Overview of malaria and dengue

Eng Eong Ooi BMBS PhD FRCPath
Professor
Programme in Emerging Infectious Diseases
Duke-NUS Medical School

Malaria

Plasmodium parasites:

P falciparum

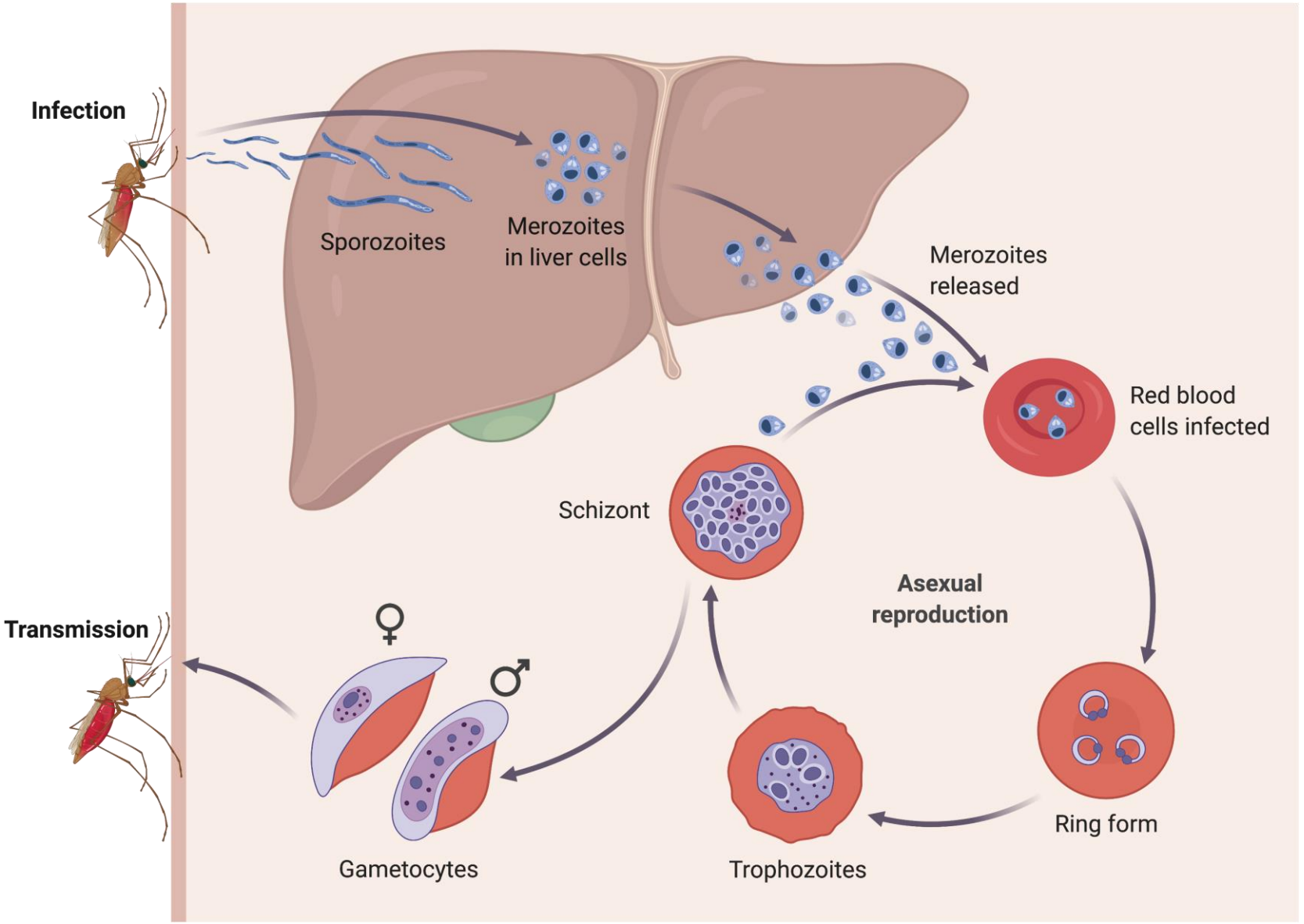
