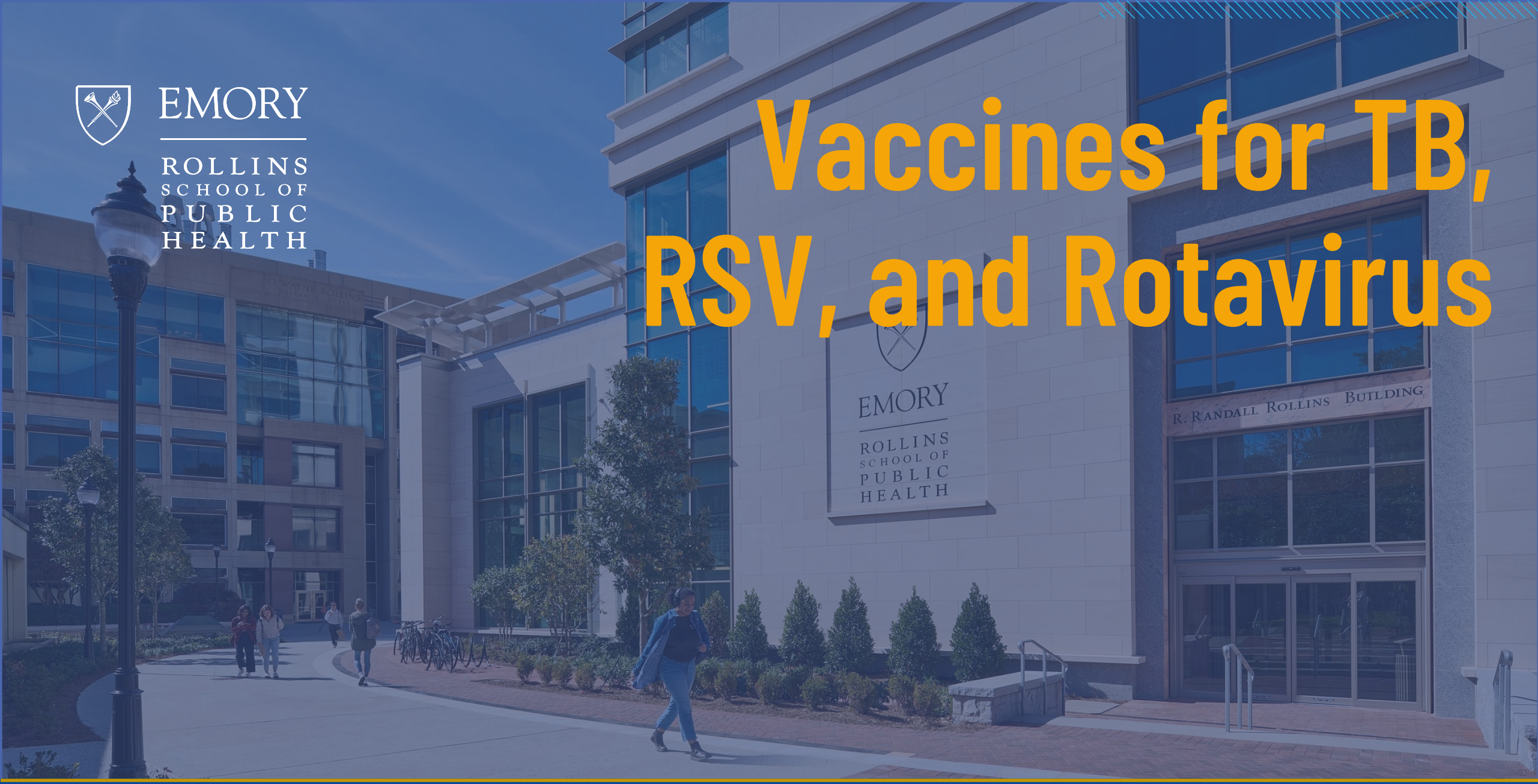
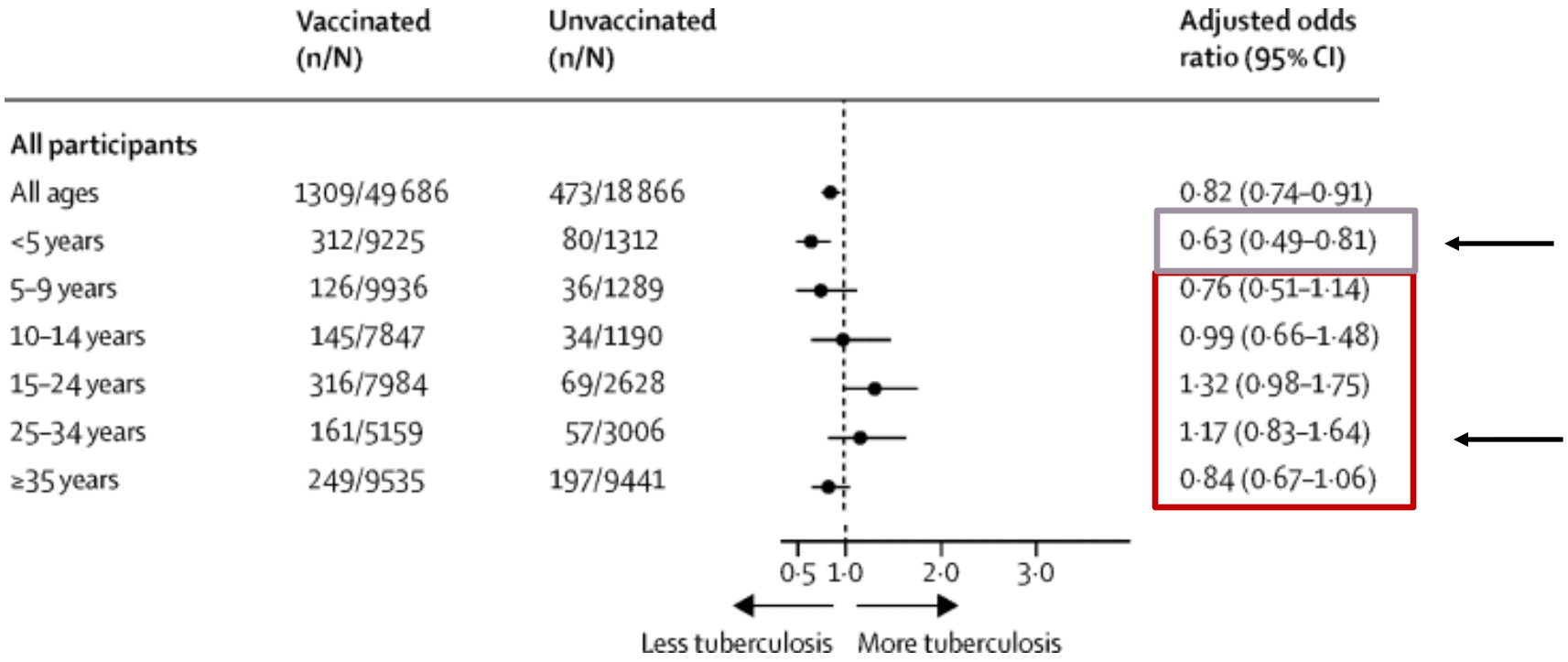


