Conceptual models of immunity

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PHAC/EMNID, Sep 2023

History of this work

- Innovative influenza cross-immunity models by Julia Gog
  - *https://pubmed.ncbi.nlm.nih.gov/11942531/*
- My attempts to understand conceptual under-pinnings
- Michael Li asking practical questions that made me share my ideas
- Daniel (Sang Woo) Park took the lead in making this a real project
  - With help from Jess Metcalf and Bryan Grenfell
- *https://www.medrxiv.org/content/10.1101/2023.07.14.23292670*

What do modelers assume about vaccines?

- Leaky model: 80% efficacy means that each individual is 80% protected (20% chance of infection relative to naive individual)
- Polarized model: 80% efficacy means that 80% of individuals are completely protected (20% are unprotected)

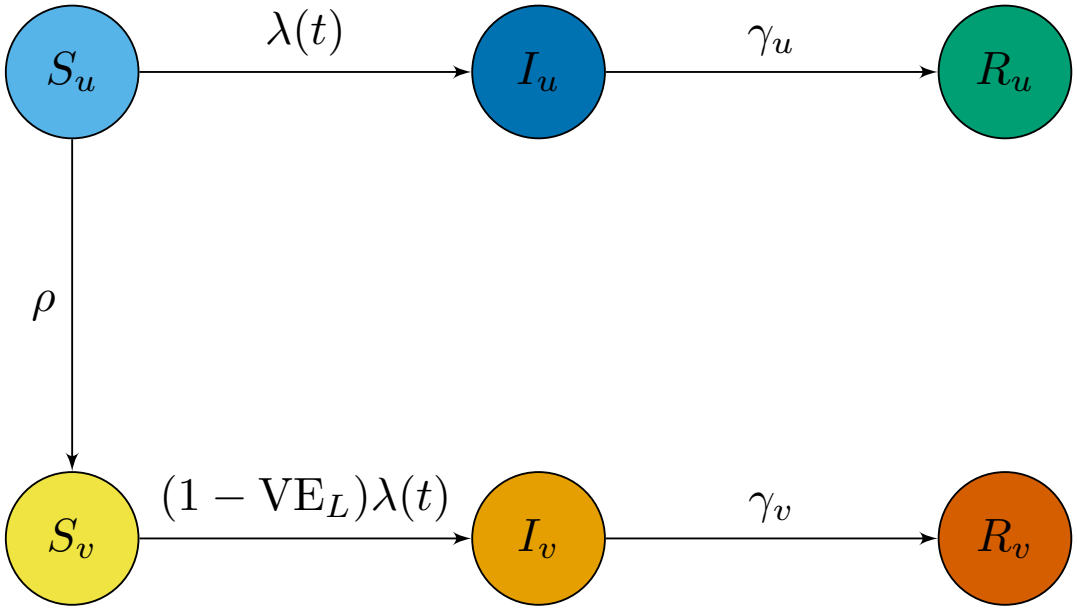
What does it mean to be protected?

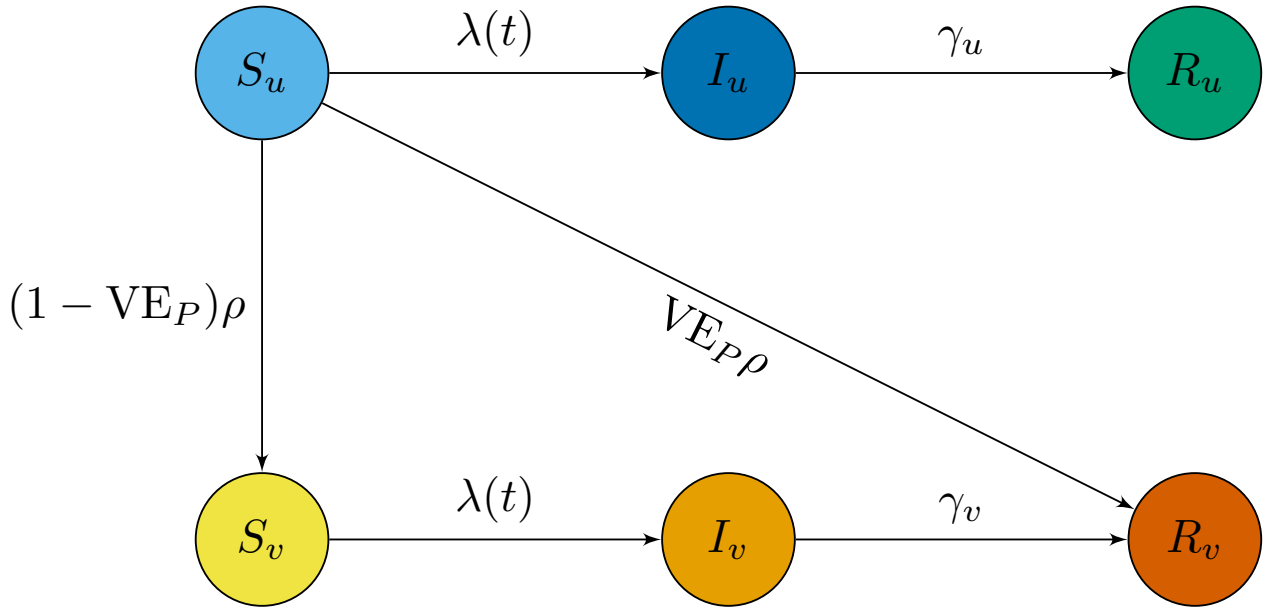
- Against death?
- Severe outcomes?
- Transmission?
- Measurable infection?
- Immune response?

