



Recent Cholera Vaccine Research at the icddr,b

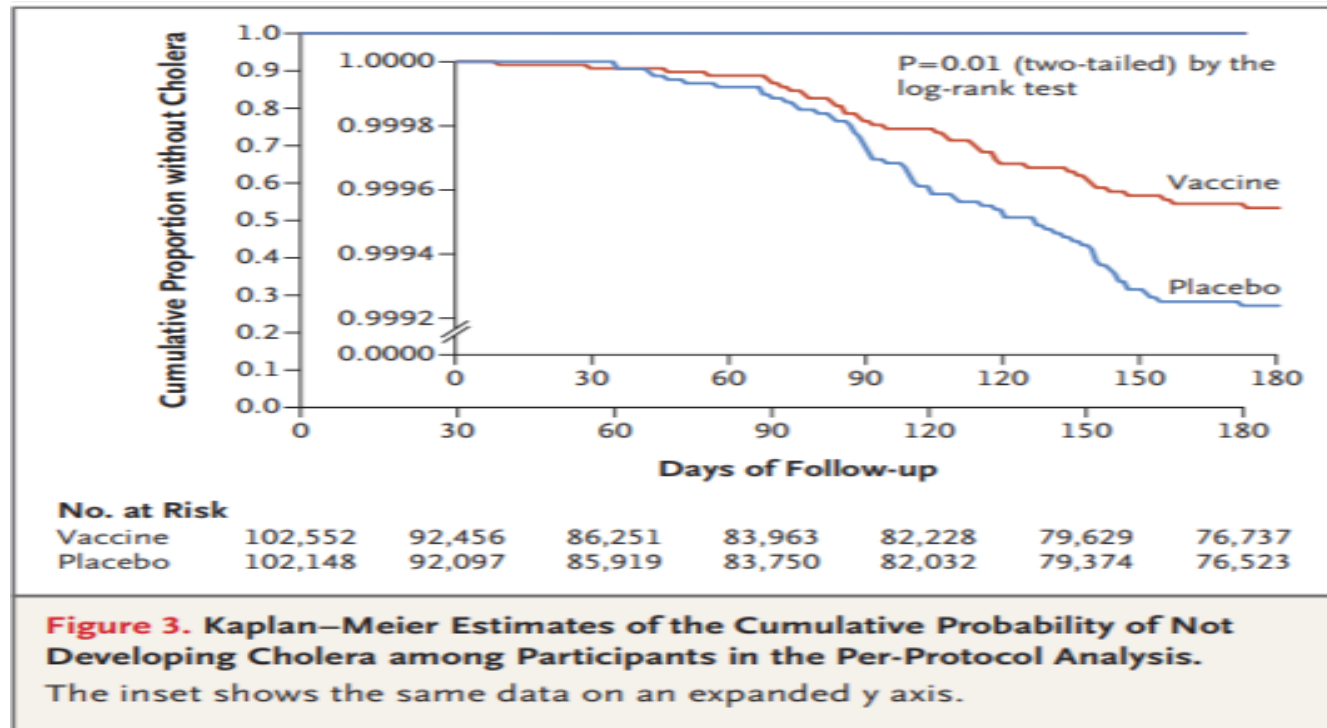
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RCT of a Single Dose of Shanchol in Urban Bangladesh

- Placebo-controlled, individually randomized, controlled clinical trial of a single dose of Shanchol administered to 205,700 non-pregnant persons aged one year and over in January-February, 2014

Results of the Single Dose OCV Trial (Qadri,2016)

