Rotavirus vaccines: Evidence from Africa

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Workshop to support accelerated Introduction of Rotavirus vaccines & PCV, N'Djamena, Tchad 13-15 Sept 2023

World Health Organization
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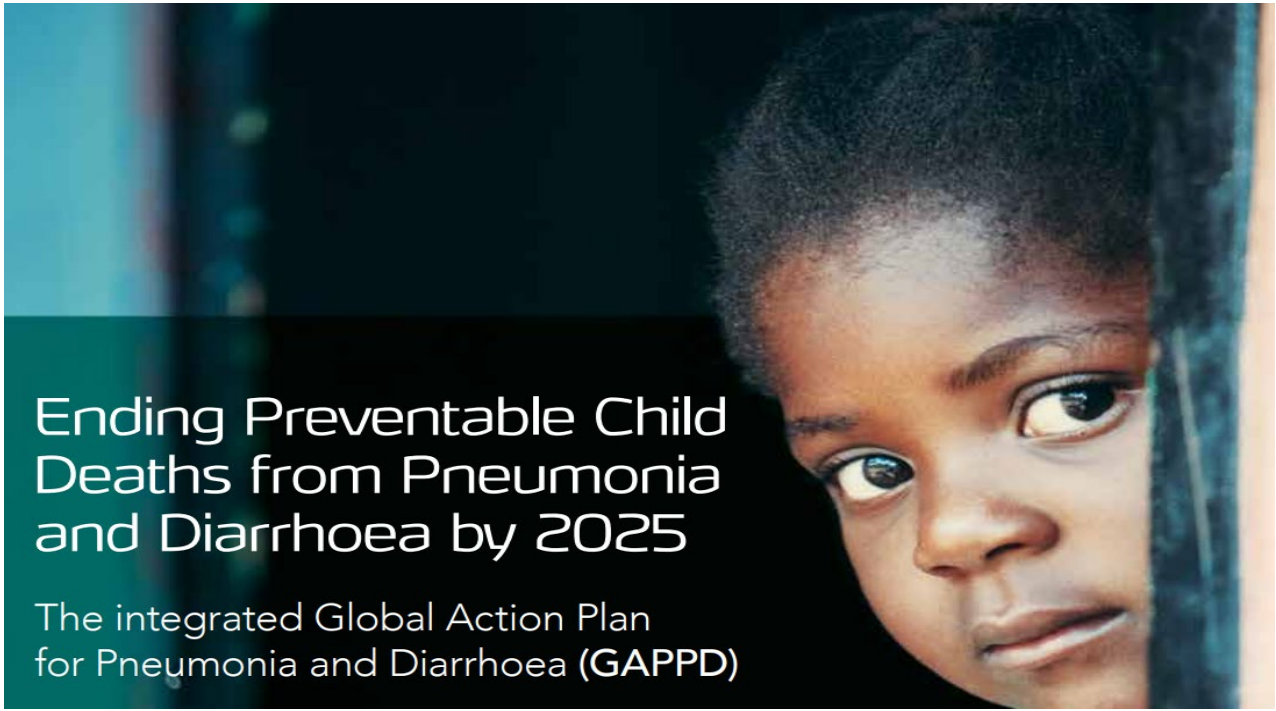
Outline

- ✓ Pneumonia and diarrhea disease burden
- ✓ WHO pre-qualified rotavirus vaccine products and policy recommendation/position paper(s)
- ✓ Progress of rotavirus introductions and coverage in Africa
- ✓ Evidence of impact and effectiveness of rotavirus vaccination in Africa using hospital based sentinel surveillance
- ✓ Summary and required actions

Pneumonia and diarrhea disease burden

- Globally, an estimated **1.22 million** young children die due to **pneumonia and diarrhea** each year, equivalent to over **140 children dying every hour** or **3,350 deaths each day**.
- Over 70% of under-5 deaths from pneumonia and diarrhea occur in just 15 countries…
- Substantial deaths due to these diseases can be prevented by vaccines – **PCV, Hib containing vaccines, rotavirus vaccines**
- **Continue and consistent disease surveillance**

Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhea (GAPPD), 2009

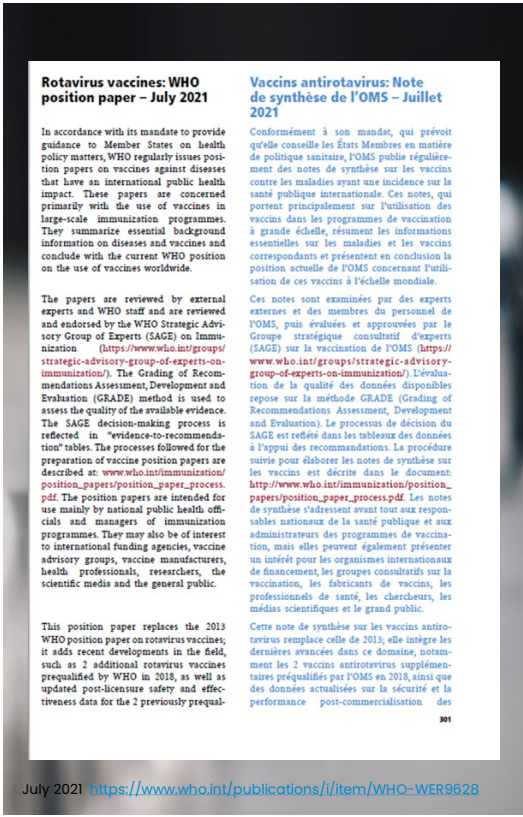


John Hopkins & IVAC PNEUMONIA & DIARRHEA PROGRESS REPORT 2022.

Rank	Country	Under-5 Pneumonia & Diarrhea Deaths	Deaths per 1,000 Live Births
1	Nigeria	321,596	43
2	India	146,558	6
3	Pakistan	76,553	13
4	Democratic Republic of the Congo	65,219	18
5	Ethiopia	45,436	13
6	Angola	28,784	22
7	Chad	28,621	43
8	Somalia	25,476	40
9	Niger	25,237	24
10	United Republic of Tanzania	24,870	12
11	Mali	24,465	30
12	Bangladesh	18,844	6
13	Cameroon	18,498	20
14	Sudan	18,431	14
15	Ivory Coast	16,586	18

Policy recommendations for Rotavirus vaccines (Position paper 2021)

- **4 oral rotavirus vaccines WHO pre-qualified as per guidance provided by SAGE – WHO position papers, 2009, 2013 & 2021**
- **RotaTeq, Rotavac and ROTASIL** should be administered in a **3-dose schedule**, while **Rotarix used in a 2-dose** schedule
- WHO recommends **countries establish sentinel surveillance** and rotavirus vaccines be **included in all national immunization programmes and monitor impact/VE and IS post introduction**
- **1st dose:** Administered as soon as possible after **6 weeks of age** with a minimum of **4 weeks between doses**
- Rotavirus vaccinations may be administered **simultaneously** with other vaccines of the childhood immunization programme



Rotavirus vaccines: WHO position paper – July 2021

In accordance with its mandate to provide guidance to Member States on health policy matters, WHO regularly issues position papers on vaccines against diseases that have an international public health impact. These papers are concerned primarily with the use of vaccines in large-scale immunization programmes. They summarize essential background information on diseases and vaccines and conclude with the current WHO position on the use of vaccines worldwide.

The papers are reviewed by external experts and WHO staff and are reviewed and endorsed by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization (https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/). The Grading of Recommendations Assessment, Development and Evaluation (GRADE) method is used to assess the quality of the available evidence. The SAGE decision-making process is reflected in "evidence-to-recommendation" tables. The processes followed for the preparation of vaccine position papers are described at: www.who.int/immunization/position_papers/position_paper_process.pdf. The position papers are intended for use mainly by national public health officials and managers of immunization programmes. They may also be of interest to international funding agencies, vaccine advisory groups, vaccine manufacturers, health professionals, researchers, the scientific media and the general public.

