Causes of Pediatric Diarrhea Hospitalizations and Deaths in Low- and Middle-Income Countries from Global Pediatric Diarrhea Surveillance, 2017-2023

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Introduction

- Data on the etiology of severe diarrhea in children in low- and middle-income countries are critical for evaluating and prioritizing public health interventions.
- Prior to establishing the Global Pediatric Diarrhea Surveillance (GPDS) network in 2017, systematically collected and analyzed data on the etiology of hospitalized diarrhea in these settings were limited.
- GPDS leverages the established sentinel-site surveillance and regional reference laboratory system from the Global Rotavirus Surveillance Network in 31 low- and middle-income countries, using a standardized protocol for qPCR testing for a broad range of enteric pathogens.

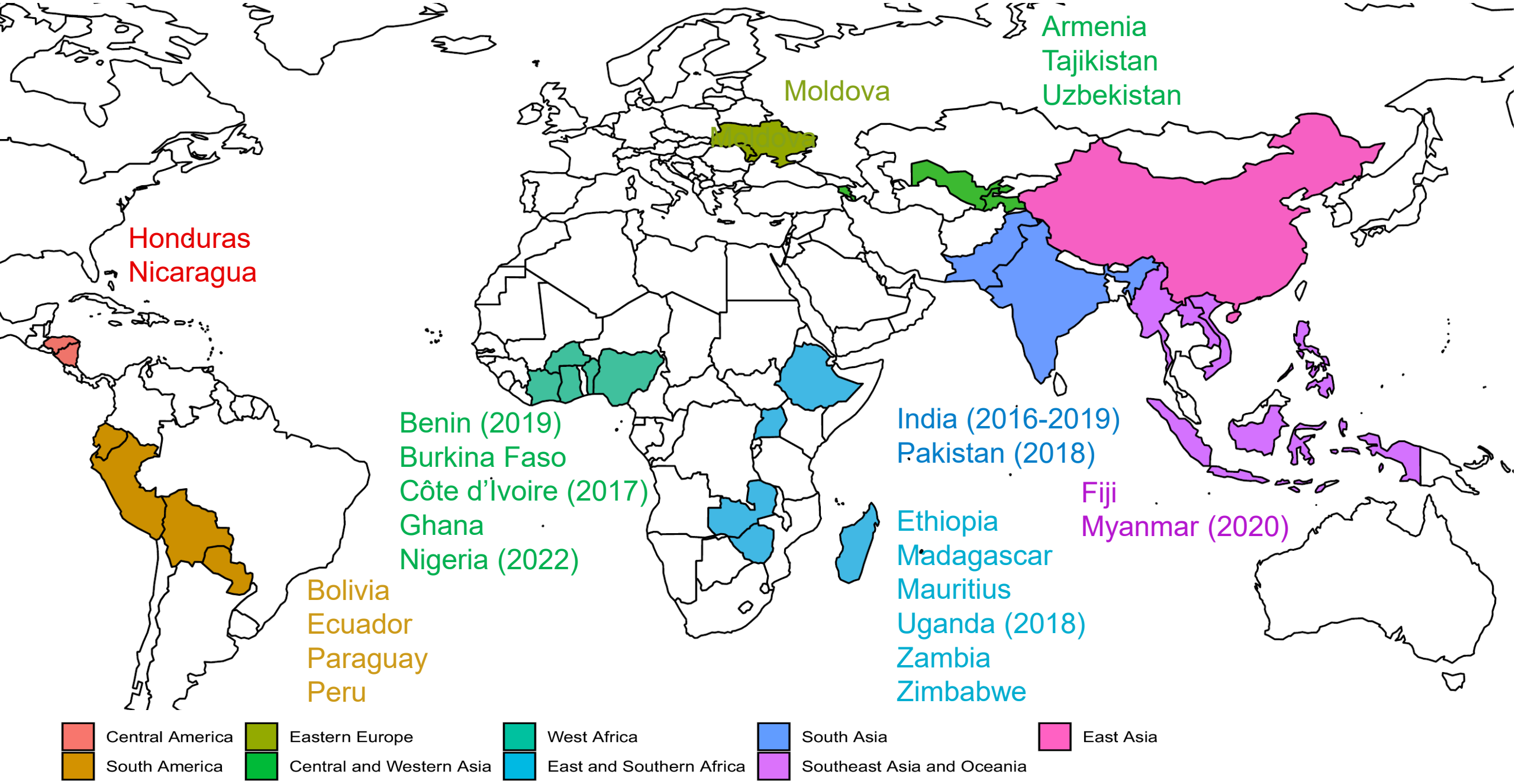
Methods

Sample selection and testing: We tested 100 random samples per site/year at Regional Reference Labs using TaqMan Array Cards. We applied inverse probability weighting to make the data representative of all enrolled children.

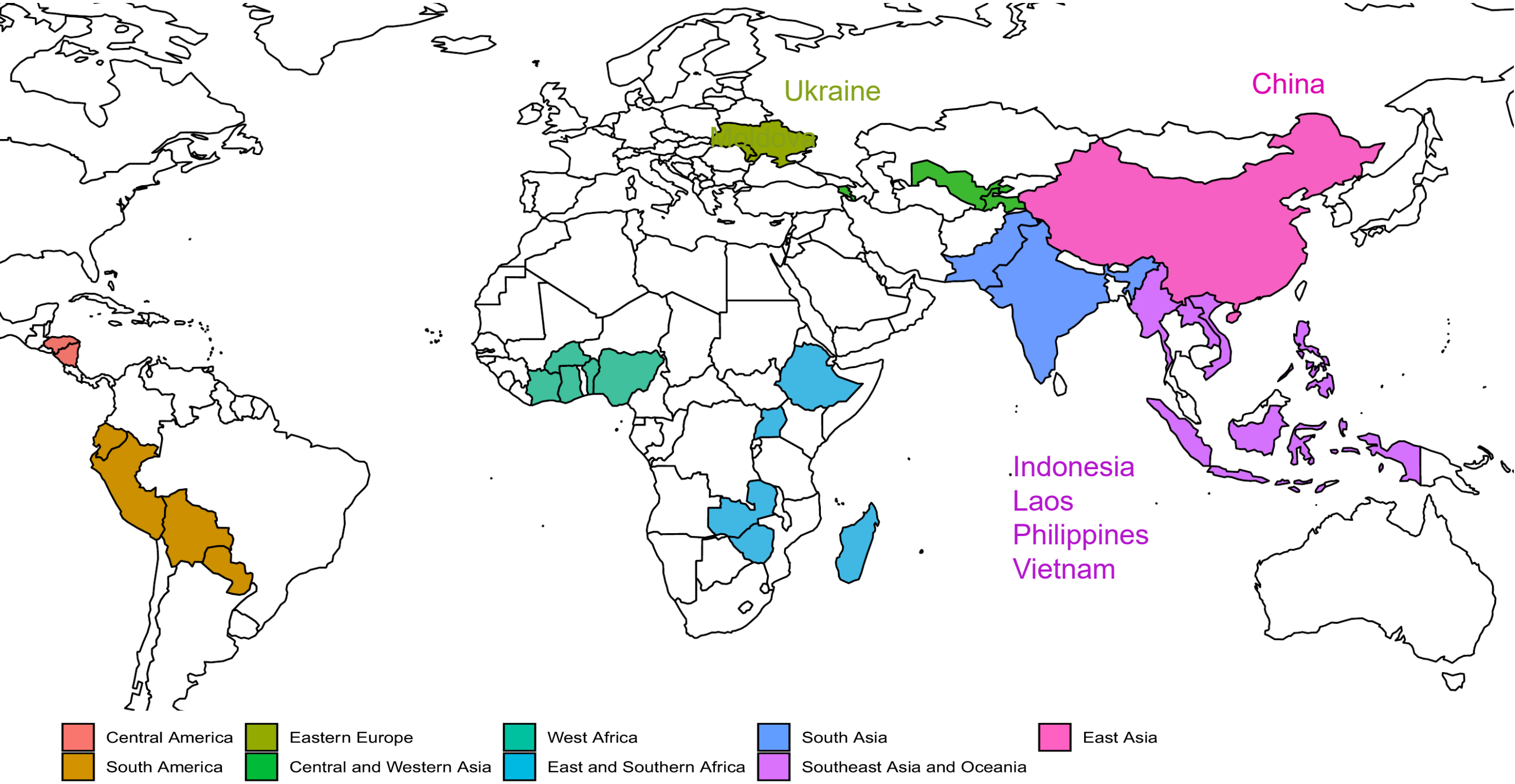
Site-level Attributable Fractions: We combined these qPCR results with associations between pathogen quantity and diarrhea from two multisite studies from similar settings (GEMS and MAL-ED) to calculate pathogen-specific attributable fractions for two-year periods starting with 2017-2018.

