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Oral cholera vaccination campaigns

This online first version has been peer-reviewed, accepted and edited,
but not formatted and finalized with corrections from authors and proofreaders.

Post-licensure deployment of oral cholera vaccines: a systematic review

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(Submitted: 13 April 2014 – Revised version received: 14 September 2014 – Accepted: 17 September 2014 – Published online: 29 September 2014)

Abstract

Objective To describe and analyse the characteristics of oral cholera vaccination campaigns; including location, target population, logistics, vaccine coverage and delivery costs.

Methods We searched PubMed, the World Health Organization (WHO) website and the Cochrane database with no date or language restrictions. We contacted public health personnel, experts in the field and in ministries of health and did targeted web searches.

Findings A total of 34 documents were included in the analysis. One country, Viet Nam, incorporates oral cholera vaccination into its public health programme and has administered approximately 10.9 million vaccine doses between 1997 and 2012. In addition, over 2 million doses of the two WHO pre-qualified oral cholera vaccines have been administered in 16 campaigns around the world between 1997 and 2014. These campaigns have either been pre-emptive or reactive and have taken place under diverse conditions, such as in refugee camps or natural disasters. Estimated two-dose coverage ranged from 46 to 88% of the target population. Approximate delivery cost per fully immunized person ranged from 0.11–3.99 United States dollars.

Conclusion Experience with oral cholera vaccination campaigns continues to increase. Public health officials may draw on this experience and conduct oral cholera vaccination campaigns more frequently.

Introduction

Vibrio cholerae causes severe diarrhoea and the main strategies to prevent the disease are to promote hygiene and to ensure safe water and sanitation. These basic needs are often not met in endemic areas with seasonal cholera outbreaks or during man-made or natural disasters in impoverished areas. An additional tool for cholera prevention and control is the oral cholera vaccine. In October 2009, the World Health Organization (WHO) Strategic Advisory Group of Experts on immunization recommended that oral cholera vaccination should be considered as a reactive strategy during outbreaks, in addition to the already recommended preventive use of oral cholera vaccine in endemic areas.¹ A vaccine stockpile was created in 2012, with an initial two million doses to be available mainly for epidemic response in low-income countries.² In November 2013, the global alliance for vaccines and immunizations (Gavi Alliance) approved a financial contribution towards the stockpile to expand its use in outbreak situations and endemic settings. With the availability of the oral cholera vaccine stockpile, more governments might consider cholera vaccination where needed.

A monovalent inactivated vaccine containing killed whole-cells of *V. cholerae* serogroup O1 and the B-subunit of cholera toxin was the first oral cholera vaccine to obtain international licensure in 1991 and WHO prequalification in 2001. The vaccine is marketed as Dukoral (Crucell, Netherlands). Randomized, placebo-controlled trials of earlier versions of Dukoral in Bangladesh and the current recombinant B-subunit whole cell vaccine in Peru showed that the vaccine is safe and confers an initial protection of approximately 85% in the first months.^{3,4} Follow-up studies in Bangladesh estimated a 62% protection during the first year, 57% during the second year and negligible thereafter.³

During the mid-1980s, the National Institute of Hygiene and Epidemiology in Viet Nam developed an oral cholera vaccine for the country's public health programme. A two-dose regimen of a first-generation of monovalent (anti-O1) cholera vaccine had an estimated efficacy of 66% against the El Tor strain of *V. cholerae*.⁵ In 1997, the vaccine was augmented with killed *V. cholerae* serogroup O139 whole cells to create a bivalent vaccine,⁶ which was locally licensed as ORC-Vax (Vabiotech, Viet Nam). After changing production procedures in 2009, the vaccine

was reformulated and licensed as mORC-Vax (Vabiotech, Viet Nam) and is currently used in Viet Nam's public health programme.⁷ However, the vaccine is not pre-qualified by WHO.

To make the mORC-Vax internationally available, manufacture of the reformulated vaccine was transferred to Shantha Biotechnics Ltd in India, where the national regulatory authority is approved by WHO.⁸ This led to the development of Shanchol, which is the third currently-available oral cholera vaccine. A randomized, placebo-controlled trial in India showed that Shanchol is safe and confers 67% protective efficacy against cholera within two years of vaccination,⁸ 66% at three years⁹ and 65% at five years¹⁰ of follow-up. Shanchol was licensed in India in 2009 and received WHO pre-qualification in 2011.

A comparison of the three oral cholera vaccines is shown in Table 1.^{11,12} The safety, relative effectiveness and duration of protection of the different types of oral cholera vaccine has previously been reviewed.¹³ Here we conduct a systematic review of post-licensure oral cholera vaccination campaigns. The objective of the review is to generate information – by describing and analysing the campaigns – that can be used to inform planning for the future use of these vaccines.

Methods

Search

We searched the Cochrane database of systematic reviews and their database of abstracts and reviews of effects from 1990 to present and found no reviews of oral cholera vaccination campaigns.

We conducted a systematic review of published documents on post-licensure vaccination campaigns using one of three oral cholera vaccines following the search and analysis process recommended in the Preferred Reporting Items for Systematic Reviews and Met-analyses guidelines. We searched PubMed and the WHO web site using “cholera vaccination”, “cholera outbreak response” and “cholera vaccination campaign” as search terms with no date or language restrictions. The bibliographies of the retrieved articles were also screened for relevant papers. Reports, presentations and international organization or company documents were obtained through targeted web searches. We also contacted public health personnel, experts in the field and in ministries of health for further information.

