



EMORY

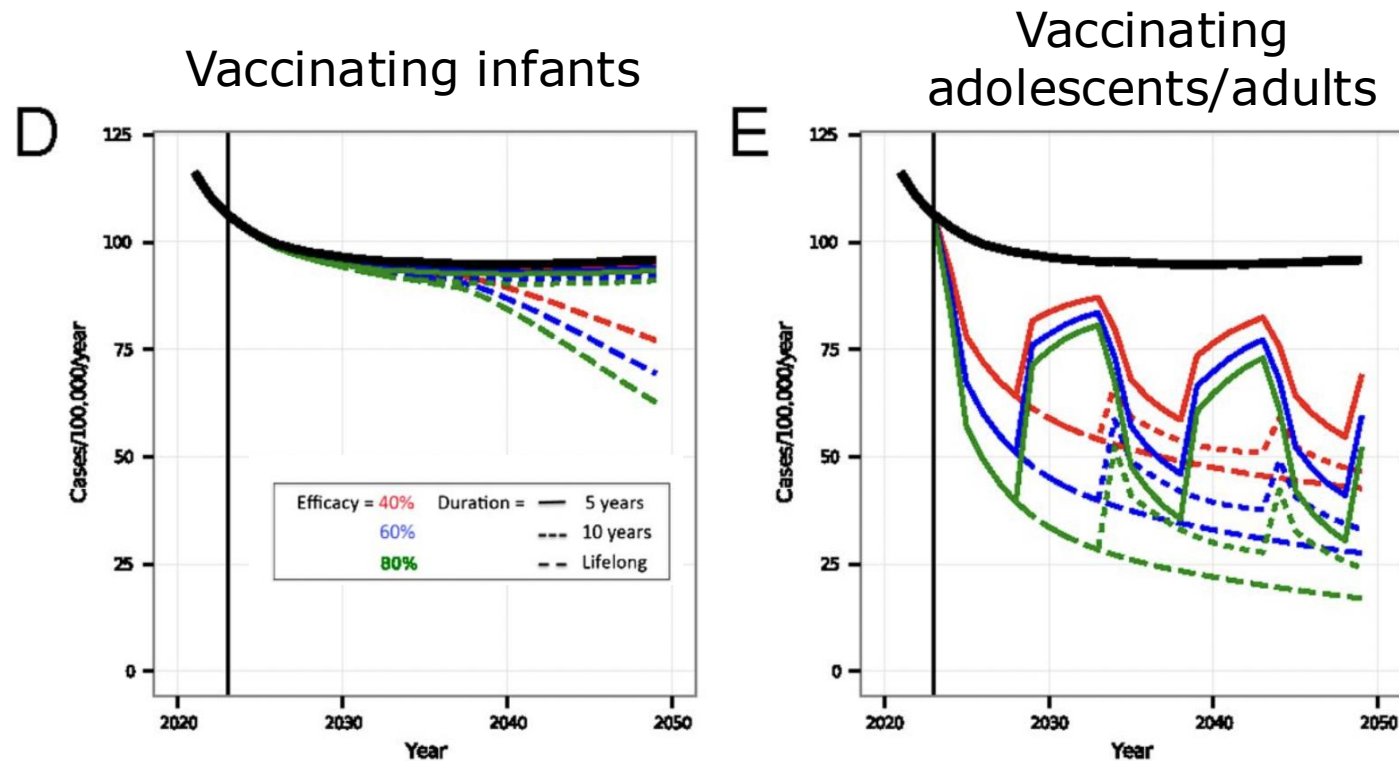
ROLLINS
SCHOOL OF
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Modelling Applications for TB, RSV, and Rotavirus



TB

Potential impact of infant vs. adolescent/adult vaccines?



Cases averted:

0.89 million
95% range: (0.42–1.58)

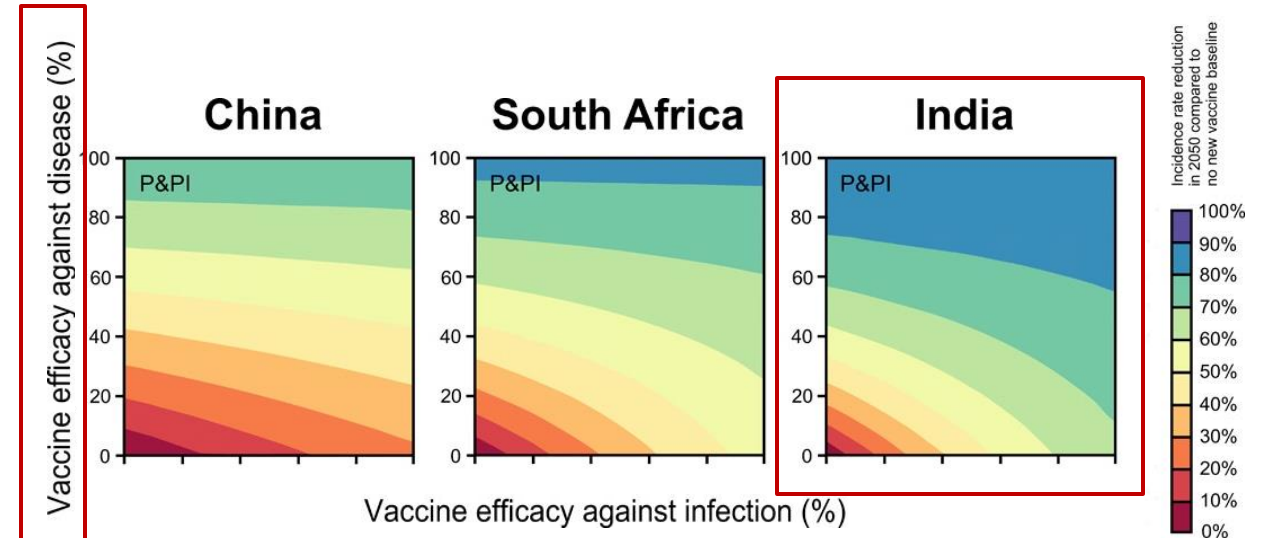
17 million
95% range: (11–24)

Preventing infection or disease?

Vaccines preventing disease, rather than infection, would **have the greatest impact in all settings**

BUT

vaccines preventing infection would have more impact in places with higher levels of transmission (more new infections, **i.e., India**, not China)



Making the investment case

50% effective vaccine for adolescents and adults could cumulatively avert

37.2–76.0 million cases and 4.6–8.5 million deaths

Also

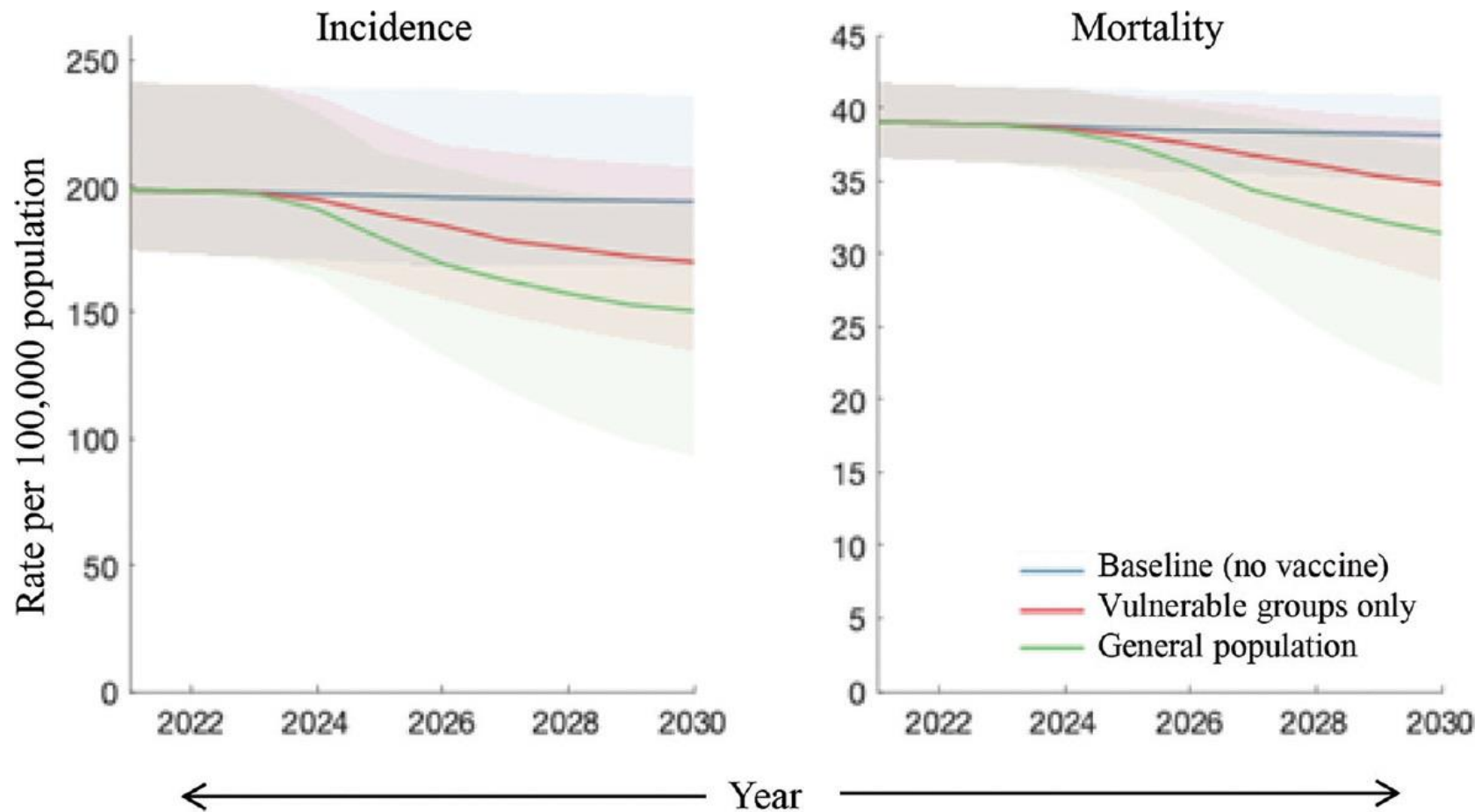
- Cost-effective and cost-saving in nearly all high-burden countries
- a significant market (5 billion adults)
- significant ROI (value of US \$70 billion)
- a boon to economic growth (US \$1.6 trillion in GDP)

An investment case
for new tuberculosis
vaccines



 World Health
Organization

Potential impact of adult / adolescent TB vaccines in India?

