Block 1.2: SIR Dynamics

NDMC Measles and Rubella Transmission Modelling Workshop

5-8 February 2024

Recap slides

- Different types of mathematical models (deterministic, compartmental, stochastic, etc)
- The structure of a model describing the transmission dynamics typically depends on the natural history of the infection
- R_0 determines the speed at which the number of infectious people increases and the epidemic size
- New susceptibles introduced by births, gives rise to cycles that decrease in magnitude over time. The cycle period depends on R_0 and birth rate

Does the SIR model feel realistic to you?

What is missing from these models??

In this session:

- We will review patterns that arise from SIR-type dynamics (mean age, cycles) that can be used to evaluate model performance
- Discuss sources of seasonality and simulate interaction with birth rate
- Review what vaccines do and how we represent vaccination in models
- Discuss herd immunity
- Simulate the impact of vaccination

R0 and Age

- Remember relationship between rate of recovery and duration of infection (or time to recovery)
  - Average time to an event is the inverse of its rate
- Relation between mean age of infection and R_0
  - R_0 reflects the rate of infection, mean age is the average time from birth to infection
  - Basic calculation requires strong assumption that age-specific force of infection is constant
- What does this mean for control?

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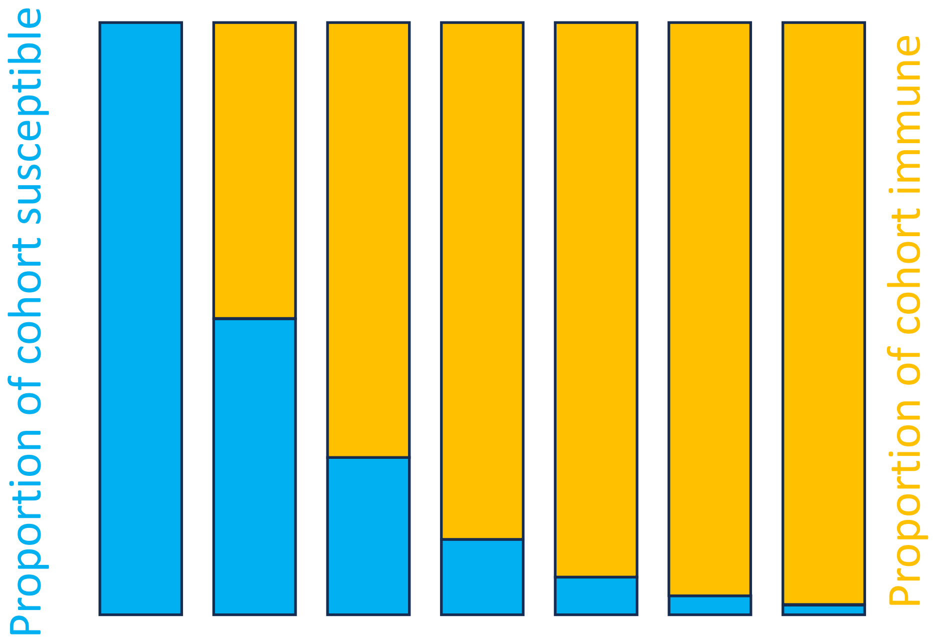
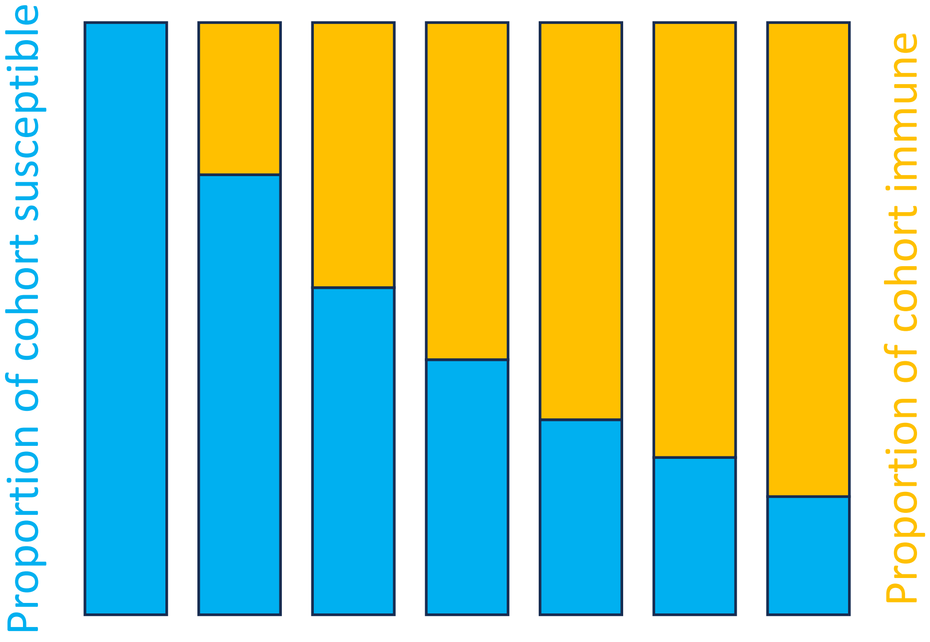
When Transmission is High



When Transmission is Low



From Pattern to Estimate

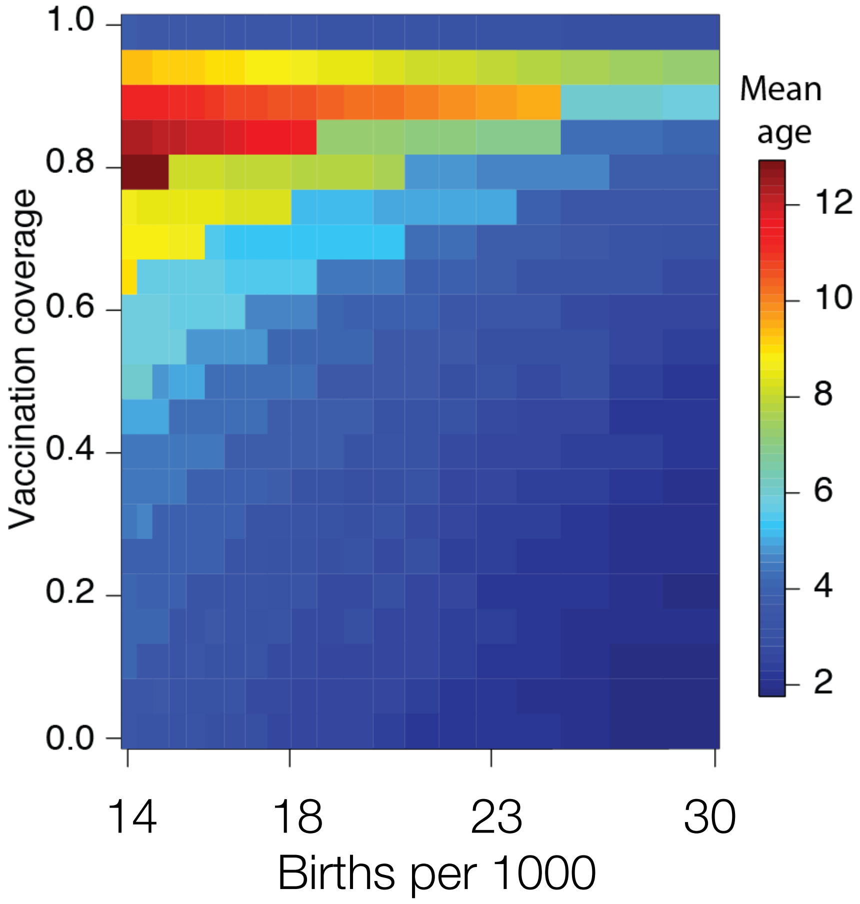
$$A = \frac{L}{R_0}$$

$$R_0 = \frac{L}{A}$$

- A is the mean age of infection
- L is the life expectancy at birth

Not a big difference, but a bias that is generated by choosing the wrong model

Intuition About Mean Age of Infection



- Reduced prevalence of infection results in lower force of infection on each susceptible individual

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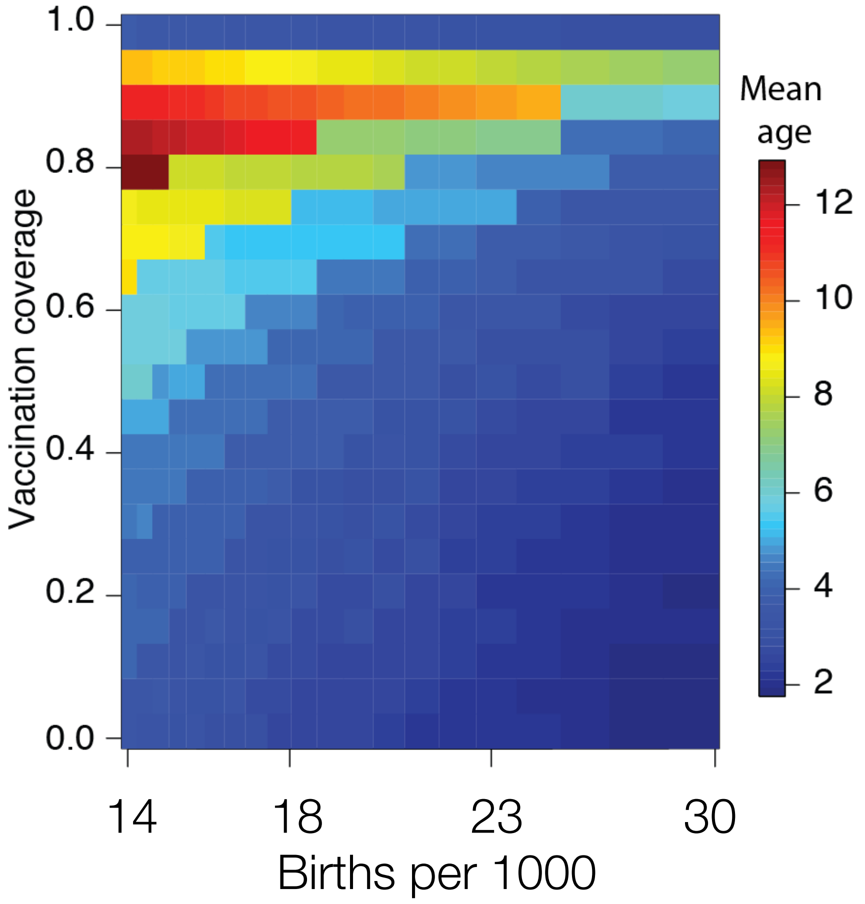

- Reduced prevalence of infection results in lower force of infection on each susceptible individual
- Longer wait until contact between susceptible and infectious individuals

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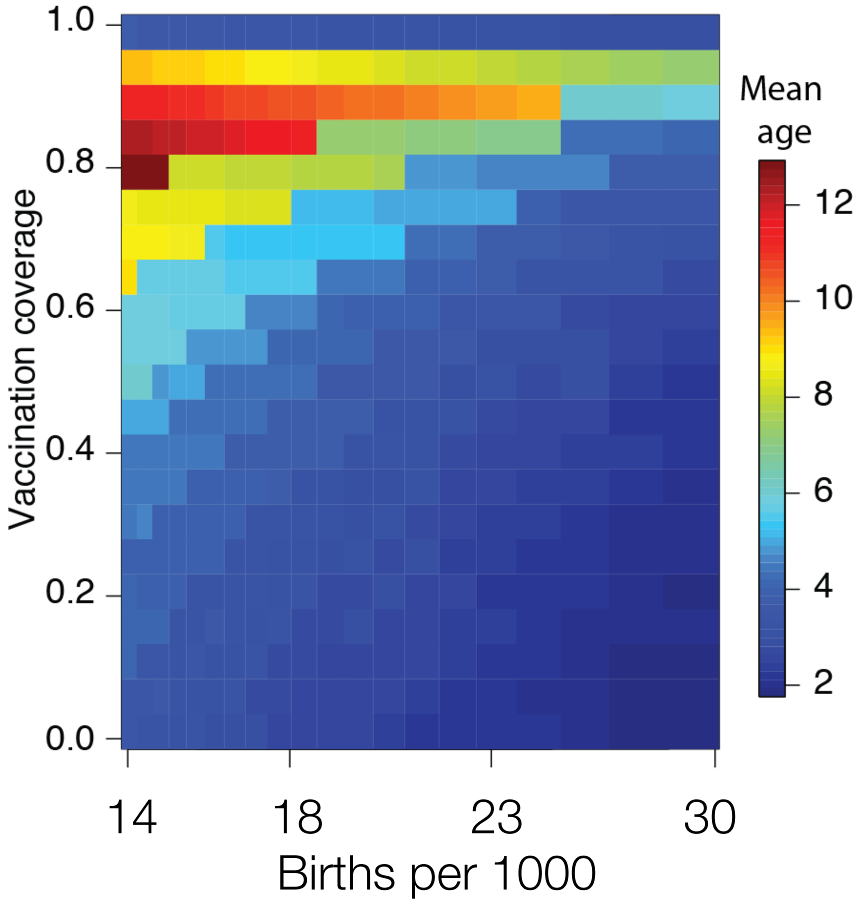

