Conceptual models of cross-immunity, and practical applications

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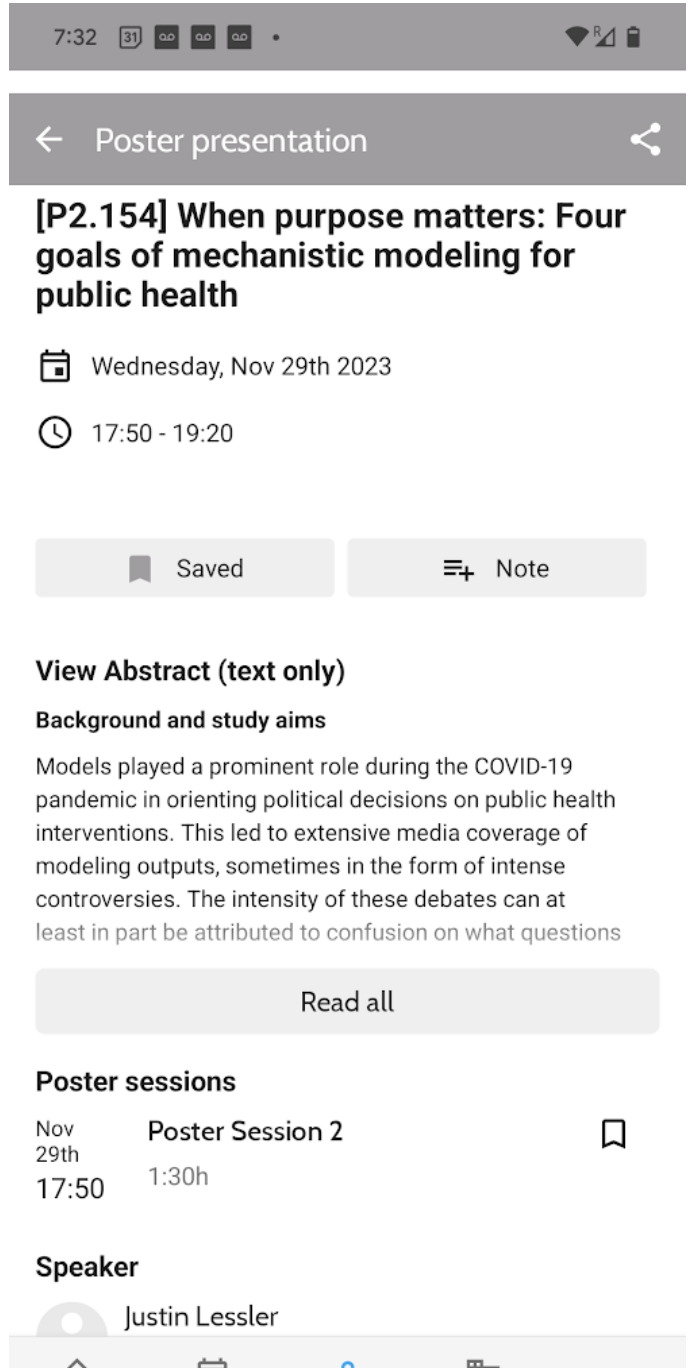
Epidemics9, Nov 2023

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



Some history

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

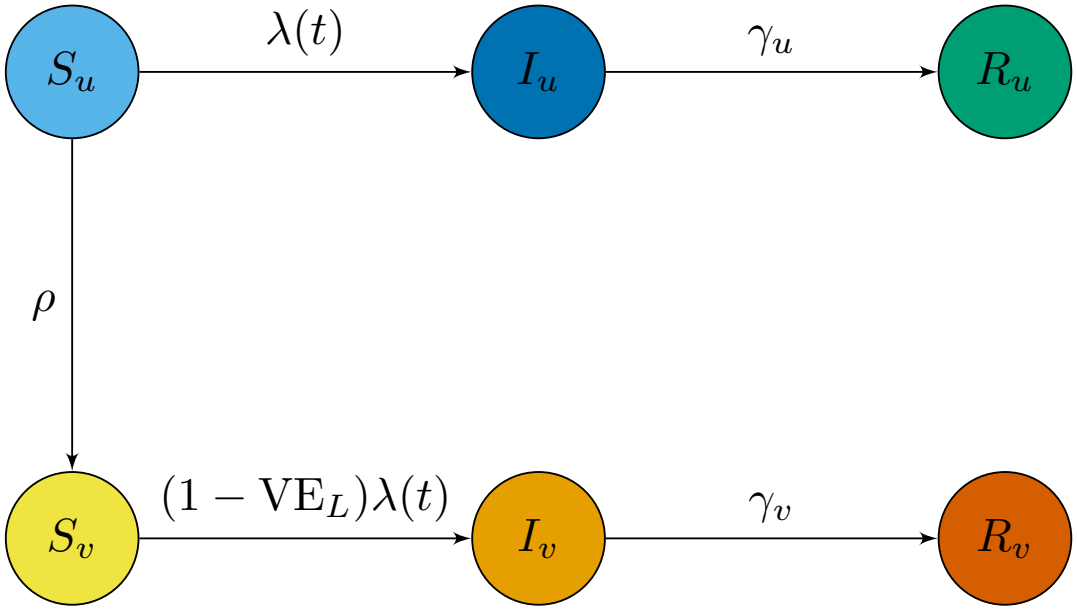
Partial protection

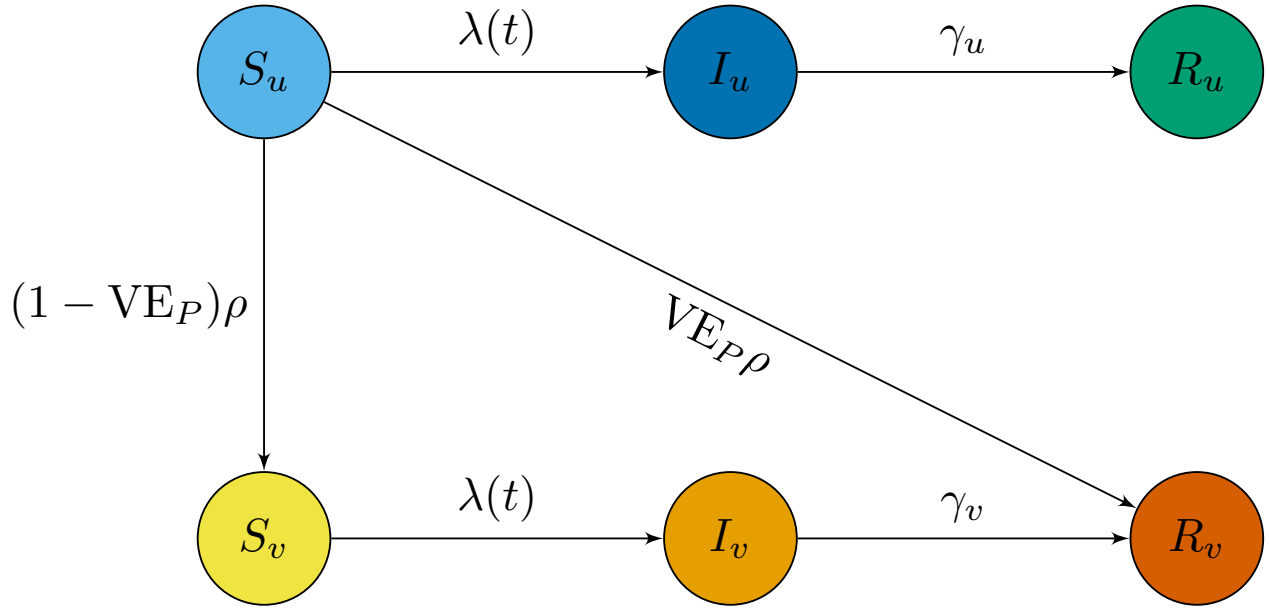
- Against which outcome?
  - Death or severe disease
  - Clinically attended disease
  - Measurable infection
  - *Transmission*
  - *Immune response*

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)

