

Supplementary tables & figures for: “Geographic and temporal trends in etiology-specific diarrhea burden among children in LMICs”

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Supplementary Table 1. Incidence per 100 person-years of moderate-to-severe diarrhea (MSD) by age group, study, and country site.

<i>Study</i>	<i>Region</i>	<i>Country</i>	<i>0-5 months</i>	<i>6-11 months</i>	<i>12-23 months</i>	<i>24-35 months</i>	<i>36-59 months</i>	<i>Rotavirus Vaccine*</i>
GEMS	Africa	Kenya	44.69 (38.31, 52.19)	70.88 (62.89, 80.06)	23.79 (21.37, 26.65)	12.08 (10.49, 13.96)	5.00 (4.22, 5.93)	No
		Mali	42.77 (29.54, 73.22)	119.12 (92.85, 186.47)	64.86 (50.98, 103.94)	29.83 (21.31, 53.28)	12.50 (7.25, 29.33)	No
		Mozambique	13.34 (10.15, 18.76)	21.46 (17.34, 28.42)	13.37 (10.63, 17.44)	6.10 (4.07, 9.71)	1.50 (0.82, 2.93)	No
		The Gambia	5.55 (3.93, 7.59)	25.73 (22.28, 30.67)	17.81 (15.90, 20.95)	5.58 (4.53, 6.91)	0.95 (0.65, 1.34)	No
	Asia	Bangladesh	18.01 (11.82, 34.29)	44.27 (32.07, 76.66)	21.91 (16.70, 36.02)	10.28 (7.57, 18.15)	3.55 (2.15, 8.24)	No
		India	49.48 (38.67, 68.40)	102.00 (83.34, 131.81)	65.08 (52.28, 84.21)	21.10 (16.08, 28.47)	9.37 (6.61, 14.74)	No
		Pakistan	24.43 (20.07, 30.18)	33.59 (28.25, 41.47)	16.91 (14.23, 20.63)	6.24 (4.97, 8.06)	2.26 (1.67, 2.96)	No
MAL-ED	Africa	Tanzania	14.35 (8.65, 23.81)	14.35 (8.65, 23.81)	1.44 (0.46, 4.45)	—	—	Partial
		South Africa	0.84 (0.12, 5.99)	1.69 (0.42, 6.75)	1.27 (0.41, 3.92)	—	—	Yes
	Asia	Bangladesh	20.95 (13.80, 31.82)	51.43 (39.39, 67.15)	26.19 (20.11, 34.11)	—	—	No
		India	5.29 (2.37, 11.77)	16.74 (10.68, 26.24)	16.30 (11.81, 22.50)	—	—	No
		Nepal	7.96 (4.14, 15.31)	32.60 (23.62, 44.99)	18.50 (13.67, 25.04)	—	—	No
		Pakistan	108.13 (91.23, 128.16)	106.50 (89.74, 126.40)	68.29 (58.71, 79.44)	—	—	No
	Latin America	Brazil	1.23 (0.17, 8.71)	0.00 (0.00, Inf)	0.61 (0.09, 4.30)	—	—	Yes
		Peru	25.77 (17.42, 38.14)	75.26 (59.83, 94.66)	70.62 (59.73, 83.49)	—	—	Yes
VIDA	Africa	Kenya	16.47 (13.49, 20.12)	26.04 (22.60, 30.77)	19.87 (17.56, 22.86)	8.85 (7.45, 10.38)	3.36 (2.75, 4.29)	Yes
		Mali	21.84 (11.41, 61.44)	77.73 (48.18, 201.53)	69.44 (45.01, 182.64)	57.52 (31.65, 182.04)	27.16 (9.93, 164.76)	Yes
		The Gambia	10.44 (7.55, 15.19)	68.54 (55.80, 87.30)	51.21 (41.70, 65.00)	14.15 (11.49, 17.90)	2.55 (1.80, 3.68)	Yes
EFGH	Africa	Kenya	—	86.17 (59.17, 141.68)	46.61 (33.18, 74.18)	24.89 (16.99, 43.94)	—	Yes
		Mali	—	21.94 (13.10, 44.24)	10.46 (6.95, 20.03)	3.02 (1.57, 6.75)	—	Yes
		The Gambia	—	20.46 (13.37, 34.00)	23.21 (15.94, 36.35)	8.49 (5.61, 14.38)	—	Yes
		Malawi	—	5.36 (3.57, 8.50)	4.44 (3.18, 6.90)	2.85 (1.84, 4.97)	—	Yes
	Asia	Bangladesh	—	17.36 (13.68, 24.85)	9.64 (7.43, 14.78)	3.76 (2.39, 6.87)	—	No
		Pakistan	—	14.66 (10.96, 20.19)	12.91 (9.94, 17.74)	4.54 (3.23, 6.58)	—	Yes
	Latin America	Peru	—	145.69 (96.01, 335.85)	132.89 (98.26, 276.21)	46.80 (29.50, 121.90)	—	Yes

*Rotavirus vaccine introduction status into national immunization program. No = vaccine not introduced at the time of the study.

