Analysis of the antimicrobial susceptibility patterns of Salmonella enterica serotype Typhi following Mass-targeted typhoid conjugate vaccine immunization campaigns in Harare City, Zimbabwe, 2023

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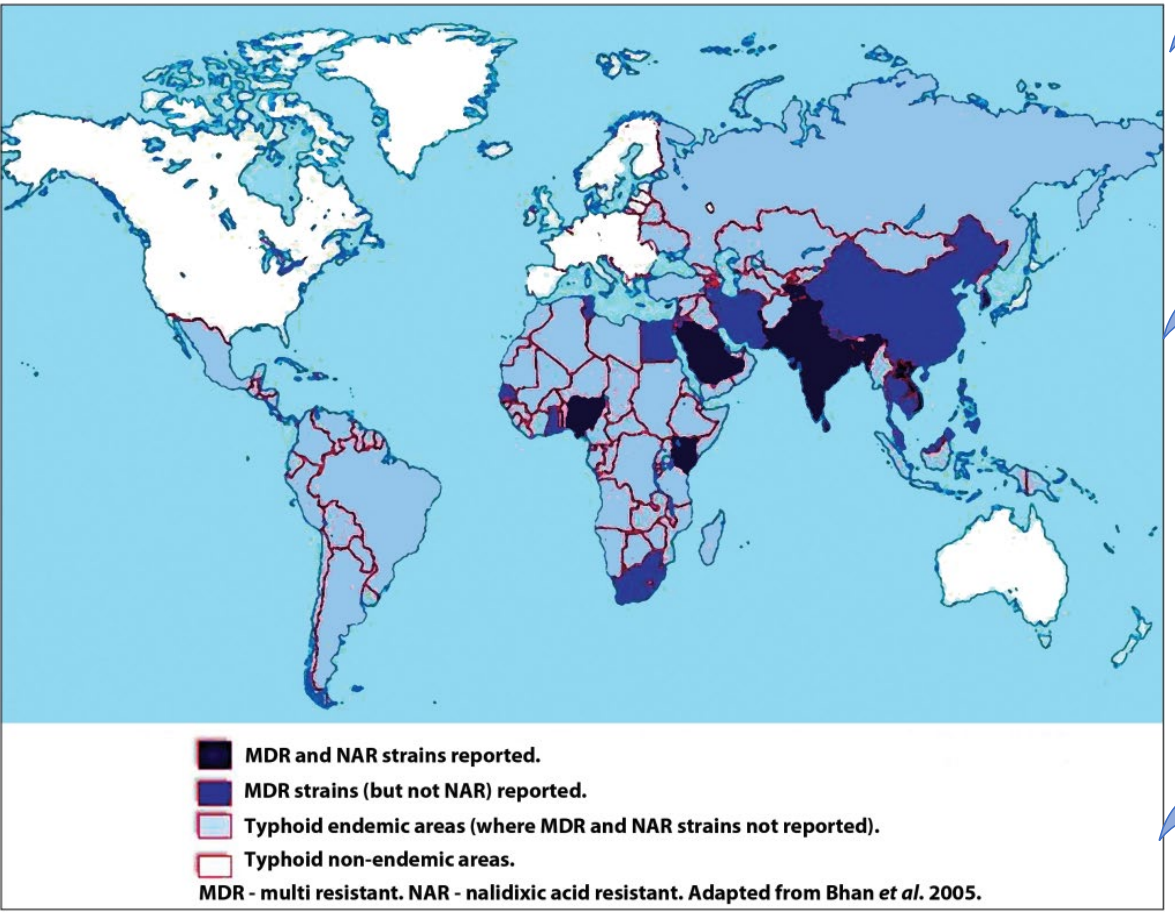
Global Epidemiology of Typhoid



- Globally, typhoid fever is a major cause of mortality and morbidity
- Annually 215,000 deaths result from over 26 million cases
- Southern Asia and sub-Saharan Africa are the most affected regions
- Up to 4% of typhoid fever patients become chronic carriers

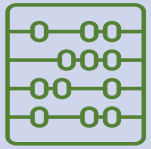
Epidemiology of Typhoid in Zimbabwe 2012 -2023

