Drinking water chlorination impact on extended-spectrum β-lactamase-producing Enterobacteriaceae in Bangladeshi children in a cluster-randomized controlled trial

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Antimicrobial resistance is rapidly increasing globally. Water, sanitation and hygiene interventions are promoted to reduce exposures (Fig. 1.). Still lack of supporting evidence.

OBJECTIVES

Hypothesis: Receiving in-line chlorinated drinking water reduces fecal carriage rates of extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-E) in Bangladeshi children
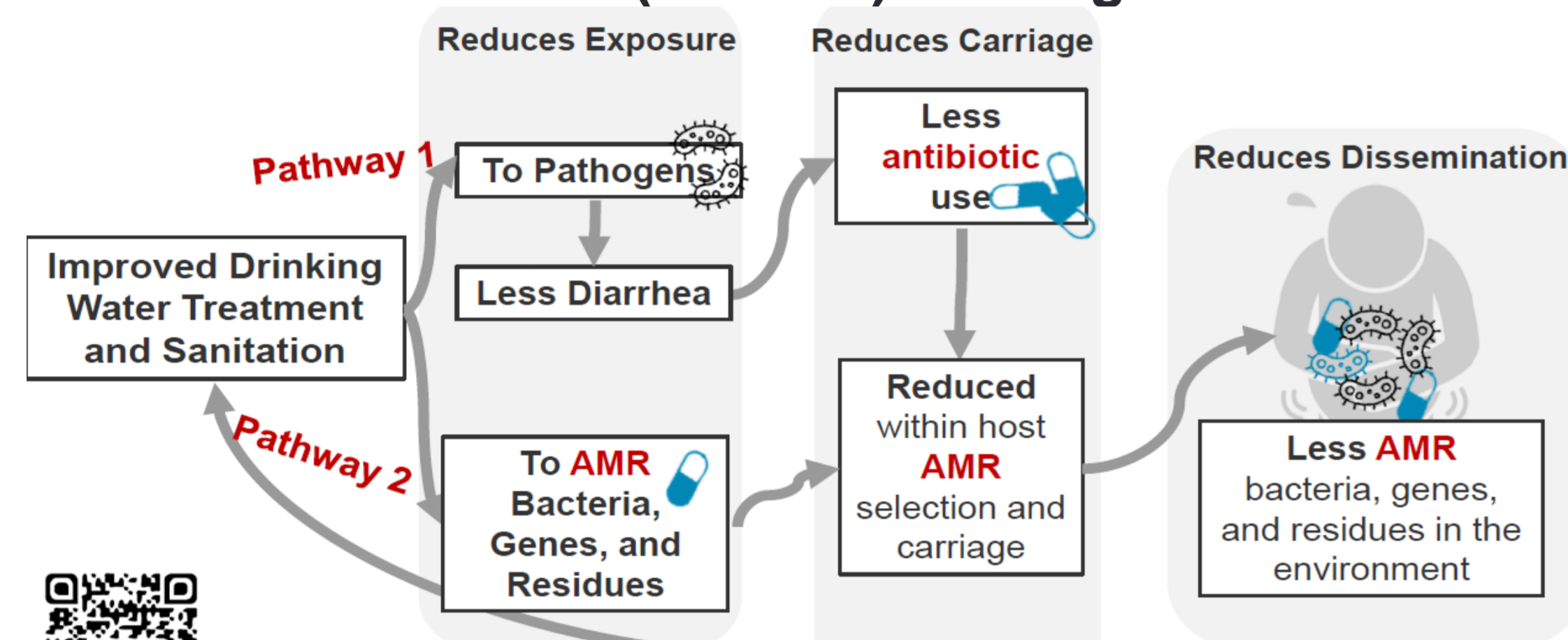

Figure 1. Nadimpalli et al. (2020) *Nature Microbiol* DOI: doi.org/10.1038/s41564-020-0722-0

