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

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 33 documents were included in the analysis. One country, Viet Nam, incorporates oral cholera vaccination into its public health programme and has administered approximately 1.09 million vaccine doses between 1997 and 2012. In addition, over 3 million doses of the two WHO-prequalified oral cholera vaccines have been administered in more than 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 O1 and O139 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. A vaccine stockpile was created in 2012, with an initial two million doses to be available mainly for epidemic response in low-income countries. In November 2013, the global alliance for vaccines and immunizations (Gavi Alliance) approved a financial contribution towards the stockpile to expand its use. 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. Follow-up studies in Bangladesh estimated a 62% protection during the first year, 57% during the second year and negligible thereafter.

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. In 1997, the vaccine was augmented with killed V. cholerae serogroup O139 whole cells to create a bivalent vaccine, 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. 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. 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, 66% at three years and 65% at five years of follow-up. Shanchol™ was licensed in India in 2009 and received WHO pre-qualification in 2011.

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A comparison of the three oral cholera vaccines is shown in Table 1. The safety, relative effectiveness and duration of protection of the different types of oral cholera vaccine has previously been reviewed. Here we conduct a systematic review of post-licensure oral cholera vaccines. 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 its database of abstracts and reviews of effects from 1990 to the 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 Meta-analyses guidelines. We searched PubMed and the WHO website 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 spreadsheet 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. 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 a 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, using ArcMap 10.0 (ESRI, 2011).

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

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dukoral®</th>
<th>ORC-Vax™ and mORC-Vax™</th>
<th>Shanchol™</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Manufacturer</strong></td>
<td>Crucell (the Netherlands)</td>
<td>Vabiotech (Viet Nam)</td>
<td>Shantha Biotechnics Ltd (India)</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Monovalent inactivated vaccine</td>
<td>Bivalent inactivated vaccine</td>
<td>Bivalent inactivated vaccine</td>
</tr>
<tr>
<td><strong>Components</strong></td>
<td>Killed whole cells of V. cholerae O1 (Classical and El Tor biotypes) and recombinant B-subunit of cholera toxin</td>
<td>Killed whole cells of V. cholerae O1 (Classical and El Tor biotypes) and V. cholerae O139</td>
<td>Killed whole cells of V. cholerae O1 (Classical and El Tor biotypes) and V. cholerae O139</td>
</tr>
<tr>
<td><strong>Recommended age</strong></td>
<td>2 years and older</td>
<td>1 year and older</td>
<td>1 year and older</td>
</tr>
<tr>
<td><strong>Delivery</strong></td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td><strong>Doses</strong></td>
<td>Two doses ≥ 1 week apart</td>
<td>Two doses ≥ 2 weeks apart</td>
<td>Two doses ≥ 2 weeks apart</td>
</tr>
<tr>
<td><strong>Buffer</strong></td>
<td>Yes. Buffer dissolved in 75 mL (2–6 years old) or 150 mL (&gt; 6 years old) water</td>
<td>Not required</td>
<td>Not required</td>
</tr>
<tr>
<td><strong>WHO prequalification</strong></td>
<td>Yes (2001)</td>
<td>No</td>
<td>Yes (2011)</td>
</tr>
<tr>
<td><strong>Storage temperature</strong></td>
<td>2–8 °C</td>
<td>2–8 °C</td>
<td>2–8 °C</td>
</tr>
</tbody>
</table>

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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 173 unique documents of potential relevance and 33 of these met the inclusion criteria (Fig. 1). In addition, we obtained information about recent campaigns through personal communications with two co-authors (DL and KA). 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). As of August 2014, 280,000 oral cholera vaccine doses from the stockpile were shipped to Ethiopia, 280,000 to Guinea, 400,000 to Haiti and 300,000 to South Sudan. For campaigns with detailed data available, the characteristics and main findings are shown in Table 2 and 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). These included two feasibility studies in refugee camps and one campaign following a natural disaster. 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, as well as herd protection. We found one document stating that 137,000 Dukoral® doses were delivered to Myanmar in 2008 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. A cold chain for vaccine delivery was reportedly maintained at 2–8 °C from storage to administration in Aceh, Indonesia, Beira, Mozambique and Zanzibar, United Republic of Tanzania. In Uganda, the vaccine was maintained at room temperature. Vaccination teams were able to vaccinate 100 to 1735 persons per day. Reported adverse events following immunization in Mozambique and Uganda were minor and non-specific. Delivery cost per fully immunized person ranged from 0.53 United States dollars (US$) to US$ 3.66 (Table 4).