Partial = vaccine introduced during the study. Yes = vaccine introduced prior to the start of the study.

Supplementary Table 2. Average attributable fractions (AFs) across studies and countries pre- and post-rotavirus vaccine introduction into the national immunization program, by age group.

Region	Rotavirus Vaccine*	Pathogen Group	Pathogen	6-11 months	12-23 months	24-35 months
Africa	No	Viruses	Adenovirus 40/41	4.63 (3.46, 6.10)	3.97 (2.81, 5.42)	2.29 (0.92, 3.90)
		Viruses	Astrovirus	3.33 (1.32, 6.52)	1.37 (0.73, 2.10)	1.27 (0.46, 2.45)
		Viruses	Norovirus GII	2.79 (1.76, 4.12)	0.57 (0.23, 0.98)	0.33 (0.00, 0.89)
		Viruses	Rotavirus	22.40 (17.97, 27.17)	17.17 (9.07, 30.87)	5.46 (3.61, 7.57)
		Viruses	Sapovirus	1.24 (0.60, 1.97)	1.33 (0.78, 1.99)	1.49 (0.54, 2.70)
		Bacteria	<i>Campylobacter jejuni</i> or <i>C. coli</i>	2.82 (1.71, 4.03)	0.98 (0.47, 1.68)	0.61 (0.00, 1.57)
		Bacteria	<i>Shigella</i> or EIEC	16.36 (11.63, 21.87)	36.65 (27.79, 50.71)	37.92 (32.96, 43.21)
		Bacteria	Typical EPEC	4.03 (1.99, 6.80)	1.45 (0.76, 2.41)	0.61 (0.00, 1.68)
		Bacteria	ST ETEC	14.54 (9.68, 19.69)	9.74 (7.81, 12.47)	10.19 (7.16, 13.06)
		Protozoa	<i>Cryptosporidium</i>	14.52 (11.18, 18.47)	7.27 (5.71, 9.30)	2.36 (1.00, 3.99)
	Yes	Viruses	Adenovirus 40/41	3.30 (2.50, 4.29)	3.71 (2.54, 5.25)	1.96 (1.07, 3.01)
		Viruses	Astrovirus	1.63 (1.08, 2.28)	8.12 (1.49, 14.83)	1.04 (0.45, 1.92)
		Viruses	Norovirus GII	4.22 (3.12, 5.52)	1.59 (1.07, 2.45)	0.17 (0.04, 0.37)
		Viruses	Rotavirus	9.74 (8.07, 12.11)	8.28 (6.81, 10.39)	8.63 (5.84, 12.08)
		Viruses	Sapovirus	1.82 (1.06, 2.69)	2.08 (1.51, 2.90)	0.96 (0.50, 1.52)
		Bacteria	<i>Campylobacter jejuni</i> or <i>C. coli</i>	9.58 (2.77, 16.53)	1.17 (0.55, 1.95)	0.98 (0.33, 1.90)
		Bacteria	<i>Shigella</i> or EIEC	16.45 (8.89, 23.98)	29.70 (27.08, 33.90)	34.95 (30.75, 39.96)
		Bacteria	Typical EPEC	3.64 (2.49, 5.13)	1.20 (0.68, 1.90)	0.44 (0.06, 1.16)
		Bacteria	ST ETEC	9.61 (7.75, 12.10)	11.03 (9.37, 13.36)	8.64 (6.75, 10.62)
		Protozoa	<i>Cryptosporidium</i>	11.78 (9.81, 14.27)	6.85 (5.56, 8.41)	3.96 (2.84, 5.34)
Asia	No	Viruses	Adenovirus 40/41	4.67 (3.38, 6.03)	4.78 (3.13, 6.74)	3.18 (1.77, 4.81)
		Viruses	Astrovirus	4.81 (3.26, 6.72)	2.82 (1.72, 4.21)	1.05 (0.32, 1.88)
		Viruses	Norovirus GII	3.05 (1.77, 4.55)	1.87 (1.00, 3.09)	0.39 (0.00, 1.25)
		Viruses	Rotavirus	28.35 (24.26, 32.80)	18.54 (15.74, 21.49)	9.14 (6.09, 12.67)
		Viruses	Sapovirus	4.74 (2.99, 6.86)	4.05 (2.33, 5.91)	0.55 (0.11, 1.24)
		Bacteria	<i>Shigella</i> or EIEC	16.24 (12.78, 19.87)	43.62 (39.62, 47.32)	56.45 (50.41, 62.20)
		Bacteria	<i>Campylobacter jejuni</i> or <i>C. coli</i>	3.60 (1.98, 5.75)	1.46 (0.78, 2.43)	0.50 (0.00, 1.19)
		Bacteria	Typical EPEC	0.99 (0.52, 1.53)	0.30 (0.07, 0.60)	0.20 (0.00, 0.65)
		Bacteria	ST ETEC	7.88 (5.65, 10.61)	10.03 (7.91, 12.64)	6.77 (4.35, 10.56)
		Protozoa	<i>Cryptosporidium</i>	4.33 (2.69, 6.30)	4.66 (3.28, 6.40)	3.21 (1.56, 5.87)
	Yes	Viruses	Adenovirus 40/41	6.17 (2.15, 11.43)	3.13 (0.39, 7.41)	1.04 (0.00, 3.60)
		Viruses	Astrovirus	1.89 (0.00, 5.14)	1.23 (0.00, 3.10)	4.49 (0.00, 14.47)
		Viruses	Norovirus GII	4.56 (1.04, 9.29)	1.95 (0.00, 6.69)	1.85 (0.00, 6.05)
		Viruses	Rotavirus	11.05 (5.50, 17.89)	5.90 (2.73, 10.04)	2.31 (0.00, 6.00)
		Viruses	Sapovirus	3.43 (0.00, 9.51)	2.32 (0.00, 6.35)	0.00 (0.00, 0.00)
		Bacteria	<i>Campylobacter jejuni</i> or <i>C. coli</i>	2.53 (0.28, 5.83)	3.12 (0.54, 6.68)	2.25 (0.00, 7.50)
		Bacteria	<i>Shigella</i> or EIEC	23.22 (15.84, 31.21)	37.46 (29.49, 45.80)	34.49 (21.46, 48.62)
		Bacteria	Typical EPEC	3.53 (0.53, 7.95)	1.37 (0.00, 3.58)	2.25 (0.00, 7.50)
		Bacteria	ST ETEC	9.65 (4.25, 16.23)	13.17 (7.95, 19.85)	19.49 (9.26, 31.30)
		Protozoa	<i>Cryptosporidium</i>	4.67 (1.67, 8.54)	5.28 (1.47, 10.75)	0.00 (0.00, 0.00)

