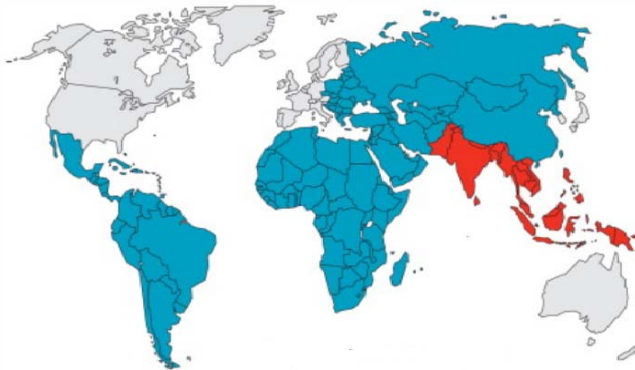


Assessment of population structure and antimicrobial resistance pattern of *Salmonella* Typhi isolates using whole genome sequencing data in Bangladesh

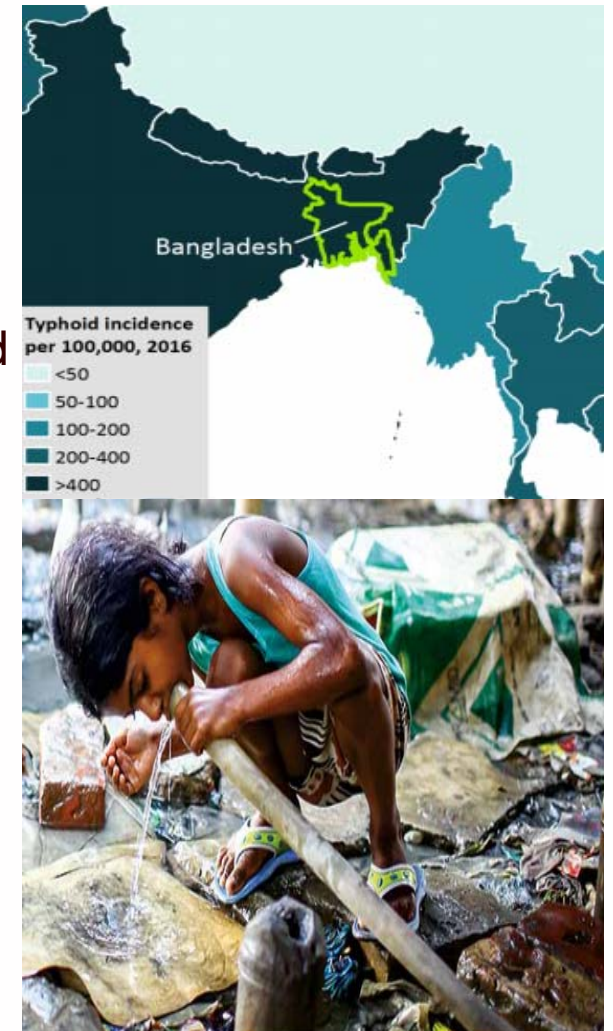
Sadia Isfat Ara Rahman
icddr,b

11th International Conference on Typhoid and other Invasive Salmonellosis
Hanoi, Vietnam
March 2019



Estimates of typhoid burden in Bangladesh

- Typhoid fever remains a public health threat especially in South Asia including **Bangladesh** due to poor access of safe water and sanitation system
- In Bangladesh, an overall population incidence of typhoid estimated between **292 - 395 per 100,000** people per year (*Theiss-Nyland et al. 2019*)
- The indiscriminate use of antibiotics is accelerating the reports of multi-drug resistance
- Whole genome sequence based study emphasizes the importance of surveillance to understand the AMR trend to facilitate patient management



S. Typhi strains isolated from Bangladesh (1998 - 2016)

A total of 818 S. Typhi strains were utilized for genomic analysis

- **202 S. Typhi strains from 3 urban areas inside Dhaka city (2003 - 2016)**

icddr,b Dhaka Hospital (n= 43)

