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Effectiveness of Rotavac[®] Against Severe Rotavirus Gastroenteritis in Indonesian Children During Early Vaccine Introduction Phase

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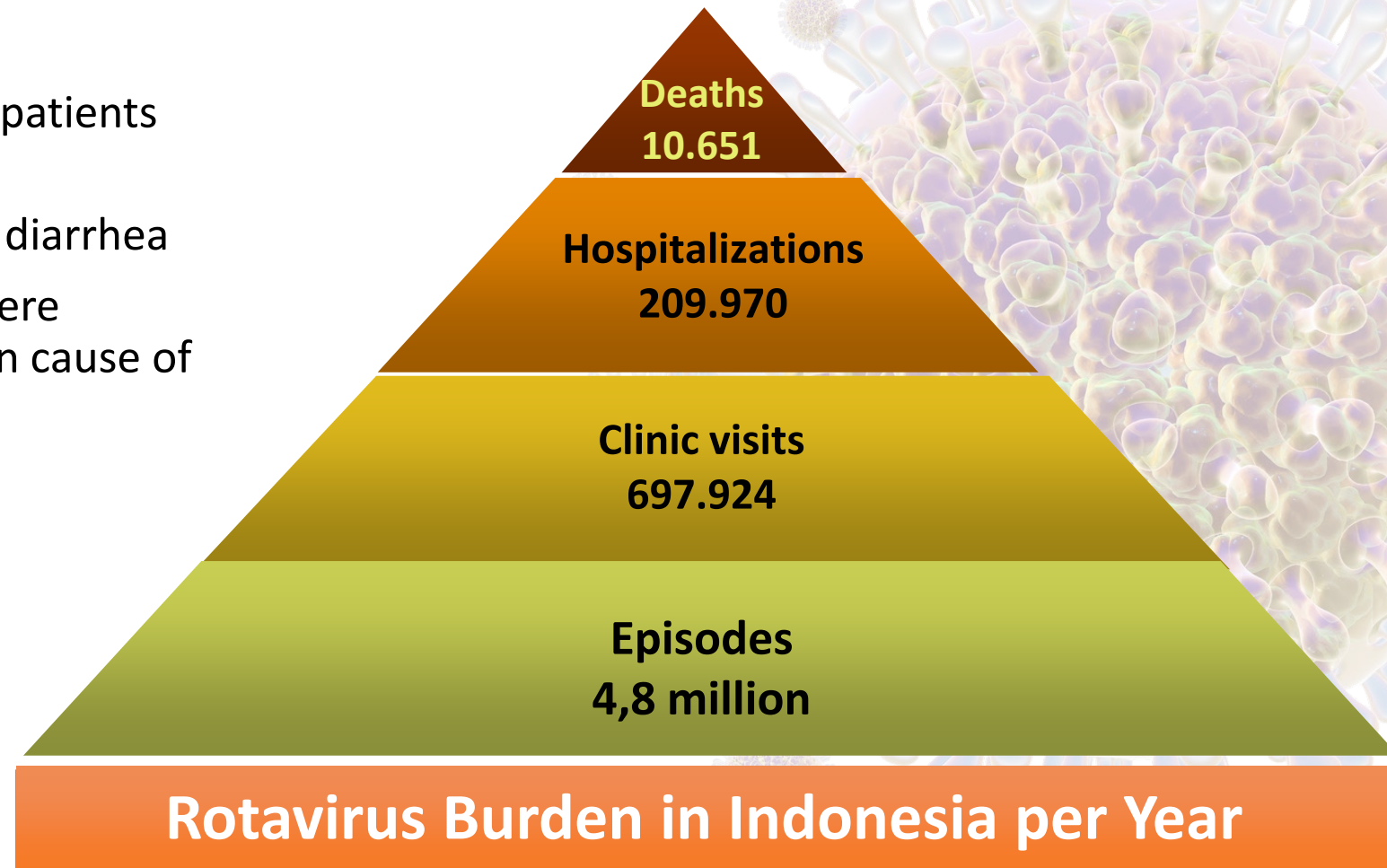
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Disease Burden of Rotavirus Children <5 years old in Indonesia



Rotavirus positive

- **60% (1345/2240)** of hospitalised patients with diarrhea
- **41% (73/176)** of outpatients with diarrhea
- 72% were 6-23 months of age; >> severe vomiting and dehydration --> common cause of death with Rotavirus
- Most common types
 - G1, G9, G2
 - P[6], P[8], P[4]



Soenarto et al. 2009, *The Journal of Infectious Diseases*, vol. 200, no. s1, pp. S188–S194.

Wilopo et al. 2009, *Vaccine*, vol. 27, pp. F67–F74.

