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Comparison of current and new pneumococcal conjugate vaccines used for infant immunisation

Submission date
15/06/2024

Recruitment status
Recruiting

Registration date
07/08/2024

Overall study status
Ongoing

Last Edited
29/06/2026

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Pneumonia, meningitis, and sepsis are serious (sometimes life-threatening) illnesses. They are particularly dangerous in young children, with babies under the age of two having the highest risk of developing severe complications. They are all forms of pneumococcal disease, which is an infection caused by the bacteria Streptococcus pneumoniae, more commonly referred to as pneumococcal bacteria. The routine vaccine used currently in babies is PCV13 (Pneumococcal Conjugate Vaccine) that protects against 13 different types of pneumococcal bacteria and has proven effectiveness. However, there are over 90 different types of pneumococcal bacteria and we have seen an increase in disease caused by types not currently covered by the PCV13 vaccine. This study aims to understand if the vaccines in the study (PCV15 and PCV20) can protect against more cases of serious disease in children and the adult population, than the existing vaccine PCV13.

Who can participate?
Healthy babies who are 8-10 weeks of age, healthy, were born after 37 weeks gestational age, and have not yet received their first vaccinations

What does the study involve?
Infants will be randomly assigned to one of four different treatment groups. If receiving two doses of either PCV 15, PCV 20, or PCV 13 they will receive PCV vaccinations at 3 or 4 months and 12 months and have two blood samples collected at 4 or 5 months and 13 months of age and three nasal samples at 3, 4 or 13 months of age. If receiving three doses of PCV20 they will receive PCV vaccinations at 2, 4 and 12 months, and have two blood samples collected at 5 and 13 months of age and four nasal samples at 2, 3, 5, and 13 months of age.

What are the possible benefits and risks of participating?
Participants in this trial will receive licensed vaccines which are already included in the childhood routine UK immunisation
schedule or licensed for use in the UK, apart from PCV20 which is licensed in the USA and EU to be used in infants. By taking part in this study the infants will receive all their routine vaccinations up to and including 12 months of age, possibly in their own home. They will also have access to a 24-hour paediatric study doctor for the duration of the study. If the infant

receives either PCV15 or PCV20 they will be immunized against more types of pneumococcal bacteria than if they had received the PCV13 only.
The risks to participants include the common side effects of each vaccination, listed within the summary of product characteristics. These include local injection site reactions such as pain, erythema, swelling, pruritis and induration and systemic side effects including fever, irritability, rash, malaise, drowsiness, vomiting and loss of appetite.
As with all vaccines, there is a small chance of an allergic reaction including severe reactions such as anaphylaxis (the risk is less than one in a million doses for existing vaccines.
The risks associated with blood sampling include bleeding, pain at the injection site, bruising and infection. Anaesthetic cream is offered to minimize any pain during venepuncture. The volume of blood taken at each visit does not exceed the recommended European limits for infants.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
June 2024 to December 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
1. Dominic Kelly, dominic.kelly@paediatrics.ox.ac.uk
2. Denis Murphy, denis.murphy@paediatrics.ox.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

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Public, Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
1009039

Central Portfolio Management System (CPMS)
59704

Protocol serial number
OVG2023/10

Study information

Scientific Title
Evaluation of higher valency pneumococcal vaccines (PCV15/PCV20) compared to PCV13 given in homologous schedules at 3/4 months and 12 months (“1+1” schedule) and 2 months, 4 months and 12 months (“2+1” schedule) in infants

Acronym
PCV15/PCV20

Study objectives
Current study hypothesis as of 30/06/2025:
Primary objective:
To determine if the PCV13 serotype-specific serum IgG concentrations are non-inferior in homologous arms 1/1r4 & 2/2r4 at 13 months in comparison to the control arm 4/4r4

Secondary objectives:
1. To determine if the PCV13 serotype-specific serum IgG concentrations are non-inferior in arm 3 at 13 months in comparison to the control arm 4/4r4
2. To characterise the seven additional PCV20 serotype-specific serum IgG concentrations at 13 months following homologous PCV schedules in arms 1/1r4, 2/2r4 and 3 in comparison to the control arm 4/4r4
3. To determine the safety and reactogenicity of different schedules with PCV15 and PCV20