P vivax

P ovale

P malariae

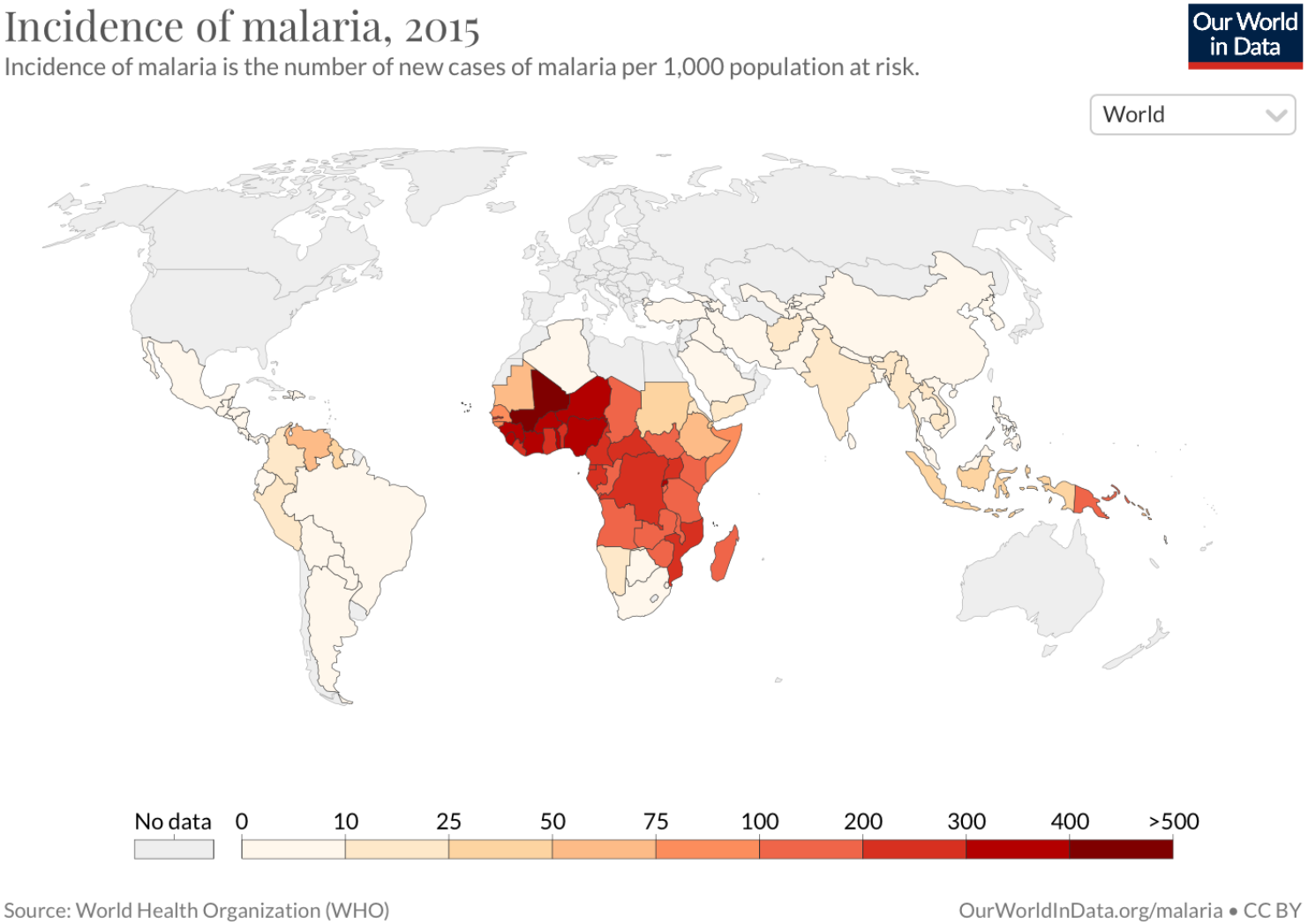
P knowlesi

Vector: *Anopheles* mosquitoes



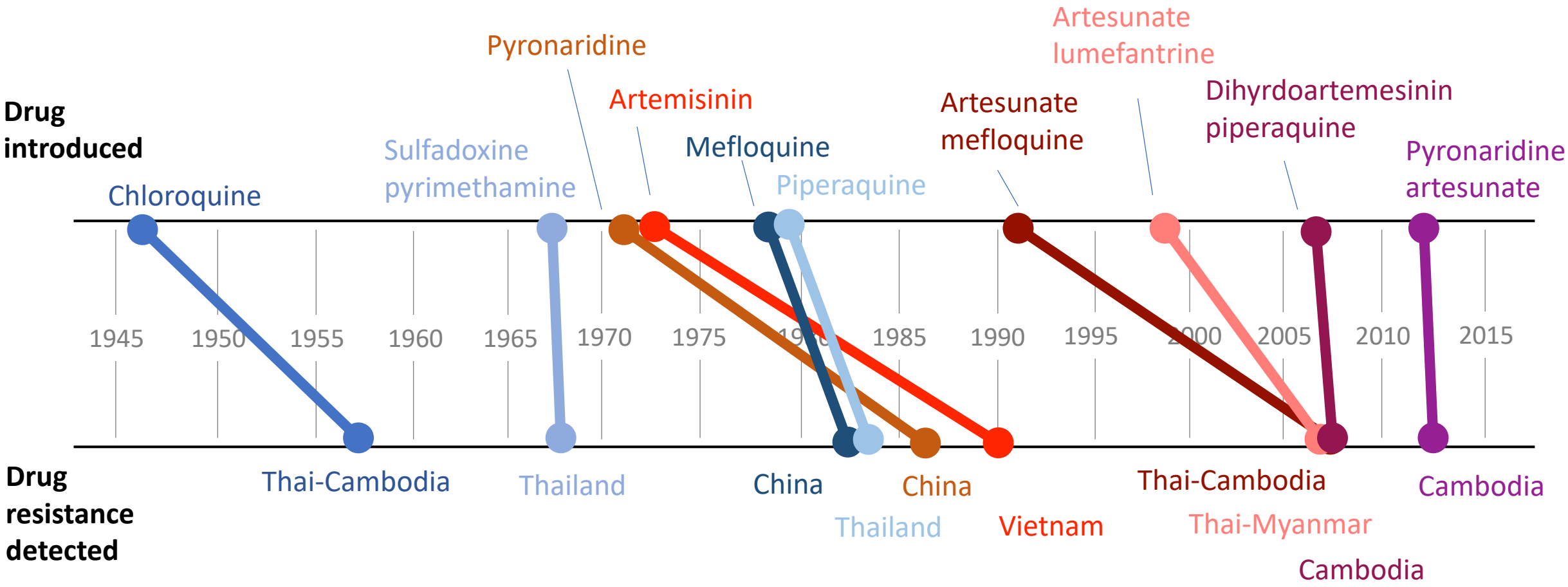
Created with BioRender.com

Global disease burden



- 300-500 million cases/year
- 1-3 million deaths
  - ~90% of deaths in Africa are of children less than 5 years old
- Economic burden of US$12 billion per year
- Most severe malaria cases are due to *P falciparum*