All identified documents in English that described campaigns using oral cholera vaccine were assessed for appropriateness using the following selection criteria. We included all documents describing campaigns using Dukoral after 1991, ORC-Vax after 1997, mORC-Vax after 2009 and Shanchol after 2009. Campaigns organized either as part of a public health response to endemic or epidemic cholera, pilot campaigns, demonstration projects, assessments of feasibility and acceptability, as well as studies of vaccine effectiveness were included. Each campaign may have more than one reference, describing different aspects of the vaccination (e.g. feasibility, coverage, cost, etc.). We excluded documents describing pre-licensure trials, reports on knowledge and perception of cholera and oral cholera vaccines, as well as planning or policy briefs that did not describe actual oral cholera vaccine deployment.

By adhering to the pre-defined inclusion and exclusion criteria, we could make a valid comparison across articles. To assess the broad picture of the vaccine campaigns, we did not exclude any document based on quality or deficiency of reporting. Information from the published and unpublished documents was extracted and entered into a spread sheet independently by two of the authors and then corroborated and summarized by a third author.

Definitions

Oral cholera vaccine campaigns can either be pre-emptive or reactive. Pre-emptive or preventive vaccination refers to campaign implementation before a cholera outbreak begins, ideally in conjunction with improved water, hygiene and sanitation. Pre-emptive vaccination may be conducted before the next seasonal outbreak in sites where cholera regularly occurs, in communities adjacent to an area with cholera or during humanitarian emergencies to prevent cholera. Reactive campaigns are those implemented after a cholera outbreak has started and while cholera cases are still being detected in the target population.¹⁴ In areas where cholera tends to occur all year-round, the distinction between pre-emptive and reactive vaccination may be difficult.

The target population was defined as the number of individuals living in a circumscribed area to whom oral cholera vaccine is offered. The target population may be an estimate based on administrative population figures or more precise figure based on a study census. Coverage was defined as the percentage of the target population who received one dose and two doses (fully immunized) of the vaccine, except when otherwise indicated (i.e. community surveys were used to calculate vaccine coverage in some campaigns particularly when a precise target population

number was not known). The approximate total number of oral cholera vaccine doses deployed was defined as the sum of the first and second dose recipients; when data on the first dose recipients were not available, we multiplied the number of fully vaccinated individuals by two. We plotted the number of approximate doses deployed in oral cholera vaccine campaigns by country. Countries were colour-coded by the number of cholera cases reported in 2005,¹⁵ using ArcMap 10.0 (ESRI, Redlands, USA). Adverse events following immunization were defined as medical incidents that take place after an immunization and cause concern. Adverse events following immunization may be coincidental or causally associated. A serious adverse event following immunization is one that requires hospitalization and/or causes birth defects, permanent damage, or death.

To allow comparison of the expenses for vaccination across various campaigns, the expenses were grouped into the following categories: vaccine and/or international shipment costs, computers and other capital expenses, international consultants, local storage and transport, meetings, social mobilization, training, local salaries, supplies and waste management and the detection and management of adverse events following immunization. The delivery cost per fully immunized person was calculated using the total local expenses (excluding vaccine, international shipment and consultant costs) as the numerator and the number of fully immunized persons as the denominator.

Results

We identified 174 unique documents of potential relevance and 34 of these met the inclusion criteria (Fig. 1).¹⁶⁻⁴⁹ In addition, we obtained information about recent campaigns through personal communications with two co-authors (Stephen Martin and Kathryn Alberti). We mapped the approximate number of doses administered in post-licensure oral cholera vaccination campaigns from 1997 to 2014 (Fig. 2) and plotted them by year (Fig. 3). The characteristics and main findings of each vaccination campaign are shown in Table 2. For campaigns with detailed data available, the vaccination logistics by target population size is shown in Table 3.

Dukoral

About 526 017 doses of Dukoral were administered in six vaccination campaigns from 1997 to 2009, all of which were pre-emptive (Table 2).¹⁶⁻³⁰ These included two feasibility studies in refugee camps^{16,17,22,23} and one campaign following a natural disaster.^{23,24} The percentage of

fully immunized persons ranged from 50–88%. There were two effectiveness studies in sub-Saharan Africa, which confirmed direct vaccine protection of 78–79%, 12 to 15 months following vaccination^{21,27}, as well as herd protection.²⁷ We found one document stating that 137 000 Dukoral doses were delivered to Myanmar in 2008²⁵ but we were unable to find more information.

The duration of the vaccination campaigns ranged from one to five months and consisted of two rounds at a 10- to 14-day interval (Table 3). Each round took 4 to 15 days.^{16,20,23,24,27} Cold chain for vaccine delivery was reportedly maintained at 2–8 °C from storage to administration in Beira, Mozambique²⁰, Aceh, Indonesia²⁴ and Zanzibar, United Republic of Tanzania.²⁷ In Uganda, the vaccine was maintained at room temperature.¹⁶ Vaccination teams were able to vaccinate 100 to 609 persons per day.^{16,20,23,24,27} Reported adverse events following immunization in Uganda and Mozambique were minor and non-specific.^{16,20} Delivery cost per fully immunized person ranged from 0.53 United States dollars (US\$) to US\$ 3.66 (Table 4).

