Case-area targeted interventions (CATI) for cholera outbreaks: protocol for a prospective observational evaluation

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CATI – Definition
CATI – Current evidence and gaps

• 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, eLife, 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, EID, 2016)

• WASH Rapid Response Teams in Haiti, Yemen, Nigeria, South Sudan (Ramos et al, UNICEF, 2019)

• Scoping review of current evidence (Ratnayake et al, Lancet ID, 2020)

• Gaps:
  • Most studies are retrospective
  • No CATI evaluations including OCV
  • Based on suspected cholera
Including OCV in CATI

• Increased effectiveness
• Longer duration of protection
• Single dose
  • Short term protection demonstrated
• But:
  • ramp-up period of protection
  • OCV needs to be combined with other, faster acting interventions
• Little experience (South Sudan, very recently in Cameroon) and limited evidence so far
• Can be complementary to mass OCV campaigns
Using CATI with OCV in outbreak response

• MSF is interested in the concept of CATI with OCV as an additional tool for cholera outbreak response
• Combining single-dose OCV with household WaSH, possibly chemoprophylaxis
• Different MSF Operational Centres involved in developing strategies
• Discussions with MoH of DRC, Zimbabwe and Cameroon about first implementations
• Evaluation using research protocol developed in collaboration with Epicentre & LSHTM
Example

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

<table>
<thead>
<tr>
<th>Primary case household</th>
<th>Adjacent households</th>
<th>Ring households</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-dose oral cholera vaccine (1-dose, oral)</td>
<td></td>
<td></td>
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<tr>
<td>Water treatment, safe storage, soap</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline or azithromycin (1-dose, oral)</td>
<td></td>
<td></td>
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<tr>
<td>Intensive hygiene promotion</td>
<td></td>
<td></td>
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<tr>
<td>Community hygiene promotion</td>
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</tbody>
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Evaluation – research questions

**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
Evaluation – principles

- Observational study of CATI performed by MSF
  - CATI can include OCV, WaSH, chemoprophylaxis
  - Evaluation can adapt to ring-size of intervention

- 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
  - CTC linelist data & location of primary cases

- Compare immediately-implemented CATIs with naturally delayed CATIs on incidence of enriched RDT-positive cholera

- Understand the pathway to impact:
  - Coverage of CATI (each individual component)
  - Impact on household transmission and ring transmission
Conclusions

• CATI is an interesting new tool for cholera response
• Including OCV could increase effectiveness
• Complementary to preventive mass OCV campaigns and long-term WaSH improvements
• MSF planning on using CATI with OCV
• Discussions ongoing with several MoH about first implementations
• Systematic and prospective evaluation to provide more evidence
• Generic study protocol for evaluation of CATI interventions developed, currently under ethical review
Thank you!

This is a large and interdisciplinary project with many contributions:

• **MSF:** Nicolas Peyraud, Iza Ciglenecki, Catherine Bachy, Andrew Azman, Isabella Panunzi, Claire Dorion, Rob D’Hondt, Caroline Henry-Ostian

• **Epicentre:** María Lightowler, Etienne Gignoux, Francisco Luquero

• **LSHTM:** Ruwan Ratnayake, Francesco Checchi, John Edmunds

• **MoH of DRC**

• **MoH of Zimbabwe**

• **UNICEF DRC**