

The RISE (RDT Implementation, Strategy, and Evaluation) Project:

a GAVI funded project to evaluate the use of cholera RDTs in Nepal

Johns Hopkins Bloomberg School of Public
Health

Baltimore, Maryland, USA



Presentation Overview

- RISE
 1. RDT distribution
 2. Nested study
 - a. Preliminary Results
 - i. Qualitative data
 - ii. Quantitative data
 - iii. Process Evaluation
 3. Year Two Plans
 - a. GAVI platform Coordination
 - b. Process Evaluation
 - c. RDT – PCR confirmation



https://commons.wikimedia.org/wiki/File:Nepal_in_Asia_%28-mini_map_-rivers%29.svg



Purpose of RISE

- 1) To evaluate the implementation and the effective use of RDT to improve understanding of disease burden, maximizing impact of future OCV campaigns.
- 2) To evaluate the RDT integration and data collection strategies at intensive surveillance sites versus sentinel sites.



Cholera RDT Pilot in Nepal

- Sporadic cases occur almost every year
 - Major outbreaks occur every 1-3 years
 - Seasonality peaks during monsoon
- Key players:
 - Epidemiology & Disease Control Division (EDCD),
 - National Public Health Lab (NPHL)
 - Group for Technical Assistance (GTA)
 - International Vaccine Institute (IVI)
 - Gavi, The Vaccine Alliance

