GLOBAL TASK FORCE ON
CHOLERA CONTROL

Case-area targeted intervention for cholera outbreaks: **protocol for an analytical observational study**

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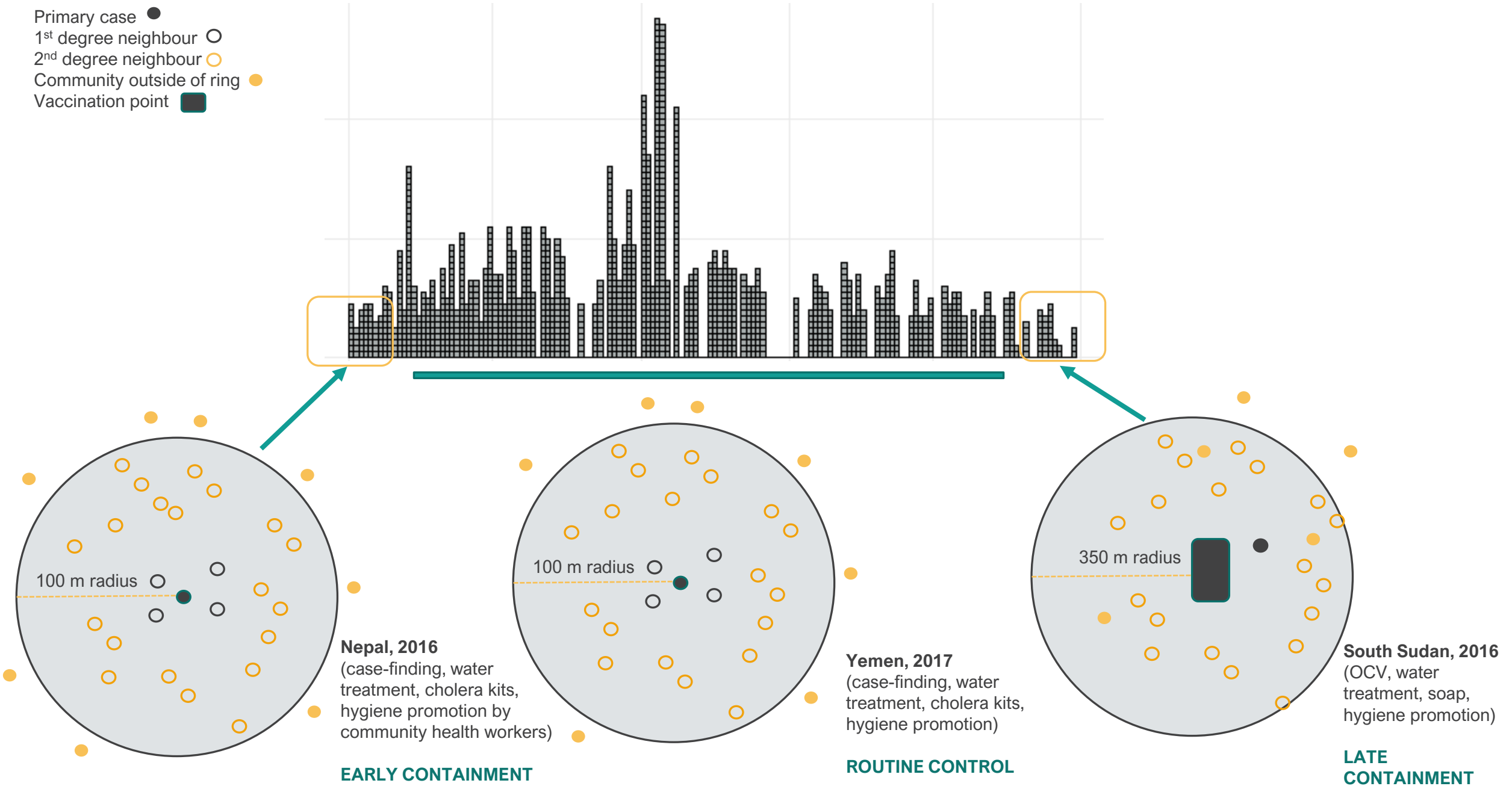
epicentre
ÉPIDÉMIOLOGIE • EPIDEMIOLOGY

