A 24-year passive surveillance study reveals trends in antimicrobial resistance amongst *Salmonella* Typhi and Paratyphi A cases in Bangladesh.

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Some enteric fever knowledge!

- Typhoid and paratyphoid fever, known as enteric fever, are often clinically indistinguishable, and similar treatment strategies are followed.
- More prevalent among school-age children.
- In Bangladesh, enteric fever patients seek care at community-based diagnostic centers or, hospital OPD.
  - complicates precise estimation of disease burden.

The big brother: typhoid fever

- Caused by *Salmonella* Typhi.
- Bangladesh has the highest reported typhoid burden, 913 per 100,000 person-years.
- Gavi application for TCV introduction in Bangladesh is ongoing.

Garrett D.O., *et al* 2022

The little brother: paratyphoid fever

- Caused by *Salmonella* Paratyphi A.
- In Bangladesh, one of six enteric fever cases is paratyphoid.
- The empirical treatment is based on the available AMR data of typhoid.
- Only a handful of reports on its AMR and most are limited by –
  - short study duration
  - small number of cases
  - lack of multi-modality surveillance platform to catch the community cases.

Filling the gaps in the data

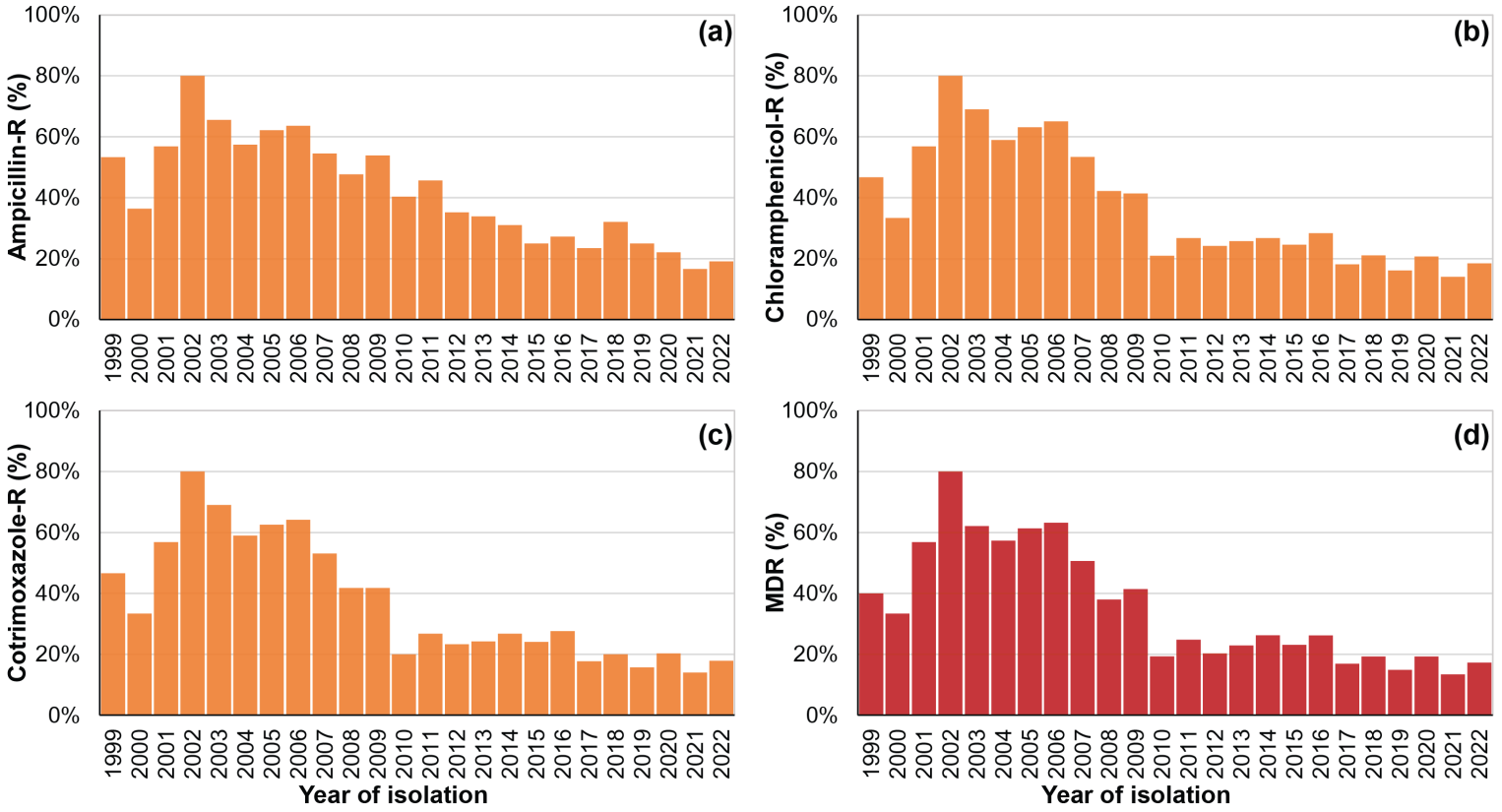
Assess AMR patterns for *Salmonella* Typhi and Paratyphi A before the introduction of typhoid-conjugate vaccine (TCV) Bangladesh.

