EMORY

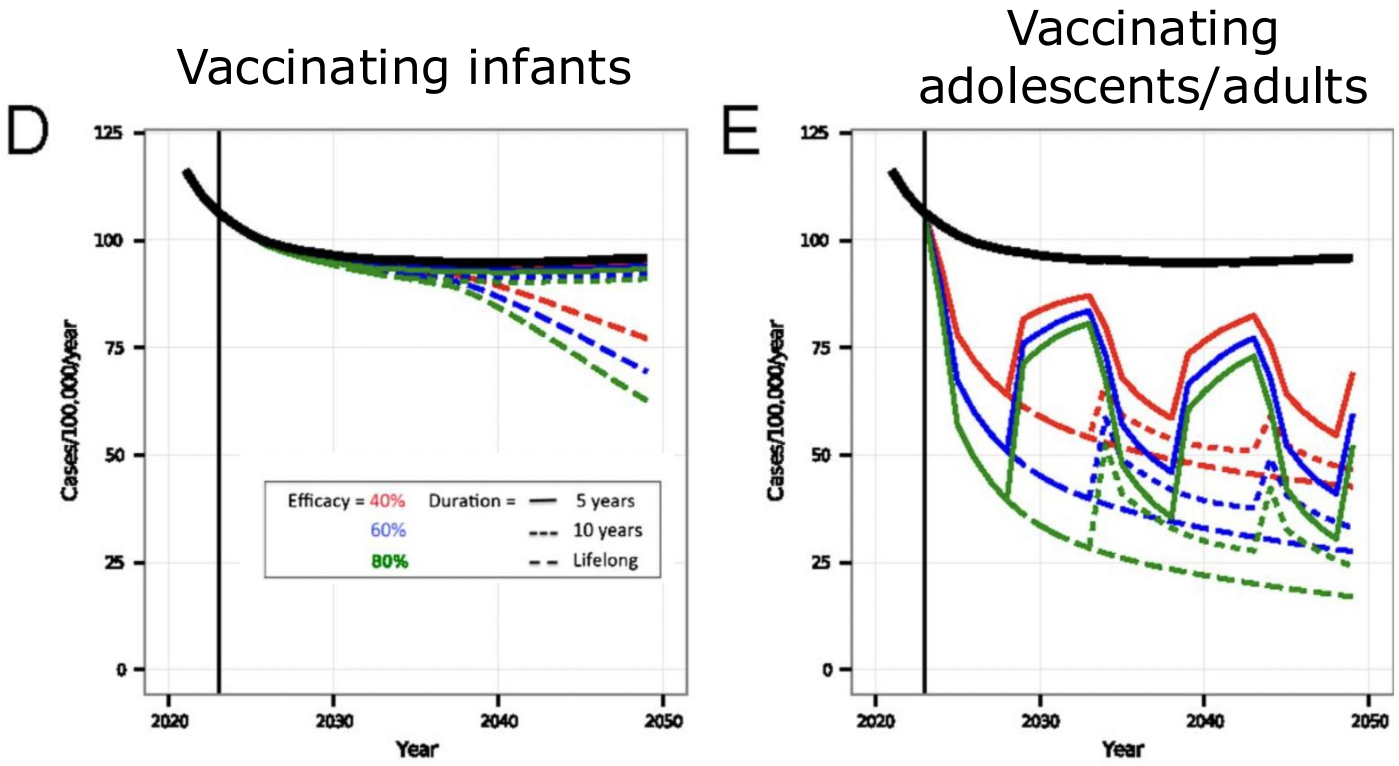
ROLLINS SCHOOL OF PUBLIC HEALTH

Modelling Applications for TB, RSV, and Rotavirus

TB

Knight et al. PNAS 2015

Potential impact of infant vs. adolescent/adult vaccines?



Cases averted:

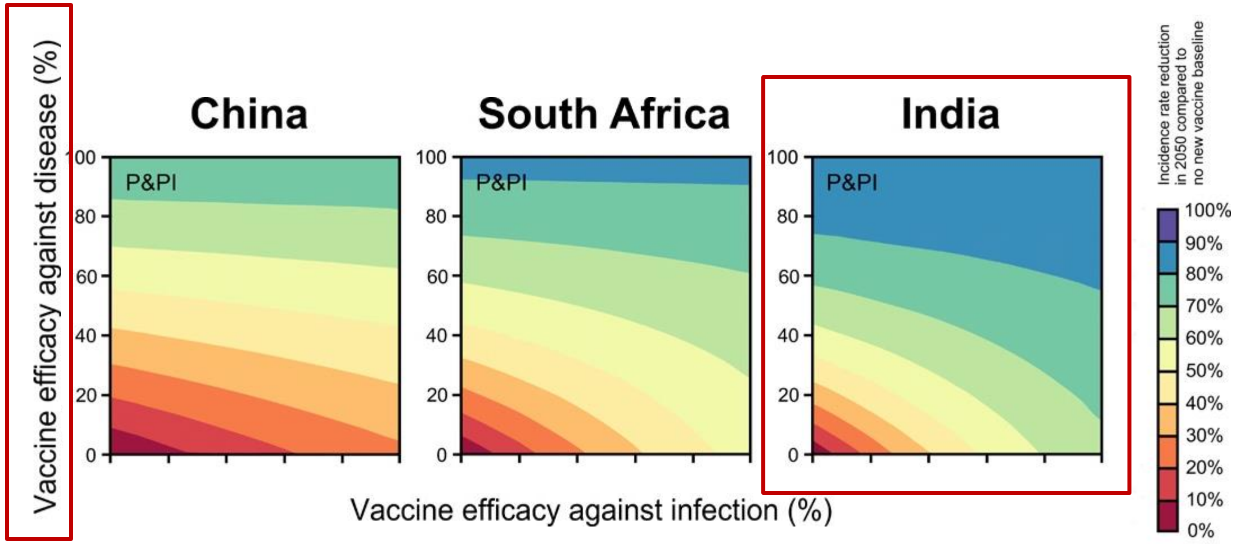
Vaccinating infants	Vaccinating adolescents/adults
0.89 million 95% range: (0.42–1.58)	17 million 95% range: (11-24)

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**)