How do we model immunity?

- History-based
  - What exposures has an individual had?
  - Maps naturally to leaky immunity (vaxxed individuals are all the same)
- Status-based
  - What is an individual immune to?
  - Maps naturally to polarized immunity

Modeling immunity

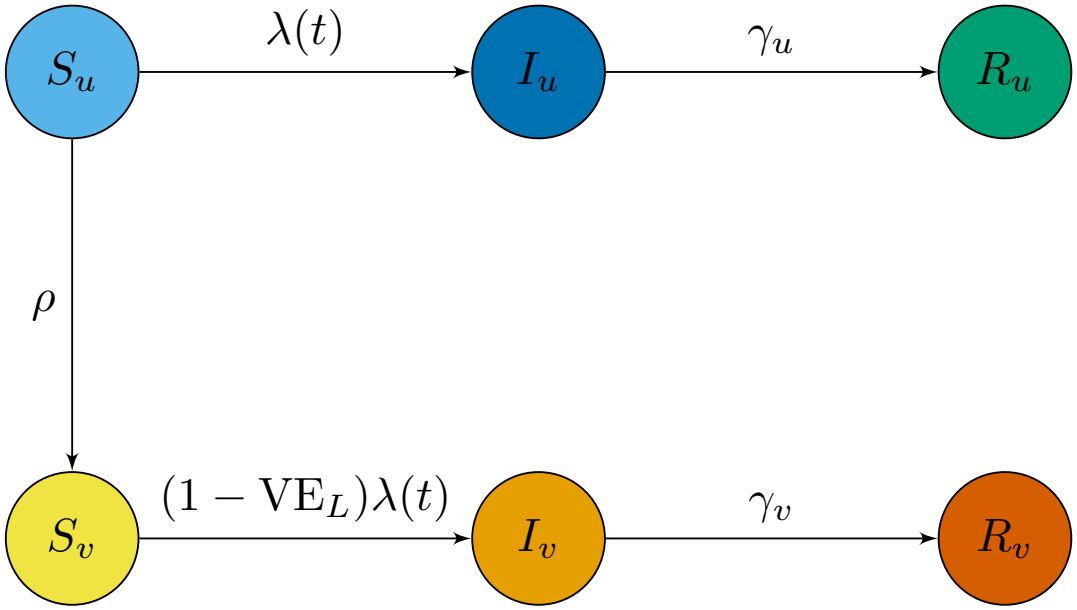


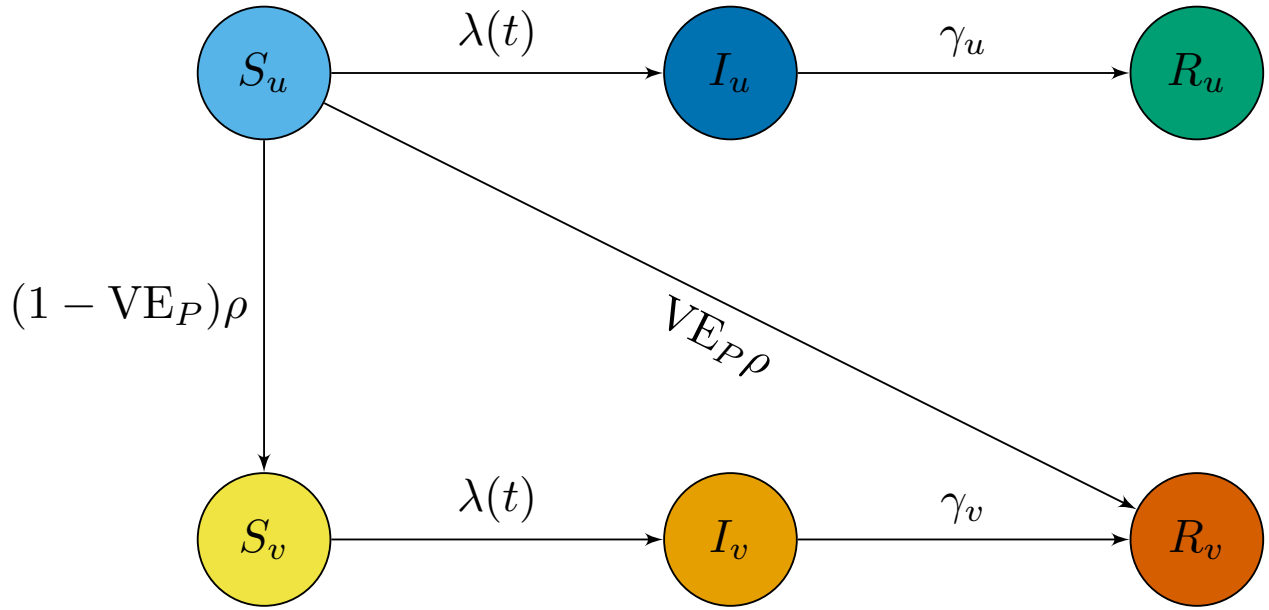


Limitations

