

# THE LANCET

## Infectious Diseases

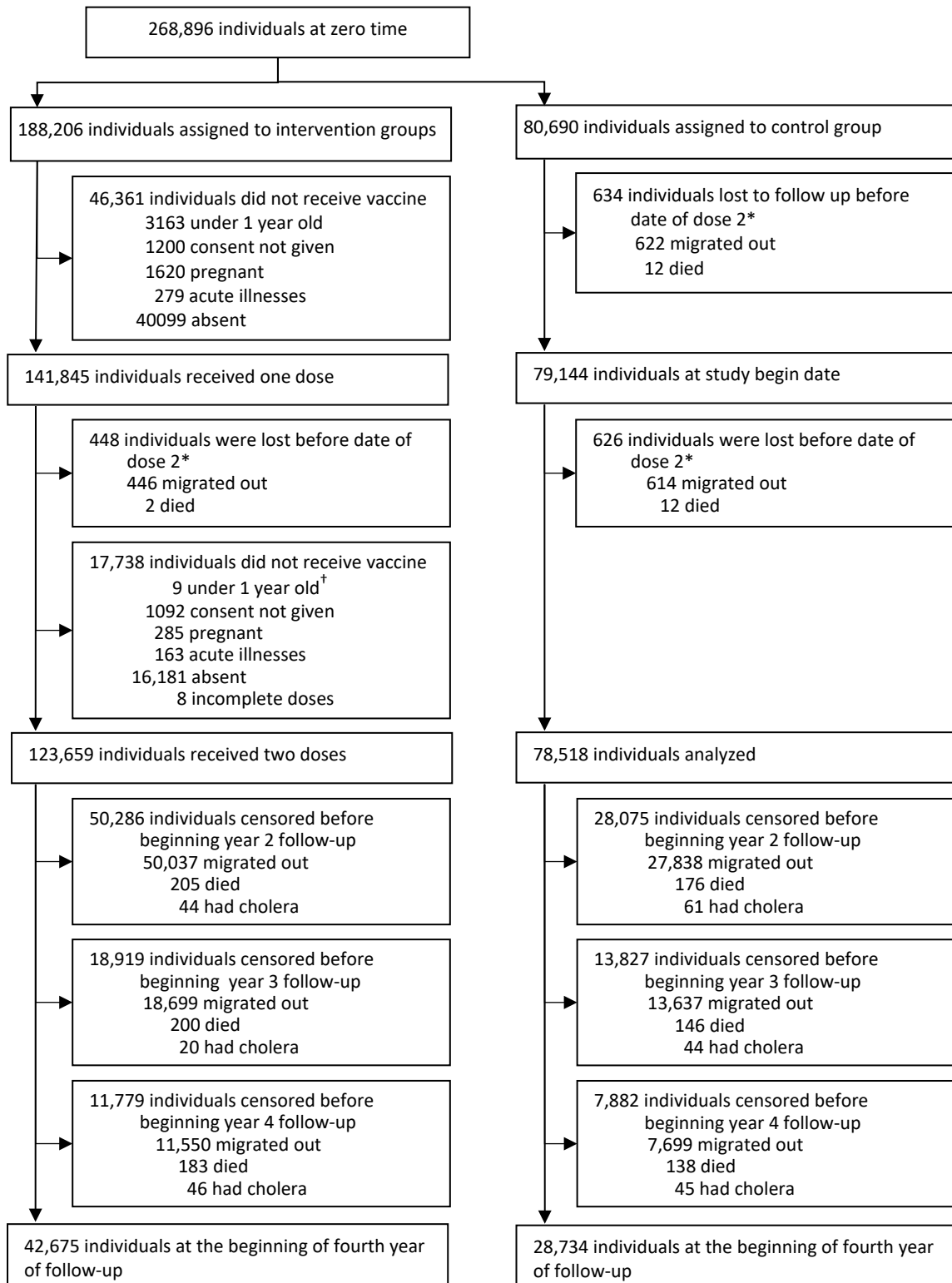
### Supplementary appendix 2

This appendix formed part of the original submission and has been peer reviewed.  
We post it as supplied by the authors.