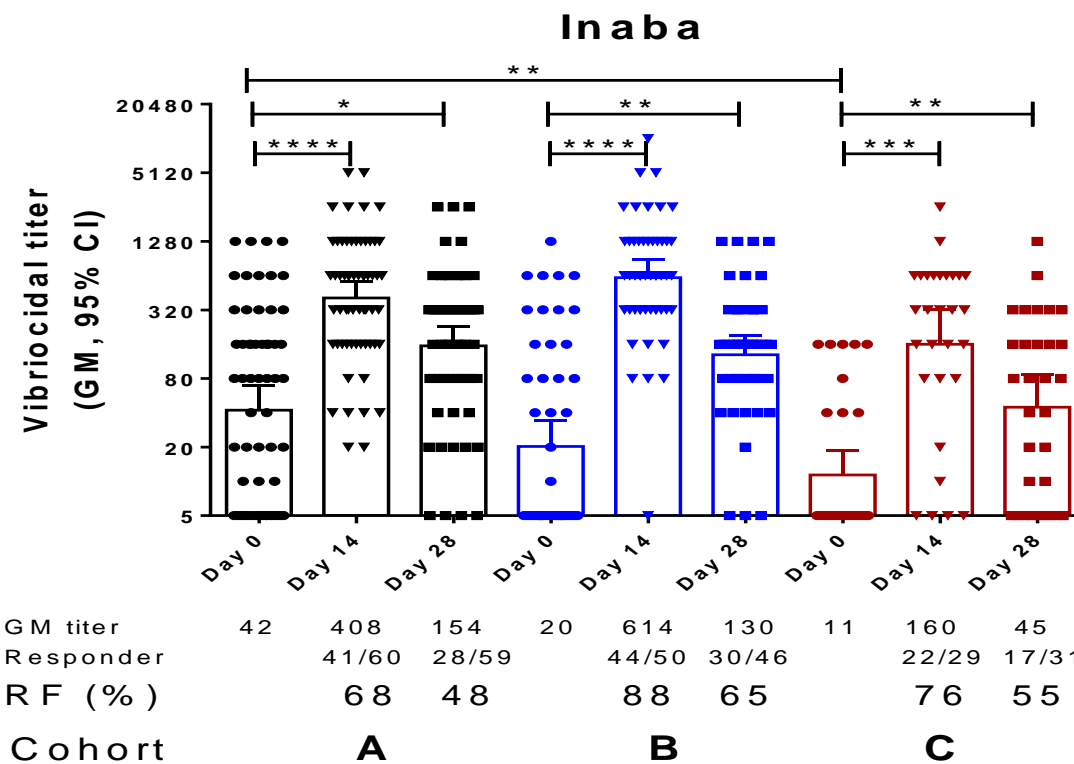


- 63% PE among 5-14 year olds; 56% PE among >14 year olds
- Nil PE in 1-4 year old age group

Rohingya Exiles: Cox's Bazaar,



Serum Vibriocidal Antibody Responses to a 2 Dose Regimen of Shanchol in the Rohingya Population



A: Adult cohort (>18 yrs)
 B: Older children cohort (6-17 yrs)
 C: Younger children cohort (1-5 yrs)

RCT of a Single Dose of Shanchol: Pregnancy Follow-up Post Dosing (Khan, 2019)

Table 2 Relative risk (RR) of having an adverse pregnancy outcome among OCV recipients compared to that of placebo recipients

Pregnancy outcome	OCV recipients		Placebo recipients		Crude RR (95% CI, <i>p</i> -value)	Adj. RR (95% CI, <i>p</i> -value)
	Cases/ Population	Rate/1000	Cases/ Population	Rate/1000		
<i>Pregnant during vaccination (Cohort 1)</i>						
Adverse pregnancy outcome	26/231	112.6	27/234	115.4	0.98 (0.58–1.62, 0.923)	0.97 ^a (0.58–1.61, 0.907)
Miscarriage	20/231	86.6	22/234	94.0	0.92 (0.51–1.64, 0.780)	0.91 ^a (0.51–1.63, 0.752)
Stillbirth	6/211	28.4	5/212	23.6	1.21 (0.37–4.13, 0.754)	– ^d
Preterm delivery	7/207	33.8	12/207	58.0	0.59 (0.22–1.43, 0.255)	0.58 ^a (0.22–1.40, 0.237)
Low birth weight	20/205	97.6	23/207	111.1	0.88 (0.49–1.55, 0.653)	0.88 ^a (0.49–1.55, 0.656)
<i>Pregnant after vaccination (Cohort 2)</i>						
Adverse pregnancy outcome	39/277	140.8	39/299	130.4	1.08 (0.71–1.63, 0.717)	1.02 ^b (0.67–1.55, 0.930)
Miscarriage	36/277	130.0	32/299	107.0	1.21 (0.78–1.91, 0.395)	1.15 ^b (0.73–1.81, 0.555)
Still birth	3/241	12.4	7/267	26.2	0.47 (0.10–1.69, 0.276)	– ^d
Preterm delivery	12/238	50.4	21/260	80.8	0.62 (0.30–1.22, 0.179)	– ^d
Low birth weight	19/238	79.8	26/260	100.0	0.80 (0.45–1.40, 0.434)	0.82 ^c (0.46–1.43, 0.477)

