

Croucher Summer Course on Vaccine Hesitancy
University of Hong Kong, 3-7 August 2026



SCHOOL
OF GLOBAL
PUBLIC HEALTH

Economics, ethics and epidemiology of vaccine decisions

The case of dengue vaccination

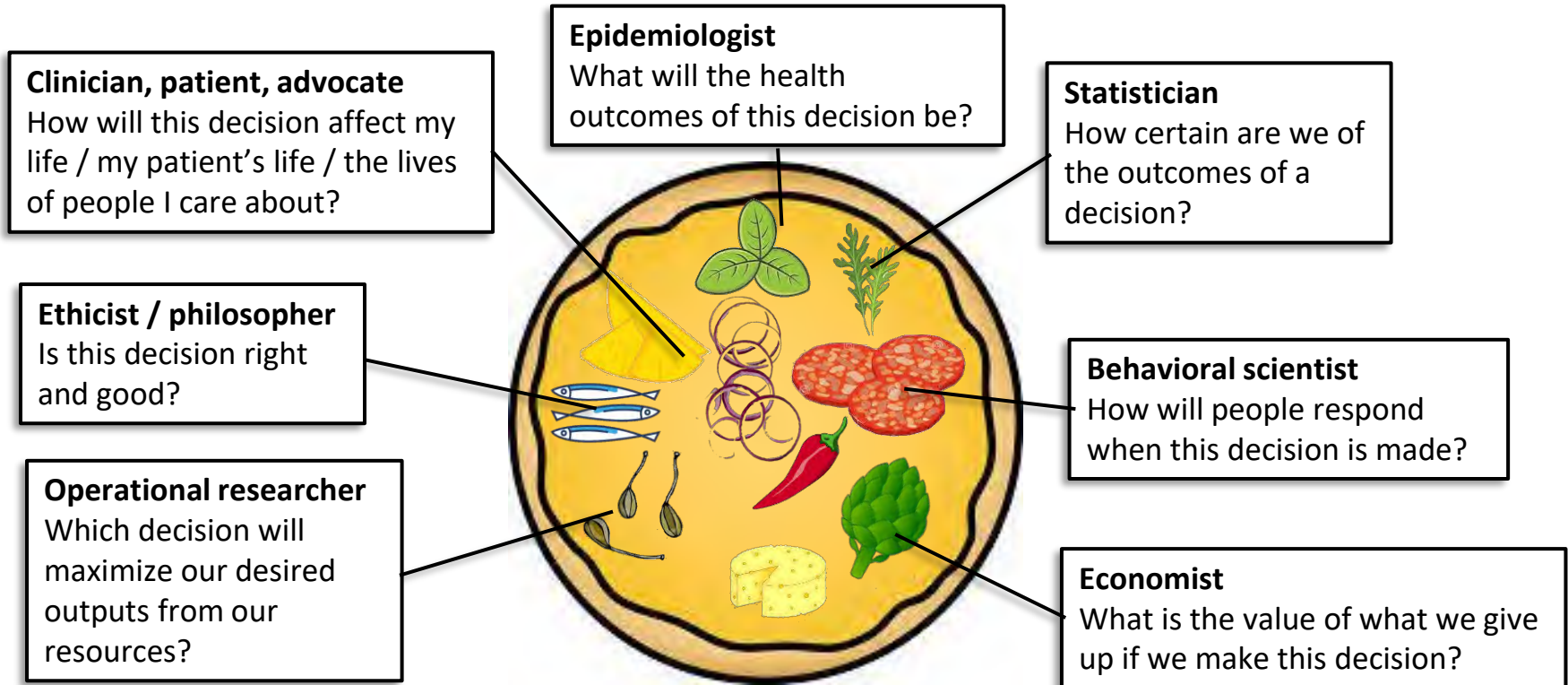
6 August 2026

Mark Jit

Lecture overview

- Recognise the contribution of key disciplines in evidence-informed vaccine decision-making
- Role play a complex public health decision process (whether to introduce dengue vaccination in 2016)
- Explore how these principles can be applied to other situations

Multiple perspectives in vaccine decision making



Structure for making evidence-informed public health decisions



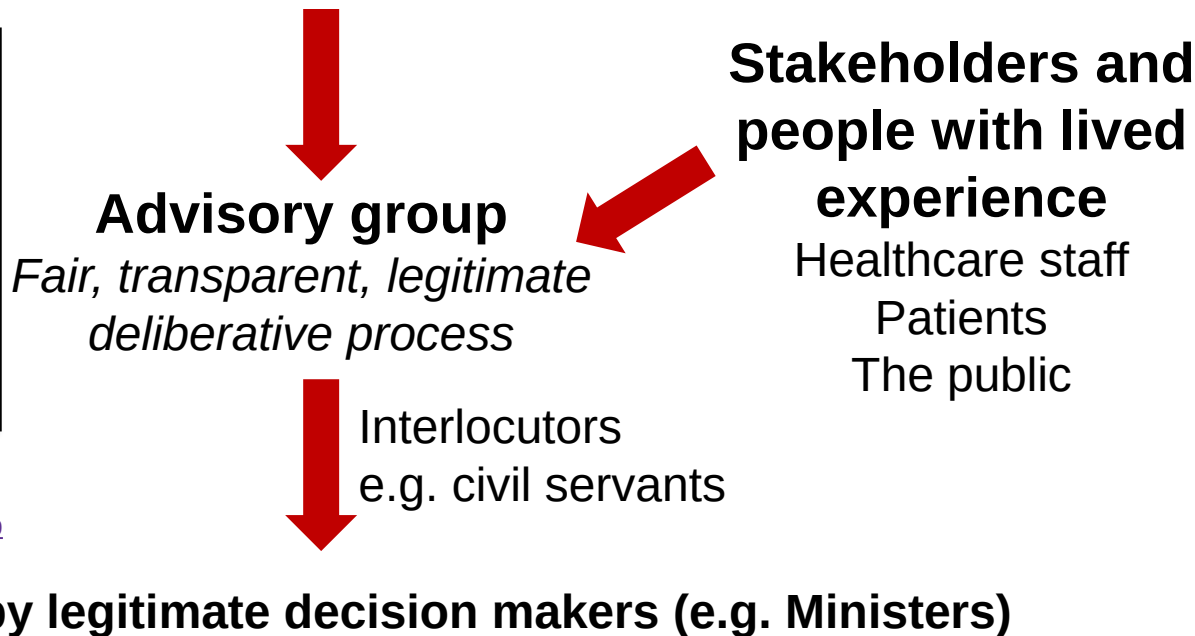
Evidence generators/interpreters

Basic science
Field epidemiology
Mathematical modelling

Health economics
Implementation science
Attitudinal research etc.



WHO Strategic Group of Experts on Immunization (SAGE) meeting, October 2018. Archived at: <https://web.archive.org/web/20190418035013/http://www.who.int/immunization/policy/sage/en/>



Recap: dengue vaccination



**What do you know
about dengue and
dengue vaccination
from your own
knowledge and from
the course so far?**

The vector and the vaccine



Aedes aegypti mosquito.

Source: Muhammad Mahdi Karim - Own work. GFDL 1.2 license.

