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

ERIC NG'ENO[1,3*], MARGARET LIND[2*], ALLAN AUDI[3], SAMUEL KIPLANGAT[3], CLIFFORD ODUOR[3],ALICE OUMA[3], GEOFFREY MASYONGO[3], NEWTON WAMOLA[3], CAROLINE OCHIENG[3], VICTOR OMBALLA[3], ELIZABETH HUNSPERGER[4], BONVENTURE JUMA[4], ERIC MINTZ[5], JENNIFER R VERANI[4]

[1]Washington State University, Global Health Program, Kenya
[2]University of Washington
[3]Kenya Medical Research Institute,
[4]Centers for Disease Control and Prevention, Nairobi, Kenya
[5]Centers for Disease Control and Prevention, Diseases, Atlanta, USA

KEMRI
Centre for Global Health Research

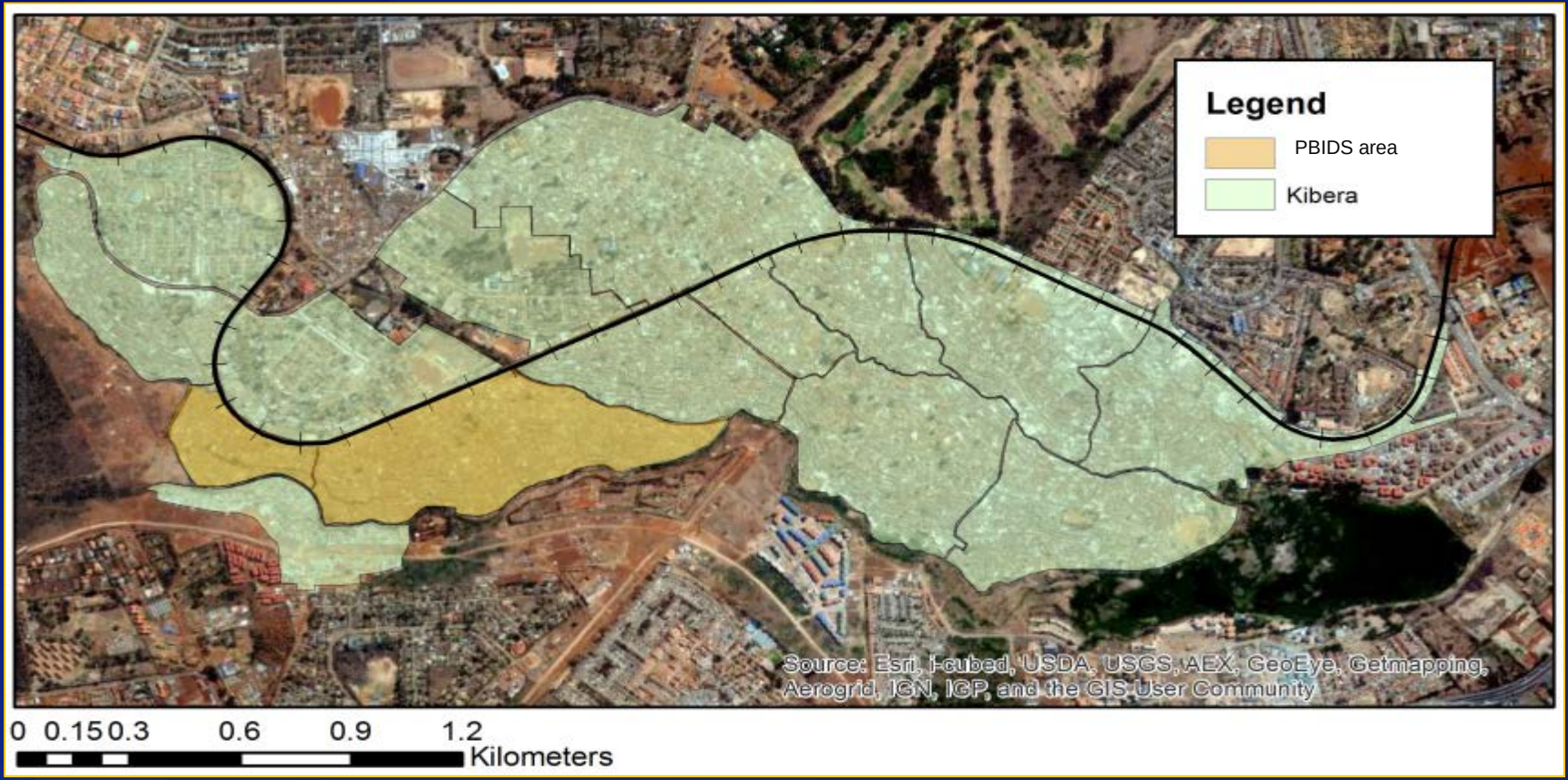
Typhoid fever in Kibera

- 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

Wikimedia commons, 2000

Breiman *at al.* (2012) PLoS ONE 7(1)