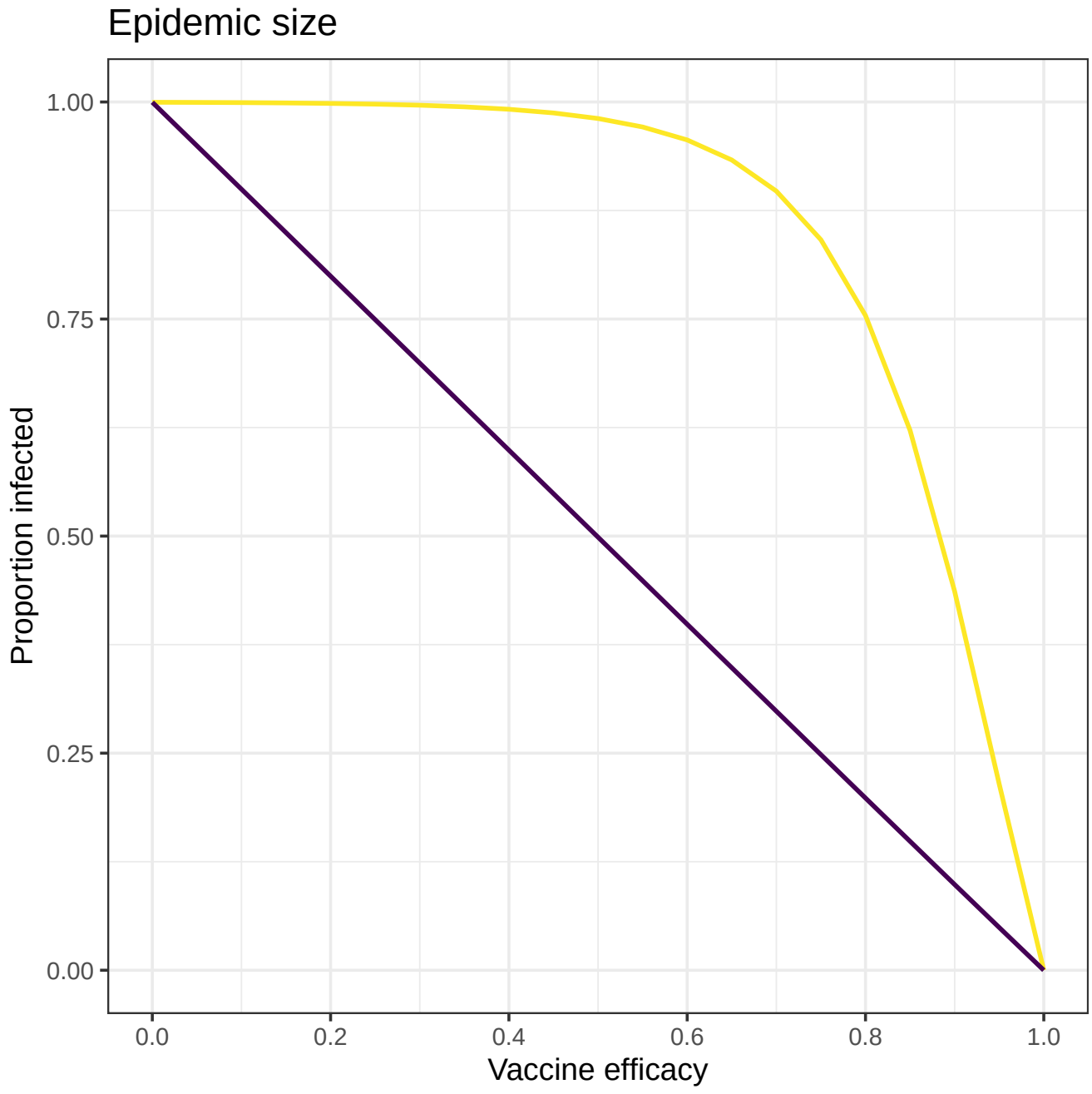
Modeling partial immunity





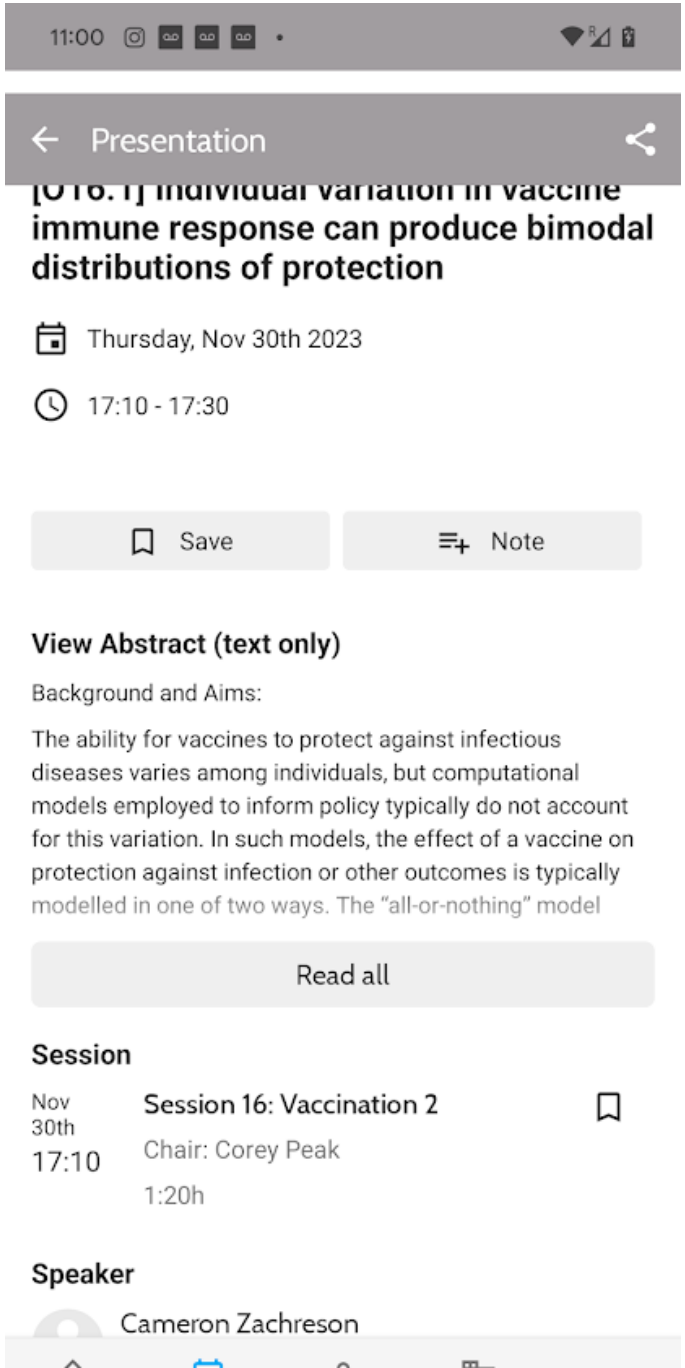
Why does it matter?

- Prediction
- Parameter estimation
- Planning


Epidemic size
Proportion infected
1.00
0.75
0.50
0.25
0.00
0.0
0.2
0.4
0.6
0.8
1.0
Vaccine efficacy

