SEROEPIDEMIOLOGY FOR EVALUATING THE IMPACT TYPHOID VACCINE INTERVENTIONS

Together We Can
Take on Typhoid

December 07, 2023

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UCDAVIS HEALTH

Mahidol University
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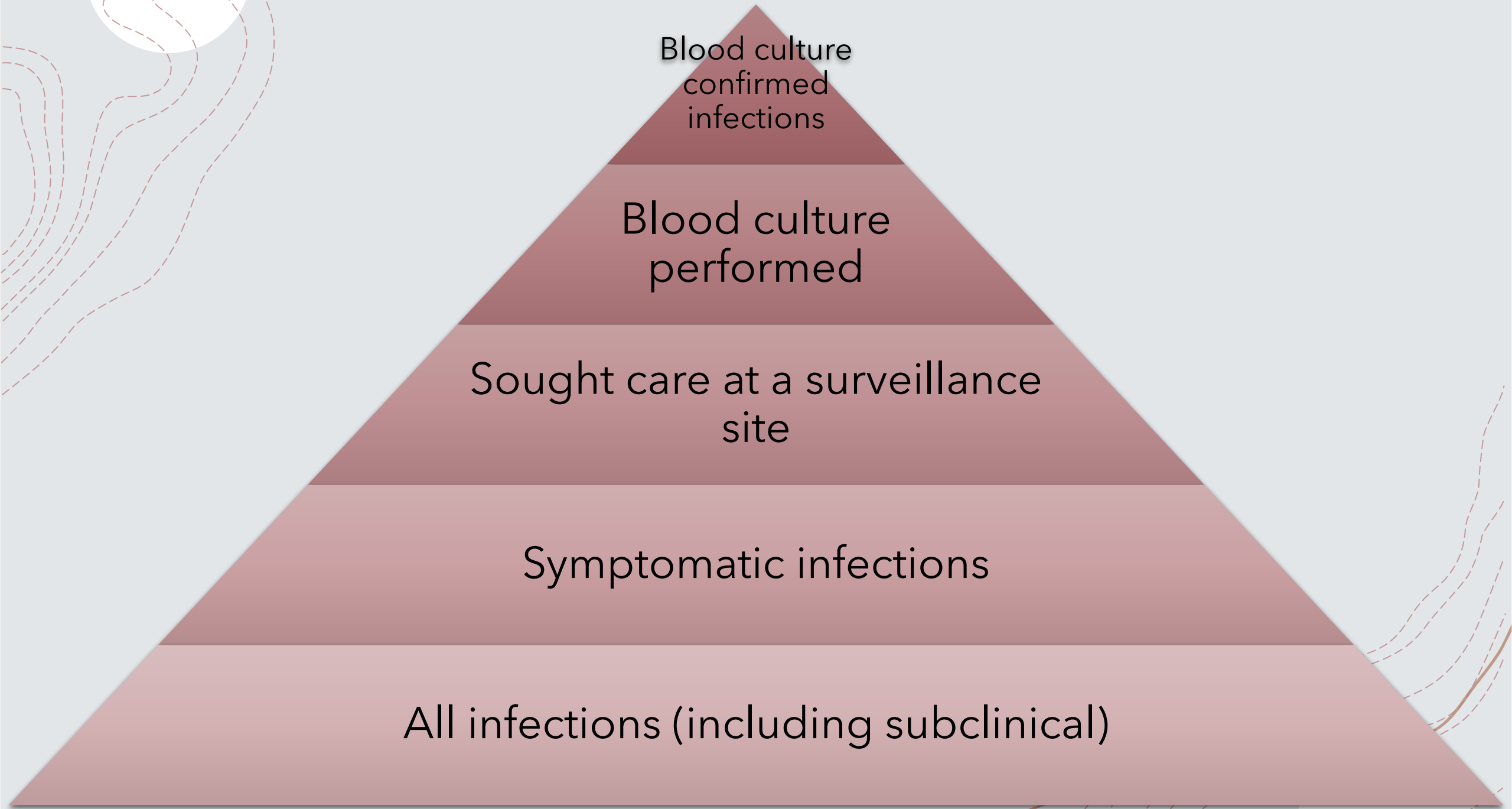
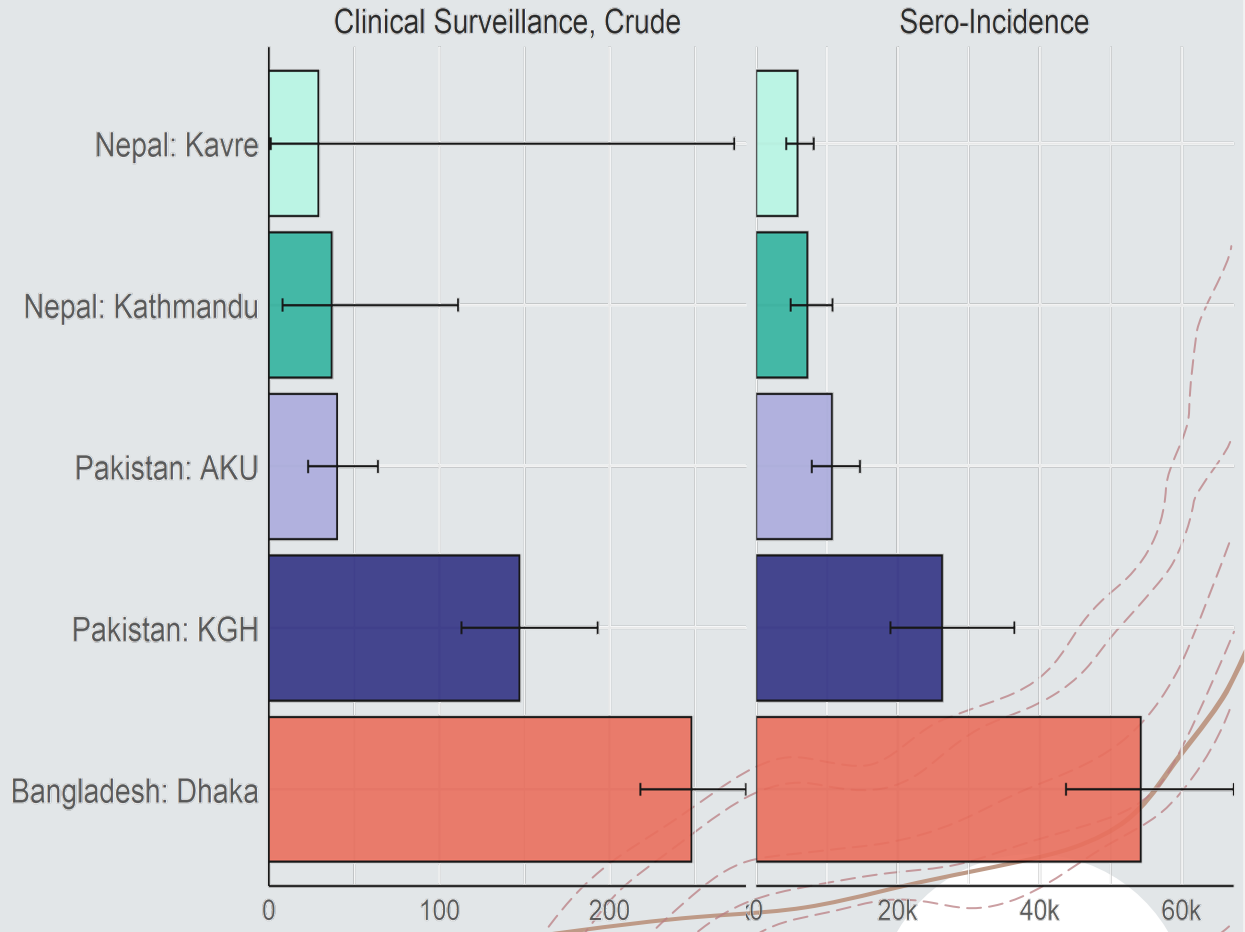
Location	Nepal		Malawi		Bangladesh	
Number of participants	20,019		27,882		61,567	
Ages of participants	9 months to <16 years		9 months to <12 years		9 months to <16 years	
Study design	**Randomized 1:1** *TCV or meningococcal A vaccine*		**Randomized 1:1** *TCV or meningococcal A vaccine*		**Cluster* randomized 1:1** *TCV or Japanese encephalitis (JE) vaccine*	
Length of follow-up	24 months		18-24 months		18 months	
Blood-culture confirmed typhoid cases	TCV: 13	Meningococcal A: 62	TCV: 10	Meningococcal A: 61	TCV: 29	JE: 192
Vaccine efficacy	**79%** *95% CI (61.9%-88.5% P<0.001)*		**84%** *95% CI (68.1%-91.6% P<0.001)*		**85%** *97.5% CI (76%-91% P<0.001)*	
Vaccine safety	Meets safety standards ✓		Meets safety standards ✓		Meets safety standards ✓	

*In cluster randomized trials, groups of participants (known as clusters) are randomized as opposed to individual participants being randomized.