Previous study hypothesis:
Primary objective:
To determine if the PCV13 serotype-specific serum IgG concentrations are non-inferior in homologous arms 1 & 2 at 13 months in comparison to the control arm 4

Secondary objectives:
1. To determine if the PCV13 serotype-specific serum IgG concentrations are non-inferior in arm 3 at 13 months in comparison to the control arm 4

2. To characterise the seven additional PCV20 serotype-specific serum IgG concentrations at 13 months following homologous PCV schedules
3. To determine the safety and reactogenicity of different schedules with PCV15 and PCV20

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 06/08/2024, South Central - Hampshire A Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8210; hampshirea.rec@hra.nhs.uk), ref: 24/SC/0222

Primary study design
Interventional

Study design
Open randomized controlled parallel-group trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Pneumococcal disease

Interventions
Current interventions as of 30/06/2025:
Arm 1: Two doses of PCV15; first dose when the infant is 3 months of age, second dose when the infant is 12 months of age
Arm 1r4: Two doses of PCV15; first dose when the infant is 4 months of age, second dose when the infant is 12 months of age
Arm 2: Two doses of PCV20; first dose when the infant is 3 months of age, second dose when the infant is 12 months of age
Arm 2r4: Two doses of PCV20; first dose when the infant is 4 months of age, second dose when the infant is 12 months of age
Arm 3: Three doses of PCV20; first dose when the infant is 2 months of age, second dose when the infant is 4 months of age and third dose when the infant is 12 months of age
Arm 4: Two doses of PCV13; first dose when the infant is 3 months of age, second dose when the infant is 12 months of age
Arm 4r4: Two doses of PCV13; first dose when the infant is 4 months of age, second dose when the infant is 12 months of age

Participants will be randomized to a 1:1:1:1: ratio before their first vaccination visit into four arms to receive the PCV vaccine. Participants randomised to Arms 1, 2 and 4 will be further randomised 1:1 to receive their first dose of PCV13 or PCV15 or PCV20 at 3 months (arm 1, 2 or 4) or at 4 months (arm 1r4, 2r4 or 4r4).

Computer-generated randomisation lists will be prepared using stratified block randomisation. Random block sizes of 2 or 4 will be used. The randomisation list will be loaded to a central randomisation system and each site user will have a unique log-in to access their corresponding randomisation list.

Six groups (1, 1r4, 2, 2r4, 4 and 4r4) will receive two PCV vaccines at 3 or 4 months and 12 months of age. One group (3) will receive three PCV vaccines at 2, 4 and 12 months of age. Blood samples will be taken after vaccination (a maximum of 4 ml and 6 ml per sample), to assess immune responses to the study vaccines. Nasal samples will be collected at the first PCV vaccination and a month after each vaccine. During the study, the children will also receive all other routine immunisations up to the age of 12 months, as per the UK immunisation programme.

Previous interventions:
Arm 1: Two doses of PCV15; first dose when the infant is 3 months of age, second dose when the infant is 12 months of age
Arm 2: Two doses of PCV20; first dose when the infant is 3 months of age, second dose when the infant is 12 months of age
Arm 3: Three doses of PCV20; first dose when the infant is 2 months of age, second dose when the infant is 4 months of age and third dose when the infant is 12 months of age
Arm 4: Two doses of PCV13; first dose when the infant is 3 months of age, second dose when the infant is 12 months of age

Participants will be enrolled in the study at the age of 2 months. They will be randomly allocated into one of four groups and vaccinated with the PCV vaccine that is assigned to each group. Three groups will receive two PCV vaccines at 3 months and 12 months of age. One group will receive three PCV vaccines at 2, 4 and 12 months of age. Blood samples will be taken after vaccination (a maximum of 4 ml and 6 ml per sample), to assess immune responses to the study vaccines. Nasal samples will be collected at the first PCV vaccination and a month after each vaccine. During the study, the children will also receive all other routine immunisations up to the age of 12 months, as per the UK immunisation programme.

