

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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S1. List of authors

Francisco J. Luquero, MD, MPH^{1*}, Lise Grout, DVM, MPH^{1,2}, Iza Ciglenecki, MD, MSc², Keita Sakoba, MD^{3,4},
Bala Traore, MD⁵, Melat Heile, NP⁷, Alpha Amadou Diallo, MSc⁶, Christian Itama, MD⁸, Anne-Laure Page, PhD¹,
Marie-Laure Quilici, PhD⁹, Martin A Menguel MD, MSc⁴, Jose Maria Eiros MD, PhD¹⁰, Micaela Serafini, MD, MPH²,
Dominique Legros, MD, MPH², Rebecca F. Grais, PhD¹.

*Corresponding Author: Francisco J. Luquero, Epicentre, 8 rue Saint Sabin, 75011 Paris France, email:

Francisco.Luquero@epicentre.msf.org

¹Epicentre, Paris, France

²Médecins sans Frontières, Geneva, Switzerland

³Ministry of Health, Conakry, Republic of Guinea

⁴African Cholera Surveillance Network, Agence de Médecine Préventive Paris, France

⁵Direction Préfectorale de la Santé, Ministry of Health, Conakry, Republic of Guinea

⁶ Research and Documentation Service, Ministry of Health, Conakry, Republic of Guinea

⁷Médecins sans Frontières, Conakry, Republic of Guinea

⁸World Health Organization, Conakry, Republic of Guinea

⁹National Reference Centre for Vibrios and Cholera, Enteric Bacterial Pathogens Research & Expertise
Unit, Institut Pasteur, Paris, France

¹⁰Department of Microbiology, University of Valladolid, Valladolid, Spain

S2. Cholera in the Republic of Guinea

The 7th cholera pandemic spread into the Republic of Guinea (Guinea) in 1970; following this event, Guinea regularly reported cholera cases to the World Health Organization (WHO). The largest outbreak was observed in 1994 with more than 30,000 cases and 670 deaths. From 2003 to 2007, the Ministry of Health (MoH) of Guinea notified cholera cases to the WHO each year, with cases consistently reported from the Capital, Conakry. The most affected areas are usually the coastal prefectures and the islands (Maritime Guinea, where the capital Conakry is located)¹. The epidemics spread in Guinea during the rainy season that lasts from July to September. From 2008 to 2011, only sporadic cases were reported².

S3. Cholera epidemic in 2012

In 2012, the first cholera case was reported in Forécariah (Maritime Guinea) on February 2. Both the Microbiology National Laboratory and the Institut Pasteur in Paris confirmed that the circulating strain was *Vibrio cholerae* O1 El Tor-Ogawa. Further studies based on genetic markers analysis showed that it was an hybrid El Tor strain possessing the classical B subunit cholera toxin gene (*ctxB1* genotype)³. From February 2 to October 31, a total of 7,350 cases including 133 deaths were reported to the WHO. This number of cases corresponds to an attack rate of 6.4 per 10,000 people. The case fatality ratio (CFR) per 100 cases was 1.8 at country level. The peak of the epidemic was observed in week 34, in which 1,152 cases were reported (MoH data, Figure S1). At country level, the vast majority of cases were reported during the rainy season.

