

FOURTEENTH INTERNATIONAL
ROTAVIRUS SYMPOSIUM

MARCH 14–16 **2023** BALI INDONESIA

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Model-based estimation of the impact on rotavirus disease of RV3-BB vaccine administered in a neonatal or infant schedule

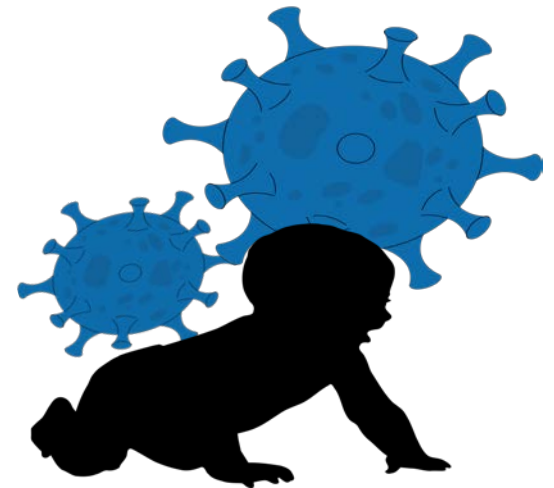
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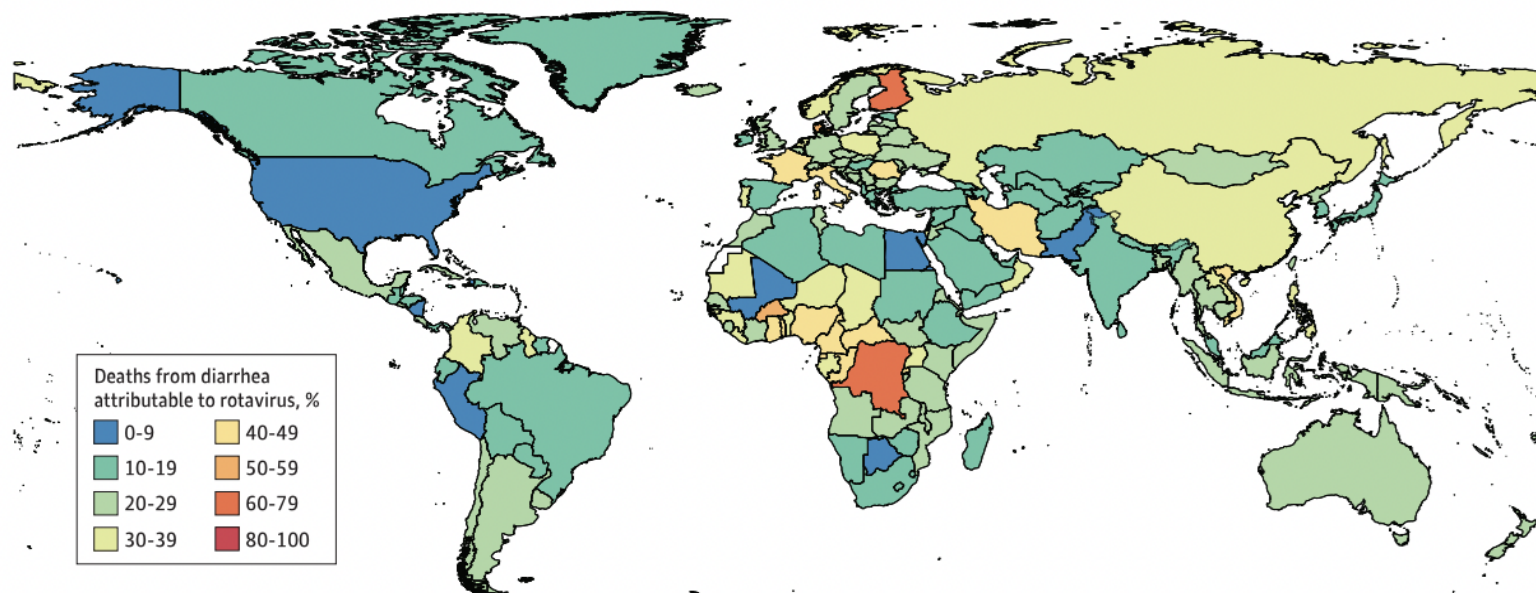
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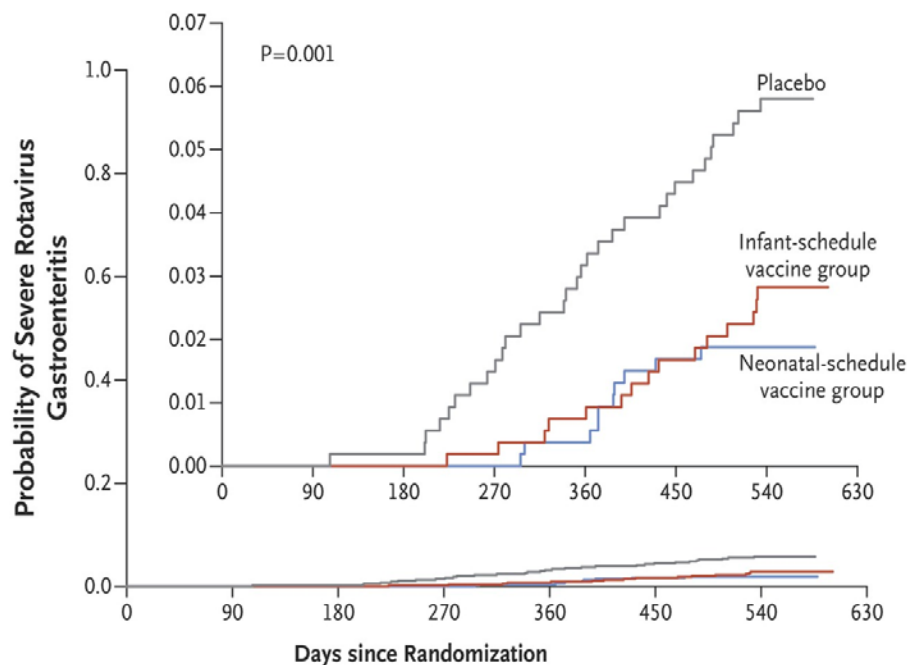
Global burden of rotavirus infections

