

Conceptual models of cross-immunity, and practical applications

Jonathan Dushoff, McMaster University





Epidemics9, Nov 2023


Conceptual talk with practical goals

- ▶ How should we incorporate partial immunity into population-level modeling?
- ▶ Why does it matter?
- ▶ How much does it matter?


Model goals


- ▶ Theoretical
- ▶ Inference
- ▶ Forecasting
- ▶ Strategic


7:32    


← Poster presentation 

[P2.154] When purpose matters: Four goals of mechanistic modeling for public health

 Wednesday, Nov 29th 2023

 17:50 - 19:20

 Saved

 Note

View Abstract (text only)

Background and study aims


Models played a prominent role during the COVID-19 pandemic in orienting political decisions on public health interventions. This led to extensive media coverage of modeling outputs, sometimes in the form of intense controversies. The intensity of these debates can at least in part be attributed to confusion on what questions

Read all


Poster sessions





Nov 29th 17:50


Poster Session 2 1:30h



Speaker

 Justin Lessler



Some history

- ▶ Halloran, Longini and others (1991-93): Leaky and “polarized” vaccines
 - ▶ [*https://pubmed.ncbi.nlm.nih.gov/1899778/*](https://pubmed.ncbi.nlm.nih.gov/1899778/)
- ▶ Gog and Swinton (2002): status-based and history-based perspectives
 - ▶ [*https://pubmed.ncbi.nlm.nih.gov/11942531/*](https://pubmed.ncbi.nlm.nih.gov/11942531/)
- ▶ Gabriela Gomes (2005): reinfection thresholds
 - ▶ [*https://pubmed.ncbi.nlm.nih.gov/15967188/*](https://pubmed.ncbi.nlm.nih.gov/15967188/)

This project

- ▶ Dormant in my files for decades
- ▶ Jump-started by practical Covid questions from Michael (WZ) Li (Public Health Agency of Canada)
- ▶ Driven forward by Daniel (Sang Woo) Park
 - ▶ With help from Jess Metcalf and Bryan Grenfell
 - ▶ *<https://www.medrxiv.org/content/10.1101/2023.07.14.23292670>*

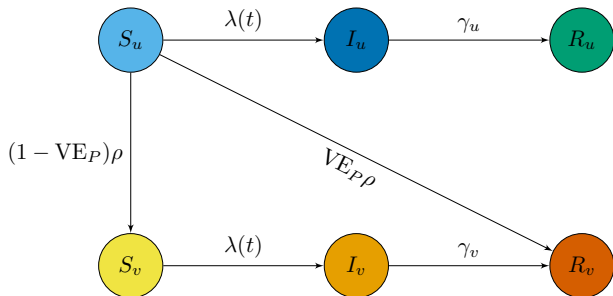
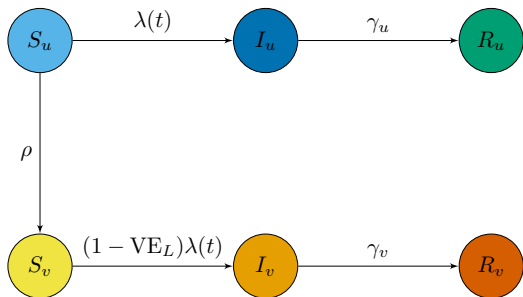
Partial protection

- ▶ Against which outcome?
 - ▶ Death or severe disease
 - ▶ Clinically attended disease
 - ▶ Measurable infection
 - ▶ *Transmission*
 - ▶ *Immune response*

Modeling partial protection

- ▶ Biological
 - ▶ Leaky vs. polarized
- ▶ Dynamical
 - ▶ History-based vs. status-based
- ▶ Link
 - ▶ With leaky protection we care what you've seen in the past (history)
 - ▶ With polarized protection, we care what your current state is (status)

