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

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Case-area targeted interventions (CATIs)

- Successfully implemented for polio or ebola outbreaks

- An old concept for cholera (1971) Voelkel *Med Trop 1971*

- Sporadically implemented but poorly documented for cholera

- "Named" in 2018 Finger *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

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Methods : settings
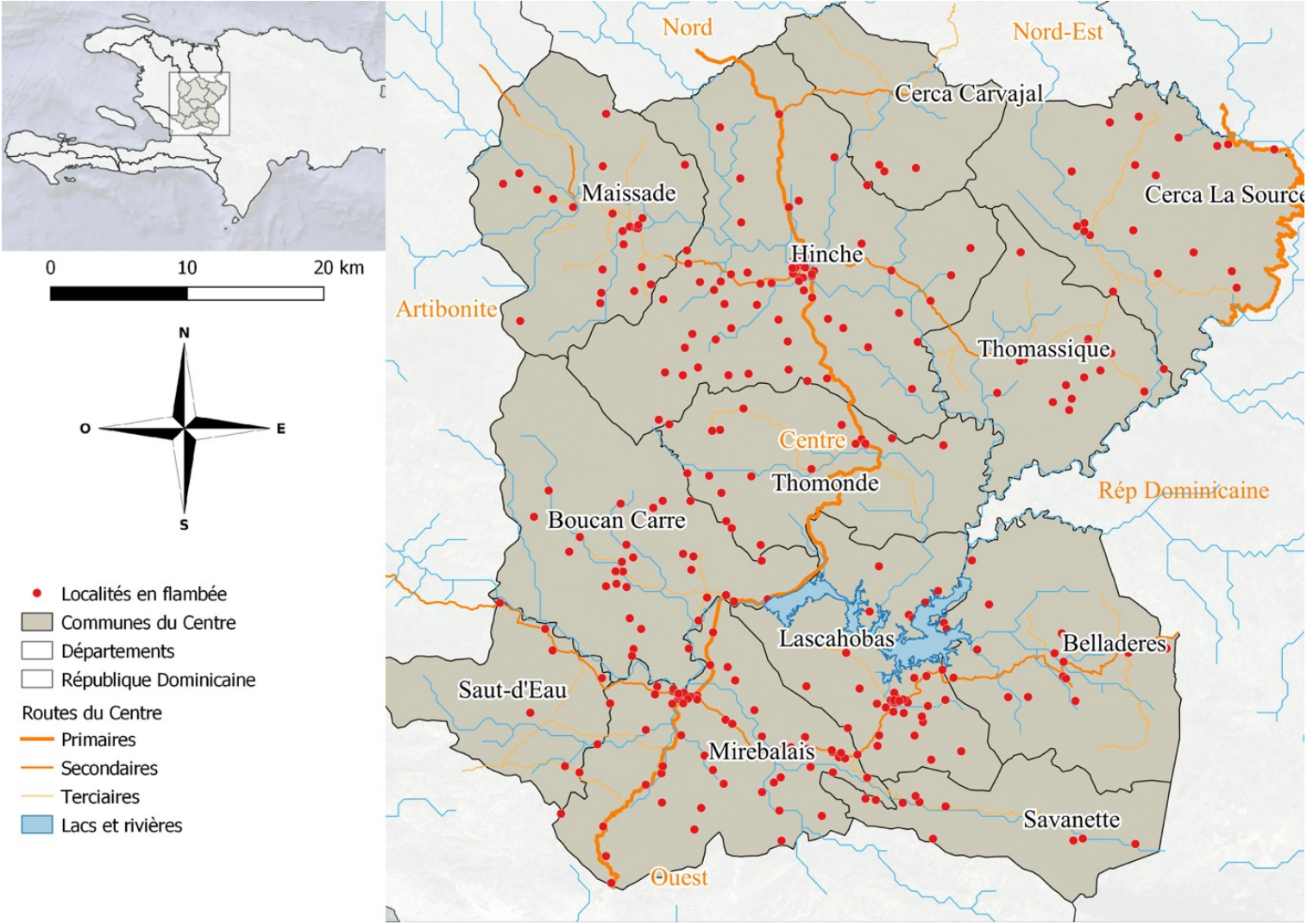
Methods : study design