Figure 2. Distribution of the Fraction of Diarrhea-Associated Mortality Attributable to Rotavirus Among Children Younger Than 5 Years in 2016



- RV incidence has declined over the last decade due to vaccine coverage, but RV remains causing morbidity and mortality in children in LMIC
- Lack of access to RV vaccines in LMIC
- Cost, suboptimal efficacy, and safety concern remain challenges of the success of RV vaccine

The efficacy human neonatal rotavirus vaccine (RV3-BB)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

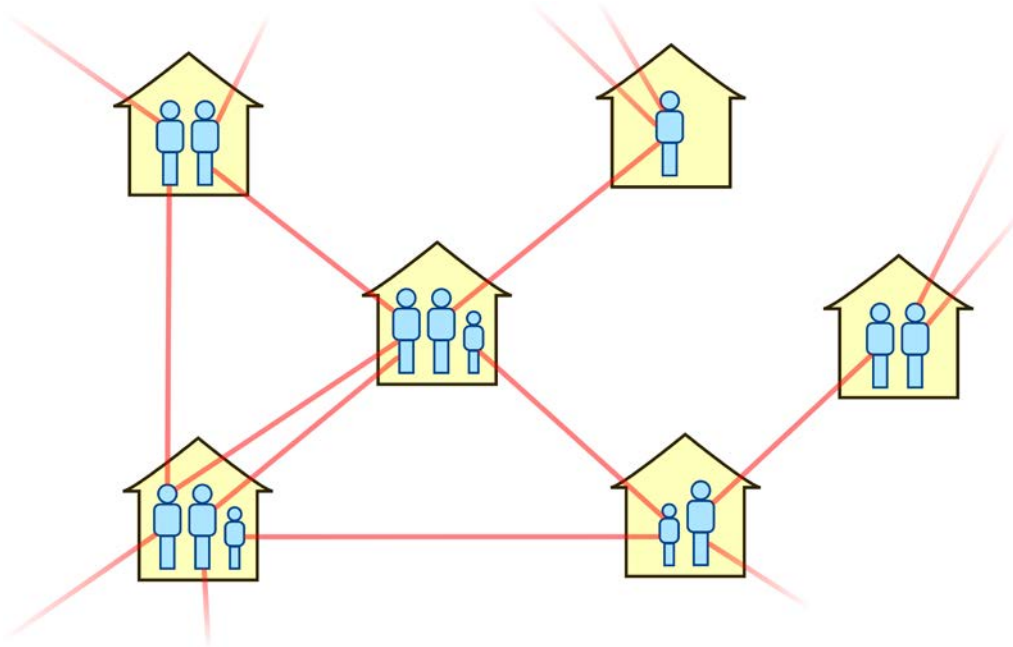
Human Neonatal Rotavirus Vaccine (RV3-BB) to Target Rotavirus from Birth

