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Typhoid conjugate vaccine booster dose study

Submission date 07/04/2025	**Recruitment status** Not yet recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 17/04/2025	**Overall study status** Ongoing	
Last Edited 09/06/2025	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims
Typhoid fever is a bacterial infection that can cause severe disease and even death. Typhoid is spread through contaminated food and water, due to poor hygiene and sanitation conditions. In Nepal, typhoid fever causes a lot of disease, mostly in children.
There is a vaccine called the typhoid conjugate vaccine that can help prevent typhoid fever. Many countries, like Nepal in 2022, have started giving this vaccine to children as part of the routine childhood immunisation programme. New information from a study in Bangladesh shows that the vaccine might not work as well after three years, especially for children who had the vaccine when they were very young (under 2 years old). This is a problem because children usually get typhoid fever when they start school (around 5-6 years old). This means they might not be protected even if they had the vaccine as infants.
This study will test whether giving children a booster (an extra dose) of the vaccine before they start school will help keep them protected from typhoid fever. The study will try two different brands of the vaccine (called Typbar or Typhibev) to see which works best. This way, if the booster works well, governments will have more choices to help protect children from typhoid fever.

Who can participate?
Children who received the Vi-TT vaccine at 9 months to 2.5 years of age as part of the TyVAC study (OxTREC 15-17; NHRC 170-2017)

What does the study involve?
There are three parts involved in the study for participants:
1. Booster vaccination: participants will receive a second dose of a typhoid conjugate vaccine. This will be one of two brands of the vaccine: either the one used in the previous TyVAC study (Typbar) or the one used in the Nepal government schedule (Typhibev). These vaccines are both licensed for use in Nepal and have a good safety record.
2. Scheduled blood draws and follow-up visits: to monitor how well the vaccine is working and to check participants' overall health, participants will undergo a few blood tests and follow-up assessments at specific times throughout the study. On the day of vaccination, a blood sample will be taken before administering the vaccine. Follow-up visits will occur at 28 days, 6 months, and 18 months post-vaccination. During these visits, a research doctor will carry out a physical examination, collect blood samples to evaluate the immune response to the vaccine, and track and document any adverse events or illnesses. Additionally, participants will be contacted

periodically via phone or home visits to ensure their well-being and address any concerns.
3. Fever clinic attendance: in addition to the above, if a participant has a fever during the study period, they should attend Patan Hospital, where there will be study clinics. At the clinic, participants will be assessed, and if they have had a fever for over 48 hours, a blood sample to look for typhoid infection will be taken.

What are the possible benefits and risks of participating?
Benefits: The booster vaccine is designed to increase and prolong protection against typhoid fever compared to the regular vaccine. It will provide participants with increased and sustained protection and contribute to improving overall public health by supporting better vaccination strategies and policies.
Participants will also receive health check-ups by a doctor at the scheduled follow up visits (four visits total). If a participant develops a fever during the 18 months of the trial, they will be able to access routine medical care (including investigations) and treatment through the study hospital, and all costs will be covered by the study. Participants will also receive 500 NRS to cover travel costs for each scheduled study visit (four in total).
Risks: When having blood samples taken, participants may develop a small bruise afterwards, which should fade in a few days. Apart from the minimal risks associated with routine childhood vaccinations, such as mild pain and acute fever, there are no additional risks to participating in the study

Where is the study run from?
Patan Academy of Health Science, Kathmandu (Nepal)

When is the study starting and how long is it expected to run for?
September 2024 to November 2026

Who is funding the study?
The Wellcome Trust (UK)

Who is the main contact?
Prof. Andrew Pollard, info@ovg.ox.ac.uk

Contact information

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Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
OVG2024/03, OxTrec 11-24

Study information

Scientific Title
Safety and immunogenicity of heterologous versus homologous prime-boost TCV schedules in Nepalese children: a non-inferiority trial

Acronym
TyBoost

Study objectives
To determine if the immunogenicity following a heterologous booster is non-inferior to a homologous booster in children who received a single dose of Vi-TT at <2.5 years old.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 17/09/2024, Oxford Tropical Research Ethics Committee (OxTREC) (University of Oxford Research Services, Research Governance Ethics & Assurance Boundary Brook House, Churchill Drive, Oxford, OX3 7GB, United Kingdom; +44 (0)1865 (2)82106; oxtrec@admin.ox.ac.uk), ref: 11-24

2. Submitted 23/01/2025, Nepal Health Research Council (NHRC) (Ramshah Path, Kathmandu, 7626, Nepal; +977 (0)1 5327460; nhrc@nhrc.gov.np), ref: -

Study design
Randomized observer and participant-blinded two-arm non-inferiority trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Safety

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Typhoid fever

Interventions
This is a randomised, observer and participant-blinded two-arm non-inferiority trial designed to compare the immunogenicity of a booster dose of either Vi-TT (homologous) or Vi-CRM197 (heterologous) vaccine given to children who received Vi-TT under 2.5 years as part of the TyVAC study (NHRC 170/2017; OxTREC 15-17). Participants vaccinated with vi-TT in the TyVAC study

who were aged 9 months to 2.5 years of age at the time of vaccination will be eligible for inclusion in the trial.