Supplement to: Ali M, Qadri F, Kim DR, et al. Effectiveness of a killed whole-cell oral cholera vaccine in Bangladesh: further follow-up of a cluster-randomised trial. *Lancet Infect Dis* 2021; published online June 16. [https://doi.org/10.1016/S1473-3099\(20\)30781-7](https://doi.org/10.1016/S1473-3099(20)30781-7).

## Appendix

Figure A1. CONSORT for assembling the population for evaluating total vaccine effectiveness



\* The date of dose 2 for the two-dose recipients, or the median date of dose 2 of the cycle of vaccination for no- or one-dose recipients.

† Assessed by the vaccinators during the time of vaccination

Figure A2. Kaplan-Meier estimates of the cumulative risk of not having severe dehydrated cholera among target population at zero time during 4 years of follow-up post-vaccination (total vaccine effectiveness analysis)

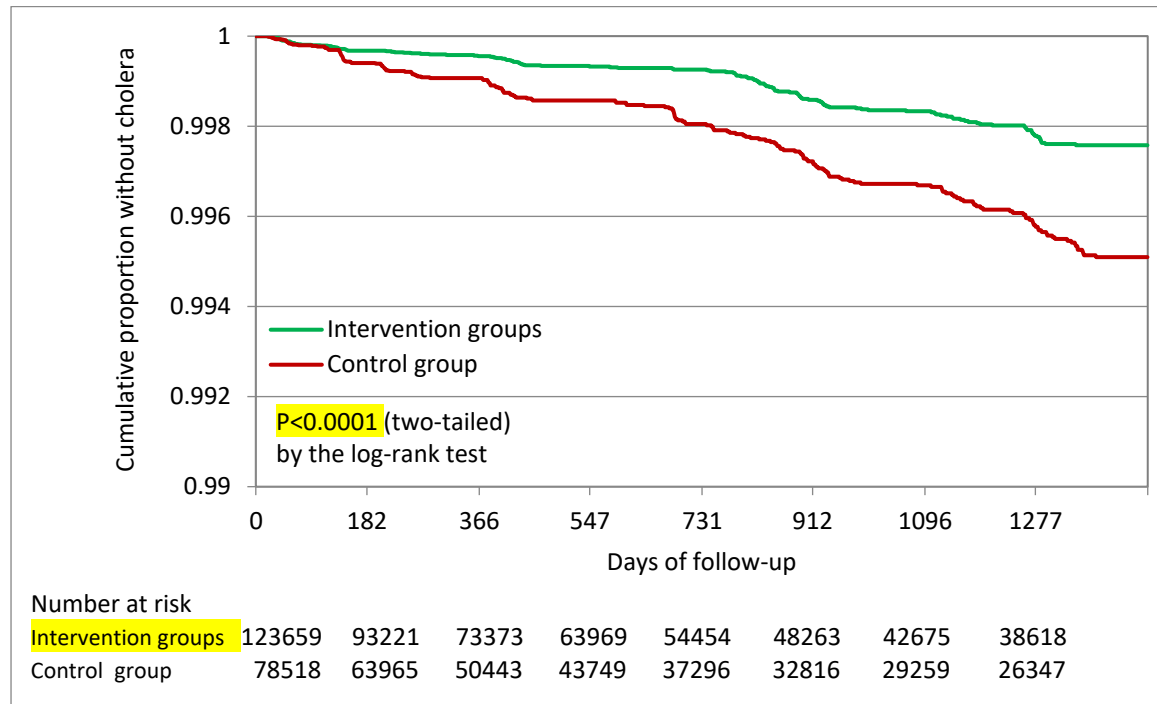


Table A1. Baseline characteristics for analysis of overall vaccine protection at the onset of the first year of follow-up