MEDECINS SANS FRONTIERES

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

OUTLINE

1. Using current evidence to define the research question
2. Principles guiding the study
3. Study design
   - CATI intervention
   - Design, control, and implementation
   - Primary and secondary outcomes
4. Collecting data during the outbreak
5. Sub-studies: coverage, household transmission, and antimicrobial resistance
6. Médecins Sans Frontières: implementation


Primary case
1st degree neighbour
2nd degree neighbour
Community outside of ring
Vaccination point
100 m radius
100 m radius
350 m radius
Nepal, 2016
(case-finding, water treatment, cholera kits, hygiene promotion by community health workers)
EARLY CONTAINMENT
Yemen, 2017
(case-finding, water treatment, cholera kits, hygiene promotion)
ROUTINE CONTROL
South Sudan, 2016
(OCV, water treatment, soap, hygiene promotion)
LATE CONTAINMENT

DEFINING THE RESEARCH QUESTION

No prospective evaluations of CATI

- **Haiti (Centre Dept, 2015-7): retrospective data analysis**

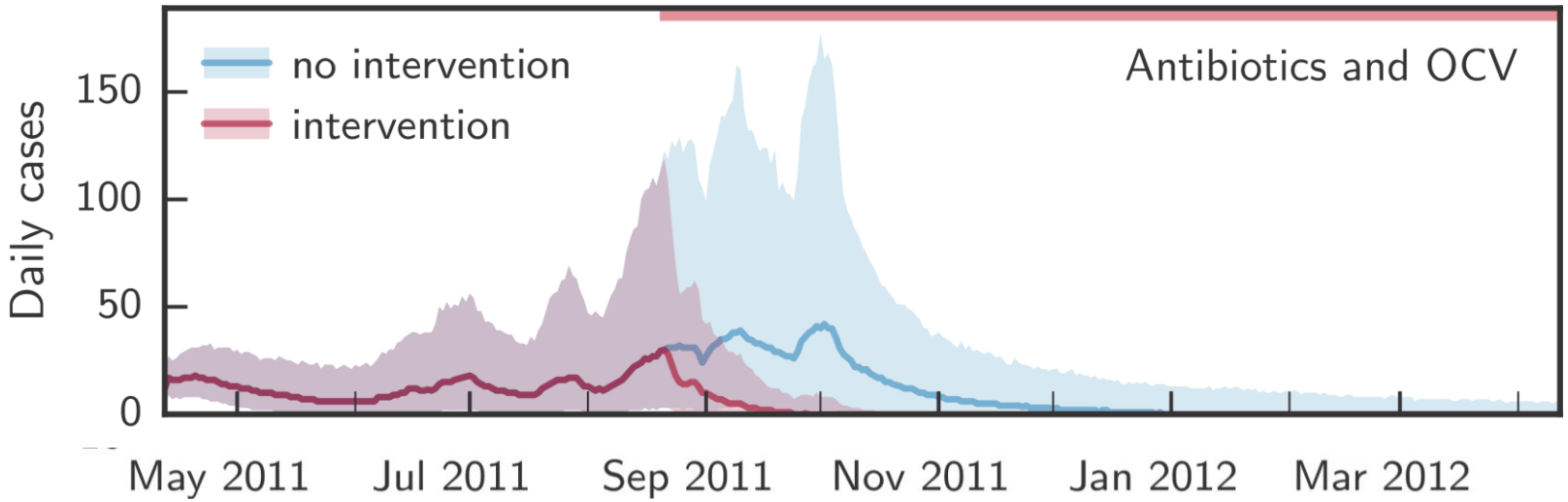
Reduction in size and duration of small-scale outbreaks when CATI was used (WASH and antibiotic chemoprophylaxis) (Michel et al, 2020)