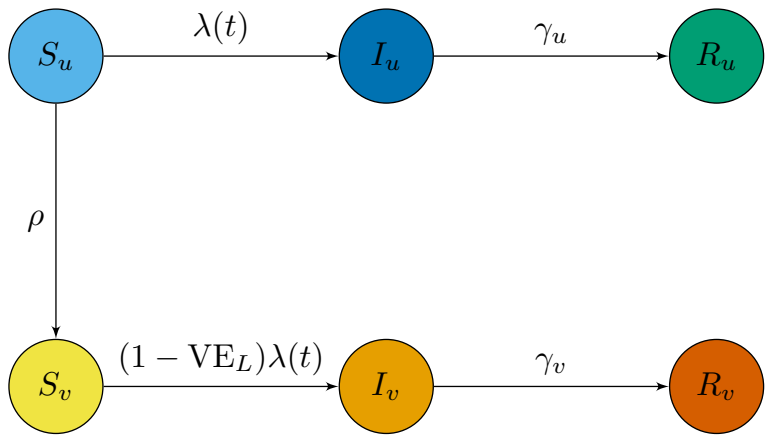
Polarized model

- 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

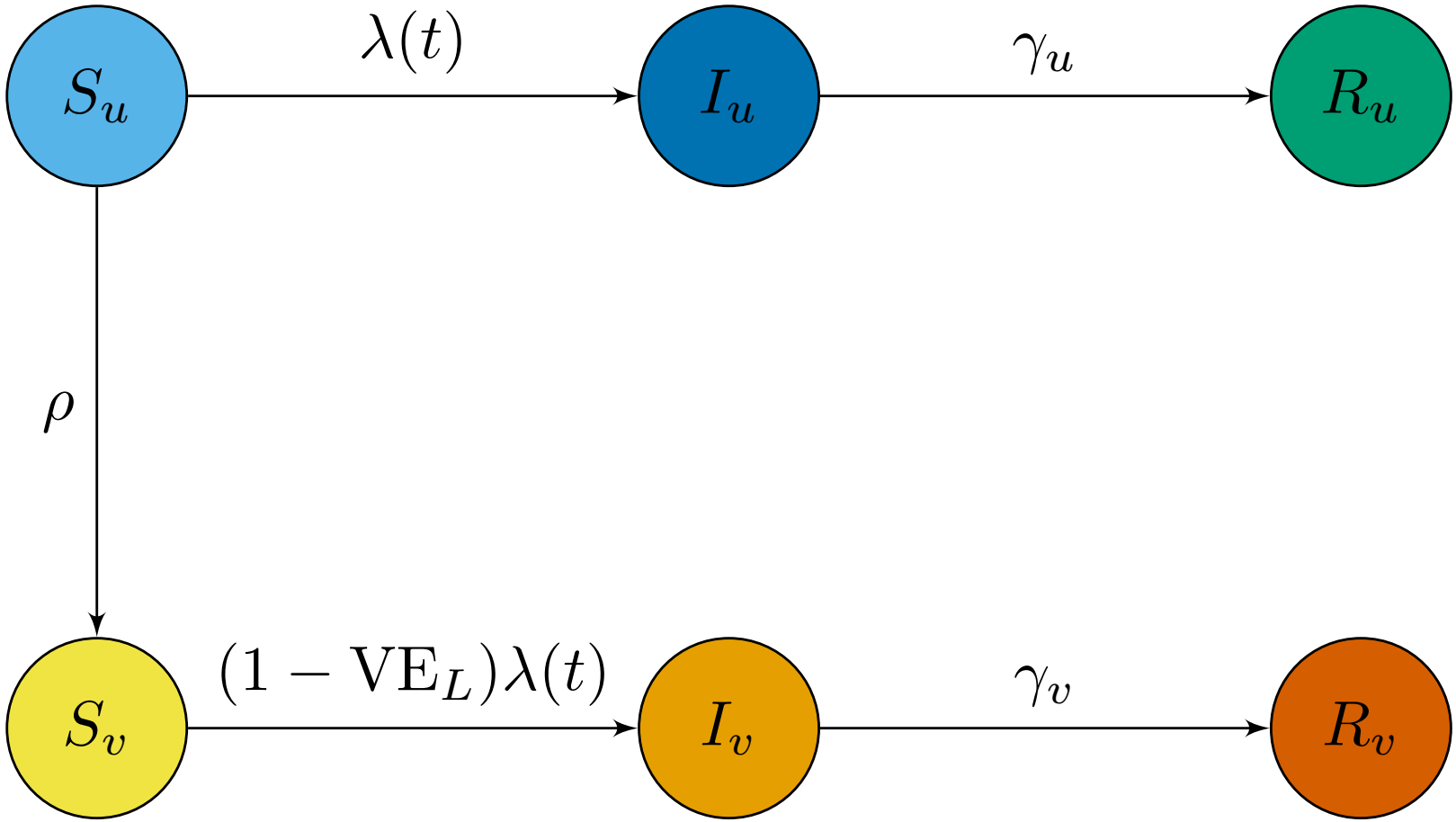


Leaky model

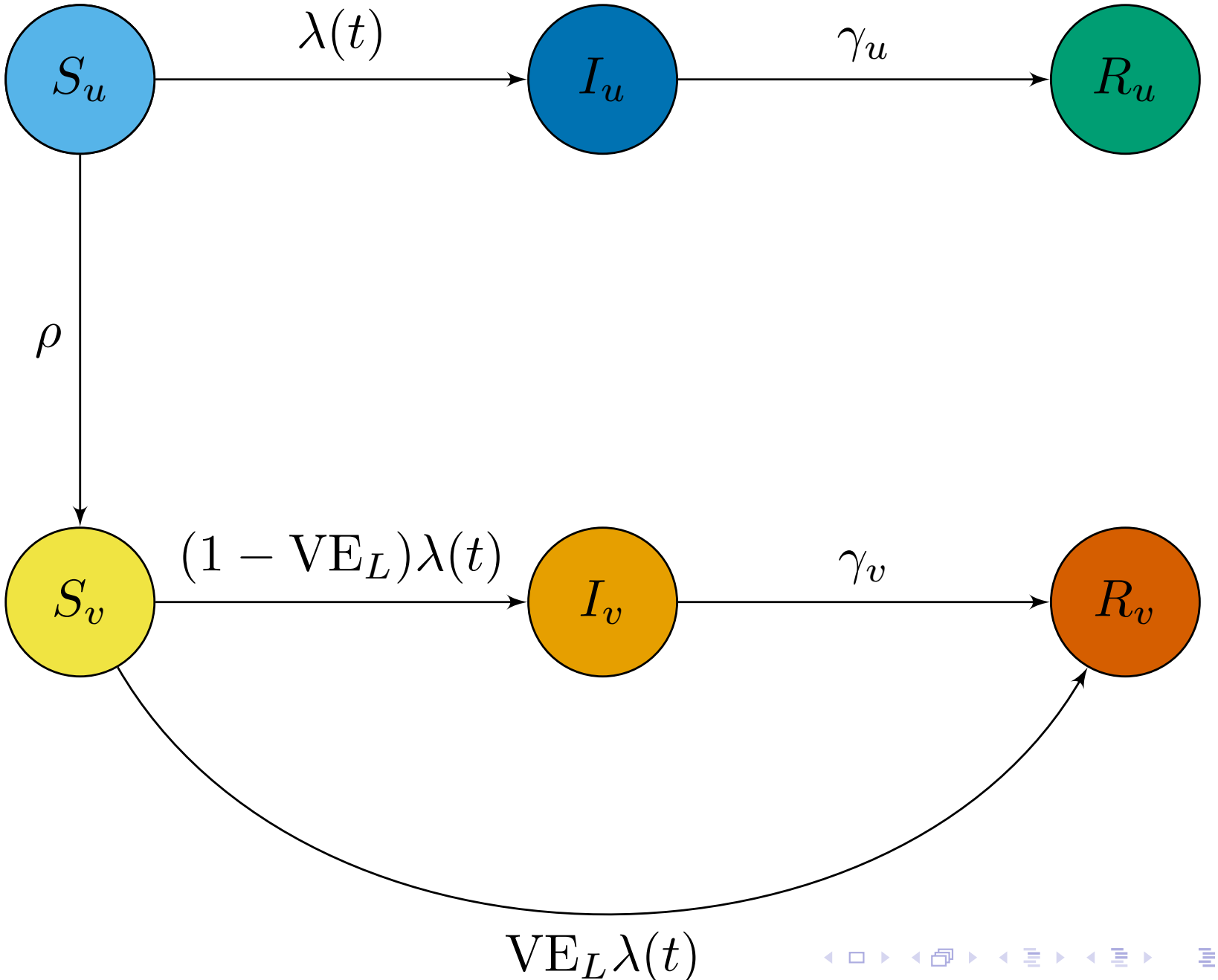
- The problem of phantom challenges
- We assume that these challenges happen, are beaten off, and have no effect
- I actively resist the flu, and then succumb to the same challenge next week!
- What if we don't do that?