Variables	Vaccine group (n=187,214)	Control group (n=80,056)
Mean age at zero time (SD; years)	23.9 (15.7)	24.1 (16.0)
Male participants (%)	90,841 (48.5)*	39,264 (49.0)
Diarrhoea within previous 6 months at the time of household registration (%)	24,800 (13.2)	11,189 (14.0)
Diarrhoea within previous 48 hours at the time of household registration (%)	2,352 (1.3)	1,003 (1.3)
Mean time living in the area (SD; months)	65.8 (113.8)	74.1 (121.7)
Lived in study area less than 1 year (%)	85,278 (45.6)	32,424 (40.5)
Live in their own house (%)	38,837 (20.7)	20,075 (25.1)
Households using safe water source (household tap, %)	9,576 (5.1)	4,228 (5.3)
Live in a household with specific place for waste disposal (%)	153,780 (82.1)	61,943 (77.4)
Live in a household with using sanitary (flushing) toilet (%)	139,759 (74.7)	62,149 (77.6)
Live in a household with a concrete roof (%)	161,502 (86.3)	67,532 (84.4)
Live in a household with only one room (%)	152,695 (81.6)	64,679 (80.8)
Sharing kitchen with other households (%)	165,693 (88.5)	66,536 (83.1)
Live in a household sharing water source with others (%)	126,892 (67.8)	48,563 (60.7)
Live in a household using treated water (boiled, filtered, or chemical treatment, %)	102,037 (54.5)	42,276 (52.8)
Live in a household that knows about cholera vaccine (%)	13,839 (7.4)	6,432 (8.0)
Live in household close (less than the median distance) to the nearest icddr,b hospital (%)	89,954 (48.0)	39,377 (49.2)
Mean number of individuals per household (SD)	4.7 (1.9)	4.8 (1.9)
Median distance to the nearest icddr,b hospitals (IQR; meters)	1792 (1229, 2282)	1802 (994, 2414)

Variables	Vaccine group (n=187,214)	Control group (n=80,056)
Mean percentage of children younger than 5 years in the cluster (SD)	10.0% (1.0)	10.1% (1.0)
Mean percentage of male participants in the cluster (SD)	48.5% (1.3)*	49.0% (0.9)
Mean percentage of individuals using safe water source in the cluster (SD)	5.1% (4.6)	5.3% (3.6)
Mean percentage of individuals living in their own house in the cluster (SD)	20.7% (17.9)	25.0% (24.7)
Mean percentage of individuals using specific place for waste disposal in the cluster (SD)	82.1% (23.4)	77.4% (24.2)
Mean percentage of individuals using sanitary (flushing) toilet in the cluster (SD)	74.6% (23.4)	77.6% (21.5)

Note, the level of significance was derived after adjustment for the design effect.

\*The difference is statistically significant ( $p < 0.05$ ) compared to the control group.

Table A2. Baseline characteristics for analysis of overall vaccine protection at the onset of the second year of follow-up