Aggregated Attributable Fractions: We used country-, year- and age-specific estimates of the incidence of hospitalized diarrhea from the Global Burden of Disease Study to aggregate attributable fractions for geographic groupings as well as across the entire network.

GPDS 2017-2023: 25/31 countries have introduced rotavirus vaccine…



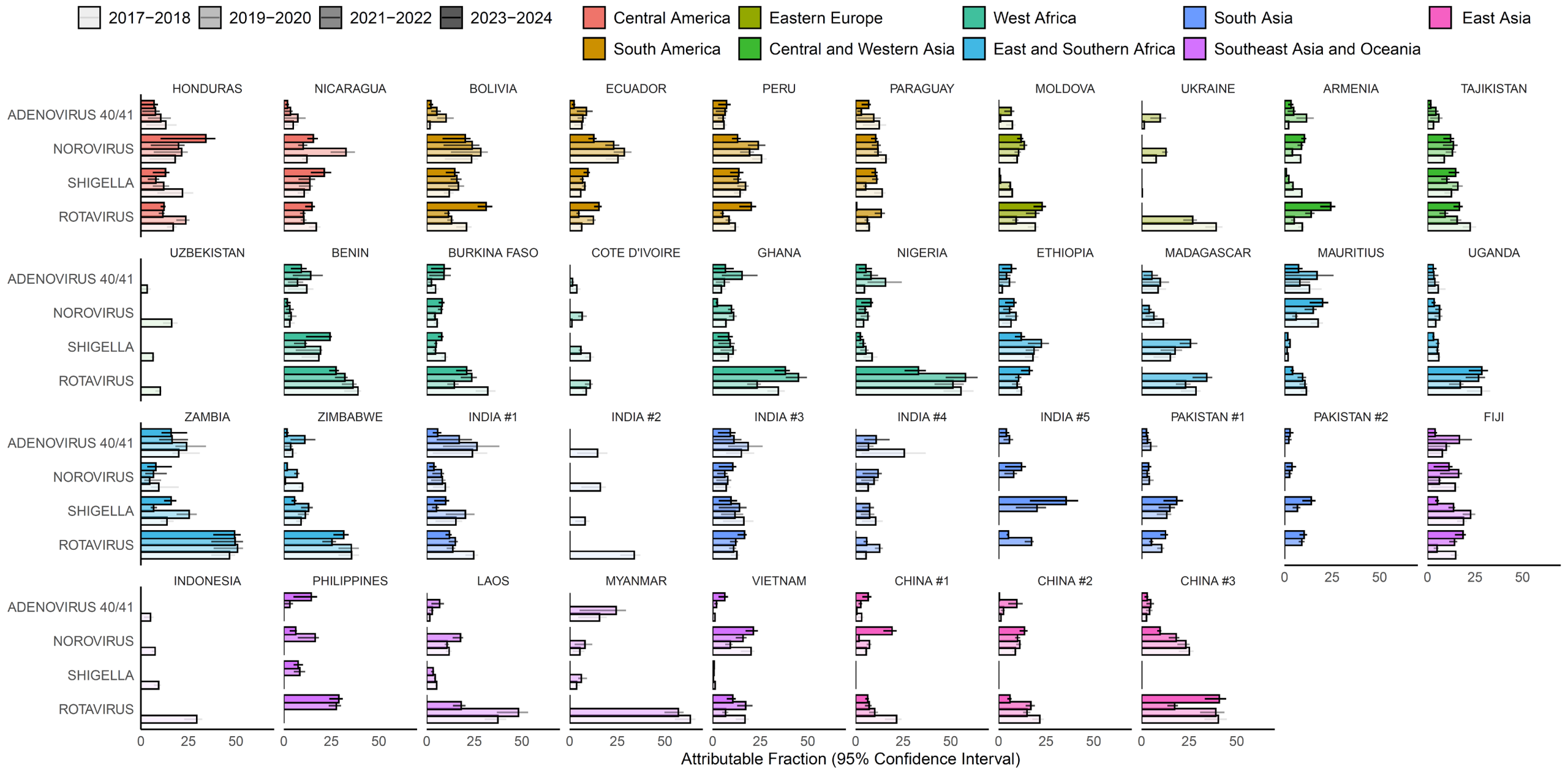
… and 6 have not



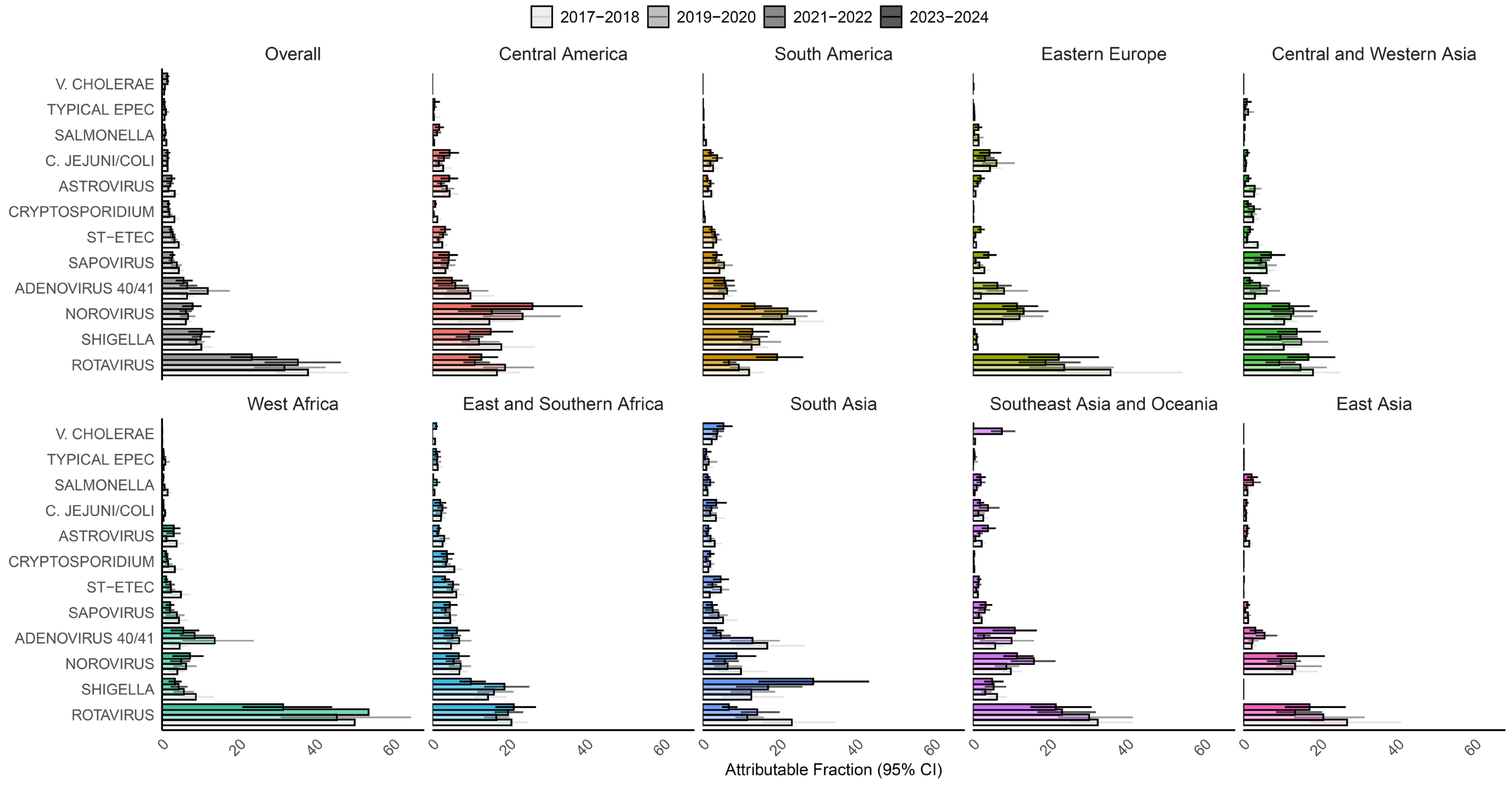
Demographic and clinical characteristics (2017-2022)

