

## Delivering Oral Vaccines Effectively (DOVE)

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- The DOVE Project and oral cholera vaccine
- Stopcholera (DOVE) toolkit
  - Cholera basics
  - OCV basics
  - Tools for deciding whether to use OCV
  - Manual for OCV campaigns



# **STOP** I The DOVE Project (Delivering Oral Vaccine Effectively)

- **Mission**: ullet
  - Ensure that populations at risk of cholera will benefit from receiving oral cholera vaccine (OCV) in an appropriate and effective manner.
- **Objectives:** ullet
  - Promote appropriate and effective use of OCV through:
    - research,
    - monitoring and evaluation,
    - technical assistance, and
    - the development of practical resources to inform the use of OCV



## **Timeline for cholera vaccines**

1980s: Oral 2000s: OCV cholera modified to comply with vaccine (Dukoral) international developed but standards and not used cheaper OCV 1900s: Injectable extensively for licensed in cholera vaccines developed and public health India (Shanchol) used use 1970s: 1990s: After Injectable tech transfer, cholera Vietnam vaccines modified OCV impractical for (ORC-Vax) and public health used this in public health Together. Stop Transmission. End Deaths. use use



## **The DOVE Project**

(Delivering Oral Vaccine Effectively)

- **Oral cholera vaccine (OCV) can save lives**. The goal of the DOVE project is to ensure that populations at risk of cholera will benefit from receiving OCV in an appropriate and effective manner.
- Working in close collaboration with WHO, UNICEF, and other key partners, the DOVE project can help countries and agencies make evidence-based decisions regarding when and how to use OCV.
- Funded by the Bill and Melinda Gates Foundation





- Cameroon
- India
- Malawi
- Nepal
- South Sudan
- Uganda
- Vietnam
- Zambia



## **STOP** How can the DOVE Project help?

- Provide operations research, monitoring and evaluation support for current and future OCV projects
  - What area is an "endemic area? "at risk?"
  - How would Ministry of Health know if the country qualifies?
  - If vaccine is being given, who should receive it?
  - How can vaccine be delivered most efficiently?
- Surveillance
  - How should vaccine programs be evaluated?
  - How can agencies and ministries learn how best to use vaccine?
  - Use of simplified methods and tools to guide the use of OCV
- Development of a rapid and practical OCV toolkit to guide decisions on use of OCV
- How to use "in conjunction with other...strategies?"



## https://www.stopcholera.org





## **StopCholera TOOLKIT**

### STOP CHOLERA

# StopCholera toolkit is a collection of practical resources and how-to guides created by the DOVE Project

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	🚔 stopcholera.org	Ċ	
STOP CHOLERA	TRANSLATI	Contact an OCV Expert Is OCV appropriate for your situation? E: Select Language	
Home About 🗸 StopCholera Toolkit	Resources 🗸 Blog Field Stories Videos	Websites FAQs	
StopCholera Toolkit			
StopCholera To	olkit	StopCholera Toolkit	
Oral cholera vaccine	saves lives: When, where, and how to use it	<ul> <li>Home</li> <li>About</li> <li>All Resources</li> </ul>	
		Cholera Basics Oral Cholera Vaccine	
Cholera is a growing threat, especially for the	hose most vulnerable. Each year about 2.7 million people	Tools for Deciding Whether to Use OCV Manual for Oral Cholera Vaccination Campaigns	



- Contains 4 modules
- <u>Cholera Basics</u>: Resources about cholera, including a glossary, fact sheets, key links, and a self-administered facility capacity assessment for cholera outbreaks.
- 2. Oral Cholera Vaccine Basics: Tools for understanding OCV and making the case for its use, including fact sheets on vaccine safety, ethical use, use in pregnancy, and approaches for integrating OCV and WASH programs.
- **3. Tools for deciding whether to use OCV:** Tools to assist the decision to use a cholera vaccine, including different scenarios, risk assessment tools, and the vaccine introduction cost-effectiveness (VICE) calculator.
- 4. Manual for OCV Campaigns: A guide for developing training sessions in preparation for carrying out OCV campaigns and a reference guide for conducting campaigns and administering the vaccine.