Latin America	Yes	Viruses	Adenovirus 40/41	4.94 (2.01, 8.45)	3.45 (2.06, 5.11)	3.79 (0.64, 8.23)
		Viruses	Astrovirus	2.14 (0.00, 4.93)	2.58 (1.18, 4.08)	1.46 (0.00, 5.11)
		Viruses	Norovirus GII	4.64 (2.13, 8.12)	1.21 (0.46, 2.37)	0.00 (0.00, 0.00)
		Viruses	Rotavirus	2.85 (0.74, 5.61)	3.08 (1.76, 4.85)	3.99 (1.67, 9.29)
		Viruses	Sapovirus	1.58 (0.00, 3.98)	3.10 (1.62, 4.70)	0.48 (0.00, 2.97)
		Bacteria	<i>Campylobacter jejuni</i> or <i>C. coli</i>	4.79 (1.82, 8.54)	0.44 (0.00, 1.18)	0.00 (0.00, 0.00)
		Bacteria	<i>Shigella</i> or EIEC	10.83 (7.36, 14.45)	17.42 (14.34, 20.60)	22.63 (15.07, 31.98)
		Bacteria	Typical EPEC	0.08 (0.00, 0.46)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
		Bacteria	ST ETEC	2.46 (0.27, 5.20)	3.77 (2.18, 5.69)	2.43 (0.00, 6.11)
		Protozoa	<i>Cryptosporidium</i>	3.16 (0.85, 6.31)	3.24 (1.74, 4.99)	0.68 (0.00, 2.37)

*Rotavirus vaccine introduction status into national immunization program. No = vaccine had not yet been introduced in study-countries included. Yes = vaccine was introduced in study-countries included. Rotavirus vaccine was introduced during MAL-ED in Tanzania; this study-site was grouped with pre-rotavirus vaccine sites.