- 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

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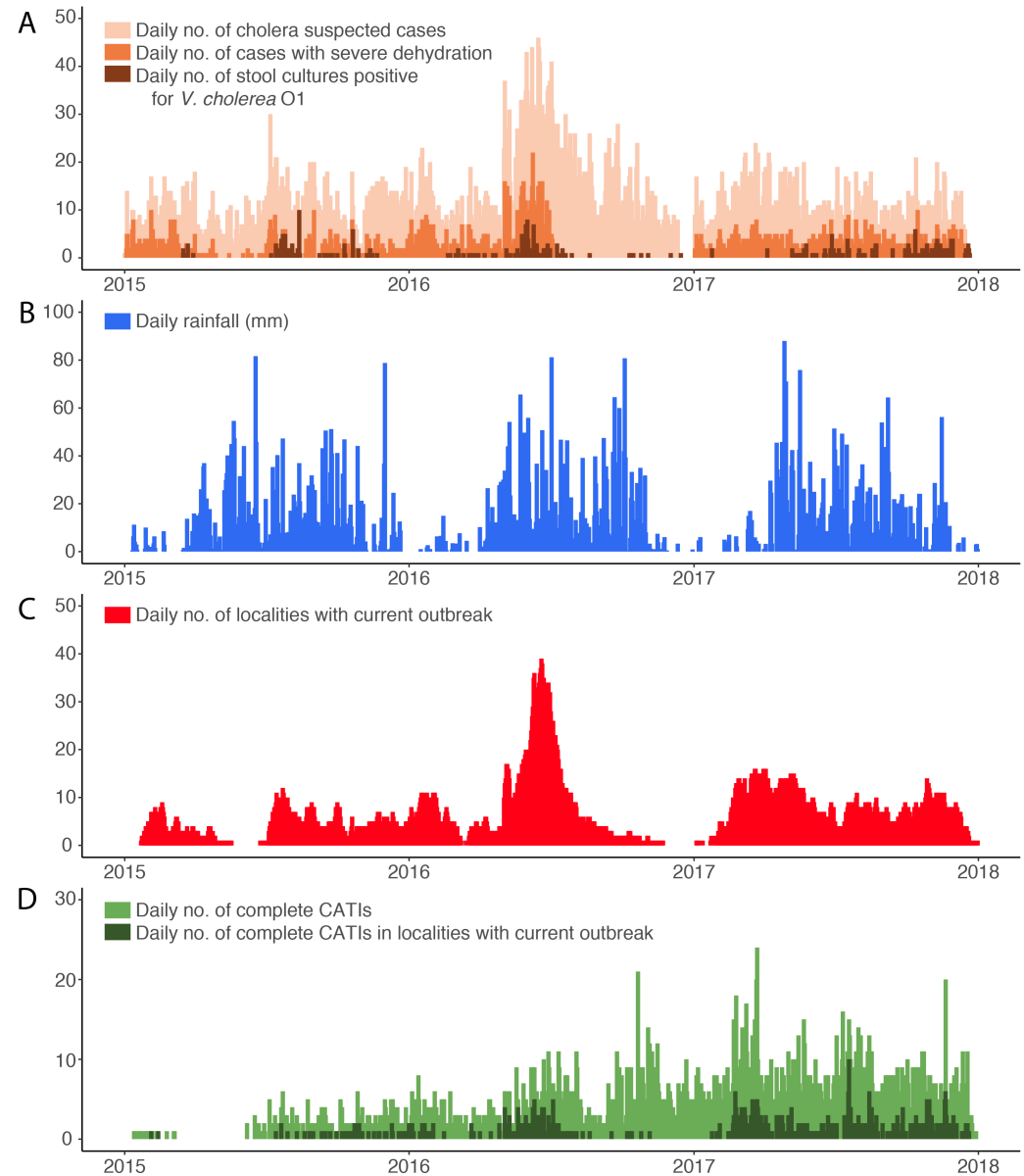
	Response promptness :	Response intensity:
	(Time to the 1st complete CATI)	(No. of CATIs/duration *or* No. of CATIs/No. of cases)
Outbreak morbidity (No. of cases from the 4th day)	Generalized linear mixed models (GLMM) Effectiveness = 1 – incidence ratio	
Outbreak duration (weeks)	Cox models for Andersen-Gill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