#### Global Burden of Cholera in Endemic Countries (PDF - 2 pages)

This fact sheet provides a revised estimate of the cholera disease burden based on recent data (from 2008-2012) using newer estimation methods.

#### An Introduction to the Infectious Disease Cost Calculator (PDF - 2 pages)

This <u>fact sheet</u> provides an introduction to the <u>Infectious Disease Cost Calculator</u>, which can be used to assess the costs associated with cholera.

#### Glossary of Terms for Cholera and Cholera Vaccine Programs (PDF - 17 pages)

This glossary is suggested as a guide to commonly used terms for cholera and cholera vaccine programs. The glossary will help to clarify the meaning of certain terms, and in the process assist in developing improved strategies for cholera control. An annex accompanies this glossary and expands the understanding and concepts of many of these terms.

#### Cholera Surveillance: Detecting and Reporting Cases (PDF - 10 pages)

This document discusses when, where and why surveillance for cholera is needed and considerations for establishing a useful and cost-effective surveillance system for cholera.

#### Manual for Detecting Vibrio Cholera (PDF - 9 pages)

This guide provides step-by-step instructions for detecting Vibrio cholera 01 from fecal samples using a modified dipstick assay, a low-cost simplified method of confirming cholera.

#### Self-Assessment Tool for Health Facilities (PDF - 20 pages)

This document is intended as a self-assessment guide to determine if preparations are adequate for a facility and community to manage a cholera outbreak. It includes questionnaires to assess community knowledge, health facility capacity, health care provider capacity and regional and district resources. It



# Cholera surveillance: Detecting and Reporting cases

- A case of cholera should be suspected when:
  - in an area where the disease is not known to be present, a patient aged 5 years or more develops severe dehydration or dies from acute watery diarrhoea;
  - in an area where there is a cholera epidemic, a patient aged 5 years or more develops acute watery diarrhoea, with or without vomiting.
- A case of cholera is confirmed when *Vibrio cholerae* O1 or O139 is isolated from any patient with diarrhoea. **Stool culture confirmation is required**
- Severe diarrheal diseases can be caused by other agents, especially ETEC
- New rapid diagnostic tests (RDT), e.g. Crystal VC has ~90% sensitivity but a specificity of ~70% ---high false negatives
  - Use of enriched dipstick (using APW as enrichment medium) method increases specificity to 99.8%

Debes AK, et al. Am. J. Trop. Med. Hyg., 94(3), 2016, pp. 537–543



## **RDT: Crystal VC kit**

https://www.stopcholera.org/content/videos

Dr. David Sack: Instructions for Using the Cholera Dipstick



This video presentation by Dr. David Sack provides easy-to-follow instructions on the use of the Crystal VC dipstick test to test a fecal specimen for the presence of vibrio cholera. The video covers direct and enriched tests (12 min).









START HERE with a fecal sample in a cup or a Cary Blair medium



Using a cotton swab, inoculate a tube of APW from the fecal sample After 6 hours incubation, test the APW using the Crystal VC



If dipstick is positive, confirm a sample of the positive samples by culturing using TCBS

OPTIONAL place 2 drops onto Protein saver card and allow to air dry to save DNA from APW for later confirmation using PCR



Detecting V. cholerae O1 from fecal samples using RDT



## Cholera Rapid Test with Enrichment Step Has Diagnostic Performance Equivalent to Culture

Table 2. Diagnostic performance of direct and enriched RDT, and of culture at National Public Health Laboratory, Juba, and at Institut Pasteur, Paris, using PCR as the reference standard in all (N = 101) or patients without prior antibiotics (N = 80).