Vaccines for TB, RSV, and Rotavirus

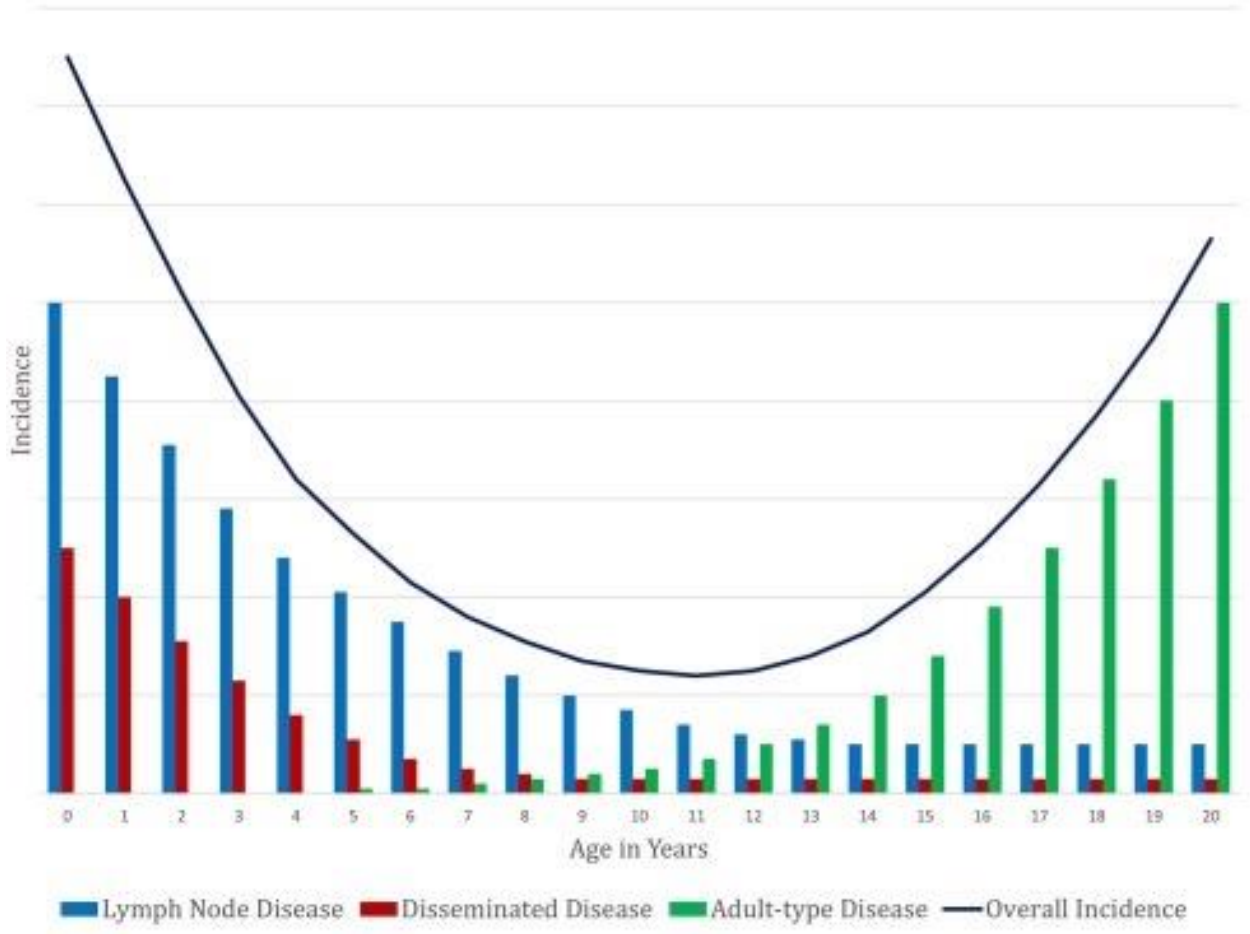
TB

Neonatal BCG vaccination does not prevent adult TB



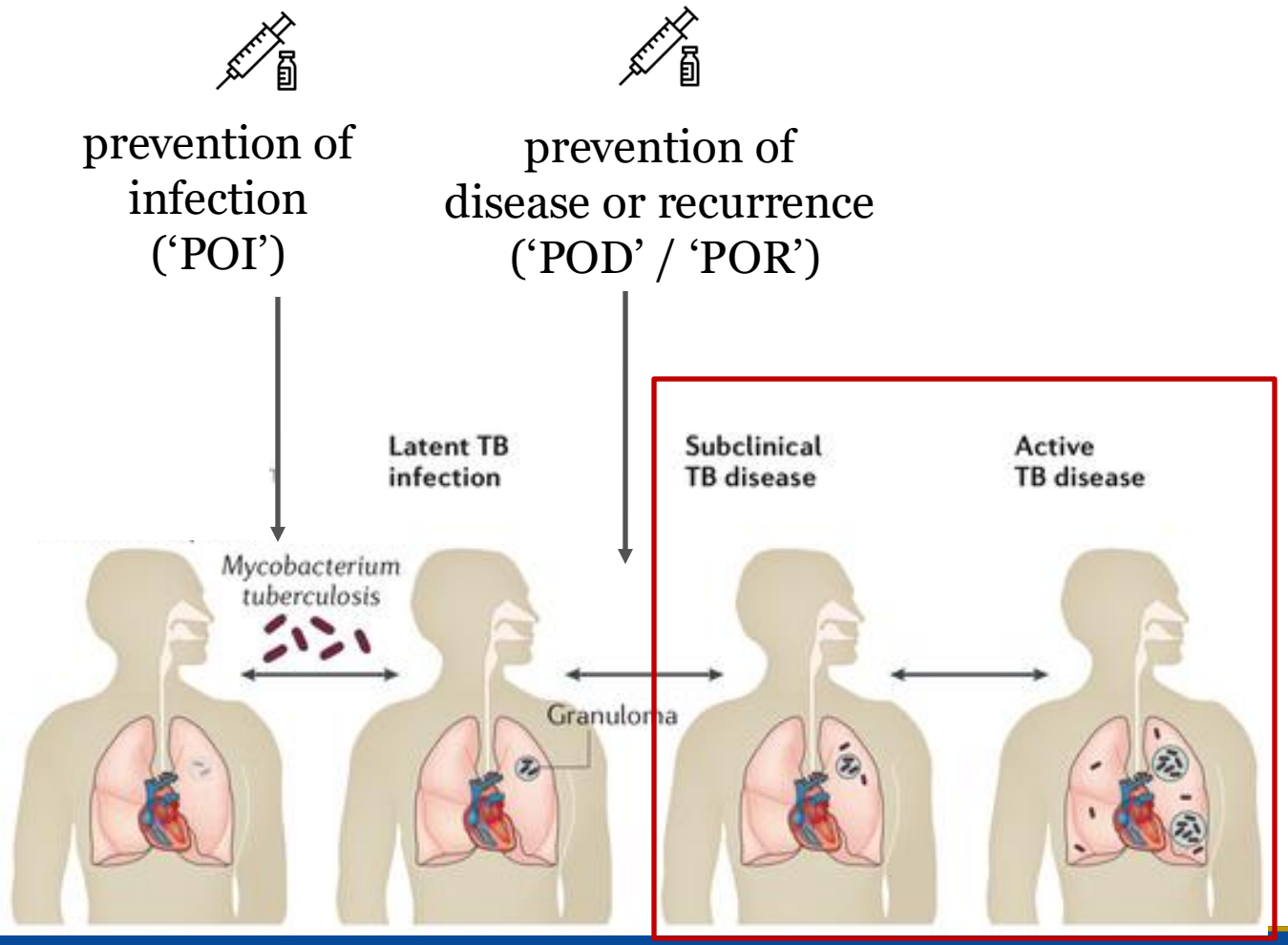
Martinez et al. Lancet ID 2022

TB infection and transmission rises in late adolescence



Seddon et al. Front Immun 2018

Target use indications guiding late-stage development



Pai et al. Nature Rev 2016

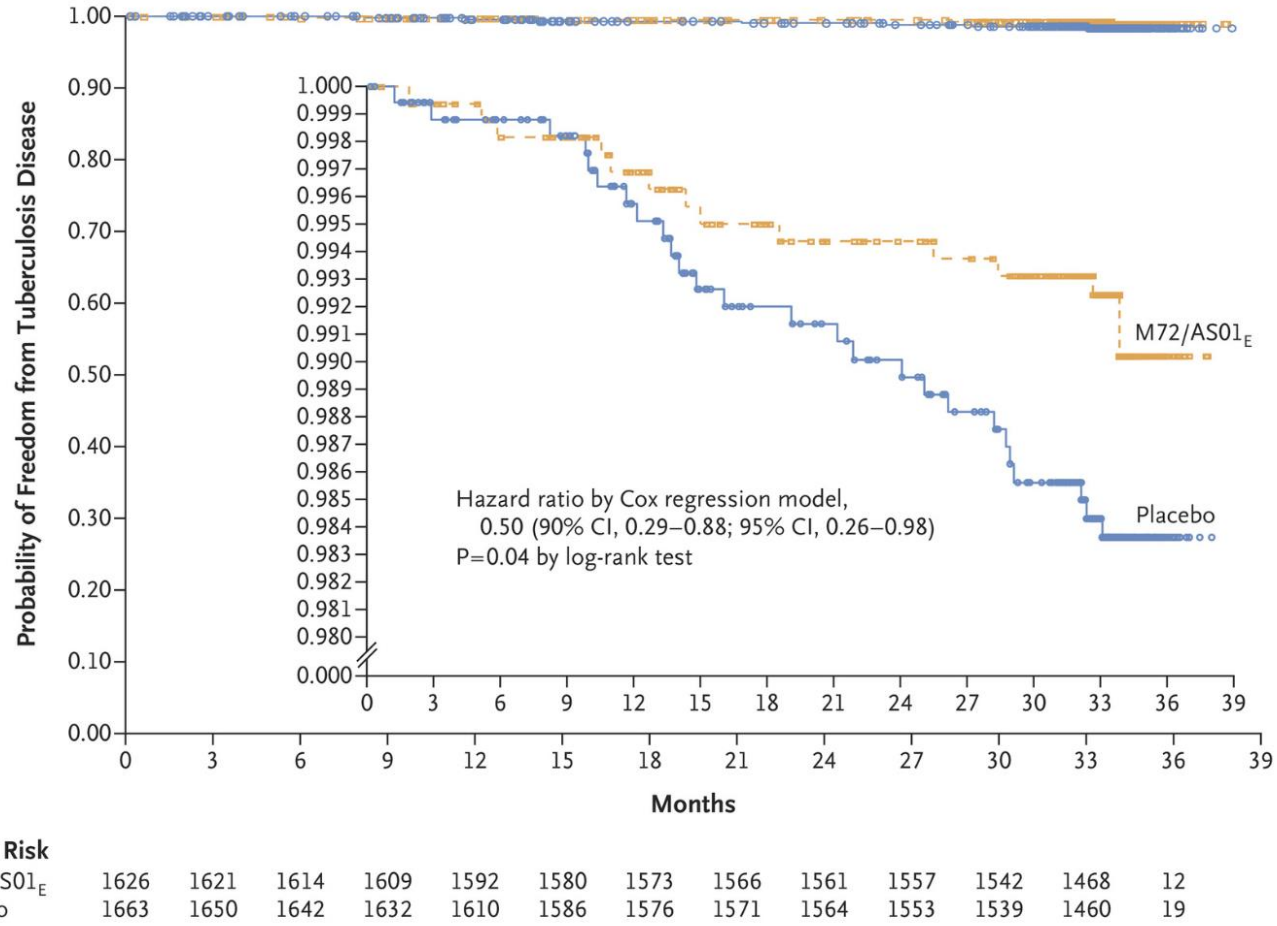
Novel vaccine candidates

M72-AS01$_E$

Protein subunit + adjuvant
(GSK, Gates MRI, Wellcome)