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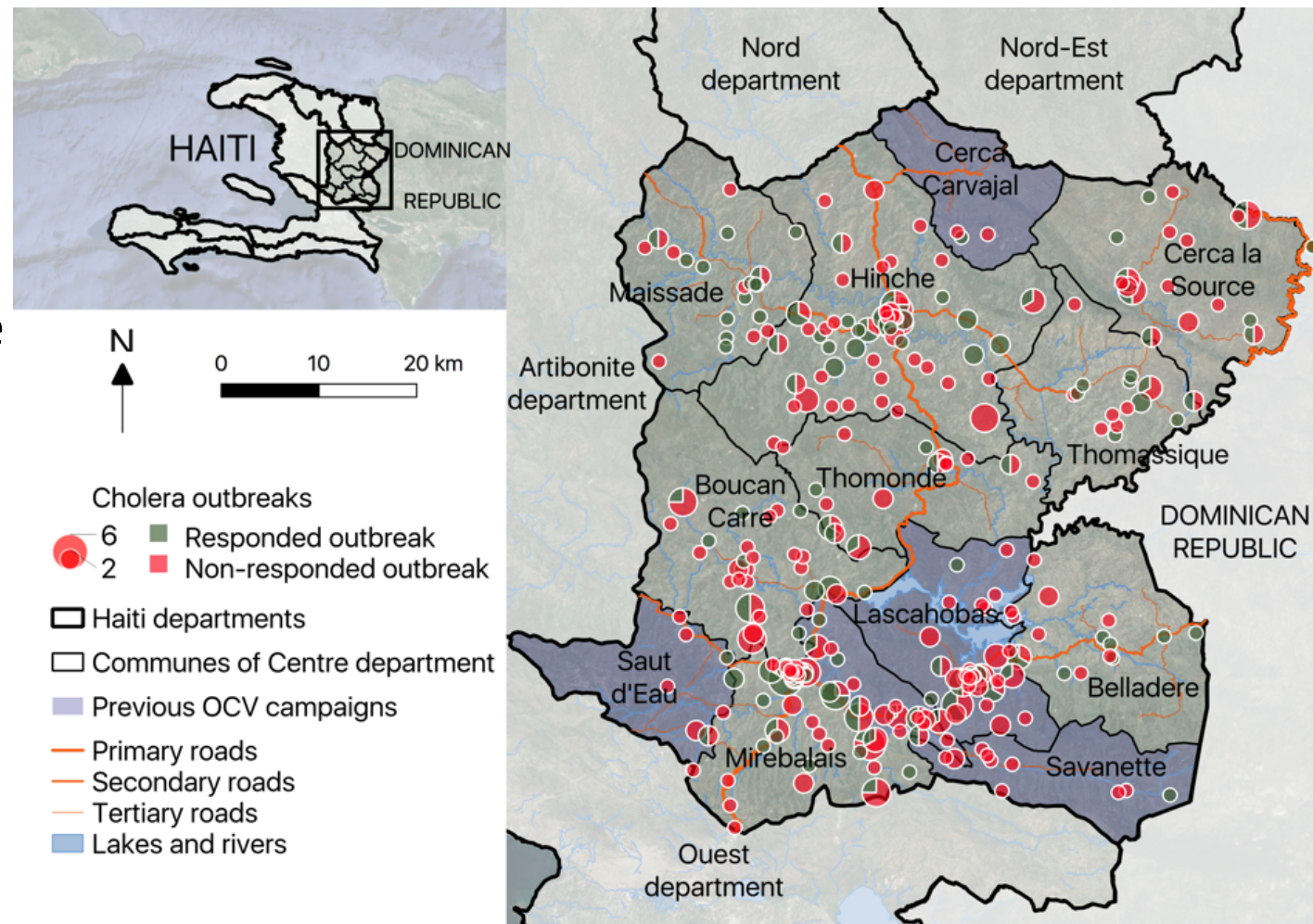
Results (1) : Data description