		Sensitivity	Specificity	PPV	NPV
		% (95% CI)	% (95% CI)	% (95% CI)	% (95% Cl)
All					
	Enriched RDT	86.1 (70.5–95.3)	100 (94.4–100)	100 (88.8–100)	92.8 (83.9–97.6)
	Culture NPHL	83.3 (67.2–93.6)	98.5 (91.7–100)	96.8 (83.3–99.9)	91.4 (82.3–96.8)
	Culture IP	72.2 (54.8-85.8)	100 (94.5–100)	100 (86.8–100)	86.7 (76.8–93.4)
No prior a	antibiotics				
	Enriched RDT	87.5 (67.6–97.3)	100 (93.6–100)	100 (83.9–100)	94.9 (85.9–98.9)
	Culture NPHL	87.5 (67.6–97.3)	98.2 (90.4–100)	95.5 (77.2 <del>-</del> 99.9)	94.8 (85.6–98.9)
	Culture IP	70.8 (48.9-87.4)	100 (93.6–100)	100 (80.5–100)	88.9 (78.4–95.4)

Ontweka LN, et al. PLoS ONE; 2016:11(12): e0168257.



### 2. Oral cholera vaccine

### **Oral Cholera Vaccine: What You Need to Know** (PDF - 3 pages) [**French**- Updated version coming soon]

This fact sheet covers the basic aspects of the currently available oral cholera vaccines, summarizing recommendations and comparing across vaccines.

#### Comparison of Currently Manufactured Oral Cholera Vaccines (PDF - 1 page)

A table comparing the different specifications of the three oral cholera vaccines currently available.

#### Integration of Oral Cholera Vaccine with Other Interventions (PDF - 2 pages)

This fact sheet outlines the need for integrating water, sanitation and hygiene (WASH) activities and other traditional cholera control interventions with oral cholera vaccination programs to improve the impact of both.

#### Oral Cholera Vaccine Safety (PDF - 2 pages)

This two-page fact sheet discusses the overall safety of oral cholera vaccine, briefly touching on vaccine safety in specific populations including pregnant women and children.

#### Cholera and the Use of OCV in Pregnant Women (PDF - 3 pages)

This document addresses the risks and benefits of cholera and the use of oral cholera vaccine in pregnant women.

#### Considerations Concerning the Ethical Use of OCV (PDF - 2 pages)

This document identifies the ethical concerns associated with oral cholera vaccine and provides guidance on some ethical issues that may arise when considering the use of oral cholera vaccine.

#### An Introductory Lecture on Oral Cholera Vaccine by Dr. David Sack (Video)



 Higher rate of miscarriage or premature delivery if pregnant women develops cholera

Table 1. Rates of fetal losses (miscarriages and stillbirths) by level of dehydration among women in Haiti treated at a specialized cholera unit for pregnant women, 2010-20116

Dehydration	No. pregnant	Fetal losses		Adjusted relative risk	
level	women	No.	%		
None	136	4	2.9	9.4 (severe vs. mild	
Moderate	110	11	10.0	dehydration) (p=0.005)	
Severe	16	6	37.5		

- "Other groups that are especially vulnerable to severe disease and for which the vaccines are not contraindicated may also be targeted, such as pregnant women and HIV-infected individuals."
  - Cholera vaccines: WHO position paper Weekly epidemiol Rec 2010;13:117–128



- Zanzibar: Out of 1,453 deliveries, no statistically significant evidence of a harmful effect of gestational exposure to the rBS-WC vaccine. Hashim R, et al PLOS Negl Trop Dis 2012;6(7): e1743.
- Guinea: Out of 2,494 pregnancies, no association between fetal exposure to BivWC and risk of pregnancy loss or malformation Grout, et al PLOS NTD 2015:9(12):e0004274.
- Bangladesh: No excess adverse fetal outcome in 69 pregnant women who received OCV Khan AI, et al. Vaccine 2017
- Malawi: No significant difference in risk of pregnancy loss, neonatal mortality, or malformation among 900 OCV-exposed and 899 non-exposed pregnant women Ali M, et al Lancet Infect Dis 2017



## **STOP** Tools for deciding whether to use OCV

#### Scenario Approach for Considering Oral Cholera Vaccination (PDF – 5 pages)

Published in The Lancet, this analysis presents a systematic classification of scenarios based on five types of cholera epidemiology and provides recommendations on when and how vaccination should be used in each scenario.

#### Vaccine Introduction Cost-effectiveness (VICE) Calculator (Excel - 4 sheets)

The VICE calculator is a user-friendly excel-based tool that estimates the cost-effectiveness of oral cholera vaccination in various settings. Clicking the link above will download the Excel file.