J.E. Bines, J. At Thobari, C.D. Satria, A. Handley, E. Watts, D. Cowley, H. Nirwati, J. Ackland, J. Standish, F. Justice, G. Byars, K.J. Lee, G.L. Barnes, N.S. Bachtiar, A. Viska Icanervilia, K. Boniface, N. Bogdanovic-Sakran, D. Pavlic, R.F. Bishop, C.D. Kirkwood, J.P. Buttery, and Y. Soenarto

Mathematical models of rotavirus transmission have been widely used to estimate the **direct** and **indirect** benefits of vaccination

The RV modelling study aims to estimate the anticipated population-level impact of RV3-BB following delivery according to either an infant (2, 4, 6 months) and neonatal (0, 2, 4 months) schedule

Model 1: Network of households - a dynamic model



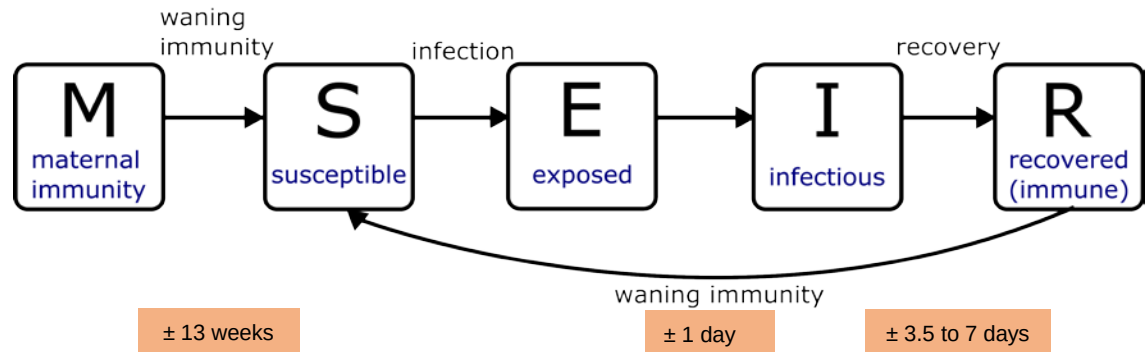
A stochastic, spatial, individual-based model characterized by age and sex (population 150k people in around 50k households ranging in size from 1 to 12 people (median 3 people))

- Each person in a population and house they live in
- Their contacts
- Their current disease status (susceptible, infected, immune, etc)
- Infections can occur within or between household

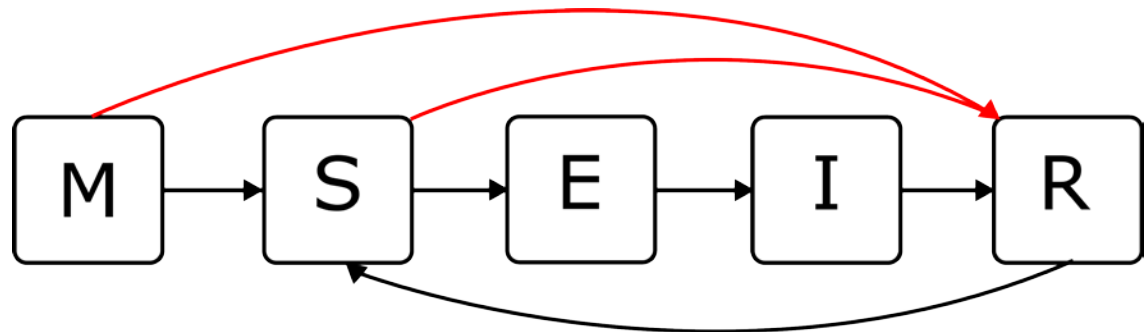
The population changes overtime: people age, die and new people born