6 provincial/teaching hospitals

Economic Burden of AGE

Direct and indirect costs of acute diarrhea in children under five years of age in Indonesia: Health facilities and community survey

Jarir At Thobari,^{a,b,*} Sutarman,^b Asal Wahyuni Erlin Mulyadi,^{b,c} Emma Watts,^{d,e} Natalie Carvalho,^e Frédéric Debellut,^g Andrew Clark,^h Yati Soenarto,^b and Julie E. Bines,^{d,f,i}

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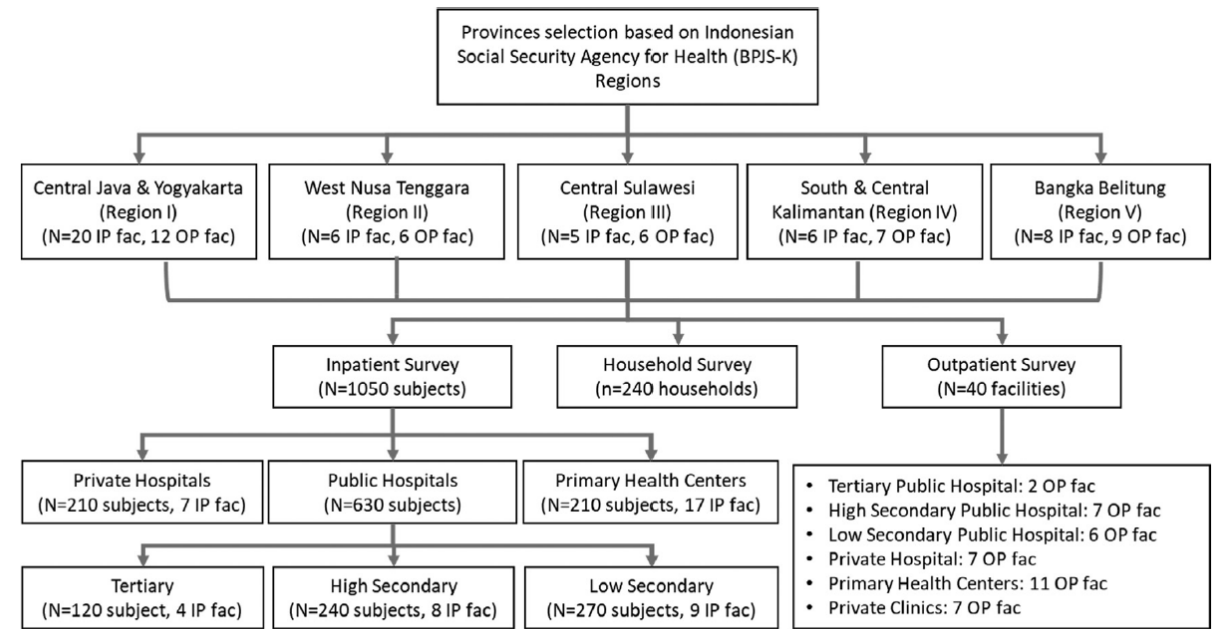


Figure 1. Study Flow Chart.

Parameter	Public Hospitals			Private Hospitals	Primary Health Centers	Private Clinic	Total
	Tertiary (Class A)	High secondary (Class B)	Low Secondary (Class C)				
Number of Facilities	2	7	6	7	11	7	40
Outpatient Direct Medical Costs (USD \$ mean ±SD)							
Registration Fee	3.7 ± 4.7	0.9 ± 0.7	1.7 ± 1.0	2.4 ± 1.8	0.4 ± 0.3	0.5 ± 0.4	
Professional Fee	1.9 ± 2.6	3.4 ± 2.4	4.4 ± 4.0	7.4 ± 3.9	0	3.5 ± 3.1	
Diagnostic cost	2.1 ± 3.0	4.0 ± 2.0	5.1 ± 1.4	7.9 ± 6.5	2.3 ± 2.0	3.7 ± 3.5	
Medication cost	1.2 ± 0.4	3.8 ± 3.2	2.3 ± 1.5	6.9 ± 5.9	0.3 ± 0.5	5.7 ± 3.8	
Total	8.9 ± 4.6	12.1 ± 2.4	13.6 ± 6.1	24.6 ± 10.4	3.0 ± 2.2	13.4 ± 7.7	
Estimated proportion of cases seeking care in each facility* (% of all cases)	0.3%	2.1%	3.4%	4.4%	59.9%	29.8%	100%
Weighted average costs (USD \$)							7.6 ± 4.3

Table 5: Outpatient direct medical costs and weighted average costs.

All costs were measured in USD 2019 (1 USD= 14,217 IDR).