- **Bangladesh (Dhaka, 2013): randomized trial of culture-confirmed cases**

Reduction in intra-household transmission when their household contacts were targeted with hygiene promotion and WASH (versus standard messaging) (George et al, 2016)

Ratnayake R, Finger F, Azman A, Lantagne D, Funk S, Edmunds WJ, Checchi F. Highly-targeted spatiotemporal interventions against cholera epidemics, 2000-2019: a scoping review. *The Lancet Infectious Diseases (in press)*

DEFINING THE RESEARCH QUESTION



Mathematical model of CATI implemented early during an outbreak (100 m around primary cases combining antibiotics and OCV) shortened epidemic duration by 68% (Finger et al, 2018)

DEFINING THE RESEARCH QUESTION

Aim: to evaluate the effectiveness of CATI in the rapid containment of case-clusters, at the start of the outbreak

Primary objective: to evaluate the effectiveness of CATI in the reduction of incidence of enriched RDT-positive cholera within targeted rings

Secondary objectives:

1. Population-based coverage
2. Spatiotemporal transmission patterns of the outbreak
3. Effectiveness in the reduction of household transmission
4. Antimicrobial resistance related to chemoprophylaxis (if used)
5. Resources and costs required

PRINCIPLES GUIDING THE EVALUATION

- Use key transmission-reducing interventions:

  Rapid impact: household WASH and antibiotic chemoprophylaxis

  Delayed but sustained protection: one-dose vaccination and household WASH

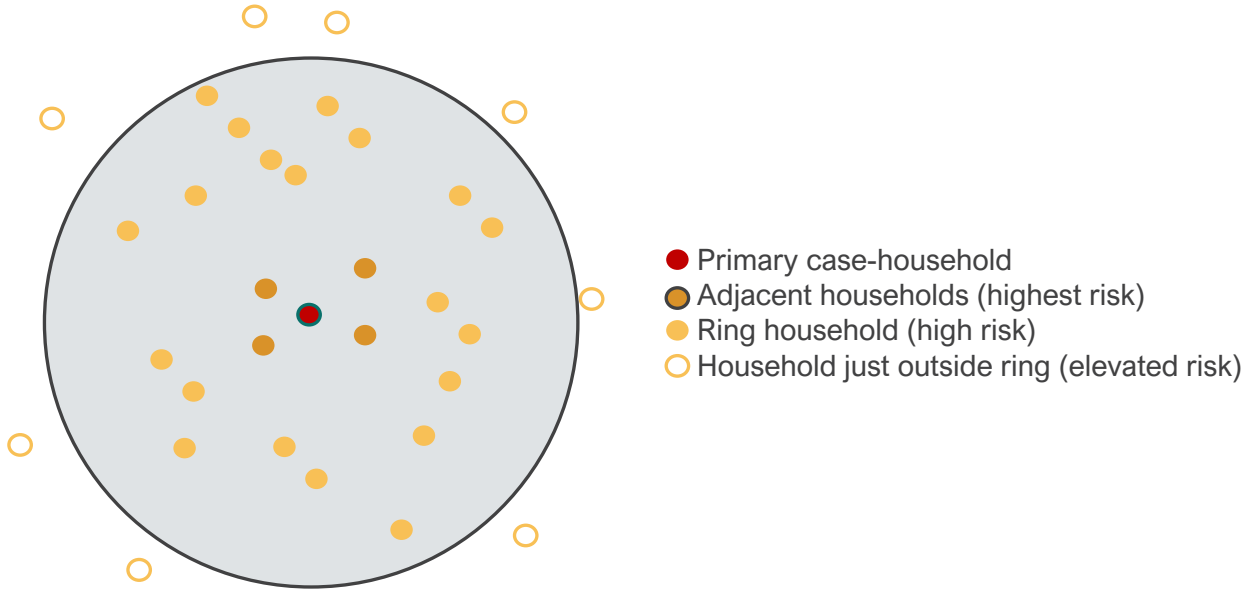
- Use a study design appropriate for an outbreak (e.g., no explicit control group)
- Use real-time data collection to evaluate a CATI strategy prospectively
- Understand the pathway to impact:

  Coverage of CATI

  Impact on household transmission and ring transmission

CATI INTERVENTION

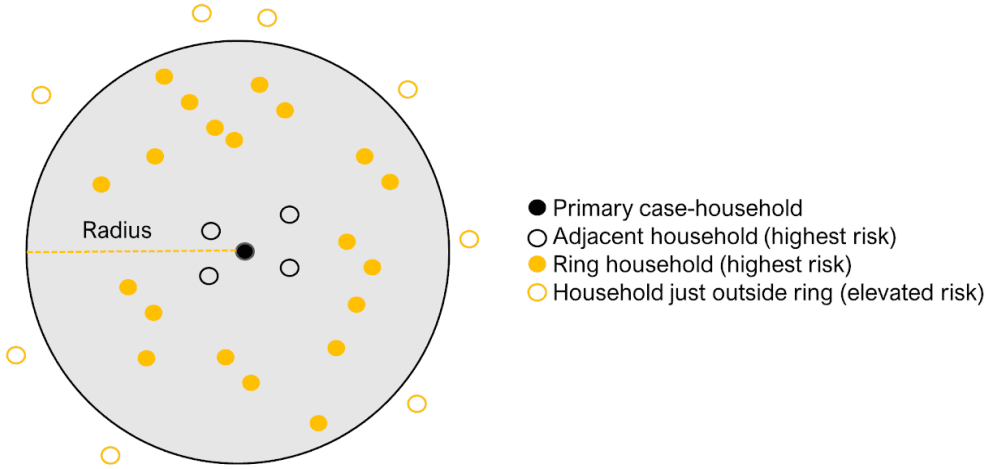
Target CATI only to enriched RDT-positive cases which are most likely to be true cases



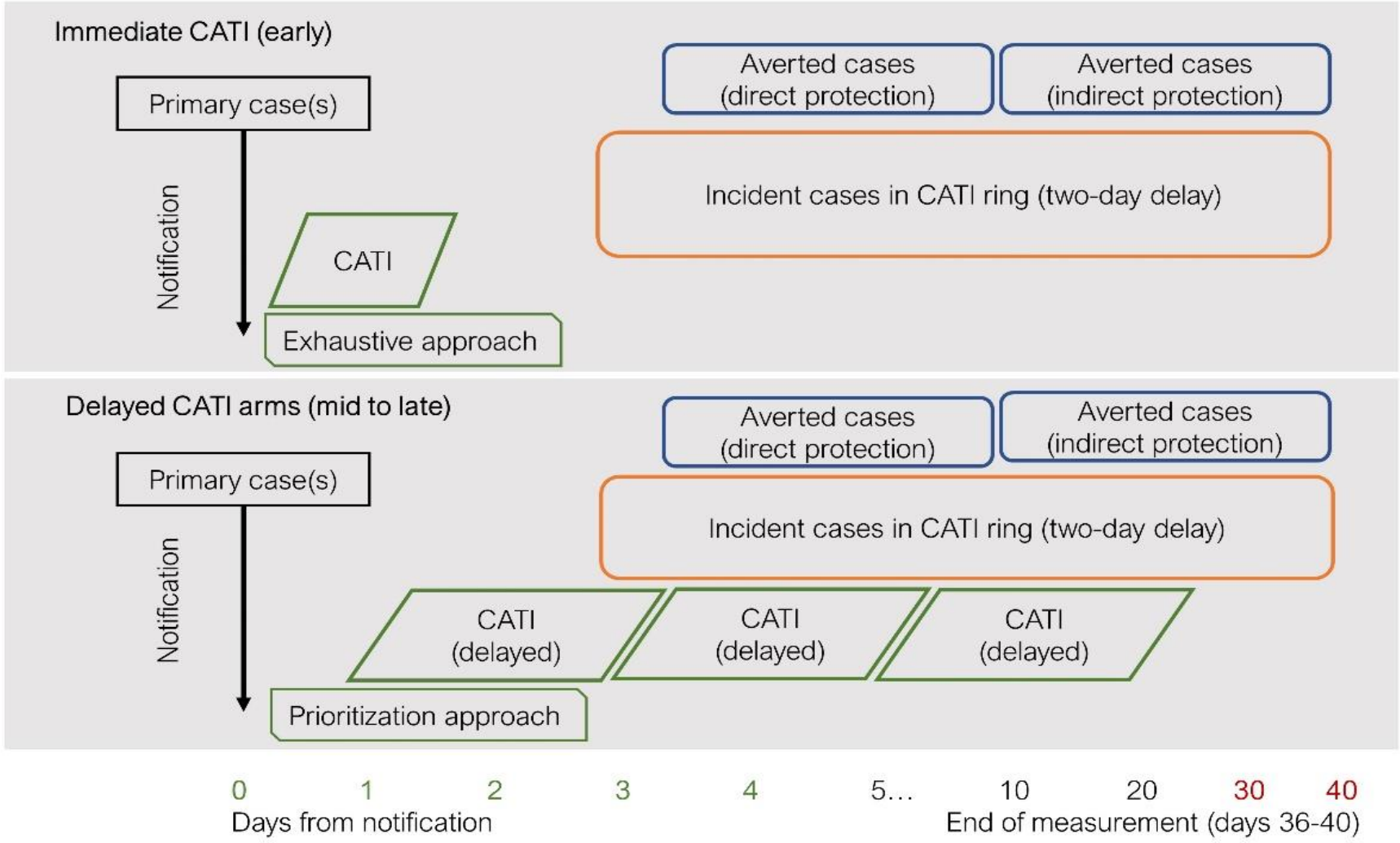
	Primary case household	Adjacent households	Ring households
Single-dose oral cholera vaccine (1-dose, oral)			
Water treatment, safe storage, soap			
Doxycycline or azithromycin (1-dose, oral)			
Intensive hygiene promotion			
Community hygiene promotion			