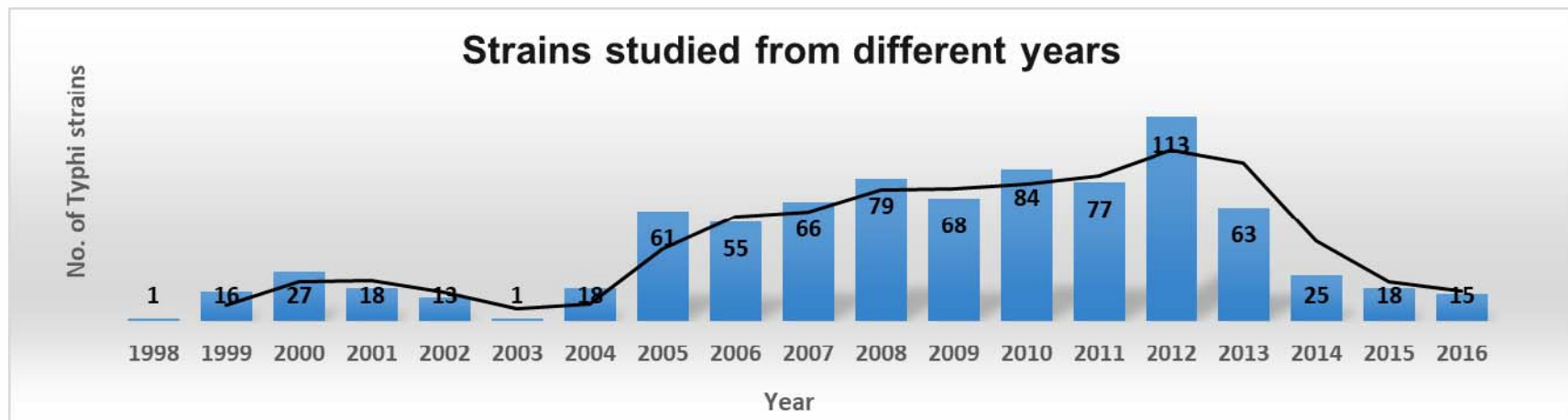
icddr,b Kamalapur field site (n= 130)

icddr,b Mirpur field site (n= 29)

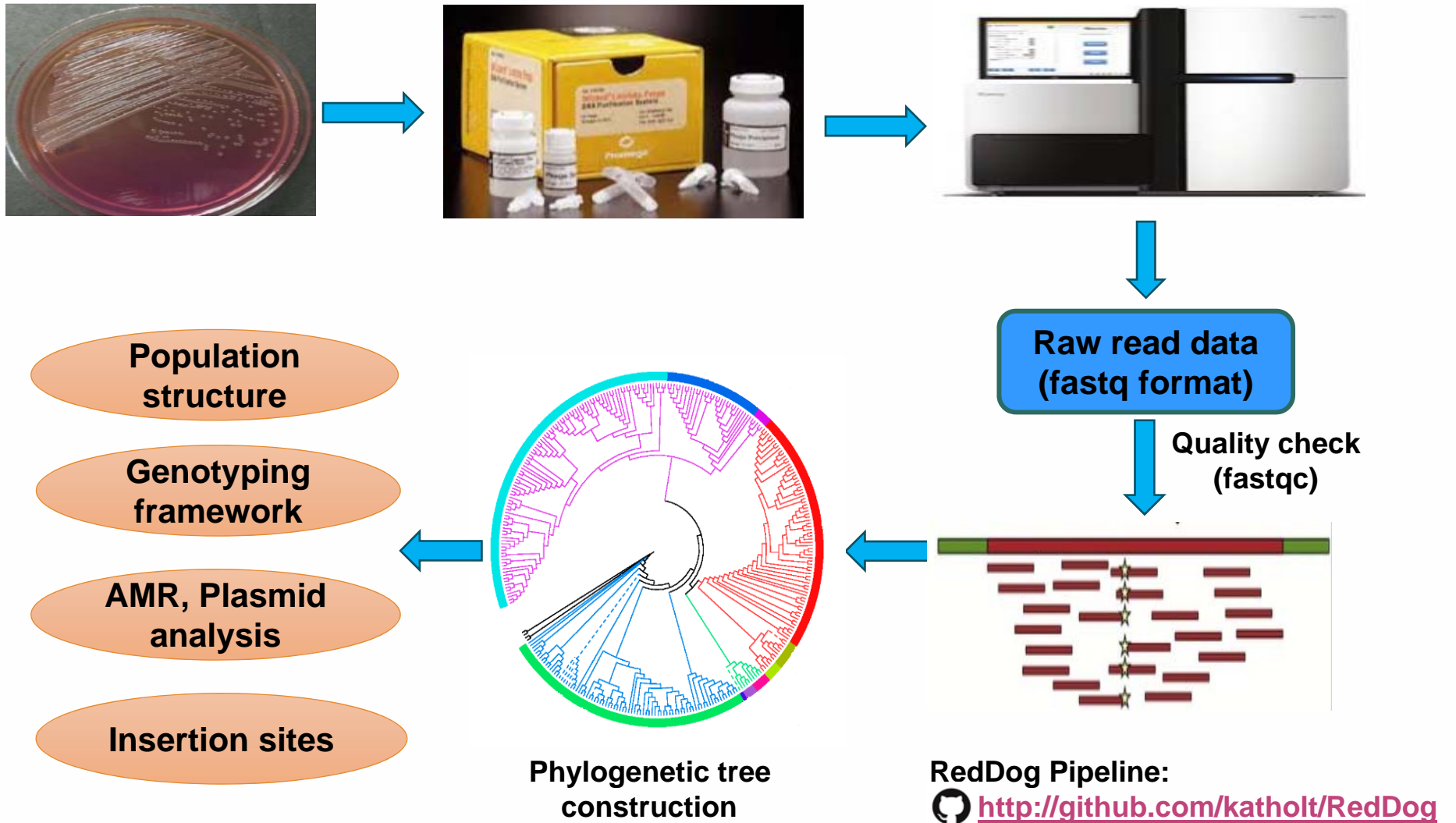
- **Also 616 previously published sequence data were included (1998 - 2016)**