* The proportions were estimated based on BPJS-K sample data (2015–2016).¹⁹

Direct and indirect costs of acute diarrhea in children under five years of age in Indonesia: Health facilities and community survey

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	Hospitals			Health Centers		
	Tertiary (Class A)	High secondary (Class B)	Low Secondary (Class C)			
Number of Facilities	4	8	9	7	17	45
Subjects (n)	120	240	270	210	210	1050
Duration of hospital stay in days: mean ±SD	3.4 ± 2.1	3.6 ± 2.4	2.9 ± 1.6	2.8 ± 1.2	2.2 ± 1.2	2.96 ± 1.78
Payment type						
JKN insurance	97 (80.8%)	152 (63.3%)	166 (61.5%)	131 (62.4%)	69 (32.9%)	625 (59.5%)
Out of pocket	23 (19.2%)	88 (36.7%)	104 (38.5%)	69 (32.9%)	131 (62.4%)	415 (39.5%)
Private insurance	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (4.8%)	0 (0.0%)	10 (1.0%)
Inpatient Direct Medical Costs (\$USD mean ±SD)						
Room costs	47 ± 51	25 ± 24	29 ± 25	74 ± 51	NA	
Professional Fee	63 ± 61	29 ± 35	20 ± 16	31 ± 28	NA	
Diagnostic cost	20 ± 25	12 ± 18	8 ± 6	10 ± 7	NA	
Medication cost	40 ± 43	29 ± 32	2.2 ± 13	29 ± 23	NA	
Total	168 ± 132	111 ± 78	79 ± 42	145 ± 78	NA	
Estimated proportion of cases seeking care in each facility* (% of all cases)	1.2%	15.3%	20.8%	41.6%	21.1%	
Weighted average costs (USD)						99.8 ± 56.8

Parameter	Public Hospitals			Private Hospitals	Primary Health Centers	Private Clinic	Total
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Number of Facilities	2	7	6	7	11	7	40
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Weighted average costs (USD \$)							7.6 ± 4.3

Economic Burden of AGE

The total costs per inpatient case of **US\$113.6** (including direct medical and non-medical costs and indirect costs) (± IDR 1.7 M per hospitalized case)

The estimation of **the total economic burden in Indonesia** hospitalization of children under five years of age due to acute diarrhea was **over \$30 million per year.** (± IDR 450 B/year)

This includes

- direct medical costs of \$26.34 million (± IDR 395 B)
- direct non-medical costs of \$1.29 million (± IDR 19 B)
- indirect medical costs of \$2.16 million (± IDR 32 B)

(Thobari, JA et al, Lancet Reg Health West Pac, 2022;19:100333)

Introduction of Rotavirus Vaccine in Indonesia is Cost Effective

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Vaccine

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



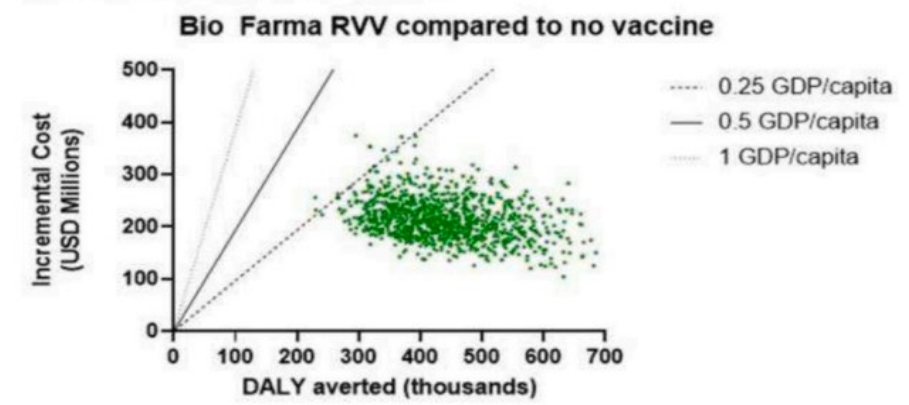
Cost effectiveness analysis of rotavirus vaccination in Indonesia

Jarir At Thobari^{a,b,*}, Emma Watts^c, Natalie Carvalho^d, Jonathan Hasian Haposan^{b,c,e}, Andrew Clark^f, Frédéric Debellut^g, Asal Wahyuni Erlin Mulyadi^{b,h}, Julitasari Sundoroⁱ, Mardiaty Nadjibⁱ, Sri Redzeki Hadinegoroⁱ, Julie Bines^{c,j}, Yati Soenarto^b

The incremental cost-effectiveness ratio (ICER) is **464 USD per DALY averted** (12 % GDP per capita) from societal perspective, and **479 USD per DALY averted** (13% GDP per capita) from health care perspective, respectively.

The introduction of **Rotavirus Vaccine into the National Immunization Program is likely to be highly cost-effective** in Indonesia

A. Cost-effectiveness plane



B. Acceptability curve

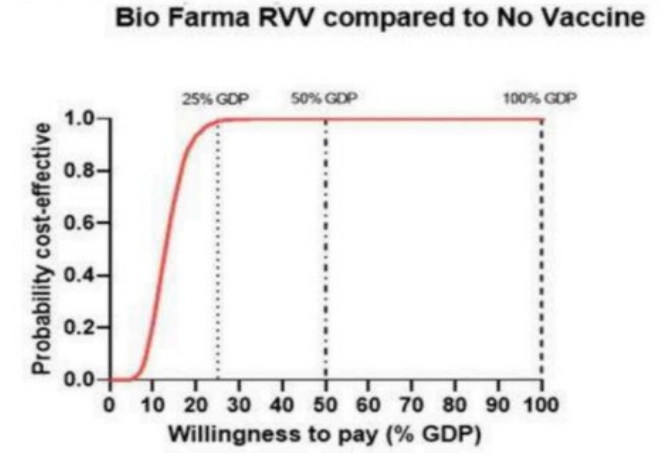


Fig. 2. Probabilistic sensitivity analyses of RVV program compared to no vaccination (societal and health care perspectives).