This position paper replaces the 2013 WHO position paper on rotavirus vaccines; it adds recent developments in the field, such as 2 additional rotavirus vaccines prequalified by WHO in 2018, as well as updated post-licensure safety and effectiveness data for the 2 previously prequal-

Vaccins antirotavirus: Note de synthèse de l'OMS – Juillet 2021

Conformément à son mandat, qui prévoit qu'elle conseille les États Membres en matière de politique sanitaire, l'OMS publie régulièrement des notes de synthèse sur les vaccins contre les maladies ayant une incidence sur la santé publique internationale. Ces notes, qui portent principalement sur l'utilisation des vaccins dans les programmes de vaccination à grande échelle, résument les informations essentielles sur les maladies et les vaccins correspondants et présentent en conclusion la position actuelle de l'OMS concernant l'utilisation de ces vaccins à l'échelle mondiale.

Ces notes sont examinées par des experts externes et des membres du personnel de l'OMS, puis évaluées et approuvées par le Groupe stratégique consultatif d'experts (SAGE) sur la vaccination de l'OMS (https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/). L'évaluation de la qualité des données disponibles repose sur la méthode GRADE (Grading of Recommendations Assessment, Development and Evaluation). Le processus de décision du SAGE est reflété dans les tableaux des données à l'appui des recommandations. La procédure suivie pour élaborer les notes de synthèse sur les vaccins est décrite dans le document: http://www.who.int/immunization/position_papers/position_paper_process.pdf. Les notes de synthèse s'adressent avant tout aux responsables nationaux de la santé publique et aux administrateurs des programmes de vaccination, mais elles peuvent également présenter un intérêt pour les organismes internationaux de financement, les groupes consultatifs sur la vaccination, les fabricants de vaccins, les professionnels de santé, les chercheurs, les médias scientifiques et le grand public.

Cette note de synthèse sur les vaccins antirotavirus remplace celle de 2013; elle intègre les dernières avancées dans ce domaine, notamment les 2 vaccins antirotavirus supplémentaires préqualifiés par l'OMS en 2018, ainsi que des données actualisées sur la sécurité et la performance post-commercialisation des

301

July 2021 https://www.who.int/publications/i/item/WHO-WER9628

WHO prequalified oral rotavirus vaccine products*

Characteristics		Rotarix™ (GlaxoSmithKline)	Rotateq™ (Merck)	Rotavac™ (Bharat Biotech International)	Rotasiil™ (Serum Institute of India Pvt Ltd)
Efficacy for severe rotavirus gastroenteritis by child mortality rate stratum of country of study site (at 2 years follow-up**)[1]	Low Mortality	90% (95% CI, 86-93%)	94% (95% CI, 61-99%)	No data available	No data available
	Medium Mortality	78% (95% CI, 70-83%)	81% (95% CI, 66-89%)	No data available	No data available
	High Mortality	54% (95% CI, 9-77%)	44% (95% CI, 23-59%)	54% (95% CI, 40-65%)	44% (95% CI, 26-58%)
	Study sites	Multiple countries at different income and mortality levels.		3 sites in India	6 sites in India; 1 center, multiple sites in Niger
Date of WHO prequalification		March 2009	October 2008	January 2018	September 2018
Recommended number of doses		*2 doses*	*3 doses*	*3 doses*	*3 doses*
Composition		*G1P[8] attenuated human strain*	*G1, G2, G3, G4, P[8] human proteins in bovine backbone*	*G9, P[11] attenuated human strain*	*G1-4, G9 human proteins with bovine P[5] in bovine backbone*

Current evidence indicates local data on **circulating rotavirus strains** should **NOT** drive product choice as all WHO prequalified rotavirus vaccines provide protection against heterologous strains

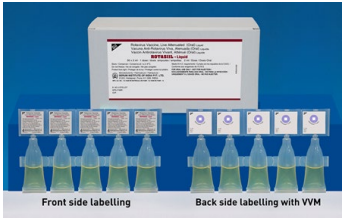
* WHO does not approve or endorse the use of specific branded products over others; this document may not be used for any commercial or promotional purposes.
** One year follow-up efficacy estimates for severe rotavirus gastroenteritis diarrhoea were reported in the 2020 Cochrane review and are similar to those for 2 year follow-up.
1. Systematic review and meta-analysis of the safety, effectiveness and efficacy of childhood schedules using Rotavirus Vaccines – Cochrane Response. October 2020 SAGE Meeting, Rotavirus Vaccines – Session 6. Background documents. https://www.who.int/publications/m/item/review-meta-analysis-rotavirus-vaccines