Demographic and clinical characteristics	2017–2018		2019–2020		2021–2022	
	All enrolled cases N = 31100	qPCR-tested cases N = 5670	All enrolled cases N = 19367	qPCR-tested cases N = 5509	All enrolled cases N = 20283	qPCR-tested cases N = 5270
Male sex	18073 (58.2)	3348 (59.1)	11194 (57.9)	3224 (58.6)	11738 (57.9)	3004 (57)
Age						
0-11 months	13706 (44.1)	2523 (44.5)	9015 (46.5)	2484 (45.1)	9127 (45)	2221 (42.2)
12-23 months	10356 (33.3)	1853 (32.7)	6210 (32.1)	1811 (32.9)	6225 (30.7)	1663 (31.6)
24-59 months	7038 (22.6)	1295 (22.8)	4142 (21.4)	1214 (22.0)	4931 (24.3)	1386 (26.3)
Acute diarrhea (<14)	30651 (98.6)	5597 (98.7)	19055 (98.4)	5409 (98.2)	20052 (98.9)	5207 (98.8)
Duration (days)	2 (1, 4)	2 (1, 4)	3 (2, 4)	3 (1, 4)	3 (2, 4)	2 (1, 3)
Bloody diarrhea	1771 (6.5)	269 (5.1)	1316 (7.1)	408 (7.7)	1010 (6.4)	331 (7.3)
Vomiting	21130 (70.6)	3785 (71.2)	12072 (65.0)	3662 (69.7)	13628 (68.1)	3523 (67.4)
In-hospital deaths	157 (0.5)	33 (0.6)	73 (0.4)	24 (0.5)	89 (0.5)	32 (0.6)

