
FOURTEENTH INTERNATIONAL
ROTAVIRUS SYMPOSIUM
MARCH 14–16 2023 BALI INDONESIA
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Changing landscape of moderate-to-severe diarrhea (MSD) among children 0-59 months old in three sub-Saharan African countries following rotavirus vaccine introduction

14th International Rotavirus Symposium
Bali, Indonesia

Dilruba Nasrin, PhD
On behalf:
Karen L. Kotloff, MD
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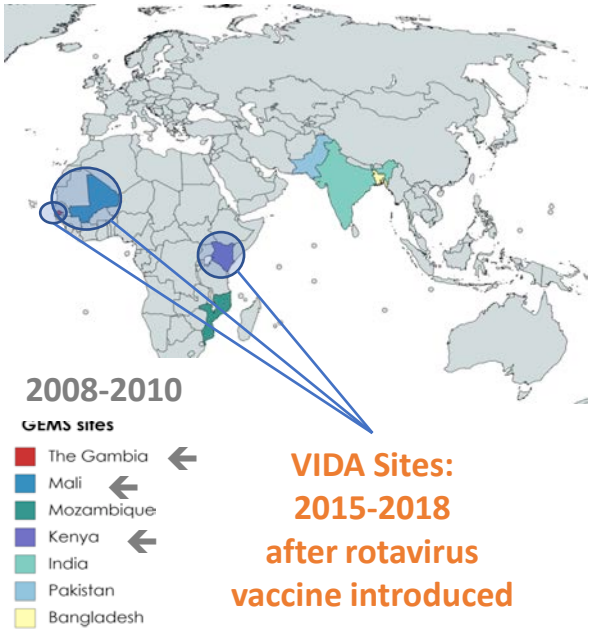
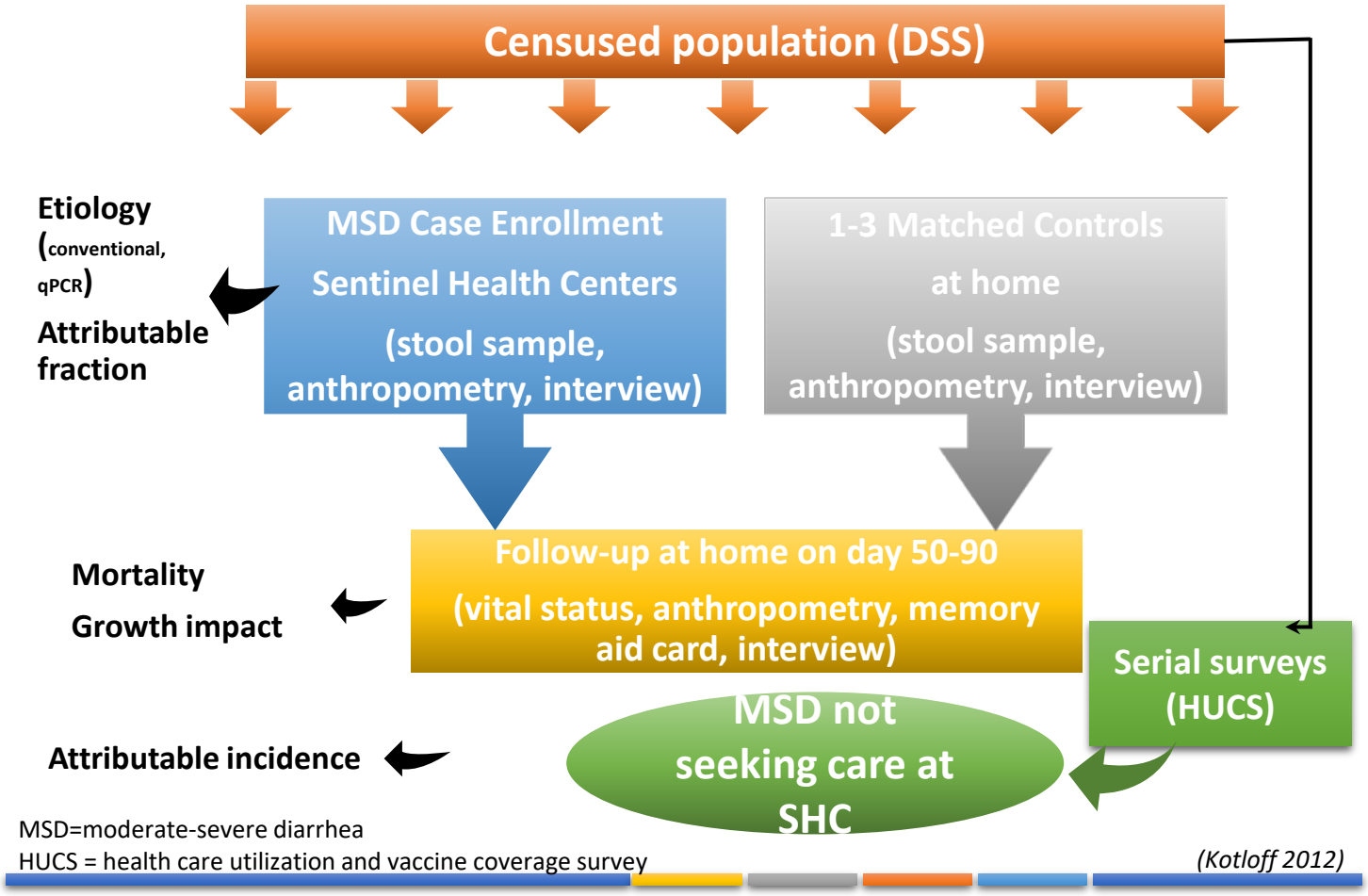
Two studies of the incidence, etiology, and adverse consequence of MSD:
GEMS (Global Enterics Multicenter Study) & **VIDA** (Rotavirus Vaccine Impact on Diarrhea in Africa)



