ISRCTN10482904 https://doi.org/10.1186/ISRCTN10482904

# The impact of BCG vaccination on the response to other vaccines among Ugandan adolescents (POPVAC C)

**Submission date**
12/03/2019

**Recruitment status**
No longer recruiting

**Registration date**
01/04/2019

**Overall study status**
Completed

**Last Edited**
21/10/2024

**Condition category**
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
Infectious diseases remain very common in low-income countries. Vaccines protect people against infectious diseases, but several important vaccines do not work as well in low-income countries compared to high-income countries. BCG is the only licensed vaccine for prevention of tuberculosis. It is given at birth in countries where tuberculosis is common and works well at preventing tuberculosis in childhood, but less well at preventing tuberculosis later in life. However, it is thought that BCG may have other effects unrelated to tuberculosis (so called “non-specific” effects”). One of these is that BCG might improve how someone responds to other unrelated vaccinations. This study aims to investigate whether giving BCG beforehand will improve the immune response to unrelated vaccines.

Who can participate?
Healthy volunteer children (aged 13-17, with no gender restriction) who are participating in the Entebbe Mother and Baby Study.

What does the study involve?
Children will be randomly allocated to receive either BCG re-vaccination or no BCG re-vaccination. Four weeks later, they will be vaccinated against yellow fever and typhoid, and against Human Papilloma Virus (which can cause cancer of the cervix [or opening] of the womb, and other cancers). Later (at 28 weeks from enrolment into the study) they will receive a booster vaccine against tetanus and diphtheria. Four weeks after receiving each of these vaccinations (eight weeks after receiving BCG), their immune responses to each vaccine will be measured.

What are the possible benefits and risks of participating?
Participants will benefit from receiving the vaccines as they are expected to provide protection against infectious diseases. Participants and their families will benefit from improved understanding of vaccines. No major risks to the participants are anticipated since all the vaccines to be given are licensed and known to be safe. The main risk to participants will be time

lost from school work, and we will work with parents to minimise this. Very rarely, a vaccine may cause a severe allergic reaction, so individuals who have previously suffered a possible allergic reaction to vaccines or their components will not be included in the study.

Where is the study run from?
The host institution for the study will be the Medical Research Council/Uganda Virus Research Institute and London School of Hygiene and Tropical Medicine Uganda Research Unit (MRC/UVRI & LSHTM), Entebbe, Uganda.

When is the study starting and how long is it expected to run for?
May 2019 to May 2021

Who is funding the study?
The study is funded by the UK Medical Research Council.

Who is the main contact?
Professor Alison Elliott, alison.elliott@lshtm.ac.uk

# Contact information

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Public

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Scientific

### Contact name
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# Additional identifiers

### Clinical Trials Information System (CTIS)
Nil known

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number
v1

# Study information

### Scientific Title
Population differences in vaccine response: the role, reversibility and mediators of immunomodulation by chronic infections in the tropics (POPVAC). Trial protocol C: The impact of BCG “pre-immunisation” on the response to vaccines among Ugandan adolescents participating in the Entebbe Mother and Baby Study

### Acronym
POPVAC C

### Study objectives
BCG “pre-immunisation” modifies the response to subsequent vaccines

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
1. Approved 05/09/2018, UVRI REC (The REC secretariat, Uganda Virus Research Institute, P.O Box 49, Entebbe, Uganda; +245 (0)414321962; directoruvri@uvri.go.ug), ref: GC/127/18/09/682
2. Approved 12/06/2019, LSHTM Ethics (LSHTM, Keppel St, London WC1E 7HT; ethics@lshtm.ac.uk; +44 (0)207 6368636), ref: 16034
3. Approved 07/05/2019, UNCST ethics (Plot 6, Kimera Road, Ntinda, P.O. Box 6884, Kampala, Uganda; +256 (0)414 705500; info@uncst.go.ug), ref: HS 2491
4. Approved 28/05/2019, NDA (Secretariat office Kampala, Plot 19 Lumumba Avenue, P.O. Box 23096, Kampala, Uganda; +245 (0) 417 788 100; ndaug@nda.or.ug), ref: CTA0094

### Study design
Single-centre individually randomized controlled open parallel-group trial

### Primary study design
Interventional

### Study type(s)
Other

### Health condition(s) or problem(s) studied
Vaccine responses

### Interventions
A randomisation code will be generated by the trial statistician using a randomly permuted block size. Participants will be allocated in a 1:1 ratio to receive either BCG pre-immunisation or no BCG pre-immunisation. Participants in the pre-immunisation arm will receive BCG vaccination (0.1 ml in the deltoid region of the right upper arm) four weeks before receiving a panel of other, unrelated, vaccines. Participants in the non BCG pre-immunisation arm will receive no BCG prior to receiving the other vaccines.

Blood, urine and stool samples will be collected from participants in order to determine the impact of the intervention on primary and secondary outcomes. Other characteristics will be determined by questionnaire and clinical examination.

