

# Using Surveillance and Targeted OCV Campaigns to End Cholera in India : A Concept

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# ICMR-NICED: Institute Brief

- ICMR-NICED is an institute of excellence with a long history of successfully undertaking operational research studies to inform policy processes in India
  - Epidemiological studies to characterize burden like cholera, typhoid and assess impact of disease-control interventions for enteric infectious diseases
  - Phase 2 and 3 clinical trials on OCV
  - 2, 3 and 5 year follow up for assessment of efficacy of OCV
  - Phase 2, 3 and 4 clinical trials on other enteric vaccines (typhoid, rotavirus)
  - Implementation research with vaccines (TCV)
  - Policy briefs to inform the implementation of OCVs in India
  - Policy advocacy with the STSC- NTAGI to present the case for targeted OCV deployment in India
  - Center of Excellence under the Prime Minister's Mission on Climate Change and Health (for Water Borne Diseases)

Facilities for multidisciplinary research under the same roof



# Presentation Context

- **Recommendations of the NTAGI STSC (28 November, 2016 and 6 July, 2018)**
  - Strengthen surveillance; improve reporting of cholera at the national level to estimate disease prevalence
  - Explore options to evaluate OCV introduction in a target population using existing public health infrastructure:  
**ICMR-NICED/MoHFW**
  - Outline vaccine stockpiling strategy at national level
  - Accurately inform on burden, geographic spread, with a focus to address frequent outbreaks



# SITUATION ANALYSIS: CHOLERA IN INDIA



# Cholera Burden in India

- Cholera continues to be a menace<sup>1</sup>
  - At risk: 400 million people
  - Likely number of cases: 675,188
  - Estimated deaths: 20,256; Case Fatality Rate: 3%
- Reported CFR: <1%
- Reported incidence: Few studies

	GEMS <sup>2</sup>	Facility-based surveillance <sup>3</sup>
<24 months	1.6/100 child-years	0.86/100 person-years
24-59 months	1.8/100 child-years	0.62/100 person-years

1. Ali M, Nelson AR, Lopez AL, Sack DA, Ope M. Updated Global Burden of Cholera in Endemic Countries. PLoS Negl Trop Dis 2015;9:e0003832.