<https://commons.wikimedia.org/w/index.php?curid=11185617>

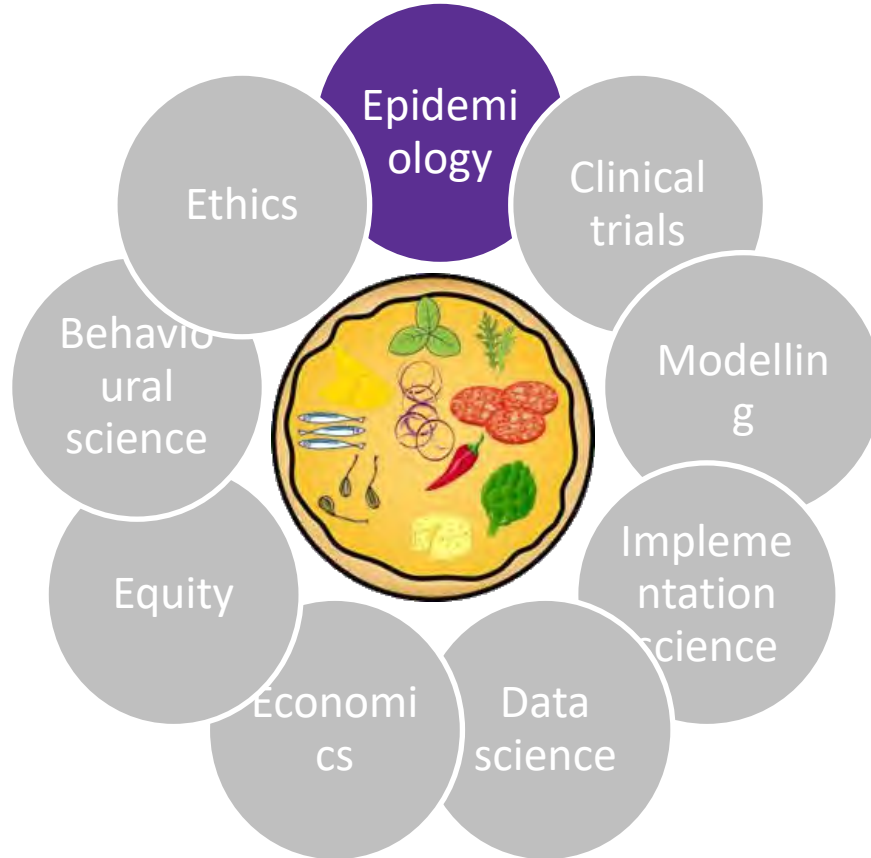


Dengvaxia vaccine against dengue

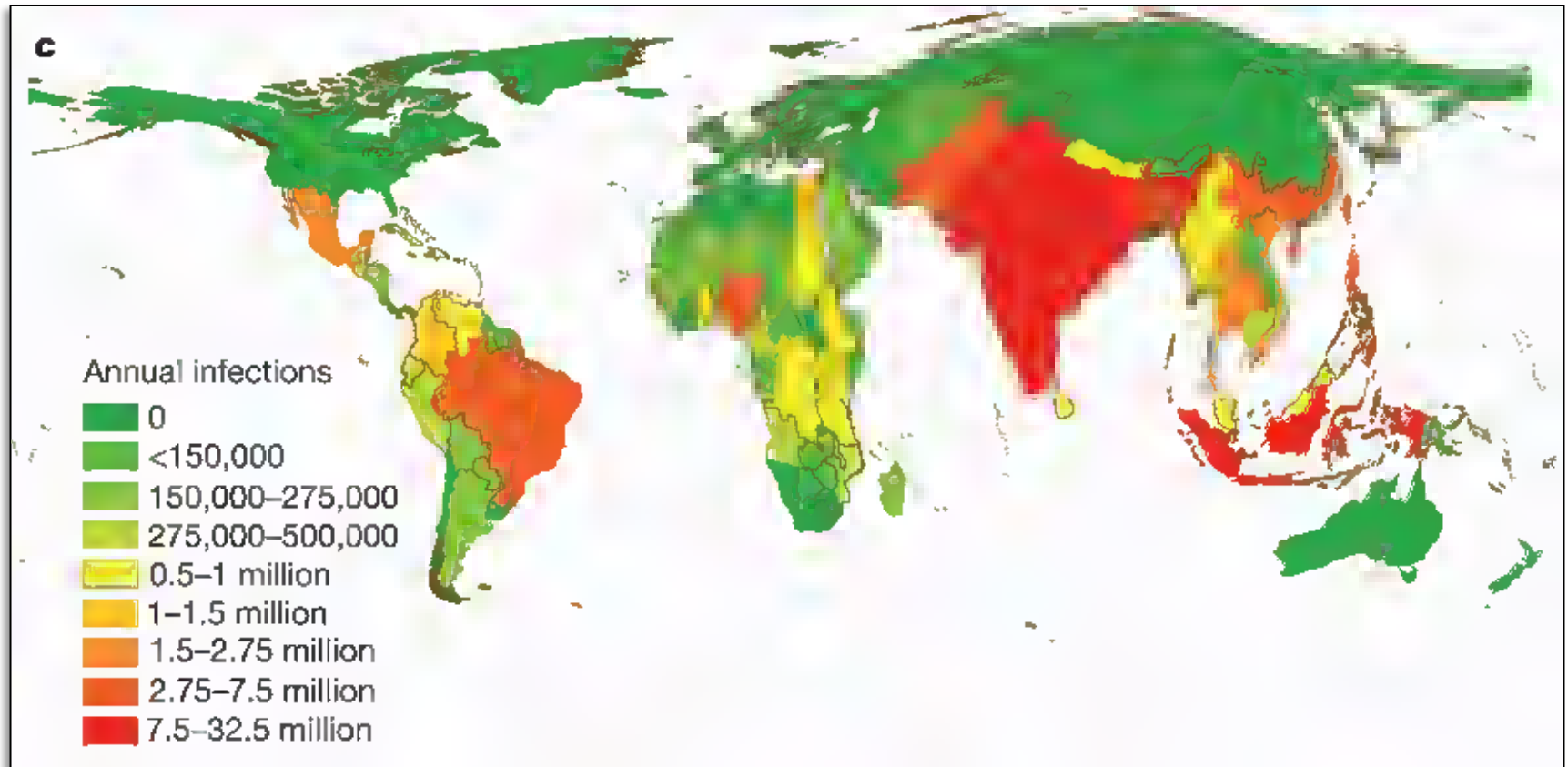
Source: National Institutes of Health

<https://www.techtransfer.nih.gov/showcase/dengvaxia-r>

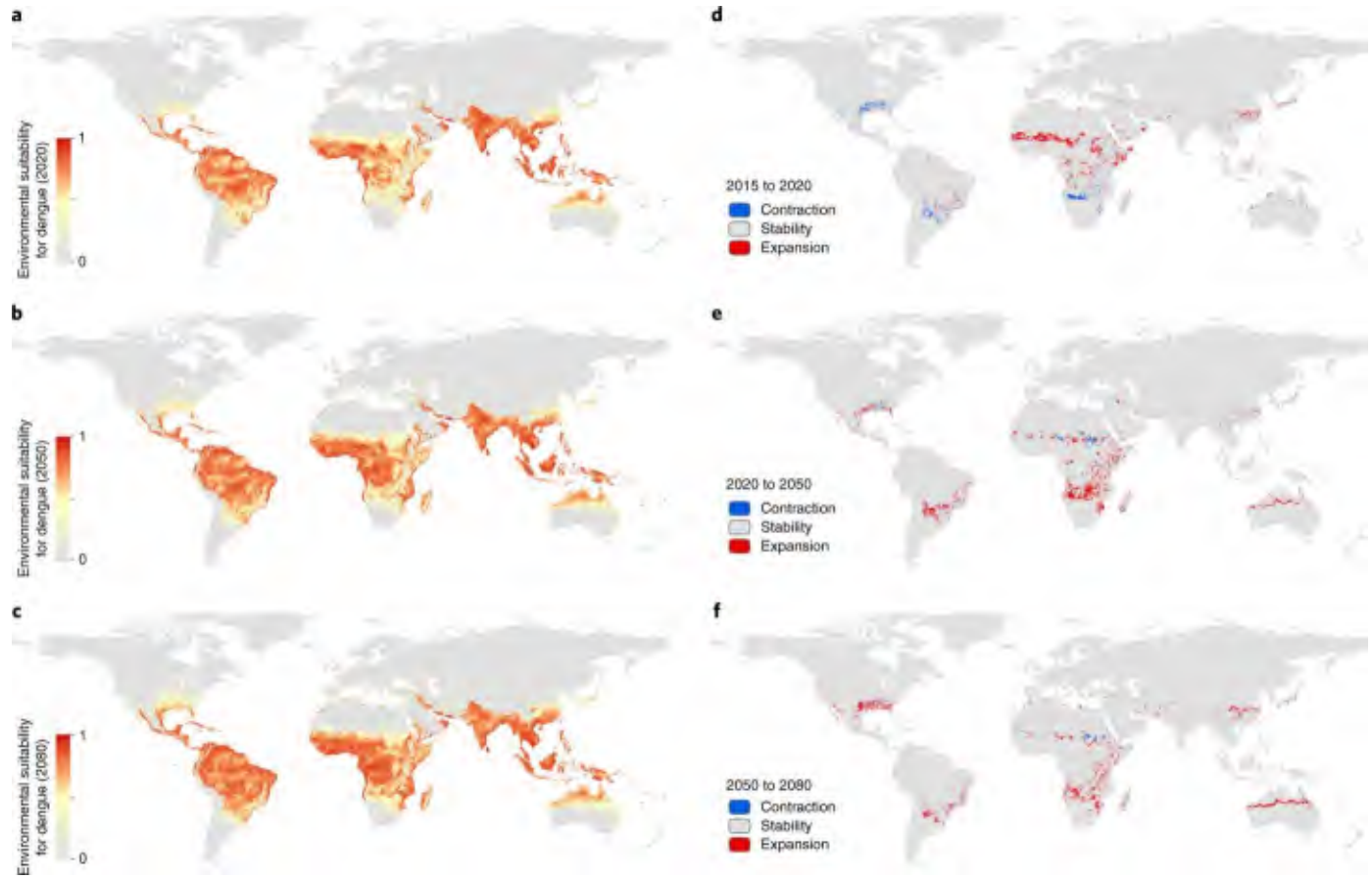
Epidemiology



Global burden of dengue (2013)

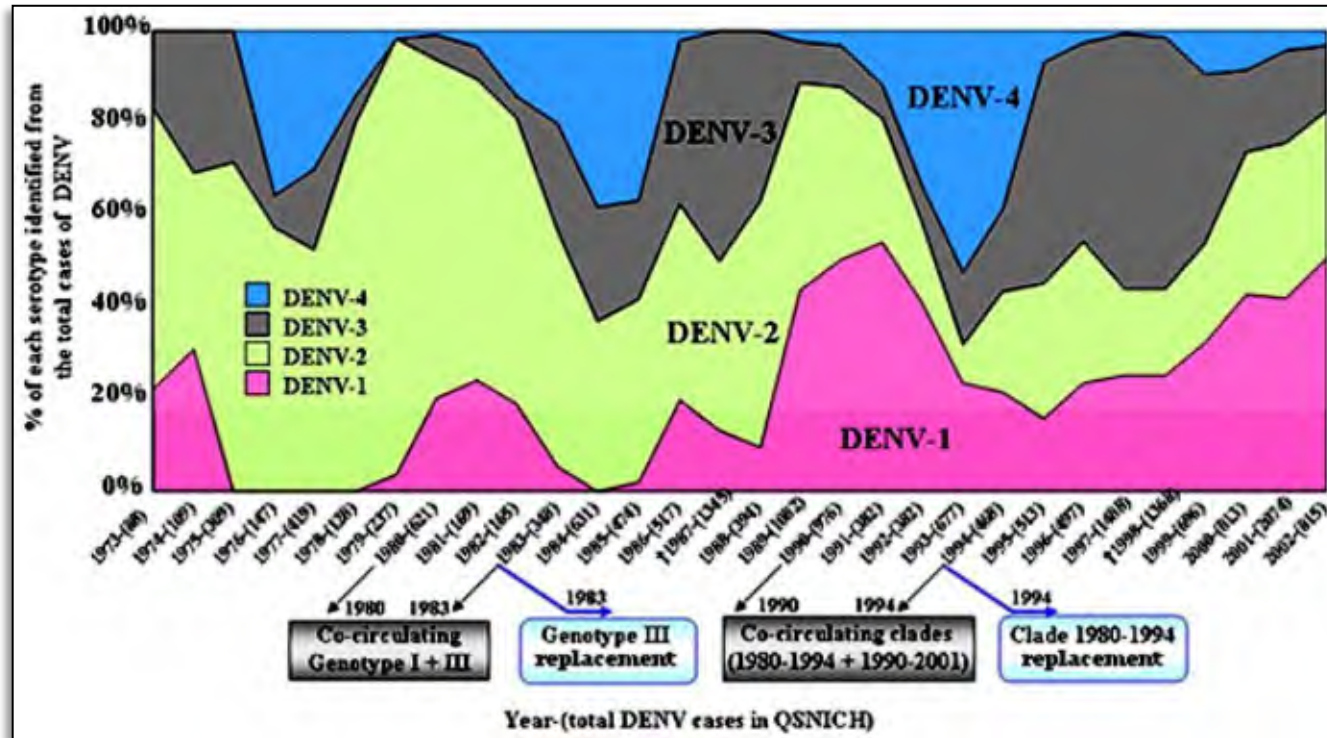


Burden likely to increase due to climate change



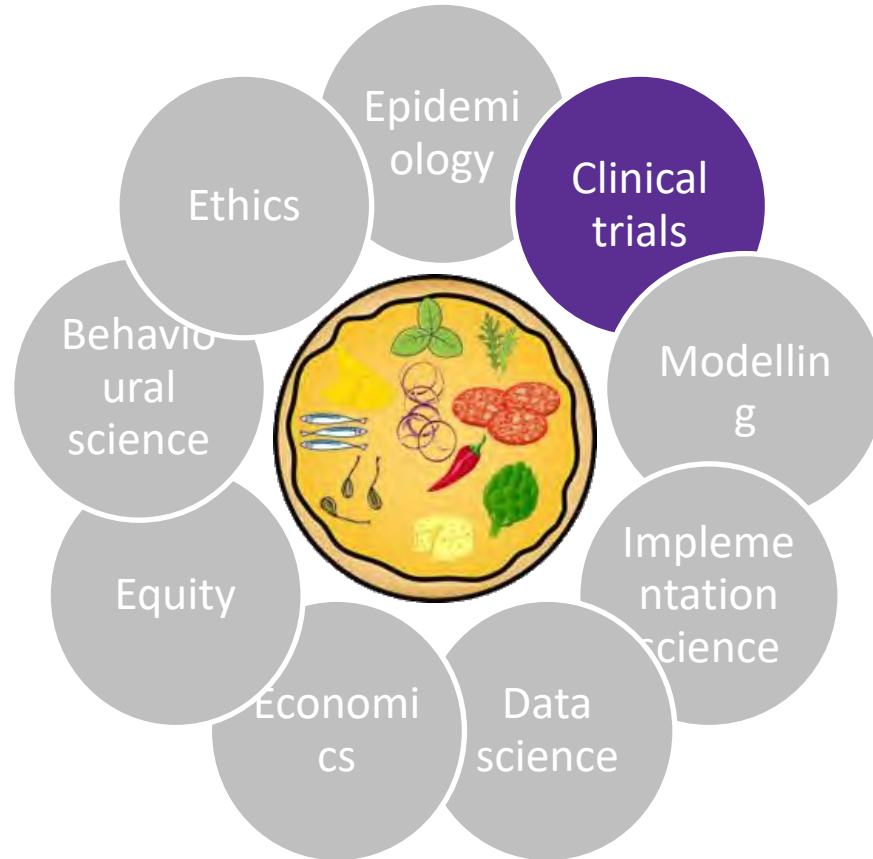
Messina JP et al. The current and future global distribution and population at risk of dengue. *Nat Microbiol* 2019; 4:1508–1515.
<https://doi.org/10.1038/s41564-019-0476-8>

