

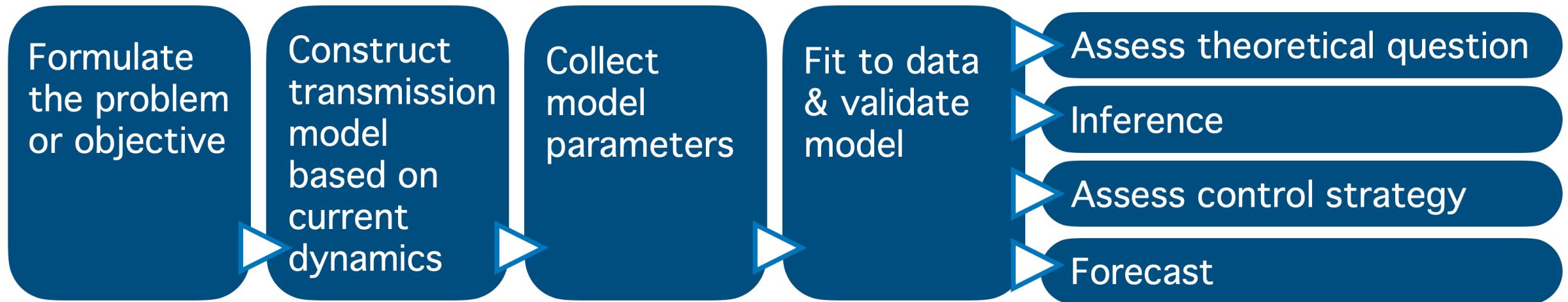
# Block 3

# Strategic Modelling and Impact Assessment

# Outline

- Interventions
- The comparator
- Impact evaluation
- Model uncertainty
- Model comparisons
- VIMC model comparisons
- Remaining M&R questions

# Reminder: ID Modelling Steps



# Reminder: Strategic Modelling

## Theoretical Modelling

*What type of emergence behavior is produced by disease systems with different properties?*

- What-if type questions
- Highly abstract
- Explore consequences of hypothetical mechanisms

## Inference Modelling

*What is the true nature of the disease processes that are producing the observed health metrics?*

- Understand specific mechanisms of transmission
- Quantify value of specific parameters
- Account for epistemic and sampling process

## Strategic Modelling

*How will an epidemic unfold and different control strategies work under various conditions?*

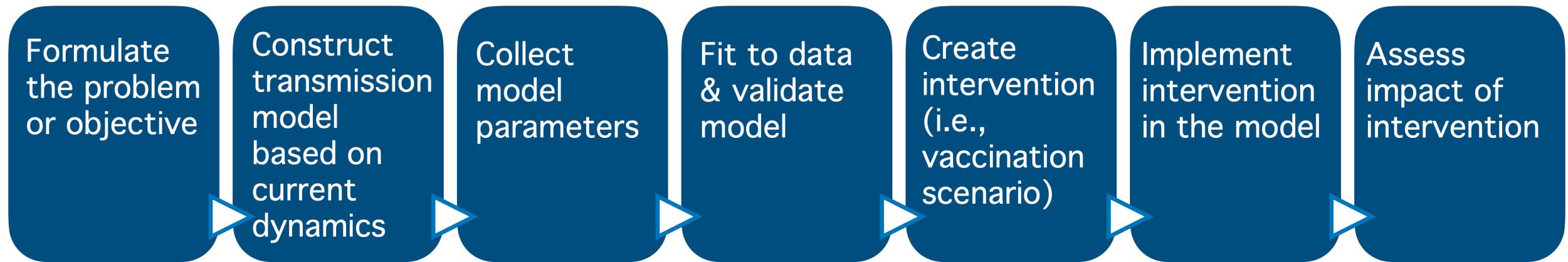
- Conditional predictions of what could happen under specific scenarios
- *Focus on contrast's between scenarios*

## Forecast Modelling

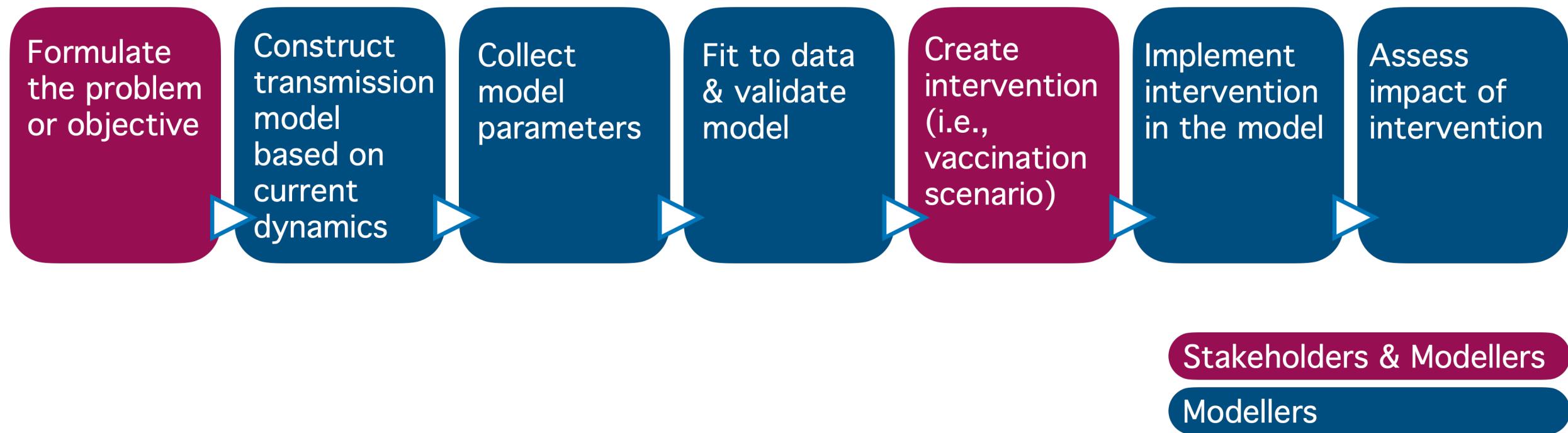
*How will an epidemic unfold in the coming weeks or months?*

- Unconditional prediction of what will happen
- Choice of specific metrics

# Strategic Modelling



# Strategic Modelling



# Learning Objectives

- What are the different interventions for measles and rubella
- What is the role of the comparator(s) in intervention scenarios
- How do we compare model output via impact metrics
- How do we incorporate different model uncertainties
- What is the role of multiple models

# Evidence – Based Medicine

## PICO

Before you start your search, it is important to have a well-built question. One way to construct a well-built question is to use the PICO model. PICO stands for patient/population, intervention, comparison and outcomes.

Patient/Population	Intervention	Comparison	Outcomes
<p>Who is your patient?</p> <ul style="list-style-type: none"><li>• Age, sex, race or patient</li><li>• Primary problem</li><li>• Health status</li></ul>	<p>What do you plan on doing for the patient?</p> <ul style="list-style-type: none"><li>• Diagnostic test</li><li>• Medication</li><li>• Procedure</li></ul>	<p>What alternative are you considering?</p> <ul style="list-style-type: none"><li>• Another test, medication or procedure</li><li>• Watchful waiting</li></ul>	<p>What do wish to accomplish?</p> <ul style="list-style-type: none"><li>• Accurate diagnosis</li><li>• Relieve or improve symptoms</li><li>• Maintain function</li></ul>

# Strategic Modelling

Population	Intervention	Comparison	Outcome
Population of India	Measles-containing vaccine at 6 months old	Measles-containing vaccine at 9 months old	Measles cases Measles deaths

# Interventions

# What **intervention**, or control strategies, do we want to evaluate?

- The type of interventions determines how we conduct the strategic modelling

# Interventions = Control Strategies



# Impact dynamics?



- Does the intervention need to feed into the model?
- Does the intervention impact transmission dynamics?