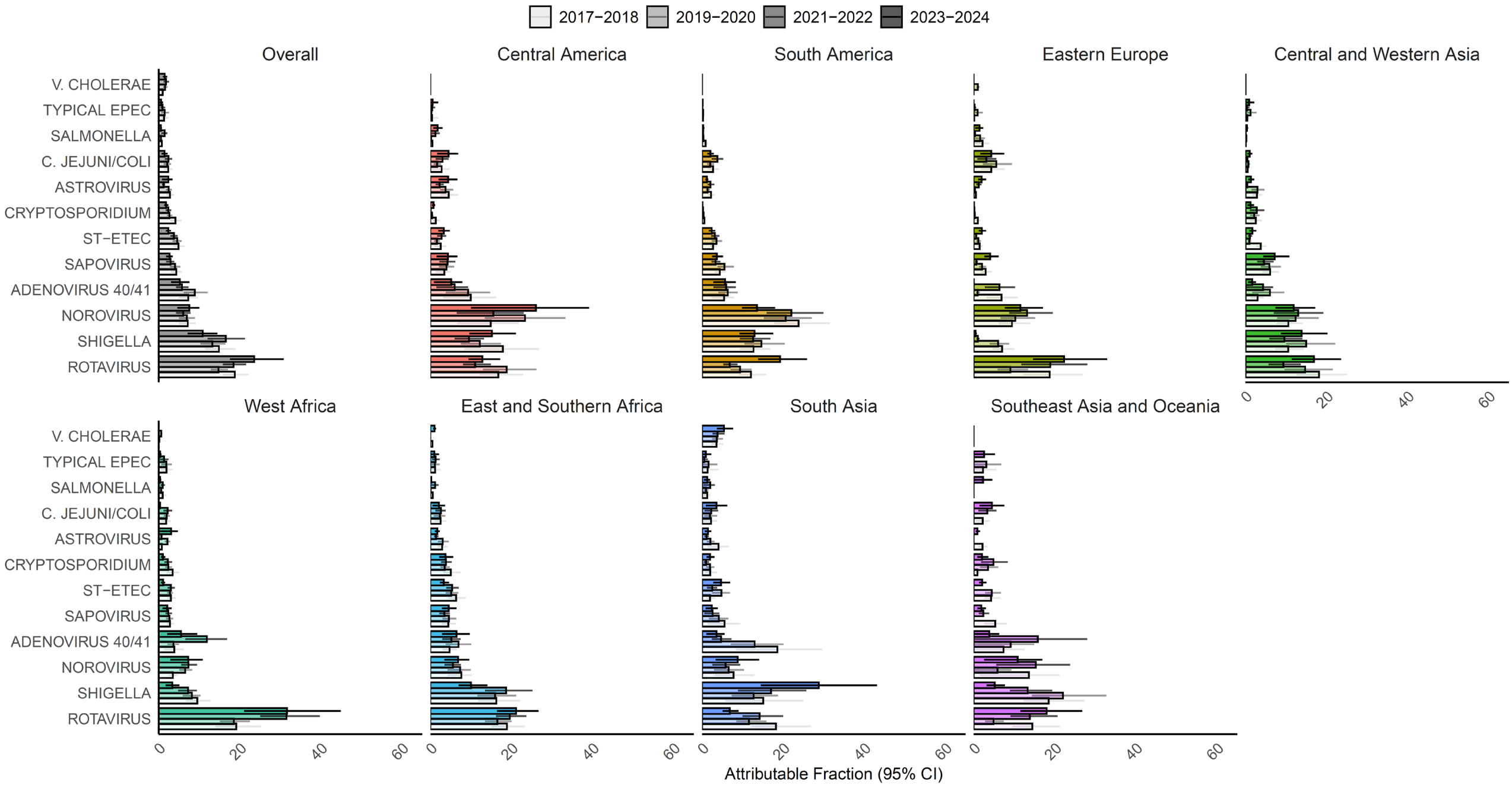
Attributable Fractions: by site (top four pathogens)



Attributable Fractions: overall and by geographic grouping



Attributable Fractions: countries that have introduced RV only



Etiology-specific mortality using GPDS data – a new approach

Because directly studying diarrheal deaths is difficult, hospitalized diarrhea has been used as a **"proxy"** -- severe enough to cause death *without access to care*. However, the etiology of deaths *despite* access to care should have a different distribution (and this subset is likely increasing). Therefore, we:

- Divided diarrheal deaths in each GPDS country into two groups: *without* and *despite* **access to care**
- Applied GPDS etiology distribution to the former, and **case fatality rate**-weighted distribution to the latter ($wAF_i = \frac{AF_i * CFR_i}{\sum_1^n AF_n * CFR_n}$)
- Summed etiology-specific death estimates for all GPDS countries in each WHO region
- Divide by the proportion of all LMIC diarrheal deaths from GPDS countries for that region (~75% of LMIC diarrheal deaths occurred in GPDS countries)

Estimating health care access among diarrheal deaths

First, we used publicly-available CHAMPS data to create a “high access” and “low access” scenario for Sub-Saharan Africa:

