazil. The mission of this alliance is to accelerate research and development and deliver dengue therapeutics through an inclusive partnership. It aims to deliver a new treatment for dengue, within 5 years, from repurposed drugs and combinations (including novel antivirals from pharmaceutical companies). This alliance is co-created, co-owned, and co-funded by dengue-endemic countries, with a tiered governance mechanism allowing

Lancet Glob Health 2023
Published Online
August 31, 2023
[https://doi.org/10.1016/S2214-109X\(23\)00362-5](https://doi.org/10.1016/S2214-109X(23)00362-5)

South-South collaboration to find a safe, affordable, and effective treatment

The first in-person Dengue Alliance meeting took place in India on 6-7 February 2023, with experts and scientists from India, Malaysia, Thailand, Brazil, Sri Lanka, and Switzerland present to kick-off plans to develop treatments for this climate-sensitive disease which causes substantial morbidity and mortality globally.






The Dengue Alliance, launched in 2022, is a global partnership led by institutions from dengue-endemic countries that aims to develop affordable and accessible treatments for dengue. The members of this alliance include the Translational Health Science and Technology Institute (THSTI), India; Siriraj Hospital, Mahidol University, Thailand; Institute of Medical Research (IMR), Ministry of Health (MOH), Malaysia; Oswaldo Cruz Foundation, Brazil; Federal University of Minas Gerais (UFMG), Brazil; and the Drugs for Neglected Diseases initiative (DNDi).



***Lancet Glob Health* 2023** Published Online August 31, 2023. [https://doi.org/10.1016/S2214-109X\(23\)00362-5](https://doi.org/10.1016/S2214-109X(23)00362-5)

[Dengue | DNDi](#)

Thank you!



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 linkedin.com/company/dndi

DNDi
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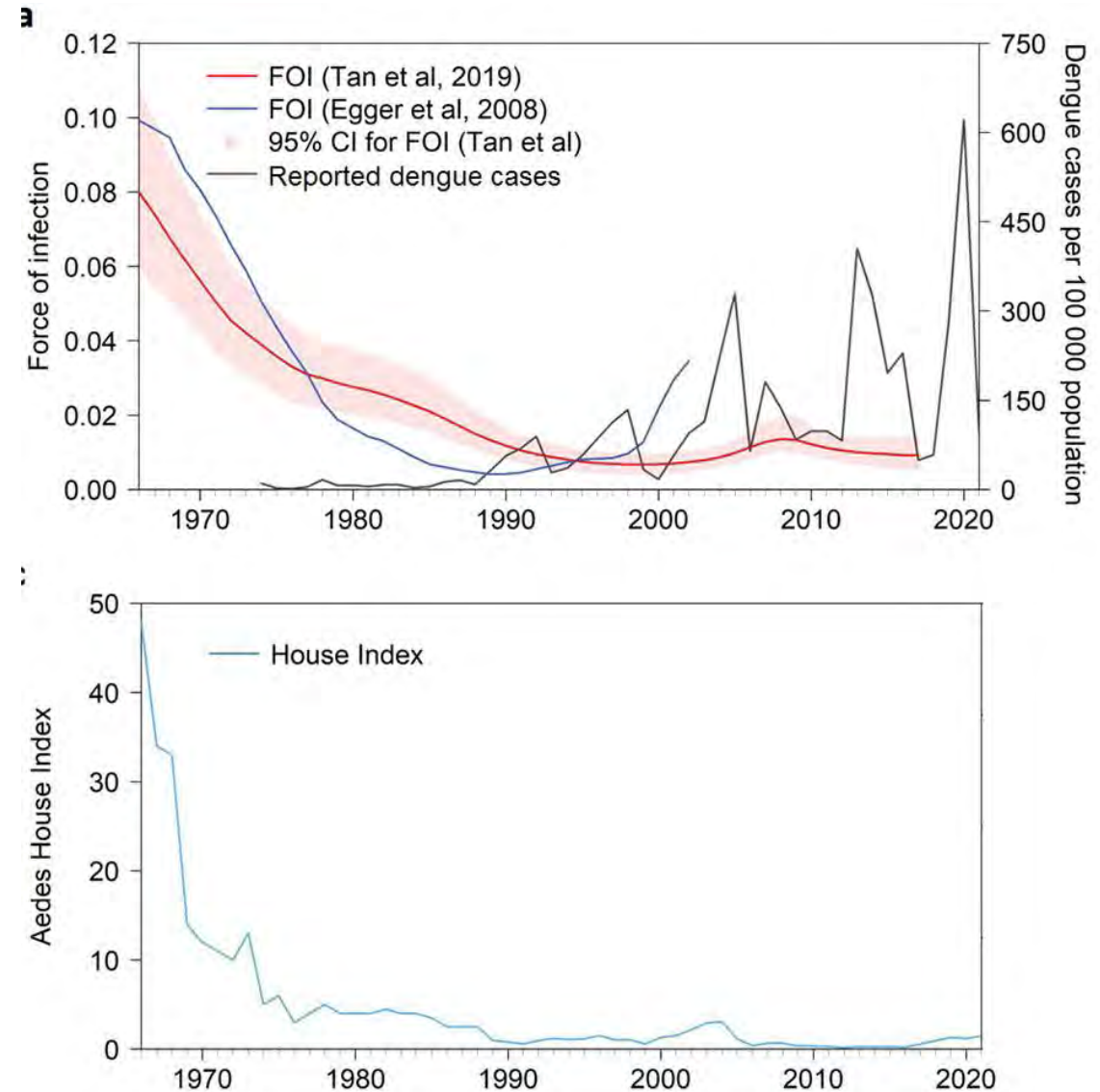
SUPPLEMENTARY SLIDES

DENGUE MANAGEMENT

Singapore's 5 decades of dengue prevention and control—Implications for global dengue control

Abstract

This paper summarises the lessons learnt in dengue epidemiology, risk factors, and prevention in Singapore over the last half a century, during which Singapore evolved from a city of 1.9 million people to a highly urban globalised city-state with a population of 5.6 million. Set in a tropical climate, urbanisation among green foliage has created ideal conditions for the proliferation of *Aedes aegypti* and *Aedes albopictus*, the mosquito vectors that transmit dengue. A vector control programme, largely for malaria, was initiated as early as 1921, but it was only in 1966 that the Vector Control Unit (VCU) was established to additionally tackle dengue haemorrhagic fever (DHF) that was first documented in the 1960s. Centred on source reduction and public education, and based on research into the bionomics and ecology of the vectors, the programme successfully reduced the *Aedes* House Index (HI) from 48% in 1966 to <5% in the 1970s. Further enhancement of the programme, including through legislation, suppressed the *Aedes* HI to around 1% from the 1990s. The current programme is characterised by 4 key features: (i) proactive inter-epidemic surveillance and control that is stepped up during outbreaks; (ii) risk-based prevention and intervention strategies based on advanced data analytics; (iii) coordinated inter-sectoral cooperation between the public, private, and people sectors; and (iv) evidence-based adoption of new tools and strategies. Dengue seroprevalence and force of infection (FOI) among residents have substantially and continuously declined over the 5 decades. This is consistent with the observation that dengue incidence has been delayed to adulthood, with severity highest among the elderly. Paradoxically, the number of reported dengue cases and outbreaks has increased since the 1990s with record-breaking epidemics. We propose that Singapore's