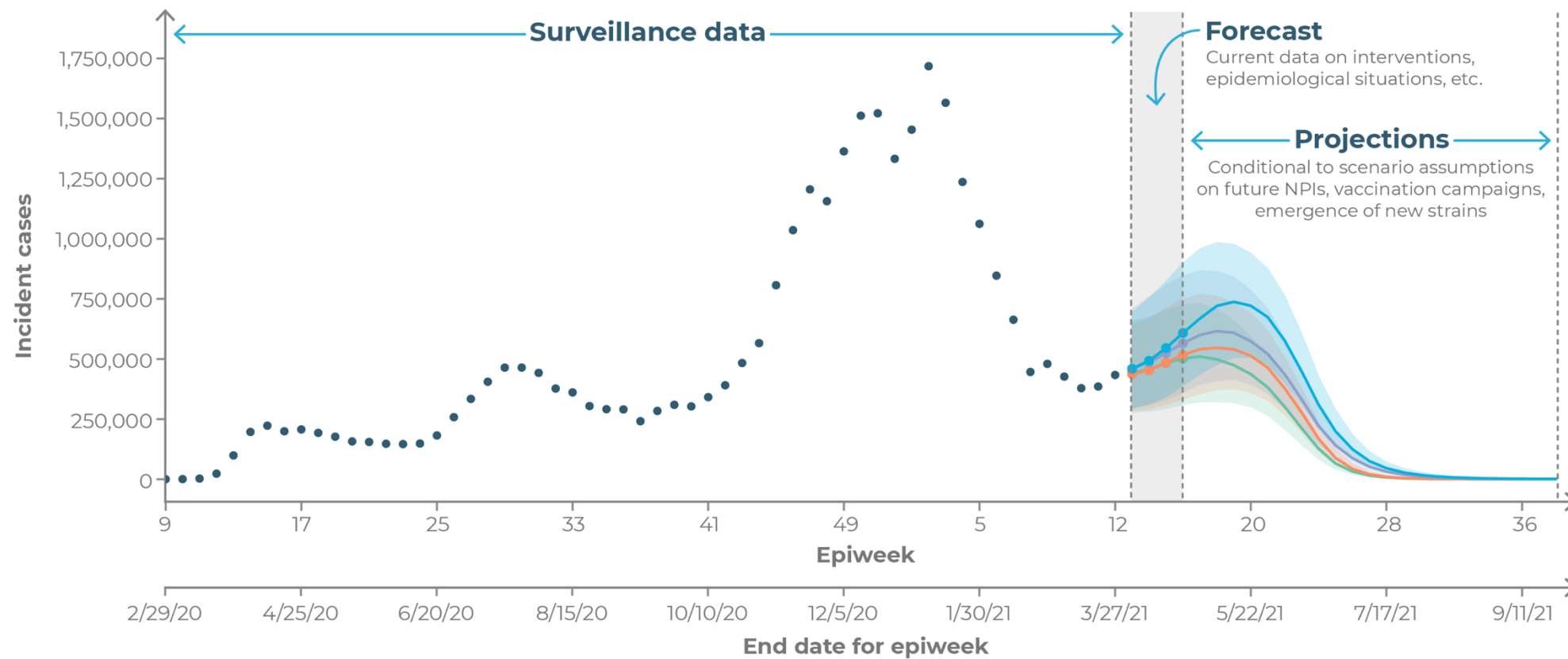


RSV

RSV Scenario Modeling Hub

- Even the best models of infectious disease transmission struggle to give accurate forecasts at time scales greater than 3-4 weeks due to unpredictable drivers like changing policy environments, behavior change, development of new control measures, and stochastic events.
- As such, long-term projections can guide longer-term decision-making while short-term forecasts are more useful for situational awareness and guiding immediate response.

RSV Scenario Modeling Hub



2024-2025 Scenarios

Specified a set of scenarios and target outcomes to allow alignment of model projections for collective insights.

Scenarios have been designed in consultation with academic modeling teams and government agencies (e.g., CDC).

	Optimistic senior waning <ul style="list-style-type: none"> Vaccine is administered from Aug to June to seniors 60+ yrs Total coverage, which includes last year and this year's vaccinations, saturates at 45% of the eligible population and is indexed on the 2021-22 state- and age-specific flu vaccine coverage VE against hospitalization is 75% at the time of vaccine receipt and is reduced by 10% in the second season after receipt, i.e., VE_year2=68%. 	Pessimistic senior waning <ul style="list-style-type: none"> Same timing and coverage assumptions as for the optimistic senior waning level VE against hospitalization is 75% in the first year after vaccination and is reduced by 50% in the second year, VE_year2=38%. 	No senior vaccination in 2023-2024 and 2024-25
Early timing of infant interventions (1.5 month earlier than usual) <ul style="list-style-type: none"> Long-acting monoclonals (nirsevimab) target infants ≤ 7 months during RSV season, starting Aug 15 ending Mar 30 <ul style="list-style-type: none"> coverage saturates at 55% nationally (+10% higher than last year) Timing of administration differs between catch-up babies born Apr 1-Aug 14, and those born during the RSV campaign Aug 15-Mar 30 VE against hospitalization is 80% Maternal vaccine given to pregnant mothers 32-36 weeks, starting July 15 ending Jan 31 <ul style="list-style-type: none"> Coverage saturates at 25% of eligible women VE against hospitalization is 60% 	Scenario A	Scenario B	
Classic timing of infant interventions <ul style="list-style-type: none"> Long-acting monoclonals (nirsevimab) as above, except that campaign starts Oct 1 and ends Mar 30 <ul style="list-style-type: none"> Timing of administration differs between babies born before the campaign Apr 1-Sep 30, and those born during the RSV campaign Oct 1-Mar 30 Other parameters (VE and vaccine coverage) unchanged Maternal vaccine as above, except that campaign starts Sep 1 and ends Jan 31 	Scenario C	Scenario D	
Nirsevimab and maternal vaccines are not available. No infant intervention beyond what was used historically, ie, limited supply of palivizumab, targeting ~2% of birth cohort at high risk			Scenario E (counterfactual)

2024-2025 Results - Overall

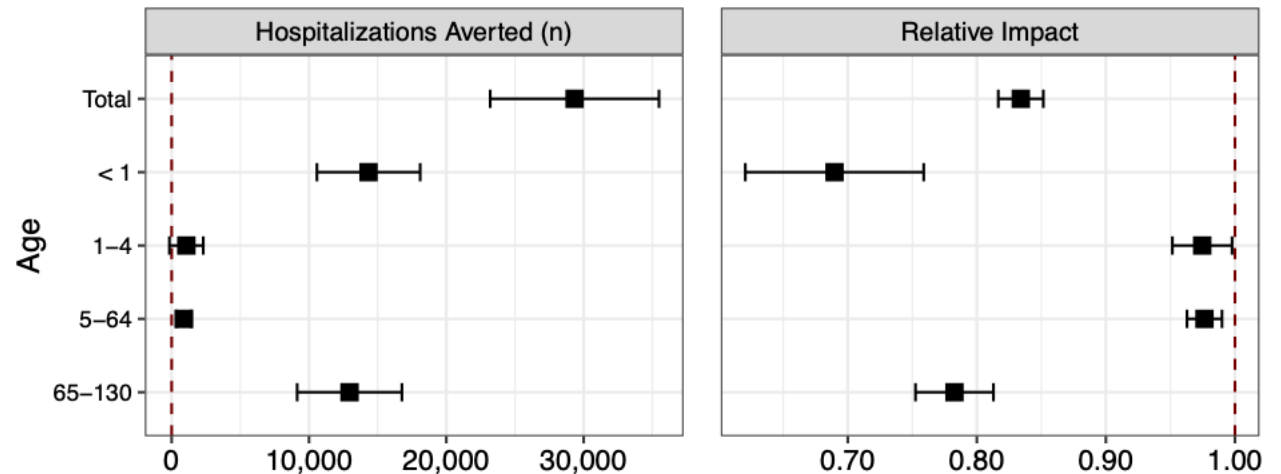
- Project that 17% (**95% CI: 15-18%**) of seasonal RSV hospitalizations, or **29,300 (23,200–35,500) hospitalizations, will be averted** in the scenario with slow vaccine waning in seniors and early timing of infant interventions (scenario A), compared to non-intervention scenario (scenario E).
- The peak and cumulative hospitalization burden of the 2024-25 RSV season is likely to remain lower than that of last season and this is consistent across all scenarios.
- The combined hospitalization impact of RSV, influenza, and COVID-19 is likely to remain below that of last season.

2024-2025 Initial Results

- Intervention benefits are projected to be highest in the targeted age groups, with **hospitalization reduction of 31% (95% CI: 24-38%) among infants and 22% (95% CI: 19-25%) among seniors** for scenario A vs E.
- Assumptions about vaccine waning among seniors affect projected intervention benefits.
- The timing of infant interventions has little impact on intervention benefits.