Multiple dengue serotypes interact

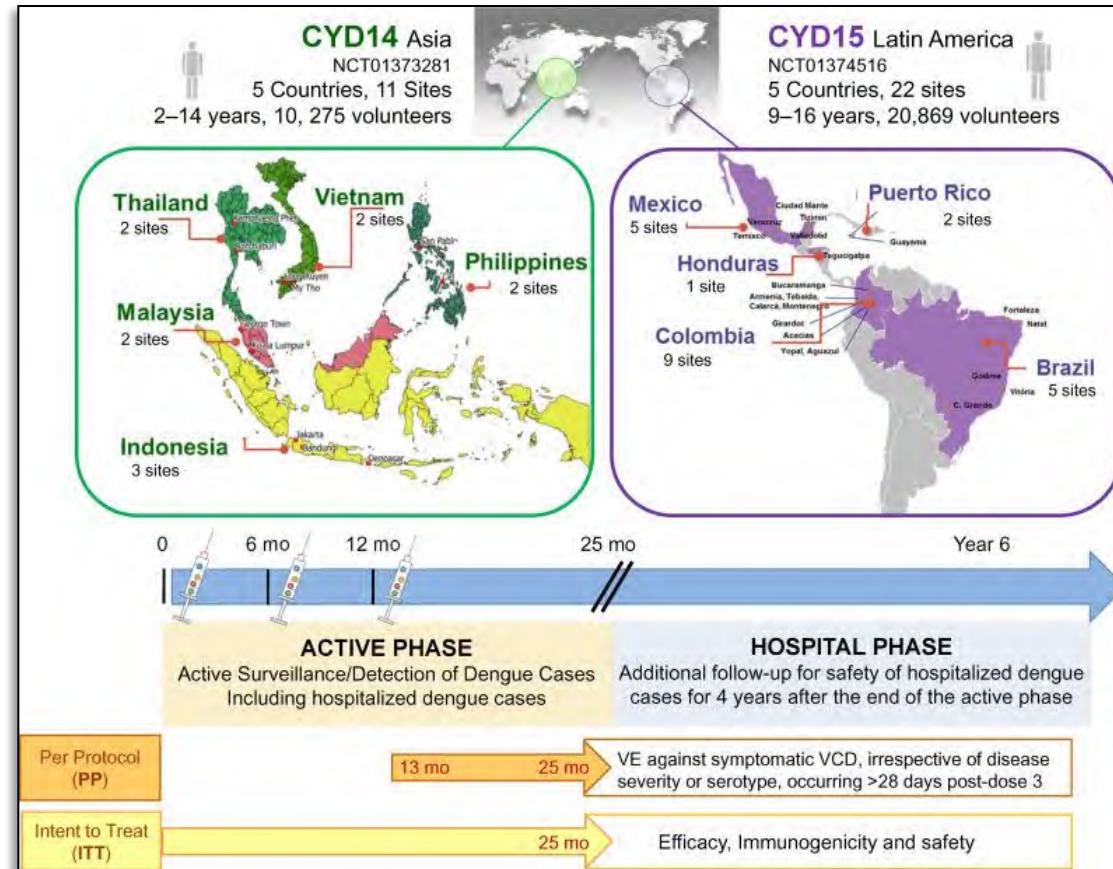


Data from patients hospitalized at Queen Sirikit National Institute of Child Health, Bangkok, Thailand.
Zhang et al. Clade Replacements in Dengue Virus Serotypes 1 and 3 Are Associated with Changing Serotype Prevalence. *J Virology* 2005; 79:15123.
<https://doi.org/10.1128/jvi.79.24.15123-15130.2005>

Clinical trials



Dengvaxia: CYD-TDV phase III trials



Guy B et al. Development of the Sanofi Pasteur tetravalent dengue vaccine: One more step forward. *Vaccine* 2015; 33(50):7100-11. <https://doi.org/10.1016/j.vaccine.2015.09.108>

Dengvaxia: CYD-TDV phase III trials

Table 1. Annual Incidence of Hospitalization for Virologically Confirmed Dengue, According to Trial, Age Group, and Study Period.*

Trial, Age Group, and Study Period	Vaccine Group			Control Group			Relative Risk (95% CI)
	Cases of Dengue	Total Participants†	Annual Incidence Rate‡	Cases of Dengue	Total Participants†	Annual Incidence Rate‡	
	no.	% (95% CI)		no.	% (95% CI)		
CYD14							
All participants§	27	6,778	0.4 (0.3–0.6)	13	3,387	0.4 (0.2–0.7)	1.04 (0.52–2.19)
2–5 yr	15	1,636	1.0 (0.6–1.6)	1	813	0.1 (0.0–0.7)	7.45 (1.15–313.80)
6–11 yr	10	3,598	0.3 (0.1–0.6)	8	1806	0.5 (0.2–1.0)	0.63 (0.22–1.83)
12–14 yr	2	1,544	0.1 (0.0; 0.5)	4	768	0.6 (0.2–1.4)	0.25 (0.02–1.74)
<9 yr	19	3,493	0.6 (0.4–0.9)	6	1741	0.4 (0.1–0.8)	1.58 (0.61–4.83)
≥9 yr	8	3,285	0.3 (0.1–0.5)	7	1646	0.5 (0.2–1.0)	0.57 (0.18–1.86)

Dengvaxia: CYD-TDV phase III trials

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Hadinegoro et al. NEJM 2015; 373:1195.

The manufacturer sought a license for everyone 9 years and over.

But a key question: is age a proxy for serostatus?

Table 2

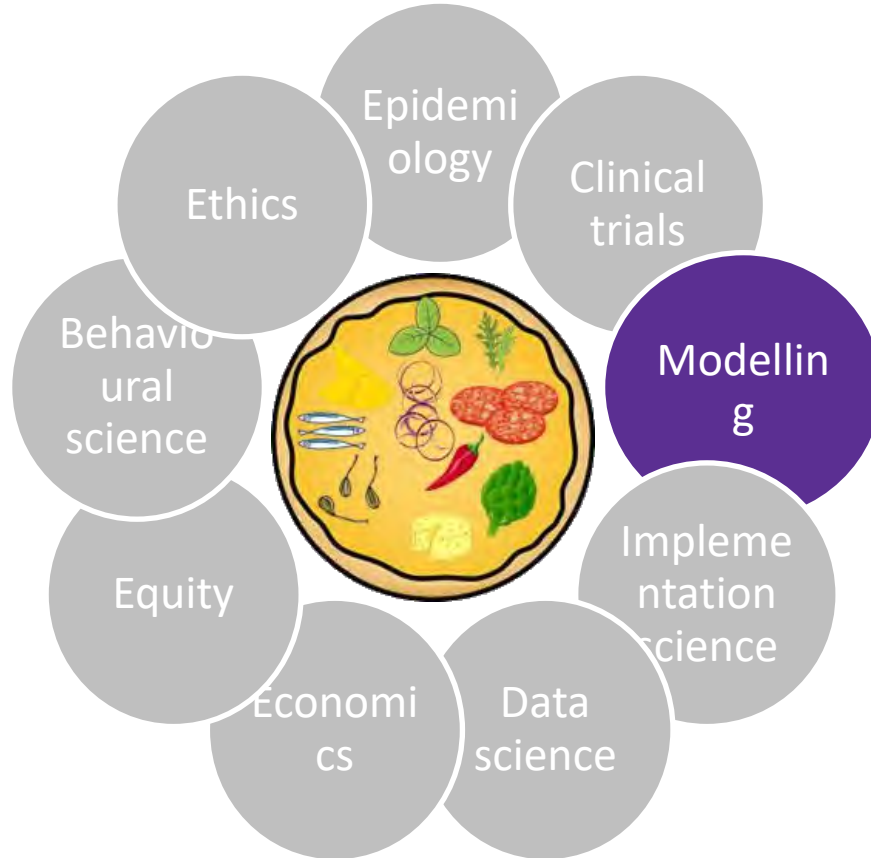
CYD vaccine efficacy, years 1–2, in seronegatives and seropositives against mild/moderate disease identified during surveillance phase in total group. From Table S6 [1].

CYD trial	Seronegatives			Seropositives		
	V	C	Efficacy	V	C	Efficacy
14 ^a	23/424	18/216	35.4 (–27.0–66.6)	18/901	37/444	74.3 (53.2–86.3)
15 ^a	9/258	9/149	43.2 (–61.6–80.0)	8/1073	23/512	83.7 (62.2–93.7)

^a = Intention to treat.

Halstead and Russell. Vaccine 2016; 34:1643.

