

Insights on cholera and control from Uvira, South Kivu, DRC

Update on Study Progress and Activities

23 May 2024



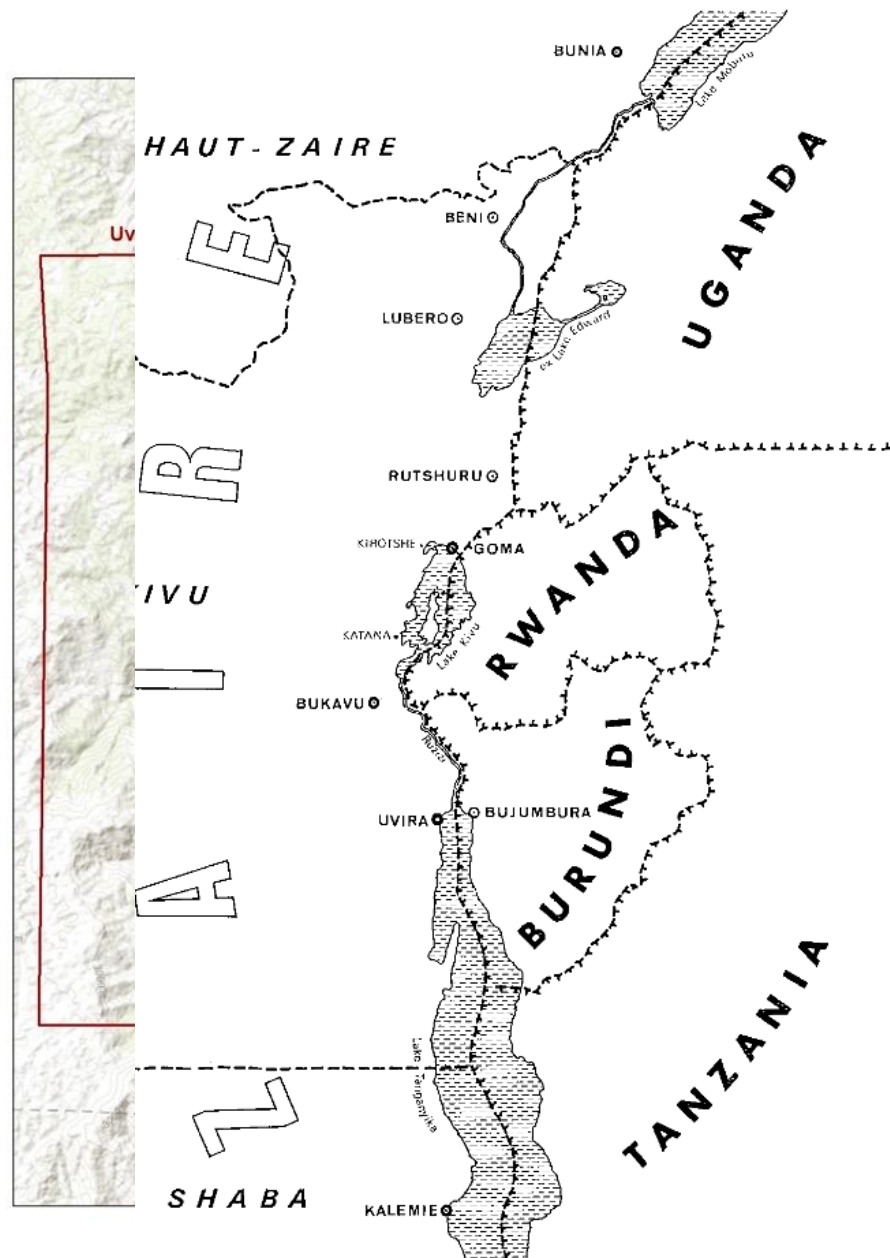


Figure 1.

Map of the area involved by cholera during 1978.

Ann. Soc. belge Méd. trop.
1979, 59, 391-400

CHOLERA IN EASTERN ZAIRE, 1978

by

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Summary — The Eastern Zaire cholera epidemic in 1978 originated in Tanzania. It was limited to the Lake areas and water played a major role in transmission of infection. Prophylactic and therapeutic measures are discussed. *Vibrio cholerae* el Tor was isolated from patients and healthy carriers. Antimicrobial susceptibility was determined.

KEYWORDS : Cholera; Zaire.

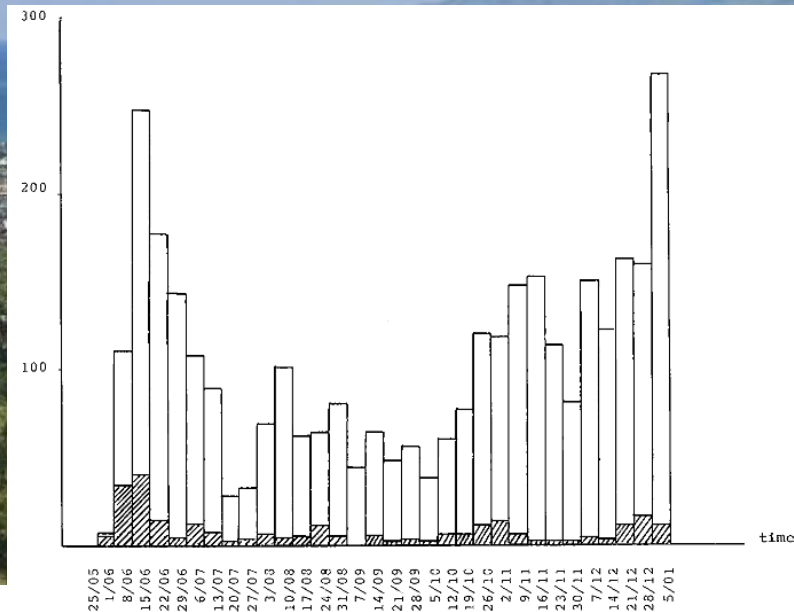
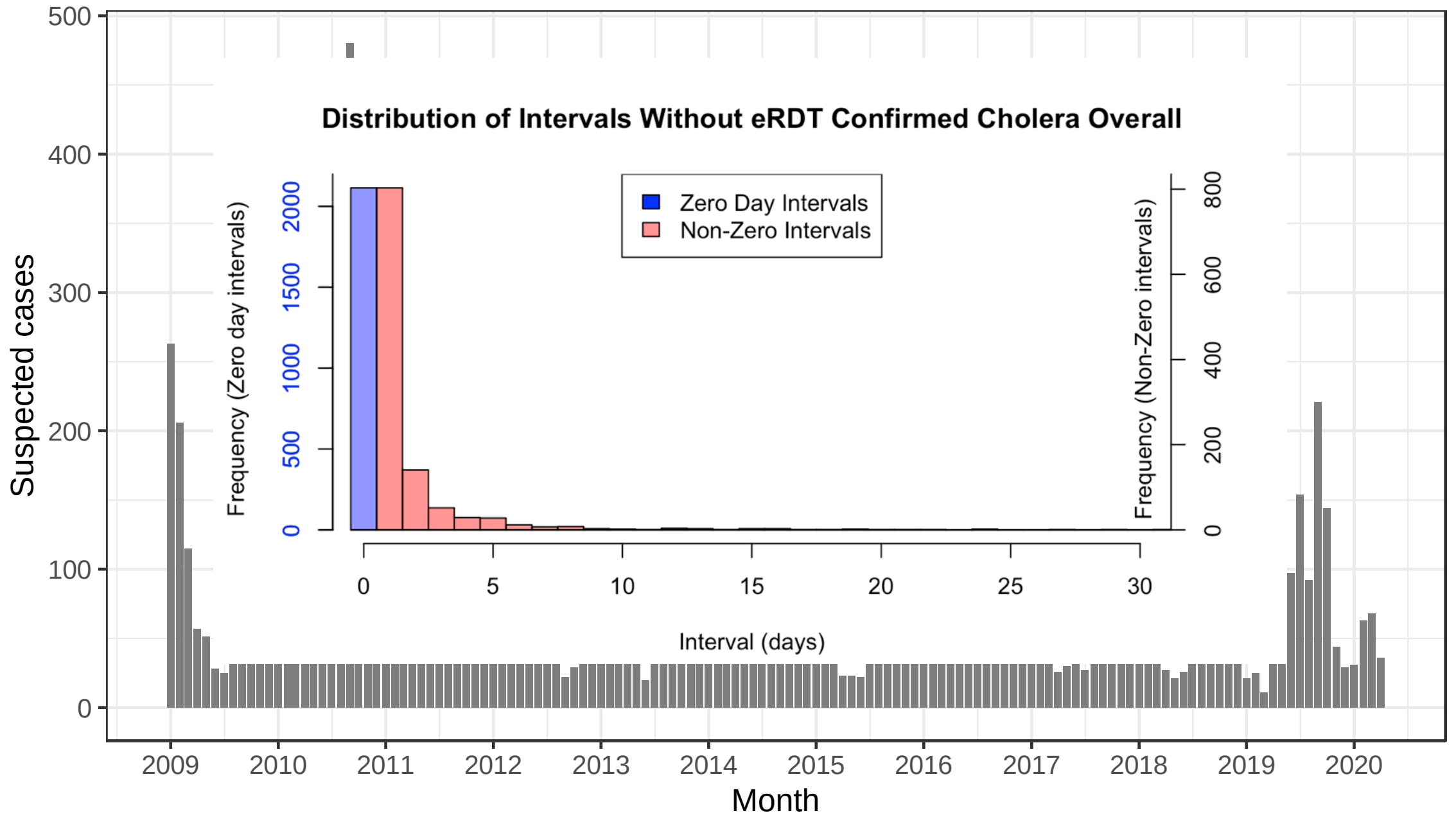