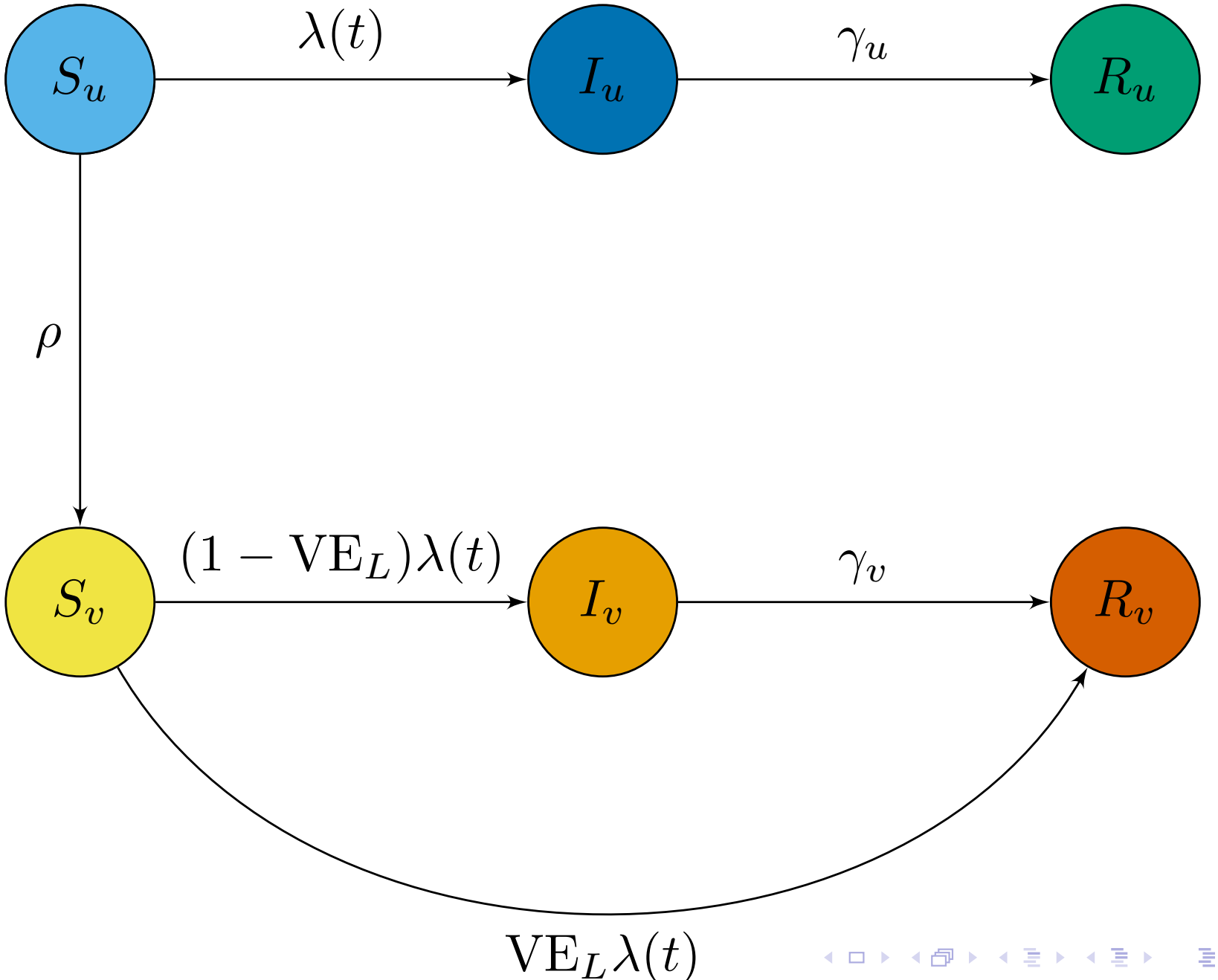
Leaky


S_u
$\lambda(t)$
I_u
γ_u
R_u
ρ
S_v
$(1 - \mathrm{VE}_L)\lambda(t)$
I_v
γ_v
R_v

Leaky with boosting



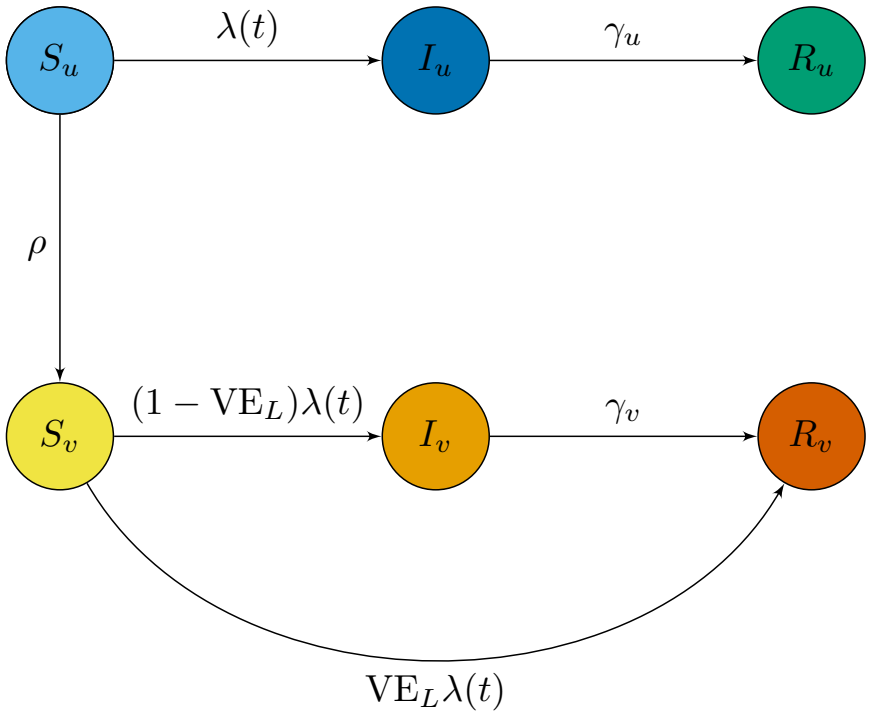
Leaky with partial boosting

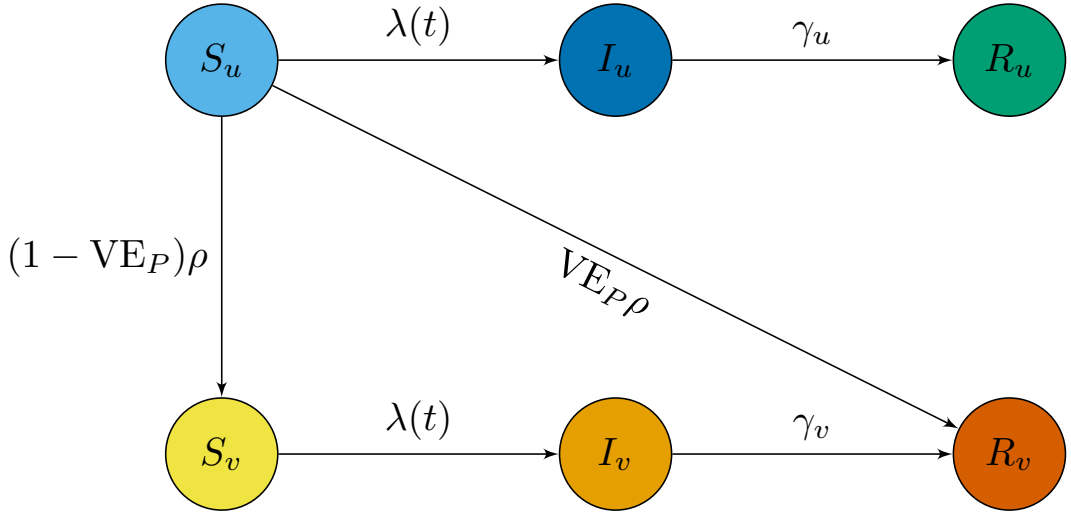


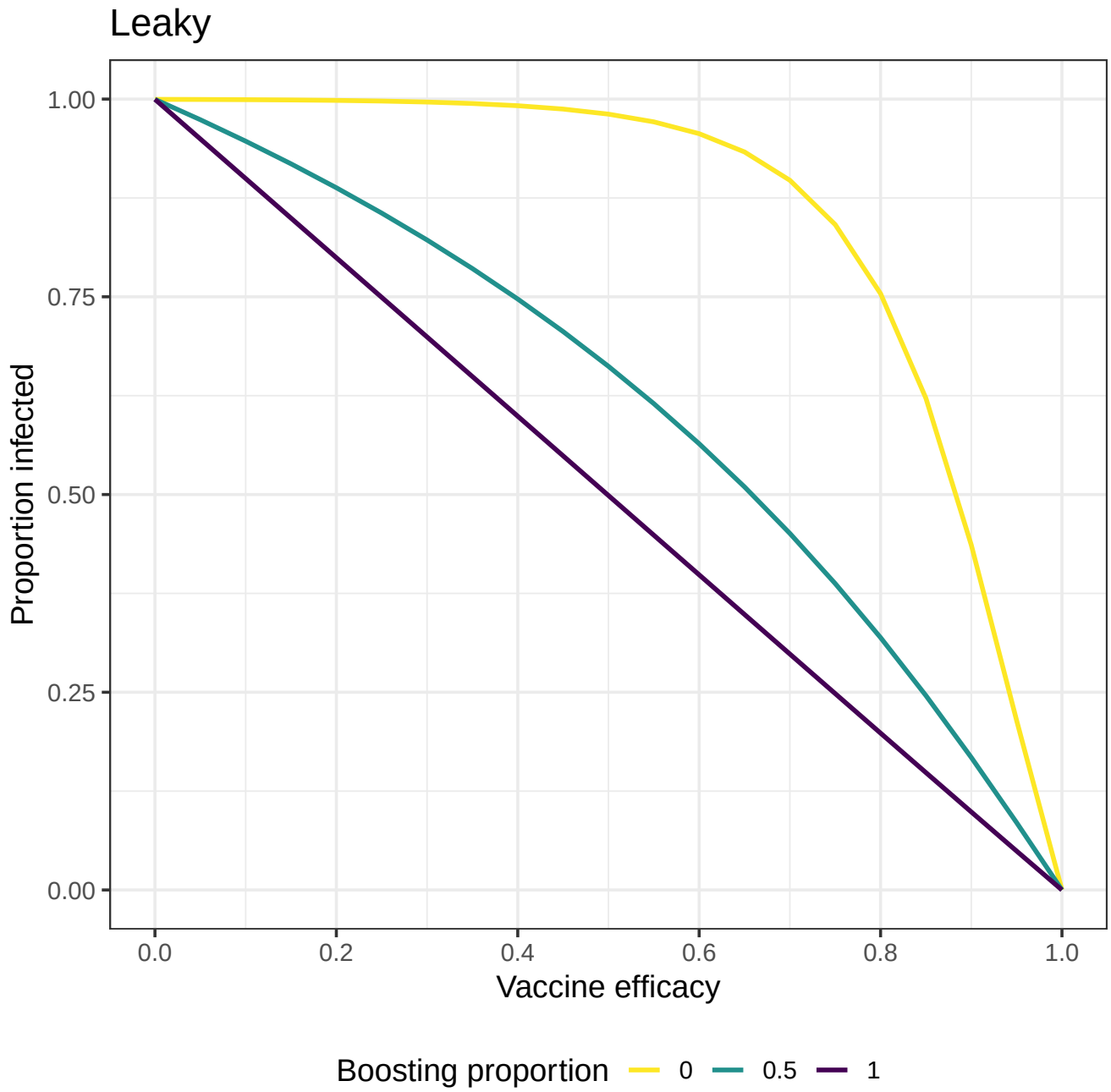
The dynamicist's perspective

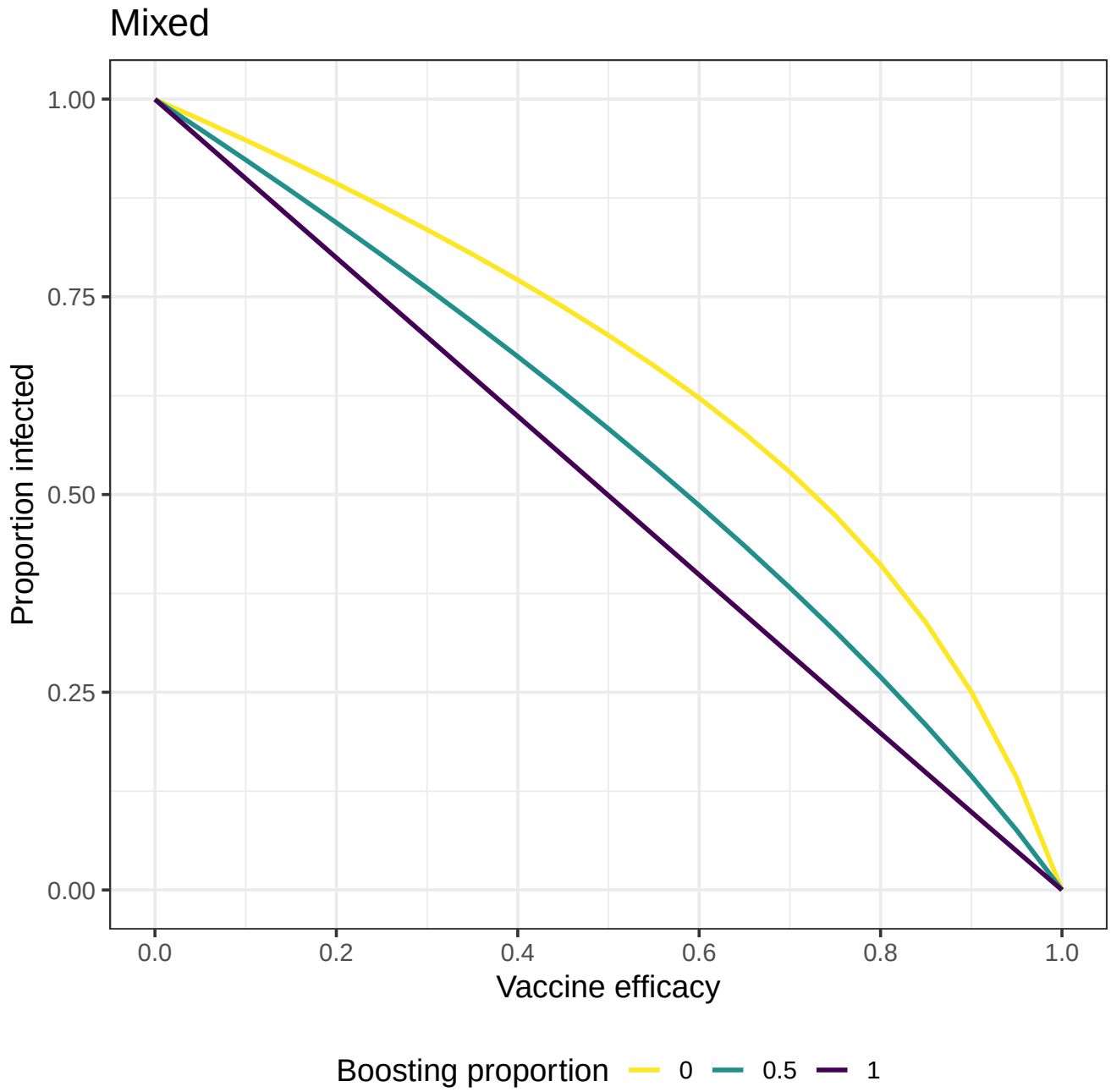
- Dynamical systems have shortcuts and dualities
- If your immunity is leaky, but is reliably boosted by challenges . . .
- The modeler can "decide" your fate when you recover
  - This is a system with equivalent dynamics

