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Protection against invasive non-typhoidal salmonella disease

Submission date 09/03/2026	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 25/03/2026	**Overall study status** Ongoing	
Last Edited 09/06/2026	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims
This is a human infection challenge and re-challenge study investigating Salmonella Typhimurium, a member of the non-typhoidal Salmonella (NTS) subgroup.

NTS typically causes gastroenteritis, with symptoms such as diarrhoea, abdominal pain, and fever that resolve within a few days. In vulnerable groups, however, infection can progress to invasive non-typhoidal Salmonella (iNTS), where bacteria spread to the bloodstream or other sites. iNTS is most common in people with weakened immunity, including those with HIV, young children, the elderly, and individuals with risk factors such as malaria or sickle cell disease.

Globally, iNTS is a major health problem, particularly in sub-Saharan Africa, where it affects an estimated half a million people each year. The disease disproportionately affects children under five, many of whom are malnourished or have coexisting conditions. Preventive strategies, including vaccines, are urgently needed.

Who can participate?
Healthy adult volunteers aged between 18 and 50 years inclusive at time of the challenge.

What does the study involve?
This study, a “challenge and re-challenge” model, will expose participants to S. Typhimurium under controlled conditions. Participants will ingest a defined dose of the bacteria during a closely monitored inpatient stay, and then 3-6 months later will be re-challenged with the same strain. The aim is to understand how the immune system responds to repeated exposure, providing insights that can guide vaccine development.

Study Procedures and Visits
• Screening: Participants first attend an outpatient clinic for eligibility assessment.
• Challenge One: Seven days before the challenge, participants attend a clinic visit. On the challenge day, they are admitted to hospital quarantine for seven days. After discharge, they will receive daily telephone follow-up for six days, followed by an outpatient visit seven days later.

Further visits occur on day 14 and day 28 post-challenge.
• Challenge Two: Conducted 3–6 months later, following the same schedule. Outpatient visits will also be held on day 14, day 28, and day 90 post-challenge.

Across both challenge periods, participants will be carefully monitored, with additional in-person assessments if symptoms occur or if the study team deems it necessary.

The study lasts approximately 6–9 months. Each participant will:
• Attend eight scheduled outpatient visits.
• Spend a total of 14 days in hospital quarantine.
• Receive 12 daily telephone calls after discharge.
• Additional visits may be arranged for safety reasons.

What are the possible benefits and risks of participating?
There is no direct health benefit to taking part in this Study. However, participants will receive information about their general health from screening tests. Participation in the Study will help improve understanding of Salmonella (NTS) and support the development of new vaccines, which will benefit our understanding and prevention of this disease.

The main risks that might affect participants include:
• developing a gut infection (gastroenteritis) with symptoms such as diarrhoea, stomach pain, fever, or vomiting.
• developing a more serious infection outside the gut, such as a blood infection (this is uncommon).
• side effects from antibiotics (for example, stomach upset, diarrhoea, or rash).
• rare complications after infection, such as irritable bowel syndrome (and other long-term bowel symptoms), carrying Salmonella in your gut for a long time, and reactive arthritis (joint pain or swelling after infection).
• passing the infection to close contacts if strict hygiene advice is not followed.

Where is the study run from?
Department of Infectious Disease, Imperial College London, UK.

When is the study starting and how long is it expected to run for?
August 2026 to December 2028.

Who is funding the study?
Wellcome Trust, UK.

Who is the main contact?
Dr Malick Gibani, m.gibani@nhs.net

Contact information

Type(s)
Principal investigator, Public, Scientific

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Additional identifiers

Wellcome Trust grant ref
310277/Z/24/Z

Study information

Scientific Title
Protection Against Invasive NTS Disease (PAiNTS) - Identifying correlates of protection and thresholds of protective immunity using a Salmonella Typhimurium challenge-rechallenge model

Acronym
PAiNTS

Study objectives
Primary objective:
To determine the attack rate of systemic Salmonellosis after challenge and re-challenge with Salmonella Typhimurium.

Secondary objectives:
1. To describe the Salmonella colonisation rate following oral challenge and re-challenge with Salmonella Typhimurium.
2. To describe the rate of gastroenteritis following oral challenge or re-challenge with Salmonella Typhimurium.
3. To determine the fever rate following oral challenge or re-challenge with Salmonella Typhimurium.
4. To describe the Salmonella bacteraemia rate following oral challenge or re-challenge with Salmonella Typhimurium.
5. To describe the rate of systemic Salmonellosis according to an alternative composite diagnostic criteria following oral challenge or re-challenge with Salmonella Typhimurium.
6. To describe the safety of challenge and re-challenge with Salmonella Typhimurium.
7. To compare clinical features following oral challenge or re-challenge with Salmonella Typhimurium.
8. To compare microbiological features of gastrointestinal infection following oral challenge or re-challenge with Salmonella Typhimurium.
9. To compare microbiological features of bloodstream infection following oral challenge and re-challenge with S. Typhimurium.

