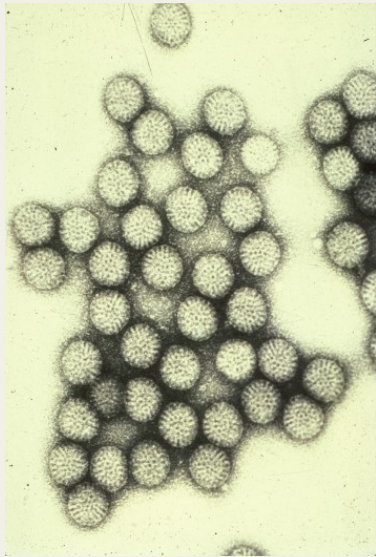


Effectiveness of Rotavirus Vaccines



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Key Efficacy Trials of RV5 and RV1

- Pivotal trials in low mortality countries – 2006
 - RV5 in USA and Finland
 - RV1 in Latin America and Europe
- Later trials in high mortality countries – 2009
 - RV5 in Africa (Kenya, Ghana, Mali) and Asia (Bangladesh, Vietnam)
 - RV1 in Africa (Malawi and South Africa)

Efficacy of Rotavirus Vaccines Against Severe Rotavirus AGE Varied by Level of Child Mortality

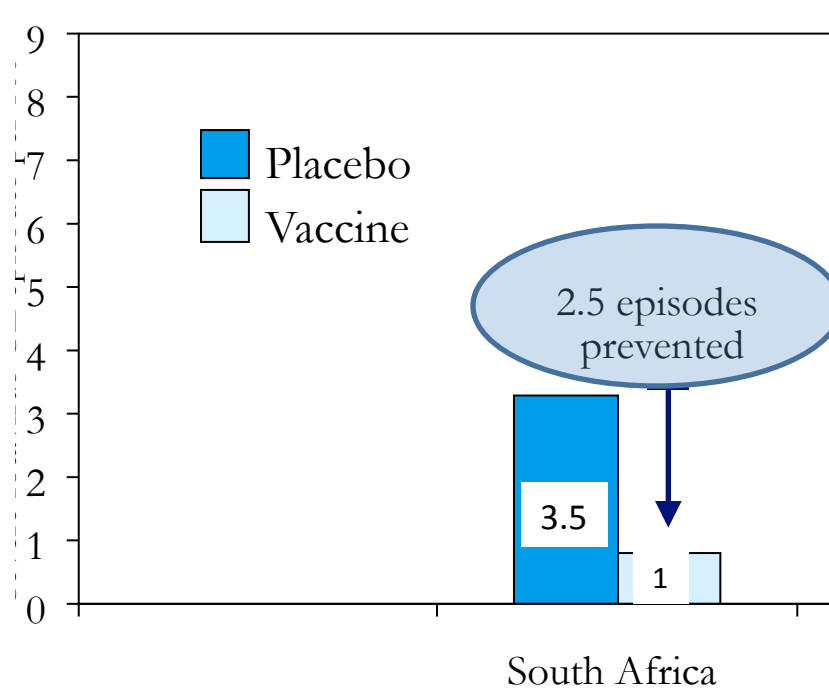
WHO Mortality Stratum	Vaccine Efficacy Against Severe Rotavirus AGE (95% CI)*
A (very low)	93% (91-95)
B & C (low)	83% (67-92)
D: Americas (high)**	69% (24-87)
D: Asia (high)	51% (13-73)
D & E: Africa (high)	61% (46-72)*

*Pooled estimates of efficacy from clinical trials for RV1 and RV5

**No RCT data from Stratum D: Americas

Impact of RV1 Vaccination Against Severe Rotavirus Gastroenteritis in South Africa and Malawi