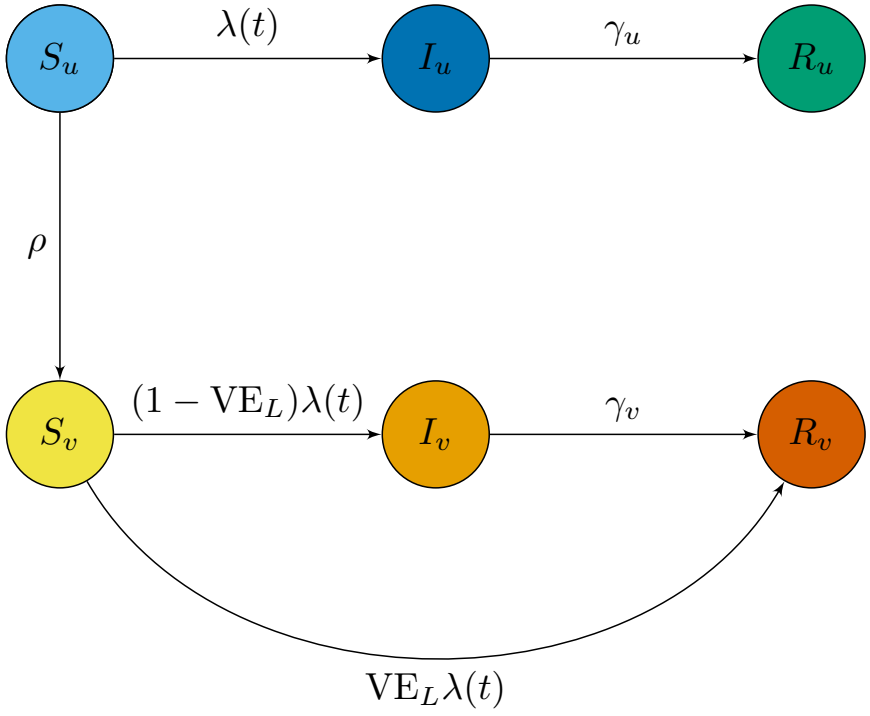
- Polarized approach assumes that a substantial proportion of the population is completely unprotected
  - Unrealistic
  - But how intrinsic is this assumption?
- Leaky approach ignores failed challenges
  - These are challenges that would counter-factually infect with protection
  - But I could resist one today and succumb next week

