Consequences of waning immunity

Population level protection vs. herd-immunity

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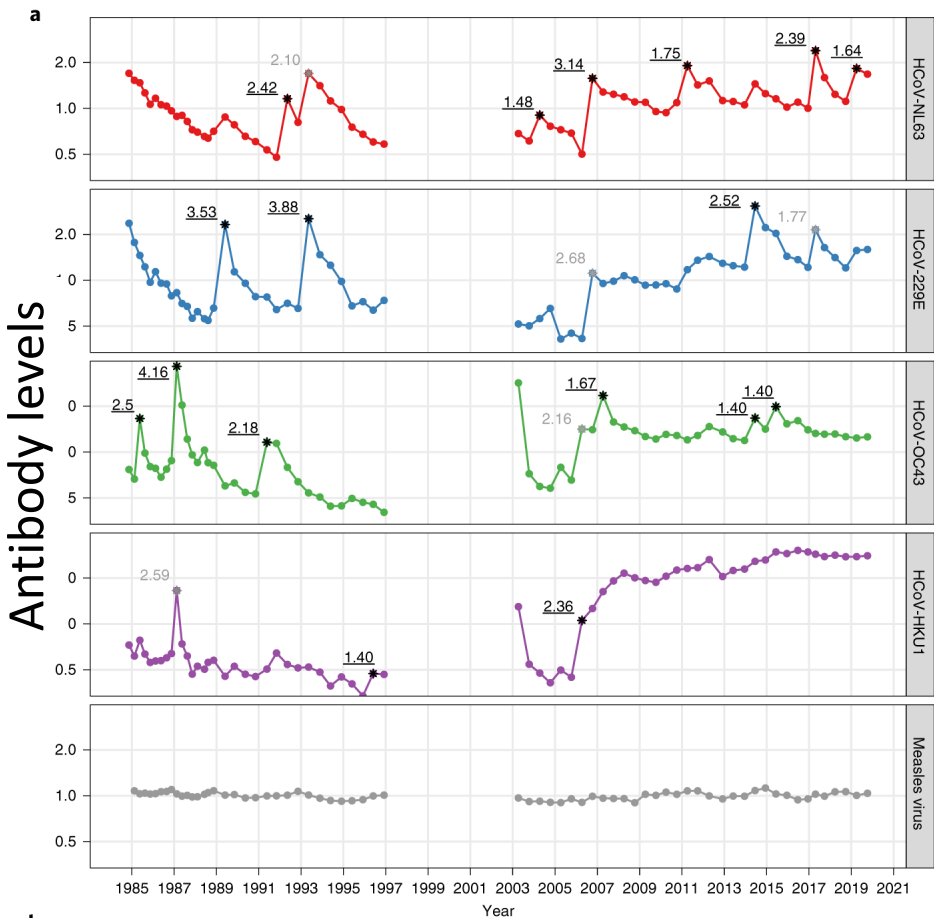
Consequences of waning immunity to respiratory viruses – Cov-2 is not measles

- Waning and boosting of immunity to influenza and CoVs
- Measures of immune efficacy <-- Halloran, Longini and others
- A toy model for the consequences of waning immunity
  - Disease prevalence vs severity
  - Antigenic changes
- Open puzzles
  - What are the rules for waning and boosting of immunity

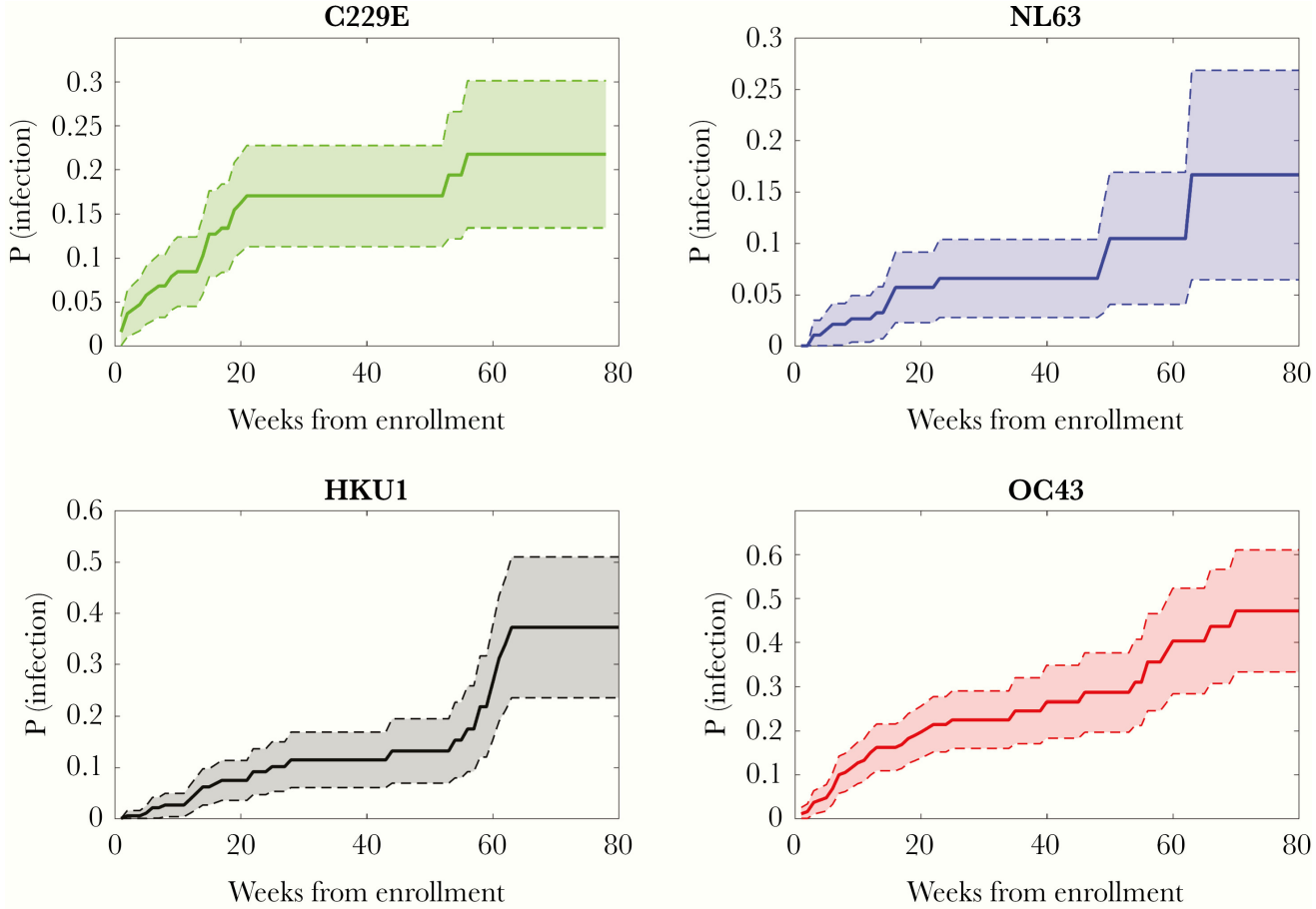
Waning immunity and reinfection for endemic hCoV's