Overview of GEMS and VIDA Study Design



MSD=moderate-severe diarrhea
HUCS = health care utilization and vaccine coverage survey

(Kotloff 2012)

Medically attended moderate-to-severe diarrhea (MSD)

- Diarrhea (≥3 abnormally loose stools/previous 24 h)
- Acute onset (<7 days)
- New episode (after ≥7 days diarrhea-free days)
- At least one of the following:
  - Sunken eyes, more than usual
  - Decreased skin turgor
  - IV hydration prescribed
  - Hospitalization recommended
  - Dysentery

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What changed between GEMS and VIDA?

Socioeconomic development over the decade

	The Gambia		Mali		Kenya	
n	GEMS	VIDA	GEMS	VIDA	GEMS	VIDA
	2,598	3,816	4,097	3,588	3,359	3,649
% caretakers 1° school	5.6	15.1*	15.0	22.9*	52.9	66.5*
% with household assets:						
Electricity	39.7	44.8*	83.9	96.0*	1.6	22.3*
Television	31.1	36.0*	78.1	89.0*	10.2	13.2*
Telephone	93.0	98.1*	95.4	97.9*	59.1	92.7*
Refrigerator	18.2	21.7*	22.4	25.0†	0.1	0.9*
Motor car / scooter	49.4	52.8†	68.1	82.8*	1.9	15.0*
Radio	95.1	82.6*	86.0	76.3*	77.8	73.2*
Bicycle	89.3	85.5*	37.9	32.4*	63.3	41.9*