Figure 2.

Morbidity (3,295 cases) and mortality (258 cases) as recorded weekly in treatment-centers in the Uvira, Ruzizi and Ubembe area, between 25 May 1978 and 5 January 1979.

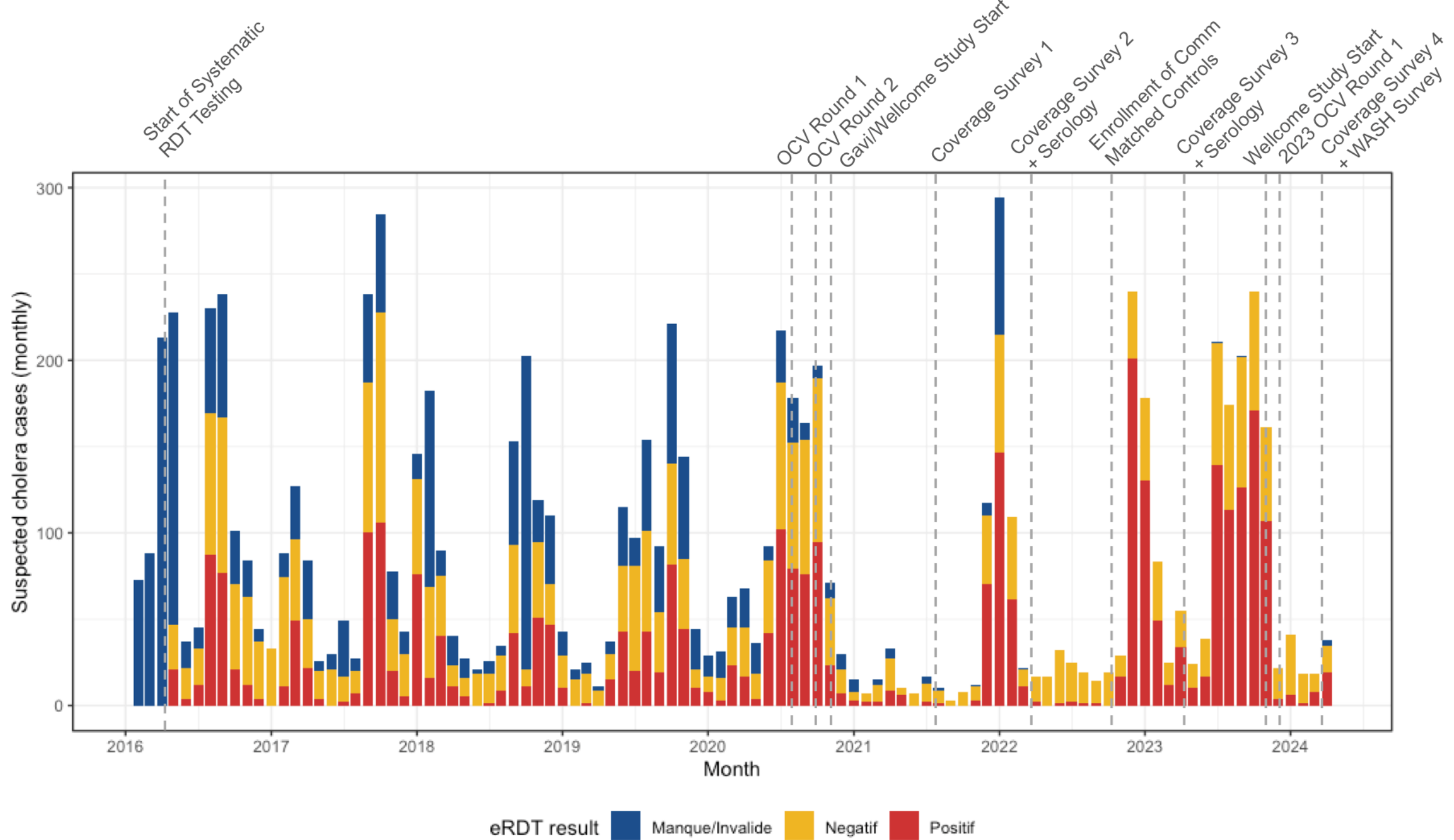




Study objectives

1. To enhance the cholera surveillance system in Uvira to estimate the impact of mass vaccination on lab-confirmed cholera incidence and mortality.
2. To conduct serial cross-sectional serosurveys after vaccination to estimate the seroincidence of *V. cholerae* infection in Uvira and contextualize the primary results based on clinical cholera cases.
3. To use phenotypic and molecular methods to describe the changes in the *V. cholerae* population after vaccination in both human and environmental samples in Uvira.
4. To estimate household transmission of *V. cholerae* and identify environmental and WASH-related risk factors for transmission & symptomatic cholera.