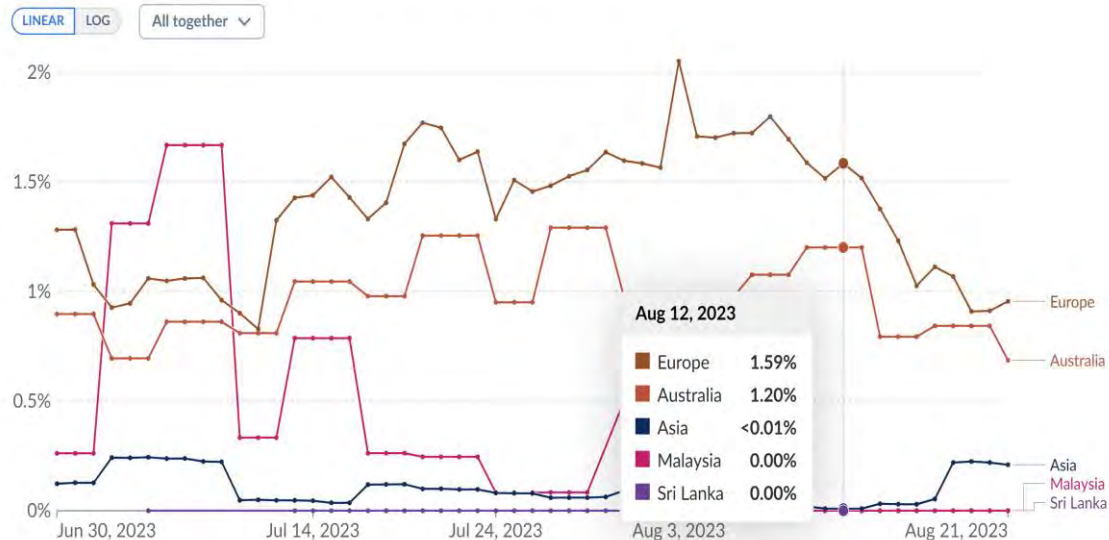


Case Fatality Rates due to Covid-19 & on-going clinical trials

Moving-average case fatality rate of COVID-19

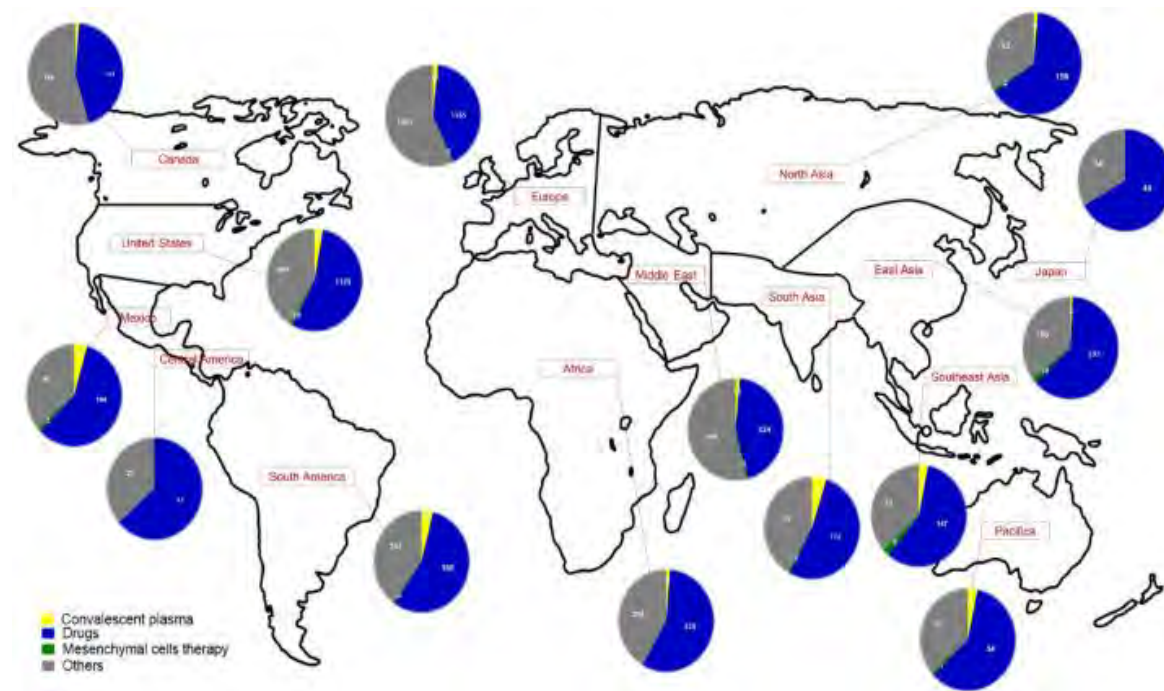
The case fatality rate (CFR) is the ratio between confirmed deaths and confirmed cases. Our rolling-average CFR is calculated as the ratio between the 7-day average number of deaths and the 7-day average number of cases 10 days earlier.

Our World in Data



Source: WHO COVID-19 Dashboard

CC BY



2,079 trials for COVID-19!

Actively recruiting: 172

Completed: 782

92 trials for dengue!

Actively recruiting: 4, active but not recruiting: 2

Completed: 62



ANRS | MIE Scientific Days in Vietnam

Towards ending epidemics

15th to 16th of November, 2023



Dengue Alliance

Đẩy mạnh phát triển
điều trị sốt xuất huyết
thông qua sự hợp tác
đa quốc gia

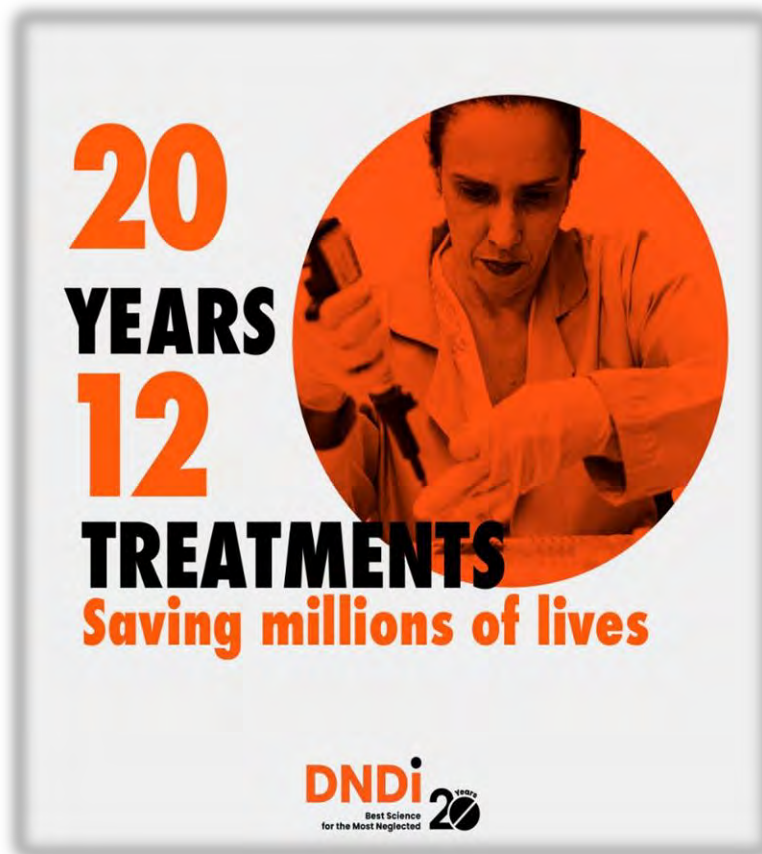
Vanessa Daniel, Alliance & Operations Lead

Drugs for Neglected Diseases initiative (DNDi)



NỘI DUNG

- Giới thiệu về DNDi
- Sốt xuất huyết: gánh nặng, tác động và quản lý
- Liên minh sốt xuất huyết: Hợp tác Nam - Nam

A large infographic on a light gray background. On the right is a circular image of a woman in a white lab coat working in a laboratory. To the left of the image, the text reads "20 YEARS 12 TREATMENTS Saving millions of lives". At the bottom right is the DNDi logo with "20 years" and "Best Science for the Most Neglected".