# Intervention based on prevention type (medical / individual perspective)

## Primary Prevention:

*Occurs prior to exposure*

*Designed to prevent disease*

## Secondary Prevention:

*Occurs during pathogenesis phase (after agent reacts with host). The disease already exists in the person.*

*Designed to reduce the progress of disease in individual*

## Tertiary Prevention:

*The disease has already occurred*

*Designed to limit disability from disease*

# Intervention based on prevention type (population perspective)

## Primary Prevention:

*Occurs prior to exposure*

*Designed to prevent disease*

## Secondary Prevention:

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*Designed to reduce the progress of disease in individual*

## Tertiary Prevention:

*The disease has already occurred*

*Designed to limit disability from disease*



direct protection from infection



surveillance as an action for indirect protection from infection



protection from death or disability

# Intervention based on prevention type

## Primary Prevention

Likely need to be incorporated into the model

### Examples:

Vaccination

## Secondary Prevention

Potentially need to be incorporated into the model

### Examples:

Surveillance interventions  
Cervical cancer screening  
STD screening

## Tertiary Prevention

Likely not need to be incorporated into the model

### Examples:

Therapeutic interventions  
Drug treatments

# Measles and Rubella Interventions

## Primary Prevention

### Vaccination

- Routine vaccination
- Supplemental Immunization Strategies (SIAs)
  - Non-Selective (i.e, give to all people in target age group)
  - Selective (i.e., only give to people without previous vaccine in the target age group)
- Periodic Intensification of Routine Immunization (PIRIs)
- School entry vaccination
- Outbreak response vaccination
- Month of SIAs
- SIA age targets
- Routine immunization age targets
- Frequency of SIAs
- Private sector vs public sector vaccination

### Lockdown/ Physical Distancing

# Measles and Rubella Interventions

Secondary Prevention

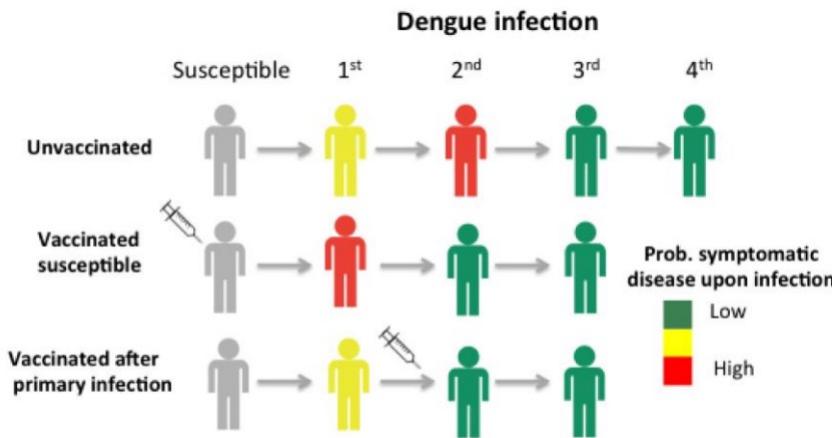
- Contact tracing
- Isolation of cases
- School closings
- Pre-natal rubella IgG testing

# Measles and Rubella Interventions

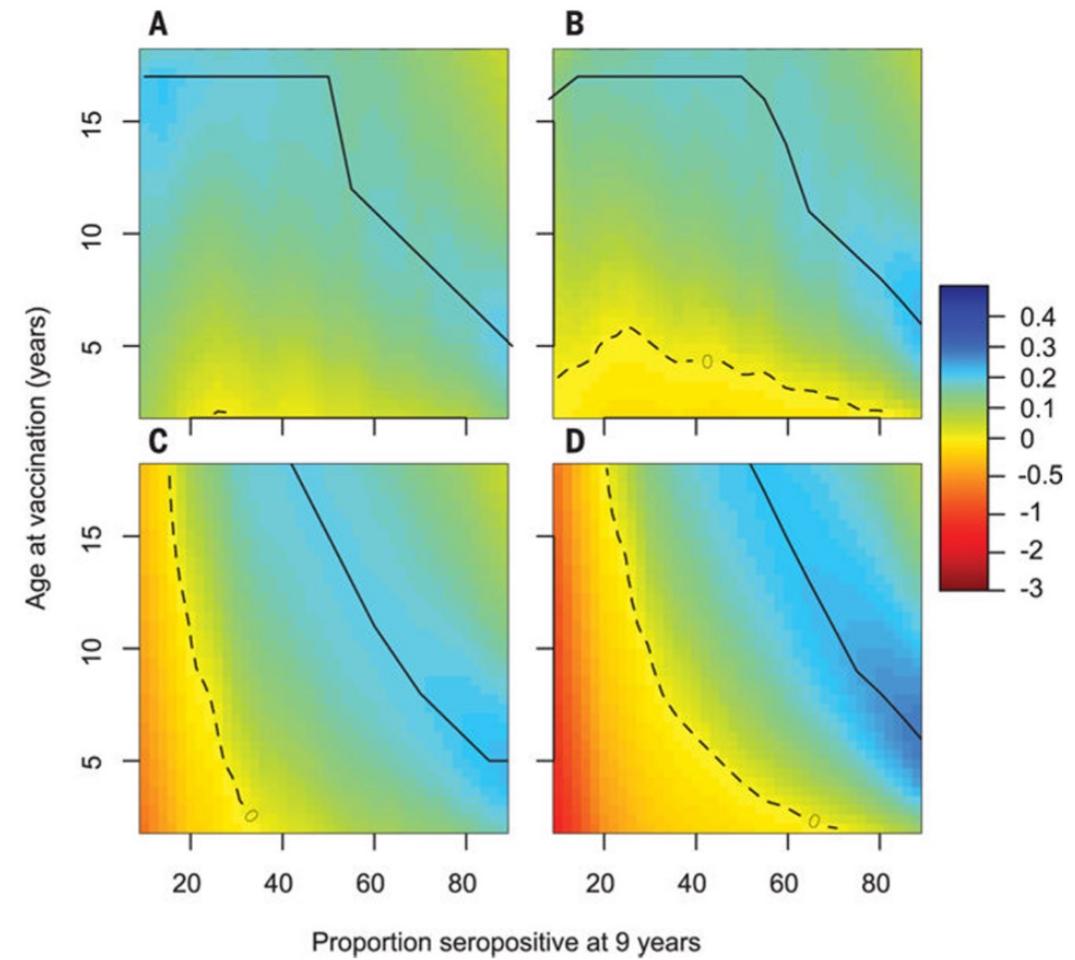
## Tertiary Prevention

- Case management
  - Vitamin A treatment
  - Fever reducing agents (e.g., paracetamol)
  - Oral rehydration

