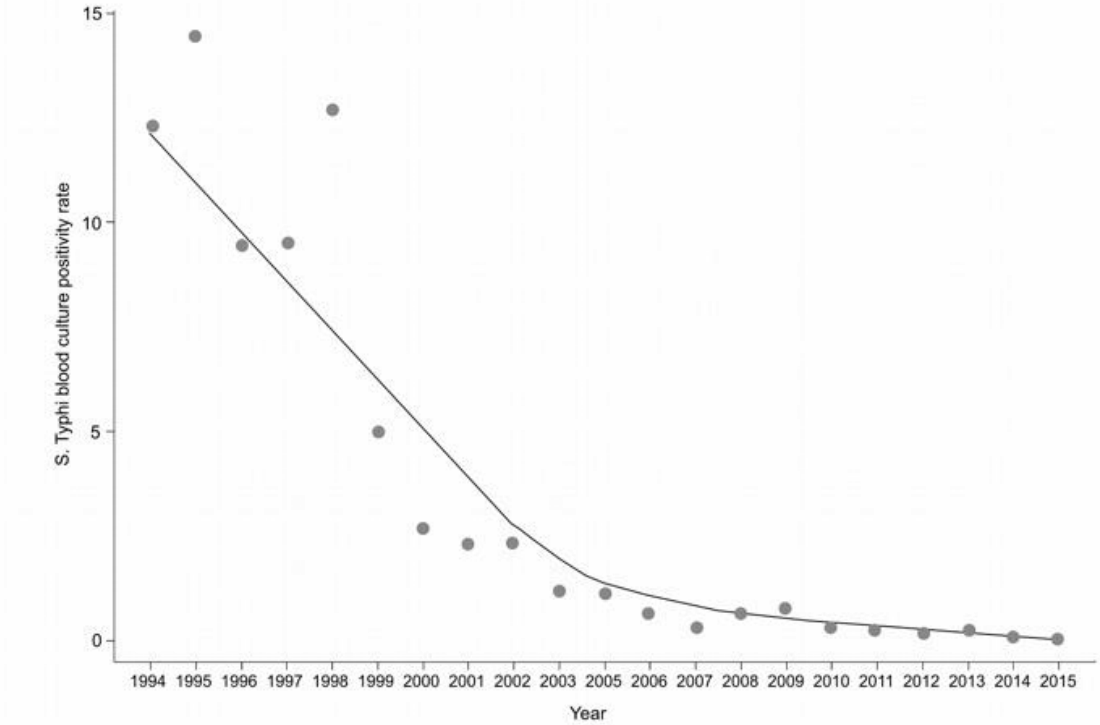
Where are we with diagnosing typhoid fever?

Stephen Baker

26th March 2019

Vietnam



Total cultures	4045	4947	3775	3640	4694	3438	3596	3444	3878	3985	4554	4764	6529	6325	4497	7543	8777	8781	9774	10346	9631
S. Typhi positive	497	716	357	346	599	171	96	80	91	49	52	30	20	40	34	24	21	14	20	9	7

The paper

Baker *et al. BMC Infectious Diseases* 2010, **10**:45
http://www.biomedcentral.com/1471-2334/10/45

BMC Infectious Diseases

COMMENTARY Open Access

Searching for the elusive typhoid diagnostic

Stephen Baker[1,2*], Michael Favorov[3], Gordon Dougan[4]

Abstract

Typhoid (enteric) fever is still a common disease in many developing countries but current diagnostic tests are inadequate. Studies on pathogenesis and genomics have provided new insight into the organisms that cause enteric fever. Better understanding of the microorganisms explains, in part, why our current typhoid methodologies are limited in their diagnostic information and why developing new strategies may be a considerable challenge. Here we discuss the current position of typhoid diagnostics, highlight the need for technological improvements and suggest potential ways of advancing this area.