Rotavirus vaccine product images (selected)

Rotateq *– liquid ready to use, plastic tube, single dose*

Rotavac 5d *– liquid ready to use, 1 or 5 dose vials with dropper*

Rotasiil *– lyophilised or liquid in vials (1 or 2 dose) or liquid in plastic tubes (single dose)*

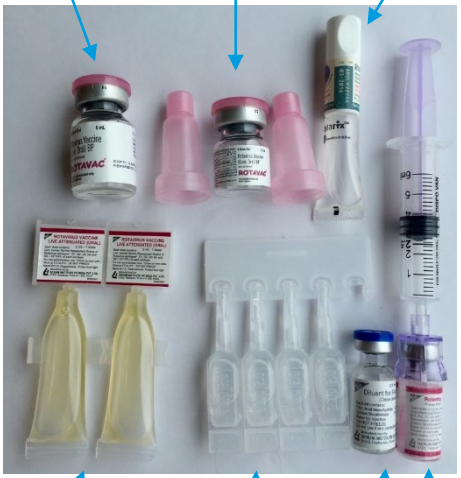


For size comparison

Rotavac *in 10d vials, with dropper*

Rotavac *in 5d vials, with dropper*

Rotarix *plastic tube, single dose*

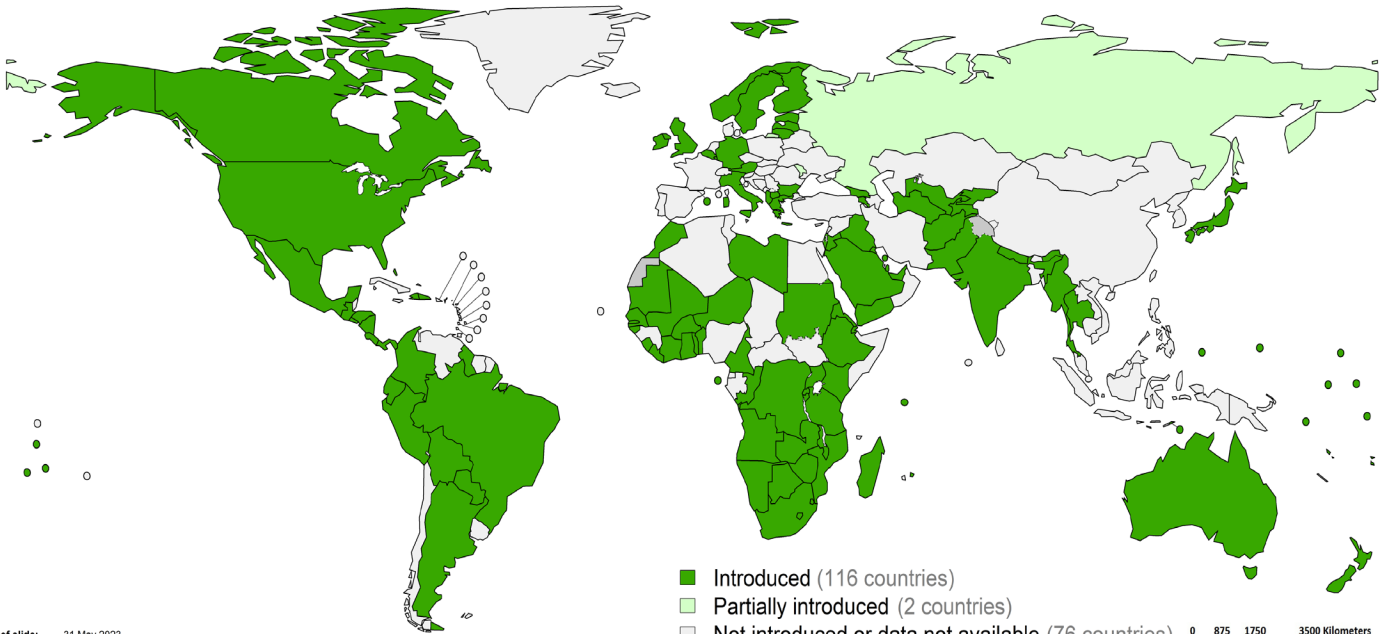


Rotasiil *liquid, plastic tube, in strip of tubes (2 of 5 tubes shown)*

Rotarix *plastic tube in strip of tubes (4 of 5 tubes shown)*

Rotasiil *lyophilised (two dose vial, after reconstitution, with oral syringe and adapter)*

Global rotavirus vaccine introduction status to the national immunization programme (118 countries)



Date of slide: 31 May 2023
Map production: Immunization, Vaccines and Biologicals (IVB), World Health Organization (WHO)
Data source: IVB database as at 31 May 2023. International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. VIEW-hub. www.view-hub.org. Accessed: 4/6/2023.

