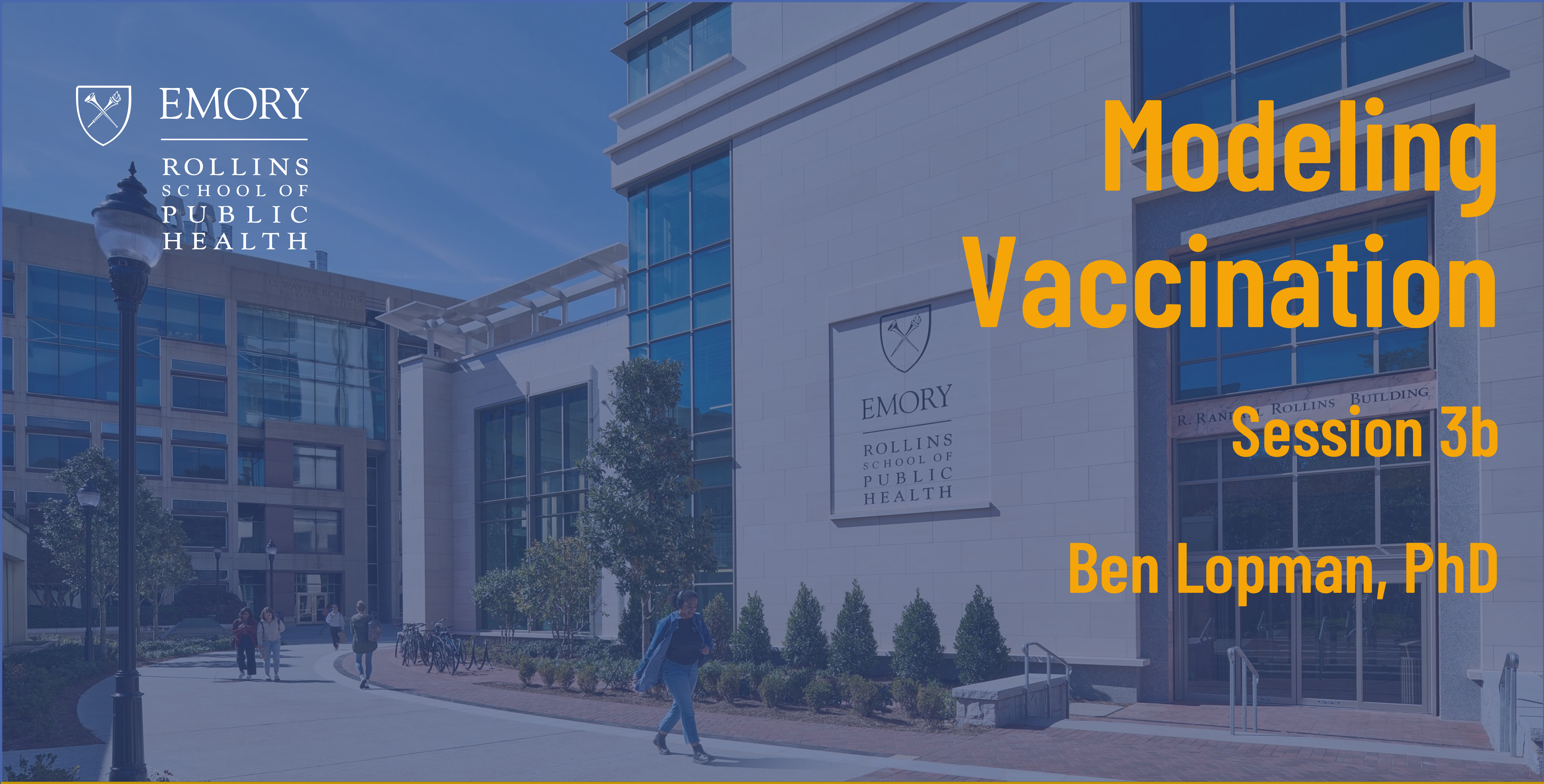
EMORY
ROLLINS SCHOOL OF PUBLIC HEALTH



Modeling Vaccination

Session 3b

Ben Lopman, PhD

Outline

1. **Representing vaccination in dynamic models**
2. **Herd immunity and the critical vaccination threshold**
3. Dynamics of vaccine introduction
4. Age-specific effects and age-targeted vaccination
   - (Sometimes) perverse effects of vaccination
5. Waning immunity

Vaccine-related questions that may be addressed by mathematical models

- What is **acceptable vaccine product profile**?
- What **coverage** must be achieved?
- What should be the **target population?**
- What should the **vaccine schedule** be?
- What is the appropriate **trial design and sample size**?
- Interpretation of **post-introduction dynamics**

… and more!