Year	Suspected Typhoid cases	Culture-confirmed Typhoid cases
2012	5829	103
2013	1707	61
2014	1653	101
2015	1236	45
2016	2352	85
2017	2032	155
2018	4195	223
2019	2137	138
2020	875	36
2021	144	7
2022	153	9

Source: District Health Information System (DHIS2)
National Microbiology Reference Laboratory

Typhoid has been endemic in Zimbabwe, particularly Harare City since 2010

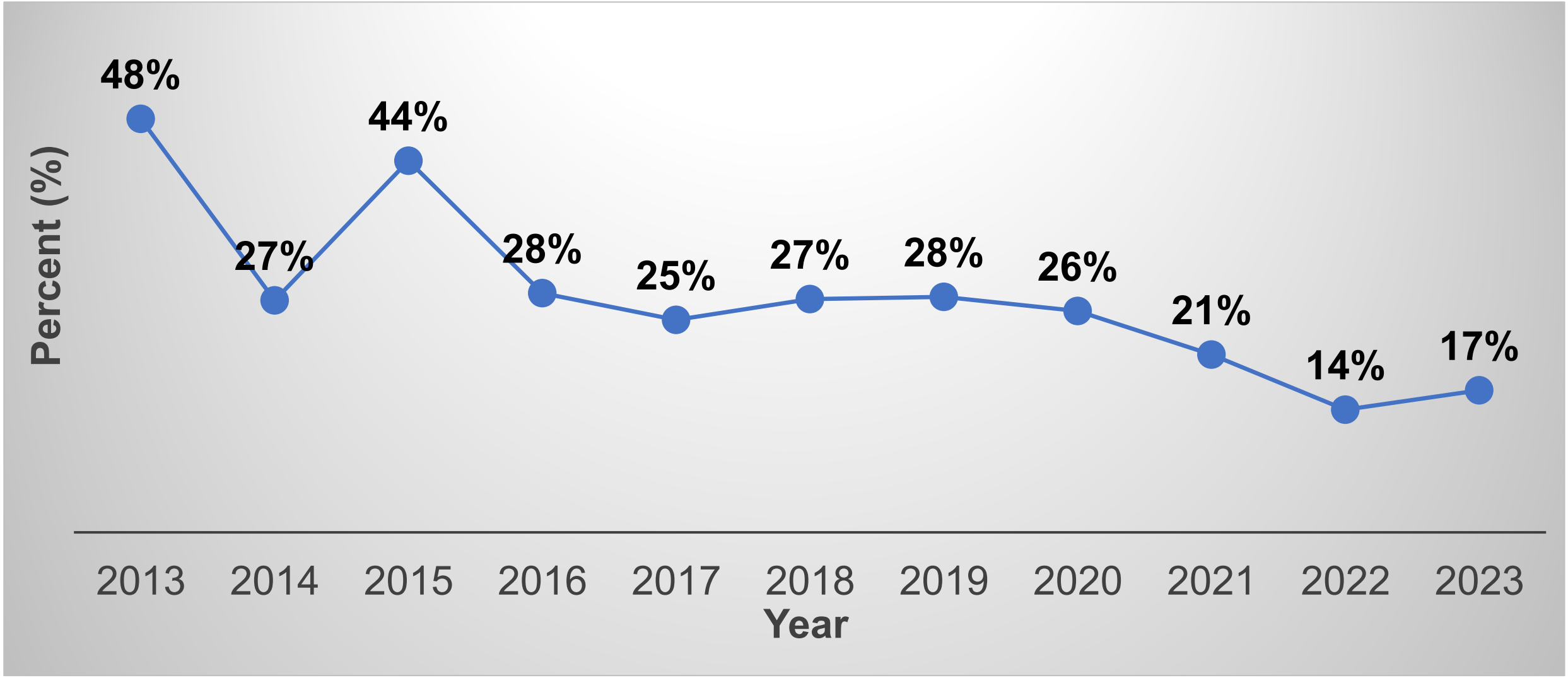
Highest number of cases in 2018



754 cases in 2023 with 29 culture confirmed cases

- Limited diagnostic capacity in Microbiology
- Limited diagnostic access

Proportion of Children under 5 years suspected of having Typhoid in Zimbabwe 2013-2023