# Dengue Example



**Figure S1:** Mechanism of action of the vaccine assumed in the default model.

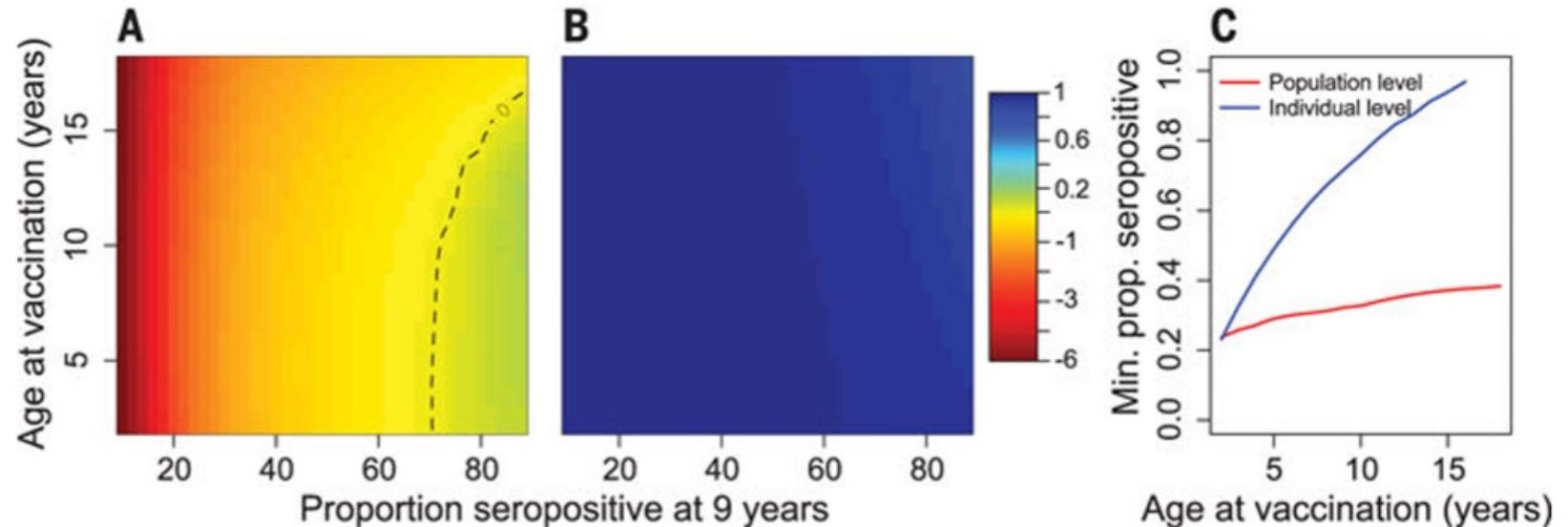


**Fig. 2. Predicted population effects of vaccination on dengue disease for a range of transmission intensities (x axes) and ages of vaccination (y axes)**

Color scale indicates proportion of cases averted in the whole population (A) over 10 years, for all symptomatic dengue; (B) over 10 years, for participants hospitalization with dengue; (C) over 30 years, for all symptomatic dengue; and (D) over 30 years, for hospitalization with dengue. Negative proportions of cases averted indicate vaccination increases risk. Solid contours indicate the optimal age of vaccination for each transmission intensity. Dashed contours indicate the youngest age group that may be targeted to avoid negative effects at the population level.