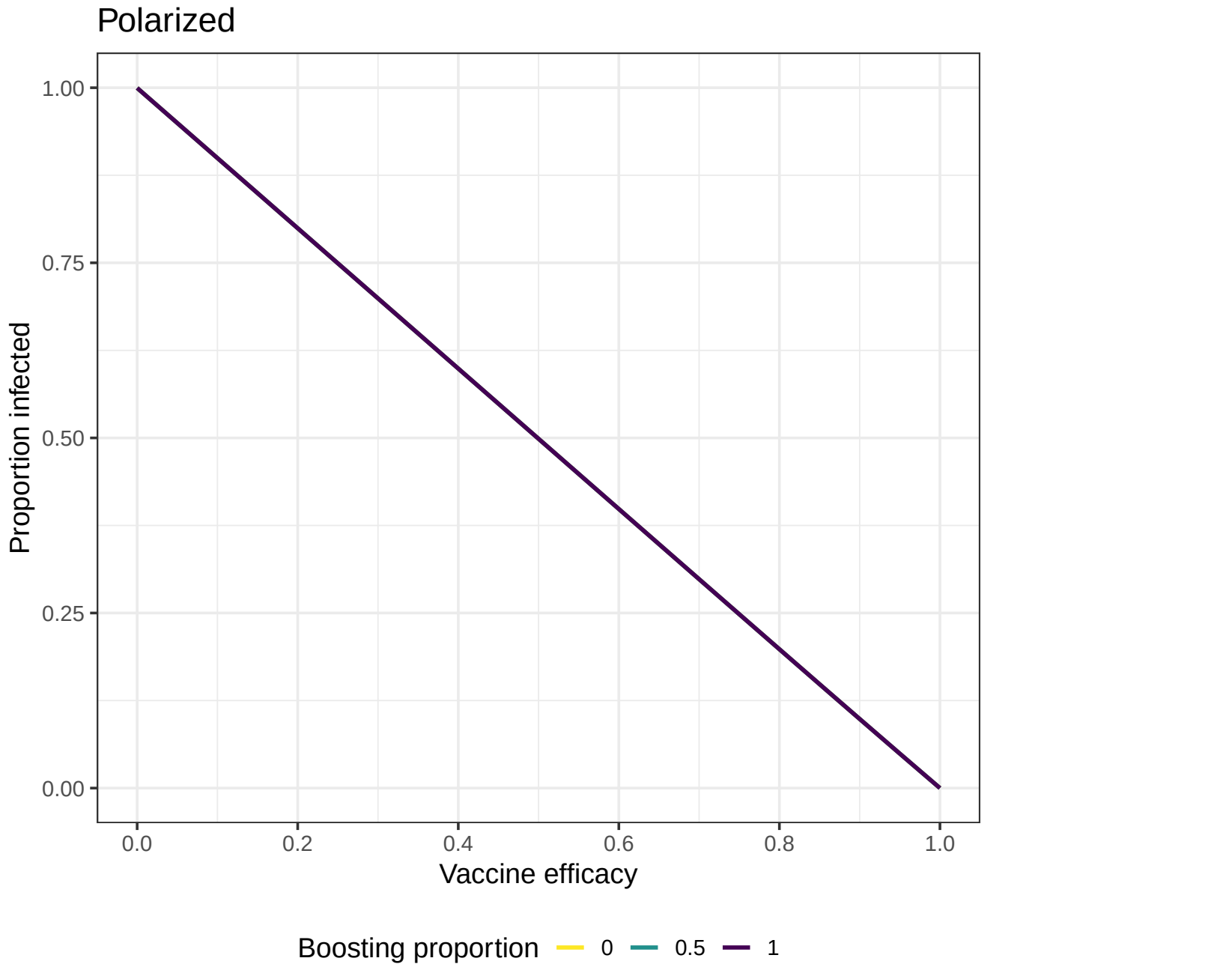
Leaky with boosting v. polarized



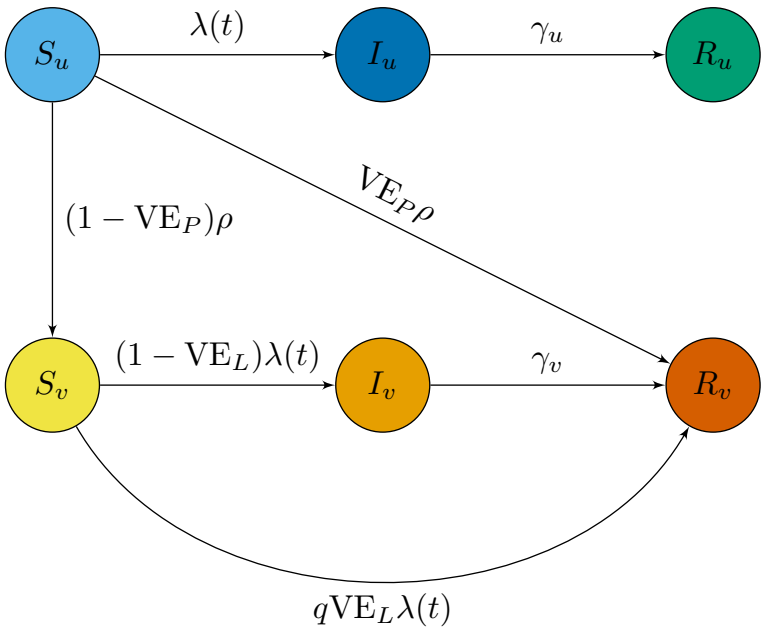



Leaky
1.00
0.75
0.50
0.25
0.00
Proportion infected
0.0
0.2
0.4
0.6
0.8
1.0
Vaccine efficacy
Boosting proportion
0
0.5
1


Mixed
1.00
0.75
0.50
0.25
0.00
Proportion infected
0.0
0.2
0.4
0.6
0.8
1.0
Vaccine efficacy
Boosting proportion
0
0.5
1

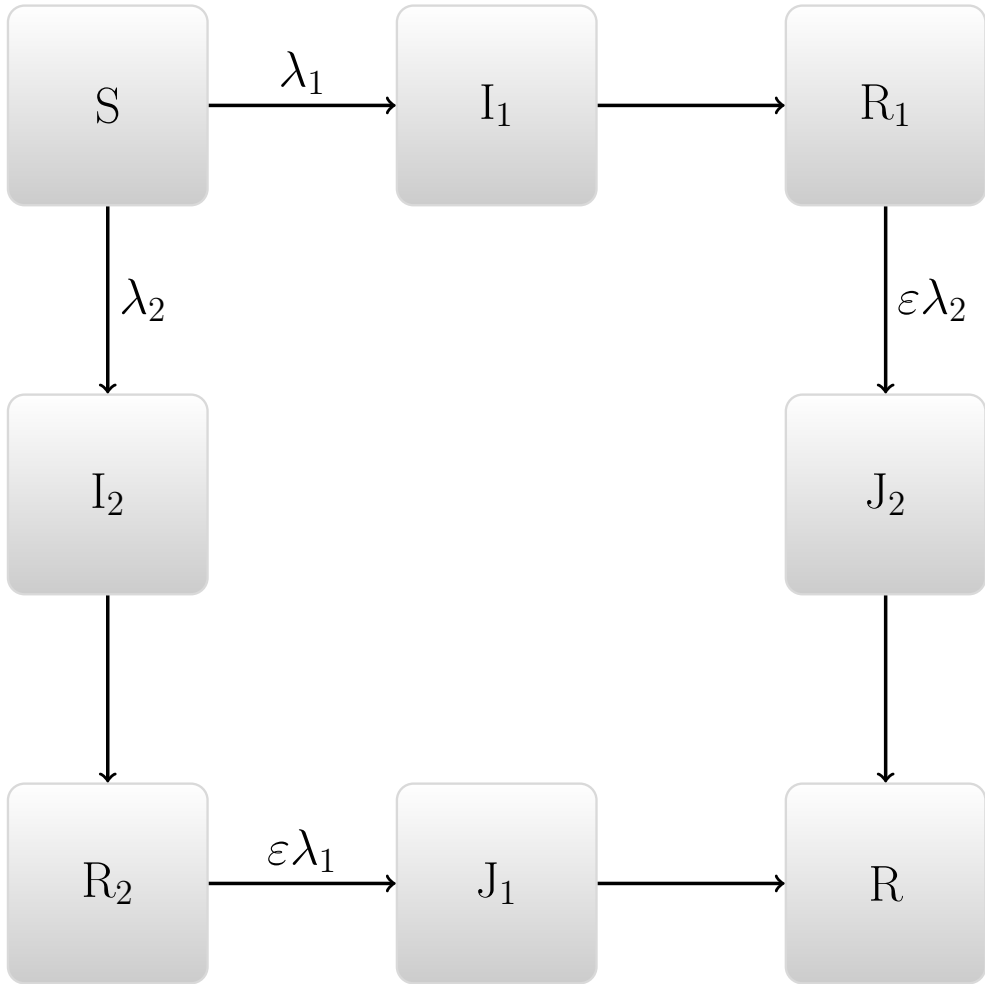

Polarized
1.00
0.75
0.50
0.25
0.00
Proportion infected
0.0
0.2
0.4
0.6
0.8
1.0
Vaccine efficacy
Boosting proportion
0
0.5
1

Transmission reduction

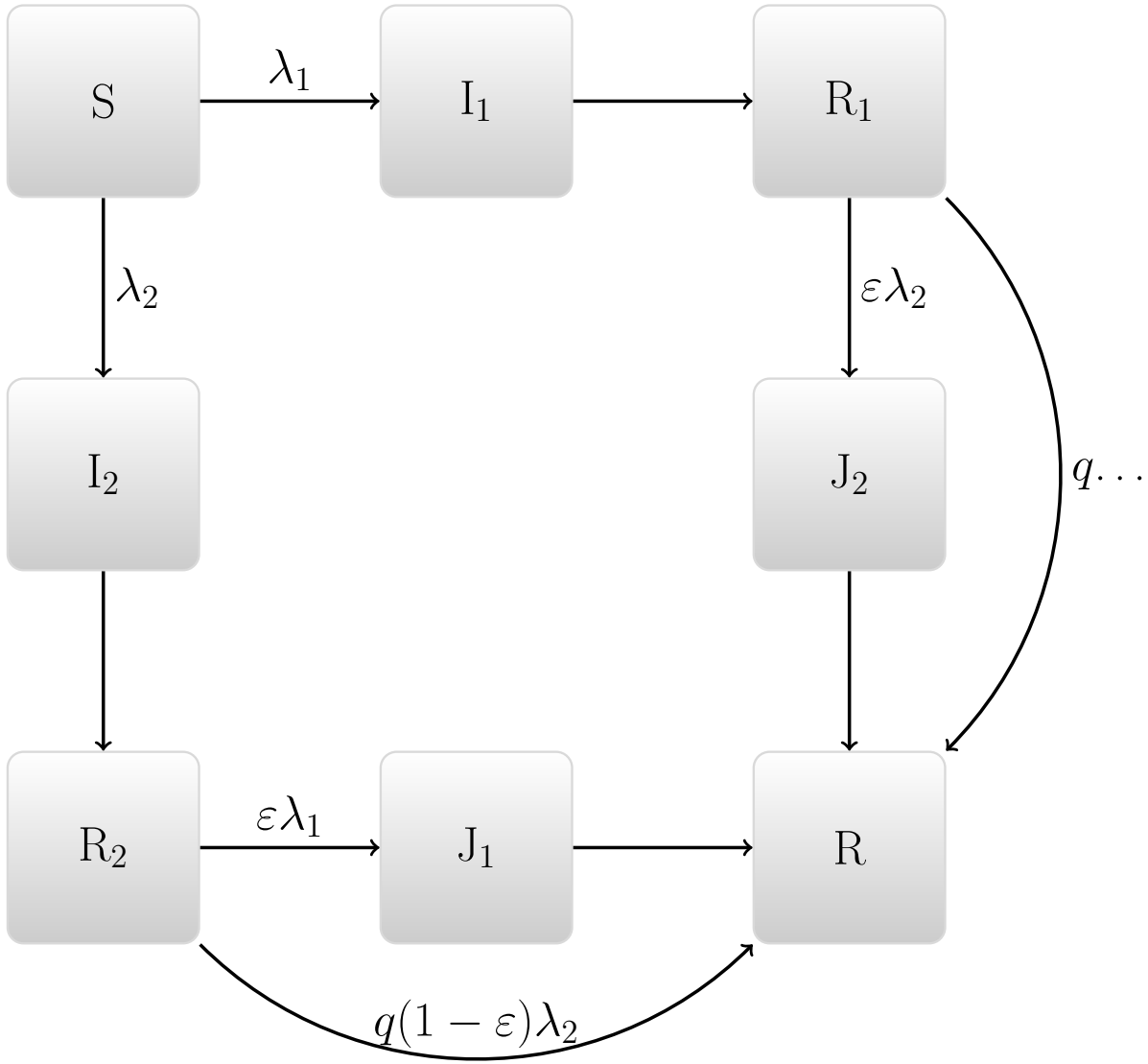


- If all breakthrough infections go through the I_v box, but only transmit a fraction q, dynamics are unchanged
- In the deterministic case!