ORC-Vax and mORC-Vax

In Viet Nam, an estimated 10.9 million doses of ORC-Vax and mORC-VAX have been deployed from 1997 to 2013 through targeted mass vaccination or – to children – through the Expanded Programme of Immunization in cholera-endemic regions.^{31–34} Documented coverage during the vaccination of half of the communes in Hue was 79% (118 703/149 557) in 1998 and 75% (103 226/137 082) in the other half in 2000; long term vaccine effectiveness (three to five years after the campaign) was 50%.^{31,32} (Table 2). Vaccine coverage was not precisely quantified in the 2008 Hanoi campaign; vaccine effectiveness was 76%.³³ The duration of the vaccination campaigns ranged from two to four weeks with each round taking 3 to 9 days (Table 3).^{31–33} Mass campaigns are held yearly in Hue and are part of the routine public health provision, requiring minimal additional costs. The delivery cost in Hue during a 2013 campaign was US\$ 0.11 per fully immunized person.³⁴

Shanchol

Since WHO pre-qualification, Shanchol has been increasingly used in campaigns.^{35–49} About 1 535 293 doses have been administered in ten campaigns (Table 2), three of which were described as reactive. The percentage of fully immunized persons ranged from approximately 46–85% (Table 2). A study in Odisha, India 2011, found that oral cholera vaccination through the Indian public health system is feasible.³⁵ The campaign in Dhaka, Bangladesh 2011, includes

an assessment of vaccine effectiveness with and without other interventions.³⁶ The two vaccination campaigns in Haiti in 2012 were pilot projects that paved the way for the launching of a national cholera vaccination programme integrated in a long-term plan to address water safety and sanitation.^{37–41} There was third campaign in Haiti in 2013. Shanchol was deployed for pre-emptive vaccination in Solomon Islands, in 2012, following reports of cholera in a nearby area.⁴² The vaccination campaign in Thailand, 2012, was conducted to prevent seasonal outbreaks in a stable camp setting.⁴³ The vaccination campaign in Guinea, 2012, was the first reactive oral cholera vaccine campaign in sub-Saharan Africa and the first time that Shanchol was used in an African setting.^{44–46} The campaigns in Guinea and in Maban county, South Sudan 2013 confirmed that large-scale vaccinations under logistically difficult conditions are feasible.^{47,48} The campaign in internally displaced persons camps in South Sudan in 2014, was the first to use the oral cholera vaccine stockpile.⁴⁹

The Shanchol campaigns were conducted in 1–3 months.^{35–49} The 2012 Haiti campaign was carried out in two phases due to an overlapping national oral polio vaccination campaign.^{37–41} The number of persons vaccinated per day ranged from 774–1150.^{36,44–49} No serious adverse events following immunization were reported. In campaigns in Odisha, Dhaka and in Haiti in 2012, cold chain for vaccine was maintained at 2–8 °C from storage to delivery at site.^{35–41} In the campaigns in Guinea and in 2013 in South Sudan cold chain was maintained until the day of vaccination, during which vaccines were transported to vaccination sites and used at ambient temperature^{44–48} (Table 3).

The delivery costs of Shanchol through the existing government health system in Bangladesh and India were US\$ 1.63 and US\$ 1.13, respectively, per fully immunized person.^{35,36} The local expenses of reactive deployment in Guinea was US\$ 1.97,⁴⁶ while costs in Maban, South Sudan were US\$ 3.99 per fully immunized person (Table 4).⁴⁸

Discussion

We estimate that about 2 061 310 doses of Dukoral and Shanchol have been deployed in vaccination campaigns in areas affected by cholera around the world from 1997 to 2014. Only one country, Viet Nam, incorporates oral cholera vaccination into its public health programme and has used more than 10 million doses since 1997. Recently larger numbers of doses have been deployed in different areas globally but the vaccine is still under-used compared to the 1.4 billion people at risk of cholera in endemic areas.¹⁵ There is a shortage of licensed, WHO-prequalified

cholera vaccines to meet global endemic and epidemic needs and insufficient supply is often cited as an obstacle to wider vaccine use.⁵⁰ Availability of an oral cholera vaccine stockpile may lead to a larger vaccine supply through more consistent and predictable demands and may help increase vaccine use. Insufficient vaccine supply can be addressed by encouraging manufacturers to increase production capacity.

The deployments of oral cholera vaccine have previously been pre-emptive but recent experiences in Guinea and Haiti have shown that reactive mass vaccinations are feasible.^{37–41,44–46} The number of cases and deaths that can be prevented by reactive vaccination depends on the characteristics of the outbreak, with greatest impact during large and long-lasting outbreaks usually seen in populations with no recent exposure to the disease.¹⁴ With the development of an oral cholera vaccine stockpile and possibility of rapid deployment, increased reactive use of oral cholera vaccine is anticipated.

To be able to compare the campaigns, we calculated the total delivery cost per fully immunized person by excluding the expenditures for vaccine, shipment and technical experts, but the estimates still varied considerably. Deployment costs were lowest in Hue, Viet Nam, where the vaccine is administered routinely through the public health system^{31,34} but a similar delivery strategy may not be possible in other cholera-endemic areas or during the acute phase of emergencies. The requirement for co-administration of a buffer with the Dukoral vaccine complicates the delivery of such vaccine and likely increases its delivery costs. Both mORC-Vax and Shanchol do not require a buffer, which should streamline the delivery and reduce logistical requirements.