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 :
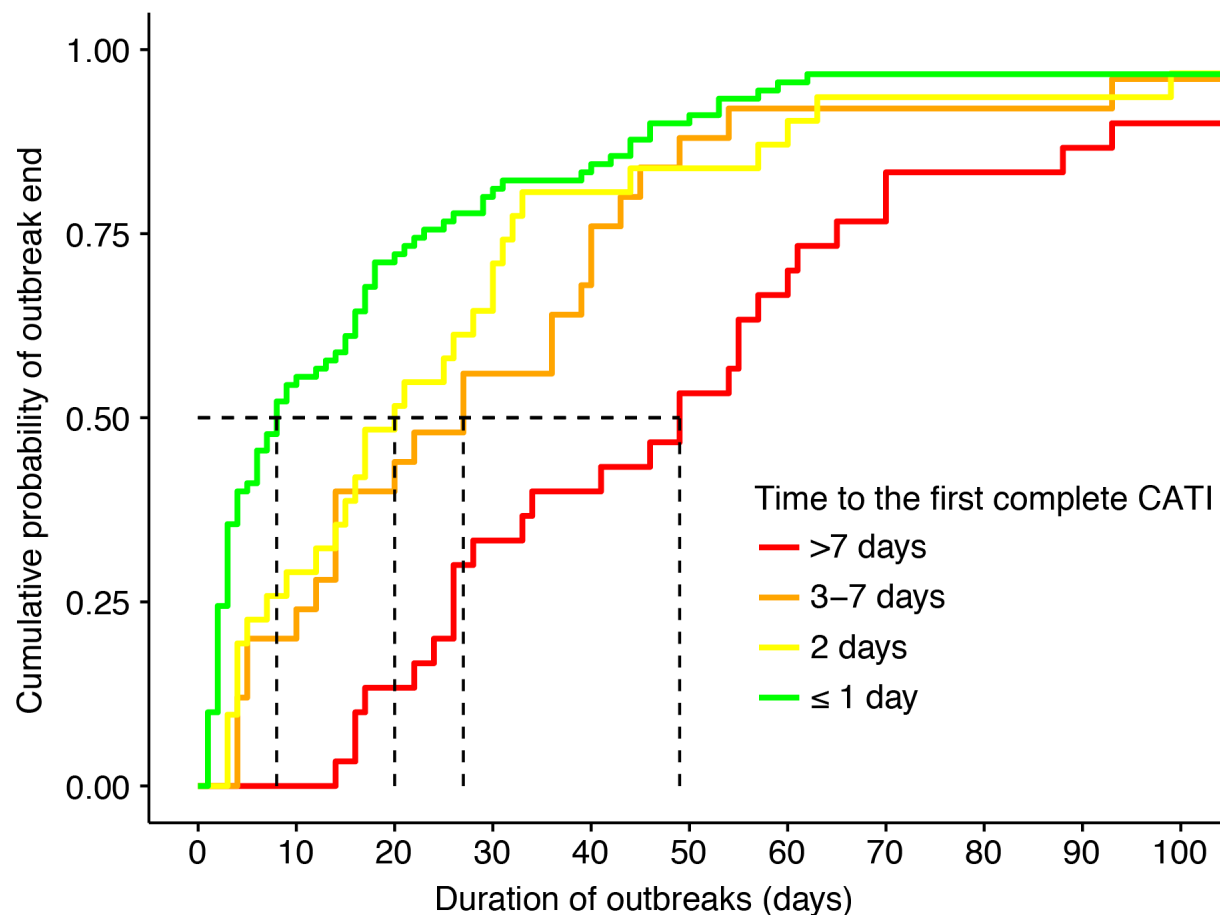
    74% (58 - 84)