Probably needs an update

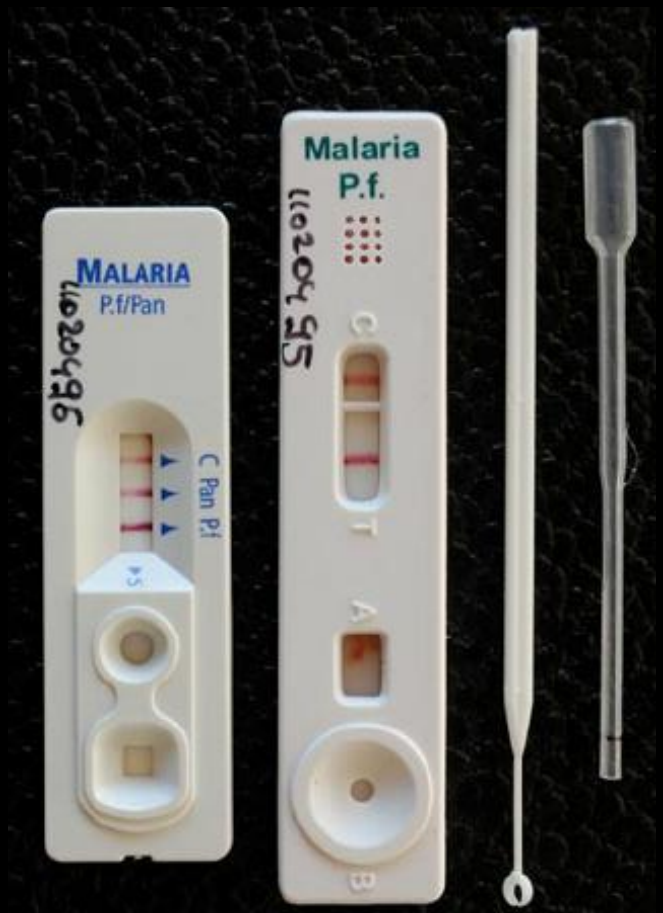
Medical advances

- We live in a period of amazing medical technology

- New generation vaccine technology
- Gene therapy
- Microbiome therapy
- Cancer diagnosis and treatment
- Hepatitis C cure
- HIV cure
- Reprogramming of T cells

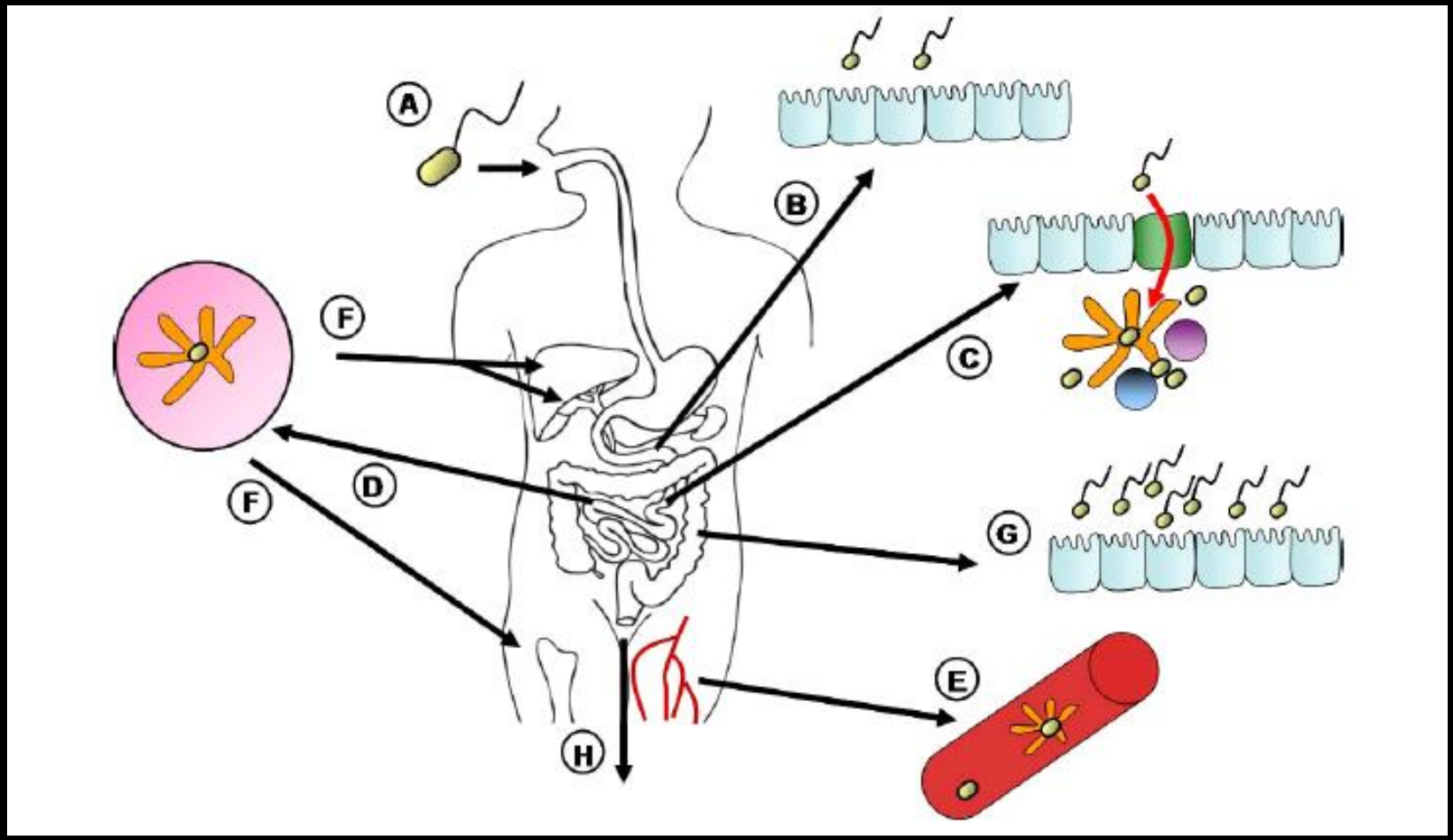
- What about typhoid?