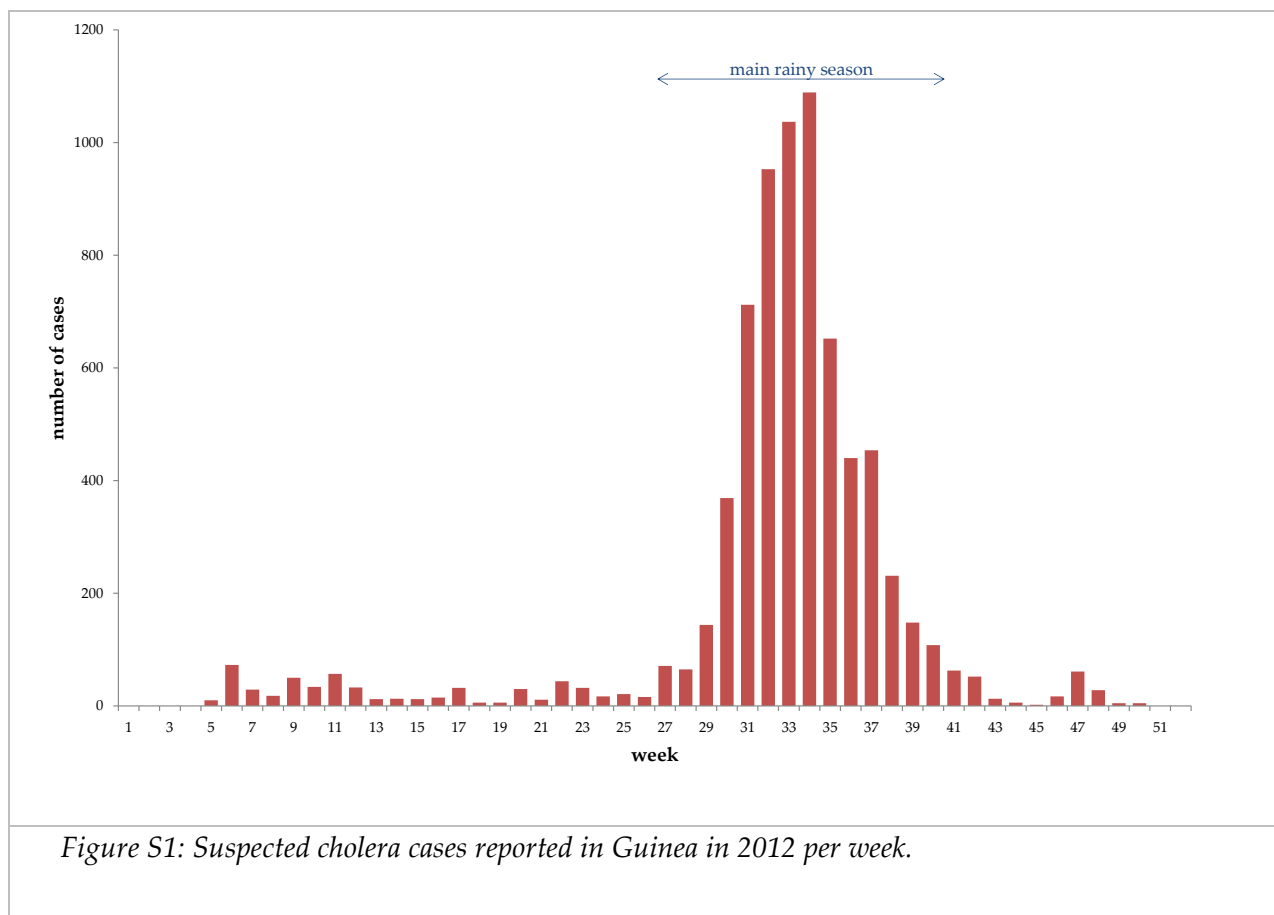


Figure S2 shows a more detailed description of the geographical distribution of the epidemic. Four prefectures had attack rates over 15 cases per 10,000 individuals (Conakry, Dubréka, Coyah and Fria); in Fria and Conakry the attack rate reached 27 and 26 cases per 10,000 respectively. In the city of Conakry, 4,617 cases were reported, which represent 63% of the total number of cases at country level. The first case was declared in Conakry in week 22 (i.e. 17 weeks after the first notification in Forécariah). In Conakry, the peak of the epidemic was observed in epidemiological week 34 in which 727 cases were reported.