Variables	Vaccine group (n=104,799)	Control group (n=51,420)
Mean age at zero time (SD; years)	24.7 (16.4)	24.6 (16.5)
Male participants (%)	51,828 (49.5)	25,511 (49.6)
Diarrhoea within previous 6 months at the time of household registration (%)	14,000 (13.4)	7,129 (13.9)
Diarrhoea within previous 48 hours at the time of household registration (%)	1,248 (1.2)	608 (1.2)
Mean time living in the area (SD; months)	93.1 (131.6)	96.2 (135.8)
Lived in study area less than 1 year (%)	34,901 (33.3)	16,049 (31.2)
Live in their own house (%)	32,866 (31.4)	17,715 (34.5)
Households using safe water source (household tap, %)	6,945 (6.6)	3,394 (6.6)
Live in a household with specific place for waste disposal (%)	85,844 (81.9)	39,346 (76.5)
Live in a household with using sanitary (flushing) toilet (%)	78,014 (74.4)	40,118 (78.0)
Live in a household with a concrete roof (%)	90,087 (86.0)	43,209 (84.0)
Live in a household with only one room (%)	79,492 (75.9)	39,176 (76.2)
Sharing kitchen with other households (%)	88,659 (84.6)	40,547 (78.9)
Live in a household sharing water source with others (%)	66,913 (63.8)	29,420 (57.2)
Live in a household using treated water (boiled, filtered, or chemical treatment, %)	57,483 (54.9)	26,661 (51.8)
Live in a household that knows about cholera vaccine (%)	8,277 (7.9)	4,393 (8.5)
Live in household close (less than the median distance) to the nearest icddr,b hospital (%)	51,200 (48.9)	25,011 (48.6)
Mean number of individuals per household (SD)	4.9 (2.0)	4.9 (2.0)
Median distance to the nearest icddr,b hospitals (IQR; meters)	1778 (1274, 2256)	1812 (1221, 2403)

Variables	Vaccine group (n=104,799)	Control group (n=51,420)
Mean percentage of children younger than 5 years in the cluster (SD)	10.0% (1.0)	10.1% (1.0)
Mean percentage of male participants in the cluster (SD)	48.6% (1.2)*	49.1% (0.9)
Mean percentage of individuals using safe water source in the cluster (SD)	5.5% (4.8)	5.5% (3.6)
Mean percentage of individuals living in their own house in the cluster (SD)	22.7% (19.4)	28.1% (26.5)
Mean percentage of individuals using specific place for waste disposal in the cluster (SD)	82.0% (23.7)	76.6% (24.3)
Mean percentage of individuals using sanitary (flushing) toilet in the cluster (SD)	74.6% (23.5)	77.5% (21.6)

Note, the level of significance was derived after adjustment for the design effect.

\*The difference is statistically significant ( $p < 0.05$ ) compared to the control group.

Table A3. Baseline characteristics for analysis of overall vaccine protection at the onset of the third year of follow-up

Variables	Vaccine group (n=75,584)	Control group (n=37,296)
Mean age at zero time (SD; years)	25.1 (16.7)	25.1 (16.8)
Male participants (%)	37,797 (50.0)	18,702 (50.1)
Diarrhoea within previous 6 months at the time of household registration (%)	10,075 (13.3)	5,174 (13.9)
Diarrhoea within previous 48 hours at the time of household registration (%)	897 (1.2)	415 (1.1)
Mean time living in the area (SD; months)	110.1 (140.5)	114.7 (145.0)
Lived in study area less than 1 year (%)	21,339 (28.2)	9,619 (25.8)
Live in their own house (%)	28,852 (38.2)	15,848 (42.5)
Households using safe water source (household tap, %)	5,671 (7.5)	2,765 (7.4)
Live in a household with specific place for waste disposal (%)	61,733 (81.7)	28,144 (75.5)
Live in a household with using sanitary (flushing) toilet (%)	55,802 (73.8)	28,636 (76.8)
Live in a household with a concrete roof (%)	64,933 (85.9)	31,460 (84.4)
Live in a household with only one room (%)	55,002 (72.8)	27,267 (73.1)
Sharing kitchen with other households (%)	61,954 (82.0)	28,068 (75.3)
Live in a household sharing water source with others (%)	45,829 (60.6)	19,880 (53.3)
Live in a household using treated water (boiled, filtered, or chemical treatment, %)	40,883 (54.1)	18,545 (49.7)
Live in a household that knows about cholera vaccine (%)	5,645 (7.5)	2,933 (7.9)
Live in household close (less than the median distance) to the nearest icddr,b hospital (%)	35,960 (47.6)	17,408 (46.7)
Mean number of individuals per household (SD)	5.0 (2.0)	5.0 (2.0)
Median distance to the nearest icddr,b hospitals (IQR; meters)	1804 (1352, 2262)	1837 (1359, 2424)