    P-value < 0.0001
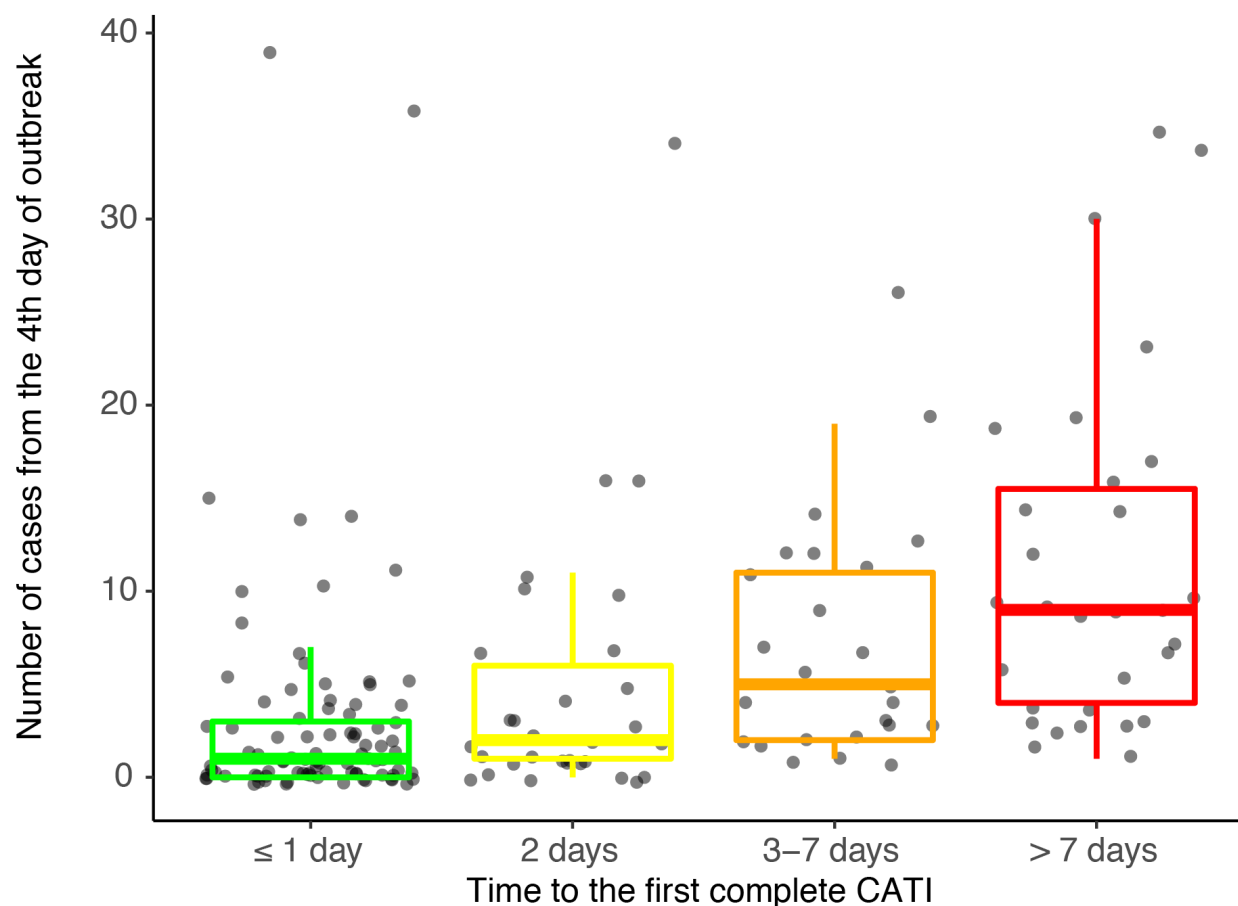
Results (4) : Outbreak duration according to the response promptness