United States

Early Infant, Optimistic Senior VS Counterfactual

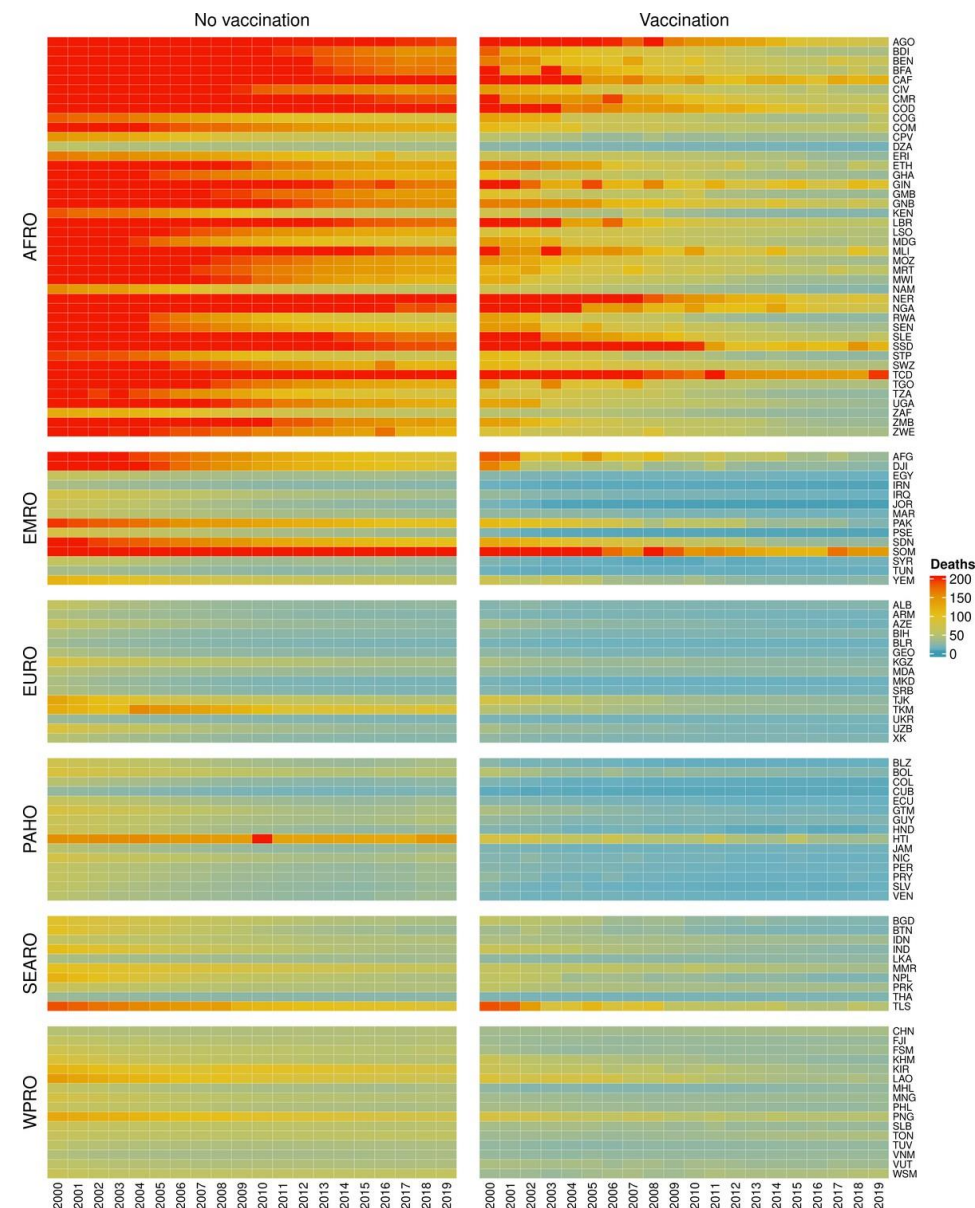


Rotavirus

Using models to predict vaccine impact

Among the greatest public health achievements

Will **prevent**
97 million deaths
from 2000-2030



Rotavirus Model – Modified for VIMC

Deterministic M-SIRS

Choose India or Mexico natural history

Age-structured

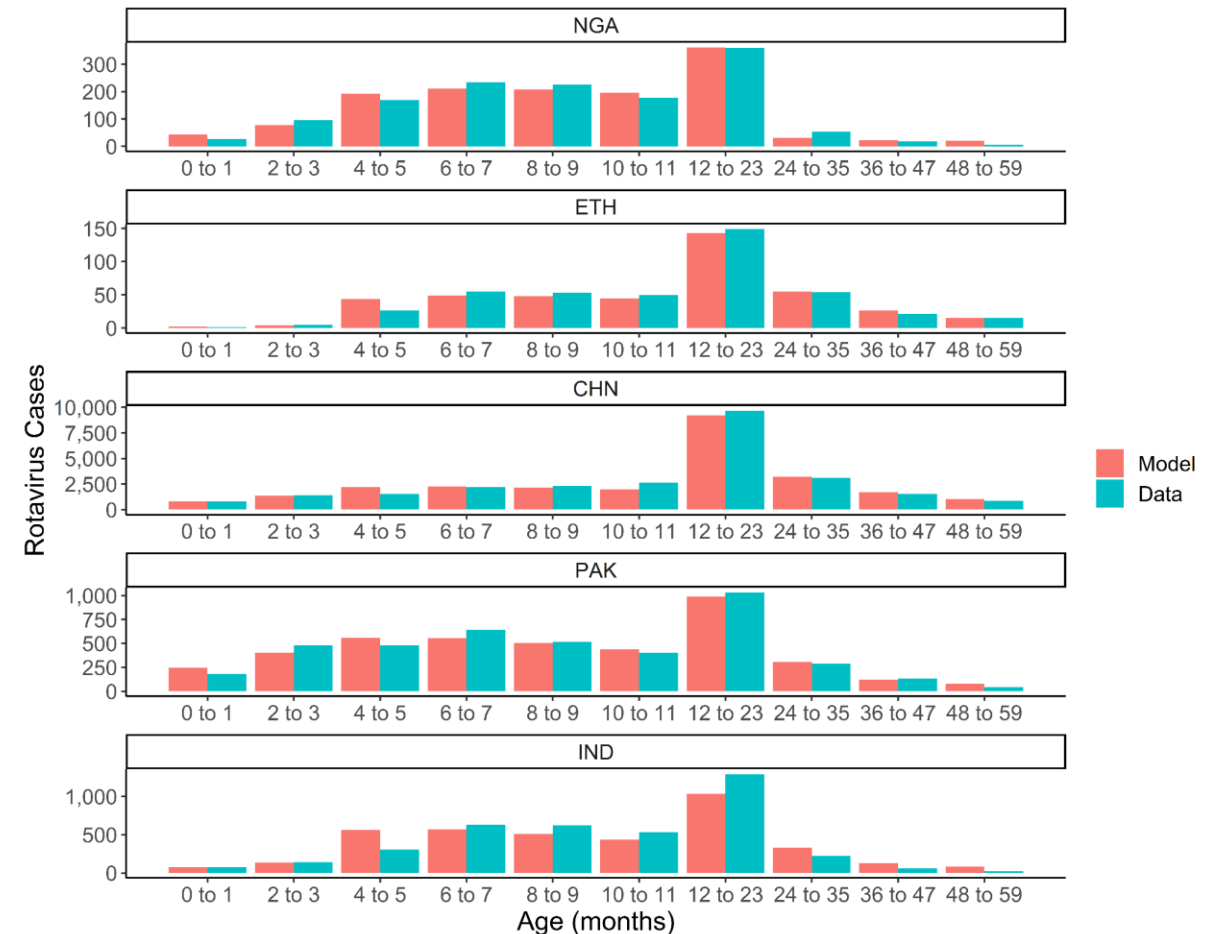
- 2 month age bands < 1 yr
- 1 year age bands for 1 to 4 year olds
- 5+ years old

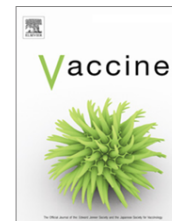
Vaccination

- Acts like natural infection -- no VE input
- 2 dose schedule at 2 and 4 months old
- Strain-agnostic

Model Calibration

1. Fit to age distribution* of rotavirus cases among < 5 yrs.
2. ML to estimate age specific transmission parameters for each country:
 1. $q_{1...3}$: 0-3; 4 to 23; ≥ 24 months
 2. Reporting rate to scale to severe cases
 3. Then, scale severe cases to GBD mortality





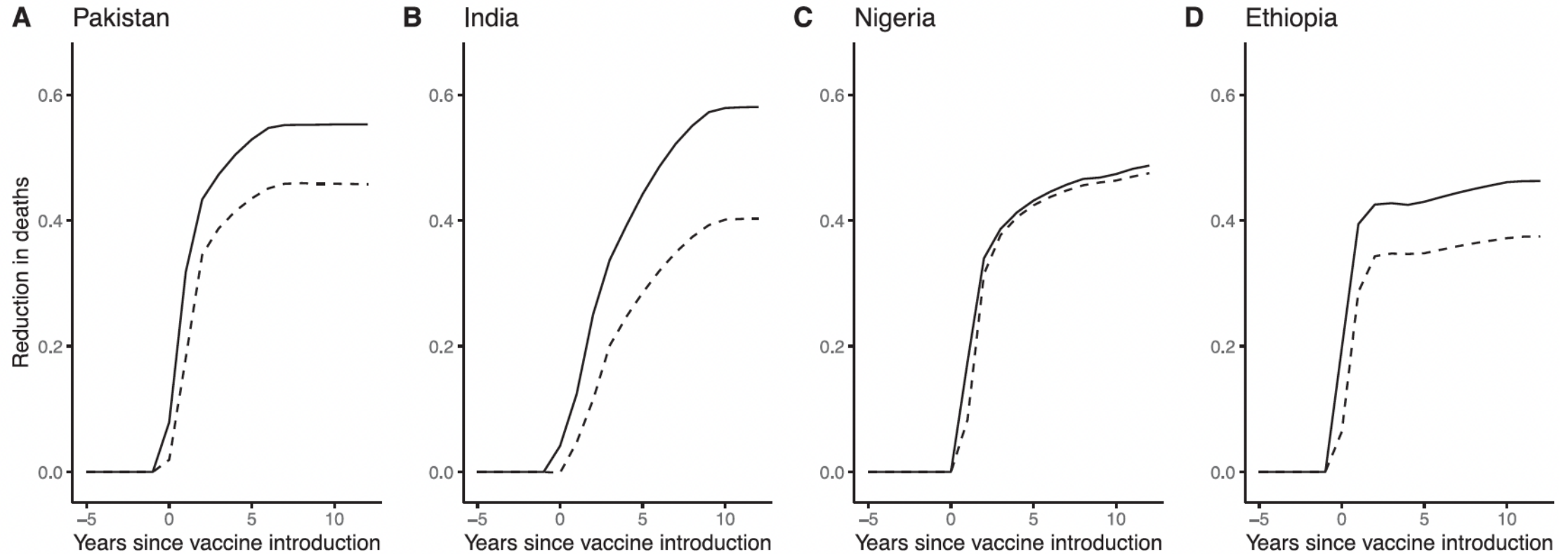
Predicting the long-term impact of rotavirus vaccination in 112 countries from 2006 to 2034: A transmission modeling analysis