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- Longer wait until contact between susceptible and infectious individuals
- Lower force of infection implies higher mean age at infection

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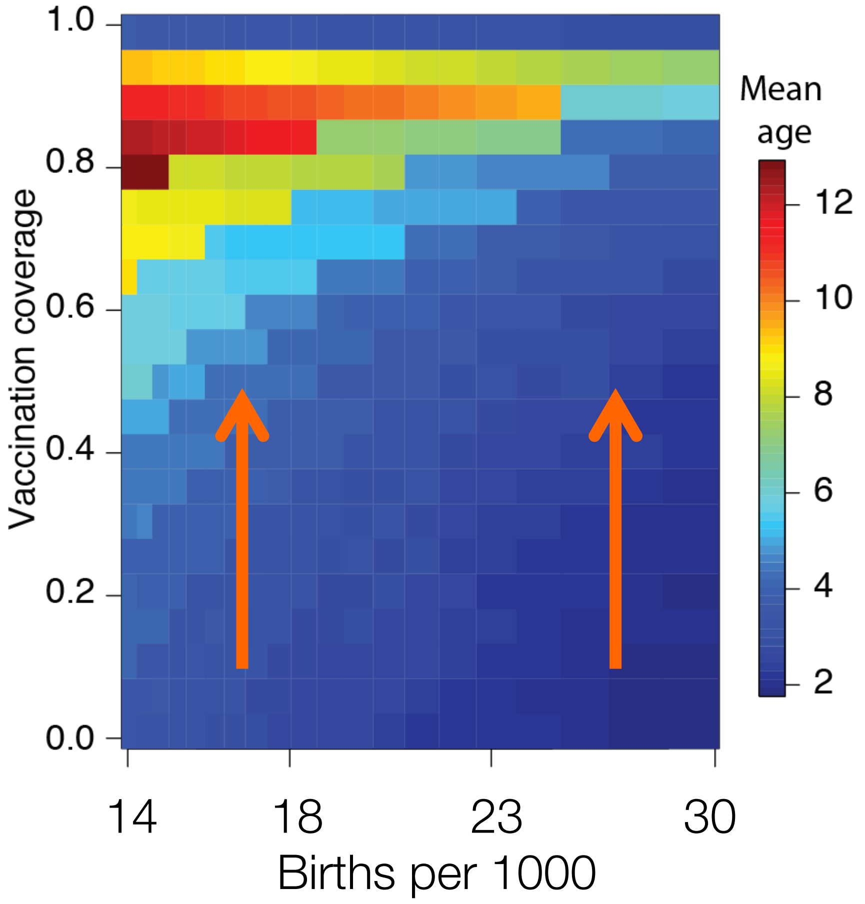

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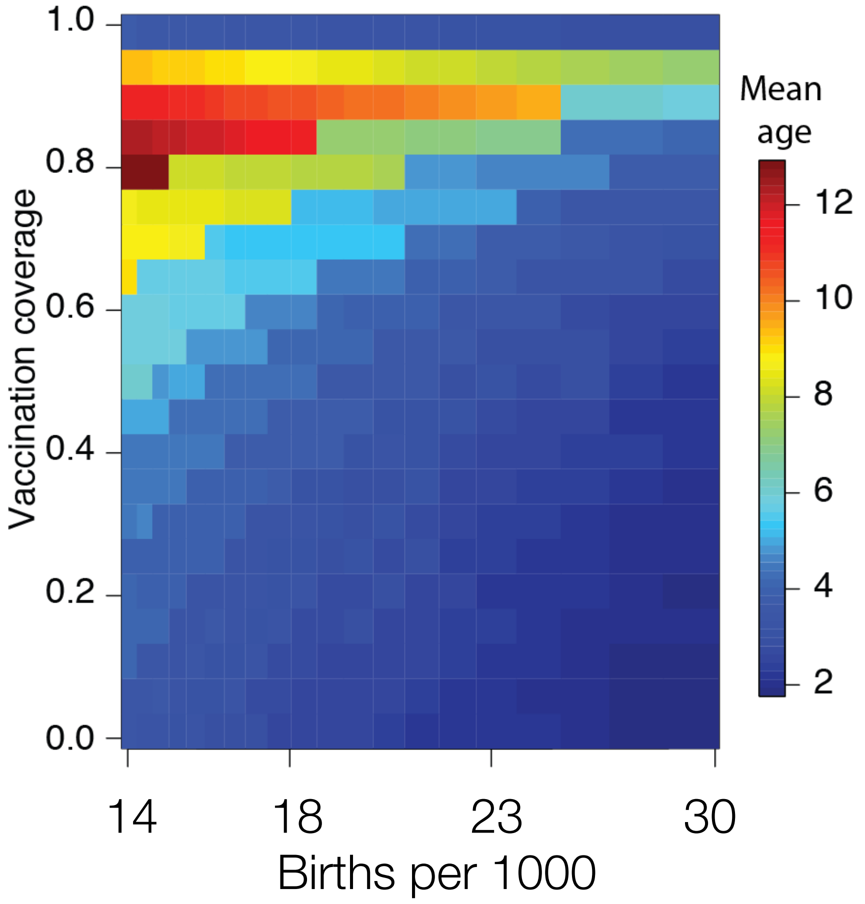
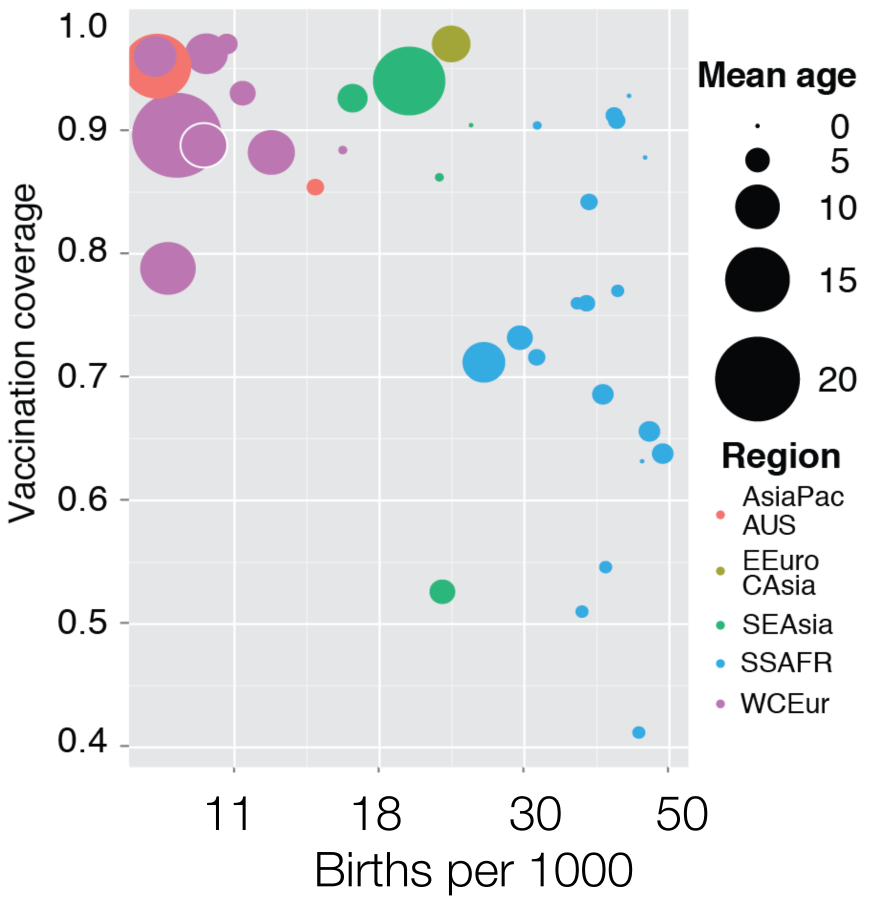
Observation About Mean Age of Infection



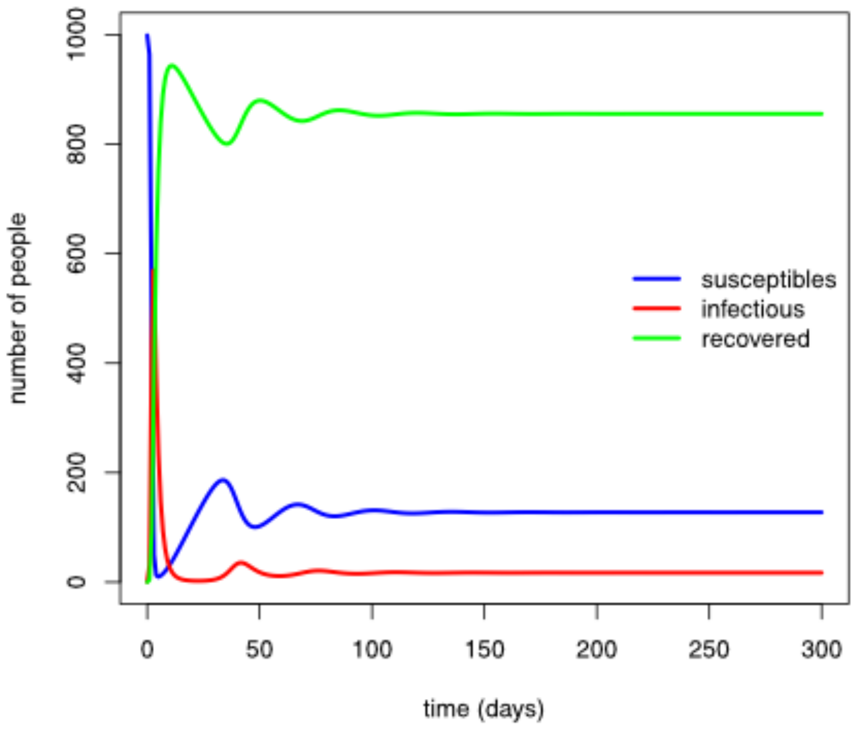
50 Countries reporting > 100 cases

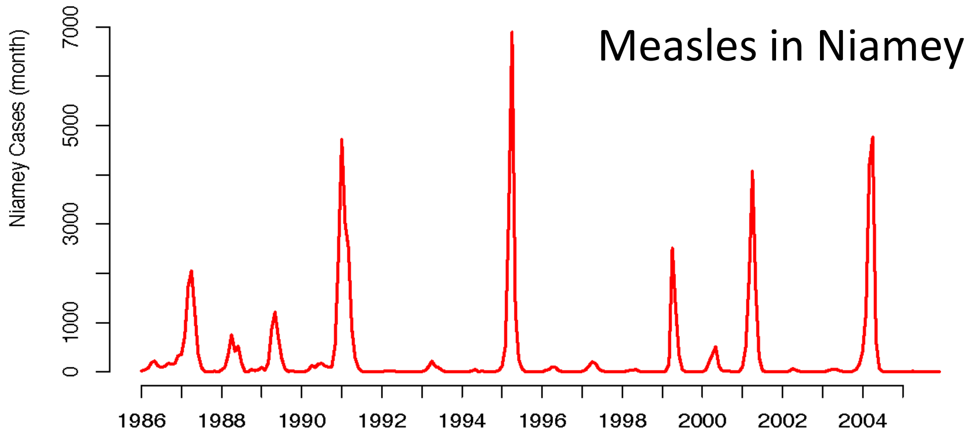


Ferrari et al 2013

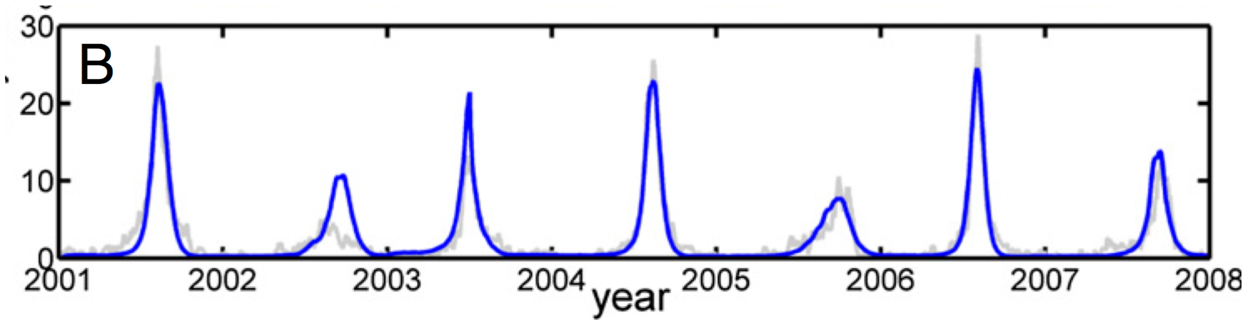
Seasonality and Cycles

Seasonality and Cycles





Measles in Niamey



Influenza in Jerusalem

Seasonality and Cycles

- Long term dynamics often exhibit regular fluctuations around the equilibrium levels because of seasonal changes in
  - Environmental conditions
  - Behavior
  - Population movement/aggregation
  - Vector seasonality