Clinical and Lab Surveillance

Recruitment of suspected cases

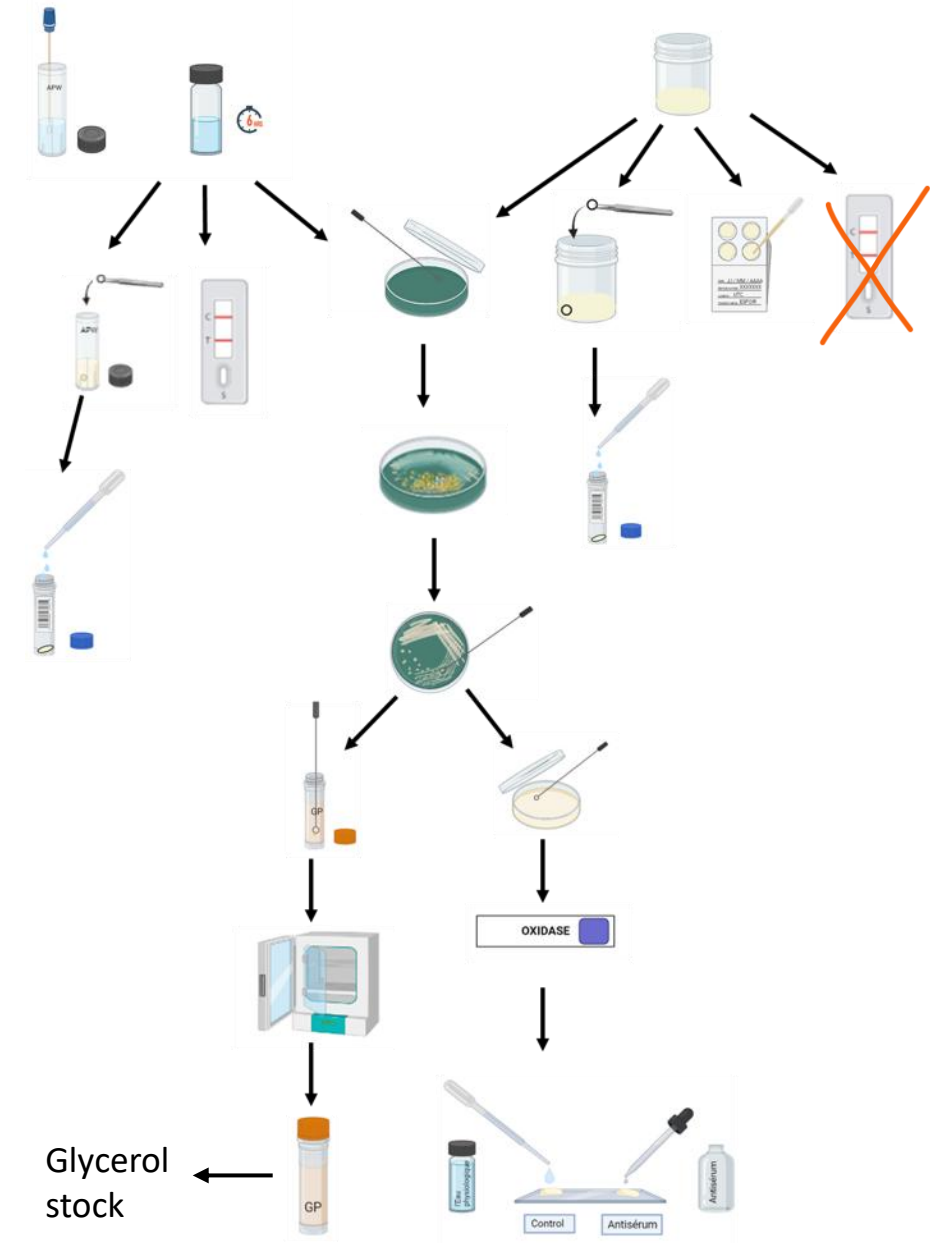
- Enrolment and testing of all acute watery diarrhea cases in the two public cholera treatment centers Uvira
- All eligible suspected cases recruited into case control study
- Stool sample and rectal swabs collected from all*

**Discussed transition away from rectal swab at last steering committee meeting and are currently testing differences between enriched rectal swabs, enriched stool and direct stool*



Testing of suspected cases

- Stool and rectal swab taken from each
- RDT from rectal swab*
- 2 x wet filter paper (*backup*)
- 1 x stool spot on dry filter paper (*qPCR*)
- Culture from both swab and stool



*Discussed transition away from rectal swab at last steering committee meeting and are currently testing differences between enriched rectal swabs, enriched stool and direct stool

Development, validation, & roll-out of qPCR

- Collaborating with Institute Pasteur, CDC National Listeria, Yersinia, Vibrio and Enterobacterales Reference Lab and MSF.
 - Analytical specificity & sensitivity being finalised on DNA libraries from the CDC and Institut Pasteur
 - Limit of detection: 7.3 gene copies per reaction
- Clinical/diagnostic sensitivity & specificity is being finalised having collaborated with Institut Pasteur on recently extracted clinical samples from the summer 2023 outbreak i.e. minimizing impact of delay in sample collection-extraction-molecular testing.
- Several months of remote training of INRB partners for quality assurance of qPCR before rolling out systematic testing.

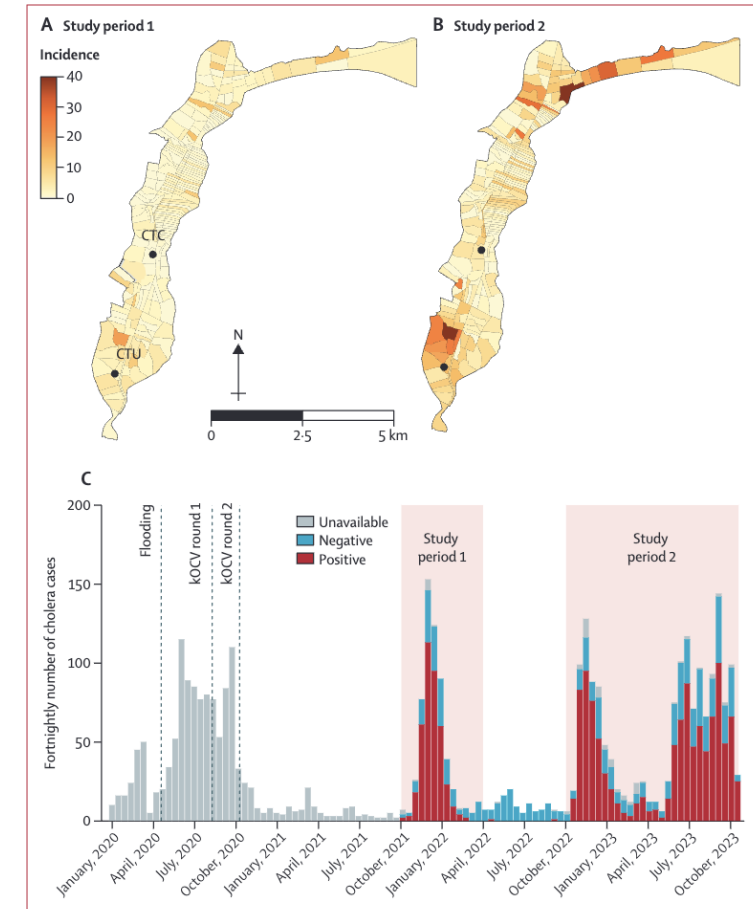
Target	Rationale	Present in	Absent in
O1-rfb	-O1 serogroup	Toxigenic <i>V. cholerae</i>	Non-O1 <i>V. cholerae</i> including -O139 strains
ctxA	Toxigenic gene	Toxigenic <i>V. cholerae</i> Some toxigenic enteropathogens including ETEC	Non-toxigenic <i>V. cholerae</i>
toxR	<i>V. cholerae</i> species specific	<u>All</u> <i>V. cholerae</i>	Non-cholerae species of vibrios and non-vibrios

Measuring direct effectiveness of one dose of Euvichol+: a matched case-control study