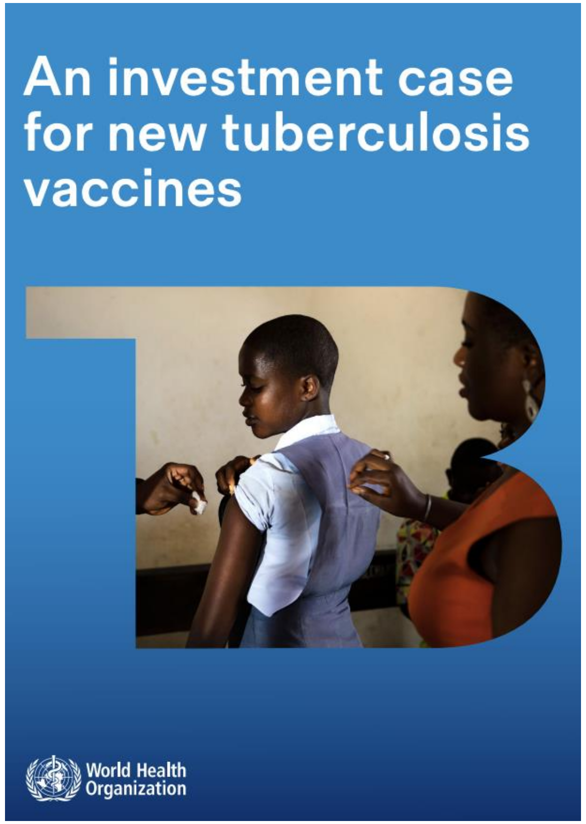
Making the investment case

50% effective vaccine for adolescents and adults could cumulatively avert

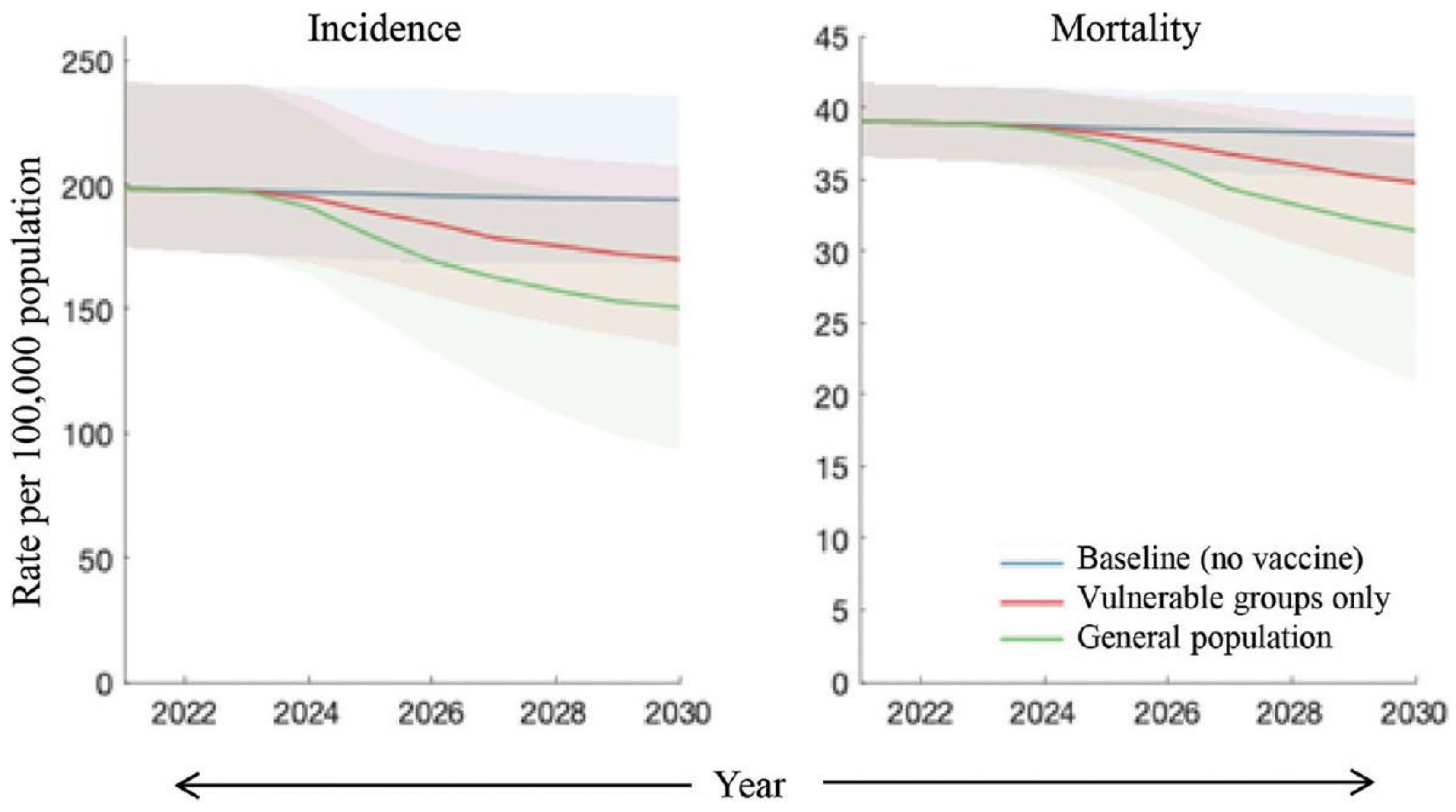
37.2–76.0 million cases and 4.6–8.5 million deaths

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)



Potential impact of adult / adolescent TB vaccines in India?



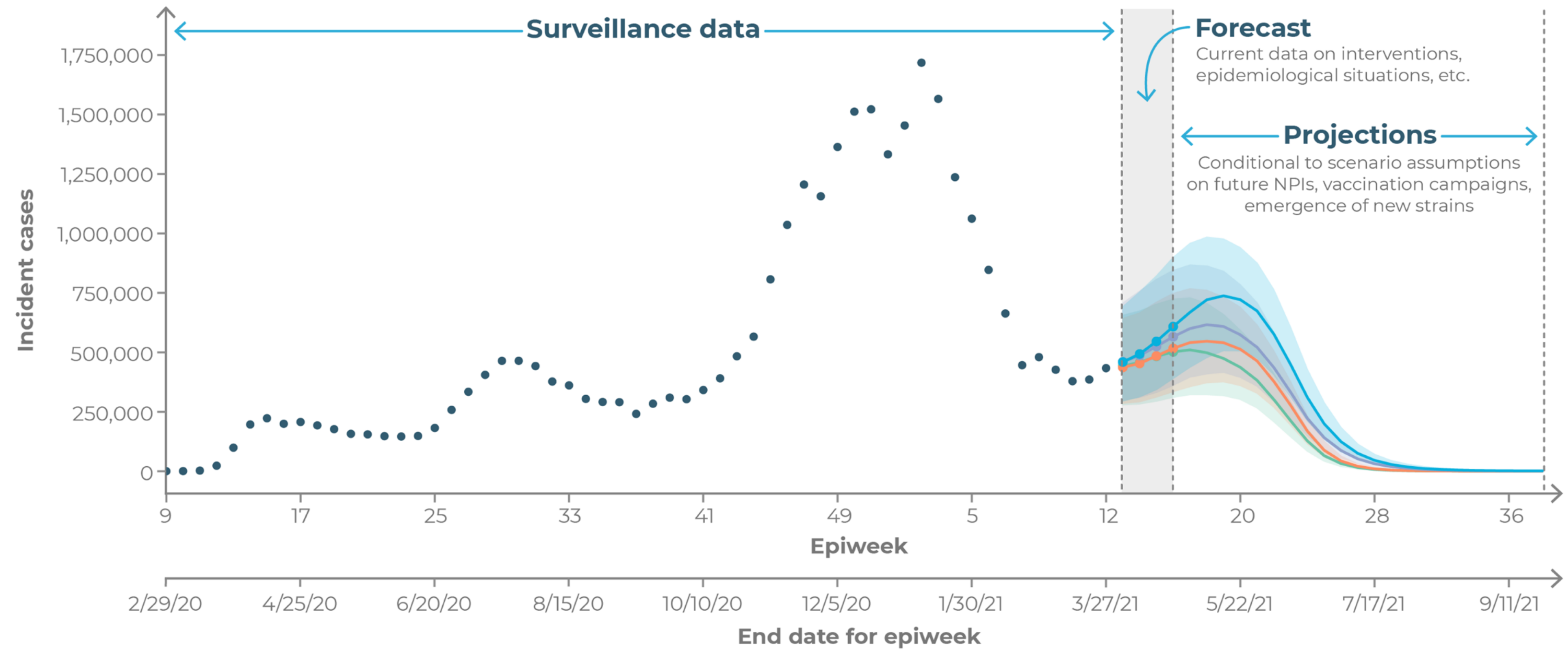
Pathy *et al*. IJMR, 2023.

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 • 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** • 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) • Long-acting monoclonals (nirsevimab) target infants ≤ 7 months during RSV season, starting **Aug 15 ending Mar 30** ◦ 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** ◦ Coverage saturates at **25%** of eligible women ◦ VE against hospitalization is **60%**	**Scenario A**	**Scenario B**	
Classic timing of infant interventions • Long-acting monoclonals (nirsevimab) as above, except that campaign **starts Oct 1 and ends Mar 30** ◦ 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

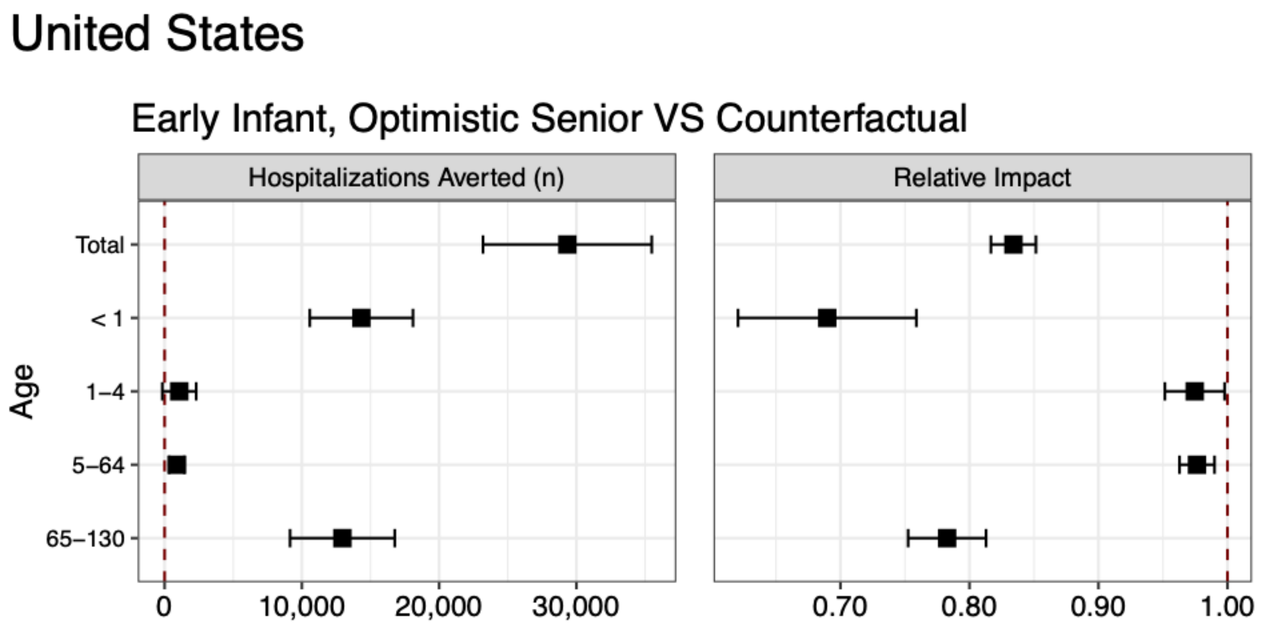
- Project that 17% **(95% CI: 15-18%) of seasonal RSV hospitalizations, or 29,300 (23,200–35,500) hospitalizations, will be averted** in the scenario with slow vaccine waning in seniors and early timing of infant interventions (scenario A), compared to non-intervention scenario (scenario E).
- The peak 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.