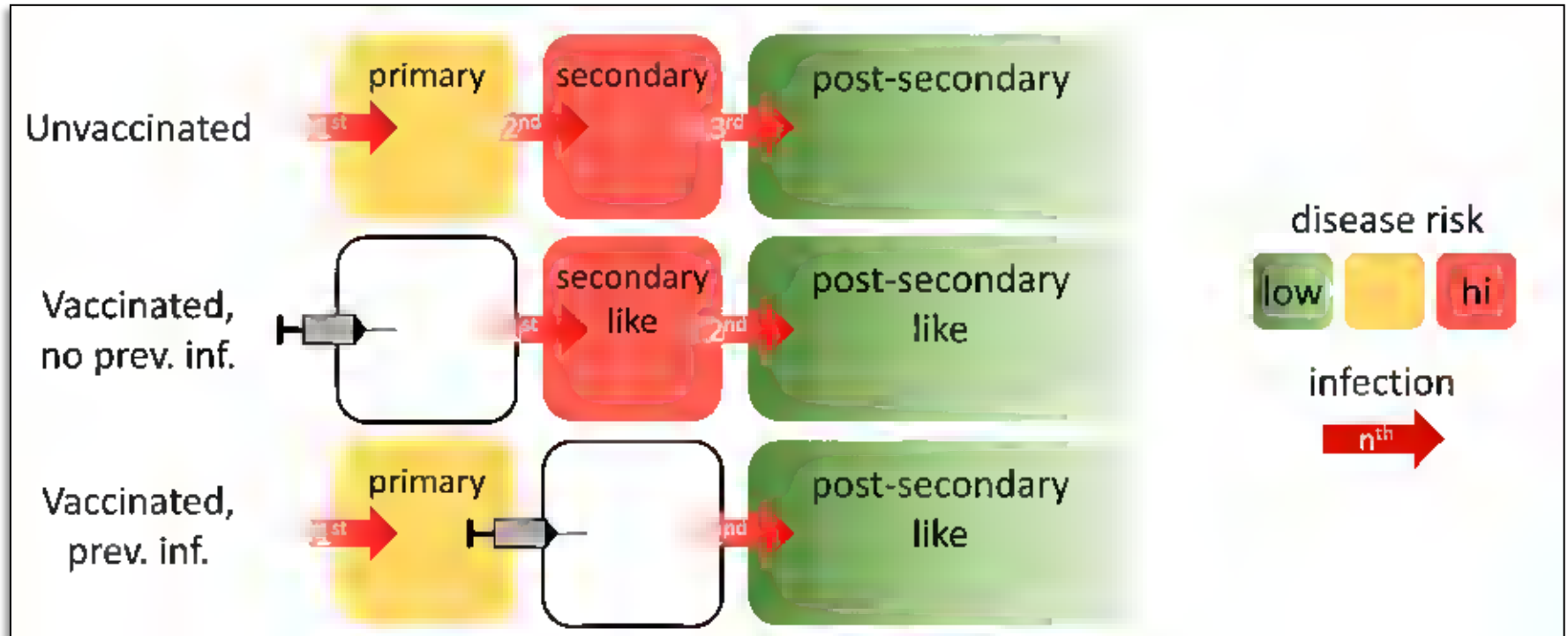
Mathematical modelling



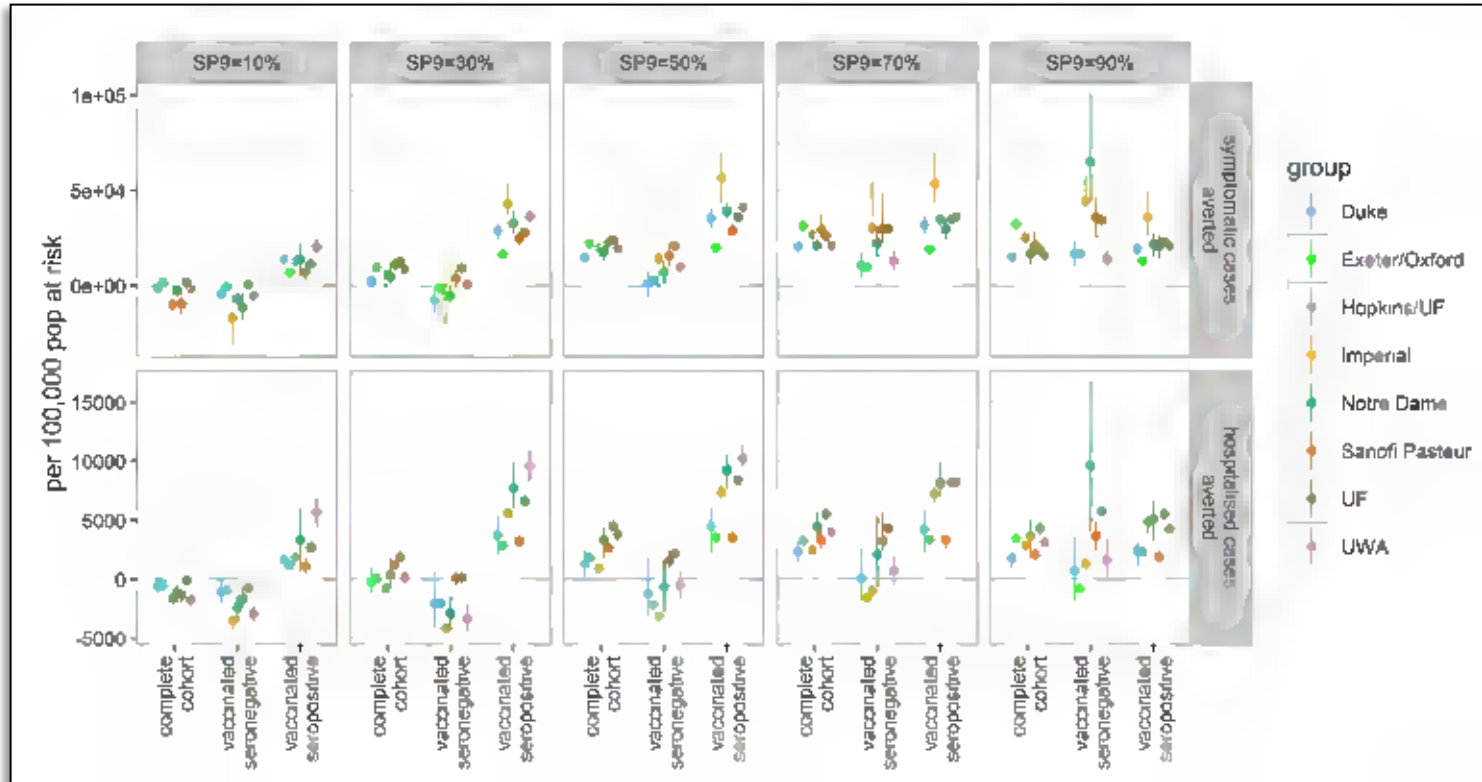
WHO Comparative Modelling of Dengue Vaccine public health Impact (CMDVI): Commissioned modeling groups

Group	Model type	Model fitted to Phase III trials?	Uncertainties represented	Seasonality	Demography
Sanofi Pasteur	Deterministic, nonspatial	Yes	Parameters and initial conditions	Biting rate, vector density	Brazil-like
Hopkins/UF		Yes	Initial conditions	Transmission	Brazil-like
Imperial		Yes	Parameters and initial conditions	Transmission	Brazil-like
Duke		Yes	Parameters	No	Brazil-like
UF	Stochastic, spatial	No	Parameters, stochasticity, and initial conditions	Vector density, incubation period	Mexico
UWA		No	Stochasticity	Vector density, incubation period	Thailand
Notre Dame		No	Parameters and stochasticity	No	Peru
Exeter/Oxford		No	Stochasticity	Vector density	Generic (67.5 y mean lifespan)

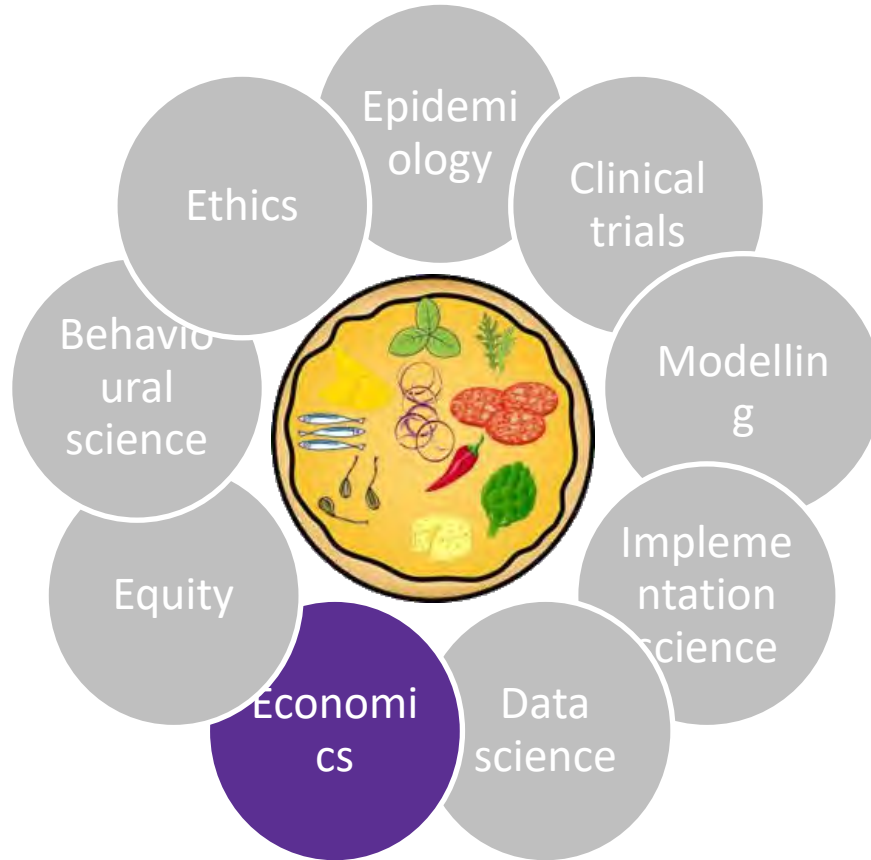
Dengvaxia proposed mechanism of action



Dengvaxia modelling consortium results

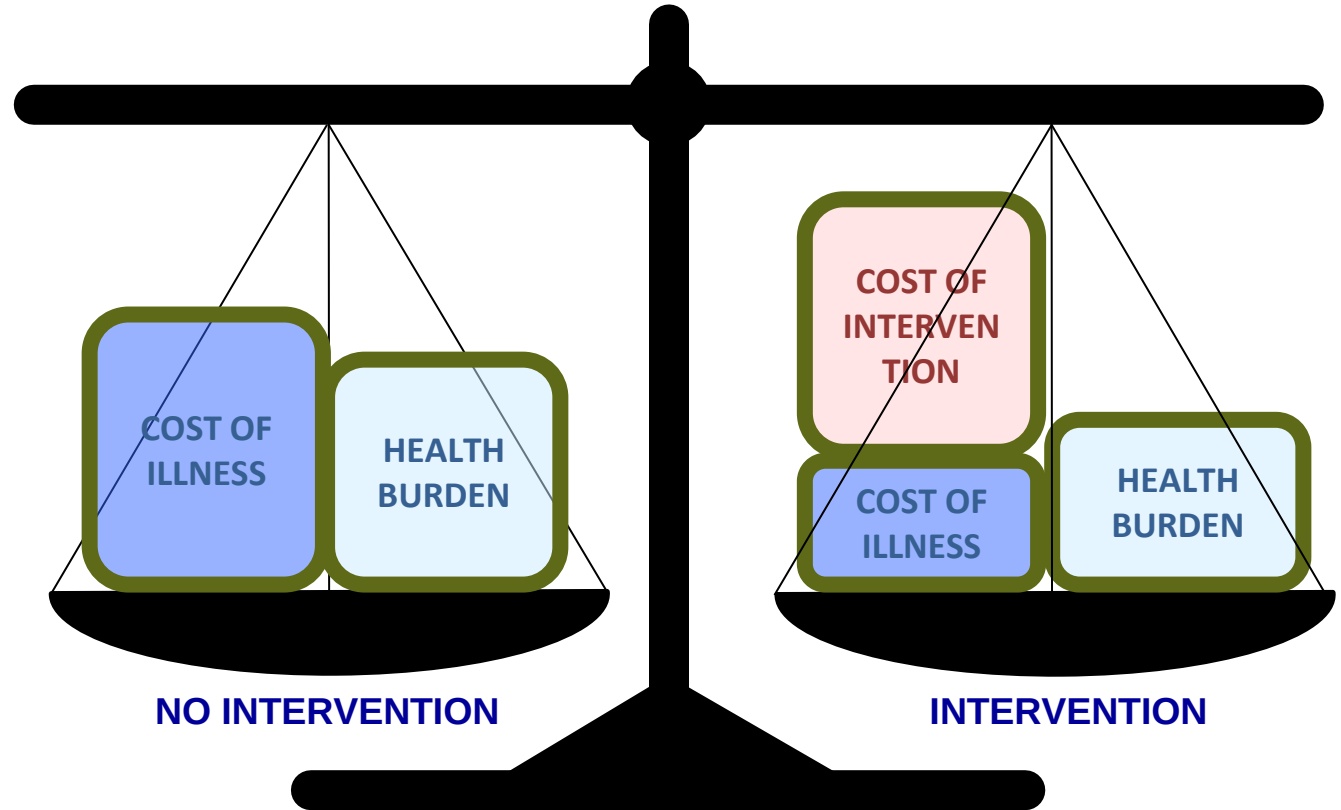


Health economics



What is an economic evaluation?