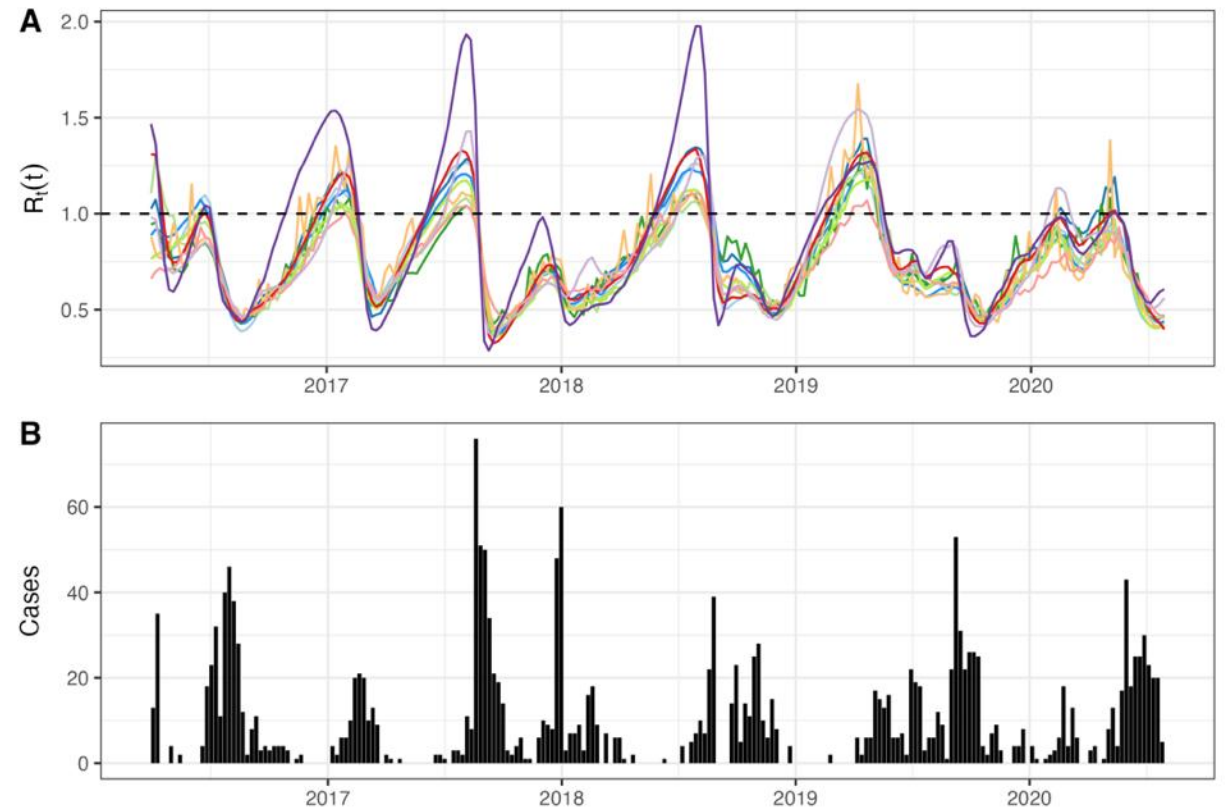
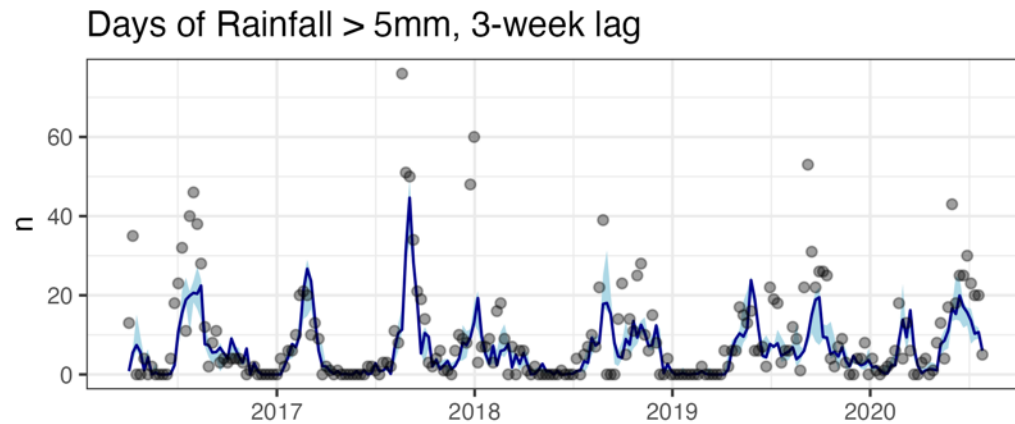
	Case group	Control group	Unadjusted vaccine effectiveness (95% CI)	Adjusted vaccine effectiveness (95% CI)
12–36 months after vaccination				
Overall	573 (419)	1998 (763)	47.8% (34.6 to 58.4)	48.2% (34.8 to 58.8)
1–4 years old	96 (61)	263 (129)	52.4% (22.5 to 70.8)	49.8% (15.6 to 70.2)
≥5 years old	463 (332)	1534 (584)	46.7% (31.8 to 58.4)	47.8% (32.8 to 59.5)
12–17 months after vaccination (study period 1)				
Overall	219 (170)	704 (300)	54.4% (34.4 to 68.3)	52.7% (31.4 to 67.4)
1–4 years old	34 (23)	83 (44)	68.3% (19.6 to 87.5)	73.5% (28.9 to 90.1)
≥5 years old	179 (141)	568 (243)	50.9% (28.0 to 66.6)	46.9% (21.0 to 64.3)
24–36 months after vaccination (study period 2)				
Overall	354 (249)	1294 (463)	43.2% (24.0 to 57.6)	44.7% (24.8 to 59.4)
1–4 years old	62 (38)	180 (85)	42.8% (–2.2 to 68.0)	32.9% (–30.7 to 65.5)
≥5 years old	284 (191)	966 (341)	43.4% (21.7 to 59.0)	47.5% (26.1 to 62.6)

Data are n (effective n) unless otherwise specified. Effective n is the sample size that effectively contributes to estimates of effectiveness in the conditional logistic regression models. Those participants in matched case-control sets where all people have the same vaccination status do not contribute to the estimates, nor do those who either do not know their vaccination status or the number of doses they received. For adjusted vaccine effectiveness, in study period 1 and in analyses combining data from both study periods, we only adjusted for age as a continuous variable.

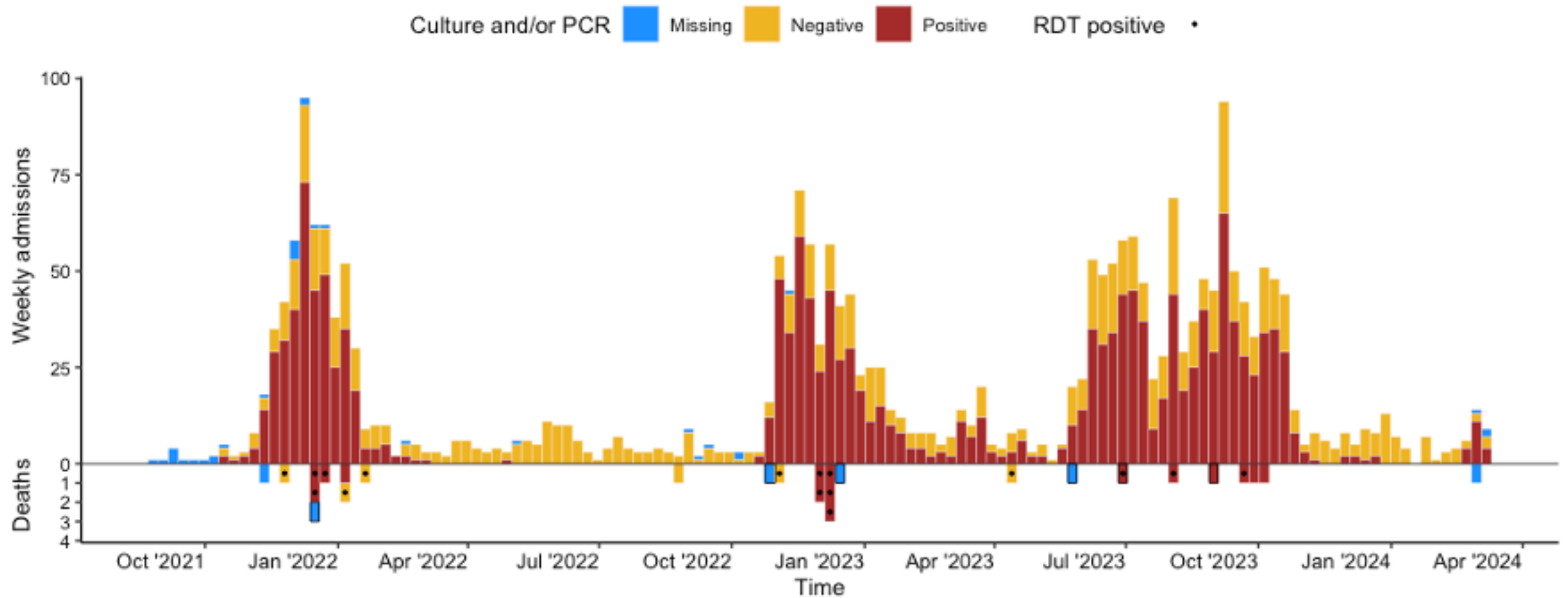
Table 3: Effectiveness of a single dose of oral cholera vaccine by age and time since vaccination