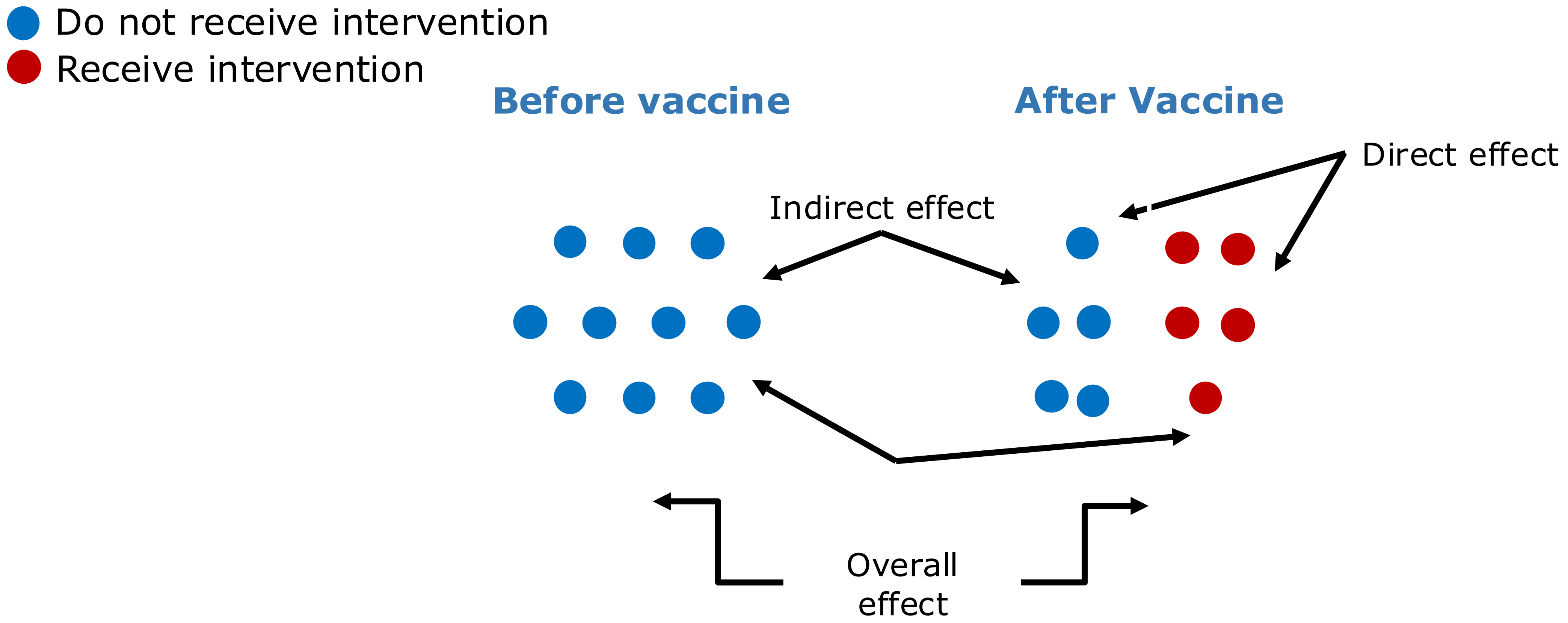
- Assumptions about vaccine waning among seniors affect projected intervention benefits.

- The timing of infant interventions has little impact on intervention benefits.

