Use of the test-negative design to estimate the protective effect of a scalar immune measure

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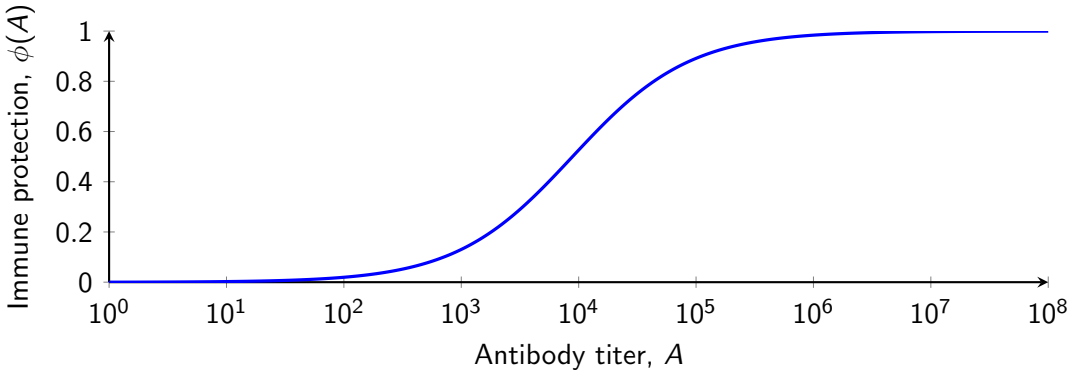
June 11, 2025

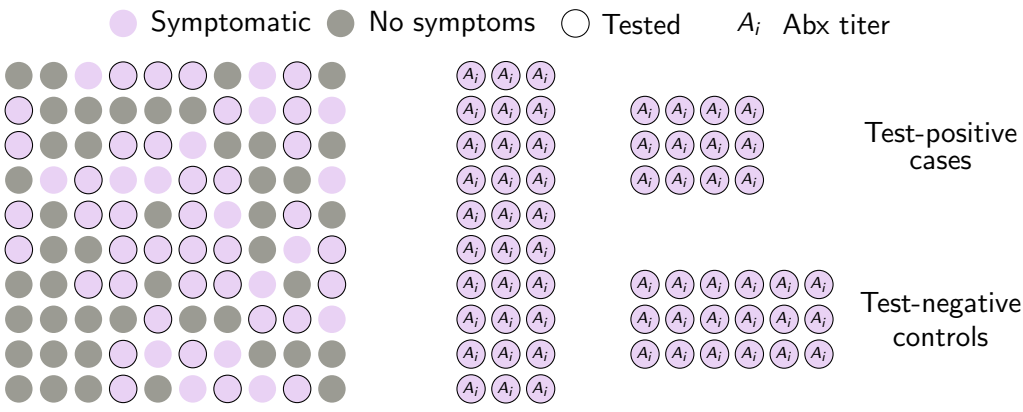
Exposure-proximal correlates of protection (COP)

The relationship between **antibody levels** and **the risk of infection** is of central interest to understand immune protection conferred by prior infection and/or vaccination.

$\Longrightarrow$ Because levels change, we want antibody levels **immediately prior to exposure**!



The test-negative design



Identification

We provide proofs that the conditional protection function $\phi(A, X)$[1] is identifiable in TND under two alternative assumptions sets:

Set A:

A1. **Equi-selection**. Conditional X, the probability of testing when symptomatic is the same for test positive and test negative illnesses.

A2. **No effect of COP on testing negative**. Conditional on X, there is no association between testing negative and A.

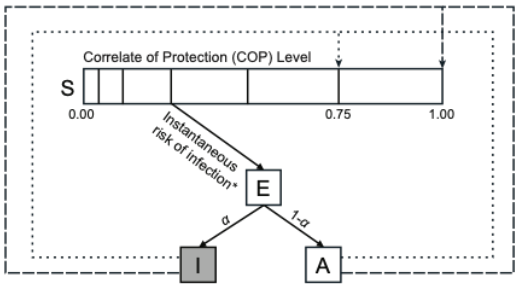
Set B:

B1. **Ignorability of test-negative sampling**. Conditional on A and X, selection is independent of symptomatic infection.

B2. **No effect of COP on testing negative**. Conditional on X, there is no association between testing negative and A.

[1] X are baseline covariates

Simulation study



Transition	Duration (day)
E to I	5
E to A	5
I to S	7
A to S	7

First-time exposure (infection or vaccination)

Subsequent exposure

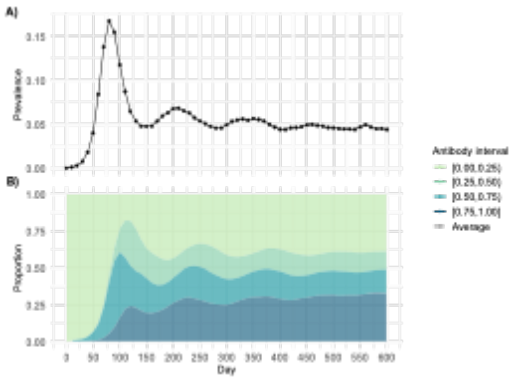


Figure: Agent based model

Simulation study

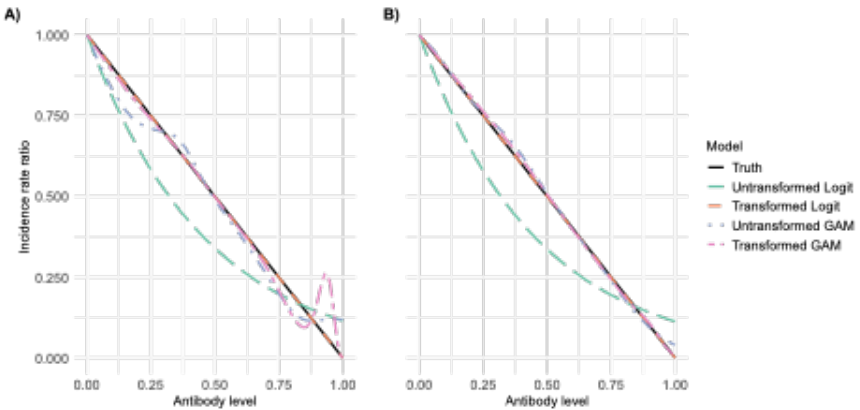


Figure: Results

Take-aways

Summary

- Exposure-proximal protection can be recovered in a TND provided conditions hold.
- COP-based TND may be more useful under waning or leaky vaccines.

Challenges

- Some interventions on antibody level may not be well-defined.
- Must correctly specify the functional form of the protection function.
- Sensitive to distribution of COP levels.

Pre-print

- Zhang, Z, Boyer, C, & Lipsitch, M. Use of the test-negative design to estimate the protective effect of a scalar immune measure: A simulation analysis. *medRxiv* https://doi.org/10.1101/2024.11.22.24317757

Collaborators

Ziyuan Zhang and Marc Lipsitch

Slide deck

https://christopherbboyer.com/talks

Funding

National Institutes of Health (U01CA261277)