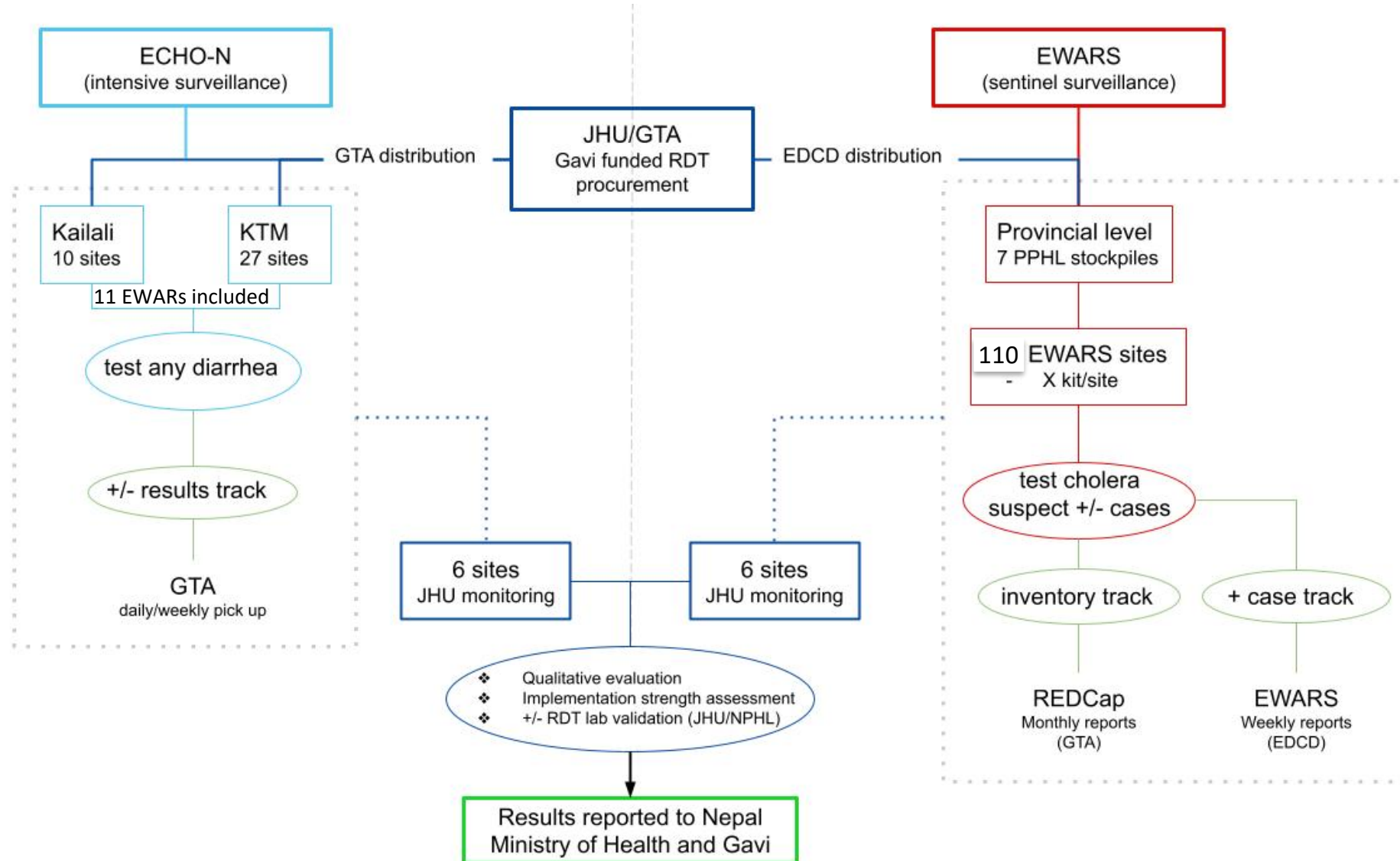


<https://www.nationsonline.org/oneworld/map/nepal-administrative-map.htm>



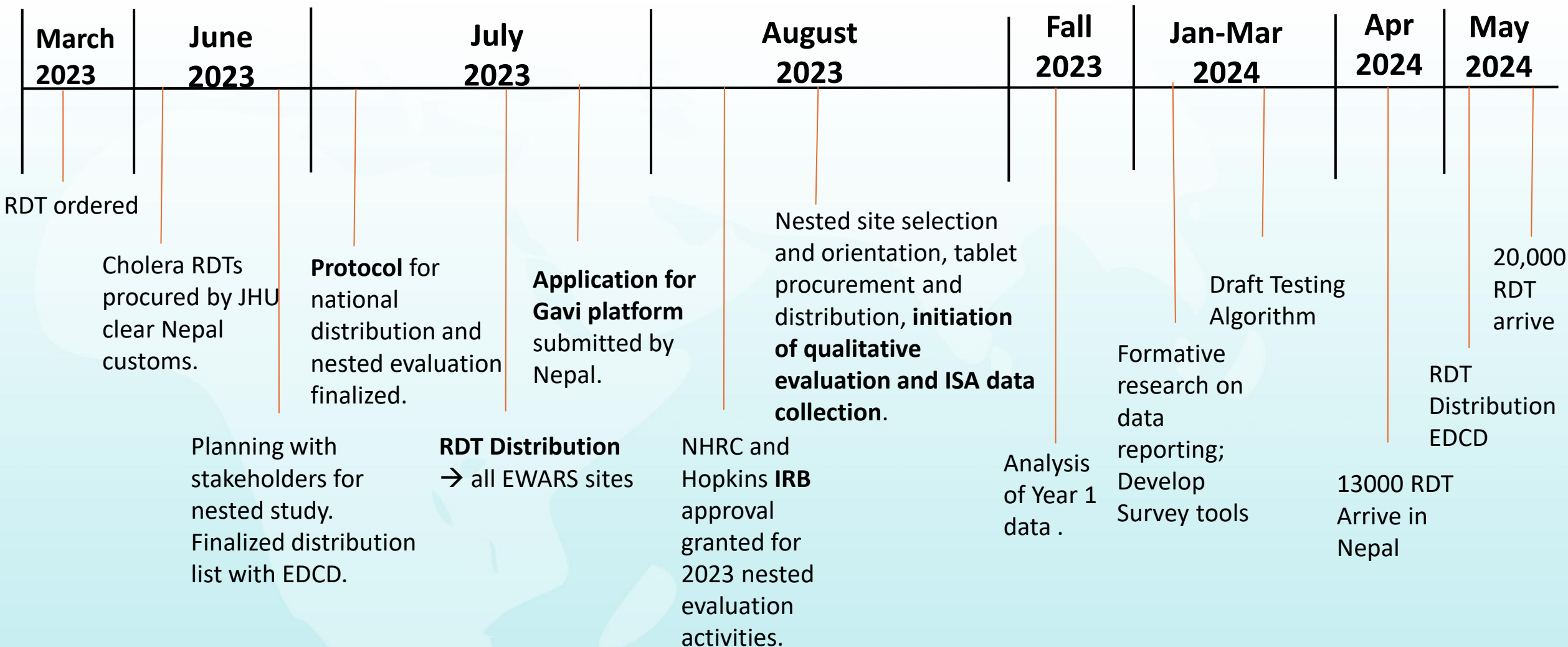
Enhancing Cholera control in Nepal (ECHO-N)