Source: District Health Information System Zimbabwe (DHIS2)

Typhoid Conjugate Vaccine Rollout in Zimbabwe

- Increased emergence and spread of drug resistance
  - Genomic characterization of 29 samples identified S. Typhi H58 with reduced susceptibility to ciprofloxacin (*T. Mashe, et al, 2021*)
- First typhoid conjugate vaccination (TCV) campaign in 2019
  - Introduced Harare's nine high-density suburbs
  - Targeted children aged 6 months -15 years
  - Extended up to 45 years in some areas due to high attack rate
- Second nationwide mass TCV was conducted in 2021
  - Incorporation of TCV in the country's routine immunisation programme

TCV Campaigns in Zimbabwe

Objectives

- Determine the antimicrobial susceptibility patterns of Salmonella Typhi isolated in Harare City from October 2022 to May 2023
- Assess the antimicrobial susceptibility pattern following two distinct TCV campaigns in Harare City
- Inform future public health interventions to control typhoid fever in Harare City

Methods

Study Location: National Microbiology Reference Laboratory (NMRL)

Salmonella Typhi Identification

- 55 blood culture isolates from suspected Salmonella cases
- BioMerieux VITEK® MS (MALDI-TOF)
- Serotyping
- 31 confirmed as Salmonella typhi