Our surveillance

- Our enteric fever surveillance at CHRF, Bangladesh started in **1999**.
- Focus on pediatric population (<18 years of age).
- Carried out at three sites in Dhaka – two major pediatric hospitals and one community-based consultation and diagnostic center.
- MIC was determined for ciprofloxacin and ceftriaxone.
- Annual antibiotic consumption data was analyzed for comparison.

Typhoid AMR: multidrug resistance (MDR)

- Total 12,489 cases were recorded during 1999-2022.
- Declining resistance for ampicillin, chloramphenicol, and cotrimoxazole.
- MDR is decreasing.
  - <25% since 2010 (avg 20%)
  - <20% since 2017 (avg 17%)



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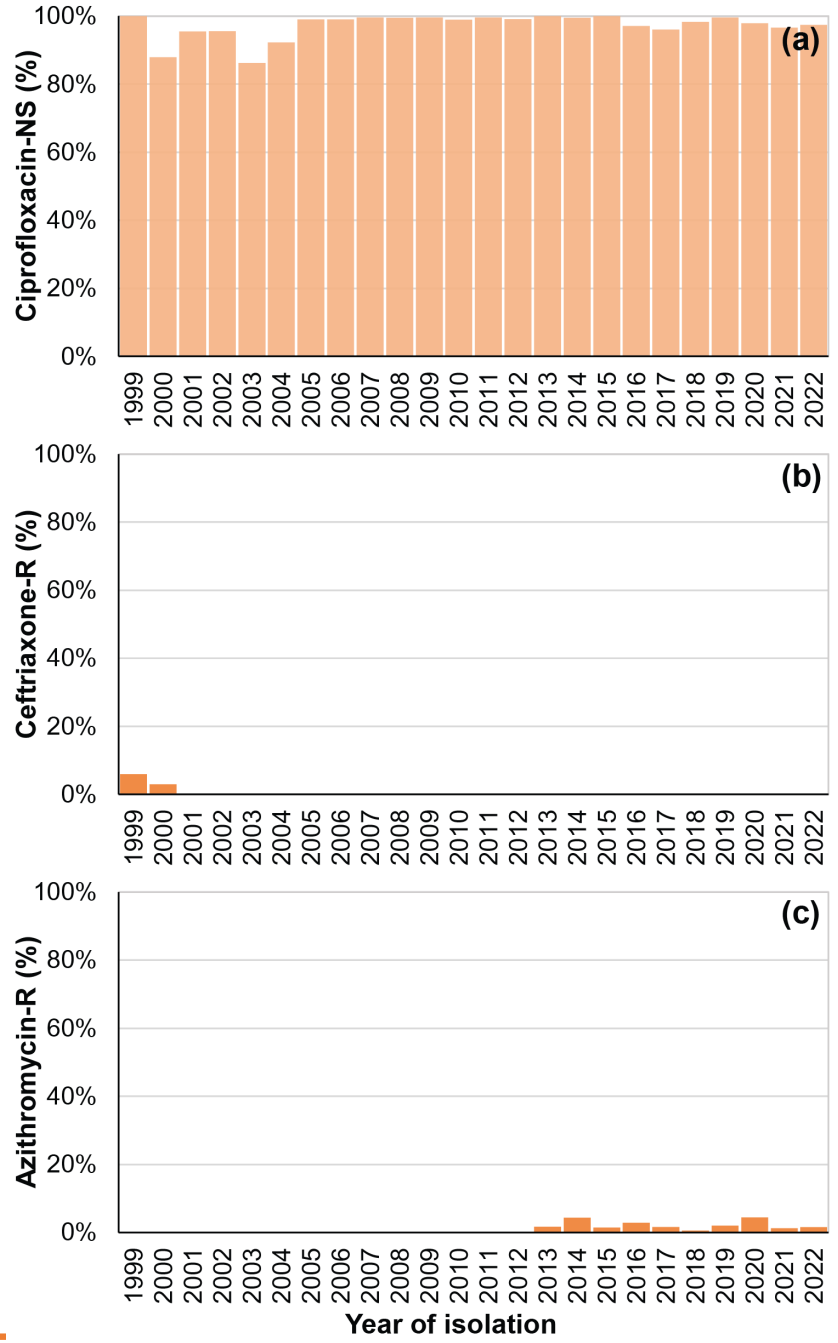
Tanmoy A.M., *et al* (Unpublished)