Recall: the SIR model

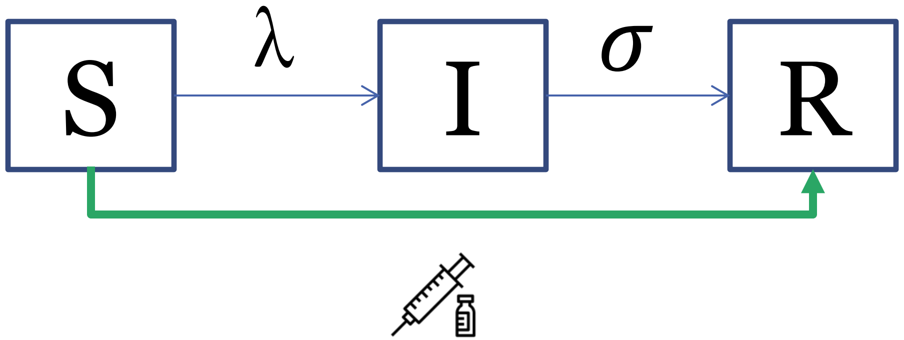
$$\boxed{S} \xrightarrow{\lambda} \boxed{I} \xrightarrow{\sigma} \boxed{R}$$

$$\frac{dS}{dt} = -\lambda_t S$$

$$\frac{dI}{dt} = \lambda_t S - I\sigma$$

$$\frac{dR}{dt} = I\sigma$$

The SIR model + vaccination



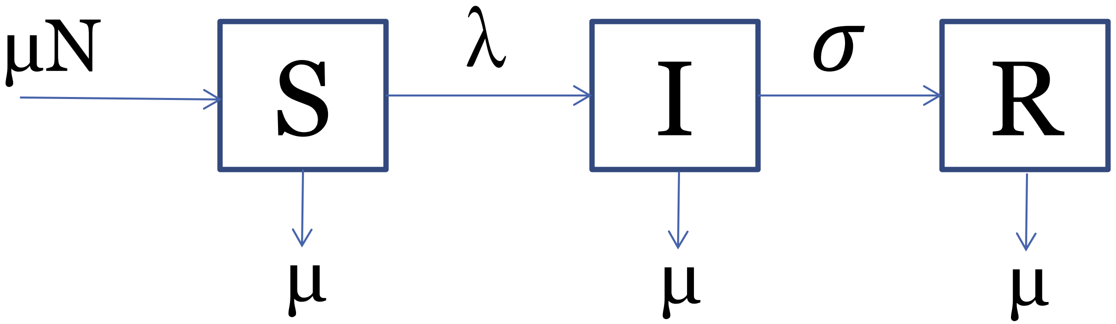
$$\frac{dS}{dt} = -\lambda_t S - xS$$

$$\frac{dI}{dt} = \lambda_t S - I\sigma$$

$$\frac{dR}{dt} = I\sigma + xS$$

x = proportion successfully immunized
= proportion receiving vaccine * vaccine efficacy
= p * VE

The SIR model – WITH DEMOGRAPHY



$$\frac{dS}{dt} = -\lambda_t S - \mu S + \mu N$$

$$\frac{dI}{dt} = \lambda_t S - I\sigma - \mu I$$

$$\frac{dR}{dt} = I\sigma - \mu R$$

A general model of vaccination

$$\frac{dS}{dt} = -\lambda S - \mu S + (1-p_1 v)\mu N - p_2 v S$$

$$\frac{dI}{dt} = \lambda S - \sigma I - \mu I$$

$$\frac{dR}{dt} = \sigma I - \mu R$$

$$\frac{dV}{dt} = p_1 v \mu N + p_2 v S - \mu V$$

Infection
Recovery
Vaccination
p_1 - fraction vaccinated **at birth**
p_2 - fraction **susceptibles (in S)** vaccinated, **at random**
v - vaccine efficacy

Draw it!

*Note that vaccinated are NOT susceptible to infection (only those in S)!

A model of leaky vaccination

$$\frac{dS_u}{dt} = -\lambda_u S_u - \mu S_u + (1-p_1)\mu N$$

$$\frac{dS_v}{dt} = -\lambda_v S_v - \mu S_v + (p_1)\mu N$$

$$\frac{dI}{dt} = \lambda_u S_u + \lambda_v S_v - \sigma I - \mu I$$

$$\frac{dR}{dt} = \sigma I - \mu R$$

$$\frac{dV}{dt} = p_1 \mu N$$

Key

Infection

Recovery

Vaccination

p_1 - fraction vaccinated at birth

v - vaccine efficacy

Where does v (VE) come in?

Vaccinated and unvaccinated subject to different force of infection.

Unvaccinated $$\lambda_u(t) = \beta \frac{I(t)}{N}$$

Vaccinated $$\lambda_v(t) = (1 - \text{v})\beta * \frac{I(t)}{N}$$

How many to vaccinate to slow an epidemic?: the herd immunity threshold (HIT)