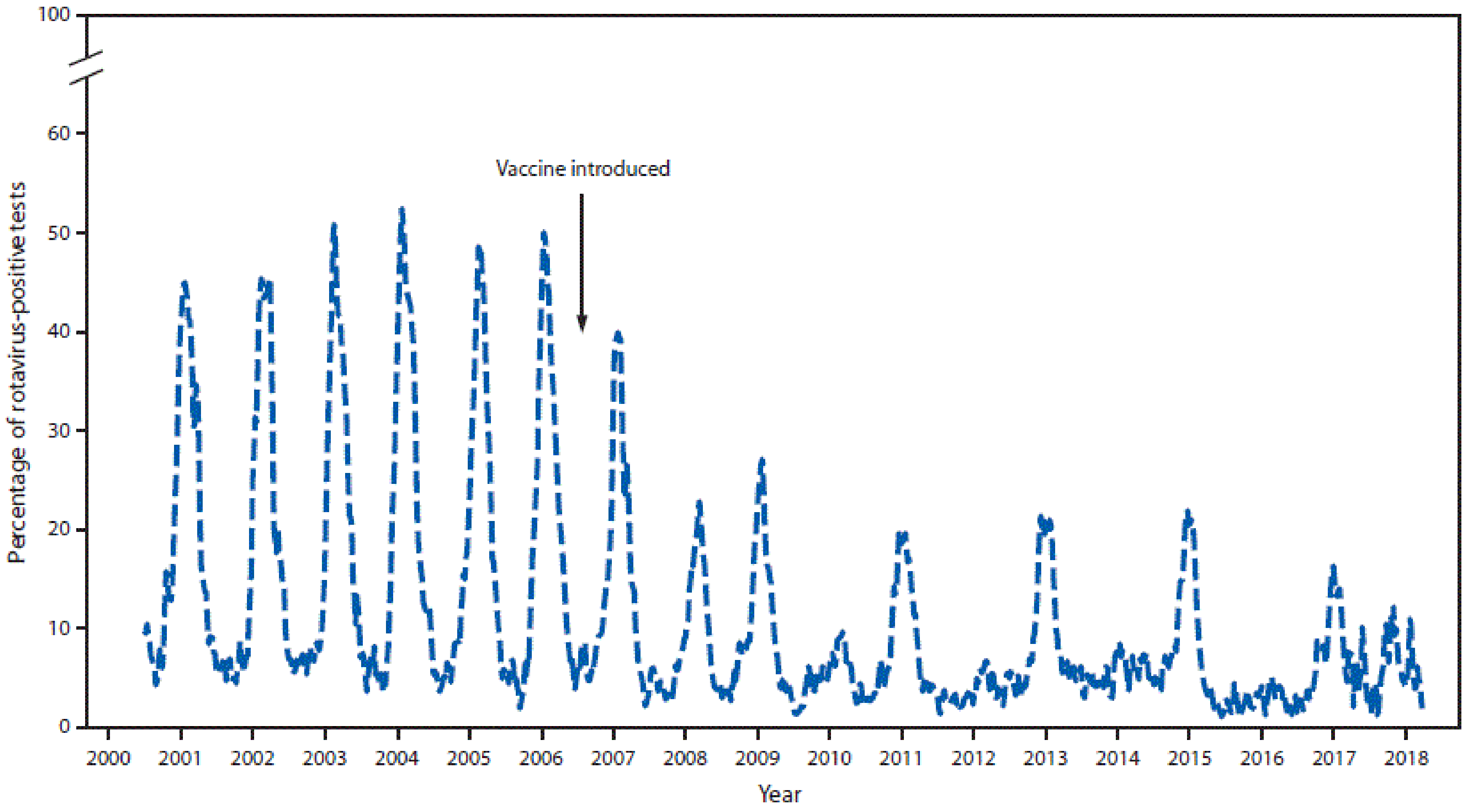


Rotavirus

Intervention effects

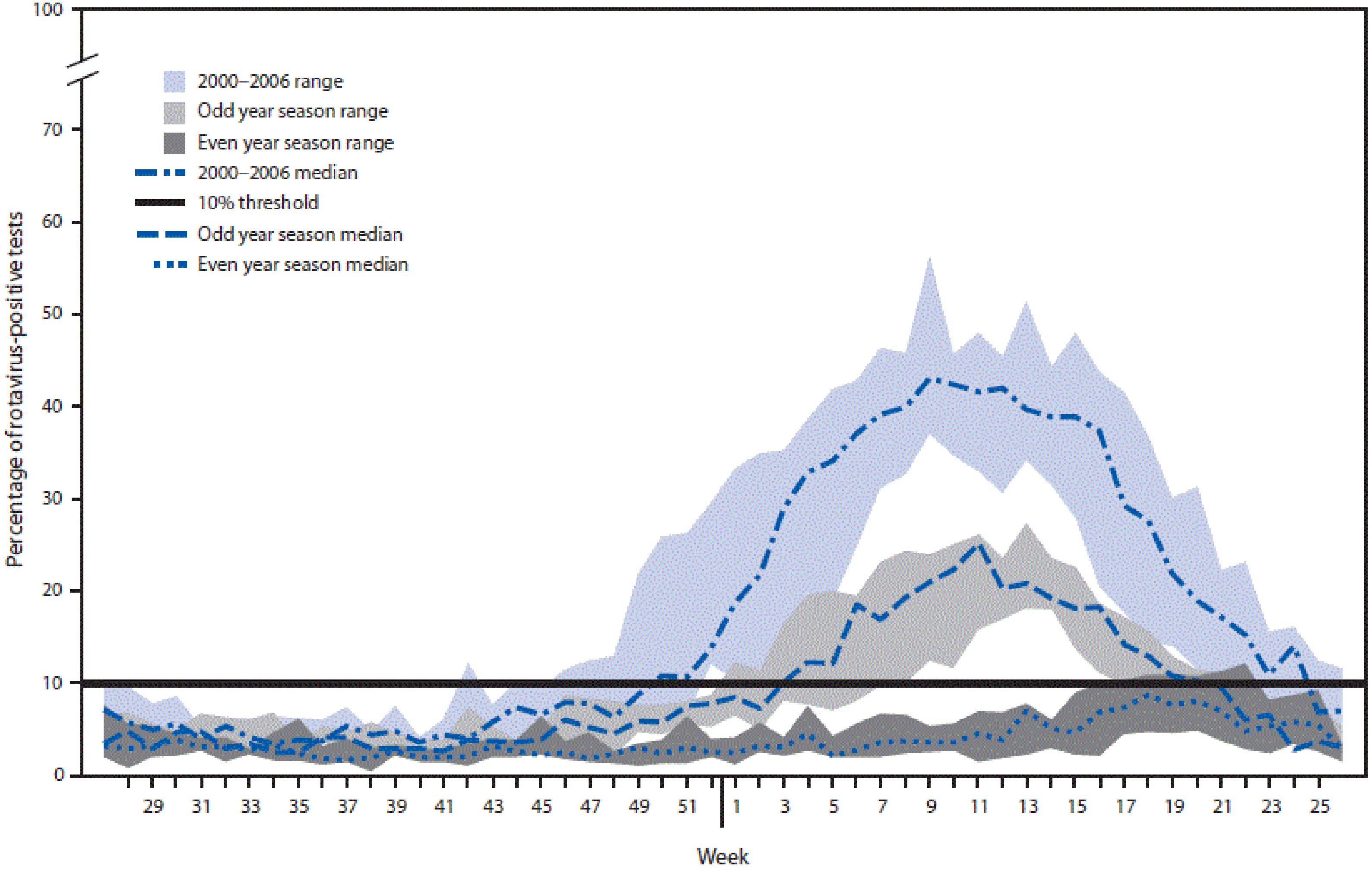


Overall effect of rotavirus vaccine in the US



Hallowell et al, *MMWR, 2021*

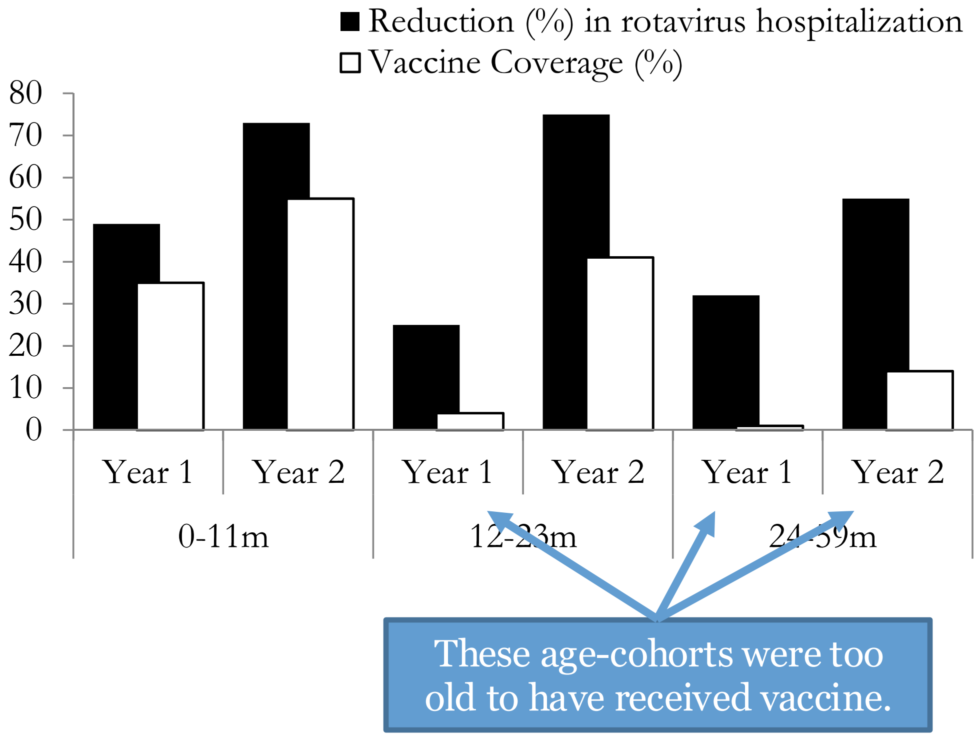
Rotavirus season duration and peak activity for pre-vaccine (2000–2006) and postvaccine years (2008–2018), stratified by even/odd year season