A (full) economic evaluation compares the **incremental costs** and **consequences** of an intervention compared to a comparator

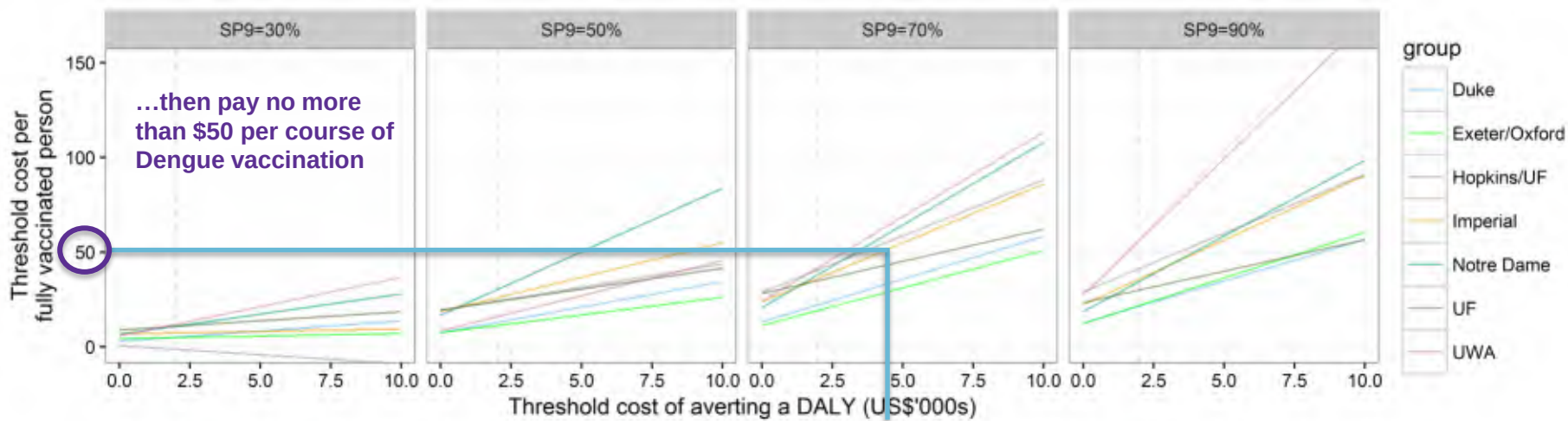


Cost-effectiveness analysis

$$\begin{aligned} \text{Incremental cost-effectiveness ratio} &= \frac{\text{Incremental costs}}{\text{Incremental health gain}} \\ &= \frac{\begin{array}{c} \text{COST OF INTERVENTION} \\ \text{COST OF ILLNESS} \end{array} - \text{COST OF ILLNESS}}{\text{INTERVENTION} - \text{NO INTERVENTION}} \\ &= \frac{\text{HEALTH BURDEN} - \text{HEALTH BURDEN}}{\text{NO INTERVENTION} - \text{INTERVENTION}} \end{aligned}$$

Measured in quantities like:
episodes of disease prevented
life years gained
QALYs gained
DALYs averted

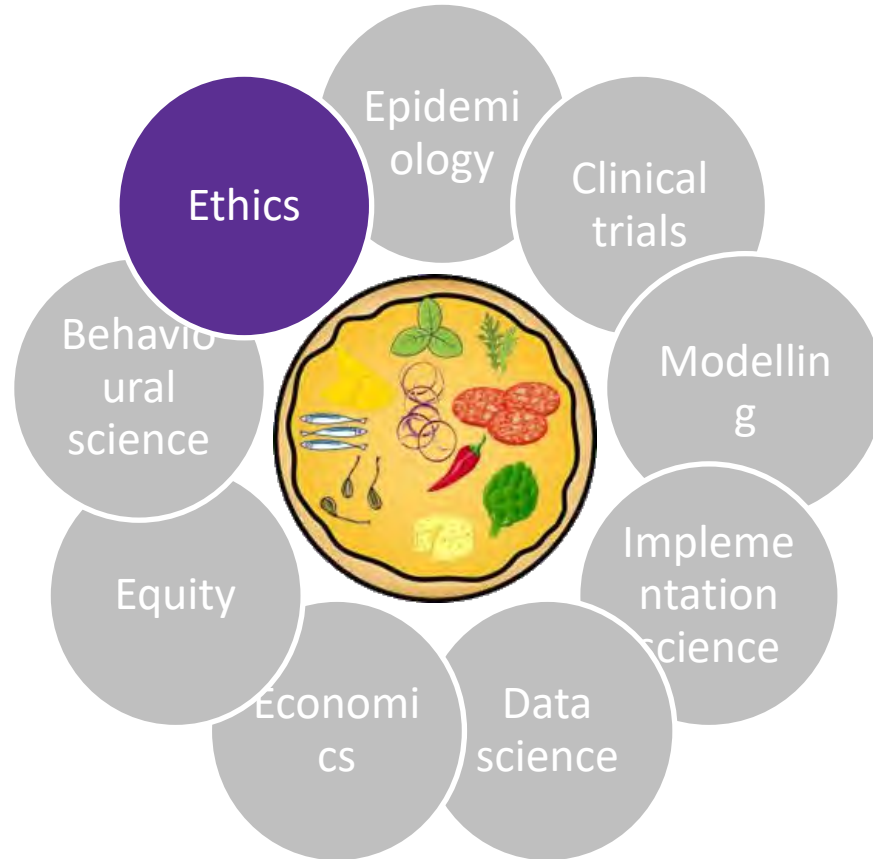
Cost-effectiveness modelling of Dengvaxia



NB: The price of a full course of Dengvaxia in the Philippines in 2016 was estimated to be 69 US\$ (España et al. PLoS Negl Trop Dis 2019; 13(7): e0007482).

If willing to pay
US\$4000 to
avert a DALY

Ethics

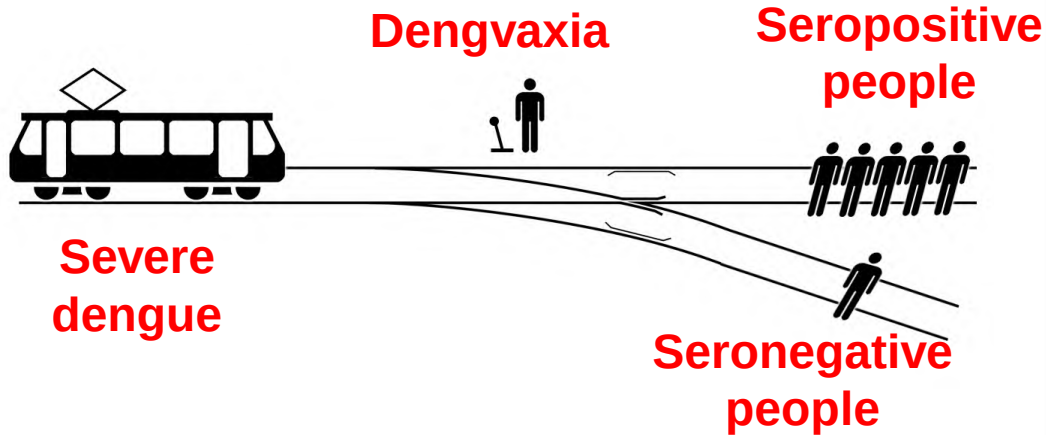


The trolley problem: good consequences vs good process



Picture: McGeddon. CCA-SA 4.0 license. Wikimedia Commons.
https://upload.wikimedia.org/wikipedia/commons/8/8c/Trolley_problem.png

Dengvaxia is a trolley problem



The NEW ENGLAND JOURNAL of MEDICINE

PERSPECTIVE

Trolleyology and the Dengue Vaccine Dilemma

Author: Lisa Rosenbaum, M.D. [Author info & Affiliations](#)

Published June 13, 2018 | N Engl J Med 2018;379:305-307 | DOI: 10.1056/NEJMp1804094 | VOL. 379 NO. 4
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"Trolleyology" refers to a series of moral dilemmas that reveal the tensions between utilitarianism — the idea that a behavior is moral if its consequences maximize public good — and our individual intuitions about right and wrong.¹ In a classic scenario, an observer is standing by a railway track where he spots a runaway trolley barreling toward five people who will soon be killed. He's standing by a switch that, if pulled, would divert the trolley away from the five but cause it to kill one person in its new path. In a related scenario, the observer is on a footbridge when he spots the trolley, and he's standing by a very large man. If he pushes the man off the bridge, the body will stop the trolley; the five people would be saved, but the man would die. What should the observer do? Most people believe he should

AUDIO INTERVIEW

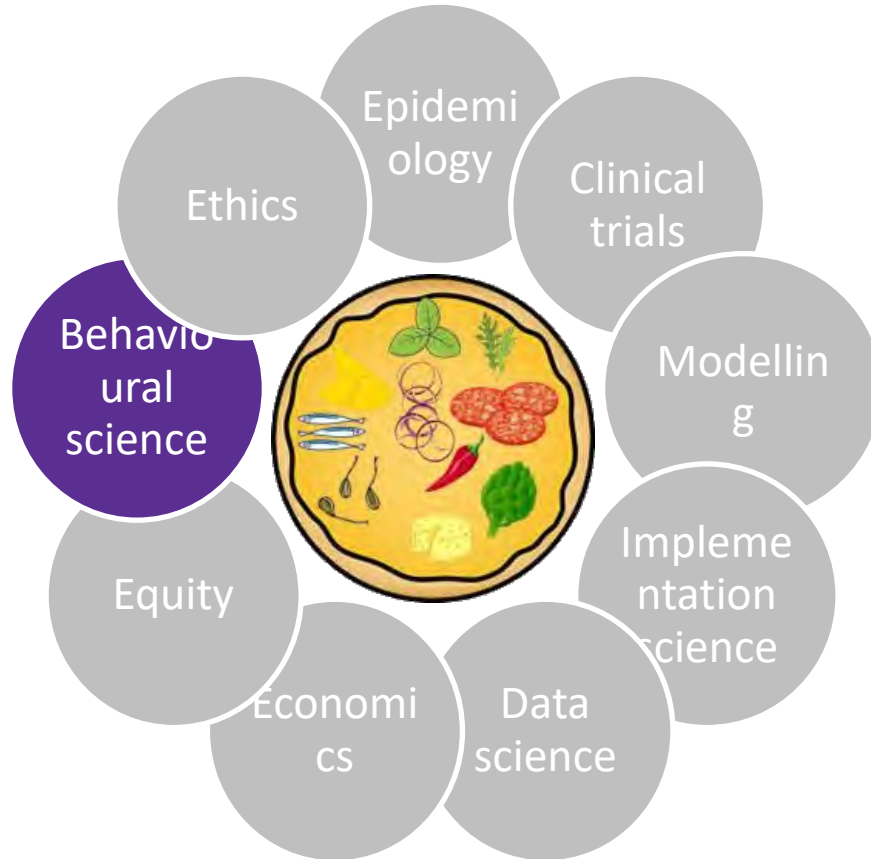
Interview with Dr. Lisa Rosenbaum on how emotion and risk perception affect decision making in public health and medicine. 8m 16s

DOWNLOAD

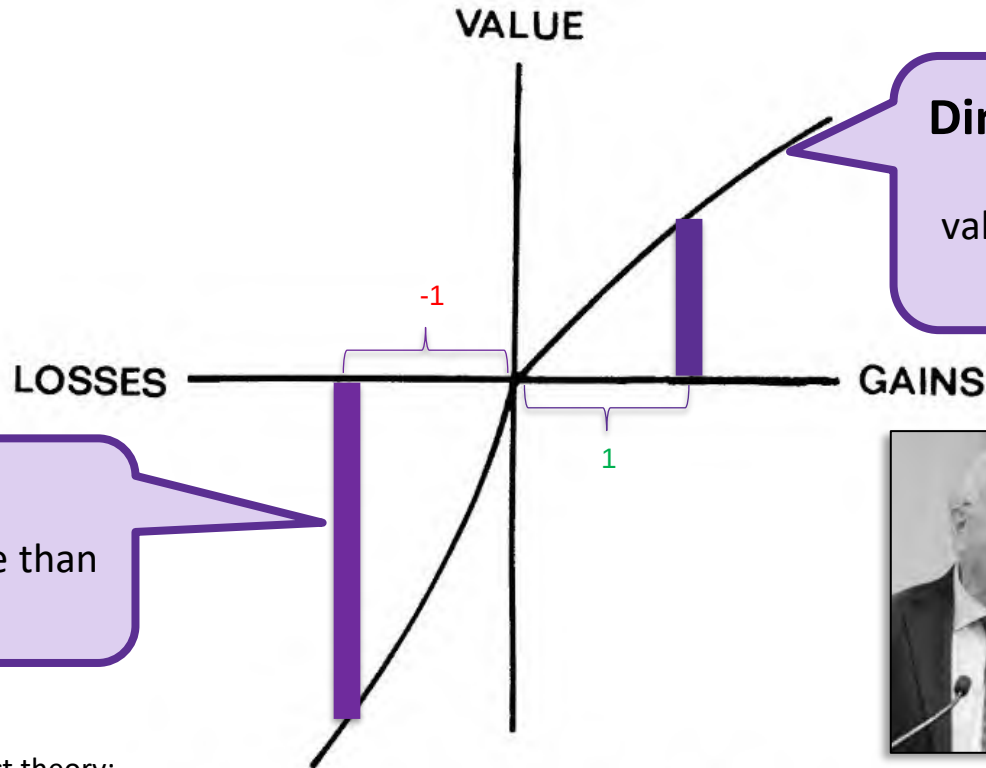
Dengvaxia: classic medical ethics principles

Principle	Meaning	Satisfied by Dengvaxia?
Benevolence	Acting in a person's best interests by promoting their well-being, providing benefits and balancing risks	☒ On average, vaccinees' risk of severe dengue decreased.
Non-maleficence	Avoiding intentional harm to patients	? The harm was not intentional, but it may have been foreseen.
Autonomy	Respecting a person's right to make fully informed decisions about their health	☐ Vaccinees did not receive full information about the potential risks of Dengvaxia.
Justice	Ensuring that everyone is treated fairly, equitably and appropriately	? The vaccinee was freely available, but it created unequal exposure to risk.