POD phase II trials showed 50% efficacy in IGRA+, HIV- persons

Phase III trial began this year, results from Phase II in PLHIV later this year (**2024**)



Tait et al. NEJM, 2018

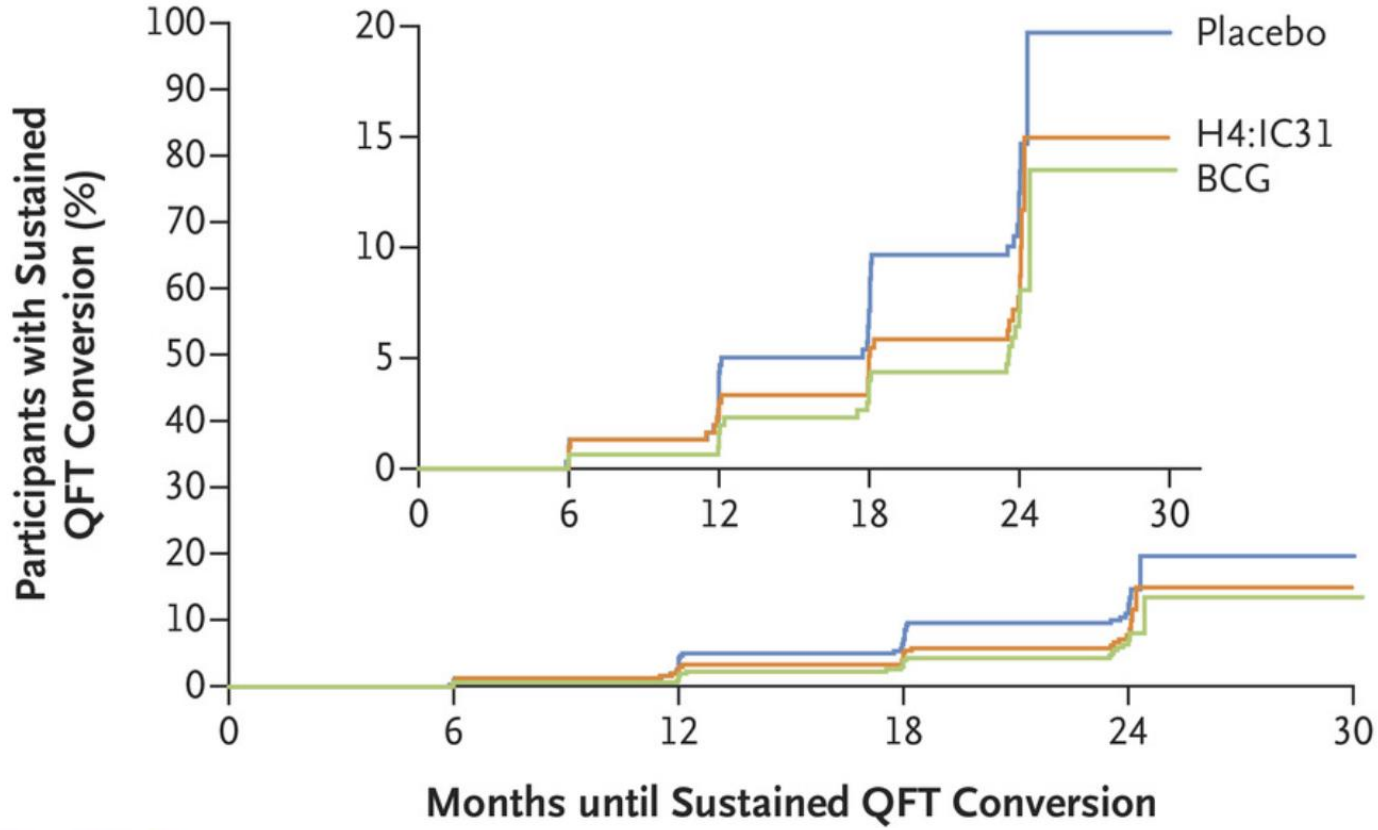
BCG revaccination

<u>BCG revaccination</u>

Whole-cell *M. bovis* (Gates MRI, ICMR, NIH)

POI phase IIb trial showed 45% efficacy against sustained QFT conversion

Phase II POI confirmatory trial completed, results later this year (2024). Trials in household contacts and preadolescents underway.



No. at Risk					
Placebo	310	302	287	263	122
H4:IC31	308	303	288	268	124
BCG	312	308	297	281	136

Nemes et al. NEJM, 2018

BCG revaccination in India

Indian J Med Res 157, February and March 2023, pp 152-159
DOI: 10.4103/ijmr.ijmr_1540_22

Revisiting the Chingleput BCG vaccination trial for the impact of BCG revaccination on the incidence of tuberculosis disease

Banurekha Velayutham[1], Kannan Thiruvengadam[2], Paramasivam Paul Kumaran[1], Basilea Watson[2], Krishnan Rajendran[2] & Chandrasekaran Padmapriyadarsini[1]

[1]*Department of Clinical Research,* [2] *Statistics Section, Epidemiology Unit, ICMR- National Institute for Research in Tuberculosis, Chennai, Tamil Nadu, India*

Table III. Incidence of tuberculosis disease and protective efficacy of BCG vaccine according to age at trial intake, sex and latent tuberculosis infection status in individuals with prior BCG vaccination at trial intake

Characteristics	Total (n)	Incident TB cases, n (%)	Hazard ratio (95% CI)	*P*	Protective efficacy % (95% CI)
Age (yr)					
<10					
Placebo	244	5 (2)	Reference		
BCG	453	9 (2)	0.96 (0.32-2.88)	0.948	4 (−188-68)
11-20					
Placebo	598	21 (3.5)	Reference		
BCG	1161	25 (2.2)	0.61 (0.34-1.09)	0.093	39 (−9-66)
21-30					
Placebo	514	24 (4.7)	Reference		
BCG	960	32 (3.3)	0.71 (0.42-1.21)	0.208	29 (−21-58)
31-40					
Placebo	129	14 (10.9)	Reference		
BCG	218	5 (2.3)	0.2 (0.07-0.57)	0.002	80 (43-93)
>40					
Placebo	61	0	-	-	-
BCG	98	6 (6.1)			
Overall					
Placebo	1546	64 (4.1)	Reference		
BCG	2890	77 (2.7)	0.64 (0.46-0.89)	0.008	36 (11-54)

<u>Programmatic study ongoing now</u>

547 districts

- 274 interventions (revax in >15yo with exposure)
- 273 comparator

Started May 2024

Velayutham *et al.* IJMR, 2023.

RSV

RSV Vaccines – Newly Available

Arexvy: inactivated protein

US, EU, UK, Canada, Australia, Japan, Hong Kong, Taiwan, Singapore, etc.

Abrysvo: non-adjuvanted bivalent vaccine

US, EU, UK, Canada, Australia, Japan, Hong Kong, Singapore, etc.

Beyfortus (nirsevimab)**:** injectable monoclonal antibody

US, EU, UK, Canada, Japan, China, Saudi Arabia, Qatar

mRESVIA: mRNA

US, EU, Canada

Potential for RSV Vaccine Approval in India

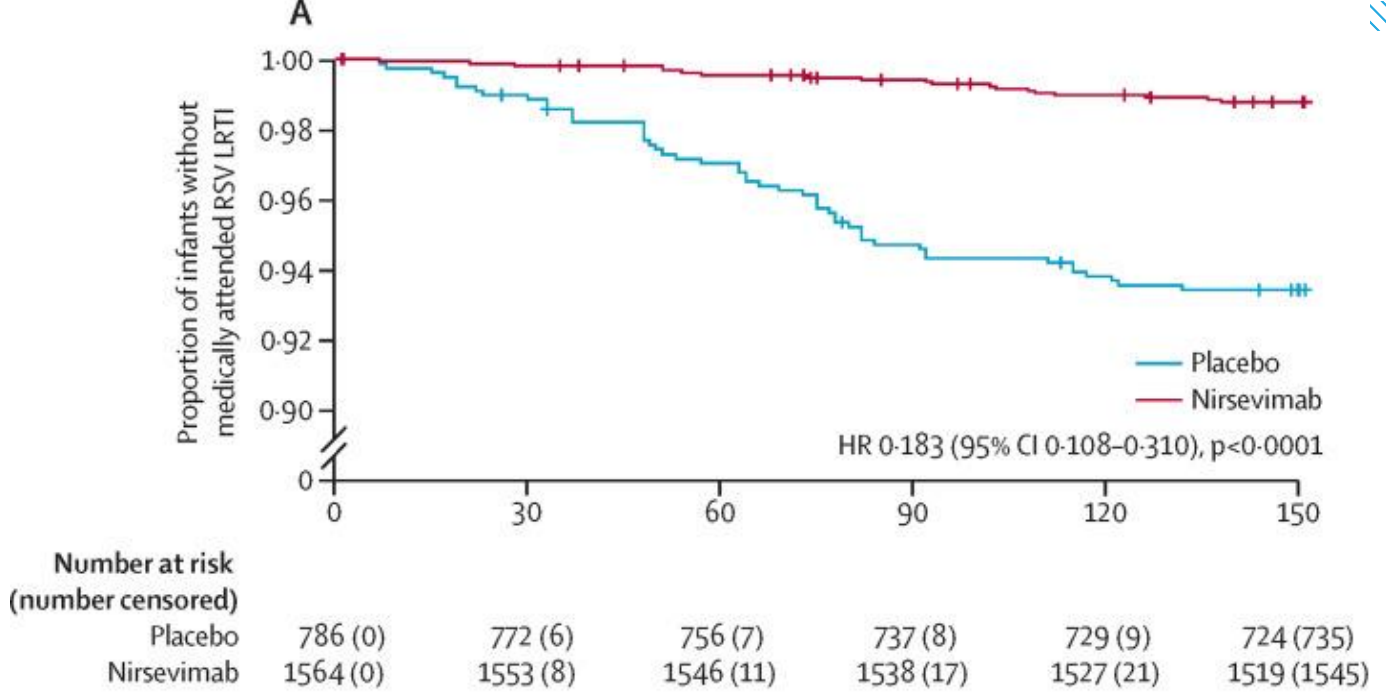
- The greatest burden of RSV-related hospitalisations and deaths in India is among children < 5
- Vaccines indicated for protection of infant are likely to be approved first in India
  - Beyfortus/nirsevimab for infants: within 1 week post-birth for births during October – March in US
  - Abrysvo for pregnant women 32 through 36 weeks gestational age

