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Pneumococcal Vaccine Schedules (PVS)

Submission date
19/09/2018

Recruitment status
No longer recruiting

Registration date
15/11/2018

Overall study status
Completed

Last Edited
05/12/2023

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Pneumococcus bacteria are the most common cause of pneumonia (lung inflammation), septicemia (bacteria in the blood) and meningitis
(inflammation of the membranes around the brain) worldwide. Many countries have introduced pneumococcal conjugate vaccines (PCV) using three or four dose schedules and this has been followed by a drop in pneumococcal disease. Herd protection effects, in which vaccinatiuon of a proportion of the population reduces the spread of a disease within the unvaccinated population, have prevented more cases than the direct effects in vaccinated children. Many African and Asian countries have now introduced PCV using the standard schedule of three doses in early infancy (3+0 schedule).
Global control of pneumococcal disease however, is hampered by the cost of PCV. Low-income countries receive subsidised vaccine through the Gavi Alliance. However, when countries' income per person exceeds the World Bank 'low-income' threshold, they 'graduate' from Gavi support and must pay a proportion of the cost. The cost of vaccine has prevented most middle-income countries from introducing PCV.
This study will test an alternative schedule that includes one early dose and a booster dose at 9 months of age, compared to the standard schedule. If this two-dose schedule is as effective as the three-dose schedule, this would make the cost of vaccinating lower. We aim to test if the impact of the alternative schedule is not worse than the standard schedule.

Who can participate?
Children aged 6 weeks to 365 days and living in the study area can receive the vaccine. The impact of the intervention will be measured in children aged 2 weeks to 59 months.

What does the study involve?
We plan to deliver two-dose (doses at age 6 weeks and 9 months, '1+1') or three-dose (doses at age 6, 10, 14 weeks, '3+0') schedules to infants resident in the study area over a period of 4 years. Vaccines will be administered at 68 immunisation clinics serving separate catchment populations. The immunisation clinic catchment population will be randomised to either group (1+1 or 3+0). We will conduct surveillance for disease in the 2 weeks to 59 months age group. After allowing time for the potentially different community-level effects of the two schedules to develop, we will measure the percentage of children with clinical pneumonia who have bacteria in their nose of the same type that is prevented by the vaccine. We will also measure the percentage of children aged 6-12 weeks presenting for their 1st dose of PCV, and the

percentage of the whole population, who have bacteria in their nose of the same type that is prevented by the vaccine.

What are the possible benefits and risks?
Potential benefits include fewer injections, more simple logistics, and less cost to the government. Potential risks are that pneumococcal disease may be more likely in one group.

Where is the study run from?
The study is located in rural Gambia and run from the Basse field station of the Medical Research Council Unit The Gambia at London School of Hygiene and Tropical Medicine.

When is the study starting and how long is it expected to run for?
November 2018 to May 2024.

Who is funding the study?
The study is funded by the MRC/Wellcome/DFID/NIHR Joint Global Health Trials scheme and the Bill and Melinda Gates Foundation.

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

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

SCC 1577 v1.2

Study information

Scientific Title
A cluster-randomised, non-inferiority trial of the impact of a two-dose compared to a three-dose schedule of pneumococcal conjugate vaccine in rural Gambia.

Acronym
PVS

Study objectives
The impact of PCV13 delivered in a 1+1 schedule is non-inferior to a 3+0 schedule.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Gambia Government/MRC Joint Ethics Committee; 19/03/201, L2018.E08, SCC1577v1.2
2. London School of Hygiene & Tropical Medicine Observational/Interventions Research Ethics Committee, 26/02/2018, 14515

Study design
Single-centre cluster-randomised non-inferiority parallel-group unmasked trial

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Community

Study type(s)
Prevention

Participant information sheet
Not available in web format.

Health condition(s) or problem(s) studied
Streptococcus pneumoniae disease and pneumococcal colonisation

Interventions
13-valent pneumococcal conjugate vaccine (PCV13) will be 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). The two schedules will be randomly allocated (1:1) to 68 geographic clusters where children attend one immunisation clinic.