Variables	Vaccine group (n=75,584)	Control group (n=37,296)
Mean percentage of children younger than 5 years in the cluster (SD)	10.0% (1.0)	10.1% (1.0)
Mean percentage of male participants in the cluster (SD)	48.6% (1.2)*	49.1% (0.9)
Mean percentage of individuals using safe water source in the cluster (SD)	5.7% (5.0)	5.6% (3.7)
Mean percentage of individuals living in their own house in the cluster (SD)	24.1% (20.1)	31.2% (27.5)
Mean percentage of individuals using specific place for waste disposal in the cluster (SD)	81.8% (23.8)	75.9% (24.5)
Mean percentage of individuals using sanitary (flushing) toilet in the cluster (SD)	74.4% (23.8)	76.7% (22.5)

Note, the level of significance was derived after adjustment for the design effect.

\*The difference is statistically significant ( $p < 0.05$ ) compared to the control group.

Table A4. Baseline characteristics for analysis of overall vaccine protection at the onset of the fourth year of follow-up

Variables	Vaccine group (n=58,315)	Control group (n=29,259)
Mean age at zero time (SD; years)	25.4 (17.0)	25.3 (17.0)
Male participants (%)	29,384 (50.4)	14,817 (50.6)
Diarrhoea within previous 6 months at the time of household registration (%)	7,830 (13.4)	4,017 (13.7)
Diarrhoea within previous 48 hours at the time of household registration (%)	672 (1.2)	306 (1.0)
Mean time living in the area (SD; months)	123.1 (145.9)	128.7 (150.5)
Lived in study area less than 1 year (%)	14,636 (25.1)	6,499 (22.2)
Live in their own house (%)	25,592 (43.9)	14,250 (48.7)
Households using safe water source (household tap, %)	4,832 (8.3)	2,299 (7.9)
Live in a household with specific place for waste disposal (%)	47,444 (81.4)	21,859 (74.7)
Live in a household with using sanitary (flushing) toilet (%)	42,909 (73.6)	22,253 (76.1)
Live in a household with a concrete roof (%)	50,171 (86.0)	24,896 (85.1)
Live in a household with only one room (%)	41,103 (70.5)	20,796 (71.1)
Sharing kitchen with other households (%)	46,444 (79.6)	21,172 (72.4)
Live in a household sharing water source with others (%)	33,781 (57.9)	14,763 (50.5)
Live in a household using treated water (boiled, filtered, or chemical treatment, %)	30,949 (53.1)	13,860 (47.4)
Live in a household that knows about cholera vaccine (%)	4,109 (7.0)	2,173 (7.4)
Live in household close (less than the median distance) to the nearest icddr,b hospital (%)	27,309 (46.8)	13,605 (46.5)
Mean number of individuals per household (SD)	5.1 (2.0)	5.1 (2.0)
Median distance to the nearest icddr,b hospitals (IQR; meters)	1831 (1402, 2270)	1838 (1373, 2448)
Mean percentage of children younger than 5 years in the cluster (SD)	10.0% (1.0)	10.1% (1.0)

Variables	Vaccine group (n=58,315)	Control group (n=29,259)
Mean percentage of male participants in the cluster (SD)	48.7% (1.2)*	49.2% (0.9)
Mean percentage of individuals using safe water source in the cluster (SD)	5.9% (5.1)	5.7% (3.7)
Mean percentage of individuals living in their own house in the cluster (SD)	25.5% (20.6)	33.6% (28.2)
Mean percentage of individuals using specific place for waste disposal in the cluster (SD)	81.6% (24.0)	75.4% (24.6)
Mean percentage of individuals using sanitary (flushing) toilet in the cluster (SD)	74.5% (23.9)	76.3% (22.9)

Note, the level of significance was derived after adjustment for the design effect.

\*The difference is statistically significant ( $p < .05$ ) compared to the control group.