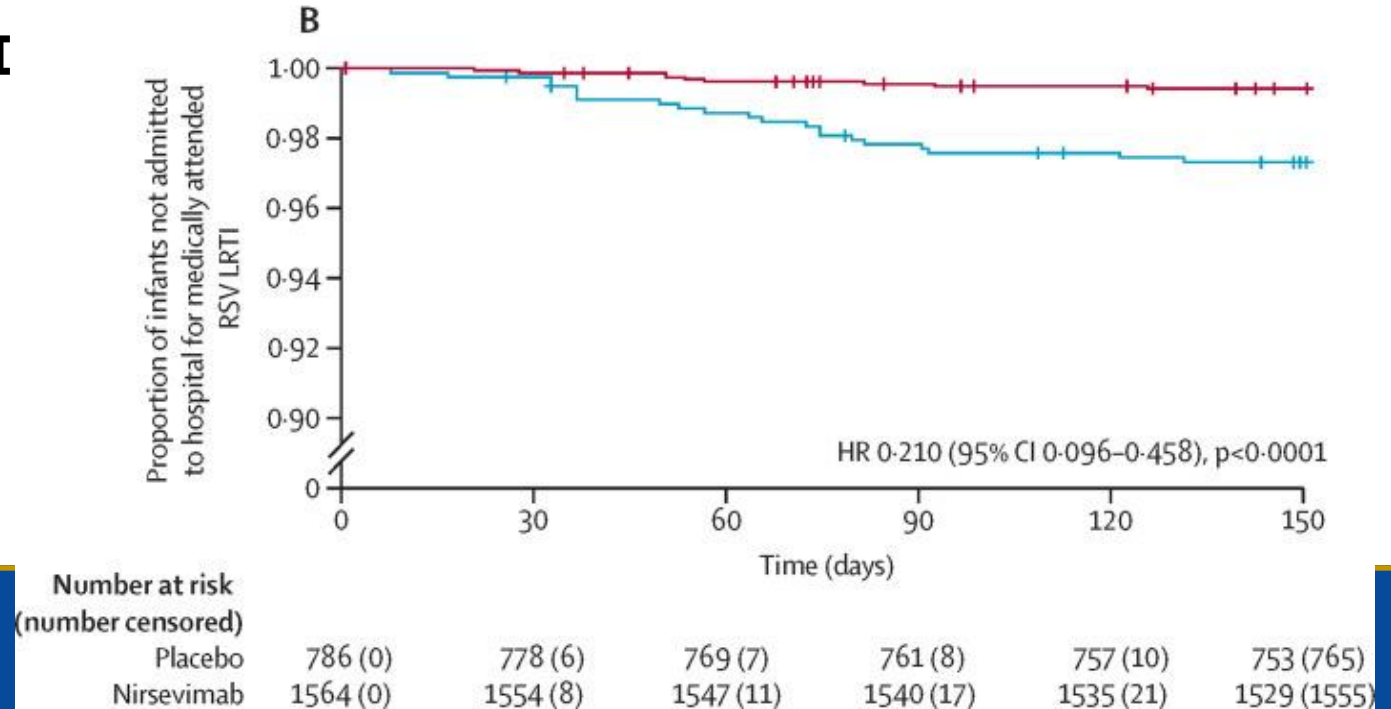
Beyfortus (nirsevimab) Efficacy

MA RSV LRTI
79.5% (95% CI: 65.9–87.7)

Hospital Admission for MA RSV LRTI
77.3% (50.3–89.7)

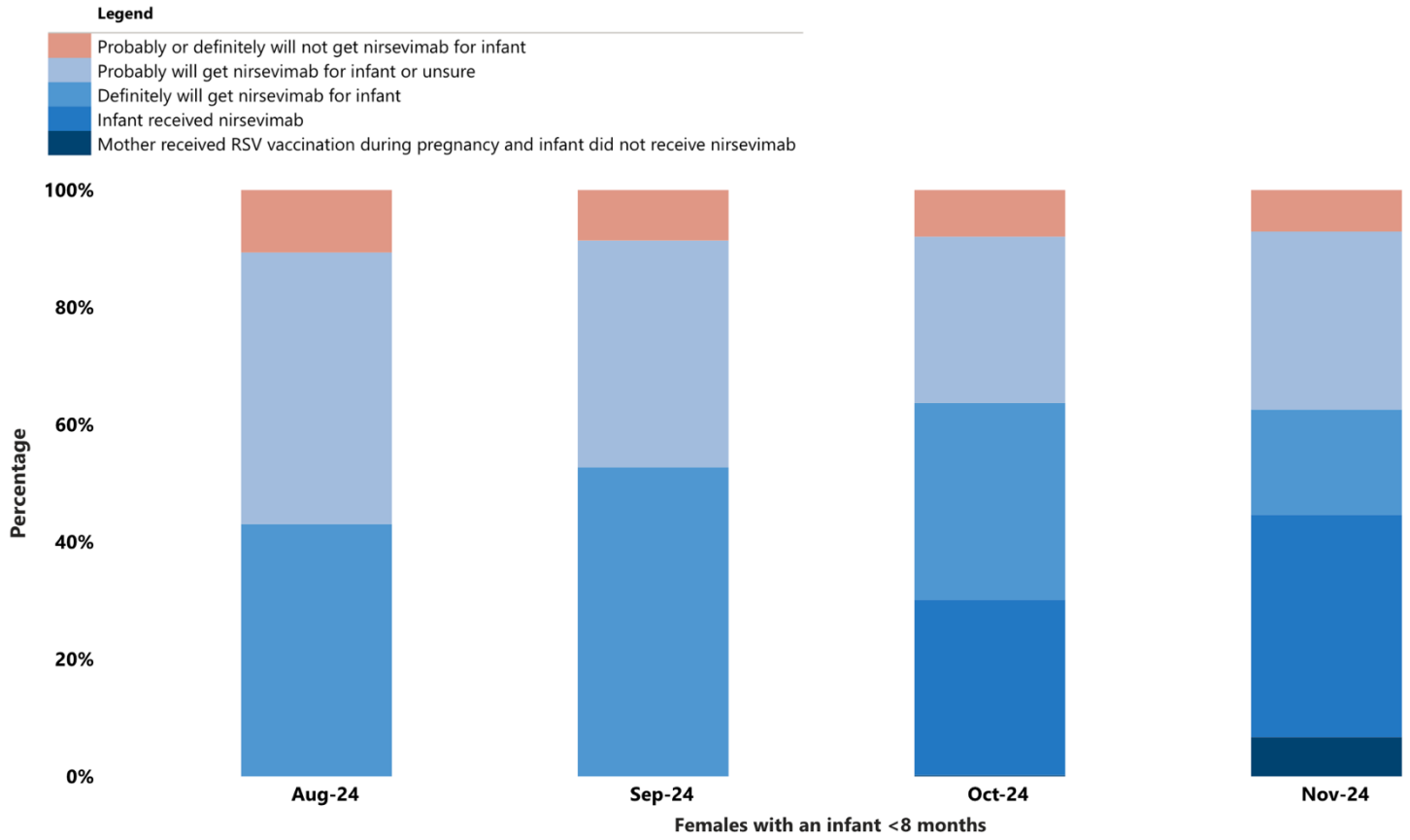
Very Severe RSV Disease
86.0% (62.5–94.8)





Uptake – Beyfortus (Nirsevimab)

Figure 6. Infant Protection Against RSV by Maternal RSV Vaccination* or Receipt of Nirsevimab,† and Intent for Nirservimab Receipt,‡ Reported By Females Aged 18–49 Years Who Have an Infant <8 Months During the RSV season (born since April 1, 2024), by Month of Interview, United States§,±
Data Source: National Immunization Survey–Adult COVID Module