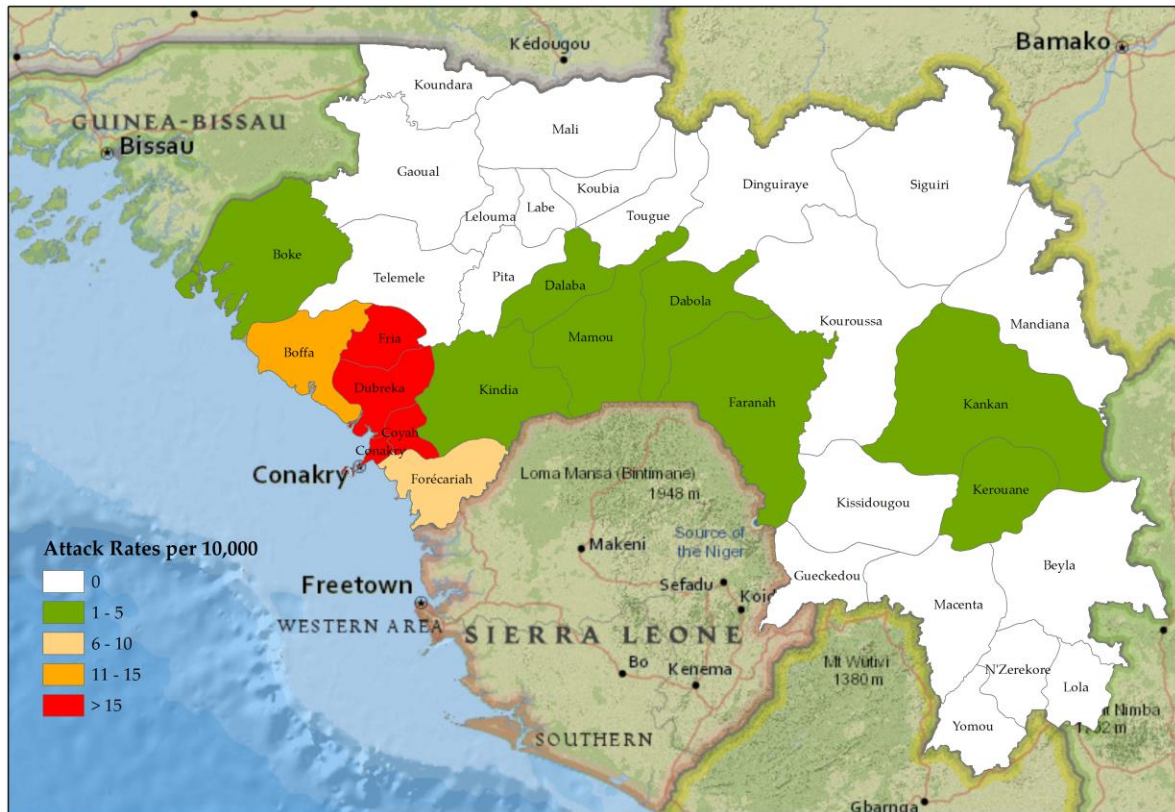


Figure S2. Cholera attack rates per sub-prefecture in Guinea 2012.

The median age of the patients was 25 years old (inter quartile range: 16-37). The number of reported cases was similar in men (49%) and women (51%).

The epidemic evolved with a different dynamic in the vaccinated areas compared with the unvaccinated areas (Figure S3). In the prefectures of Boffa and Forécariah, 283 and 344 cases were respectively reported in 2012.

In the country as a whole, 93% of the cases were reported after week 24, when the implementation of the vaccination campaigns ended. Conversely, in the vaccinated areas of Boffa and Forécariah the percentage of cases reported after the implementation of the vaccination campaigns was respectively 45% and 16% (Figure S4).