Supplementary Table 3. Top ranked pathogen and attributable fraction for each study site and age group, by rotavirus vaccine introduction status.

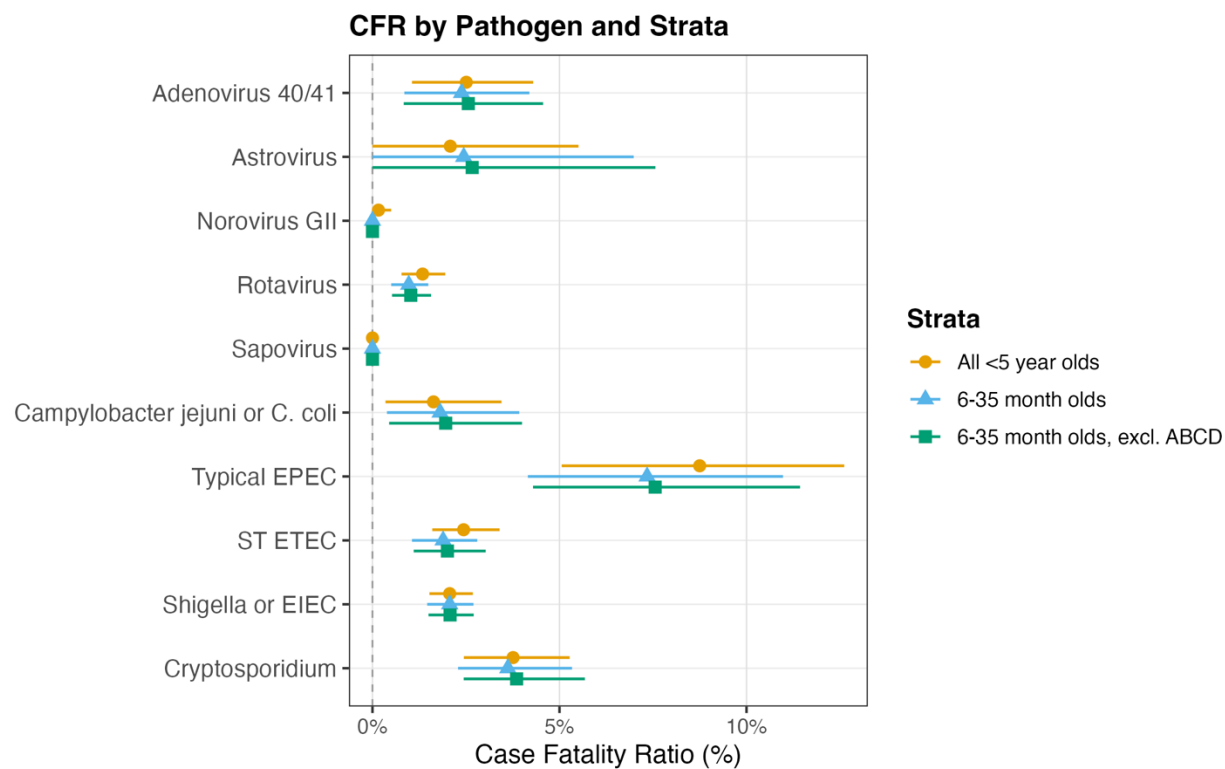
<i>Rotavirus vaccine introduction status</i>	<i>Study</i>	<i>Country</i>	<i>6-11 months</i>	<i>12-23 months</i>	<i>24-35 months</i>
Pre-rotavirus vaccine introduction	GEMS	Bangladesh	Rotavirus (27.26%; 95% CI: 19.06 - 37.33)	<i>Shigella or EIEC</i> (64.36%; 95% CI: 54.68 - 73.39)	<i>Shigella or EIEC</i> (82.24%; 95% CI: 71.26 - 90.82)
	GEMS	India	Rotavirus (34.31%; 95% CI: 26.83 - 41.80)	Rotavirus (28.39%; 95% CI: 22.79 - 34.44)	<i>Shigella or EIEC</i> (45.76%; 95% CI: 37.64 - 53.52)
	GEMS	Kenya	Rotavirus (19.27%; 95% CI: 13.50 - 25.42)	<i>Shigella or EIEC</i> (23.01%; 95% CI: 17.94 - 28.33)	<i>Shigella or EIEC</i> (24.55%; 95% CI: 17.97 - 31.65)
	GEMS	Mali	<i>Cryptosporidium</i> (21.60%; 95% CI: 13.85 - 31.70)	<i>Shigella or EIEC</i> (43.79%; 95% CI: 33.97 - 55.51)	<i>Shigella or EIEC</i> (30.86%; 95% CI: 22.33 - 41.03)
	GEMS	Mozambique	Rotavirus (35.72%; 95% CI: 27.03 - 45.16)	<i>Shigella or EIEC</i> (40.71%; 95% CI: 31.07 - 51.05)	<i>Shigella or EIEC</i> (53.53%; 95% CI: 39.40 - 68.44)
	GEMS	Pakistan	Rotavirus (29.16%; 95% CI: 22.72 - 35.99)	<i>Shigella or EIEC</i> (43.58%; 95% CI: 37.56 - 49.92)	<i>Shigella or EIEC</i> (42.21%; 95% CI: 33.08 - 51.59)
	GEMS	The Gambia	Rotavirus (25.12%; 95% CI: 18.46 - 31.94)	<i>Shigella or EIEC</i> (42.40%; 95% CI: 35.50 - 49.27)	<i>Shigella or EIEC</i> (42.72%; 95% CI: 33.17 - 52.07)
	MAL-ED	Bangladesh	Rotavirus (38.46%; 95% CI: 26.33 - 52.22)	<i>Shigella or EIEC</i> (50.91%; 95% CI: 37.94 - 63.76)	--
	MAL-ED	India	<i>Shigella or EIEC</i> (29.41%; 95% CI: 12.80 - 54.19)	<i>Shigella or EIEC</i> (66.67%; 95% CI: 49.23 - 80.49)	--
	MAL-ED	Nepal	Rotavirus (24.32%; 95% CI: 13.17 - 40.52)	<i>Shigella or EIEC</i> (40.48%; 95% CI: 26.86 - 55.74)	--
	MAL-ED	Pakistan	Sapovirus (12.00%; 95% CI: 7.37 - 18.95)	<i>Shigella or EIEC</i> (13.33%; 95% CI: 8.94 - 19.42)	--
	MAL-ED	Tanzania*	ST ETEC (33.33%; 95% CI: 14.60 - 59.40)	Rotavirus (33.33%; 95% CI: 4.34 - 84.65)	--