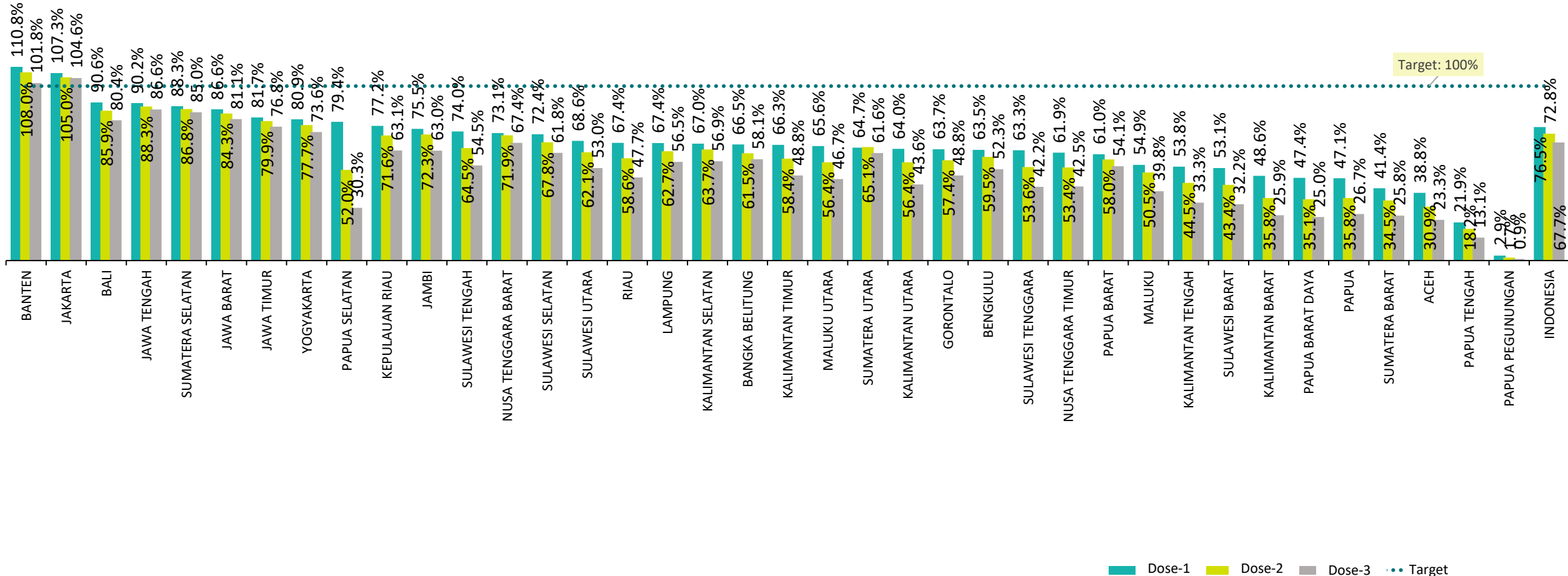
Rotavirus Vaccine Implementation in Indonesia