Examples
Influenza
Lassa fever
Legionellosis
Leptospirosis
Meningococcal meningitis
Polio
Typhoid

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Examples
Chickenpox
Measles
Pertussis
Rubella

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Modeled as a temporal change in β

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Meningococcal meningitis

Modeled as a temporal change in β ***or*** S

Seasonality and Cycles

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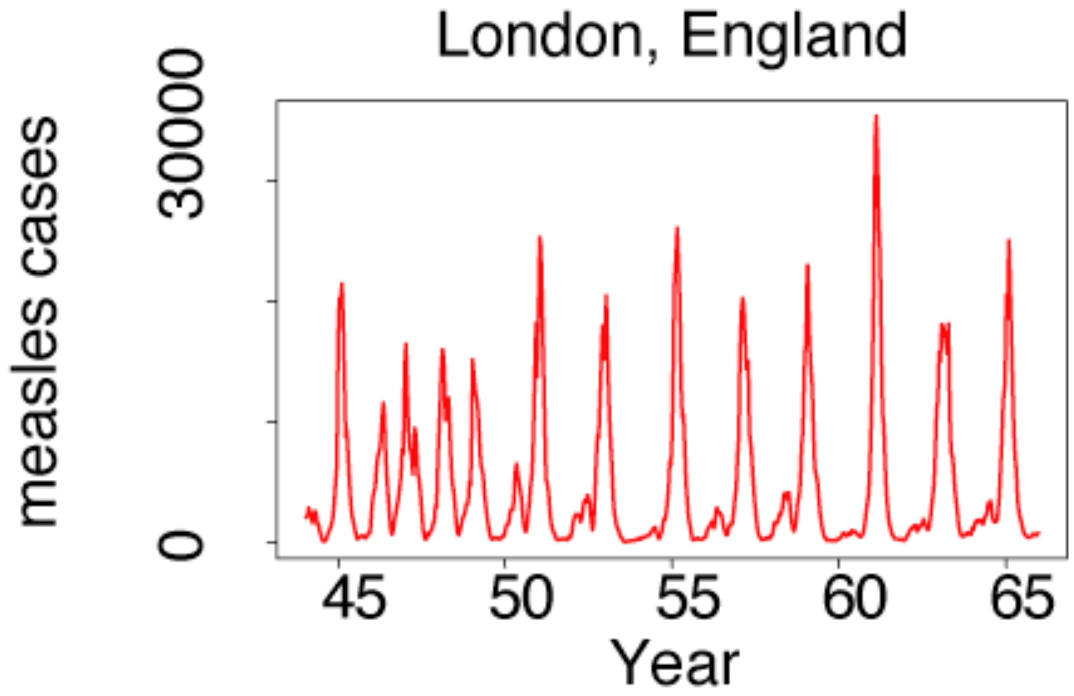
  - Behavior
  - Population movement/aggregation
  - Vector seasonality

Examples
Chikungunya
Dengue
Malaria
Trypanosomiasis
West Nile Virus
Yellow Fever

Requires a new compartment for the vector populations

Measles and Seasonality



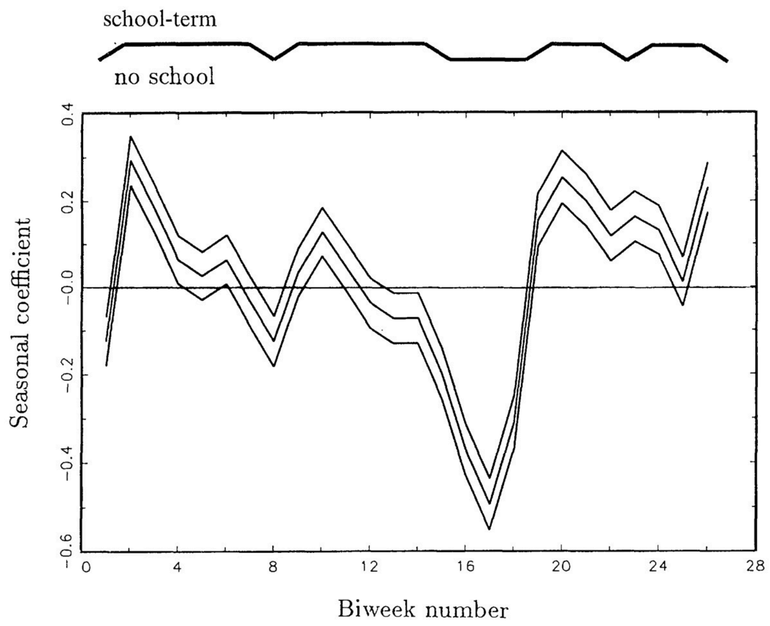
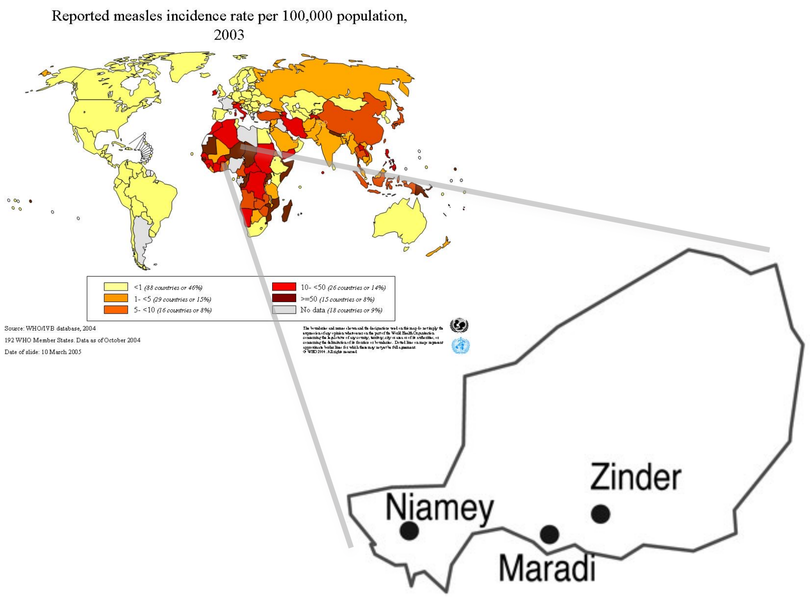
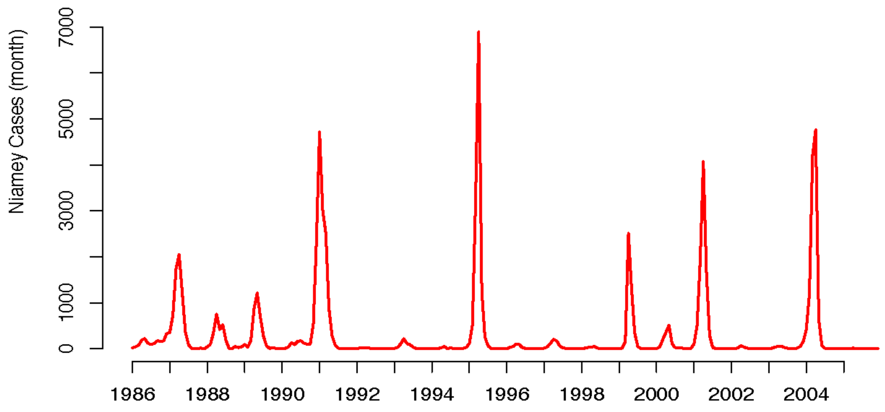


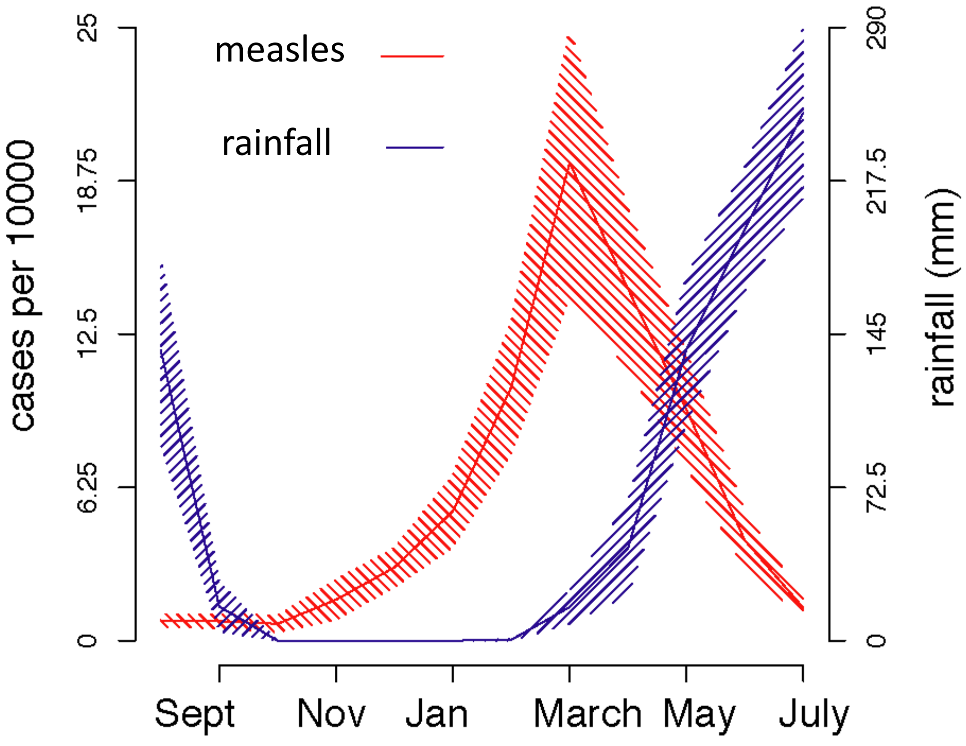
Fig. 7. Estimates of seasonal coefficients (mean centred) of measles in England and Wales within a confidence band of width two standard deviations: the uppermost graph shows the school-term indicator function (high level, school-term; low level, no school) for England and Wales

Finkenstadt and Grenfell 2000

Measles Dynamics in Niger



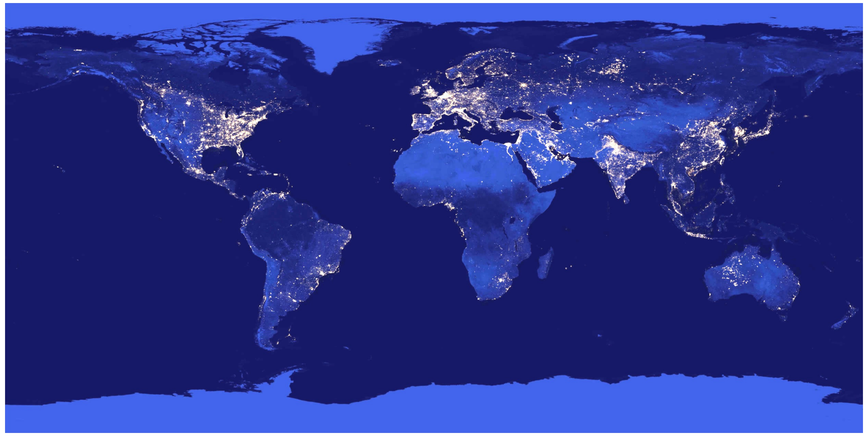


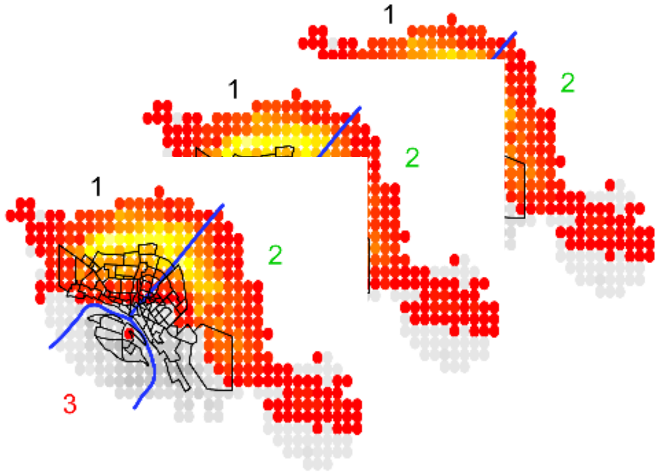


Seasonality of measles is very regular, yet the dynamics in any individual district are very episodic, with long periods of measles absence