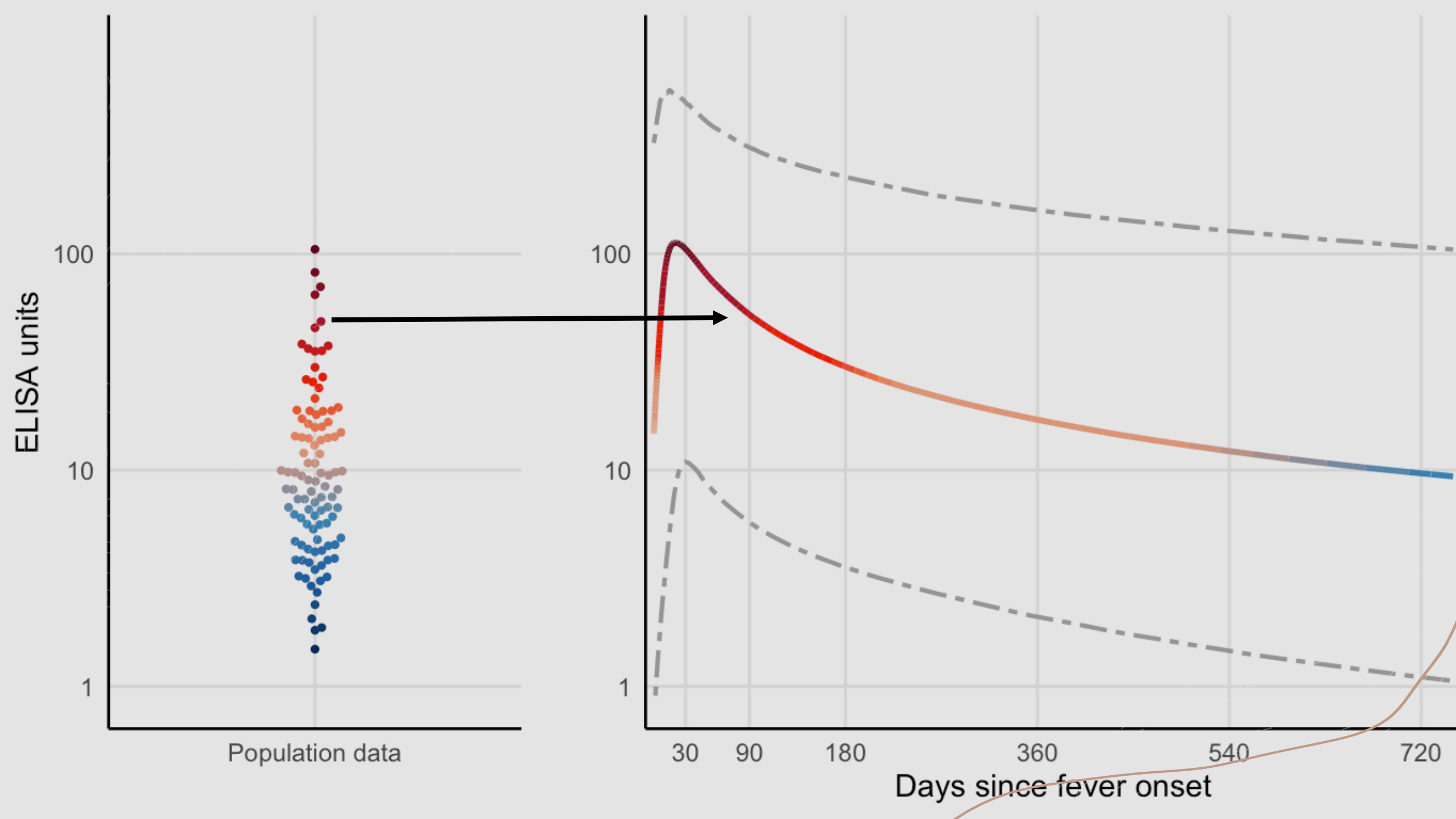
TyVAC Typhoid Vaccine Acceleration Consortium


Blood culture confirmed infections
Blood culture performed
Sought care at a surveillance site
Symptomatic infections
All infections (including subclinical)

Seroincidence: a new tool for capturing enteric fever infection burden based on anti-HLyE antibody responses



SABIN VACCINE INSTITUTE

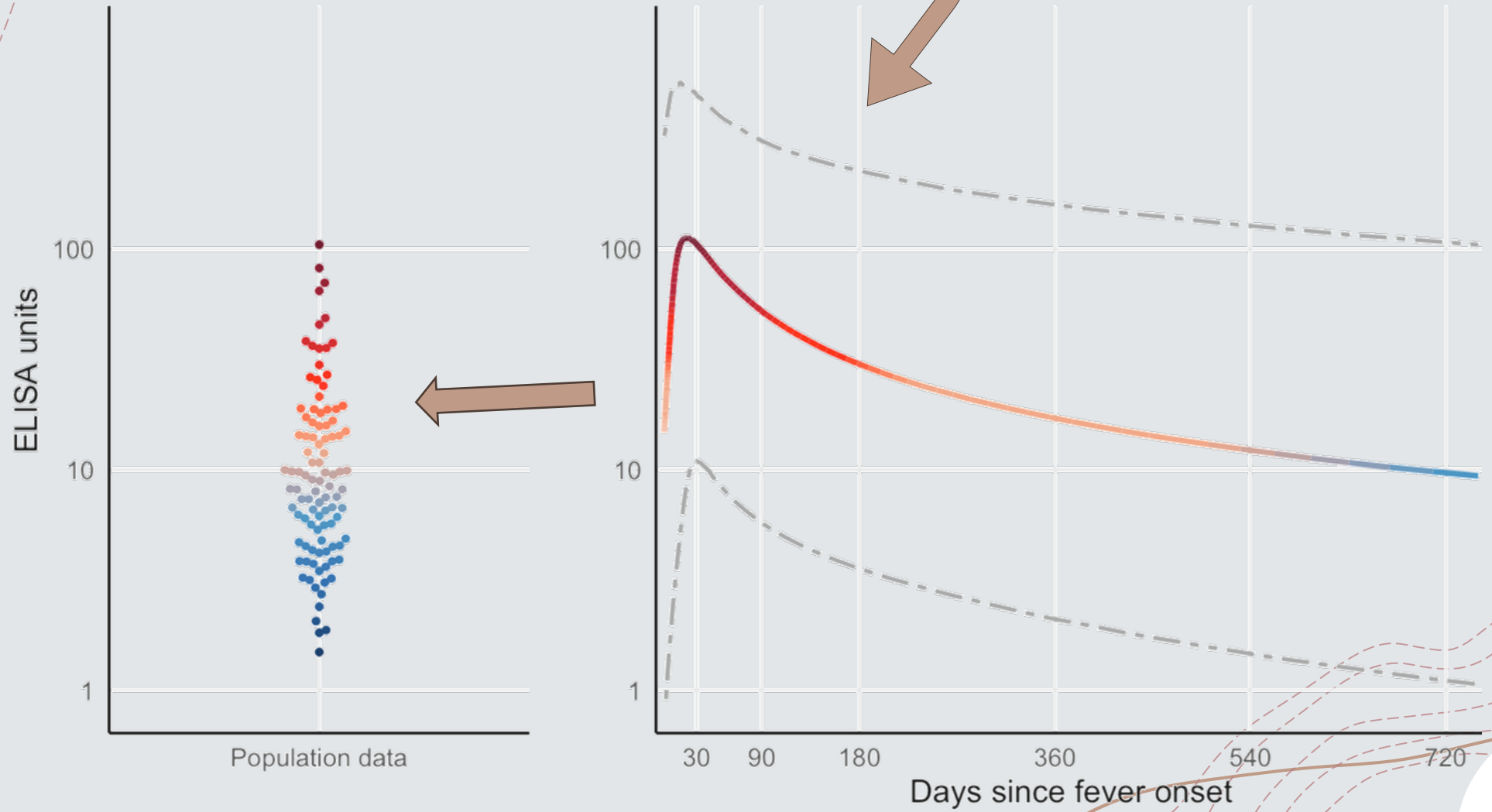

ELISA units
100
10
1
Population data
100
10
1
30
90
180
360
540
720
Days since fever onset

Can seroepidemiology be used to efficiently characterize overall/total/ indirect effects of TCV introduction?