This analysis has several limitations. First, there was a wide variation in the methods used to calculate coverage and costs in the vaccination campaigns. Some coverage estimations were precise, while others were approximations. Although we attempted to make the costing comparable, the calculated figures should be interpreted with caution. There are large variations in the costing of some items that cannot merely be explained by differences in site conditions and access. There are also local variables such as distance from central storage to the vaccine administration sites, campaign duration and vaccine storage conditions that affect the costs. Variations in campaign logistics also influence the estimates. Differences may also arise from the methods used to calculate expenses. For future campaigns, estimating cost using a standardized method would be very useful. Second, reporting was not consistent, as some information about

the campaign, such as coverage, delivery, adverse events following immunization monitoring and other details, were not always measured or reported. We obtained the least information on the oral cholera vaccine campaigns in the Comoros and the Solomon Islands. Third, the more recent post-licensure vaccination campaigns (for example in Ethiopia and Nepal) have not been included and will require updated reporting as information becomes available. Fourth, 29% (10/35) of documents included in the analysis were not published in peer-reviewed journals but were the only available sources of data for some of the vaccination campaigns. Fifth, many of the campaigns are done in collaboration between ministries of health and external health agencies (e.g. Médecins Sans Frontières, WHO, Partners for Health, United States' Centers for Disease Control and Prevention). It will be important to continue to monitor and evaluate future campaigns using vaccine from the stockpile and implemented mainly by ministries of health.

Despite these limitations, our findings provide important lessons. The number of oral cholera vaccination campaigns is increasing and experience has been documented in a variety of settings. The increasing use of oral cholera vaccine is reassuring but more needs to be done to encourage its use where needed. This increase will likely continue with the availability of an oral cholera vaccine stockpile and as more experience is gained with campaigns. Data from the deployments confirm the effectiveness, safety and feasibility of mass oral cholera vaccination. While the two-dose vaccination schedule may be perceived as an impediment to delivery and coverage, the experience with both Dukoral and Shanchol disproves this perception. In addition, community education on cholera control and distribution of other preventive measure such as soap and chlorine solution were feasibly integrated into recent vaccination campaigns.^{36,38–40,44–46} We also found that there were substantial differences in how the campaigns were reported making comparisons difficult. A more systematic approach to decision-making – such as a rapid assessment tool – and a standardized method for data collection, monitoring and evaluation should be pursued, supported and published. This will ensure appropriate documentation of future campaigns.

Funding

This research was supported by the World Health Organization and by the Delivering Oral Vaccine Effectively (DOVE) project. DOVE is supported by the Bill and Melinda Gates Foundation and administered through the Johns Hopkins Bloomberg School of Public Health.

Competing interests:

None declared.

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Table 1. **Oral cholera vaccines, 2014**

Vaccine	Dukoral¹¹	ORC-Vax and mORC-Vax^{11,12}	Shanchol¹¹
Manufacturer	Crucell (the Netherlands)	Vabiotech (Viet Nam)	Shantha Biotechnics Ltd (India)
Description	Monovalent inactivated vaccine	Bivalent inactivated vaccine	Bivalent inactivated vaccine
Components	Killed whole-cells of <i>V. cholerae</i> O1 (Classical and El Tor biotypes) and recombinant B-subunit of cholera toxin	Killed whole cells of <i>V. cholerae</i> O1 (Classical and El Tor biotypes) and <i>V. cholerae</i> O139	Killed whole cells of <i>V. cholerae</i> O1 (Classical and El Tor biotypes) and <i>V. cholerae</i> O139
Recommended age	2 years and older	1 year and older	1 year and older
Delivery	Oral	Oral	Oral
Doses	Two doses \geq 1 week apart	Two doses \geq 2 weeks apart	Two doses \geq 2 weeks apart
Buffer	Yes. Buffer dissolved in 75 mL (2–6 years old) or 150 mL (> 6 years old) water	Not required	Not required
Booster dose	Every 2 years (every 6 months for children 2–5 years)	Every 3 years	Every 3 years
Licensure	International (1991)	Viet Nam (1997/2009)	India (2009)
WHO pre-qualification	Yes (2001)	No	Yes (2011)
Storage temperature	2–8 °C	2–8 °C	2–8 °C

Table 2. **Characteristics and main findings of post-licensure oral cholera vaccination campaign studies, 1997–2014**