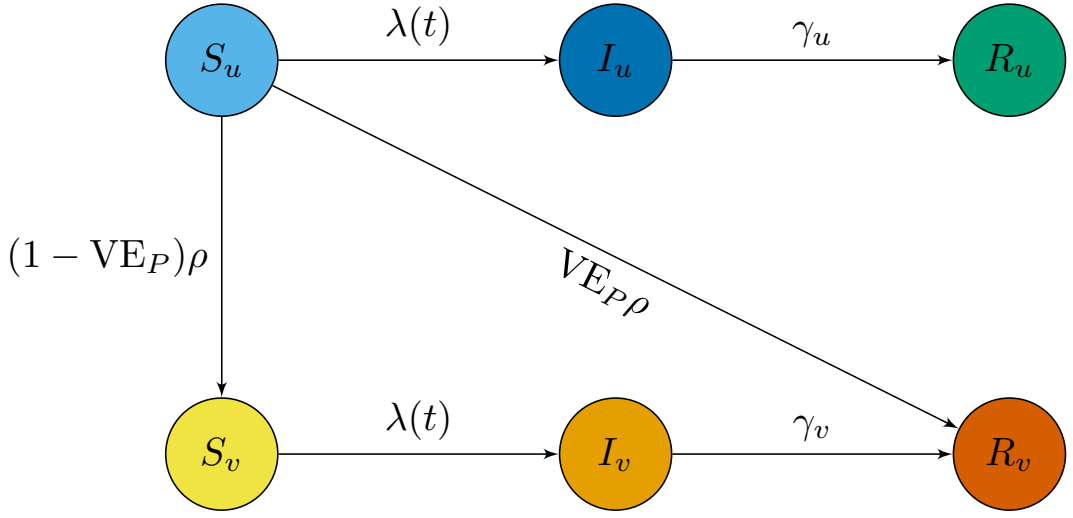
Leaky v. polarized



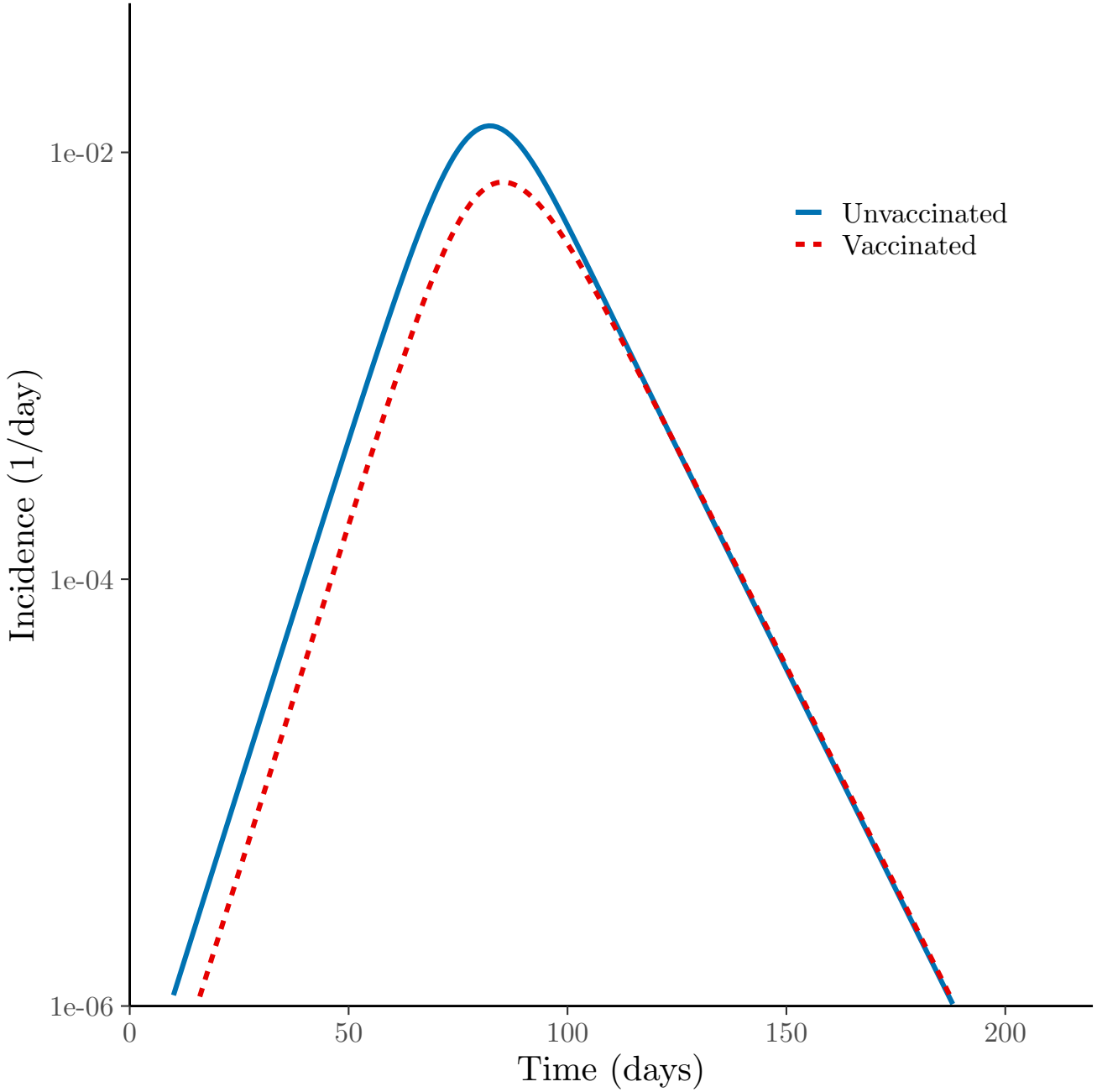


Leaky with boosting v. polarized

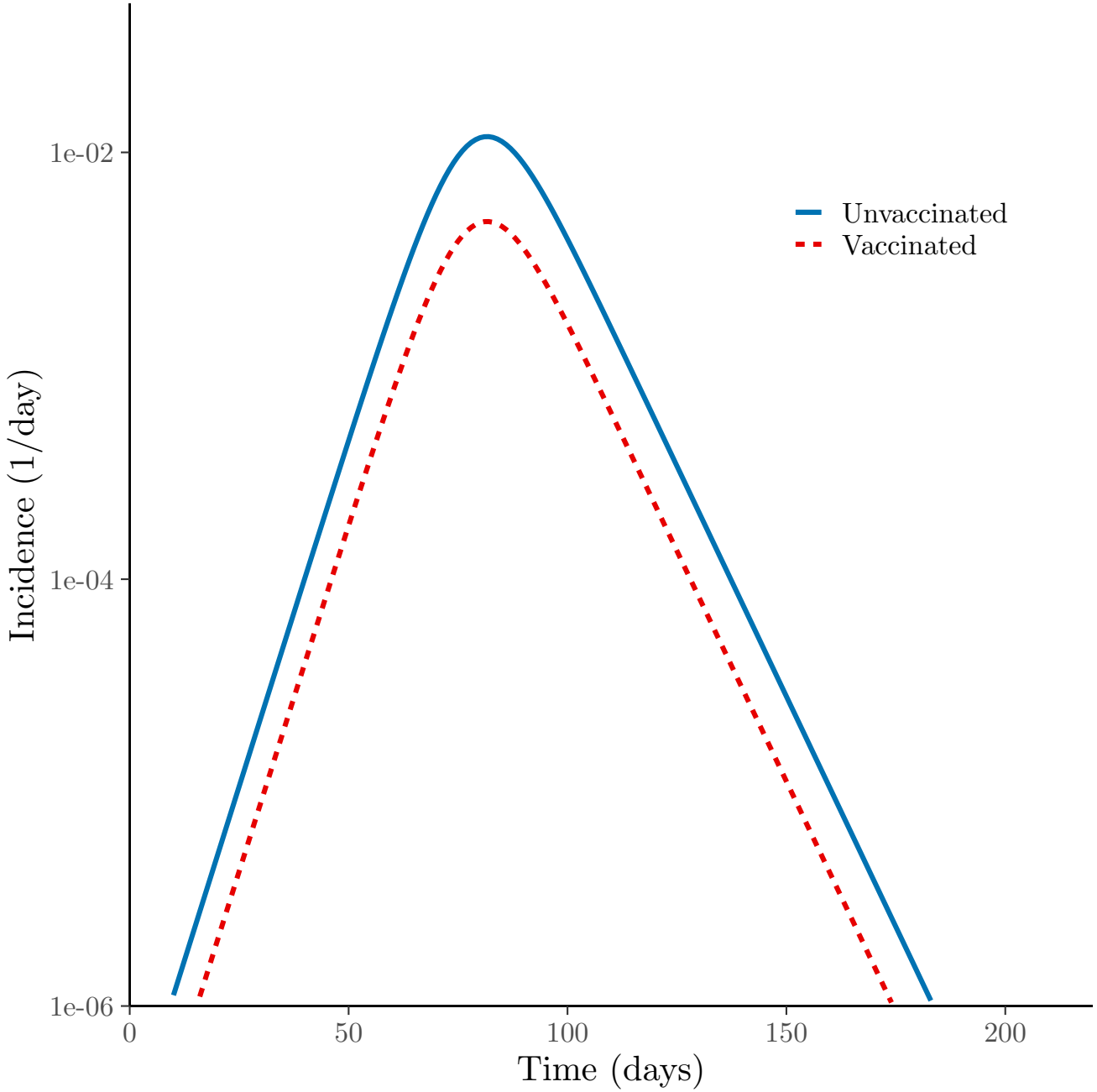