Initial model fits to understand impact of 2020 vaccination campaign



Mortality surveillance



Lessons learned about mortality

- Older individuals far more likely to die of cholera in CTC
- Many dying long after admission
- CFR among those taking antibiotics before admission appears lower than others
- Vaccine effectiveness against death 85.5% (95% CI 49.0-97.7%)

Table 1. Characteristics of Patients With Suspected Cholera who Died and Survived in the Cholera Treatment Facilities, Uvira, September 2021 to September 2023

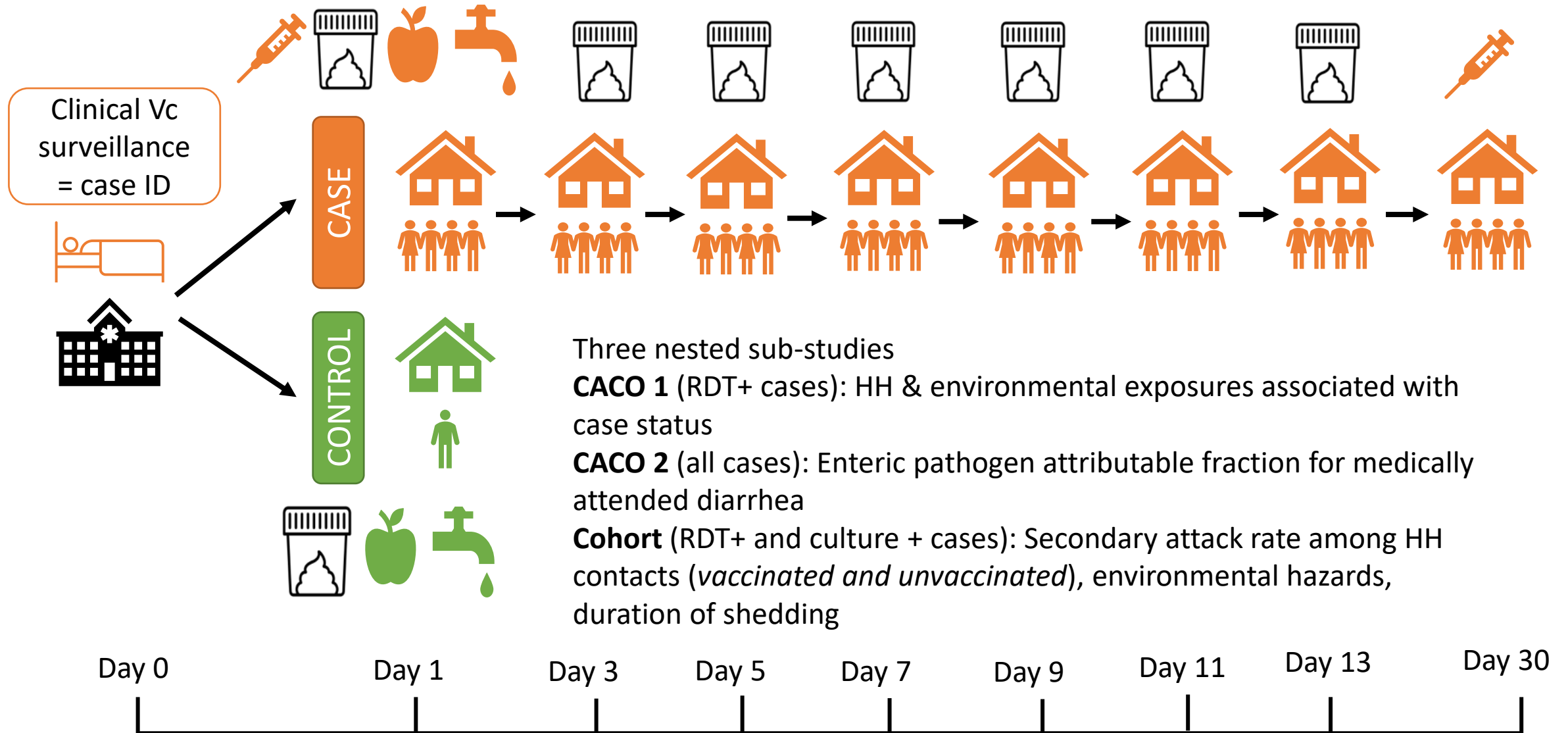
Characteristic	Overall, N = 2209	Suspected Cholera Deaths, N = 18	Suspected Cholera Cases (Survivors), N = 2191	PValue	Suspected Case Fatality Ratio
Age (y), median (IQR)	17.0 (7.0, 34.0)	40.0 (21.0, 67.8)	17.0 (7.0, 34.0)	<.001	0.81%
Age group (y)				<.001	
<5	384 (17.4%)	1 (5.6%)	383 (17.5%)		0.26%
5-14	608 (27.5%)	1 (5.6%)	607 (27.7%)		0.16%
15-59	1024 (46.4%)	8 (44.4%)	1016 (46.4%)		0.78%
≥60 y	193 (8.7%)	8 (44.4%)	185 (8.4%)		4.12%
Duration of hospitalization, d				<.001	
<1	130 (6.0%)	7 (38.9%)	123 (5.7%)		5.38%
1	542 (24.8%)	6 (33.3%)	536 (24.7%)		1.11%
≥2	1512 (69.2%)	5 (27.8%)	1507 (69.6%)		0.33%
Missing	25	0	25		
Comorbidities ^b				.490	
No	1449 (91.9%)	7 (87.5%)	1442 (92.0%)		0.48%
Yes	127 (8.1%)	1 (12.5%)	126 (8.0%)		0.79%
Missing	633	10	623		
Use of antibiotics before admission ^d				.232	
No	1163 (52.6%)	12 (66.7%)	1151 (52.5%)		1.03%
Yes	1046 (47.4%)	6 (33.3%)	1040 (47.5%)		0.57%
APW-enriched RDT				.081	
Negative	807 (38.1%)	3 (17.6%)	804 (38.2%)		0.37%
Positive	1312 (61.9%)	14 (82.4%)	1298 (61.8%)		1.07%
Missing	90	1	89		
Culture/PCR-confirmed cholera				.818	
Negative	751 (34.5%)	6 (35.3%)	703 (34.5%)		0.80%
Positive	1428 (65.5%)	11 (64.7%)	1417 (65.5%)		0.77%
Missing	30	1	29		
Vaccination status				> .999 ^e	
Not vaccinated	1688 (81.0%)	11 (84.6%)	1677 (80.9%)		0.65%
At least 1 dose	397 (19.0%)	2 (15.4%)	395 (19.1%)		0.50%
Missing	124	5	129		



A photograph showing three men in blue Johns Hopkins University polo shirts. The man on the left is wearing a face mask and blue gloves, looking down at his hands. The man in the middle is sitting on the floor, looking at papers. The man on the right is sitting on a yellow plastic chair, looking at a tablet. They are all wearing lanyards with ID badges. The background is a plain, light-colored wall.

