# Change in *Salmonella* Typhi incidence and antimicrobial resistance patterns following mass vaccination with the new typhoid conjugate vaccine

**Ioana D Olaru**

N. Feasey, R. Ferrand, J. Martin, D. Mabey,
H. Hopkins, S. Zinyowera, P. Chonzi, K. Kranzer

UKaid from the British people

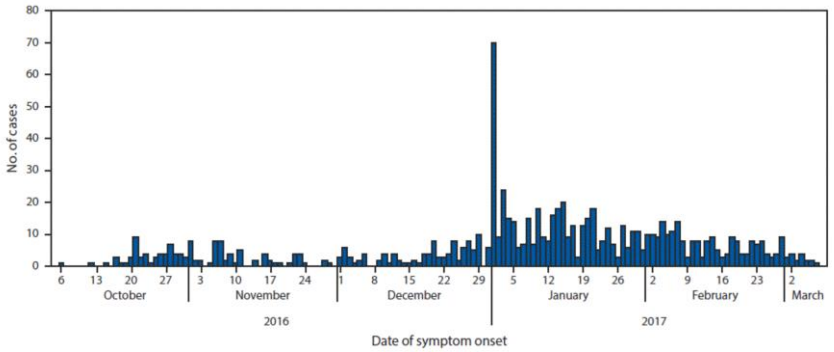
FIEBRE Febrile Illness Evaluation in a Broad Range of Endemicities

wellcome

BRTI Biomedical Research and Training Institute

# Typhoid fever in Harare

- Typhoid fever outbreak in Harare since 2016
- Usually seasonal with more cases in the rainy season
- Main causes:
  - inappropriate disposal of sewage
  - contaminated communal boreholes
  - water shortages




*Davis et al. MMWR 2018*

# FIEBRE Study


**Recruiting adults and children ≥2 months presenting with fever at primary care clinics and hospitals in Harare**

# FIEBRE Study

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**AIMS**

To identify the causes of fever, and the antimicrobial susceptibility of bacterial pathogens causing fever, in low- and middle-income countries from where few data are available.

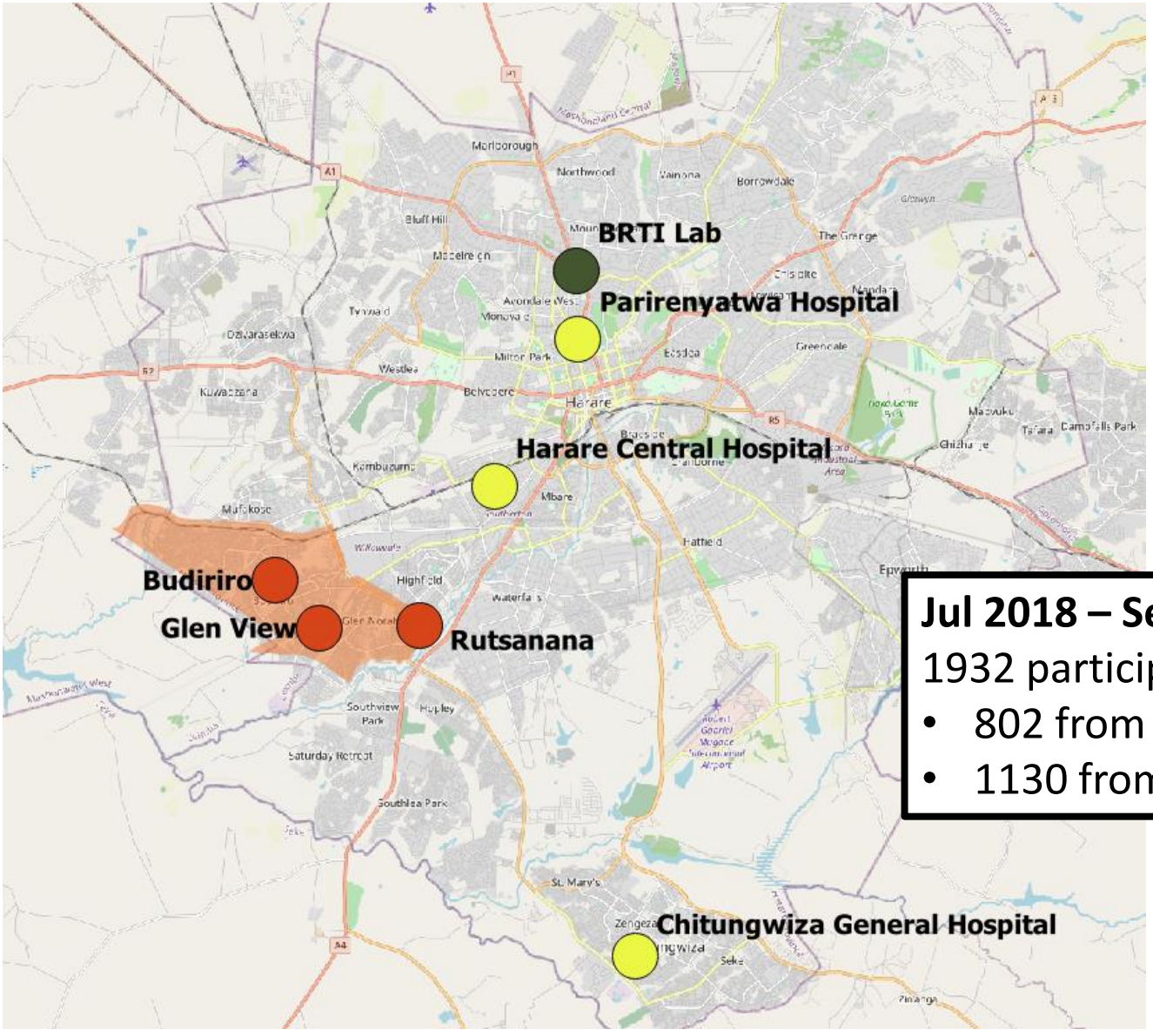
**4 countries:** Lao PDR, Malawi, Mozambique and Zimbabwe