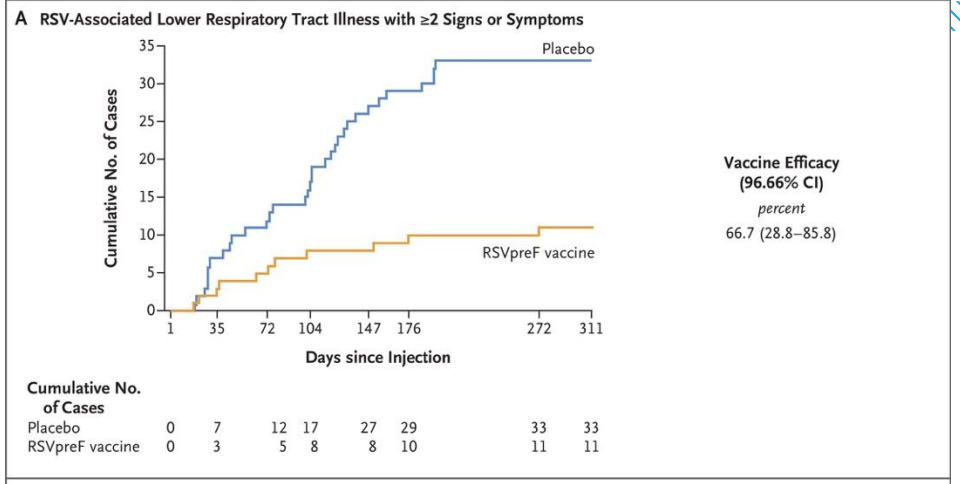
https://www.cdc.gov/rsvvaxview/dashboard/nirsevimab-coverage-infants.html

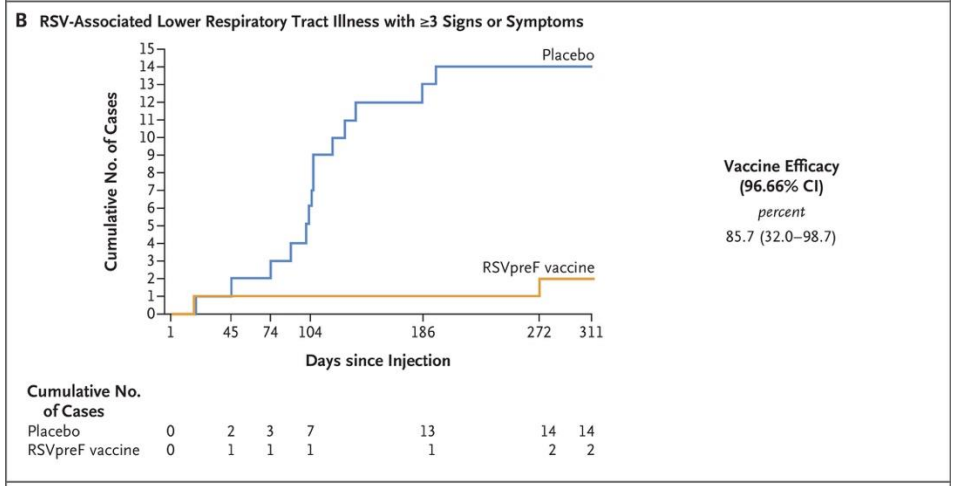
Abrysvo Efficacy

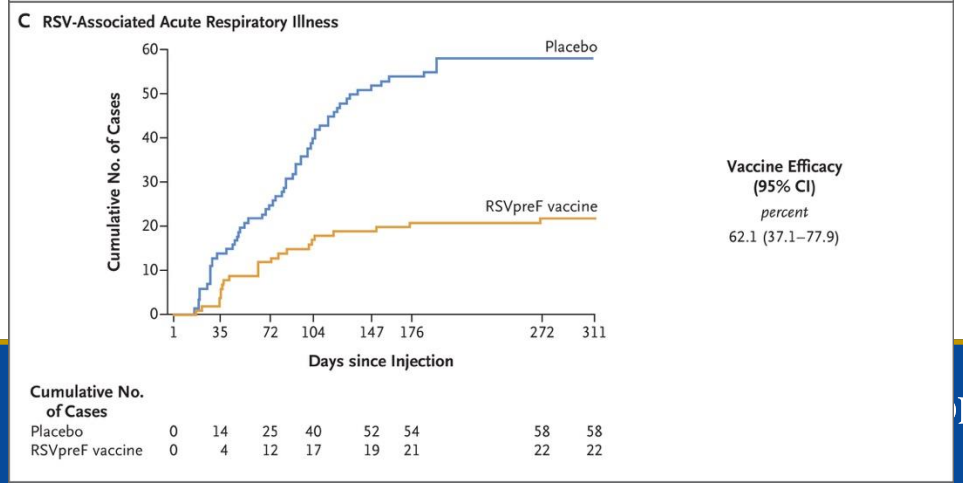
RSV LRTI 2+ Symptoms
66.7% (96.66% CI: 28.8-85.8)

RSV LRTI 3+ Symptoms
85.7% (32.0-98.7)

RSV ARI
62.1% (37.1-77.9)







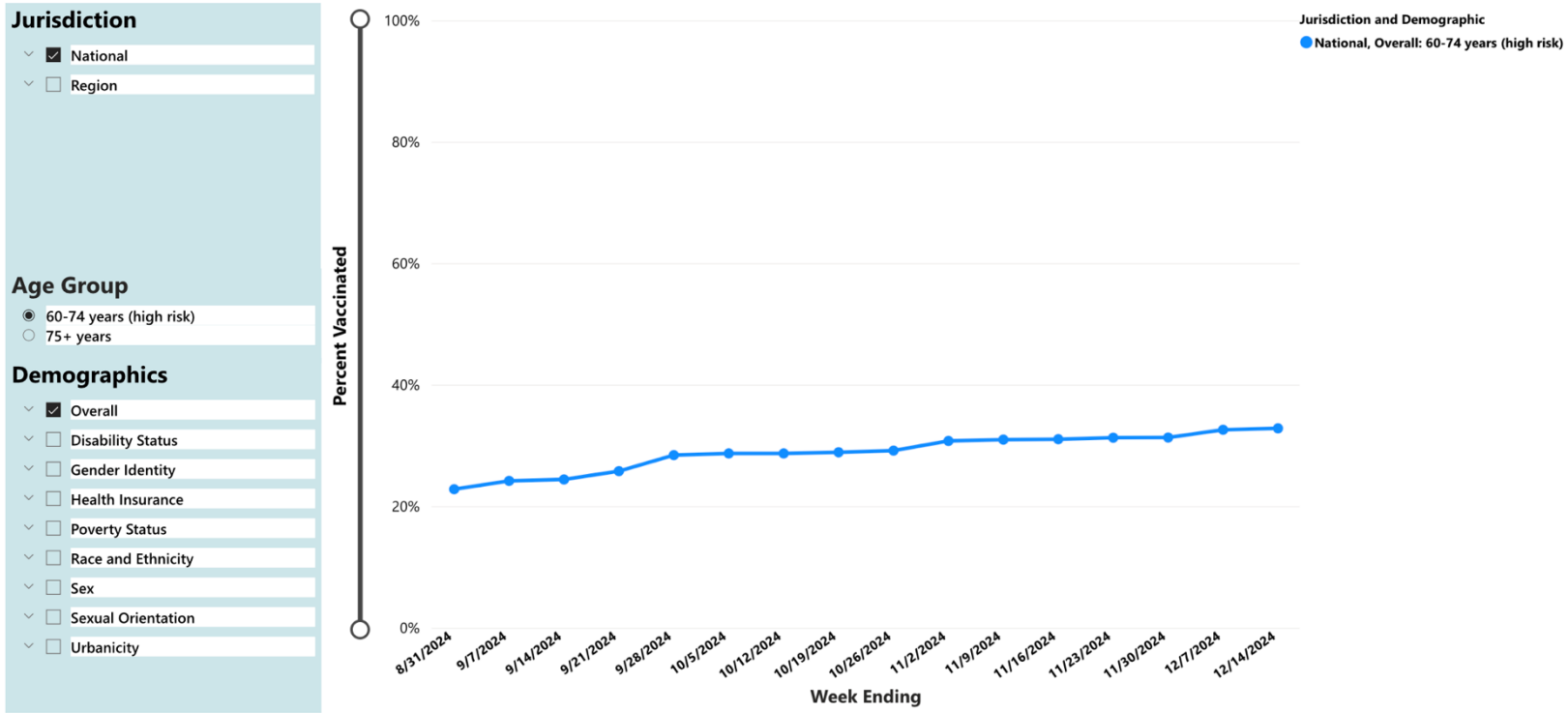
Uptake – Older Adult Vaccines

Fig. 1A: RSV Vaccination Coverage

Fig. 1B: RSV Vaccination and Intent

Fig. 1C: RSV Comparison Tables

Figure 1A. Cumulative Percentage of Adults 75 Years and Older and Adults 60–74 Years with High-Risk Conditions Ever Vaccinated with RSV Vaccine, 2024—2025*,†,‡,§,^
Data Source: National Immunization Survey–Adult COVID Module



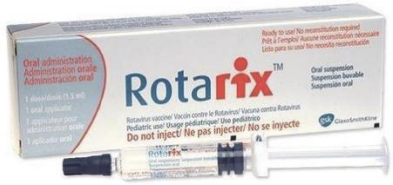
https://www.cdc.gov/rsvvaxview/dashboard/adults-60-coverage-intent.html

Rotavirus

WHO-prequalified Rotavirus vaccines

Rotarix® (RV1)

- GlaxoSmithKline Biologicals
- Monovalent G1P8
- 2 doses
  - 6 & 10 weeks



RotaTeq® (RV5)