Ferrari et al 2008
Bharti et al 2010

Seasonality in Niger

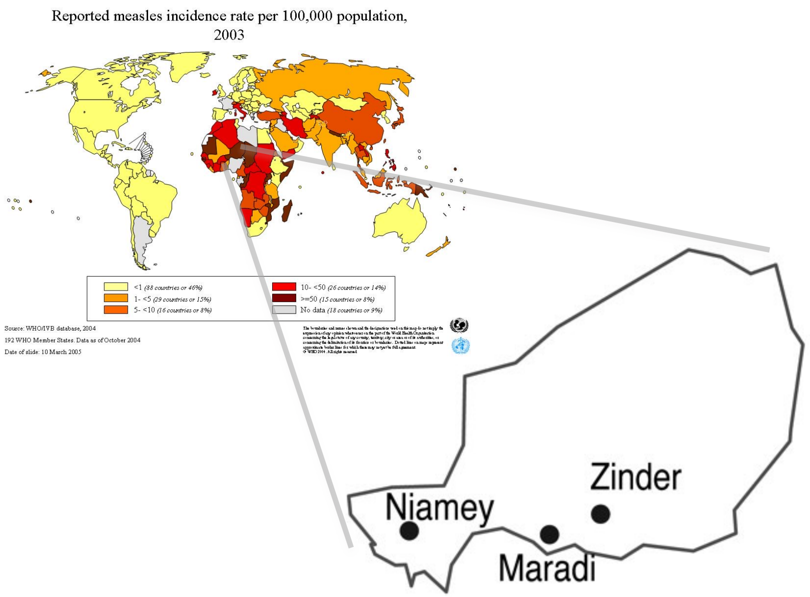


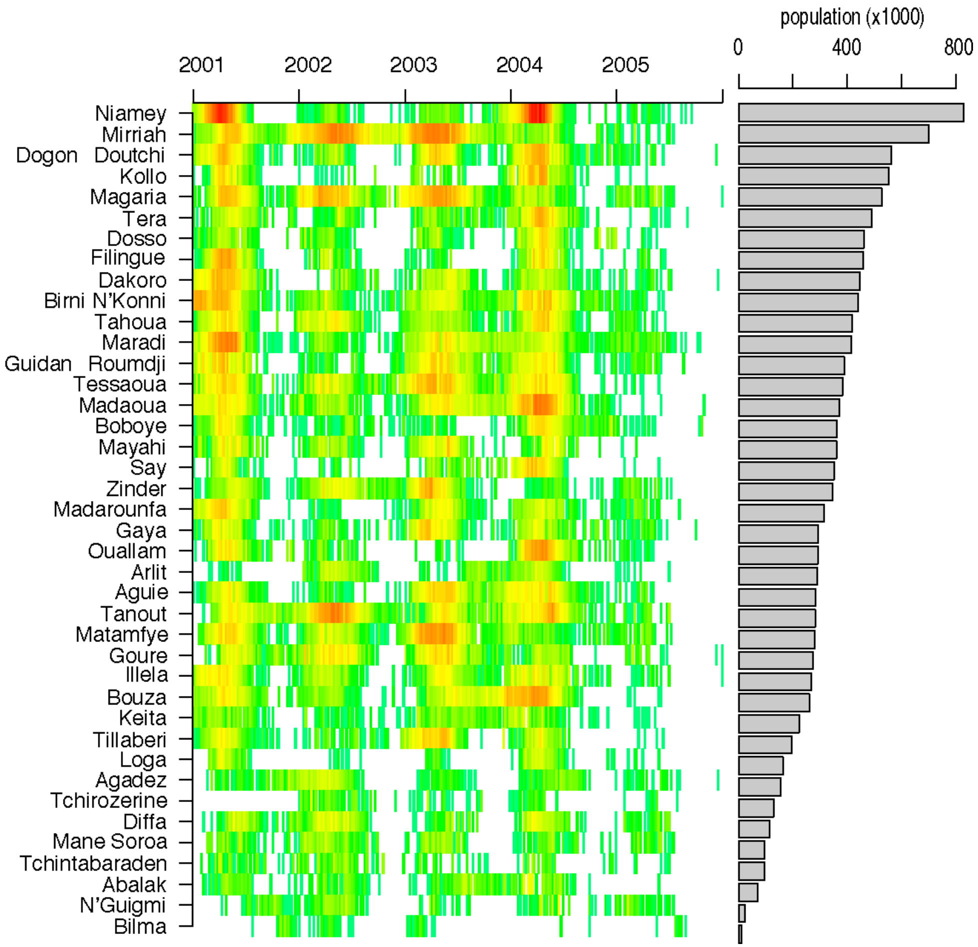


- Rural to urban migration in Niger drives increased population density in cities during the dry season
- Serial images of night time brightness indicate seasonal seasonal change in human distribution

Bharti et al, 2011

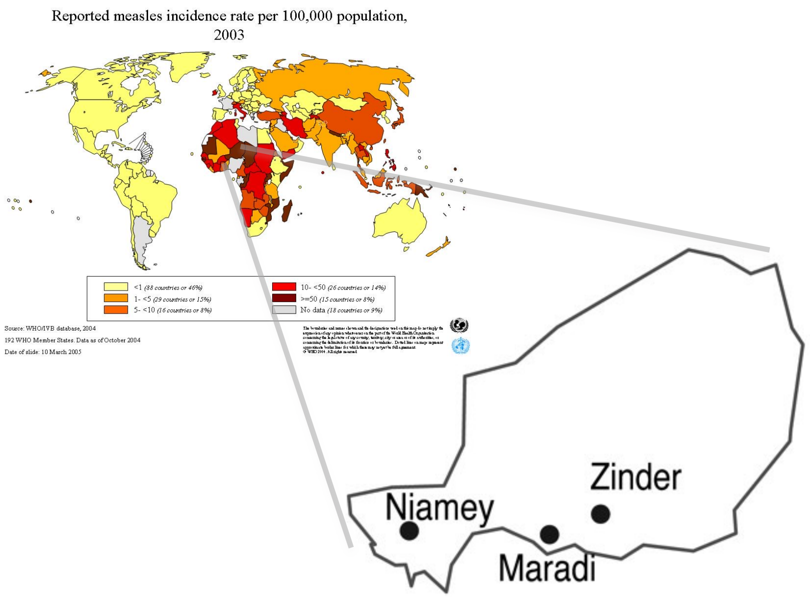
Measles Dynamics in Niger





- Measles persistence scales with population size
- Nowhere is measles endemic

Measles Dynamics in Niger



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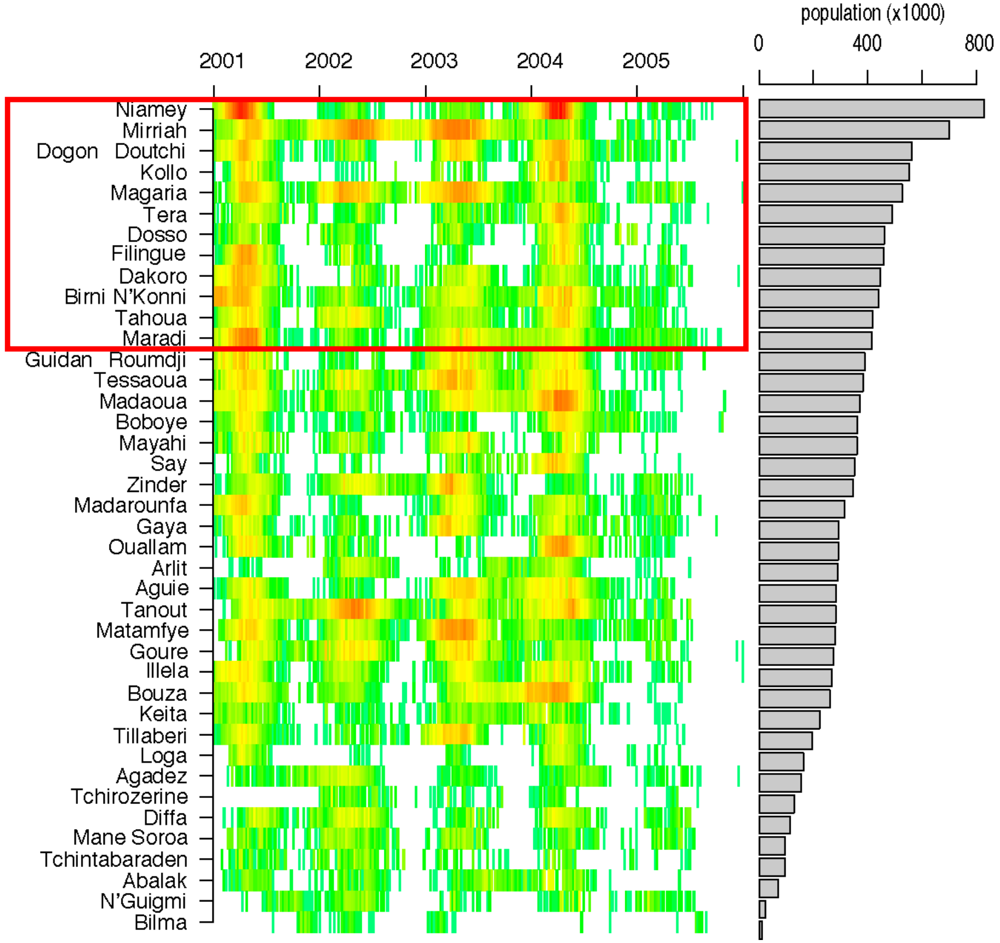

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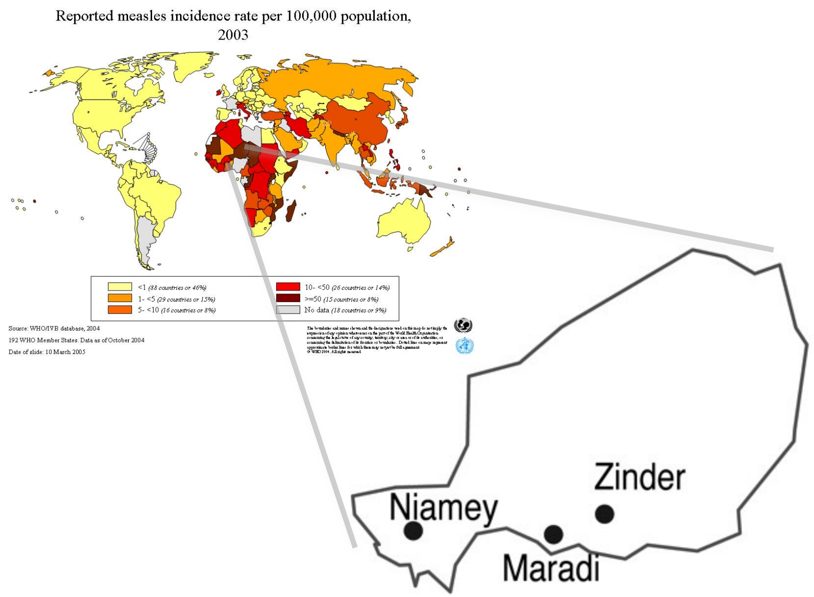