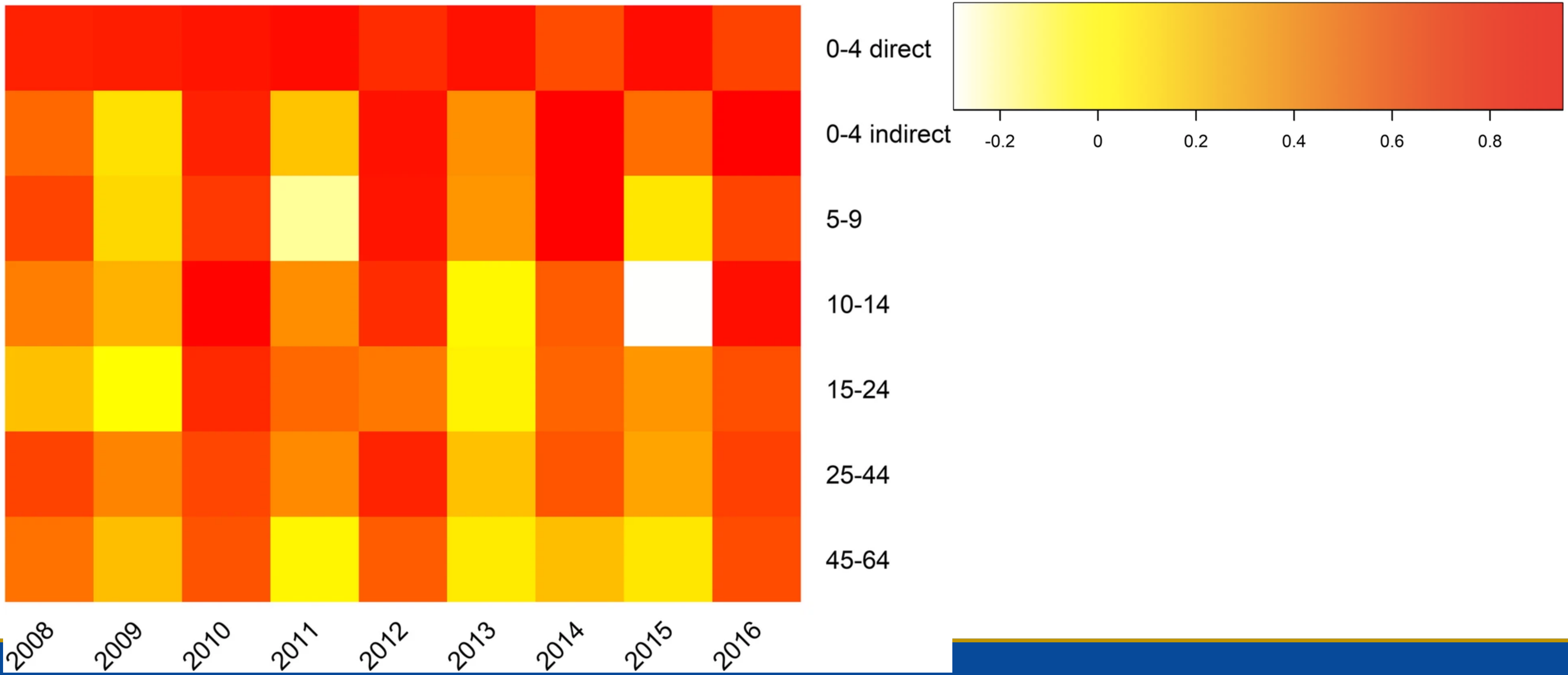
Hallowell et al, *MMWR, 2021*

Rotavirus vaccine in Moldova: 2009 to 2014

Indirect effect

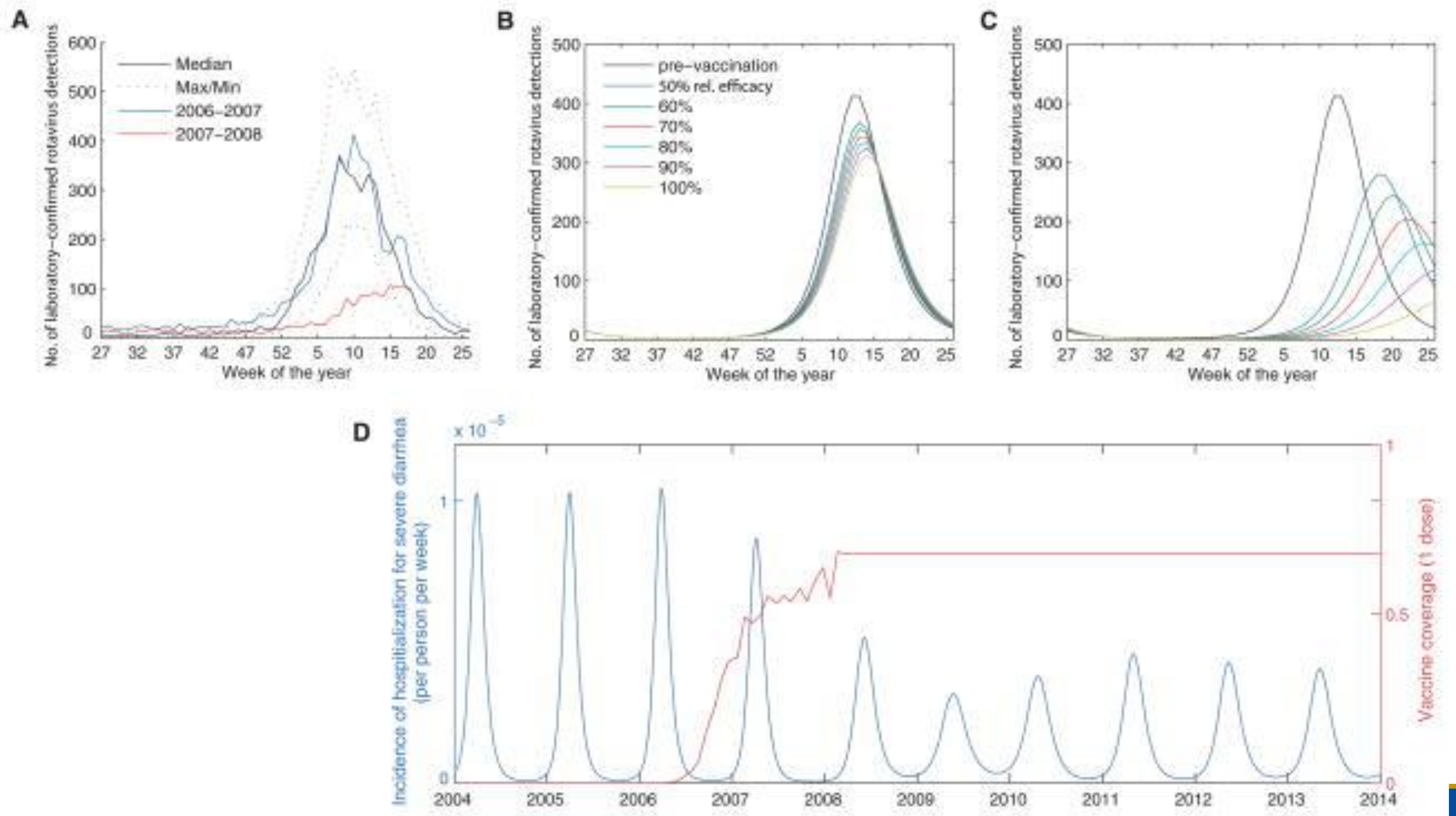


Direct and indirect VE against rotavirus for each post-vaccine year, United States, by age group



Gastañaduy et al, JAMA 2014. Baker et al, BMCID 2019

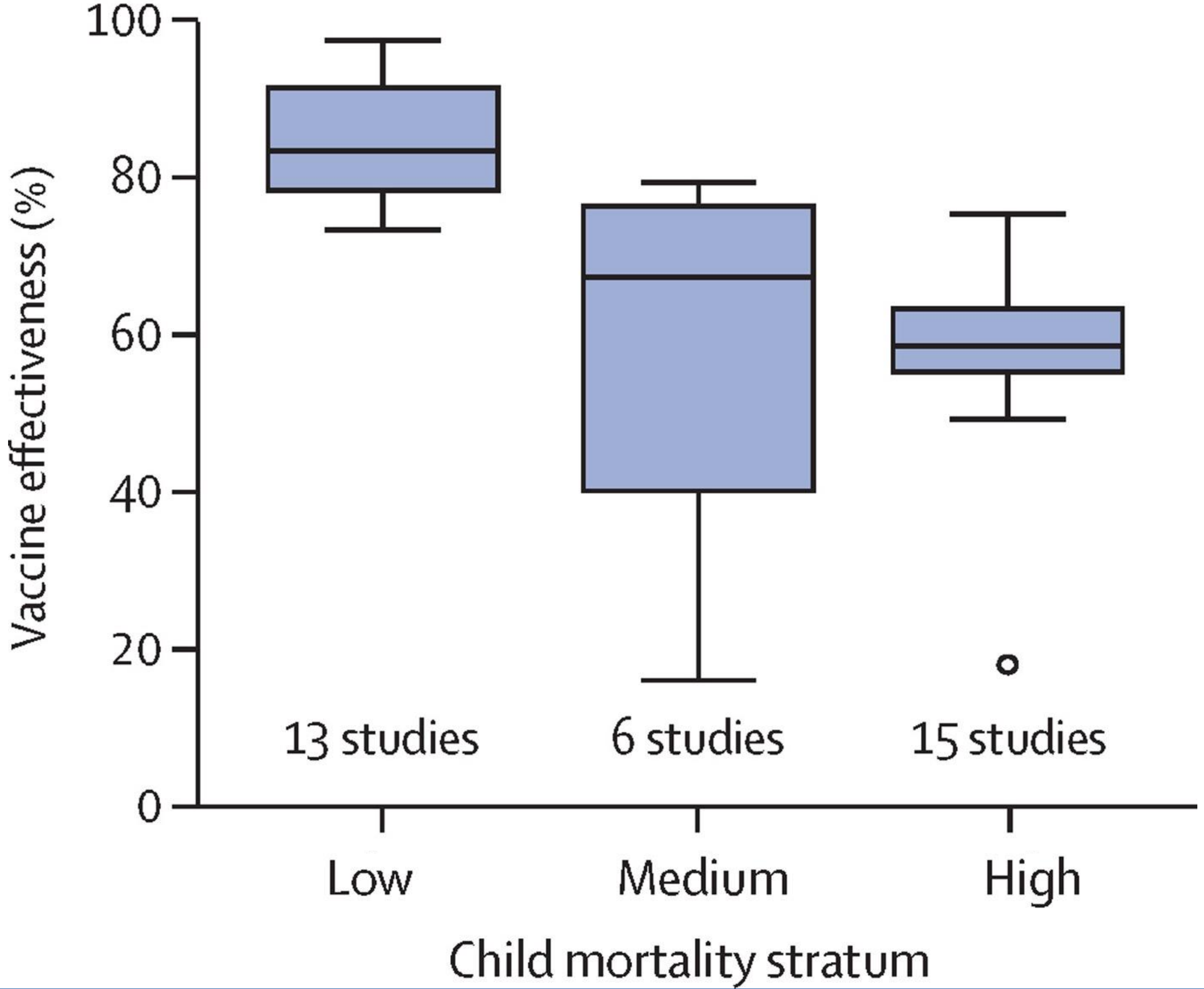
Models predicts (some) of these vaccine effects



Pitzer et al, Science 200

Rotavirus Vaccines are Less Efficacious in LMICS

Direct effect



Burnett et al, *Lancet GH 2020*

Why do rotavirus vaccine work less well in LMICs?

Pre-parturition → Pre-vaccination → Peri-vaccination → Post-vaccination

Pre-parturition
- Maternal exposure
- Transplacental antibody
- Genetic factors (HBGA)

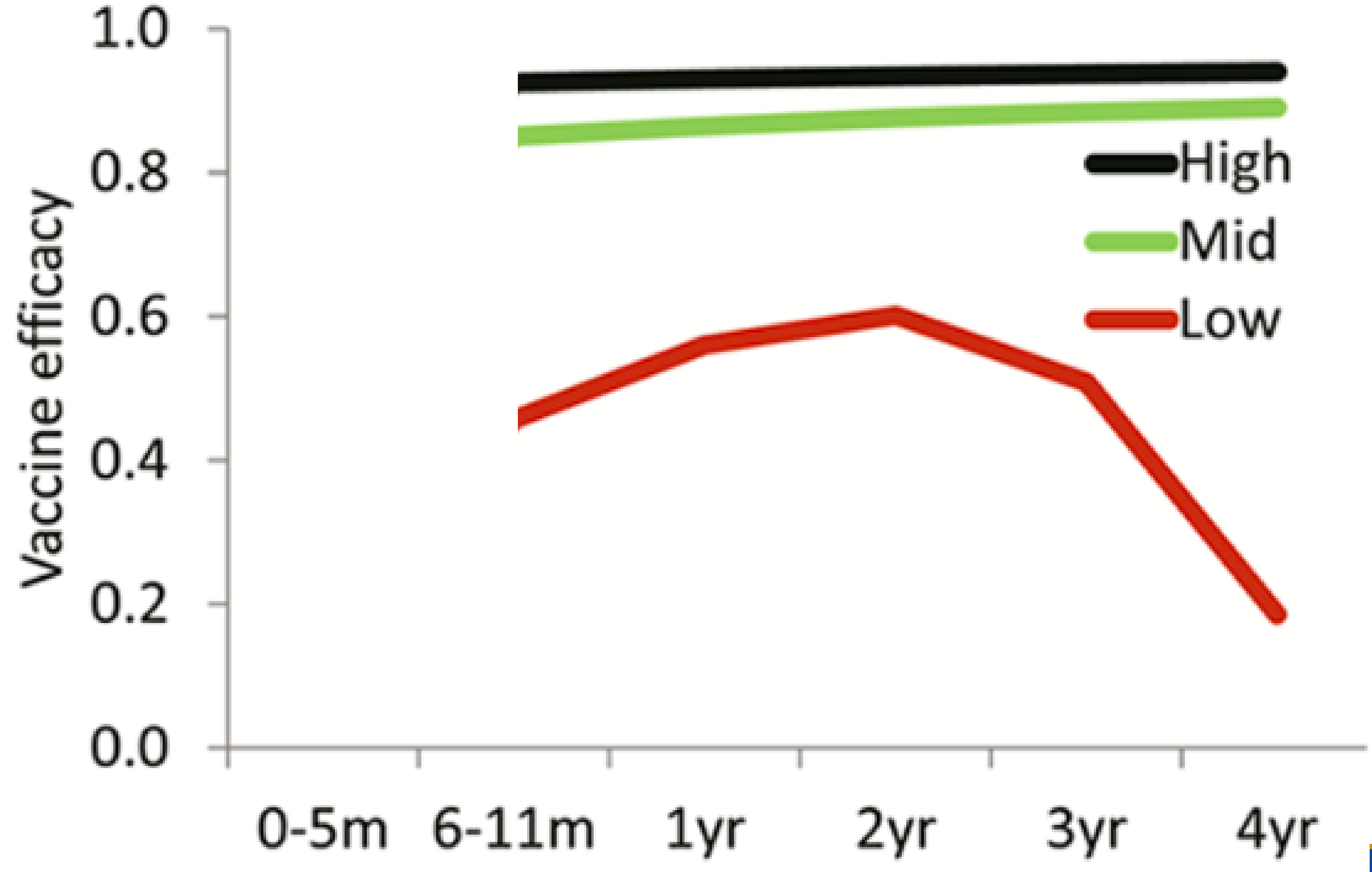
Pre-vaccination
- Innate immunity training
- History of exposure
- Enteric enteropathy
- Malnutrition