ITAGI recommendation to introduce rotavirus vaccine

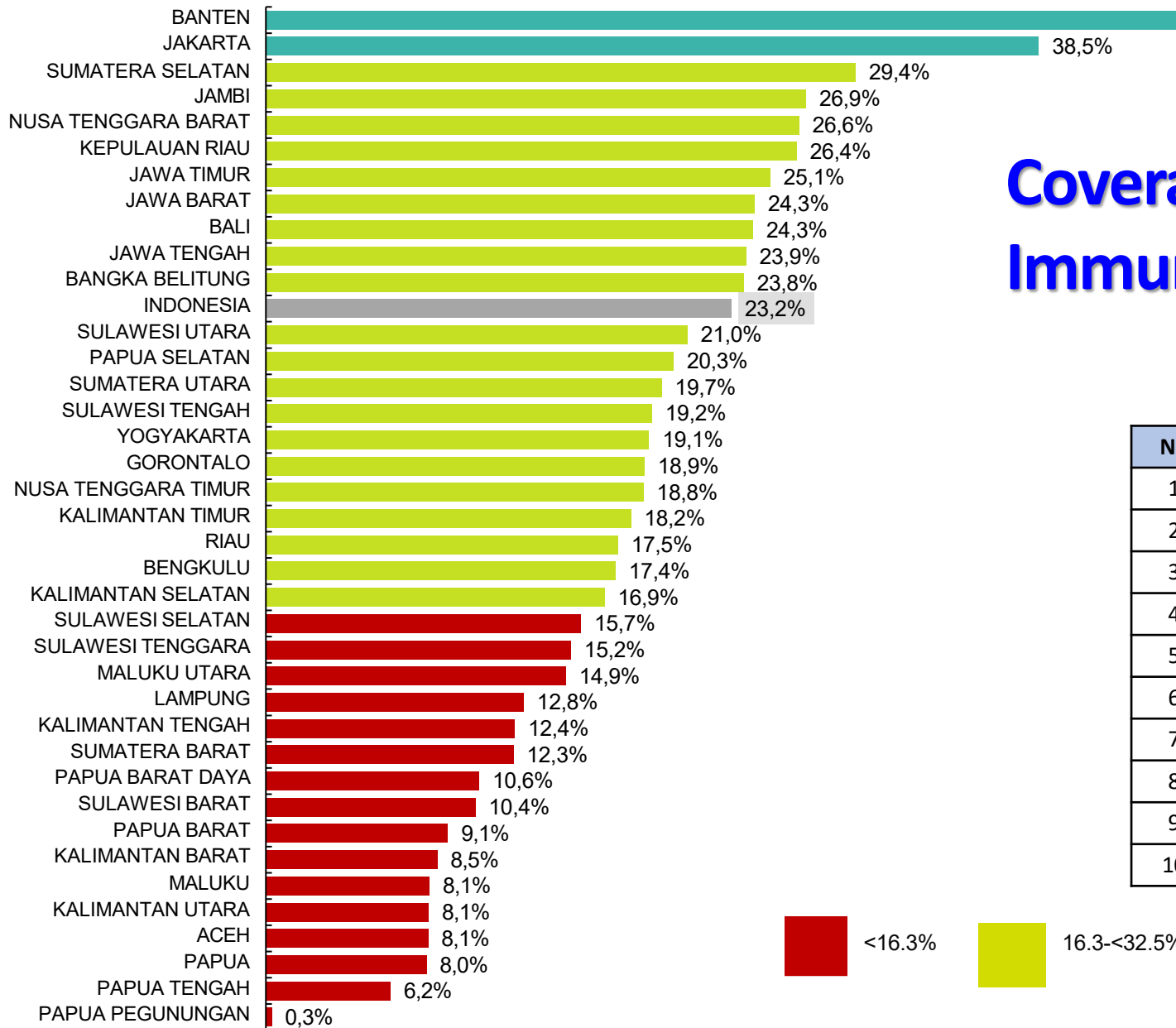
MoH is now in revise cMYP 2022-2024.

Introduce Rota-vaccine in 21 cities/districts in 18 provinces in 2022 and implementation nationwide in August 2023

Coverage of rotavirus immunization in 2024



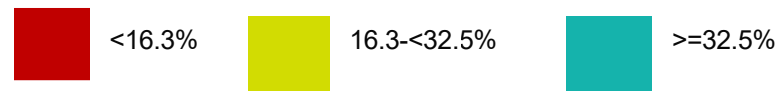
Source MoH



Coverage of full three dose Rotavirus Immunisation (June 2025)

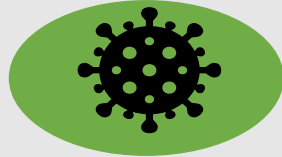
Top 10 Districts/Cities with the Highest RV3 Coverage

No	KABUPATEN/KOTA	RV3
1	TANGERANG	90.5%
2	KOTA SURAKARTA	68.4%
3	PANDEGLANG	68.4%
4	KOTA BLITAR	50.4%
5	KOTA TANGERANG SELATAN	49.3%
6	KOTA PALU	44.5%
7	PADANG LAWAS	43.7%
8	KUDUS	43.0%
9	KOTA SEMARANG	42.9%
10	KOTA SURABAYA	42.8%



Source MoH June 2025

The Surveillance Rotavirus Acute Gastroenteritis (RVGE) in Children U5 Years of Age and Effectiveness of RV Vaccination against Hospitalised RVGE in Indonesia



Conducted during the early phase of vaccine introduction at selected sentinel sites



Prospective hospital-based observational study design



Analysis focused on children U5 years hospitalized with GEA



Provides early real-world evidence of Rotavac® effectiveness & Supports the potential scale-up of national rotavirus vaccination programs

Rotavirus Vaccine Implementation in Indonesia

ITAGI recommendation to introduce rotavirus vaccine (import vaccine) and gradually implement vaccine RV3 Biofarma



MoH revised c-MYP (comprehensive Multi Years Planning) for Immunization 2022-2025.