	EFGH	Bangladesh	Rotavirus (48.45%; 95% CI: 38.67 - 58.54)	<i>Shigella or EIEC</i> (43.35%; 95% CI: 32.69 - 53.30)	<i>Shigella or EIEC</i> (55.56%; 95% CI: 37.75 - 72.90)
	MAL-ED	Brazil	[no MSD cases detected]	Astrovirus (0.00%; 95% CI: 0.00 - 100.00)	--
	MAL-ED	Peru	<i>Campylobacter jejuni or C. coli</i> (8.57%; 95% CI: 3.90 - 17.79)	<i>Shigella or EIEC</i> (33.83%; 95% CI: 26.31 - 42.28)	--
Post-rotavirus vaccine introduction	MAL-ED	South Africa	<i>Campylobacter jejuni or C. coli</i> (50.00%; 95% CI: 5.89 - 94.11)	Astrovirus (50.00%; 95% CI: 5.89 - 94.11)	--
	VIDA	Kenya	ST ETEC (11.12%; 95% CI: 7.99 - 14.49)	<i>Shigella or EIEC</i> (29.27%; 95% CI: 25.48 - 33.57)	<i>Shigella or EIEC</i> (26.35%; 95% CI: 20.75 - 32.31)
	VIDA	Mali	<i>Cryptosporidium</i> (18.22%; 95% CI: 13.88 - 23.06)	<i>Shigella or EIEC</i> (26.91%; 95% CI: 22.59 - 31.19)	<i>Shigella or EIEC</i> (25.15%; 95% CI: 19.09 - 31.64)
	VIDA	The Gambia	<i>Shigella or EIEC</i> (20.72%; 95% CI: 15.25 - 26.41)	<i>Shigella or EIEC</i> (48.09%; 95% CI: 41.35 - 54.25)	<i>Shigella or EIEC</i> (43.26%; 95% CI: 37.29 - 49.12)
	EFGH	Kenya	Rotavirus (11.13%; 95% CI: 7.93 - 14.79)	<i>Shigella or EIEC</i> (20.89%; 95% CI: 16.01 - 26.45)	<i>Shigella or EIEC</i> (24.98%; 95% CI: 16.95 - 33.32)
	EFGH	Malawi	Rotavirus (12.91%; 95% CI: 4.67 - 24.20)	<i>Shigella or EIEC</i> (16.93%; 95% CI: 8.20 - 26.23)	<i>Shigella or EIEC</i> (24.62%; 95% CI: 12.14 - 39.08)
	EFGH	Mali	<i>Cryptosporidium</i> (23.26%; 95% CI: 14.14 - 33.04)	<i>Shigella or EIEC</i> (43.54%; 95% CI: 30.29 - 55.72)	<i>Shigella or EIEC</i> (27.36%; 95% CI: 6.49 - 52.78)
	EFGH	Pakistan	<i>Shigella or EIEC</i> (23.22%; 95% CI: 15.84 - 31.21)	<i>Shigella or EIEC</i> (37.46%; 95% CI: 29.49 - 45.80)	<i>Shigella or EIEC</i> (34.49%; 95% CI: 21.46 - 48.62)
	EFGH	Peru	<i>Shigella or EIEC</i> (15.94%; 95% CI: 11.23 - 21.00)	<i>Shigella or EIEC</i> (18.42%; 95% CI: 14.01 - 23.46)	<i>Shigella or EIEC</i> (22.63%; 95% CI: 15.07 - 31.98)
	EFGH	The Gambia	<i>Shigella or EIEC</i> (17.38%; 95% CI: 10.00 - 25.91)	<i>Shigella or EIEC</i> (51.93%; 95% CI: 43.82 - 60.80)	<i>Shigella or EIEC</i> (72.95%; 95% CI: 58.93 - 86.15)