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

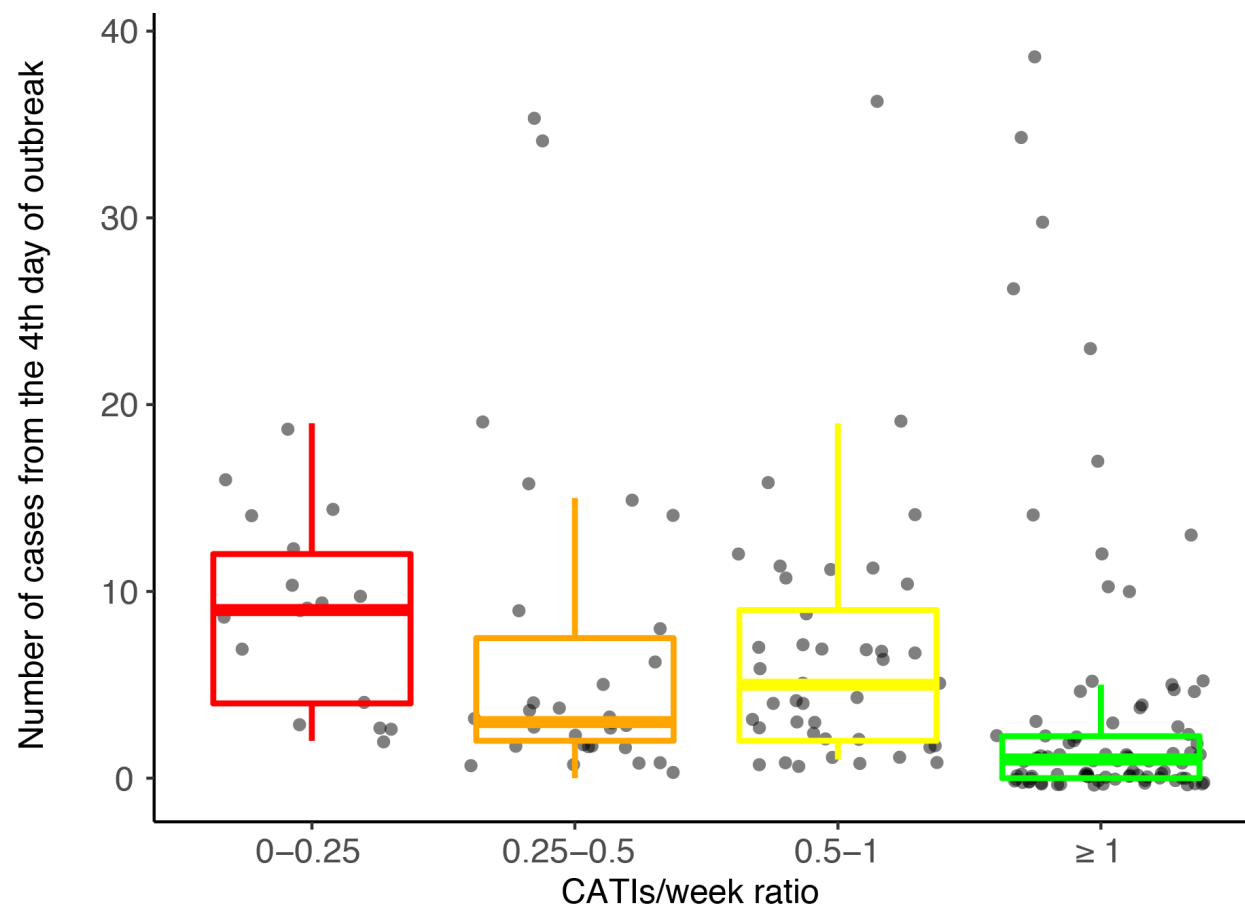- Adjusted effectiveness of a response in ≤1 day VS >7 days :