20
YEARS
12
TREATMENTS
Saving millions of lives

DNDi
Best Science
for the Most Neglected **20**^{years}

NGUỒN GỐC CỦA DNDi



DNDi được tạo ra để đáp lại sự thất vọng của bác sĩ lâm sàng và sự tuyệt vọng của bệnh nhân khi phải đối mặt với các loại thuốc không hiệu quả, không an toàn, không có sẵn, không đủ khả năng chi trả hoặc chưa bao giờ được phát triển.

Gốc rễ của vấn đề?

Mô hình nghiên cứu và phát triển y tế (R&D) hướng tới lợi nhuận phổ biến không tạo ra nhiều động lực phát triển thuốc cho các cộng đồng nghèo nhất và dễ bị tổn thương nhất.

TẠI SAO LẠI LÀ DNDi?

For neglected diseases, a fatal imbalance remains

1975- 1999



1.1% of the 1,393 new drugs were for neglected diseases that represent **12%** of the global disease burden*



> 1 IN 5 PEOPLE worldwide are affected by diseases you may never have heard of

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MỘT SỰ HỢP TÁC TOÀN CẦU THẬT SỰ


A patient needs-focused, globally networked R&D organization

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12 


field-adapted and affordable treatments
for 6 deadly diseases

R&D pipeline replenished

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9 projects in Phase III and registration

A healthy pipeline of drug candidates for
9 deadly diseases

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 An average of 20 active
clinical studies per year



KẾ HOẠCH CHIẾN LƯỢC

SUMMARY



DNDi Strategic Plan

Deliver 15 - 18 treatments from 2021 - 2028*
for a total of 25 treatments in our first 25 years
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3 Contribute to building a proactive agenda for maternal and child health and gender-responsive R&D



4 Champion open science and transparency



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INNOVATE TO SAVE LIVES

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- Develop strategies tailored to target diseases and countries' specific needs to ensure **equitable and affordable access and delivery of new treatments**



FOSTER INCLUSIVE & SUSTAINABLE SOLUTIONS

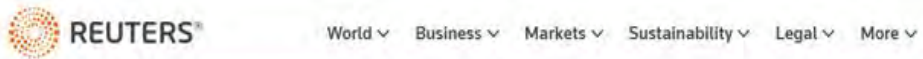
- Grow partnerships for **'end-to-end' R&D** in LMICs
- **Proactively collaborate** with LMIC pharmaceutical and other partners
- Conduct **half of first-in-human Phase I studies** in LMICs
- Train **600 to 1,000 frontline clinicians and researchers** every year



ADVOCATE FOR CHANGE

- **Secure concrete policy changes** to make the innovation system more needs-driven, collaborative, equitable, open and transparent, inclusive, and sustainable
- **Engage with 50+ strategic advocacy partners** to build stronger coalitions and networks of influence
- **Document and share key lessons** from DNDi's model

GÁNH NẶNG CỦA SỐT XUẤT HUYẾT

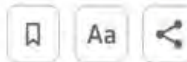


Asia Pacific

Bangladesh grapples with record deadly outbreak of dengue fever

By Ruma Paul

August 5, 2023 12:43 PM GMT+5:30 · Updated a month ago



Mosquito-borne dengue grows deadlier in South Asia as planet warms



Mosabber Hossain, Aadesh Subedi

Published: September 08, 2023

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NEWS | 27 July 2023

Dengue is breaking records in the Americas – what’s behind the surge?

Increasing temperatures contribute to longer dengue seasons, and could drive the geographical expansion of the disease.

The Daily Star

Sports Business Entertainment Life & Living Youth Tech & Startup

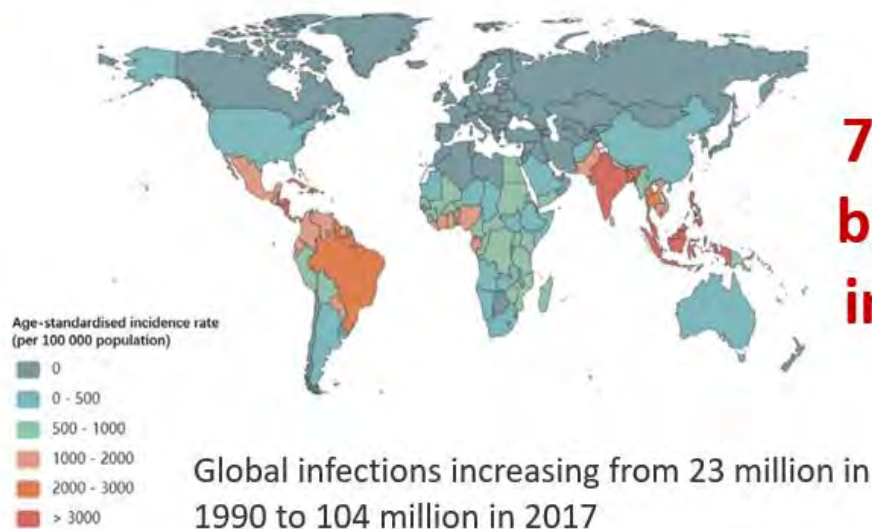
Dengue Outbreak: 2023 already the deadliest year

GÁNH NẶNG CỦA SỐT XUẤT HUYẾT



Global, regional, and national dengue burden from 1990 to 2017: A systematic analysis based on the global burden of disease study 2017

Zhilin Zeng ¹ • Juan Zhan ¹ • Liyuan Chen • Huilong Chen   • Sheng Cheng • [Show footnotes](#)



Age stratified deaths and DALYs also increased (DALYS by 109%)

70% of burden in Asia



Although the incidence of dengue is similar in Latin America and Asia, the mortality rates are higher in Asia

GÁNH NẶNG CỦA SỐT XUẤT HUYẾT



Why is there a sudden surge of dengue in 2022/2023?

- It is not sudden!
- WHO named dengue as one of the top ten threats to global health in 2019
- Reasons for gradual increase in dengue
 - Increase temperatures
 - Erratic rains
 - Urbanization
 - Overcrowding and population expansion