s = proportion susceptible

To stop epidemic, R_e must be < 1

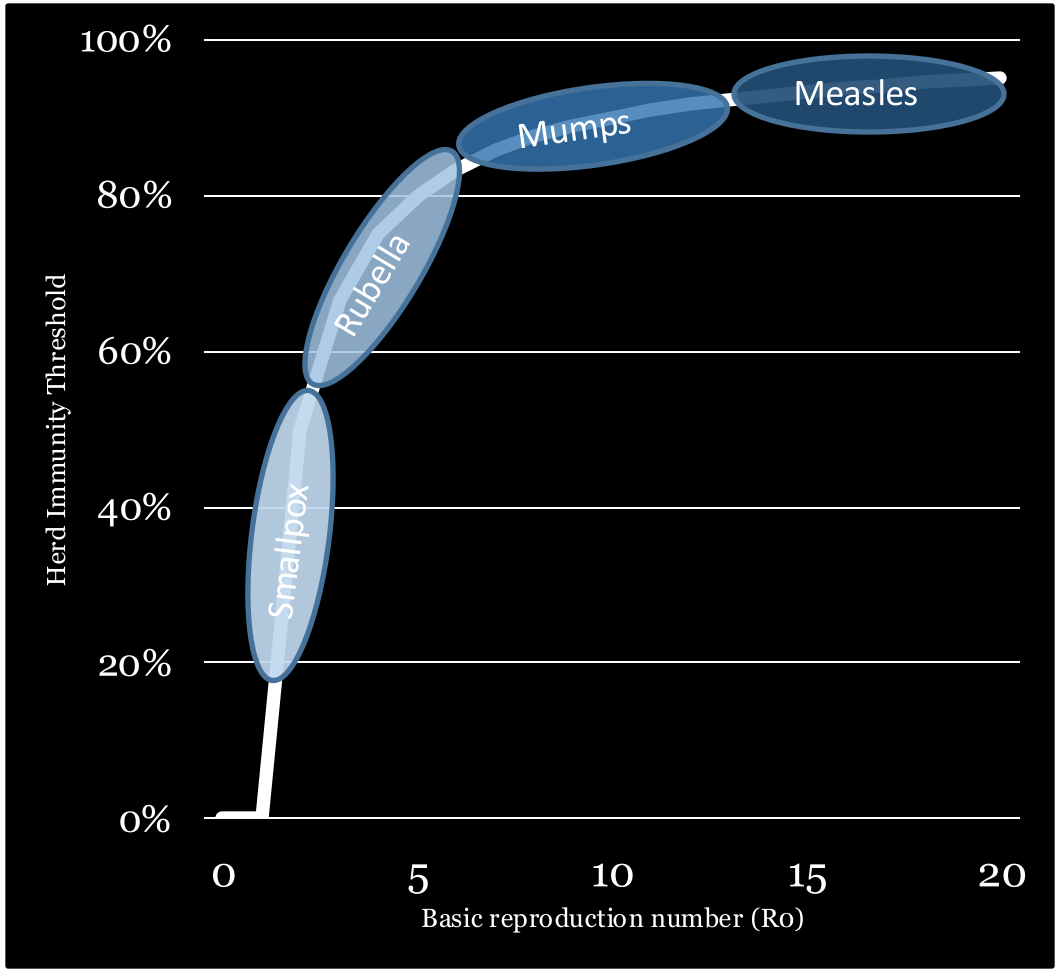
means R_0 * s < 1

Rearranging, s must be < $1/R_0$

In words:

fraction of susceptibles in population must be lower than $1/R_0$ to slow transmission

- HIT = 1 - $1/R_0$



How many to vaccinate to slow an epidemic?: critical vaccine coverage (p_c)

Vaccines are not perfect!

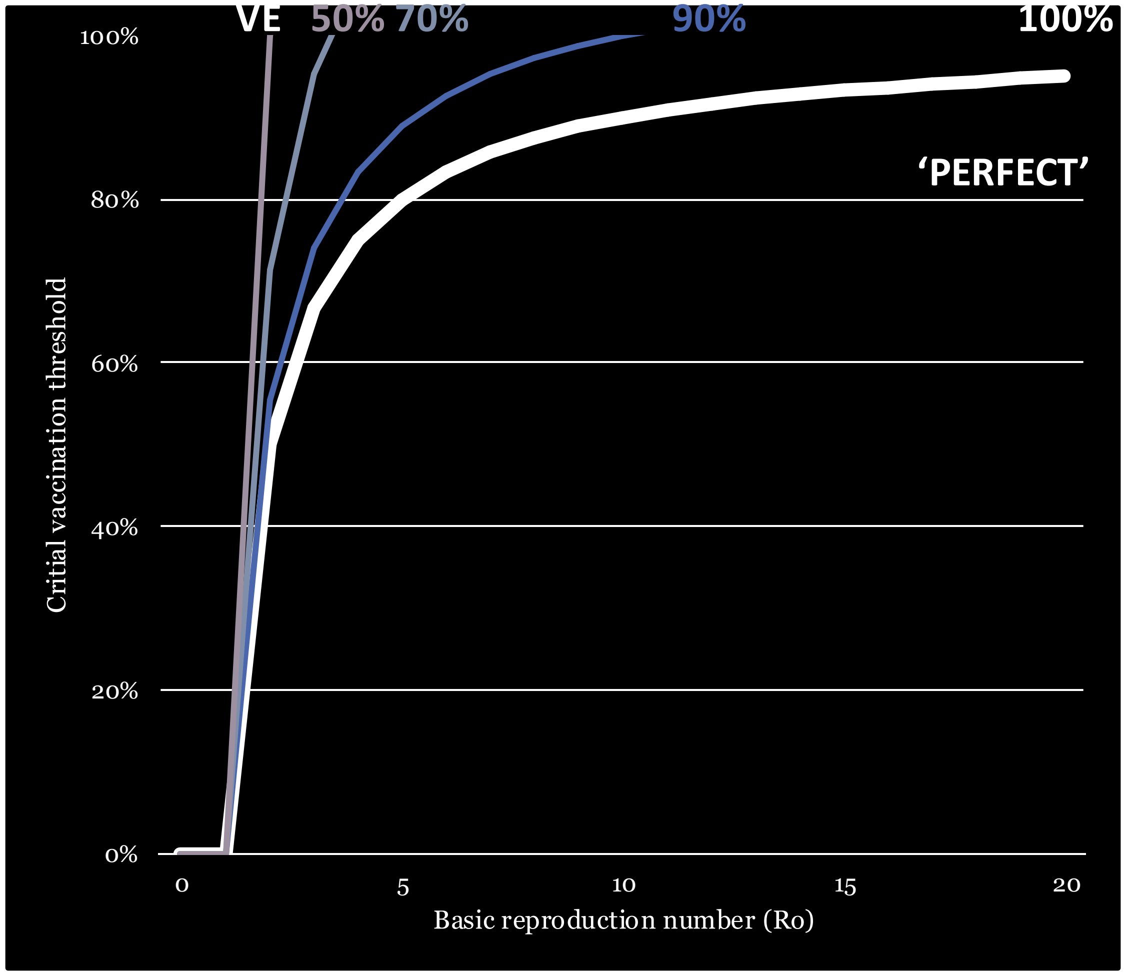
Proportion of the population that must be vaccinated to achieve herd immunity threshold

