

Advances in serology for enteric fever diagnostics and sero-surveillance

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Impact of lack of rapid diagnostics for enteric fever

Over diagnosis and over-prescribing of anti-typhoid antimicrobials

- **Driven emergence of antimicrobial resistance**
 - Specifically, fluoroquinolone resistance in Asia
 - Now there is emergence of extensively drug resistant *Salmonella* Typhi (XDR) = MDR + FQ + 3rd gen. cephalosporin resistance

Surveillance equity gaps

- Many LMICs lack incidence data
- Major gaps exist across Africa, Asia, and the Middle East and central America.
- May lead to vaccine equity gaps

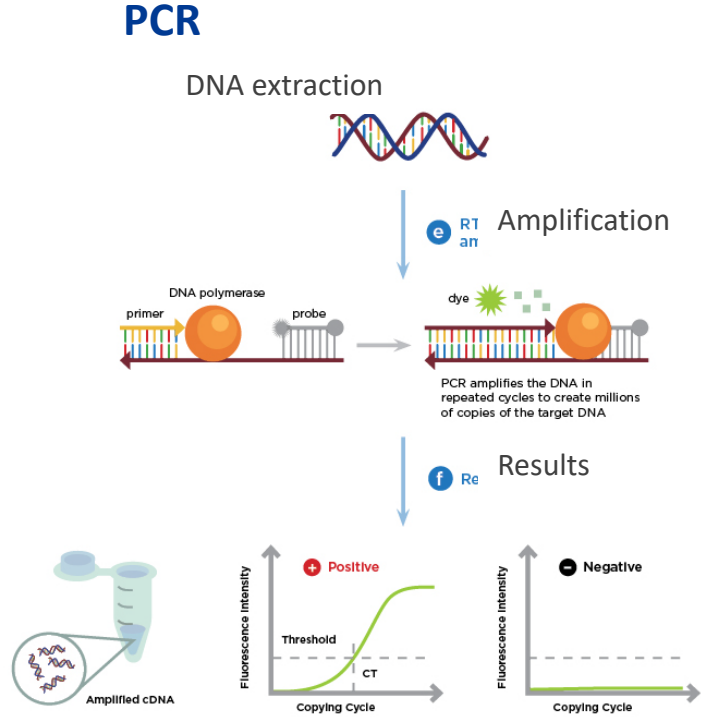


Current enteric fever diagnostics lack sensitivity and specificity

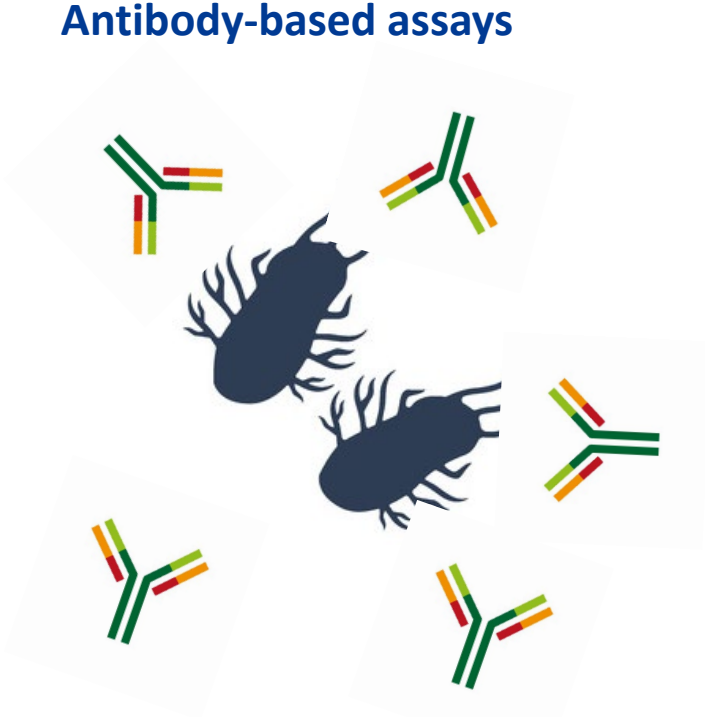
Blood Culture



Result takes 2 days
Requires laboratory capacity
60% sensitive



Requires laboratory capacity



Lack of specificity

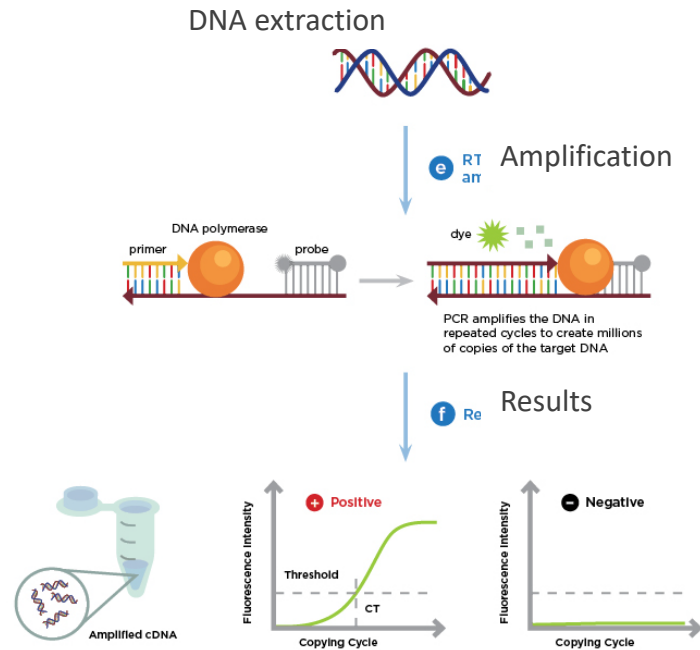
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PCR



Requires laboratory capacity

Antibody-based assays



Lack of specificity

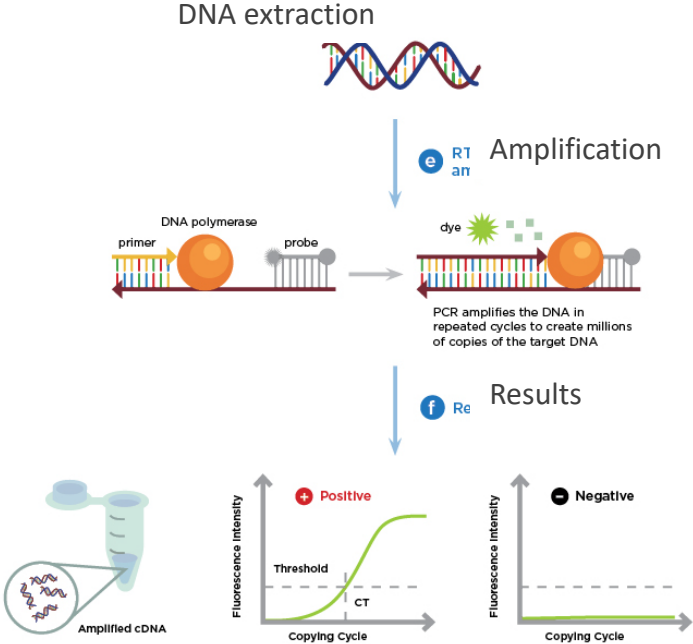
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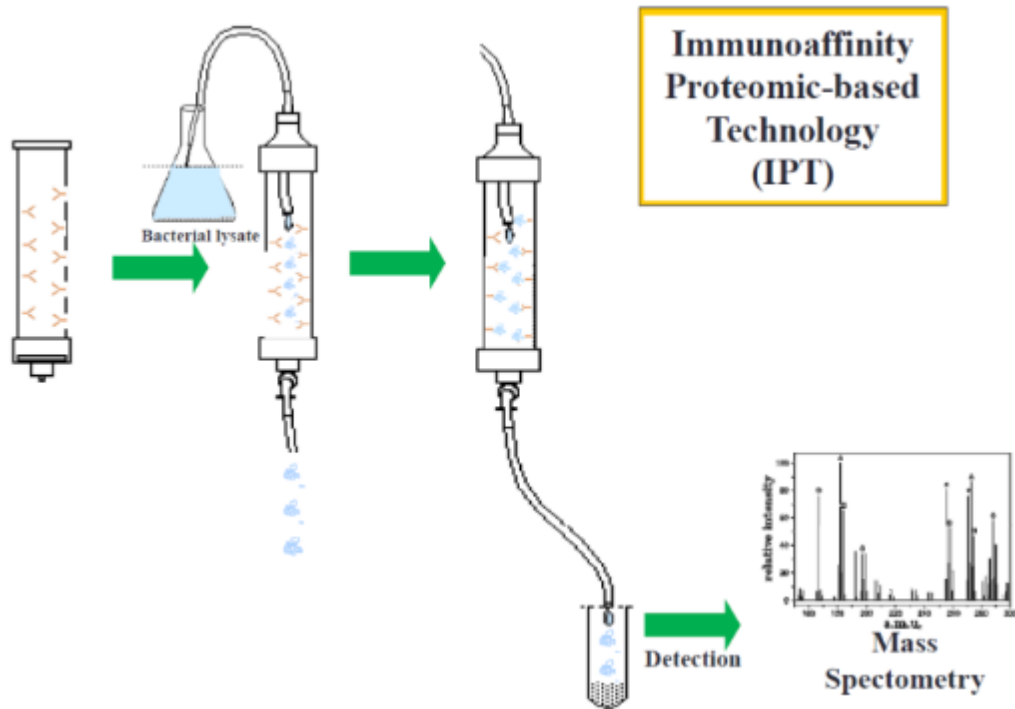
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Antibody-based assays