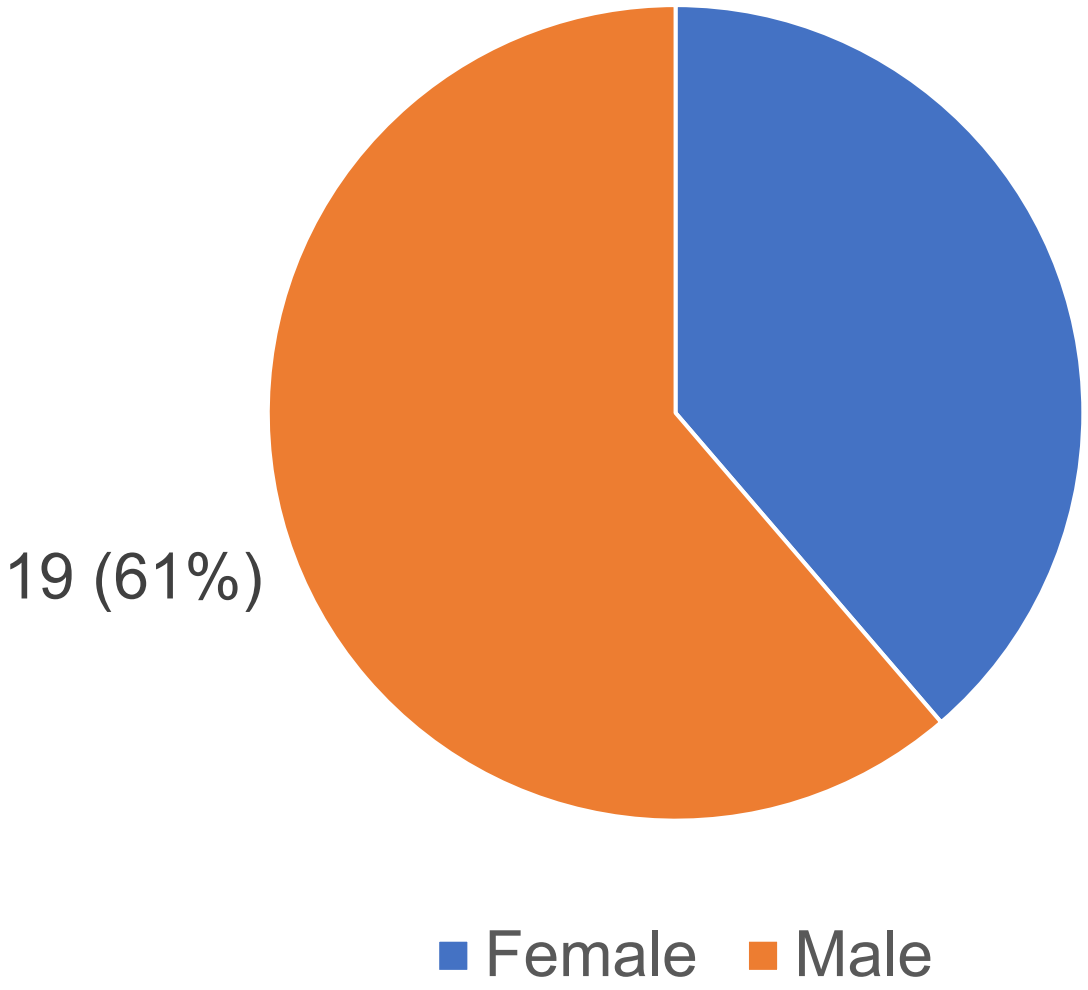
Antimicrobial Susceptibility Testing

- BioMerieux VITEK® 2 COMPACT
- To determine Minimum Inhibitory Concentration

Statistical Analysis

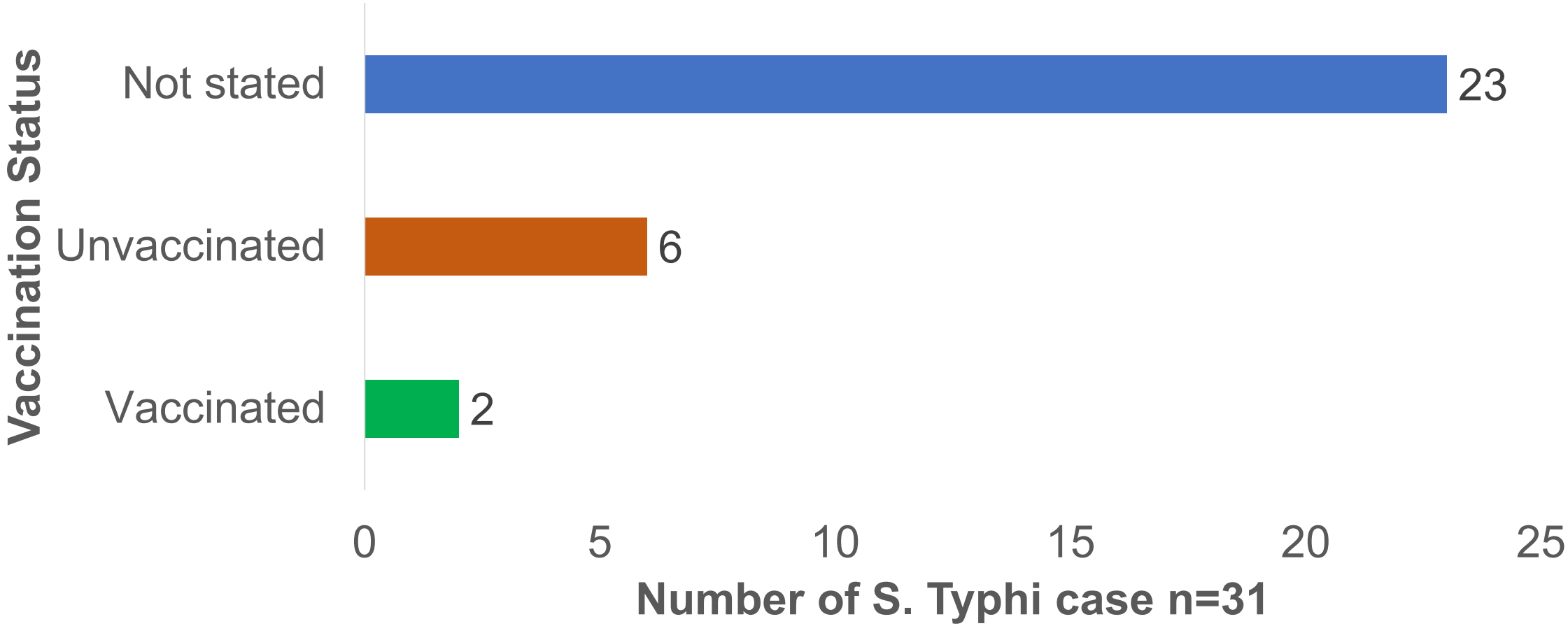
- Stata® to calculate frequencies and proportions