Typhoid AMR: ciprofloxacin, ceftriaxone & azithromycin

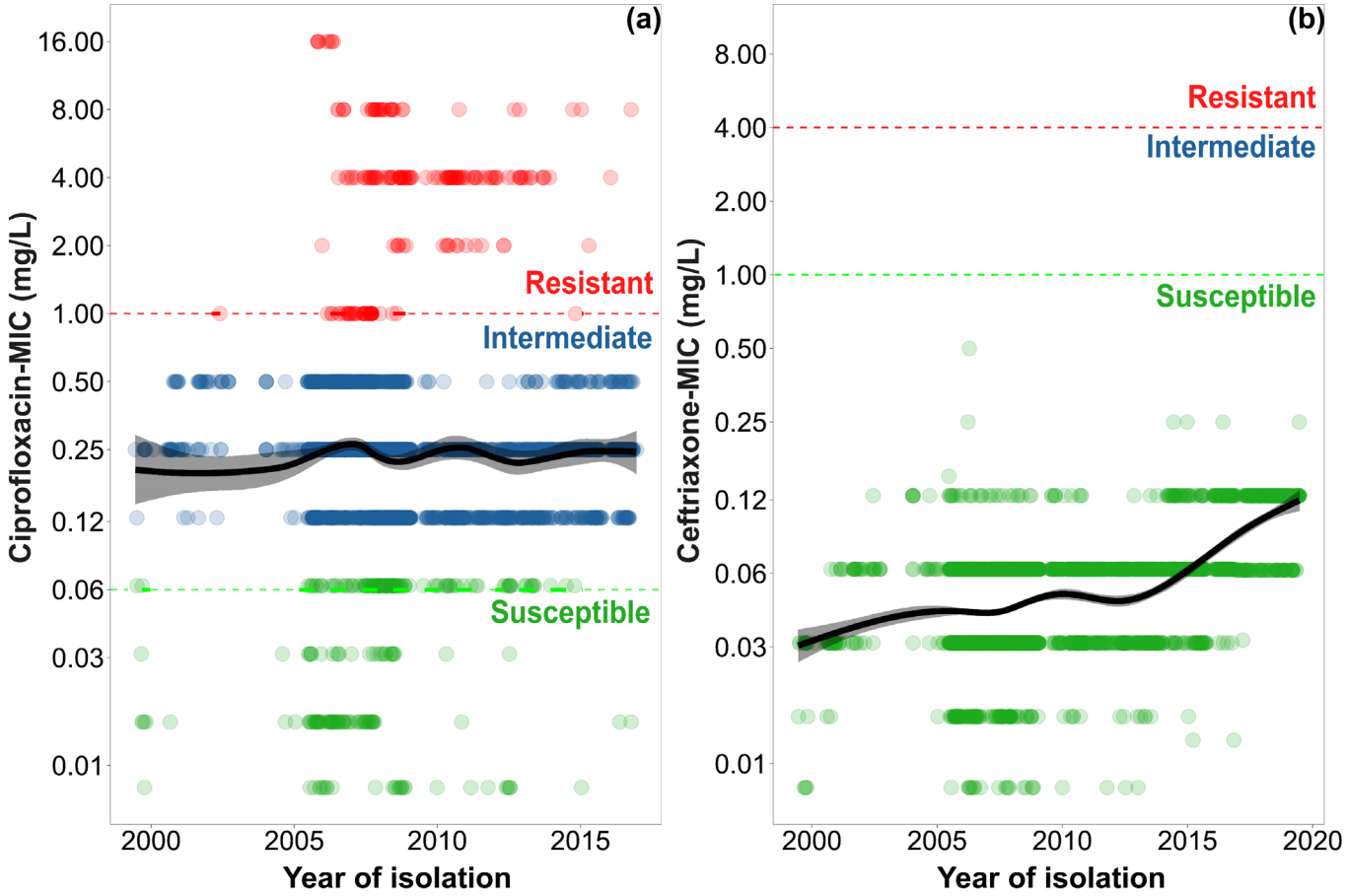
- Non-susceptibility to ciprofloxacin remained >90%.
- No ceftriaxone resistance, except for one isolate in 1999 and another in 2000.
- Azithromycin resistance was first identified in 2013.
  - average yearly resistance of 2% (1%–3%).



