ISRCTN12884329 https://doi.org/10.1186/ISRCTN12884329

# Examining exhaled breath for the presence of the bacteria pneumococcus

**Submission date**
23/07/2019

**Recruitment status**
No longer recruiting

**Registration date**
30/08/2019

**Overall study status**
Completed

**Last Edited**
09/05/2022

**Condition category**
Infections and Infestations

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

## Plain English summary of protocol

Background and study aims
The aim of this study is to assess whether two devices, 'BreathSpec' and the 'Exhaled Detection Facemask' (EDF) are able to identify and quantify Streptococcus pneumoniae (pneumococcus) in exhaled breathe from participants who have had the bacteria experimentally introduced into their nose. Antimicrobial resistance is a growing problem all over the world. In order to address this, better diagnostic tests are urgently needed to improve the use of antibiotics. Currently doctors only find the bacteria or virus causing the pneumonia in 50-73% of patients even with extensive investigation, which leads to poor antibiotic prescribing. This study uses two new diagnostic devices that could identify the presence of the leading cause of pneumonia, Streptococcus pneumoniae. The first device, BreathSpec, analyses chemicals that are present in exhaled breath for a specific 'signature' that indicates the presence of pneumococcus. The second, EDF, is a facemask that collects samples from exhaled breath. The 'Experimental Human Pneumococcal challenge' (EHPC) model is used to perform both BreathSpec and EDF before and after the pneumococcus is experimentally introduced into a participant's nose. As a result, the two devices can be used to assess the changes occuring when the pneumococcus is present.

Who can participate?
Healthy volunteers aged 18-50

What does the study involve?
The plan is to perform BreathSpec (breathing into a machine) and EDF (wearing a facemask for 30-60 minutes) with 50 participants who have had pneumococcus put up their nose. Samples are then collected intermittently for the following month.

What are the possible benefits and risks of participating?
In future these data may contribute to the development of devices that better identify the cause of pneumonia and guide targeted antibiotic treatment. There are no direct benefits to taking part in the study but it is hoped that participants will feel that they have contributed to a research project that could inform pneumonia diagnosis in the future. The risks associated with the research relate to the sampling methods and the exposure to live bacteria. Nasal wash: samples involve squirting some sterile saline inside the nose, this is then expelled and collected for processing. Some participants may swallow some of the saline but this is not uncomfortable.

Blood sampling: a very small sample of blood is taken at the beginning of the study (3 ml). Some participants may find this temporarily uncomfortable but the staff that perform this are trained and experienced in this process. On occasions, blood sampling can cause a small bruise or make the participant feel light headed. The volume taken during this study is highly unlikely however to make participants feel light headed. Throat swab(s): The throat is swabbed with a cotton stick. It can make you gag a little. Nasosorption: This involves a small blotting paper that is placed up a nostril for two minutes. This can tickle but is not painful. There are no risks involved in the saliva or urine sampling. BreathSpec: participants are asked to provide two breaths into a tube. A forced breath may cause temporary dizziness. There are no risks involved. EDF: Participants are asked to wear a mask that covers the mouth for between 15-30 minutes. Participants may feel a little claustrophobic when wearing the mask over their mouth but there are no risks involved with the sampling. The risks associated with the exposure to live bacteria include pneumonia, meningitis or sepsis. The researchers have however inoculated over 1400 healthy participants in 9 years and have not experienced a single case of these diseases. They reduce the risk by providing the participant with 24/7 access to a member of the research team, a course of antibiotics to be taken in case of illness (under specific guidance of the research team), a safety information leaflet and a digital thermometer to check their temperature daily for the first 3-4 days and in the case of feeling unwell.

Where is the study run from?
Accelerator Research Clinic (UK)

When is the study starting and how long is it expected to run for?
September 2019 to April 2021

Who is funding the study?
Centre of Excellence in Infectious Disease Research (CEIDR) grant

Who is the main contact?
Dr Ryan Robinson
2volresearch@lstmed.ac.uk

# Contact information

### Type(s)
Scientific

### Contact name
Dr Ryan Robinson

### ORCID ID
http://orcid.org/0000-0003-0871-4780

### Contact details
Accelerator Research Clinic
Liverpool School of Tropical Medicine
1 Daulby Street
Liverpool
United Kingdom

L7 8XZ
+44 (0)151 702 9468
2volresearch@lstmed.ac.uk

# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
Version 1; 22/07/2019

# Study information

### Scientific Title
The PneumEx study: experimental human pneumococcal challenge and exhaled pneumococcal biomarkers

### Acronym
PneumEx

### Study objectives
To determine if there is an exhaled biomarker for nasopharyngeal colonisation by pneumococcus

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 23/10/2019, North West- Liverpool Central Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8197; nrescommittee.northwest-liverpoolcentral@nhs.net), ref: 19/NW/0586

### Study design
Experimental cohort study

### Primary study design
Interventional

### Secondary study design
Non randomised study

### Study setting(s)
Hospital

### Study type(s)

Diagnostic

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

### Health condition(s) or problem(s) studied
Nasopharyngeal colonisation by pneumococcus

### Interventions
Nasal exposure with Streptococcus pneumoniae SPN6B. Participants will undergo exhaled assessment via the BreathSpec and 'exhaled detection facemask' pre- and post pneumococcal inoculation. Samples will then be collected intermittently for the following month.