Model 2:
Epidemiological
dynamic of
rotavirus
infection and
disease model

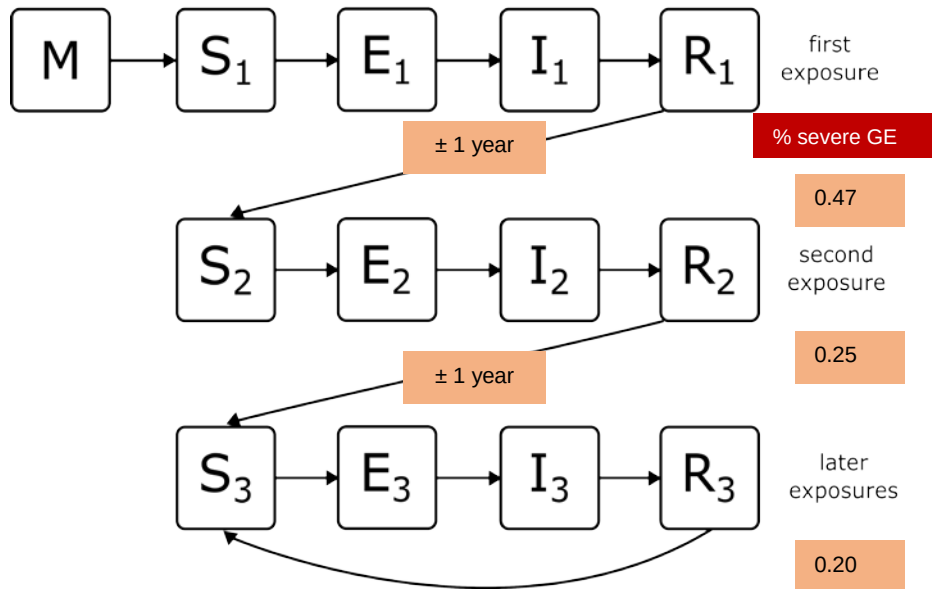
Scenario 1 : with natural infections



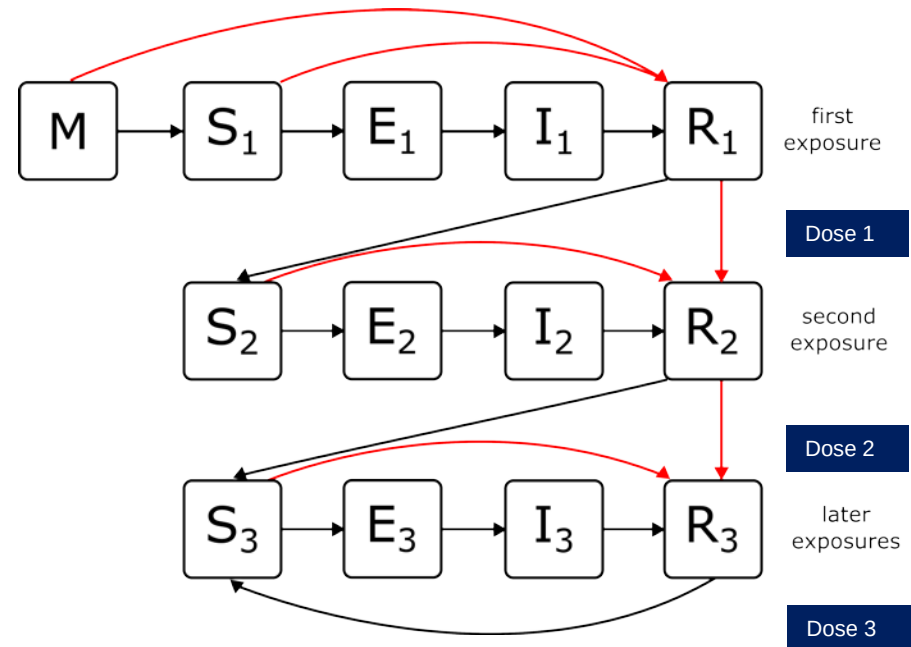
Scenario 2: with vaccination



with natural infections

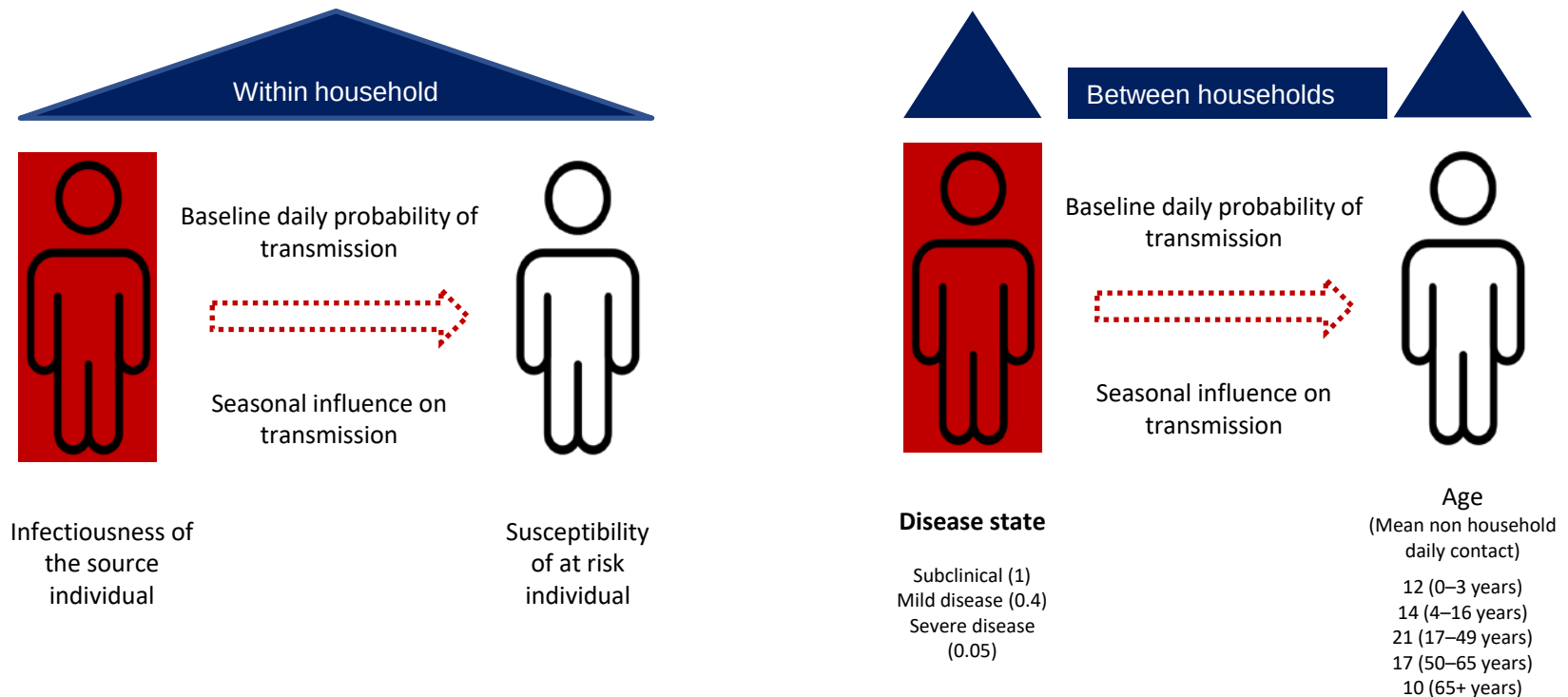


with vaccination



- RR: first infections 0.62, second and subsequent infections 0.37
- Proportion with any RVG (severe RVEG)E: first 0.47, second 0.25 and third and subsequent 0.2

Model 3: Rotavirus transmission model





Model 4: Rotavirus vaccination model

Table 3. Cumulative vaccine response

	 INFANT SCHEDULE	 NEONATAL SCHEDULE
DOSE 1	42%*	23%
DOSE 2	87%	53%*
DOSE 3	99%	94%

- **Assumption:** successive RV infections with rotavirus induce increased protection? successful vaccine doses contribute to immune maturation
- For example, in Neonatal schedule:
 - **Dose 1:** 23% infants will have immunity equivalent to R1
 - **Dose 2 :** 30 % infants will have immunity equivalent to R1 and 23% equivalent to R2