Behavioral science



Prospect theory: loss aversion, diminishing sensitivity

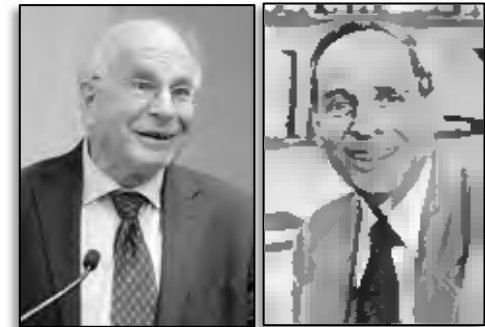


Diminishing sensitivity

Large gains/losses are valued proportionately less than smaller ones.

Loss aversion

Losses are valued more than equivalent gains



Daniel Kahneman (left) and Amos Tversky (right).
<https://www.amacad.org/news/two-systems-mind>

FIGURE 3.—A hypothetical value function.

Kahneman D, Tversky A. Prospect theory:
An analysis of decision under risk.
Econometrica 1979; 47:263-291.

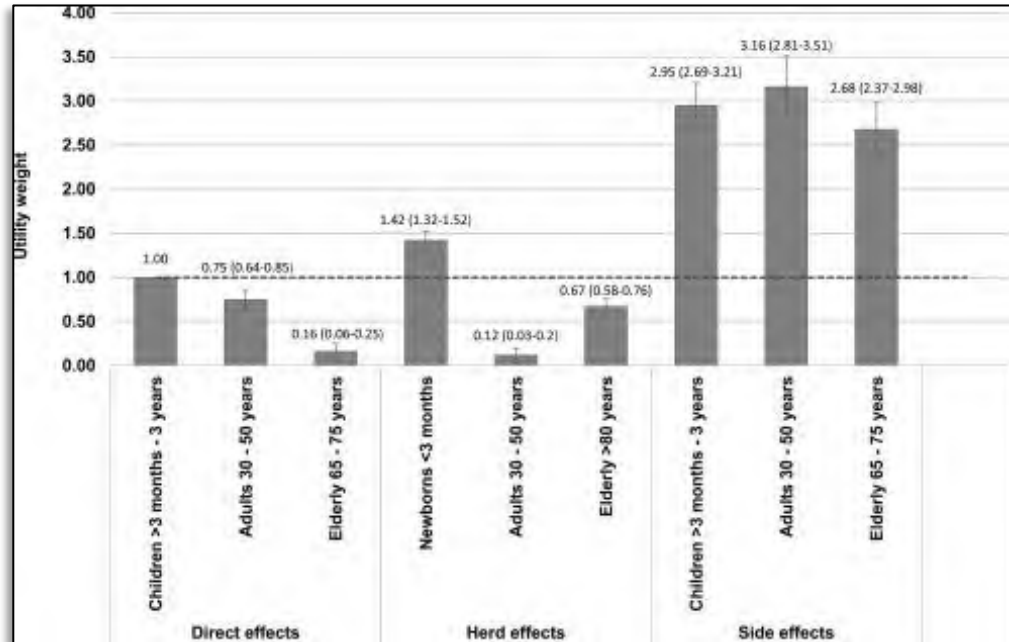
Expected utility theory vs prospect theory

	Expected utility theory (von Neumann and Morgenstern, 1944)	Prospect theory (Kahneman and Tversky, 1979)
Goal	Describes how rational people should make choices under uncertainty.	Describes how real people actually make choices under uncertainty.
Key concept	How to maximize the expected utility you gain from a decision (i.e. sum of utility gains times probability of that gain).	People don't actually maximise their expected utility – they evaluate compared to a reference point (usually the status quo), and put more weight on losses than gains.

Prospect theory in practice: vaccine trade-offs

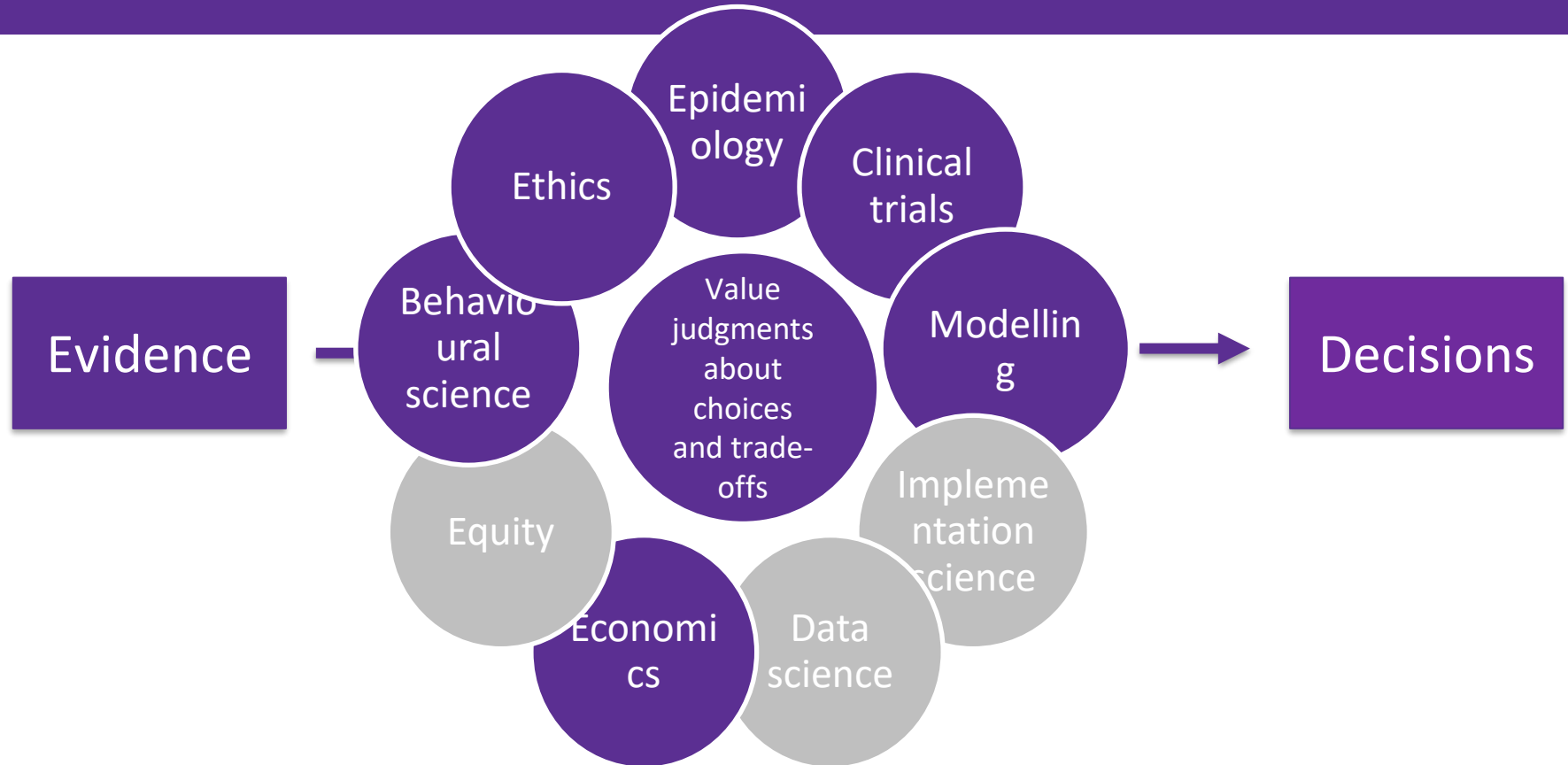
Based on prospect theory, what results do you think this discrete choice experiment showed?

	PROGRAM A	PROGRAM B
TOTAL NUMBER OF PREVENTED CASES (per 100,000)	7500	7700
Direct effects <i>How old are the 100,000 people who will become vaccinated?</i>	Adults (30-50 years) 	Adults (30-50 years) 
<i>How many cases of disease will be prevented in the 100,000 who become vaccinated?</i>	5000 cases prevented 	3000 cases prevented 
Side-effects <i>How many of the 100,000 vaccinated persons will get the disease through side effects of vaccination?</i>	500 cases occurring 	300 cases occurring 
Indirect effects <i>How old are those who will benefit from the indirect protection but are not vaccinated themselves?</i>	Infants (Under 3 months) 	Infants (Under 3 months) 
<i>How many cases of disease will be prevented via indirect protection in those who will not be vaccinated?</i>	3000 cases prevented 	5000 cases prevented 



Luyten J et al. Quantifying the public's view on social value judgments in vaccine decision-making: A discrete choice experiment. *Soc Sci Med* 2019; 228:181-193.