Disclaimer:

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area nor of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

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New vaccines inject hope

- ✓ **12 Sep 2008 – 1st rotavirus vaccines given in EPI, Eastern Cape, SA**
- ✓ **National roll-out August 2009**

~ coverage stagnated at ~70% last 3 years

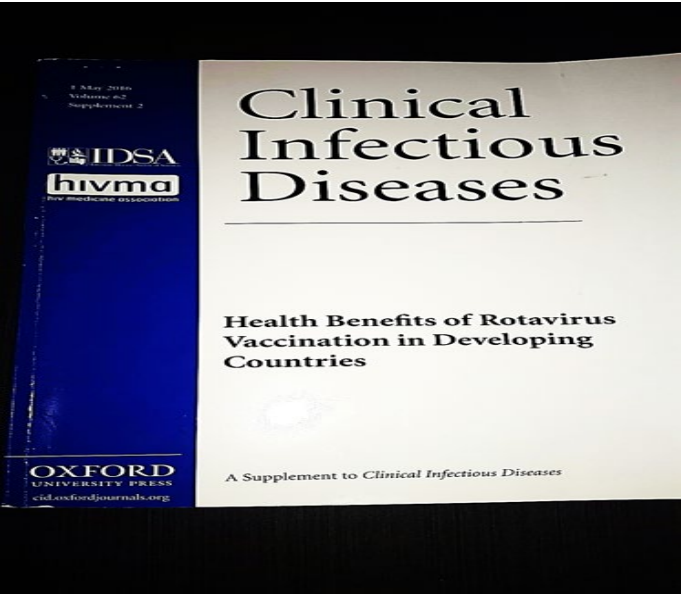
Rotavirus vaccine performance in Africa –

"Public health officials must make difficult trade-off decisions about which new vaccines to introduce into already crowded immunization schedule"

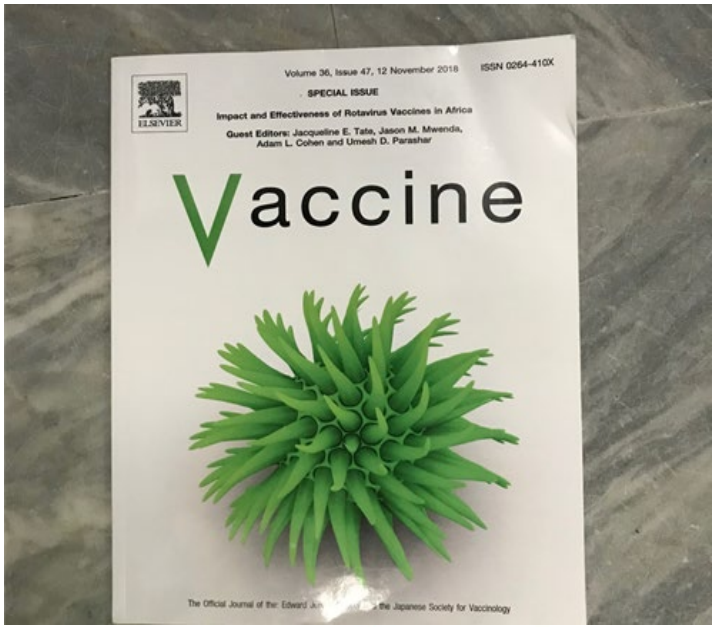
Documentation of early impact of Rotavirus vaccines in EPI in Africa

7 African countries published data showing early impact of rotavirus vaccination in Africa and rotavirus VE in the African countries;