Pakistan floods: Dengue cases soaring after record monsoon

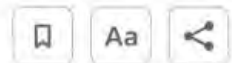
© 15 September 2022



El Nino rains intensify record dengue outbreak in Peru

By Marco Aquino

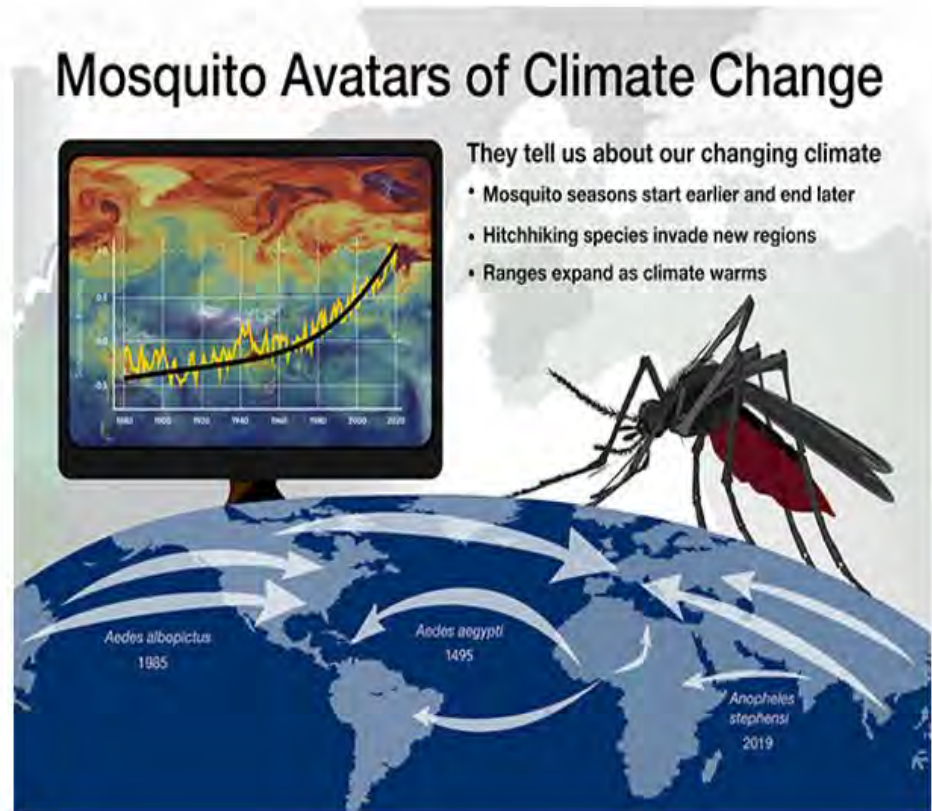
June 9, 2023 2:35 AM GMT+5:30 · Updated 20 days ago



How does climate change affect *Aedes* mosquitoes?

Increase in temperature:

1. Stimulates egg hatching and accelerates growth of larva. Development of *Aedes* from egg to adult was:
 - 7.2 days at 35 °C
 - 39.7 days at 15°C
2. The mosquito gonadotropic cycle shortens:
 - more time for the female mosquito to be in contact with host (longer duration of the ability to infect)
3. At higher temperatures, the mosquitoes bite more frequently
4. Increased virus replication within the mosquito at higher temperatures



GÁNH NẶNG CỦA SỐT XUẤT HUYẾT



Change in the epidemiology of dengue and implications



Dengue infections in pregnancy



- Dengue increases maternal death by 3 times and DHF increases maternal death by 450 times, compared to pregnant women without dengue (Paixao et al,2018).
- Pregnant women were more likely to require ICU admission, ventilatory support and multiorgan failure (Brar et al, 2021)
- Foetal complications: still birth, low birth weight, preterm delivery, foetal distress, miscarriages (Martin et al, 2023).

Comorbidities Associated with Severe Dengue

Diabetes, cardiac disorders and asthma as risk factors for severe organ involvement among adult dengue patients: A matched case-control study

Junxiong Pang^{1,2}, Jung Pu Hsu¹, Tsin Wen Yeo^{1,3}, Yee Sin Leo^{1,2,4} & David C. Lye^{1,3,5}

SCIENTIFIC REPORTS | 7:39872 | DOI: 10.1038/srep39872

The association between diabetes and obesity with Dengue infections

S. D. Sekaran^{1*}, Z. M. Liew², H. C. Yam² and C. S. Raju³

Sekaran et al.
Diabetology & Metabolic Syndrome (2022) 14:101

Is Diabetes a Risk Factor for a Severe Clinical Presentation of Dengue? - Review and Meta-analysis

Nan Shwe Nwe Htun^{1,2}, Peter Odermatt^{1,2}, Ikenna C. Eze^{1,2}, Noémie Boillat-Blanco^{1,2,3}, Valérie D'Acremont^{1,2,4}, Nicole Probst-Hensch^{1,2*}

PLOS Neglected Tropical Diseases | DOI:10.1371/journal.pntd.0003741

Original Article

Diabetic patients suffering dengue are at risk for development of dengue shock syndrome/ severe dengue: Emphasizing the impacts of co-existing comorbidity(ies) and glycemic control on dengue severity

Ing-Kit Lee^{a,b}, Ching-Jung Hsieh^{c,†}, Chien-Te Lee^{b,d}, Jien-Wei Liu^{a,b,*}

Journal of Microbiology, Immunology and Infection (2020) 53, 69–78

Diabetes with Hypertension as Risk Factors for Adult Dengue Hemorrhagic Fever in a Predominantly Dengue Serotype 2 Epidemic: A Case Control Study

Junxiong Pang^{1,2*}, Agus Salim², Vernon J. Lee^{2,3}, Martin L. Hibberd^{1,2}, Kee Seng Chia², Yee Sin Leo^{4,5}, David C. Lye^{4,5}

www.plosntds.org

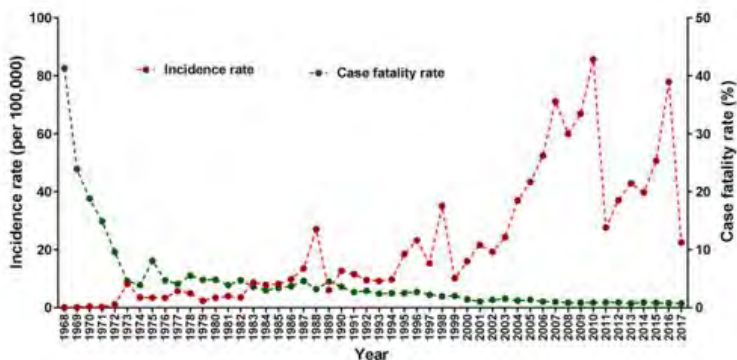
May 2012 | Volume 6 | Issue 5 | e1641

With the rise in diabetes, obesity and metabolic disease in our countries, we are likely to see more people developing severe dengue

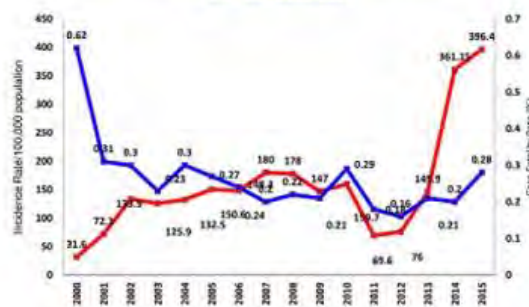
GÁNH NẶNG CỦA SỐT XUẤT HUYẾT



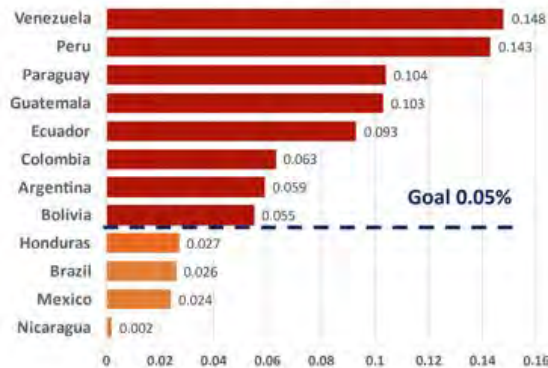
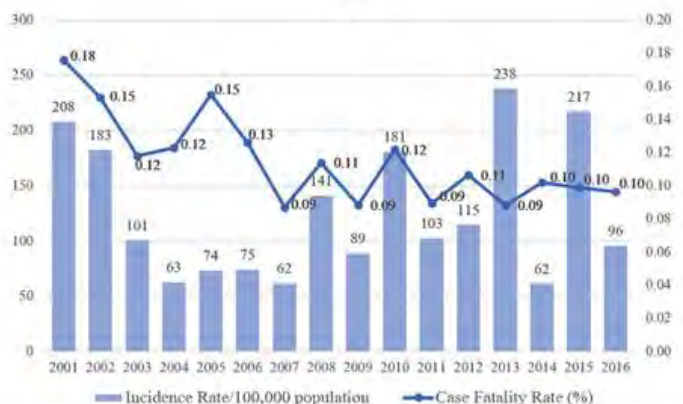
But isn't dengue mild in most..?