- 2022: 27 sites in Kathmandu Valley
- 2023: 10 more sites were added in a western district, Kailali
- All patients ≥ 2 y.o. with AWD or suspect cholera eligible to enroll
 - Consent
 - Case Report Forms (CRFs)
- Enrolled patients → direct RDT, sample preserved in CB and on filter paper
- Dipstick, filter paper, CB swab are sent to NPHL to be culture and PCR confirmed
 - All RDT positive samples
 - Clinically cholera suspect
 - 10% RDT negative samples

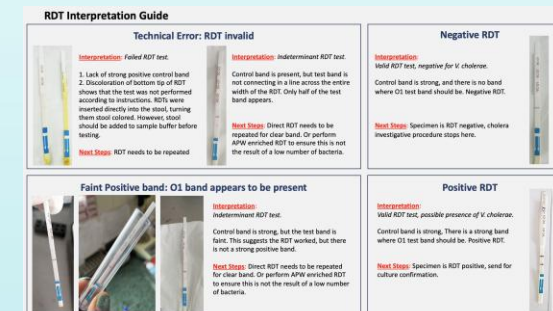
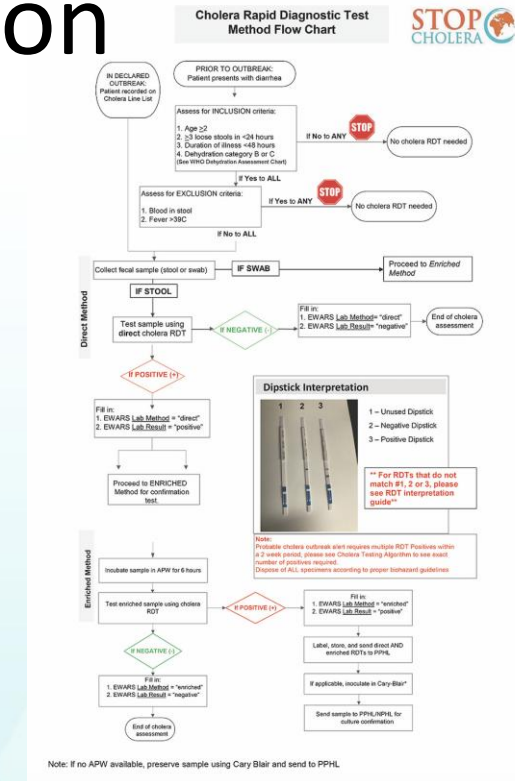




Year 1 Overview



- Allocation of RDT kits was done in collaboration with the EDCCD
 - Crystal VC O1
- Provincial-level stockpiles
 - Finalized list made by the end of June
- Printed training materials provided with initial shipment
- RDTs sent July 13th
 - Initial shipment via private courier due to monsoon season
 - EDCCD agreed to support subsequent shipments and restocks
 - (eLIMS)