   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
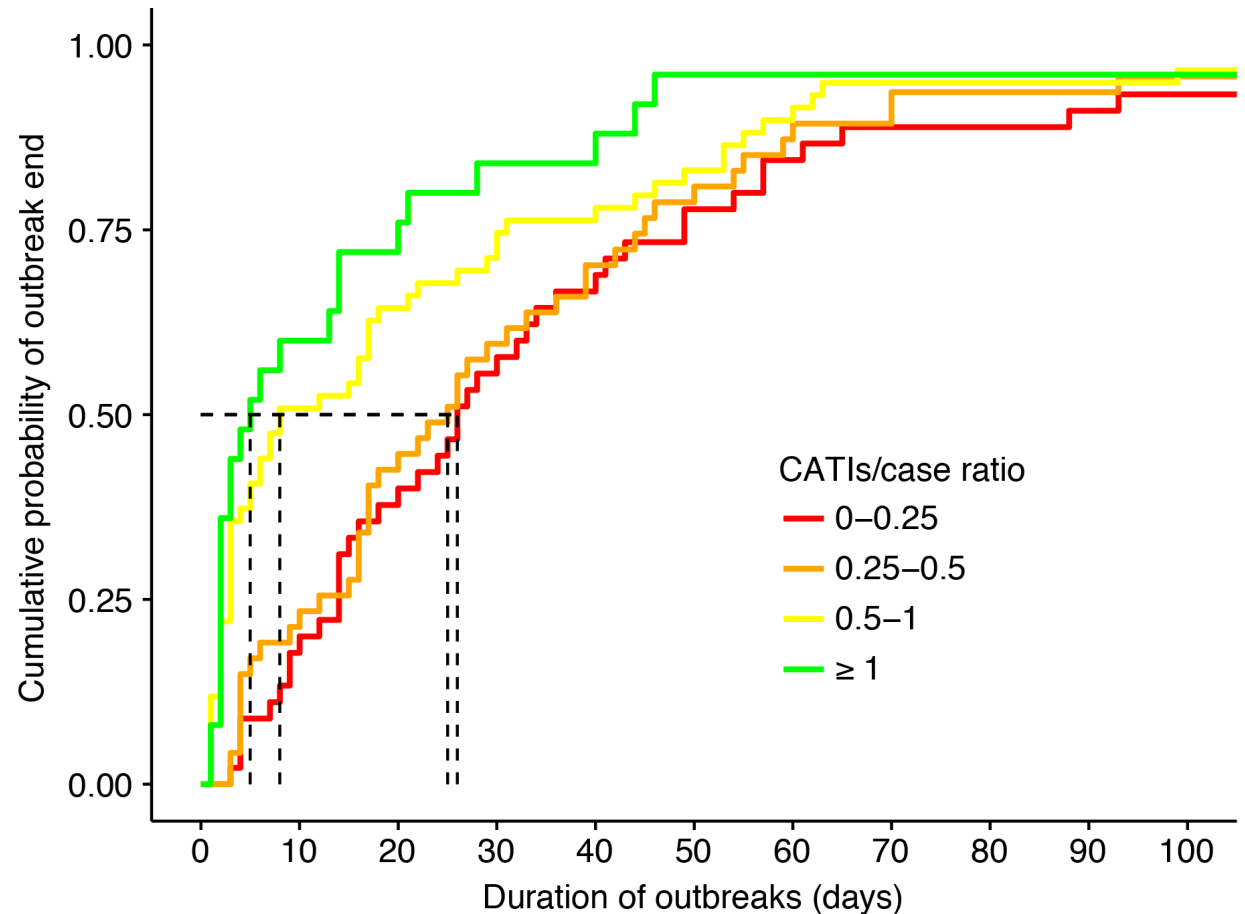
Conclusion

- 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

Preprints with THE LANCET

Effectiveness of Case-Area Targeted Response Interventions Against Cholera: A Quasi-Experimental Study in Haiti

32 Pages · Posted: 21 Dec 2018

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https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3304278

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Thank you for your attention

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Annex: confounding by indication

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

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