- assuming that vaccination takes place at random

Fraction immune by vaccination = fraction vaccinated * VE

HIT = $1 – 1/ R_0$

$p_c = (1 – 1/ R_0) / VE$



*If VE = 100%, p_c = HIT, but lower VE means p_c is higher

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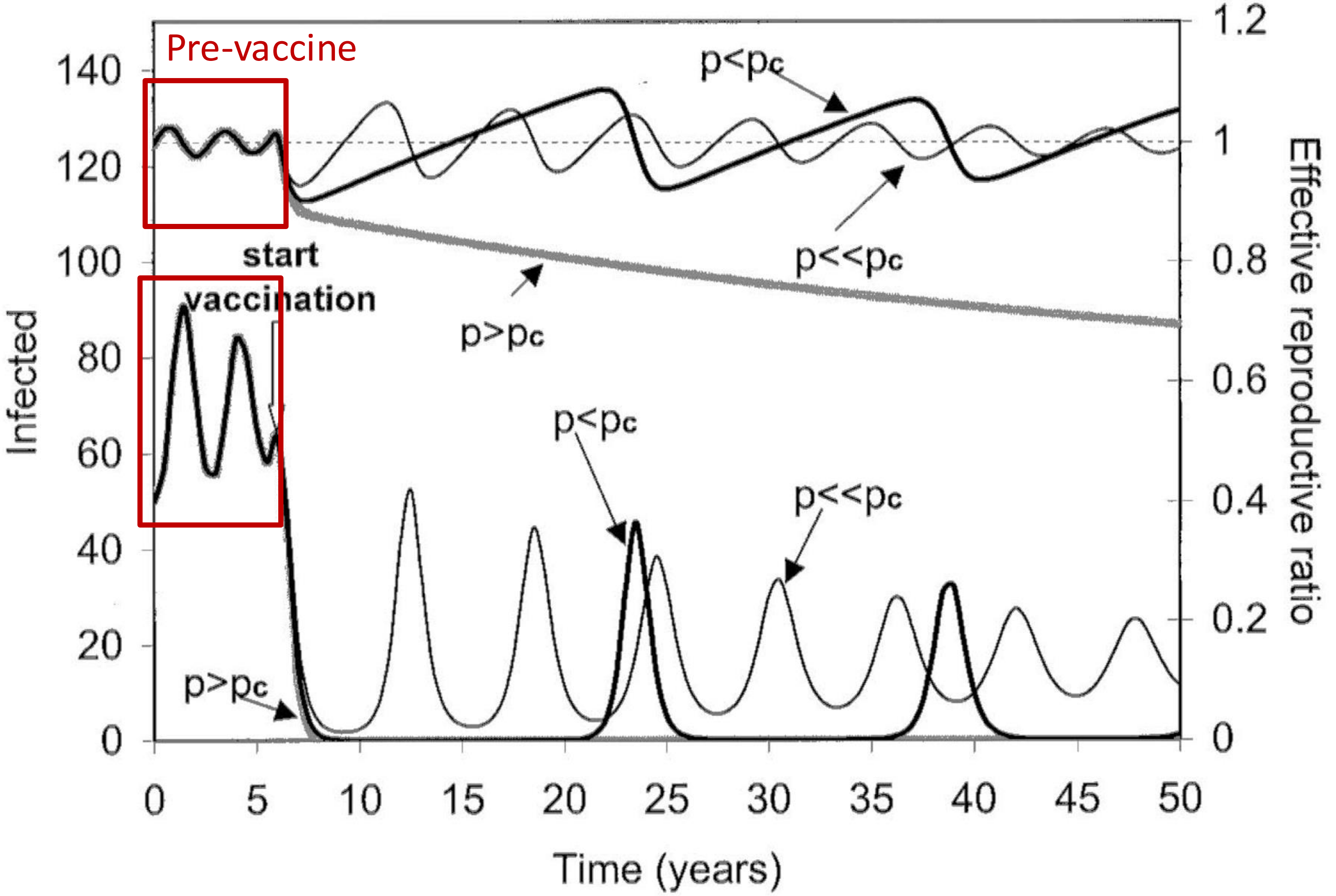
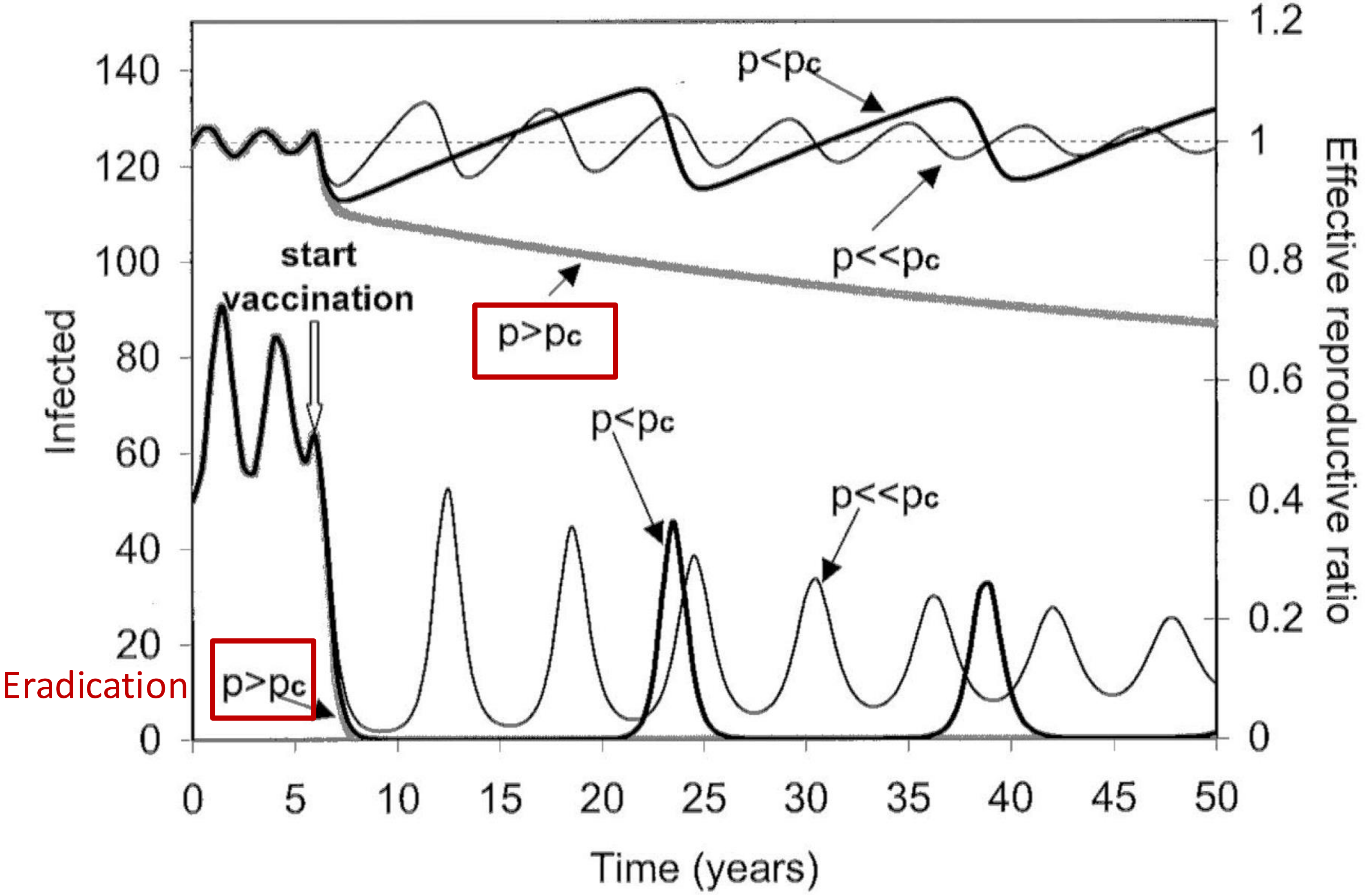
Dynamics of vaccine introduction: the effect of a vaccine program