Tanmoy A.M., *et al* (Unpublished)

Focus: resistance to ciprofloxacin, ceftriaxone

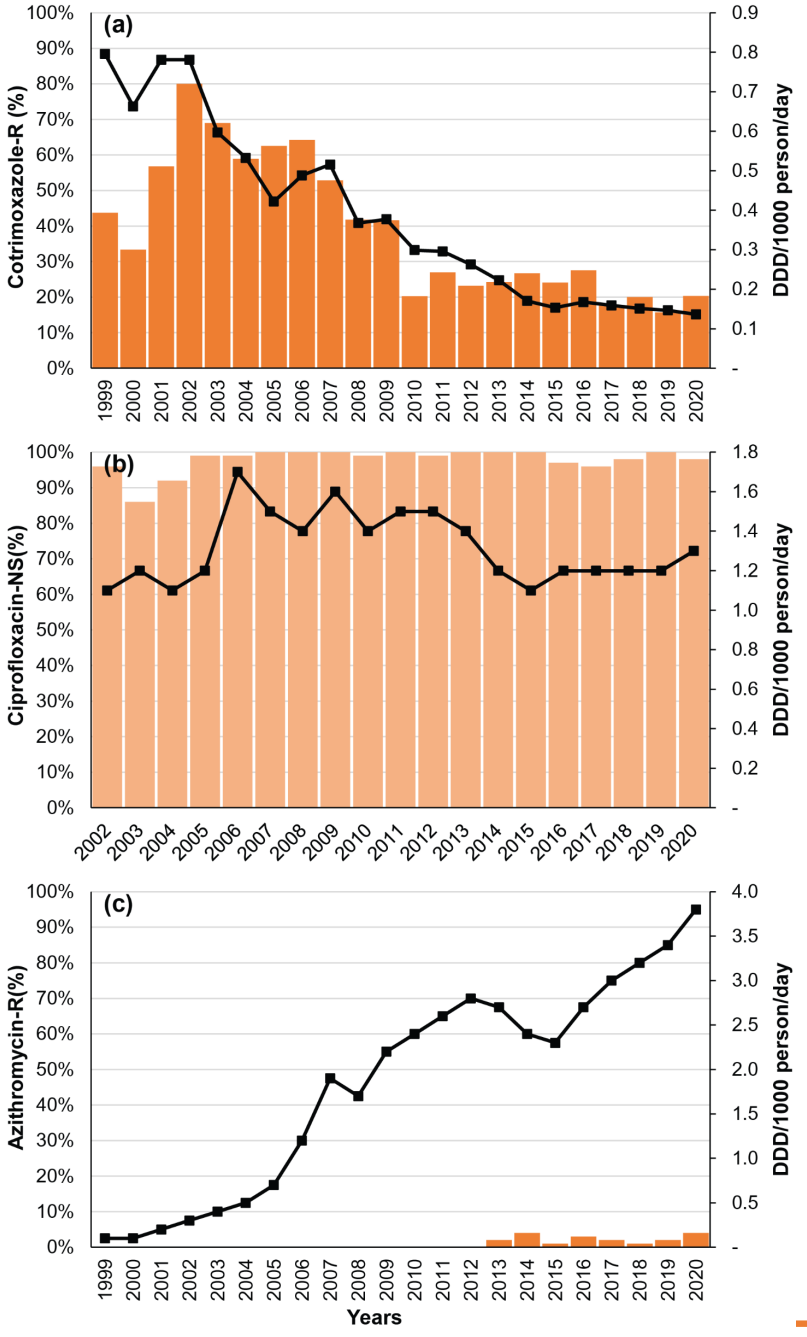
- Ciprofloxacin MIC data showed no significant changes.*
  - Average ~0.25 µg/mL
- Ceftriaxone MIC showed a gradual increase in MIC.*
  - From 0.03 µg/mL in 2001 to 0.12 µg/mL in 2019.
  - MIC_{50} increased by 4-fold.