Introduce RV in 21 cities/districts in 18 provinces in 2022-2023
Nation Wide implementation August 2023 (as Program 3 in CEA study)

*** STUDY DESIGN ***



Hospitalized Severe Rotavirus Gastroenteritis



Indonesian Children aged under 5 years

- Demographic Data
- Clinical Profile
- Vaccine Information
- Sampel Collected:
- Genotype analysis



Medical Record, Vaccinee Card/ASIK, and Sample Collected

***** TIMELINE *****

- February 2023**
Signing of study agreement with Pediatric Research Office – Universitas Gadjah Mada
- June 2023**
Training from UGM center research team to site research team
- July 2023**
Site Initiation Visit
- August 2023**
First subject recruitment
- September 2023-June 2024**
Site Monitoring Visit
- July 2024**
Cut-off for recruitment in year one



Effectiveness of Rotavac® Against Severe Rotavirus Gastroenteritis in Indonesian Children During Early Vaccine Introduction Phase

Objective

To evaluate the effectiveness of the RV3 vaccine against hospitalized rotavirus AGE in children <5 years of age in the selected surveillance sites.

Study Design

Case-control study nested within a rotavirus surveillance cohort in 16 sentinel hospitals and Located in 8 provinces across **Indonesia**.



Study Population



Hospitalized children ≤ 1 year with acute gastroenteritis



Enrolment period: **August 2023 – July 2024**

Sample Collection & Testing

Stool specimens collected within 48 hours of admission
Tested for rotavirus using *Premier® Rotaclone® EIA kit*.

Disease Severity Assessment

Vesikari scoring system: Severe AGE: score ≥ 11

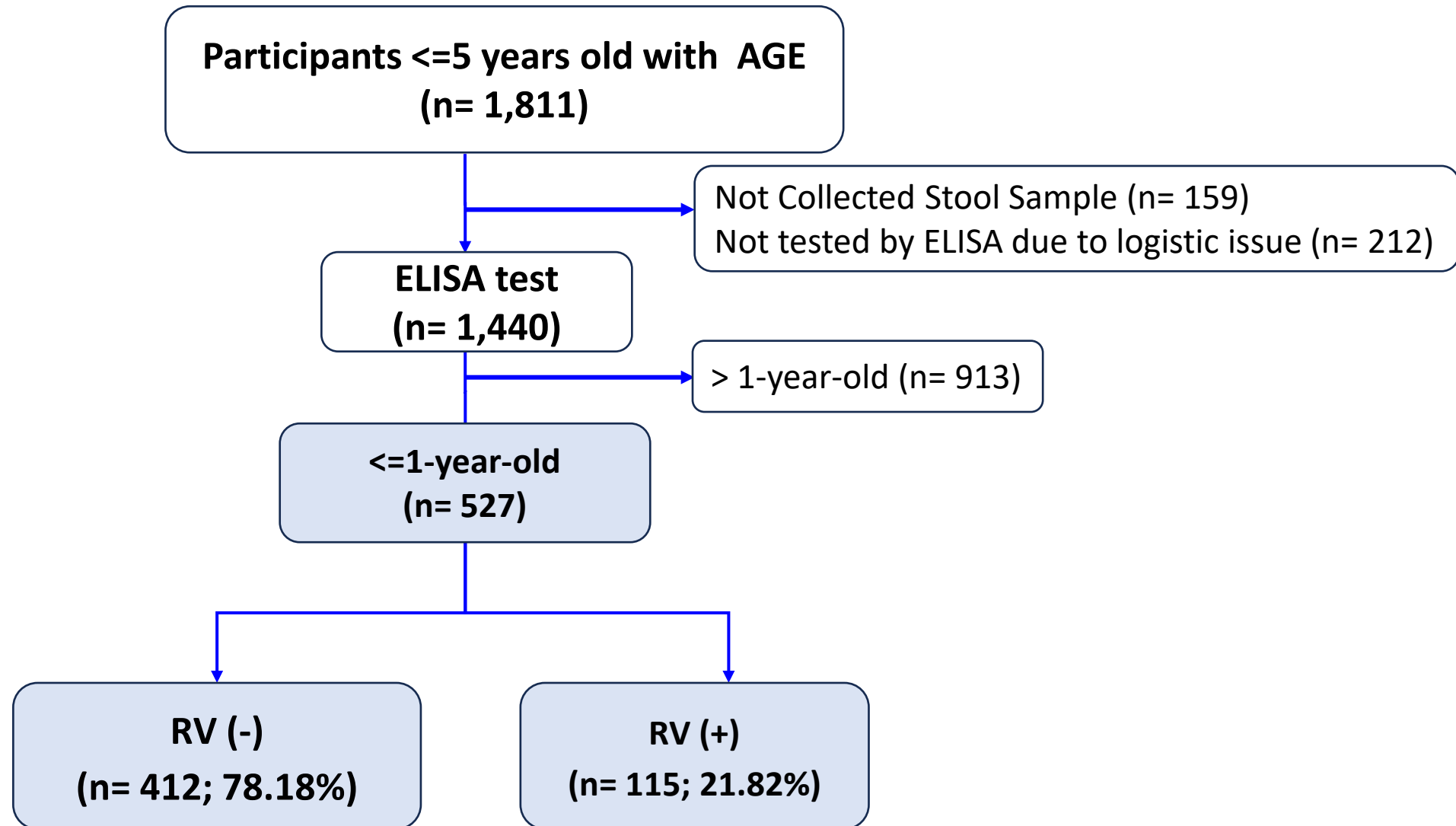
Vaccine Effectiveness (VE) = $(1 - OR) \times 100\%$