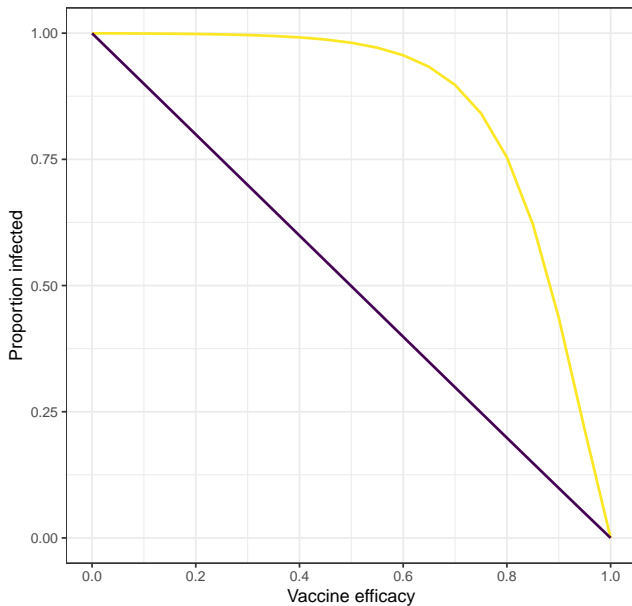
Modeling partial immunity



Why does it matter?

- ▶ Prediction
- ▶ Parameter estimation
- ▶ Planning





Epidemic size






Polarized model

- ▶ Also known as “all or none”:
 - ▶ Assumes that a substantial proportion of the population is completely unprotected
- ▶ Can be seen as a limit of broad distribution of susceptibilities


11:00





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← Presentation



 Thursday, Nov 30th 2023

 17:10 - 17:30

 Save

 Note

View Abstract (text only)

Background and Aims:

The ability for vaccines to protect against infectious diseases varies among individuals, but computational models employed to inform policy typically do not account for this variation. In such models, the effect of a vaccine on protection against infection or other outcomes is typically modelled in one of two ways. The “all-or-nothing” model