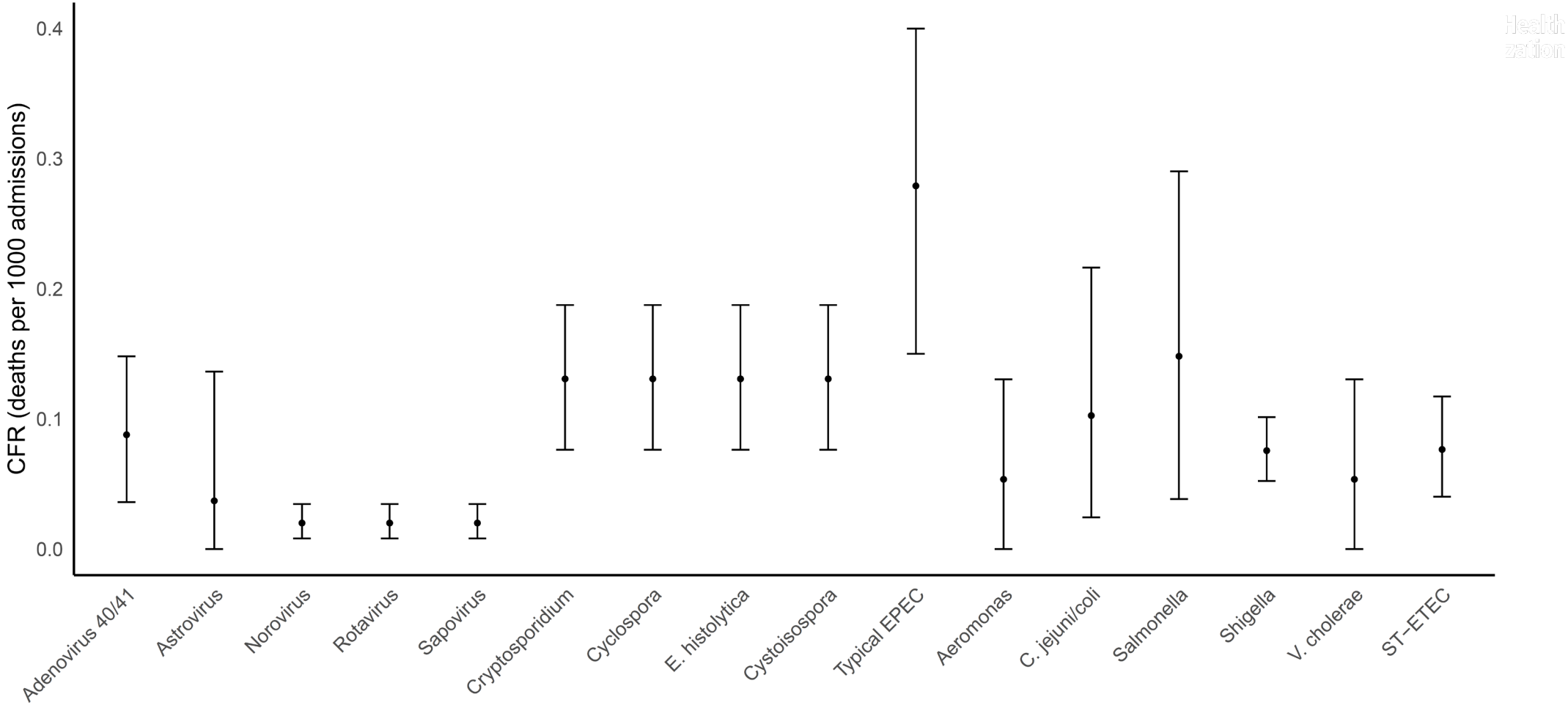
- High Access: Proportion of diarrheal deaths with maternal report of seeking care
- Low Access: Proportion with documented receipt of IV fluids

We assumed 100% access (High) and 95% access (Low) for the European region and then scaled between these extremes using the average Healthcare Access and Quality Index (HAQI; Lancet Global Health 2022) in each region.