Anti-malarial drug resistance



Adapted from *The Scientist* 2019

NEWS | 30 June 2021

Vaccine made of live malaria parasites shows early success

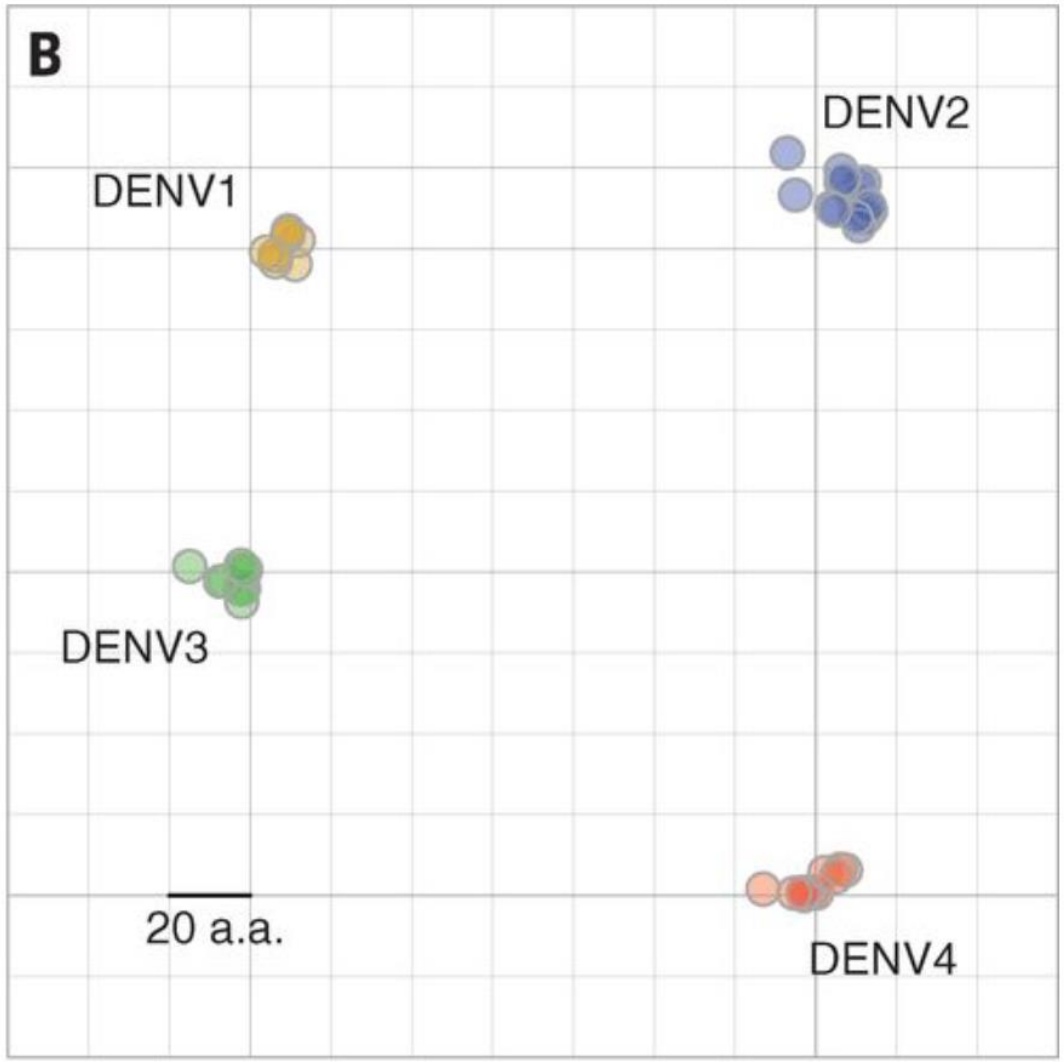
Strategy uses a combination of parasites and medicines to generate immunity while avoiding symptoms.