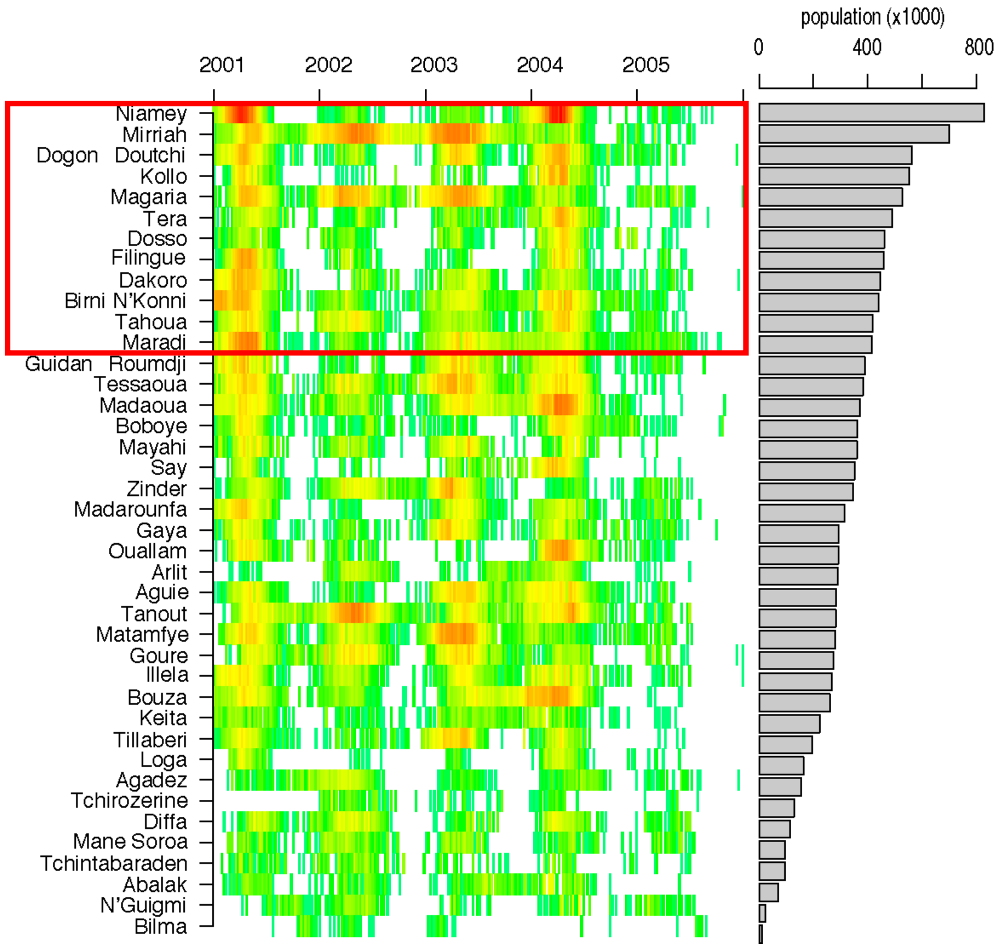

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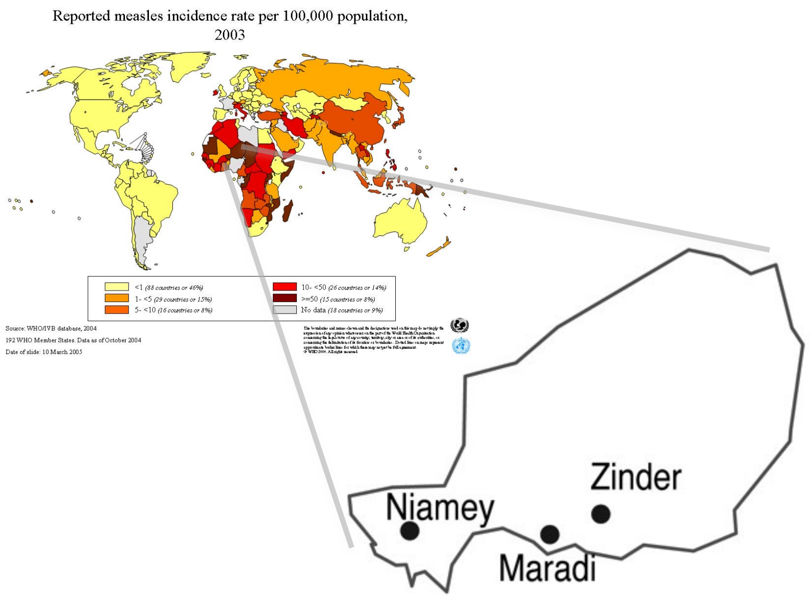
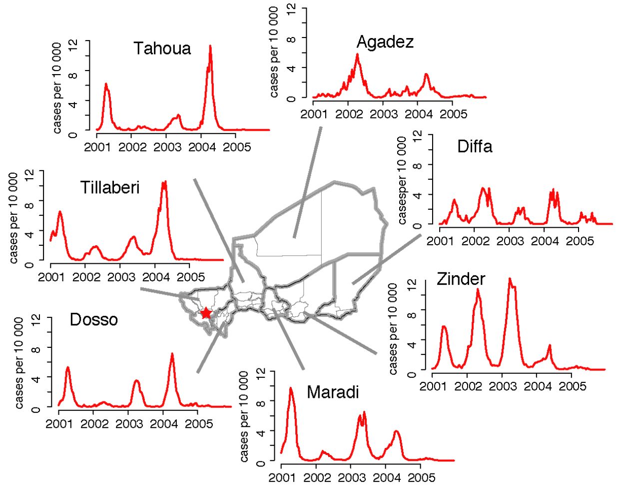
- Even for large populations
- Impacts the choice of models

Measles Dynamics in Niger





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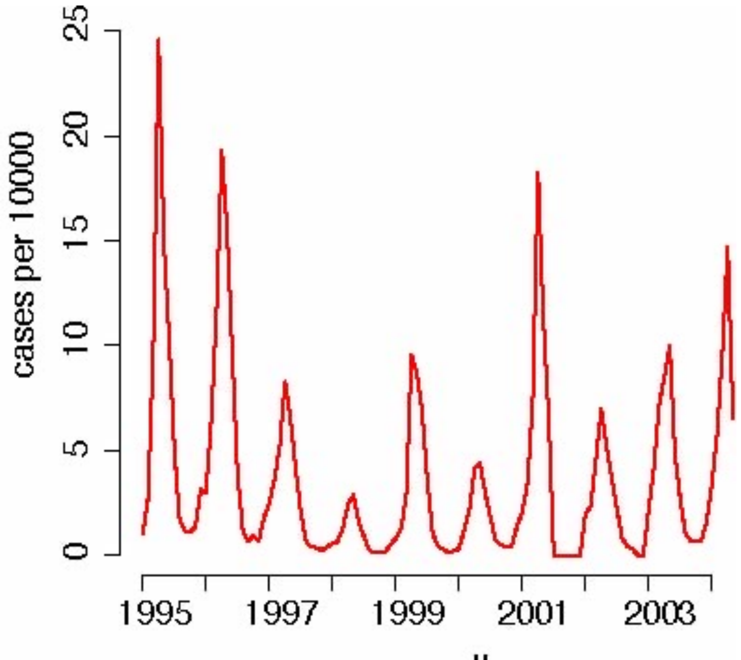

Interactive Session: simulating seasonality

R-file: SIRModel 2birthsdeaths_seasonality.r

Vaccination

What do vaccines do?

- **Vaccine:** A preparation that is used to stimulate the body's immune response against diseases.
- **Efficacy:** measured in a controlled clinical trial and is based on how many people who got vaccinated developed the 'outcome of interest' (usually disease) compared with how many people who got the placebo developed the same outcome.
- **Effectiveness:** a measure of how well vaccination works under real-world conditions to protect people against health outcomes such as infection, symptomatic illness, hospitalization, and death.

What do vaccines do?

- **Prevent infection** – move you from S -> R
  - Measles, Oral polio vaccine
- **Prevent illness** – perhaps still transmission?
  - Inactivated polio vaccine, diptheria
- **Prevent/reduce transmission** –> reduce Beta
  - SARS-CoV-2, RTS,s
- **Accelerate clearance** –> shorten L
  - SARS-CoV-2

How long does immunity last?
For simplicity now, we'll assume that immunity is lifelong

Herd Immunity

- Indirect protection to non-immune individuals due to the presence of immune individuals in the population

Critical Herd Immunity Threshold

- When indirect protection is high enough, the risk to non-immune individuals falls to 0 because the endemic equilibrium is 0

Critical Herd Immunity Threshold

$$R_0 = \frac{\beta S}{\gamma} = \beta S L$$

$$R_0 = \beta S L$$

$$1 = \frac{\beta S L}{R_0}$$

$$1 = \frac{1}{R_0} S \beta L$$

What fraction of Susceptibles need to be immune in order for

$$\frac{1}{R_0} S$$

to remain?

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What fraction of Susceptibles need to be immune in order for

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to remain?

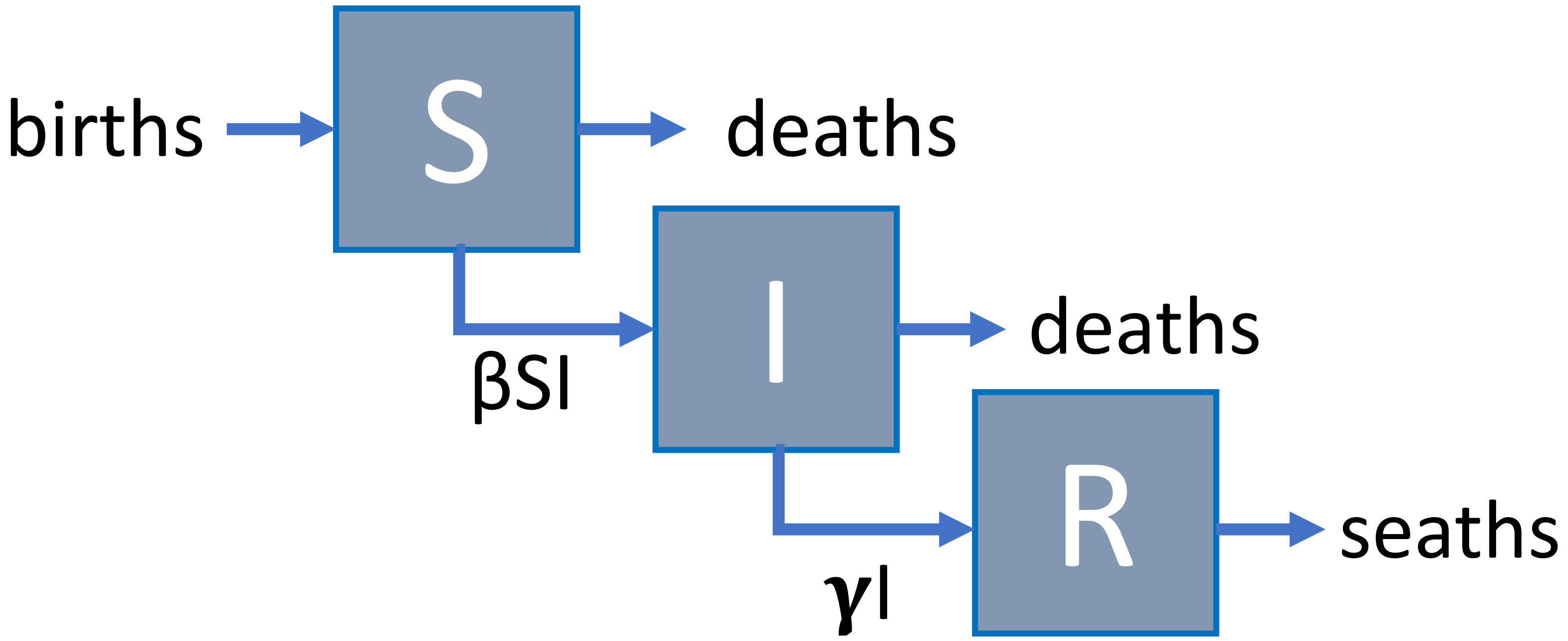
$$T_c = 1 - \frac{1}{R_0}$$

How is vaccination delivered?

- Routine
  - 1st dose
  - 2nd dose … second opportunity
- Supplemental immunization activities
- Outbreak response immunization

Vaccination with a single dose

How do we represent vaccination in models?