Patient recruitment started in June 2018 in Zimbabwe

Broad range of diagnostic tests for bacteria, viruses, fungi and parasites

**1 aerobic blood culture is collected for all study participants**

# FIEBRE study clinics




**Jul 2018 – Sep 2020:**

1932 participants recruited

- 802 from 3 hospitals
- 1130 from 3 primary care clinics

# Methods

- **AIM:** describe the impact of typhoid conjugate vaccine (TCV) mass vaccination on *S.* Typhi cases and antimicrobial resistance (AMR) in Harare

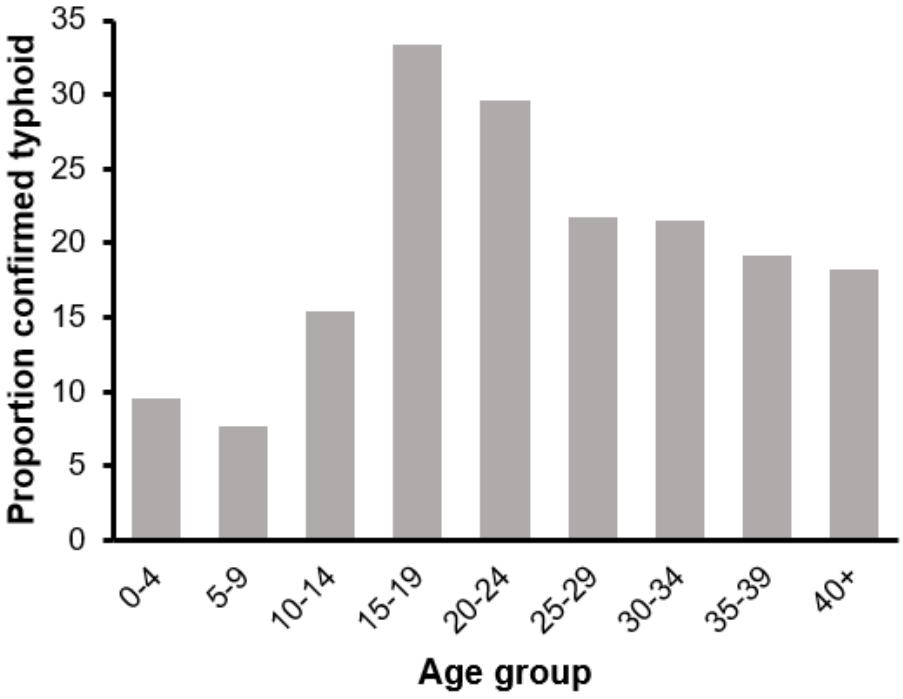
- Automated blood culture system (BacT/ALERT, Biomerieux)
- Identification of isolates using biochemical tests (API 20E, Biomerieux)
- Suspected *S.* Typhi isolates confirmed by serotyping at the National Microbiology Reference Laboratory
- Drug susceptibility testing: EUCAST standards
  - Disc-diffusion for ampicillin, chloramphenicol, co-trimoxazole, ceftriaxone
  - Pefloxacin discs were used to screen for fluoroquinolone resistance.
  - E-Tests were used for azithromycin and ciprofloxacin.