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
      - < 5 years: indrawing or O2 saturation <90% or danger sign
      - ≥ 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

$$\textit{Crude rate} = \left(\frac{\#\ \text{bacteremic } \textit{S}.\ \text{Typhi cases per year}}{\text{annual person-years-observation (pyo)}}\right) \times 100{,}000$$

Breiman, RF., et al. (2012). PLoS ONE 7(1):

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

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

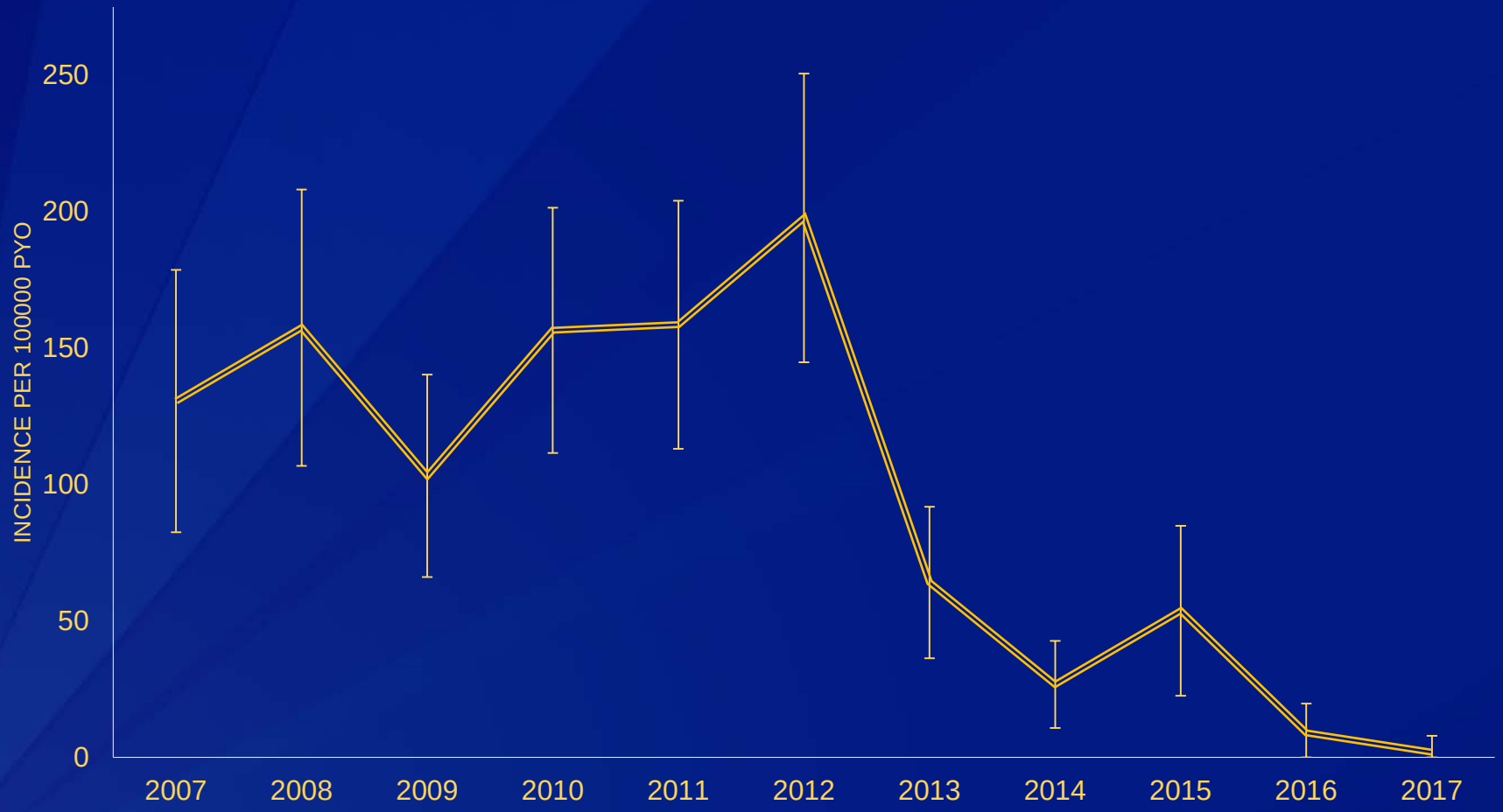
- Used bootstrapping to account for uncertainty in adjusted incidence rates