^a Adjusted for gestational age at vaccination

^b Adjusted for time of vaccination prior to pregnancy (included by choice due to biological plausibility), diarrhoea in past 6 months and roof material of household

^c Adjusted for diarrhoea in the past 6 months

^d Number of cases was not sufficient to perform a multivariable model

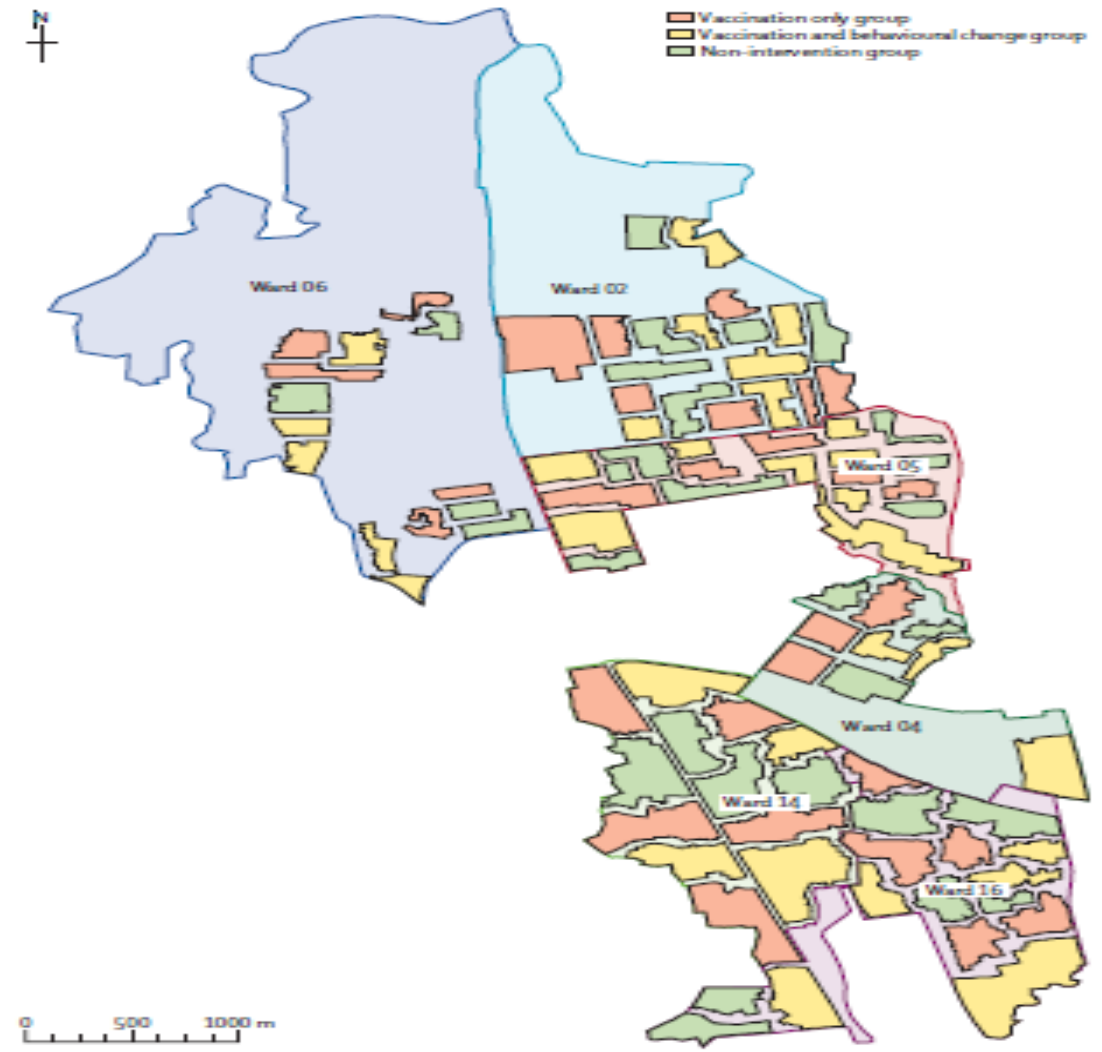
Self-Administration of Second Dose of Shanchol in Urban Slums of Dhaka, Bangladesh (Khan, 2018)