# Results

| OUTPATIENTS | Children (<15 years) N=525 | Adults (≥15 years) N=605 | Total N=1130 |
|---|---|---|---|
| **Confirmed** | 50 (9.5%) | 147 (24.3%) | 197 (17.4%) |
| **Suspected or confirmed** | 183 (34.9%) | 291 (48.1%) | 474 (41.9%) |

*Confirmed typhoid fever case – positive blood culture with S. Typhi*
*Suspected typhoid fever case – according to the diagnosis made at the clinic*

# Participant characteristics




| | Typhoid | Blood culture negative |
|---|---|---|
| Male | 47% | 47% |
| Age (median) | 21 | 18 |
| HIV+ | 3% | 6% |

**Symptoms**

Headache 94%

Abdominal pain 73%

Vomiting 13%

# Typhoid fever cases according to age

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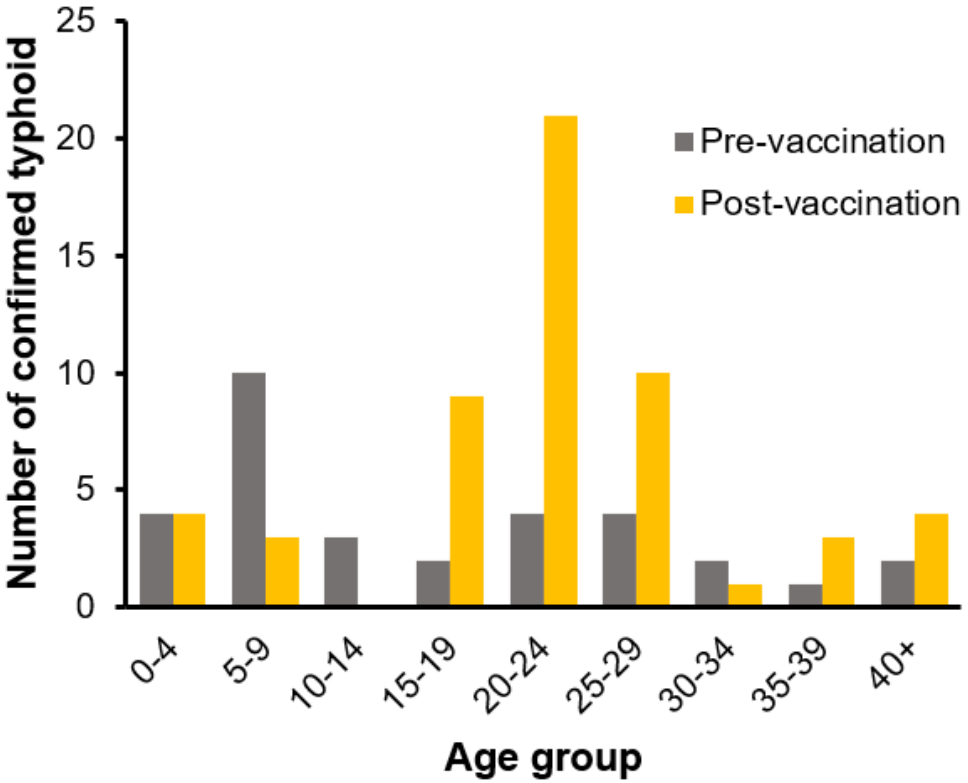
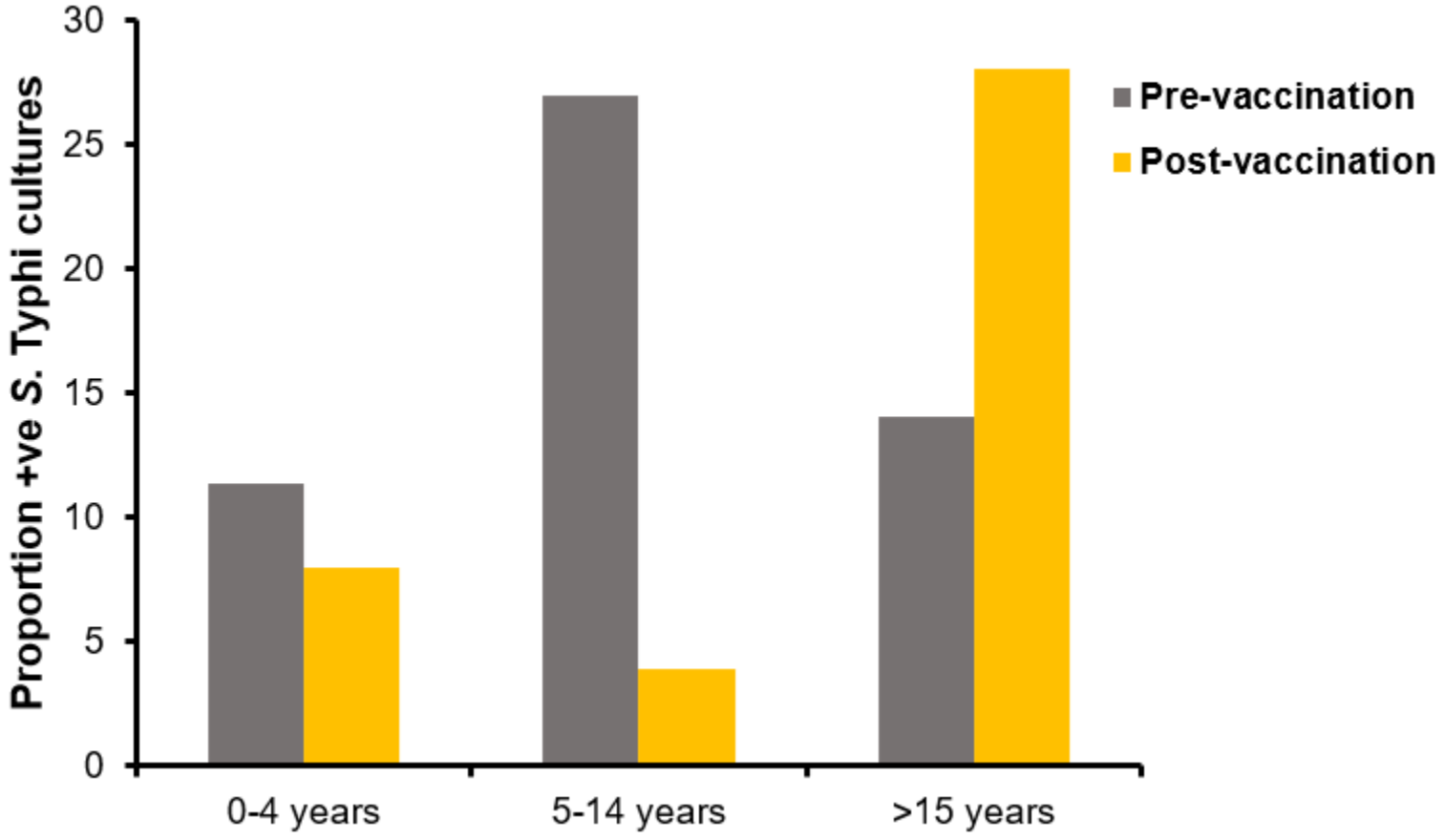
**Mass vaccination campaign of children <15 years with the typhoid conjugate vaccine (TCV) in March 2019**