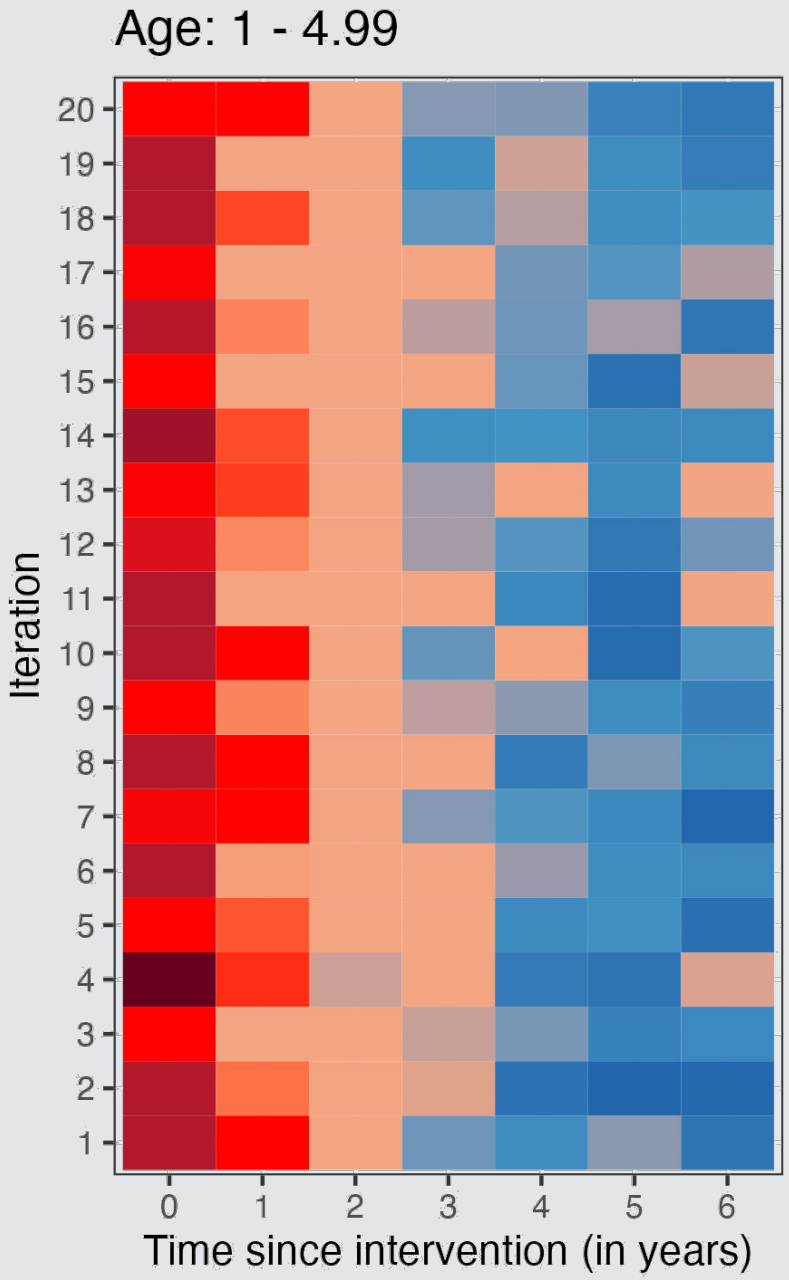
Outcomes

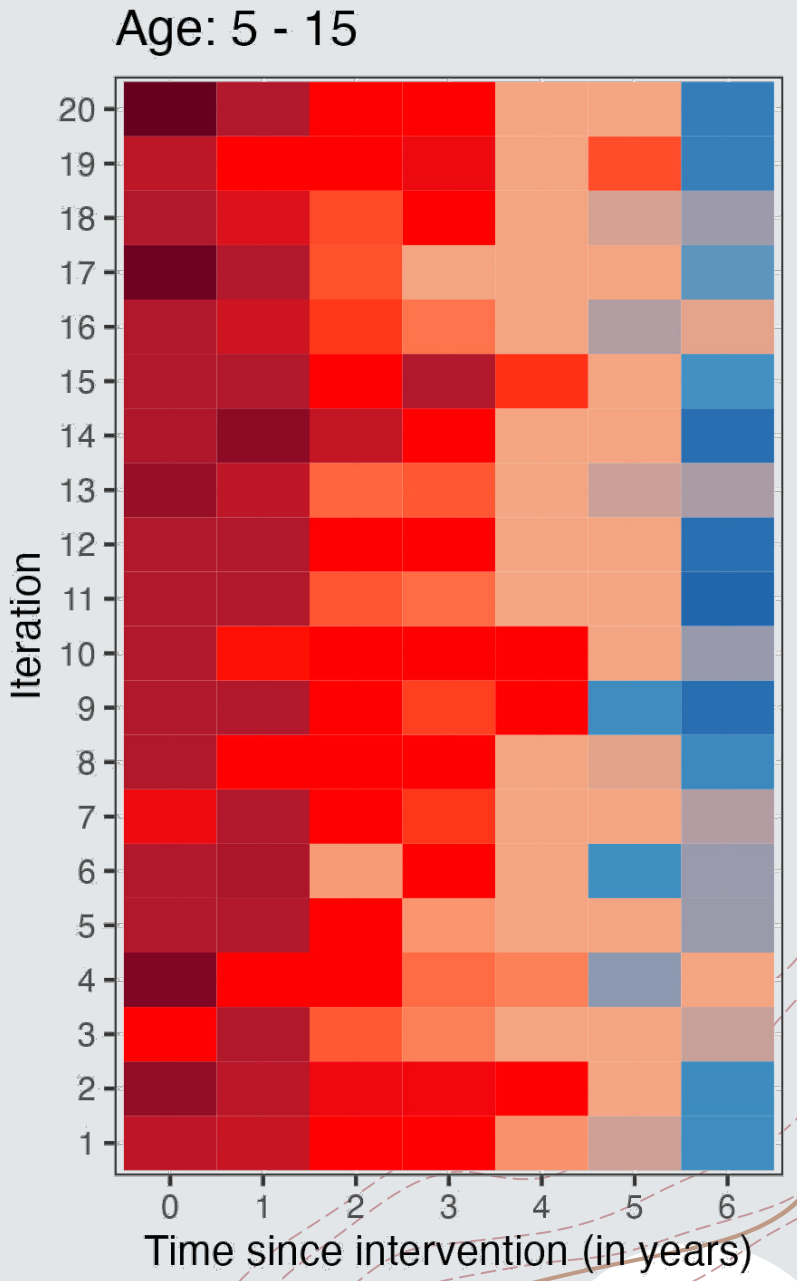
- **Overall effect**: Seroincidence in intervention arm vs. control arm
- **Total effect**: Seroincidence among vaccinated individuals in the intervention arm vs. unvaccinated individuals in the control arm
- **Indirect effect:** Seroincidence incidence in unvaccinated individuals in the intervention arm vs. control arm

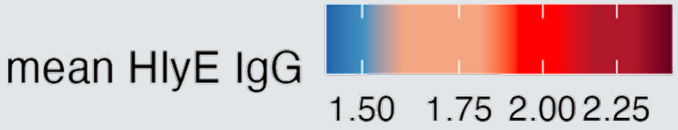
Seroincidence of X per 1000 person-years



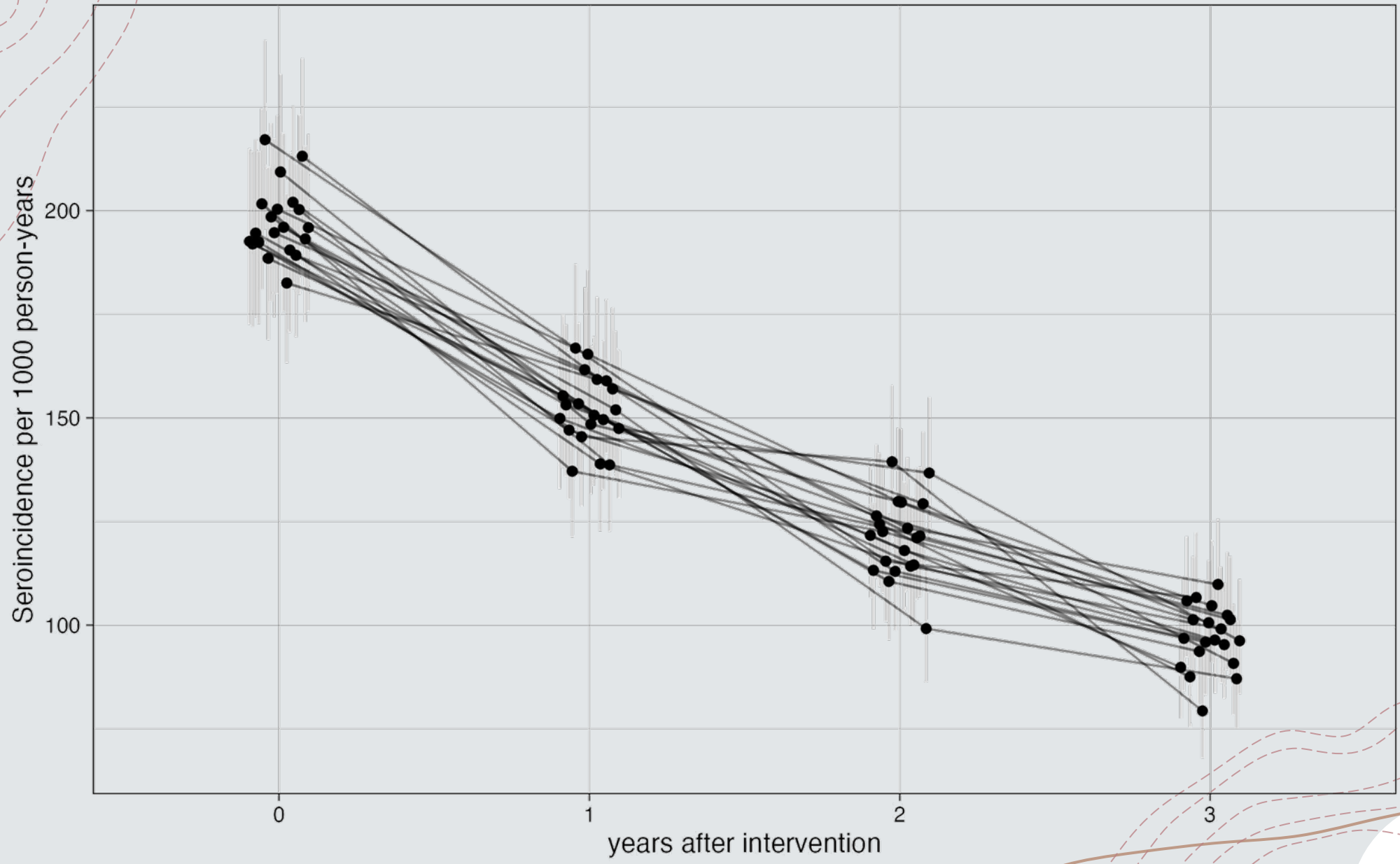
Effect size = 60%
Sample size = 500
Starting seroincidence =
200 per 1000