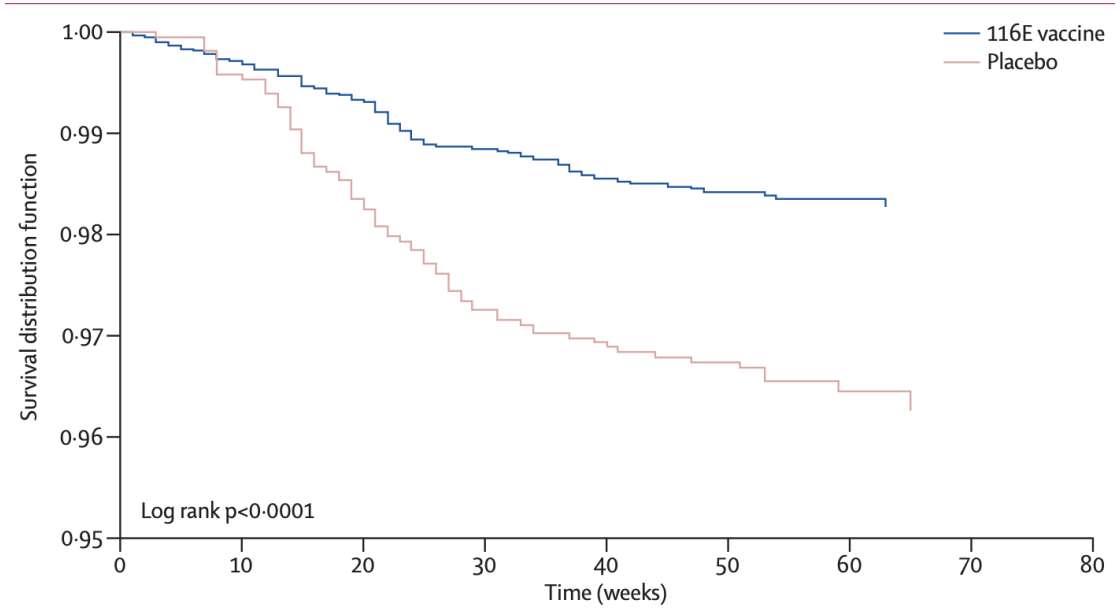
- Merck & Co. Inc.
- G1, G2, G3, G4, and G9 reassortant
- 3 doses
  - 6, 10 and 14 weeks

Rotavac

- Bharat Biotech International Limited
- Natural reassortant neonatal G9P[11]
- 3 doses
  - 6, 10 and 14 weeks

Rotasil

- Serum Institute of India
- G1, G2, G3, G4, and G9 reassortant
- 3 doses
  - 6, 10 and 14 weeks



Efficacy of a monovalent human-bovine (116E) rotavirus vaccine in Indian infants: a randomised, double-blind, placebo-controlled trial

Nita Bhandari, Temsunaro Rongsen-Chandola, Ashish Bavdekar, Jacob John, Kalpana Antony, Sunita Taneja, Nidhi Goyal, Anand Kawade, Gagandeep Kang, Sudeep Singh Rathore, Sanjay Juvekar, Jayaprakash Muliyil, Alok Arya, Hanif Shaikh, Vinod Abraham, Sudhanshu Vrati, Michael Proschan, Robert Kohberger, Georges Thiry, Roger Glass, Harry B Greenberg, George Curlin, Krishna Mohan, G V J A Harshavardhan, Sai Prasad, T S Rao, John Boslego, Maharaj Kishan Bhan, for the India Rotavirus Vaccine Group†*

	Vaccine (n=4354)	Placebo (n=2187)	Vaccine efficacy (% [95% CI])	p value
Severe rotavirus gastroenteritis				
Overall*	71 (2%)	76 (3%)	53·6% (35·0 to 66·9)	0·0013
At 1 year of age	56 (1%)	64 (3%)	56·4% (36·6 to 70·1)	<0·0001
Severe rotavirus gastroenteritis needing hospital admission† or supervised rehydration therapy‡				
Overall*	71 (2%)	76 (3%)	53·6% (35·0 to 66·9)	<0·0001
At 1 year of age	56 (1%)	64 (3%)	56·4% (36·6 to 70·1)	<0·0001
Very severe rotavirus gastroenteritis				
Overall*	10 (<1%)	11 (<1%)	54·4% (−18·3 to 82·6)	0·1130
At 1 year of age	9 (<1%)	9 (<1%)	49·8% (−42·6 to 82·4)	0·2176
Rotavirus gastroenteritis of any severity				
Overall*	287 (7%)	216 (10%)	34·6% (21·6 to 45·3)	<0·0001
At 1 year of age	226 (5%)	171 (8%)	34·6% (19·7 to 46·6)	<0·0001
Rotavirus gastroenteritis of any severity needing hospital admission† or supervised rehydration‡ therapy				
Overall*	277 (6%)	201 (9%)	32·0% (18·0 to 43·5)	<0·0001
At 1 year of age	218 (5%)	161 (7%)	32·9% (17·2 to 45·5)	0·0002
Severe gastroenteritis of any cause				
Overall*	308 (7%)	188 (9%)	18·6% (1·9 to 32·3)	0·0305
At 1 year of age	221 (5%)	145 (7%)	24·1% (5·8 to 38·7)	0·0123

Data are n (%), unless otherwise indicated. We defined severe gastroenteritis as episodes with a Vesikari score of 11 or greater. Episodes of severe rotavirus gastroenteritis had a Vesikari score of 11 or greater and presence of rotavirus (rotaclone positive and VP6 or VP4 and VP7 positive by RT-PCR) strains; includes all cases except those for which G9P[11] was isolated. Episodes of very severe gastroenteritis had a Vesikari score of 16 or greater. *Median age was 17·2 months (range 13·4–21·7) at the time of analyses. †Inpatient admission for at least 6 h in a treatment facility or hospital. ‡Administration of oral rehydration salts or intravenous fluids.

Table 2: **Efficacy of the vaccine against gastroenteritis in the per-protocol population**

Efficacy of a monovalent human-bovine (116E) rotavirus vaccine in Indian infants: a randomised, double-blind, placebo-controlled trial

Nita Bhandari, Temsunaro Rongsen-Chandola, Ashish Bavdekar, Jacob John, Kalpana Antony, Sunita Taneja, Nidhi Goyal, Anand Kawade, Gagandeep Kang, Sudeep Singh Rathore, Sanjay Juvekar, Jayaprakash Muliyil, Alok Arya, Hanif Shaikh, Vinod Abraham, Sudhanshu Vrati, Michael Proschan, Robert Kohberger, Georges Thiry, Roger Glass, Harry B Greenberg, George Curlin, Krishna Mohan, G V J A Harshavardhan, Sai Prasad, T S Rao, John Boslego, Maharaj Kishan Bhan, for the India Rotavirus Vaccine Group†*

Summary of vaccine efficacy at the time of final analysis.

	Per protocol analysis			
	BRV-PV	Placebo	Vaccine efficacy	
	N = 3533	N = 3502	%	95% CI
SRVGE	171	275	39.5	26.7, 50.0
Very severe RVGE	29	63	54.7	29.7, 70.8
RVGE of any severity	492	614	22.6	12.9, 31.3
SRVGE in first year of life	85	125	32.9	11.6, 49.1
SRVGE against vaccine serotypes	170	271	38.9	26.0, 49.6
SRVGE requiring hospitalization	95	140	33.4	13.6, 48.7
Severe GE of any etiology	804	832	4.6	−5.1, 13.4

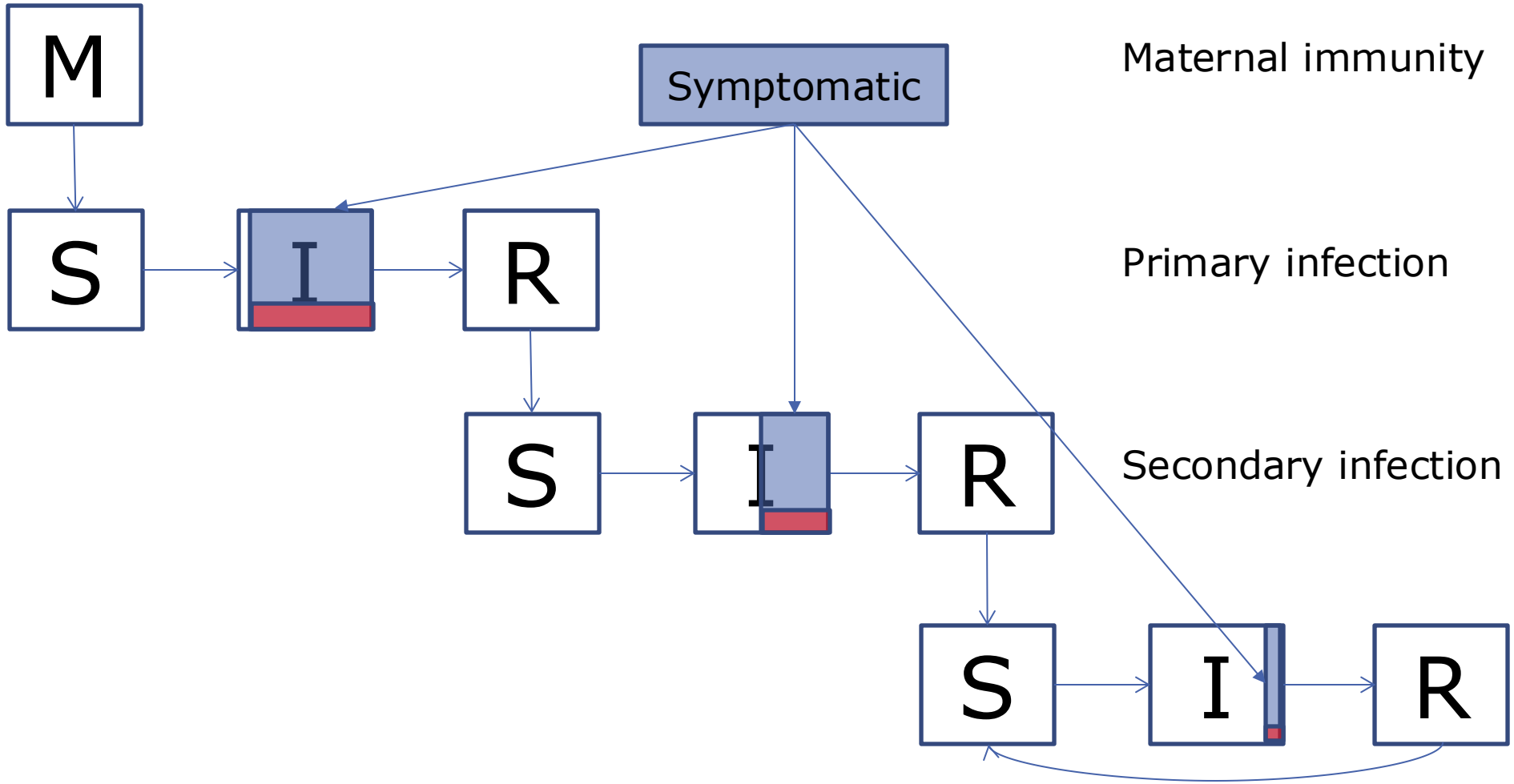
Contents lists available at ScienceDirect