# Dengue Example

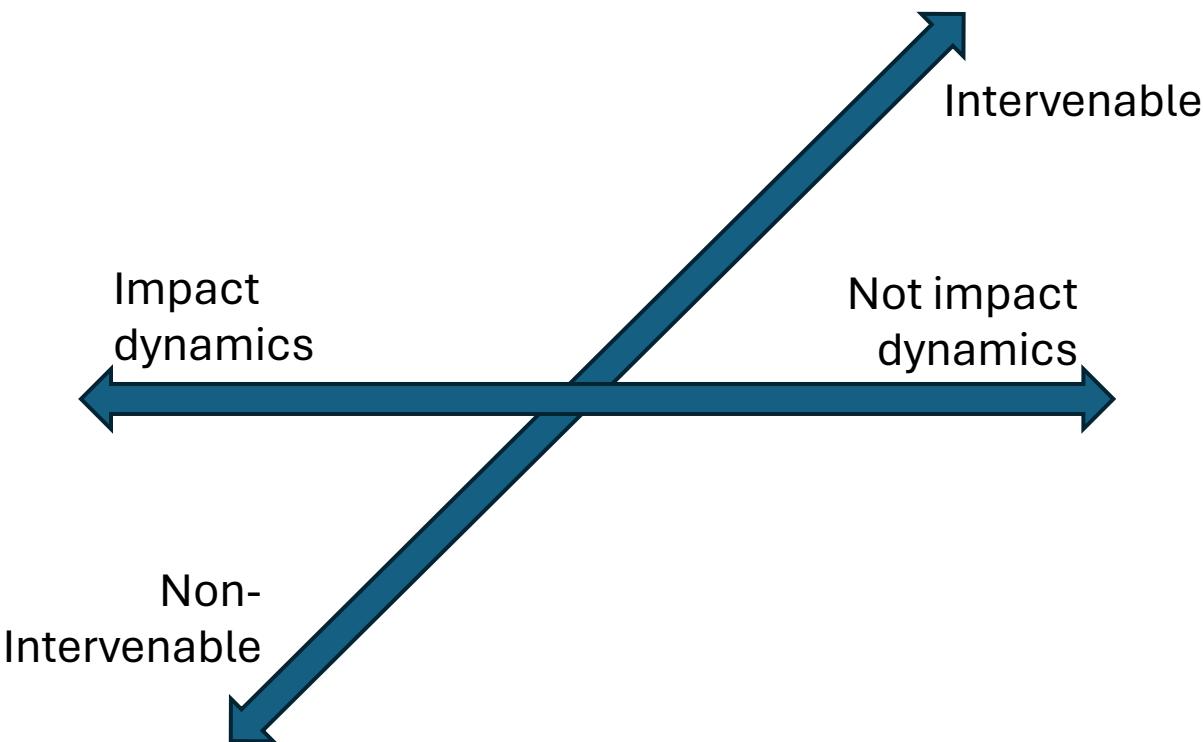
Ferguson et al 2016



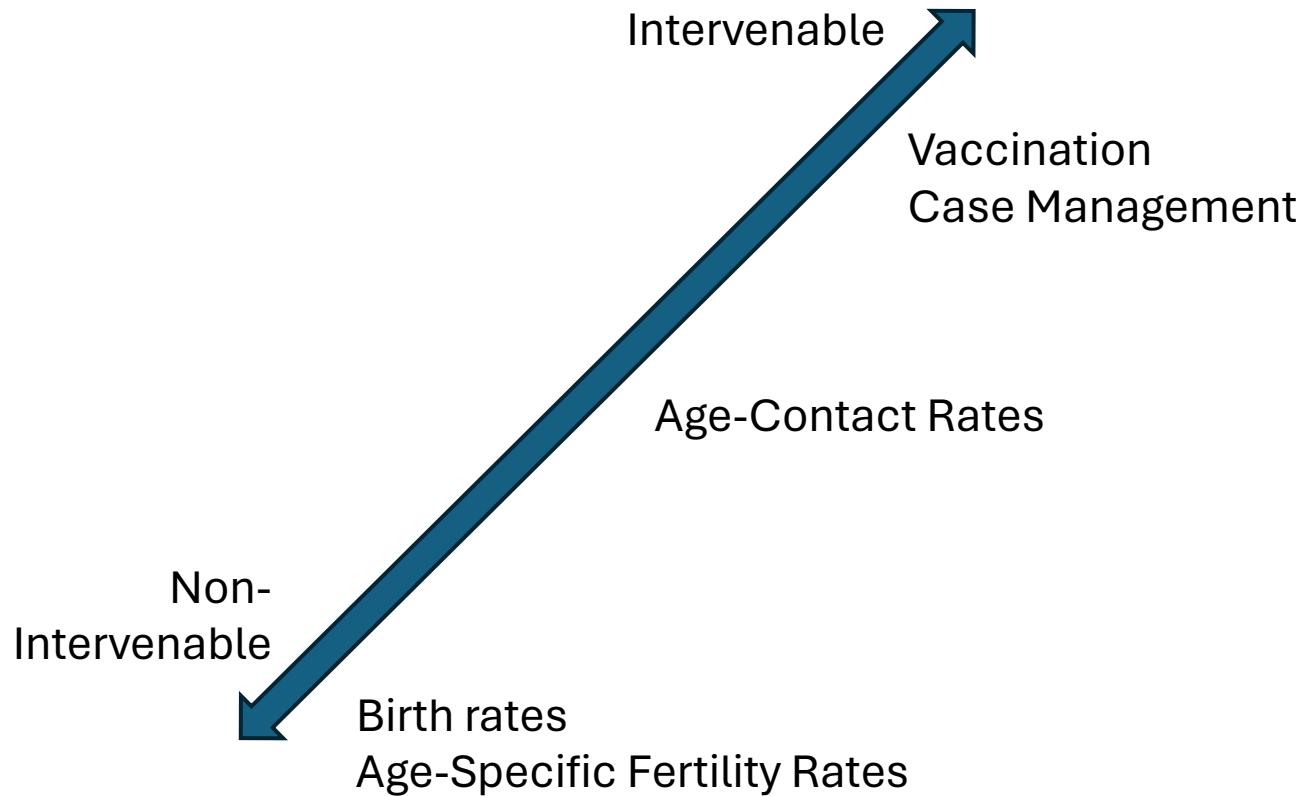
**Fig. 3. Predicted individual effects of vaccination over 30 years**

Proportion of hospitalized cases averted among individual vaccine recipients who are vaccinated: (A) when seronegative and (B) when seropositive. Dashed contour indicates the youngest age group that may be targeted to avoid negative effects at the individual level. (C) Minimum proportion of the age group (1-year age band) targeted for routine vaccination that should be seropositive before introduction of vaccination to avert negative impacts (over a 30-year time frame) at the population (red) and individual (blue) level.

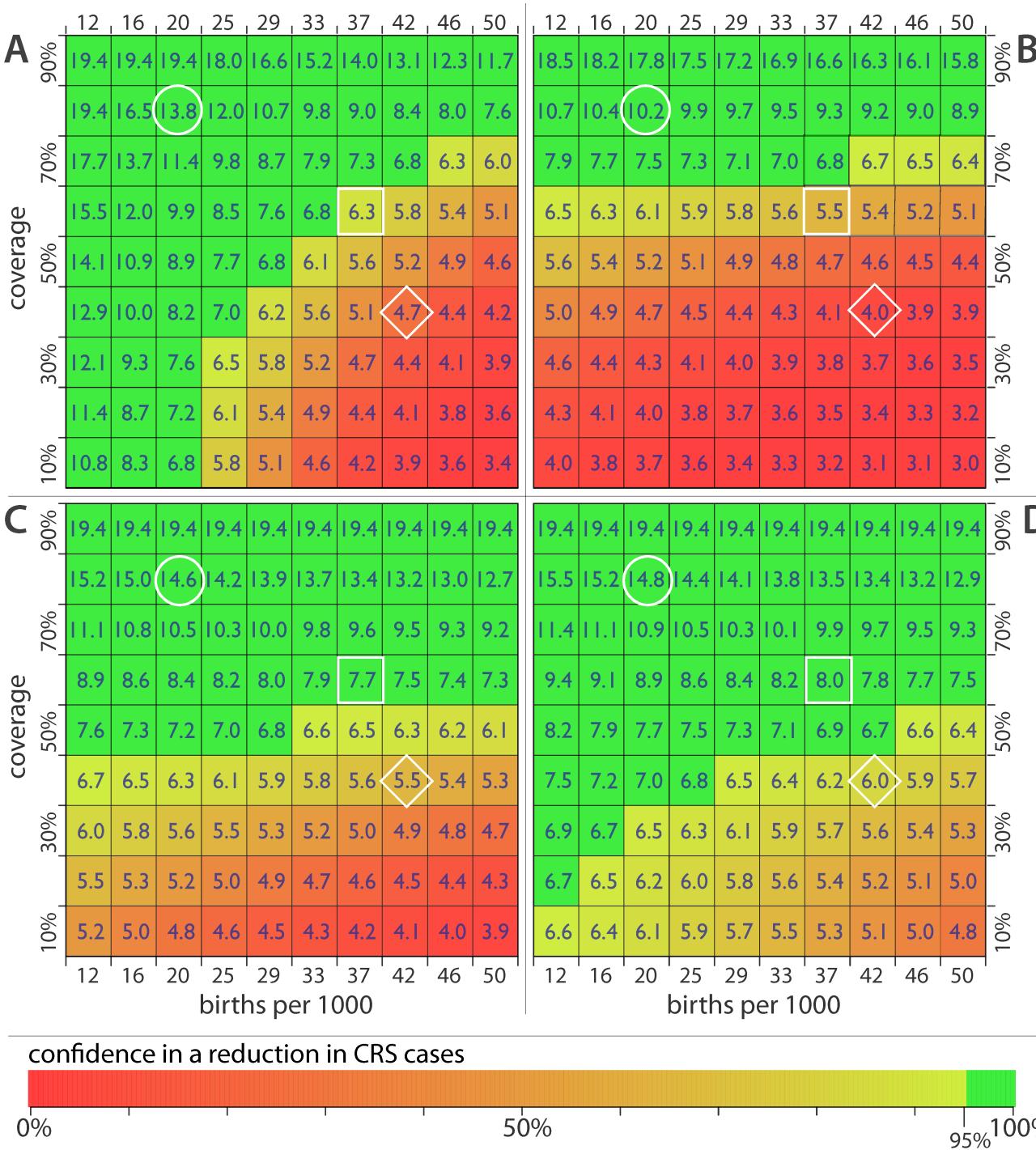
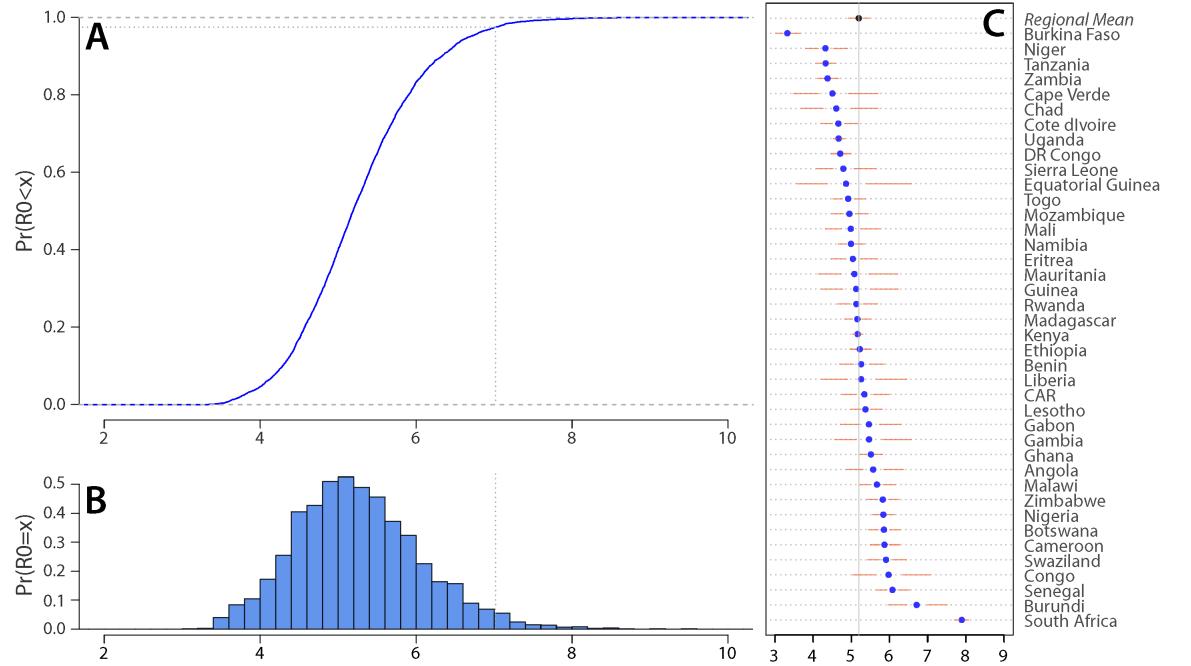
# Interventions = Control Strategies