Sup 2 CID vol 62, May 2016



15 African countries published data showing sustained impact of rotavirus vaccines and VE in Africa; supplement Vaccine Vol 36 (43), November 2018



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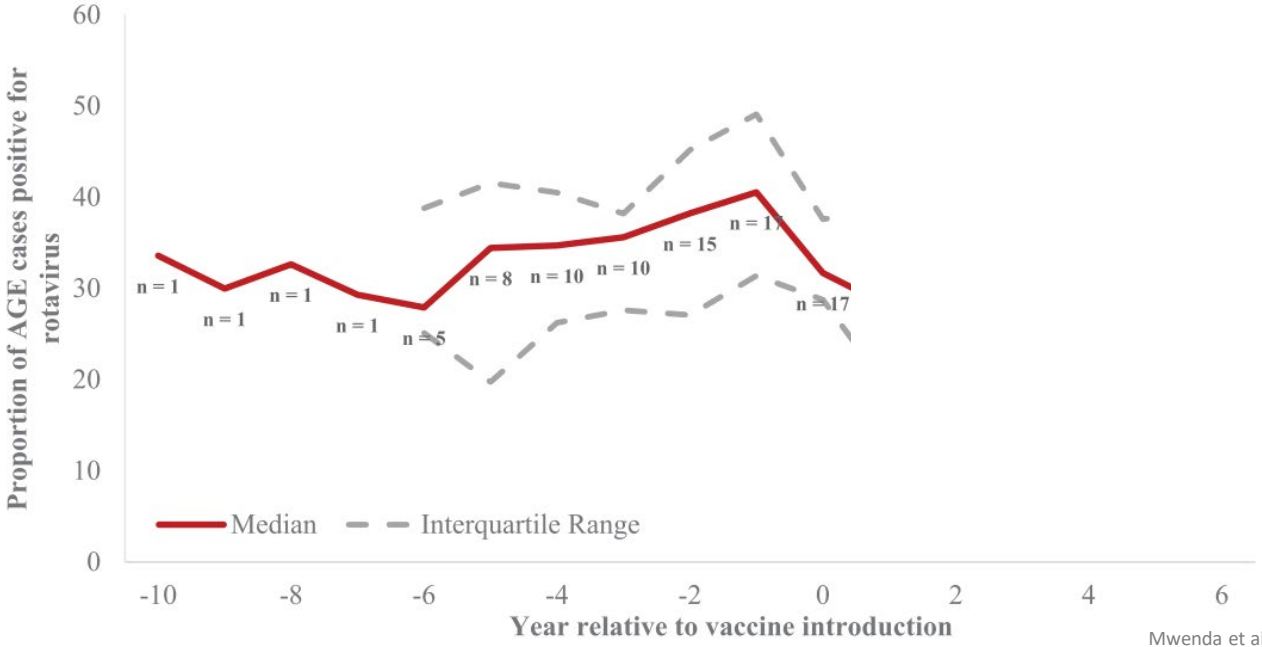
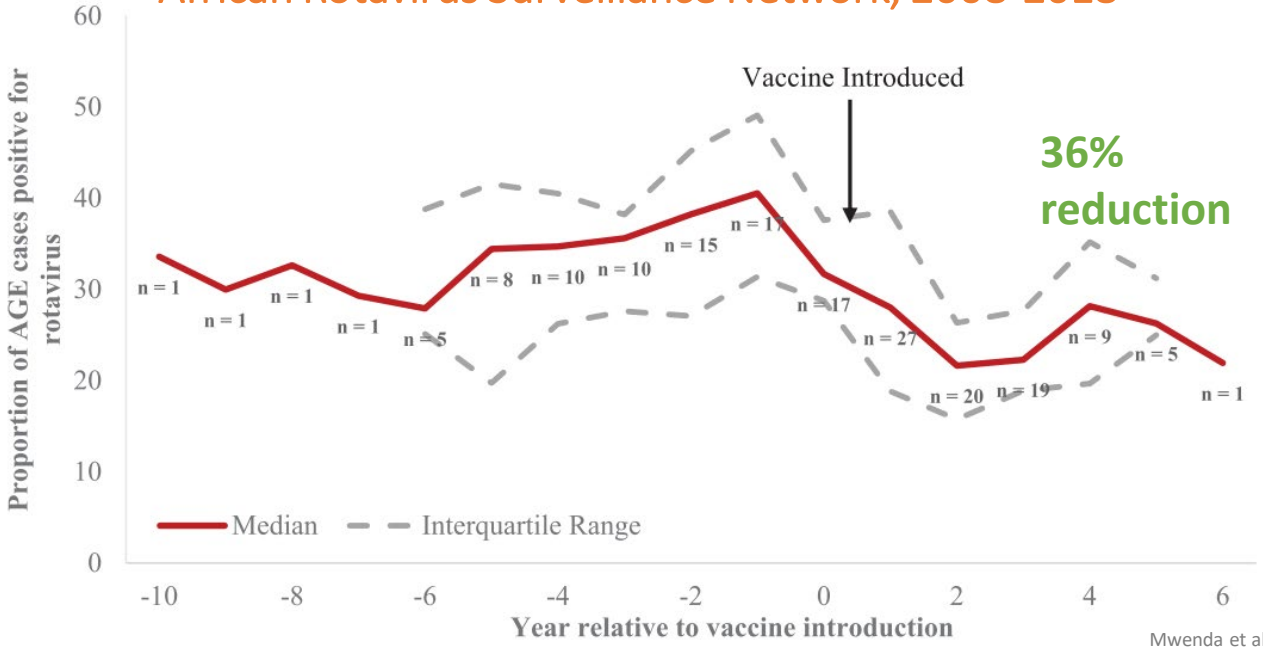
African Rotavirus Surveillance Network, 2008-2018