ANALYTICAL OBSERVATIONAL DESIGN

- Compare immediately-implemented CATIs with naturally delayed CATIs on incidence of enriched RDT-positive cholera
- Study units are the CATI rings (100-250 meters around primary case-household(s), depending on context, or an entire rural settlement
- Regression will model the incidence of enriched RDT-positive cholera by the delay to intervention (delay groups serve as an internal control)



DESIGN, CONTROL, AND IMPLEMENTATION



PRIMARY OUTCOMES

1. Incidence of enriched RDT-positive cholera within the rings after the implementation of CATI
   Suspected cholera (including RDT-positive, RDT-negative, untested)

2. Reduction in spatiotemporal clustering of cases throughout the whole outbreak

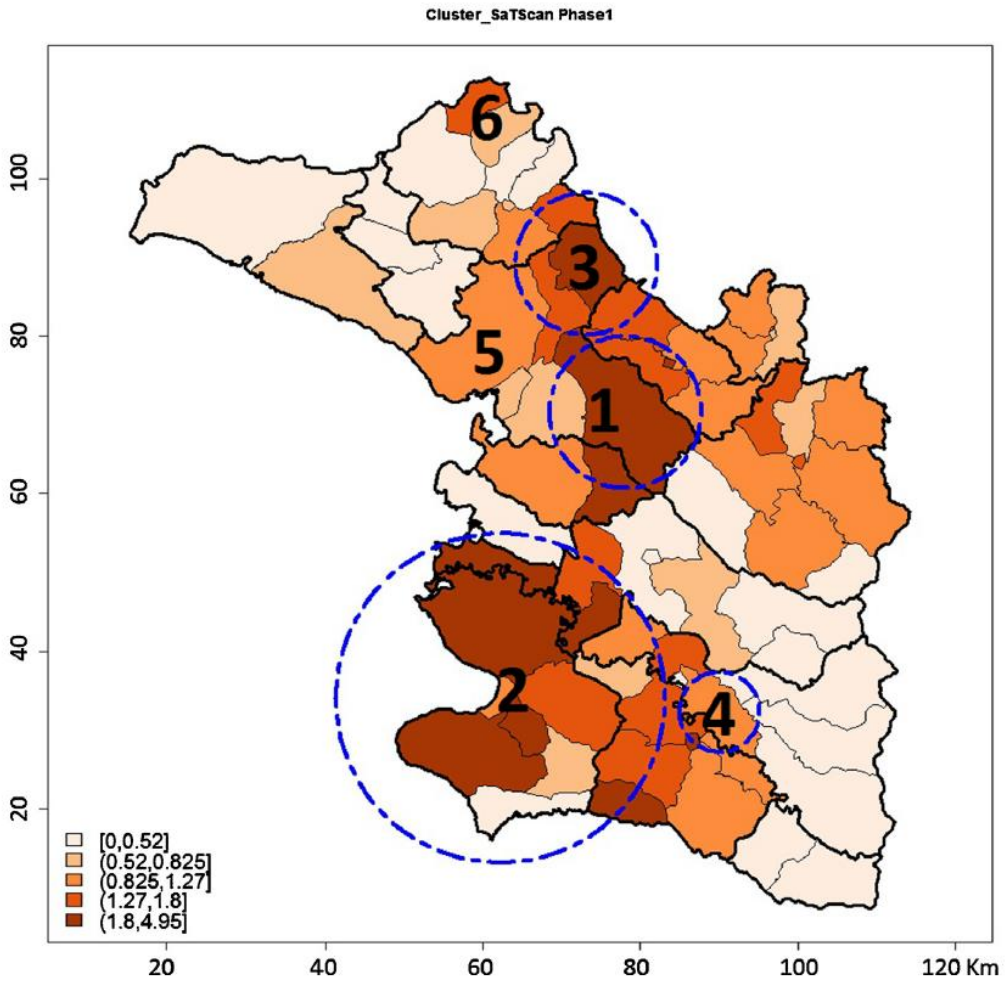


Fig. 7. Significantly high-risk clusters ($p < 0.05$): Phase 1 (2010—Week 42 to 2011—Week 12).

(Allan et al, 2016)

DATA COLLECTION

Patient-level line-list data from CTC

GIS data to link primary case household and households in the ring

Ring-level data to collect information on implementation in the ring

SUB-STUDIES

1. **Cohort study of household transmission** reduction among household contacts
2. **Coverage surveys** to measure coverage and reported uptake of CATI's interventions at a time point after implementation in the ring.