**Vaccination coverage:**

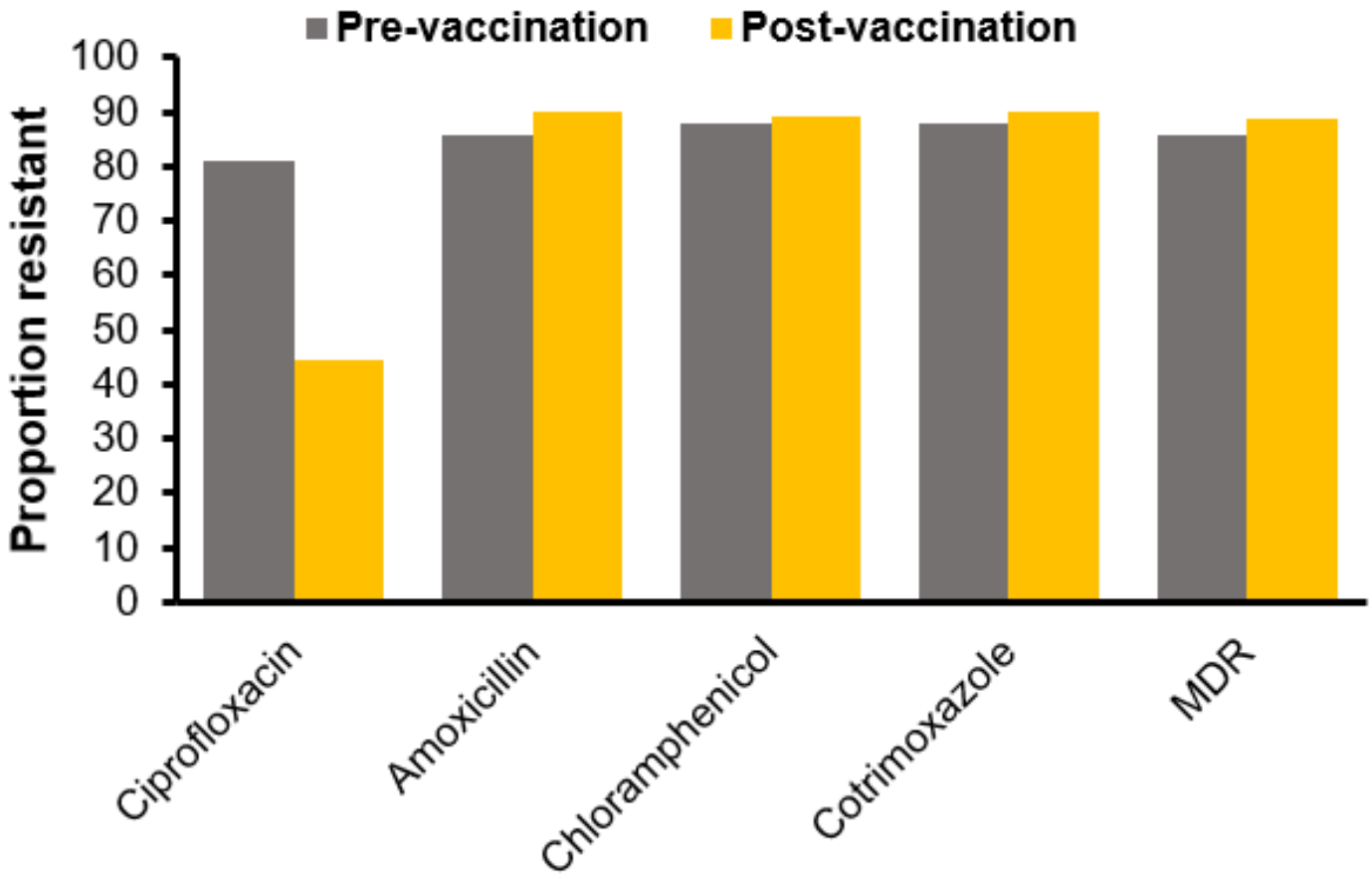
- 72% in pre-school children
- 97% in school going children