10. To compare biochemical and haematological laboratory parameters following oral challenge or re-challenge with S. Typhimurium.
11. To describe and compare the serum antibody response following oral challenge and re-challenge with S. Typhimurium.

Exploratory objectives:
1. To investigate how the human microbiota interacts with oral challenge of S. Typhimurium.
2. To investigate the impact of diet on the outcome of Salmonella challenge.
3. To describe and compare cell-mediated immune response following oral challenge with S. Typhimurium.
4. To describe and compare the mucosal antibody response following oral challenge and re-challenge with S. Typhimurium.
5. To investigate novel diagnostic methods for detecting S. Typhimurium infection.
6. To describe and compare additional host immune responses following oral challenge and re-challenge of S. Typhimurium D23580 strains.
7. To evaluate host-pathogen interactions following Salmonella infection including the presence and mechanisms of Salmonella persister infected macrophages.
8. To describe participant experience following oral challenge or re-challenge with S. Typhimurium.
9. To described epigenetic markers associated with susceptibility to Salmonella infection.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 24/04/2026, London - Riverside Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 0207 104 8000; riverside.rec@hra.nhs.uk), ref: 26/LO/0316

Primary study design
Interventional

Allocation
N/A: single arm study

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Single

Purpose
Basic science

Study type(s)

Health condition(s) or problem(s) studied
Non-typhoidal Salmonella infection in healthy volunteers.

Interventions
This study is a challenge-rechallenge controlled human infection model of S. Typhimurium infection. After screening and a pre-challenge visit, participants will undergo their first challenge with S. Typhimurium D23580 at a dose of 1-5 x 10^5 Colony Forming Units (CFUs), termed the primary challenge. After a period of 3-6 months, participants will undergo a second challenge with S. Typhimurium D23580 at a dose of 1-5 x 10^5 CFU. The total study duration will be 6 – 9 months.

Based on data from the first-in-human S. Typhimurium challenge study (CHANTS study; https://clinicaltrials.gov/study/NCT05870150), the dose used for the challenge will be 1-5 x 10^5 CFU. In volunteers without prior exposure to Salmonella, this dose is estimated to cause an attack rate of 57.9% (95%CI 37.3-73.8%) using a primary endpoint of fever ≥38°C and/or bacteraemia, when administered with sodium bicarbonate.

This study will use the ST313 Lineage D23580 strain of S. Typhimurium. We will use GMP grade frozen batches of challenge stocks used in the CHANTS study. Stability testing has confirmed stable challenge doses over 2 years since manufacture.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
Salmonella Typhimurium

Primary outcome(s)
1. Sustained fever measured using tympanic temperature at daily assessments from day 0 to 7

2. Salmonella Typhimurium bacteraemia measured using blood culture positive at daily testing from day 0 to 14

Key secondary outcome(s)
1. Salmonella Colonisation measured using stool culture positive at daily testing from day 0 to 90

2. Salmonella gastroenteritis measured using clinical diagnosis at daily assessments from day 0 to 14

3. Mild, moderate or severe diarrhoea measured using the Bristol Stool Chart observation at daily assessments from day 0 to 14

4. Fever ≥38°C on ≥2 occasions ≥12 hours apart measured using tympanic temperature at daily assessments from day 0 to 14

5. Any fever measured using tympanic temperature at daily assessments from day 0 to 14

6. Salmonella bacteraemia alone measured using blood culture positive at daily tests from day 0 to 14

7. Salmonella Typhimurium bacteraemia with or without fever measured using blood culture positive, tympanic temperature at daily assessments from day 0 to 14