Serology – antibody titers



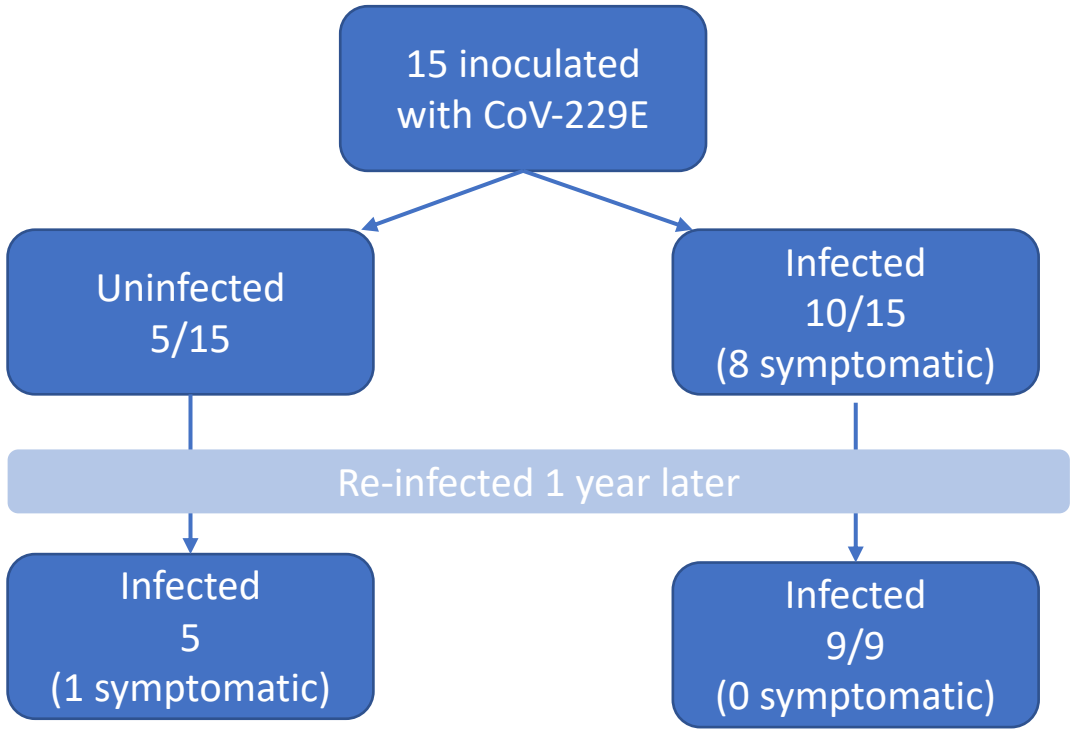
Edridge et al Nat. Med. 2020

Virus spikes indicate reinfections every few years

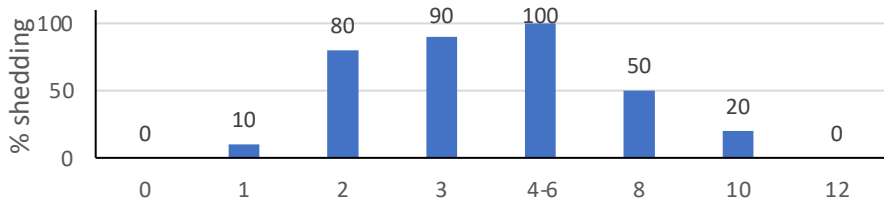


Galanti et al JID 2020

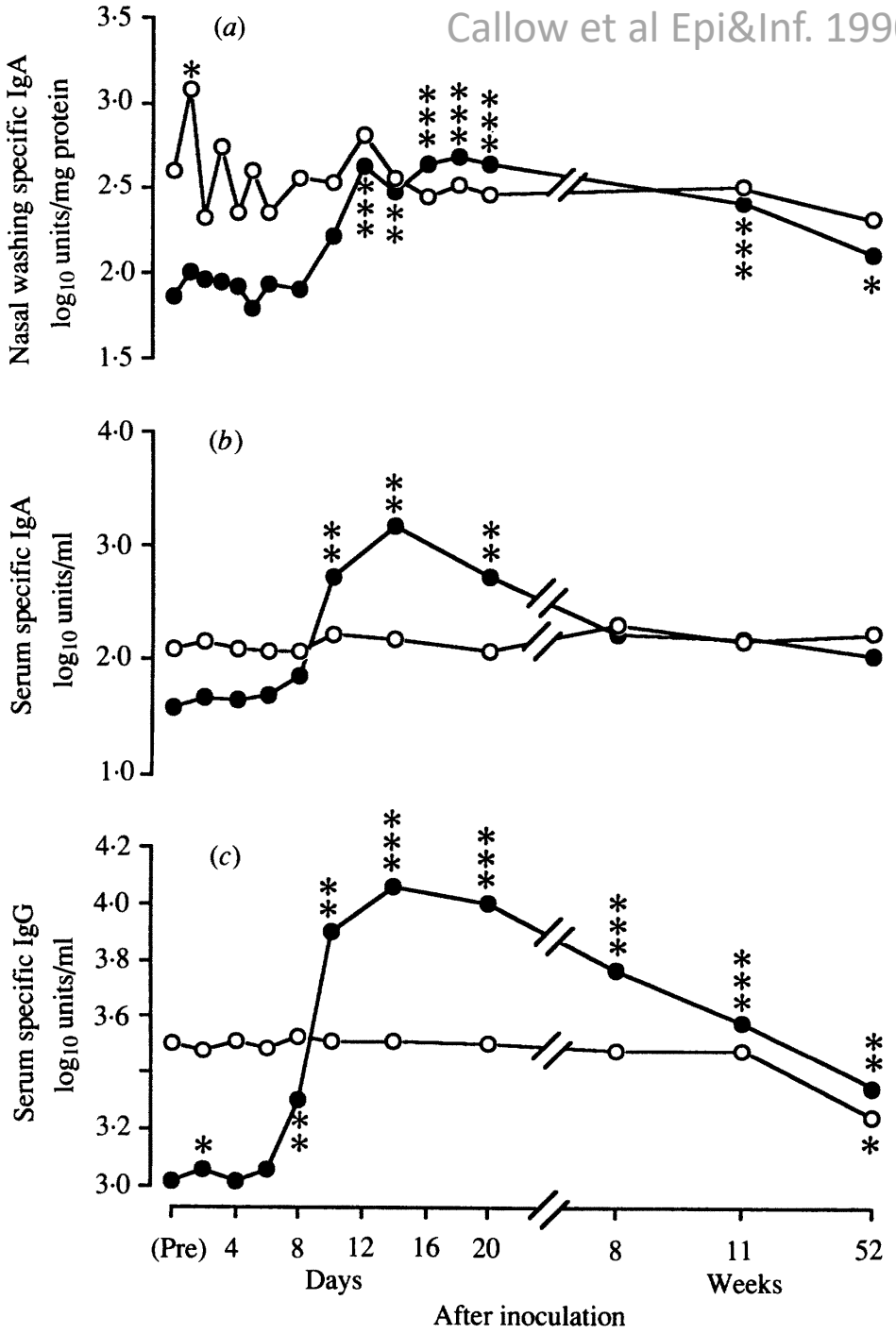
Experimental infections



Shedding after first innoculation

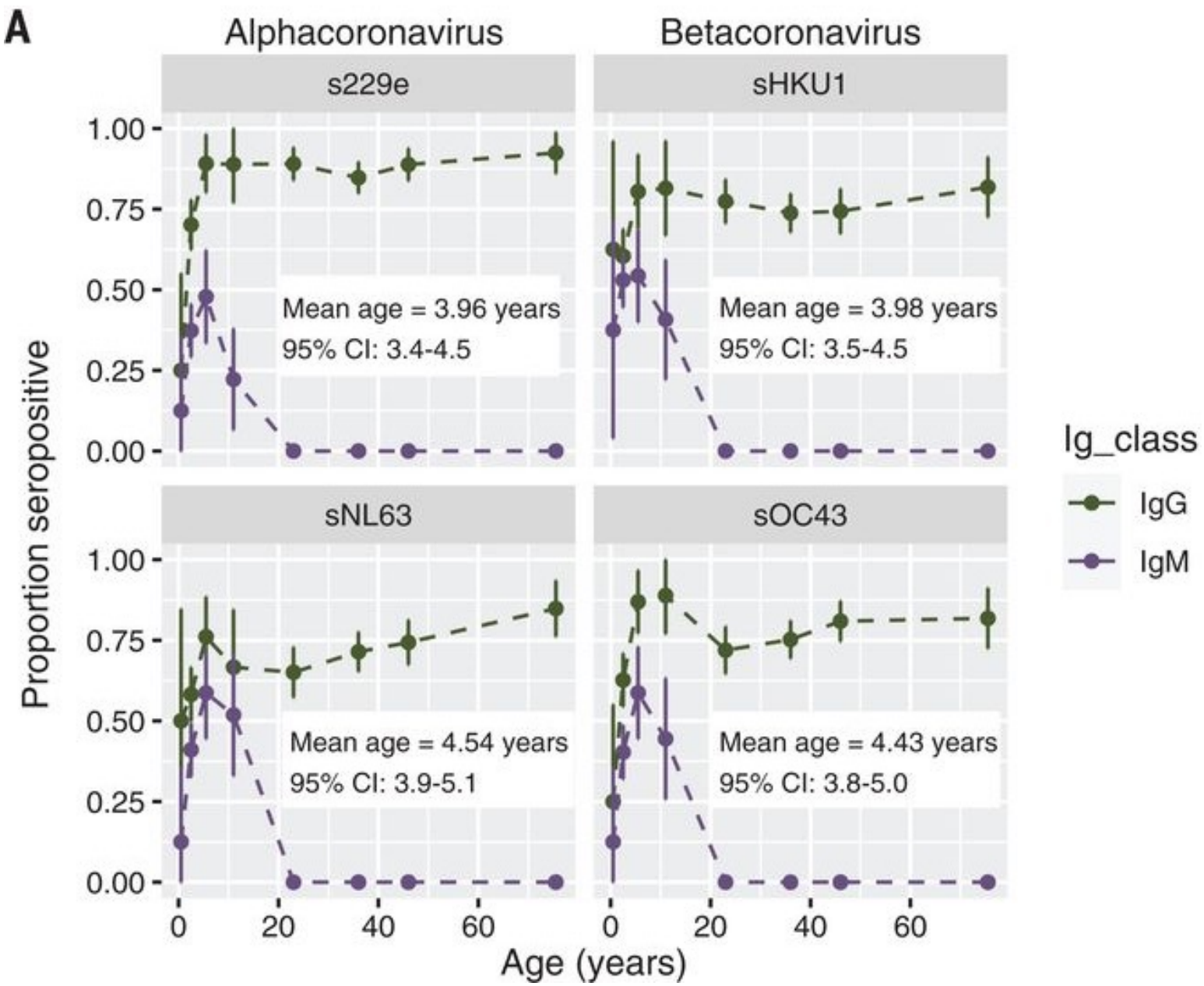


Callow et al Epi&Inf. 1990



Seroprevelance

From Zhou et al 2013 plotted in Lavine et al 2021



Individuals cannot rely on COVID-19 herd immunity: Durable immunity to viral disease is limited to viruses with obligate viremic spread

Jonathan W. Yewdell

Virus	Initial Infection Site	Lymph/Blood Dissemination for Disease/ Transmission	Durable Immunity Infection	Durable Immunity Vaccination
Corona	Airway	No	No	N/A
Influenza A, B	Airway	No	No	No
Metapneumonia	Airway	No	No	No
Parainfluenza 1–3	Airway	No	No	N/A
Respiratory Syncytial	Airway	No	No	N/A
Rhino	Airway	No	No	N/A
Ebola	Airway	Yes	Yes	Yes
Measles	Airway	Yes	Yes	Yes
Mumps	Airway	Yes	Yes	Yes
Parvovirus	Airway	Yes	Yes	N/A
Rubella	Airway	Yes	Yes	Yes
Varicella	Airway	Yes	Yes	Yes
Variola	Airway	Yes	Yes	Yes
Noro	Gastrointestinal	No	No	
Rota	Gastrointestinal	No	No	No
Hepatitis A	Gastrointestinal	Yes	Yes	Yes
Polio	Gastrointestinal	Yes	Yes	Yes
Dengue fever	Blood	Yes	Yes	Yes
Hepatitis B	Blood	Yes	Yes	Yes
Yellow Fever	Blood	Yes	Yes	Yes

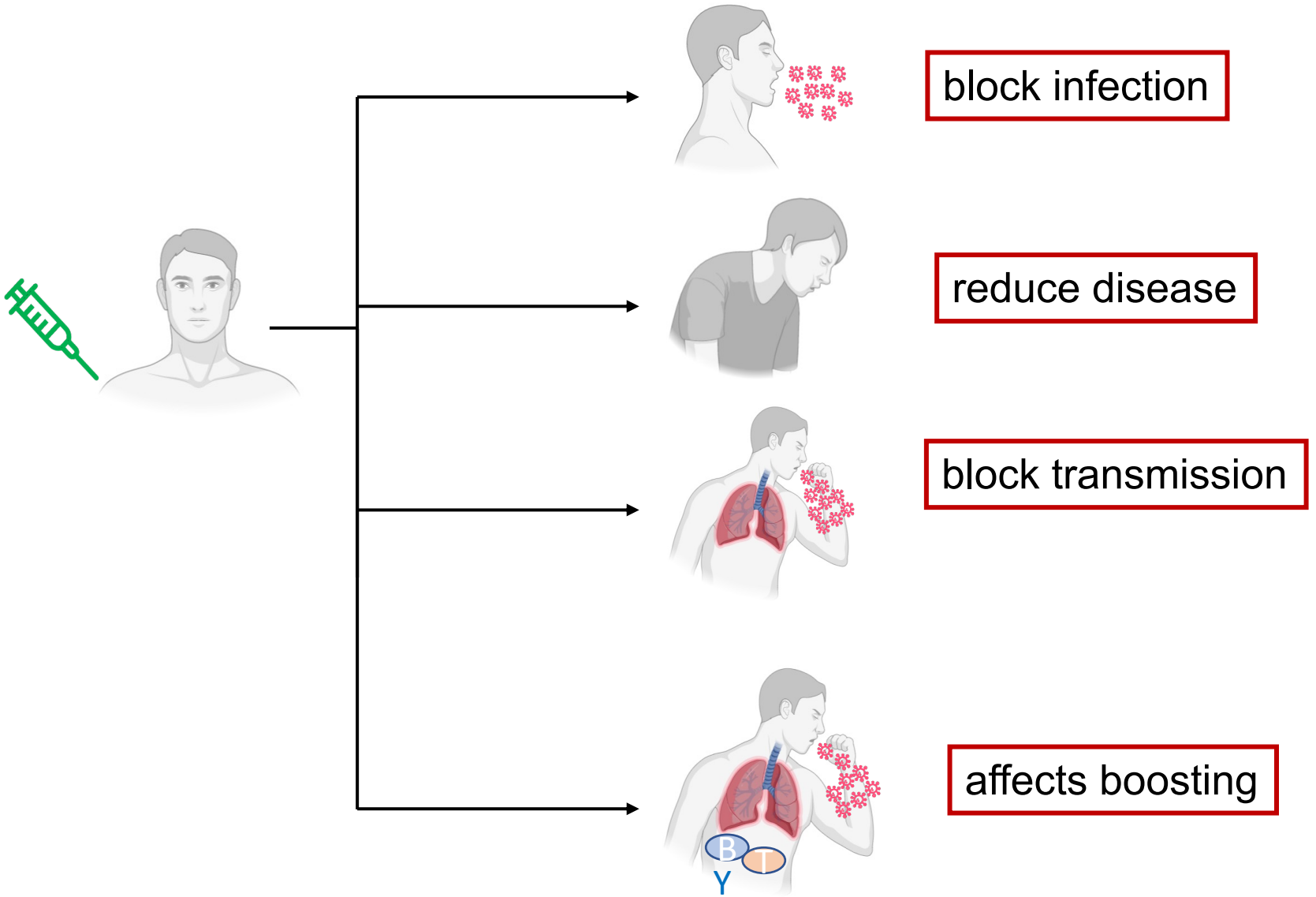
https://doi.org/10.1371/journal.ppat.1009509.t001