Using Generalized Additive Model (GAM) in R.

Comparing typhoid AMR with antimicrobial consumption

- Cotrimoxazole consumption is declining.
  - from 0.8 DDD per 1,000 persons/day (1999) to 0.1 DDD/1,000 persons/day (2020)
  - significant correlation with cotrimoxazole resistance (p = 0.00, 95% CI).
- Azithromycin consumption increased by 38-fold.
  - from 0.1 to 3.8 DDD/1,000 persons/day
  - average annual increase was 0.18 DDD/1,000 persons/day
  - Azithromycin resistance remained <4%.



Tanmoy A.M., *et al* (Unpublished)

Typhoid vaccine, TCV is coming…

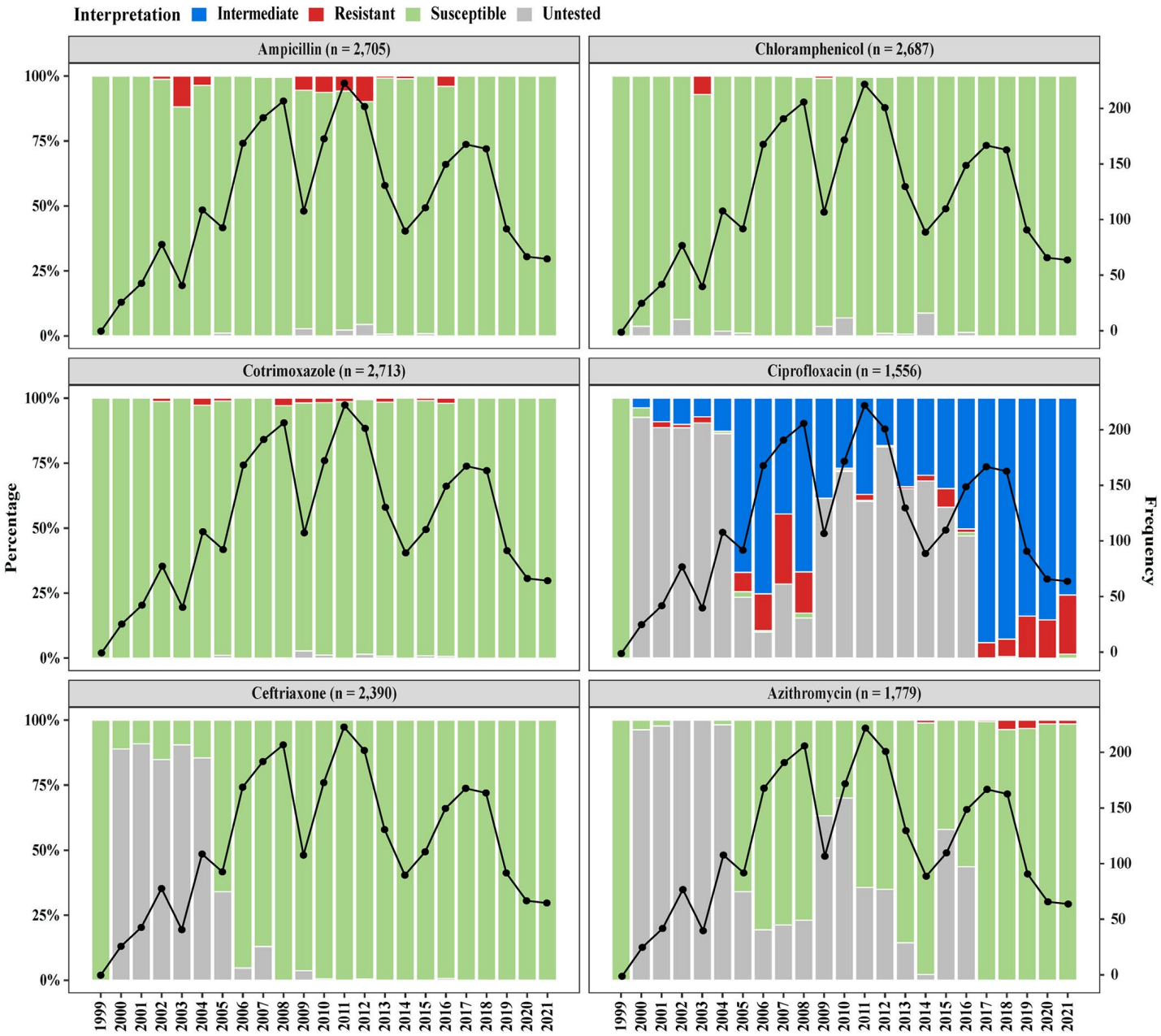
Burden and AMR of Paratyphoid fever may change.

Paratyphoid fever: focusing on AMR

How much do we know?

Paratyphoid AMR

- Total 2,725 cases across sites during 1999-2021
- >97% were susceptible to ampicillin, chloramphenicol, and cotrimoxazole.
- **No MDR cases**
- ~99% non-susceptibility for ciprofloxacin
- <1% resistance to azithromycin
- No ceftriaxone-resistant cases