Vaccine and year of the campaign	Site	Setting	Type and purpose of the vaccination campaign	Eligibility criteria	Target population, No.	Coverage		Main findings
						Received 1 st dose, No. (%)	Received 2 nd dose, No. (%)	
Dukoral 1997	Adjumani district, Uganda	Refugee camp, rural	Pre-emptive vaccination to assess feasibility in a stable refugee camp setting ^{16,17}	≥ 1 year old	44 000	35 613 (81)	27 607 (62)	Oral cholera vaccination of a large refugee population is feasible. ¹⁶ During a cholera epidemic in the area the following year, cholera attack rates were 0.59% in the non-refugee Ugandan villages, 0.04% in the 30 non-vaccinated refugee camps and 0.00% in the six vaccinated refugee camps ¹⁷
2000	Mayotte Island, Comoros	Urban and rural	Pre-emptive vaccination campaign to prevent a cholera epidemic ¹⁸	N/A	145 000	NA	93 000 (64)	N/A
2003–2004	Beira, Mozambique	Urban	Pre-emptive vaccination in an endemic area with seasonal outbreaks. Effectiveness study in an HIV-endemic sub-Saharan African site ^{20,21}	Non-pregnant, ≥ 2 years old	19 550	14 164 (72)	11 070 (57)	Mass vaccination was feasible but required considerable logistic support and planning. ²⁰ One or more doses conferred 78% protection (95% CI: 39–92) against cholera during the year post vaccination ²¹
2004	South Darfur, Sudan	Refugee camp, rural	Pre-emptive vaccination to assess feasibility during the acute phase of an emergency (i.e. refugee camp of internally displaced persons) ^{22,23}	≥ 2 years old	45 825	42 502 (93)	40 330 (88%)	Although planning and implementation requirements were significant, the campaign was successful because of the strong support and commitment of the refugee community and collaborators ^{22,23}
2005	Aceh, Indonesia	Site of internally displaced persons	Pre-emptive vaccination to assess feasibility during the acute phase of an emergency (i.e. post-tsunami) ^{23,24}	≥ 2 years old	78 870	62 505 (79%)	54 627 (69%)	Challenges in the coordination, heavy logistics and frequent aftershocks complicated and delayed implementation. Difficulties in maintaining cold chain resulted in 11.7% vaccine losses ^{23,24}

2009	Zanzibar, the United Republic of Tanzania	Urban and rural	Pre-emptive vaccination in an endemic area with seasonal outbreaks. Effectiveness study to measure direct and indirect protection ^{27–29}	Non-pregnant, ≥ 2 years old	48 178	27 678 (57%)	23 921 (50%)	Confirmed direct vaccine effectiveness of 79% (95% CI: 47–92). First study to show vaccine herd protection in an African setting: 75% (95% CI: 11–93%) indirect protection in the higher coverage group compared with the lower coverage group ²⁷ No evidence of a harmful effect of gestational exposure to the vaccine ²⁸ First use of personal digital assistants for direct data entry during a survey enumeration and mass vaccination ²⁹
ORC-Vax and mORC-Vax 1998–2012	Viet Nam	Endemic urban and rural areas	Pre-emptive and reactive vaccinations of children integrated into the country's public health program ³⁴	Non-pregnant, ≥ 1 year old	≈10.9 million doses	N/A	N/A	Viet Nam is the only country in the world to regularly use oral cholera vaccinations. Since 1997, the number of cholera cases in Viet Nam has declined, in association with increased vaccination use as well as improvements in socioeconomic and water and sanitation conditions ³⁴
1998 and 2000	Hue, Viet Nam	Urban and rural	Pre-emptive vaccination campaign in a cholera-endemic area. Study to assess long term effectiveness ^{31,32}	Non-pregnant, ≥ 1 year old	149 557 (1998) and 137 082 (2000)	In 1998: 125 135 (84%) and in 2000:104 706 (76%)	In 1998:118 703 (79%) and in 2000:103 226 (75%)	Mass immunization is feasibly administered through the public health system. ³¹ Direct vaccine effectiveness 3 to 5 years after vaccination was 50% (95% CI: 9–63) ³²
2008	Hanoi, Viet Nam	Urban	Reactive vaccination campaign during an ongoing outbreak ³³	Non-pregnant, ≥ 1 year old	≈370 000 > 10 years old	N/A	≈80% vaccinated	Protective effectiveness of 76% (95% CI: 5–94). First study to document reactive use of oral cholera vaccination during an outbreak ³³
Shanchol 2011	Odisha, India	Rural	Pre-emptive vaccination campaign and feasibility study ³⁵	Non-pregnant, ≥ 1 year old	51 488	31 552 (61%)	23 751 (46%)	Feasible to vaccinate using governmental set-up ³⁵

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2011	Dhaka, Bangladesh	Endemic urban areas	Pre-emptive vaccination. Cluster randomized study with three arms: vaccine, vaccine plus safe water and hand washing practice and no intervention ³⁶	Non-pregnant, ≥ 1 year old	172 754	141 839 (82%)	123 666 (72%)	Feasible to us the national immunization setup. ³⁶ On-going study of vaccine effectiveness.
2012	Port-au-Prince, Haiti	Urban	Reactive vaccination campaign. Pilot study ³⁷	≥ 1 year old	70 000	52 357 (75%)	47 540 (68%)	Effort, community mobilization and organizational capacity needed for a successful campaign where there were logistical and security challenges ³⁷
2012	Bocozel and Grand Saline, Haiti	Rural	Reactive vaccination campaign. Pilot study ^{38–41}	≥ 1 year old	N/A	45 417	41 238	The campaign integrated with the other components of cholera control was found to be feasible and acceptable ^{38–41}
2012	Choiseul and Shortland, Solomon Islands	Rural	Pre-emptive vaccination campaign near an area with a cholera outbreak ⁴²	Children 1–14 years old in high-risk areas	N/A	11 888	11 318	N/A
2012	Tak Province, Thailand	Refugee camps, rural	Pre-emptive vaccination campaign with a knowledge, attitudes and practices survey ⁴³	Non-pregnant, ≥ 1 year old	43 968	36 325 (83%)	26 753 (61%)	First use of Shanchol in a stable refugee camp setting ⁴³
2012	Boffa and Forecariah regions, Guinea	Rural	Reactive vaccination campaign during an on-going outbreak and feasibility study ^{44–46}	≥ 1 year old	$\approx 209\ 000$ ($\approx 163\ 000$ in Boffa and $\approx 46\ 000$ Forecariah)	172 544	143 706 (Based on administrative population figures, 68% in Boffa and 51% in Forecariah. Household survey immediately after campaign 76%.) ⁴⁴	First use of Shanchol in sub-Saharan Africa. The campaign was successful despite short preparation time, remote rural setting and highly mobile population. ^{44,45} Protective effectiveness of 87% (95% CI: 56–96) ⁴⁶
2013	Maban county, South Sudan	Refugee camps, rural	Pre-emptive vaccination campaign in an area with escalating Hep E outbreak ^{47,48}	≥ 1 year old	146 317	N/A	132 000 (> 85% by survey)	The campaign was successful despite logistical challenges ^{47,48}
2013	Petite Anse, Haiti	Urban and rural	Pre-emptive vaccination campaign in a cholera-endemic area ^a	≥ 1 year old	110 000	N/A	80 000	N/A