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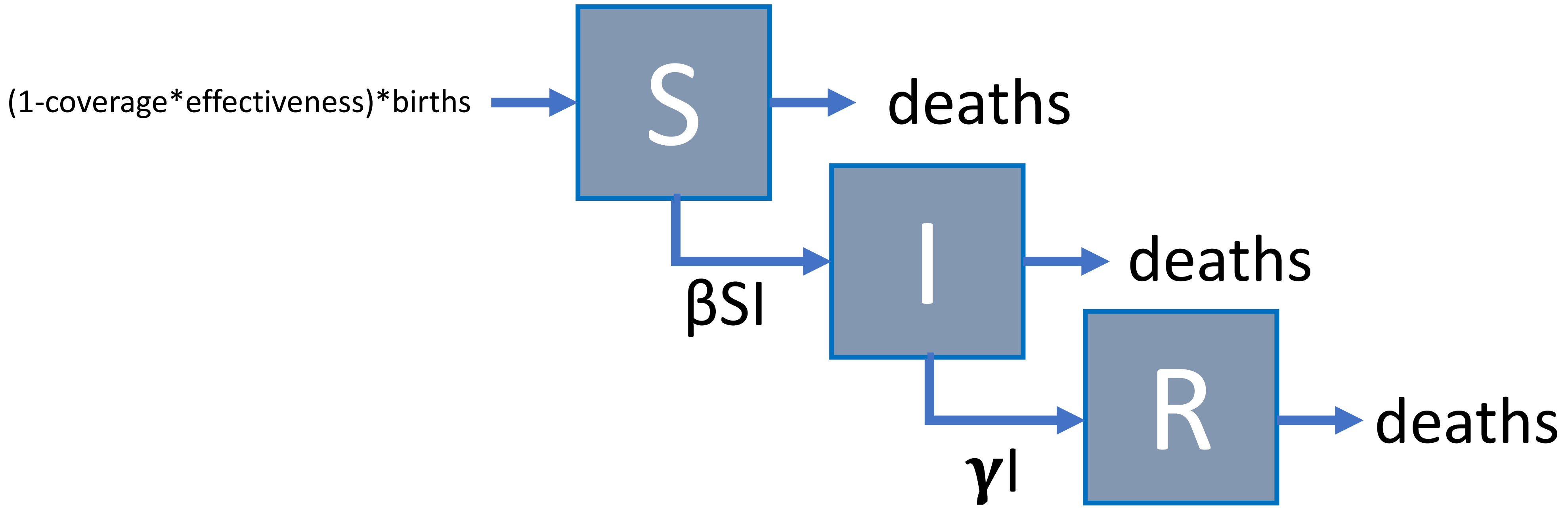

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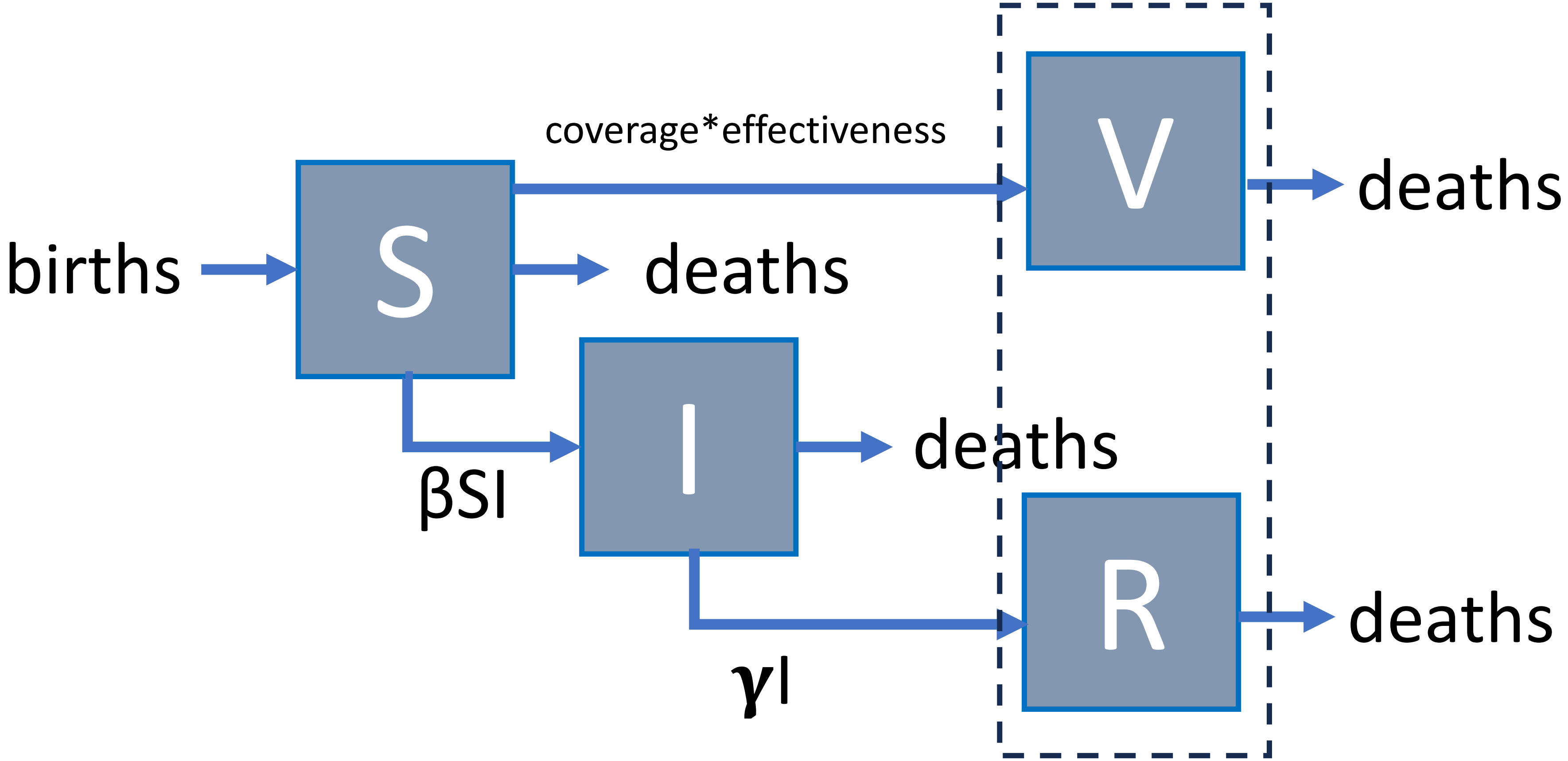
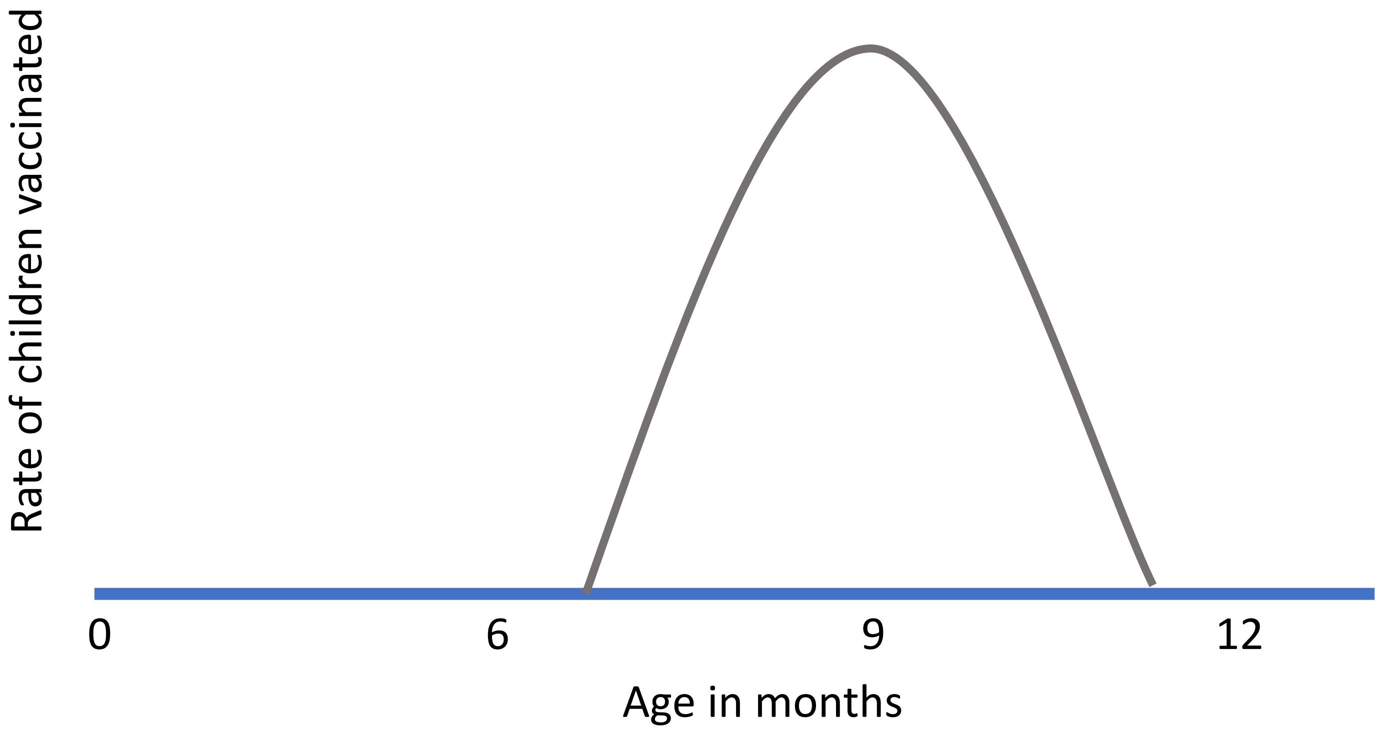


Interactive Session: simulating vaccination

R-file: SIRModel 2birthsdeaths_seasonality_vaccination.r

Vaccination at Age

Vaccination at specific ages



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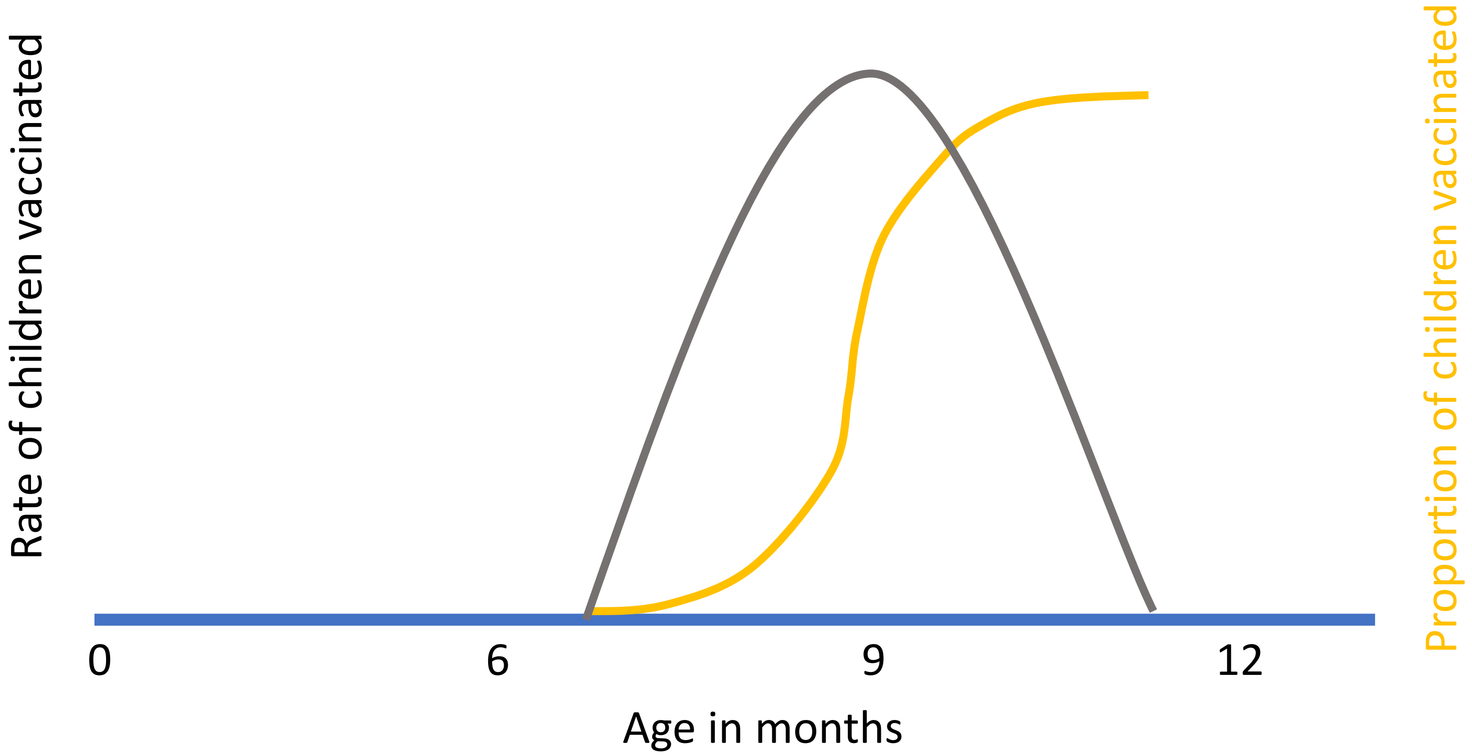

