ISRCTN72821613 https://doi.org/10.1186/ISRCTN72821613

Pneumococcal vaccine schedules acquisition, immunogenicity, and pneumococcal conjugate and yellow fever vaccine co-administration study

Submission date
08/10/2019

Recruitment status
No longer recruiting

Registration date
28/11/2019

Overall study status
Completed

Last Edited
14/01/2025

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
Global control of pneumococcal disease is limited by the cost of pneumococcal conjugate vaccines (PCV). In 2009, The Gambia introduced PCV using a routine three-dose schedule without a booster dose (a '3+0' schedule). The introduction of PCV has led to large reductions in invasive pneumococcal disease due to serotypes included in the vaccine and severe pneumonia. Now that vaccine-type invasive pneumococcal disease is controlled, the Pneumococcal Vaccine Schedules (PVS) study will compare the ongoing use of the 3+0 schedule with transition to an alternative two-dose schedule that includes a booster dose one early dose and one booster dose. This proposed PVS sub-study aims to evaluate the effect of the booster dose on nasopharyngeal pneumococcal acquisition, the immunogenicity of the two schedules, and the co-administration of PCV with Yellow Fever vaccine.

Who can participate?
Infants aged 0-6 weeks resident in the PVS-AcqImm study area

What does the study involve?
PCV13 will be administered through the structures of the national immunisation programme with delivery of each schedule in two groups of 14 clusters. Sub-study participants in the alternative schedule clusters will be further allocated to two groups, one receiving co-administered PCV13 and Yellow Fever vaccine and one receiving PCV13 and Yellow Fever vaccine separated by one month. The researchers will measure the rate of pneumococcal nasopharyngeal acquisition in the 5 months after administration of the PCV13 booster dose. They will also measure pneumococcal antibody concentrations at 18 months of age and the proportion of children with protective Yellow Fever antibody levels one month after administration of Yellow Fever vaccine.

What are the possible benefits and risks of participating?
The possible benefits are enhanced clinical care for participants and the potential future

benefits for the population of reduced numbers of immunization injections and a more sustainable EPI. The possible risks of participating are that the risk of pneumococcal disease may be different in the two groups. Both immunization schedules will provide significant protection against vaccine-type pneumococcal disease. It is difficult to estimate the magnitude of this potential risk, but it is very small and in the order of one excess case of vaccine-type disease during the course of the study.

Where is the study run from?
This is a collaborative study between the Gambia Government Ministry of Health and the Medical Research Council Unit, The Gambia at the London School of Hygiene & Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
January 2018 to June 2025

Who is funding the study?
1. Bill and Melinda Gates Foundation
2. Mucosal Pathogens Research Unit, National Institutes of Health Research (UK)
3. Medical Research Council
4. Wellcome Trust
5. UKAID

Who is the main contact?
Dr Grant Mackenzie
gmackenzie@mrc.gm

Contact information

Type(s)
Scientific

Contact name
Dr Grant Mackenzie

ORCID ID
https://orcid.org/0000-0002-4994-2627

Contact details
MRCG at LSHTM Field Station
Basse
Gambia
273
+220 (0)7207826
gmackenzie@mrc.gm

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
17683

Study information

Scientific Title
The effect of a two-dose compared to a three-dose schedule of pneumococcal conjugate vaccine on pneumococcal acquisition, immunogenicity, and co-administration of pneumococcal conjugate and yellow fever vaccines

Acronym
PVS-AcqImm

Study objectives
The hypothesis of the acquisition sub-study is that the PCV13 booster dose at 9 months of age in the 1+1 schedule reduces acquisition of VT pneumococci compared to the 3+0 schedule. The hypotheses of the immunogenicity/co-administration sub-study are that VT specific IgG responses are superior at 18 months of age following administration of the PCV13 booster dose at 9 months of age in the 1+1 schedule compared to the 3+0 schedule and that immune responses to YF vaccine are non-inferior when administered with compared to separately from PCV13.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 14/08/2019, Gambia Government/Medical Research Council Unit Joint Ethics Committee (MRC Unit The Gambia at LSHTM, Fajara, PO Box 273 Banjul, The Gambia; Tel: +220 (0)4495442 ext. 2308; Email: ethics@mrc.gm), ref: 17683
2. Approved 20/08/2019, London School of Hygiene & Tropical Medicine Interventions Research Ethics Committee (Keppel St, London, WC1E 7HT, UK; Tel: +44 (0)20 76368636, Email: ethics@lshtm.ac.uk), ref: 17683