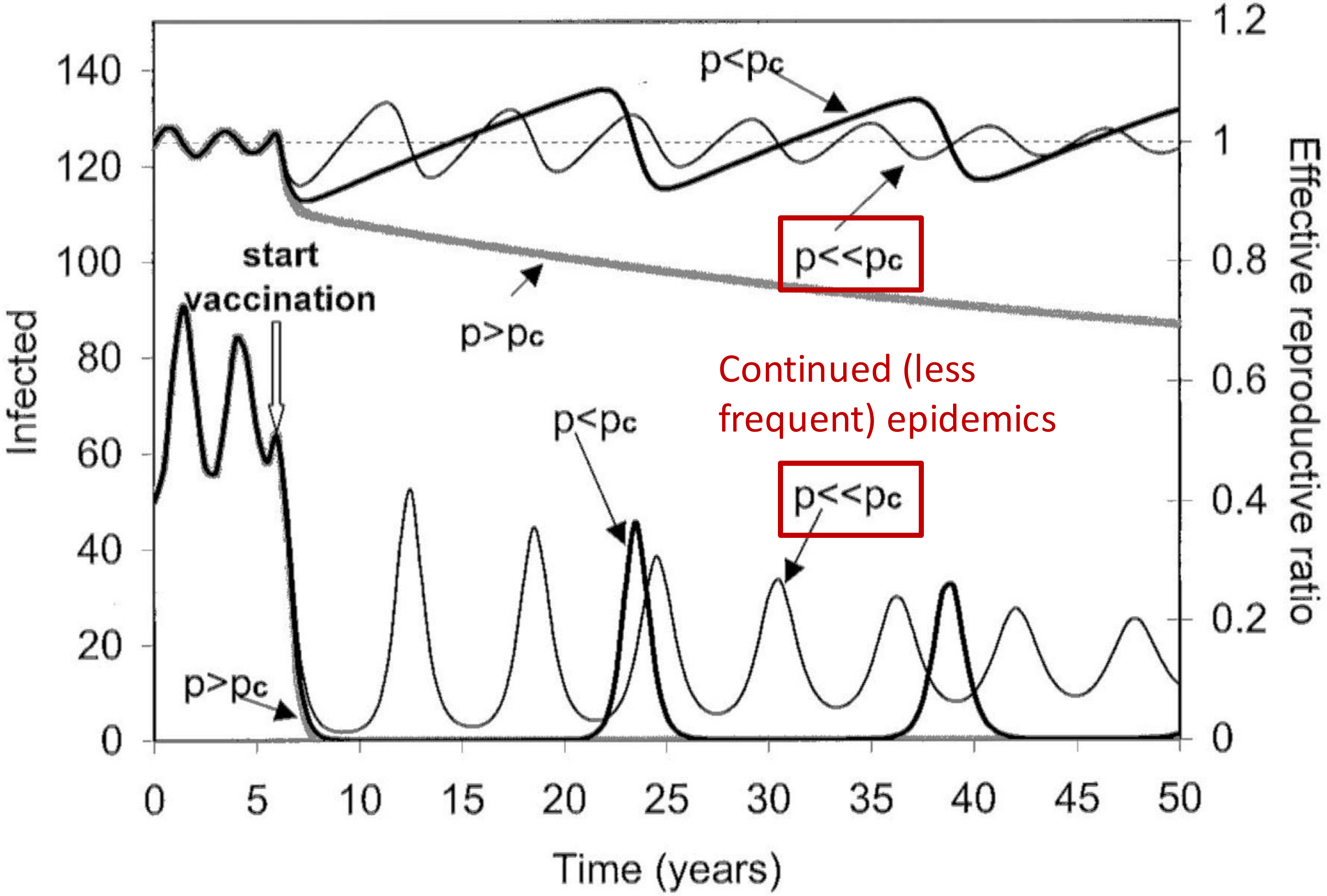
Dynamics of vaccine introduction: scenario 1