Read all


Session

Nov 30th
17:10


Session 16: Vaccination 2

Chair: Corey Peak

1:20h

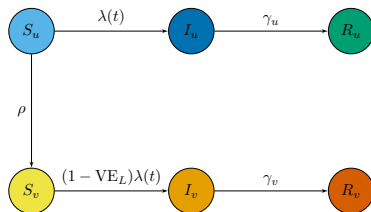


Speaker

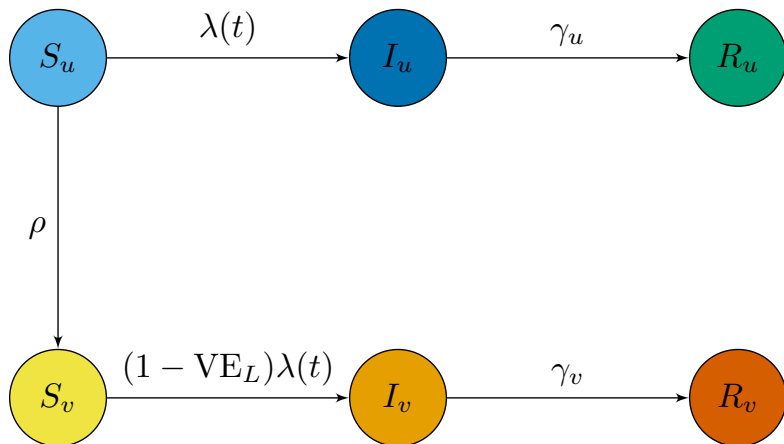
 Cameron Zachreson

Leaky model

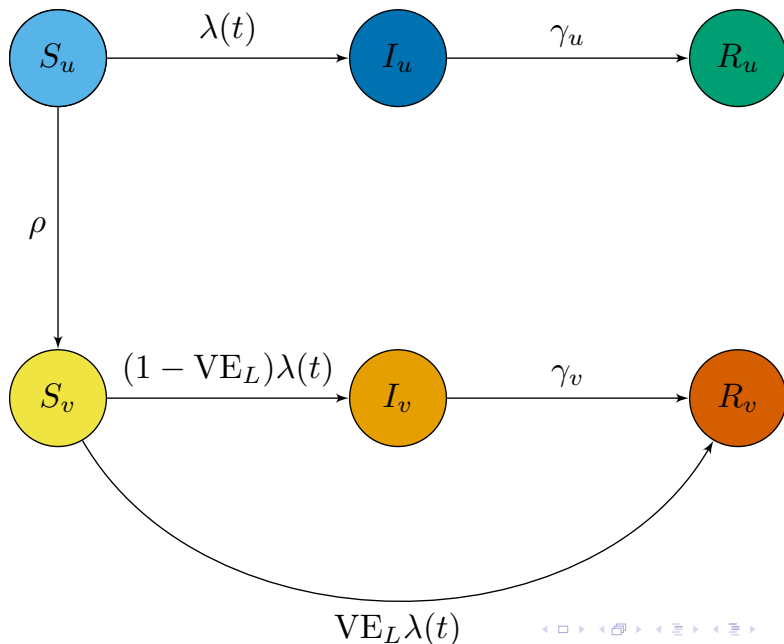
- ▶ The problem of phantom challenges
- ▶ We assume that these challenges happen, are beaten off, and have no effect
- ▶ I actively resist the flu, and then succumb to the same challenge next week!
- ▶ What if we don't do that?



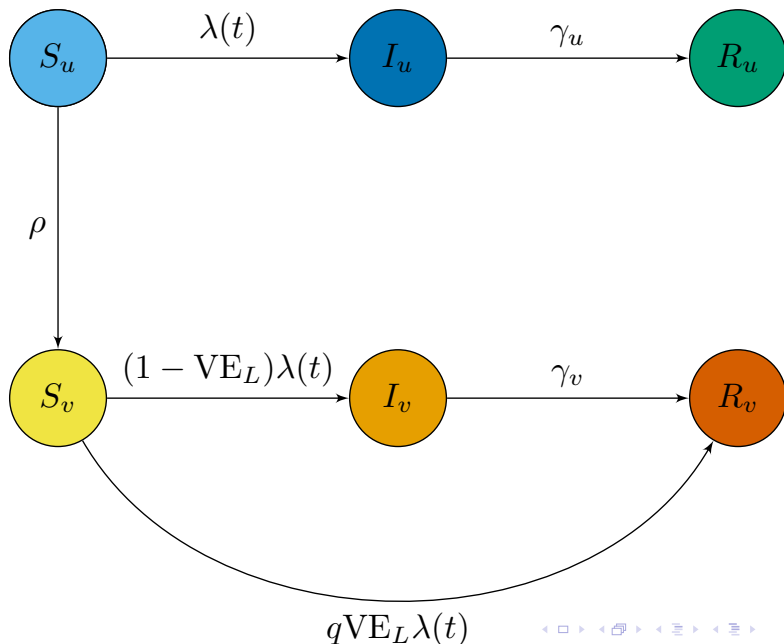
Leaky



Leaky with boosting



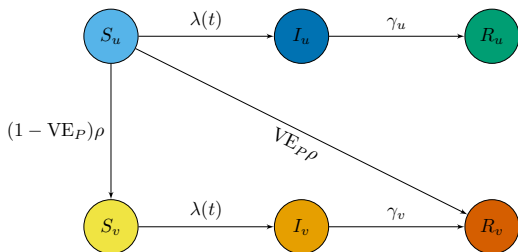
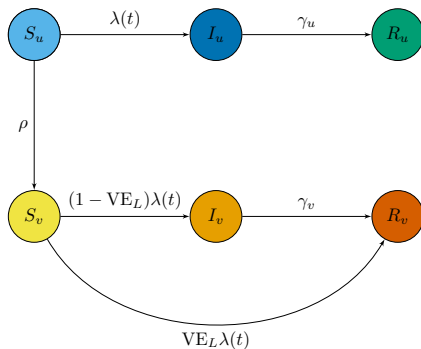
Leaky with partial boosting [corrected]