Things didn't really work out as we hoped



Non specific febrile diseases

Typhoid isn't so easy



What do we need?

- A POC test that can identity Typhi/Paratyphi/NTS
- A POC test that can identify viral/bacterial/parasitic infections
- A POC test that can identify MDR/XDR organisms

- A test than can help us measure disease burden and incidence
- A test that can identify and estimate carriage
- A test that can identify environmental circulation

- It is unlikely that one can do all

POC tests

eLIFE elifesciences.org

RESEARCH ADVANCE

Reproducible diagnostic metabolites in plasma from typhoid fever patients in Asia and Africa

Elin Näsström[1], Christopher M Parry[2,3], Nga Tran Vu Thieu[4,5], Rapeephan R Maude[6], Hanna K de Jong[7,8], Masako Fukushima[2], Olena Rzhepishevska[1], Florian Marks[9], Ursula Panzner[9], Justin Im[9], Hyonjin Jeon[9], Seeun Park[9], Zabeen Chaudhury[9], Aniruddha Ghose[10], Rasheda Samad[10], Tan Trinh Van[4], Anders Johansson[11], Arjen M Dondorp[6], Guy E Thwaites[4,12], Abul Faiz[13], Henrik Antti[1]*, Stephen Baker[4,12,14]*

JEM

Article

Interferon-driven alterations of the host's amino acid metabolism in the pathogenesis of typhoid fever

Christoph J. Blohmke,[1] Thomas C. Darton,[1] Claire Jones,[1] Nicolas M. Suarez,[2] Claire S. Waddington,[1] Brian Angus,[3] Liqing Zhou,[1] Jennifer Hill,[5] Simon Clare,[5] Leanne Kane,[5] Subhankar Mukhopadhyay,[5] Fernanda Schreiber,[5] Maria A. Duque-Correa,[5] James C. Wright,[6] Theodoros I. Roumeliotis,[6] Lu Yu,[6] Jyoti S. Choudhary,[6] Asuncion Mejias,[2] Octavio Ramilo,[2] Milensu Shanyinde,[4] Marcelo B. Sztein,[7] Robert A. Kingsley,[5] Stephen Lockhart,[10] Myron M. Levine,[7] David J. Lynn,[8,9] Gordon Dougan,[5] and Andrew J. Pollard[1]

AMERICAN SOCIETY FOR MICROBIOLOGY | Clinical and Vaccine Immunology

CrossMark

Development of a Simple, Peripheral-Blood-Based Lateral-Flow Dipstick Assay for Accurate Detection of Patients with Enteric Fever