Participants will be randomised (block randomisation) 1:1 to receive a dose of either:
1. Vi polysaccharide-tetanus toxoid conjugate vaccine (Vi-TCV). Trade name: Tybar-TCV, Bharat-Biotech or
2. Vi polysaccharide conjugated to CRM197 (Vi-CRM197). Trade name: TYPHIBEV®, Biological E. Limited

Participants will be followed up for 18 months. Blood samples will be collected at four timepoints to assess immunogenicity. If participants develop a fever during that time, they will be asked to come to the hospital for review. If they have a fever over 38 degrees C, or if they have had a fever for 2 or more days, they will get treatment and a blood test to check if they have typhoid fever. The cost of treatment for suspected or confirmed typhoid will be covered by the trial. All participants will also be monitored for safety outcomes associated with the vaccine.

Intervention Type
Biological/Vaccine

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Phase III

Drug/device/biological/vaccine name(s)
Vi polysaccharide-tetanus toxoid conjugate vaccine (Vi-TCV), trade name: Tybar-TCV, Bharat-Biotech; Vi polysaccharide conjugated to CRM197 (Vi-CRM197), trade name: TYPHIBEV®, Biological E.Limited

Primary outcome measure
Current primary outcome measure as of 09/06/2025:

The immunogenicity following a homologous or heterologous booster vaccination in children who received a single dose of Vi-TT at <2.5 years old is measured using anti-Vi IgG levels in a blood sample taken at 28 days post booster vaccination.

Previous primary outcome measure:

The immunogenicity following a homologous or heterologous booster vaccination in children who received a single dose of Vi-TT at <2.5 years old is measured using anti-Vi IgG and anti-Vi IgA levels in a blood sample taken at 28 days post booster vaccination.

Secondary outcome measures
1. Vaccine safety, measured as the proportion of participants developing all adverse events within the first 7 days post-vaccination, and serious adverse events within 6 months of vaccination as determined through self-reporting at follow-up contacts at 7 days, 28 days and 6 months post booster vaccination
2. The kinetics of immunogenicity following heterologous and homologous boosters in children

who received a single dose of Vi-TT at <2.5 years old will be measured using anti-Vi IgG and anti-Vi IgA levels in blood samples taken at Day 0 (pre booster), Day 28, 6 months and 18 months post booster vaccination.
3. The incidence of typhoid and paratyphoid disease in the boosted participants measured through blood culture confirmed cases of typhoid or paratyphoid fever from passive surveillance in participants throughout the study period

Overall study start date
17/09/2024

Completion date
30/11/2026

Eligibility

Key inclusion criteria
The participant must satisfy all the following criteria to be eligible for enrolment:
1. Parent/legal guardian is willing and competent to provide informed consent. If the participant is 7 years of age or older, assent will also be sought
2. Between 9 months and 2.5 years of age at time of initial vaccination with Vi-TT
3. In good health on the day of vaccination according to the attending doctor
4. Parent/legal guardian confirms that their child will be willing and able to comply with study requirements including follow-up contact, according to the schedule
5. Live within the study catchment area at the time of booster vaccination

Participant type(s)
Other

Age group
Child

Lower age limit
5 Years

Upper age limit
10 Years

Sex
Both

Target number of participants
240 (120 in each arm)

Key exclusion criteria
The participant will not be enrolled if any of the following criteria apply:
1. They have a known allergy to any of the vaccine components
2. Any medical or social reasons that will prevent the participant from conforming to the study requirements as judged by a medical professional
3. Any congenital or acquired immunodeficiency that could impact vaccine responses
4. They are planning to move away from the catchment area within the next 6 months

Date of first enrolment
01/12/2025

Date of final enrolment
02/01/2026

Locations

Countries of recruitment
Nepal

Study participating centre
Patan Academy of Health Services, Patan Hospital
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Sponsor type
University/education

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ROR
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Funder(s)

Funder type
Research organisation

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

Publication and dissemination plan
It is planned that the results of this trial will be published in high-impact peer-reviewed journals within 1 year of the conclusion of the trial, around November 2027.

Intention to publish date
30/11/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Andrew Pollard (info@ovg.ox.ac.uk).

IPD sharing plan summary
Available on request, Published as a supplement to the results publication