Bringing the evidence together for decision making



Role play (15 mins)



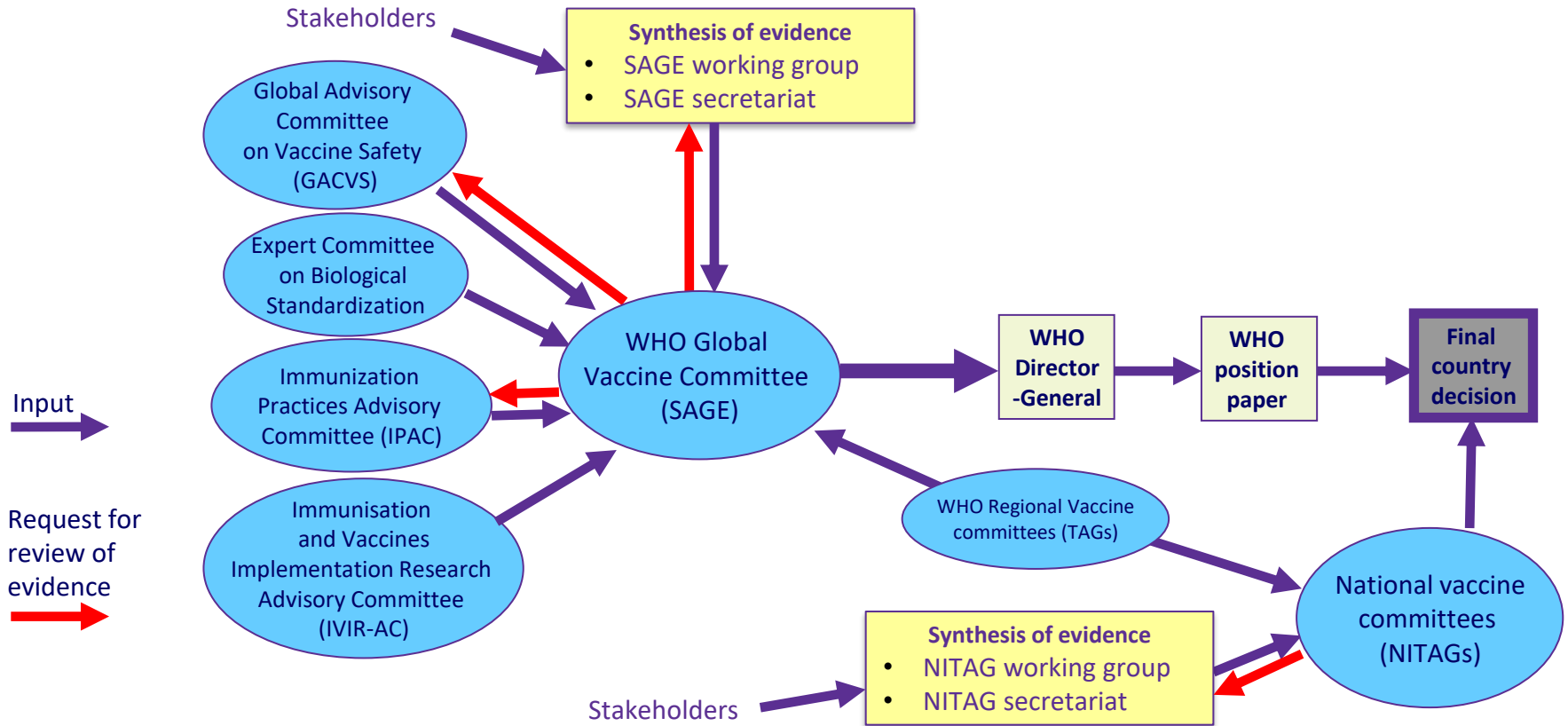
A dengue vaccine with the characteristics you just saw has just been licensed. The Health Minister of a country in South-East Asia is deciding whether or not to introduce the vaccine and proposes to set up an expert committee to evaluate this question.

In your groups, split yourself into people on the expert committee with different roles: an epidemiologist, a vaccine trialist, a modeller, an ethicist, a behavioural scientist, an economist and a chairperson. If there are not enough people, pick any roles you think are most relevant.

Agree on rules by which the discussion should be conducted and the final recommendation reached.

What conclusion did your committee reach?

WHO decision-making processes about vaccination



Dengvaxia: 2016 WHO recommendations

“SAGE recommended countries consider introduction...only in geographic settings (national or subnational) with...seroprevalence of approximately 70% or greater in the age group targeted for vaccination.....decisions about introduction require careful assessment at the country level...”

Summary of the April 2016 meeting of SAGE.

https://www.who.int/immunization/sage/meetings/2016/april/SAGE_April_2016_Meeting_Web_summary.pdf

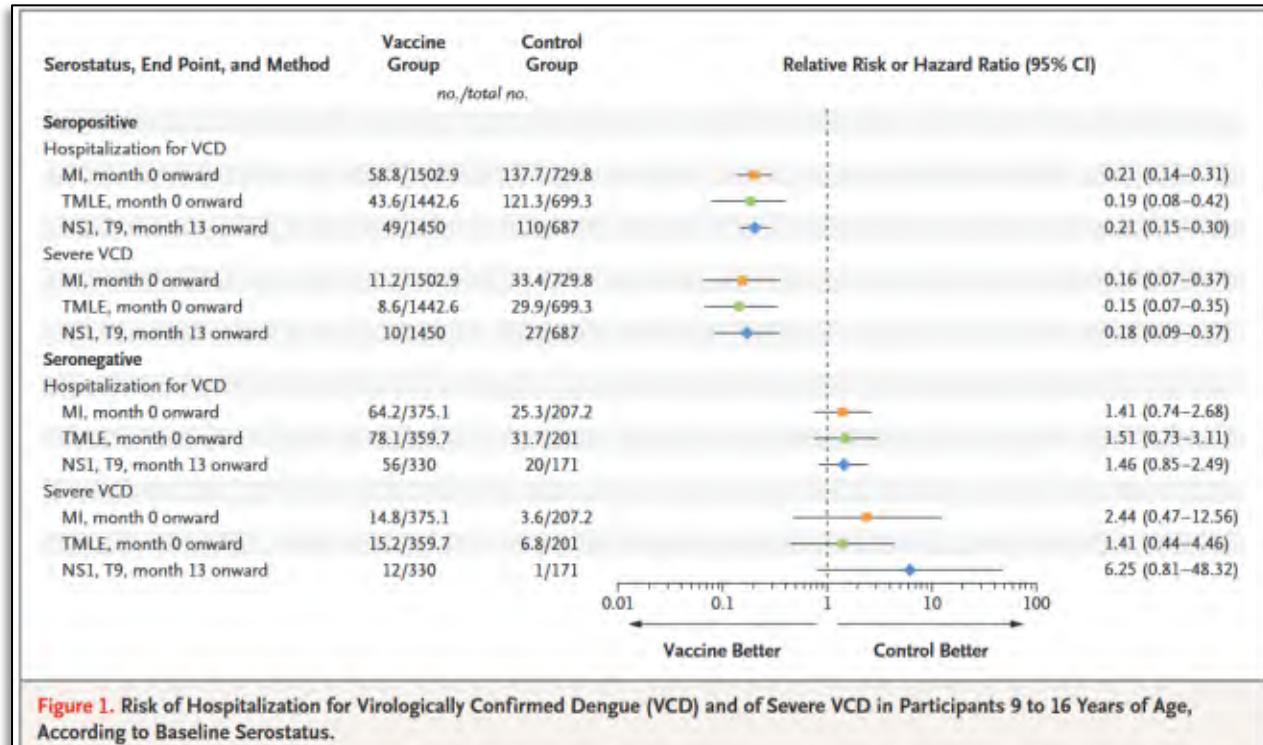


WHO Strategic Group of Experts on Immunization (SAGE) meeting, October 2018. Archived at:
<https://web.archive.org/web/20190418035013/https://www.who.int/immunization/policy/sage/en/>

Dengvaxia was subsequently licensed in 20 dengue-endemic countries

Dengvaxia: further data in 2018

In 2018, the manufacturer conducted a post-hoc study with a newly developed assay that allowed retrospective testing of blood samples of vaccinees to recover baseline serostatus.



Sridhar et al. Effect of Dengue Serostatus on Dengue Vaccine Safety and Efficacy. *N Engl J Med* 2018; 379:327-340.
<https://doi.org/10.1056/nejmoa1800820>

Dengvaxia: Philippines public response

The Manila Times

Govt delists Dengvaxia
BY CATHERINE A. MODESTO
FEBRUARY 20, 2019

HOME / NEWS / TOP STORIES / GOVT DELISTS DENGVAXIA



The Food and Drug Administration (FDA) registration (CPR) of Dengvaxia, which was used to boost immunization rates in the Philippines.



Science

Home

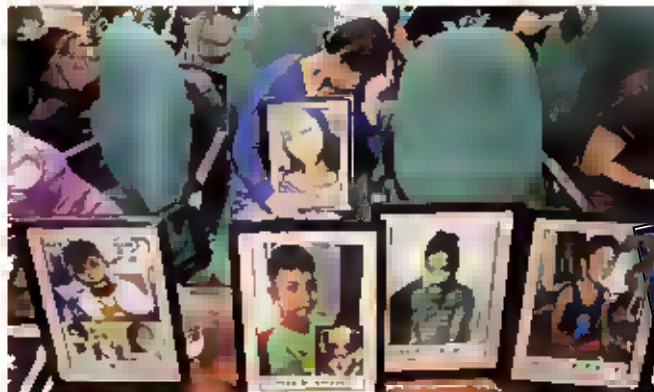
News

Journals

Topics

Careers

SHARE



Parents brought pictures of children immunized with Dengvaxia to a 2018 hearing in the Philippine Senate. NOEL CELIS/AP - GETTY IMAGES

Dengue vaccine fiasco leads to criminal charges for researcher in the Philippines



This file photo shows Public Attorney's Office chief Persida Acosta checking the rashes of a 12-year-old girl during a press conference with the alleged victims of Dengvaxia. The STAR/Boy Santos, File

How the Dengvaxia scare helped erode decades of public trust in vaccines

by Katreena Cabico (Philstar.com) - February 6, 2019



PHILIPPINE DAILY INQUIRER
BALANCED NEWS • FEARLESS VIEWS
PH TO SUE MAKER OF DENGUE VACCINE
STORY BY FRANCES MANGOSING
The health secretary says the government may ask Sanofi to refund P1.4 billion worth of unused vaccines and demand the drug maker set up an 'indemnity fund' to cover the hospitalization of vaccinated kids who will fall ill.



Dengvaxia: Halstead et al. analysis

Four year projections of occurrence of dengue hospitalizations and severe cases among 880,464 Philippine children who were either given or not given Dengvaxia.

Serostatus	At risk	DENV infected	Vaccinated		Not Vaccinated	
			Hospitalized	Severe cases	Hospitalized	Severe Cases
Seroneg	132,070	63,129 ^a	2241	480	1547	75
Seropos	290,553 ^b	138,884 ^c	2917	597	13,958	3472
Totals	422,623	202,013	5158	1077	15,505	3547

a = monotypic DENV infections.

b = monotypic-immunes.

c = secondary DENV infections.

“In 2016, Dengvaxia given to 880,464 nine-year-old children...

...After this program was initiated a novel serological test, applied retrospectively, generated data for entire phase 3 population discovering that ...seronegative children given Dengvaxia were at significant risk to severe dengue. This news resulted in cancelation of the vaccination program in the Philippines and in widespread public alarm.”

...during the first four years after complete Dengvaxia immunization...nearly 500 vaccinated seronegative children are expected to acquire severe dengue.”

Dengvaxia: 2018 WHO recommendations (revised)

“For countries considering vaccination as part of their dengue control programme, pre-vaccination screening is the recommended strategy...With this strategy, only persons with evidence of a past dengue infection would be vaccinated...

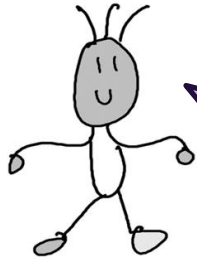
If pre-vaccination screening is not feasible, vaccination without individual screening could be considered in areas with...seroprevalence rates of at least 80% by age 9 years.”

Dengue vaccine: WHO position paper - Sept 2018. Available at:
<https://apps.who.int/iris/bitstream/handle/10665/274315/WER9336.pdf?ua=1>



WHO Strategic Group of Experts on Immunization (SAGE) meeting, October 2018. Archived at:
<https://web.archive.org/web/20190418035013/https://www.who.int/immunization/policy/sage/en/>

Every actor has an important perspective



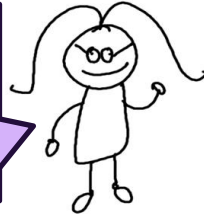
Epidemiologist

Global dengue burden is high.
We need a vaccine!



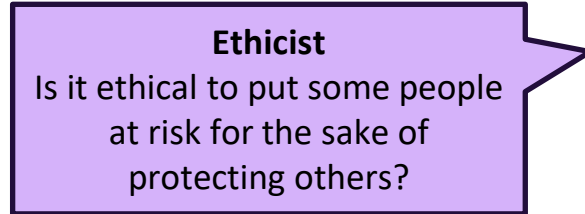
Economist

The vaccine might not be cost-effective in some countries at current prices ...