Heidi Ledford

Dengue virus (DENV)

Aedes aegypti

Aedes albopictus

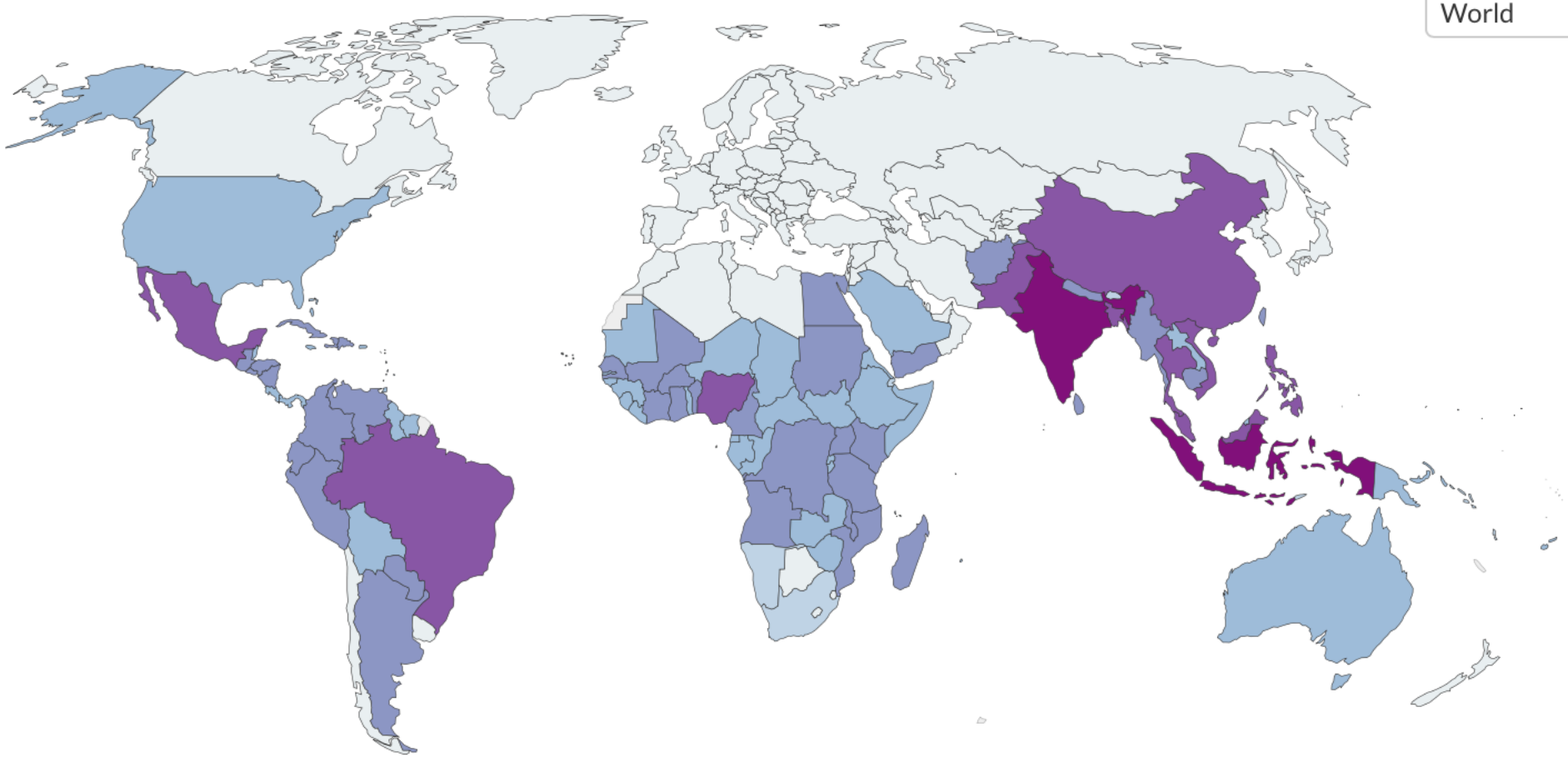


Katzelnick et al, Science 2015

Number of dengue fever infections, 2017

Our World in Data

World

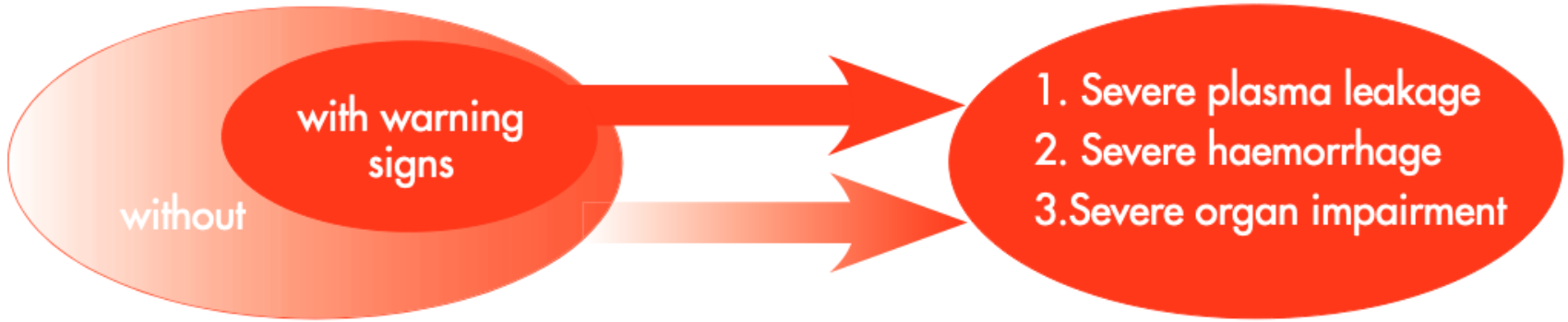


No data | No infections <1 | 10,000 | 100,000 | 1 million | 10 million | 100 million

Source: IHME, Global Burden of Disease

DENGUE ± WARNING SIGNS

SEVERE DENGUE



CRITERIA FOR DENGUE ± WARNING SIGNS

Probable dengue

live in /travel to dengue endemic area.
Fever and 2 of the following criteria:

- Nausea, vomiting
- Rash
- Aches and pains
- Tourniquet test positive
- Leukopenia
- Any warning sign

Laboratory-confirmed dengue

(important when no sign of plasma leakage)

Warning signs*

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargment >2 cm
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

*(requiring strict observation and medical intervention)

CRITERIA FOR SEVERE DENGUE

Severe plasma leakage

leading to:

- Shock (DSS)
- Fluid accumulation with respiratory distress

Severe bleeding

as evaluated by clinician

Severe organ involvement

- Liver: AST or ALT >=1000
- CNS: Impaired consciousness
- Heart and other organs