A.N.M. Kraay^{a,b,*}, M.K. Steele^b, J.M. Baker^b, E.W. Hall^b, A. Deshpande^b, B.F. Saidzosa^c, A. Mukaratirwa^d, A. Boula^e, E.M. Mpabalwani^f, N.M. Kiulia^g, E Tsolenyanu^{h,i}, C. Enweronu-Laryea^j, A. Abebe^k, B. Beyene^k, M. Tefera^k, R. Willilo^l, N. Batmunkh^m, R. Pastoreⁿ, J.M. Mwenda^o, S. Antoni^p, A.L. Cohen^p, V.E. Pitzer^q, B.A. Lopman^b

**105,000 (95% UI: 99,000 to 115,000) deaths averted per year
a reduction of 50.4% (95%UI:47.4%–55.2%)
compared to no vaccination**

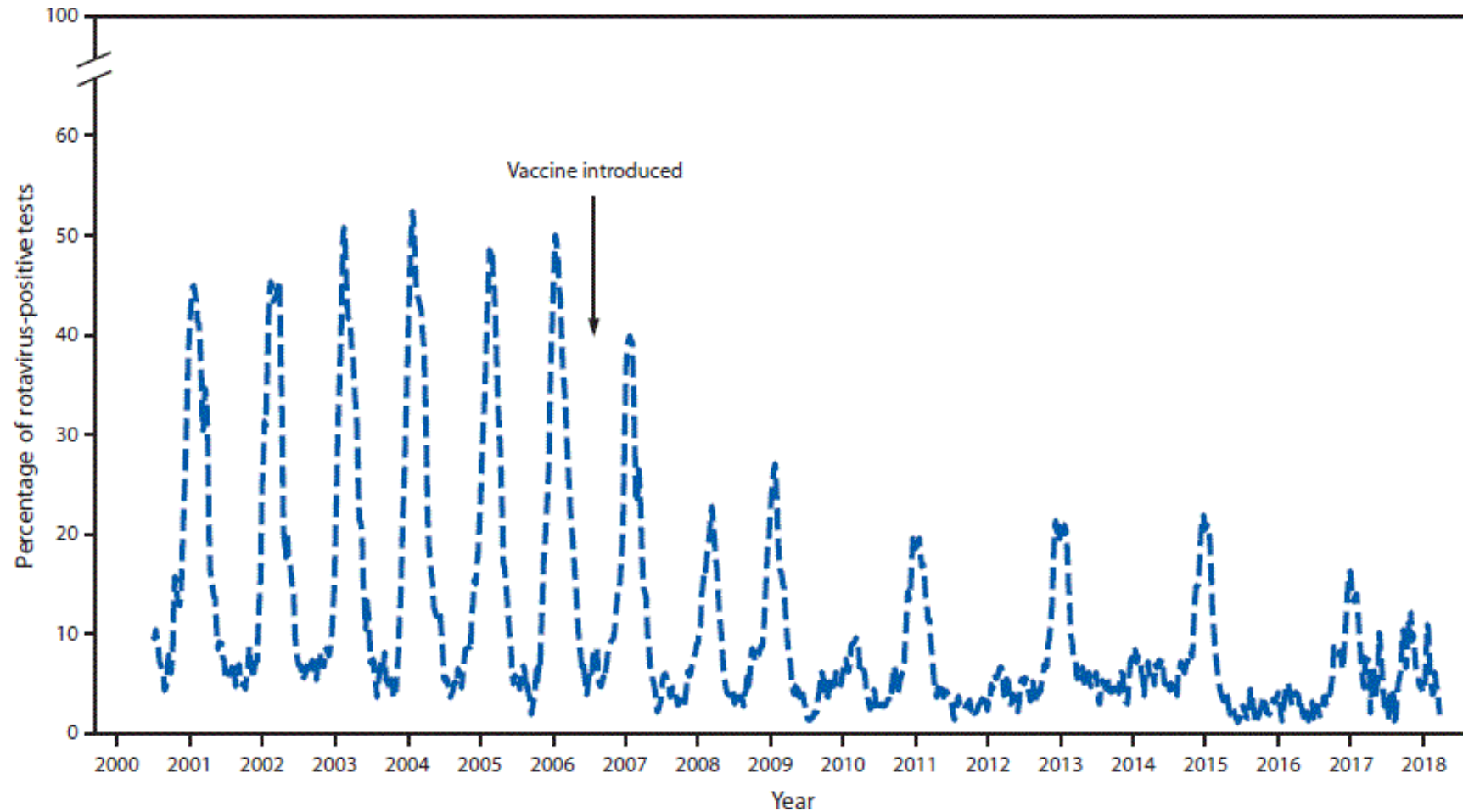
Direct and Indirect Effects of Rotavirus vaccination



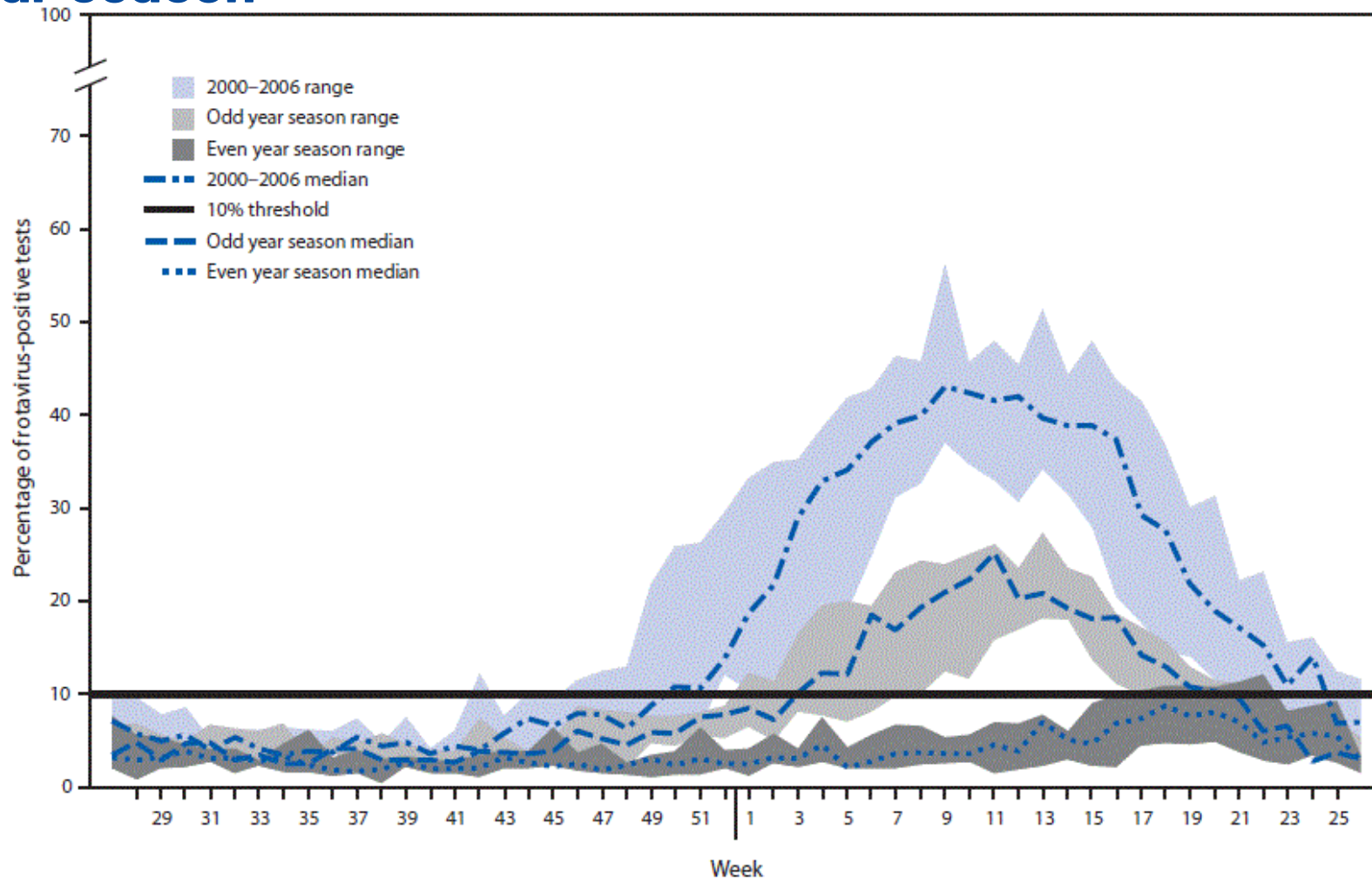
Solid: Overall Effect, Dashed: Direct Effect

Using models to interpret post-vaccination dynamics

Overall effect of rotavirus vaccine in the US

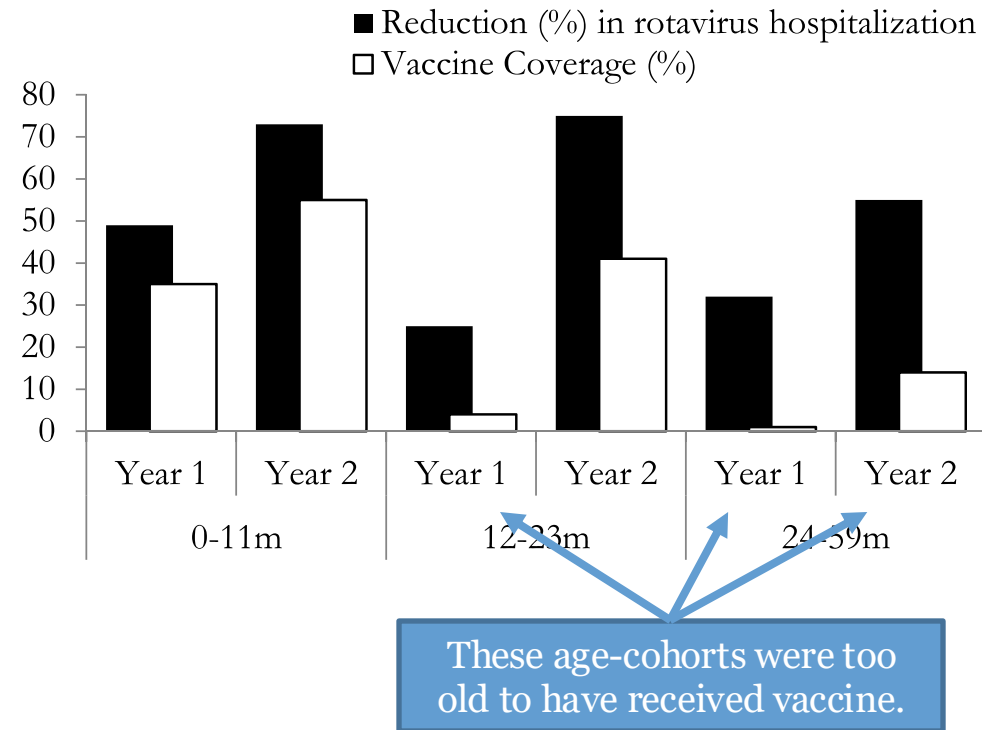


Rotavirus season duration and peak activity for pre-vaccine (2000–2006) and postvaccine years (2008–2018), stratified by even/odd year season