From Wong *et al.* 2016 (n= 88)

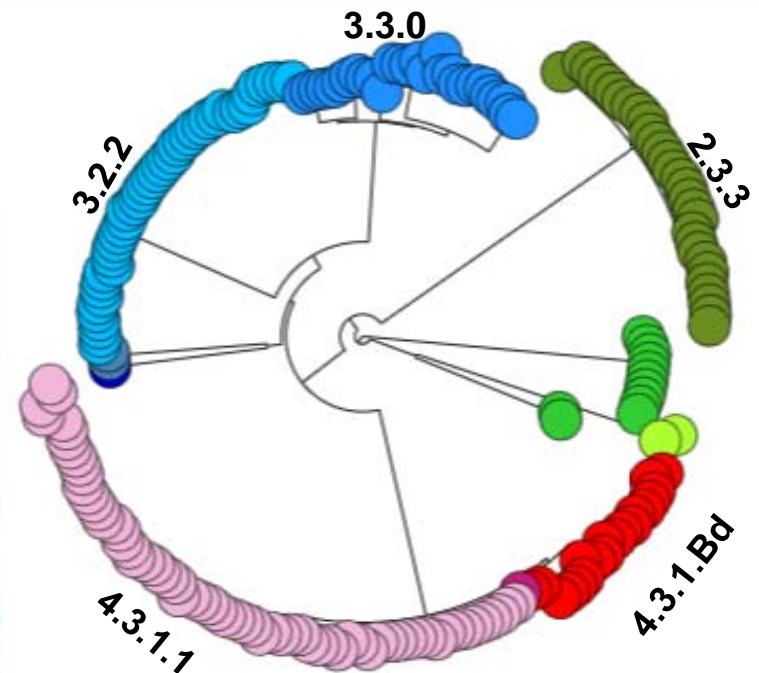
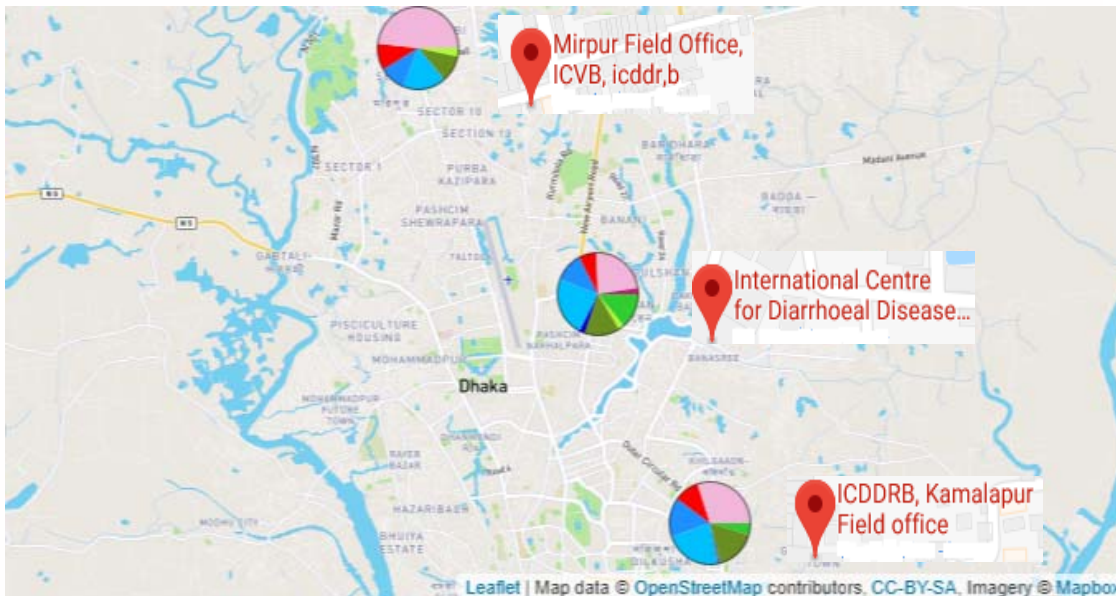
From Tanmoy *et al.* 2018 (n= 528)