Demographic Distribution of Salmonella Typhi Confirmed Cases



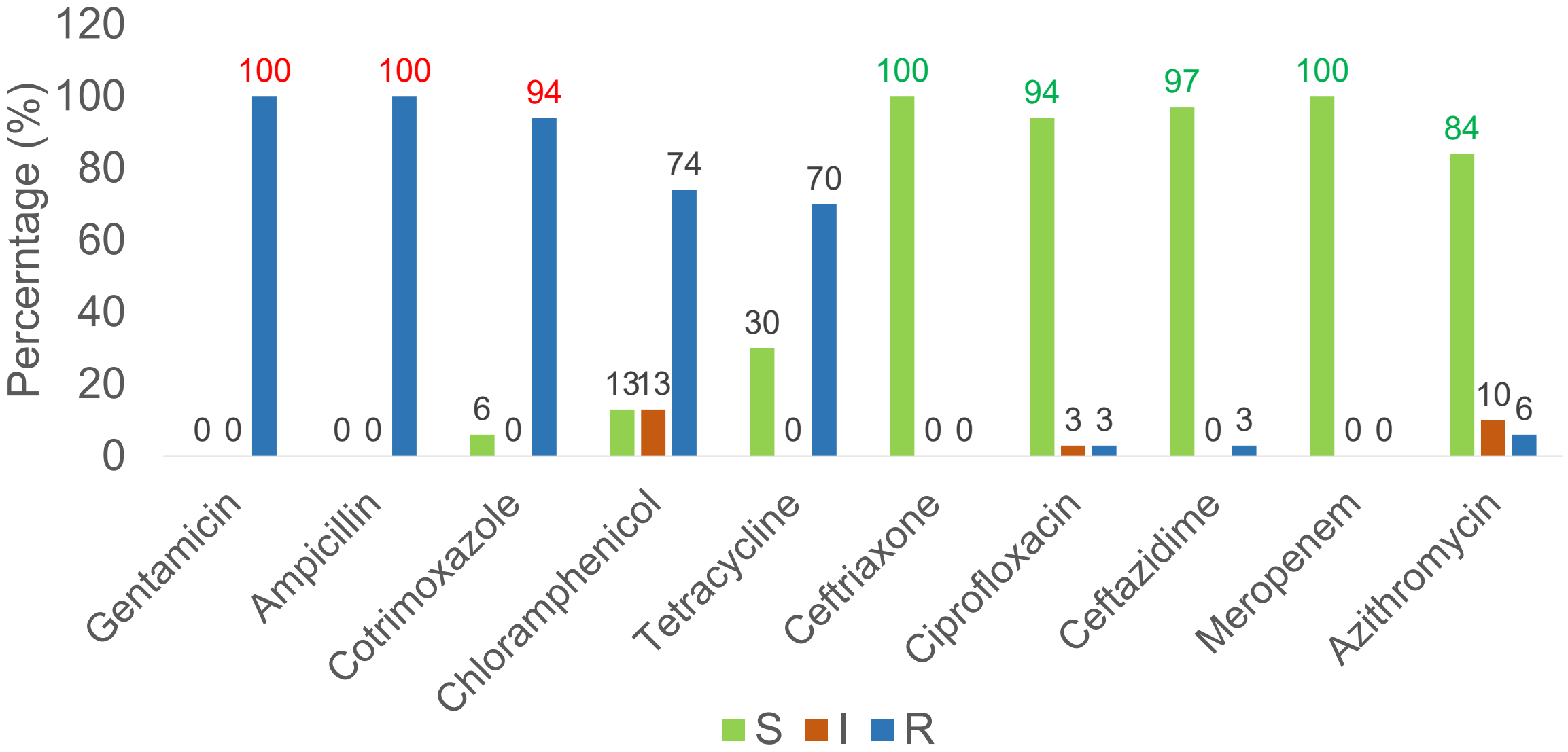
- Males were 19/31 (61%)
- Median age was19 years (IQR,12-24)