3. **Systematic monitoring of antimicrobial resistance** among *V. cholerae* isolates (potential description of AMR at baseline and post-administration in commensal *E. coli* using rectal samples

IMPLEMENTATION

- Focus on **OCV**, preventive **antibiotics**, and **household WASH**
- CATI implementation by MSF (different operational centres)
- Evaluation using research protocol developed by Epicentre & Ruwan
- MSF operational centres involved in protocol development

- **Potential sites:** Cameroon, Democratic Republic of the Congo, Zimbabwe, …
- Generic protocol subsequently adapted to local situation
- **Timeline:** end 2020 through 2021

- **Acknowledgements**

MSF: Andrew Azman, Nicolas Peyraud, Iza Ciglenecki, Catherine Bachy, Isabella Panunzi, Claire Dorion, Rob D'hondt, Caroline Henry-Ostian, María Lightowler, **LSHTM:** Francesco Checchi, John Edmunds

JHU STUDY

- **Three implementing partners:** Action Contre La Faim, Solidarités International, and Medair
- Flexibility in **research protocol** to incorporate partners' CATI implementation guidelines and country contexts
- WASH, health, and surveillance **interventions** will be selected by partners and/or national cholera outbreak response policy
- **Collaboration** with MSF/LSHTM to complement results and avoid study site overlap
- Timeline: 2021-2022

JHU will not change partners' CATI interventions, but will provide technical and financial support related to the research