Genomic analysis workflow

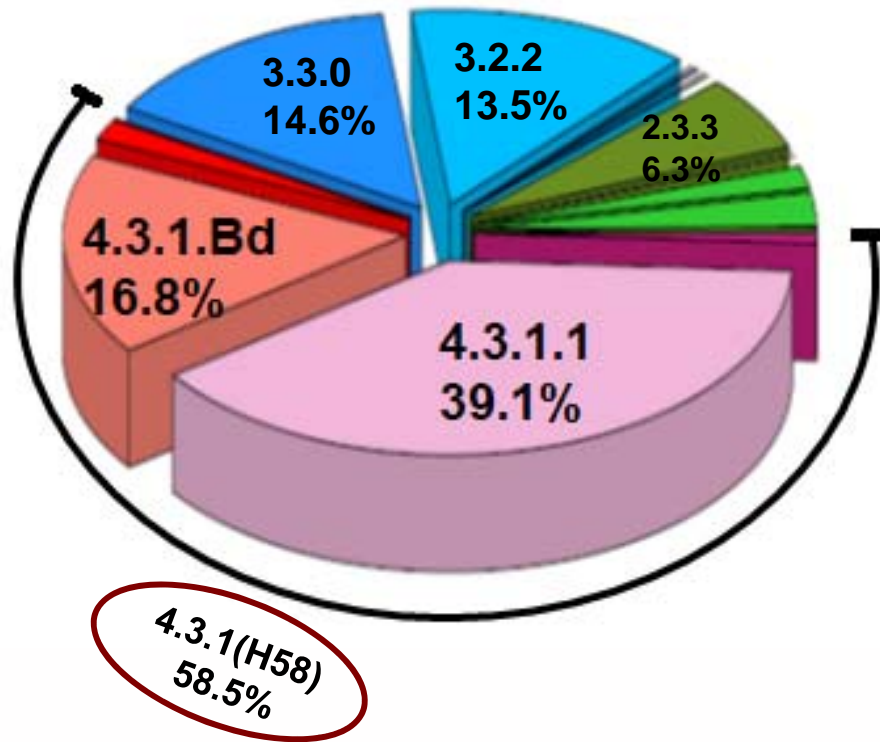


Spatial analysis of 202 S. Typhi strains of this study



Microreact: <https://microreact.org/project/S1a1IWN7N>

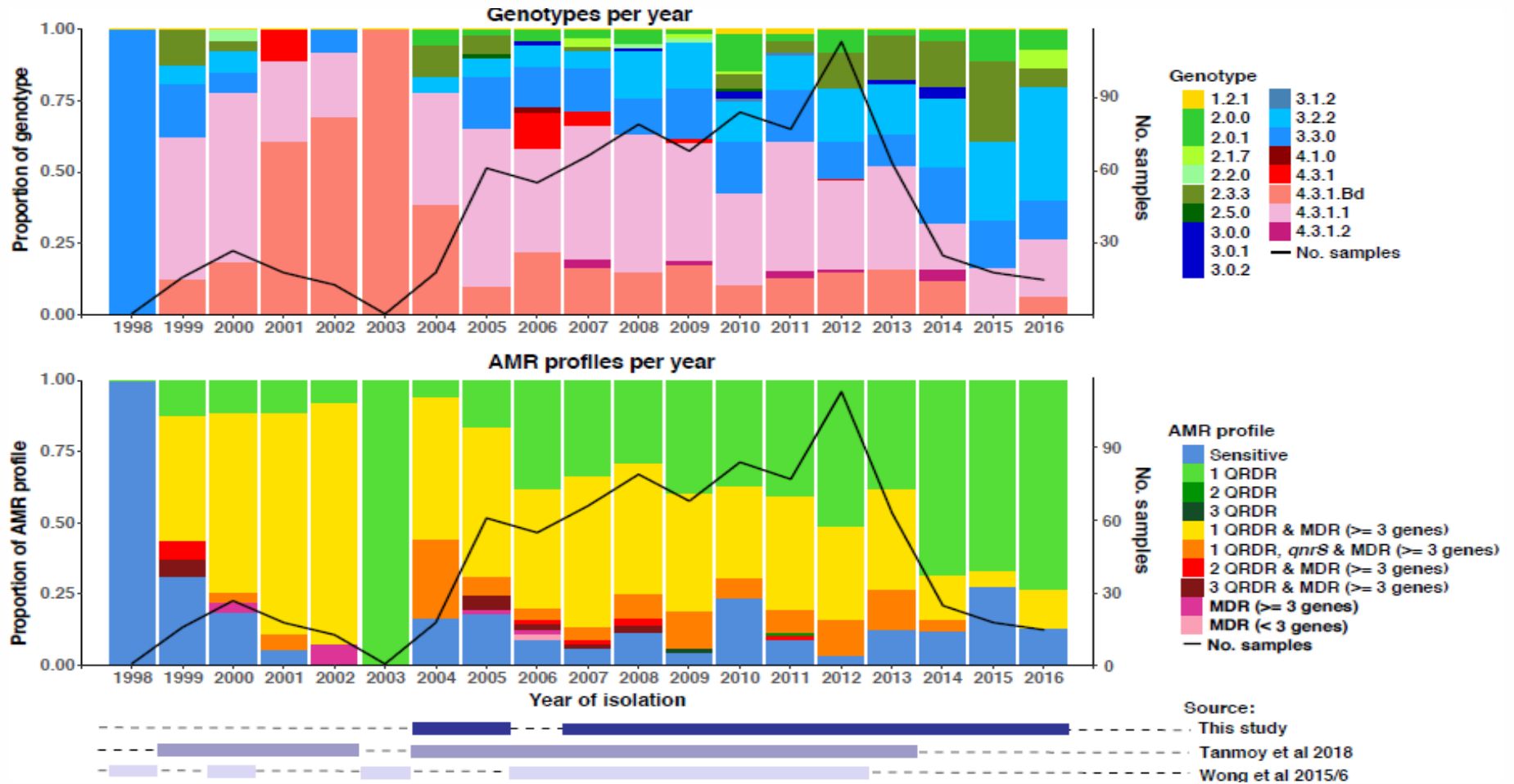
Genotypic distribution of 818 *S. Typhi* strains