Table A5. Baseline characteristics for analysis of total vaccine protection at the onset of the first year of follow-up

Variables	Vaccine group (n=123,659)	Control group (n=78,518)
Mean age at zero time (SD; years)	23.2 (15.8)*	24.6 (15.8)
Male participants (%)	56,196 (45.4)*	38,485 (49.0)
Diarrhoea within previous 6 months at the time of household registration (%)	17,717 (14.3)	11,050 (14.1)
Diarrhoea within previous 48 hours at the time of household registration (%)	1,652 (1.3)	973 (1.2)
Mean time living in the area (SD; months)	72.7 (118.5)	74.3 (121.9)
Lived in study area less than 1 year (%)	51,903 (42.0)	31,725 (40.4)
Live in their own house (%)	28,011 (22.7)	19,714 (25.1)
Households using safe water source (household tap, %)	6,821 (5.5)	4,157 (5.3)
Live in a household with specific place for waste disposal (%)	101,172 (81.8)	60,744 (77.4)
Live in a household with using sanitary (flushing) toilet (%)	92,190 (74.6)	60,942 (77.6)
Live in a household with a concrete roof (%)	107,465 (86.9)	66,249 (84.4)
Live in a household with only one room (%)	99,805 (80.7)	63,389 (80.7)
Sharing kitchen with other households (%)	108,766 (88.0)	65,258 (83.1)
Live in a household sharing water source with others (%)	81,844 (66.2)	47,616 (60.6)
Live in a household using treated water (boiled, filtered, or chemical treatment, %)	68,138 (55.1)	41,457 (52.8)
Live in a household that knows about cholera vaccine (%)	5,873 (4.7)*	6,306 (8.0)
Live in household close (less than the median distance) to the nearest icddr,b hospital (%)	60,644 (49.0)	38,637 (49.2)
Mean number of individuals per household (SD)	4.8 (1.9)	4.8 (1.9)
Median distance to the nearest icddr,b hospitals (IQR; meters)	1773 (1220, 2268)	1802 (991, 2414)
Mean percentage of children younger than 5 years in the cluster (SD)	10.0% (1.0)	10.1% (1.0)

Variables	Vaccine group (n=123,659)	Control group (n=78,518)
Mean percentage of male participants in the cluster (SD)	48.5% (1.2)*	49.0% (0.9)
Mean percentage of individuals using safe water source in the cluster (SD)	5.2% (4.6)	5.3% (3.6)
Mean percentage of individuals living in their own house in the cluster (SD)	21.2% (18.4)	24.9% (24.7)
Mean percentage of individuals using specific place for waste disposal in the cluster (SD)	82.1% (23.4)	77.4% (24.1)
Mean percentage of individuals using sanitary (flushing) toilet in the cluster (SD)	74.8% (23.1)	77.6% (21.5)

Note, the level of significance was derived after adjustment for the design effect.

\*The difference is statistically significant ( $p < .05$ ) compared to the control group.

Table A6. Baseline characteristics for analysis of total vaccine protection at the onset of the second year of follow-up