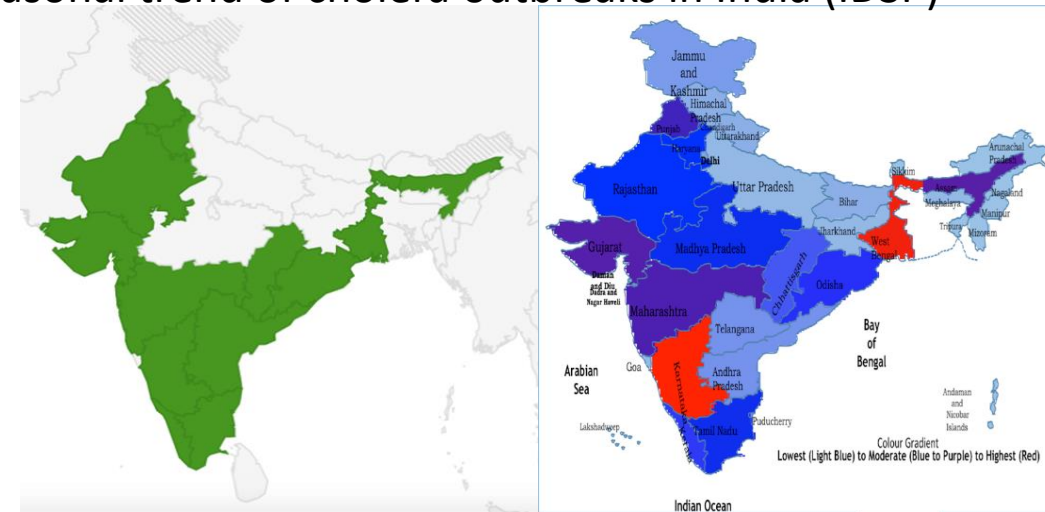
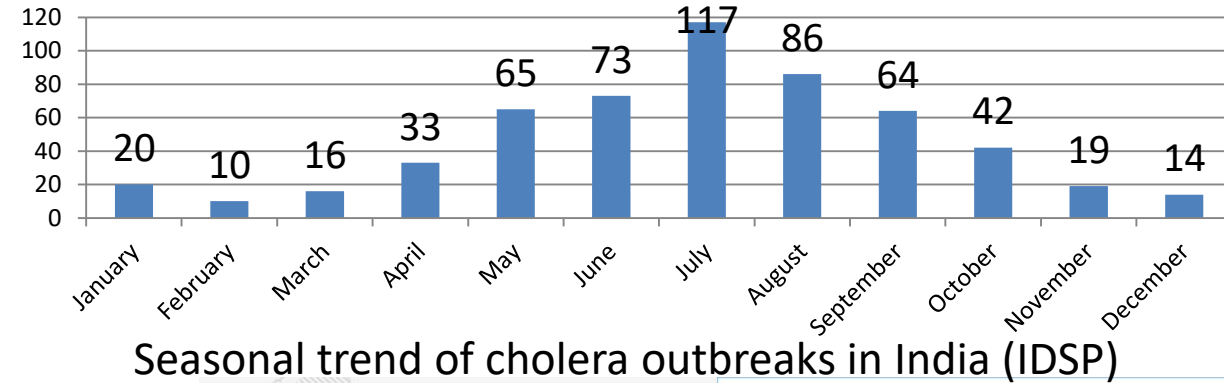
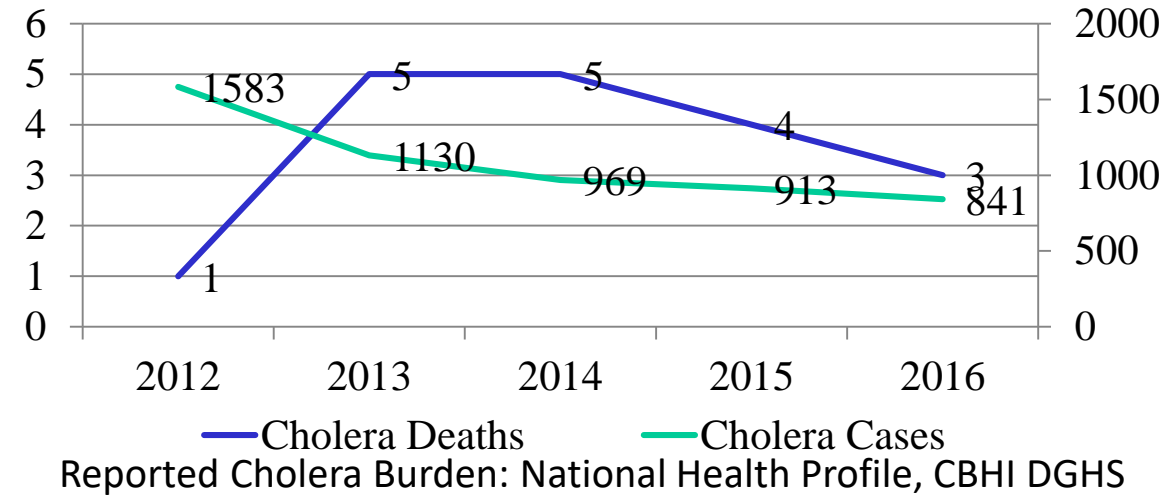
2. Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, et al. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): A prospective, case-control study. Lancet 2013;382:209–22.

3. Deen JL, von Seidlein L, Sur D, Agtini M, Lucas MES, Lopez AL, et al. The High Burden of Cholera in Children: Comparison of Incidence from Endemic Areas in Asia and Africa. PLoS Negl Trop Dis 2008;2:e173.