Intervention effect of 60%; Sample size = 800; Age 1-5



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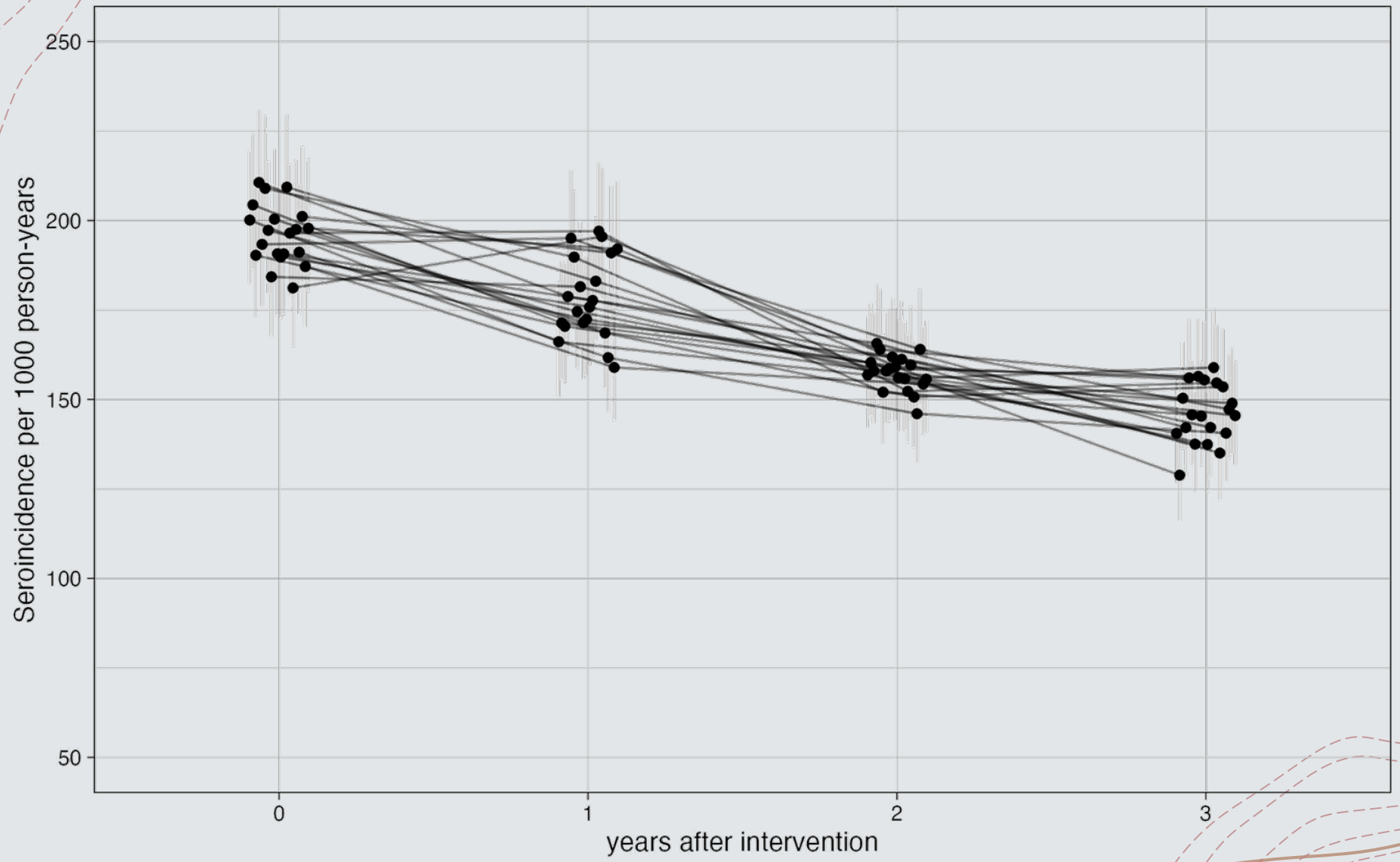
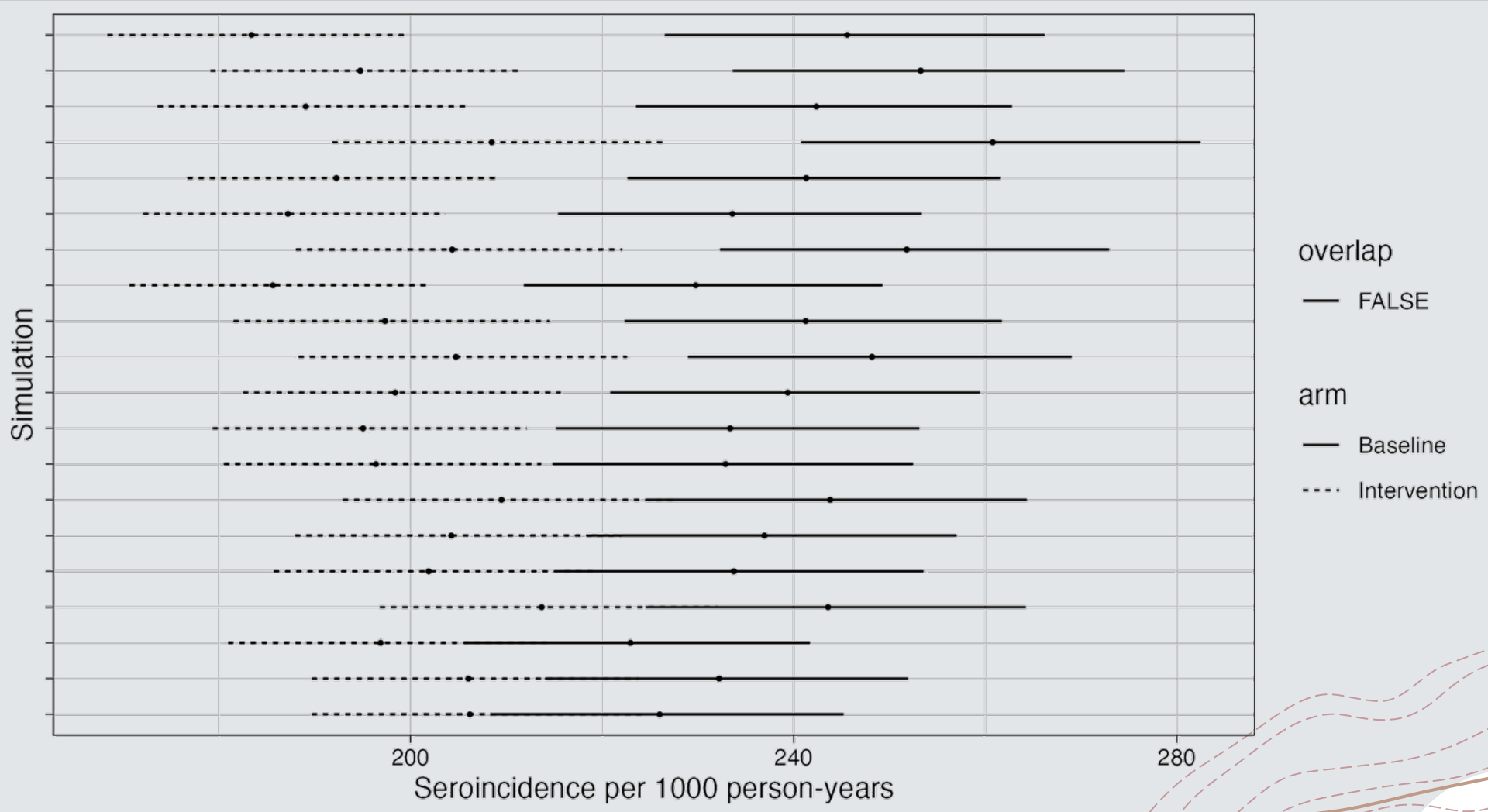
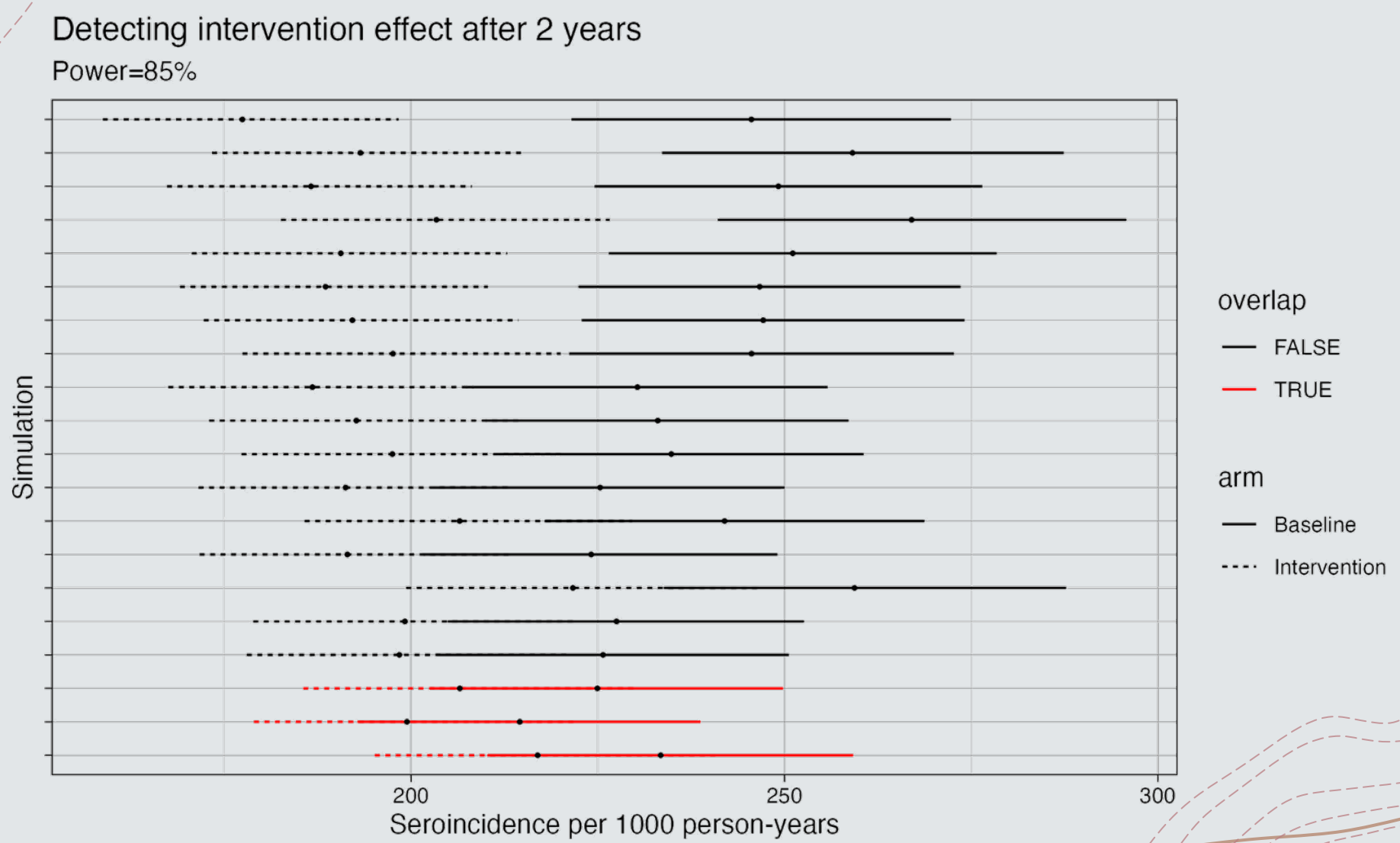