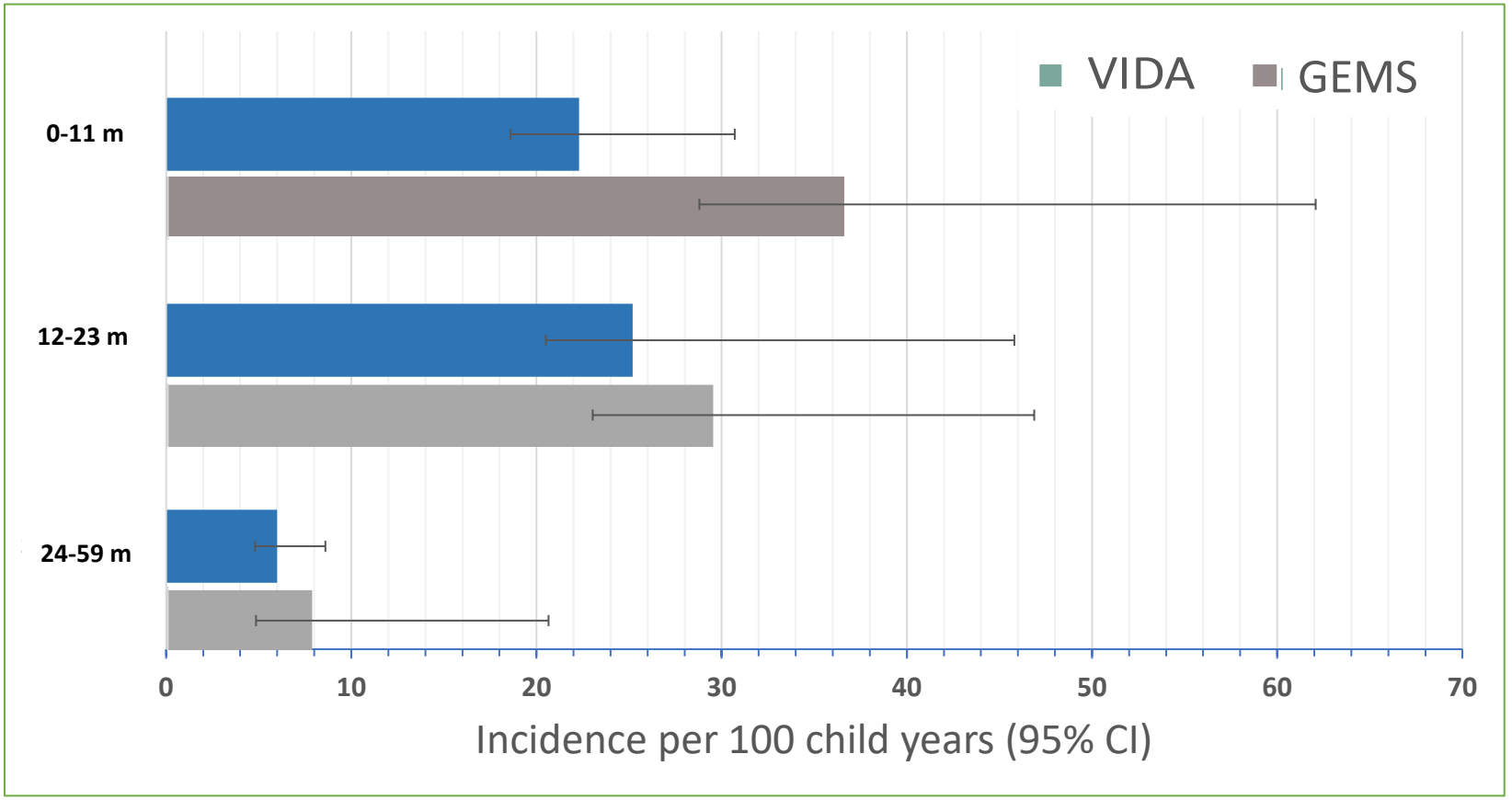
*p<0.001; †0.01<p>0.001 = increase = decrease

High Vaccine coverage

(Among those who were eligible to be vaccinated and eligible to be fully vaccinated (plus 14 days) at enrollment –VIDA)

Age stratum:	0-11 mo.		12-23 mo.		24-59 mo.	
	Case	Control	Case	Control	Case	Control
% fully vaccinated						
The Gambia	81.8	82.6	92.8	92.5	91.2	91.6
Mali	86.2	85.9	83.4	88.9	81.1	82.5
Kenya	90.9	88.2	89.0	87.7	83.5	82.8
% partially vaccinated						
The Gambia	17.8	17.1	7.2	7.5	8.8	8.4
Mali	10.3	10.7	8.2	6.1	10.8	6.9
Kenya	4.5	6.3	3.1	3.2	2.0	1.9

Incidence of MSD in GEMS vs VIDA*



*Adjusted for site

Pathogen-specific attributable fraction: GEMS vs. VIDA

Infants:

- **Highest: rotavirus**

(21.5% in GEMS vs. 14.5% in VIDA)

- ***Cryptosporidium***

(12.8% in GEMS vs. 12.0% in VIDA)