*Cumulative vaccine response – proportion of participants have either serum immune response (a serum rotavirus IgA antibody titer or a serum neutralizing antibodies titer 3 times as high as titer at baseline) 28 days after administration of vaccine and or shedding RV3-BB between days 3 and 7 after vaccine was received

3.98 km

seeding mode: manual (1 seed)

scenario max length: 3650 days

spread pathways: Jump Diffusion

fixed start date: Mon. 01 May 201

current date: Thu. 29 Apr. 2027

elapsed real time: 6 hours 0 mins

currently infected people: 3474

hiwater people infections: 12170
scenario status: completed

scenario status: completed
sim day: 3650 (10.0 sim years)

sim day: 3650 (10.0 s)
run number: 10 of 10

run number: 10 of 10

susceptible: 94122 (55%)

(lost maternal immunity:

infected: 3474 (2.03%)

(latent: 107)

(infectious: 3367)

recovered: 73765 (43.05%)
(maternally immune: 3101)

(naturally immune: 73047)

(naturally immune: 73047)
(vaccine immune: 0)

(dead: 10)

population: 171361

(deaths: 12937)

(births: 31255)

households: 113

(home leavers: 908
(=arrivals: 10300)

(marriages: 10208)

- **Grey dots** are household
- **Red dots** are infected person
- **Green dots** are newborn and infants with maternal immunity

Cases everyday for 10 years



Simulation of alternate vaccination scenarios

Three scenarios were simulated



Scenario 1

Baseline:

No vaccination
Burn in 30 years
period to
establish
endemic



Scenario 2

Infant:

Vaccination
according to the
infant schedule (2,
4, and 6 months).



Scenario 3

Neonatal:

Vaccination
according to the
neonatal
schedule (0, 2,
and 4 months).

- 153,000 individuals, 96% had some immunity and 4% susceptible
- Assumption 85 % vaccine coverage
- Three scenarios were simulated in 10 stochastic runs