Iqbal Hassan Khan,[a] M. Abu Sayeed,[b] Nishat Sultana,[a] Kamrul Islam,[b] Jakia Amin,[a] M. Omar Faruk,[b] Umama Khan,[a] Farhana Khanam,[b] Edward T. Ryan,[c,d,e] Firdausi Qadri[b]

Incepta Pharmaceuticals Ltd, Savar, Dhaka, Bangladesh[a]; International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh[b]; Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts, USA[c]; Department of Medicine, Harvard Medical School, Boston, Massachusetts, USA[d]; Department of Immunology and Infectious Diseases, Harvard School of Public Health, Boston, Massachusetts, USA[e]

Journal of Infection (2017) 75, 104–114

ELSEVIER

BIAM British Infection Association

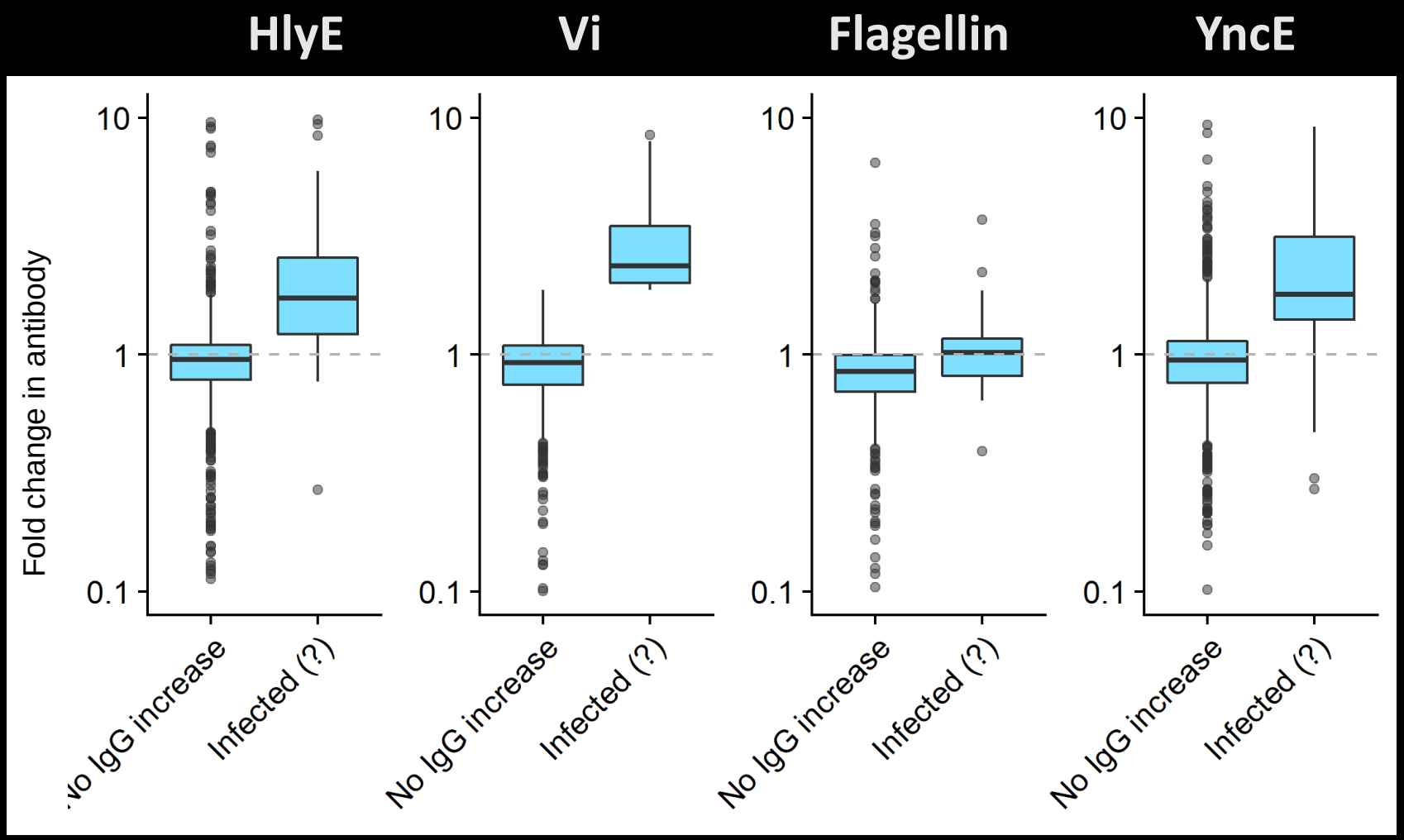
www.elsevierhealth.com/journals/jinf

An evaluation of purified *Salmonella* Typhi protein antigens for the serological diagnosis of acute typhoid fever

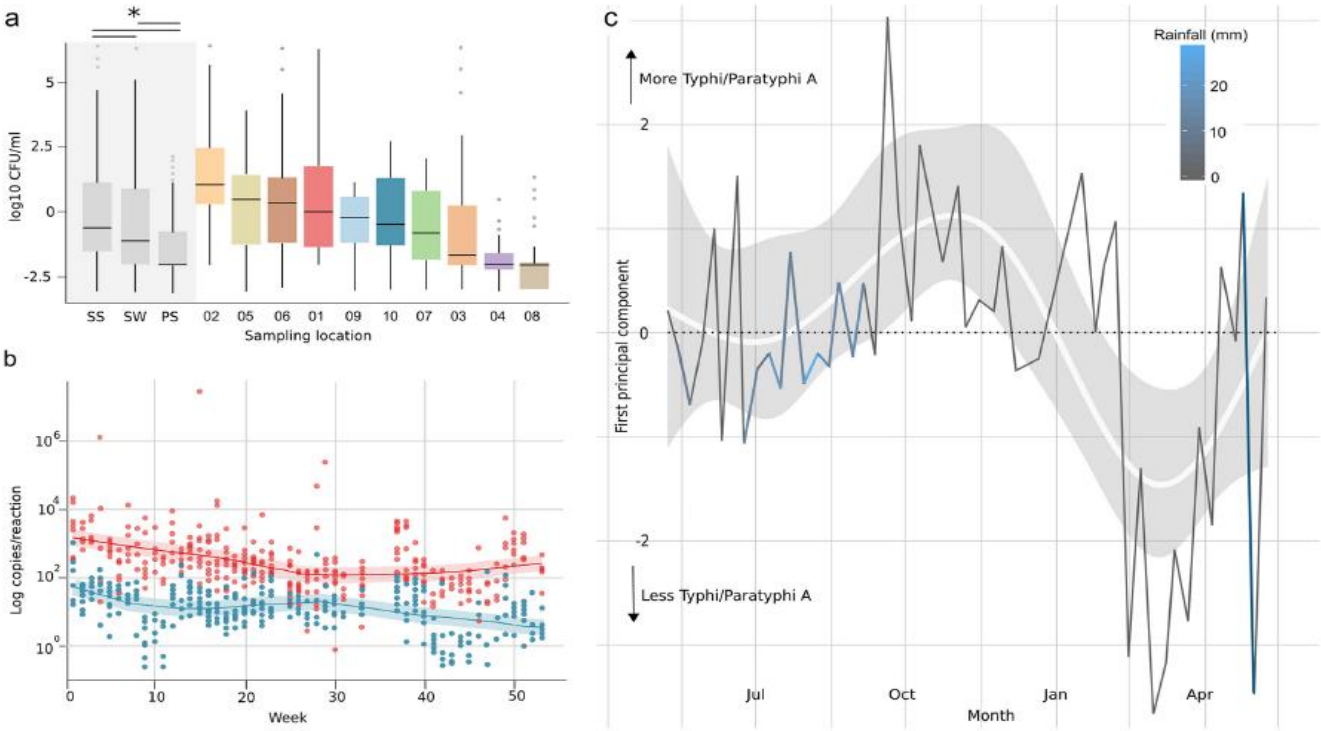
CrossMark

Incidence/Burden

"Infection" defined as increase in **CdtB** in paired samples (3 months apart)