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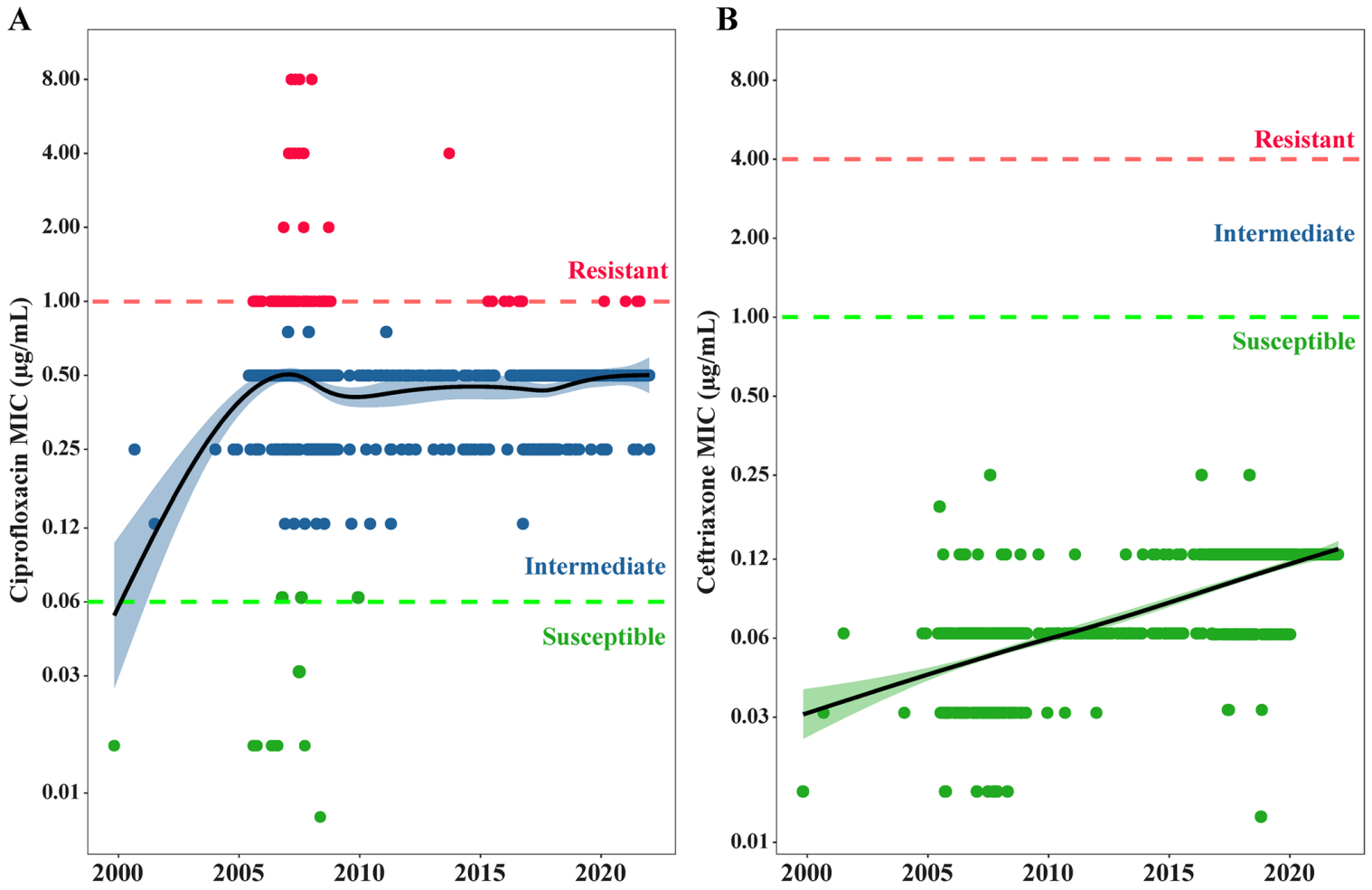
Sajib M.S.A., *et al* 2023. (Plos NTD)

Focus: resistance to ciprofloxacin, ceftriaxone

- Ciprofloxacin MIC data showed no changes.
  - 0.25 → 0.5 µg/mL
- Ceftriaxone MIC showed a slow increasing trend
  - 4-fold increase in 23 years (0.03 → 0.12 µg/mL).
- CLSI resistance cut-off is 4 µg/mL.



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Sajib M.S.A., *et al* 2023. (Plos NTD)

What we learned…

- Study provides the AMR patterns against *Salmonella* Typhi and Paratyphi A isolates in Bangladesh over the last 24 years.
- MDR is <20% and decreasing for Typhi, while it is not present for Paratyphi A in Bangladesh.
- Paratyphi A overall exhibits higher susceptibility to most antibiotics.
- This study suggests evidence-based changes to the empirical treatment of enteric fever in Bangladesh.
  - favoring first-line antimicrobials: ampicillin/amoxicillin, chloramphenicol, and cotrimoxazole

Tanmoy A.M., *et al* (Unpublished);
Sajib M.S.A. *et al.* 2023. (Plos NTD)

Acknowledgement

Funded by

BILL & MELINDA GATES foundation

CHRF

Surveillance for Enteric Fever in Asia Project

Poster: 95) Genomic Epidemiology of *Salmonella* Paratyphi B isolates from Bangladesh

Poster: 110) Paratype 1.1: Recent updates to the genotyping tool for Paratyphoid fever surveillance

Preonath Chandrow Dev

Thank you

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