- Revealed 17 distinct genotypes
- Genotype 4.3.1 (H58) dominant
- H58 lineage I (4.3.1.1) more common among Bangladeshi strains than lineage II
- New H58 lineage called “lineage Bd” (**4.3.1.Bd**) reported in Tanmoy *et al.* 2018 was also found in our collection

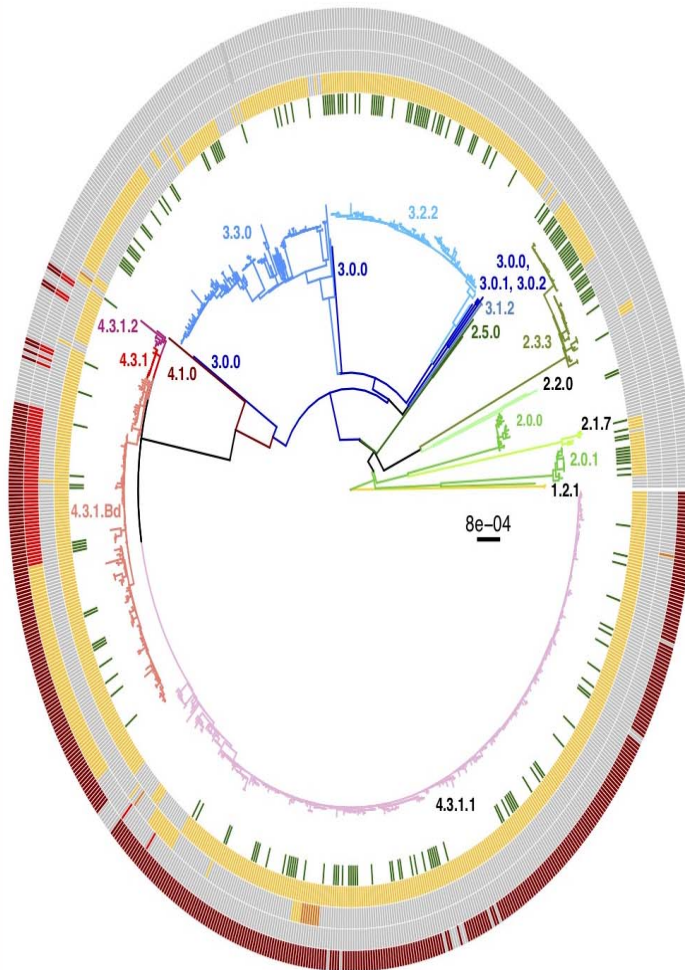
Genotyphi tool: <http://github.com/katholt/genotyphi/>

Timeline of Bangladeshi Typhi strains sequenced from 1998 - 2016



- Rapid increase of genotypes **3.3.0**, **3.2.2**, and **2.3.3** carrying only 1 QRDR in recent years