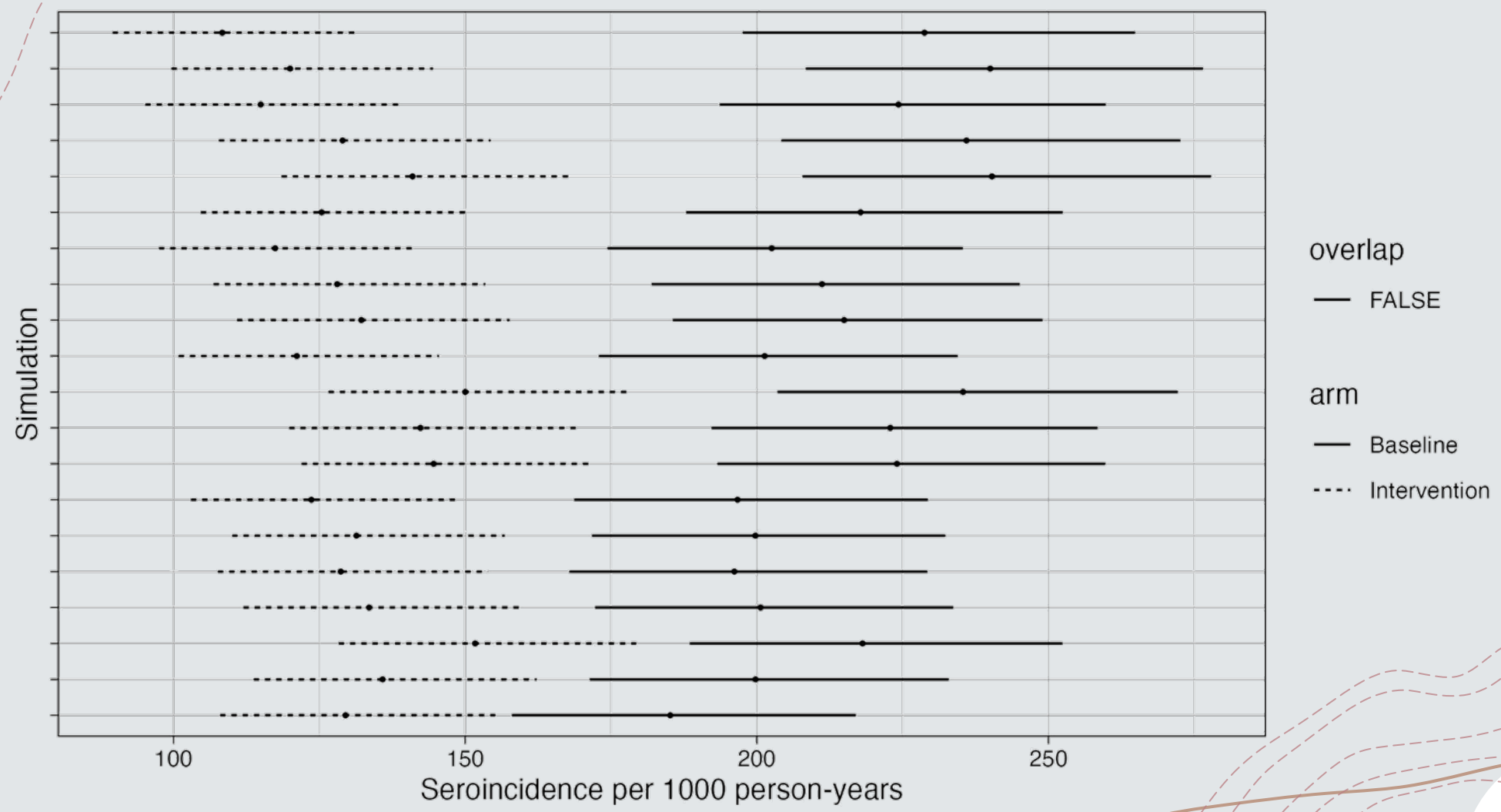
100% power to detect an intervention effect of 60% 2 years post-intervention with a sample size of 2000 1-15 year-olds (1000 per arm)



85% power to detect an intervention effect of 60% 2 years post-intervention with a sample size of 1200 1-15 year-olds (600 per arm)



100% power to detect an intervention effect of 60% 2 years post-intervention with a sample size of 800 1-5 year-olds (400 per arm)



serocalculator

Antibody levels measured in a cross–sectional population sample can be translated into an estimate of the frequency with which seroconversions (infections) occur in the sampled population. In other words, the presence of many high antibody titres indicates that many individuals likely experienced infection recently and the burden of disease is high in the population, while low titres indicate a low frequency of infections in the sampled population and therefore a lower burden of disease.