Result: Incidence of infection and disease by age

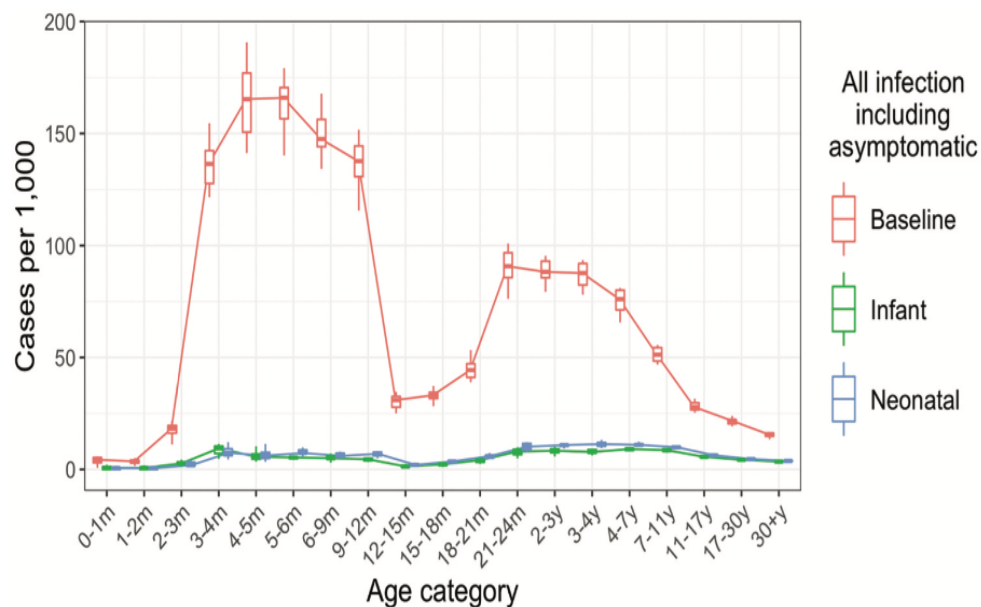


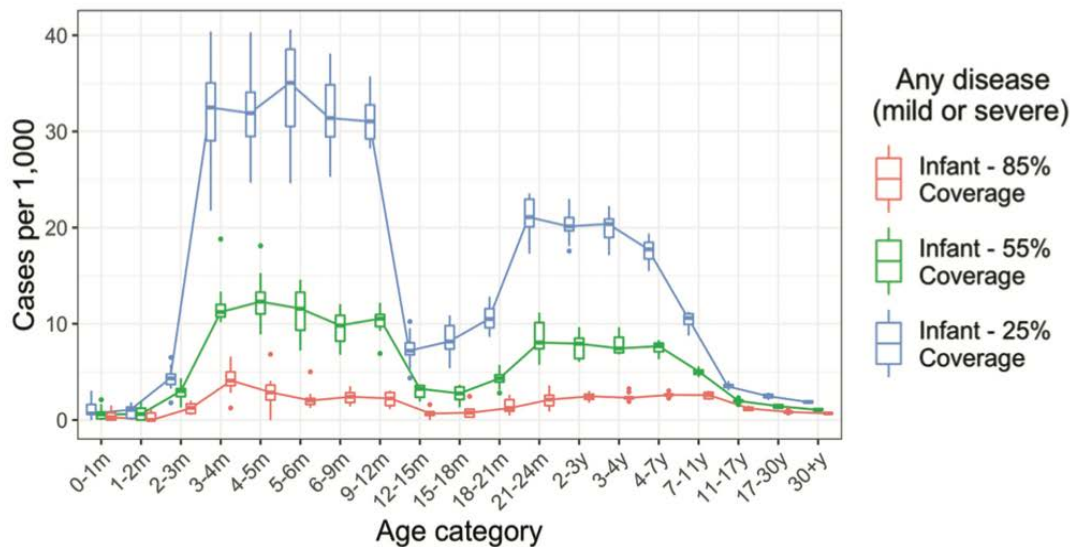
Figure 2. Annual incidence of all rotavirus infections, including asymptomatic infections, by age in the baseline, infant schedule and neonatal schedule scenarios. Incidence values are calculated over a five-year period, five years after the introduction of vaccination. Each boxplot shows the median, IQR and range over 10 simulation runs.

	 INFANT SCHEDULE	 NEONATAL SCHEDULE
Annual incidence of <u>infections</u>	↓96% (112.9 to 4.4 per 1000)	↓95% (112.9 to 5.4 per 1000)
Annual incidence of <u>severe disease</u>	↓96% (14.8 to 0.6 per 1000)	↓95% (14.8 to 0.7 per 1000)
Annual incidence of infection and any diseases (> 17 yo)	↓78% (16.7 to 3.6 per 1000)	↓78% (3.3 to 0.73 per 1000)

Both vaccine schedules produced substantial reductions compared with no vaccination



Result - Sensitivity analysis of different vaccine coverage scenario



	55% Vaccination coverage
Annual incidence of <u>infection*</u>	↓84% (112.9 to 18.1 per 1000)
Annual incidence of <u>severe disease*</u>	↓84% (14.8 to 2.4 per 1000)

*In infants under 12 months of age

Figure 3. Impact of lower vaccine coverage. Annual incidence of all rotavirus infections, including asymptomatic infections, by age for baseline assumption of 85% vaccine coverage, and alternative moderate (55%) and low (25%) vaccine coverage scenarios. Incidence values are calculated over a five-year period, five years after the introduction of vaccination.

Conclusion

- RV3-BB vaccination in LMIC would reduce rotavirus infection and disease by >95% in young infants with vaccine coverage of 85%
- Model-based estimation
 - to assess cost-effectiveness of vaccination
 - to help decision-making process for introduction of RV vaccine into the national immunization program
- Sensitivity analysis: even if high vaccine coverage levels were not reached, moderate coverage could provide sufficient direct and indirect protection

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Richard Bradhurst

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Amanda Handley

Julie E. Bines

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References

1. Geard, N., Bradhurst, R., Tellioglu, N., Oktaria, V., McVernon, J., Handley, A., & Bines, J. E. (2022). Model-based estimation of the impact on rotavirus disease of RV3-BB vaccine administered in a neonatal or infant schedule. *Human Vaccines & Immunotherapeutics*, 18(6), 2139097
2. Bines, J. E., At Thobari, J., Satria, C. D., Handley, A., Watts, E., Cowley, D., ... & Soenarto, Y. (2018). Human neonatal rotavirus vaccine (RV3-BB) to target rotavirus from birth. *New England Journal of Medicine*, 378(8), 719-730
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