Breiman, RF., et al. (2012). PLoS ONE 7(1):

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

Years	*S.* Typhi isolated	Person-year-observation
2007	59	21401
2008	53	21941
2009	21	24224
2010	69	25912
2011	42	24971
2012	62	23831
2013	8	22983
2014	9	22888
2015	9	17608
2016	4	20132
2017	2	14138
Total	338	240029

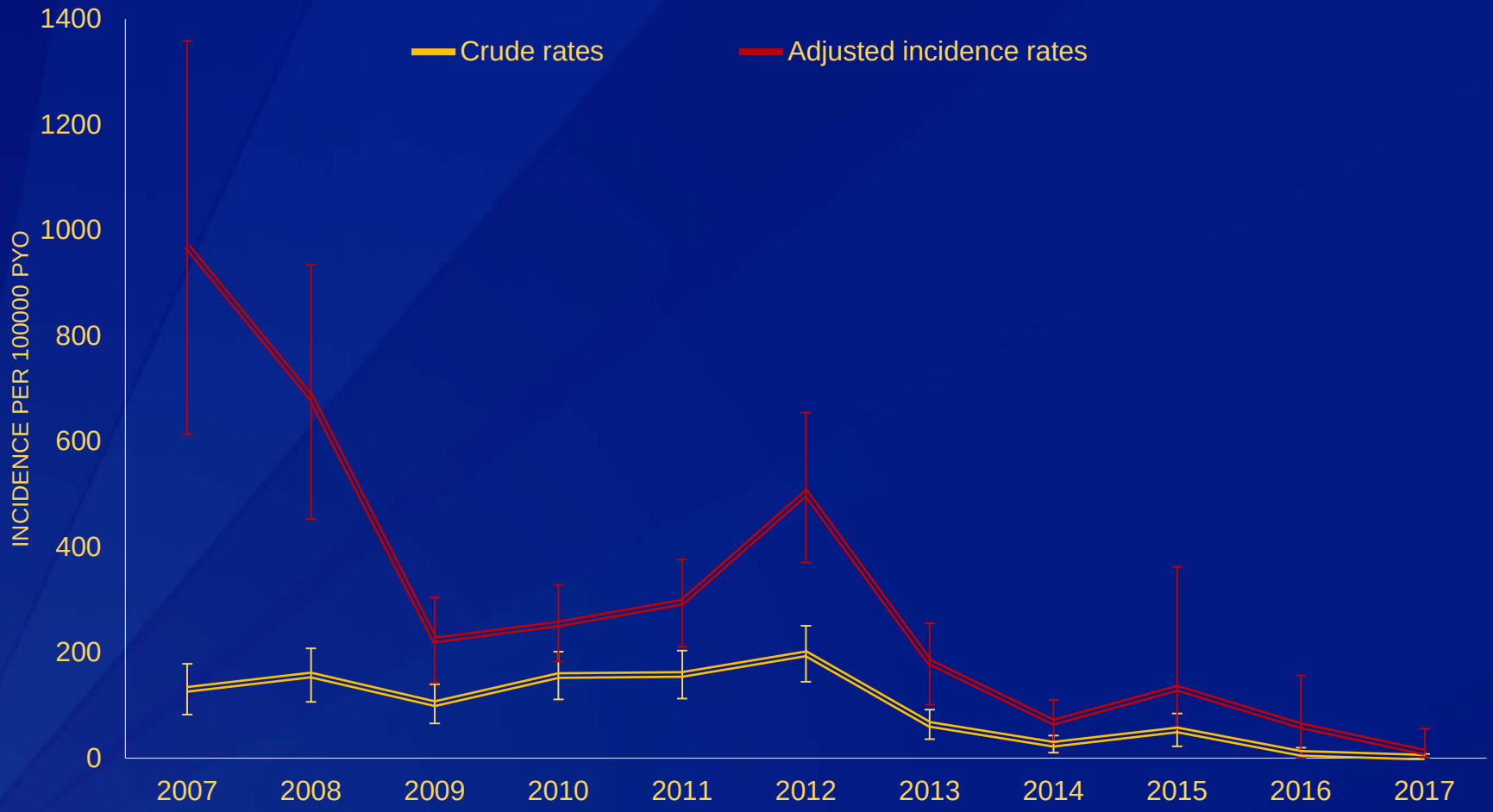
Crude typhoid fever incidence by year, Kibera, 2007-2017