Mwenda et al CID 2021

Decline in proportion of diarrhea hospitalizations due to rotavirus in *AFRO countries with rotavirus vaccine*

African Rotavirus Surveillance Network, 2008-2018



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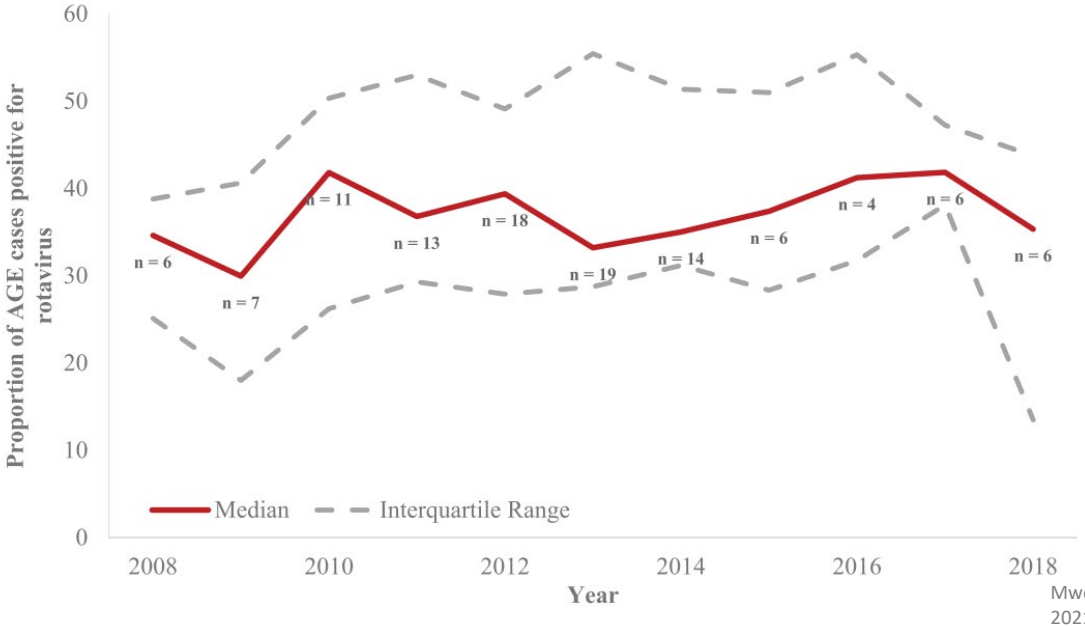
No change in proportion of diarrhea hospitalizations due to rotavirus in *AFRO countries without rotavirus vaccine*