Reported Vaccination Status among Confirmed Cases



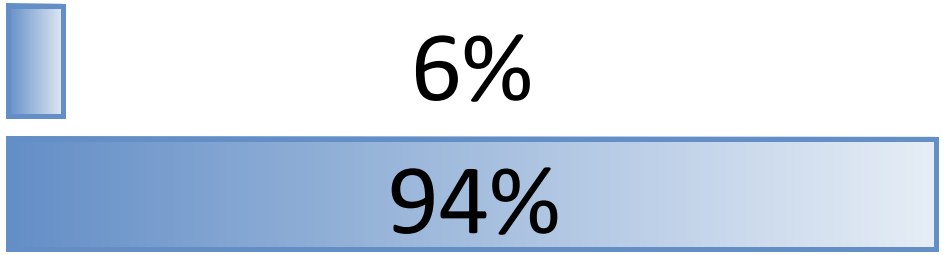
- 23/31 (74.2%) did not have their vaccination status stated
- 6/31 (19.4%) were unvaccinated whilst 2/31 (6.4%) reported previous vaccination

Antimicrobial resistance pattern in Zimbabwe, 2022-2023



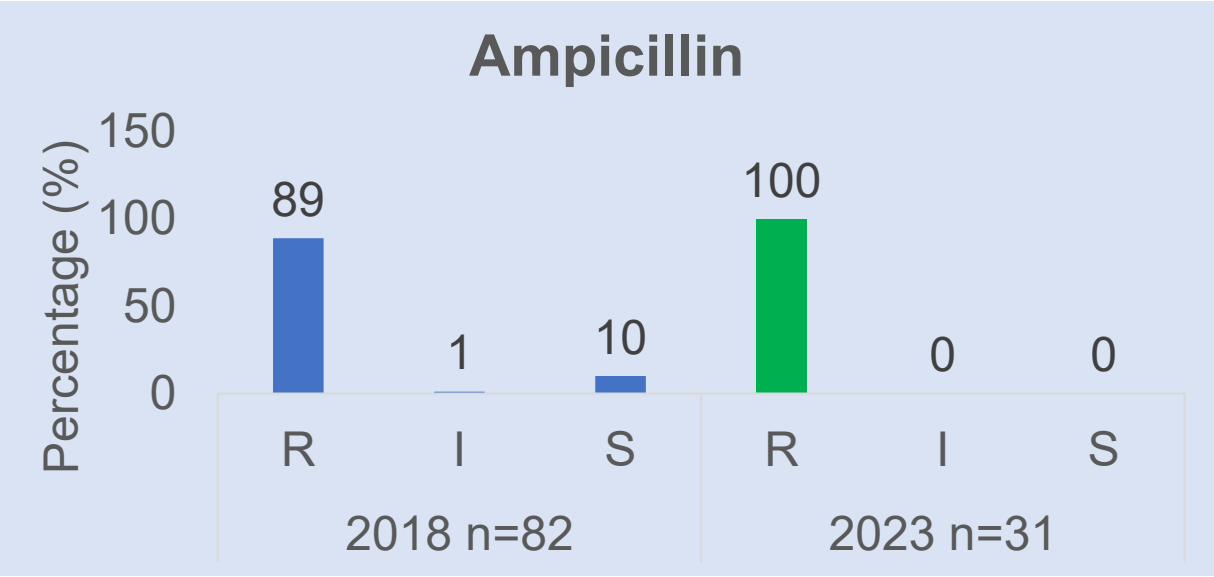
Ratio of MDR Salmonella Typhi in Zimbabwe, 2023