Yewdell PLOS pathogens 2020

Measures of immune efficacy

Immune efficacy IE

$$IE = 1 - RR$$



block infection

IE_S: Protection from infection

reduce disease

IE_P: Protection from disease

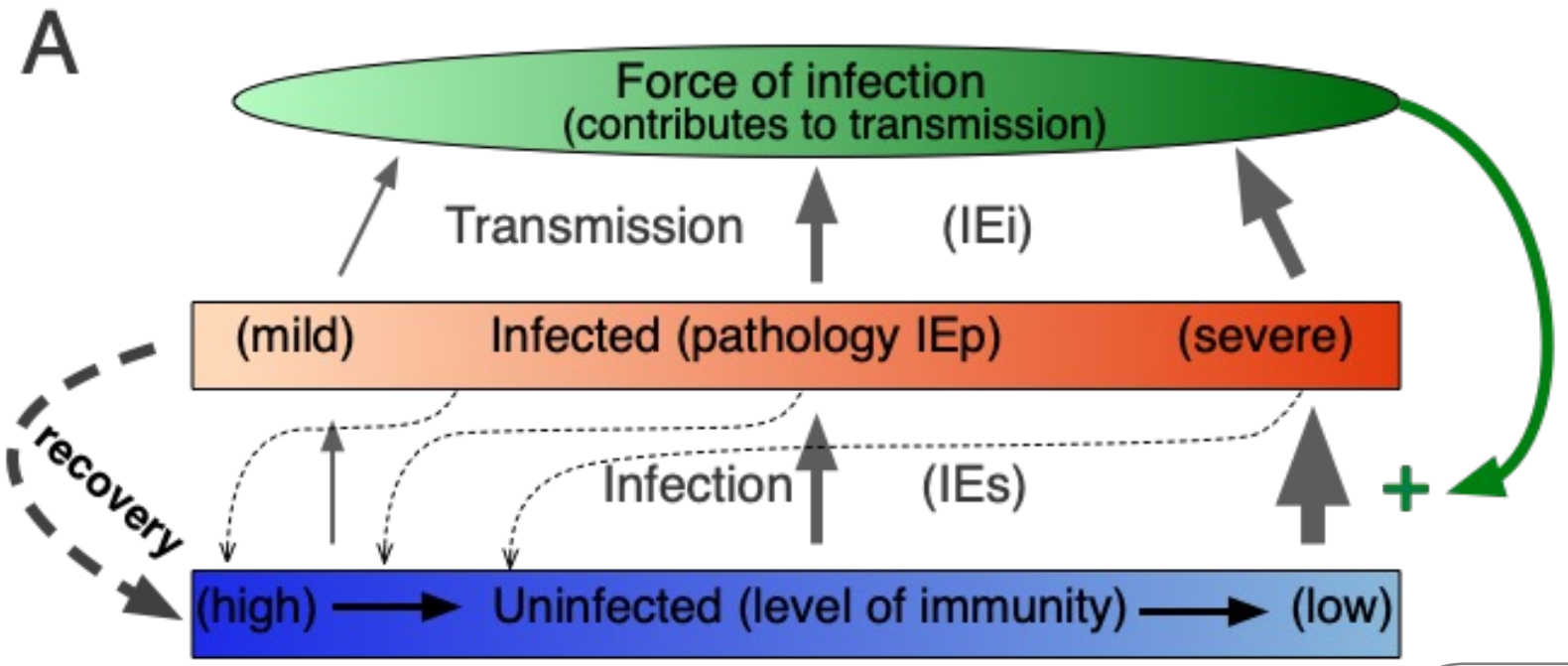
block transmission

IE_I: Reduction in transmission

affects boosting

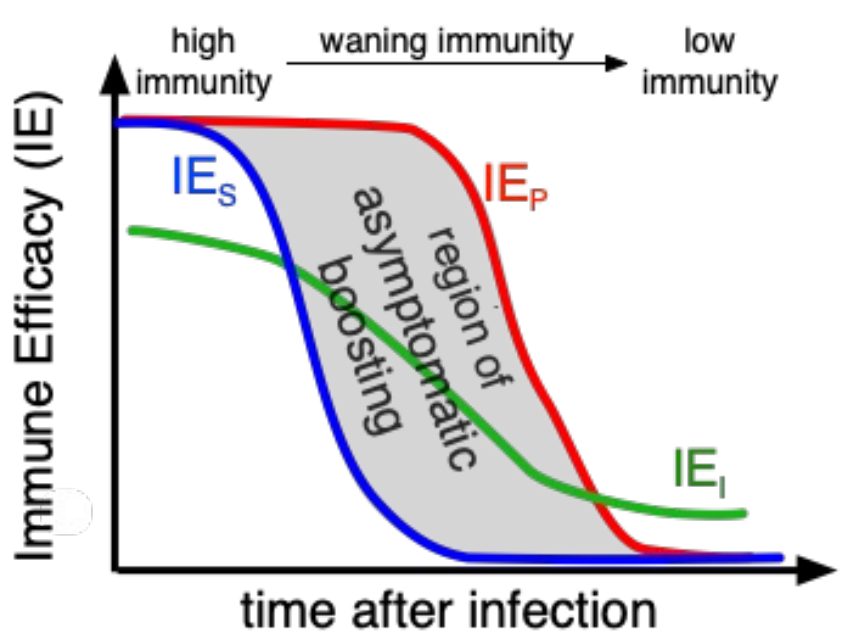
IE_B: Affect on boosting

Outline of the model



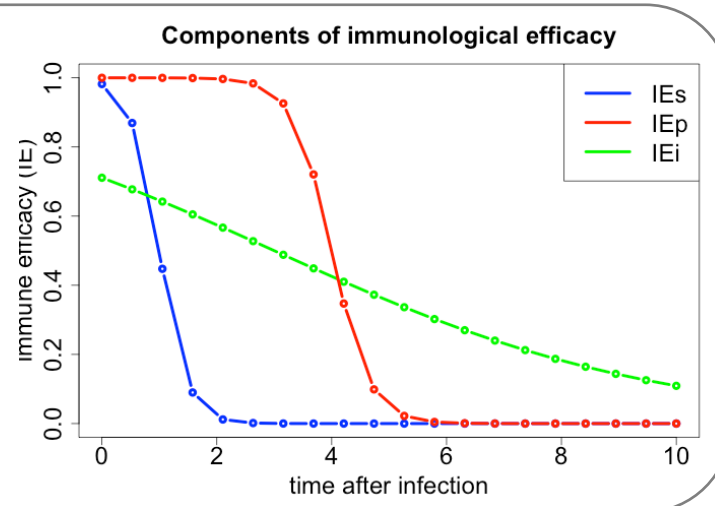
Level of immunity

immune waning
antigenic drift

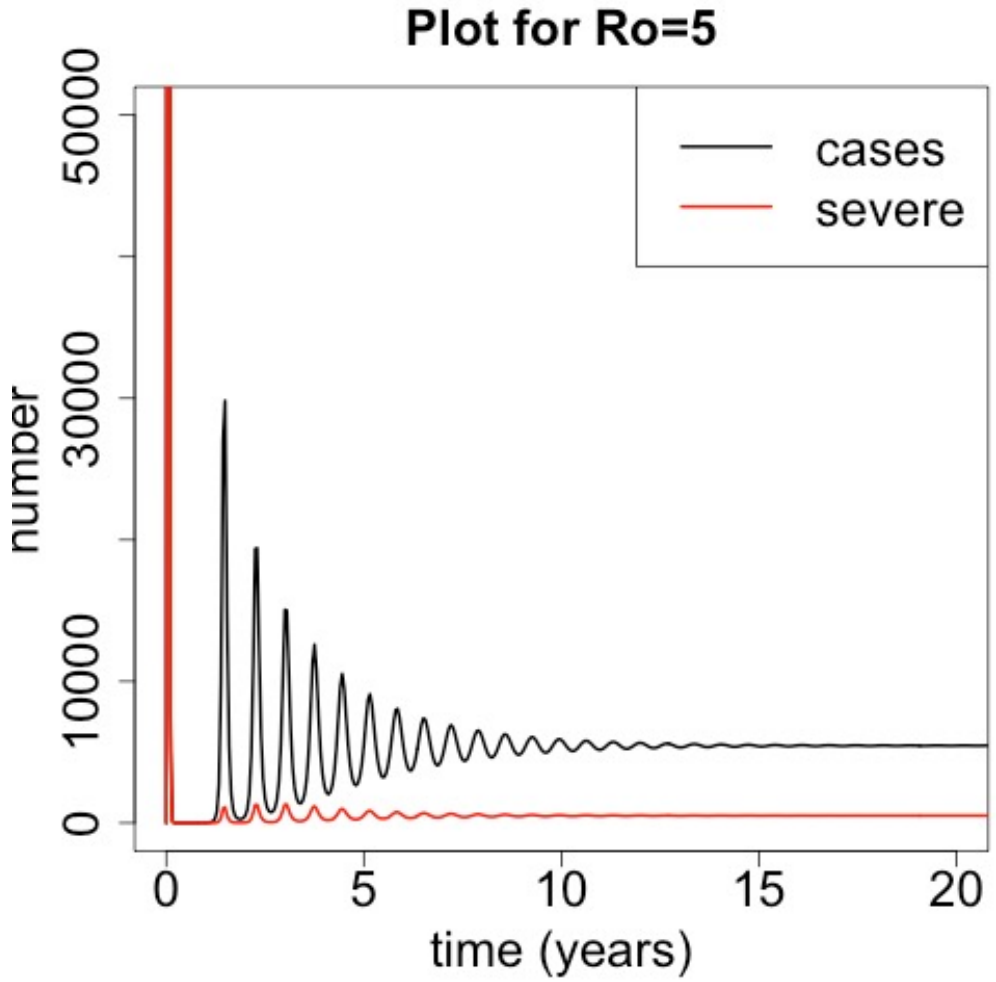


Acute infection

duration 4 days
Ro = 5
Const. pop size
(10^6 individuals)



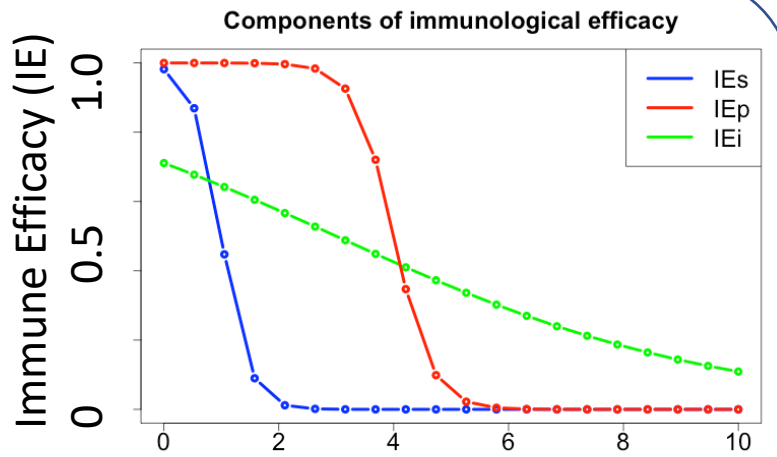
Transition from epidemic to endemicity



Transition from severe epidemic to relatively mild endemicity (as individuals acquire immunity against disease)