MALAYSIA
DENGUE INCIDENCE RATE & CASE FATALITY RATE FOR YEAR 2000-2015



Country	2023 CFRs
Malaysia	0.06
Sri Lanka	0.06
Thailand	0.08
Indonesia	0.93
Bangladesh	0.46
Philippines	0.39

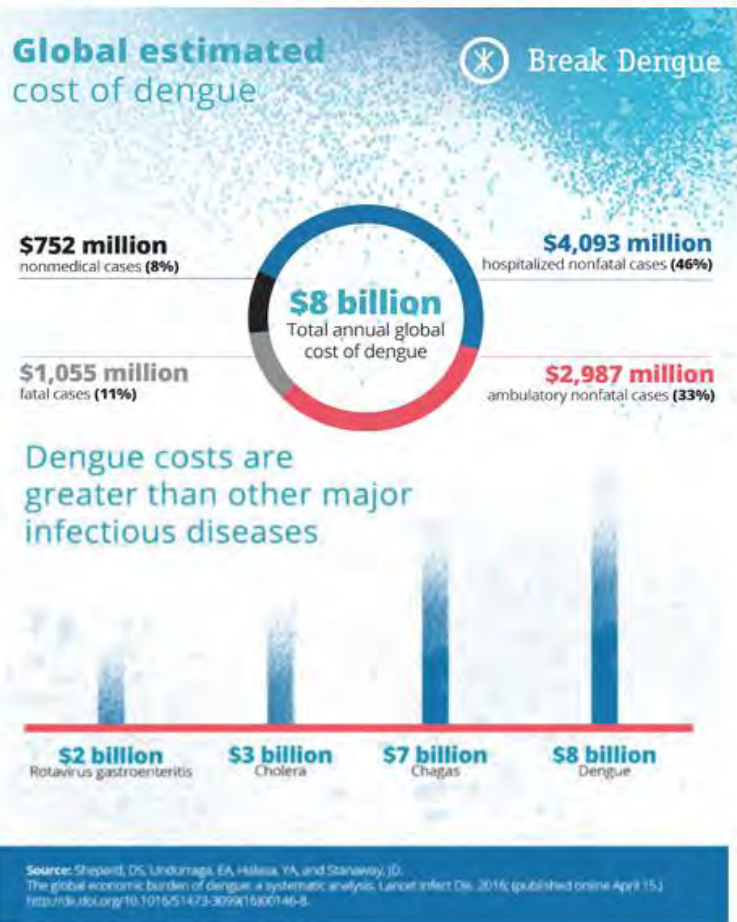


Many of our countries have CFRs of > 0.1%

TÁC ĐỘNG ĐẾN KINH TẾ CỦA SỐT XUẤT HUYẾT



Economic burden of dengue



Economic burden of dengue illness in India from 2013 to 2016: A systematic analysis

Dhwani Hariharan^a, Manoja Kumar Das^b, Donald S. Shepard^a, Narendra Kumar Arora^b

^a Heller School for Social Policy and Management, Brandeis University, Waltham, MA, USA
^b The INCLEN Trust International, New Delhi, India

Global costs of USD 8 billion in 2014 is a gross under estimation, when the costs in India alone in 2018 was **USD 5.71 billion**

Productivity costs from a dengue episode in Asia: a systematic literature review

A review of 31 studies

- Outpatient: USD 3.8 to 1332
- Hospitalized: USD 6.7 to 1445.9
- Fatal dengue: USD 12.035 to 1,453,237

Loss of workdays (Thailand)

Dengue fever: 8.4

Dengue hemorrhagic fever: 9.7

Shock: 12.3

TÁC ĐỘNG ĐẾN KINH TẾ CỦA SỐT XUẤT HUYẾT



How can we face these challenges?