MATERIAL & METHODS

Samples. We analysed 479 fecal samples of children <5 years of age previously enrolled in a **double-blind cluster randomized controlled trial** of in-line water chlorination conducted at two low-income communities in Bangladesh (Dhaka city and Tongi) between July 2015 and December 2016 (Pickering et al.)
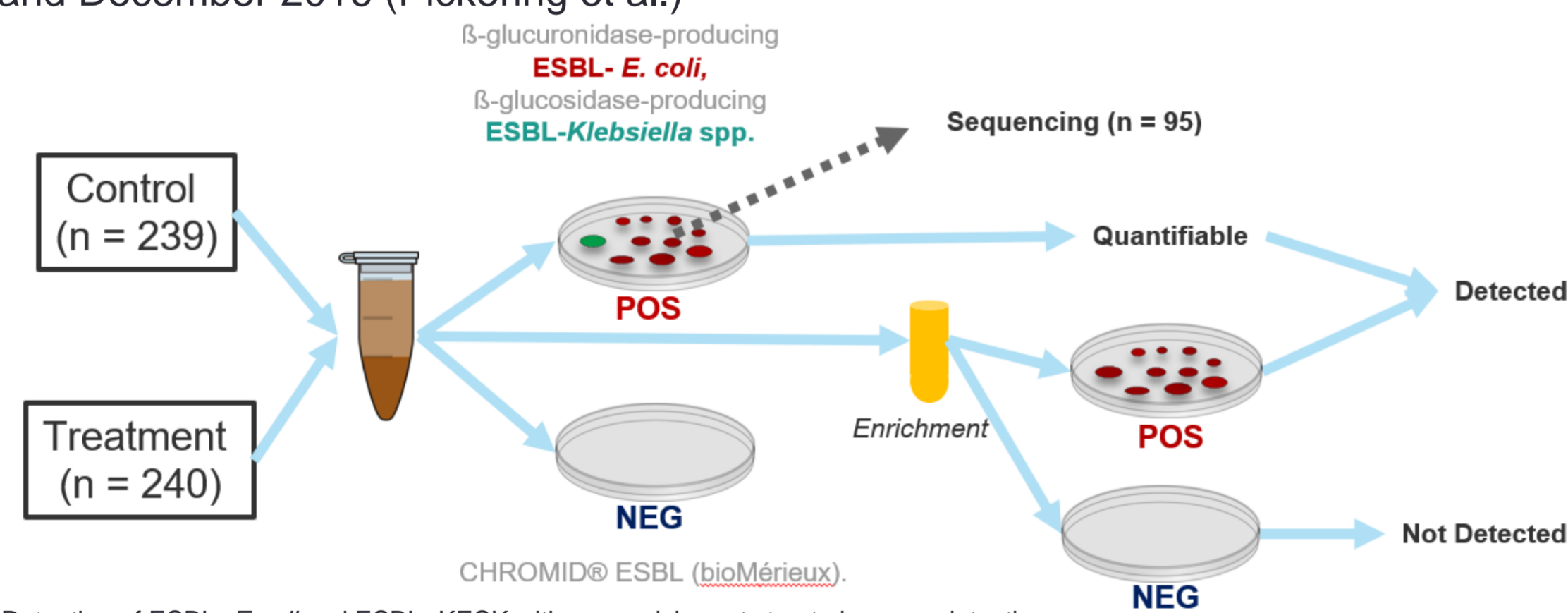

Figure 2. Detection of ESBL- *E.coli* and ESBL- KESK with pre-enrichment step to improve detection

- Detected and enumerated ESBL- *E.coli* and ESBL- KESK on CHROMID® ESBL
- Modeled impact of intervention, controlling for study site and age
- Sequenced E. coli genomes from 86 child fecal samples (n = 43 control, n = 43 intervention)
- Characterized occurrence of β-lactamase genes using short-read metagenomic sequencing on 97 fecal samples (children >6 months, n=50 control, n=47 treatment)

REFERENCES

Pickering AJ, Crider Y, Sultana S, et al. Effect of in-line drinking water chlorination at the point of collection on child diarrhoea in urban Bangladesh: a double-blind, cluster-randomised controlled trial. Lancet Glob Health 2019; 7: e1247–56.

Nadimpalli, Maya L., et al. "Urban informal settlements as hotspots of antimicrobial resistance and the need to curb environmental transmission." *Nature microbiology* 5.6 (2020): 787-795.

In-line drinking water chlorination is insufficient to meaningfully impact the carriage of ESBLs in children in low income communities in urban Bangladesh.