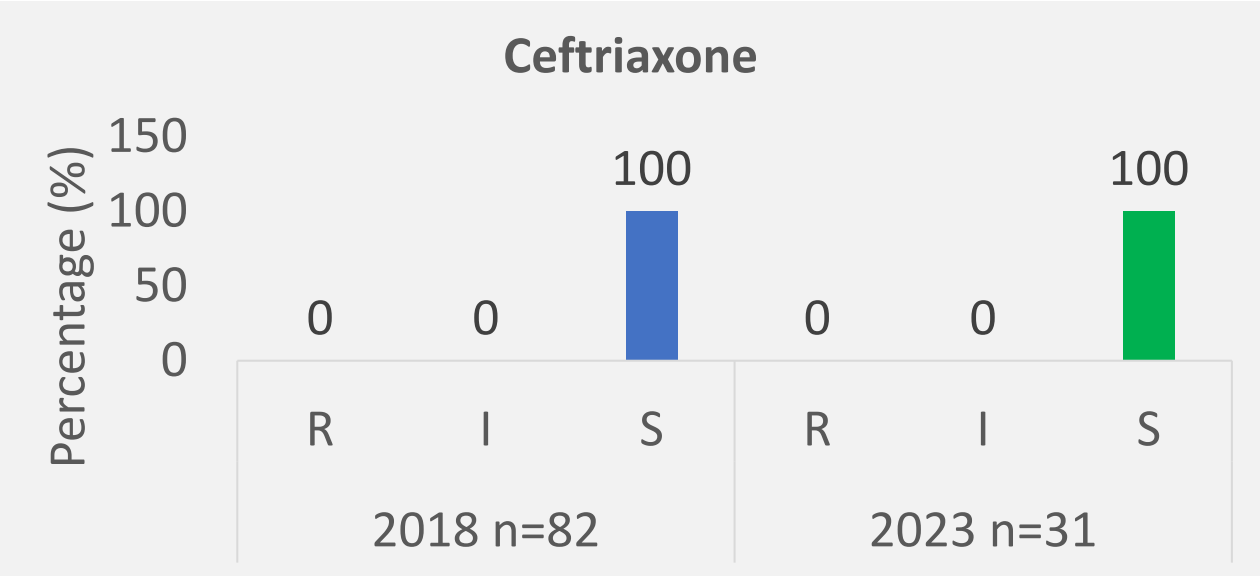
	n/N	Frequency (%)
MDR	2/31	6%
Non MDR/XDR	29/31	94%