Healthcare & Pharmaceuticals | Public Health

Bangladesh fears record high death toll from dengue outbreak



Dengue fever crisis forces Peru minister to resign

🕒 16 June



Slide credits: Prof Neelika Malavige, DNDi

QUẢN LÝ SỐT XUẤT HUYẾT



Vector Control



Use insect repellent



Cover skin

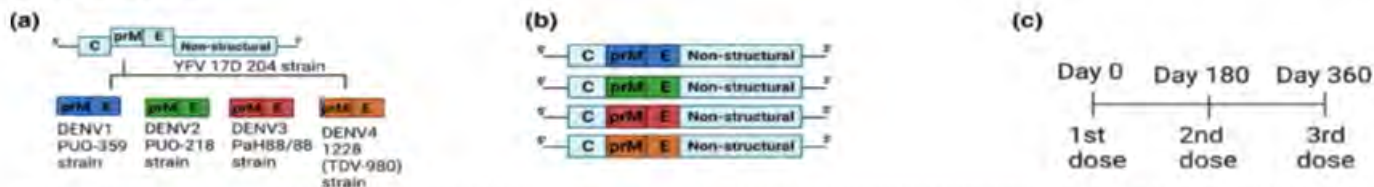


QUẢN LÝ SỐT XUẤT HUYẾT

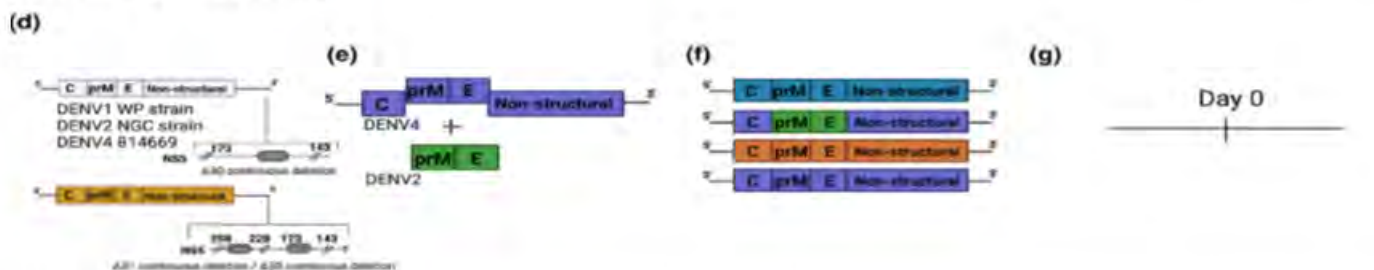


Dengue vaccines currently in Phase 3 trials or approved

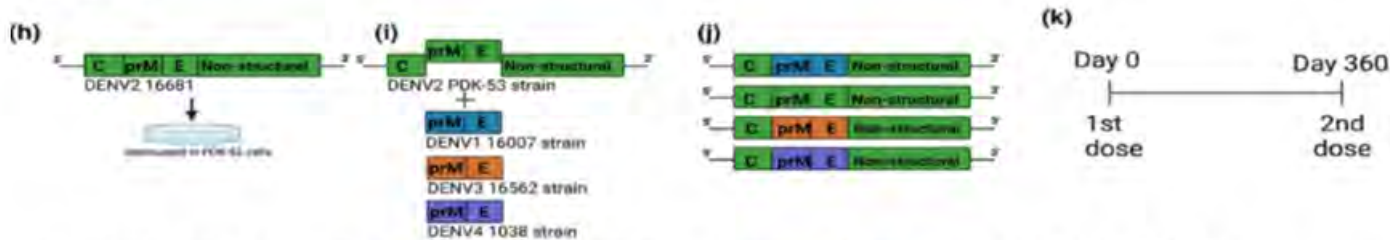
Dengvaxia®



NIAID LATV TV003



TAK-003



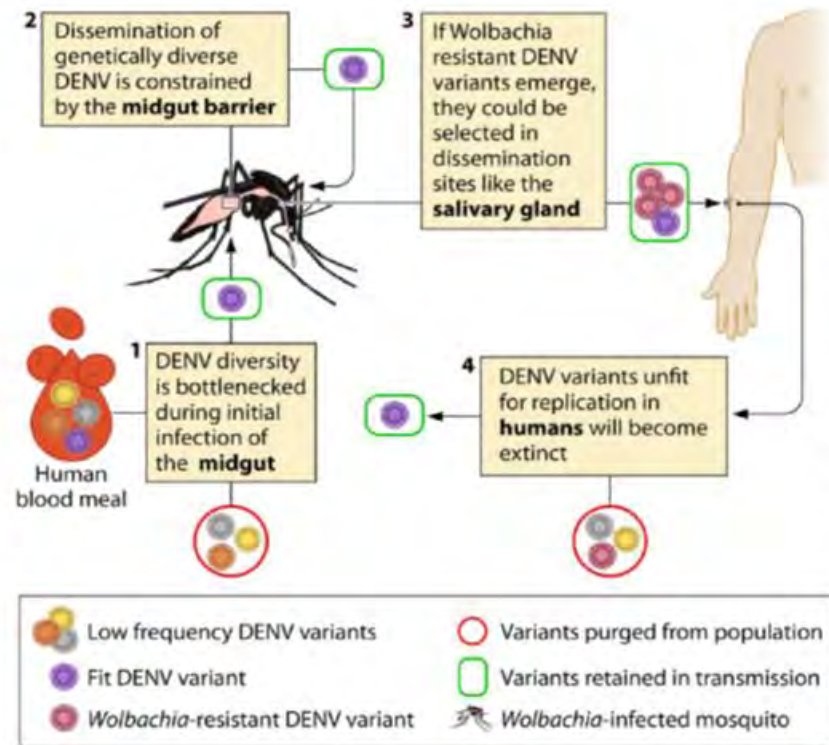
Pintado Silva and Fernandez-Sesma, *Journal of General Virology* 2023;104:001831

QUẢN LÝ SỐT XUẤT HUYẾT



Using *Wolbachia* to Eliminate Dengue: Will the Virus Fight Back?

Kathryn M. Edenborough,^a Heather A. Flores,^a Cameron P. Simmons,^{b,c,d} Johanna E. Fraser^{a,e}



CONCLUDING REMARKS

With a body of evidence now demonstrating that *Wolbachia*-*Ae. aegypti* introgression methods can substantially reduce the burden of dengue in areas of endemicity, it is expected that application of this technology will undergo a major expansion in coming years (17, 19, 24, 26). The intention is that this will lead to long-term control or local elimination of human-pathogenic arboviruses. Achieving long-term suppression in the field would be dependent upon the evolutionary stability of the *Wolbachia*, *Ae. aegypti*, and DENV tripartite interaction. *Wolbachia* and *Ae. aegypti* evolve slowly compared to DENV, and *Wolbachia*-carrying mosquitoes collected years after release have so far retained their antiviral profile. Yet the rapid mutation rate of RNA viruses suggests it is inevitable that viruses like DENV will eventually adapt to *Wolbachia*'s selective pressure and become resistant to the intervention. The question is, how long will this take?

ABSTRACT Recent field trials have demonstrated that dengue incidence can be substantially reduced by introgressing strains of the endosymbiotic bacterium *Wolbachia* into *Aedes aegypti* mosquito populations. This strategy relies on *Wolbachia* reducing the susceptibility of *Ae. aegypti* to disseminated infection by positive-sense RNA viruses like dengue. However, RNA viruses are well known to adapt to antiviral pressures. Here, we review the viral infection stages where selection for *Wolbachia*-resistant virus variants could occur. We also consider the genetic constraints imposed on viruses that alternate between vertebrate and invertebrate hosts, and the likely selection pressures to which dengue virus might adapt in order to be effectively transmitted by *Ae. aegypti* that carry *Wolbachia*. While there are hurdles to dengue viruses developing resistance to *Wolbachia*, we suggest that long-term surveillance for resistant viruses should be an integral component of *Wolbachia*-introgression biocontrol programs.

QUẢN LÝ SỐT XUẤT HUYẾT



Why Aren't We Focusing on a treatment for dengue?

- Dengue is mild. Really?
- It costs too much to develop a treatment?
- We have managed to reduce dengue fatalities with monitoring and fluid replacement?



A hospital ward in the dengue outbreak in Sri Lanka 2017. Photo: courtesy Dr. Lakkumar Fernando

Slide credits: Prof Neelika Malavige, DNDi

CHIẾN LƯỢC SỐT XUẤT HUYẾT



Dengue Strategy: An Oral Treatment for Patients of All Ages, with Acute Dengue Infection to Prevent progression to Severe Disease

Correctly identify patients with dengue



Identify those who need it most (risk stratification)



Treat to prevent progression to severe disease

Point-of-care (POC) testing available but lack sensitivity especially after day 3 of illness

No test to identify who will progress to plasma leakage

Prevent progression to severe disease
Reduce hospitalizations
Return to work/school/day to day activities sooner

Need proper diagnostics!



Need a biomarker to predict severe disease!



Need effective drugs!



Establish a clinical network for conducting phase 2 and 3 trials and validate POC diagnostics and biomarkers to predict progression to severe disease

CHIẾN LƯỢC SỐT XUẤT HUYẾT



DENGUE

FORGING GLOBAL PARTNERSHIPS TO TACKLE
A RAPIDLY SPREADING CLIMATE-SENSITIVE DISEASE

FACTS

3.9 billion
people at risk

About
390 million
infections per
year

Endemic in
129
countries around
the world

CHALLENGES

- **Most prevalent** mosquito-borne viral disease
- **Climate sensitive:** rising burden of disease
- **No existing treatments for uncomplicated dengue fever** to prevent progression to severe disease and complications

OPPORTUNITIES

- **Window of opportunity** to meet growing medical need
- **Well-defined populations** for clinical trials and endpoints to define success
- **Opportunities in small-molecule drugs and/or biologicals**
- **COVID-19 learnings** and opportunities for cross-fertilization

OUR GOALS

2021- 2028: Advance treatment solutions that can prevent progression to severe disease and reduce burden on public health systems

- Together with leaders in endemic countries, coordinate **public-private partnerships for dengue R&D**
- Accelerate evaluation of **candidate repurposing agents** as well as **novel treatments**, in monotherapy and in combination
- **Antiviral + host-directed therapy combination**, to be deployed with rapid diagnostic tests at point of care
- **Affordable, sustainable, and adapted** for use in resource-limited settings, suitable for children/adults/elderly



MAIN PARTNERS: Ministry of Health Malaysia, Mahidol University (Faculty of Medicine Siriraj Hospital) - Thailand, Oswaldo Cruz Foundation (*Fiocruz*) - Brazil, Translational Health Science and Technology Institute - India