Study design
Phase IV parallel unmasked cluster-randomised trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Pneumococcal acquisition and vaccine immunogenicity

Interventions

13-valent pneumococcal conjugate vaccine (PCV13) is a licenced product, procured by the Gambia Government EPI, delivered in two schedules, one with doses scheduled at ages 6, 10 and 14 weeks (3+0 schedule) and the other with doses scheduled at ages 6 weeks and 9 months (1+1 schedule). In one arm of this substudy, PCV13 will be given at 9 months of age and YF vaccine at 10 months of age. YF vaccine is a licenced product procured by the Gambia Government EPI. Participants will be selected from the 28 clusters closest to Basse. Thus, individual participants in this acquisition/immunogenicity sub-study will not be individually randomised as their group allocation will be determined by their village of residence and cluster allocation in the larger PVS trial. Of these 28 clusters, 14 are allocated to each of the 1+1 and 3+0 groups, four of these 28 clusters include health facilities (two in the 1+1 group), and 14 are stratified as high clinical pneumonia incidence (seven in the 1+1 group).

Intervention Type
Biological/Vaccine

Phase
Phase IV

Drug/device/biological/vaccine name(s)
13-valent pneumococcal conjugate vaccine (PCV13); Yellow fever vaccine

Primary outcome(s)
1. Nasopharyngeal acquisition of vaccine-type pneumococci measured using latex sweep serotyping at five timepoints between 9 and 14 months of age
2. Concentration of pneumococcal vaccine-type serotype-specific IgG measured by enzyme-linked immunosorbent assay at 18 months of age
3. Yellow fever neutralizing antibody titre expressed as the serum dilution that yields neutralisation of greater than or equal to 50% of virus infections of a standard cell line, measured 1 month after administration of yellow fever vaccine

Key secondary outcome(s))
1. Rate of non-vaccine type pneumococcal nasopharyngeal acquisition between 9 and 14 months of age
2. Proportion with vaccine-type pneumococcal colonisation at 6, 9 and 18 months of age
3. Proportion with geometric mean concentration of pneumococcal vaccine-type serotype-specific IgG ≥0.35 µg/ml, 4 weeks after the primary series and 4 weeks after the booster dose at age 9 months, and at 18 months of age
4. Pneumococcal vaccine-type opsonophagocytic antibody titres following a single dose of PCV13 at age 6 weeks, following three primary doses, following the booster dose at age 9 months, and at 18 months of age
5. Geometric mean concentrations of pneumococcal vaccine-type serotype-specific IgG 4 weeks after administration of PCV13 at 9 months of age with and without co-administration with yellow fever vaccine

Completion date
30/06/2025

Eligibility

Key inclusion criteria

1. Resident in the study area (PVS-AcqImm trial)
2. Age 0-6 weeks
3. Intention to reside in cluster until 18 months of age

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Lower age limit
0 weeks

Upper age limit
6 weeks

Sex
All

Total final enrolment
827

Key exclusion criteria
1. Intent to move out of the study area before 18 months of age
2. Age greater than 6 weeks
3. Prematurity <34 weeks gestation
4. Birth weight <2.0kg or weight <2.5 kg
5. History of invasive bacterial infection or measles
6. Receiving long-term antibiotic therapy, defined as greater than 4 weeks
7. HIV infection in the infant or mother
8. Chronic debilitating illness
9. Immunosuppressive therapy or immunodeficiency disorder
10. Contraindication to PCV13 – severe hypersensitivity to a previous dose of PCV13
11. Contraindication to YF vaccine

Date of first enrolment
14/09/2020

Date of final enrolment
28/10/2021

Locations

Countries of recruitment
Gambia

Study participating centre
MRC Unit, The Gambia at LSHTM
Basse Field Station
Basse
Gambia
273

Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

ROR
https://ror.org/00a0jsq62

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

Funder Name
Mucosal Pathogens Research Unit, National Institutes of Health Research (UK)

Funder Name

Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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

Funder Name
UKAID

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from MRC Unit The Gambia at LSHTM (archives@mrc.gm). Data will be available indefinitely after all study publications have been accepted although earlier requests will be considered on a case by case basis, data requests will be reviewed by the MRC Unit The Gambia at LSHTM Scientific Coordinating Committee and the Gambia Government/MRC Joint Ethics Committee, consent from participants has been obtained for data sharing, data will be anonymised.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		10/10/2025	14/01/2025	Yes	No
Protocol article		15/01/2022	24/05/2022	Yes	No
Participant information sheet	version 4.0	17/02/2021	17/01/2024	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan		26/03/2024	27/03/2024	No	No