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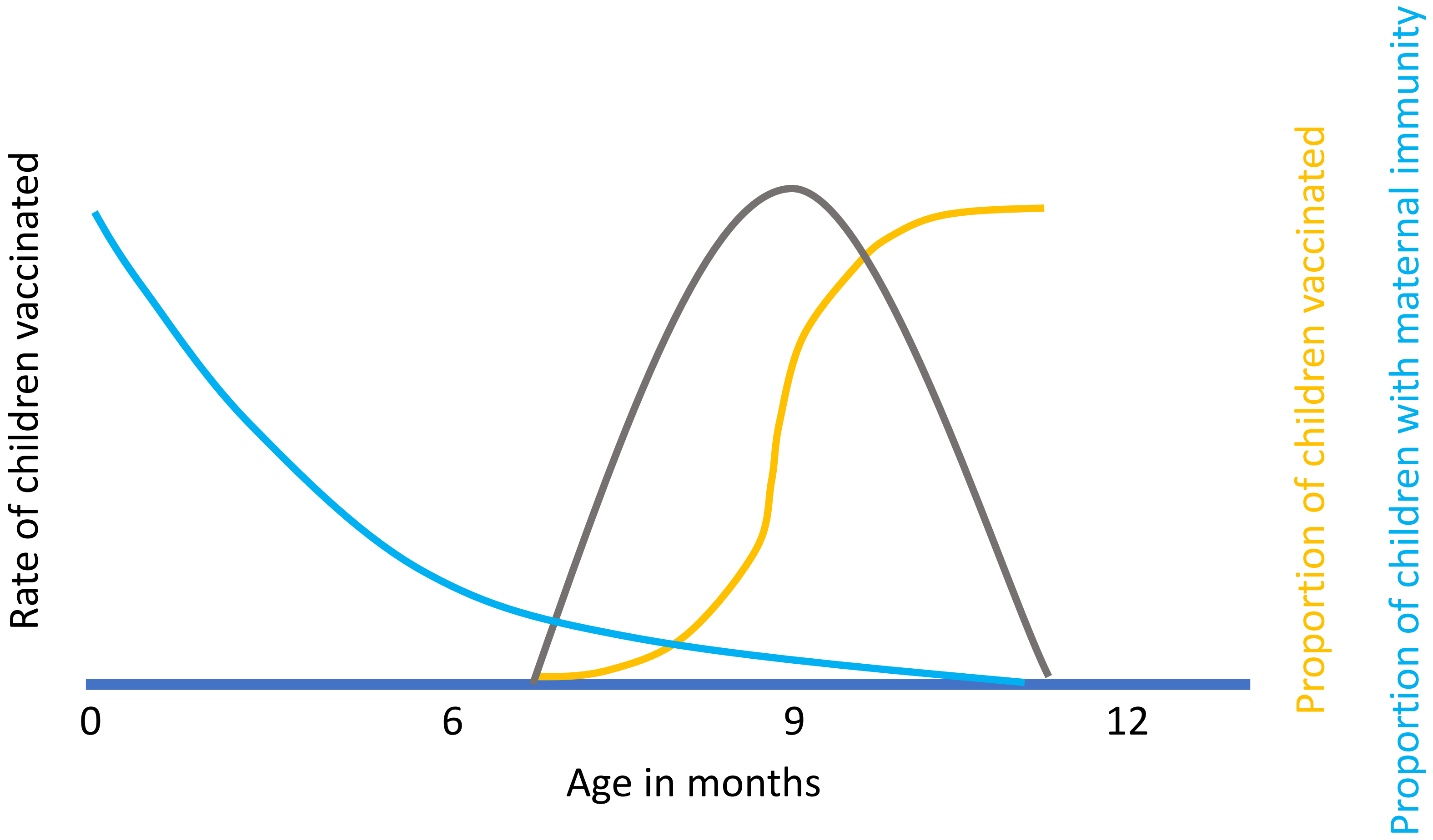


Maternal Immunity

- Antibodies from immune mothers are passively transferred to infant
- Infant cannot produce new antibodies. Transferred antibodies (and immunity) degrades approximately exponentially.

Immunogenicity, effectiveness, and safety of measles vaccination in infants younger than 9 months: a systematic review and meta-analysis

Laura M Nic Lochlainn, Brechje de Gier, Nicoline van der Maas, Peter M Strebel, Tracey Goodman, Rob S van Binnendijk, Hester E de Melker, Susan J M Hahné

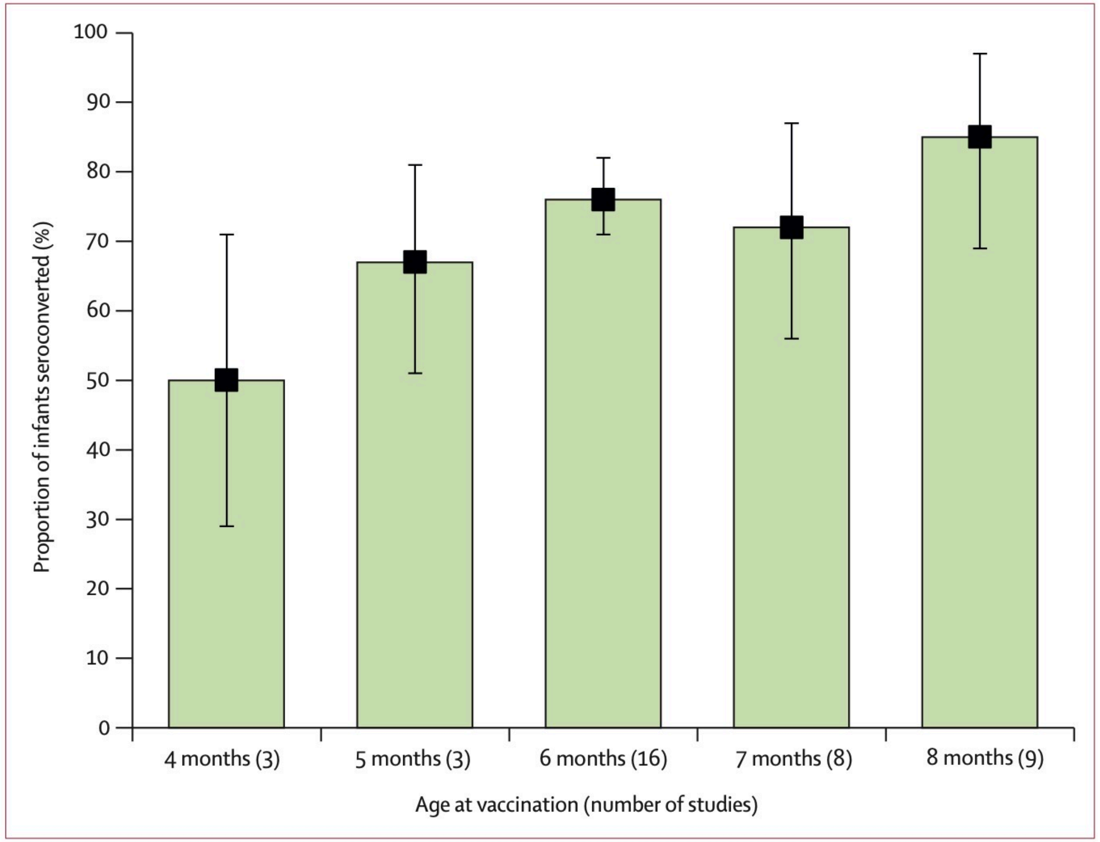
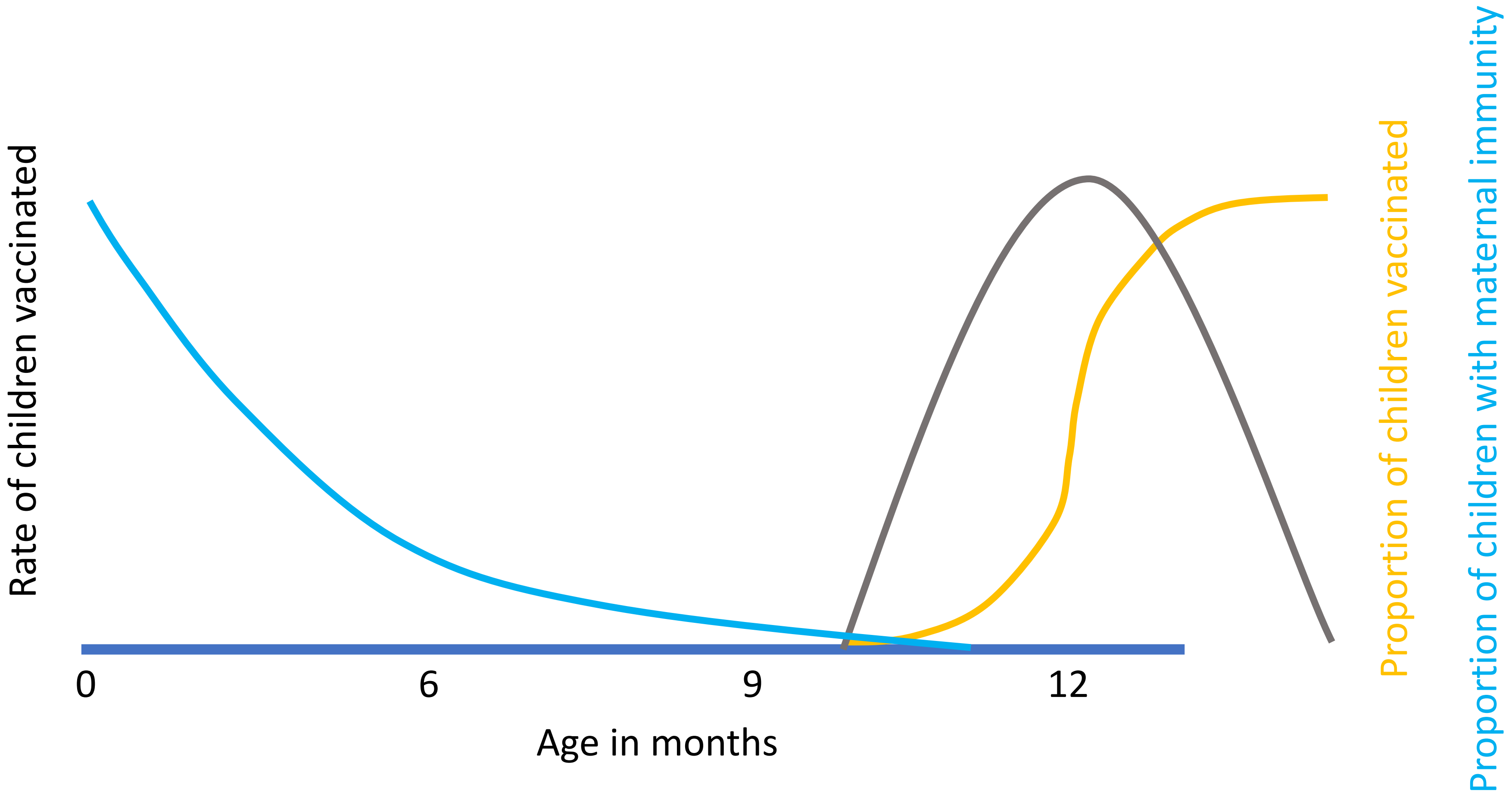


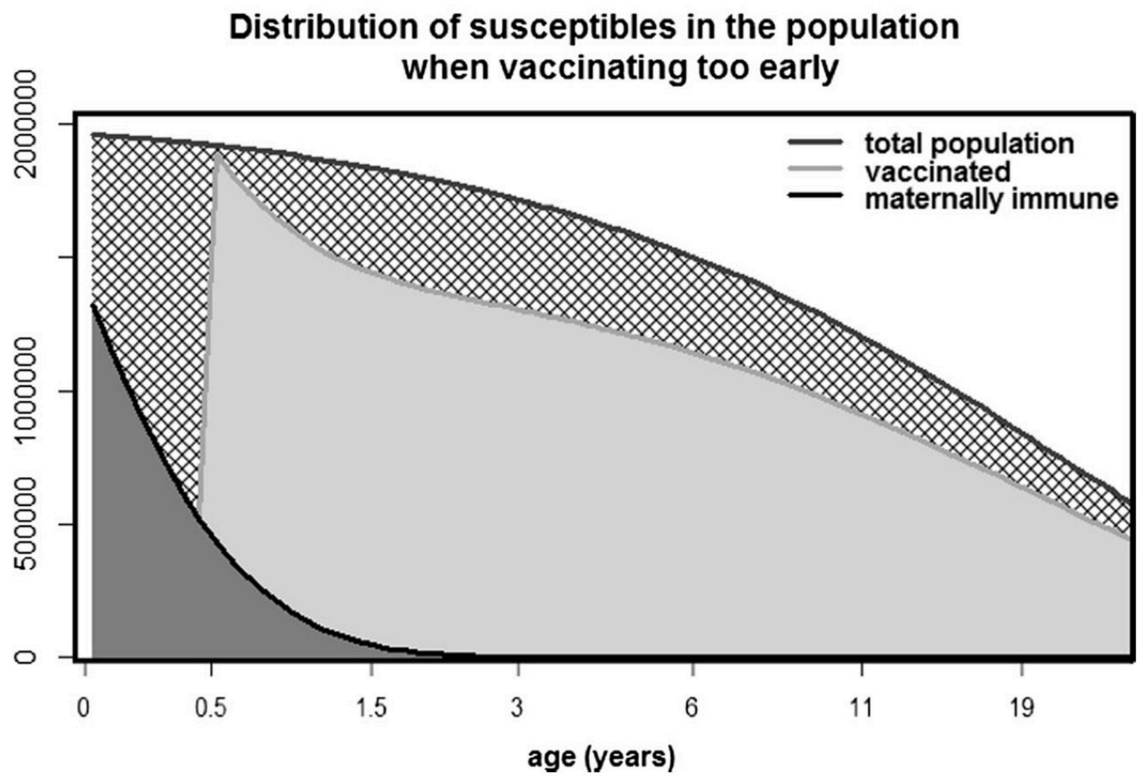
Figure 2: **Pooled estimates of proportion of infants seroconverted, by age of MCV1 (4–8 months) with 95% CIs**
MCV1=first dose of measles-containing vaccine.