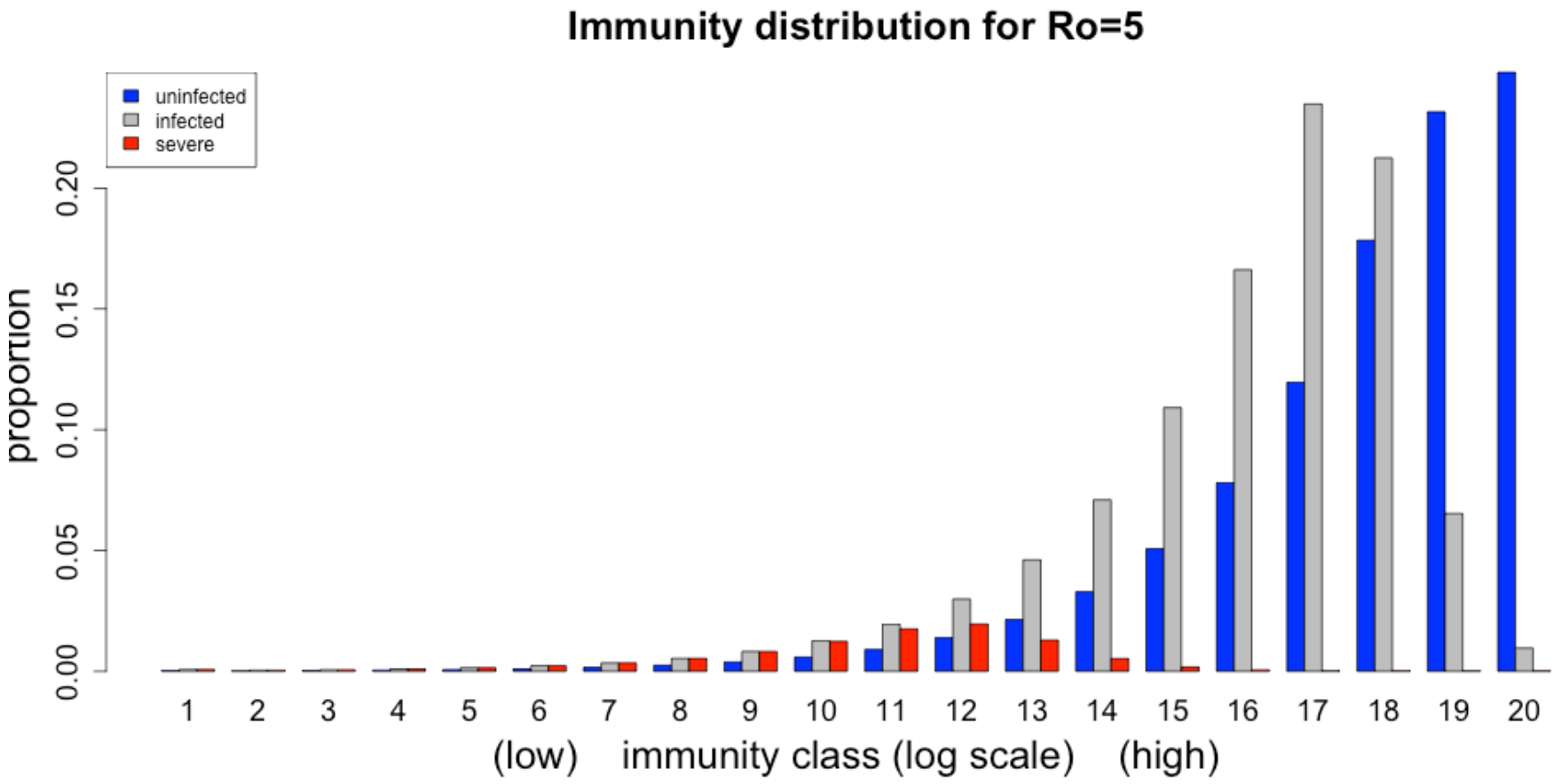
Acute infection

duration 4 days
Ro = 5
Const. pop size
(10^6 indiv)

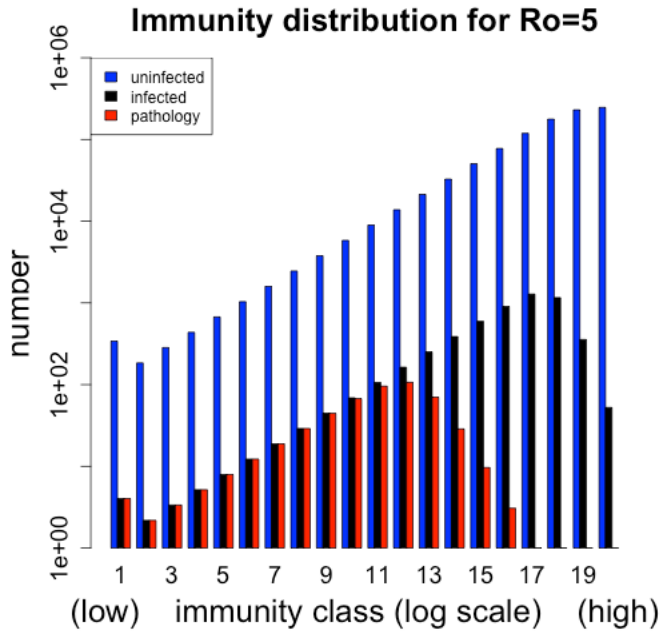


(high) immunity (low)

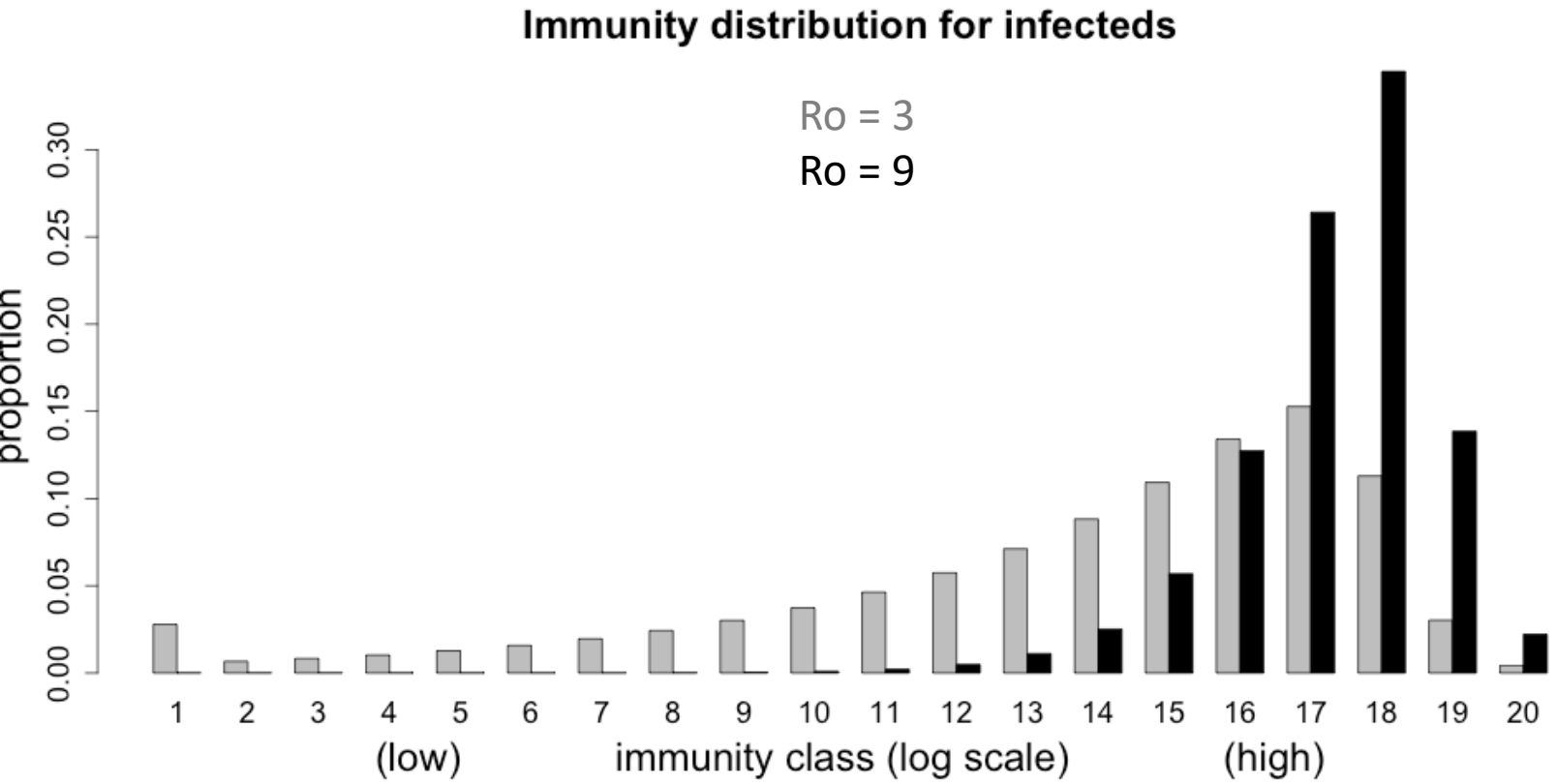
Distribution of immunity in the population



Cases:
uninfected
infected
severe



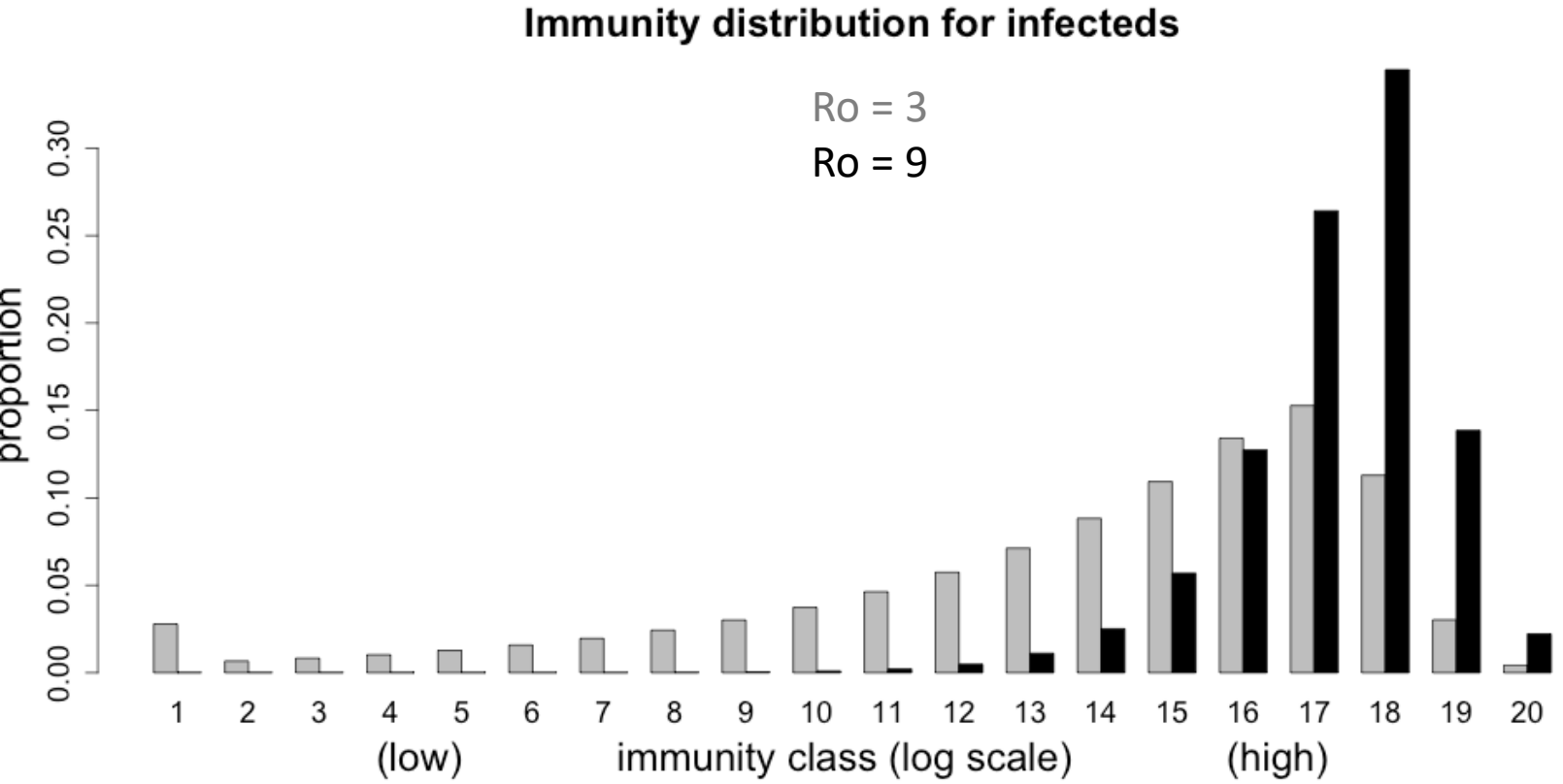
Comparison of infecteds for low and high Ro