### Intervention Type
Biological/Vaccine

### Phase
Not Applicable

### Drug/device/biological/vaccine name(s)
BCG vaccine

### Primary outcome(s)
1. BCG: BCG-specific IFN-gamma ELIspot response eight weeks post BCG immunisation
2. YF-17D: neutralising antibody titres (plaque-reduction neutralisation test) at four weeks post YF immunisation
3. Ty21a: Salmonella typhi lipopolysaccharide (LPS)-specific immunoglobulin(Ig)G concentration at four weeks post Ty21a immunisation
4. HPV: IgG specific for L1-proteins of HPV-16/18 at four weeks post HPV priming immunisation
5. Td: tetanus and diphtheria toxoid-specific IgG concentration at four weeks post Td immunisation

### Key secondary outcome(s))
1. Protective immunity. Proportions with protective neutralising antibody (YF); protective IgG levels (TT); seroconversion rates (Ty21a) at four weeks post the corresponding immunisation.
2. Response waning. Primary outcome measures (all vaccines) repeated at week 52, and area-under-the curve (AUC) analyses.
3. Priming versus boosting. Effects on priming versus boosting will be examined for HPV only, comparing outcomes four weeks after the first, and four weeks after the second vaccine dose.

### Completion date
30/04/2022

## Eligibility

### Key inclusion criteria
Participants must meet all of the following criteria to enter the trial:
1. A participant in the Entebbe Mother and Baby Study. Participants will be aged 13-17 years of age.
2. Written informed consent by parent or guardian
3. Written informed assent by participant

4. Willing to remain in the study area for the duration of the study
5. Willing to provide locator information and to be contacted during the course of the trial
6. Agree to avoid pregnancy for the duration of the trial (female only)
7. Able and willing (in the investigator's opinion) to comply with all the study requirements

## Participant type(s)
Healthy volunteer

## Healthy volunteers allowed
No

## Age group
Child

## Lower age limit
13 years

## Upper age limit
17 years

## Sex
All

## Total final enrolment
300

## Key exclusion criteria
1. Concurrent enrolment into another clinical trial. Of note, EMaBS participants enrolled into trial TB042 “Open label, dose escalation and age de-escalation for ChAdOx1 85A in Ugandan adults and adolescents, followed by a Phase IIa randomised, open-label trial among adolescents comparing ChAdOx1 85A prime followed by MVA85A boost versus BCG re-vaccination” will not be eligible to enrol into this study. If they have not already received the vaccines offered in this study, they will be given the opportunity to receive them, as a service (not as part of a study) once TB042 follow up has been completed.
2. Clinically significant history of immunodeficiency (including HIV), cancer, cardiovascular disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder and neurological illness
3. History of serious psychiatric condition or disorder
4. Previous immunisation with YF, oral typhoid or HPV vaccine; previous immunisation with BCG or Td at age >5 years
5. Concurrent oral or systemic steroid medication or the concurrent use of other immunosuppressive agents within 2 months prior to enrolment
6. History of allergic reaction to immunisation or any allergy likely to be exacerbated by any component of the study vaccines including egg or chicken proteins
7. Tendency to develop keloid scars
8. Positive HIV serology
9. Positive pregnancy test
10. Female currently lactating, confirmed pregnancy or intention to become pregnant during the trial period
11. Use of an investigational medicinal product or non-registered drug, live vaccine, or medical device other than the study vaccines for 30 days prior to dosing with the study vaccine, or

planned use during the study period
12. Administration of immunoglobulins and/or any blood products within the three months preceding the planned trial immunisation date

**Date of first enrolment**
01/06/2019

**Date of final enrolment**
26/02/2021

# Locations

**Countries of recruitment**
Uganda

**Study participating centre**
**MRC/UVRI and LSHTM Uganda Research Unit**
Plot 51-59 Nakiwogo Road
Entebbe
Uganda
NA

# Sponsor information

**Organisation**
London School of Hygiene and Tropical Medicine

**ROR**
https://ror.org/00a0jsq62

# Funder(s)

**Funder type**
Research council

**Funder Name**
Medical Research Council

**Alternative Name(s)**
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

### Funding Body Type
Government organisation

### Funding Body Subtype
National government

### Location
United Kingdom

# Results and Publications

### Individual participant data (IPD) sharing plan
The de-identified individual participant data that underlie the results reported in journal articles will be stored in a non-publically available repository (LSHTM Data Compass), together with a data dictionary. This will be done at the time of publication. Each dataset will be allocated a unique digital object identifier (DOI). Researchers who would like to access the data may submit a request through LSHTM Data Compass, detailing the data requested, the intended use for the data, and evidence of relevant experience and other information to support the request. The request will be reviewed by the Principal Investigator in consultation with the POPVAC Steering Committee, with oversight from the UVRI and LSHTM ethics committees. In line with the MRC policy on Data Sharing, there will have to be a good reason for turning down a request. Patient Information Sheets and consent forms specifically referenced making anonymised data available and this has been approved by the relevant ethics committees. Researchers given access to the data will sign data sharing agreements which will restrict the use to answering pre-specified research questions.

### IPD sharing plan summary
Stored in non-publicly available repository

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 01/11/2024 | 21/10/2024 | Yes | No |
| Protocol article | | 16/02/2021 | 05/05/2022 | Yes | No |
| Protocol article | | 16/02/2021 | 03/05/2024 | Yes | No |
| Statistical Analysis Plan | version v1.0 | 26/01/2021 | 27/01/2021 | No | No |