Peri-vaccination
- Breastmilk
- Concurrent infections
- Diarrhea
- Co-administration of other oral

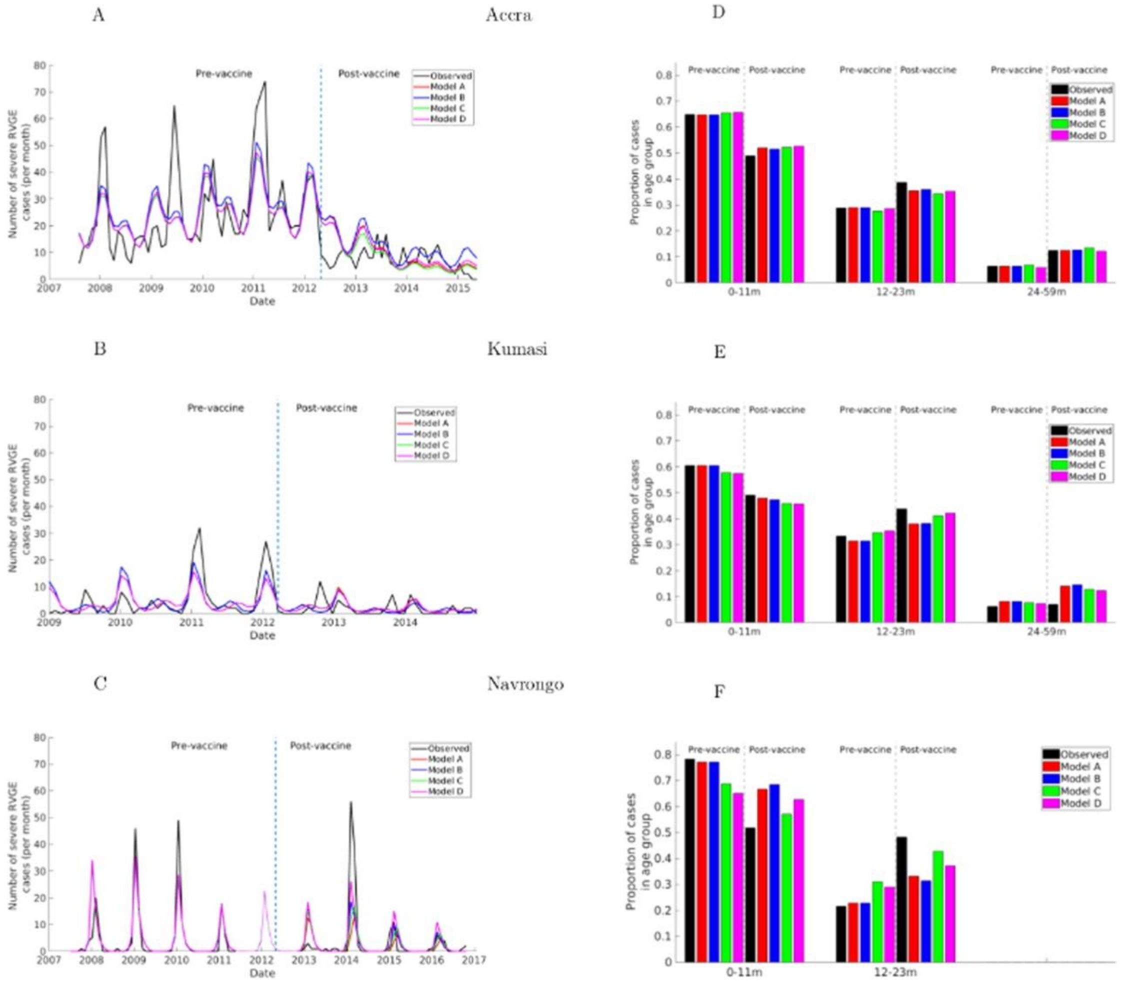
Post-vaccination
- Heterotypic strains
- Breakthrough infection

Parker et al, Future Micro, 201

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



Lopman et al, PLoS One 2012



Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

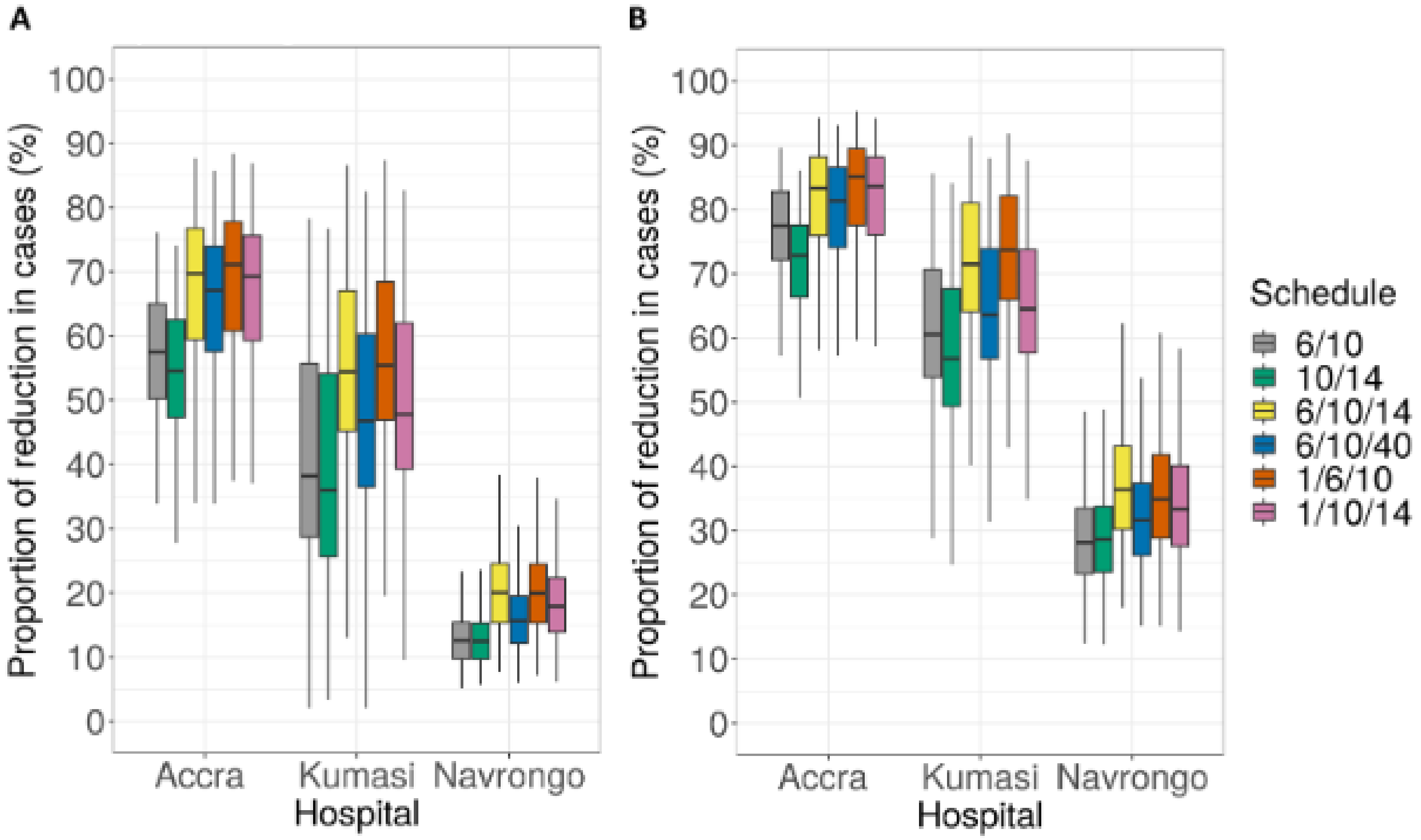
Modeling of rotavirus transmission dynamics and impact of vaccination in Ghana