Bangladeshi 818 *S. Typhi* population structure with AMR



Ring 1: Study

- This study
- Previous study

Ring 2: QRDR *gyrA* codon 83

- Ns mutation (S83F or S83Y)
- No mutation

Ring 3: Other QRDR mutations

- 1 other ns mutation
- 2 other ns mutations
- No mutation

Ring 4: Plasmids

- IncHI1
- IncFIBK (carrying *qnrS*) & MDR transposon
- IncFIBK (carrying *qnrS*)

Ring 5: AMR genes

- MDR (>= 3 genes)
- AMR (2 genes)
- AMR (1 gene)
- 0 AMR genes

Acquired AMR genes (defined as MDR)

- *bla*_{TEM-1} (ampicillin)
- *catA1* (chloramphenicol)
- *dfrA7, sul1, sul2* (cotrimoxazole)
- MDR genes without evidence of IncHI1 plasmids observed in only H58 lineage I isolates
- QRDR mutation in *gyrA* (S83F or S83Y) was the most prevalent

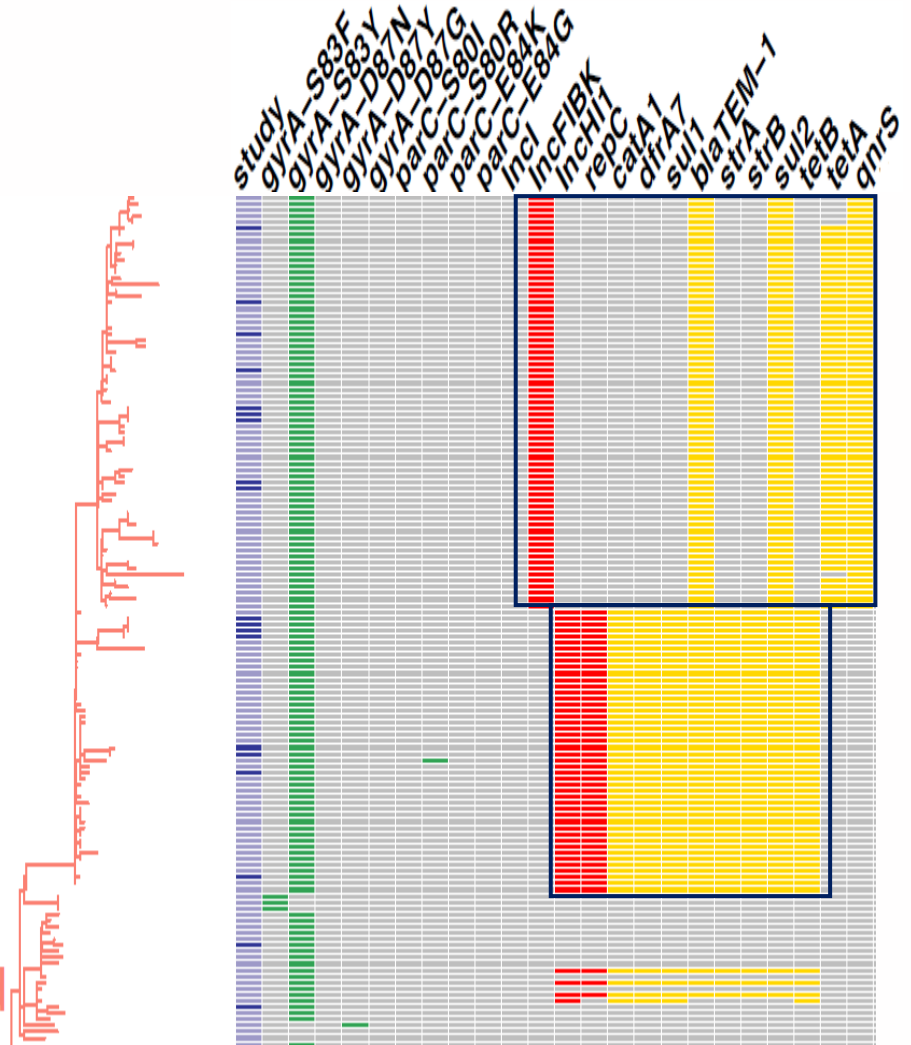
AMR and plasmid analysis:

- ariba: <https://github.com/sanger-pathogens/ariba>
- SRST2: <https://github.com/katholt/SRST2>