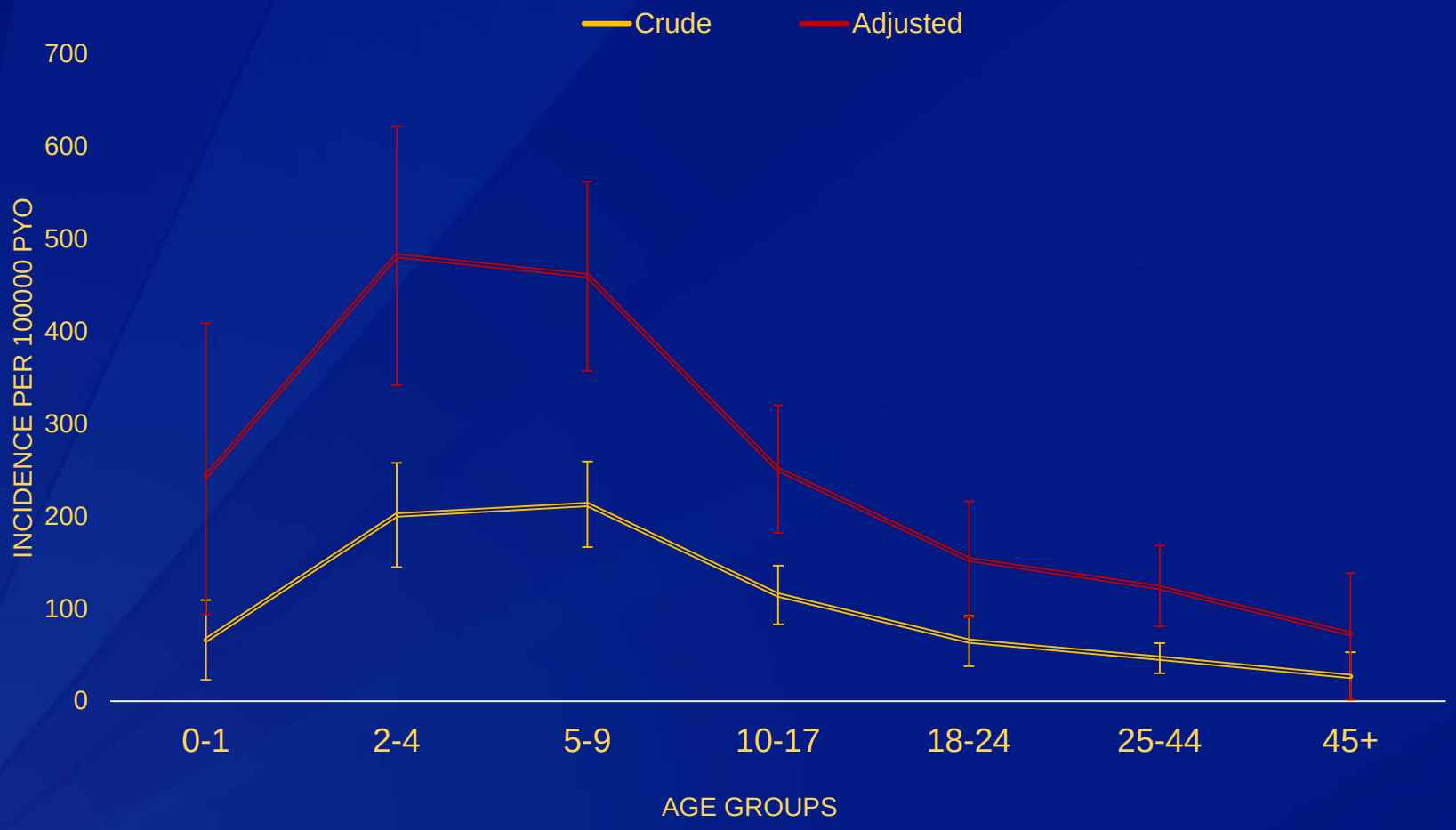
Crude typhoid fever incidence by year, Kibera, 2007-2017