# Impact of vaccination with typhoid conjugate vaccine



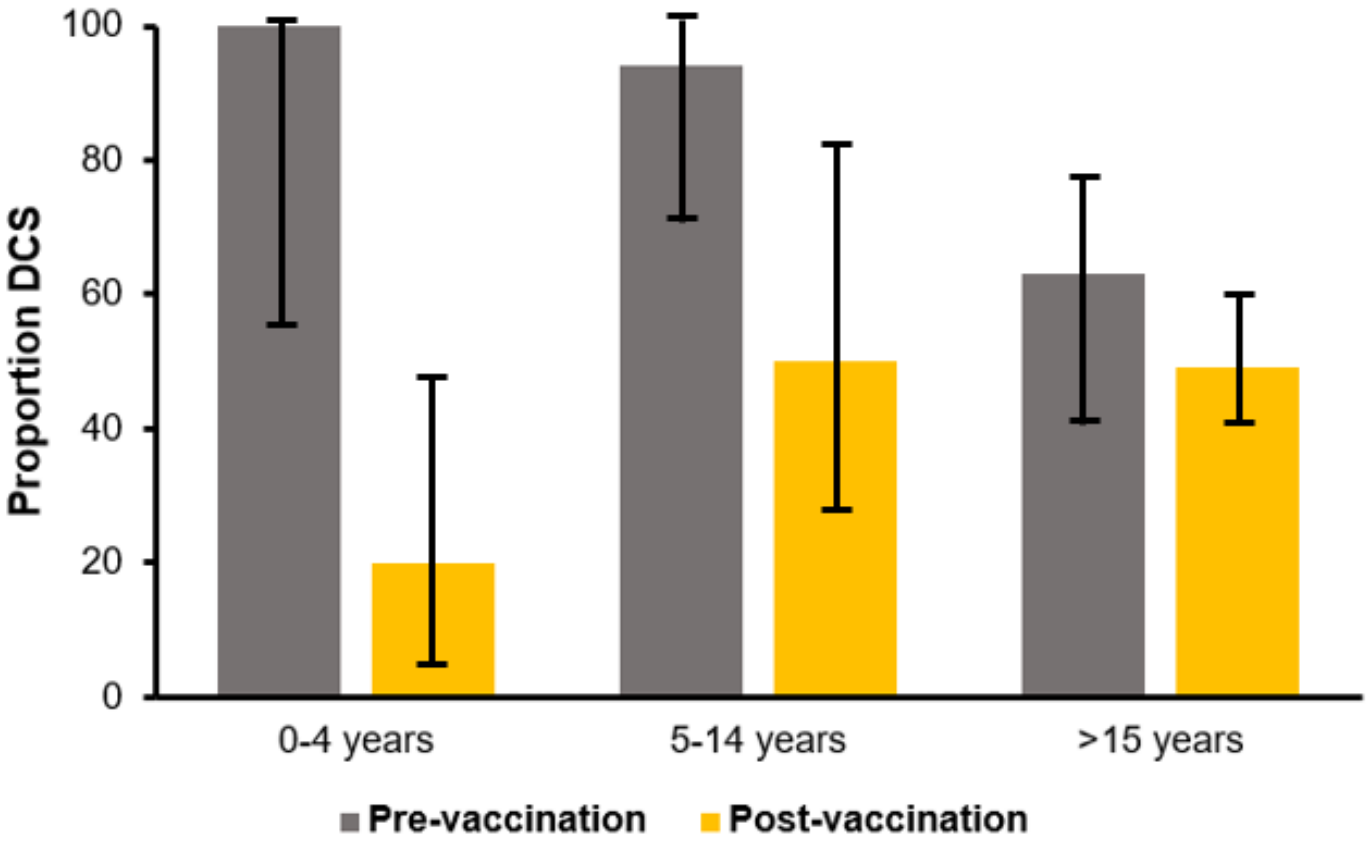
# Drug susceptibility testing




**No *S.* Typhi isolates were resistant to ceftriaxone or azithromycin**

*MDR = resistance to amoxicillin + chloramphenicol + co-trimoxazole*

# Decreased ciprofloxacin susceptibility according to age




*DCS: decreased ciprofloxacin susceptibility*

# MIC distribution for ciprofloxacin

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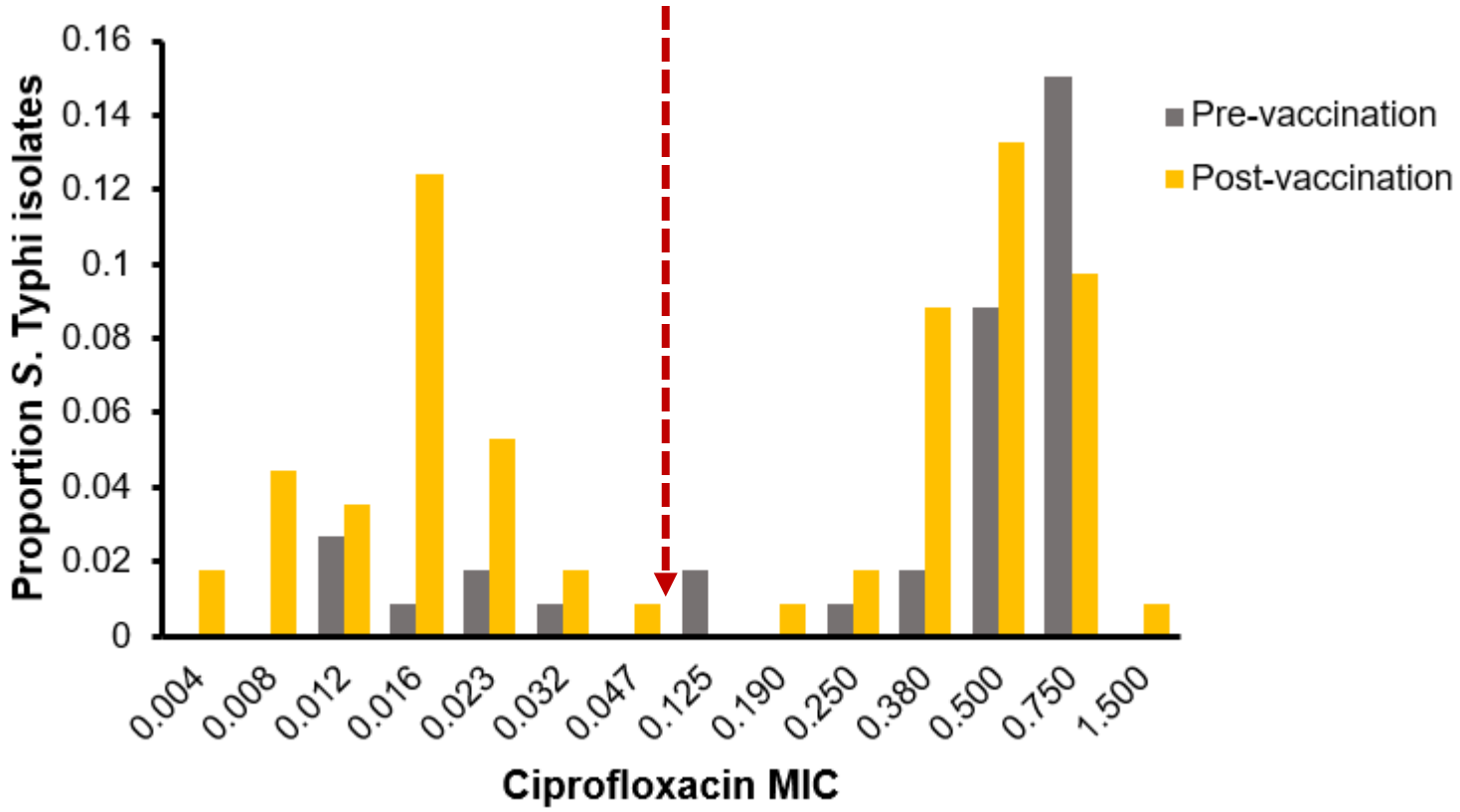