Newly defined “lineage Bd” in Bangladeshi *S. Typhi* strains

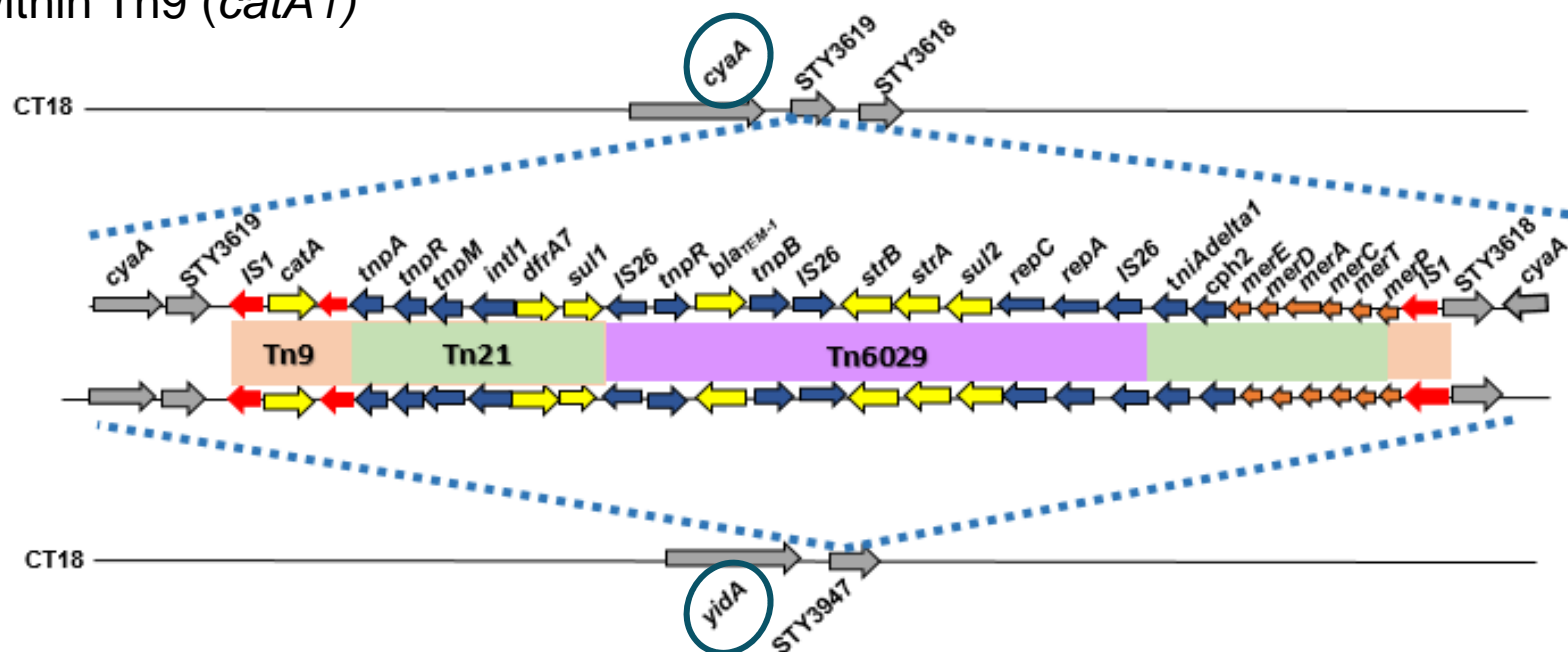
- A newly defined H58 lineage reported in Tanmoy *et al.* 2018 as “**lineage Bd**” (4.3.1.Bd) was found in 138 Typhi strains
- Revealed **two major patterns** in terms of AMR gene and plasmid association
 - ❑ Strains harbouring IncHI1-PST6 plasmid contained 8 AMR genes *catA1*, *dfrA*, *sul1*, *bla_{TEM-1}*, *strAB*, *sul2*, *tetB*
 - ❑ Strains carrying IncFIBK plasmid associated with only 4 AMR genes *bla_{TEM-1}*, *sul2*, *qnrS1*, *tetA*