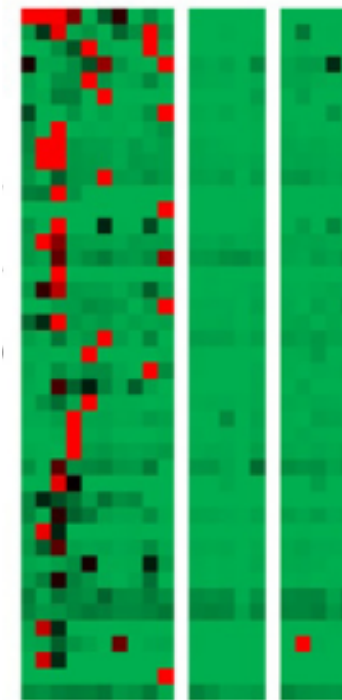


Lack of specificity

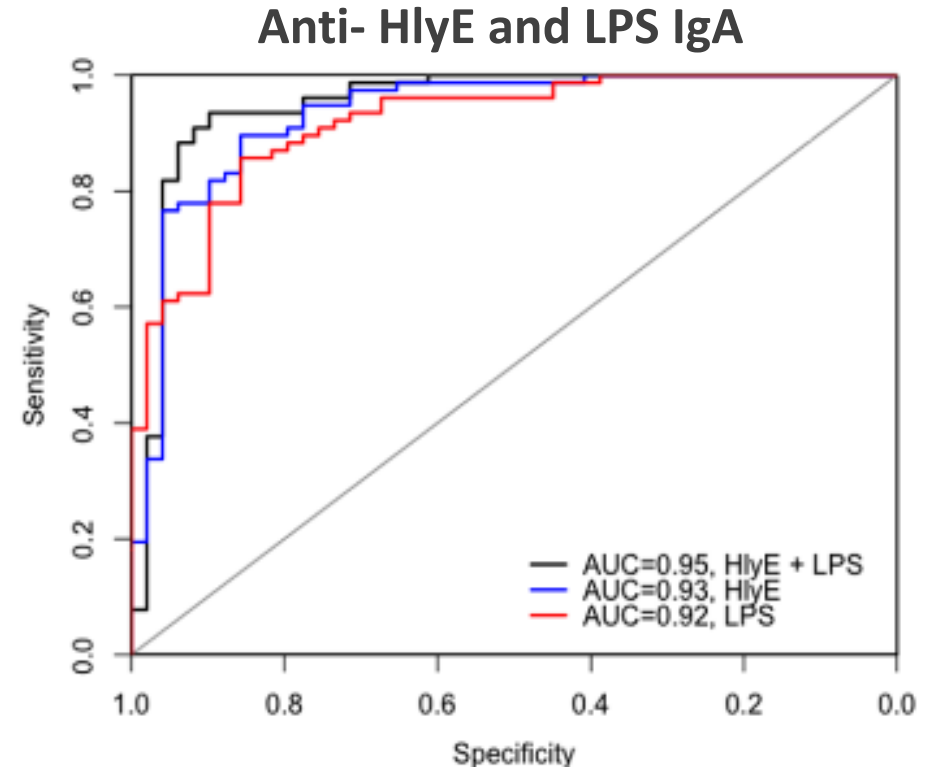
Biomarker screens identified seroresponses with better diagnostic accuracy



Charles RC et al., CVI 2010 Aug;17(8):1188-95



Charles RC, et al. CVI. 2014;21(3):280-5



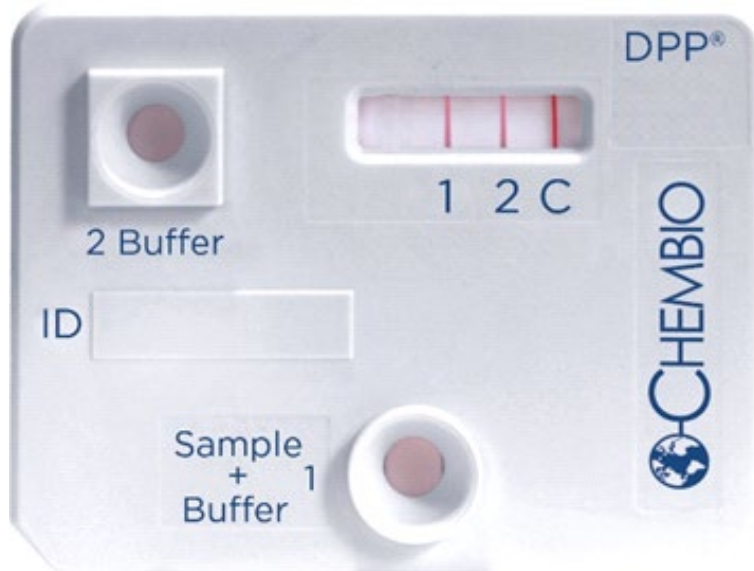
Andrews JR, Clin Infect Dis. 2019 Mar 5;68(6):949-955.

sensitivity of 90% and specificity of 92%

DPP Typhoid Assay

- Generate a rapid test on detecting IgA antibody responses targeting LPS and HlyE of *S. Typhi* and *S. Paratyphi A*