**Shanchol**

Since WHO pre-qualification, Shanchol™ has been increasingly used in campaigns. About 2,649,189 doses have been administered in more than 10 campaigns (Table 2; data from the most recent campaigns in Ethiopia, Guinea and Haiti are not yet available), 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. The campaign in Dhaka, Bangladesh 2011, includes an assessment of vaccine effectiveness with and without other interventions. The two vaccination campaigns in Haiti in 2012 were pilot projects that paved the way for the launching of a national
Fig. 2. Post-licensure oral cholera vaccination campaigns, 1997–2014

* Number of vaccines in 2014 counted from January to August.
cholera vaccination programme integrated in a long-term plan to address water safety and sanitation.46–48 There was a third campaign in Haiti in 2013 that was part of this plan. Shanchol™ was deployed for pre-emptive vaccination in the Solomon Islands in 2012, following reports of cholera in a nearby area.49 The vaccination campaign in Thailand, 2012, was conducted to prevent seasonal outbreaks in a stable camp setting.50 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.43–45 The campaigns in Guinea and in Maban county, South Sudan 2013 confirmed that large-scale vaccinations under logistically difficult conditions are feasible.46–48 The campaign in internally displaced persons camps in South Sudan in 2014, was the first to use the oral cholera vaccine stockpile.16

The Shanchol™ campaigns were conducted in 1–3 months.14–16 The 2012 Haiti campaign was carried out in two phases due to an overlapping national oral polio vaccination campaign.16–18 The number of persons vaccinated per day ranged from 774–1150.35,43–48 No serious adverse events following immunization were reported. In campaigns in Odisha, Dhaka and in Haiti in 2012, acold chain for vaccine was maintained at 2–8 °C from storage to delivery on site.14–16 In the campaigns in Guinea and in South Sudan cold chain was maintained until the day of vaccination, during which vaccines were transported to vaccination sites and used at ambient temperature43–47 (Table 3).

The delivery costs of Shanchol™ through the existing government health system in Bangladesh15 and India14 were US$ 1.63 and US$ 1.13, respectively, per fully immunized person. The local expenses of reactive deployment in Guinea were US$ 1.97,45 while costs in Maban, South Sudan were US$ 3.99 per fully immunized person (Table 4).47