Participants will be randomized to a 1:1:1:1: ratio before their first vaccination visit into four arms to receive the PCV vaccine. Computer-generated randomisation lists will be prepared using stratified block randomisation. Random block sizes of 2 or 4 will be used. The randomisation list will be loaded to a central randomisation system and each site user will have a unique log-in to access their corresponding randomisation list.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Prevenar 13, pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) [pneumococcal polysaccharide conjugate vaccine containing 1, 3, 4, 5, 6A, 6B 7F, 9V, 14, 18C, 19A, 19F, and 23F serotypes], Vaxneuvance® suspension for injection in pre-filled syringe [Pneumococcal polysaccharide conjugate vaccine containing 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F], Apexxnar / PREVENAR 20 suspension for injection in pre-filled syringe [Pneumococcal polysaccharide conjugate vaccine containing 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F], Prevenar 20 suspension for injection in pre-filled syringe [Pneumococcal polysaccharide conjugate vaccine containing 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F]

Primary outcome(s)

PCV13 serotype-specific serum IgG concentration measured using Enzyme-Linked Immunoassay at 13 months of age (at least 4 weeks after administration of the last dose of PCV vaccine)

Key secondary outcome(s)
1. PCV20 serotype-specific serum IgG concentrations measured using Enzyme-Linked Immunoassay at 13 months of age (at least 4 weeks after administration of the last dose of PCV vaccine)
2. Solicited adverse events (AEs) collected using e-Diary recordings within 7 days
3. Unsolicited AEs and serious adverse events (SAEs) recorded when observed by the Investigator or reported by the participant's parent/guardian during the whole study period

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. Infants due to receive their primary immunizations, aged up to 2 months (+ 2 weeks) at first vaccinations
2. Infants born at ≥37 weeks of gestational age
3. Parent(s) or legal guardian(s) willing and able to follow the requirements of the protocol for the duration of the study
4. Written informed consent given by parent(s) or legal guardian(s) who is aged ≥16 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 Months

Upper age limit
2.5 Months

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Prior receipt of vaccines (except for Hepatitis B or BCG vaccine)
2. Prior planned receipt of Investigation vaccines.
3. Current participation in another research study, except if the study is solely observational.
4. Children of parents who are on the delegation log for this study

5. A confirmed anaphylactic reaction to neomycin, streptomycin or polymyxin B (which may be present in trace amounts in the tetanus vaccine) and/or kanamycin, histidine, sodium chloride or sucrose (which may be present in trace amounts in the MenB vaccine).
6. Latex hypersensitivity (the syringe cap of Bexsero may contain natural rubber latex)
7. Major congenital defects or serious chronic illness
8. Presence of an evolving or changing neurological disorder
9. Presence of central nervous system disease or convulsions in the infant.
10. Bleeding disorder
11. Confirmed or suspected immunodeficiency
12. A family history of congenital or hereditary immunodeficiency
13. Receipt of more than 1 week of immune-suppressants or immune-modifying drugs (e.g., oral prednisolone >0.5 ml/kg/day or intravenous glucocorticoid steroid). Nasal, topical or inhaled steroids are allowed
14. Administration of immunoglobulin and/or any blood products since birth or planned administration during the study period
15. History of allergy to any component of the vaccines. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk through participation in the study, or may influence the result of the study or the participant's ability to participate in the study

Date of first enrolment
03/12/2024

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Bristol Vaccine Centre
L6 Education & Research Centre
Upper Maudlin Street
Bristol
England
BS2 8AE

Study participating centre
The University of Nottingham Health Service Cripps Health Centre
University Park Nottingham
Nottingham
England
NG7 2QW

Study participating centre
St George's University Hospitals NHS Foundation Trust and St. George's Vaccine Institute (SGVI) Centre for Neonatal and Paediatric Infection Diseases
St George's University of London
Cranmer Terrace
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SW17 0RE

Study participating centre
Southampton General Hospital
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SO16 6YD

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care 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

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 4.1	06/08/2025	15/09/2025	No	No
Protocol file	version 5.0	02/10/2025	18/12/2025	No	No
Protocol file	version 6.0	21/01/2026	23/04/2026	No	No