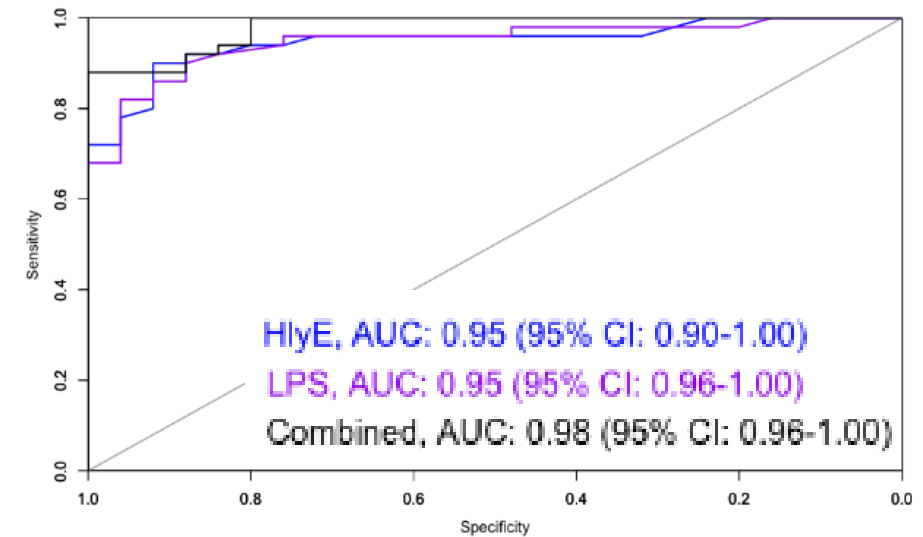
DPP[®] Test Cassette



DPP[®] Micro Reader



Specificity of 96% and sensitivity of 90%.



*Kumar et al. 2020. mSphere 5:e00253-20.