Severe rotavirus gastroenteritis per 100

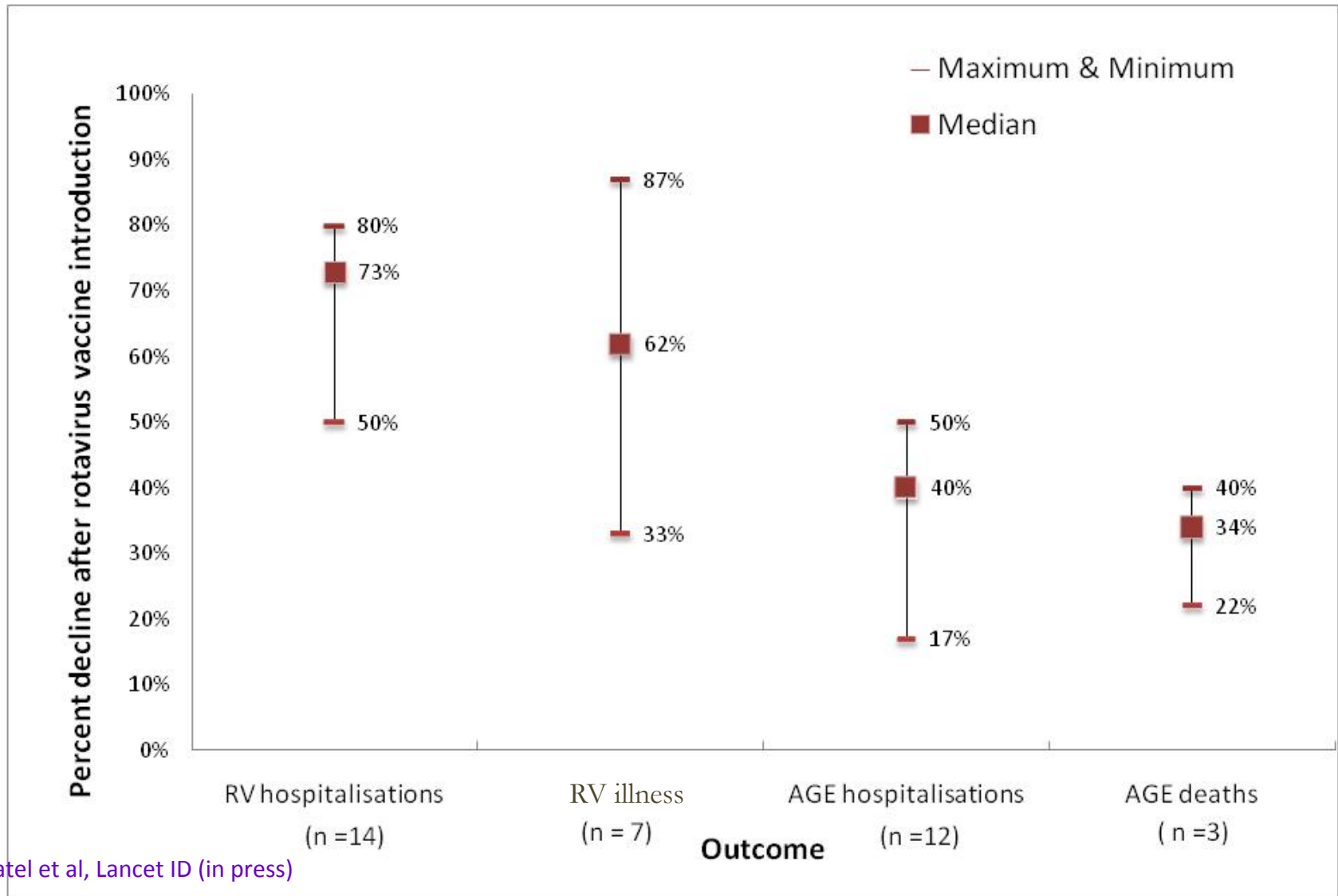


RV1 Efficacy

77%

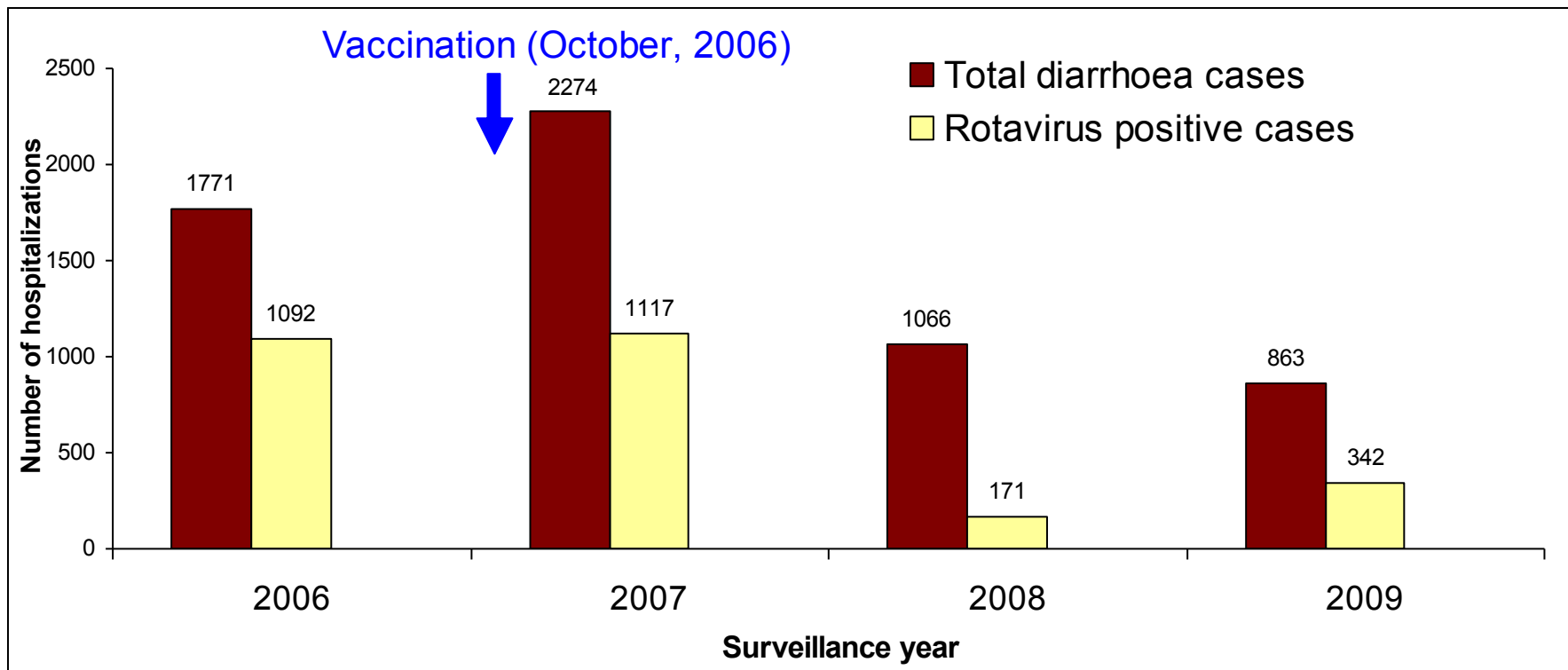
Impact of Rotavirus Vaccination in Different Settings

Impact Against Severe Rotavirus and All-Cause Gastroenteritis in High & Middle income Countries after Routine Introduction