Relative Risk 0.87 (95%CI 0.83-0.91); 13% reduction per year

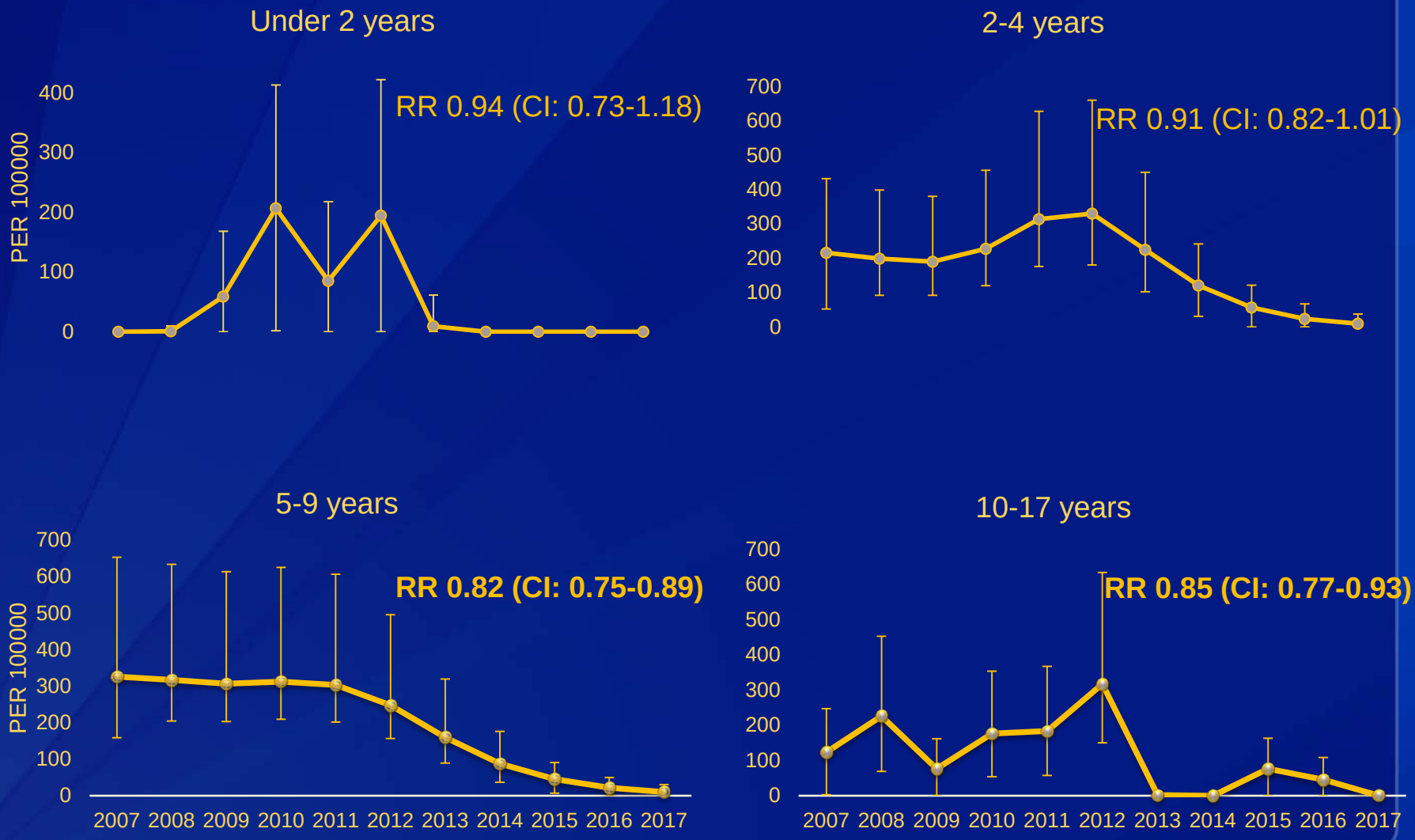
Crude and adjusted typhoid fever incidence by year, Kibera, 2007-2017