Variables	Vaccine group (n=73,373)	Control group (n=50,443)
Mean age at zero time (SD; years)	23.9 (16.4)*	25.1 (16.3)
Male participants (%)	33,908 (46.2)*	25,016 (49.6)
Diarrhoea within previous 6 months at the time of household registration (%)	10,675 (14.5)	7,038 (14.0)
Diarrhoea within previous 48 hours at the time of household registration (%)	936 (1.3)	586 (1.2)
Mean time living in the area (SD; months)	99.7 (134.3)	96.5 (136.0)
Lived in study area less than 1 year (%)	22,296 (30.4)	15,707 (31.1)
Live in their own house (%)	24,150 (32.9)	17,400 (34.5)
Households using safe water source (household tap, %)	5,090 (6.9)	3,335 (6.6)
Live in a household with specific place for waste disposal (%)	59,765 (81.5)	38,598 (76.5)
Live in a household with using sanitary (flushing) toilet (%)	54,374 (74.1)	39,347 (78.0)
Live in a household with a concrete roof (%)	63,738 (86.9)	42,396 (84.0)
Live in a household with only one room (%)	55,280 (75.3)	38,391 (76.1)
Sharing kitchen with other households (%)	61,740 (84.1)	39,767 (78.8)
Live in a household sharing water source with others (%)	45,484 (62.0)	28,857 (57.2)
Live in a household using treated water (boiled, filtered, or chemical treatment, %)	40,387 (55.0)	26,156 (51.9)
Live in a household that knows about cholera vaccine (%)	3,131 (4.3)*	4,307 (8.5)
Live in household close (less than the median distance) to the nearest icddr,b hospital (%)	36,459 (49.7)	24,539 (48.6)
Mean number of individuals per household (SD)	5.0 (2.0)	5.0 (2.0)
Median distance to the nearest icddr,b hospitals (IQR; meters)	1766 (1264, 2248)	1812 (1221, 2400)
Mean percentage of children younger than 5 years in the cluster (SD)	10.0% (1.0)	10.1% (1.0)

Variables	Vaccine group (n=73,373)	Control group (n=50,443)
Mean percentage of male participants in the cluster (SD)	48.6% (1.2)*	49.1% (0.9)
Mean percentage of individuals using safe water source in the cluster (SD)	5.6% (4.9)	5.5% (3.6)
Mean percentage of individuals living in their own house in the cluster (SD)	23.2% (19.8)	28.1% (26.4)
Mean percentage of individuals using specific place for waste disposal in the cluster (SD)	82.0% (23.6)	76.6% (24.3)
Mean percentage of individuals using sanitary (flushing) toilet in the cluster (SD)	74.7% (23.2)	77.5% (21.7)

Note, the level of significance was derived after adjustment for the design effect.

\*The difference is statistically significant ( $p < .05$ ) compared to the control group.

Table A7. Baseline characteristics for analysis of total vaccine protection at the onset of the third year of follow-up

Variables	Vaccine group (n=54,454)	Control group (n=36,616)
Mean age at zero time (SD; years)	24.3 (16.7)*	25.5 (16.6)
Male participants (%)	25,460 (46.8)*	18,340 (50.1)
Diarrhoea within previous 6 months at the time of household registration (%)	7,908 (14.5)	5,120 (14.0)
Diarrhoea within previous 48 hours at the time of household registration (%)	697 (1.3)	401 (1.1)
Mean time living in the area (SD; months)	116.2 (142.3)	114.9 (145.2)
Lived in study area less than 1 year (%)	14,022 (25.8)	9,429 (25.8)
Live in their own house (%)	21,389 (39.3)	15,569 (42.5)
Households using safe water source (household tap, %)	4,208 (7.7)	2,719 (7.4)
Live in a household with specific place for waste disposal (%)	44,340 (81.4)	27,633 (75.5)
Live in a household with using sanitary (flushing) toilet (%)	40,143 (73.7)	28,100 (76.7)
Live in a household with a concrete roof (%)	47,278 (86.8)	30,887 (84.4)
Live in a household with only one room (%)	39,495 (72.5)	26,744 (73.0)
Sharing kitchen with other households (%)	44,506 (81.7)	27,550 (75.2)
Live in a household sharing water source with others (%)	32,163 (59.1)	19,518 (53.3)
Live in a household using treated water (boiled, filtered, or chemical treatment, %)	29,571 (54.3)	18,214 (49.7)
Live in a household that knows about cholera vaccine (%)	2,244 (4.1)*	2,869 (7.8)
Live in household close (less than the median distance) to the nearest icddr,b hospital (%)	26,367 (48.4)	17,098 (46.7)
Mean number of individuals per household (SD)	5.1 (2.0)	5.1 (2.0)
Median distance to the nearest icddr,b hospitals (IQR; meters)	1790 (1335, 2255)	1837 (1359, 2423)
Mean percentage of children younger than 5 years in the cluster (SD)	10.0% (1.0)	10.1% (1.0)