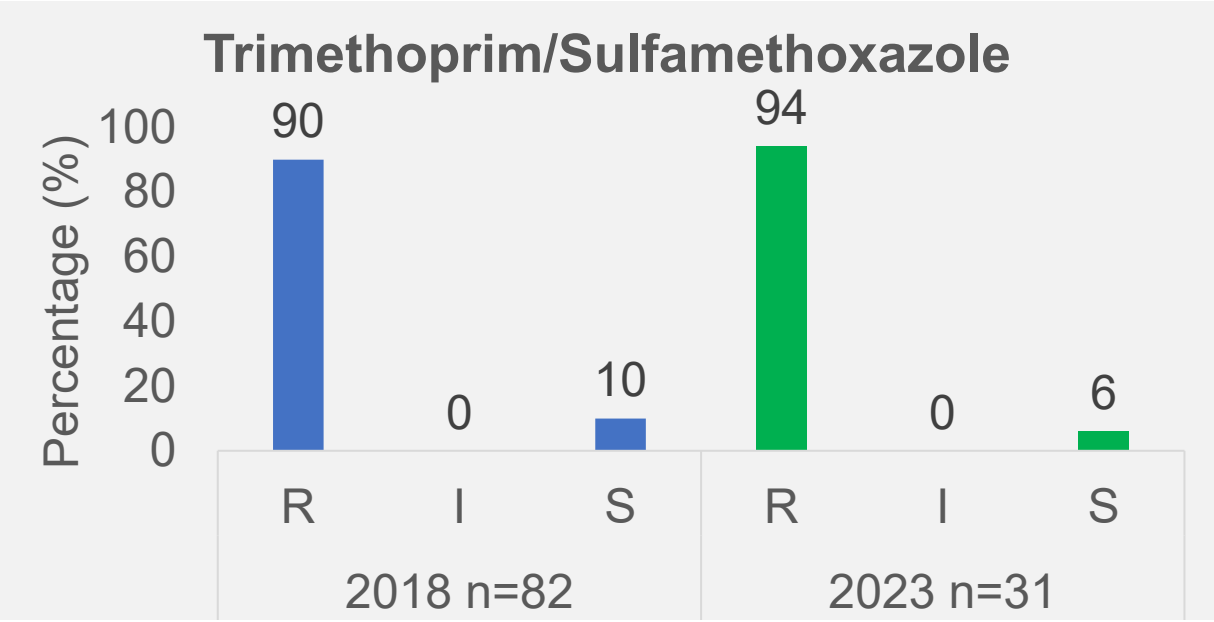


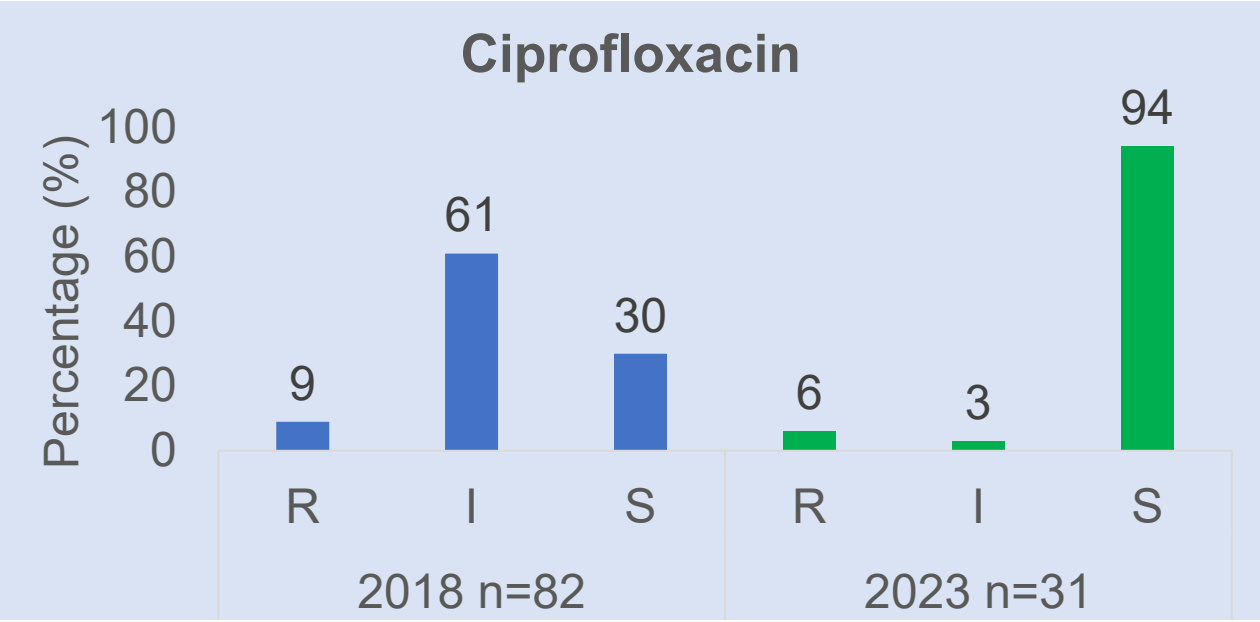
- Overall, 2/31 (6%) of analysed isolates had multi-drug resistance
- No isolates phenotypically showed extensive drug resistance

Comparison of antibiograms 2018 versus 2023









Study Limitations

- Limited statistical power inference based on a small sample size
- Small sample size may be more susceptible to selection bias
- Confounding variables (eg different Salmonella Typhi strains)

Conclusions

The study suggests increased susceptibility to ciprofloxacin following the introduction and integration of TCV in Harare City

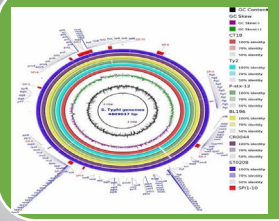
- **Previous studies conducted in Zimbabwe have shown increased resistance to ciprofloxacin *(Mashe et al, 2019)***
- **Zimbabwe treatment guidelines:**
- **1st line – Ciprofloxacin, Ceftriaxone**
- **2nd line - Azithromycxin**

Ampicillin and cotrimoxazole resistance in Salmonella Typhi isolates has remained persistent in Zimbabwe between 2018 and 2023

Recommendations

Continued integration of TCV in the national immunization program

Whole-genome sequencing to identify the presence and mechanisms of antimicrobial resistance



Genetic characterization to determine phylogenetic relatedness

Acknowledgements


Thank you