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Assessing optimal timing for childhood vaccines in Uganda

Submission date
05/02/2021

Recruitment status
No longer recruiting

Registration date
17/02/2021

Overall study status
Completed

Last Edited
28/06/2024

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Vaccines help protect our bodies against diseases. When a child comes into contact with a disease against which they have been vaccinated, their body will be able to recognise and fight the disease. Without vaccines, children are at increased risk of catching many serious diseases.

The World Health Organization (WHO) recommends that all children receive a number of different vaccines at specific ages. One of the vaccines recommended protects against 5 diseases called diphtheria, tetanus, whooping cough, hepatitis B and Haemophilus influenzae type b (Hib) infection, which can cause pneumonia and meningitis. This vaccine is sometimes called a DTP-containing vaccine. Many countries around the world gives this vaccine at different time points and it is not known which schedule is best. This study aims to determine the best schedule for the DTP-containing vaccine.

Who can participate?
Children aged between 42 and 50 days

What does the study involve?
Participants will be randomly allocated to one of five groups which will each involve different immunisation schedules of the vaccine containing DTP. Participants will have an equal chance of being allocated to each group. The timing of doses, and whether a child receives two or three doses (as both have been shown to be effective), will vary between each group. Children will then have blood tests taken to see whether they have antibodies for DTP before they receive their booster doses.

What are the possible benefits and risks of participating?
The benefits include the opportunity to receive vaccines for Typhoid and Varicella which are not currently included as part of the Expanded Programme on Immunisation. The risks are those associated with phlebotomy (blood-drawing), and include pain and discomfort.

Where is the study run from?
The Masaka Field site, managed by the MRC/UVRI and LSHTM Uganda Research Unit (Uganda)

When is the study starting and how long is it expected to run for?
June 2019 to June 2024

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?
1. Professor Andrew Pollard (scientific), andrew.pollard@paediatrics.ox.ac.uk
2. Sarah Kelly (public), sarah.kelly@paediatrics.ox.ac.uk

Contact information

Type(s)
Scientific

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
V1.3 November 2019

Study information

Scientific Title
Optimising diphtheria, tetanus toxoids and pertussis (DTP)-containing vaccine infant immunisation schedules in Uganda

Acronym
OPTIMMS-Uganda

Study objectives
To identify an optimal immunisation schedule for infants by comparing the immunogenicity of 5 different immunisation schedules (each based on positive immunogenicity data from previous research) including the current WHO recommended 'accelerated' schedule, investigating the effect of number, spacing and timing of doses of routine infant vaccines in the different schedule using the WHO recommended EPI schedule as the reference schedule

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 16/12/2019, Uganda Virus Research Institute (UVRI) Research Ethics Committee (Plot 51-59, Nakiwogo Rd, Entebbe, Uganda; +256 414 320 385; fayebazibwe@uvri.go.ug), ref: GC /127/19/12/754
2. Approved 24/07/2020, Uganda National Council for Science & Technology (UNSCT, Plot 6 Kimera Road, Ntinda, P.O. Box 6884, Kampala, Uganda; +256 414 705500; info@unsct.go.ug), ref: SS 5205
3. Approved 04/02/2021, National Drug Authority (Plot 19 Lumumba Avenue, P.O. Box 23096, Kampala, Uganda; +256 417 788 100/1; ndaug@nda.or.ug), ref 686/NDA/DPS/09/2020.
4. Approved 03/03/2021, OxTREC (Research Services, University Of Oxford, University Offices, Oxford, OX1 2JD, UK; +44 (0)1865 282585; oxtrec@admin.ox.ac.uk), ref: 13-20.

Study design
Multi-site randomized 5-arm non-inferiority clinical trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied

Diphtheria, tetanus toxoids and pertussis (DTP) immunity through infant immunisation schedules in Uganda

Interventions
Infants will be enrolled at study “hub” sites, located in busy and centrally located health facilities and clinics, in Masaka District, Uganda. Potential participants will be identified throughout a broader catchment area, through antenatal clinics (ANC), and early vaccination visits, and invited to come of one of the hub sites to enrol in the study, if interesteds. The study will be open-label for participants and clinical trial staff but blinded for laboratory staff. The study will assess the immunogenicity of the current DTP-Hib-HBV-containing vaccine administered in 5 different immunisation schedules

Following informed parent/legal guardian consent, enrolled infants will be randomly allocated to one of 5 main vaccination groups, and one of four booster dose schedule. Randomisation will occur electronically via a plugin on RedCAP.