#### Introduction to the Vaccine Introduction Cost-effectiveness (VICE) Calculator (PDF - 2 pages)

This fact sheet provides a guick introduction to the VICE calculator for estimating the cost-effectiveness of oral cholera vaccination.

#### Determining the Feasibility of an Oral Cholera Vaccination (OCV) Campaign (PDF - 5 pages)

Several factors must be considered to determine whether oral cholera vaccination is feasible in a given setting. This short document describes a series of feasibility factors and includes a feasibility assessment that results in a clear decision on whether or not to move forward with the vaccination plan.



		Characteristics	Oral cholera vaccination recommendation	Other considerations
S	cenario 1	Ongoing cholera outbreak in areas where water and sanitation conditions have deteriorated severely as a result of natural or man-made disasters	Recommend oral cholera vaccination	Populations with no recent cholera outbreaks are especially at risk; oral cholera vaccination campaigns under diverse and difficult conditions have been shown to be feasible; use oral cholera vaccination as part of an integrated strategy to reduce transmission and prevent cholera deaths; enhance cholera surveillance to monitor course of the outbreak
Sce	cenario 2	Areas where sanitation and water conditions have deteriorated severely as a result of natural or man-made disasters, increasing the risk for cholera	If no recent or nearby cholera outbreaks, implement oral cholera vaccination quickly if cholera occurs; if with recent or nearby cholera and if the situation suggests rapid spread should a cholera outbreak occur, implement pre-emptive oral cholera vaccination	Difficult to predict outbreak, reactive vaccination could be more feasible; if oral cholera vaccination is used, ensure an integrated strategy with other cholera interventions; enhance cholera surveillance so that an outbreak can be detected early
Sce	cenario 3	Areas with endemic cholera	Recommend oral cholera vaccination for populations with high incidence rate	Ensure access to care to reduce case-fatality rate; enhance surveillance to guide use of oral cholera vaccination to populations at highest risk
	cenario 4	Cholera has not been identified in areas with poor water and sanitation infrastructure	Implement oral cholera vaccination if an outbreak occurs; oral cholera vaccination should be considered if cholera occurs at an adjacent site	This scenario describes most developing countries; it is not possible to use oral cholera vaccines in all such areas; consider antibiotics with or without oral cholera vaccination for groups of high-risk travellers coming from cholera-endemic countries; a surveillance system should be in place to detect cases should they occur
	c <b>enario 5</b> n J, et al Lan	Cholera has not been identified in areas in which water and sanitation standards are high neet Infect Dis 2016;16: 125–29	Oral cholera vaccination not recommended	The vaccine might be regarded as useful for special groups, such as workers from cholera-endemic countries, but cholera outbreaks do not occur in areas where water and sanitation standards are high; no special precautions needed but individual cases should be reported



Determining feasibility of OCV campaign

## **Key Factors for OCV Feasibility:**

- Vaccine availability
- Importation regulations
- Commitment of Partners
- Funding availability
- Competing priorities
- Cold chain capacity
- Human resources
- Transport needs
- Security concerns
- Acceptability of communities
- Timeliness



#### Manual for Oral Cholera Vaccination Campaigns: For adaptation by program managers for training health care workers (PDF - 61 pages, including annexes)

This manual is meant to be used by immunization program managers to develop training sessions in preparation for carrying out oral cholera vaccine (OCV) campaigns. It is also intended to serve as a reference guide for health care workers conducting the campaigns and administering the vaccine. The manual should enable program managers to prepare quality training sessions and their own training materials in a relatively short period of time.

#### Annexes:

Annex A: OCV Vaccination Card (PDF - 1 page) [French] Annex B: Vaccination Tally Sheets (PDF - 3 pages) [French] Annex C: Daily Logistic Supply and Return Form (PDF - 1 Page) [French] Annex D: Supervisor Checklist (PDF - 1 page) Annex E: Daily Reporting Form (PDF - 1 page) [French]



# Continue to follow developments on OCV at our website and on Twitter

## www.stopcholera.org

## Follow @STOPCholera





## Thank you!