

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

Submission date 15/06/2024	Recruitment status Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 07/08/2024	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 30/06/2025	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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 June 2026

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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Type(s)

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

1009039

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

OVG2023/10, IRAS 1009039, CPMS 59704

Study information

Scientific Title

Evaluation of higher valency pneumococcal vaccines (PCV15/PCV20) compared to PCV13 given in homologous schedules at 3 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

Study design

Open randomized controlled parallel-group trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Safety, Efficacy

Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

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 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 measure

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)

Secondary outcome measures

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

Overall study start date

12/06/2024

Completion date

30/06/2026

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

Age group

Child

Upper age limit

2 Months

Sex

Both

Target number of participants

600

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

31/08/2024

Date of final enrolment

28/02/2026

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Bristol Vaccine Centre

L6 Education & Research Centre

Upper Maudlin Street

Bristol
United Kingdom
BS2 8AE

Study participating centre

The University of Nottingham Health Service Cripps Health Centre
University Park Nottingham
Nottingham
United Kingdom
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
London
United Kingdom
SW17 0RE

Study participating centre

Southampton General Hospital
Tremona Road
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SO16 6YD

Sponsor information

Organisation

University of Oxford

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Sponsor type

University/education

Website

<http://www.ox.ac.uk/>

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

Publication and dissemination plan

1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Other publication
5. Submission to regulatory authorities

Participants will not be identifiable from shared or published data. De-identified participant data will be made available upon requests directed to the chief investigator. Proposals will be reviewed and approved by the sponsor, chief investigator, and collaborators on the basis of scientific merit. After approval of a proposal, data can be shared through a secure online platform after signing a data access agreement.

Intention to publish date

30/06/2027

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date