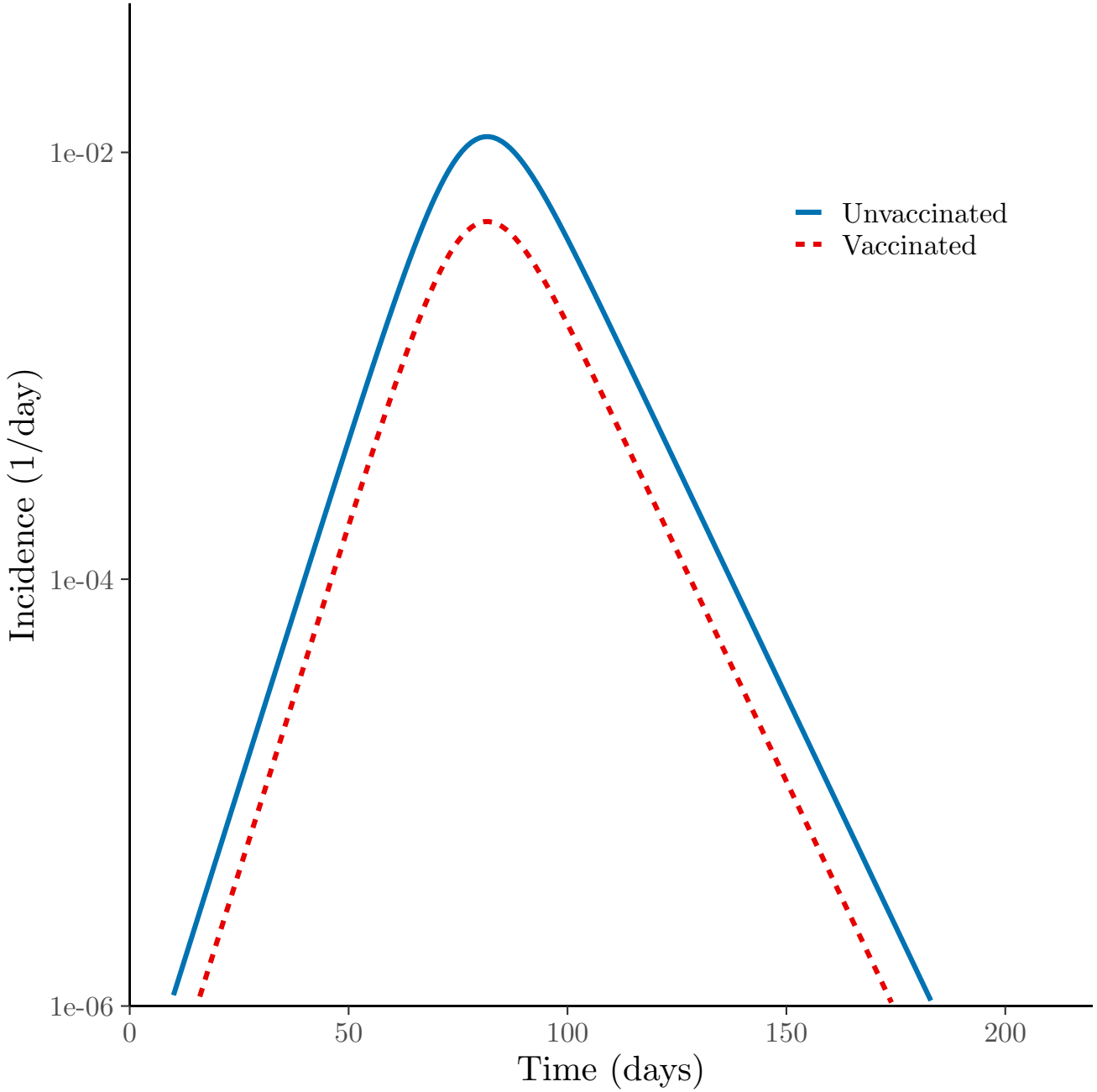
Leaky vaccine



Polarized vaccine



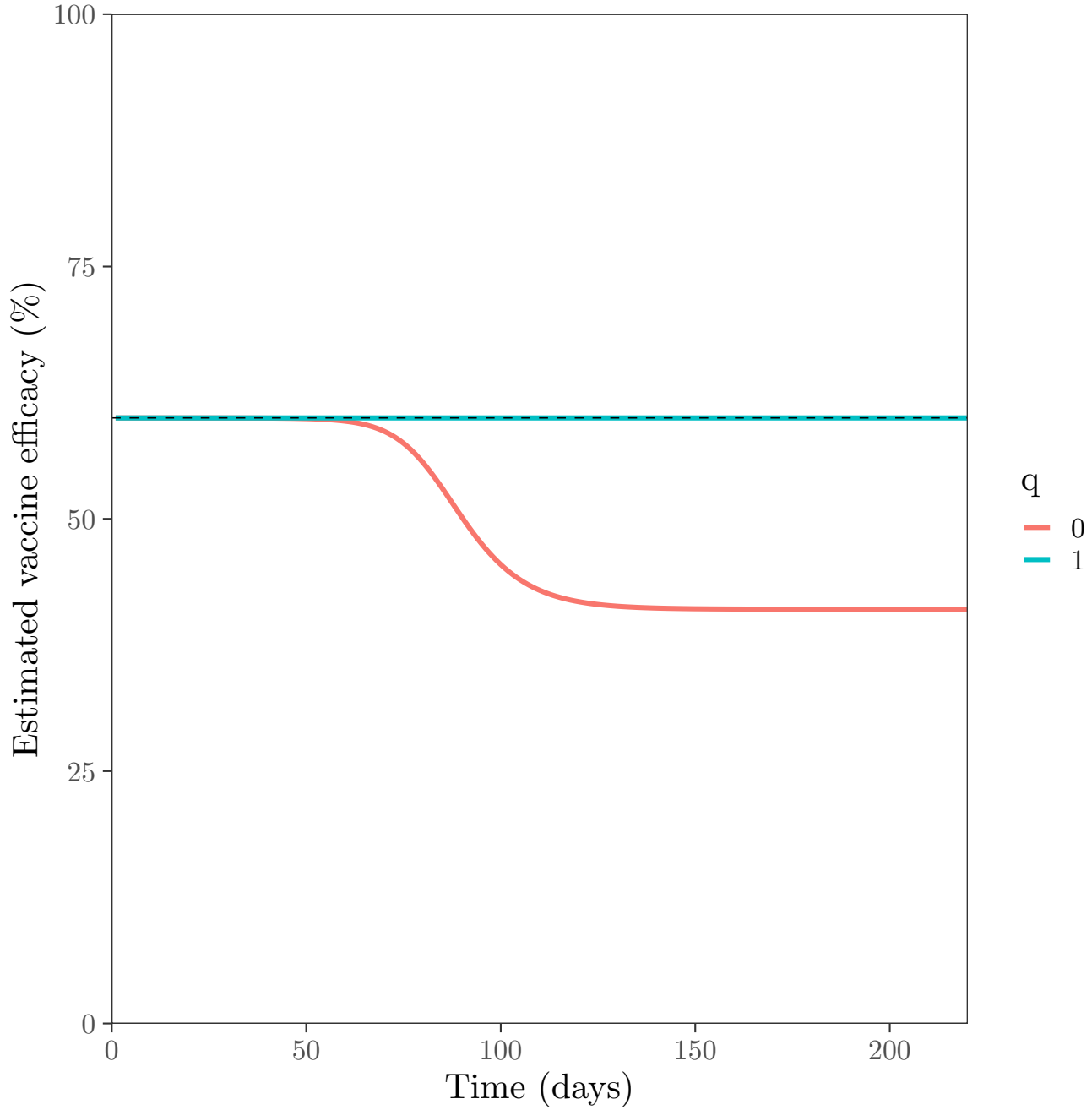
Leaky vaccine with boosting