Intervention Type

Biological/Vaccine

Pharmaceutical study type(s)
Not Applicable

Phase
Phase IV

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

Primary outcome measure
Nasopharyngeal (NP) carriage of vaccine-type (VT) pneumococci in children aged 2 weeks to 59 months with clinical pneumonia will be measured in the 2nd and 4th year of the trial. Measurement in the 4th year is the primary analysis. Measurement in the 2nd year is a secondary analysis.

Secondary outcome measures
1. NP carriage of non-vaccine-type (NVT) pneumococci in children aged 2 weeks to 59 months with clinical pneumonia measured in the 4th year of the trial
2. Population-based NP prevalence of VT and NVT pneumococci
3. NP prevalence of VT and NVT pneumococci in infants presenting for the first dose of PCV aged 6-12 weeks measured in the 4th year of the trial
4. Incidence of radiological pneumonia in children aged 2 weeks to 59 months will be measured by facility-based surveillance throughout the trial
5. Incidence of clinical pneumonia in children aged 2 weeks to 59 months will be measured by facility-based surveillance throughout the trial
6. Incidence of serotype-specific invasive pneumococcal disease (IPD in children aged 2 weeks to 59 months will be measured by facility-based surveillance throughout the trial
7. Incidence of hospitalisation in children aged 2 weeks to 59 months will be measured by facility-based surveillance throughout the trial
8. Mortality in children aged 2 weeks to 59 months will be measured by facility-based and demographic surveillance throughout the trial

Overall study start date
09/06/2017

Completion date
31/05/2024

Eligibility

Key inclusion criteria
1. Resident in the study area
2. Children aged 6 weeks to 365 days will be eligible to receive the intervention
3. Children aged 2 weeks to 59 months will be eligible for measurement of the primary endpoint and disease endpoints by disease surveillance

Participant type(s)
Mixed

Age group
Child

Lower age limit
2 Weeks

Upper age limit
59 Months

Sex
Both

Target number of participants
68 clusters; birth cohort approximately 10,000 per year

Key exclusion criteria
1. Intent to move out of the study area before 4 months of age
2. Aged over 364 days
3. Contraindication to vaccination with PCV13, including severe hypersensitivity to a previous dose of PCV13

Date of first enrolment
22/08/2019

Date of final enrolment
31/10/2023

Locations

Countries of recruitment
Gambia

Study participating centre
Basse Field Station, Medical Research Council Unit The Gambia at London School of Hygiene & Tropical Medicine
Basse Field Station, MRCG at LSHTM
Upper River Region
Basse
Gambia
NA

Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

Sponsor details
Keppel Street
London
England
United Kingdom
WC1E 7HT

Sponsor type
University/education

Website
https://www.lshtm.ac.uk

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, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype

International organizations

Location
United Kingdom

Funder Name
Department for International Development

Alternative Name(s)
Department for International Development, UK, DFID

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, 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

Publication and dissemination plan
Current publication and dissemination plan as of 03/03/2023:
The protocol and statistical analysis plan were published in a peer-reviewed open-access journal in 2022. The final results will be published in a peer-reviewed open-access journal in 2025.

Previous publication and dissemination plan:
The protocol will be published in a peer-reviewed open-access journal in 2020. The final results will be published in a peer-reviewed open-access journal in 2023.

Intention to publish date
02/02/2025

Individual participant data (IPD) sharing plan
Anonymised datasets will be available indefinitely after publications of results. Data will be accessible by application to the MRCG at LSHTM scientific coordinating committee. Participant consent will be obtained. Approval of the Gambia government/MRCG at LSHTM joint ethics committee is required for data to be sent out of the country.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		24/01/2022	24/05/2022	Yes	No
Statistical Analysis Plan	statistical analysis plan article	28/12/2022	03/03/2023	Yes	No