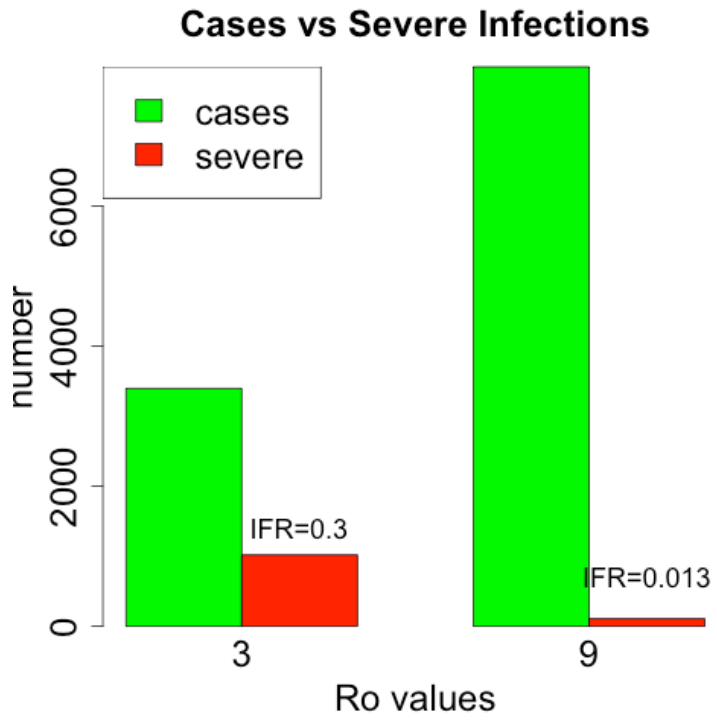


these infections will be severe

these infections will be mild

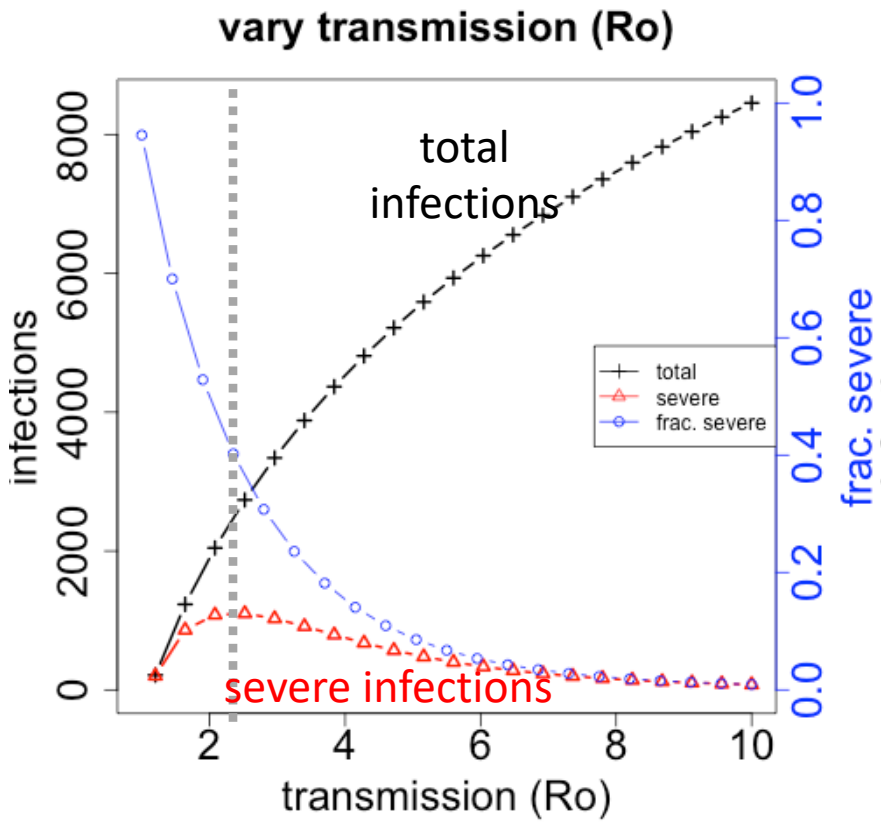
Comparison of infecteds for low and high Ro

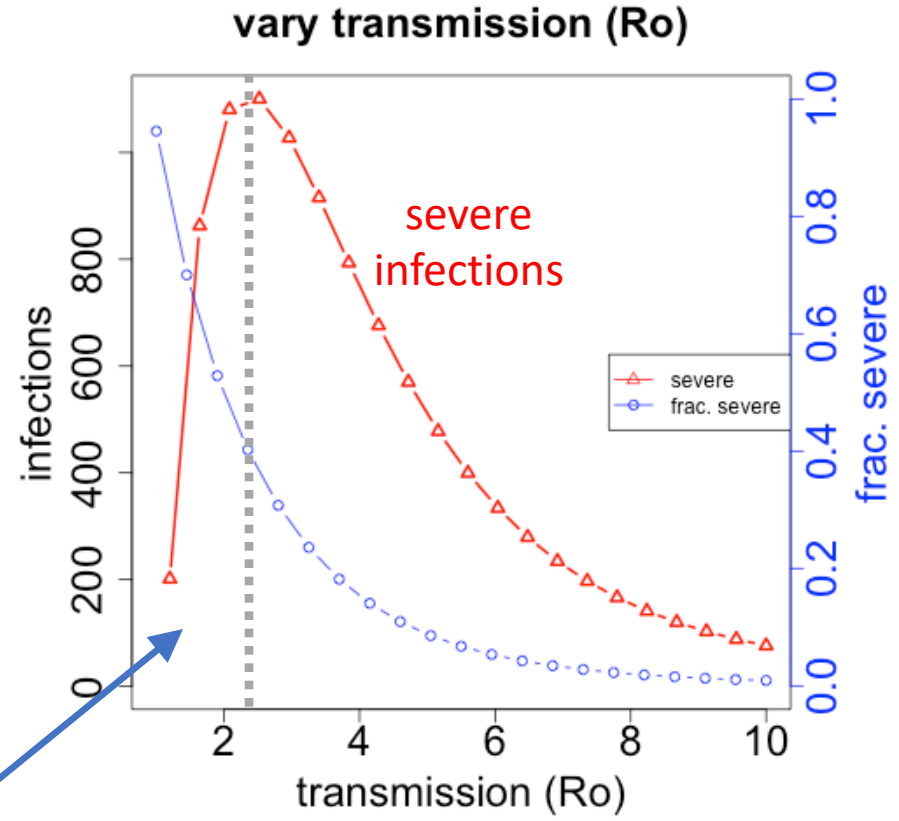




Increasing transmission
increases infection prevalence but decreases disease burden

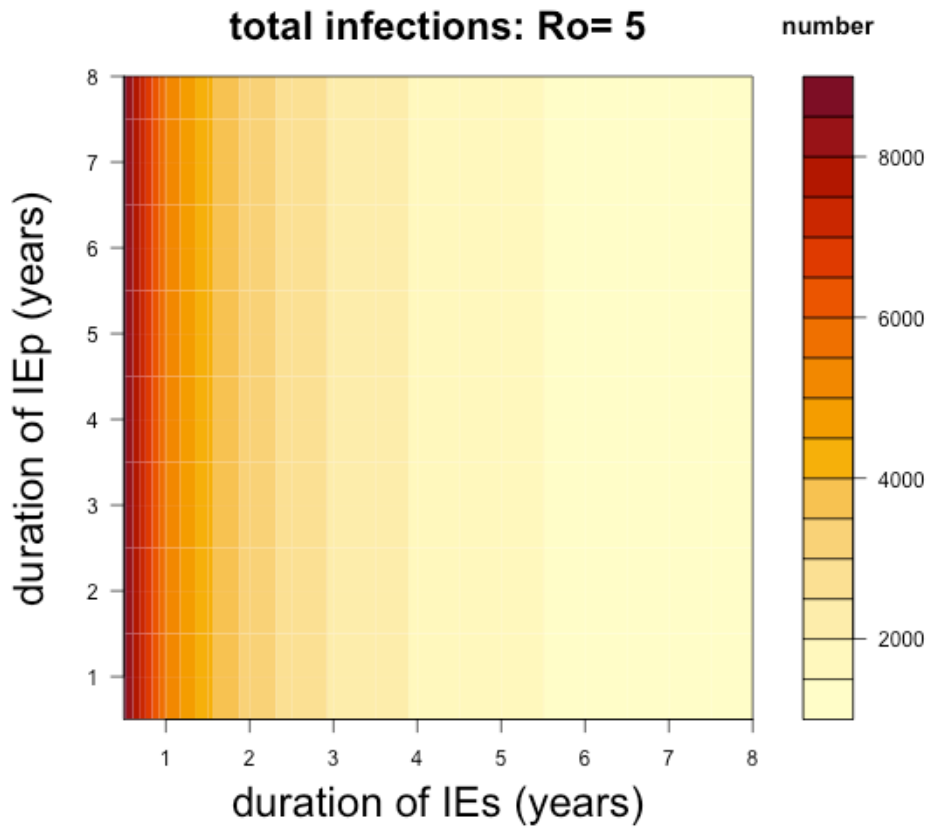
Relationship between transmission and disease