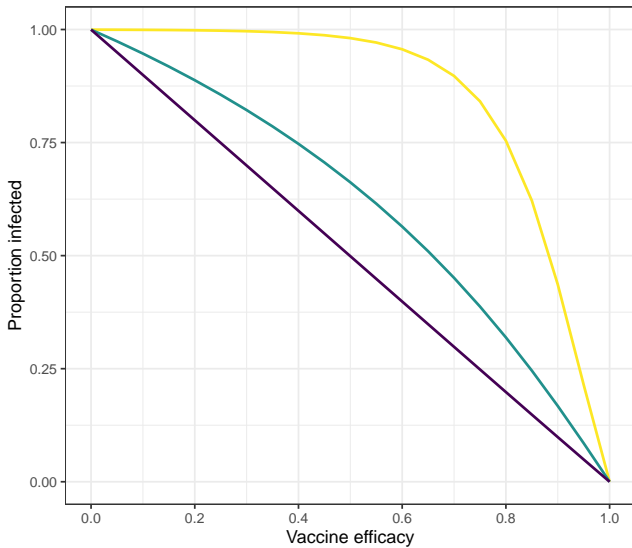
The dynamicist's perspective

- ▶ Dynamical systems have shortcuts and dualities
- ▶ If your immunity is leaky, but is reliably boosted by challenges
...
- ▶ The modeler can “decide” your fate when you recover
 - ▶ This is a system with equivalent dynamics