Distribution Challenges

- 35/103 sites confirmed arrival of RDTs within 2 weeks
 - Private Courier – priced based on weight
 - Geography
 - Monsoon
- ~2 months for all sites to receive the RDT kits (early September)
 - Monsoon (cholera) season over by late September
- Important lessons:
 - Private vs. Government delivery
 - Logistics/supply chain

Formative Findings: Qualitative interviews

Perceived benefits of RDTs

- Facilitate cholera surveillance and outbreak detection
 - RDTs are fast with immediate results
 - Can be rolled out widely
 - Better data on disease burden and increased awareness of cholera in Nepal
 - Less expensive than other alternatives
- RDTs easy to use; can be used by unskilled personnel in facilities with limited capacity
 - Can be used in remote areas
 - RDT results more reliable when done by unskilled personnel
 - Reduce burden on lab techs
- Limits need for confirmatory testing- only on positive RDTs

Formative Findings: Qualitative interviews

Perceived negatives of RDTs

- Perceived high False Positivity
 - False Positive rate only 1.6%, demonstrates high capability by Nepali personnel limited laboratory training
- Familiarity using other tests (i.e., hanging drop)
 - RDT is simple, deployable, less expensive, and no lab or technical ability required
- Concerns about RDT cost and accessibility
 - 43,000 RDT Provided through GAVI Platform
- Some concern that RDTs could be misused
 - clear case definition needed
- Perception that RDTs could increase workload
 - RDT are low effort

Formative Findings: Qualitative interviews

Challenges with implementing RDTs

- Lack of awareness of RDTs for cholera
 - Training materials available to those receiving RDT
 - WHO, JHU, UNICEF
- Cholera RDTs not integrated into health facility systems
 - Cholera Testing Algorithm and NCP
- Physicians must order RDTs before labs can perform
 - Educate Physicians on RDT availability/Testing Algorithm
- Transport challenges affect ability to conduct culture to confirm RDT results
 - RDT reduces transport challenges by 98%
- Lack of knowledge regarding cholera data reporting
 - Lack of knowledge about who is responsible for reporting
 - Reporting delays



Lessons Learned from Qualitative Evaluation

- Concerns regarding RDT quality and validity
 - False positives cited as causing a lack of confidence in the tests
 - The lack of trust in the RDTs led some lab technicians to perform confirmatory tests alongside all samples (+ and -)
 - Cholera RDTs were adding to their workload rather than increasing efficiency
- RDTs for surveillance rather than cholera treatment
 - Interviewees felt positive about the use of RDT to improve case management
 - Reasoning-- reduction in antimicrobial resistance through targeted antibiotic use
- RDT distribution without utilization
 - Ensuring that there is guidance on standard reporting protocols
 - Understanding the current gaps in surveillance systems prior to distributing RDTs



Lessons Learned from Qualitative Evaluation

- Variability in RDT experiences and usage seen across the nested sites
 - Sensitization of cholera RDTs
 - Built into distribution and training plans
- All interview groups expressed the desire for training around cholera RDTs
 - Major topics requested include:
 - the clinical and epidemiological characteristics of cholera
 - the availability of the RDTs
 - understanding the sensitivity and specificity of the RDTs especially in the context of false positives
 - reporting mechanisms and timeline
 - what to do based on RDT outcome
 - Training for overcoming personnel turnover

RISE Data Reporting sources

- 3 sources of national-level data:
 - EWARS weekly reports (select variables)
 - EDCCD EWARS supplemental survey
 - Monthly RISE EWARS distribution survey
- 4 sources of intensive & nested-site data:
 - Individual RDT Tablet forms
 - IVI CRF
 - Qualitative Evaluations
 - Process Evaluation Tools
 - ISA formative research
 - Year 2 tools