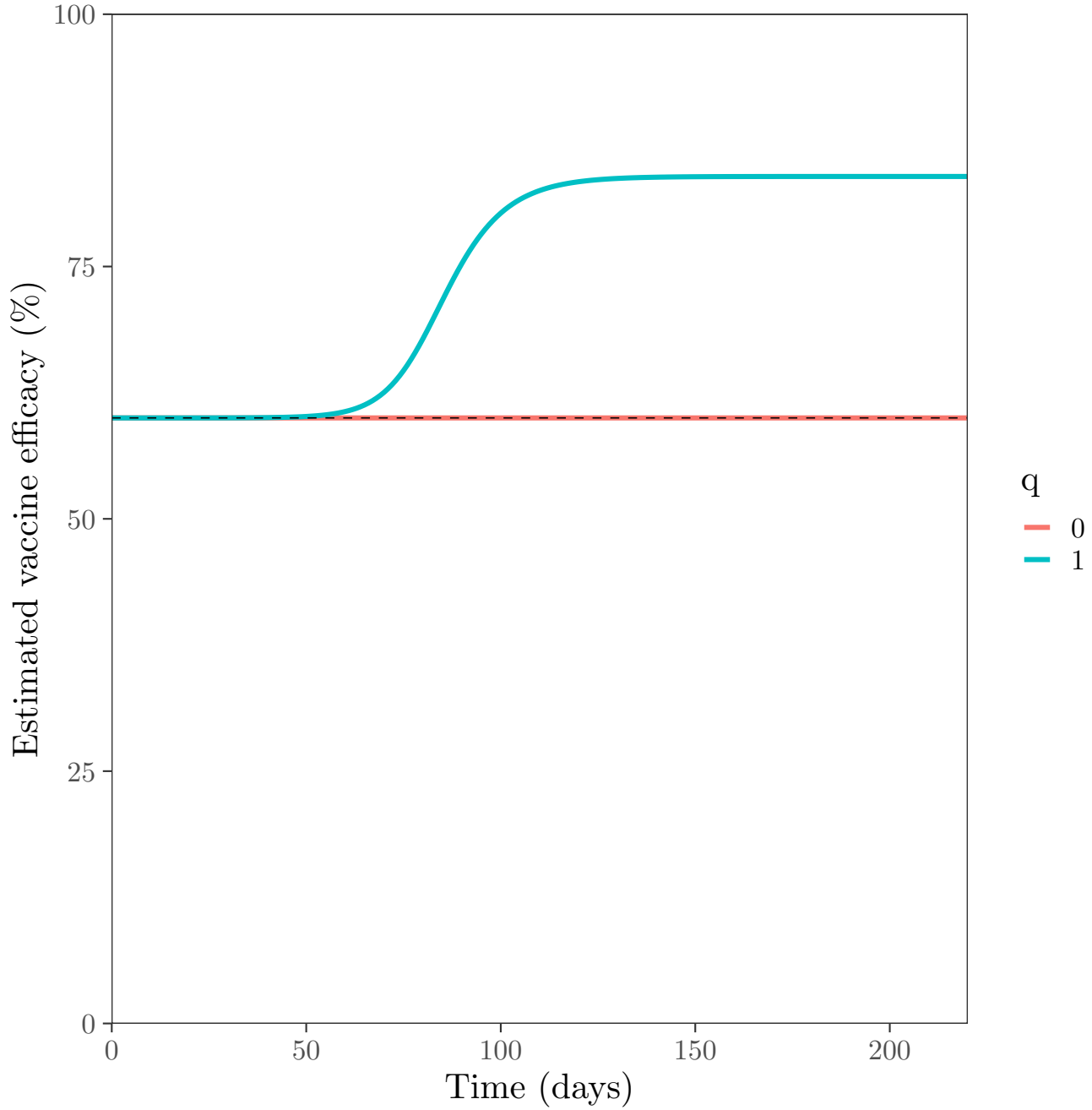
Vaccine effectiveness

- Efficacy: how protective the vaccine is in theory with a controlled exposure
- Effectiveness: how protective it will in a population
- We can project theoretical effectiveness under different assumptions
  - Cumulative incidence
  - Instantaneous hazard