* Rotavirus vaccine was introduced during MAL-ED in Tanzania.

Supplementary Table 4. Average case fatality ratios (CFR) for pathogen classes and individual pathogens across studies.

<i>Pathogen Group</i>	<i>Pathogen</i>	<i>14-day CFR % (95% CI)</i>	<i>90-day CFR % (95% CI)</i>	<i>90-day Hospitalized CFR % (95% CI)</i>
Viruses	All viruses	0.95 (0.62, 1.37)	1.42 (0.97, 2.01)	3.78 (2.05, 6.10)
Bacteria	All bacteria	1.46 (1.05, 1.91)	2.52 (2.02, 3.06)	10.06 (7.64, 12.72)
Protozoa	All protozoa	2.01 (1.01, 3.27)	3.55 (2.34, 4.96)	12.95 (7.38, 18.20)
Viruses	Adenovirus 40/41	1.97 (0.67, 3.63)	2.51 (1.06, 4.30)	11.03 (4.35, 19.26)
Viruses	Astrovirus	0.00 (0.00, 0.00)	2.08 (0.00, 5.51)	15.08 (0.00, 39.78)
Viruses	Norovirus GII	0.00 (0.00, 0.00)	0.16 (0.00, 0.50)	0.00 (0.00, 0.00)
Viruses	Rotavirus	1.06 (0.58, 1.64)	1.34 (0.78, 1.95)	2.24 (0.91, 3.76)
Viruses	Sapovirus	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Bacteria	<i>Campylobacter jejuni</i> or <i>C. coli</i>	0.85 (0.00, 2.23)	1.63 (0.35, 3.45)	12.18 (2.38, 25.00)
Bacteria	ST ETEC	1.25 (0.65, 2.03)	2.44 (1.60, 3.40)	7.59 (3.56, 11.99)
Bacteria	<i>Shigella</i> or EIEC	1.21 (0.77, 1.70)	2.06 (1.52, 2.68)	9.57 (6.47, 12.95)
Bacteria	Typical EPEC	5.14 (2.56, 8.06)	8.75 (5.06, 12.61)	27.85 (15.73, 41.62)
Protozoa	<i>Cryptosporidium</i>	2.13 (1.08, 3.41)	3.76 (2.44, 5.27)	13.09 (7.85, 19.20)

CFRs for bacteria also include *Salmonella*, *V. cholerae*, and *Aeromonas*, and CFRs for protozoa also include *Isospora*, *E. histolytica*, and *Cyclospora*. Studies include GEMS, VIDA, ABCD, and EFGH.



Supplementary Figure 1. Sensitivity analysis of the 90-day CFRs, comparing including the full age range (<5 years), restricting to the age range in EFGH (6-35 months), and excluding ABCD given differing eligibility criteria for cases.