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RESULTS

Negative = no growth observed after direct plating onto the selective ESBL agar or after the pre-enrichment step; **Enrichment** = presumptive *E. coli* colonies after the pre-enrichment step; **Quantifiable** = presumptive ESBL-*E. coli* colonies after direct plating onto the selective ESBL agar.
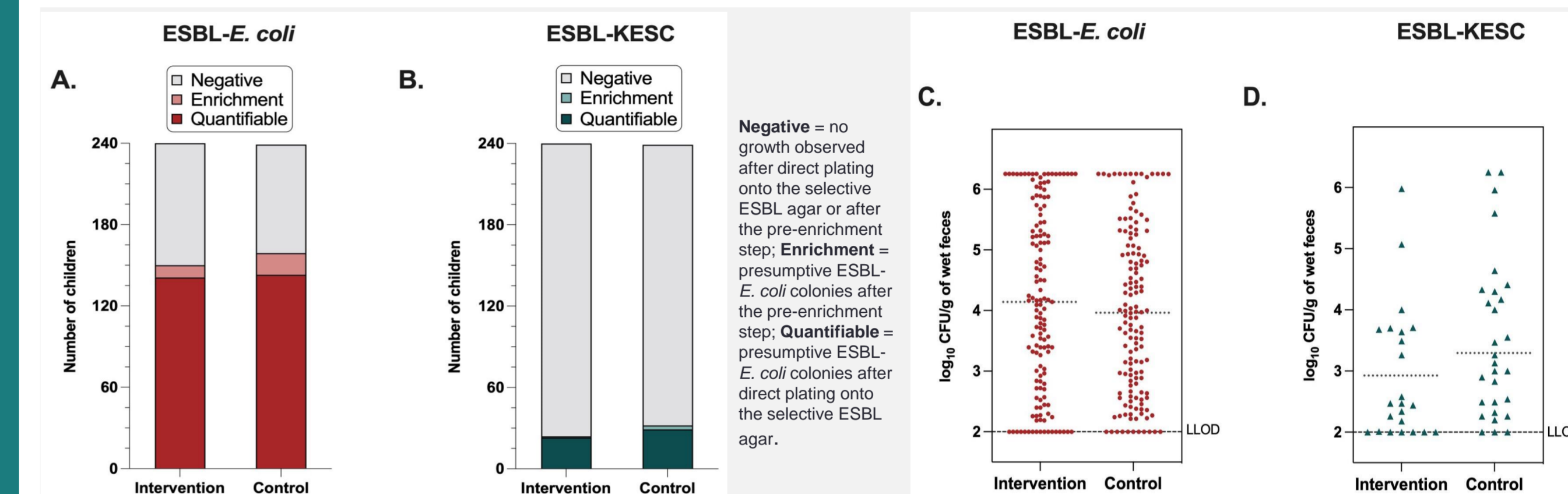
Figure 3. Fecal carriage rates of A) ESBL-*E. coli* and B) ESBL-KESC and concentrations of C) ESBL-*E. coli* and D) ESBL-KESC amongst samples with direct positive cultures (quantifiable) in the intervention and control groups. The dotted horizontal line is the mean log10 CFU/g-wet feces in the intervention and control groups; the lowest limit of detection (LLOD) is indicated.

Model	Variable	RR	95% CI	Pr(>|z|)	Model Fit
A	**ESBL-*E. coli*, Carriage**				AIC: 892
	Constant	0.73	[0.50, 1.03]	0.09	
	Intervention	0.98	[0.78, 1.23]	0.87	
	Dhaka	**0.77**	**[0.61, 0.98]**	**0.03**	
	Age (16-32 mo)	0.88	[0.59, 1.33]	0.52	
	Age (>32 mo)	1.04	[0.73, 1.52]	0.84	
B	**ESBL-KESC, Carriage**				AIC: 359
	Constant	**0.17**	**[0.07, 0.34]**	**<0.001**	
	Intervention	0.76	[0.44, 1.29]	0.31	
	Dhaka	0.83	[0.47, 1.42]	0.50	
	Age (16-32 mo)	1.03	[0.46, 2.62]	0.95	
	Age (>32 mo)	0.74	[0.35, 1.85]	0.48	