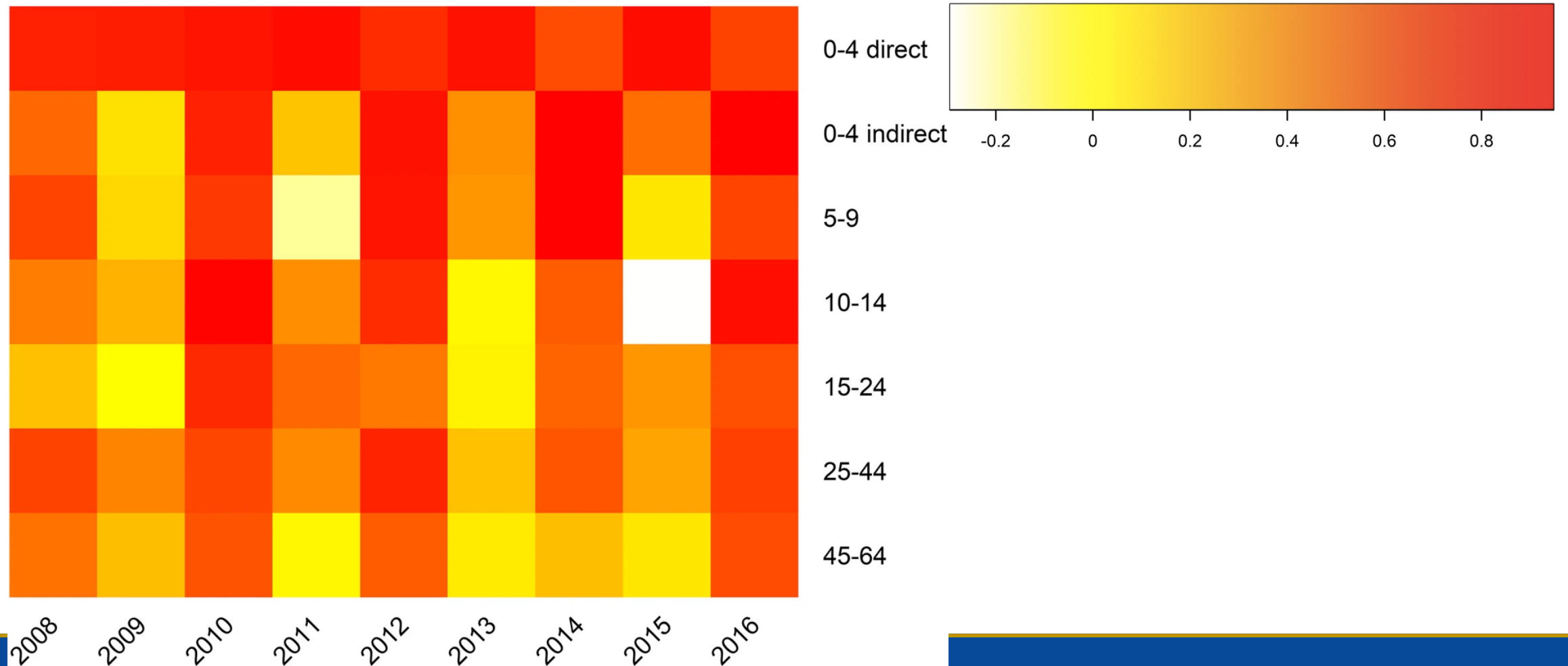


Rotavirus vaccine in Moldova: 2009 to 2014

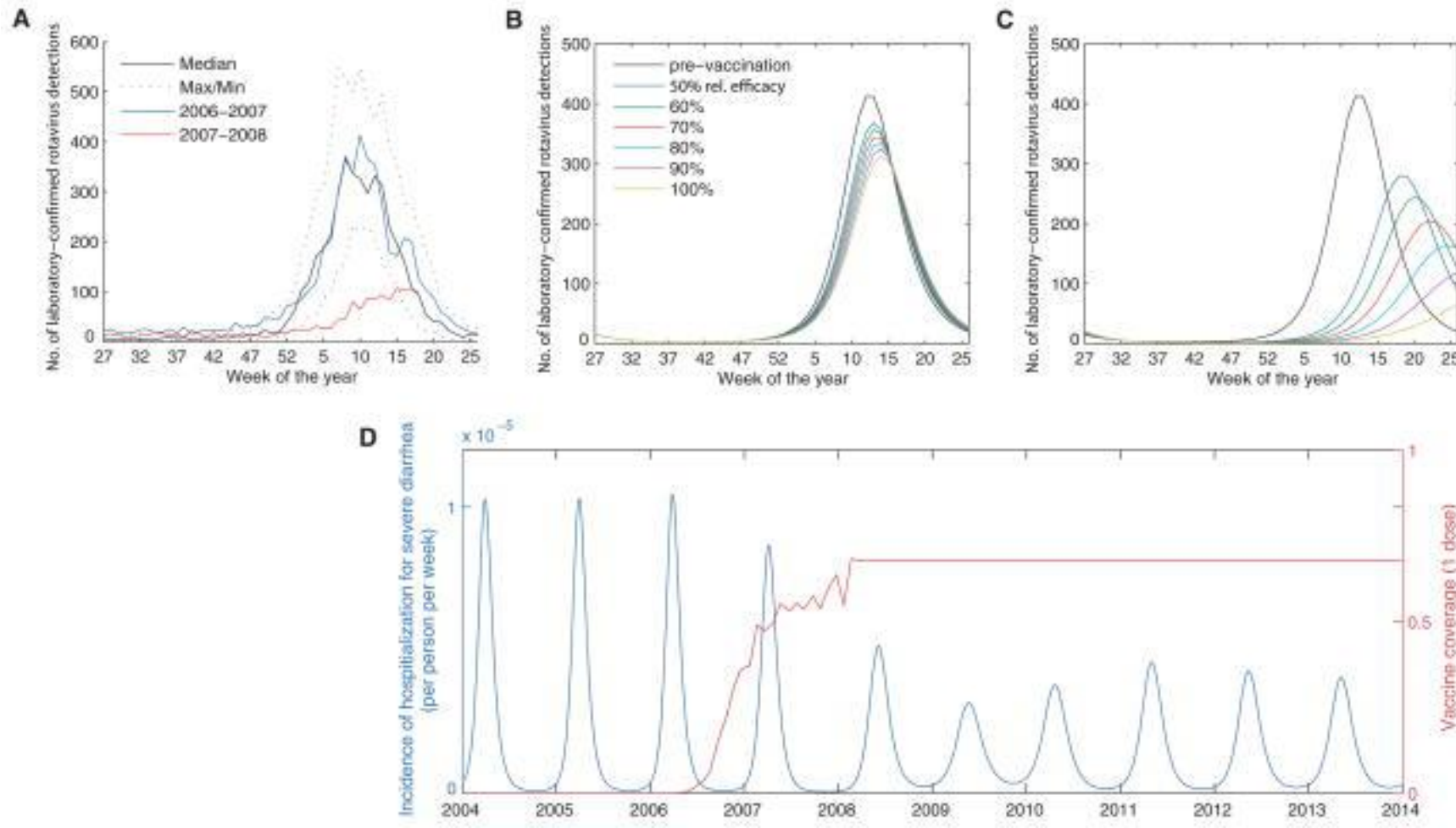
Indirect effect



Direct and indirect VE against rotavirus for each post-vaccine year, United States, by age group