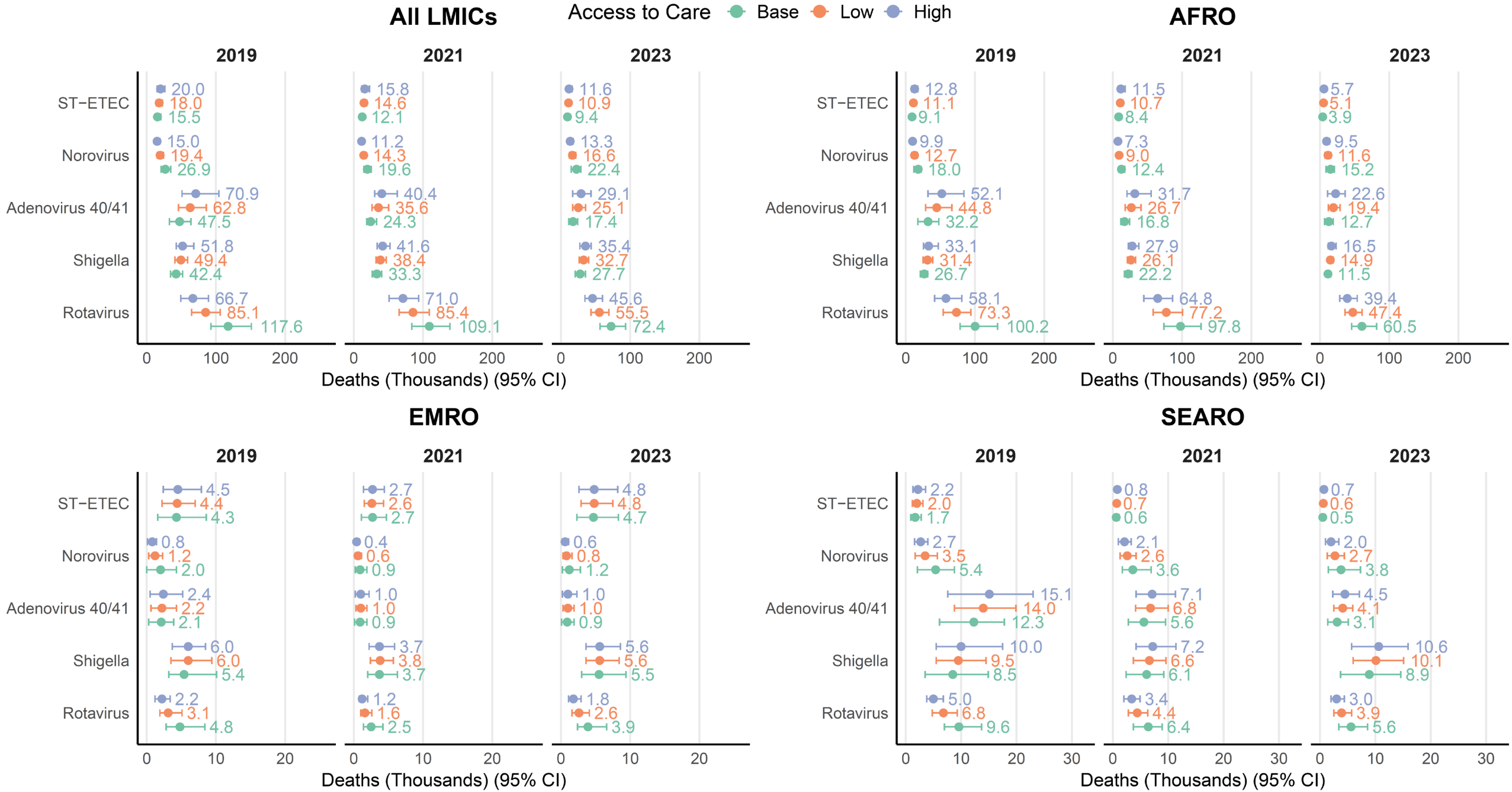
Region	Low Access Scenario	High Access Scenario
African	47.3	73.7
American	76.9	90.0
Eastern Mediterranean	51.3	75.9
European	95	100
Southeast Asia	67.3	84.7
Western Pacific	74.1	88.4

Derivation of pathogen-specific Case Fatality Rates (CFRs)

Individual-level meta-analysis of hospitalized children from three multisite diarrhea studies that used the same diagnostic platform (GEMS, VIDA, EFGH). For pathogens with insufficient deaths, we applied the lowest CFR from a pathogen in the same class (virus, bacteria, protozoa).



Etiology-specific diarrheal death estimates for 2019, 2021, 2023*



Conclusions

- Despite the impact of rotavirus vaccine introduction, **rotavirus remained the leading cause of under 5 hospitalizations and deaths** (under varying assumptions about access to care). Ongoing rotavirus vaccine introductions as well as improvement in the efficacy and coverage of rotavirus vaccination could further reduce diarrhoea morbidity and mortality.
- ***Shigella*, norovirus, and adenovirus** were other important causes of diarrhea hospitalizations in these settings.
- Looking forward, this network can provide a platform for understanding the impact of the ongoing introduction and optimization of rotavirus vaccines, as well as provide support for future enteric vaccines.

Acknowledgements

GPDS Network

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