Population: **children < 1 year**

Exposure: **at least 1 dose of Rotavac®**

Comparison: **RV+ (cases) vs RV- (controls)**

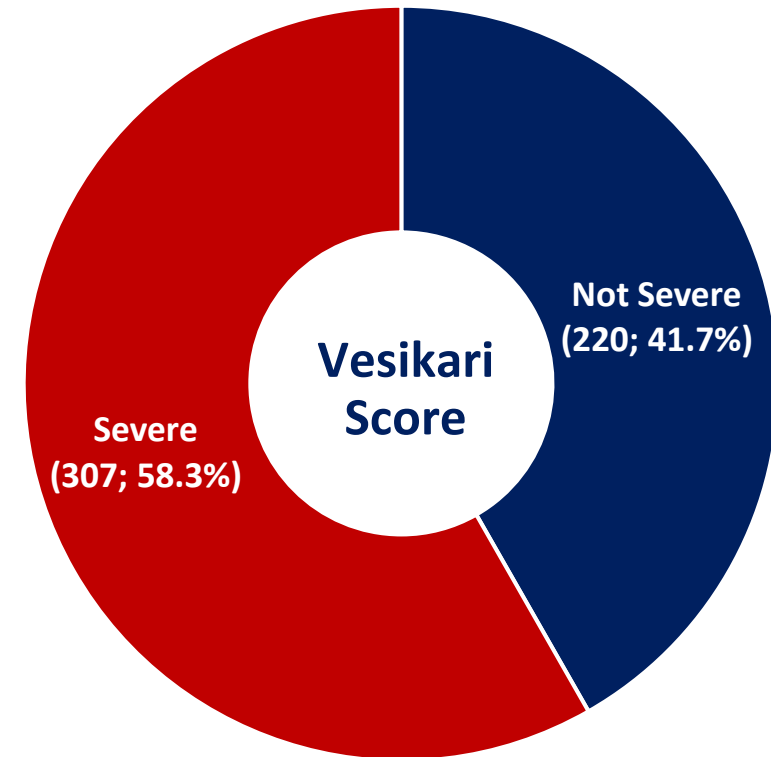
Rotavirus Status (RV⁺ vs RV⁻) in Infants ≤1 Year of Age (N = 527)



Study Results

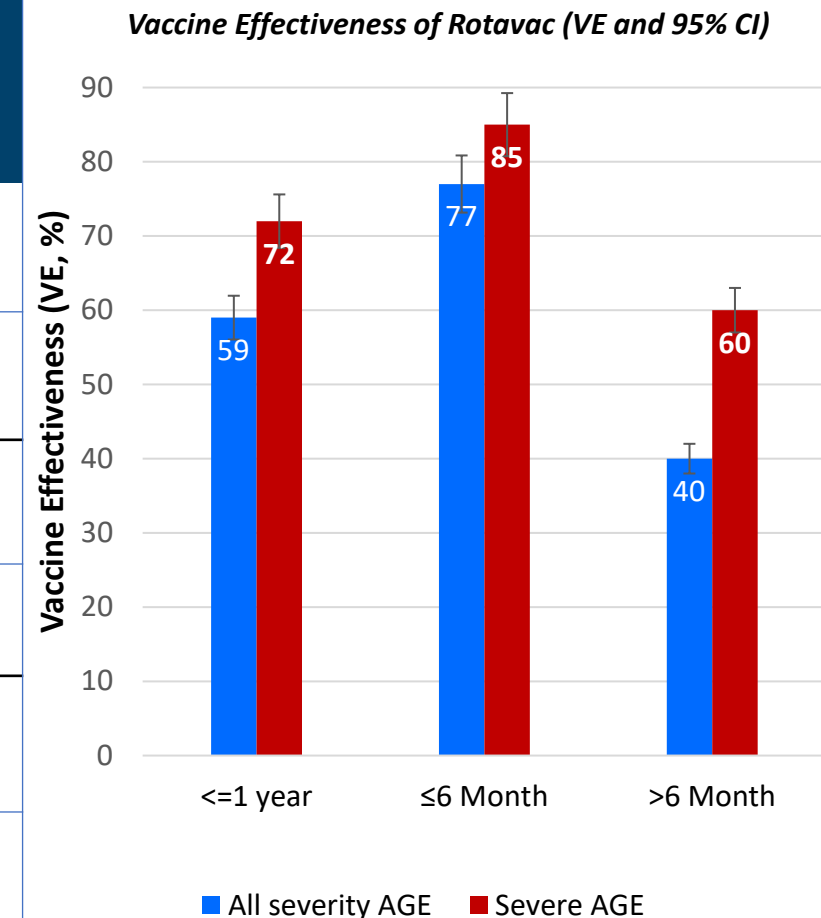
Baseline Characteristics by Rotavirus Status (RV+ vs RV-) and Disease Severity in Infants ≤1 Year Old