- ***Campylobacter***
- **Norovirus GII**
- ***Shigella***
- **Adenovirus 40/41**

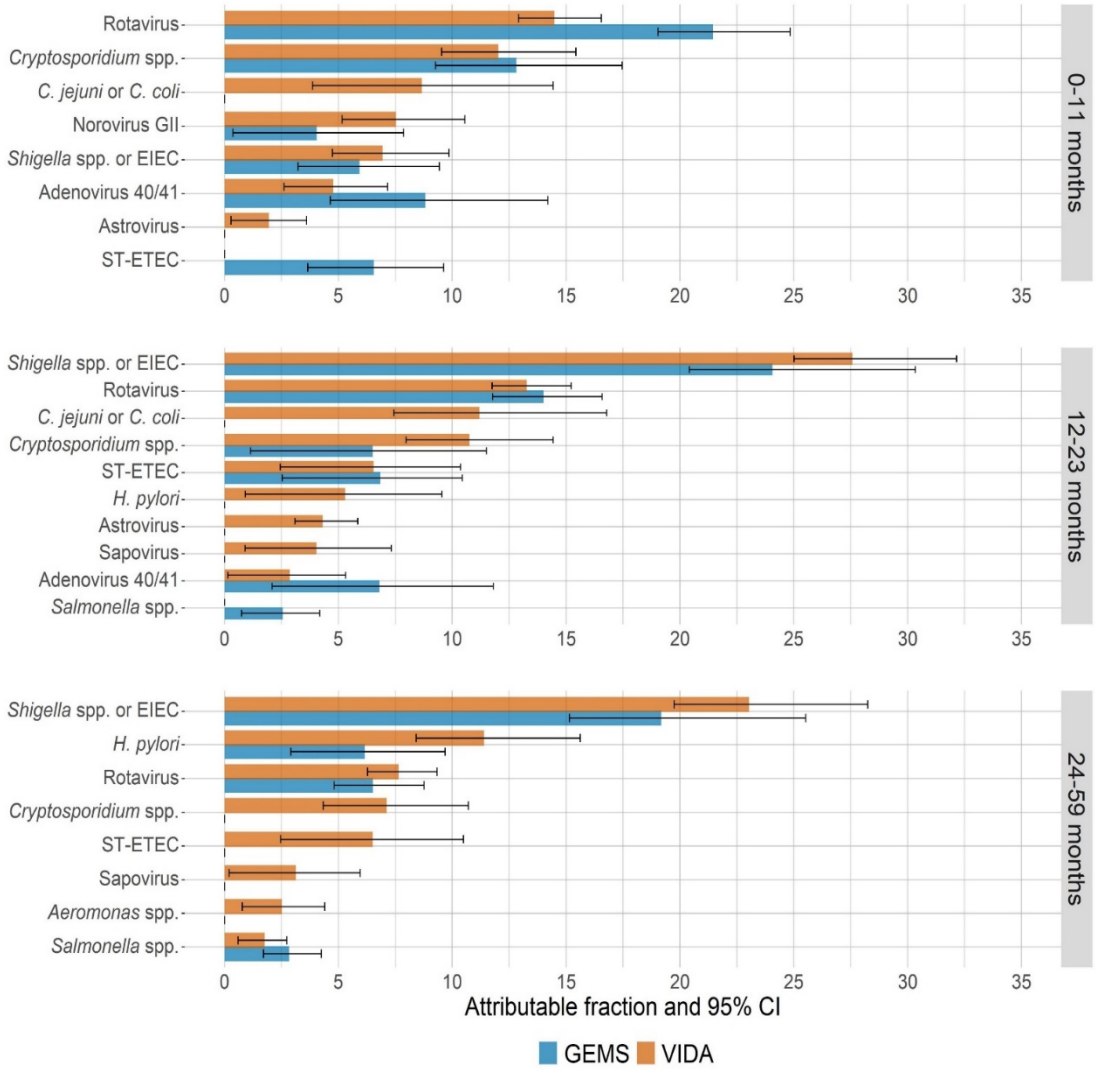
12-59 months:

- **Highest: *Shigella***

peaked at 12-23 months

(24% in GEMS, 28% in VIDA)

- **Rotavirus**
- ***Cryptosporidium***
- ***Campylobacter***
- ***ST-ETEC***
- ***H. pylori***



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Pathogen specific attributable incidence (qPCR) of MSD by age group, all sites combined, GEMS vs VIDA

Infants:

- **Highest: rotavirus**

(5.9 in GEMS vs. 3.1 in VIDA)

- ***Cryptosporidium***

(3.5 in GEMS vs. 2.5 in VIDA)

- ***Campylobacter*, norovirus GII, *Shigella,* adenovirus 40/41**

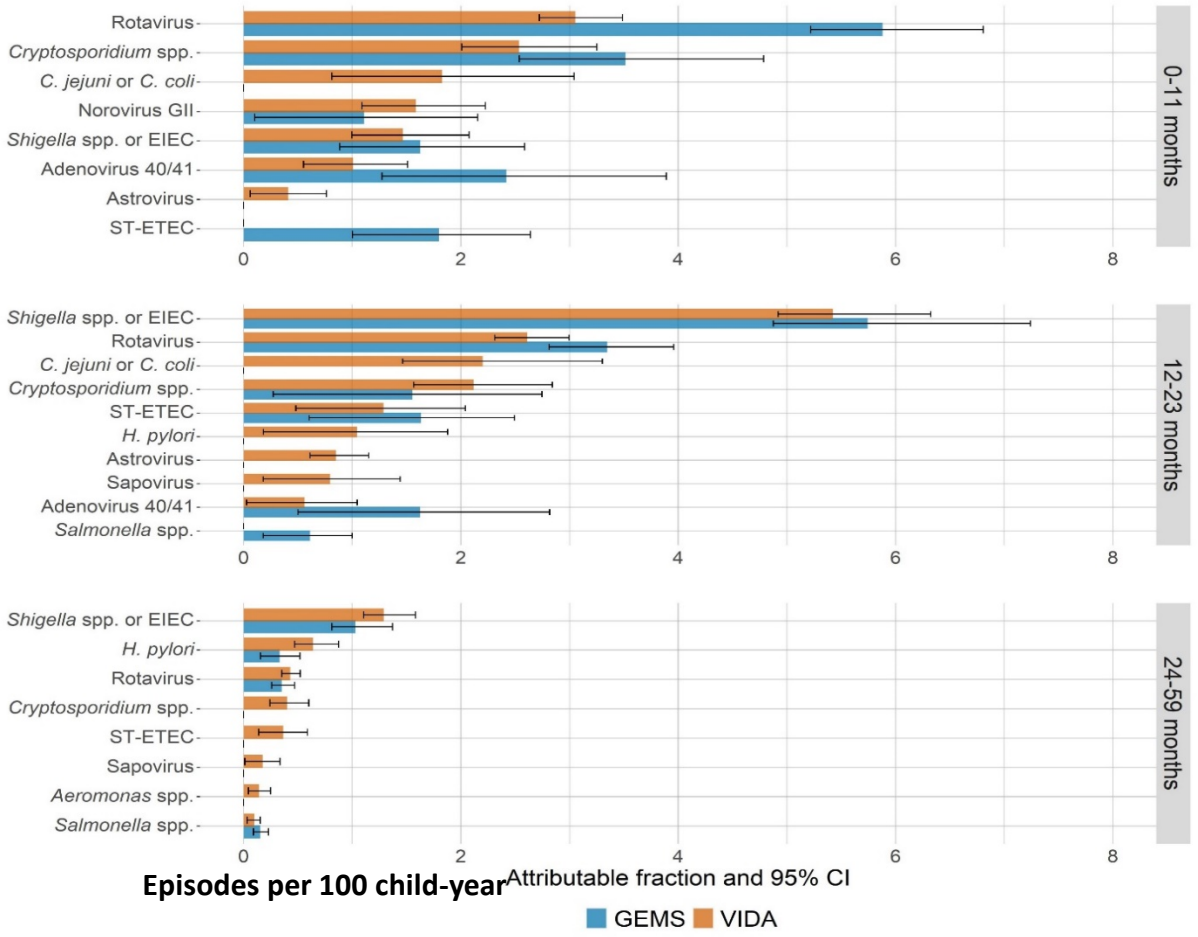
12-59 months:

- **Highest: *Shigella***

peaked at 12-23 months

(5.7 in GEMS vs. 5.4 in VIDA)

- **Rotavirus**
- ***Cryptosporidium***
- ***Campylobacter***
- ***ST-ETEC***
- ***H. pylori***



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Changes in Rotavirus AF and AI between GEMS and VIDA, all sites combined

Rotavirus	GEMS	VIDA	Change
Attributable fraction (AF)			
0-11 months	21.5 (19.0-24.8)	14.5 (12.9-16.6)	32.6%
12-23 months	14.0 (11.8-16.6)	13.3 (11.8-15.2)	5.0%
24-59 months	6.5 (4.8-8.8)	7.7 (6.3-9.3)	-18.5%
Attributable incidence (AI)			
0-11 months	5.9 (5.2-6.8)	3.1 (2.7-3.5)	47.5%
12-23 months	3.4 (2.8-4.0)	2.6 (2.3-3.0)	23.5%
24-59 months	0.35 (0.26-0.47)	0.43 (0.35-0.52)	-22.9%

= decrease = increase

Changes in progression of MSD cases to persistent diarrhea (PD) between GEMS and VIDA

	GEMS (%)	VIDA (%)	Change (%)
The Gambia	5.3	8.8	-66.0
Mali	10.3	4.2	59.2
Kenya	20.6	14.7	28.6
Combined sites	12.5	9.2	26.4

- Proportion of MSD episodes progressing to PD remains high
- Proportion decreased in Mali and Kenya, but increased in The Gambia

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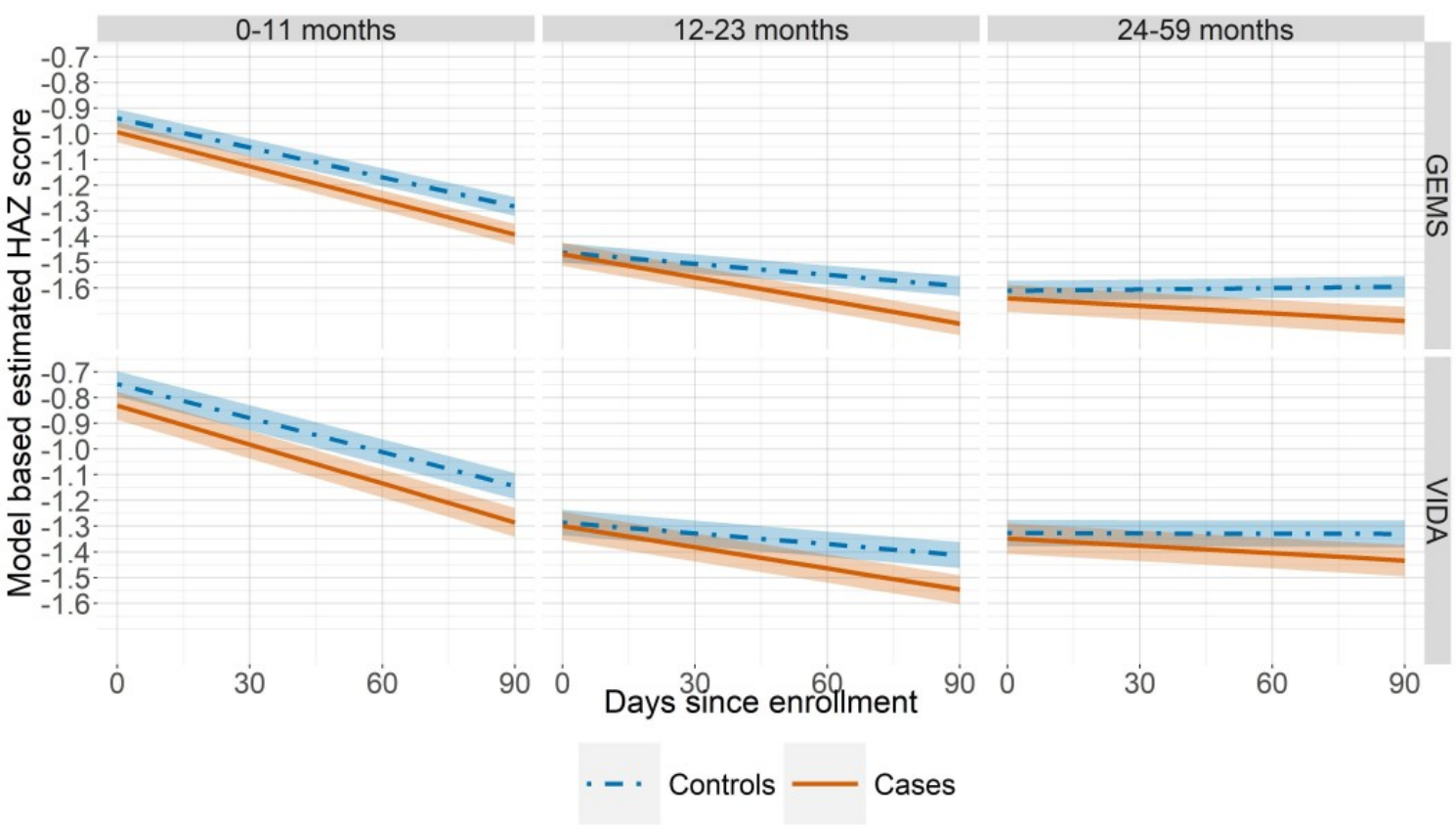
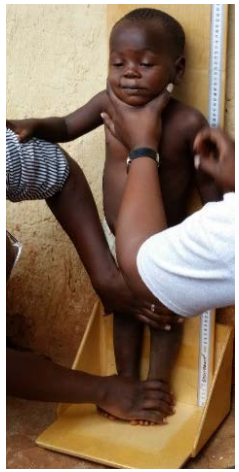
Changes in the impact of MSD on linear growth: GEMS vs VIDA





- **Linear mixed effects model (controlling for age, gender, SES, maternal education, site)**
- **HAZ at enrollment was not significantly different between cases and controls in GEMS or VIDA in any age group.**
- **In both studies, the decline in HAZ (slope) was significantly greater in cases vs controls over the follow-up period for all 3 age groups ($p<0.001$ for all).**
- **However, in GEMS, the effect of MSD on the slope (negative impact on HAZ trajectory) is significantly stronger compared to VIDA ($p=0.03$)**

Relationship between an episode of MSD and death

	GEMS			VIDA		
	Cases	**Controls**	**OR**	**Cases**	**Controls**	**OR**
The Gambia	3.8%	0.4%	7.5 (3-8)	1.0%	0.05%	20.6 (3-162)
Mali	1.1%	0.2%	4.3 (1-7)	0.4%	0.05%	7.4 (1-64)
Kenya	3.5%	0.6%	5.3 (3-11)	1.1%	0.05%	22.0 (3-173)
Total	2.5%	0.4%	5.9 (4-9)	0.8%	0.05%	16.4 (5-55)

- 68% reduction case mortality
- 88% reduction control mortality
- An episode of MSD continues to be associated with increased mortality

SUMMARY AND CONCLUSIONS (1)

- GEMS and VIDA
  - **Standardized** clinical, epidemiological, and microbiological methods
  - **Sub-Saharan Africa** where mortality is concentrated
  - **Population-based** to calculate incidence
  - **Broad panel** of pathogens
  - **Controls** allowed calculations of attributable fraction/incidence
  - Directly measured impact of MSD on **growth and mortality**
  - Directly measured rotavirus **vaccine coverage** (written documentation)

SUMMARY AND CONCLUSIONS (2)

- **Changing epidemiology**
  - Marked socio-economic development over time
  - Rotavirus incidence declined: 48% decline among infants
  - In these high-risk settings, *Cryptosporidium* and *Shigella* dominate strains, on par with rotavirus
  - Other viral agents (adeno 40/41, norovirus, astrovirus, sapovirus) follow in importance
- Proportion of MSD episodes progressing to PD remains high
- The detrimental impact of MSD on linear growth persists
- An episode of MSD continues to be associated with increased mortality

THANK YOU

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