2014	South Sudan	Internally displaced persons camps	Pre-emptive vaccination campaign ⁴⁹	Non pregnant, ≥ 1 year old	152 000	125 311 (72%)	76 088 (awaiting coverage surveys)	Humanitarian crisis. First use of global OCV stockpile, Fixed and mobile teams. Second round in one site was co-administered with meningitis vaccine ⁴⁹
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CI: confidence interval; Hep E: Hepatitis E; N/A, information not available.

^a Information obtained through personal communications with Kathryn Alberti, UNICEF, New York, USA.

Table 3. **Logistics of oral cholera vaccination campaigns, 1997–2013**

Target population size	Site, year	Vaccine	Max. days per round	Total duration	Delivery method	Approximate doses delivered/day	Staff
< 50 000	Adjumani district, Uganda, 1997 ¹⁶	Dukoral	4	Just over 1 month	15 vaccination sites	250–1735	114 persons: 19 nurses/midwives, 21 nursing aides, 44 community health workers and 30 persons without qualifications
	Esturro, Beira, Mozambique, 2003–2004 ²⁰	Dukoral	9	1 month	Outposts in churches and schools 8am–3pm 6 days/week	Average 609	One supervisor and 15–23 members per outpost
	Zanzibar, the United Republic of Tanzania, 2009 ²⁷	Dukoral	15	Just over 1 month	Eight vaccination posts on each of the two islands. 8 hours daily.	N/A	Local health care workers and villagers
	Aceh, Indonesia, 2005 ^{23,24}	Dukoral	N/A	5 months	Three-phase approach, three different geographical areas with approximately one month between each phase. Fixed vaccination sites with some door to door mop-up.	100–250	4 members per team
50 000 to 100 000	Odisha, India, 2011 ³⁵	Shanchol	3	1 month	Vaccination booths within 10–15 minute walking distance from villagers open 7am–5pm daily.	N/A	At each booth: 1 midwife and 5–6 community health workers/volunteers
	City of God, Port-au-Prince and Bocozele and Grand Saline, Artibonite Department, Haiti, 2012 ^{37,39}	Shanchol	Urban: N/A Rural: 10	3 months per site	Urban: door to door pre-registration and vaccination at 9 fixed sites. Rural: fixed posts, mobile posts and door to door	N/A	Urban campaign: 500 staff, 75 teams of 4 workers, plus 15 supervisors Rural: 40 teams of 4 workers each led by 20 supervisors
> 100 000	Viet Nam 1998 and 2000 ^{31,32}	ORC-Vax	9	1 month	Specifically designated sites, also used by EPI. 90 sites.	139 (max)	90 teams
	Viet Nam 2008 ³³ Mirpur, Dhaka, Bangladesh 2011 ³⁶	ORC-Vax Shanchol	3 3-day cycles	13 days One and half months	Commune health centres Fixed outreach vaccination sites. Sixty vaccine clusters were grouped into five cycles. In each 3-day vaccination cycle, 12 clusters were covered. The teams then moved on to the next cycle and thus all clusters were covered two times in two rounds.	N/A 900–1000	N/A 76 vaccinators, 220 volunteers and 12 first line supervisors

Publication: Bulletin of the World Health Organization; Type: Systematic reviews
 Article ID: BLT.14.139949

Boffa and Forecariah regions, Guinea 20 124 ^{44,45}	Shanchol	6	3 months	Decentralized semi-mobile strategy. Most sites in place for only 1 day. In rural areas, teams could cover three sites in one day.	774 (avg)	43 teams of 9 to 20 people
Maban county, South Sudan 2013 ^{47,48}	Shanchol	7	Just over 1 month	Semi-mobile strategy, fixed points for first days of round, then mix of fixed sites and mop-up for last days of round. Also, in each MSF clinic.	1150	Teams of 10 people at each site, plus 14 people per camp for mobilization

EPI: Expanded Program on Immunization; MSF: Médecins Sans Frontières; N/A: not available; OCV: oral cholera vaccine.