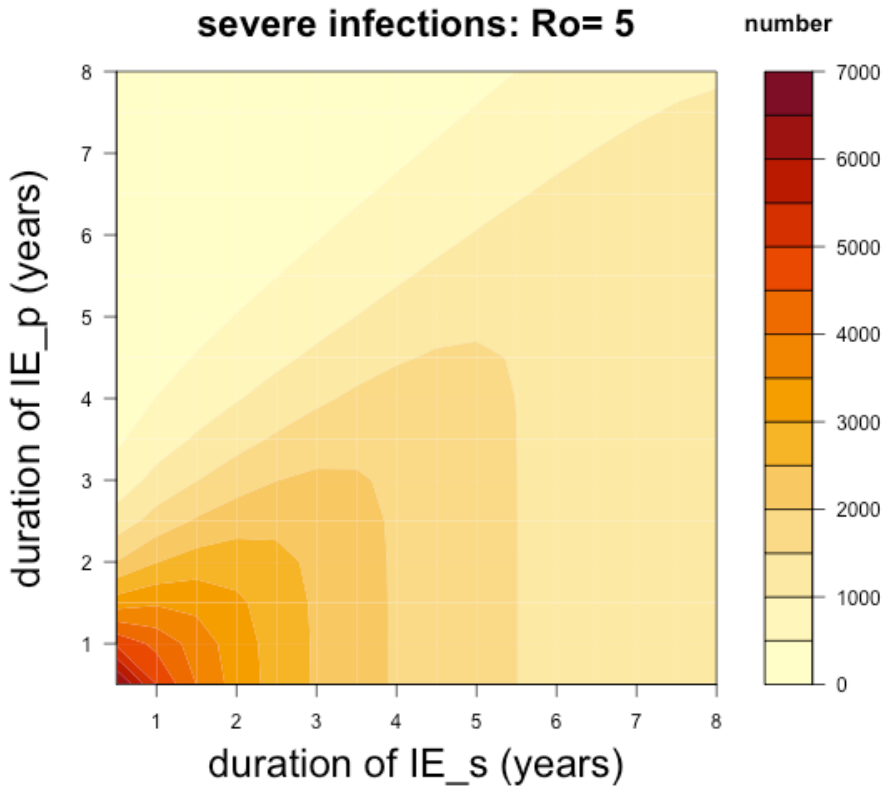




very low prevalence

Reduce susceptibility vs protection from disease





Implications for NPIs and vaccination

- For highly transmissible respiratory infections reducing transmission will reduce infection prevelance but **may** not reduce disease

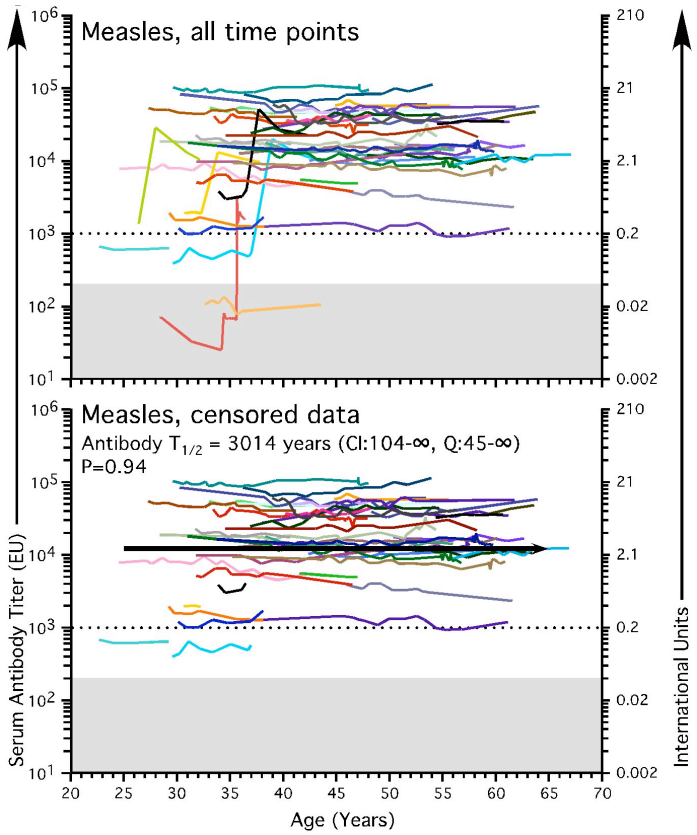
- Vaccines
  - Focus on reducing disease rather than reducing community transmission (herd immunity)
  - Focus on the vaccinating high-risk individuals
  - Natural infection automatically keeps immunity abreast with currently circulating strains

- Similar patterns have been suggested for Dengue (Nagao and Koelle 2008 PNAS)