The **serocalculator** package was designed to use the longitudinal response characteristics using a set of modeled parameters characterizing the longitudinal response of the selected serum antibodies.

Installing R

The **serocalculator** package is written in R, a free, open-source software program. The end user of this package must have access to a working installation of the R software. We recommend installing base R and a Graphical User Interfaces (GUI) for R such as RStudio.

If you need to download and install R and/or RStudio, we recommend following the tutorial below from *Hands On Programming in R* by Garrett Grolemund:

Installing R and RStudio: https://rstudio-education.github.io/hopr/starting.html

Installing the Serocalculator Package

The **serocalculator** package must be installed in R before first use. As of November 21, 2023, **serocalculator** is still in development. To install the development version, you must

Links

Browse source code

License

GPL-3

Community

Contributing guide

Code of conduct

Citation

Citing serocalculator

Developers

Peter Teunis

Author, copyright holder

Kristina Lai

Author

Kristen Aiemjoy

Author

Douglas Ezra Morrison

Author, maintainer

More about authors...

Dev status

R-CMD-check passing

Generate a simulated cross-sectional sample and estimate seroincidence

Enteric Fever using HlyE IgG and/or HlyE IgA

Source: vignettes/articles/simulate_xsectionalData.Rmd

This vignette shows how to simulate a cross-sectional sample of seroresponses for incident infections as a Poisson process with frequency `lambda`. Responses are generated for the antibodies given in the `antigen_isos` argument.

Age range of the simulated cross-sectional record is `lifespan`.

The size of the sample is `nrep`.

Each individual is simulated separately, but different antibodies are modelled jointly.

Longitudinal parameters are calculated for an age: `age.fx` (fixed age). However, when `age.fx` is set to NA then the age at infection is used.

The boolean `renew.params` determines whether each infection uses a new set of longitudinal parameters, sampled at random from the posterior predictive output of the longitudinal model. If set to `FALSE` a parameter set is chosen at birth and kept, but: 1. the baseline antibody levels (`y0`) are updated with the simulated level (just) prior to infection, and 2. when `is.na(age.fx)` then the selected parameter sample is updated for the age when infection occurs.

There is also a variable `n.mc`: when `n.mc==0` then a random MC sample is chosen out of the posterior set (1:4000). When `n.mc` is given a value in 1:4000 then the chosen number is fixed and reused in any subsequent infection. This is for diagnostic purposes.

On this page

https://ucd-serg.github.io/serocalculator/articles/simulate_xsectionalData.html

Conclusions

- Through simulation, we show that seroepidemiology could be an efficient and rapid way to evaluate TCV interventions
- Young children provide the most informative data for detecting intervention effects
- Approach for both trials and pre/post designs

ACKNOWLEDGEMENTS

National Institute of Allergy and Infectious Diseases

Bill & Melinda Gates foundation

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Stanford University

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Extra slides

Outcomes

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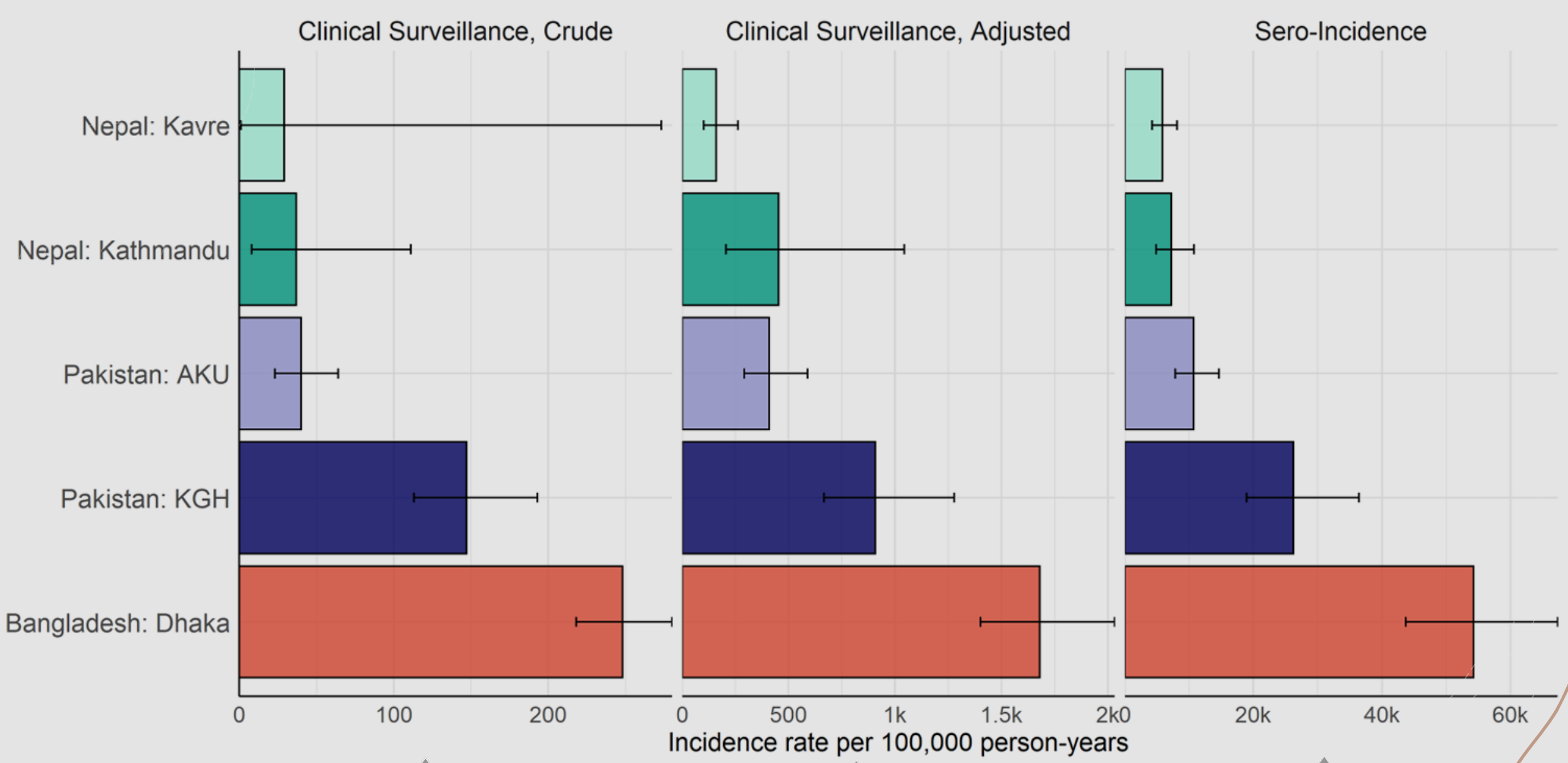
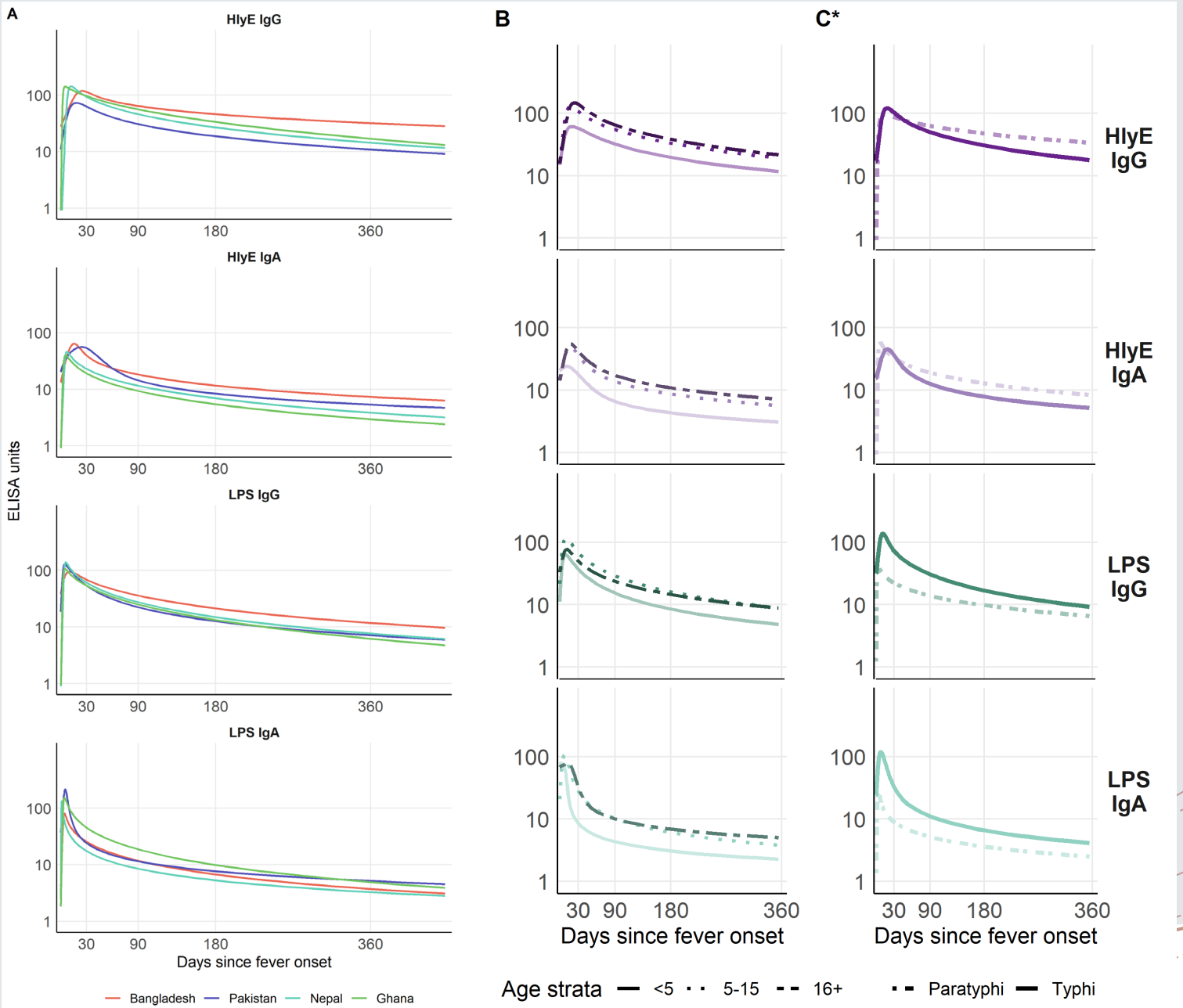