Ongoing RISE Activities

- Monthly survey
 - Sent to all EWARS facilities monthly
 - Includes data on # RDTs available, # RDTs used, # RDTs positive, availability and use of APW, availability and use of Cary Blair
- Individual RDT survey
 - Completed by sample of 12 selected EWARS facilities (6 participating in ECHO study, 6 not ECHO)
 - Completed each time an RDT is used
 - Includes data on patient age/sex, RDT result, confirmatory testing done, patient symptoms and antibiotic use, final diagnosis, and reporting to EWARS

Formative Findings: Quantitative Data

Results for 2022

Culture Results				Total
RDT Results		Positive	Negative	
	Positive	43	8	51
	Negative	0	545	545
	Total	43	553	596

Results for 2023

Culture Results				Total
RDT Results		Positive	Negative	
	Positive	5	44	49
	Negative	0	2289	2334
	Total	5	2333	2338

Results for 2024

Culture Results				Total
RDT Results		Positive	Negative	
	Positive	2	21	23
	Negative	0	1281	1281
	Total	2	1302	1304

False Positive Rate (FPR)=

$$\frac{\text{False Positive}}{\text{True Negatives} + \text{False Positives}} \times 100\%$$

FPR 2022: 8/553=1.4%

FPR 2023: 44/2333=1.9%

FPR 2024: 21/1302=1.6%

RISE EVALUATION: YEAR 2 PLANS

RISE Evaluation Plans

- Ongoing monitoring of RDT usage
 - Quantitative data analysis and RDT validation
- April-July 2024: Planning phase for the RISE Process evaluation
 - Interviews, meetings/workshops, reports, and document review
 - Observe trainings (FETP, RRT)/EWARS orientations led by EDCCD
- August-September 2024: Evaluate cholera RDT implementation
 - In-depth interviews with:
 - Representatives from EDCCD, NPHL, PPHL
 - Physicians, laboratory technicians, and medical reporters at ~12 health facilities in Kathmandu
 - Facility survey conducted by phone with EWARS health facilities and PPHL personnel (at end of cholera season)
 - Clinical and laboratory vignettes to evaluate quality of RDT use and reporting at health facilities

Process Evaluation: Facility Survey

- Goal: Understand RDT distribution, implementation, and cholera results reporting
- Method of administration: Phone survey
- Topics to be covered:
 - Process of receiving RDTs
 - Availability/stock-outs of RDTs and related supplies
 - Effectiveness of cholera RDTs
 - Adoption of RDTs in health facility systems
 - Training and capacity for RDT use
 - Processes for using RDTs
 - Knowledge about RDT guidance documents and training materials



Process Evaluation: Clinical and Laboratory Vignettes

- Goal: Assess quality of RDT use and knowledge base
- Present scenarios of common cholera case presentations to providers and lab technicians and ask how they would respond
 - 1-3 providers and 1-3 laboratory technicians per facility
- Observe use of RDT to test provided stool specimens (both positive and negative for cholera)
- Assess knowledge and practices around correct testing, referral strategies, and reporting procedures

Year 2 Qualitative Interviews

- Year 2 Goals:
 - Including medical recorders, who are responsible for reporting data on cholera diagnoses and test results
 - Providing a detailed understanding of the successes and challenges related to national-level cholera RDT implementation v. Pilot study efforts.
 - Enabling an understanding of how cholera RDTs are perceived and used one year after their initial introduction
 - Focusing on facilities that have not received intensive training through research efforts to determine how RDTs are perceived and used outside of the research context
 - Informing sustainability by identifying what works well and what can be improved within the nationally-implemented system

- Improved estimates of cholera disease burden in Nepal
- Enhanced data to inform hotspot mapping
- Understand facilitators and barriers to national RDT roll-out to improve implementation and usage of RDTs
- Quantitative assessment of RDT use nationwide
 - PCR validation in nested cohort
- Contribute to planning for cholera elimination in Nepal

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