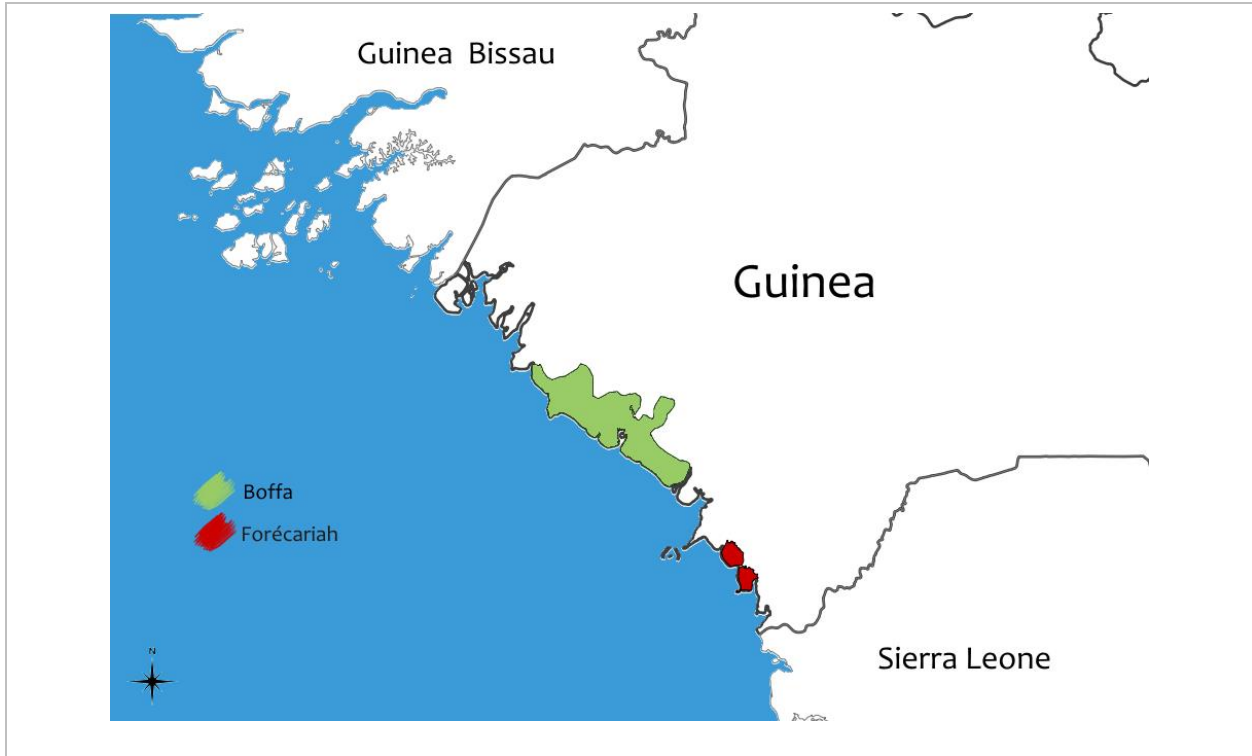


Figure S3: Target areas for the non-selective mass vaccination campaigns, Guinea, 2012.