Coverage: 95%



Dynamics of vaccine introduction : scenario 2

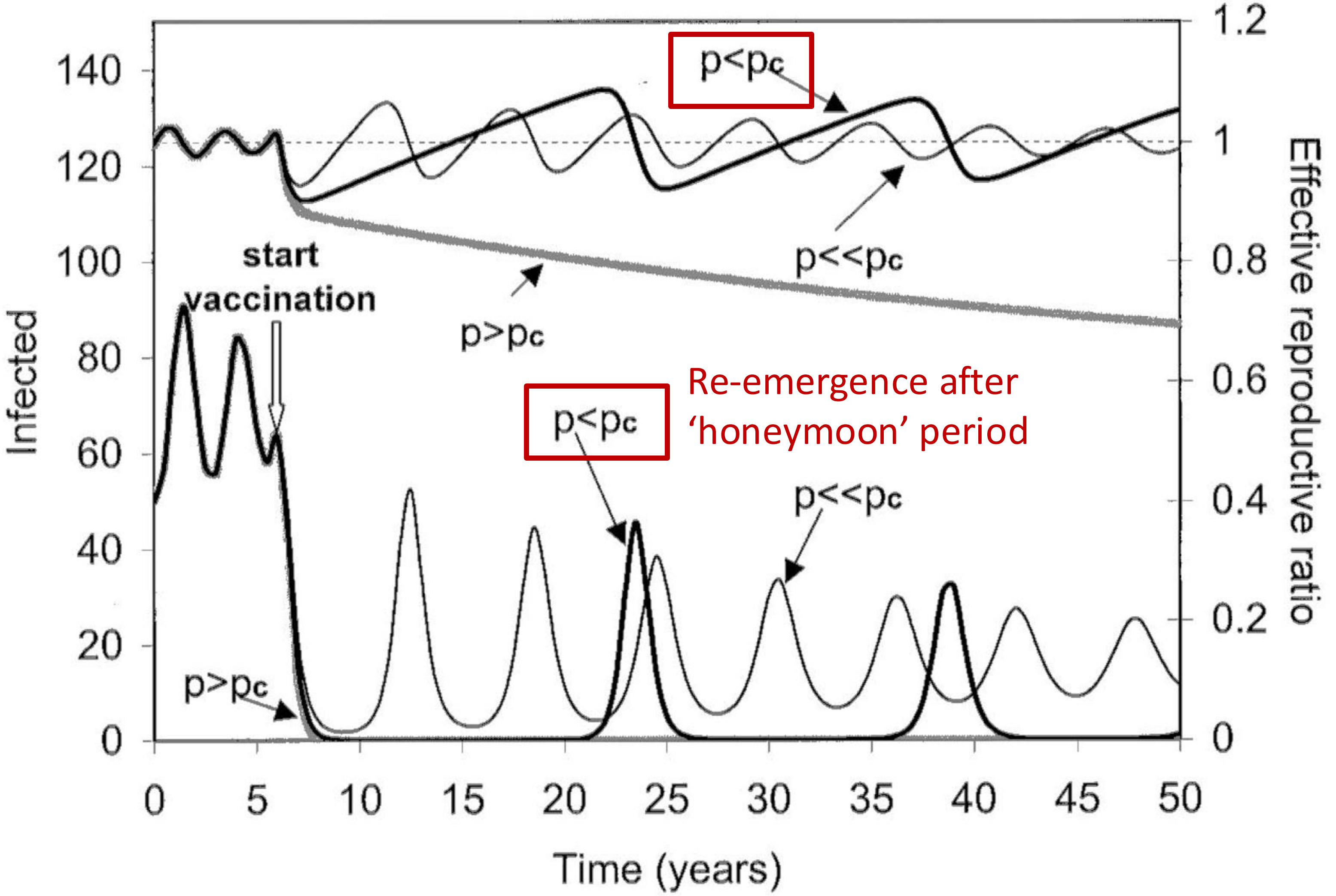
Coverage: 70%



nd McLean, BMB 2002

Dynamics of vaccine introduction : scenario 3

Coverage: 85%



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Infant vaccination always* acts to increase mean age of infection