The environment



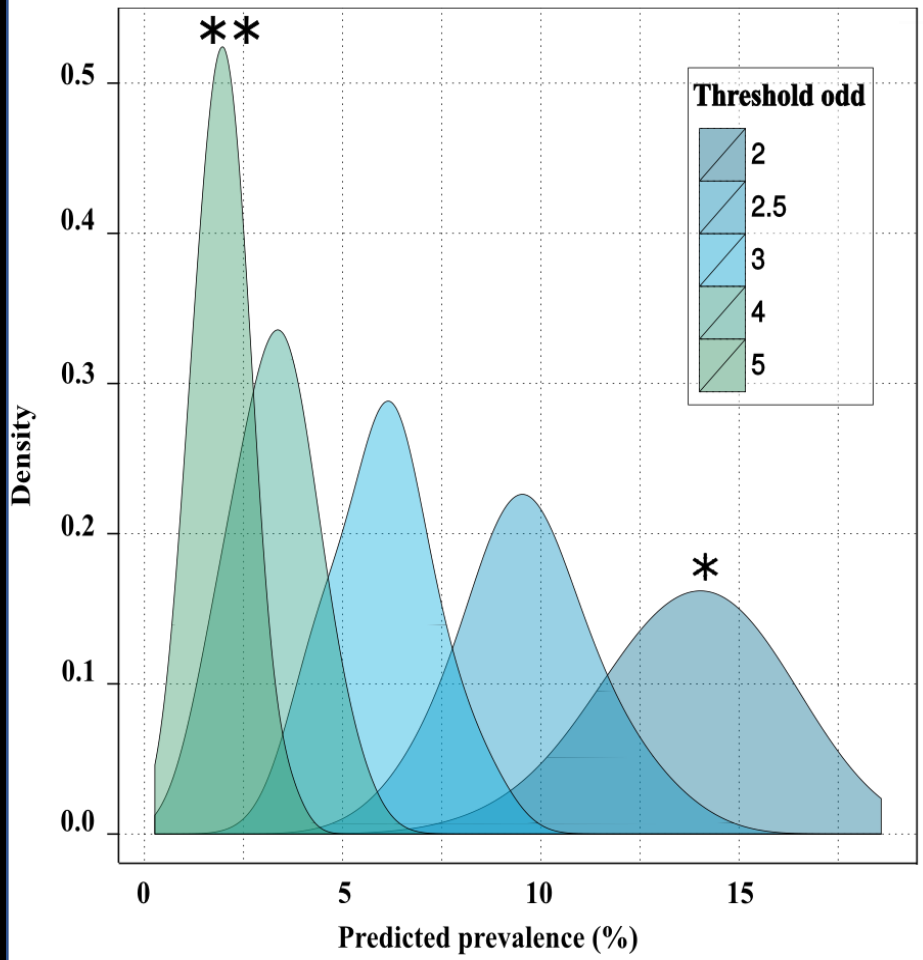
Am. J. Trop. Med. Hyg., 100(1), 2019, pp. 43–46
doi:10.4269/ajtmh.18-0428

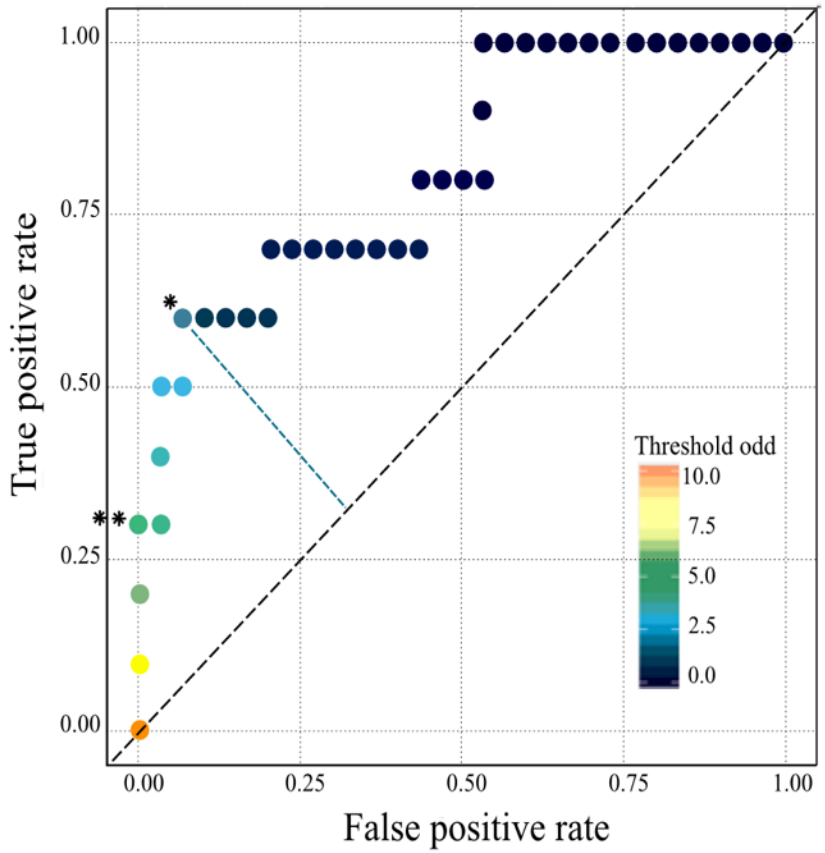
Evaluating PCR-Based Detection of *Salmonella* Typhi and Paratyphi A in the Environment as an Enteric Fever Surveillance Tool