Vaccine

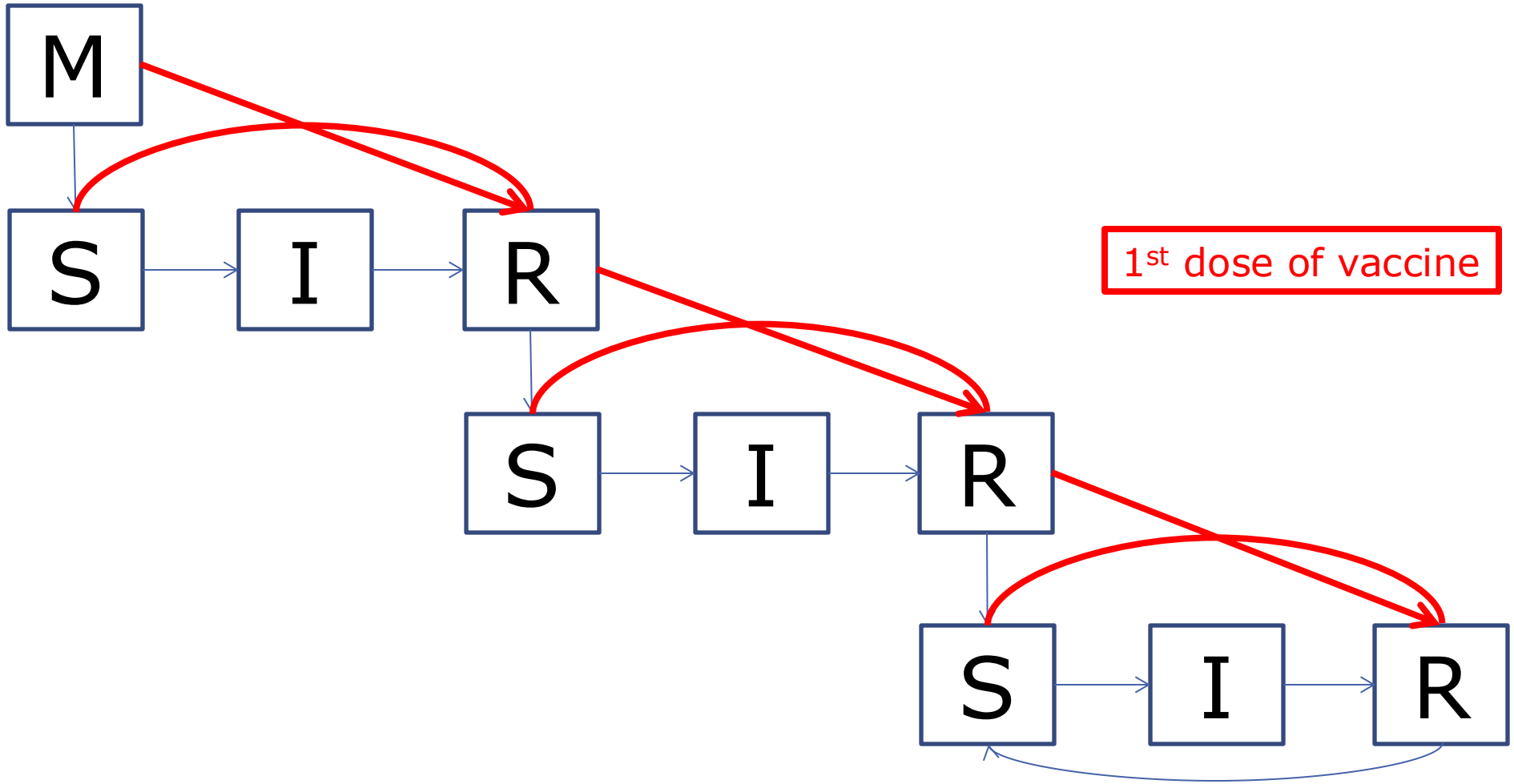
journal homepage: www.elsevier.com/locate/vaccine

A randomized Phase III clinical trial to assess the efficacy of a bovine-human reassortant pentavalent rotavirus vaccine in Indian infants

Prasad S. Kulkarni[a,*], Sajjad Desai[a], Tushar Tewari[b], Anand Kawade[c], Nidhi Goyal[d], Bishan Swarup Garg[e], Dinesh Kumar[f], Suman Kanungo[g], Veena Kamat[h], Gagandeep Kang[i], Ashish Bavdekar[c], Sudhir Babji[i], Sanjay Juvekar[c], Byomkesh Manna[g], Shanta Dutta[g], Rama Angurana[f], Deepika Dewan[f], Abhijeet Dharmadhikari[a], Jagdish K. Zade[a], Rajeev M. Dhere[a], Alan Fix[j], Maureen Power[j], Vidyasagar Uprety[b], Varsha Parulekar[k], Iksung Cho[j], Temsunaro R. Chandola[d], Vikash K. Kedia[d], Abhishek Raut[e], Jorge Flores[j], SII BRV-PV author group[1]



Pitzer et al, Science 2009
Atchison et al, Vaccine 2010
Lopman et al, PLoS One 2012