Leaky with boosting v. polarized

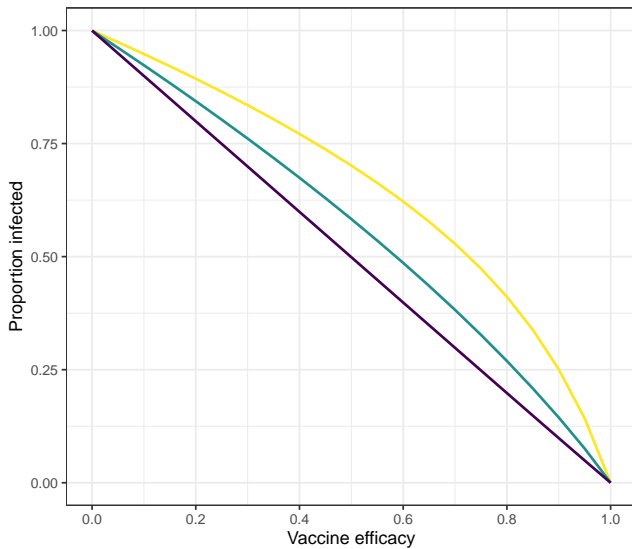


Leaky



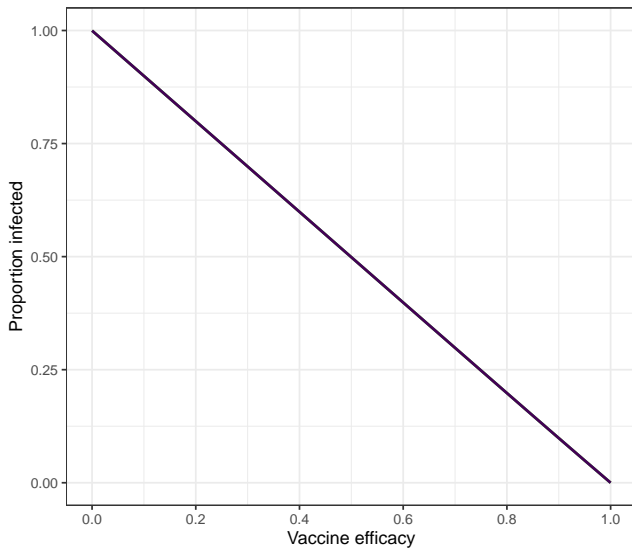
Boosting proportion — 0 — 0.5 — 1

Mixed



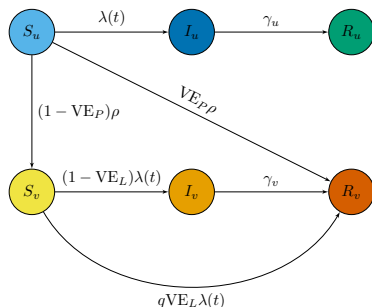
Boosting proportion — 0 — 0.5 — 1

Polarized



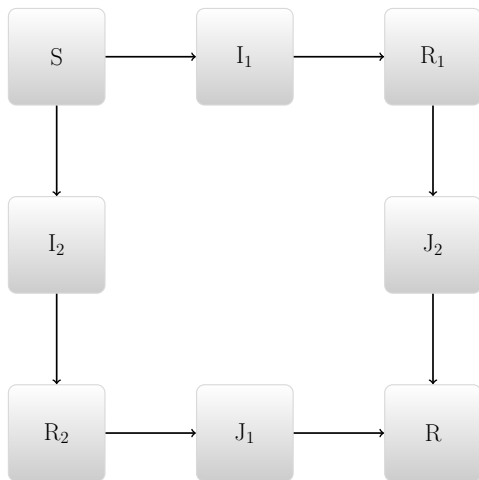
Boosting proportion 0 0.5 1

Transmission reduction

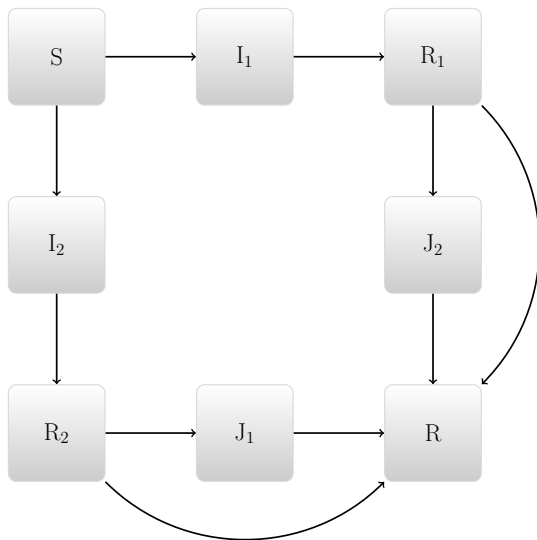


- ▶ If all breakthrough infections go through the I_v box, but only transmit a fraction q , dynamics are unchanged
- ▶ In the deterministic case!

Interacting strains



Interacting strains with boosting



Deterministic coexistence

- ▶ As long as both strains can invade:



$$R_{\text{inv}}(1/R_{\text{res}} + \varepsilon(1 - 1/R_{\text{res}})) > 1$$

- ▶ Depends only on parameters (not on paradigm) ...
- ▶ but how are they estimated?

Stochastic coexistence

- ▶ Leaky dynamics lead to giant epidemics
- ▶ Lots of overshoot
- ▶ Greater likelihood of stochastic extinction
- ▶ Probably

Estimating parameters is practically hard

- ▶ Cobey presentation
 - ▶ Antigenic evolution is extremely complicated
 - ▶ Immune responses as well

11:06

Presentation

Wednesday, Nov 29th 2023

09:10 - 09:50

Save

Note

View Abstract (text only)

Vaccination is a popular strategy to control pathogens, and yet vaccine performance remains difficult to explain. The less than stellar protection conferred by seasonal influenza vaccines is often attributed to the challenge of matching vaccine strains to strains that will be circulating after the vaccine is distributed. Evidence has been accumulating for decades that past infections and vaccinations also