### Discussion

We estimate that about 3 175 206 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.11 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.16 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 Guinea43–45 and Haiti36–46 have shown that reactive mass vaccinations are feasible. 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 system30,31 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
<table>
<thead>
<tr>
<th>Vaccine and year of the campaign</th>
<th>Site</th>
<th>Setting</th>
<th>Type and purpose of the vaccination campaign</th>
<th>Eligibility criteria</th>
<th>Target population</th>
<th>Coverage</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dukoral*</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>Adjumani district, Uganda</td>
<td>Refugee camp, rural</td>
<td>Pre-emptive vaccination to assess feasibility in a stable refugee camp setting[15,17]</td>
<td>≥ 1 year old</td>
<td>44 000</td>
<td>35 613 (81)</td>
<td>27 607 (62)</td>
</tr>
<tr>
<td>2000</td>
<td>Mayotte Island, Comoros</td>
<td>Urban and rural</td>
<td>Pre-emptive vaccination campaign to prevent a choler a epidemic[18]</td>
<td>NA</td>
<td>145 000</td>
<td>NA</td>
<td>93 000 (64)</td>
</tr>
<tr>
<td>2003–2004</td>
<td>Beira, Mozambique</td>
<td>Urban</td>
<td>Pre-emptive vaccination in an endemic area with seasonal outbreaks. Effectiveness study in an HIV-endemic sub-Saharan African site[19,20]</td>
<td>Non-pregnant women, ≥ 2 years old children</td>
<td>19 550</td>
<td>14 164 (72)</td>
<td>11 070 (57)</td>
</tr>
<tr>
<td>2004</td>
<td>South Darfur, Sudan</td>
<td>Refugee camp, rural</td>
<td>Pre-emptive vaccination to assess feasibility during the acute phase of an emergency (i.e. refugee camp of internally displaced persons)[22,23]</td>
<td>≥ 2 years old</td>
<td>45 825</td>
<td>42 502 (93)</td>
<td>40 330 (88)</td>
</tr>
<tr>
<td>2005</td>
<td>Aceh, Indonesia</td>
<td>Site of internally displaced persons</td>
<td>Pre-emptive vaccination to assess feasibility during the acute phase of an emergency (i.e. post-tsunami)[24,25]</td>
<td>≥ 2 years old</td>
<td>78 870</td>
<td>62 505 (79)</td>
<td>54 627 (69)</td>
</tr>
<tr>
<td>2009</td>
<td>Zanzibar, the United Republic of Tanzania</td>
<td>Urban and rural</td>
<td>Pre-emptive vaccination in an endemic area with seasonal outbreaks. Effectiveness study to measure direct and indirect protection[26–28]</td>
<td>Non-pregnant women, ≥ 2 years old children</td>
<td>48 178</td>
<td>27 678 (57)</td>
<td>23 921 (50)</td>
</tr>
<tr>
<td>Vaccine and year of the campaign</td>
<td>Site</td>
<td>Setting</td>
<td>Type and purpose of the vaccination campaign</td>
<td>Eligibility criteria</td>
<td>Target population</td>
<td>Coverage</td>
<td>Main findings</td>
</tr>
<tr>
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<td>--------------</td>
</tr>
<tr>
<td><strong>ORC-Vax™ and mORC-Vax™</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1998–2012 Viet Nam</td>
<td>Endemic urban and rural areas</td>
<td>Pre-emptive and reactive vaccinations of children integrated into the country’s public health programme[1]</td>
<td>Non-pregnant women, ≥ 1 year old children</td>
<td>≈10.9 million doses</td>
<td>NA</td>
<td>NA</td>
<td>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[2]. Mass immunization is feasibly administered through the public health system[3]. Direct vaccine effectiveness 3 to 5 years after vaccination was 50% (95% CI: 9–63)[4].</td>