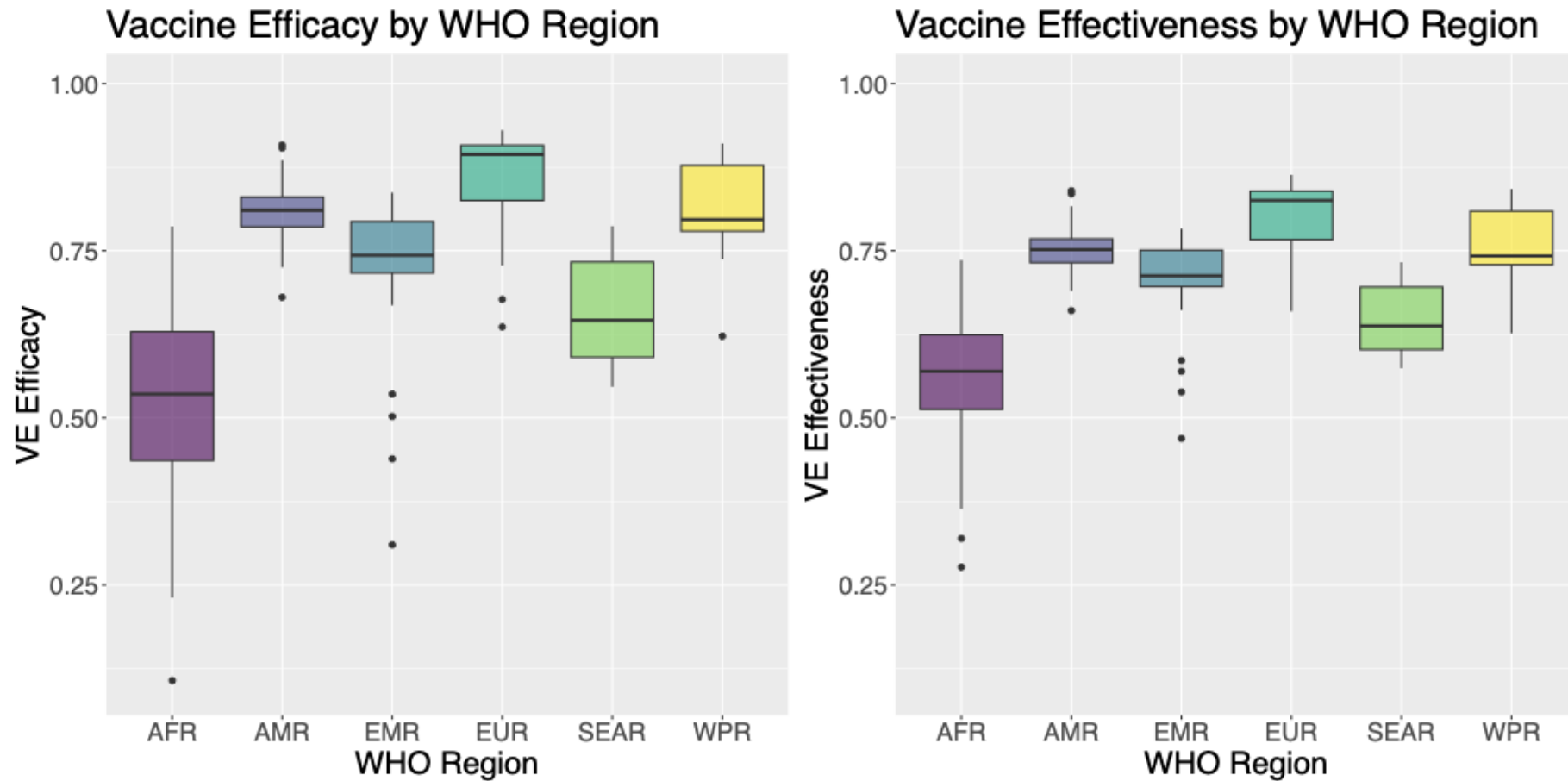


Models predicts (some) of these vaccine effects



Using models to understand lower vaccine performance and examine new strategies

Global estimates of rotavirus vaccine efficacy and effectiveness: a meta-regression analysis