African Rotavirus Surveillance Network, 2008-2018



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Vaccine effectiveness (VE) against rotavirus hospitalizations during the first year of life in low-income countries

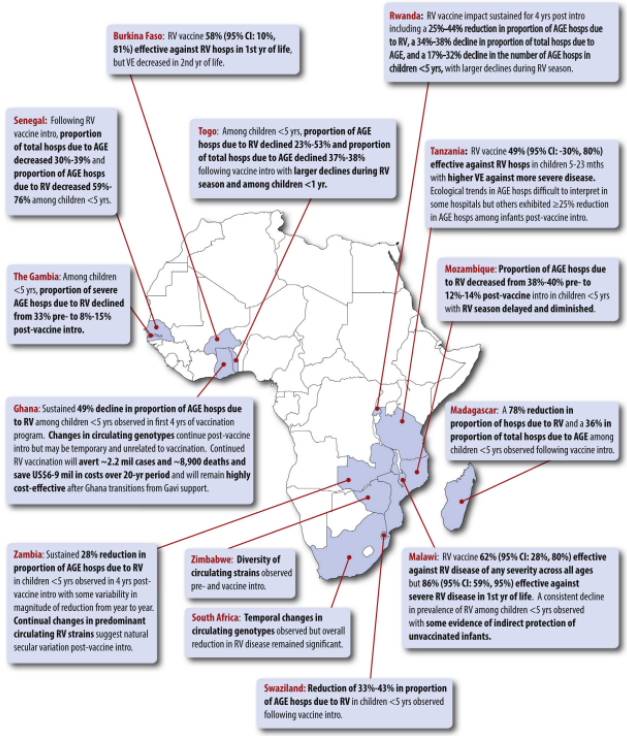
Country	Year of evaluation	Vaccine – Year intro	VE (95% CI)
Mozambique	2017-2019	RV1 - 2015	52 (-11-79)
Botswana	2013-2015	RV1 – 2012	52 (8-75)
South Africa	2010-2012	RV1 – 2009	54 (32-68)
Burkina Faso	2013-2017	RV5 - 2013	58 (10-81)
Zimbabwe	2014-2017	RV1 - 2014	61 (21-81)
Rwanda	2012-2015	RV5 - 2012	65 (-80-93)*
Tanzania	2013-2015	RV1 - 2013	66 (-2-89)**
Kenya	2014-2017	RV1 - 2014	67 (30-84)
Malawi	2012-2015	RV1 – 2012	71 (34-87)
Ghana	2013-2015	RV1 – 2012	78 (2-95)***

*Vaccine administered at ~10, 14, 18 weeks; **Age 5-23 months; Vesikari score >=11 **Any dose

Groome Lancet ID 2014; Bar-Zeev CID 2016; Gastanaduy CID 2016; Armah CID 2016; Tate CID 2016; Jani Vaccine 2018; Bonkoungou Vaccine 2018; Majuru Vaccine 2018; Khagayi CID 2020; Chissaque Vaccines 2022

A wealth of data available about rotavirus vaccine performance in Africa

- Data from >14 countries on performance of rotavirus vaccine under conditions of routine use
  - Vaccine effectiveness
  - Vaccine impact
  - Genotype trends over time
  - Cost burden and cost effectiveness
- All available data is for Rotarix and RotaTeq
  - Limited data available for Rotavac and Rotasiil under conditions of routine use – evaluations on going in several African countries



Mwenda et al Vaccine 2018

Summary and required actions

- Commendable progress in rotavirus introduction (42/54; 78%) countries, but support needed for 12 (22%) countries are yet to introduce rotavirus vaccine.
- In 29 African countries that had introduced rotavirus vaccine by the end of 2014, ~135,000 rotavirus hospitalizations and 21,000 rotavirus deaths were prevented in 2016 – use existing sentinel surv to continue monitoring impact/VE & safety and document
- 36% reduction in rotavirus confirmed diarrhea hospitalizations in < 5 children; need to sustain rotavirus surveillance
- 51 % regional rotavirus vaccine coverage – lower than other vaccines in EPI
- Millions of children in Africa have missed out on lifesaving rotavirus vaccine because of recent vaccine global vaccine supply constraints and decision delays, COVID-19 impact, switch disruptions

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THANK YOU

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