# Reviewing the Epidemiology Data

- **India has no National Cholera Control Program/Plan**
- Under IDSP outbreaks of acute watery diarrhea reported & investigated
- Cholera morbidity/mortality reported through CBHI, DGHS – evidence of massive under-reporting
- 559 outbreaks, affecting 27 States/UTs between 2009-2017
- Hotspots susceptible to cholera outbreaks identified in 16 S/UTs (in green in adjacent map)
- Clear seasonal trend in cholera outbreaks reported
- Very low CFRs; reported case loads reducing over the years
- No cholera specific objective at the national level; although improved water & sanitation facilities ensured through Swachcha Bharat Abhiyan



IDSP Reported:  
Cholera Vulnerable States (left)  
Cholera Endemic States (right)



# Rationale for Proposed Surveillance- Control Activities

- Available data, modeling approaches unlikely to reflect the true reality of the situation
- Fragmentation of data: outbreaks (IDSP), isolated case counts (hospital surveillance, ICMR-NICED), reports (outbreaks, publications, reports) and case/death reports (CBHI, DGHS) available: all likely underestimates
- Approaches based on reported data likely to underestimate magnitude; approaches based on adjusted models likely to overestimate magnitude
- Sentinel surveillance approaches necessary to get more robust estimates of vulnerability



# Goal and Objectives

- Goal:
  - To identify cholera vulnerable areas by deploying an effective, facility- and indicator-based hybrid surveillance system and implement and evaluate the programmatic introduction of Oral Cholera Vaccine as a control measure to meet the End Cholera targets set up by the GTFCC
- Objectives
  - Primary Objective-
    1. To estimate rates and seasonality of cholera in selected regions of India through a sentinel, facility based surveillance system accompanied by a health care utilization survey
  - Secondary Objectives
    1. To identify cholera hotspots in endemic states of India.
    2. To evaluate the acceptability, effectiveness and impact of the programmatic introduction of OCVs in cholera hotspots under ongoing cholera surveillance.





# Method 1: Plan for Surveillance

- Multiple partner institutions across India with competency in identifying cholera as a causative agent of acute diarrhea
- A systematic, passive, facility-based, indicator-based, hybrid surveillance system for burden estimation
- Systematically choosing of  $n^{\text{th}}$  patient from line list of diarrhea patients reporting to participating facilities
- Extraction of demographic and epidemiologic information from participating patients
  - Development of models to estimate cholera burden in areas where surveillance is not ongoing but other data are available through representative surveys (DLHS/DHS/NFHS4)
- **Online data entry using REDCap** for easy and immediate access to data
- Surveillance will be combined with healthcare utilization survey – hybrid surveillance
  - Identify a catchment area from where a majority of patients arrive at the participating facilities
  - Multistage, cluster sampling design approach to select a representative subset of all households in the catchment area
  - 8-week recall for healthcare utilization pattern



# Method 2: Laboratory Activities

- Culture confirmation of *Vibrio cholerae* in clinical samples
- Biochemical characterization
- Serotyping scheme
- Drug sensitivity testing
- PCR based assays to check for virulence genes of *V. cholerae*
- Whole Genome Sequencing to characterize circulating cholera strains



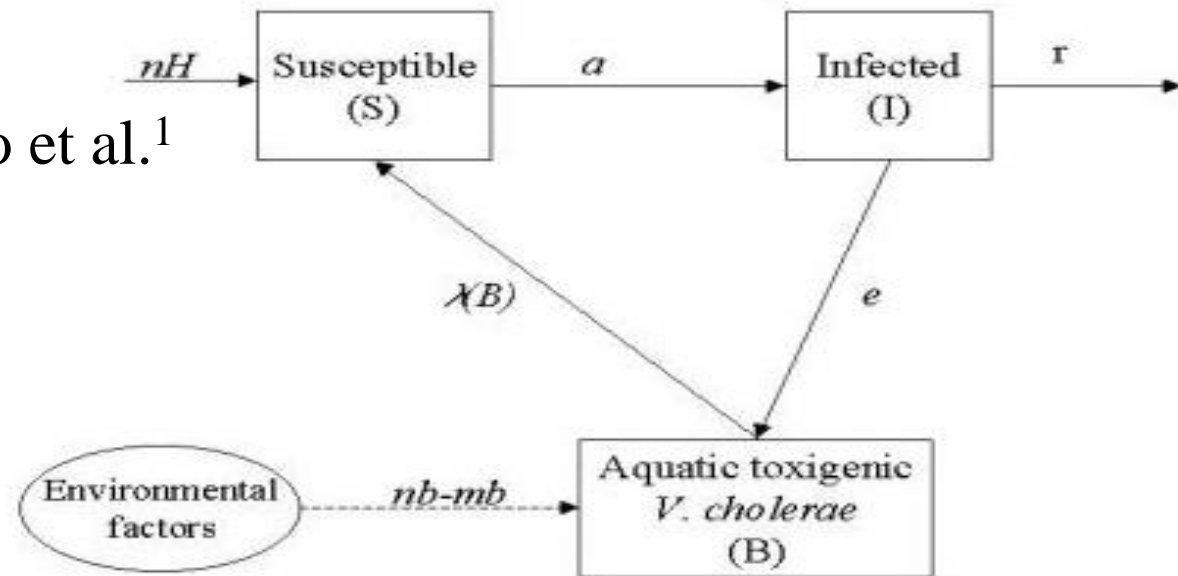
# Method 3: Hotspot Mapping and Forecast Modelling