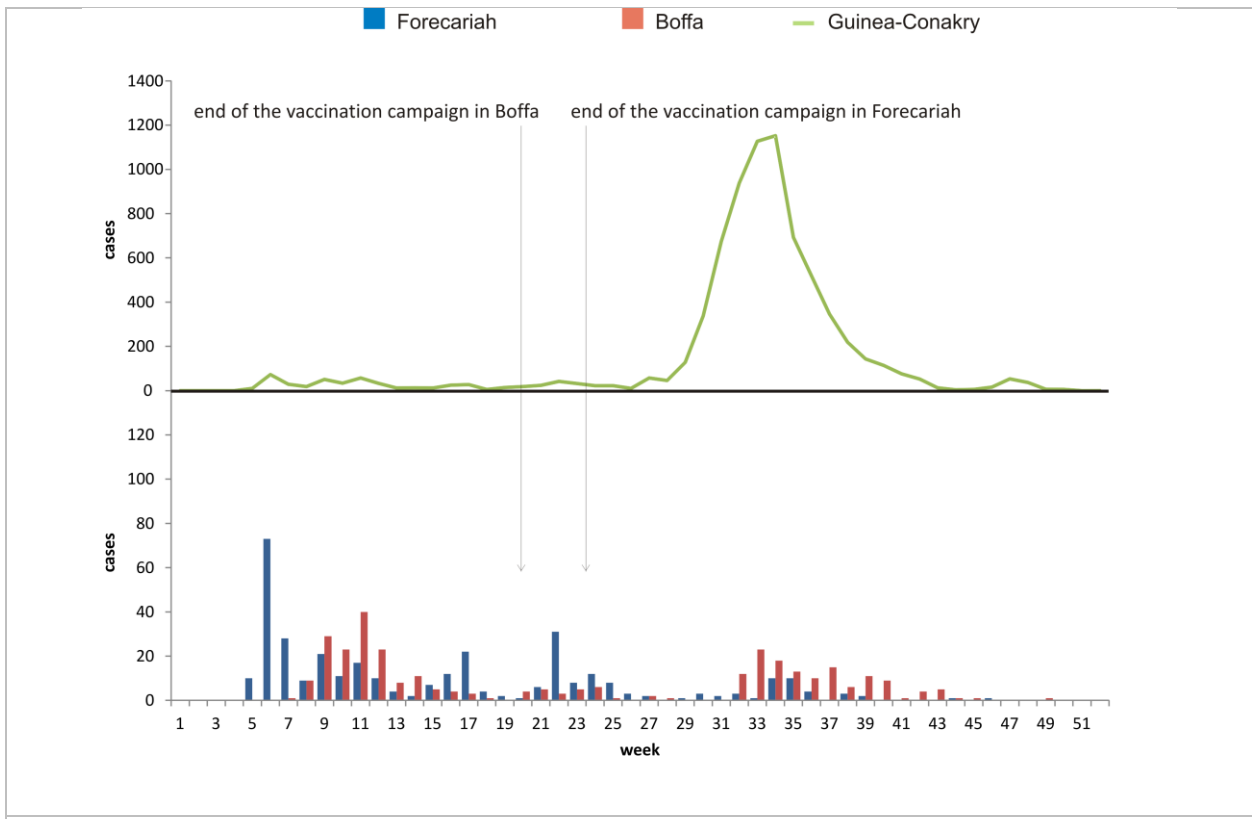


Figure S4. Evolution of the outbreak in the country and in the vaccinated prefectures.

S4. Description of the case-patient and control-subjects characteristics included in the primary effectiveness analysis.

The Table S1 shows the socio-economic characteristics and the exposure to different risk factors for cholera among case-patients and control individuals. We observed a statistical association between being a case-patient and eating in public places and sharing the latrine with a cholera case. The potential confounding effect of factors with P values lower than 0.2 was assessed in the multivariate conditional logistic regression analysis.

Table S1. Characteristics of the case-patients and control-subjects included in the vaccine effectiveness study, Boffa and Forécariah, Guinea, 2012.

	Controls		Cases		P value
	n	(%)	n	(%)	
Profession					0.18
Trader	29	(18.1)	8	(20.0)	
Farmer	37	(23.1)	16	(40.0)	
Pupil / student	29	(18.1)	3	(7.5)	
Fisherman	10	(6.3)	3	(7.5)	
Housewife	10	(6.3)	1	(2.5)	
Unemployment	22	(13.8)	6	(15.0)	
Other	23	(14.4)	3	(7.5)	
Head of the household's educational degree					0.13
Non	43	(27.2)	13	(32.5)	
Primary	5	(3.2)	4	(10.0)	
Secondary	21	(13.3)	2	(5.0)	
University	5	(3.2)	0	(0.0)	
Literate	84	(53.2)	21	(52.5)	
Radio	113	(70.6)	27	(67.5)	0.68
Bicycle	82	(51.2)	19	(47.5)	0.64
Telephone	128	(80.0)	27	(67.5)	0.10
Generator	36	(22.5)	6	(15.0)	0.28
Television	36	(22.5)	6	(15.0)	0.27
Fridge	1	(0.6)	0	(0.0)	0.50
Boat	26	(16.3)	9	(22.5)	0.29
Household size					0.06
0-4 members	34	(21.3)	17	(42.5)	
5-7 members	40	(25.0)	7	(17.5)	
8-12 members	49	(30.6)	9	(22.5)	
>12 members	37	(23.1)	7	(17.5)	
Proportion of children attending school in the household					0.13
None of them	33	(22.9)	14	(37.8)	
Less than half	42	(29.2)	11	(29.7)	
More than half	51	(35.4)	8	(21.6)	
All of them	18	(12.5)	4	(10.8)	
Distance to the closet health center					0.10
Need of transport	107	(66.9)	31	(77.5)	
Walking distance	53	(33.1)	9	(22.5)	
Other cholera cases in the household	4	(2.5)	3	(7.5)	0.15