Higher incidence -> earlier in life infection occurs

Quantifying this: in an unvaccinated population

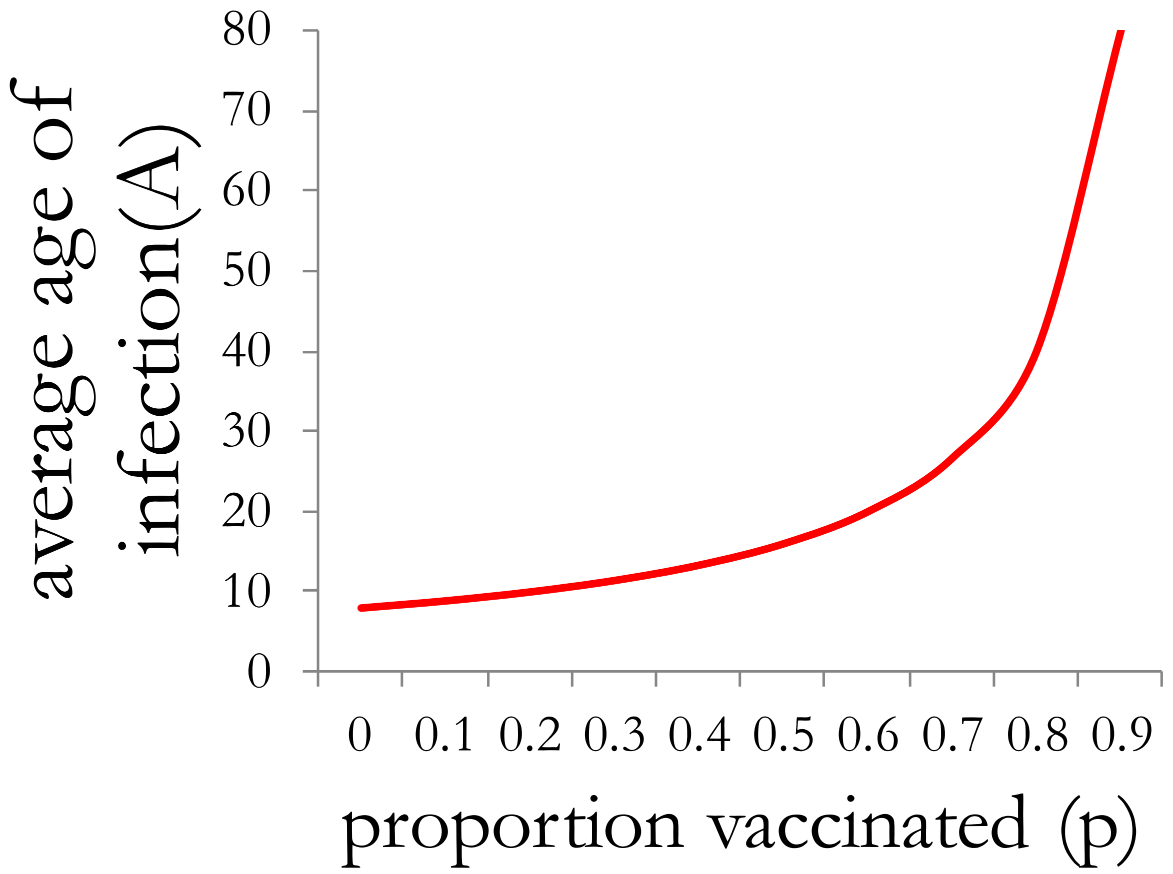
average age of infection, A

$A \approx L / R_0$

When a proportion, x, is vaccinated at birth

$A \approx L / R_E = L / R_0(1-x)$

**except when infection is eliminated*



For many childhood infections, a shift in the age distribution will **shift burden into older, less vulnerable children**