# Intervenable?



# Rubella CBR and Vaccination Example



# The Comparator

# How do we create the intervention scenario(s) to compare?

- To estimate the impact of an intervention using strategic modelling we need to compare outcomes from different intervention scenarios
- Each strategic modelling exercise needs at least one comparator
- The comparator intervention does not have to be realistic, it is all about pulling out the impact of interest
  - For decision-making (don't use unrealistic) or other uses

# Rubella Vaccine Intro?

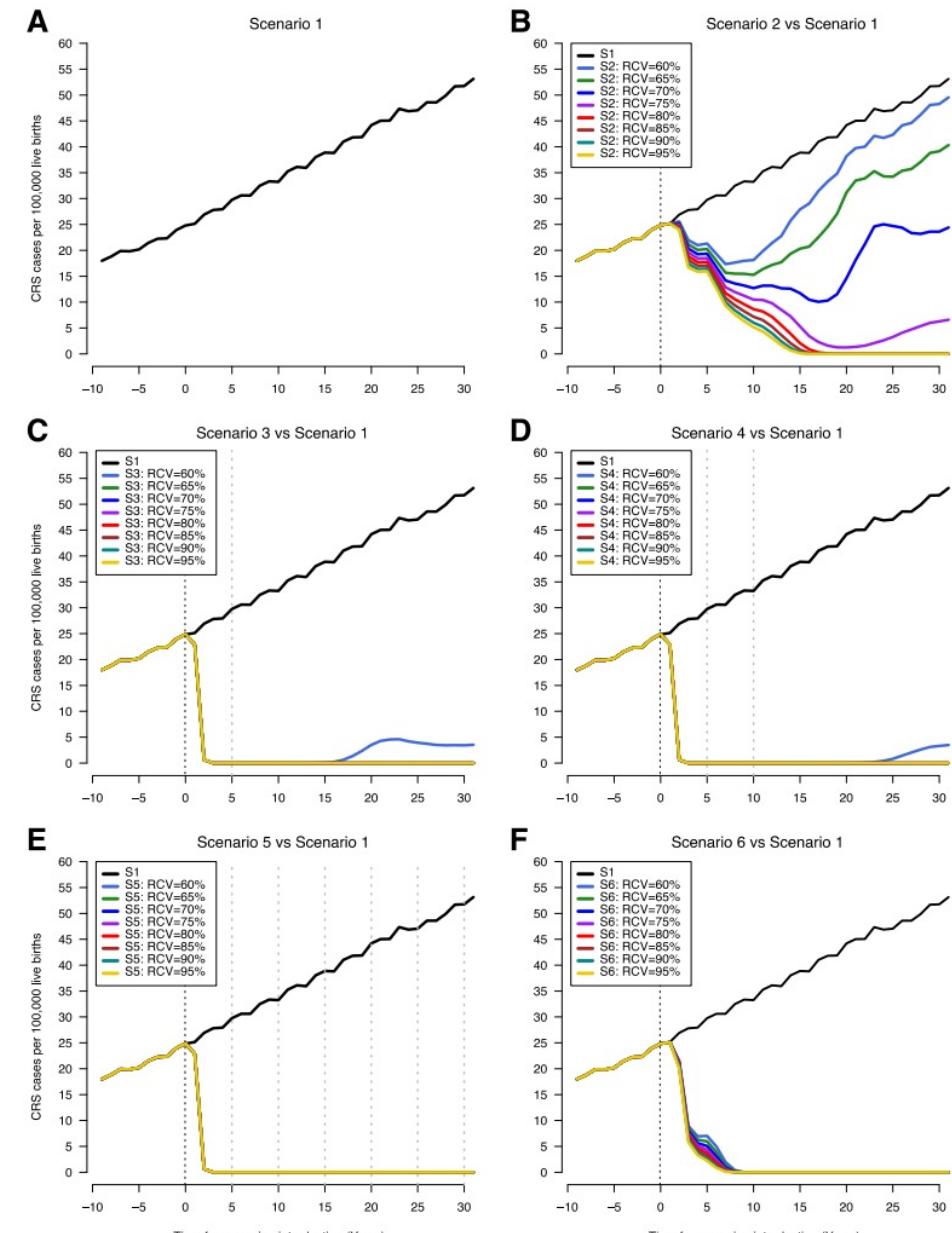


Article

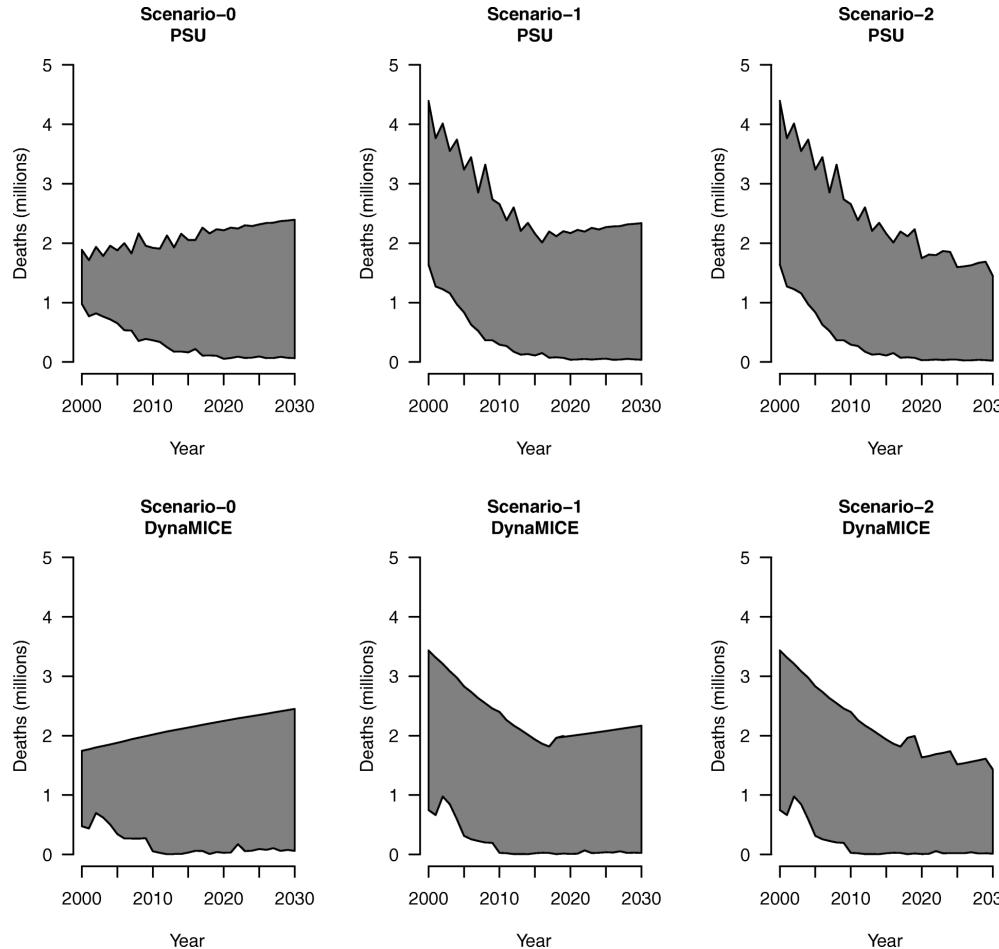
## Rubella Vaccine Introduction in the South African Public Vaccination Schedule: Mathematical Modelling for Decision Making