Table 4. Cost of post-licensure oral cholera vaccinations, 1997–2013

Cost	Uganda, 1997¹⁶	Mozambique^a, 2003–2004²⁰	Indonesia, 2005^{23,24}	United Republic of Tanzania, 2009³⁰	India^a, 2011³⁵	Bangladesh, 2011³⁶	Guinea, 2012⁴⁵	South Sudan, 2013⁴⁷
Oral cholera vaccine	Dukoral	Dukoral	Dukoral	Dukoral	Shanchol	Shanchol	Shanchol	Shanchol
Price per vaccine dose, US\$	Free	Free	4.70	5.00	2.22	1.00	1.85 ^c	2.40 ^c
Number fully immunized persons	27 607	44 156	54 627	23 921	23 751	123 666	143 706	71 912
Vaccine and/or international shipment costs, US\$	4 421	6 608	665 247	555 000	122 629	284 529	632 782 ^c	661 690 ^c
Computers and other capital expenses, US\$	1 600	900	4 738	N/A	N/A	N/A	N/A	N/A
International consultants, US\$	N/A	N/A	124 230	110 000	N/A	N/A	N/A	133 917 ^c
Local storage and transport, US\$	3 239	33 510	5 159	N/A	2 081	43 701	175 930 ^c	115 428 ^c
Meetings, community mobilization, training, local salaries, supplies and waste management, US\$	5 395	54 269	159 275	87 500	20 625 ^b	157 932	106 630 ^c	171 766 ^c
Adverse event following immunization monitoring and management, US\$	N/A	N/A	N/A	N/A	4 237	N/A	N/A	N/A
Total cost for the vaccination campaign, US\$	14 655 (0.53)	95 287 (2.16)	958 649 (17.55)	752 500 (31.46)	149 572 (6.30)	486 162 (3.93)	915 342 (6.37) ^c	1 082 801 (15.06) ^c
Total local delivery cost (per person), US\$ ^d	14 655 (0.53)	88 679 (2.01)	169 172 (3.10)	87 500 (3.66)	26 943 (1.13)	201 633 (1.63)	282 560 (1.97) ^c	287 197 (3.99) ^c

N/A: not available; US\$: United States dollar.

^a Including vaccinations outside the study target population

^b Itemized as follows: Social mobilization US\$ 5603 and vaccine administration US\$ 15 022

^c Costs originally reported in Euro. US\$ was calculated using the conversion rate as of 1 February 2013: 1 Euro to US\$ 1.37.

^d Excluding vaccine, international shipment and consultant costs.

Fig. 1. **Flowchart for the selection of documents on oral cholera vaccination campaigns**