</tr>
<tr>
<td>2008 Hanoi, Viet Nam</td>
<td>Urban</td>
<td>Reactive vaccination campaign during an ongoing outbreak[7]</td>
<td>Non-pregnant women, ≥ 1 year old children</td>
<td>≈37,000 &gt; 10 years old</td>
<td>NA</td>
<td>≈80% vaccinated</td>
<td>Protective effectiveness of 76% (95% CI: 5–94). First study to document reactive use of oral cholera vaccination during an outbreak[8].</td>
</tr>
<tr>
<td><strong>Shanchol™</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012 Port-au-Prince, Haiti</td>
<td>Urban</td>
<td>Pre-emptive vaccination campaign. Pilot study[10]</td>
<td>≥ 1 year old children</td>
<td>70,000</td>
<td>52,357 (75)</td>
<td>47,540 (68)</td>
<td>Effort, community mobilization and organizational capacity needed for a successful campaign where there were logistical and security challenges[10]. The campaign integrated with the other components of cholera control was found to be feasible and acceptable[11].</td>
</tr>
</tbody>
</table>
| 2012 Bocozel and Grand Saline, Haiti | Rural | Pre-emptive vaccination campaign. Pilot study[12,13] | ≥ 1 year old children | ≈50,000 | 45,417 | 41,238 (Estimated 77–79% in Bocozel and 63% in Grand Saline) | (continues . . )
<table>
<thead>
<tr>
<th>Vaccine and year of the campaign</th>
<th>Site</th>
<th>Setting</th>
<th>Type and purpose of the vaccination campaign</th>
<th>Eligibility criteria</th>
<th>Target population</th>
<th>Coverage</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Received 1st dose, no. (%)</td>
<td>Received 2nd dose, no. (%)</td>
</tr>
<tr>
<td>2012</td>
<td>Choiseul and Shortland, Solomon Islands</td>
<td>Rural</td>
<td>Pre-emptive vaccination campaign near an area with a cholera outbreak(^1)</td>
<td>Children 1–14 years old in high-risk areas</td>
<td>NA</td>
<td>11 888</td>
<td>11 318</td>
</tr>
<tr>
<td>2012</td>
<td>Tak Province, Thailand</td>
<td>Refugee camps, rural</td>
<td>Pre-emptive vaccination campaign with a knowledge, attitudes and practices survey(^2)</td>
<td>Non-pregnant women, ≥ 1 year old children</td>
<td>43 968</td>
<td>36 325 (83)</td>
<td>26 753 (61)</td>
</tr>
<tr>
<td>2012</td>
<td>Boffa and Forecariah regions, Guinea</td>
<td>Rural</td>
<td>Reactive vaccination campaign during an on-going outbreak and feasibility study(^3)</td>
<td>≥ 1 year old children</td>
<td>209 000 (=163 000 in Boffa and =46 000 Forecariah)</td>
<td>172 544</td>
<td>143 706 (Based on administrative population figures, 68% in Boffa and 51% in Forecariah. Household survey immediately after campaign 76%)</td>
</tr>
<tr>
<td>2013</td>
<td>Maban county, South Sudan</td>
<td>Refugee camps, rural</td>
<td>Pre-emptive vaccination campaign in an area with escalating Hep E outbreak(^8),(^9)</td>
<td>≥ 1 year old children</td>
<td>146 317</td>
<td>NA</td>
<td>132 000 (&gt; 85% by survey)</td>
</tr>
<tr>
<td>2013</td>
<td>Petite Anse and Cerca Carvajal, Haiti</td>
<td>Urban and rural</td>
<td>Pre-emptive vaccination campaign in a cholera-endemic area(^5)</td>
<td>≥ 1 year old children</td>
<td>&gt; 110 000</td>
<td>113 045</td>
<td>102 250</td>
</tr>
<tr>
<td>2014</td>
<td>South Sudan Internally displaced persons camps</td>
<td></td>
<td>Pre-emptive vaccination campaign(^10)</td>
<td>Non pregnant women, ≥ 1 year old children</td>
<td>152 000</td>
<td>125 311 (72)</td>
<td>76 088 (awaiting coverage surveys)</td>
</tr>
</tbody>
</table>