DNDi

LIÊN MINH SỐT XUẤT HUYẾT: HỢP TÁC NAM - NAM



An Endemic Country-Led Collaboration to Accelerate Development of Dengue Treatment

Treatments for dengue: a Global Dengue Alliance to address unmet needs



Dengue is currently the most rapidly spreading mosquito-borne viral infection in the world, with half of the world's population at risk of becoming infected.¹ As a result of climate change, rapid urbanisation, and widespread international travel, the incidence of dengue is rapidly increasing, overwhelming health-care systems in many lower-income countries. Climate change has increased the burden of dengue in endemic countries and has also led to expansion of this infection to new territories in Europe and North America.²

in India; the Oswaldo Cruz Foundation in Brazil; and the Federal University of Minas Gerais in Brazil. The mission of this alliance is to accelerate research and development and deliver dengue therapeutics through an inclusive partnership. It aims to deliver a new treatment for dengue, within 5 years, from repurposed drugs and combinations (including novel antivirals from pharmaceutical companies). This alliance is co-created, co-owned, and co-funded by dengue-endemic countries, with a tiered governance mechanism allowing

Lancet Glob Health 2023
Published Online
August 31, 2023
[https://doi.org/10.1016/S2214-109X\(23\)00362-5](https://doi.org/10.1016/S2214-109X(23)00362-5)

South-South collaboration to find a safe, affordable, and effective treatment

The first in-person Dengue Alliance meeting took place in India on 6-7 February 2023, with experts and scientists from India, Malaysia, Thailand, Brazil, Sri Lanka, and Switzerland present to kick-off plans to develop treatments for this climate-sensitive disease which causes substantial morbidity and mortality globally.



The Dengue Alliance, launched in 2022, is a global partnership led by institutions from dengue-endemic countries that aims to develop affordable and accessible treatments for dengue. The members of this alliance include the Translational Health Science and Technology Institute (THSTI), India; Siriraj Hospital, Mahidol University, Thailand; Institute of Medical Research (IMR), Ministry of Health (MOH), Malaysia; Oswaldo Cruz Foundation, Brazil; Federal University of Minas Gerais (UFMG), Brazil; and the Drugs for Neglected Diseases initiative (DNDi).

Lancet Glob Health 2023 Published Online August 31, 2023. [https://doi.org/10.1016/S2214-109X\(23\)00362-5](https://doi.org/10.1016/S2214-109X(23)00362-5)
[Dengue](#) | [DNDi](#)

LIÊN MINH SỐT XUẤT HUYẾT: HỢP TÁC NAM - NAM



Dengue Alliance and Supporting Ecosystem



LIÊN MINH SỐT XUẤT HUYẾT: HỢP TÁC NAM - NAM



Key Objectives of The Dengue Alliance



Create a joint & collaborative agenda for the development of affordable dengue therapeutics



Promote & foster collaborative non-for-profit medical R&D environment



Implement research activities with the partners



Engage in joint fundraising to support the Alliance and R&D activities



Encourage, support, & develop research knowledge & skills of personnel



Engage additional partners/service providers required to fulfil Alliance objectives

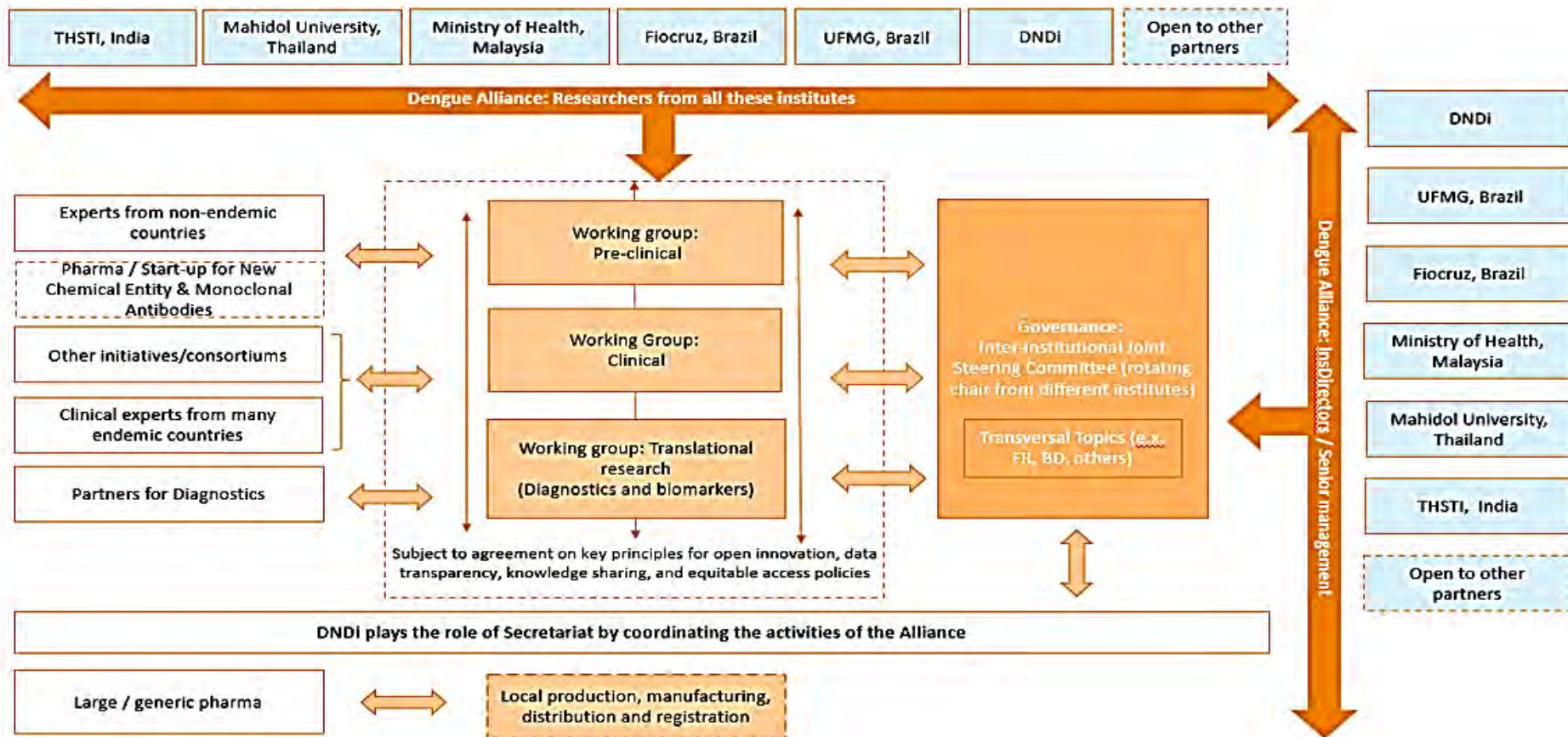


Encourage & promote the use & sharing of the research results (including intellectual property) & products, created under this collaboration, for an equitable & affordable access, policy-making & other public purposes