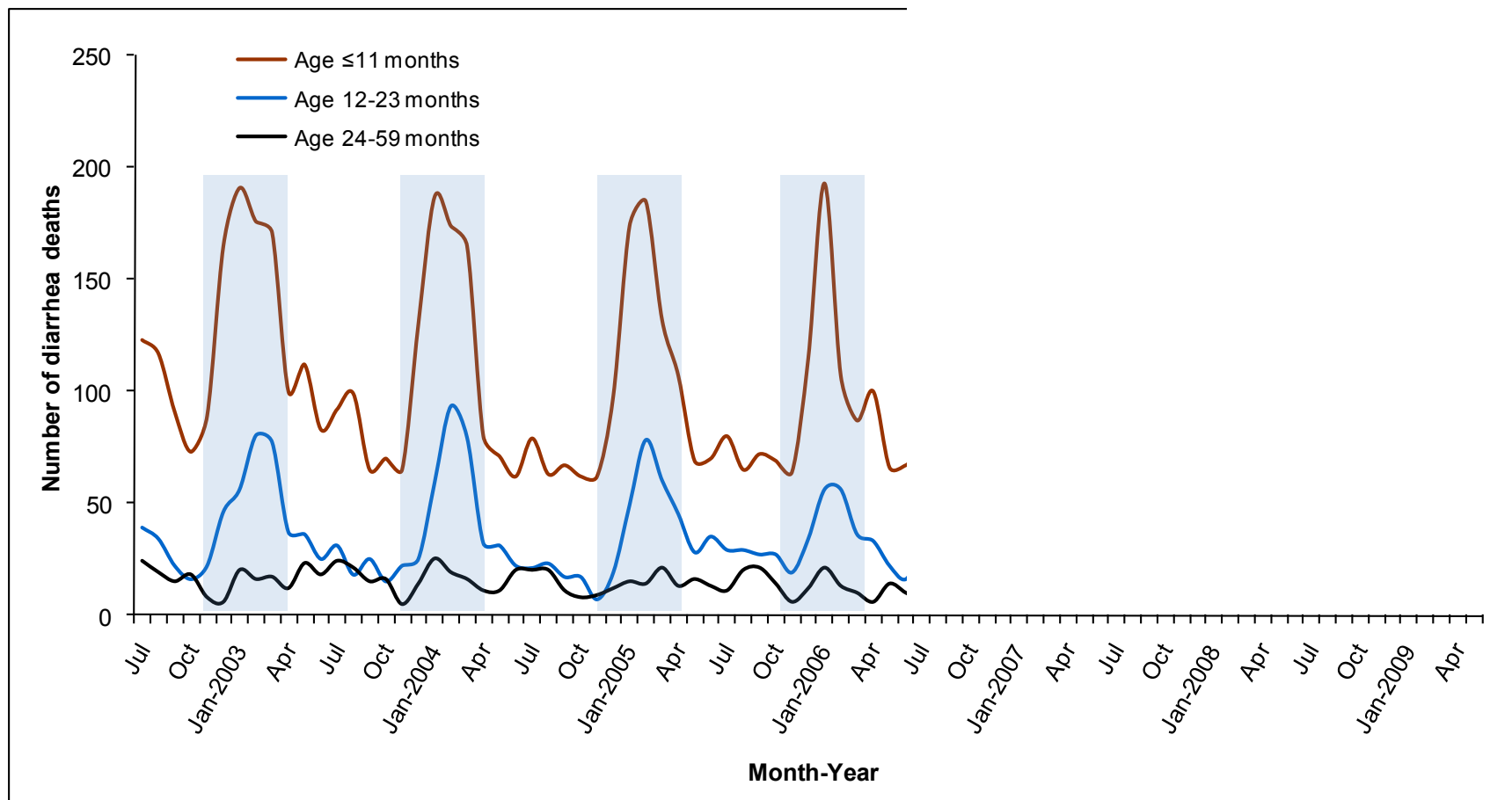


Impact on Rotavirus and All-Cause Gastroenteritis Hospitalizations in Children in El Salvador

70-80% reduction in rotavirus hospitalizations children < 5 years



ORIGINAL ARTICLE

Effect of Rotavirus Vaccination on Death
from Childhood Diarrhea in Mexico

Schedules -- What is the optimal number of RV1 doses for developing countries?

Could a third RV1 dose improve efficacy?

First Year Efficacy of 3 RV1 Doses vs 2 RV1 Doses in African Trial

	South Africa	Malawi
2 dose (10,14 weeks)	72 (40-88)	49 (11-72)
3 dose (6, 10, 14 weeks)	82 (55-94)	50 (11-72)

Recommended 2 dose RV1 schedule is 6,10 weeks

Immunogenicity of 2 RV1 Doses given with OPV at 6,10 versus 10,14 weeks in South Africa

2 Dose RV1 Schedule	IgA Seroconversion Rate
6 and 10 weeks	36% (26%-50%)
10 and 14 weeks	61% (43%-76%)

6 week dose potentially more prone to interference by higher maternal antibody and first OPV dose

In Addition.....

- New data from RV1 trial in Africa indicates lower 2nd year efficacy of 2 doses (at 10,14 weeks) vs 3 doses
 - Trial not adequately powered to make firm conclusions about efficacy by year of life
- Two ongoing studies (Pakistan & Ghana) on immunogenicity of different RV1 schedules
- Economic and logistical considerations

Schedules -- Interval Between Vaccine Doses & Co-administration

- Minimum 4 week interval recommended between doses
 - Limited data on other intervals
- Co-administer other recommended vaccines (including OPV)
 - OPV impacts seroconversion of 1st rota dose
 - No adverse impact on immunogenicity or efficacy of rotavirus or other vaccines after full series

Summary

- Efficacy of rotavirus vaccines varies in different WHO mortality strata
 - Public health impact of vaccines substantial in high mortality countries despite lower efficacy
- Marked reductions in severe diarrhea in countries using vaccine
 - Including mortality benefits in Mexico and Brazil
- Need to assess the potential benefits and costs of a third dose of RV1 for developing countries