Interacting strains



Interacting strains with boosting



Deterministic coexistence

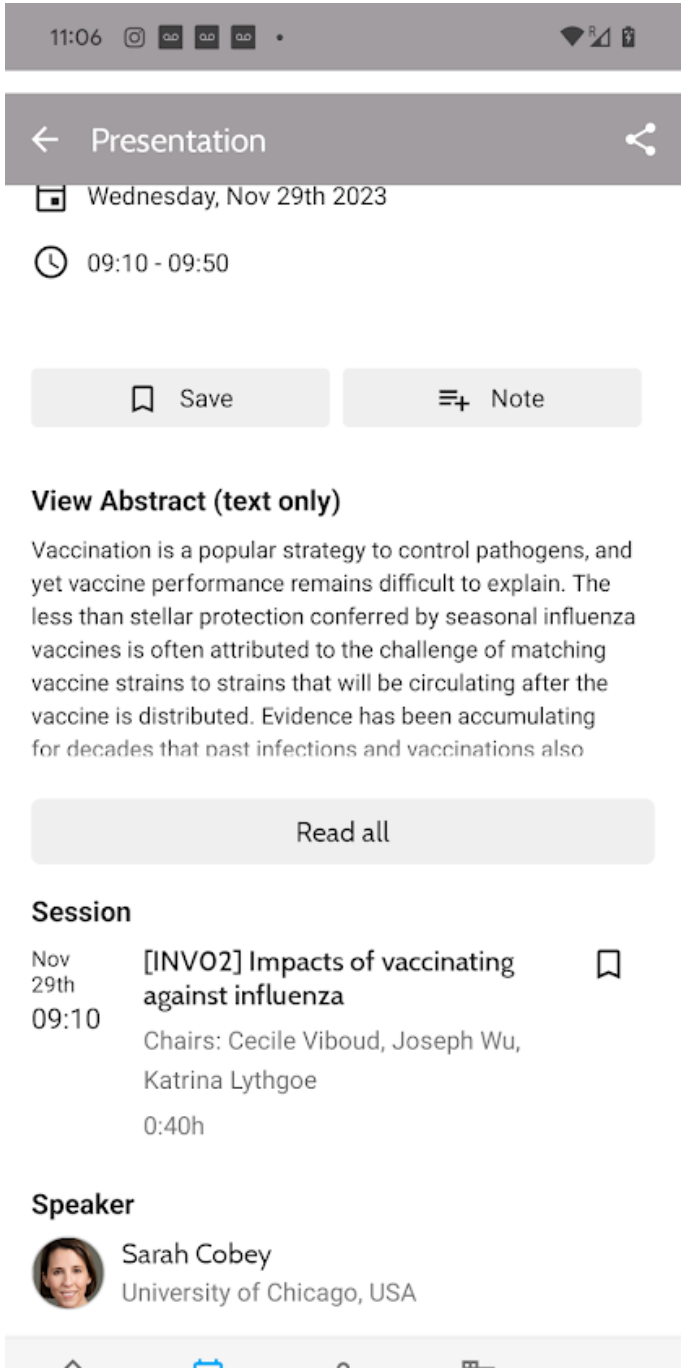
- As long as both strains can invade:
  - $$R_{\text{inv}}(1/R_{\text{res}} + \varepsilon(1 - 1/R_{\text{res}}) > 1$$
- Depends only on parameters (not on paradigm) ...
- but how are they estimated?

Stochastic coexistence

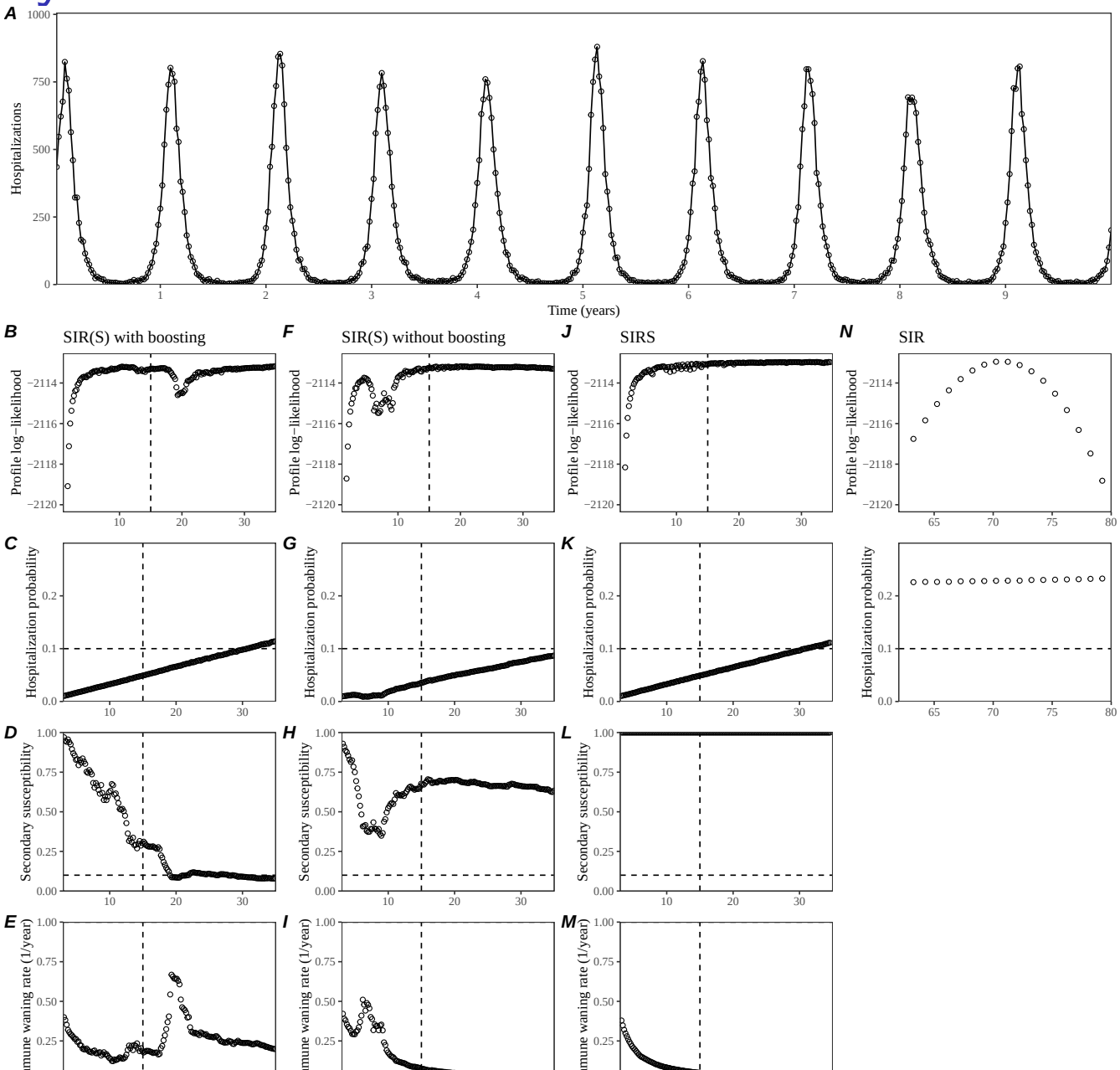
- Leaky dynamics lead to giant epidemics
- Lots of overshoot
- Greater likelihood of stochastic extinction
- Probably

Estimating parameters is practically hard

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



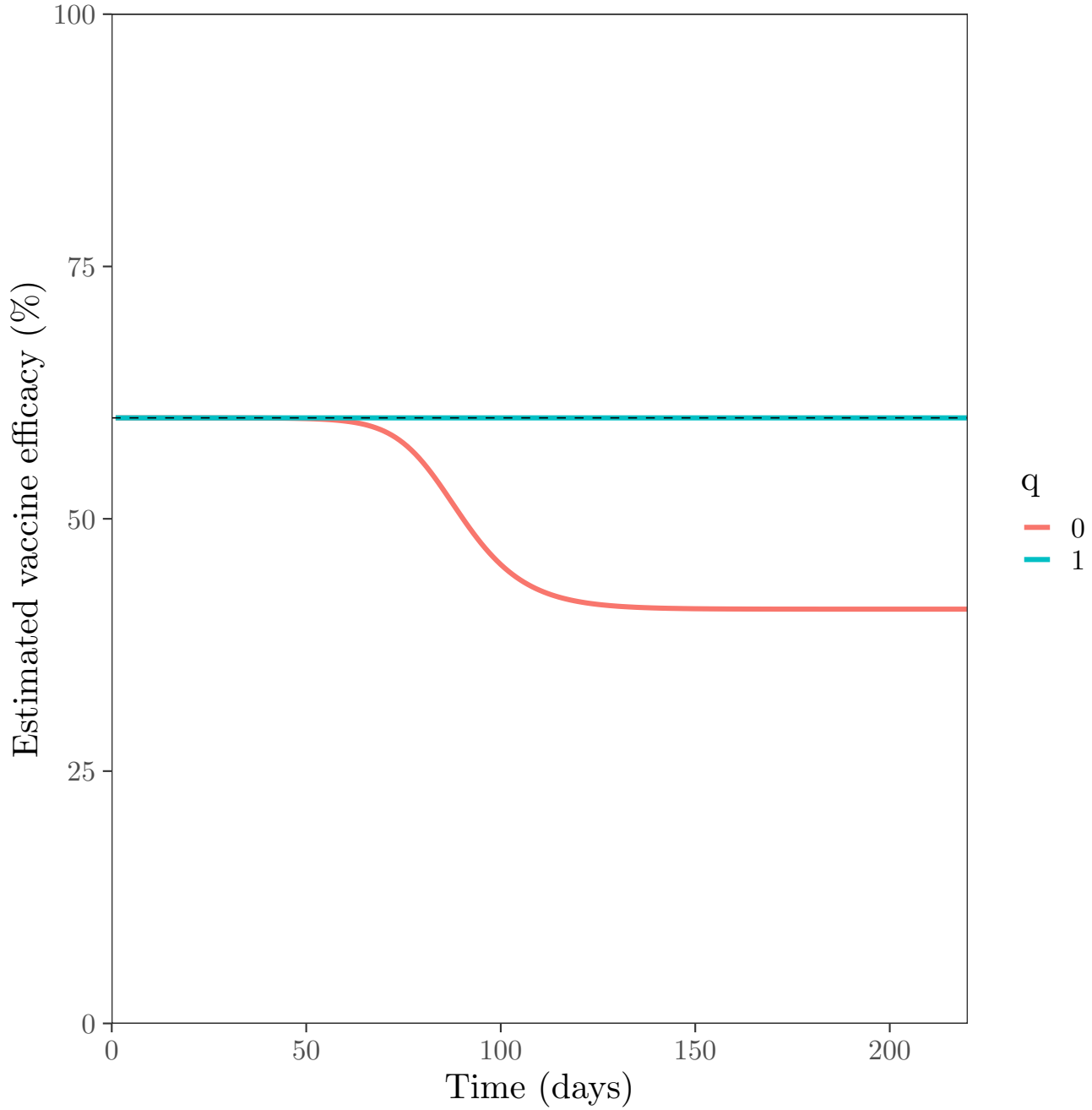
Estimating parameters from population-level data is intrinsically hard