Prospective Study of DPP in Bangladesh

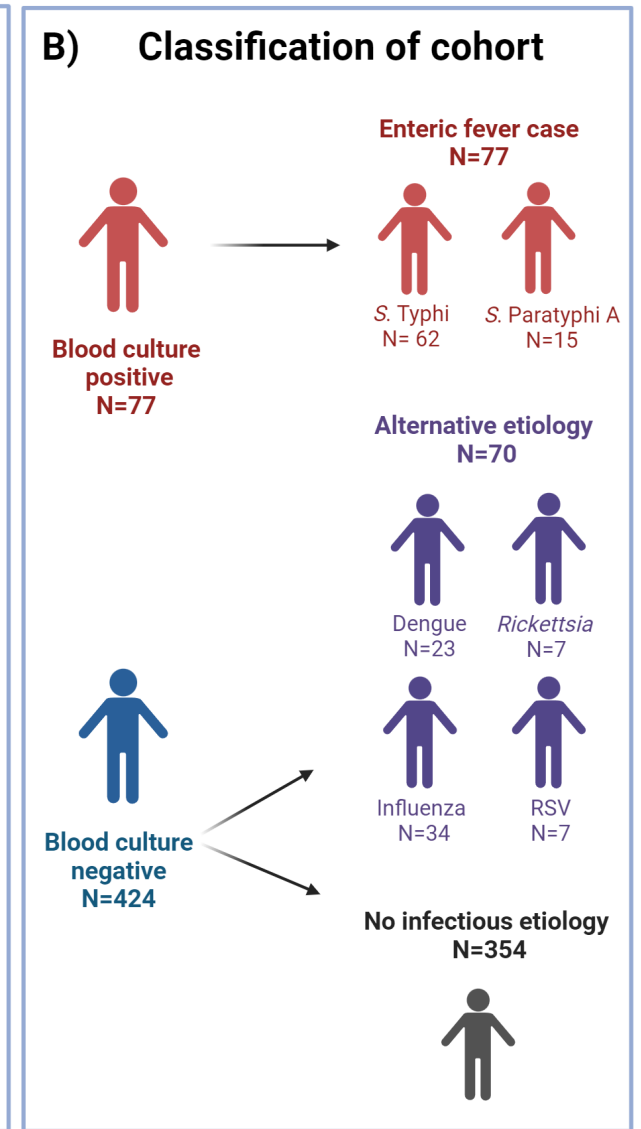
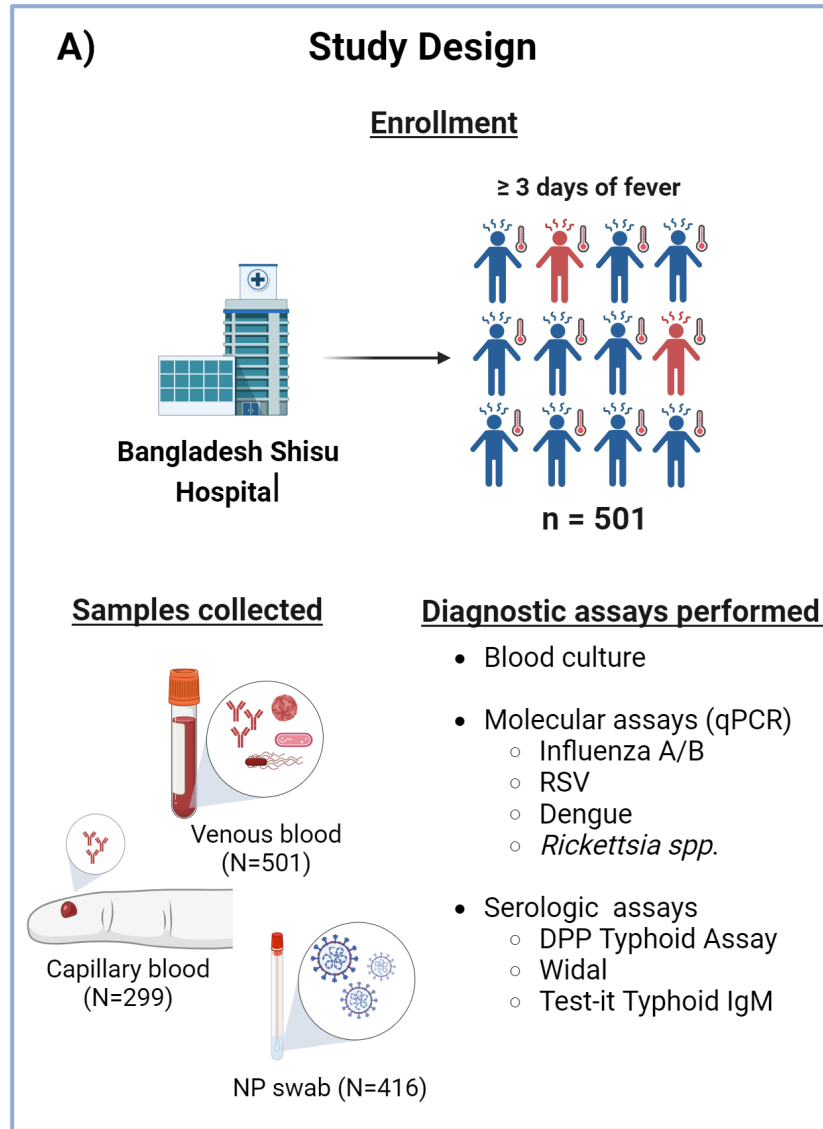


Poster #70

Dr. Sira Jam Munira



CHRF team



DPP Typhoid Assay

- We used Bayesian latent class models incorporating the results from all the typhoid and alternative etiology diagnostics to estimate the true sensitivity and specificity of DPP Typhoid
- The AUC for the DPPT in distinguishing typhoid from alternative etiologies was 97% (95% CI: 94-99%).

Dr. Sira Jam
Munira
Poster #70

Test	Sensitivity	Specificity	Balanced accuracy
DPPT assay	93% (87 - 97)	89% (85- 93)	91% (87 - 94)
Test-It	54% (49 - 59)	100% (100 – 100)	77% (74 - 79)
Widal \geq 1:160	48% (43 - 53)	92% (90 – 94)	70% (67 - 73)
Blood culture	62% (55 - 69)	100% (100 – 100)	81% (78 - 85)