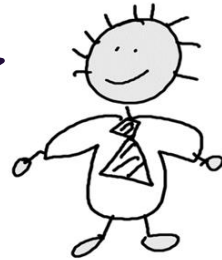
Clinical trialist

The trials showed good results! But the <5 data are worrying...



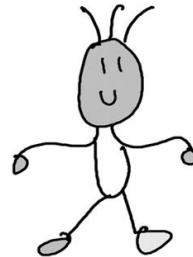
Ethicist

Is it ethical to put some people at risk for the sake of protecting others?



Modeller

The data are consistent with vaccination acting like a silent infection... which means it will harm some people ... but protect more people than it harms in high-transmission settings.



Behavioural scientist

If parents find out their kids have been put at risk by the vaccine, this could affect their trust in vaccines.

Another difficult decisions: **varicella vaccination**

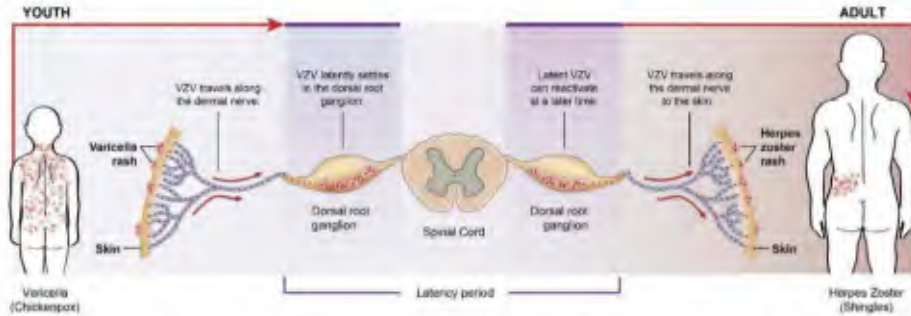


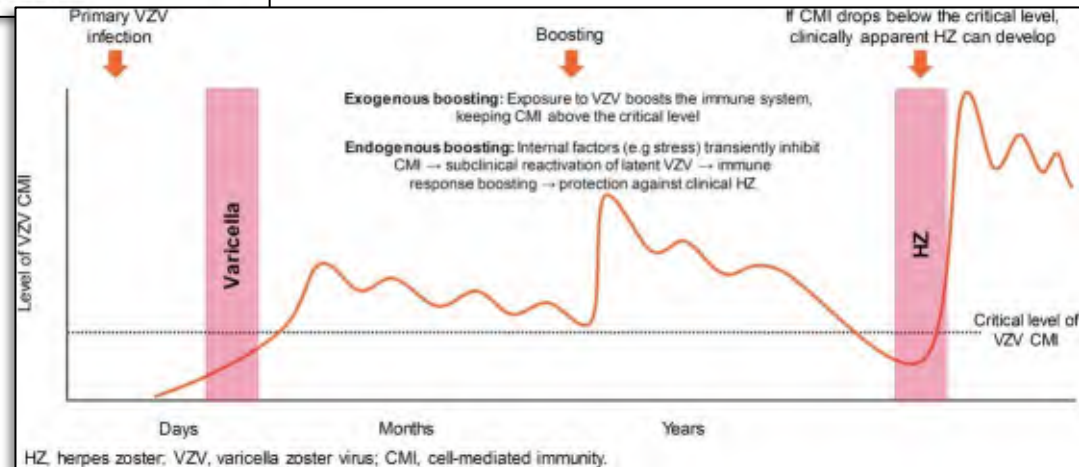
Figure 1. Physiological mechanism of HZ via reactivation of VZV. HZ = herpes zoster; VZV = varicella-zoster virus. Note: Factors impacting reactivation of VZV include fever, trauma, stress, and decreases in VZV cell-mediated immunity due to aging (immunosenescence), immunocompromising health conditions (e.g. cytomegalovirus), or use of immunosuppressing therapies. Exogenous boosting (or lack thereof) may also be a determinant of VZV reactivation.

Wutzler P et al. Herpes zoster in the context of varicella vaccination - An equation with several variables. *Vaccine* 2018; 36(46):7072-7082.

<https://doi.org/10.1016/j.vaccine.2018.09.013>

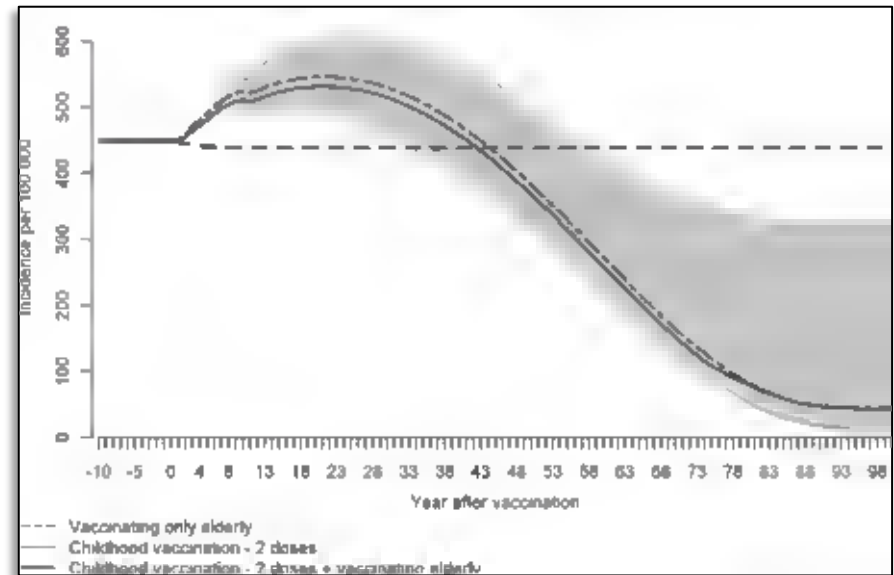
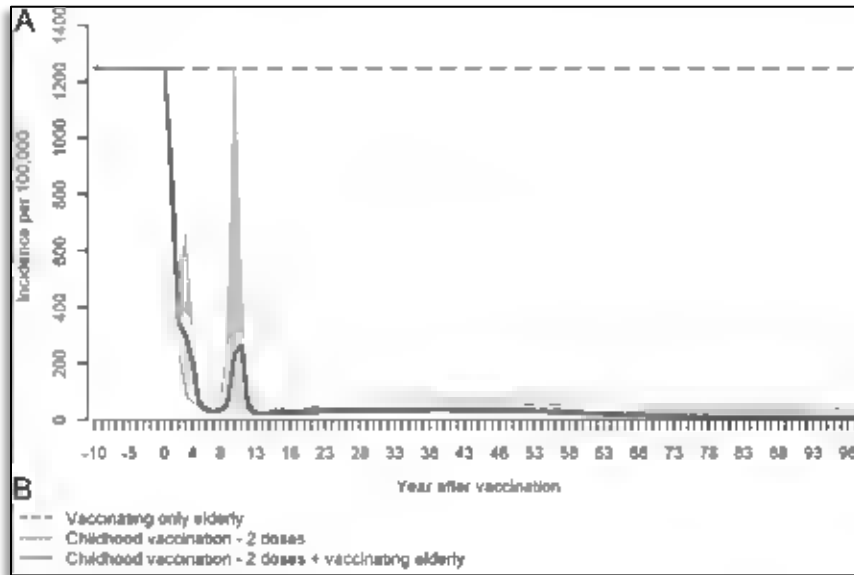
Talbird SE et al. Understanding the role of exogenous boosting in modeling varicella vaccination. *Expert Rev Vaccines* 2018; 17(11):1021-1035.

<https://doi.org/10.1080/14760584.2018.1538801>



Another difficult decisions: **varicella vaccination**

Impact of childhood varicella vaccination in the UK on varicella (left) and zoster (right) incidence



Role play (5 mins)



Go back to your committee.

What would the epidemiologist, modeller, ethicist, behavioural scientist and economist say about introducing varicella vaccination in the UK?

What conclusion would your committee reach overall?

[Make this a briefer discussion since I've given you much less information]

Summary of perspectives

Perspective	Key issues
Epidemiology	• Varicella is highly infectious and usually mild in children but can cause severe disease in immunocompromised individuals. • Reduced varicella circulation may decrease natural immune boosting in adults, potentially causing a temporary increase in zoster, which is more severe (but evidence is contested).
Modelling	• Transmission models suggest that varicella vaccination will cause a temporary increase in zoster incidence, but in the long-term will reduce both varicella and zoster incidence. • Predictions are sensitive to the assumed strength and duration of exogenous boosting.
Economics	• Varicella vaccination could be cost-effective in the short-term (reduced disease and health care costs), but in the medium-term will depend on how much increase in zoster is anticipated.
Ethics	• Vaccination protects children from disease and complications (beneficence) but may expose current adults to higher shingles risk (non-maleficence). • Raises issues of justice and intergenerational fairness.
Behaviour	• Public concern that vaccination could increase shingles may contribute to vaccine hesitancy or resistance if uncertainty is poorly communicated.

Epilogue: what happened in the UK?

The “exogeneous boosting effect” was found to be shorter than previously estimated (3-5 years), based on fitting a model to zoster incidence in the USA following the introduction of varicella vaccination in 1995.

This means that the effect of varicella vaccination on zoster incidence is smaller than previously thought.

Based on new health and economic modelling, the UK’s vaccine committee recommended introducing varicella vaccination in 2023.

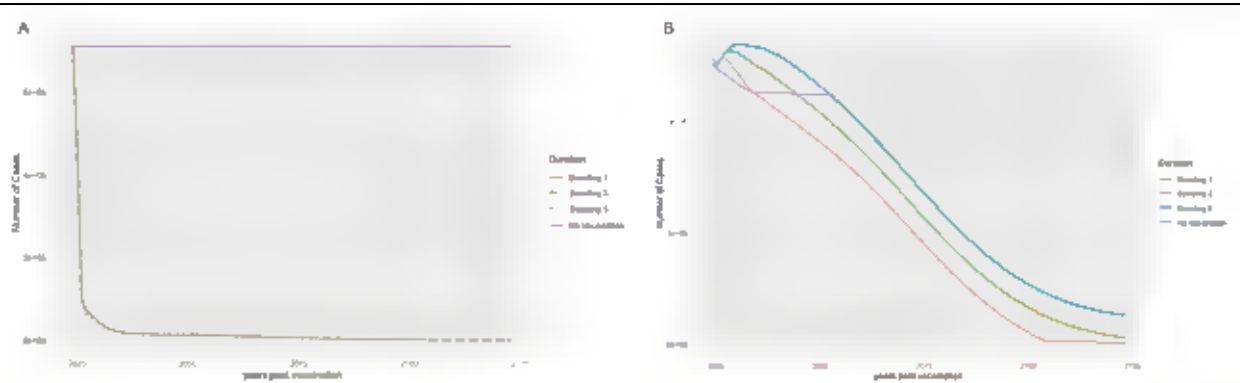


Fig. 4. A: Predicted varicella incidence from 2024 to 2124 for each duration of exogenous boosting in the routine scenario. No varicella vaccination (purple solid line), boosting duration 1 (red solid line), boosting duration 3 (green dashed line) and boosting duration 5 (blue dotted line). B: Predicted zoster incidence from 2024 to 2124 for each duration of exogenous boosting in the routine scenario. No varicella vaccination (purple), boosting duration 1 (red), boosting duration 3 (green), boosting duration 5 (blue). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Adams L et al. Modelling the impact and cost effectiveness of universal varicella vaccination in England. *Vaccine* 2025; 50:126831. <https://doi.org/10.1016/j.vaccine.2025.126831>

Take home messages

- **Vaccine decision making** integrates evidence and perspectives from a variety of disciplines: epidemiology, implementation science, mathematics, economics, behavioural science, ethics etc.
- Ignore any of these perspectives at your peril!