- 56,000 persons 1 year of age and older targeted
- 41,694 (74%) received dose 1 through mass immunization delivered by routine public health system (Government and NGOs) on June 6-19, 2017
- Ziplock bag with second dose and immunization card given at time of first dose, with instructions on home storage of vaccine and instructions for self-administration of second dose two weeks later
- Histories taken at homes shortly after 2 weeks revealed that 93% had taken second doses

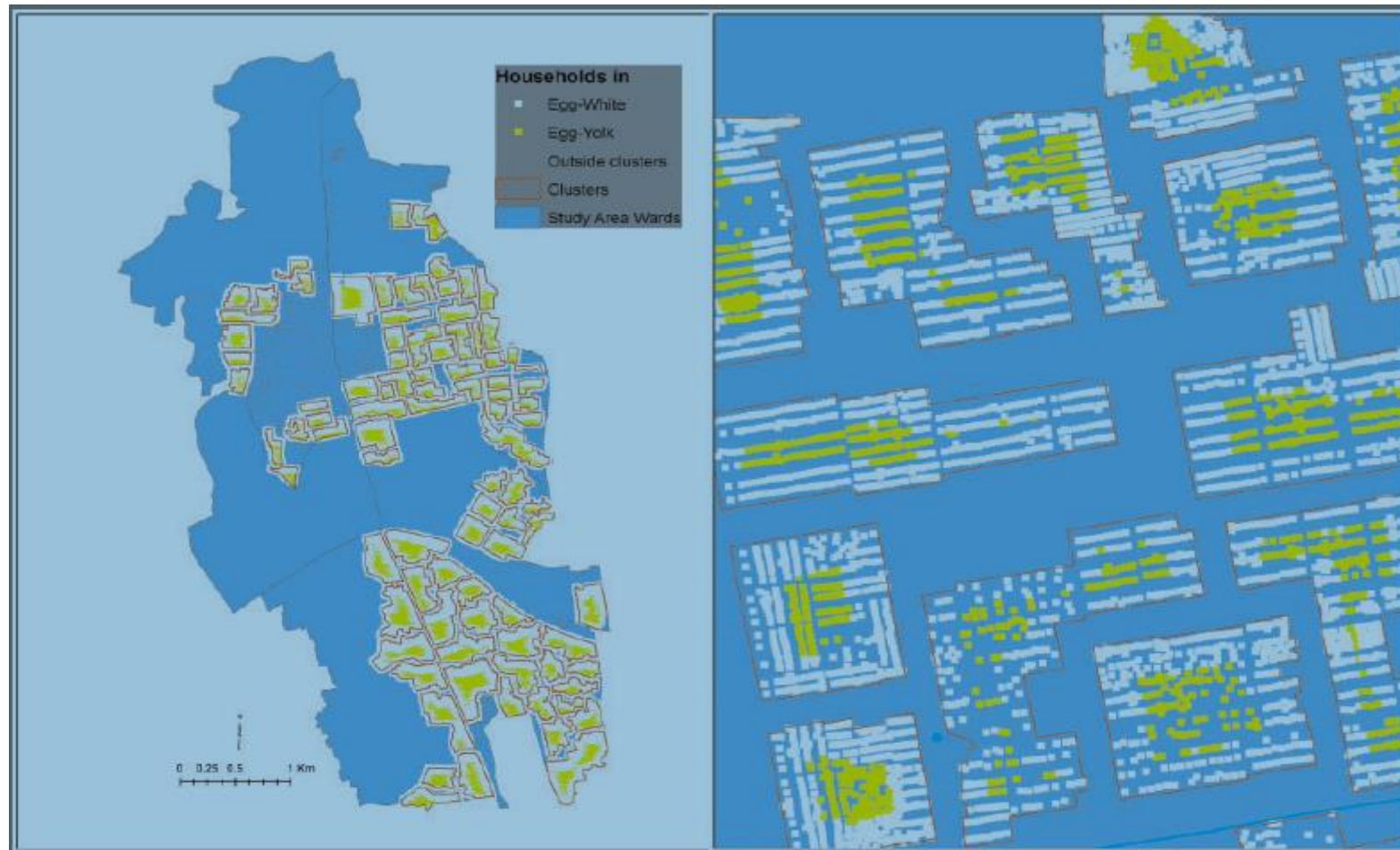
Could a Cluster Randomized Trial of Shanchol in Urban Dhaka Have Underestimated Vaccine Protection?