Completion date
30/12/2028

Eligibility

Key inclusion criteria
1. Agree to give informed consent for participation in the study.
2. Aged between 18 and 50 years inclusive at time of challenge.
3. In good health as determined by medical history, physical examination, and clinical judgment of the study team.
4. Agree (in the study team's opinion) to comply with all study requirements, including capacity to adhere to good personal hygiene and infection control precautions.
5. Agree to allow his or her General Practitioner to be contacted regarding participation in the study.
6. Agree to allow study staff to access their medical history and vaccination records via a shared electronic health record and/or to contact their GP to access medical records.
7. Agree to allow UKHSA and the local health protection team to be informed of their participation in the study.
8. Agree to give his or her close contacts written information informing them of the participant's involvement in the study.
9. Agree to a period of inpatient quarantine in accordance with study protocols.
10. Agree to make every effort to be contactable 24/7 by study staff during the four weeks post challenge and re-challenge.
11. Agree to allow the study team to hold the name and 24-hour emergency contact number of a close friend, relative or housemate.
12. Agree to avoid antipyretic/anti-inflammatory treatment from the time of challenge (Day 0) until advised by a study doctor or until 14 days after challenge and re-challenge.
13. Agree to refrain from donating blood for the duration of the study.
14. Agree to provide their National Insurance/Passport number for the purposes of Trial over-volunteering prevention system (TOPS) registration and for payment of reimbursement expenses.
15. Be able to understand, retain, weigh up and communicate the study details as outlined in the participant information sheet.

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. History of microbiologically confirmed Salmonella infection prior to the primary challenge.
2. History of significant organ-specific and/or systemic disease that could interfere with trial conduct or completion. Including, but not restricted to: Cardiovascular disease, vascular disease, respiratory disease, haematological disease, endocrine disorders, renal/bladder disease, biliary tract disease, previous cholecystectomy, gastro-intestinal disease (including specifically a current requirement for antacids, H2-receptor antagonists, proton pump inhibitors or laxatives, inflammatory bowel disease and confirmed diagnosis of irritable bowel syndrome), neurological disease, metabolic disease, autoimmune disease, psychiatric illness requiring hospitalisation, known or suspected drug and/or alcohol misuse disorder, chronic/active infectious disease, severe infection requiring hospitalisation for intravenous antibiotics within the last 10 years, history of recent malaria infection, joint replacement, any orthopaedic/osseous implanted prosthesis, other internal implanted devices e.g. permanent pacemaker, any known or suspected impairment/alteration of immune function (including Human Immunodeficiency Virus infection, recent treatment for malignant disease with immunosuppressive chemotherapy or radiotherapy, solid organ or bone marrow transplant, recent high-dose steroid treatment).
3. Receipt of immunoglobulin or any blood product transfusion within 3 months of study start.
4. History of cancer (except squamous cell or basal cell carcinoma of the skin and cervical carcinoma in situ).
5. Moderate or severe depression or anxiety at screening or challenge.
6. Weight less than 50kg.
7. Anyone taking long-term medication (e.g. analgesia, anti-inflammatories or antibiotics) that may affect symptom reporting or interpretation of the study results.
8. Contraindication to cephalosporin, fluroquinolone, or macrolide antibiotics.
9. Female participants who are pregnant, lactating, or unwilling to ensure that they or their partner use effective contraception during the study.
10. Have a full-time, part-time, voluntary occupations or studies involving: Clinical healthcare work, social work with direct contact with young children (attending pre-school groups or nursery or aged under 2 years) or other clinically vulnerable children/adolescents, clinical or social work with direct contact with highly susceptible patients or persons, commercial food handling.
11. Have close household contact with: young children (attending pre-school groups, nursery or those aged less than 2 years), immunocompromised individuals, pregnant women, people over 70 years old.
12. Scheduled elective surgery or other procedures requiring general anaesthesia during the study period.
13. Participants who have participated in another research study involving an investigational product that might affect risk of Salmonella infection or compromise the integrity of the study within the 30 days prior to enrolment (e.g. significant volumes of blood already taken in previous study).
14. Detection of any abnormal results from screening investigations, unless deemed not clinically significant.
15. Any other social, psychological or health issues which, in the opinion of the study staff, may: put the participant or their contacts at risk because of participation in the study, adversely affect the interpretation of the primary endpoint data, impair the participant's ability to participate in the study.
16. Have previously received any experimental Salmonella vaccine as part of a clinical trial or

participated in previous Salmonella challenge studies (with ingestion of challenge agent).
17. Have a prolonged corrected QT interval (>450 milliseconds) on ECG screening.
18. Screening blood test positive for HLA-B27.

Date of first enrolment
14/08/2026

Date of final enrolment
01/08/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
England
W2 1BL

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type

Funder Name
Wellcome Trust

Alternative Name(s)

Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository to be created during the study as part of the program of activities. The datasets generated and/or analysed during the current study will be published as a supplement to the results publication.

IPD sharing plan summary
Published as a supplement to the results publication, Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	24/04/2026	09/06/2026	No	Yes
Protocol file	version 1.1	24/04/2026	09/06/2026	No	No