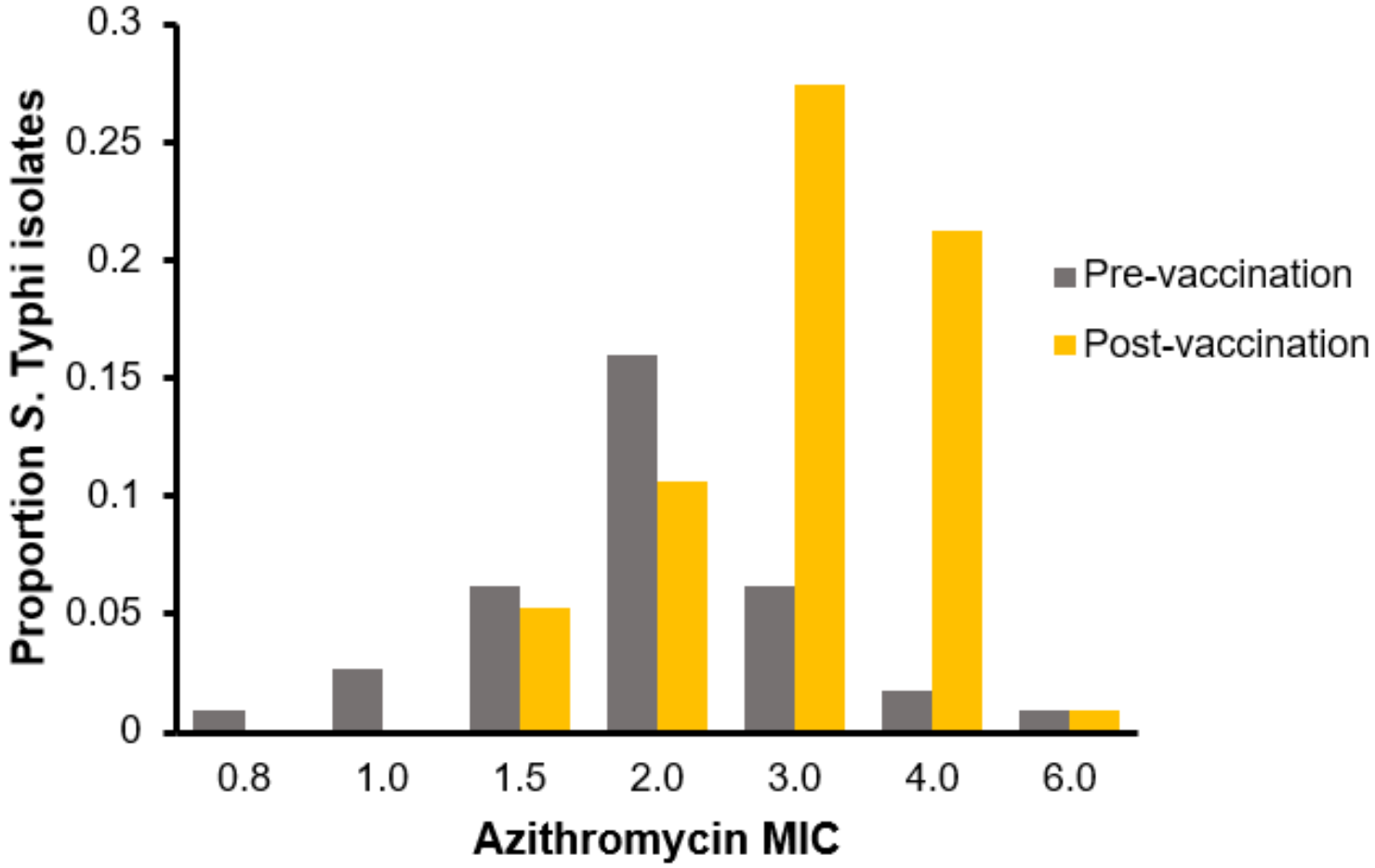
**Decreased susceptibility to ciprofloxacin (DCS) if MIC >0.06 (poor treatment response)**




*All isolates with pefloxacin resistance by disc diffusion had ciprofloxacin MICs >0.06*

# MIC distribution for azithromycin



# Conclusion

- Decrease in the prevalence of DCS following the TCV mass vaccination campaign.
  - ? localized point-source outbreak ended by vaccination
- Vaccination led to a reduction of typhoid fever cases among children presenting to primary healthcare
- High number of cases identified post-vaccination campaign (mostly adults)
  - need for further control measures to control the outbreak

# Acknowledgements

**BRTI laboratory**
Janice Martin
Forget Makoga
Beauty Makamure

**Harare City Health**
Prosper Chonzi
The doctors and nurses from the clinics
**National Microbiology Reference Laboratory**

**LSHTM**
David Mabey
Heidi Hopkins
Katharina Kranzer
Rashida Ferrand

**FIEBRE Field team**
**The study participants**

# Thank you!

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