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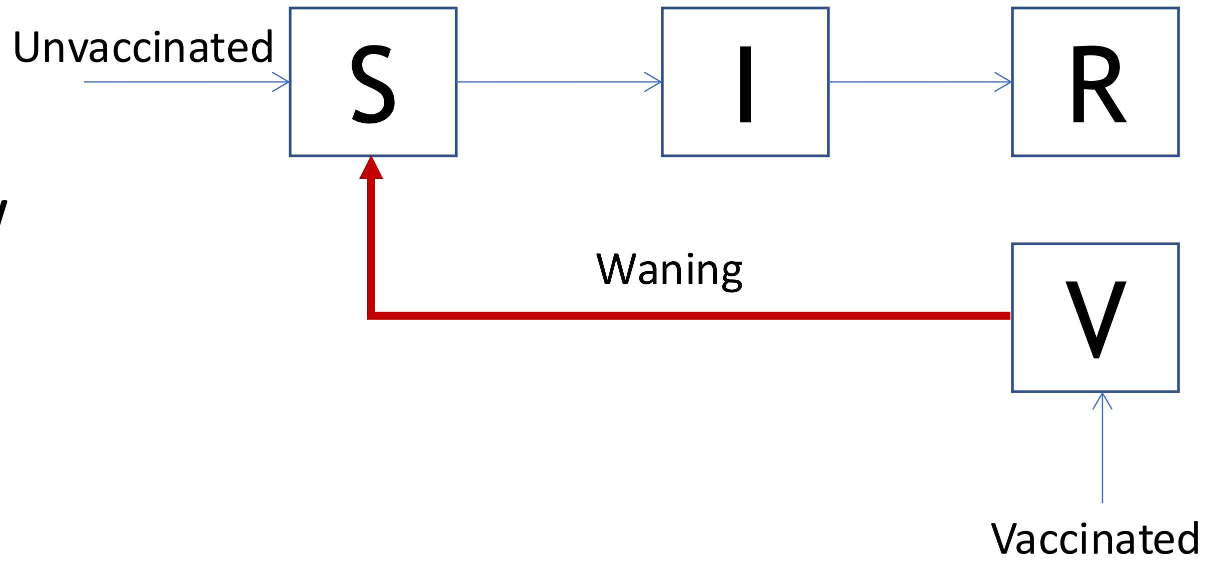
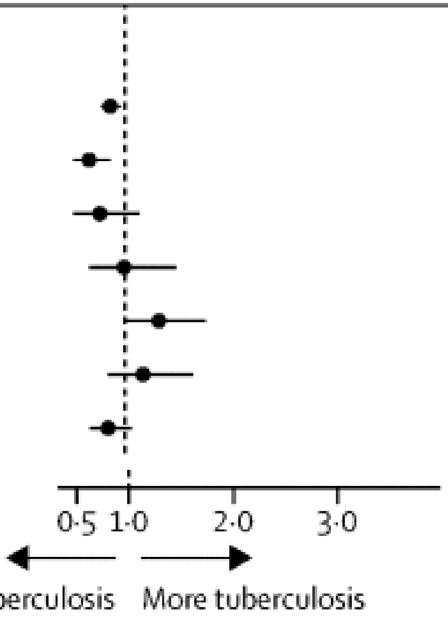
Waning immunity ('secondary vaccine failure')

- Models we have discussed so far, vaccine protection is considered lifelong
- To represent loss of immunity with time, need to allow for flow back to 'S'
- Hard to observe/measure directly
- BUT important!



Measuring waning vaccine immunity: in years

	Vaccinated (n/N)	Unvaccinated (n/N)	Adjusted odds ratio (95% CI)
All participants			
All ages	1309/49 686	473/18 866	0·82 (0·74–0·91)
<5 years	312/9225	80/1312	0·63 (0·49–0·81)
5–9 years	126/9936	36/1289	0·76 (0·51–1·14)
10–14 years	145/7847	34/1190	0·99 (0·66–1·48)
15–24 years	316/7984	69/2628	1·32 (0·98–1·75)
25–34 years	161/5159	57/3006	1·17 (0·83–1·64)
≥35 years	249/9535	197/9441	0·84 (0·67–1·06)



Infant BCG vaccination and risk of pulmonary and extrapulmonary tuberculosis throughout the life course: a systematic review and individual participant data meta-analysis

Martinez et al. Lancet GH 2022

Measuring waning vaccine immunity: in months

JOURNAL ARTICLE

Waning Vaccine Effectiveness Against Influenza-Associated Hospitalizations Among Adults, 2015–2016 to 2018–2019, United States Hospitalized Adult Influenza Vaccine Effectiveness Network FREE

Jill M Ferdinands, Manjusha Gaglani, Emily T Martin, Arnold S Monto, Donald Middleton, Fernanda Silveira, H Keipp Talbot, Richard Zimmerman, Manish Patel

Clinical Infectious Diseases, Volume 73, Issue 4, 15 August 2021, Pages 726–729, https://doi.org/10.1093/cid/ciab045

Influenza Type/Subtype	Influenza Seasons Included	No. of Cases/Controls	Estimated VE Decline per Month, Absolute % (95% CI)	*P* Value[a]
Influenza A(H3N2)[b]				
Aged ≥18 y	2016–2017, 2017–2018	754/2262	7.5 (.3–16.3)	.05
Aged ≥65 y	2016–2017, 2017–2018	395/1185	10.8 (2.6–23.8)	.02

A model of vaccination with waning vaccine immunity

$$\frac{dS}{dt} = -\lambda S - \mu S + (1-p_1)\mu N - p_2 S + \omega V$$

$$\frac{dI}{dt} = \lambda S - \sigma I - \mu I$$

$$\frac{dR}{dt} = \sigma I - \mu R$$

$$\frac{dV}{dt} = p_1 \mu N + p_2 S - \mu V - \omega V$$

<u>Key</u>

Infection

Recovery

Vaccination

p_1 - fraction vaccinated at birth

p_2 - fraction susceptibles (in S) vaccinated, at random

Loss of (waned) immunity

The reproductive number with waning immunity (R_v)

Where:

- ω is average duration of (vaccine) protection
- μ is death rate (inverse of average life expectatncy)
- e is vaccine efficacy
- p is proportion vaccinated

$$R_v = \left(1 - e \boxed{\frac{\mu}{(\mu + \omega)}} p\right) R_0$$

the fraction of a lifetime for which an individual is protected by a vaccine