Read all

Session

Nov 29th 09:10

[INV02] Impacts of vaccinating against influenza

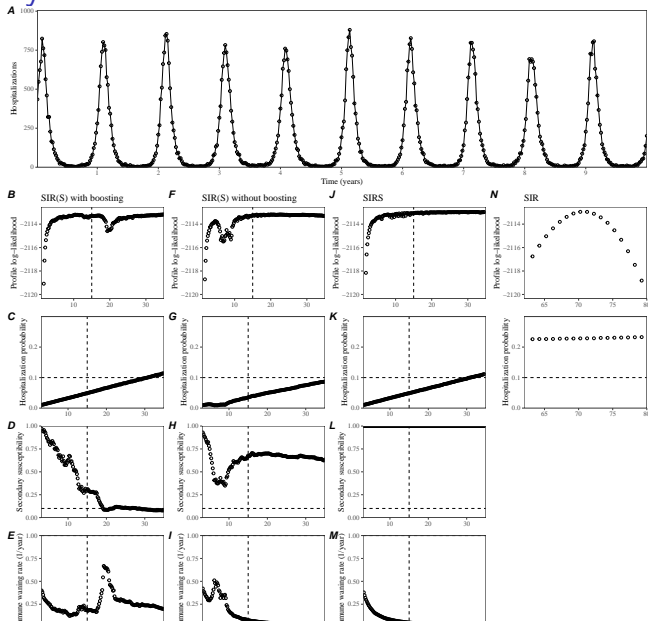
Chairs: Cecile Viboud, Joseph Wu, Katrina Lythgoe

0:40h

Speaker

Sarah Cobey
University of Chicago, USA

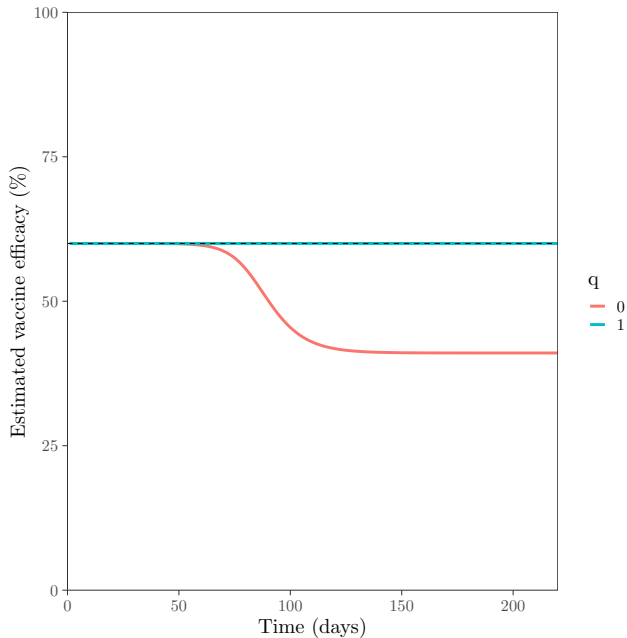
Estimating parameters from population-level data is intrinsically hard



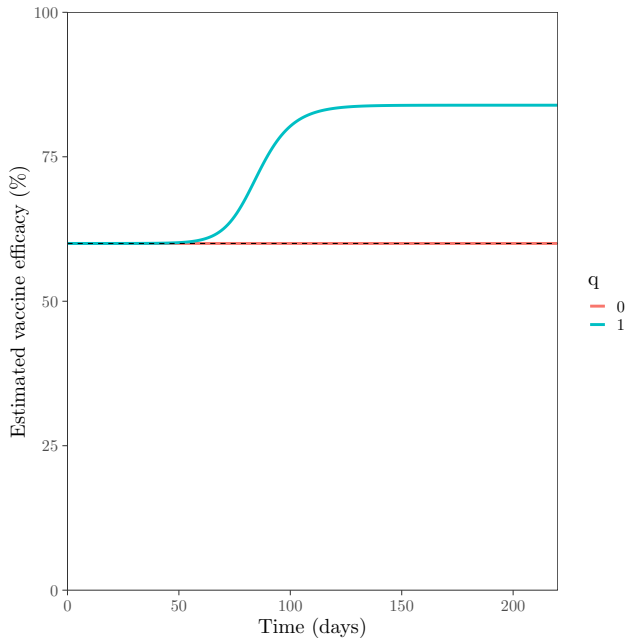
Individual-level inference depends on paradigm