The first two schedules (Groups 1 and 2) are two 'Early Pertussis' schedules and correspond to the WHO standard, and a modified, EPI schedules (two rather than 3 early doses).

Group 3 will be vaccinated according to the OptImms-proposed schedule (which is also the E-CDC recommended schedule).

Groups 4 and 5 correspond to the programs currently in use in the UK and Americas.

Blood tests will be performed at standard time points considered necessary for evaluation of vaccine responses.

The primary outcome Pertussis IgG immune response will be measured at the pre-booster dose time point, at 9 or 12 months of age. Children will receive varicella and typhoid vaccination as a benefit of participation in the study.

Vaccinations will occur over a 15-month time period, with a 24-month follow-up period for all study arms.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
DTwP-HBV-Hib vaccine (Serum Institute of India), Oral Polio Vaccine – Bi-valent, Injectable Polio Vaccine, Pneumococcal conjugate vaccine (Synflorix), Measles Rubella vaccine, Typhoid conjugate vaccine (Typbar-TCV®, Bharat-Biotech.), Yellow fever vaccine (Stamaril live attenuated, Sanofi Pasteur)

Primary outcome(s)
Pertussis IgG immune response measured using Multiplexed Immune Assay (MIA)-5 plex at the pre-booster dose time point (aged 9 or 12 months)

Key secondary outcome(s))

Current secondary outcome measures as of 28/06/2024:

1. Pertussis IgG immune response measured using MIA 4-plex at the post-prime dose time point, (aged 10, 12, 14 or 16 weeks), 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months
2. Diphtheria IgG immune response measured using MIA 5-plex using in-house reference sera calibrated against the WHO standard, at age 14 or 16 weeks, 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months. The MIA 5-plex uses in-house reference sera as standard, which are calibrated against the WHO standard.
3. Tetanus IgG immune response measured using MIA 5-plex using in-house reference sera calibrated against the WHO standard, at age 14 or 16 weeks, 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months
4. Hepatitis B virus S antigen measured using an assay currently under development at the Dutch Institute of Public Health, at age 14 or 16 weeks, 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months
5. Polyribosylribitol phosphate (PRP) Haemophilus influenzae type b (Hib) IgG immune response measured using a multiplexed immune assay, at age 14 or 16 weeks, 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months
6. Serotype specific anti-pneumococcal IgG measured in an MIA x-plex, in 1a, 2, 3 and 4 blood samples in all arms and booster groups . IVIG that has been calibrated against the 89-S serum is used as reference serum
7. Polio type I-III IgG immune response measured using a 3-plex inhibition assay, at the pre-booster timepoint (aged 9 or 12 months) and aged 24 months
8. Typhoid vi-IgG will be measured using an assay currently under development at the Dutch Institute of Public Health, in blood 2 in Arm 5 at 28 weeks , in blood 3&4b in booster group 2, 3, and 4 (12 and 24 months).
9. Serum volumes permitting YF response will be measured using plaque reduction neutralization titre (PRNT) assays, by ELISA and/or indirect fluorescent antibody test (IFA) in blood 2 in Arm 5 at 28 weeks , in blood 3&4b in booster group 2, 3, and 4 (12 and 24 months).
10. Measles IgG antibody concentrations are measured in an MIA 4-plex at all time points up to the first measles and rubella vaccine dose, if possible given blood sample volumes
11. Measles titre measured using plaque reduction neutralization titre (PRNT) assay, if possible given blood sample volume, at all time points up to the first measles and rubella vaccine dose
12. Rubella IgG response measured using MIA 4-plex, if possible given blood sample volume, at all time points up to the first measles and rubella vaccine dose. As standard, the international rubella standard (RUBI-1-94) is used, which has been calibrated against the international reference serum for measles.
13. Descriptive summary of self-reported local and systemic vaccine reactions occurring within 7 days post-vaccination collected verbally at each point of contact, using Brighton Collaboration case definitions
14. Rota virus IgG will be measured using MIA 4-plex in all blood samples of all arms and booster groups.
15. SARS-COV2 IgG and RSV IgG will be measured using MIA 4-plex in all blood samples of all arms and booster groups.