LIÊN MINH SỔ XUẤT HUYẾT: HỢP TÁC NAM - NAM





Governance Structure



THANK YOU



 facebook.com/dndi.org
 youtube.com/dndiconnect
 twitter.com/dndi

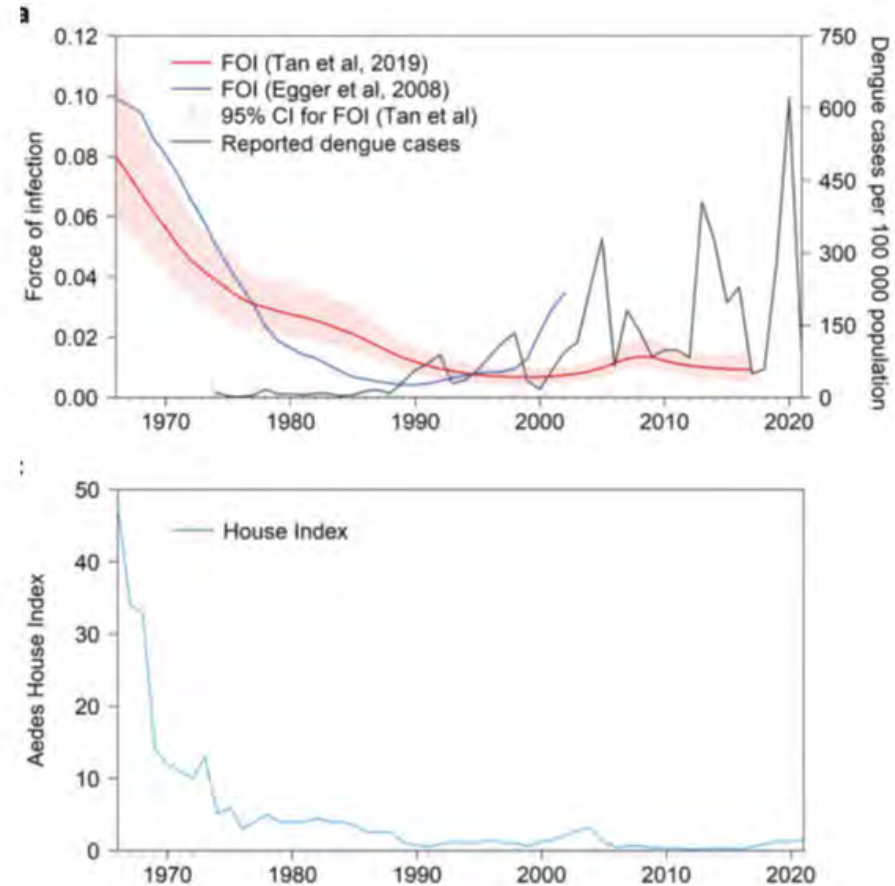
 instagram.com/drugsforneglecteddiseasesinitiative
 linkedin.com/company/dndi



Singapore's 5 decades of dengue prevention and control—Implications for global dengue control

Abstract

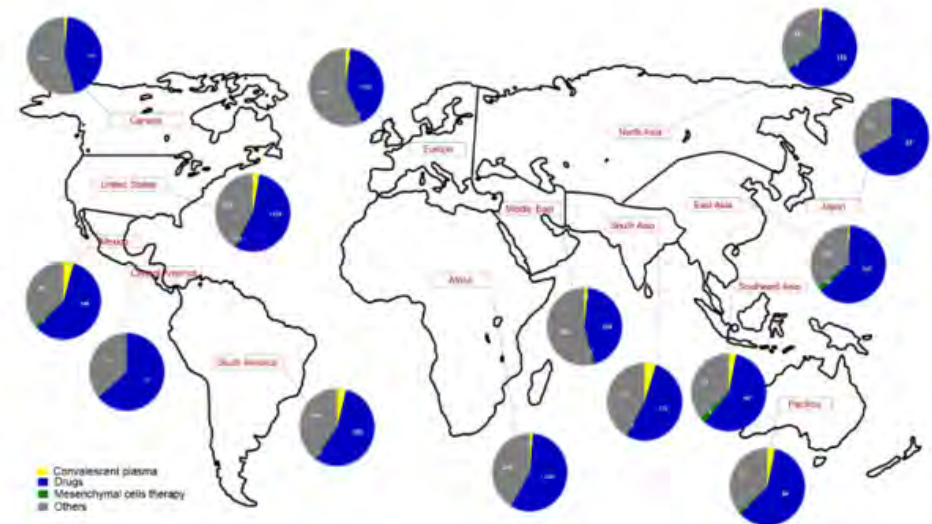
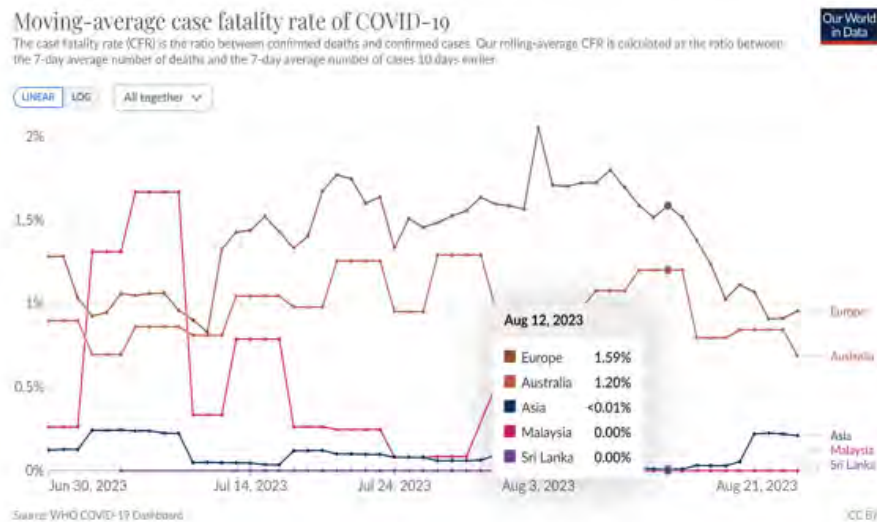
This paper summarises the lessons learnt in dengue epidemiology, risk factors, and prevention in Singapore over the last half a century, during which Singapore evolved from a city of 1.9 million people to a highly urban globalised city-state with a population of 5.6 million. Set in a tropical climate, urbanisation among green foliage has created ideal conditions for the proliferation of *Aedes aegypti* and *Aedes albopictus*, the mosquito vectors that transmit dengue. A vector control programme, largely for malaria, was initiated as early as 1921, but it was only in 1966 that the Vector Control Unit (VCU) was established to additionally tackle dengue haemorrhagic fever (DHF) that was first documented in the 1960s. Centred on source reduction and public education, and based on research into the bionomics and ecology of the vectors, the programme successfully reduced the *Aedes* House Index (HI) from 48% in 1966 to <5% in the 1970s. Further enhancement of the programme, including through legislation, suppressed the *Aedes* HI to around 1% from the 1990s. The current programme is characterised by 4 key features: (i) proactive inter-epidemic surveillance and control that is stepped up during outbreaks; (ii) risk-based prevention and intervention strategies based on advanced data analytics; (iii) coordinated inter-sectoral cooperation between the public, private, and people sectors; and (iv) evidence-based adoption of new tools and strategies. Dengue seroprevalence and force of infection (FOI) among residents have substantially and continuously declined over the 5 decades. This is consistent with the observation that dengue incidence has been delayed to adulthood, with severity highest among the elderly. Paradoxically, the number of reported dengue cases and outbreaks has increased since the 1990s with record-breaking epidemics. We propose that Singapore's



PLOS Neglected Tropical Diseases | <https://doi.org/10.1371/journal.pntd.0011400> June 22, 2023

Slide credits: Prof Neelika Malavige, DNDi

Case Fatality Rates due to Covid-19 & on-going clinical trials



2,079 trials for COVID-19!

Actively recruiting: 172

Completed: 782

92 trials for dengue!

Actively recruiting: 4, active but not recruiting: 2

Completed: 62