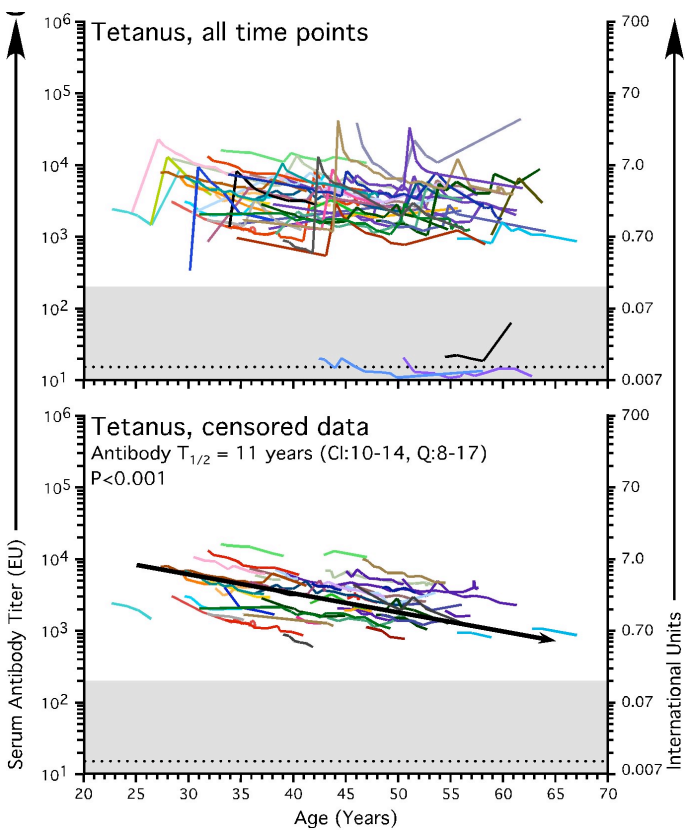
Waning of immunity

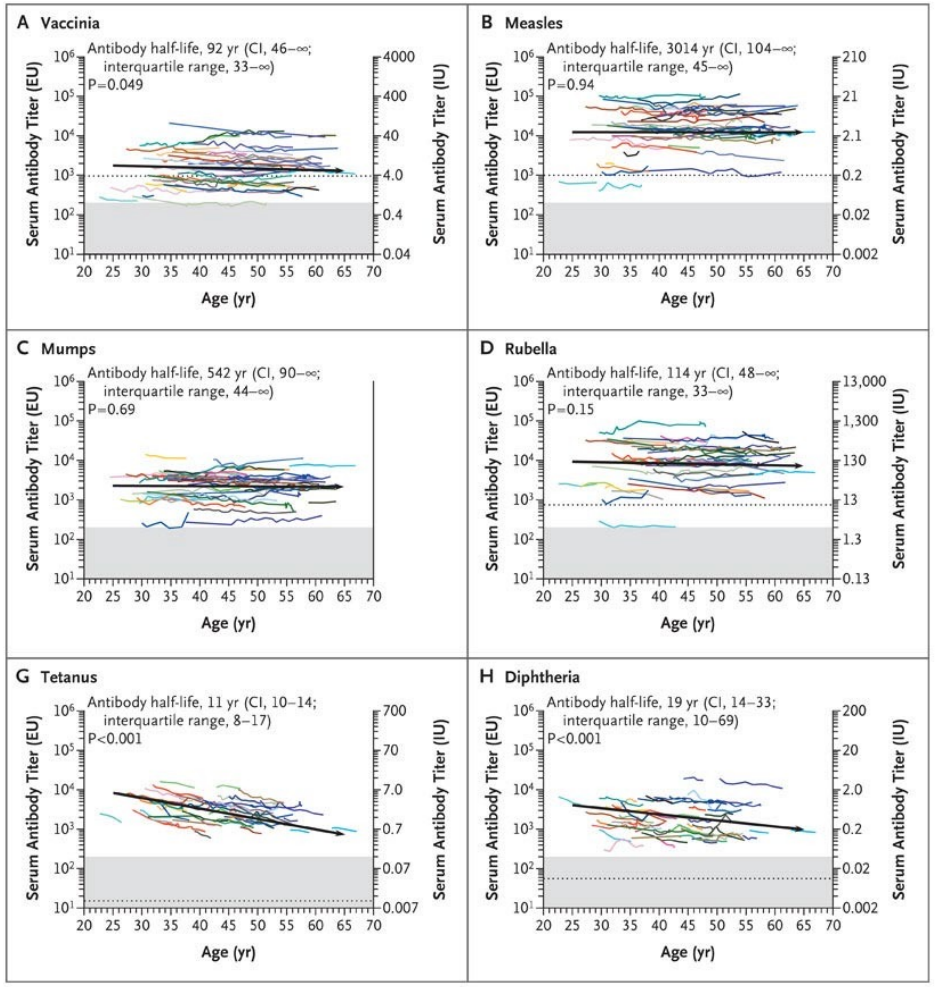
Quantifying the waning of immunity

Measles



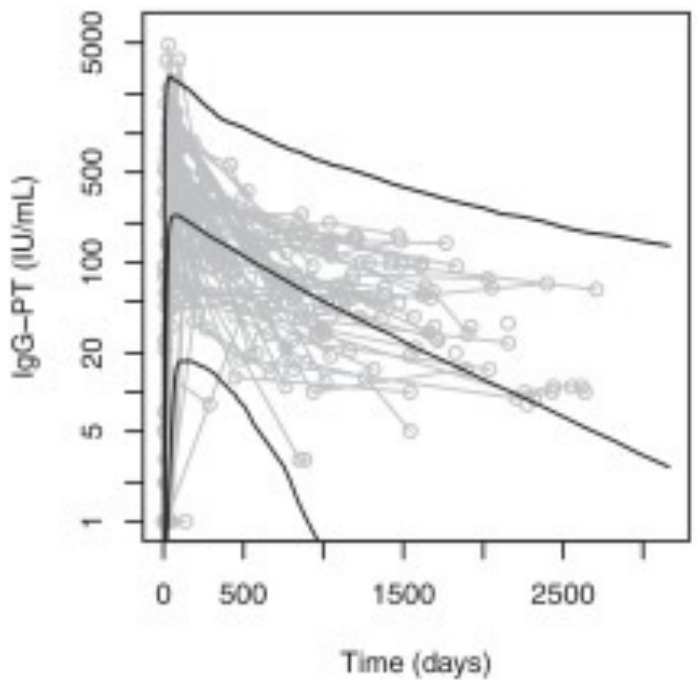
Tetanus



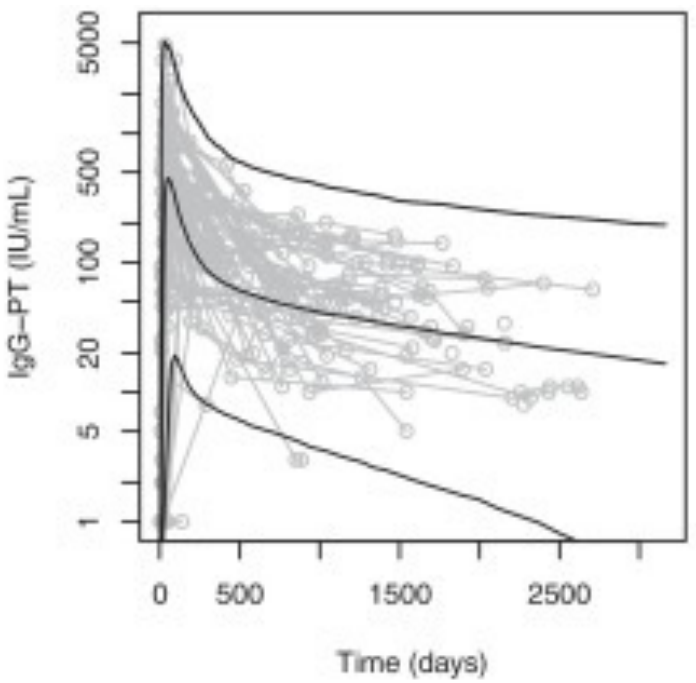


Amanna et al NEJM 2007

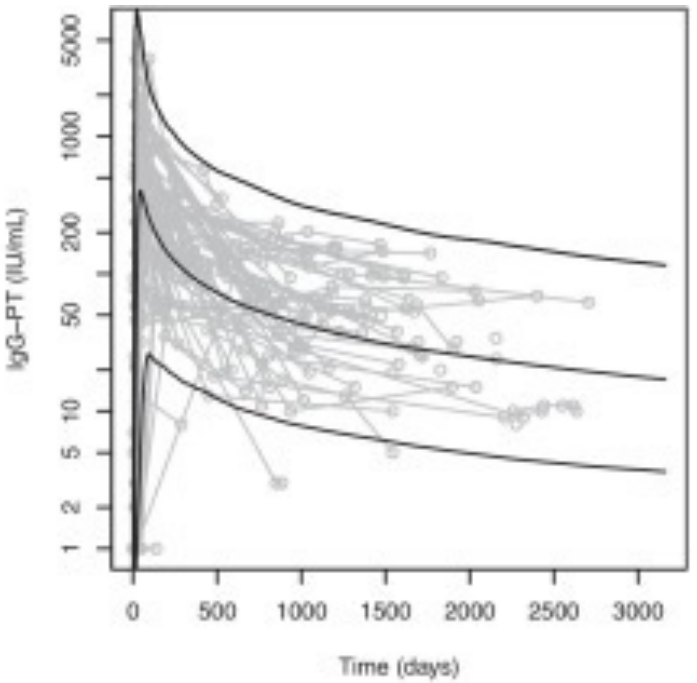
Teunis et al suggest waning follows a power-law