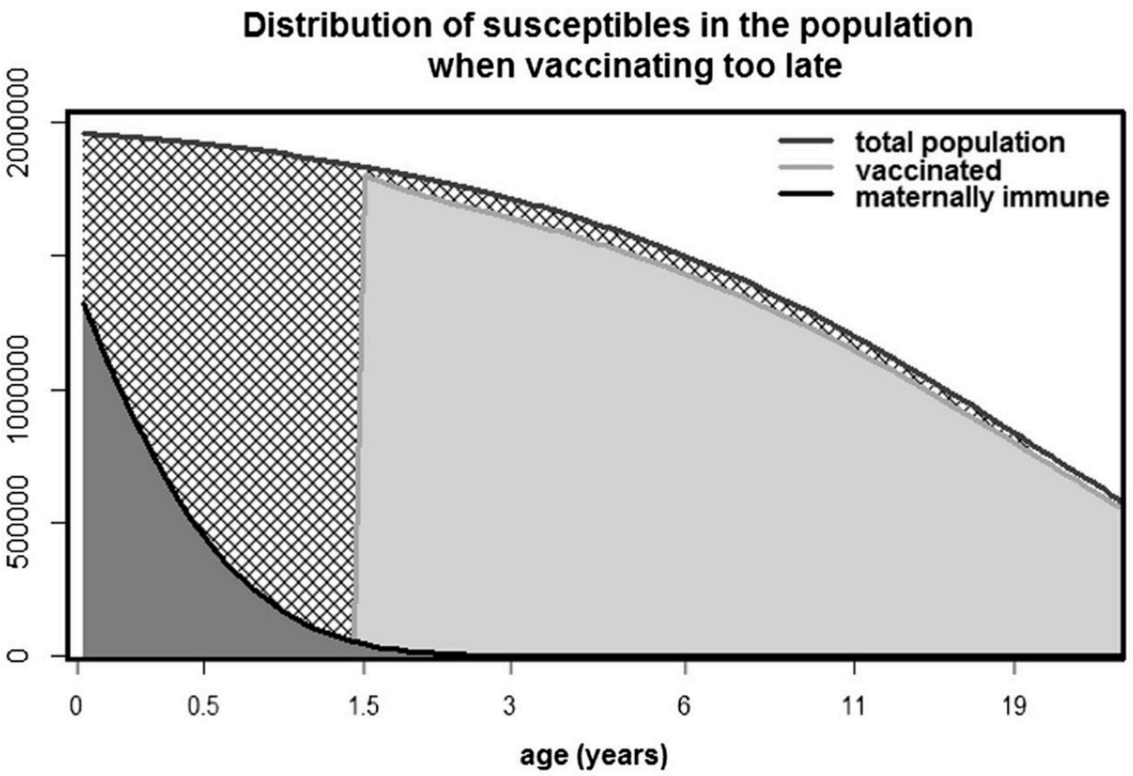
Vaccination at specific ages



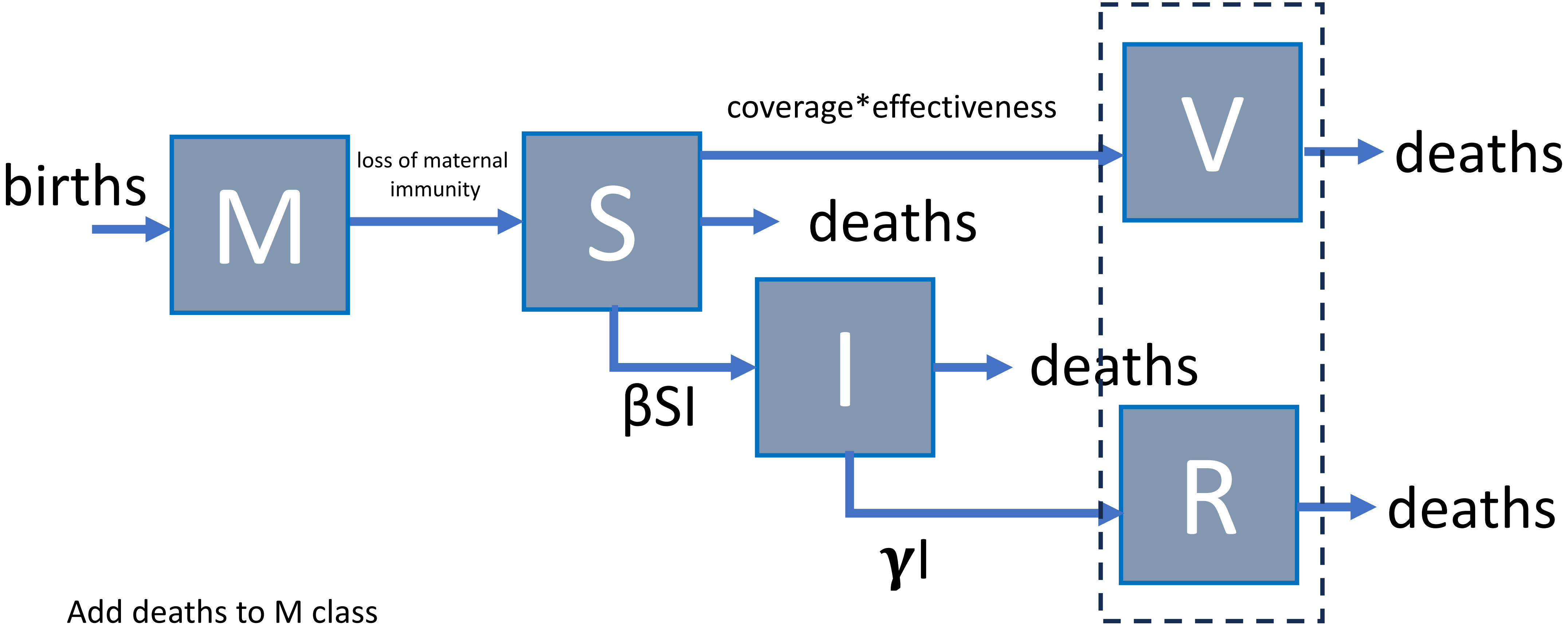
Timing of the First Dose

Label y axis



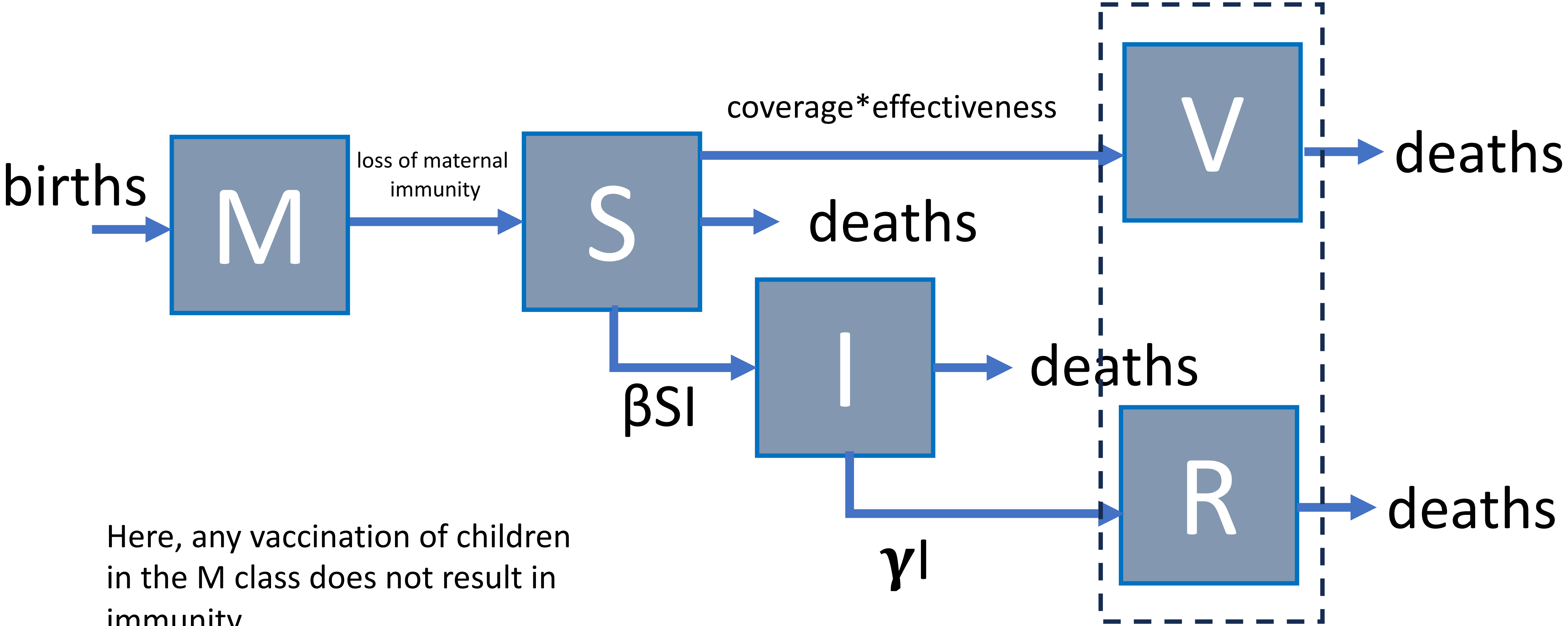


Adding a Maternal Immunity Class



Add deaths to M class

Adding a Maternal Immunity Class



Here, any vaccination of children in the M class does not result in immunity

Second Doses

Second Doses

- Routine Immunization
- Supplemental Immunization
- Outbreak Response Immunization

Second Doses

- Routine Immunization
  - Delivered through “well-child” visits at targeted ages
  - 1st dose recommended at 9-12 months, timing dependent on prevalence
  - 2nd dose recommended at 24 months or higher, varies by country. Goal is immunize those who failed to seroconvert with first dose
  - Formally, 2nd dose coverage is recorded as the fraction of children with 1st dose that receive a 2nd dose. However, this convention is not universal.
- Supplemental Immunization
- Outbreak Response Immunization

Second Doses

- Routine Immunization
- Supplemental Immunization (SIA)
    - Periodic, large-scale vaccination of all children (regardless of prior vaccination) within a target age group.
    - Modeled after PAHO strategy of “catch up”, “keep up”, ”follow up”
    - Models have been useful in determining the frequency and age targets for these campaigns
    - Implementation in models as a single time point move from S to R, resulting in a large reduction in S class in the target age groups.
- Outbreak Response Immunization

Second Doses

- Routine Immunization
- Supplemental Immunization (SIA)
- Outbreak Response Immunization
  - Vaccination activities that are triggered by the occurrence of an outbreak
  - Indiscriminate targeting of all children within an age window (e.g. 6-59m)
  - Triggers (e.g. number of cases), speed, scale, and coverage of response varies by country and the organization conducting the ORI
  - Modelling has been useful in identifying age targets and evaluating the potential trade-offs between speed and coverage. As outbreak progresses there is less indirect (herd) benefit of each dose.

Interactive session: SIAs

R-file: SIRModel 2birthsdeaths_seasonality_vaccination_SIA.r

What have we learned?