Ernest O. Asare [a,*], Mohammad A. Al-Mamun [a], George E. Armah [b], Benjamin A. Lopman [c], Umesh D. Parashar [d], Fred Binka [e], Virginia E. Pitzer [a]

EPIDEMIOLOGY

Impact of dosing schedules on performance of rotavirus vaccines in Ghana

Ernest O. Asare[1,2]*, Mohammad A. Al-Mamun[3], George E. Armah[4], Benjamin A. Lopman[5], Virginia E. Pitzer[1,2]



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

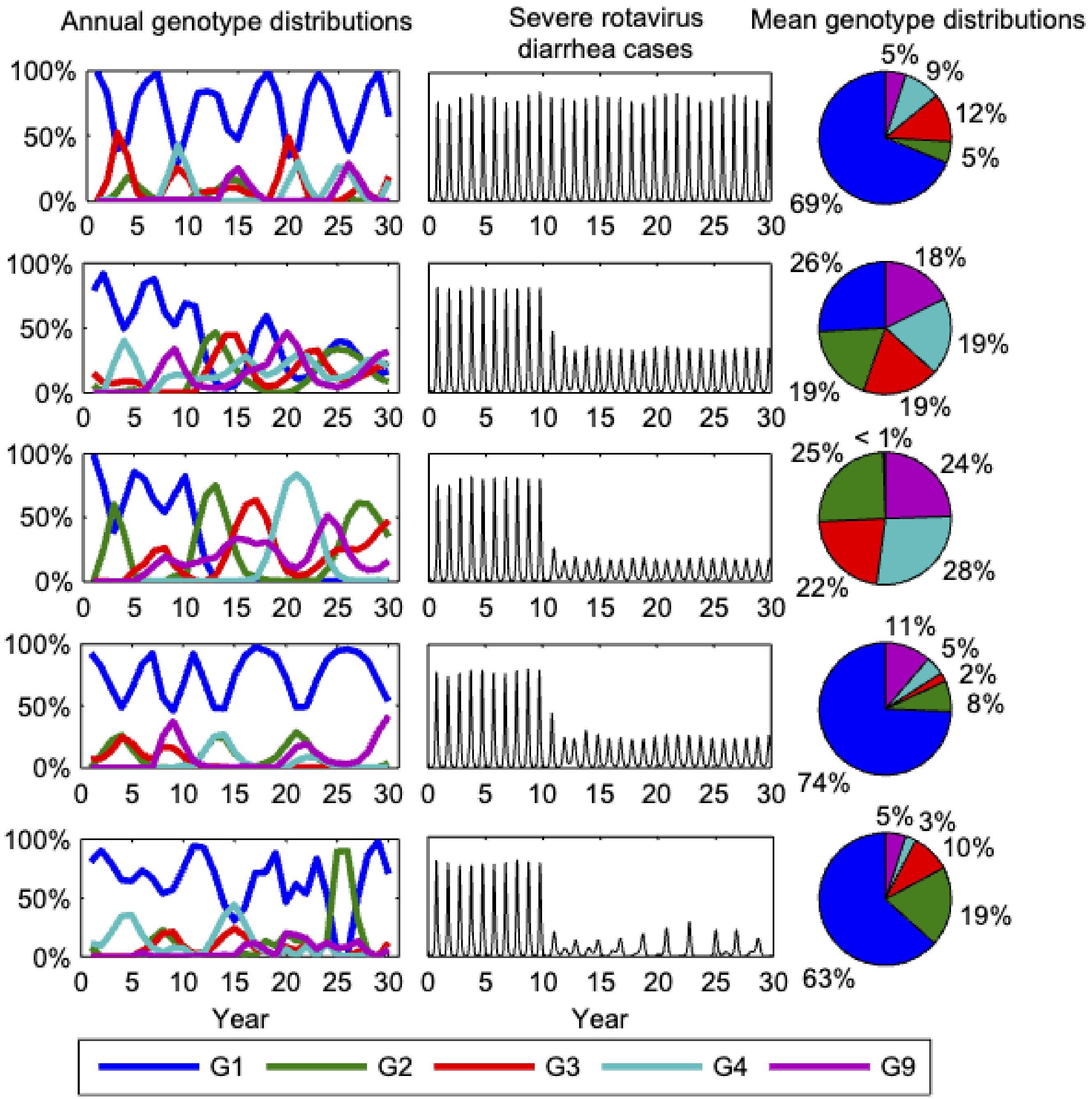
A) Pre-vaccination

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



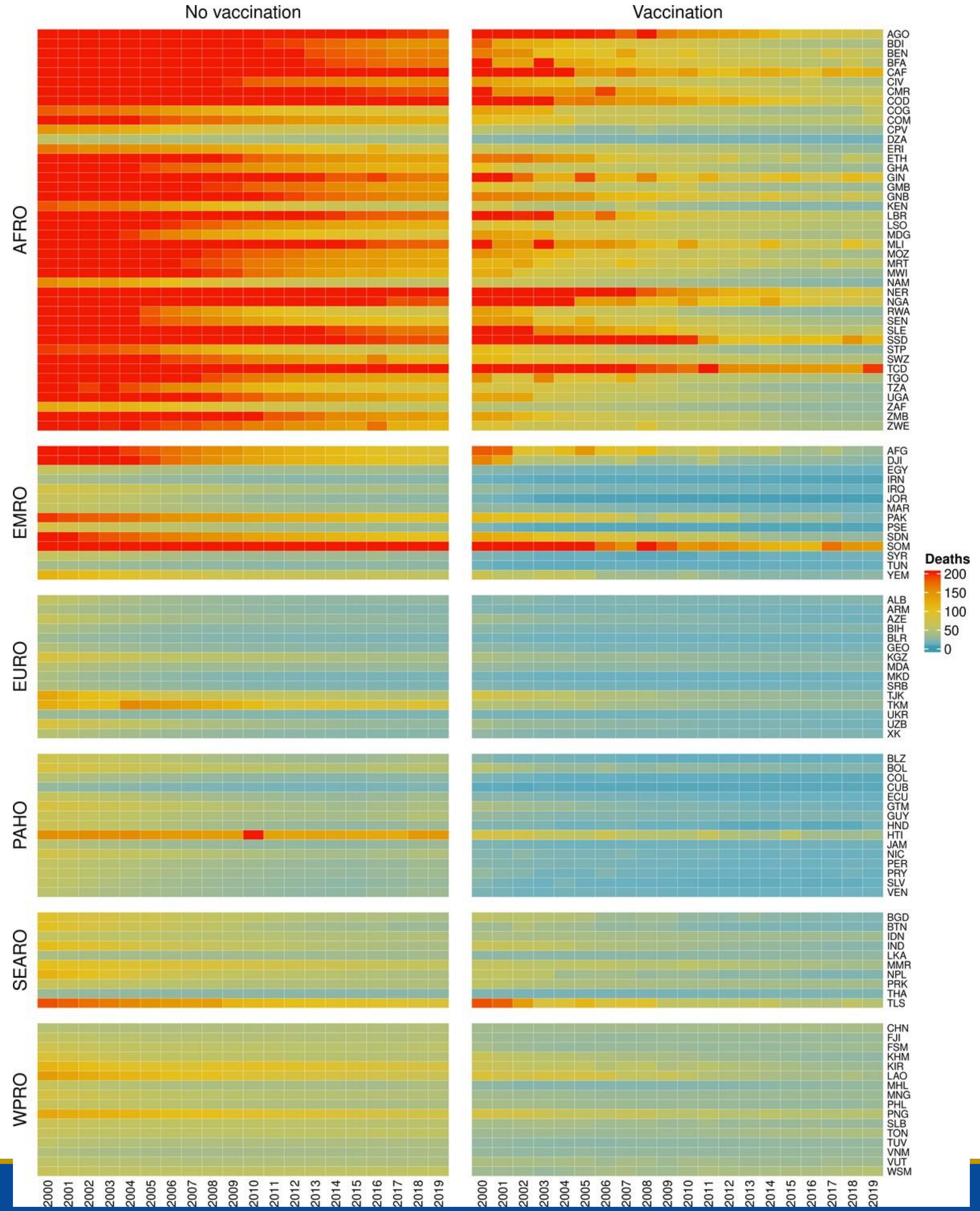
Among the greatest public health achievements

