Effectiveness of case-area targeted interventions (CATI) including vaccination on the control of cholera in the DRC

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Photo: Lisa Véran, MSF
CATI: Case-area targeted intervention

- **Highest risk of cholera infection**: 100 to 500m around **household of cases** during 5 **first days** after case presentation

- **CATI = Multi-pillar reactive intervention**

- Within a **fixed radius around** the household of cholera cases

- Package for **all ring households** with additional items for **primary household** and **direct neighbours**

- **Reactivity** is the main objective

- CATI used by UNICEF, MSF and others in Haiti, Bangladesh, Yemen, Zimbabwe, Nigeria, South Sudan, Cameroon, …

- CATI **with vaccination** is recent and never evaluated
CATI project in the Democratic Republic of the Congo (DRC)

- **CATI package**
  - Single-dose oral cholera vaccine (OCV)
  - Hygiene kit (soap, Aquatabs/chlorine, water storage container, handwashing station)
  - Hygiene promotion
  - Antibiotic chemoprophylaxis (single-dose oral doxycycline) to primary household and direct neighbours

- **Case-ascertainment** with enriched RDTs (Rapid Diagnostic Tests)

- **Ring-radius** between 100 and 500m depending on population density
Epicentre prospective observational study - Endpoints

- **Reactivity**: Timing of each intervention after primary case presentation
- **Coverage & Adherence**: Survey in 30 households in every ring, around 3 weeks after CATI
- **Effectiveness**: Number of cholera cases reported within rings after CATI
- **(Resources)**

Study protocol approved by the MSF ERB & the CNES of the DRC

Photo: Flavio Finger, Epicentre
CATI implementation

- April 2022 to April 2023
- 5 sites in 4 provinces of the DRC
- 118 CATI rings completed
- 104 rings included in effectiveness analysis
  - Main exclusion criterion: surveillance not maintained during 30 days after CATI

<table>
<thead>
<tr>
<th>Ring radius</th>
<th>Hour (IQR)</th>
<th>Population (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100m</td>
<td>84 (71%)</td>
<td>331 (IQR 151, 566)</td>
</tr>
<tr>
<td>50m</td>
<td>34 (29%)</td>
<td></td>
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</tbody>
</table>
Reactivity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N = 118†</th>
</tr>
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<tbody>
<tr>
<td>Symptoms onset to reporting</td>
<td>0.00 (0.00, 1.00)</td>
</tr>
<tr>
<td>Reporting to start of CATI</td>
<td>2.00 (1.00, 3.00)</td>
</tr>
<tr>
<td>Reporting to start of Vaccination</td>
<td>3.0 (2.0, 6.0)</td>
</tr>
<tr>
<td>Duration of Vaccination</td>
<td>4.0 (2.0, 6.0)</td>
</tr>
</tbody>
</table>

† Median (IQR)

### Délai et durée des interventions CATI

- **Minova Sud Kivu**
- **Mbuji-Mayi Kasai Oriental**
- **Masisi Nord Kivu**
- **Katuba Haut Katanga**
- **Kasika Nord Kivu**
- **Buhimba & Mugunga Nord Kivu**

0 10 20 30

jours depuis le début des symptômes du cas primaire
Coverage

Household survey in 30 randomly selected households in every ring, about 3 weeks after CATI.
Adherence

Household survey in 30 randomly selected households in every ring, about 3 weeks after CATI.
How we measure effectiveness

• **Hypothesis:** The shorter the delay to CATI the fewer secondary cases observed in the rings

• **Comparison** between rings where we were fast and ones where we were slow

• **Exposure:** Delay between primary case presentation and start of CATI

• **Outcome:** Secondary cases that are
  - in a CATI ring
  - Reported within 1 to 30 days after primary case presentation
  - Positive to enriched RDTs

• Bayesian **multivariate Poisson regression** adjusting for population density, population <5, water and sanitation, receipt of CATI components, adherence (FRC), random effect for study site
Effectiveness

- **No secondary case** within 30 days in 81 of 104 rings (78%)
- Total of **51** secondary cases, **less than expected**
- Low statistical power

<table>
<thead>
<tr>
<th>Delay to CATI</th>
<th>2 days</th>
<th>5 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of seeing at least one secondary case in a ring</td>
<td>17.9% (1.3 - 42.7%)</td>
<td>26.4% (0.4 - 66.2%)</td>
</tr>
<tr>
<td>Number of secondary cases expected per ring</td>
<td>0.53 (0.027 - 2.01)</td>
<td>1.33 (0.01 - 4.85)</td>
</tr>
</tbody>
</table>

**Trend**: the earlier the CATI, the less secondary cases we see
Study conclusions

• CATI shown to be **feasible**

• **Reactivity:** rapid implementation of CATI possible
  • CATI initiation within 2 days (median)
  • Vaccination started within 3 days (median)
  • Heterogeneity between sites

• **Good coverage:** >85% coverage of full package

• **Adherence** is variable and requires more in-depth analysis

• **Less secondary cases than expected**

• **Effectiveness:**
  • Results show that with a delay to CATI between 0 and 5 days the number of secondary cases expected is low
  • Within this range, we show a trend towards less secondary cases with a quicker implementation of CATI
  • Main limitation is the little variation in delay that we observed

Photo: Lisa Véran, MSF
Operational learnings

• **When and where** is CATI the most appropriate strategy?
  • Containment at **start or end of outbreaks**
  • May prevent expansion in **highly endemic areas** (year-round cholera transmission), but also consider **preventive mass interventions**

• **Reliant on preparedness:**
  • Requires **operating procedures ready, teams trained** and all necessary **approvals** before outbreak starts
  • Clearly defined **trigger criteria**
  • Functioning **surveillance** is key to reactivity, case definitions and/or RDT

• **Resource and labour intensive**
  • Possible **collaborations** with other actors, community health workers
  • **Ring size** is a trade-off between resource need and area covered
  • **Water and sanitation technician on site** can adapt hygiene kit to local conditions

• **Vaccination** is a useful addition to CATI
  • Requires **stock of OCV** in country
  • **Small number of doses** needed (<40K first doses for 118 rings in this study)
  • CATI is a multi-pillar package, **not about vaccination alone**

• **Overall, CATI is an excellent way of quickly providing protection to people most at risk to get infected with cholera**
Merci!

• Équipe d’étude CATI en RDC, en particulier Nana et Innocent
• Les équipes opérationnelles de MSF en RDC
• Le PNECHOL-MD & et le PEV de la RDC et les autorités provinciaux et locaux
• Les relais communautaires
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• Ruwan Ratnayake, LSHTM
• L’équipe de l’étude Wellcome
• Sophie Meakin d’Epicentre
• Les co-investigateurs d’Epicentre MSF, LSHTM et du MSP