Nkengafac Villyen Motaze <sup>1,2,\*</sup>, Ijeoma Edoka <sup>3</sup>, Charles S. Wiysonge <sup>2,4,5</sup>**Table 1.** Possible scenarios for rubella-containing vaccine (RCV) introduction in South Africa.

Scenario	Routine Vaccination in Expanded Program on Immunization (EPI)	Target Age Group for Routine Vaccination	Target Age Group for Initial Mass Campaign	Follow-Up Mass Campaigns	
				Target Age Group	Timing
1			No RCV in EPI		
2	RCV introduction	1 year	No initial campaign	No follow-up campaign	N/A
3	RCV introduction	1 year	1 to 14 years	No follow-up campaign	N/A
4	RCV introduction	1 year	1 to 14 years	1 to 4 years	One follow-up campaign 5 years after initial campaign
5	RCV introduction	1 year	1 to 14 years	1 to 4 years	Six follow-up campaigns every 5 years after initial campaign for 30 years
6	RCV introduction	1 year and 9 years	No initial campaign	No follow-up campaign	N/A

**Figure 2.** Time series of congenital rubella syndrome (CRS) incidence (CRS cases per 100,000 live births) showing scenario 1 (A) and comparing scenario 1 with scenarios 2–6 (B–F). The vertical black dotted

# Estimating the Impact of Measles Vaccination

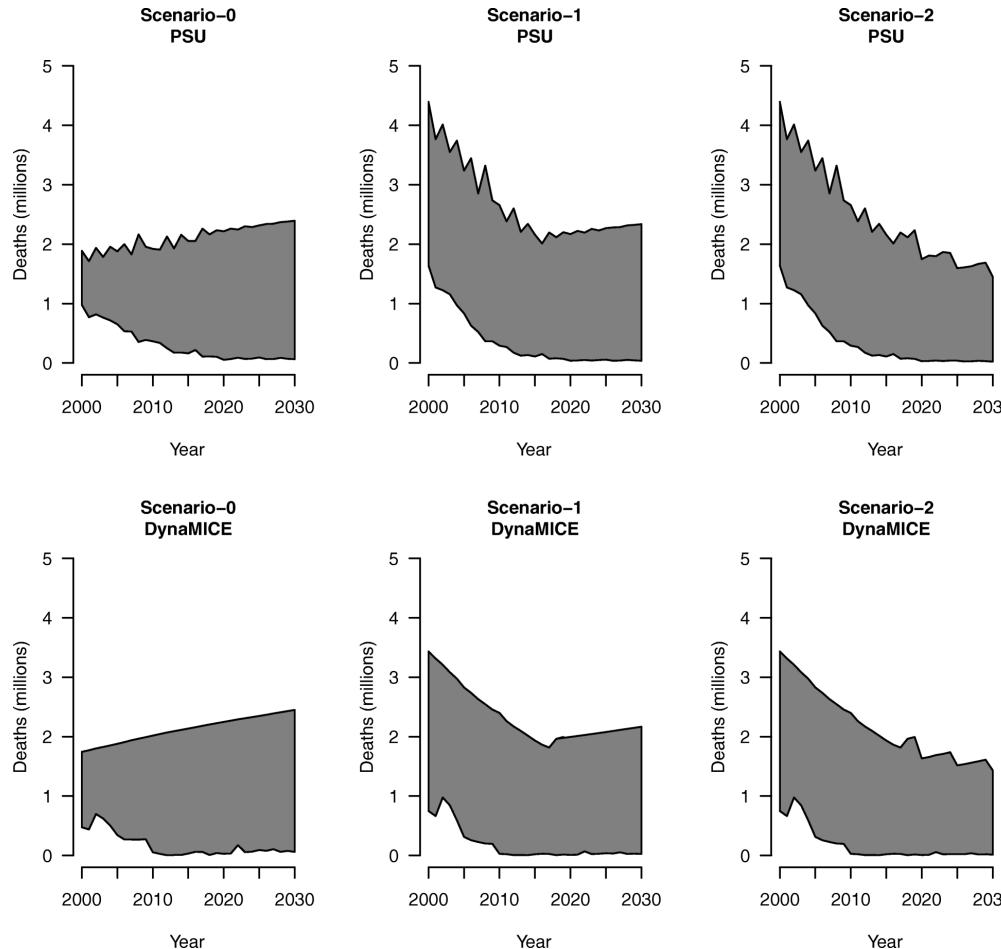


In collaboration with Mark, we did an evaluation of the impact of Gavi supported vaccination on mortality due to measles – in the past AND into the future.

We fitted models to the impact of vaccination (bottom of grey area) AND to a counterfactual scenario as though there was no measles vaccination (top of grey area)

BUT, it is unclear how we should treat the mortality attributable to measles ...

# Estimating the Impact of Measles Vaccination



Estimates of case-fatality ratios of measles in low-income and middle-income countries: a systematic review and modelling analysis

Allison Portnoy, Mark Jit, Matthew Ferrari, Matthew Hanson, Logan Brenzel, Stéphane Verguet

Portnoy et al. BMC Medicine (2022) 20:113  
https://doi.org/10.1186/s12916-022-02242-2

BMC Medicine

RESEARCH ARTICLE

Open Access



Differential health impact of intervention programs for time-varying disease risk: a measles vaccination modeling study

Allison Portnoy<sup>1\*</sup>, Yuli Lily Hsieh<sup>2</sup>, Kaja Abbas<sup>3</sup>, Petra Klepac<sup>3</sup>, Heather Santos<sup>4</sup>, Logan Brenzel<sup>5</sup>, Mark Jit<sup>3†</sup> and Matthew Ferrari<sup>4†</sup>