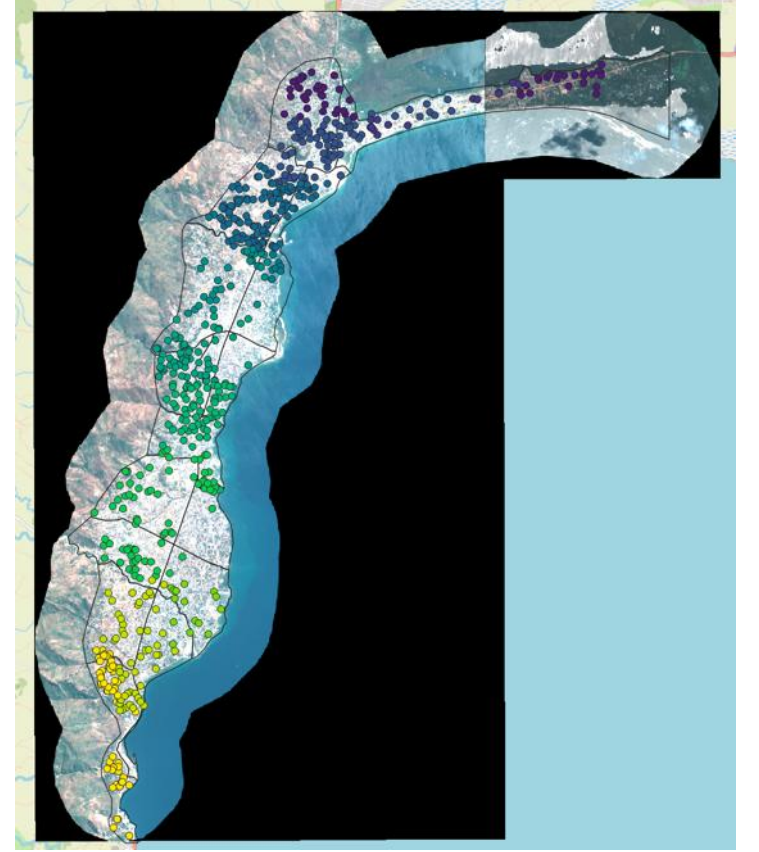
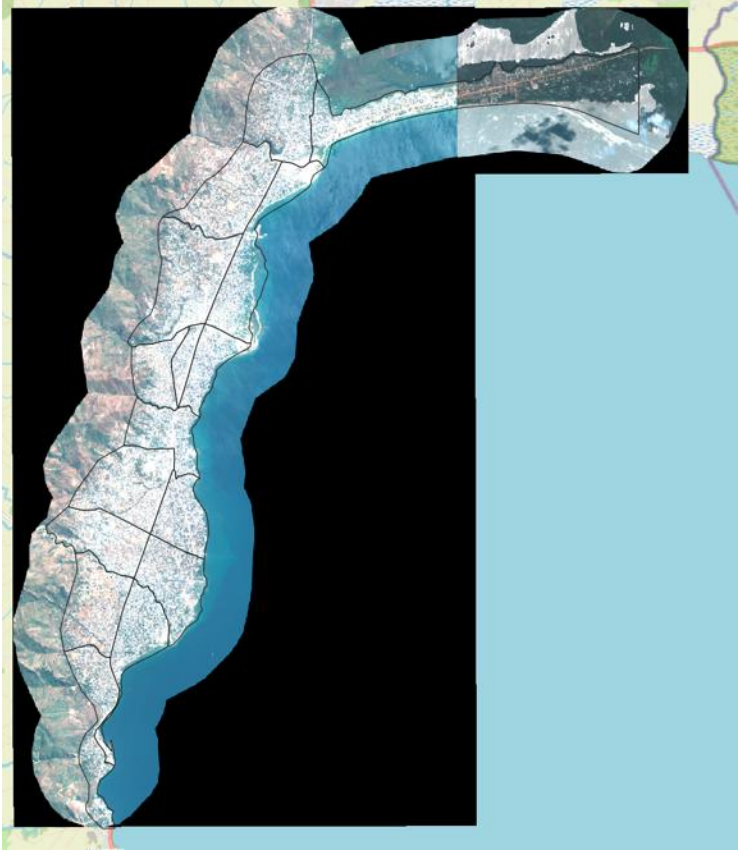
Household Studies

Household sub-studies



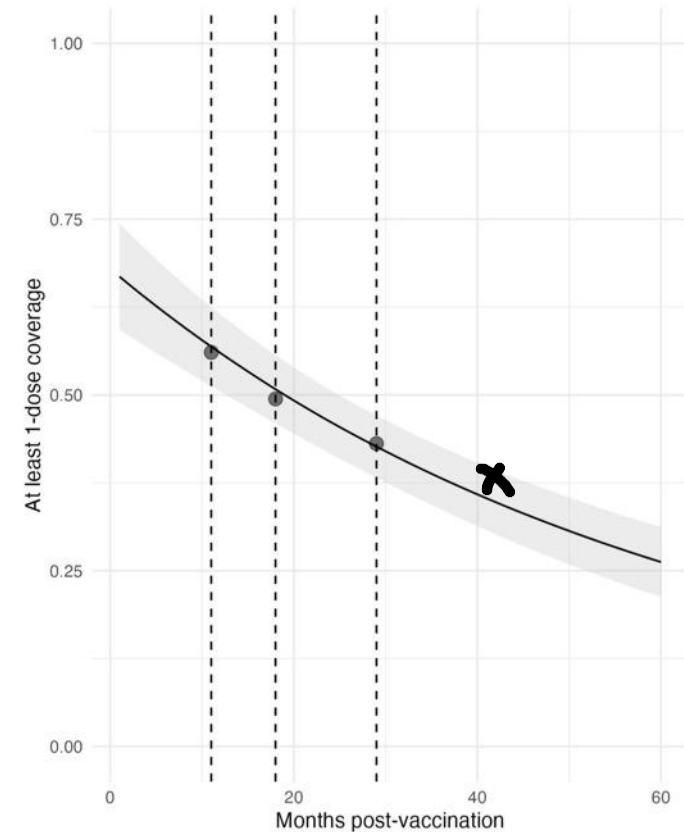
A photograph of three people in a rural setting. A woman in a green shirt and patterned skirt sits on a wooden chair, facing a man in a blue polo shirt who is sitting on a red plastic chair. They are both looking down at a small object in the man's hands. A woman in a blue shirt and black headwrap sits on a green plastic chair, also looking down. In the background, there are brick buildings, a stone wall, and a tree. The text "Community Surveys" is overlaid in white.