Will **prevent**

97 million deaths

from 2000-2030

VACCINE IMPACT MODELLING CONSORTIUM



Toor et al, eLife, 202

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

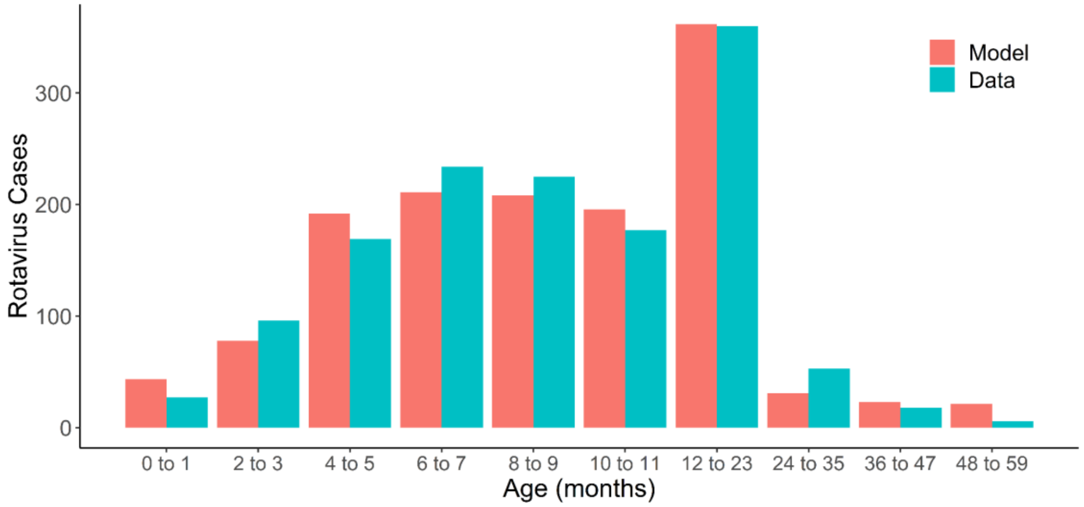
Model Calibration

Fit to age distribution* of rotavirus cases among < 5 yrs.

ML to estimate age specific transmission parameters for each country:

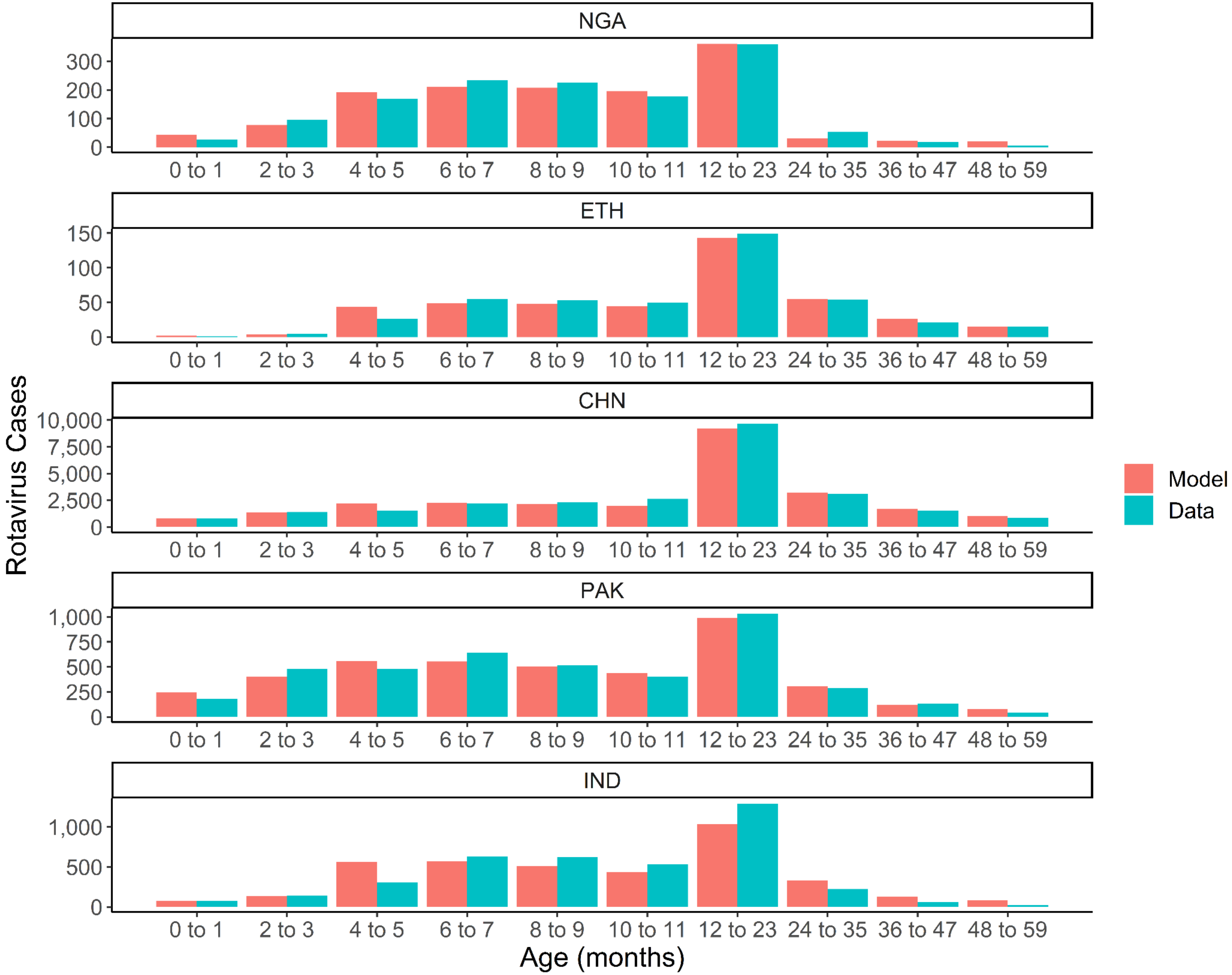
- $q_{1...3}$: 0-3; 4 to 23; >=24 months
- Reporting rate to scale to severe cases
- Then, scale severe cases to GBD mortality

Nigeria



*Hasso-Agopsowicz et al, CID 20

Model Calibration



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

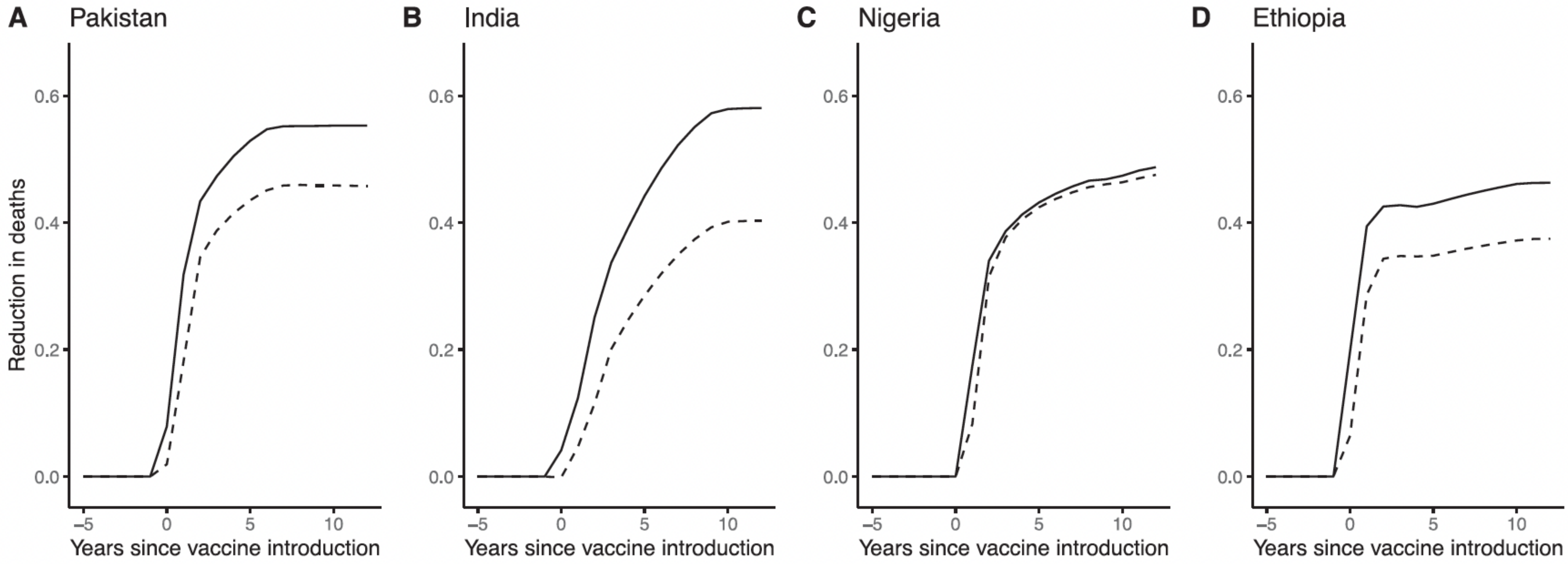
A.N.M. Kraay[a,b,*], M.K. Steele[b], J.M. Baker[b], E.W. Hall[b], A. Deshpande[b], B.F. Saidzosa[c], A. Mukaratirwa[d], A. Boula[e], E.M. Mpabalwani[f], N.M. Kiulia[g], E Tsolenyanu[h,i], C. Enweronu-Laryea[j], A. Abebe[k], B. Beyene[k], M. Tefera[k], R. Willilo[l], N. Batmunkh[m], R. Pastore[n], J.M. 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

Comparison of Direct vs. Indirect Effects in Pakistan, India, Nigeria, and Ethiopia



Solid: Overall Effect, Dashed: Direct Effect

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