Reasons for lower VE in LMICs

Concomitant oral polio vaccine

Nutritional deficiencies

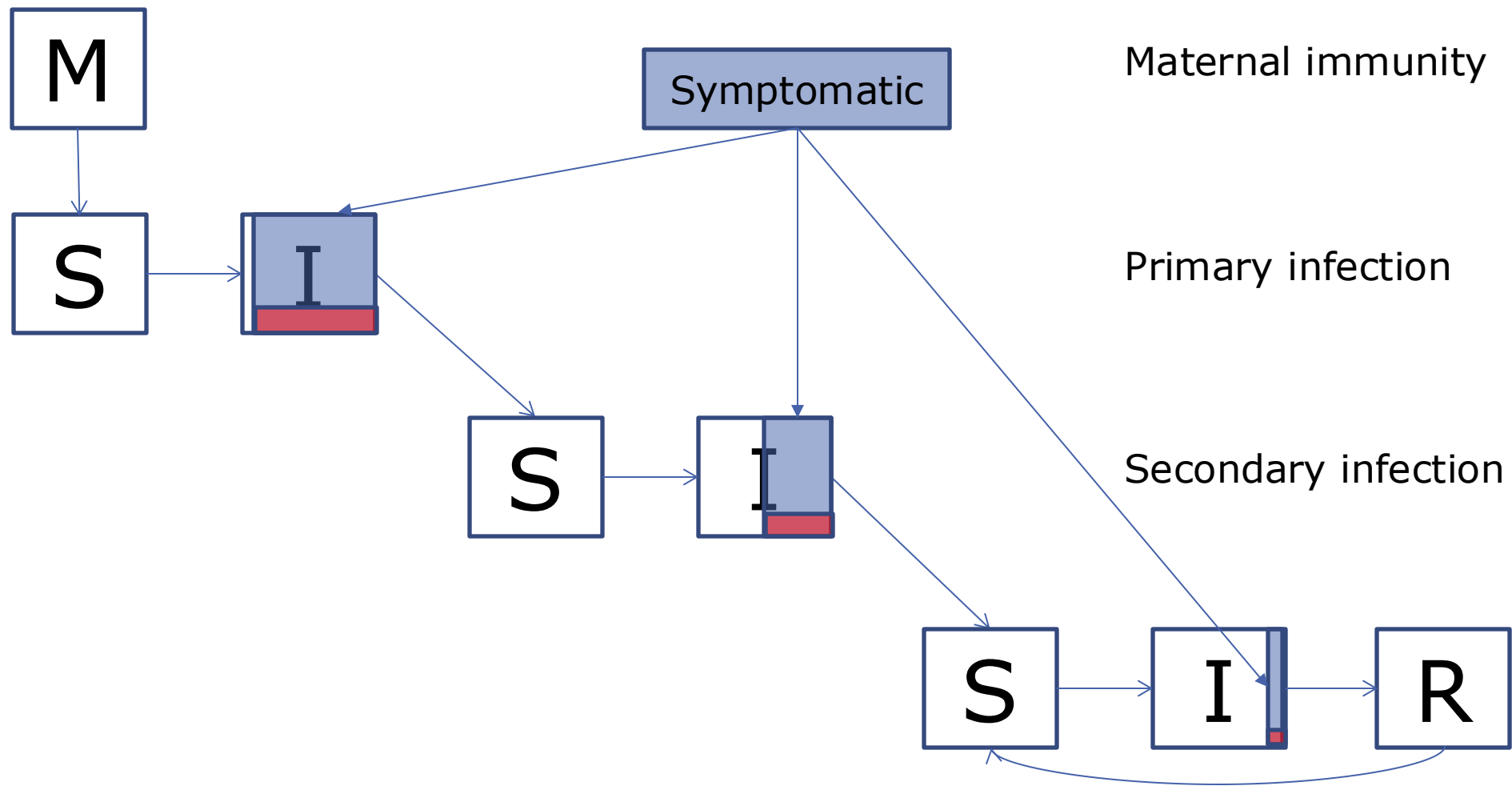
Gut microbiome composition

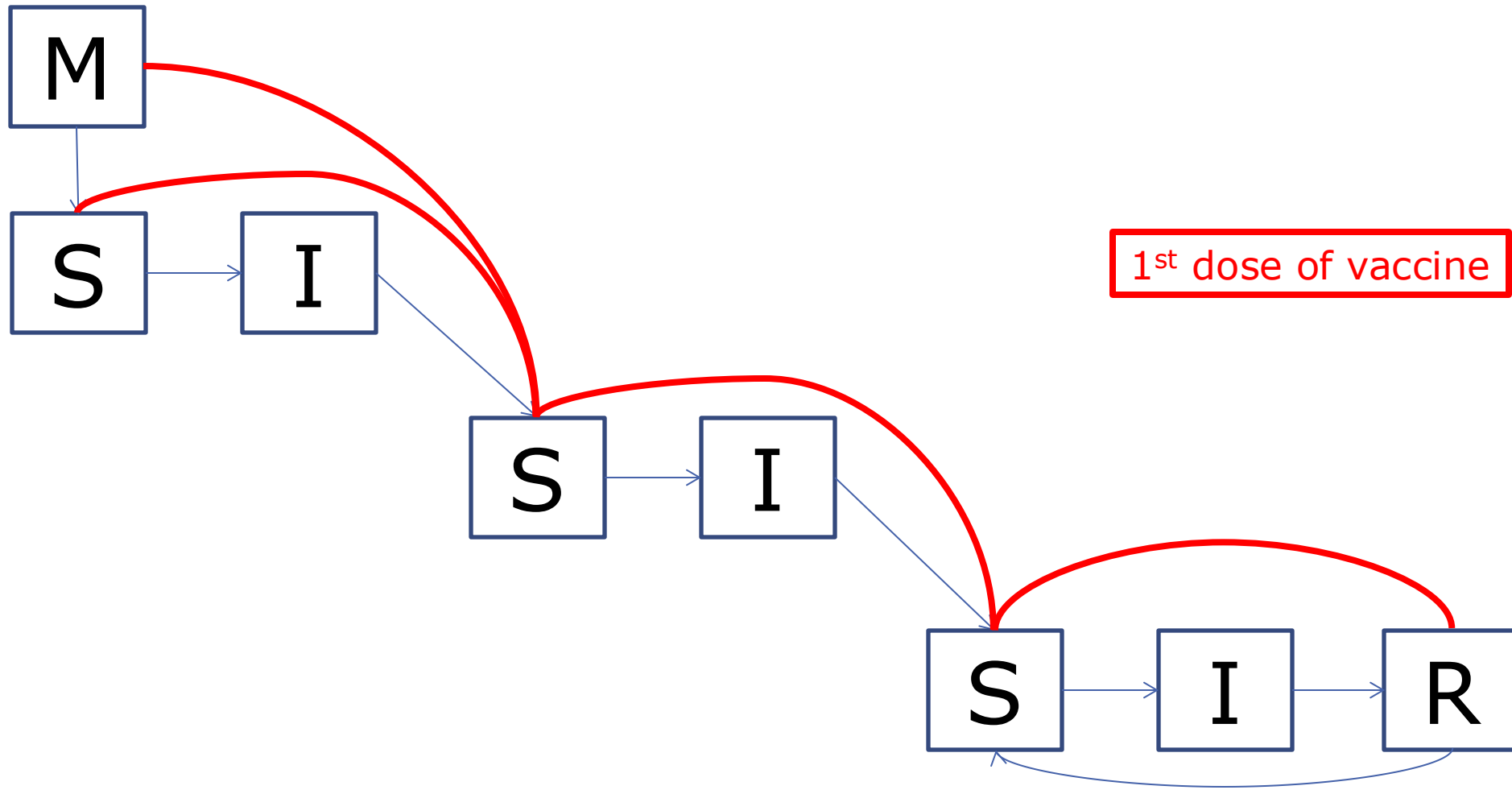
Co-infections

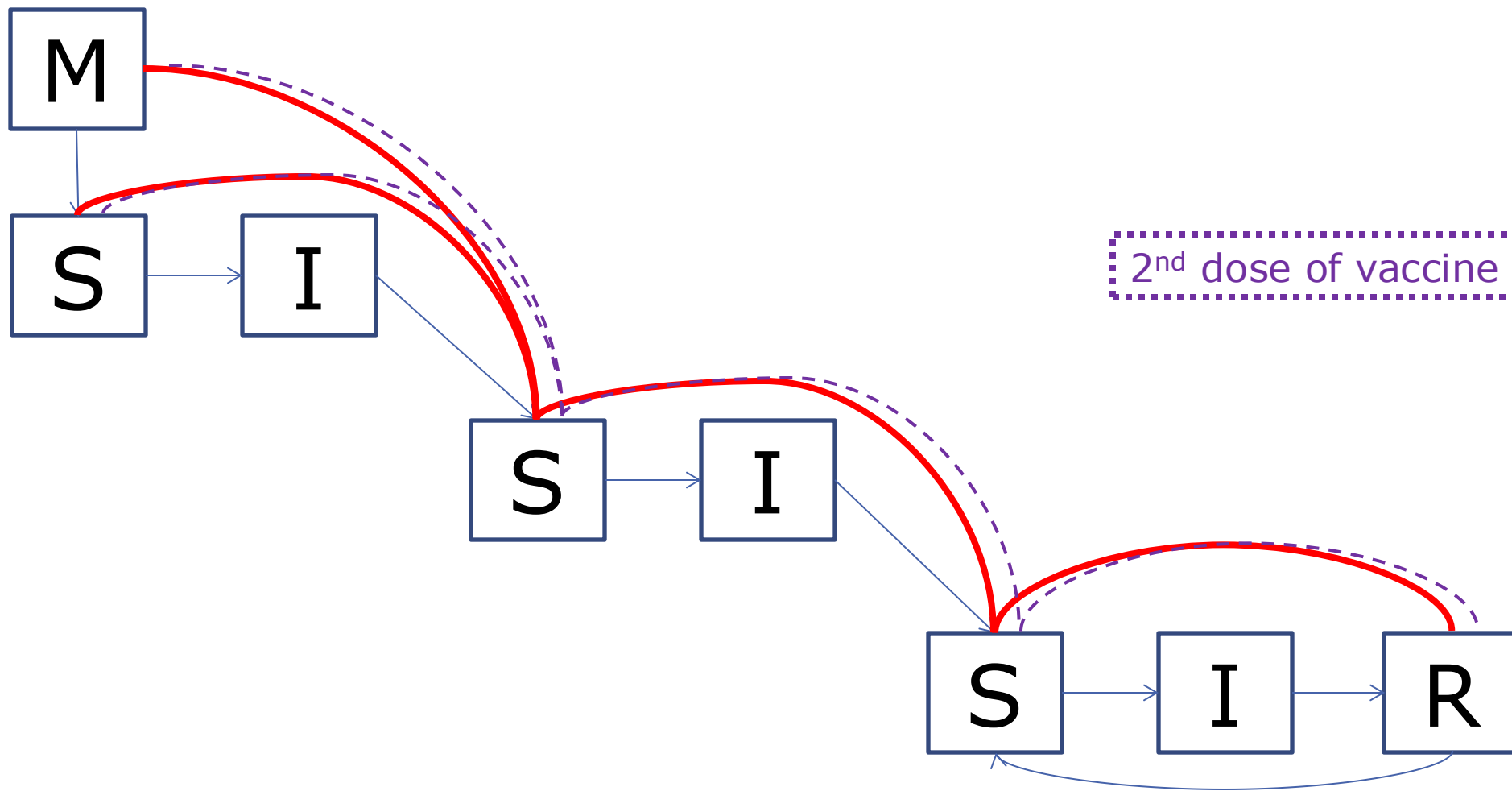
Maternal antibody interference

Genotype-specific VE

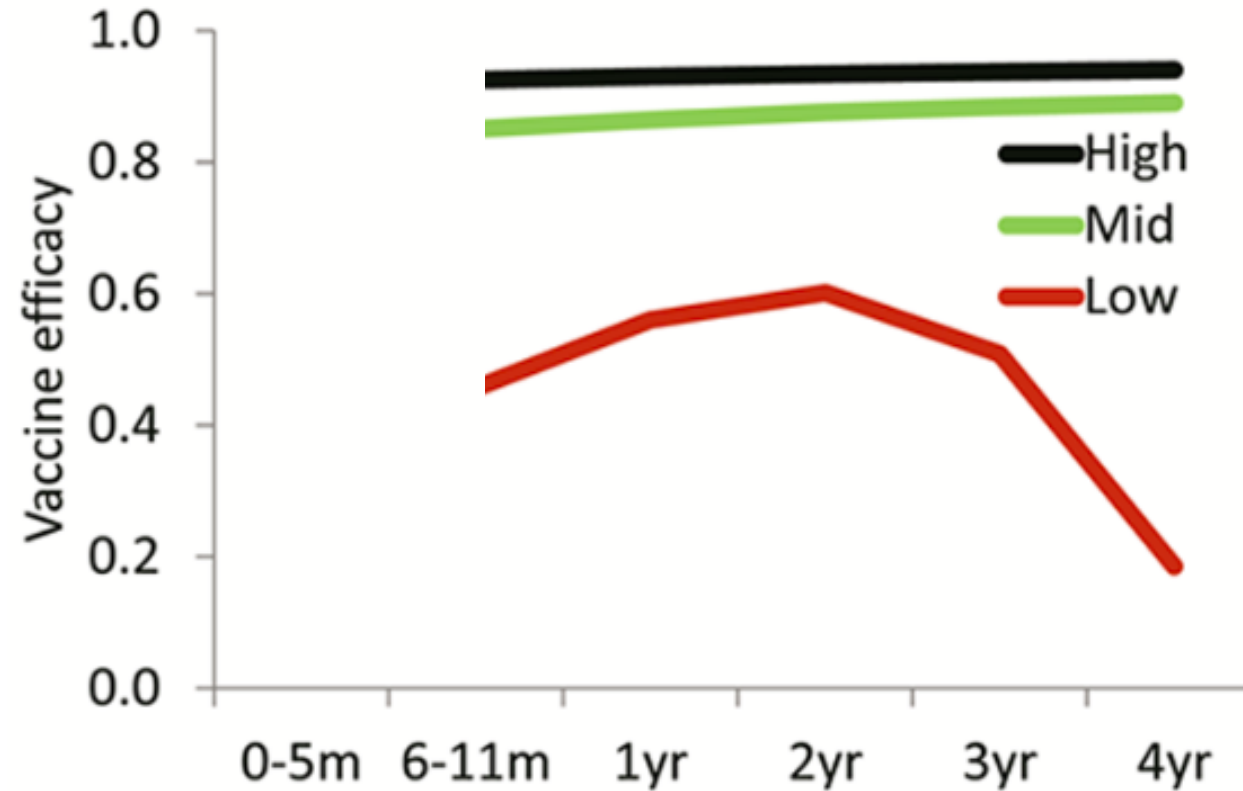
Measurement bias



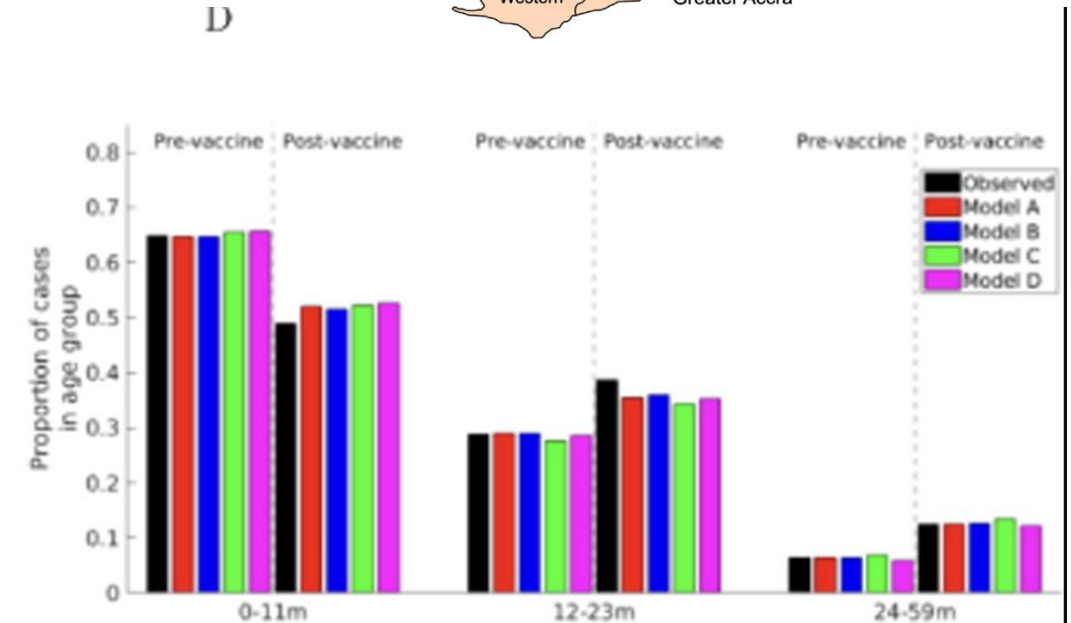
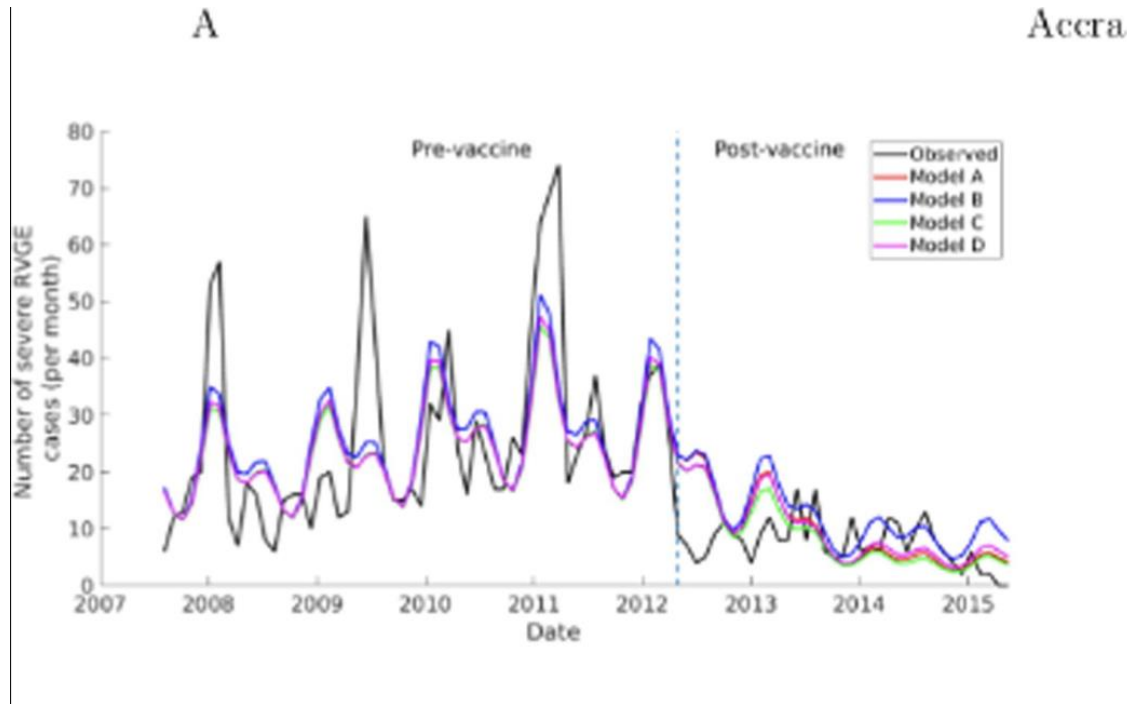
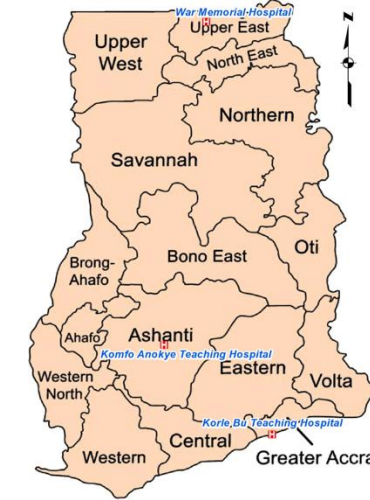