## • Hotspot Mapping

- One state partner to be identified
- Multiple healthcare facilities from partner states will provide surveillance data on occurrence of cholera
- Spatio-temporal clustering techniques will be used to identify hotspots centering participating facilities

## • Forecast Modelling

- Based on previous work done by Codeço et al.<sup>1</sup>
- Correlations with meteorological data
  - In partnership with Indian Met Dept.
- Correlations with outbreaks
  - Reported by the IDSP



1. Codeço CT. Endemic and epidemic dynamics of cholera: the role of the aquatic reservoir. BMC Infect Dis. 2001;1:1.



# Method 4: Targeted OCV Introduction

- Deployment of OCVs targeting known areas of **high vulnerability, covered by ongoing facility-based surveillance**, Cover all eligible persons, aged  $\geq 1$  year, residing in the hotspots
- Vaccine deployment using **door-to-door delivery strategy** as in polio vaccination, with similar microplans
- Partnering with **civic authorities (municipal corporations, etc.)** to leverage existing systems and human resources available
- Community mobilization and IEC using **extension workers** (ASHA, ANMs)
- Home-based screening, verbal assent/consent and vaccination, as appropriate, using the existing systems
- **Monitoring immediate reactogenicity** after vaccine delivery and **AEFIs** through existing systems
- Additional vaccination drives in the evenings, and on Sundays to cover working males
- **Vaccination cards** issued to each vaccinated individual
- **Second dose given at least 14 days after first**; only those who received the first dose eligible for the second
- **Evaluation end-points**: vaccination coverage in each round; acceptability of vaccine to the community; drop-out rates between the two doses; reasons for drop-out and declining/accepting vaccination; and impact on cholera burden in the pre- and post-vaccination period in the cholera hotspots.
- **Assessing logistic feasibility**: describe and quantify resources, including personnel, needed for vaccine procurement, storage, and transport and vaccine delivery; and vaccine storage, transport and handling requirements/barriers.

# Expected Outcomes

- Facility-based surveillance
  - Burden of cholera in areas under surveillance
  - Models for estimating cholera burden in other areas
  - Developing models for estimating cholera burden
  - Hotspot mapping
- Molecular characterization of circulating *V. cholerae* in India
  - Including AMR profiles
- Vaccine introduction
  - Vaccine effectiveness, costs, barriers to implementation
  - Vaccine acceptability, reasons for non-acceptance/attrition
  - Strategies for improved social mobilization for improving vaccine uptake
- Pilot studies
  - Forecasting models for cholera outbreaks
  - Diagnostic accuracy of RDTs
  - Diagnostic yield of dry, filter paper specimen

How to implement targeted, OCV campaigns to meet the End Cholera goals in India?



# Way Forward: The Last Pieces of the Puzzle

- Funding
- Access to OCVs
  - The STSC of the NTAGI suggested that the introduction of OCVs in vulnerable areas should be further explored by identifying hotspots
  - The MOHFW has not agreed yet for central procurement of OCV
  - Major cost consideration for local partners
- Identification of a credible, willing state partner
  - Identified High-burden states willing to invest in the programmatic introduction of OCVs



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**THANK YOU!**