Travelling or receiving a visit in the last week	42	(26.3)	13	(32.5)	0.41
Participation in a burial ceremony	3	(1.9)	0	(0.0)	-
Water source					0.98
Pump	63	(39.4)	17	(42.5)	
Protected well	21	(13.1)	5	(12.5)	
Unprotected well	10	(6.3)	2	(5.0)	
Water from natural source	47	(29.4)	11	(27.5)	
Other	19	(11.9)	5	(12.5)	
Treatment of the drinking water	34	(21.3)	5	(12.8)	0.15
Recipient to store drinking water with a lid	158	(98.8)	40	(100.0)	0.35
Eating food in a public space					0.02
Never	72	(45.0)	11	(28.2)	
Sometimes	49	(30.6)	20	(51.3)	
Soap available in the household	78	(49.1)	16	(40.0)	0.30
Washing hands before eating	143	(89.4)	33	(82.5)	0.22
Washing hands after eating	24	(15.0)	4	(10.0)	0.37
Washing hands after going to the toilet	72	(45.0)	17	(42.5)	0.77
Washing hands after cleaning a baby after defecation	12	(7.5)	1	(2.5)	0.20
Washing hands before cooking	21	(13.1)	5	(12.5)	0.90
Usual place of defecation					0.12
Latrine	81	(50.6)	17	(42.5)	
Pit in the yard	56	(35.0)	14	(35.0)	
In the ground	23	(14.4)	9	(22.5)	
Sharing the latrine					0.71
Just for the household	31	(22.3)	6	(18.8)	
Several households	59	(42.4)	13	(40.6)	
Anybody	49	(35.3)	13	(40.6)	
Sharing the latrine with someone suffering from cholera	5	(3.7)	6	(20.0)	0.001
Flooding latrine	13	(9.5)	4	(12.9)	0.54

S5. Description of the case-patient and control-subjects characteristics included in the indicator bias effectiveness analysis.

The Table S2 shows the socio-economic characteristics and the exposure to different risk factors for cholera among non-cholera watery diarrhea case-patients and control-subjects included in the indicator bias analysis. In this analysis, cases were defined as individuals with non-cholera watery diarrhea who: (i) gave written informed consent, (ii) resided in the study areas since April 16, 2012 and their residence could be located after discharge for acquisition of information about vaccination and other data, (iii) were older than 12 months and (iv) had a negative cholera RDT result. Four matched controls by age, sex and residence place were recruited for each case. The non-cholera watery diarrhea case-patients and the matched control-subject showed similar socio-economic characteristics and had similar exposure to different risk factors for cholera infection (Table S2).

Table S2. Characteristics of the non-cholera watery diarrhea case-patients and control-subjects included in the indicator bias analysis, Boffa and Forécariah, Guinea, 2012.

	Controls		Cases		P value
	n	(%)	n	(%)	
Profession					0.50
Trader	22	(12.8)	8	(18.6)	
Farmer	48	(27.9)	9	(20.9)	
Pupil / student	19	(11.0)	3	(7.0)	
Fisherman	5	(2.9)	2	(4.7)	
Housewife	26	(15.1)	8	(18.6)	
Unemployment	36	(20.9)	11	(25.6)	
Other	16	(9.3)	2	(4.7)	
Head of the household's educational degree					0.24
Non	34	(19.9)	13	(31.0)	
Primary	16	(9.4)	3	(7.1)	
Secondary	11	(6.4)	4	(9.5)	
University	5	(2.9)	3	(7.1)	
Literate	105	(61.4)	19	(45.2)	
Radio	123	(71.5)	28	(65.1)	0.30
Bicycle	91	(52.9)	21	(48.8)	0.55
Telephone	124	(72.1)	31	(72.1)	1.00
Generator	27	(15.7)	11	(25.6)	0.20
Television	23	(13.4)	13	(30.2)	0.03
Fridge	1	(0.6)	1	(2.3)	0.35
Boat	31	(18.0)	8	(18.6)	0.71
Household size					0.61
0-4 members	23	(13.5)	3	(7.0)	
5-7 members	41	(24.1)	9	(20.9)	
8-12 members	57	(33.5)	15	(34.9)	
>12 members	49	(28.8)	16	(37.2)	
Proportion of children attending school in the household					0.60
None of them	29	(17.6)	4	(9.8)	
Less than half	63	(38.2)	17	(41.5)	
More than half	54	(32.7)	13	(31.7)	
All of them	19	(11.5)	7	(17.1)	
Distance to the closet health center					0.15
Need of transport	51	(29.7)	17	(39.5)	
Walking distance	121	(70.3)	26	(60.5)	
Other cholera cases in the household	6	(3.5)	2	(4.7)	0.69
Travelling or receiving a visit in the last week	35	(20.3)	11	(25.6)	0.34
Participation in a burial ceremony	2	(1.2)	1	(2.3)	0.23
Water source					0.11
Pump	84	(48.8)	20	(46.5)	
Protected well	39	(22.7)	14	(32.6)	
Unprotected well	6	(3.5)	2	(4.7)	
Water from natural source	42	(24.4)	7	(16.3)	
Other	1	(0.6)	0	(0.0)	
Treatment of the drinking water	43	(25.4)	11	(25.6)	0.66
Recipient to store drinking water with a lid	170	(98.8)	43	(100.0)	0.35