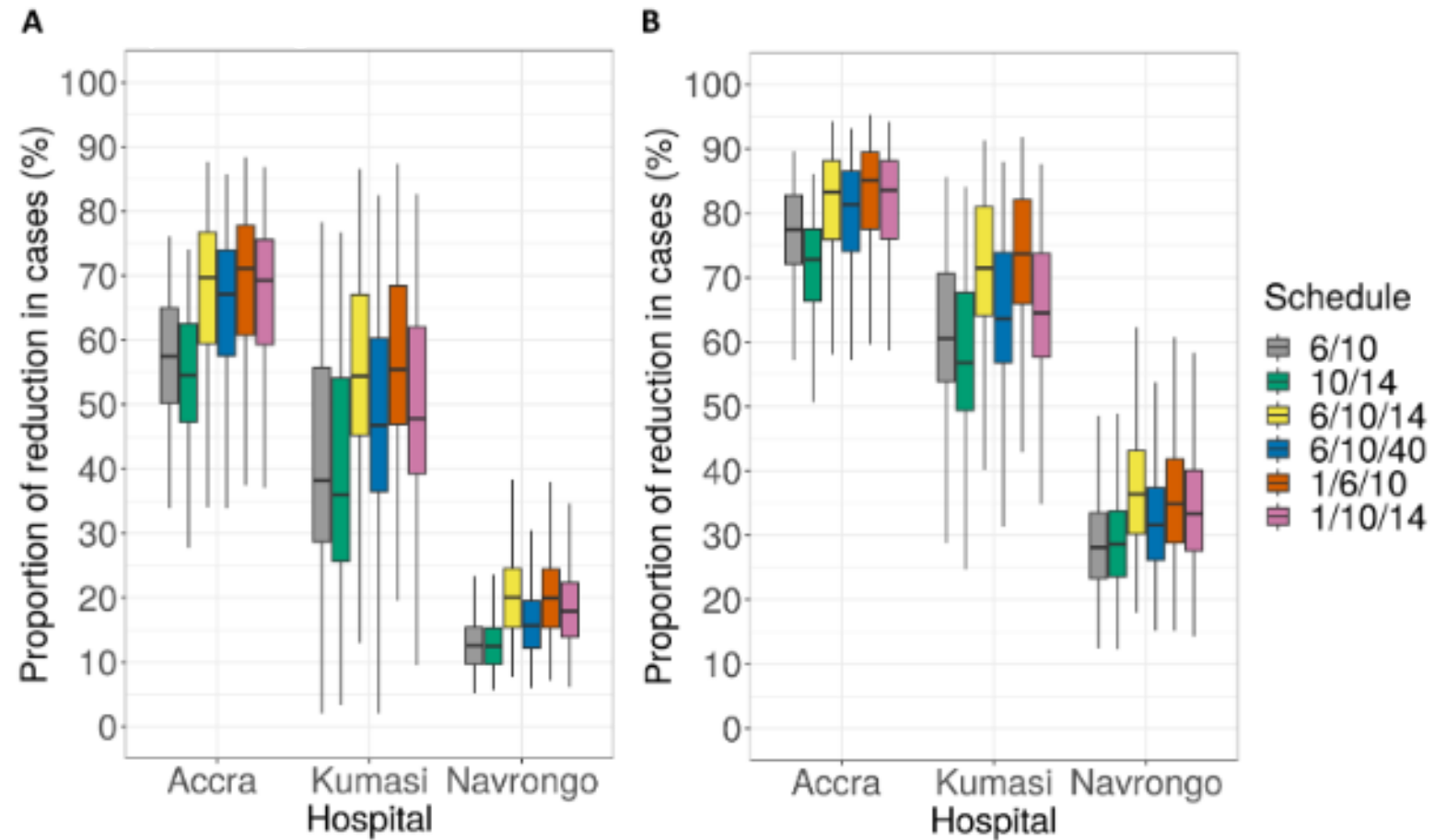
Assuming vaccine acts like natural infection, model framework can predict VE



Modeling of rotavirus transmission dynamics and impact of vaccination in Ghana




Impact of dosing schedule on performance of vaccines in Ghana

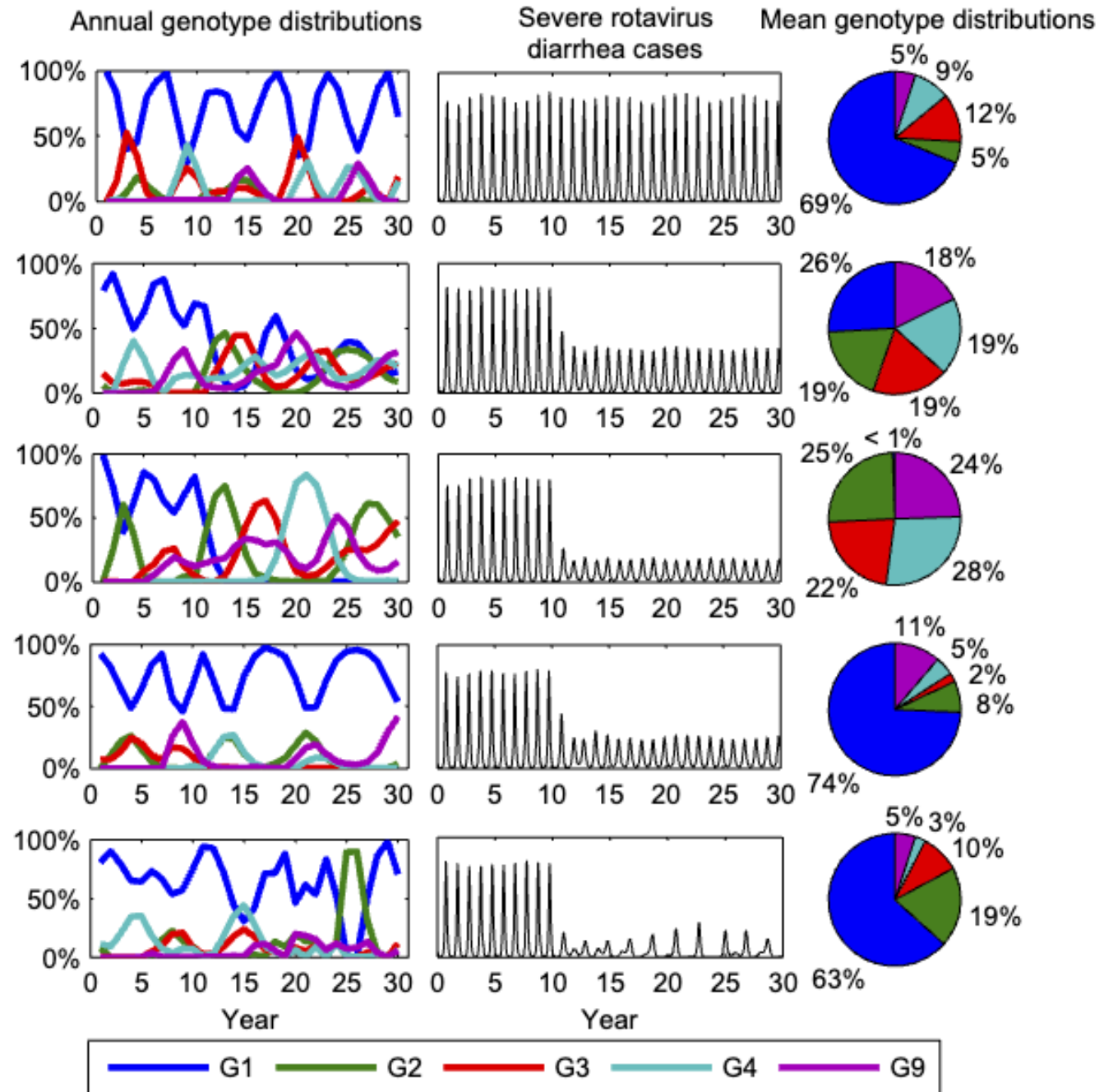




To what extent can vaccine impact be affected by and affect rotavirus strain dynamics?



- A) Pre-vaccination
- B) 50% coverage with a vaccine that provides strong protection against G1 and weaker protection against other genotypes
- C) 80% coverage with such a vaccine
- D) 50% coverage with a vaccine that provides strong protection against all genotypes
- E) 80% coverage with such a vaccine





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in Infectious Diseases

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