

Cholera spatial clustering and the use of case-area targeted interventions for cholera control

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BACKGROUND

- Cholera transmission is thought to occur through two modes of exposure:
 - environmentally-mediated exposure, often due to fecal contamination in the broader environment, and
 - "direct" exposure to an infected individual (e.g., being served food directly contaminated by a case).
- The mix of environmentally-mediated and direct exposure shapes the spatiotemporal distribution of cases within an epidemic.

RESULTS

MICRO-HOTSPOT ANALYSIS

- We found zones of increased risk of at least 200-meters during the 5-days immediately following case presentation to a clinic. Risk was highest for those living closest to cases and diminished in time and space similarly across settings.
- Evidence from Bangladesh and other locations have shown that direct transmission plays an important role in cholera transmission leading to elevated risk when residing close to an incident case. Likewise, those living close together will often share risk factors and access shared water sources
- Therefore cholera prevention and control interventions targeted to neighbors of cholera cases (case-area targeted interventions [CATIs]), including improved water, sanitation, and hygiene, oral cholera vaccine (OCV), and prophylactic antibiotics, may be able to efficiently avert cholera cases and deaths while saving scarce resources during epidemics.
- Efforts to quickly target interventions to neighbors of cases have been made in recent outbreaks, but little empirical evidence related to the effectiveness, efficiency, or ideal design of this approach exists.
- Here, we aim to provide practical guidance on how CATIs might be used by exploring key determinants of intervention impact, including the mix of interventions, "ring" size, and timing, in simulated cholera epidemics fit to data from an urban cholera epidemic in Africa.

METHODS

MICRO-HOTSPOT ANALYSIS

• Data sources

– Médecins Sans Frontières (MSF) assisted the Chad Ministry of Health (MoH) to respond to a cholera outbreak that started in mid-April. On 22-June-2011 the MSF team, with the assistance of other collaborating agencies, began systematically collecting household GPS coordinates through a home visit to each suspected cholera case presenting at one of the official cholera treatment centers/units in N'Djamena. As the number of cases per day began to rapidly increase in early October, MSF modified their protocol to collect household coordinates for one out of every three cases.

- Clear zones of increased risk suggest that highly targeted interventions may provide an efficient means of limiting transmission in outbreaks across different settings.



Figure 1. Estimates of the relative risk of the next cholera case occurring at different distances from a primary case by days since primary case presentation (x-axis) and distance from primary case (panels). N'Djamena estimates and 95% confidence intervals are shown in green and those from Kalemie are shown in orange.

CATI MODELING

- -OCV was the most effective single intervention, followed by POUWT and antibiotics. Although any combination increased the number of cases adverted, adding POUWT or antibiotics to OCV provided only marginal improvements.
- Kalemie is located on Lake Tanganyika in eastern D.R. Congo and serves as a large urban trading center for the region. From 1-Jan-2013 to 15-Jan-2014, MSF and the MoH collected the household coordinates for each suspected cholera case seeking care at the main diarrhea treatment center in Kalemie.

• Data analysis

- -To characterize the spatiotemporal clustering of cases, we calculated, a global clustering statistic estimating the relative risk of the next case occurring at a distance d, within t days after a suspected ('primary') case presents at a health facility compared to the risk of the next case occurring anywhere in the population (i.e., the entire city) during the same period.
- -We calculated tau functions using the IDSpatialStats package, with a 50 meter moving window estimated every 10-meters and 95% confidence intervals as the 2.5th and 97.5th quantiles from 1,000 bootstrap replicates.
- -We focused at distances up to 500m from a 'primary' case and within 5-day windows up to 30-days after a primary case presented to a facility. We considered the zones of increased risk around incident cases to extend until the 95% confidence intervals cross unity for at least two consecutive points (i.e., ≥ 20) consecutive meters).

- -CATIs shorten the duration of epidemics and are more resource-efficient than mass campaigns.
- -CATIs used late in epidemics, even after the peak, were estimated to avert relatively few cases but substantially reduced the number of epidemic days (e.g., by 28% [IQR 15% to 45%] for OCV in a 100-m radius).



Figure 2. Outcome of the 3 main interventions with case-area targeted allocation in a 100-m radius.



CATI MODELING

- -We developed a micro-simulation model from the GPS data collected in N'Djamena, Chad.
- -We calibrated the model to both the epidemic curve and the small-scale spatiotemporal clustering pattern of case households from the 2011 cholera outbreak in N'Djamena (4,352 reported cases over 232 days).
- We explored the potential impact of CATIs in simulated epidemics.
- -CATIs were implemented with realistic logistical delays after cases presented for care using different combinations of prophylactic antibiotics, OCV, and/or pointof-use water treatment (POUWT) starting at different points during the epidemics and targeting rings of various radii around incident case households.

Acknowledgments

CONCLUSION

- CATIs using OCV, antibiotics, and water treatment interventions at an appropriate radius around cases could be an effective and efficient way to fight cholera epidemics.
- They can provide a complementary and efficient approach to mass intervention campaigns and may prove particularly useful during the initial phase of an outbreak, when there are few cases and few available resources, or in order to shorten the often protracted tails of cholera epidemics.

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