\(^1\) Confidence interval; Hep E: Hepatitis E; NA: information not available; OCV: oral cholera vaccination.
\(^2\) Information obtained through personal communications with Kathryn Alberti, UNICEF, New York, USA.
### Table 3. Logistics of oral cholera vaccination campaigns, 1997–2013

<table>
<thead>
<tr>
<th>Target population size</th>
<th>Site, year</th>
<th>Vaccine</th>
<th>Max. days per round</th>
<th>Total duration</th>
<th>Delivery method</th>
<th>Approximate doses delivered/day</th>
<th>Staff</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50000</td>
<td>Adjumani district, Uganda, 1997</td>
<td>Dukoral®</td>
<td>4</td>
<td>Just over 1 month</td>
<td>15 vaccination sites</td>
<td>250–1735</td>
<td>114 persons: 19 nurses/midwives, 21 nursing aides, 44 community health workers and 30 persons without qualifications</td>
</tr>
<tr>
<td>Esturro, Beira, Mozambique, 2003–2004</td>
<td>Dukoral®</td>
<td>9</td>
<td>1 month</td>
<td>Outposts in churches and schools 08:00–15:00 6 days/week</td>
<td>Average 609</td>
<td>One supervisor and 15–23 members per outpost</td>
<td></td>
</tr>
<tr>
<td>Zanzibar, the United Republic of Tanzania, 2009</td>
<td>Dukoral®</td>
<td>15</td>
<td>Just over 1 month</td>
<td>Eight vaccination posts on each of the two islands. 8 hours daily</td>
<td>NA</td>
<td>Local health care workers and villagers</td>
<td></td>
</tr>
<tr>
<td>Aceh, Indonesia, 2005–2006</td>
<td>Dukoral®</td>
<td>NA</td>
<td>5 months</td>
<td>Three-phase approach, three different geographical areas with approximately one month between each phase. Fixed vaccination sites with some door-to-door mop-up</td>
<td>NA</td>
<td>Local health care workers and villagers</td>
<td></td>
</tr>
<tr>
<td>50000 to 100,000</td>
<td>Odisha, India, 2011</td>
<td>Shanchol™</td>
<td>3</td>
<td>1 month</td>
<td>Vaccination booths within 10–15 minute walking distance from villagers open 07:00–17:00 daily</td>
<td>NA</td>
<td>At each booth: 1 midwife and 5–6 community health workers/volunteers</td>
</tr>
<tr>
<td>City of God, Port-au-Prince and Bocouz and Grand Saline, Artibonite Department, Haiti, 2012</td>
<td>Shanchol™ Urban: NA Rural: 10</td>
<td>3 months per site</td>
<td>Urban: door-to-door pre-registration and vaccination at 9 fixed sites Rural: fixed posts, mobile posts and door-to-door</td>
<td>NA</td>
<td>Urban campaign: 500 staff, 75 teams of 4 workers, plus 15 supervisors Rural: 40 teams of 4 workers each led by 20 supervisors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viet Nam 1998 and 2000</td>
<td>ORC-Vax™</td>
<td>9</td>
<td>1 month</td>
<td>Specifically designated sites, also used by EPI. 90 sites</td>
<td>139 (max)</td>
<td>90 teams</td>
<td></td>
</tr>
<tr>
<td>Viet Nam 2008</td>
<td>ORC-Vax™</td>
<td>3</td>
<td>13 days</td>
<td>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</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Mirpur, Dhaka, Bangladesh 2011</td>
<td>Shanchol™ 3-day cycles</td>
<td>1</td>
<td>One and half months</td>
<td>NA</td>
<td>76 vaccinators, 220 volunteers and 12 first line supervisors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 100,000</td>
<td>Boffa and Forecariah regions, Guinea 2012–2013</td>
<td>Shanchol™</td>
<td>6</td>
<td>3 months</td>
<td>Decentralized semi-mobile strategy. Most sites in place for only 1 day. In rural areas, teams could cover three sites in one day</td>
<td>774 (avg)</td>
<td>43 teams of 9 to 20 people</td>
</tr>
<tr>
<td>Maban county, South Sudan 2013</td>
<td>Shanchol™</td>
<td>7</td>
<td>Just over 1 month</td>
<td>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</td>
<td>1150</td>
<td>Teams of 10 people at each site, plus 14 people per camp for mobilization</td>
<td></td>
</tr>
</tbody>
</table>

EPI: Expanded Programme on Immunization; MSF: Médecins Sans Frontières; NA: OCV: oral cholera vaccine.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Uganda, 1997(^a)</th>
<th>Mozambique, 2003–2004(^a)</th>
<th>Mozambique, 2005–2009(^a)</th>
<th>United Republic of Tanzania, 2009(^a)</th>
<th>Bangladesh, 2011(^a)</th>
<th>Guinea, 2012(^a)</th>
<th>South Sudan, 2013(^a)</th>
<th>India, 2011(^a)</th>
<th>Indonesia, 2012(^a)</th>
<th>Comoros and the Solomon Islands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number fully immunized persons</td>
<td>607</td>
<td>44,136</td>
<td>27,607</td>
<td>2,318</td>
<td>3,359</td>
<td>3,239</td>
<td>14,655</td>
<td>14,655</td>
<td>9,532</td>
<td>902</td>
</tr>
<tr>
<td>Vaccines and/or international shipment costs, US$</td>
<td>Free</td>
<td>4,700</td>
<td>5,462</td>
<td>1,600</td>
<td>1,600</td>
<td>1,600</td>
<td>1,600</td>
<td>1,600</td>
<td>1,600</td>
<td>1,600</td>
</tr>
</tbody>
</table>

**Notes:**
- NA: not available
- US$: United States dollar
- Including vaccinations outside the study target population.
- Costs originally reported in Euro were calculated using the conversion rate as of 1 February 2013 ($1 Euro = $1.37).
- Including vaccinations outside the study target population.
- Itemized as follows: Social mobilization US$ 560 and vaccine administration US$ 592.