### Intervention Type
Device

### Phase
Not Applicable

### Primary outcome measure
Exhaled biomarker analysis performed by BreathSpec post-inoculation at D0+4, D2, D7, D14, then D14+4, D15, D16, D21 post booster inoculation

### Secondary outcome measures
BreathSpec:
1. The density and duration of pneumococcal colonisation as defined by nasal wash and BreathSpec post-inoculation at D0+4, D2, D7, D14, then D14+4, D15, D16, D21 post booster inoculation

Exhaled Detection Facemask:
1. The rate of pneumococcal bacterial shedding as defined by exhaled detection facemask and cough-plate based assessment post- inoculation at D2, D7, D16, D21 (presence and density (CFU /ml)
2. Pneumococcal carriage density as defined by the exhaled detection facemask and cough-plate based assessment post-inoculation at D2, D7, D16 and D21

### Overall study start date
01/09/2019

### Completion date
01/04/2021

## Eligibility

### Key inclusion criteria
1. Adults aged 18-50 years
2. Fluent spoken English
3. Access to mobile telephone – to ensure safety and timely communication
4. Capacity to give informed consent

**Participant type(s)**
Healthy volunteer

**Age group**
Adult

**Lower age limit**
18 Years

**Upper age limit**
50 Years

**Sex**
Both

**Target number of participants**
48

**Total final enrolment**
41

**Key exclusion criteria**
1. Research participant:
1.1. Currently involved in another study unless observational or non-interventional except for the EHPC bronchoscopy study
1.2. Participant in a previous EHPC trial within the last 3 years (at the discretion of the study team, i.e. not inoculated nasally with pneumococcus)
2. Vaccination: previous pneumococcal vaccination PPV23 or PCV13 (routine in UK babies born since 2005 or US 2001)
3. Allergy: to penicillin/amoxicillin and clarithromycin (or other macrolides)
4. Health history:
4.1. Chronic ill health including immunosuppressive history, diabetes, asthma (on regular medication), recurrent otitis media or other respiratory disease
4.2. Medication that may affect the immune system e.g. steroids, inflammation altering (e.g. nasal steroids, roacutane) or disease-modifying anti-rheumatoid drugs.
4.3. Recent antibiotics (within the last 28 days or long term for known active chronic infection)
4.4. Current illness or acute illness within 14 days prior to inoculation
4.5. Major pneumococcal illness requiring hospitalisation
4.6. Other conditions considered by the clinical team as a concern for participant safety or integrity of the study
5. Direct caring role or close contact: with individuals at higher risk of infection:
5.1. Children under 5 years age
5.2. Chronic ill health or immunosuppressed adults
6. Smoker:
6.1. Current or ex-smoker (regular cigarettes, regular e-cigarette/vaping and regular smoking of recreational drugs) in the last 6 months
6.2. Previous significant smoking history - more than 20 cigarettes per day for 20 years or the equivalent (>20 pack years)
7. Women of childbearing potential (WOCBP): who are:
7.1. Not deemed to have sufficient/effective birth control or confirmed abstinence
7.2. Pregnant

8. History or current drug or alcohol abuse: (frequently drinking alcohol: men and women should not regularly drink >3 units/day and >2 units/day respectively) at the discretion of the clinician
9. Overseas travel planned in the follow-up period of the study visits

### Date of first enrolment
01/10/2019

### Date of final enrolment
01/10/2020

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**Accelerator Research Clinic**
3rd Floor Liverpool Life Sciences Accelerator Building
1 Daulby Street
Liverpool
United Kingdom
L7 8XZ

## Sponsor information

### Organisation
Liverpool School of Tropical Medicine

### Sponsor details
Research Governance Team
Liverpool Life Sciences Accelerator Building
1 Daulby Street
Liverpool
England
United Kingdom
L7 8XZ
+44 (0)151 705 3794
lstmgov@lstmed.ac.uk

### Sponsor type
University/education

### ROR

https://ror.org/03svjbs84

# Funder(s)

### Funder type
Research organisation

### Funder Name
Centre of Excellence in Infectious Disease Research (CEIDR) grant

# Results and Publications

### Publication and dissemination plan
The researchers plan to publish the results in scientific peer-reviewed journals, national and international conferences, on their website and summaries to be included in our yearly newsletter that is used at public engagement events and sent to all participants electronically.

### Intention to publish date
01/10/2023

### Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication.

### IPD sharing plan summary
Other

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| HRA research summary | | | 28/06/2023 | No | No |