Eating food in a public space					0.21
Never	117	(68.0)	28	(65.1)	
Sometimes	27	(15.7)	10	(23.3)	
Soap available in the household	113	(65.7)	31	(72.1)	0.29
Washing hands before eating	144	(83.7)	37	(86.0)	0.83
Washing hands after eating	87	(50.6)	22	(51.2)	0.69
Washing hands after going to the toilet	93	(54.1)	25	(58.1)	0.47
Washing hands after cleaning a baby after defecation	16	(9.3)	3	(7.0)	0.59
Washing hands before cooking	23	(13.4)	6	(14.0)	0.91
Usual place of defecation					0.28
Latrine	61	(35.5)	15	(34.9)	
Pit in the yard	81	(47.1)	17	(39.5)	
In the ground	30	(17.4)	11	(25.6)	
Sharing the latrine					0.17
Just for the household	73	(48.7)	13	(38.2)	
Several households	48	(32.0)	11	(32.4)	
Anybody	29	(19.3)	10	(29.4)	
Sharing the latrine with someone suffering from cholera	9	(7.1)	5	(16.7)	0.23
Flooding latrine	11	(7.4)	4	(11.8)	0.39

S6. Sensitivity analysis of the vaccine coverage estimates considering the uncertainty about the vaccination status.

In the Scenario 1 of the sensitivity analysis individuals reporting vaccination but without cards are considered as unvaccinated and in Scenario 2 are considered as vaccinated

Table S3. Sensitivity analysis of the vaccine effectiveness (VE) considering the uncertainty of vaccination status among those reporting vaccination but without vaccination cards.

	controls		cases		VE	95%CI		P value	
	N	(%)	N	(%)	%				
Vaccination status									
Unvaccinated	23	(14.4)	15	(37.5)					
Incomplete course (with card)	22	(13.8)	7	(17.5)					
Incomplete course (without card)	14	(8.8)	7	(17.5)					
Full course (with card)	68	(42.5)	6	(15.0)					
Full course (without card)	33	(20.6)	5	(12.5)					
Scenario 1: those without cards as unvaccinated									
Unvaccinated	70	(43.8)	27	(67.5)	Ref				
Incomplete course (with card only)	22	(13.8)	7	(17.5)	11.8%	(-140.1%	-	67.6%)	0.80
Full course (with card only)	68	(42.5)	6	(15.0)	81.9%	(49.2%	-	93.6%)	0.001
Scenario 2: those without cards as vaccinated									
Unvaccinated	23	(14.4)	15	(37.5)	Ref				
Incomplete course (with and without card)	36	(22.5)	14	(35.0)	38.9%	(-55.2%	-	76.0%)	0.30
Full course (with and without card)	101	(63.1)	11	(27.5)	84.0%	(59.7%	-	93.6%)	<0.001

S7. Adverse events following immunization

Surveillance of adverse events following immunization (AEFI) was implemented at vaccination sites, health centers and health posts in the areas targeted for the cholera vaccination campaign. An AEFI was defined as a medical occurrence detected by the vaccination site supervisor or a physician with an onset up to 14 days after receipt of a dose of vaccine. During the awareness campaign and at the time of vaccination, participants were told to report to a vaccination site or a health center if they felt ill after receiving the vaccine. The following data were collected using a standardized form: age, sex, pregnancy, history of allergies, vaccination date, consultation date, date of onset of the symptoms, type of symptoms, and clinical outcome (recovery, transfer or death).

Overall, 48 individuals spontaneously reported symptoms that were linked with the vaccine by the health personnel and considered as AEFI with 35 after the first round and 13 after the second round. In total, 29 were women (60%) and the median age was 27 years (IQR: 16–36 years). Seven patients reported having a history of allergies (15%). The delay between vaccination and symptom onset is shown in Figure S5, the median delay was 7 hours (IQR: 1–24 hours). The symptoms reported were mainly gastro-intestinal (Table S4). Most of the patients (n=33, 69%) reported more than one symptom.