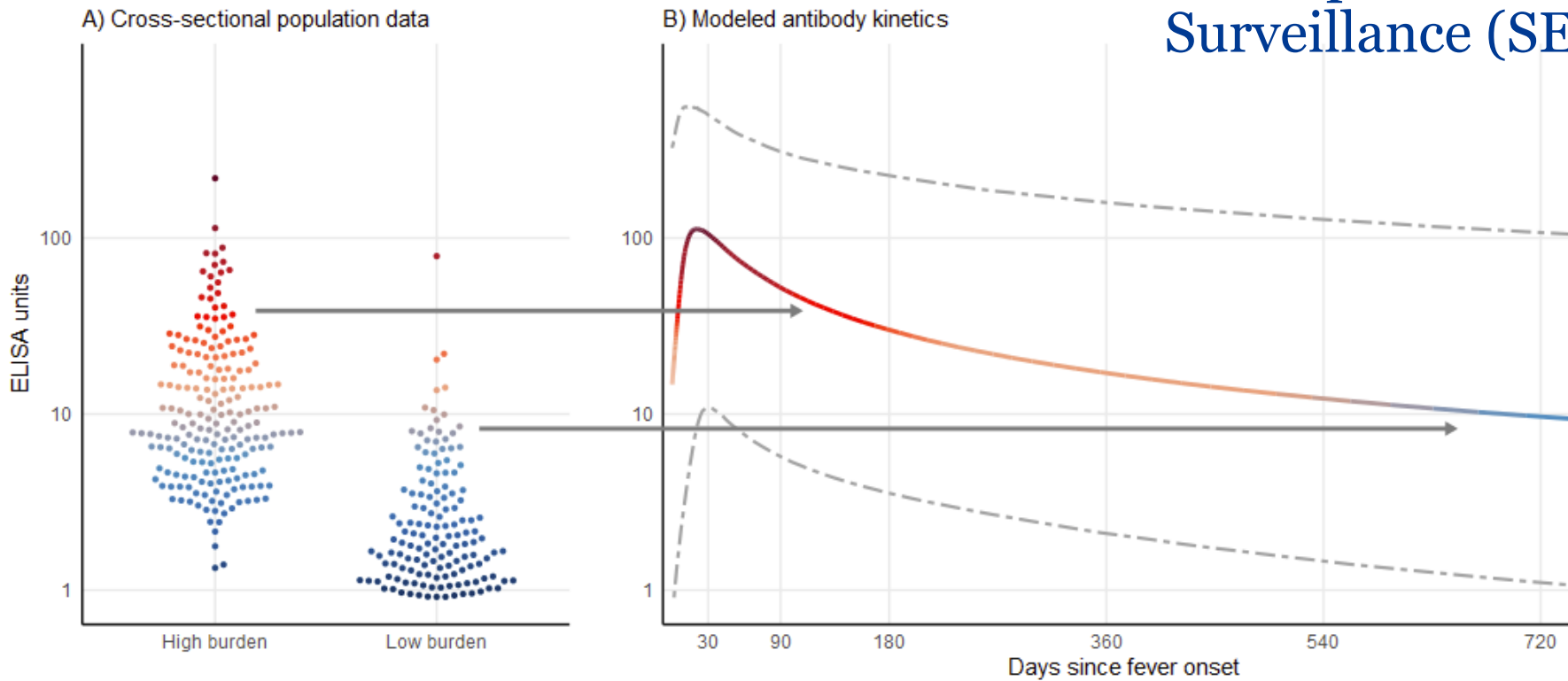
Dr. Zahida Azizullah
will share the FIND
analysis of the DPP
Typhoid Assay

11 am tomorrow

Using HlyE Ig for sero-surveillance

- Serological surveillance may be a more versatile and cost-effective approach to evaluating the burden of disease
- Overcomes some of the limitations of current culture-based surveillance
- Available for countries that lack infrastructure for culture-based surveillance