- ▶ Co-existence doesn't depend on leaky vs. polarized *once parameters are known*
- ▶ But *effective* cross immunity will differ
- ▶ So *estimates* will depend on immune assumptions
 - ▶ Leaky protection matches instantaneous hazard
 - ▶ Polarized protection matches cumulative hazard

Incidence-based cross-protection



Hazard-based cross-protection



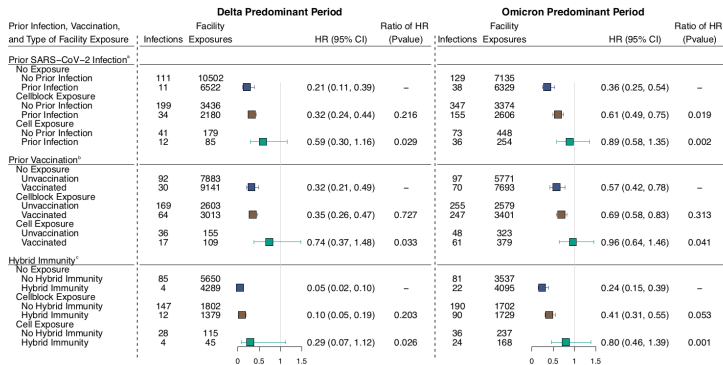
Skimming the surface

- ▶ Relationship to serology
- ▶ Different outcomes (severe illness)
- ▶ Immune waning

Thanks

- ▶ Organizers and audience
- ▶ Daniel, Mike and other collaborators
- ▶ PHAC, CIHR

Connecticut correctional study



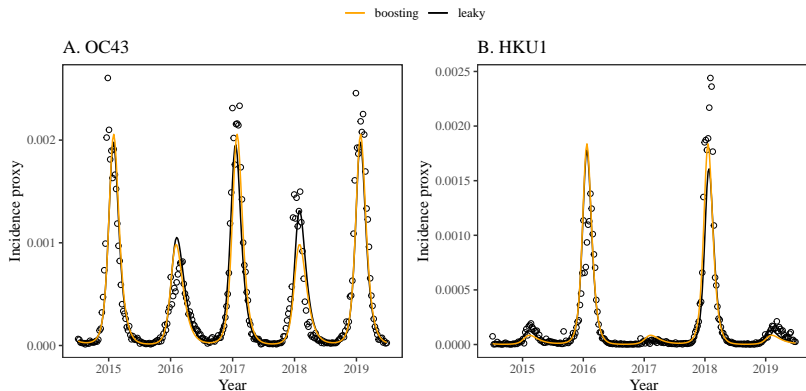
Lind et al., Nat Commun, 2023.