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Previous secondary outcome measures:

1. Pertussis IgG immune response measured using MIA 4-plex at the post-prime dose time point, (aged 10, 12, 14 or 16 weeks), 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months
2. Diphtheria IgG immune response measured using MIA 5-plex using in-house reference sera calibrated against the WHO standard, at age 14 or 16 weeks, 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months. The MIA 5-plex uses in-house reference sera as standard, which are calibrated against the WHO standard.
3. Tetanus IgG immune response measured using MIA 5-plex using in-house reference sera calibrated against the WHO standard, at age 14 or 16 weeks, 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months
4. Hepatitis B virus S antigen measured using an assay currently under development at the Dutch Institute of Public Health, at age 14 or 16 weeks, 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months
5. Polyribosylribitol phosphate (PRP) Haemophilus influenzae type b (Hib) IgG immune response measured using a multiplexed immune assay, at age 14 or 16 weeks, 1 month post-primary series (aged 18, 20, or 28 weeks), pre-booster timepoint (aged 9 or 12 months), post-booster timepoint (aged 10 or 13 months), and aged 24 months
6. Serotype specific anti-pneumococcal IgG measured in an MIA x-plex, at the pre-booster timepoint (aged 9 months), post-booster timepoint (aged 10 months), and aged 24 months. IVIG that has been calibrated against the 89-S serum is used as reference serum
7. Polio type I-III IgG immune response measured using a 3-plex inhibition assay, at the pre-booster timepoint (aged 9 or 12 months) and aged 24 months
8. Typhoid vi-IgG will be measured using an assay currently under development at the Dutch Institute of Public Health, at age 13 and 24 months
9. Serum volumes permitting JE response will be measured using plaque reduction neutralization titre (PRNT) assays, by ELISA and/or indirect fluorescent antibody test (IFA) at age 13 and 24 months
10. Measles IgG antibody concentrations are measured in an MIA 4-plex at all time points up to the first measles and rubella vaccine dose, if possible given blood sample volumes
11. Measles titre measured using plaque reduction neutralization titre (PRNT) assay, if possible given blood sample volume, at all time points up to the first measles and rubella vaccine dose
12. Rubella IgG response measured using MIA 4-plex, if possible given blood sample volume, at all time points up to the first measles and rubella vaccine dose. As standard, the international rubella standard (RUBI-1-94) is used, which has been calibrated against the international reference serum for measles.
13. Descriptive summary of self-reported local and systemic vaccine reactions occurring within 7 days post-vaccination collected verbally at each point of contact, using Brighton Collaboration case definitions

Completion date
30/06/2024

Eligibility

Key inclusion criteria

1. Aged between 42 and 50 days at the time of the first visit
2. Generally healthy as determined by a medical history and examination
3. Resident in the greater Masaka, Uganda study area and planning to remain in the study area for the 2 years of the study

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Child

Lower age limit
42 days

Upper age limit
50 days

Sex
All

Key exclusion criteria
1. Born at <37 weeks gestation
2. Birth weight <2.5 kg, or a current weight of <3 kg at 6 weeks of age, as determined by a medical professional
3. Prior receipt of any vaccination except polio, hepatitis B, or BCG
4. Planned administration of vaccines other than the study vaccines (with the exception of vaccines against rotavirus, hepatitis A & B, inactivated influenza and varicella, which can be administered 14 days before or after study vaccines; polio and measles/rubella vaccines as part of national campaigns; and BCG vaccines which will be administered when indicated by national programme)
5. Parents who plan to move out of the geographical study area
6. Concurrently participating in another clinical study, which includes blood draws or IMPs, at any time during the study period, in which the participant has been or will be exposed to an investigational or a non-investigational product (pharmaceutical product or device)
7. Any major congenital defects, serious chronic illness, significant disease, disorder, family history or diagnosis of immunosuppressive condition, or medical treatments which, in the opinion of the Investigator, may either put the participants at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study
8. Use of any investigational or non-registered product (drug or vaccine) within 30 days preceding the vaccination, or planned use during the study period
9. Known allergy to any vaccine components

Date of first enrolment
01/10/2021

Date of final enrolment
31/07/2022

Locations

Countries of recruitment
Uganda

Study participating centre
MRC/UVRI and LSHTM Uganda Research Unit (Entebbe)
Plot 51-59
Nakiwogo Road
Entebbe
Uganda
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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

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

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to their size, but analyses will be published with summary data.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		21/07/2023	24/07/2023	Yes	No
Participant information sheet	version V2.1	17/02/2020	01/03/2021	No	Yes
Participant information sheet	version 3.0	24/02/2021	11/02/2022	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes