

# Vaccine Impact on Diarrhea in Africa (VIDA)

UMB/CVD ♦ CVD-Mali ♦ MRC/The Gambia ♦ KEMRI/CDC

## Prevalence, antimicrobial resistance, and distribution of *Shigella* among children under five in three sub-Saharan African countries in the Vaccine Impact on Diarrhea in Africa Study

Henry Badji<sup>1</sup>, Irene Kasumba<sup>2</sup>, Sunil Sen<sup>2</sup>, Shamima Nasrin<sup>2</sup>, Jennifer Jones<sup>2</sup>, Jasnehta Permala-Booth<sup>2</sup>, Helen Powell<sup>2</sup>, M. Jahangir Hossain<sup>1</sup>, Jennifer R. Verani<sup>3</sup>, Marc-Alain Widdowson<sup>3</sup>, James Platts-Mills<sup>4</sup>, Anna Roose<sup>2</sup>, Richard Omoro<sup>5</sup>, Ben Ochieng<sup>5</sup>, Samba Sow<sup>6</sup>, Sanogo Doh<sup>6</sup>, Boubou Tamboura<sup>6</sup>, Joquina Chiquita M. Jones<sup>1</sup>, Syed M.A. Zaman<sup>1</sup>, Dilruba Nasrin<sup>2</sup>, Catherine Okoi<sup>1</sup>, Martin Antonio<sup>1</sup>, Jie Liu<sup>4</sup>, Eric Houpt<sup>4</sup>, Ciara Sugerman<sup>7</sup>, Karen L. Kotloff<sup>2</sup> and Sharon M. Tennant<sup>2</sup>

<sup>1</sup>Medical Research Council Unit The Gambia at the London School of Hygiene & Tropical Medicine, Banjul, The Gambia, <sup>2</sup>Center for Vaccine Development and Global Health, University of Maryland School of Medicine, Baltimore, Maryland, United States, <sup>3</sup>Global Disease Detection Division, Kenya Office of the US Centers for Disease Control and Prevention, Nairobi, Kenya, <sup>4</sup>Division of Infectious Diseases and International Health, Department of Medicine, University of Virginia, Charlottesville, VA, United States, <sup>5</sup>Kenya Medical Research Institute, Center for Global Health Research, Kisumu, Kenya, <sup>6</sup>Center for Vaccine Development-Mali, Bamako, Mali, <sup>7</sup>Division of Foodborne, Waterborne, and Environmental Diseases, US Centers for Disease Control and Prevention, Atlanta, GA, United States

### Background

- Shigellosis, caused by *Shigella*, is a leading cause of diarrheal morbidity and mortality worldwide.
- In the Global Enteric Multicenter Study (GEMS), *Shigella* was the second leading cause of moderate-to-severe diarrhea (MSD) in children aged less than 5 years and the most important bacterial pathogen in 12-23 and 24-59 month old children.
- A follow-up 36-month prospective, matched, case-control study called Vaccine Impact on Diarrhea in Africa (VIDA) assessed the impact of rotavirus vaccine introduction on moderate-to-severe diarrhea (MSD) in children <5 years in Kenya, Mali and The Gambia.
- Here, we describe the prevalence of *Shigella* and distribution of serogroups, serotypes and antimicrobial resistance (AMR) using standard microbiological culture during VIDA.

### Methods

**Enrollment:** We enrolled 4840 MSD cases and 6213 healthy matched controls and collected stool and epidemiological data for all cases and controls. Cases were matched with controls by age, sex and proximity.

**Molecular detection of *Shigella*:** TaqMan Array Card (TAC) quantitative PCR was performed to detect *Shigella* directly from stool and to calculate the attributable fraction (AF<sub>e</sub>) for *Shigella*. AF<sub>e</sub> was calculated for each case with respect to age group, site and quantity of *Shigella* DNA detected in stool, and cases with an AF<sub>e</sub> ≥ 0.5 were considered to have *Shigella* attributable MSD.

**Identification & Isolation:** Conventional microbiological culture was used to identify and isolate *Shigella* from stool samples.

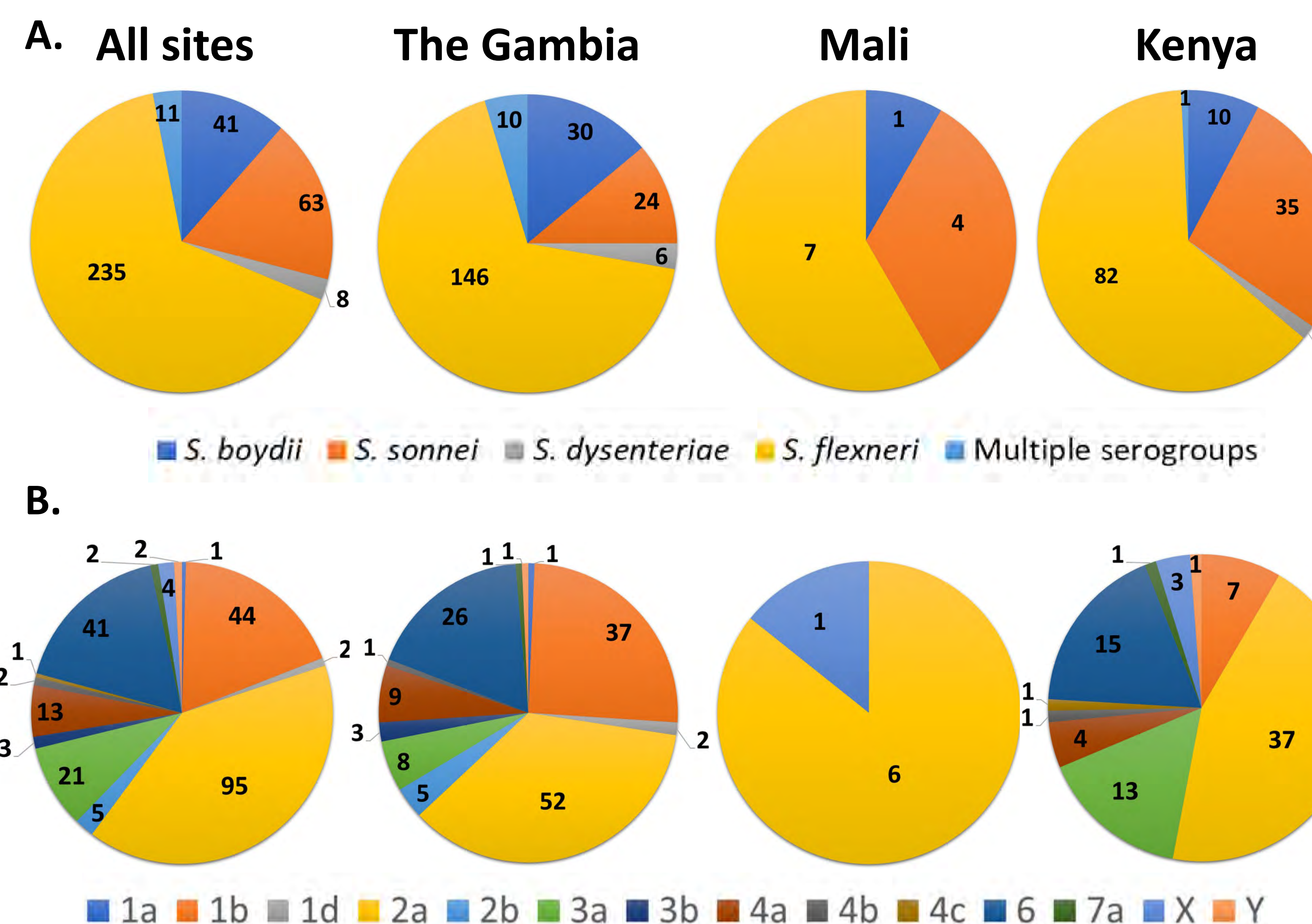
**Antimicrobial resistance testing:** Antimicrobial resistance was determined using the Kirby-Bauer disc diffusion method.

### Results

***Shigella* detection:** *Shigella* was detected in 355 (7.4%) MSD cases by conventional culture and in 1641 (34.2%) cases by TAC (using a cycle threshold less than 35 cutoff).

**Table 1.** Stool positivity by culture and TAC, and etiologic detection of *Shigella* among MSD cases and controls.

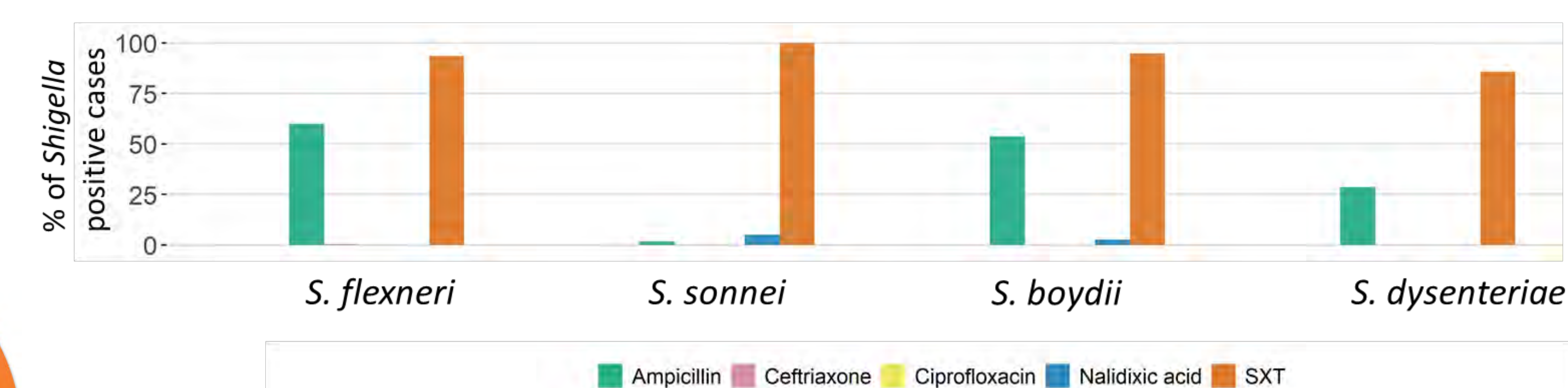
	All sites		The Gambia		Mali		Kenya	
	Cases (N=4804)	Controls (N=4803)	Cases (N=1665)	Controls (N=1665)	Cases (N=1601)	Controls (N=1600)	Cases (N=1538)	Controls (N=1538)
Stool culture	355 (7.4%)	72 (1.5%)	215 (12.9%)	42 (2.5%)	12 (0.7%)	5 (0.3%)	128 (8.3%)	25 (1.6%)
TAC Results Positive (Ct < 35)	1641 (34.2%)	1084 (22.6%)	770 (46.2%)	507 (30.5%)	438 (27.4%)	334 (20.9%)	433 (28.2%)	243 (15.8%)
Etiologic detection (AF <sub>e</sub> ≥ 0.5)	944 (19.7%)		515 (30.9%)		150 (9.4%)		279 (18.1%)	



**Figure 1.** Distribution of **A)** *S. flexneri*, *S. sonnei*, *S. boydii* and *S. dysenteriae*; and **B)** *S. flexneri* serotypes isolated from MSD cases in the VIDA study.

**Table 2.** Antimicrobial resistance of *Shigella* isolates from MSD cases in the VIDA study.

Antibiotic	All sites (N=342)	The Gambia (N=202)	Mali (N=11)	Kenya (N=129)
Ampicillin	164 (48.0%)	83 (41.1%)	6 (54.5%)	75 (58.1%)
Ceftriaxone	1 (0.3%)	1 (0.5%)	0 (0%)	0 (0%)
Nalidixic Acid	4 (1.2%)	0 (0%)	2 (18.2%)	2 (1.6%)
Sulfamethoxazole	322 (94.2%)	187 (92.6%)	9 (81.8%)	126 (97.7%)
Ciprofloxacin	0 (0%)	0 (0%)	0 (0%)	0 (0%)



**Figure 2.** Antimicrobial resistance by serogroup.

### Conclusion

*Shigella* continues to be a major pathogen causing MSD among children under five years in sub-Saharan Africa. A high burden of *Shigella*-associated diarrhea was seen among the three African sites. Preventive strategies focusing on *Shigella* could further reduce the burden of under-five diarrhea.

### Acknowledgments

We wish to thank all the clinical, field, epidemiological and lab staff of all the VIDA sites and the Center for Vaccine Development and Global Health, University of Maryland School of Medicine, Baltimore. We also thank the study participants and their care givers for participating in the study. The VIDA study was funded by the Bill & Melinda Gates Foundation.