(a) Exponential decay



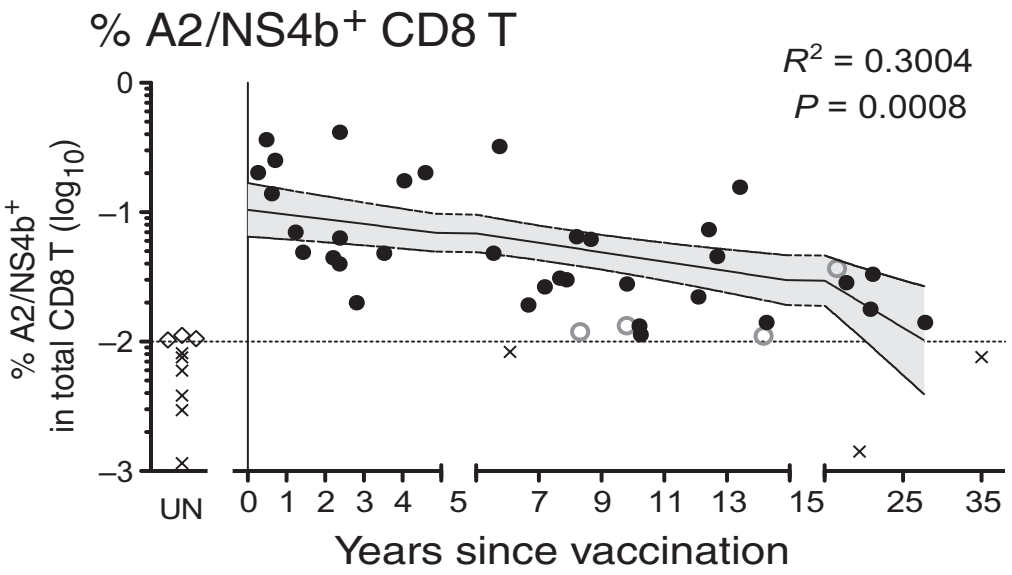
(b) Bi–exponential decay



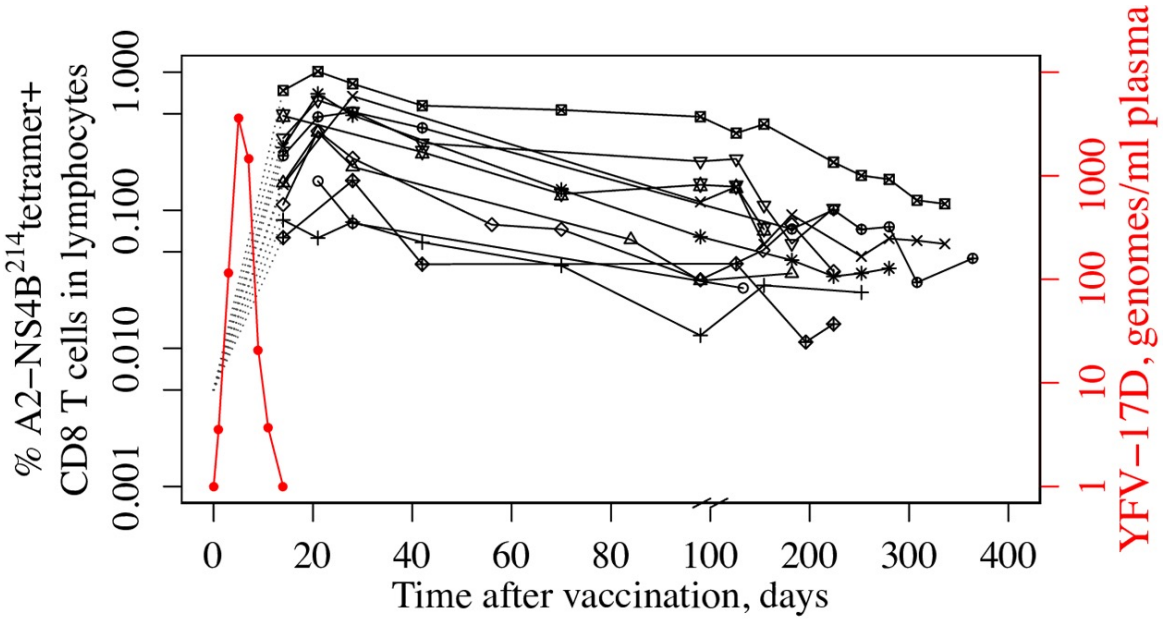
(c) Power function decay

Teunis et al Epidemics 2016

Waning of CD8 T cell immunity to YFV

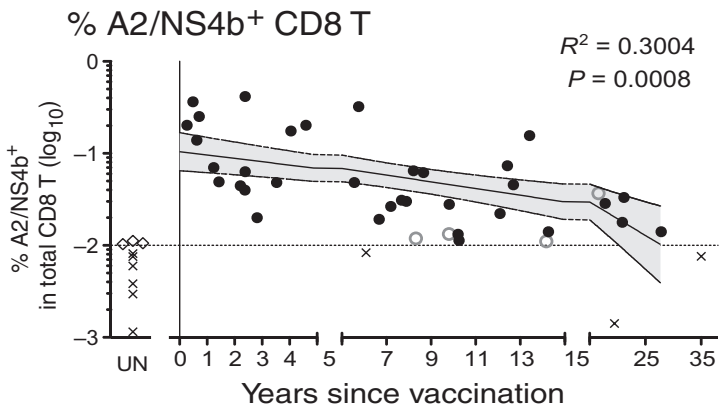


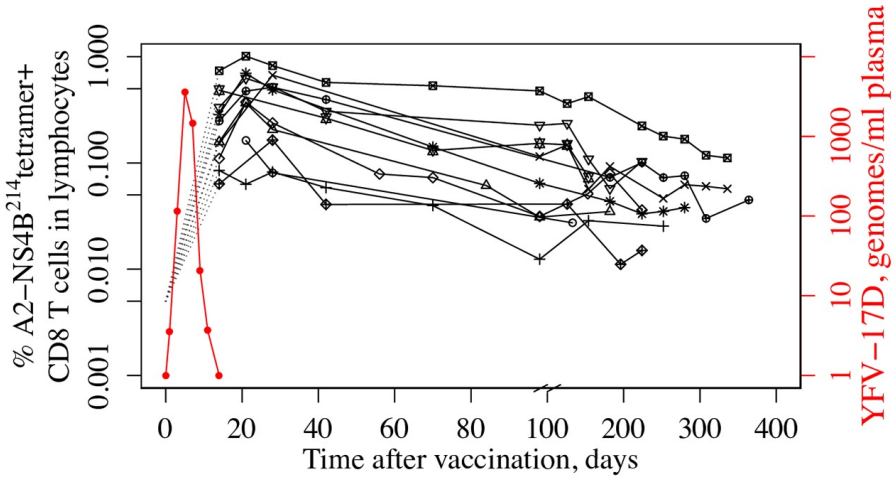
Fuertes Marraco et al 2014

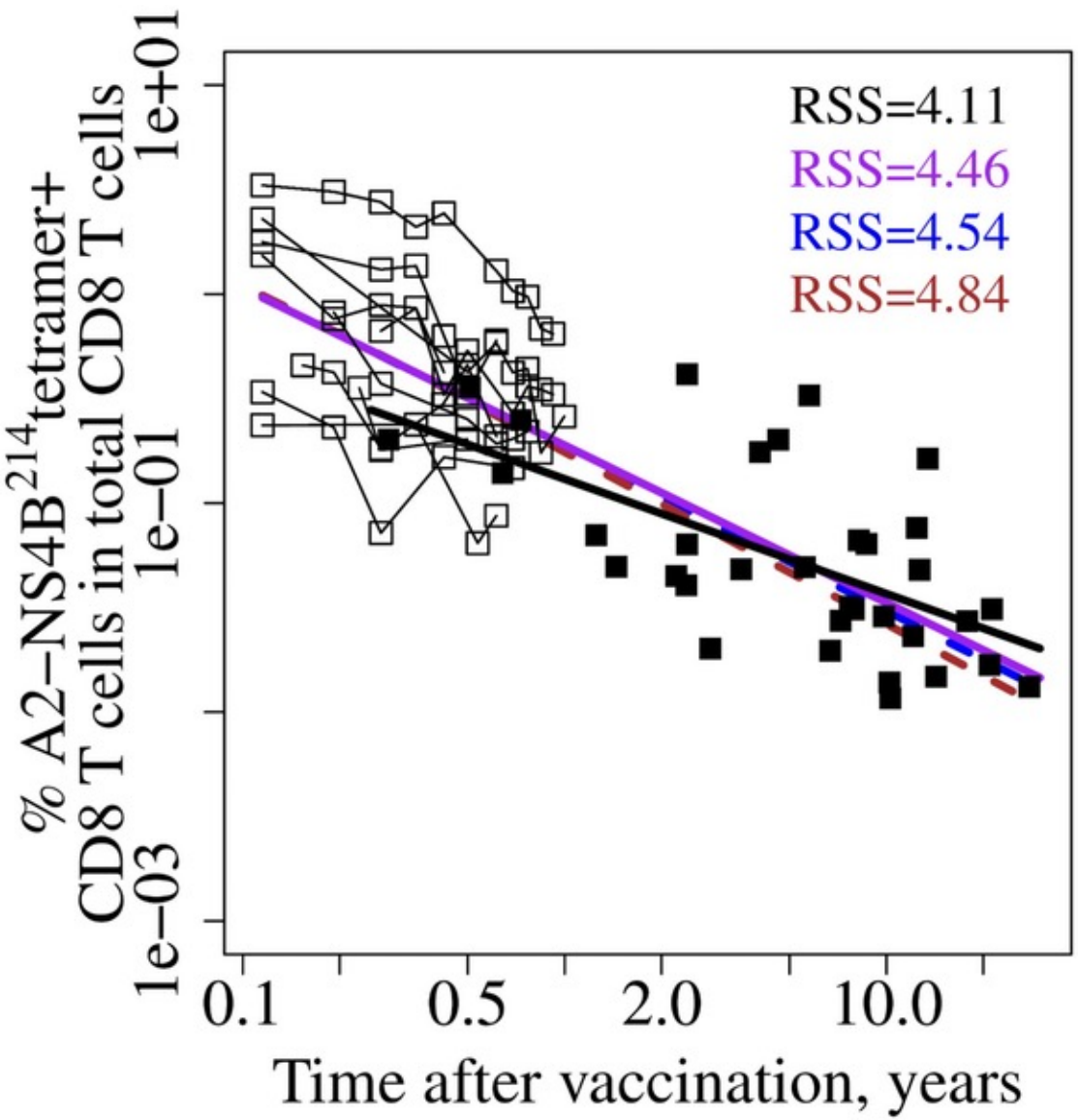


Akondy et al 2014

Power-laws work astonishingly well

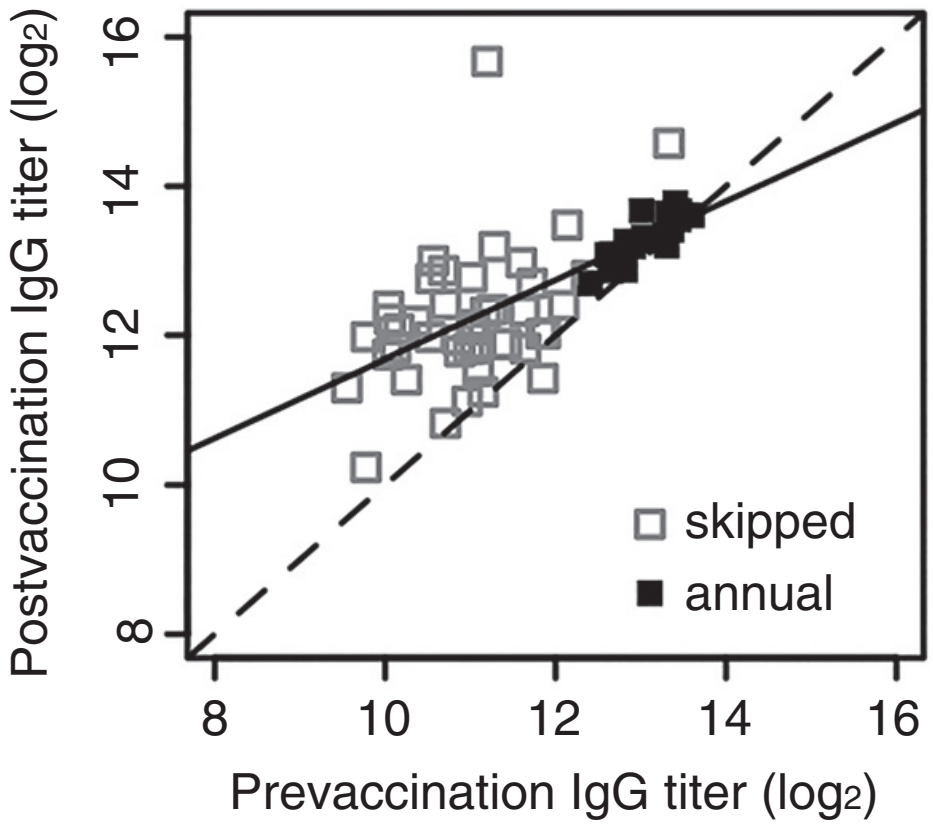






Zarnitsyna et al 2021 PLOS CB

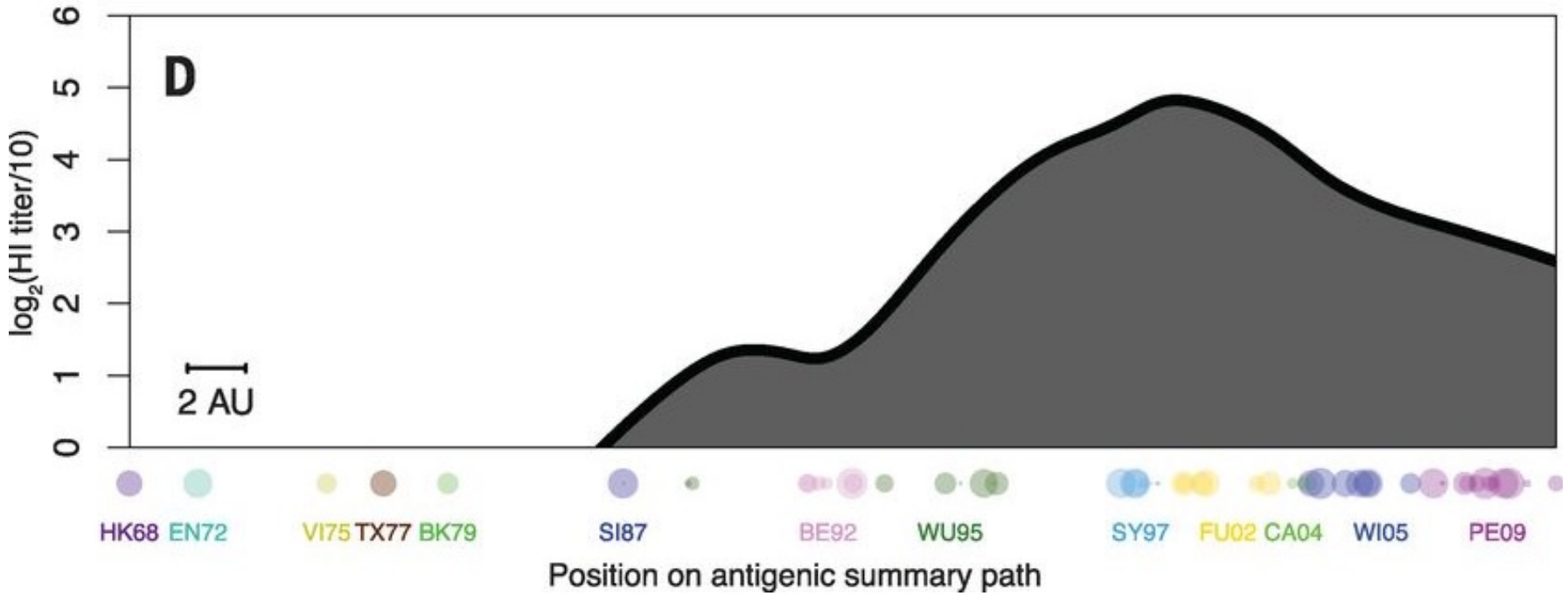
Boosting of immunity



Saturation in the magnitude of responses following vaccination with influenza

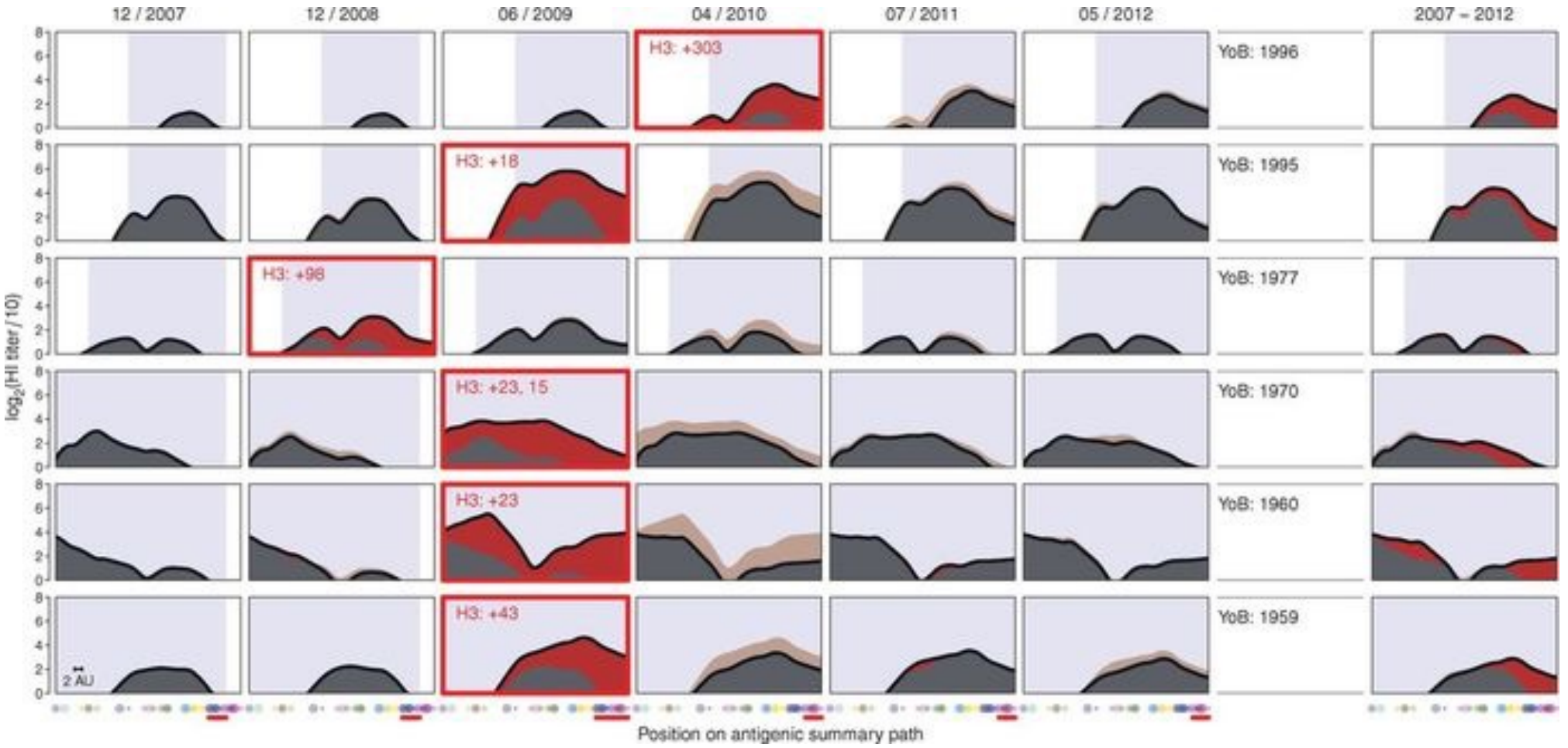
Linderman et al 2020 Cold Spring Harbor

Strain variation gives rise to complex patterns of boosting



Fonville et al 2014 Science

Strain variation gives rise to complex patterns of boosting



Fonville et al 2014 Science

Summary

- Responses to respiratory viruses show waning of immunity and reinfections
- It is important to consider different measures of protection (from infection vs disease)
- Reducing the force of infection will decrease the number of cases but may increase the frequency and number of severe infetions

- We are only just beginning to get a quantitative understand the immunological mechanisms for the waning and boosting of immunity to respiratory infections

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