Effectiveness of case-area targeted response interventions against cholera: a quasi-experimental study in Haiti

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Annecy
13 February 2019
Case-area targeted interventions (CATIs)

- Successfully implemented for polio or ebola outbreaks
- An old concept for cholera (1971)  
  *V*oelkel Med Trop 1971
- Sporadically implemented but poorly documented for cholera
- “Named” in 2018  
  *F*inger *PLoS Med* 2018; Azman *JID* 2018
- But nearly forgotten in all official cholera “cookbooks”
Rationale for case-area targeted interventions (CATIs) against cholera

• Supported by:
  • frequent household transmission of *V. cholerae* O1
    - Weil *CID* 2009; Taylor *PLoS one* 2015; Domman *Nat Genet* 2018
  • transitory increased cholera risk among neighbors of cholera cases
    - Debes *Int J Epidemiol* 2016; Azman *JID* 2018
  • significant protection of household contacts of cases by promoting hand washing with soap and treatment of water
    - Georges *EID* 2016
  • micro-simulation modeling study
    - Finger *PLoS Med* 2018

• But case-area targeted interventions (« CATIs ») at case households and neighbors have rarely been documented and never evaluated
Since mid-2013, a nationwide alert-response strategy against cholera in Haiti

• Surveillance improvement (case line-lists)

• Case-area targeted interventions (« CATIs ») in max 48h :
  • Implemented by mobile teams : NGOs + MOH (+ DINEPA)
  • WaSH package at case households and neighbors :
    - Education sessions
    - House decontamination
    - Distribution (soaps, chlorine tablets, ORS) +/- Water chlorination points
    - +/- chemoprophylaxis for close contacts

• Study objective : evaluate the effectiveness of complete CATIs against cholera outbreaks between January 2015 and December 2017 in the Centre department, Haiti
Methods: settings
Methods: study design

• Quasi-experimental observational study (2015-2017)

• Identification of outbreaks at locality level:
  • Cases line-lists and stool cultures positive for *Vibrio cholerae* O1
  • Mixed criteria with: number of cases, severity, cultures, detection window, refractory period

• Initial outbreak severity: no. of cases and positive stool cultures during the first 3 days

• Response characterization:
  • *Response promptness* = time to the first complete CATI (days)
  • *Response intensity* = CATIs / weeks ratio; CATIs / cases ratio

• Outbreak outcome:
  • *Outbreak morbidity* = Number of cases from the 4th day of outbreak
  • *Outbreak duration* = Number of days

• Other covariates: locality, altitude, distance to main roads, OCV, no. of previous cases, population density, rainfall
Methods: statistical analyses

1. Assessment of a confounding by indication effect ➔ confirmed
2. Comparison of the outcome of responded outbreaks (morbidity and duration) according to the response promptness and the response intensity:

<table>
<thead>
<tr>
<th></th>
<th>Response promptness:</th>
<th>Response intensity:</th>
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<tbody>
<tr>
<td></td>
<td>(Time to the 1st complete CATI)</td>
<td>(No. of CATIs/duration or No. of CATIs/No. of cases)</td>
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<tr>
<td>Outbreak morbidity</td>
<td>Generalized linear mixed models (GLMM)</td>
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<tr>
<td>(No. of cases from the 4th day)</td>
<td>Effectiveness = 1 – incidence ratio</td>
<td></td>
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<tr>
<td>Outbreak duration</td>
<td>Cox models for Andersen-Gill counting process (AG-CP)</td>
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<tr>
<td>(weeks)</td>
<td>Effectiveness = 1 – (1/hazard ratio)</td>
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</table>

Effectiveness adjustment on covariates using multivariate models
Results (1) : Data description

Daily evolution of :
- 10 428 cholera cases (2144 severe)
- 509 positive cultures
- Rainfall
- 456 outbreaks
- 3887 complete CATIs
Results (2) : Spatial Distribution of cholera outbreaks

- 456 outbreaks
- in 290 localities
- 176 responded before the last case of the outbreak
Results (3): Outbreak morbidity according to the response promptness

- The sooner the first complete CATI was implemented, the fewer cholera suspected cases were recorded from the 4th day of outbreak.

- Adjusted effectiveness of a response in ≤1 day VS >7 days:
  - 74% (58 - 84)
  - $P$-value < 0.0001
Results (4) : Outbreak duration according to the response promptness

• The sooner the first complete CATI was implemented, the shorter the duration of outbreaks

• Adjusted effectiveness of a response in ≤1 day VS >7 days :
  64% (42 to 78)
  $P$-value < 0.0001
Results (5) : Outbreak morbidity according to the response intensity

• The higher the CATIs/week ratio, the fewer cholera suspected cases were recorded from the 4th day of outbreak

• Adjusted effectiveness of a CATIs/weeks ratio ≥1 VS <0.25 :
  76% (54 to 87)
  $P$-value < 0.0001
Results (6) : Outbreak duration according to the response intensity

• The higher the CATIs/cases ratio, the shorter the duration of outbreaks

• Adjusted effectiveness of a CATIs/cases ratio ≥1 VS <0.25 :
  37% (-29 to 69)
  $P$-value = 0.21
Conclusion

• Prompt and repeated case-area targeted interventions (CATIs) significantly effective to mitigate and shorten local cholera outbreaks in the real epidemic setting of rural and semi-urban Haiti

• New consistent preliminary results over 4.5 years throughout Haiti, at the weekly and commune scale. Need to replicate in other contexts.

• Need to assess the impact of each component of the CATI package and optimize the radius of response

• CATIs contributed to get close to cholera elimination in Haiti

• CATI would warrant a better integration within cholera “cookbooks”:
  • Cholera Outbreak Response Field Manual
  • Framework for the Development and Monitoring of Multi-Sectoral NCP
Effectiveness of Case-Area Targeted Response Interventions Against Cholera: A Quasi-Experimental Study in Haiti

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Thank you for your attention

M’di ou mèsi anpil pou koute’ m
Annex: confounding by indication

If CATIs were significantly more likely implemented in more severe outbreaks, estimates of CATI effectiveness could be underestimated.  

Remschmidt BMC Infect Dis 2015

Three supporting results:
1. Onset of responded outbreaks significantly more severe than onset of non-responded ones
2. Paradoxically, worse outcome of responded outbreaks than non-responded outbreaks (negative estimated effectiveness)
3. Better adjusted effectiveness than crude effectiveness

Interpretation:
- Numerous little outbreaks ended automatically, often before mobile teams arrived for the response.
- In absence of randomization, response teams tended to give priority to initially more severe outbreaks.
Annex: limitations

• CATIs not randomized : effectiveness biased by unmeasured confounders ?
  ➢ Models adjusted of on initial outbreak severity and taking into account the heterogeneity between localities
  ➢ Stratified models yielding consistent response effectiveness estimates

• Missing epidemiological data ?
  ➢ Would lead to underestimate the effectiveness

• Impact of chosen outbreak definition ?
  ➢ Sensitivity analysis showing consistent results

• Missing CATI data ?
  ➢ Most CATIs conducted jointly by several organizations (NGOs+EMIRA)

• Respective effectiveness of each component of the CATI package ?
  ➢ Sensitivity analysis on “complete CATI” definitions showing consistent results
  ➢ Additional studies
Annex : example of intervention (CATI)

https://www.youtube.com/watch?v=KOYRX4Fmabo