Efficacy trials of anti-dengue therapeutics

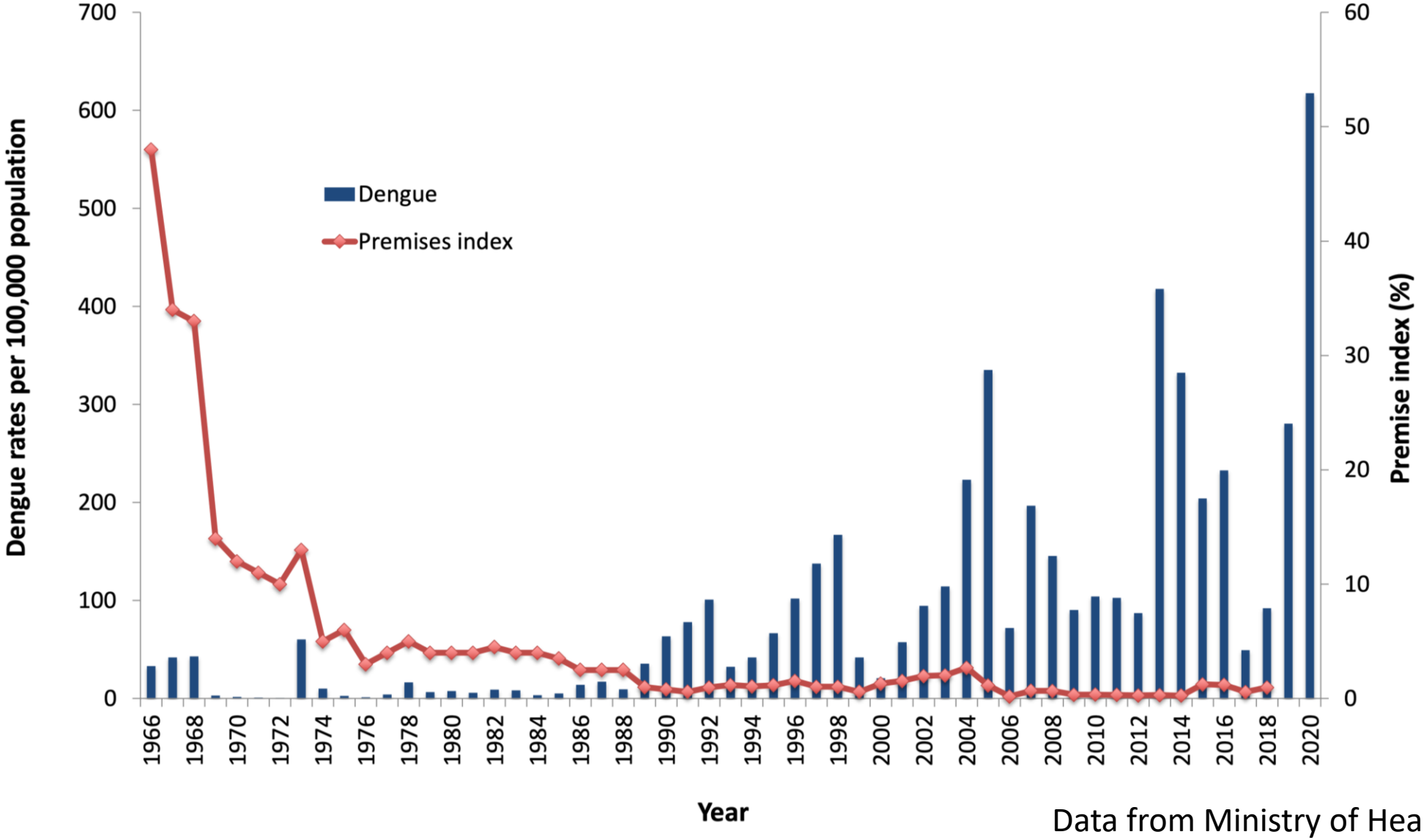
Compound	Trial design	Primary endpoint	Efficacy
Chloroquine	Randomised, placebo controlled	Viremia resolution	None
Balaparivir	Randomised, double-blind, placebo controlled	Viral log reduction	None
Celgosivir	Randomised, double-blind, placebo controlled	Viral log reduction	None
Prednisolone	Randomised, double-blind, placebo controlled	Safety Viral log reduction	Safe None
Lovastatin	Randomised, double-blind, placebo controlled	Safety	Good safety but no efficacy signal
Ivermectin	Randomised, double-blind, placebo controlled	Viral log reduction	None
VIS513	Randomised, double-blind, placebo controlled (trial on-hold due to covid)	Viral log reduction	?

Clinical phase dengue vaccine/candidates

Vaccine	Type	Stage	Efficacy outcome	Status
Dengvaxia (Sanofi Pasteur	Chimeric	Completed phase 3	Bi- to tri-valent?	Licensed for use in those with prior dengue infection (PDI)
TAK003 (Takeda)	LAV/Chimeric	Completed phase 3	Bi-valent. Possibly tri-valent.	No ADE thus far. Appears safe in those without PDI
TV003 (NIH/Butantan/Merck)	LAV/Chimeric	Phase 3	?	
TDEN (GSK/WRAIR)	Inactivated	Phase 1	Poor immunogenicity	Abandoned
V180 (Merck)	Subunit	Phase 1	Poor immunogenicity	Abandoned
D1ME100 (US Navy)	DNA	Phase 1	?	Likely abandoned

The challenge of dengue control

Mosquito population and population immunity



Data from Ministry of Health, Singapore