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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. Since the creation of the stockpile, a higher number of doses have been used and 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\(^b\) and Shanchol\(^b\) disproves this perception. In addition, community education on cholera control and distribution of other preventive measures such as soap and chlorine solution were feasible integrated into recent vaccination campaigns.\(^33,34,35,36,41,42\) 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
Nurturing and supported by published. This will ensure appropriate documentation 
of future campaigns.

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Bloomberg School of Public Health.

Competing interests: None declared.

ملخص
نشر لقاحات الكوليرا الفموية بعد ترخيص استخدامها: استعراض منهجي

الصحة العالمية في أكثر من 16 حملة في جميع أرجاء العالم بين عامي 
1997 و2014. وكانت هذه الحملات إما وقائية أو تفاعلية 
وتتم تنفيذهم في ظروف شتى، مثل مخيمات اللاجئين أو الكوارث الطبيعية، وتوفر نطاق التغطية المقدرة ثنائي الجرعة من 46 إلى 
88% للسكان المستهدفين، وتراوحت تكلفة الإتيان المقدرة لكل 
شخص يحصل على التطعيم الكامل من 0.11 إلى 3.99 دولاراً. 

استنتاج ما زالت خبرات حملات التطعيم بلقاحات الكوليرا الفموية في تزايد، وبمعدل متعددة الصورية الأسابيع، ويعتبر تكاليف الإتيان المقدرة لكل 
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Résumé
Déploiement après homologation des vaccins oraux contre le choléra: une revue systématique

Objectif Décrire et analyser les caractéristiques des campagnes de vaccination orale contre le choléra; y compris le site, la population cible, 
la logistique, la couverture vaccinale et les coûts de distribution.

Méthodes Nous avons effectué des recherches dans PubMed, le site 
Internet de l'Organisation mondiale de la Santé (OMS) et la base de 
données Cochrane sans aucune restriction de date ou de langue. Nous 
avons contacté des membres du personnel de la santé publique, des 
experts travaillant dans le domaine et dans les ministères de la Santé 
and nous avons cité les recherches sur Internet.

Résultats Nous avons inclus 33 documents au total dans l'analyse. Un 
seul pays, le Viet Nam, inclut la vaccination orale anticholérique dans 
sa programme de santé publique et a administré environ 10,9 millions 
de doses de vaccins entre 1997 et 2012. En outre, plus de 3 millions de 
doses de deux vaccins oraux anticholériques préqualifiés de l'OMS 
ont été administrés dans plus de 16 campagnes de vaccination dans 
le monde entier entre 1997 et 2014. Ces campagnes ont été menées 
in prévention ou en réaction et ont eu lieu dans diverses conditions, 
car dans des campes de refugiés ou lors de catastrophes naturelles. La couverture estimée des deux doses était comprise entre 46 et 88% de 
la population cible. Les frais de distribution approximatifs par personne 
ettément vaccinée sont compris entre 0,11 et 3,99 dollars.

Conclusion L'expérience avec les campagnes de vaccination orale 
contre le choléra continue à se développer. Les responsables de la 
santé publique peuvent tirer profit de cette expérience et mener plus 
fréquemment des campagnes de vaccination orale contre le choléra.
Results and we conducted specific searches on the web.

Personal of public health, experts of the sector and the ministries of health, without limitations of dates or language. We got in contact with the objective, the logistics, the costs of coverage and the delivery of vaccines.

We reviewed 33 documentary. In one country, in Vietnam, oral vaccination against cholera is a part of the health program, and in the period from 1997 to 2012, it was given in about 10.9% of target population. Besides, more than 3 million doses of each of the two oral cholera vaccines that meet the requirements of the WHO were administered.

References