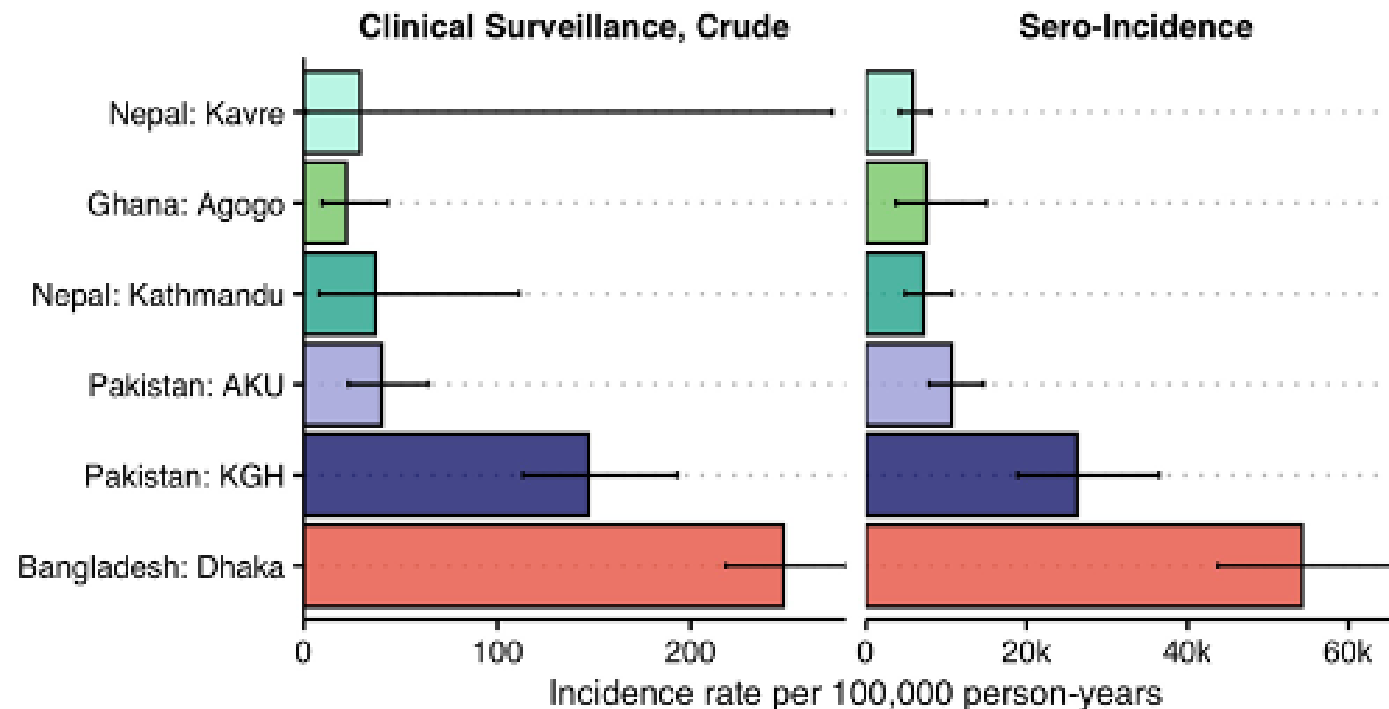
Sero-epidemiology and Environmental Surveillance (SEES) Study



- Took longitudinal data from >1400 cases and used Bayesian hierarchical modeling to estimate the antibody kinetics of HlyE
- We then apply the cross-sectional data to estimate time-since infection and incidence

Aiemjoy et al, *Lancet Microbe*, 2022

Comparison of estimates for crude and adjusted clinical enteric fever incidence with typhoidal *Salmonella* seroincidence



Conclusion

Diagnostics

- We have promising new diagnostic tools based on the detection of IgA responses to LPS and HlyE
- Today Poster #70
- December 7th at 11 am

Serosurveillance

- We have a new tools for sero-surveillance tools for enteric fever based on the antibody detection
- Today at 1:30
 - Bridging the gap: environmental and sero-surveillance for estimating typhoid burden and supporting vaccine introduction.

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