Variables	Vaccine group (n=54,454)	Control group (n=36,616)
Mean percentage of male participants in the cluster (SD)	48.6% (1.2)*	49.1% (0.9)
Mean percentage of individuals using safe water source in the cluster (SD)	5.8% (5.0)	5.6% (3.7)
Mean percentage of individuals living in their own house in the cluster (SD)	24.5% (20.4)	31.2% (27.5)
Mean percentage of individuals using specific place for waste disposal in the cluster (SD)	81.9% (23.7)	76.0% (24.5)
Mean percentage of individuals using sanitary (flushing) toilet in the cluster (SD)	74.7% (23.5)	76.6% (22.5)

Note, the level of significance was derived after adjustment for the design effect.

\*The difference is statistically significant ( $p < .05$ ) compared to the control group.

Table A8. Baseline characteristics for analysis of total vaccine protection at the onset of the fourth year of follow-up

Variables	Vaccine group (n=42,675)	Control group (n=28,734)
Mean age at zero time (SD; years)	24.5 (16.9)*	25.7 (16.8)
Male participants (%)	20,131 (47.2)*	14,537 (50.6)
Diarrhoea within previous 6 months at the time of household registration (%)	6,209 (14.5)	3,978 (13.8)
Diarrhoea within previous 48 hours at the time of household registration (%)	537 (1.3)	296 (1.0)
Mean time living in the area (SD; months)	128.9 (146.9)	129.0 (150.6)
Lived in study area less than 1 year (%)	9,653 (22.6)	6,375 (22.2)
Live in their own house (%)	19,149 (44.9)	14,000 (48.7)
Households using safe water source (household tap, %)	3,630 (8.5)	2,262 (7.9)
Live in a household with specific place for waste disposal (%)	34,595 (81.1)	21,472 (74.7)
Live in a household with using sanitary (flushing) toilet (%)	31,330 (73.4)	21,847 (76.0)
Live in a household with a concrete roof (%)	37,039 (86.8)	24,452 (85.1)
Live in a household with only one room (%)	29,993 (70.3)	20,401 (71.0)
Sharing kitchen with other households (%)	33,882 (79.4)	20,786 (72.3)
Live in a household sharing water source with others (%)	24,082 (56.4)	14,502 (50.5)
Live in a household using treated water (boiled, filtered, or chemical treatment, %)	22,695 (53.2)	13,618 (47.4)
Live in a household that knows about cholera vaccine (%)	1,676 (3.9)*	2,128 (7.4)
Live in household close (less than the median distance) to the nearest icddr,b hospital (%)	20,308 (47.6)	13,382 (46.6)
Mean number of individuals per household (SD)	5.1 (2.0)	5.1 (2.0)
Median distance to the nearest icddr,b hospitals (IQR; meters)	1819 (1397, 2260)	1837 (1372, 2446)
Mean percentage of children younger than 5 years in the cluster (SD)	9.9% (1.0)	10.1% (1.0)

Variables	Vaccine group (n=42,675)	Control group (n=28,734)
Mean percentage of male participants in the cluster (SD)	48.7% (1.2)*	49.2% (0.9)
Mean percentage of individuals using safe water source in the cluster (SD)	6.0% (5.2)	5.7% (3.7)
Mean percentage of individuals living in their own house in the cluster (SD)	26.0% (20.9)	33.6% (28.2)
Mean percentage of individuals using specific place for waste disposal in the cluster (SD)	81.7% (23.8)	75.5% (24.6)
Mean percentage of individuals using sanitary (flushing) toilet in the cluster (SD)	74.7% (23.6)	76.3% (22.9)

Note, the level of significance was derived after adjustment for the design effect.

\*The difference is statistically significant ( $p < .05$ ) compared to the control group.