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The transmission of pneumococcus in family units study

Submission date
04/11/2019

Recruitment status
No longer recruiting

Registration date
25/11/2019

Overall study status
Completed

Last Edited
15/01/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Pneumococcus is a bacterium that frequently lives in the noses of young children without causing any illness. Occasionally, it causes disease like ear infections and pneumonia (chest infection) and very rarely meningitis (infection around the surface of the brain). Viral infections, like influenza (flu), seem to help pneumococcus to spread from one person to another and may contribute to these diseases. Flu is a common viral illness spread by coughing, sneezing and direct contact that causes sore throat, cough, fever, runny nose and muscle aches.
The nasal flu vaccine is the licensed vaccine that all 2- to 10-year-old children are routinely offered in the UK every autumn which is known to be safe and effective. The vaccine causes a very mild flu infection and so protects against real flu but the mild infection can change the numbers of other bugs in the nose too without causing any illness. We are conducting this study to find out whether those changes result in those bugs being passed around within the family differently. Nothing in the study changes anything that would be happening anyway, it just tracks what is going on. By understanding how these bugs are spread, we will be able to plan more effective strategies to prevent infections in the future.

Who can participate?
To take part, a family must live near to the study centre, have a healthy child who has turned 2 years of age between January 1st and August 31st (2017 if participating in season 1 or 2018 if participating in season 2) who is eligible to receive their first nasal flu vaccine during the study period and have 2 other household members (adults and/or children) that are willing and able to take part in the study. All those taking part in the study must be willing and able to provide nasal and saliva samples and complete a survey about their recent contacts with household members and other people on five occasions over about 2 months (about every 2 weeks).

What does the study involve?
The 2-year-old child in each family enrolled receives one dose of the flu vaccine that is routinely offered to children aged 2-10 years of age in the UK. Saliva samples and nose swabs are taken from the 2-year-old and all participating family members at each of 5 study visits between September and December to track the spread of bacteria within the family. Participants are also asked to complete a contact survey at each visit. Each family is involved in the study for about 3 months, and visits are carried out as home visits.

What are the possible benefits and risks of participating?
Children participating in the study who are eligible for the nasal flu vaccine receive it at home which may be more convenient and receiving the nasal flu vaccine is the best way to protect them against flu.
Participation will help further understanding in how viruses interact with bacteria that normally live in children's noses and how these bacteria are transferred from one person to another. This will be useful in developing more effective ways to prevent infections.
There is a reimbursement of £15 per family for each of 5 sampling visits (£75 in total) in the form of vouchers to compensate for the time and trouble in participating in the study.
The most common mild symptoms that a minority of children may develop after nasal flu vaccination are runny nose/nasal congestion, cough, wheezing, fever, headaches and malaise, abdominal pain, vomiting and diarrhoea which may last for 1-2 days and are self-limiting. The vaccine has not been related to severe side effects but, as with all vaccines and medications, severe allergic reactions may occur very rarely. The study staff are trained to manage such a reaction in the unlikely event that it should occur.
Participants may feel mild discomfort for a few seconds while nasal swabs are taken. Saliva samples are easy to get and the process does not have any risks.

Where is the study run from?
Bristol Children's Vaccine Centre at the University of Bristol (UK)

When is the study starting and how long is it expected to run for?
August 2017 to December 2023

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

Who is the main contact?
1. Dr Jennifer Oliver, jennifer.oliver@bristol.ac.uk
2. Dr Jane Metz, jane.metz@bristol.ac.uk

Contact information

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

CPMS 35674

Study information

Scientific Title
Evaluation of the relationship between pneumococcal colonisation density in 2-year-old children and rates of transmission to family contacts using live attenuated intranasal influenza vaccine as a probe. A randomised prospective step-wedge multicentre study

Acronym
TOP

Study objectives
Increased carriage density of Streptococcus pneumoniae (Sp) in the upper respiratory tract of young children following the live attenuated influenzae vaccine (LAIV) will lead to increased rates of Sp transmission to close household contacts.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/09/2017, West - Cornwall & Plymouth Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol BS1 2NT; +44 (0)207 104 8059; nrescommittee.southwest-cornwall-plymouth@nhs.net), ref: 17/SW/0190

Study design
Multi-centre prospective randomized stepped-wedge trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

Study type(s)
Other

Participant information sheet
As we are enrolling families, there are information sheets for the index child, children and adults.