Senjuti Saha,[1]*† Arif M. Tanmoy,[1,2]† Jason R. Andrews,[3] Mohammad S. I. Sajib,[1] Alexander T. Yu,[3] Stephen Baker,[4] Stephen P. Luby,[3] and Samir K. Saha[1,5]*

[1]*Child Health Research Foundation, Department of Microbiology, Dhaka Shishu Hospital, Dhaka, Bangladesh;* [2]*Department of Medical Microbiology and Infectious Diseases, Erasmus University Medical Centre, Rotterdam, The Netherlands;* [3]*Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University, Stanford, California;* [4]*Enteric Infections, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam;* [5]*Bangladesh Institute of Child Health, Dhaka Shishu Hospital, Dhaka, Bangladesh*

Carriage


**
*
Threshold odd
2
2.5
3
4
5
Density
0.0
0.1
0.2
0.3
0.4
0.5
0
5
10
15
Predicted prevalence (%)


True positive rate
False positive rate
0.00
0.25
0.50
0.75
1.00
Threshold odd
10.0
7.5
5.0
2.5
0.0
*
**

Outlook?

- We have made substantial inroads into assessing various aspects of typhoid detection
- We are in a good position to take some of these methods forwards into the typhoid elimination era
- We have the tools and new ones are coming

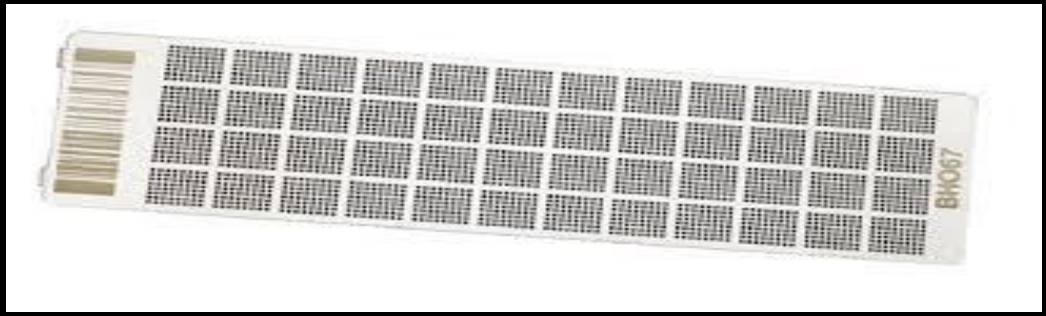
- However
  - We still lack important data
  - We lack standardized approaches
  - We lack a consensus of what is needed
  - We need to focus our efforts on the best approach

  - A POC test for typhoid?

What next?

- We need to capitalize on existing momentum
- Fill some important knowledge gaps
- Use the roll out of TCV as a mechanism to develop appropriate tests
  - Disease burden
  - Impact of vaccine
  - Replacement of Paratyphi A

- Non specific febrile disease/vaccines/AMR



Many thanks

- To the various contributors in the room
- Look forward to seeing more advances in the coming days