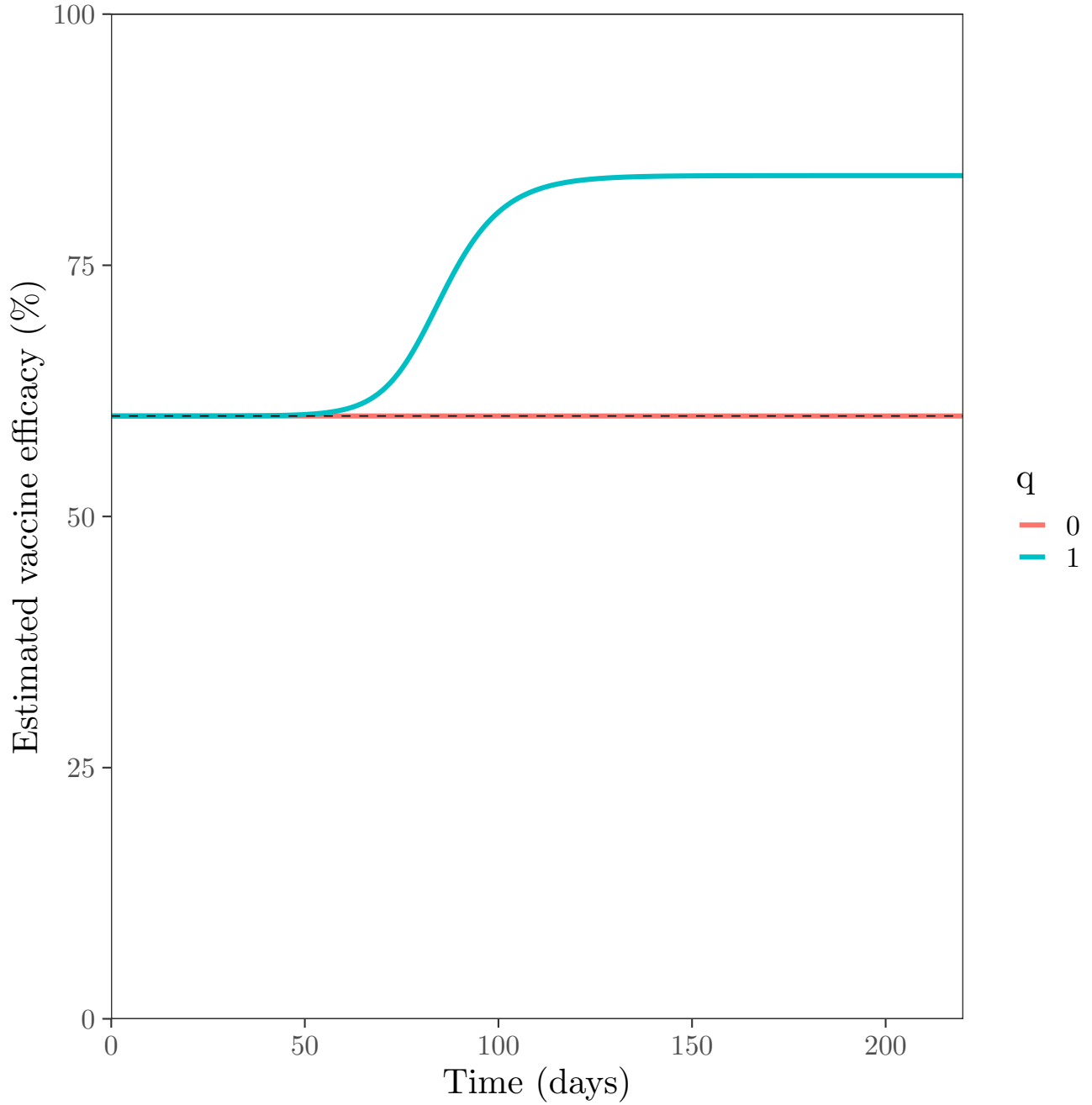
Individual-level inference depends on paradigm

- 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



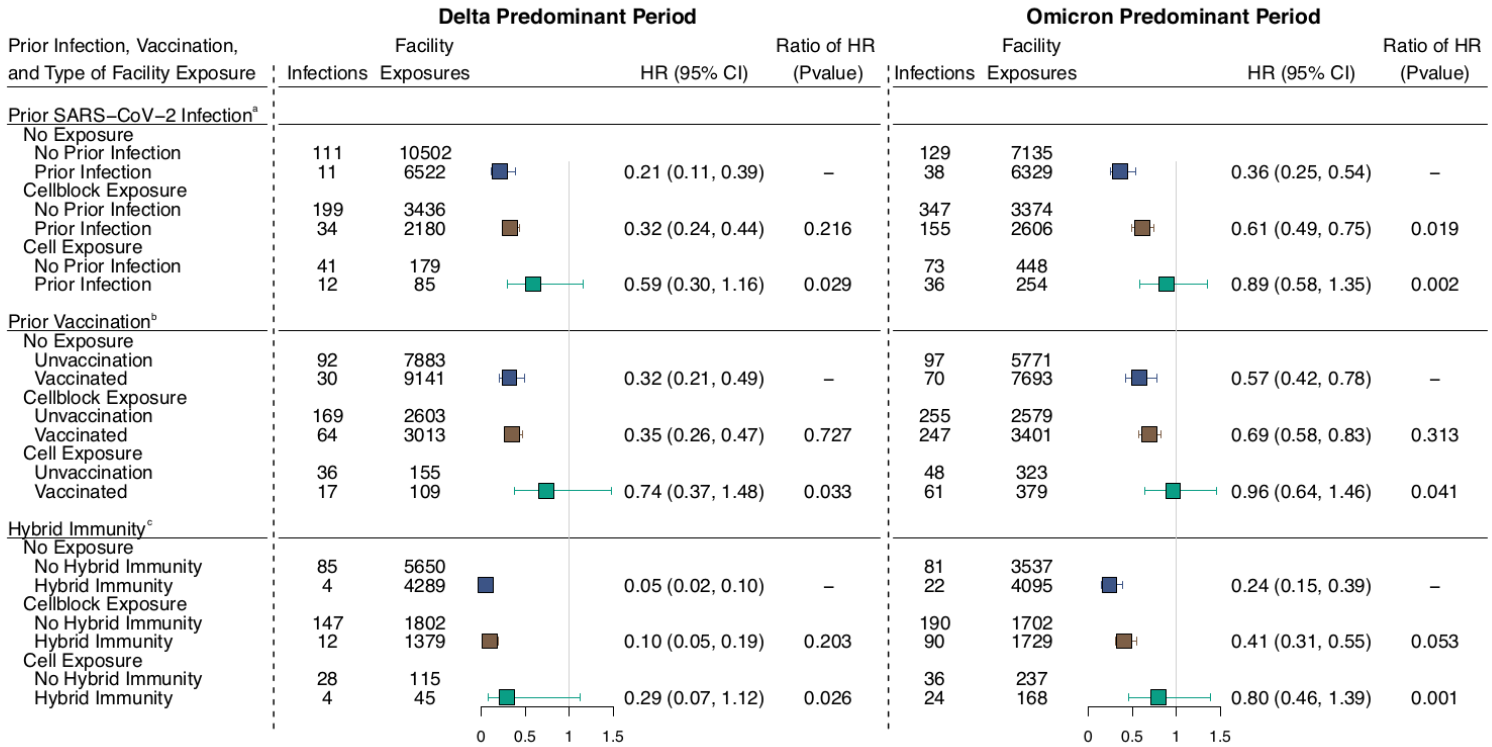
Skimming the surface

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

Thanks

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

Connecticut correctional study



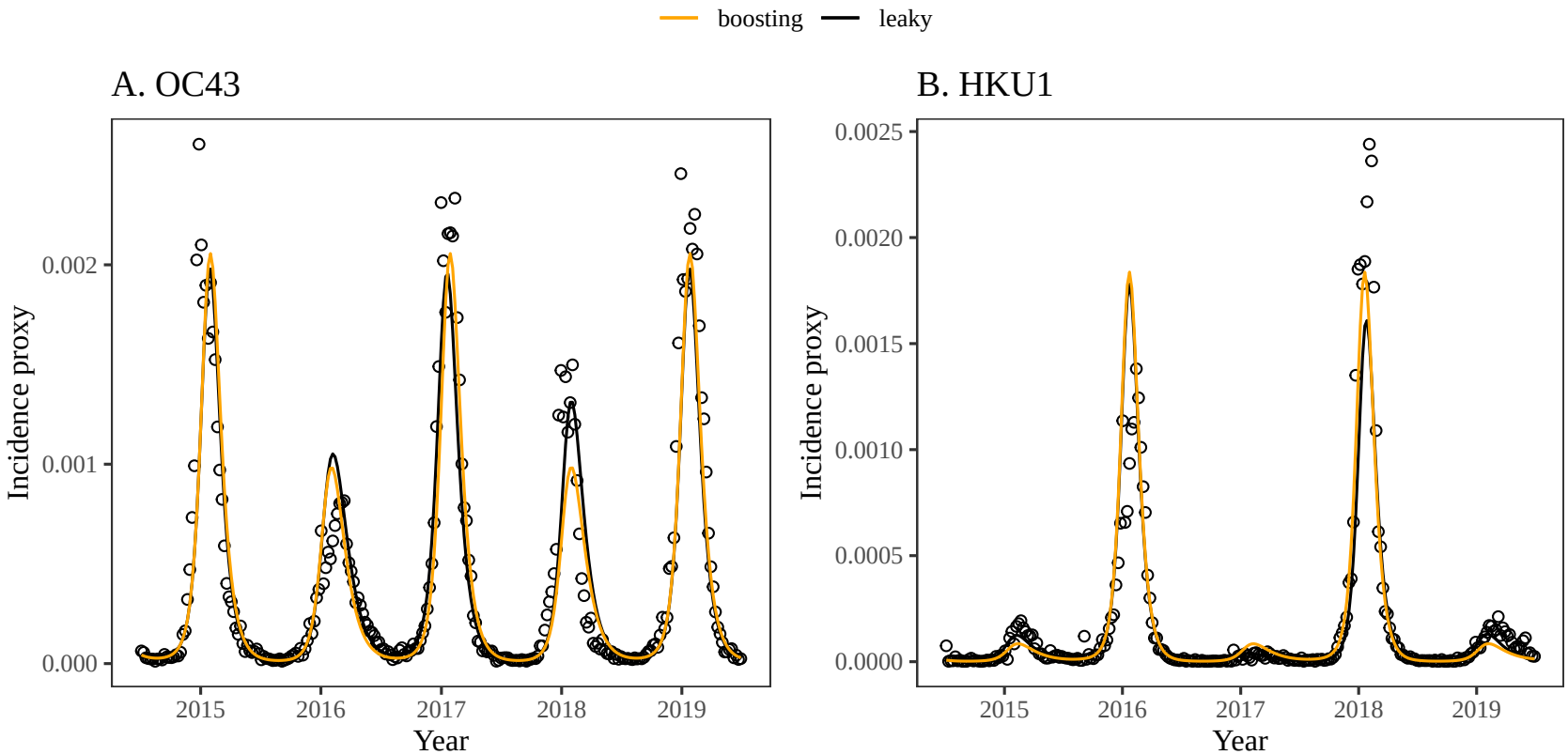
Lind et al., Nat Commun, 2023.