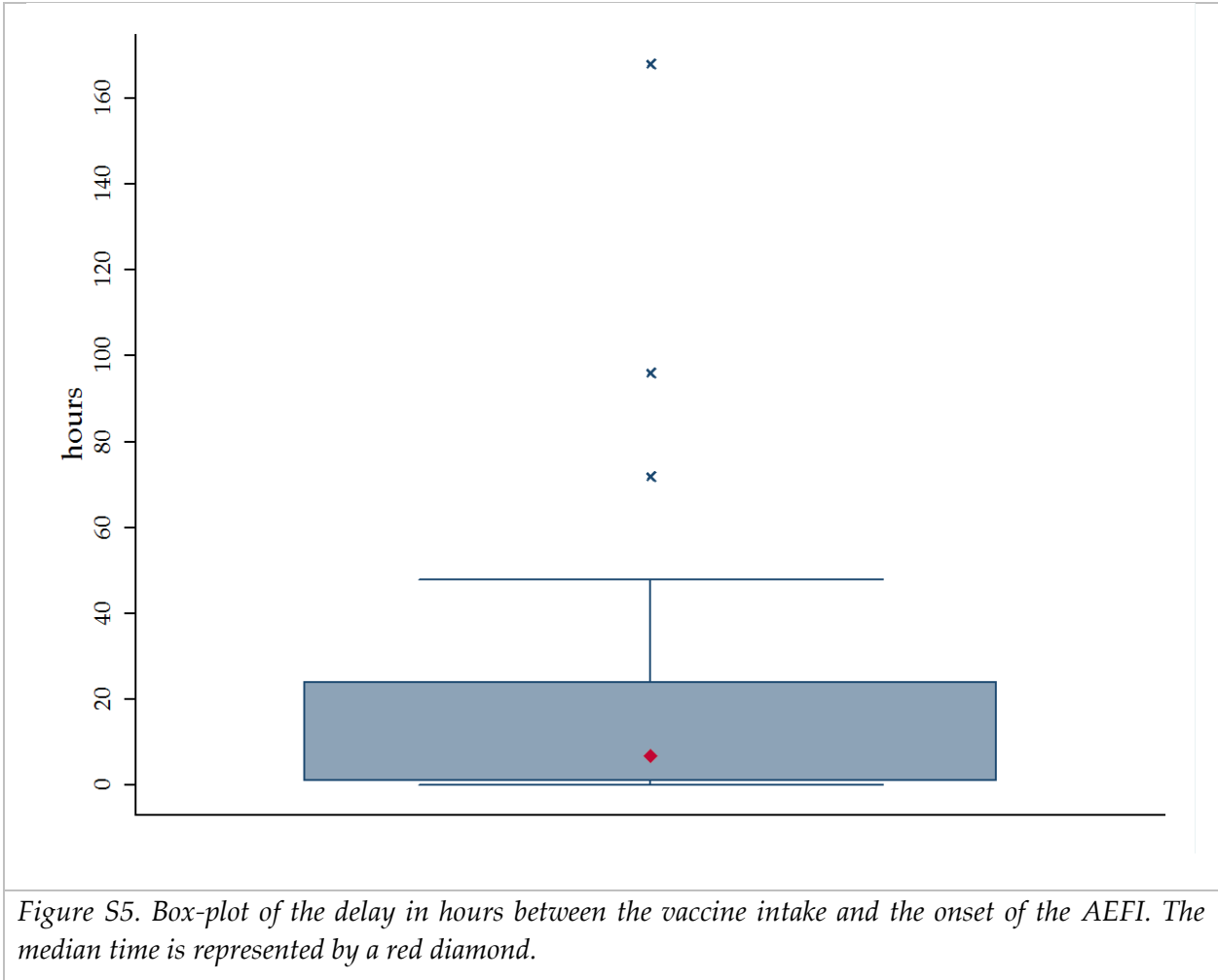


Table S4. Symptoms reported by the forty-eight patients reporting adverse events following immunization.

Symptom	n = 139	%
Diarrhea	28	(20.1)
Vomiting	22	(15.8)
Stomachache	14	(10.1)
Fever	15	(10.8)
Weakness	15	(10.8)
Nausea	12	(8.6)
Dizziness	9	(6.5)
Headache	5	(3.6)
Borgorygms	2	(1.4)
Anorexia	2	(1.4)
Other	15	(10.8)

S8. References

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