Crude and adjusted typhoid fever incidence by age group, Kibera, 2007-2017



Crude age-stratified typhoid fever incidence by year, Kibera, 2007-2017



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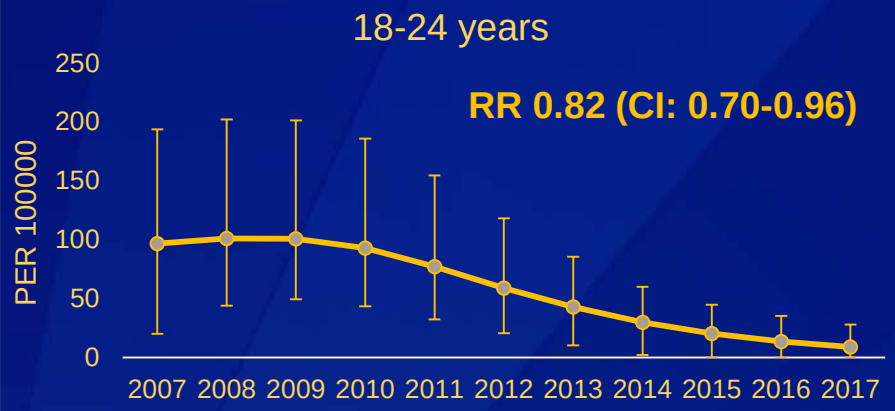
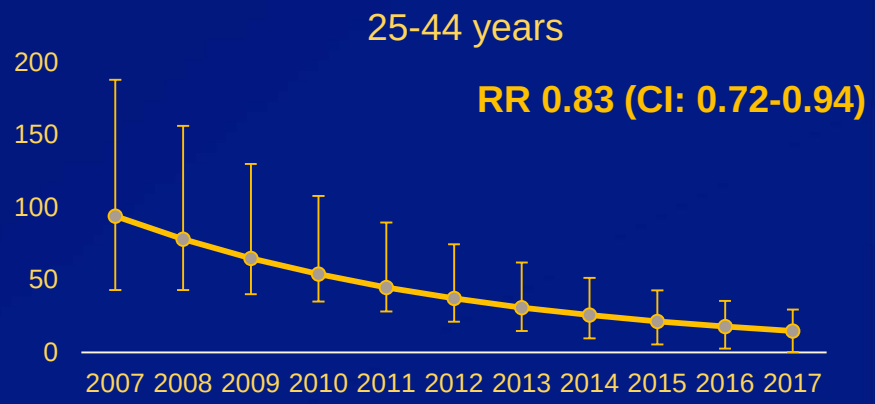
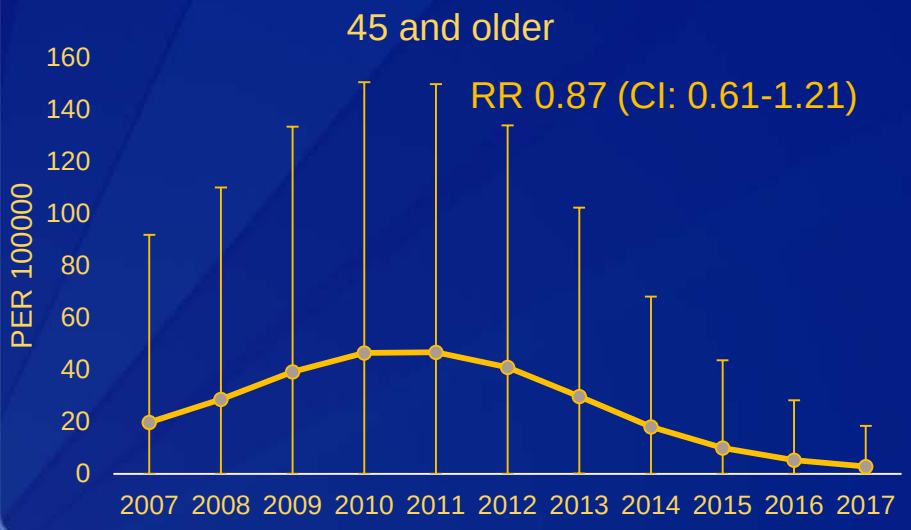
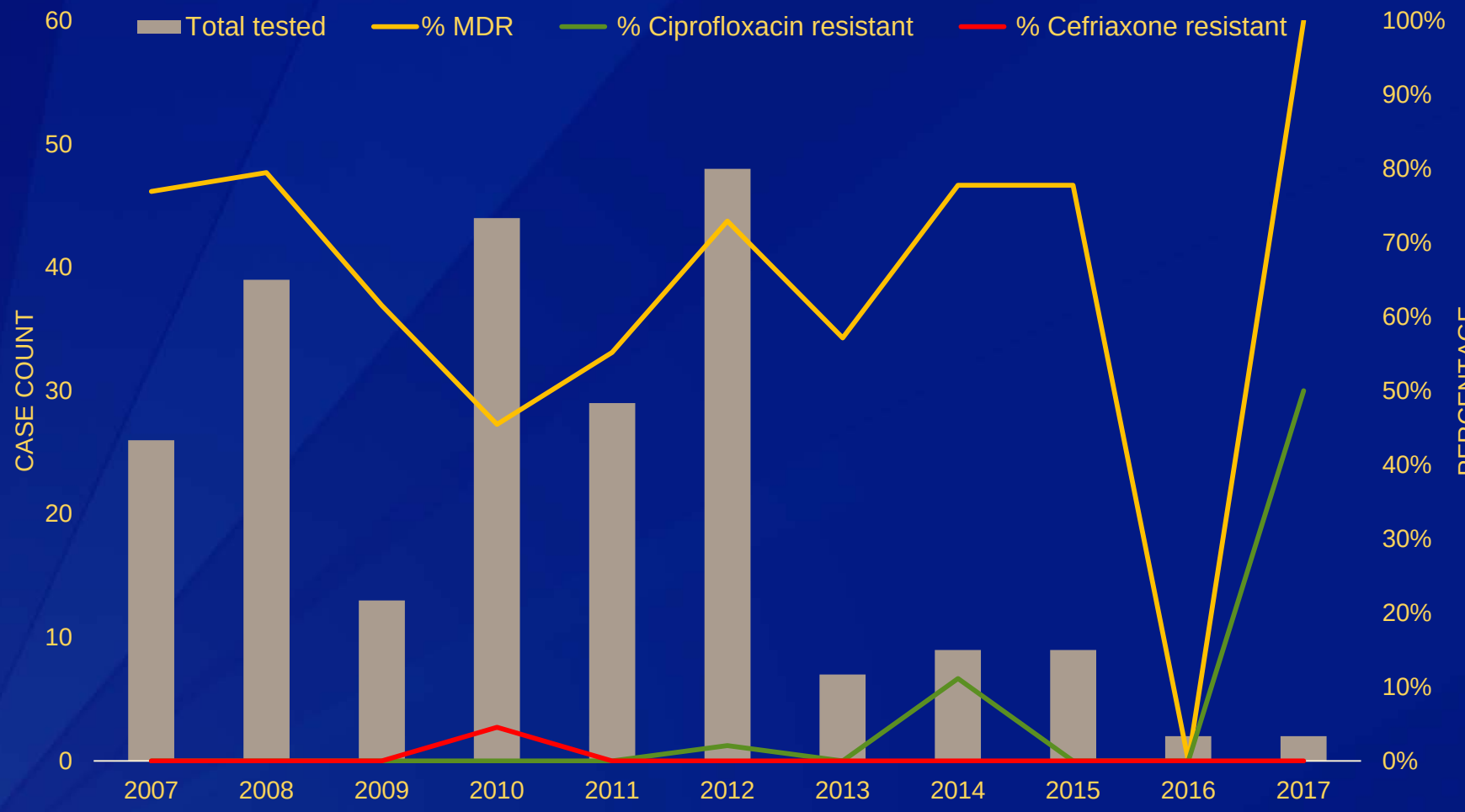






Resistance phenotypes



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

Acknowledgment

- CDC-Kenya
- KEMRI field, data and laboratory staff
- Institute for Disease Modeling

Funding:

- Active population-based surveillance for major infectious disease syndromes in Kenya (CDC)

- This work is supported in part by the Bill and Melinda Gates Foundation

Thank you

engeno@kemricdc.org

For more information please contact:

KEMRI CGHR
P.O. Box 1578
Kisumu, Kenya
E-mail: info@kemricdc.org

254.572.022.929
254.720.374.226
254.734.512.232

Nalidixic Acid resistance