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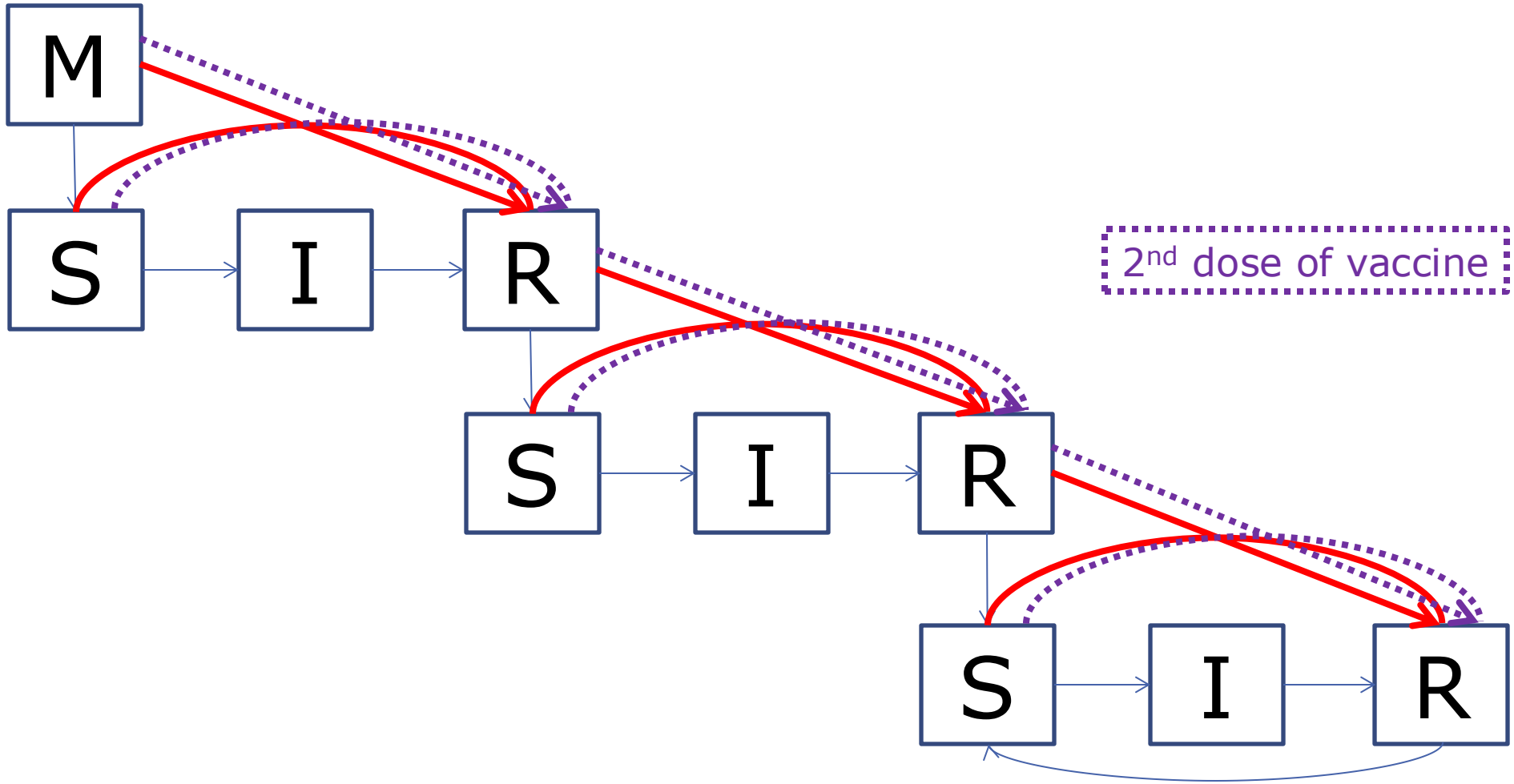
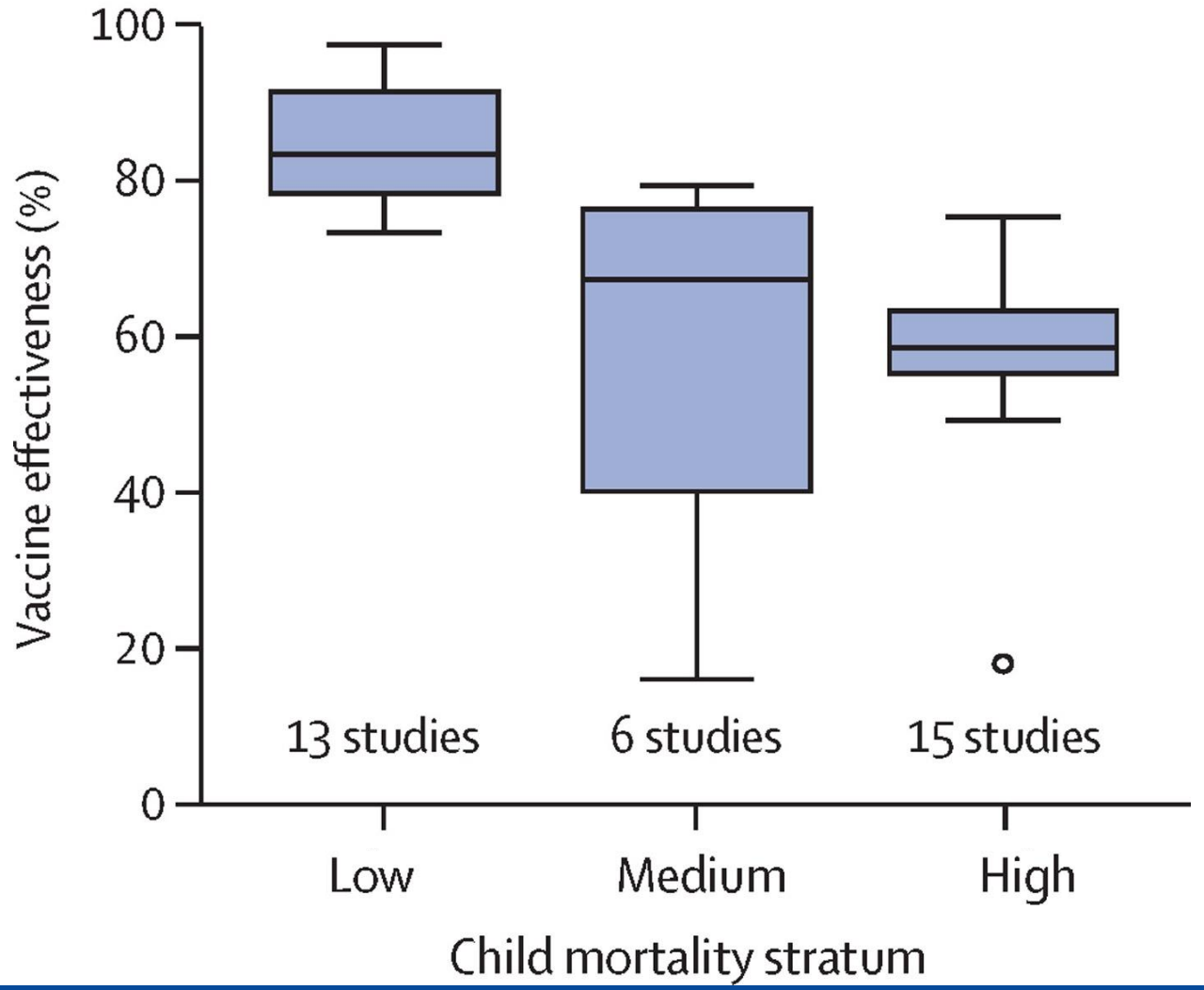


Pitzer et al, Science 2009
Atchison et al, Vaccine 2010
Lopman et al, PLoS One 2012

Rotavirus Vaccines are Less Efficacious in LMICS

Direct effect



Burnett et al, *Lancet GH 2020*

Why do rotavirus vaccine work less well in LMICs?

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

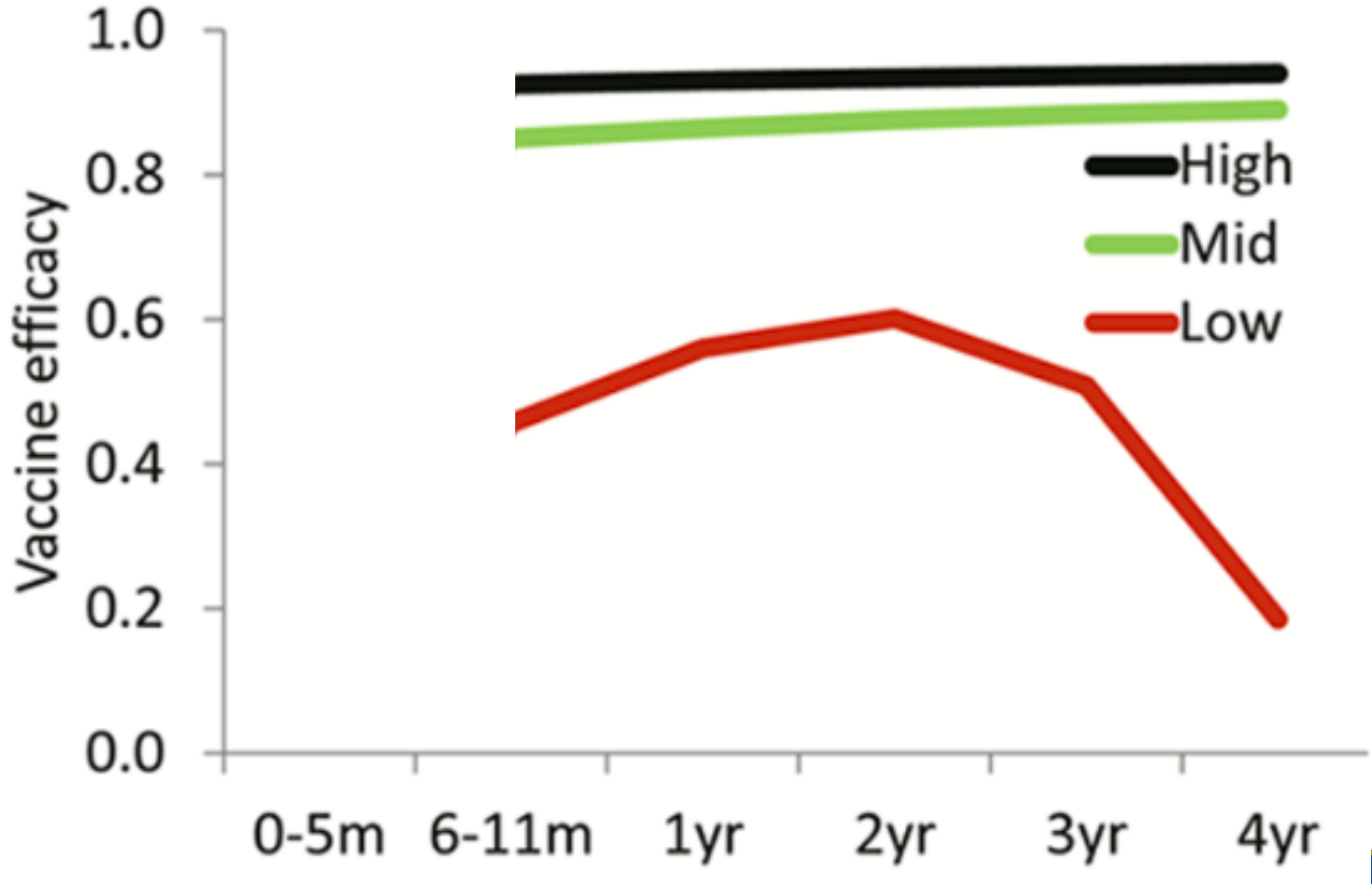
- Innate immunity training
- History of exposure
- Enteric enteropathy
- Malnutrition

- Breastmilk
- Concurrent infections
- Diarrhea
- Co-administration of other oral vaccines

- Heterotypic strains
- Breakthrough infection

Parker et al,
Future Micro, 2017

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



Lopman et al, PLoS One 2012

EMORY

ROLLINS
SCHOOL OF
PUBLIC
HEALTH