<https://doi.org/10.1038/s41467-023-40750-8>

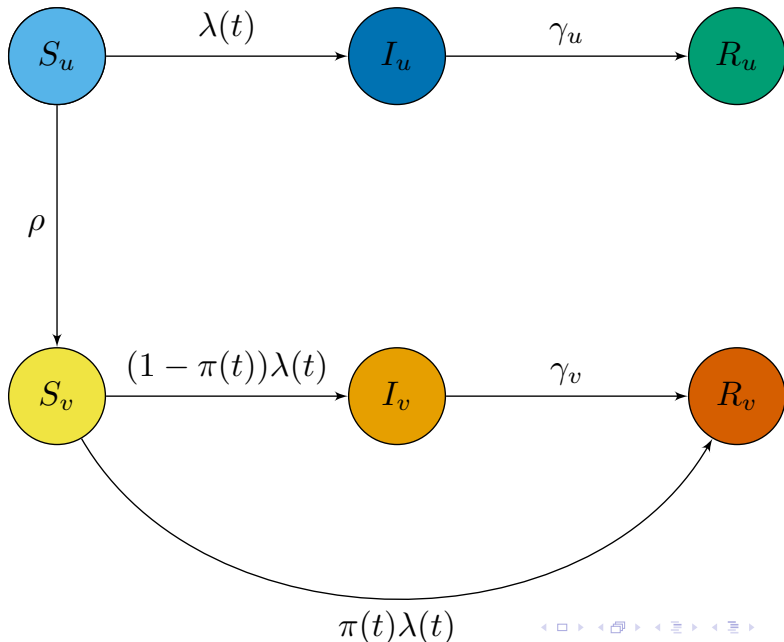
Time scales of challenge

- ▶ Challenges a week apart are likely antagonistic
 - ▶ Immune boosting, polarized-like dynamics
- ▶ Challenges an hour apart are likely *synergistic*
 - ▶ Potentially overwhelming, leaky-like dynamics
- ▶ Work on getting lessons from individual-level models

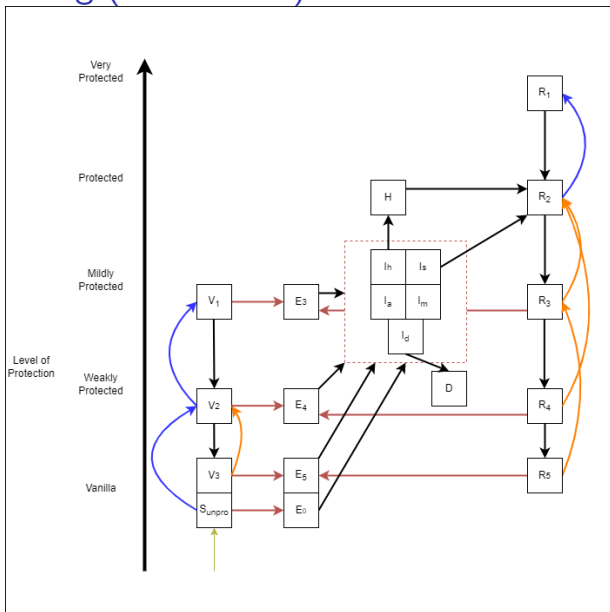
Coronavirus fits



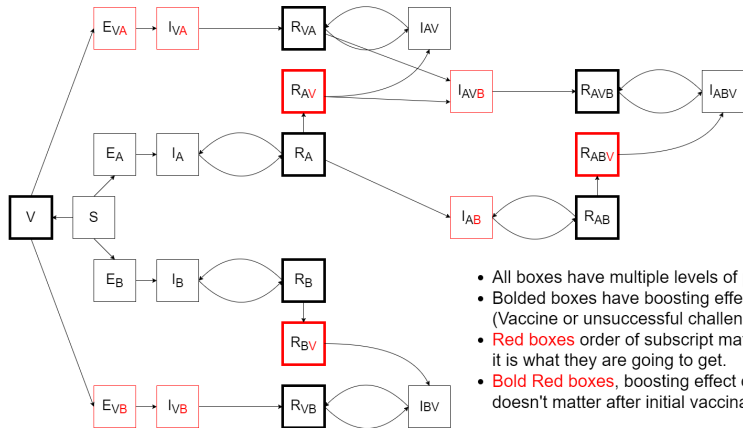
Dose dependence



Immune waning (whiteboard)



Cross immunity (whiteboard)



- All boxes have multiple levels of protection
- Bolded boxes have boosting effect (Vaccine or unsuccessful challenge)
- Red boxes order of subscript matters and it is what they are going to get.
- Bold Red boxes, boosting effect order doesn't matter after initial vaccination.

Michael WZ Li, PHAC