Health condition(s) or problem(s) studied
Streptococcus pneumoniae (Sp), Haemophilus influenzae (Hi) and Moraxella catarrhalis (Mc)

Interventions
This is a step-wedge design so that both index children of group 1 and group 2 (randomly allocated at a 1:1 ratio) receive the standard dose of LAIV but at different times. The group number determines whether the two-year-old (index) child receives LAIV at the first study visit

(Group 1) or at the third study visit, 4 weeks later (Group 2). Serial saliva and nasopharyngeal swabs taken every 2 weeks over an 8-week period will be analysed for Streptococcus pneumoniae using real-time PCR. Standard statistical methods including generalised linear mixed models and individual-based mathematical modelling of transmission dynamics will be used for analysis.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
-

Primary outcome measure
Streptococcus pneumoniae carriage and transmission events in family units measured using real-time PCR on serial nasopharyngeal and saliva samples taken every 2 weeks over an 8-week period

Secondary outcome measures
1. Haemophilus influenzae carriage and transmission events in family units measured using real-time PCR on serial nasopharyngeal and saliva samples taken every 2 weeks over an 8-week period.
2. Moraxella catarrhalis carriage and transmission events in family units measured using real-time PCR on serial nasopharyngeal and saliva samples taken every 2 weeks over an 8-week period

Overall study start date
22/08/2017

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. Healthy male or female child
2. Who will be 2 years of age between 1st January and 31st August of the year of recruitment
3. Who is resident near the recruiting centres
4. Who have at least two other people, either adults or children, resident in the house where they live that are willing and able to take part

Participant type(s)
Healthy volunteer

Age group
Mixed

Sex

Both

Target number of participants
500 families

Key exclusion criteria
Exclusion criteria include all contra-indications in the vaccine licence, in addition:
1. Children currently enrolled in another clinical trial or study which, in the opinion of the investigator might interfere with their likelihood of completing either or both studies or which might confound outcomes of either study. Families participating in the first year of the study who have another child of the right age and are otherwise eligible and who wish to participate again in the second year will be permitted to do so
2. Confirmed or suspected primary or secondary immunodeficiency OR known to be severely immunosuppressed due to any condition or recent (in the last 6 months) therapy (eg leukaemia, HIV infection, organ or bone marrow transplant)
3. Severely immunocompromised household member or close contact (because of potential for transmission of live attenuated virus)
4. Receipt of immunosuppressants or immune modifying drugs including oral or parenteral steroids (at a dose equivalent of prednisolone >0.5mg/kg/day for more than 1 week within the 3 months prior to enrolment). Inhaled steroids are not a contraindication (although see below re asthma and wheezing)
5. Current hospital-based management of asthma
6. Previous receipt of, or intended immunisation with any other influenza vaccine(s)
7. Children who are in risk groups for severe influenza (e.g. chronic respiratory (but for severe asthma see above), cardiac, renal, hepatic or neurological diseases and diabetes) can be enrolled and immunized in the study provided they are eligible to receive LAIV following the guidance published in the Green Book (ref: www.gov.uk/government/uploads/system/uploads /attachment_data/file/456568/2904394_Green_Book_Chapter_19_v10_0.pdf)
8. Children with other chronic, stable medical illnesses that do not result in immunosuppression and are not risk groups indicating receipt of seasonal flu vaccine (e.g. epilepsy, metabolic disorders) may participate in the study, unless their condition or circumstances will in some way interfere with the completion of study procedures
9. Children receiving salicylate therapy (Aspirin)
10. Previous anaphylactic reaction to any component of the nasal flu vaccine (including gelatine or gentamicin), or to eggs or egg proteins (eg ovalbumin)
11. Any other condition or circumstances which, in the opinion of the investigator, might put the index subject or family members or research team members at risk or which might interfere with the likelihood of successful of study procedures and sampling per protocol or which might prevent the results obtained from contributing in any way with successful achievement of the study objectives

Date of first enrolment
04/10/2017

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Bristol Children's Vaccine Centre
University Hospitals Bristol NHS Foundation Trust
Level 6, UH Bristol Education and Research Centre
Upper Maudlin Street
Bristol
United Kingdom
BS2 8AE

Study participating centre
St Georges Hospital, University of London
Paediatric Infectious Diseases Research Group
Jenner Wing, Level 2, Room 2.216F, Mail Point J2C
London
United Kingdom
SW17 0RE

Study participating centre
University of Oxford
Oxford Vaccine Group
Department of Paediatrics
Centre for Clinical Vaccinology and Tropical Medicine (CCVTM)
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre
Southampton General Hospital
Southampton National Institute for Health Research Clinical Research Facility
University Hospital Southampton NHS Foundation Trust
Mailpoint 218
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre

Royal Manchester Children's Hospital
Paediatric Research Team
Clinical Trial Management Office (ICON Building)
Manchester University Hospitals NHS Foundation Trust
North Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Royal United Hospital
Paediatric Clinical Research Team
Children’s Centre Outpatient’s Department B11
Royal United Hospital Bath NHS Foundation Trust
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Musgrove Park Hospital
Department of Clinical Research
Starling Clinic
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
NIHR Clinical Research Network: South West Peninsula
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Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Sheffield Children's Hospital
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D Floor, Stephenson Wing
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Study participating centre
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Sponsor type
University/education

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Industry

Funder Name
Pfizer

Alternative Name(s)

Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

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
The researchers intend to present data at conferences over the next few years including at the International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD) and the European Society of Paediatric Infectious Diseases (ESPID).
Written publications are intended when all results are available.

Intention to publish date
01/06/2024

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

HRA research summary	28/06/2023	No	No