- ICVB study
 - 267,270 people residing in 90 geographic clusters in urban Dhaka randomized in 2011 (1:1:1) to:
 - * 2 doses of Shanchol (1 yr and older)
 - * Shanchol (1 yr and older) plus WASH
 - * Control
- Ca. 65% OCV coverage
- 2 years of follow up for severe cholera (primary outcome) with passive surveillance
- WASH added little to the protection by Shanchol
- Overall protection in the 2 intervention arms combined was 46%

Map of the Clusters in the ICVB Trial



Analysis Using the “Fried Egg Approach” (Ali, 2019)



Overall, Total, and Indirect OCV Protection against Severe Cholera in Populations Defined by Different Sized “Yolks” (Ali, 2019)

Measures of protection	Intervention arm (no. of clusters = 60)			Non-intervention arm (no. of clusters = 30)			Protective effectiveness (PE) ^a		
	No. of persons	No. of cases	Rate/1000 person-years	No. of persons	No. of cases	Rate/1000 person-years	PE (%)	95% CI	<i>P</i> value
P100 clusters									
Overall	187 214	120	0.53	80 056	106	0.98	46	30 to 59	<0.0001
Total	123 659	64	0.41	78 518	105	0.99	58	43 to 70	<0.0001
Indirect	45 784	43	0.83	80 056	106	0.98	16	-20 to 41	0.3502
P75 clusters									
Overall	143 915	97	0.56	61 398	78	0.95	41	21 to 56	0.0005
Total	95 254	56	0.46	60 196	77	0.95	51	30 to 65	<0.0001
Indirect ^b	35 039	32	0.81	61 398	78	0.95	12	-31 to 43	0.5000
P50 clusters									
Overall	95 310	62	0.54	40 758	55	1.00	47	23 to 63	0.0007
Total	63 185	31	0.38	39 960	55	1.02	62	40 to 75	<0.0001
Indirect ^b	23 156	25	0.95	40 758	55	1.00	1	-60 to 39	0.9557
P25 clusters									
Overall	45 748	18	0.32	20 725	31	1.13	72	49 to 84	<0.0001
Total	30 342	11	0.28	20 343	31	1.16	75	50 to 87	<0.0001
Indirect	11 192	7	0.56	20 725	31	1.13	52	-9 to 79	0.0783