Clinical Surveillance, Crude
Clinical Surveillance, Adjusted
Sero-Incidence
Nepal: Kavre
Nepal: Kathmandu
Pakistan: AKU
Pakistan: KGH
Bangladesh: Dhaka
0
100
200
0
500
1k
1.5k
2k0
20k
40k
60k
Incidence rate per 100,000 person-years
Culture positive
Culture positive
Blood culture performed
Sought care
Symptomatic infections
Culture positive
Blood culture performed
Sought care
Symptomatic infections
All infections
Age 2 to <5

Variation in antibody kinetics by:

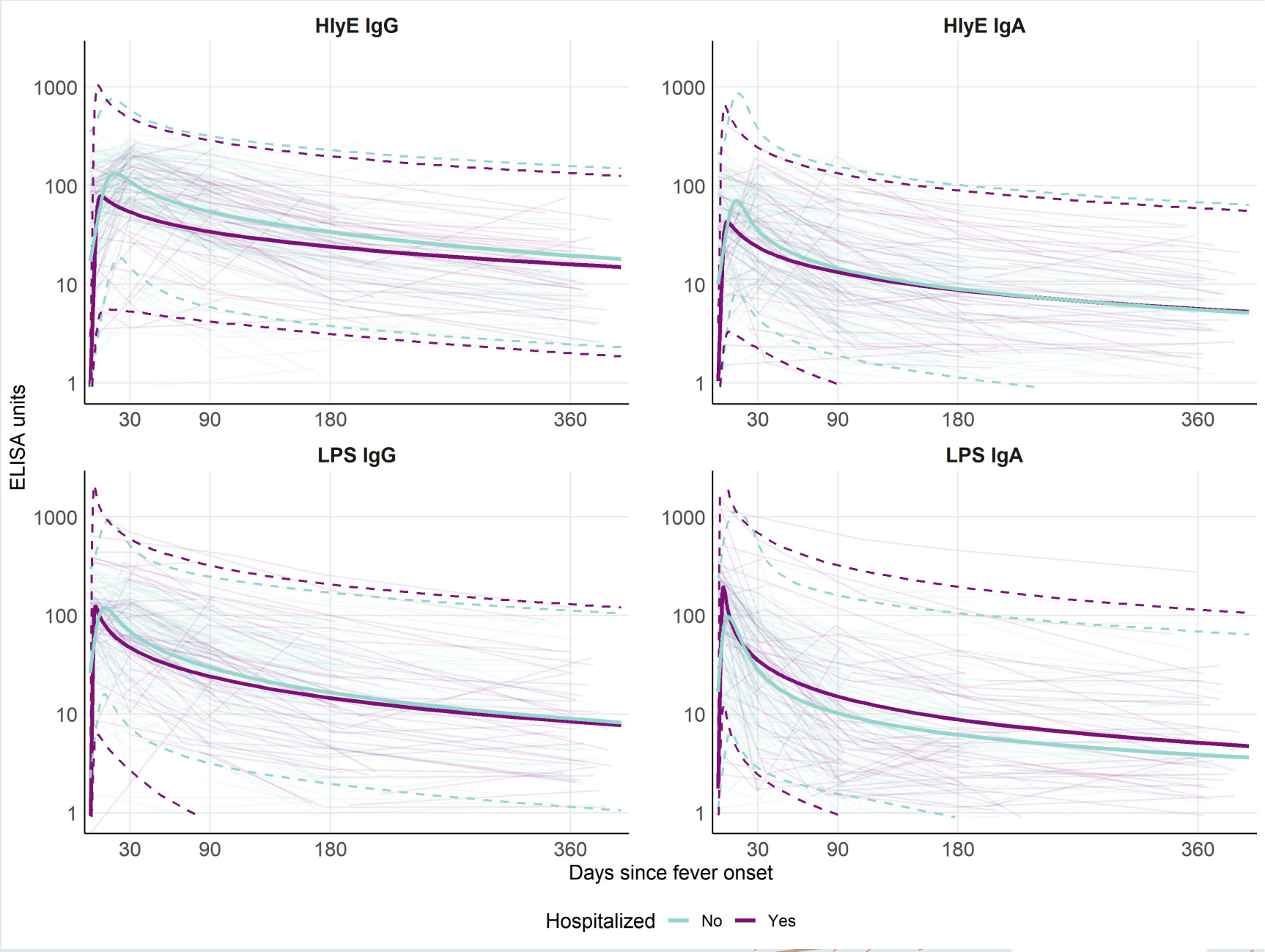
Country

Age

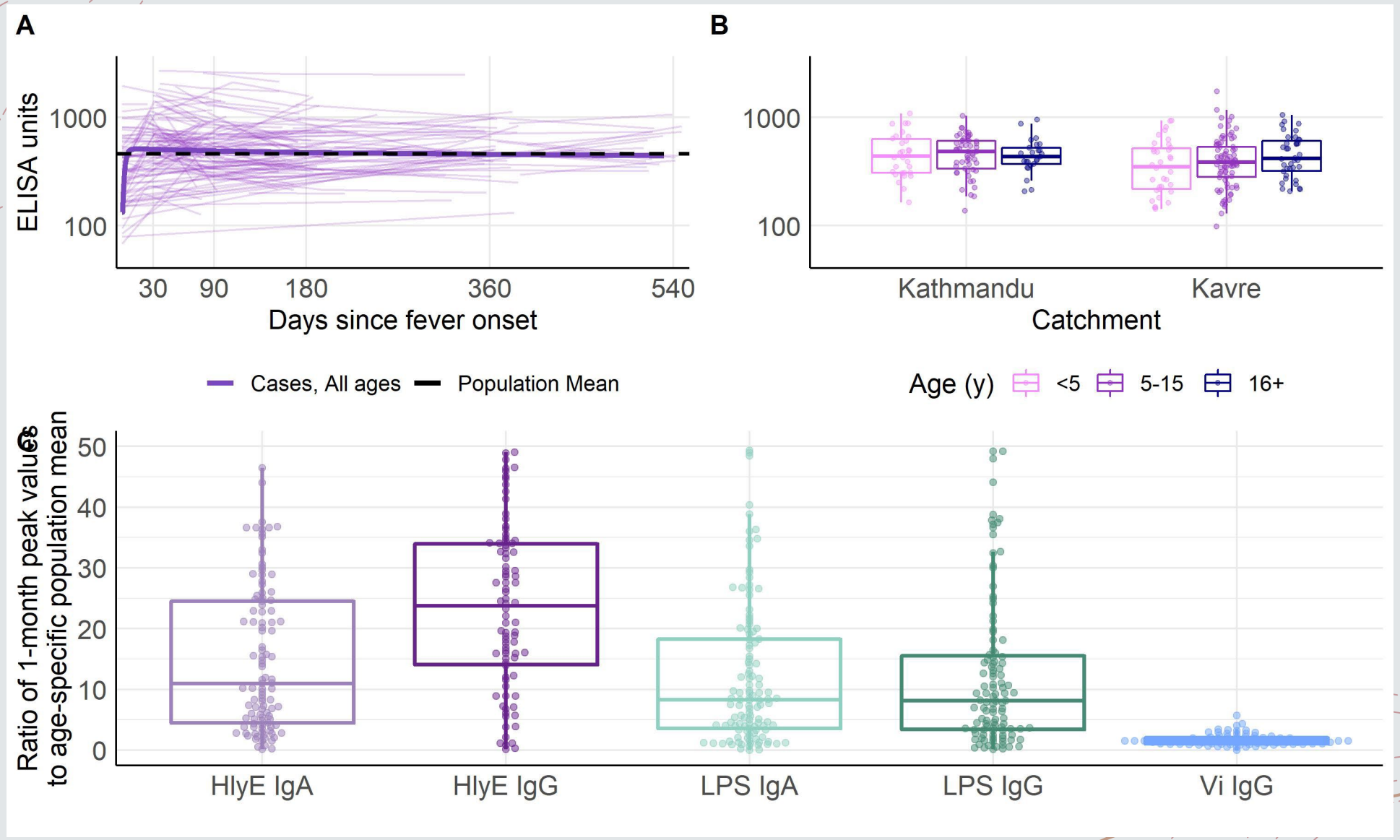
Typhi/Paratyphi A



No differences in antibody responses among hospitalized vs non-hospitalized cases