Characteristic	RV + N=115	RV – N=412	Total N=527	P-Value
Age (month) (Mean ± SD)			6.99 ± 3.30	0.001
- ≤6 month	34 (30.43%)	198 (48.06%)	233 (44.21%)	
- >6 month	80 (69.57%)	214 (51.94%)	294 (55.79%)	
Gender (%)				0.664
- Boys	72 (62.61%)	267 (64.81%)	339 (64.33%)	
- Girls	42 (37.39%)	145 (35.19%)	188 (35.67%)	
Severity (%)				0.001
- Not severe	32 (27.83%)	188 (45.63%)	220 (41.75%)	
- Severe	83 (72.17%)	224 (54.37%)	307 (58.25%)	
Vaccine (%)				0.001
- Rotavac	17 (14.78%)	123 (29.85%)	140 (26.57%)	
- No vaccine	98 (85.22%)	289 (70.15%)	387 (73.43%)	



Rotavirus Vaccine Effectiveness Against Hospitalised AGE in Infant

		Cases (Rotavirus +)		Control (Rotavirus -)		OR (95% CI)	VE (95% CI)
		Vaccine (Rotavac)	No Vaccine	Vaccine (Rotavac)	No Vaccine		
<=1-year	All severity AGE	17	98	123	289	0.41 (0.23 – 0.71)	59% (29% – 77%)
	Severe AGE	10	73	73	151	0.28 (0.13 – 0.61)	72% (39% – 87%)
0-6 months	All severity AGE	4	31	71	127	0.23 (0.08 – 0.68)	77% (32% – 92%)
	Severe AGE	2	23	37	62	0.15 (0.03 – 0.65)	85% (35% – 97%)
6–12 months	All severity AGE	13	67	52	162	0.60 (0.31 – 1.18)	40% (-18% – 69%)
	Severe AGE	8	50	36	89	0.40 (0.17 – 0.92)	60% (8% – 83%)



Rotavirus Vaccine Effectiveness Against Hospitalised AGE in Infant (≤ 1 Year of Age), partial and full doses for any severity

		Rotavirus		OR	VE
		Positive	Negative	(95% CI)	(95% CI)
≤ 1-year	Partial (1-2 doses)	10	65	0.34 (0.15 – 0.78)	66% (22% – 85%)
	Full (3 doses)	7	58	0.26 (0.10 – 0.68)	74% (32% – 90%)
0-6 month	Partial (1-2 doses)	3	46	0.27 (0.08 – 0.88)	73% (12% – 92%)
	Full (3 doses)	1	25	0.16 (0.02 – 1.29)	84% (-29% – 98%)
6–12 months	Partial (1-2 doses)	7	19	0.31 (0.12 – 0.80)	69% (20% – 88%)
	Full (3 doses)	6	33	0.17 (0.06 – 0.47)	83% (53% – 94%)

*Reference = Unvaccinated

Rotavirus Genotype Distribution In Vaccinated vs Unvaccinated Infants

Genotype	Vaccinated	Unvaccinated	Total
G1P8	1 (5.6%)	1 (1.0%)	2 (1.7%)
G3P8	2 (11.1%)	35 (35.7%)	37 (31.9%)
G4P6	1 (5.5%)	0 (0.0%)	1 (0.9%)
G9P6	2 (11.1%)	4 (4.1%)	6 (5.2%)
G9P8	9 (50.0%)	45 (45.9%)	54 (46.6%)
Untypeable	3 (16.7%)	13 (13.3%)	16 (13.8%)

Discussion

- First real-world evaluation of Rotavac[®] in Indonesia in early post-introduction evidence supports its inclusion in the national immunisation program
- Significant protection observed in infants against hospitalised AGE (in severe cases and in any severity).
- These findings strengthen confidence in the national rotavirus vaccine rollout and provide valuable guidance for targeted efforts to increase uptake in areas with low coverage
- This study will be updated to assess the long-term impact of rotavirus vaccines in Indonesia, and similar studies will be undertaken for RV3-BB following its introduction.

Discussion

- Limitations
 - Uneven vaccine coverage across provinces may affect generalizability
 - Limited sample size for detailed subgroup analysis (e.g., malnutrition, preterm birth)
 - No testing for other diarrheal pathogens limits the ability to rule out non-rotavirus causes
 - Hospital-based data only may not fully reflect community-level impact
 - Possible inaccuracies in vaccination records could bias estimates
 - Short observation period captures only the first-year post-introduction

Conclusions

- This study demonstrated the effectiveness of the implementation of the rotavirus vaccine (Rotavac) against both all-severity and severe hospitalised rotavirus AGE in infants during the early phase of vaccine introduction in Indonesia
- Findings were consistent with international evidence, reinforcing the value of rotavirus vaccination in low- and middle-income settings and supporting the RV vaccine's role in reducing hospitalisations and severe disease burden.

Acknowledgments



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Gates Foundation

Gates Foundation, Seattle, USA

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2. Carl Kirkwood



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