4.3.1.Bd



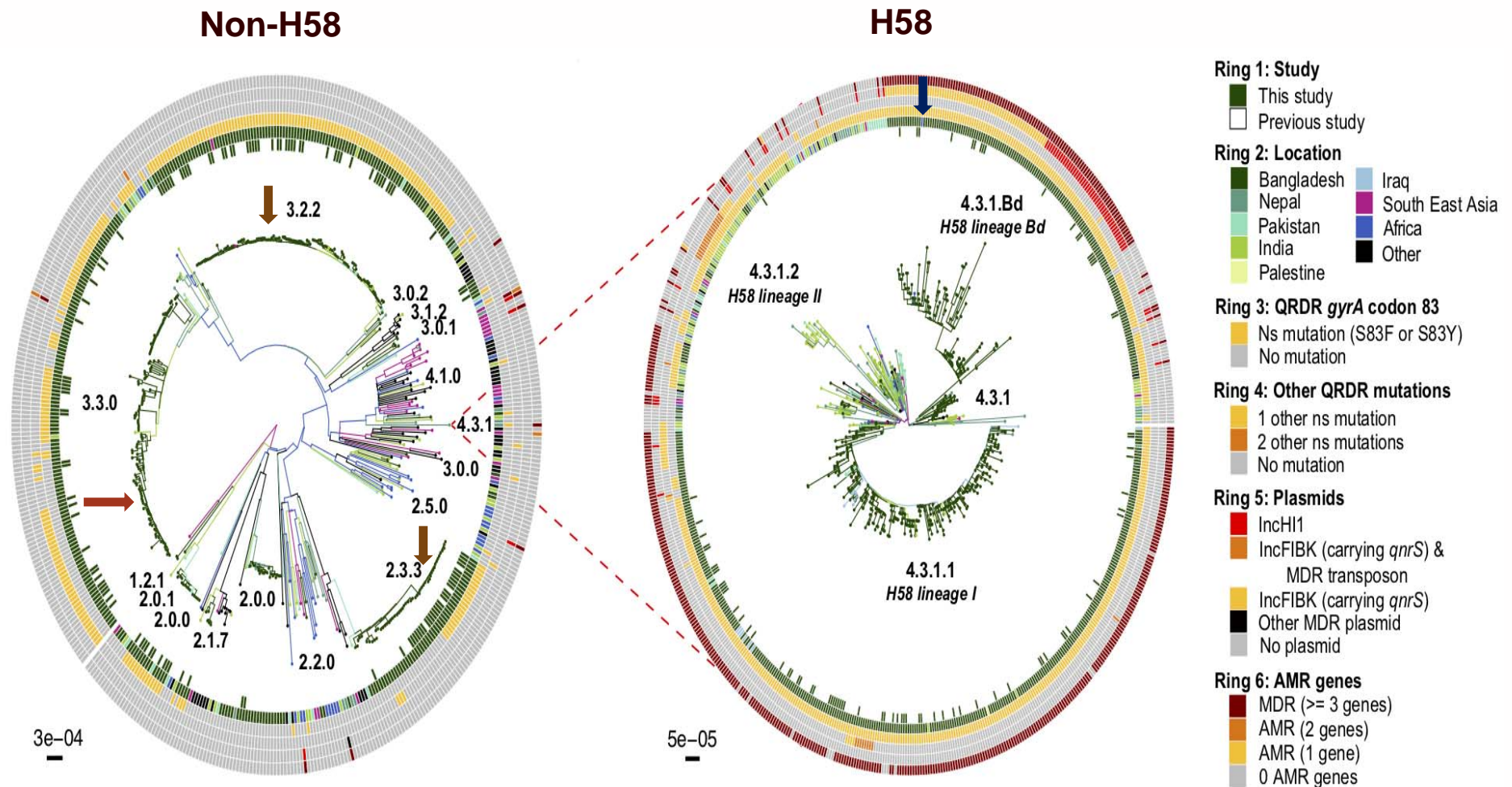
Insertion sites of transposons in *S. Typhi* isolates

- Two separate integration event of *IS1* site observed in H58 lineage I isolates
 - STY3618 and STY3619 locus near gene *cyaA*
 - STY3947 locus near gene *yidA*
- Acquired AMR genes encoded within **Tn2670 composite transposon**, comprising Tn6029 (*bla*_{TEM-1}, *strB*, *strA*, *sul2*) and Tn21 (*dfrA7*, *sul1*) inserted within Tn9 (*catA1*)



ISMMapper: https://github.com/jhawkey/IS_mapper

Global and regional S.Typhi strain circulation patterns



Conclusions

WGS data of *S. Typhi* strains representative of the past 18 years from Bangladesh suggest that :

- H58 lineage I (39.1%) most common in Bangladeshi strains followed by H58 lineage Bd strains (16.8%)
- MDR phenotype strongly correlated with H58 isolates than non-H58 isolates
- Reported for the first time two different patterns of AMR and plasmid association in lineage Bd isolates (4.3.1.Bd)
- Rapid spread of genotype 2.3.3, 3.2.2,3.3.0 carrying only QRDR mutation led to reduce fluoroquinolone susceptibility
- Highlights the need for laboratory and molecular based surveillance to monitor acquisition of AMR and ongoing evolution in endemic regions

Acknowledgments

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**15th International Asian Scientific Conference on Diarrheal Disease & Nutrition
(ASCODD)**

Date: January 28-30, 2020

Venue: icddr,b, Dhaka, Bangladesh

Theme: Humanitarian Crisis and Impact on Diarrhoeal diseases and Nutrition