Table 1. Impact of the drinking water chlorination intervention on children's carriage of ESBL-*E. coli* and ESBL-KESC controlling for study site and age, as determined using modified Poisson regression. RR is Relative Risk and CI is the 95% Confidence Interval. Emboldened variables are statistically significant as defined at α = 0.05.
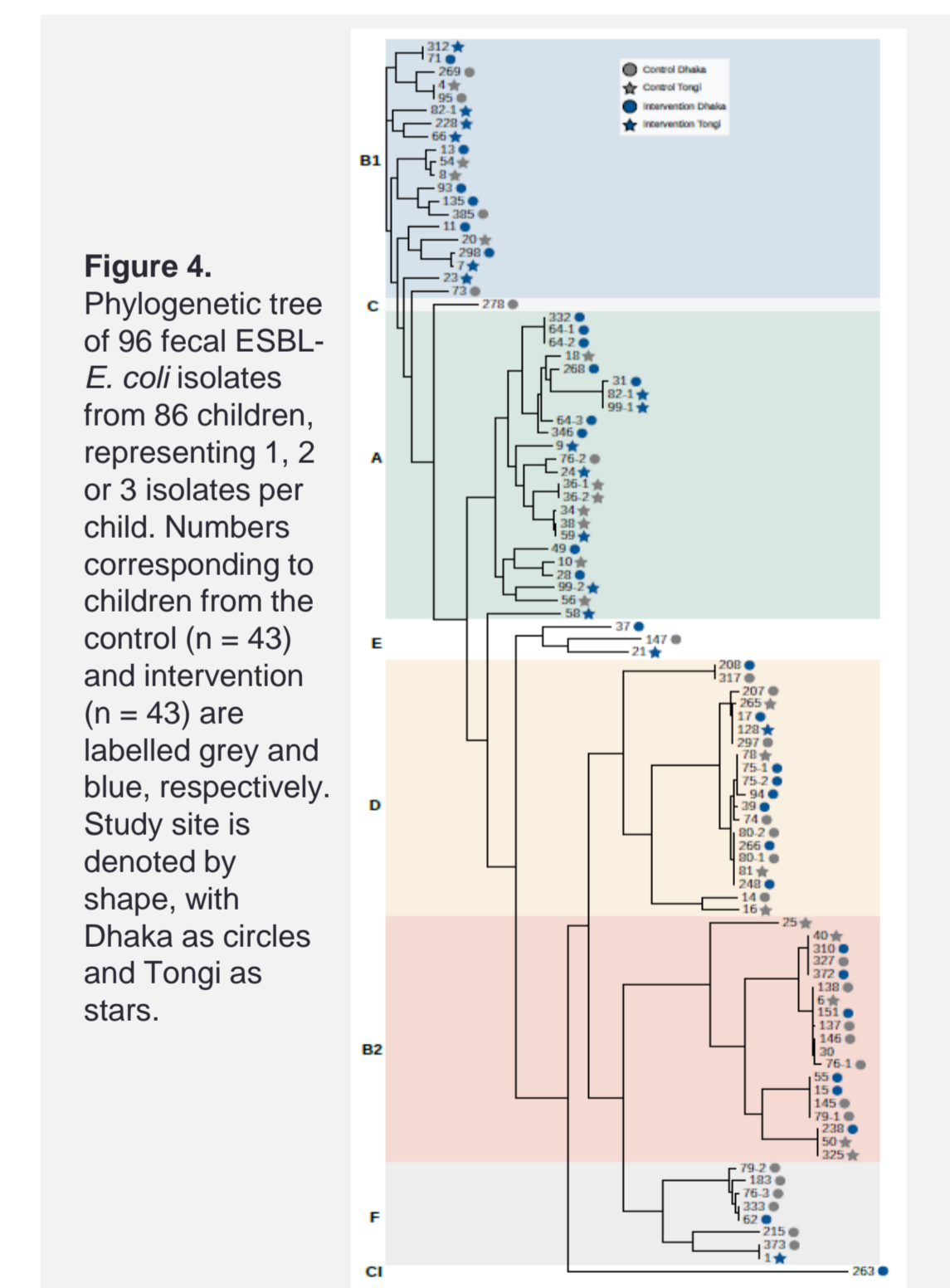
Figure 4. Phylogenetic tree of 96 fecal ESBL-*E. coli* isolates from 86 children, representing 1, 2 or 3 isolates per child. Numbers corresponding to children from the control (n = 43) and intervention (n = 43) are labelled grey and blue, respectively. Study site is denoted by shape, with Dhaka as circles and Tongi as stars.

SUMMARY / CONCLUSION

- **In-line drinking water chlorination did not significantly reduce fecal carriage of ESBL-E in the gut of Bangladeshi children.**

- Lack of an impact on ESBL-E contrasts with impact of same intervention on diarrhea (Pickering et al.)
- Observed rates of culturable ESBL-*E. coli* carriage are high, but nevertheless may underestimate the true carriage rate.
- Geographic differences in ESBL-*E. coli* carriage rates highlight the influence of environmental exposures on health risks.
- The *E. coli* circulating amongst the children in Dhaka and Tongi are major drivers of AMR extraintestinal infections in Bangladesh.
- The primary limitation of the study was the limited exposure time of the children to the intervention.

- **Development and evaluation of effective interventions to control AMR carriage are needed to support National and Global AMR Action Plans.**