

## The Strategic Typhoid Alliance across Africa and Asia; A Study of Burden, Transmission, Anti-Microbial Resistance and Improved Diagnostics in Enteric Fever across Africa and Asia

James E. Meiring,<sup>1</sup> Deus Thindwa,<sup>2</sup> Mila Shakya,<sup>3</sup> Md Arifuzzman Khan,<sup>4</sup> Thomas C. Darton,<sup>1, 6</sup> Stephen Baker,<sup>6, 7, 8</sup> Buddha Basnyat,<sup>3, 7</sup> John D. Clemens,<sup>4</sup> Gordon Dougan,<sup>8</sup> Christiane Dolecek,<sup>7, 9</sup> Sarah J. Dunstan,<sup>10</sup> Melita A. Gordon,<sup>2, 11</sup> Robert S. Heyderman,<sup>2, 12</sup> Kathryn E. Holt,<sup>13, 14</sup> Virginia E. Pitzer,<sup>15</sup> Firdausi Qadri,<sup>4</sup> and Andrew J. Pollard<sup>1</sup>

<sup>1</sup>Oxford Vaccine Group, Department of Paediatrics, University of Oxford, and the NIHR Oxford Biomedical Research Centre, Oxford, United Kingdom; <sup>2</sup>Malawi Liverpool Wellcome Trust Clinical Research Programme, University of Malawi College of Medicine, Blantyre, Malawi; <sup>3</sup>Oxford University Clinical Research Unit, Patan Academy of Health Sciences, Kathmandu, Nepal; <sup>4</sup>International Centre for Diarrhoeal Diseases Research, Bangladesh (icddr,b), Dhaka, Bangladesh; <sup>5</sup>Oxford University Clinical Research Unit, Patan Academy of Health Sciences, Kathmandu, Nepal; <sup>6</sup>The Hospital for Tropical Diseases, Wellcome Trust Major Overseas Programme, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam; <sup>7</sup>Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, United Kingdom; <sup>8</sup>The Wellcome Trust Sanger Institute, Hinxton, Cambridgeshire, United Kingdom; <sup>9</sup>Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; <sup>10</sup>The Peter Doherty Institute for Infection and Immunity, The University of Melbourne, Melbourne, Australia; <sup>11</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, United Kingdom; <sup>12</sup>Division of Infection and Immunity, University College London, London, United Kingdom; <sup>13</sup>Centre for Systems Genomics, University of Melbourne, Parkville, Victoria, Australia; <sup>14</sup>Department of Biochemistry and Molecular Biology, University of Melbourne, Parkville, Victoria, Australia; <sup>15</sup>Department of Epidemiology of Microbial Diseases, Yale School of Public Health, Yale University, New Haven, Connecticut, United States of America

**Background:** With an estimated 21 million infections globally each year, typhoid fever is a significant public health problem. Recently published mathematical models have highlighted limitations in our current understanding of typhoid biology that hinder the design of effective control strategies. These data gaps include a lack of accurate age stratified incidence for disease or sub-clinical infection across different endemic settings; little understanding of the natural immunity that follows infection and the rate at which this immunity wanes; and uncertainty around the relative importance of shedding during acute disease and chronic typhoid carriage in transmission.

**Methods:** Three urban sites with known high rates of typhoid disease but with differing endemic/epidemic transmission status were selected: Blantyre (Malawi), Kathmandu (Nepal) and Dhaka (Bangladesh). A census of 100,000 people has been enumerated from which a two-year period of passive surveillance for acute cases of typhoid fever is being performed. Within these populations, ~8500 age stratified individuals will be enrolled into serological surveys to assess the rate of sub-clinical infection/exposure and enable the identification of chronic carriers. Household level studies for serological and microbiological evidence of transmission will be performed around acute and chronic cases. Healthcare utilization and water, sanitation and hygiene surveys will be performed in 735 households providing data on the percentage of population seeking healthcare at our study sites. Census and survey data is collected electronically using ODK, and data are uploaded onto

MySQL databases. Host and bacterial genetics; transcriptomic; metabolomic; microbiome; and diagnostic sub-studies are also underway.

**Results:** Census enumeration is complete. Passive and serological surveillance are ongoing, along with clinical samples for a package of novel diagnostics. Data from healthcare utilization and household transmission studies are currently being captured. A detailed quality assurance programme with appropriate quality controls has been put in place.

**Conclusion:** The STRATAA study will provide key data on age stratified incidence, transmission dynamics, sub-clinical infection, host and bacterial genetics and new diagnostics that will inform the development of typhoid control strategies through the implementation of vaccine programmes.