Incidence-based effectiveness



Hazard-based effectiveness



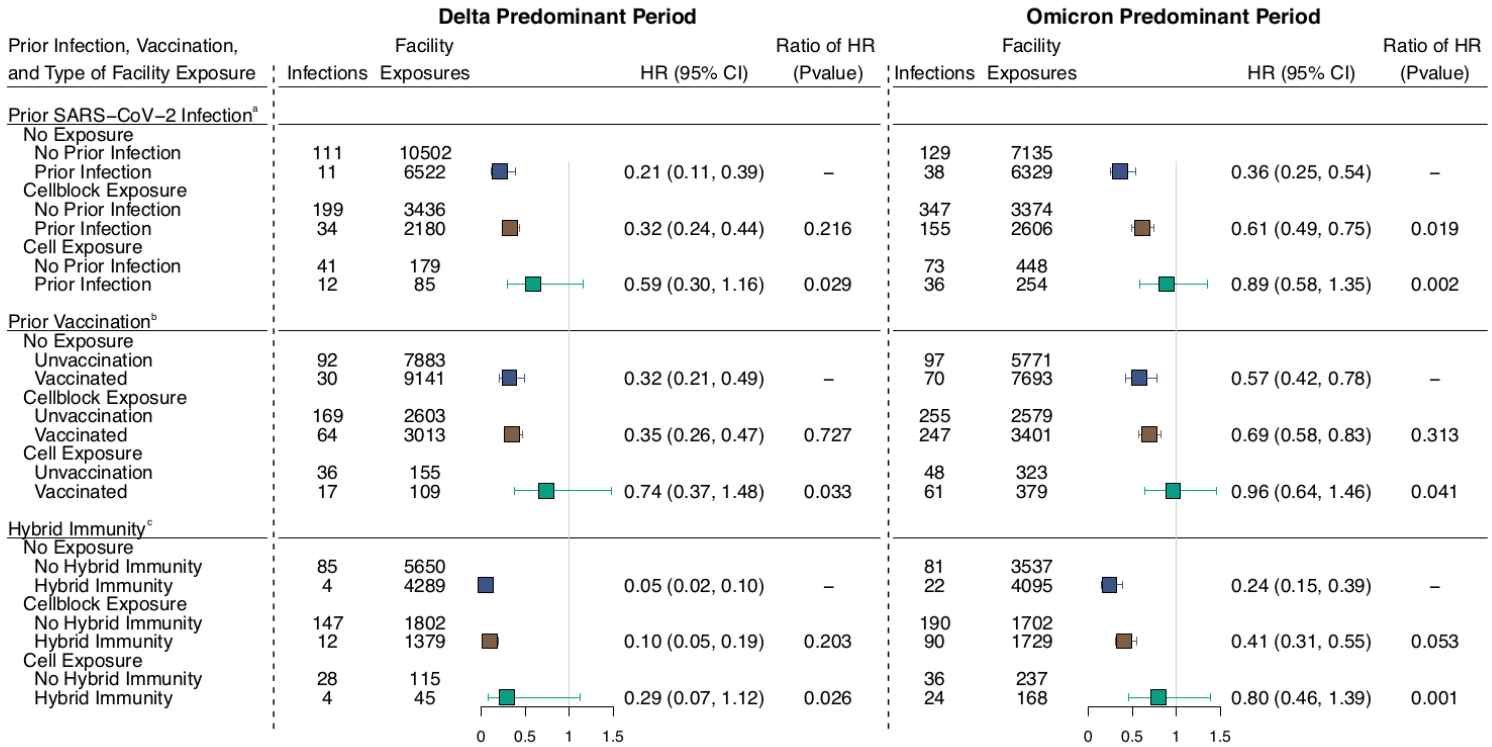
Questions going forward

- Vaccine vs infection-driven immunity
- Protection against what?
- Immune waning
- A broader view of leakiness

Leakiness

- We can define leakiness as any gap between efficacy and effectiveness
  - We can imagine different standard challenges for efficacy
- Should we be thinking only about number of challenges?
  - What about dose-dependence?
  - Can these be cleanly disentangled?

Connecticut correctional study



Lind et al., Nat Commun, 2023.

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