Vi IgG responses barely elevated in cases compared with population No increase across age



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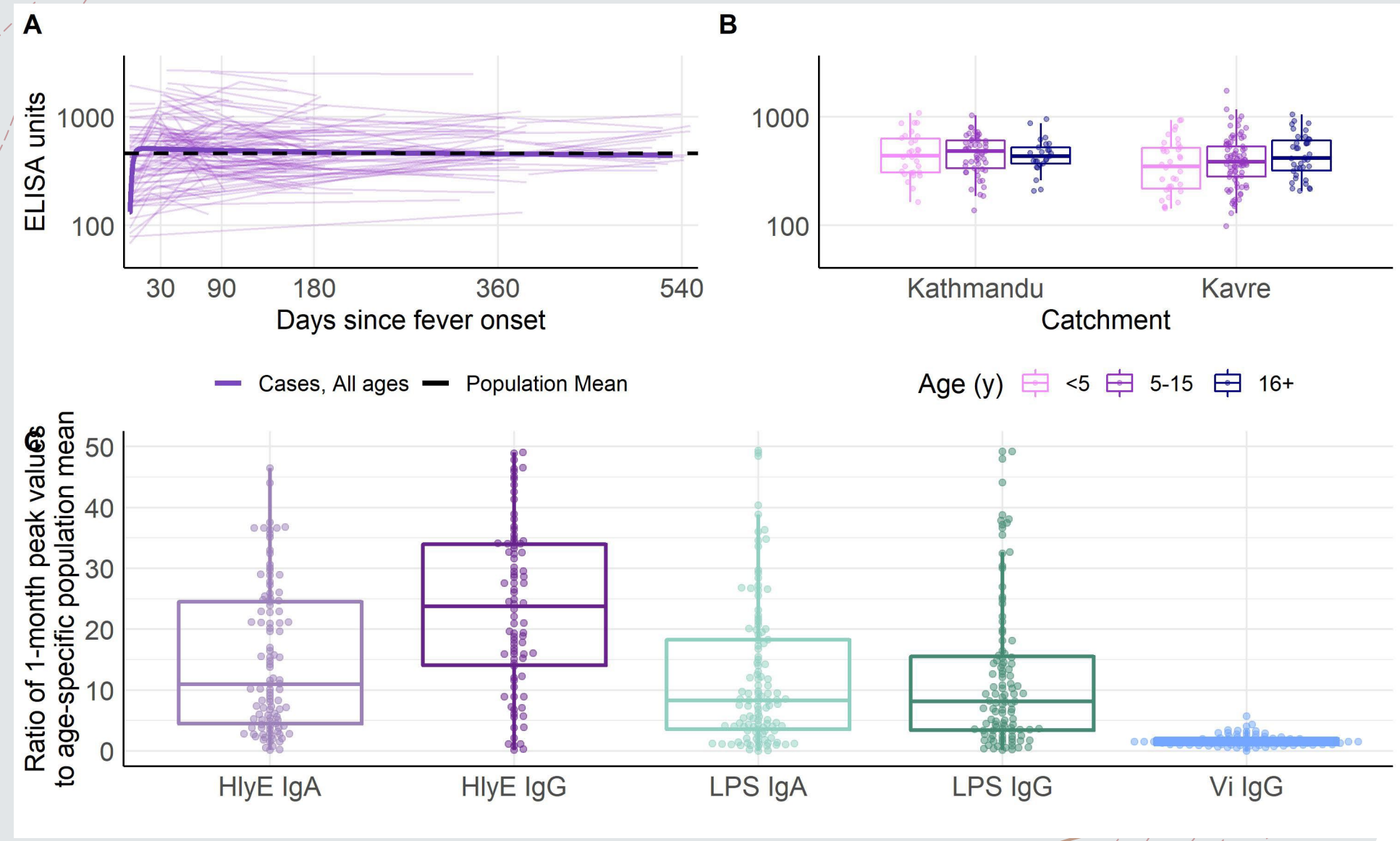
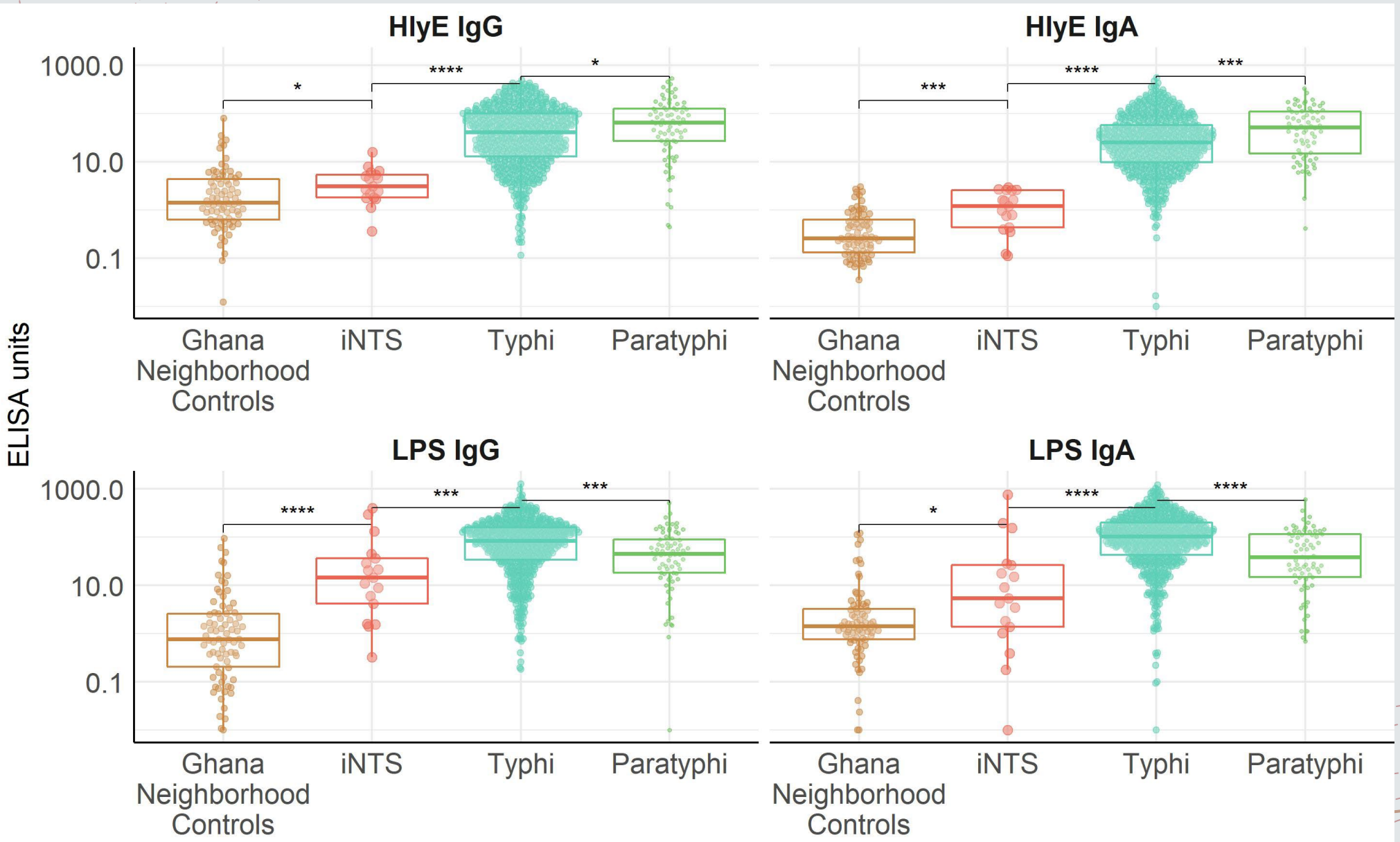


Cross-reactive antibody responses in iNTS?



HlyE IgA
Typhi vs iNTS
AUC: 0.97
(95% CI: 0.96-0.99)

LPS IgA
Typhi vs iNTS
AUC: 0.88
(95% CI: 0.78-0.99)

No differences in antibody responses among hospitalized vs non-hospitalized cases