Community Surveys



Coverage over time since vaccination

Round	Months after 2nd dose campaign**	Sample Size	Coverage, at least one dose (95% CI)	Coverage, at least two doses (95% CI)
Survey 1	11	2292	55% (51-60)	23% (20-27)
Survey 2	19	3583	47% (44-50)	20% (18-23)
Survey 3	32	2864	39% (36-43)	10% (8-12)
Survey 4	41	2257	37% (33-41)	11% (9-14)



Koyuncu A, Bugeme P et al, 2024

Serologic surveys to measure infection incidence

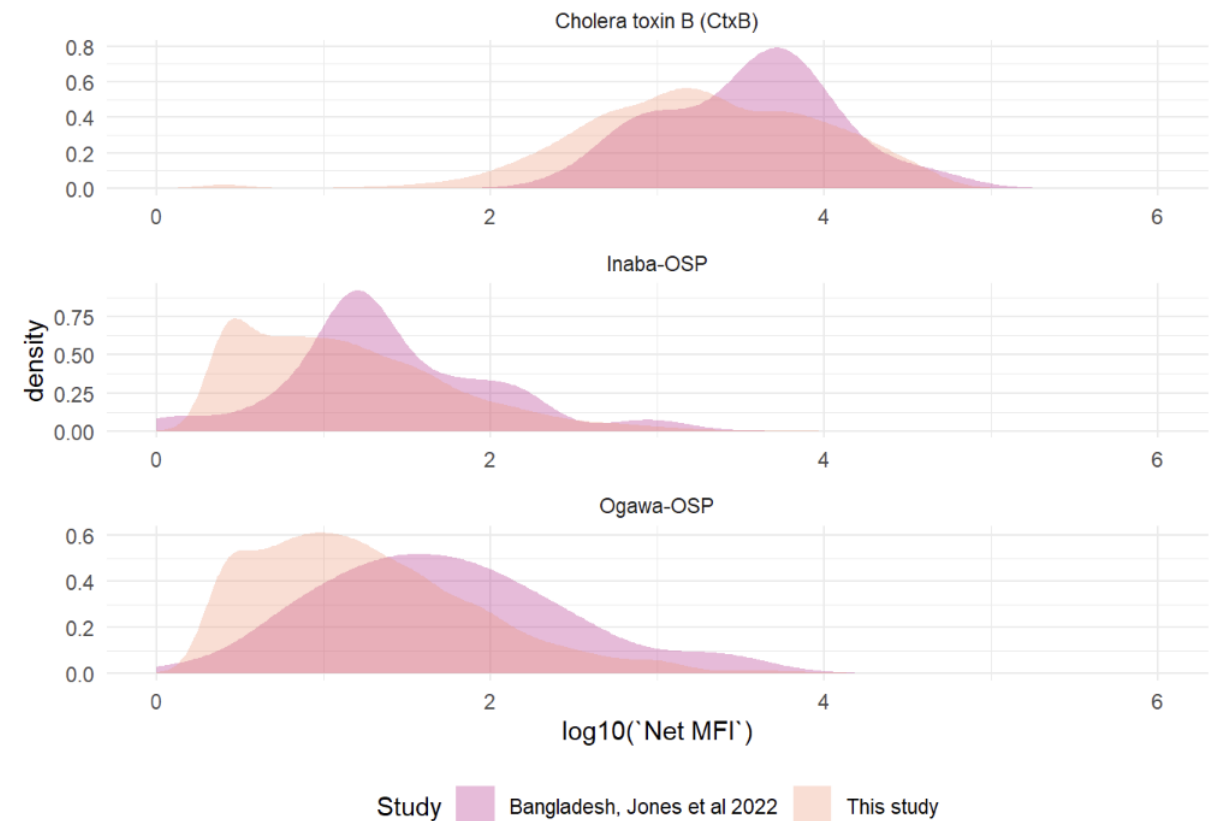
Round	Months after 2nd dose campaign	Persons enrolled	Under 5 year olds enrolled
Survey 1	11.0 - 11.7	-	-
Survey 2	19.5 - 20.6	2,376	197
Survey 3	32.5 - 33.2	2,208	254



Seroincidence R1

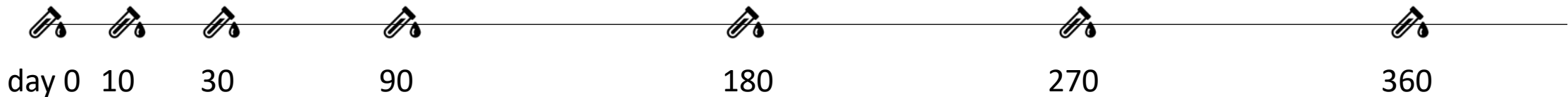
- Unadjusted 200-day seroincidence of ~20% (very preliminary) based on model fit to data from severe cases in Bangladesh
- Concerns about generalizability of post-infection anti-body kinetics between Bangladesh and Uvira

Net MFI



Longitudinal serologic follow-up

- **No data on post-infection kinetics of anti-VC antibodies in African populations available**
- 100 cases in each age group (<5, 5-15, 15+) with 7 follow-up visits
- Will test with Luminex and vibriocidal assays and compare with responses from other populations in Bangladesh
- Enrollment nearly complete



Data Sharing

Weekly report for local actors

Évolution de la situation épidémiologique du choléra dans la ville d'Uvira

ZONE DE SANTE D'UVIRA ET JOHNS HOPKINS UNIVERSITY
SURVEILLANCE CLINIQUE DU CHOLERA

Rapport du 25/03/2024

Préambule

Ce bref rapport résume la situation épidémiologique actuelle du choléra dans la ville d'Uvira, sur base de données issues du système de surveillance du choléra mis en place dans le cadre du projet d'évaluation d'impact de la vaccination orale de masse contre le choléra à Uvira.

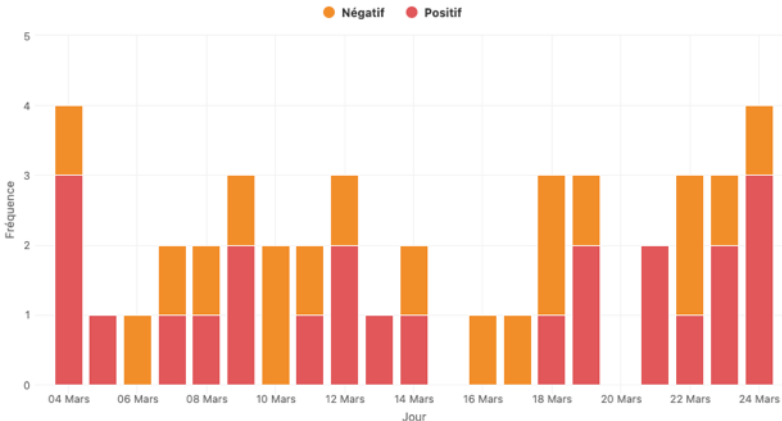
Incidence du choléra à Uvira

Durant la semaine épidémiologique 12 (Jan 12 - Jan 18), 18 cas suspects de choléra ont été enregistrés dans la ville d'Uvira, dont 40% (n=2/5) étaient positifs à la culture, 61% (n=11/18) positifs au test de diagnostic rapide (TDR) après enrichissement dans l'eau peptonée alcaline (Alkaline Peptone Water, APW), et 0 décès.

Graphique 1. Courbe épidémique du choléra dans la ville d'Uvira à partir de la semaine du 29 Feb, 2024 au 25 Mar, 2024

La courbe épidémiologique en haut (A) montre l'évolution journalière de l'incidence des admissions pour suspicion choléra, avec confirmation des cas par TDR enrichis dans l'eau peptonée alcaline. En bas (B), la confirmation du choléra est faite par culture réalisée sur place à Uvira. Notons que la culture est en cours pour 13 (n=13/43) cas. En bas (C), le choléra est sérotypé dans les laboratoires d'Uvira et de l'INRB.