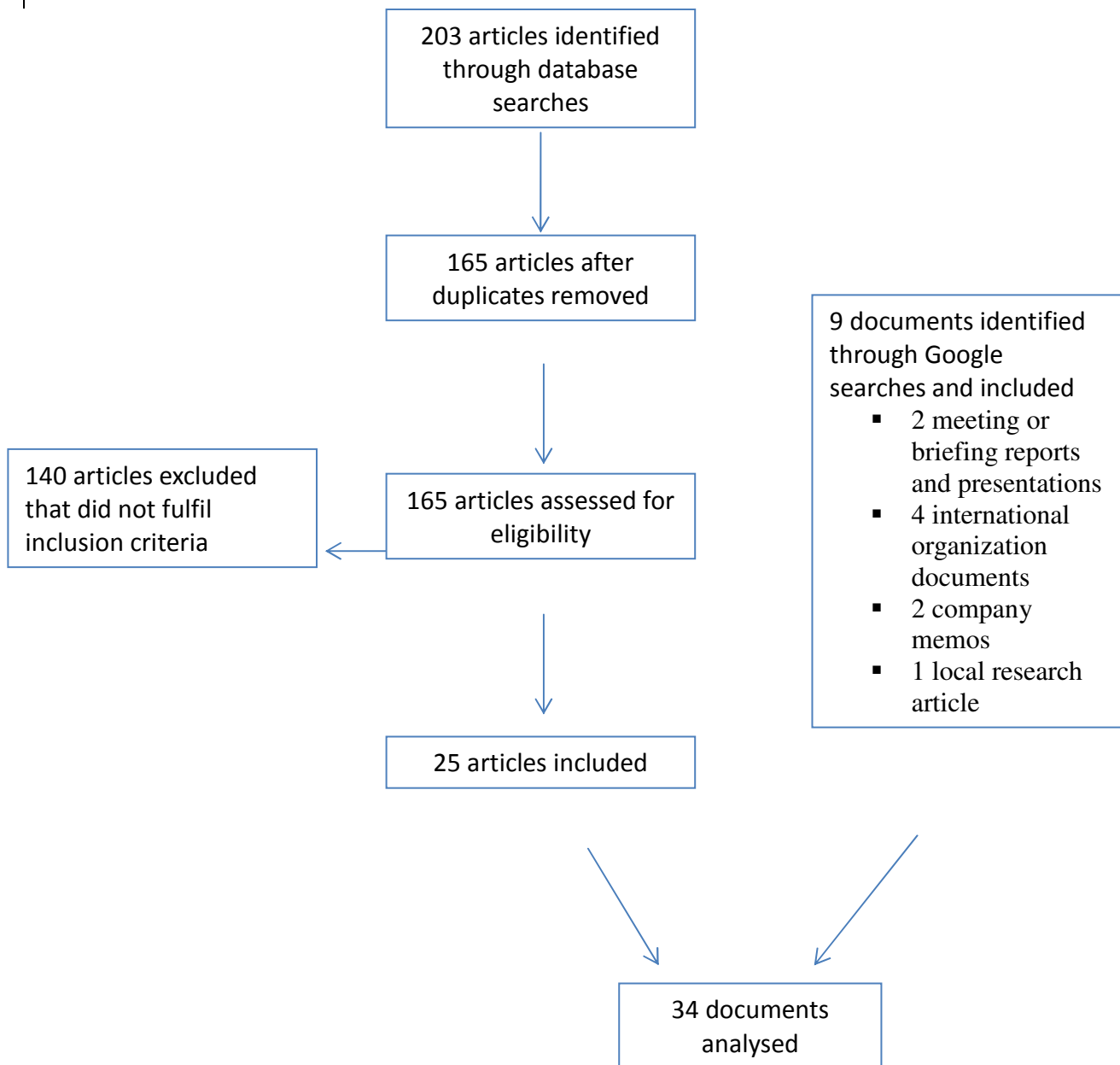


Fig. 2. Post-licensure oral cholera vaccination campaigns, 1997–2014

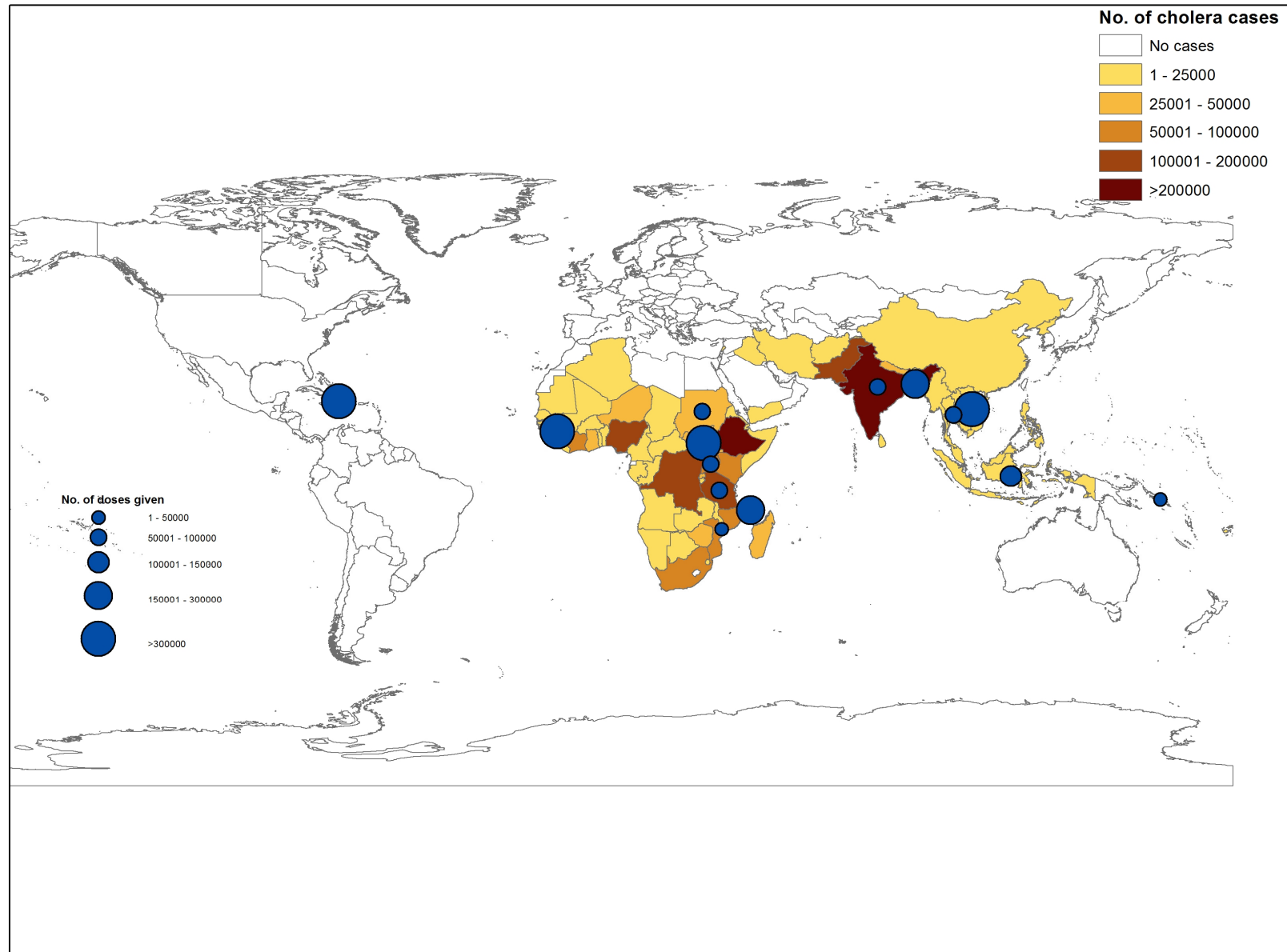


Fig. 3. Administration of Dukoral or Shanchol in post-licensure oral cholera vaccination campaigns globally, 1997–2014