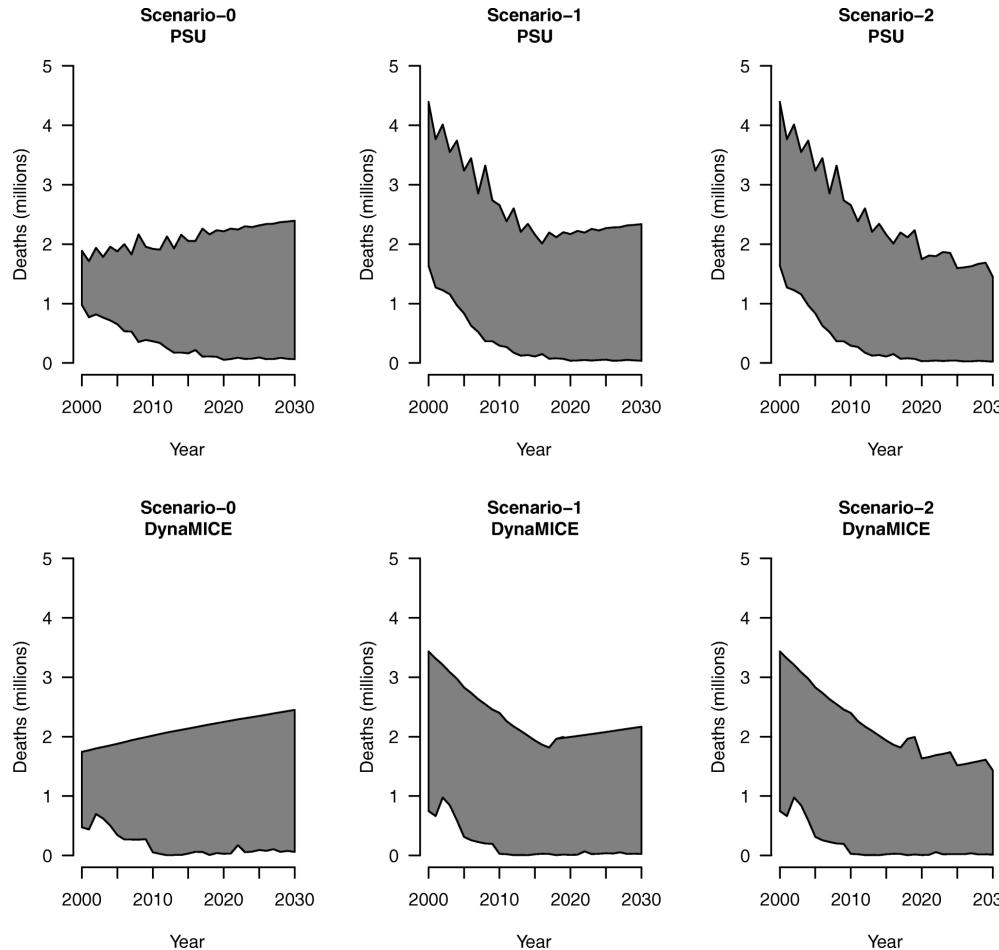
Portnoy et al 2019 showed that the CFR of measles depends on many things:

- wealth
- maternal education
- incidence of measles (more cases -> higher CFR)
- time

“time” may reflect overall increases in primary health care



# Estimating the Impact of Measles Vaccination



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Each column at left presents a different assumption about the CFR in the counterfactual

1. CFR stays the same over all time in the no vaccination setting
2. CFR decreases per the Portnoy model until present, and stays the same thereafter
3. CFR decreases per the Portnoy model and projects additional reductions into the future



# Outcome / Impact Metric

# How to evaluate the **impact** of intervention scenarios?

- We need to determine
  1. Difference metric
  2. Burden metric
- This will depend on the strategic modelling question at hand
- The relative and burden metric will also determine features of the model
  - For example, CRS means must incorporate age structure

# Difference (or comparison) metrics

- Rank order
  - scenario C burden < scenario B burden < scenario A burden
- Relative difference
  - Ratios, Percent Relative Difference
- Absolute difference

# Measles and Rubella Burden Metrics

Measles & Rubella	Rubella Specific
Infections	Congenital rubella syndrome cases
Cases	Congenital rubella syndrome deaths
Deaths	Congenital rubella infection deaths
DALYs	
QALYs	
Cost effectiveness measures	
<ul style="list-style-type: none"><li>• Cost to vaccinate one child</li><li>• Cost to prevent one death</li><li>• Cost to vaccinate one unvaccinated child</li></ul>	

# Estimating Congenital Rubella Syndrome

## Age-Specific CRS Rate

$$CRS(a) = (1 - \pi(a)) \times (1 - e^{-\lambda(a)\frac{16}{52}}) \times 0.65 \times 100,000$$