(A) TDR enrichis



II. Description des cas de choléra enregistrés dans la ville d'Uvira

Tableau 1. Évolution de l'incidence de choléra à Uvira au cours de 8 dernières semaines

Semaine	Cas suspects de choléra admis	Cas avec TDR enrichis (%)	TDRs positifs (Positivité)	Cultures réalisées	Cultures positives (Positivité)	Décès (taux de létalité)	Enfants de < 5 ans (%)	Déshydratation sévère (%)
18/03/2024	18	18 (100%)	11 (61%)	5 (28%)	2 (40%)	0	6 (33%)	8 (44%)
11/03/2024	10	10 (100%)	5 (50%)	10 (100%)	6 (60%)	0	3 (30%)	5 (50%)
04/03/2024	15	15 (100%)	8 (53%)	15 (100%)	8 (53%)	0	3 (20%)	8 (53%)
26/02/2024	14	14 (100%)	9 (64%)	14 (100%)	11 (79%)	1	5 (36%)	8 (57%)
19/02/2024	6	6 (100%)	4 (67%)	6 (100%)	4 (67%)	0	2 (33%)	4 (67%)
12/02/2024	4	4 (100%)	0 (0%)	4 (100%)	0 (0%)	0	0 (0%)	1 (25%)
05/02/2024	3	3 (100%)	0 (0%)	3 (100%)	0 (0%)	0	1 (33%)	1 (33%)
29/01/2024	1	1 (100%)	1 (100%)	1 (100%)	0 (0%)	0	0 (0%)	0 (0%)
22/01/2024	7	7 (100%)	0 (0%)	7 (100%)	0 (0%)	0	1 (14%)	4 (57%)

Tableau 2. Distribution des cas de choléra par âge et sévérité

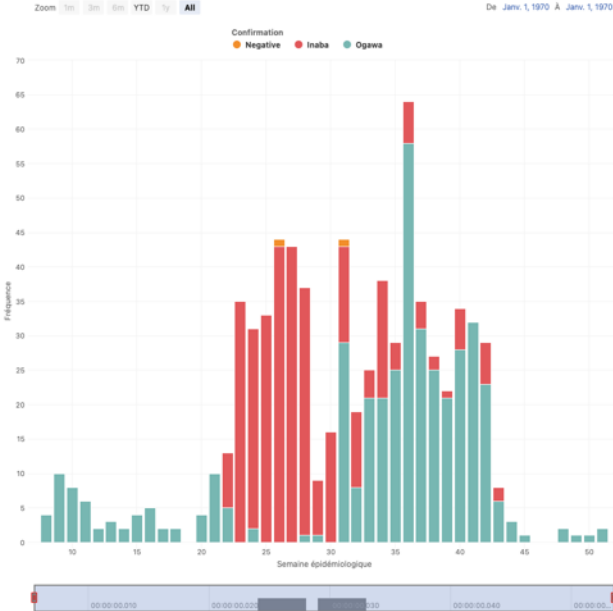
Tranche d'Âge	Cette semaine (19 Mar-25 Mar)				365 derniers jours (27 Mar 2023-25 Mar 2024)			
	Simple	Modérée	Sévère	Manquant	Simple	Modérée	Sévère	Manquant
0-11 mois								
12-59 mois					10	107	92	0
5-14 ans					14	145	186	0
15-59 ans					23	202	324	0
60+ ans					4	33	68	0
Total	0	0	0	0	51	487	670	0

Tableau 3. Distribution des cas par âge et positivité au test de diagnostic rapide après enrichissement dans APW

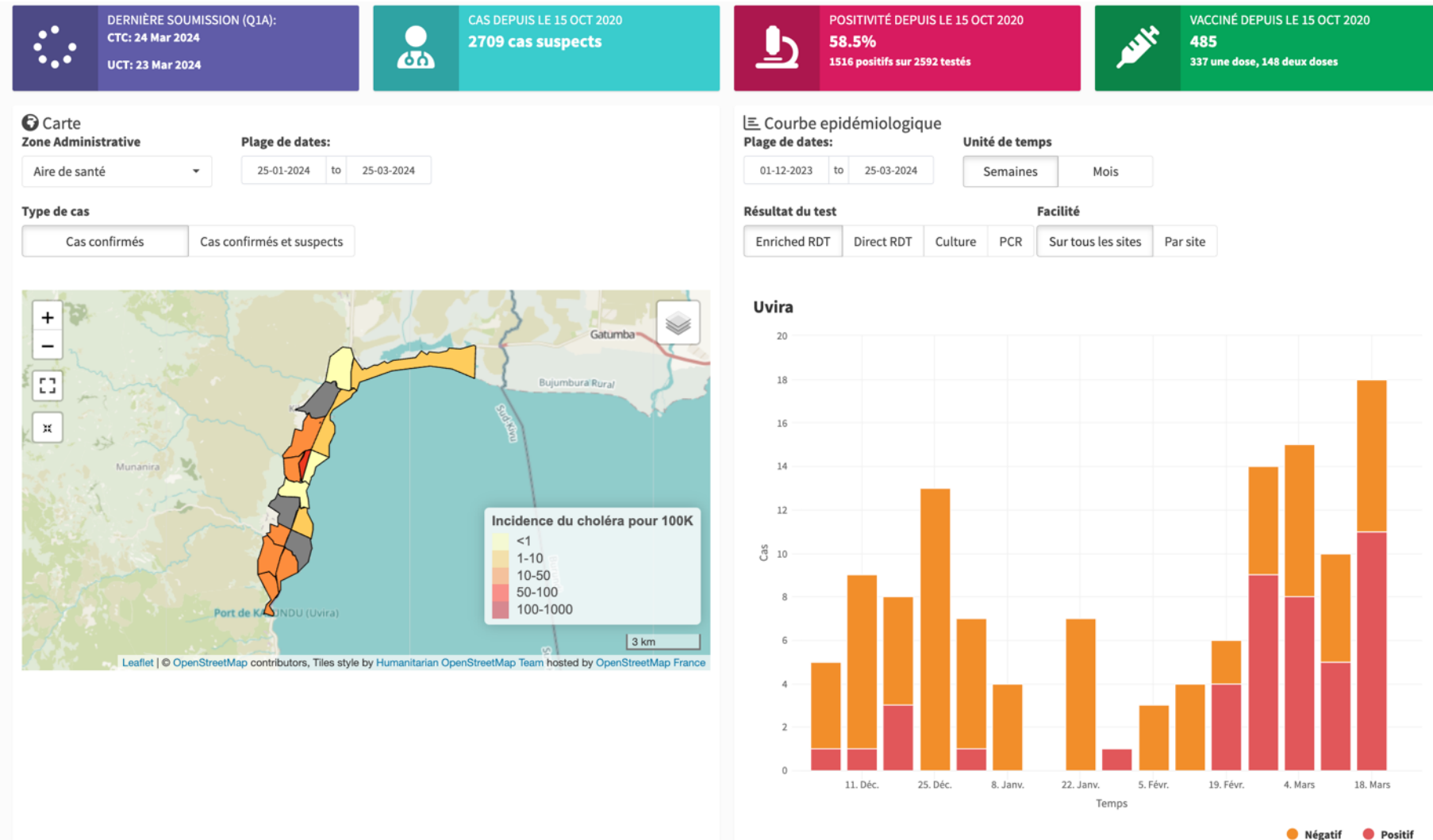
Tranche d'Âge	Cette semaine (19 Mar-25 Mar)				365 derniers jours (27 Mar 2023-25 Mar 2024)			
	Cas	Tests faits (%)	Positivité (%)	Décès	Cas	Tests faits (%)	Positivité (%)	Décès
0-11 mois								
12-59 mois					209	209 (100%)	121 (58%)	1
5-14 ans					345	345 (100%)	250 (72%)	1
15-59 ans					549	549 (100%)	318 (58%)	5
60+ ans					105	105 (100%)	48 (46%)	0
Total	0	0	0	0	1208	1208	737	7

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Live dashboard





Ministère de la Santé
République Démocratique du Congo



**Programme National d'Elimination du Choléra et de lutte
contre les autres Maladies Diarrhéiques
(PNECHOL-MD)**

Placide Welo Okitayemba
Bodiongo Landu

Uvira Health Zone
Jaime Saidi Mufitini
Panzu Nimi

Daniel Lung
Christy Clutter



Thank you!



Espoir B Malembaka
Patrick Musole Bugeme
Juan Dent Hulse
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Jules Jackson
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Andrew Azman

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