Decline in typhoid fever incidence in Kibera, an urban informal settlement in Nairobi, Kenya

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Typhoid fever in Kibera

- Large slum in Nairobi, Kenya
  - Densely populated
  - Poor water and sanitation infrastructure

- Population-based infectious disease surveillance system (PBIDS) in the area (since 2007)

- High burden of typhoid fever observed (03/2007-02/2009)
  - Crude incidence 247/100,000
  - Adjusted incidence 822/100,000

- Children at highest risk
  - 2-4 years 2,242/100,000
  - 5-9 years 1,788/100,000
Updated analysis of Typhoid fever in Kibera

- Typhoid fever burden can vary over time
- Analyzed PBIDS data from 2007 to September 2017
- About 20,000-25,000 enumerated Kibera residents surveyed
Household-based surveillance

- Demographic
  - Migrations
  - Pregnancies
  - Births
  - Deaths

- Assessed for
  - Recent illness
  - Healthcare seeking

- Frequency of home visits
  - Biweekly (01/2007-03/2010)
  - Weekly (04/2010-04/2011)
  - Biweekly (05/2011-03/2015)
  - Biannual (04/2015-present)

- Re-consenting and re-enumeration in 2015-2016

Photo credit: Alice Auma, 2013
Clinic-based surveillance

• Free care for acute illness at Tabitha clinic
  ▪ PBIDS households within ~1km

• Blood culture for patients with
  ▪ Acute febrile illness (AFI)
    • Documented fever
    • Onset <14 days prior
  ▪ Severe acute respiratory infection (SARI)
    • Cough or difficulty breathing, plus
      o < 5 years: indrawing or O2 saturation <90% or danger sign
      o ≥ 5 years: documented fever or O2 saturation <90%
Laboratory methods

• Collected samples incubated in BACTEC System

• *Salmonella* isolation and identification through standard microbiology techniques

• Serotyping by *Salmonella* antisera and/or genomic sequencing

• Antimicrobial susceptibility testing by Kirby-Bauer disc diffusion
  - Multi-drug resistance (MDR) = non-susceptibility to ampicillin, trimethoprim-sulfamethoxazole and chloramphenicol
Crude incidence calculation

\[
\text{Crude rate} = \left( \frac{\# \text{ bacteremic } S. \text{Typhi cases per year}}{\text{annual person-years-observation (pyo)}} \right) \times 100,000
\]
Typhoid fever crude incidence trend estimates

- Used smoothed spline, regression model
  - Accounts for continuous nature of categorized prediction variables (e.g. time)

- Used Poisson regression with continuous time variable to test for risk reduction over time
### Adjusted incidence calculation

#### Adjustment 1 for sample collection among patients eligible for blood culture

\[
\text{Adjustment 1} = \frac{\text{crude incidence}}{\left( \frac{\text{number patients with blood culture performed}}{\text{total eligible for blood culture}} \right)}
\]

#### Adjustment 2 for healthcare seeking among people with medically-attended AFI or SARI in household data

\[
\text{Adjustment 2} = \frac{\text{adjusted incidence}}{\left( \frac{\text{number people with AFI or SARI at household who sought care at surveillance clinic}}{\text{total people with AFI or SARI at household who sought care}} \right)}
\]

- Used bootstrapping to account for uncertainty in adjusted incidence rates

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### Isolation of *Salmonella enterica* serovar Typhi (S. Typhi) from blood cultures in Kibera, 2007-2017

<table>
<thead>
<tr>
<th>Years</th>
<th>S. Typhi isolated</th>
<th>Person-year-observation</th>
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<td>14138</td>
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<tr>
<td>Total</td>
<td>338</td>
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</table>
Crude typhoid fever incidence by year, Kibera, 2007-2017
Crude typhoid fever incidence by year, Kibera, 2007-2017

Relative Risk 0.87 (95%CI 0.83-0.91); 13% reduction per year
Crude and adjusted typhoid fever incidence by year, Kibera, 2007-2017
Crude and adjusted typhoid fever incidence by age group, Kibera, 2007-2017
Crude age-stratified typhoid fever incidence by year, Kibera, 2007-2017

- Under 2 years: RR 0.94 (CI: 0.73-1.18)
- 2-4 years: RR 0.91 (CI: 0.82-1.01)
- 5-9 years: RR 0.82 (CI: 0.75-0.89)
- 10-17 years: RR 0.85 (CI: 0.77-0.93)
Crude age-stratified typhoid fever incidence by year, Kibera, 2007-2017

18-24 years
RR 0.82 (CI: 0.70-0.96)

25-44 years
RR 0.83 (CI: 0.72-0.94)

45 and older
RR 0.87 (CI: 0.61-1.21)
Discussion

• Burden of typhoid fever in Kibera declined
  ▪ Sharp decline in 2013; remained low
  ▪ Investigating possible drivers of decline
    ○ Posters 41, 105 and 113

• No significant decline in children < 5 year
  ▪ Relative increase in cases 2010-2012
  ▪ Consistent with genomic data suggesting possible outbreak

• Generally common resistant to ampicillin, chloramphenicol and trimethoprim sulfamethoxazole
  ▪ Sporadic resistance to ceftriaxone and ciprofloxacin
Limitations

- Relatively small population size and case counts
- Assumptions about patients with no blood culture or who seek care elsewhere may not be accurate
- Changes in frequency of household visits
  - Might have impacted case detection
  - However, care at surveillance clinic free of charge and nearby, thus minimize barriers to care seeking
- Drop in pyo in 2015
  - Issue with linking between old an new demographic data being resolved; in the meantime may inflate incidence for 2015
Conclusions

• The burden of typhoid fever has declined

• Modelling and environmental surveillance for typhoid to improve understanding of typhoid dynamics in Kibera

• Continued surveillance to monitor for resurgence of disease and antimicrobial resistance

• Potential for further reduction with intervention
  ▪ Particularly for children < 5 years
  ▪ New generation typhoid vaccine
  ▪ Improved water and sanitation
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the KEMRI Center for Global Health Research.
Nalidixic Acid resistance

Total tested for Nalidixic resistance

% Nalidixic Acid resistance

CASE COUNT

PERCENTAGE


0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%


0 5 10 15 20 25 30 35 40 45 50