↑  
age  $a$   
15-44 years old

↑  
Proportion  
seropositive  
at age  $a$

↑  
Force of  
infection  
at age  $a$

↑  
Probability child born  
with CRS given CRI in  
the 16 weeks pregnancy

Piecewise constant  
Generalized additive models  
Penalized regression splines

# Model Uncertainty

# Uncertainty can arise from

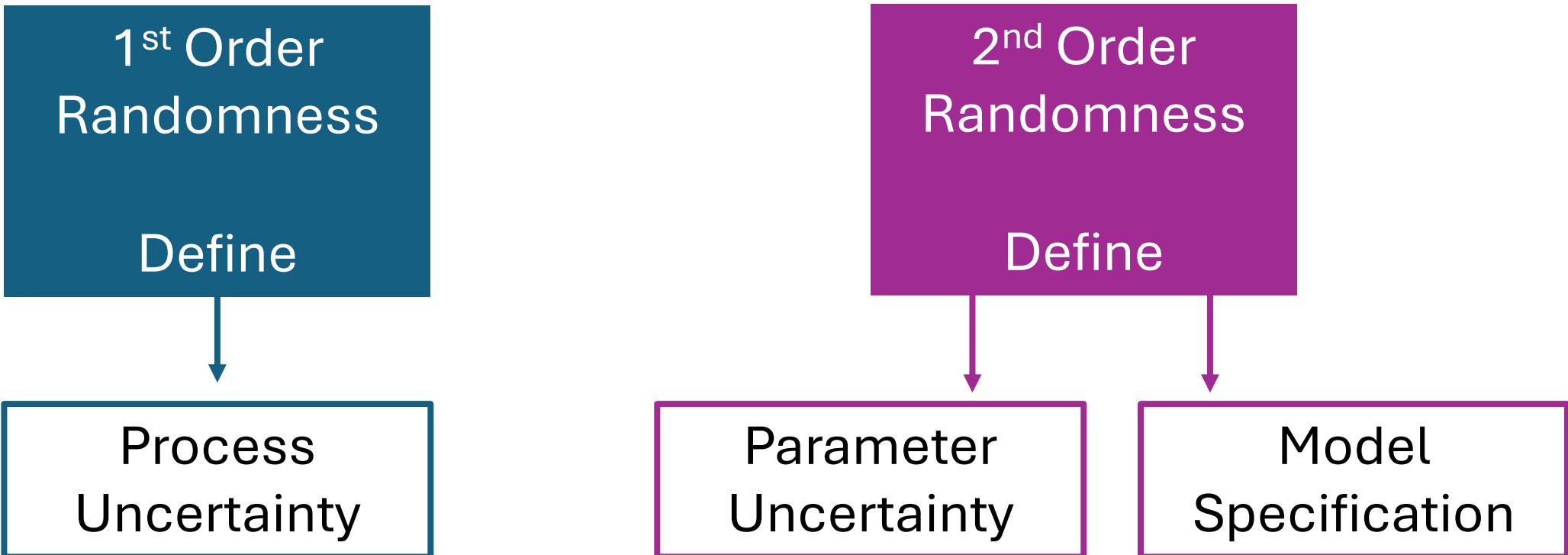
1<sup>st</sup> Order  
Randomness

Define

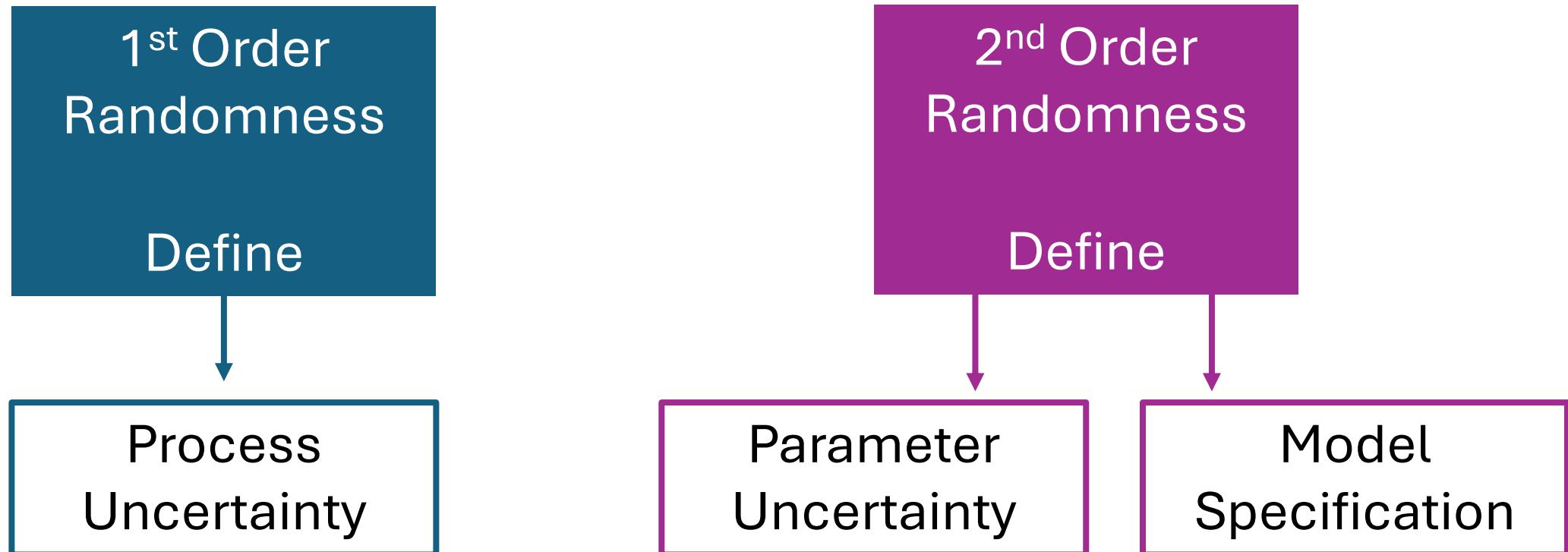
2<sup>nd</sup> Order  
Randomness

Define

This uncertainty is incorporated into the model as...



# In practice, this looks like...

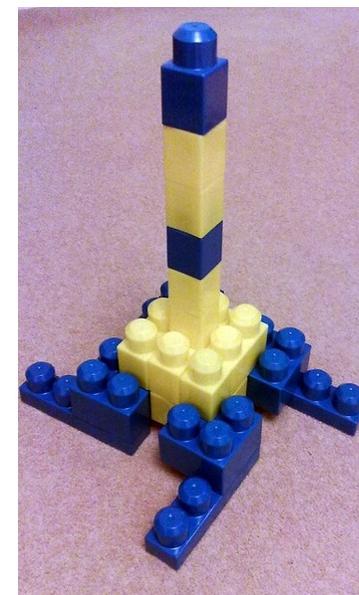


- *Random draw from distributions conditional on known parameter*

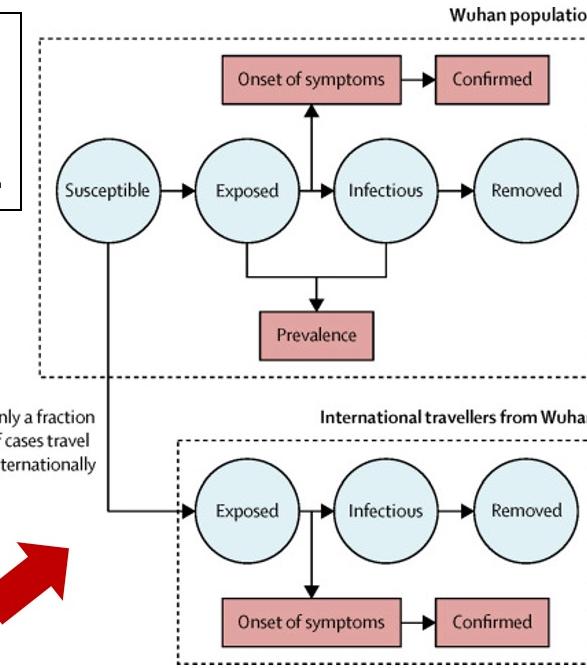
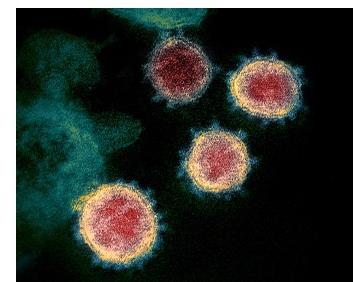
- *Random draw from a distribution of parameters*
- *Sensitivity Analysis*

- *Model structure*
- *Model assumptions*

# Reminder: Why do we incorporate uncertainty?



A model is a simplified representation  
of a more complex object/process,  
*designed to address specific questions.*



# Interactive Session II

# Model uncertainty → Outcome uncertainty

How do we get impact assessment given outcome uncertainty?

- Difference in means
- Difference in upper uncertainty bound and lower uncertainty bounds
- Bootstrapping approach of random simulation from each for distribution of differences (issue negative impact which is more an artifact of the approach)

# Model Comparison

Taking into account uncertainty via model specification

# Vaccine Impact Modelling Consortium (VIMC)

## Who, What, When, Where, Why

- VIMC is an **international community of modellers** providing high-quality estimates of the public health impact of vaccination, to inform and improve decision making.
- The Consortium was established at the end of 2016 for a period of five years, and **is coordinated by secretariat based at Imperial College London**.
- As its core objective, the Consortium aims to **deliver more sustainable, efficient, and transparent approach to generating disease burden and vaccine impact estimates** of twelve vaccine-preventable diseases.
- **Funded by Gavi, the Vaccine Alliance and the Bill & Melinda Gates Foundation**, to support the evaluation of the two organisations' existing vaccination programmes, and inform potential future investments and vaccine scale-up opportunities.



# VIMC

## Measles and Rubella Modelling Teams

- We conduct **strategic modelling** based on defined vaccination scenarios for >100 countries
- We compare direct model outputs (i.e., infections) as well as its sequel (i.e., deaths, congenital rubella syndrome cases, DALYs) across vaccination scenarios in order to answer questions for Gavi such as:
  - What is the impact of a vaccination strategy X compared to vaccination strategy Y on the number of infections and number of death?