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

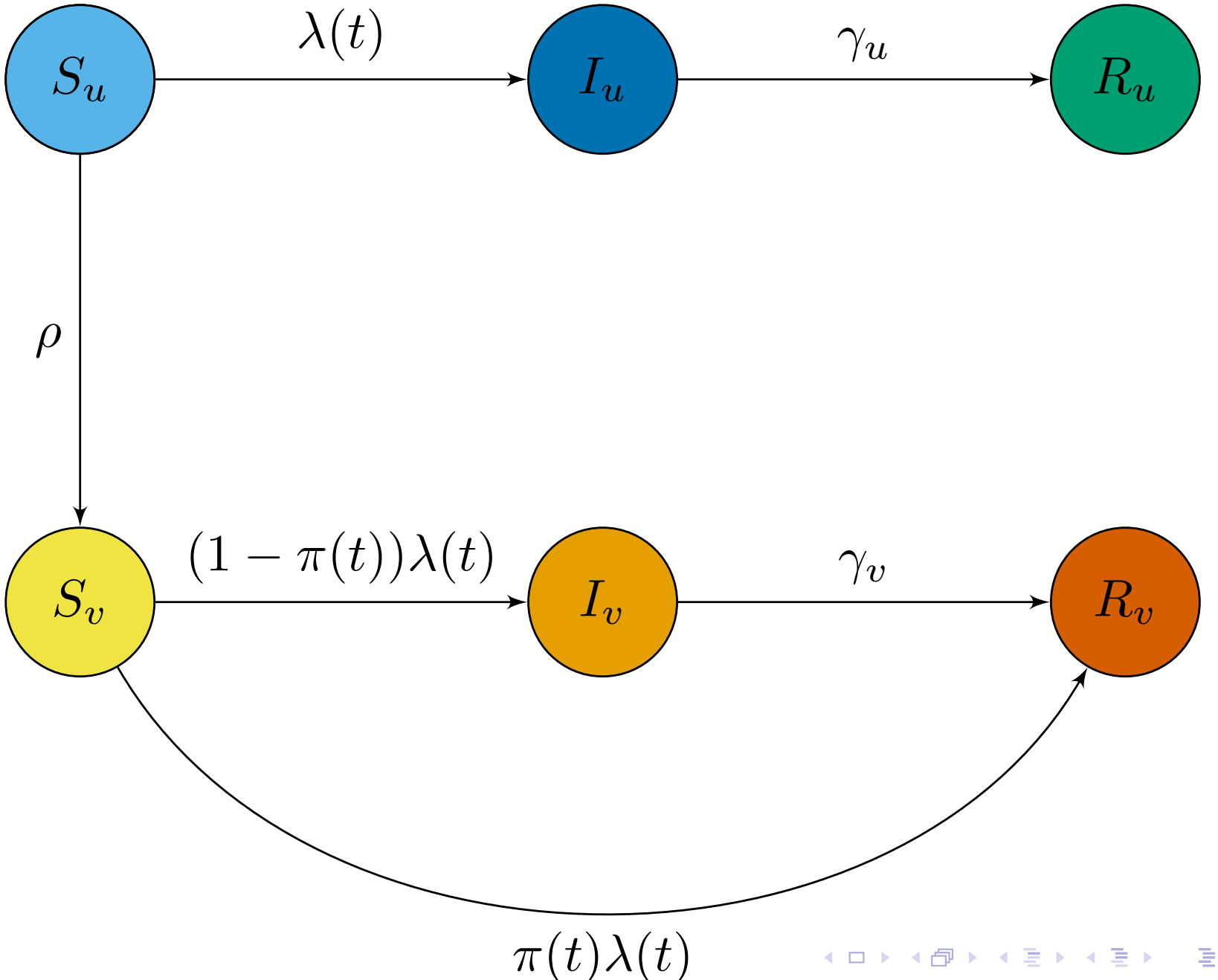
Time scales of challenge

- 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

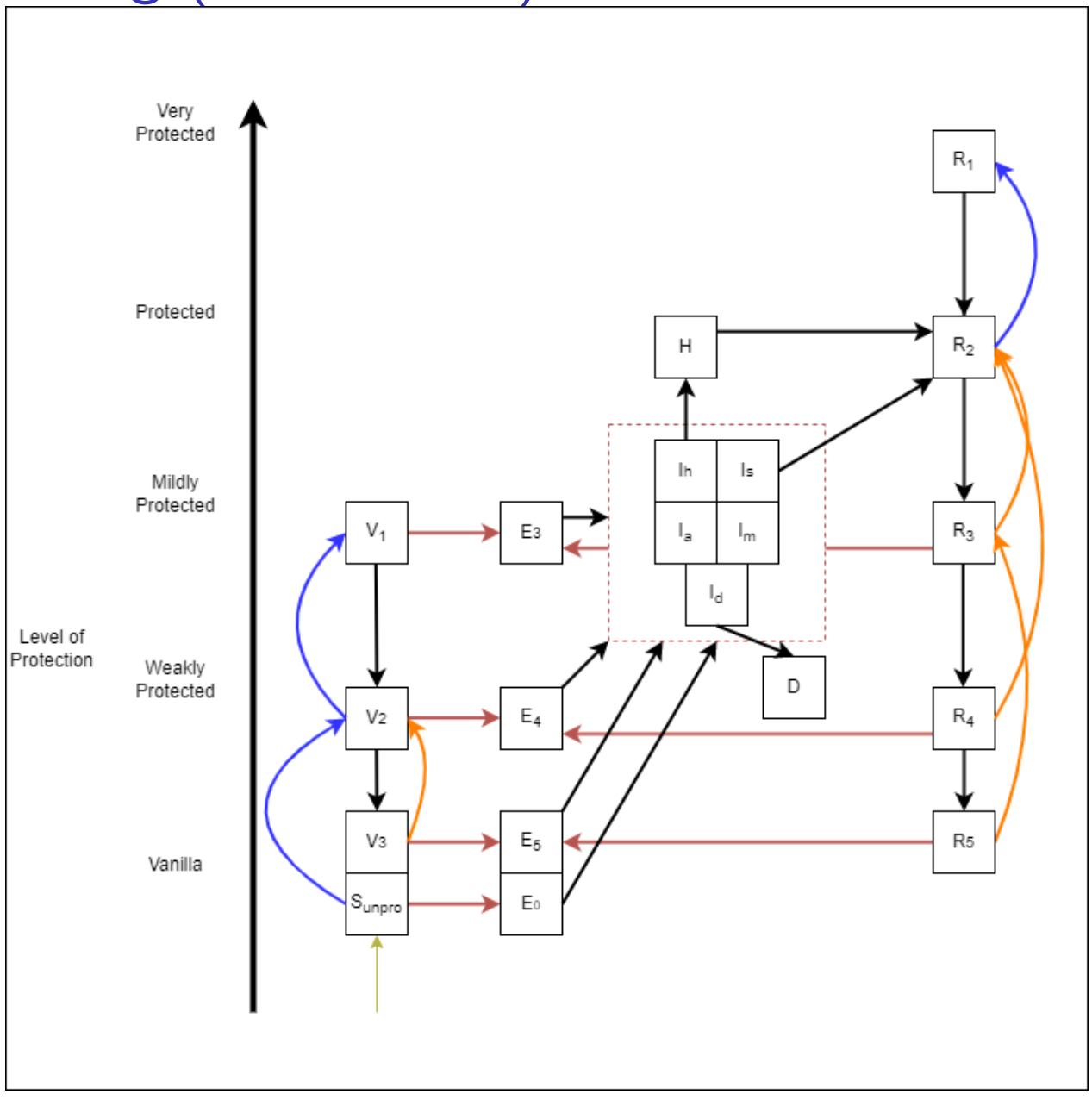
Coronavirus fits



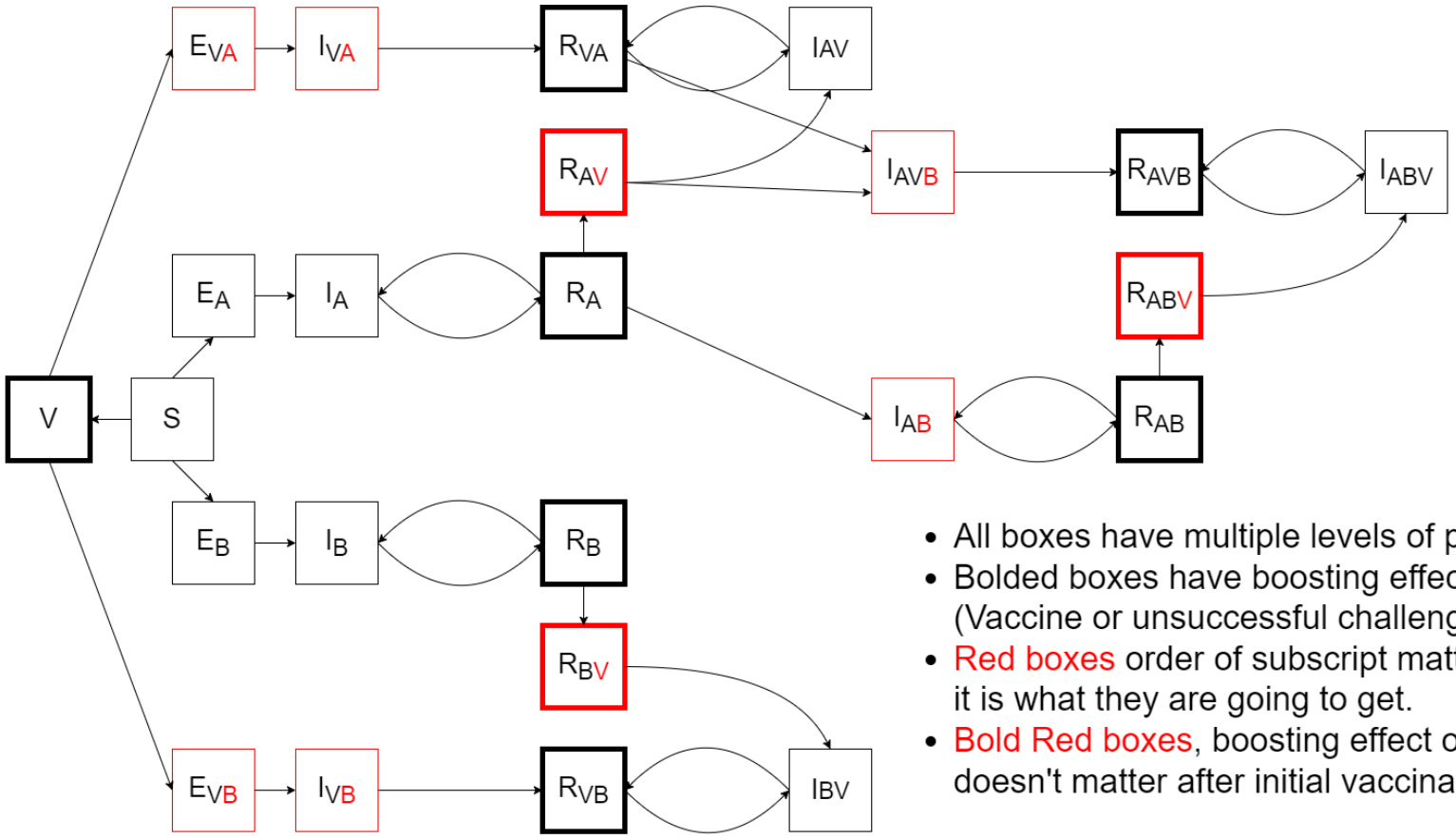
Dose dependence



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.

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