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Predicting the outcomes from acute lower respiratory tract infections at the point of need

Submission date 19/10/2021	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 11/07/2024	**Overall study status** Completed	
Last Edited 11/07/2024	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims
SARS-CoV-2 (COVID-19) has emerged as a major cause of acute lower respiratory infection (ALRTI) and death. Patients who develop symptoms and signs of ALRTI are at a higher risk of deterioration due to sepsis and its adverse outcomes. Diagnostic tests for COVID-19 and other bacteria and viruses causing ALRTIs may misdiagnose patients, but gene expression host response biomarker signatures may be used to identify patients at risk of disease progression to multi-organ failure irrespective of diagnosis or treatment. The aims of this study are to determine the accuracy of the GADx multi-channel lateral flow device to detect bacterial infection and differentiate it from viral infection or no infection, and to determine the accuracy of Presymptom Health gene host response and biomarker signatures to predict organ dysfunction in ALRTI patients.

Who can participate?
Patients aged 18 years or older who present to the emergency department with symptoms associated with an ALRTI

What does the study involve?
The study involves the collection of blood samples from patients who are admitted to the emergency department with a suspected chest infection which occasionally could develop into sepsis. Blood samples are taken daily from the day of admission (Day 0) for 4 days or until discharge (whichever occurs first).

What are the possible benefits and risks of participating?
By helping with the study, the team can learn how to identify sepsis early before the symptoms occur. This may help family, friends and others in the future. The patient may feel slight discomfort during the blood collection with a small risk of bruising and a rare risk of infection from the blood collection.

Where is the study run from?
Queen Alexandra Hospital (UK)

When is the study starting and how long is it expected to run for?
February 2021 to April 2024

Who is funding the study?
Presymptom Health & Global Access Diagnostics Ltd (formerly Mologic) (UK)

Who is the main contact?
Portsmouth Research office, Research.Office@porthosp.nhs.uk

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
292720

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number
CPMS 48422, IRAS 292720

Study information

Scientific Title
An observational study of host biomarker signatures that predict the onset of sepsis in patients with lower respiratory tract infections including COVID-19: Utility in managing patients at risk of multi organ failure

Acronym
PRECISION

Study objectives
Gene signatures and protein biomarker signatures that predict the onset of sepsis in an infected patient cohort may be able to differentiate between COVID-19 and general acute lower respiratory tract infection (ALRTI) patients who are likely to deteriorate over time with organ dysfunction and multi-organ failure.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 19/02/2021, South Central – Berkshire Research Ethics Committee (Bristol REC Centre Whitefriars Level 3, Block B Lewins Mead , Bristol , BS1 2NT, United Kingdom; +44 (0)207 104 8178; Berkshire.rec@hra.nhs.uk), ref: 21/SC/0048

Study design
Observational cohort study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Sepsis in patients with lower respiratory tract infections

Interventions
Patients admitted through the ED/COVID reception area with symptoms suggestive of acute lower respiratory tract infection, namely fever, cough, or breathlessness will be assessed for eligibility. The COVID status of all patients admitted to the study will be confirmed through testing for SARS-CoV-2 using the gold standard PCR test of either nasal swab or sputum samples. It is envisaged that there will be two cohorts of patients, defined by the results of a COVID PCR test, within an anticipated 24 hours after admission.
• COVID-19- other infection+
• COVID-19+ infection-

Following written consent and review of inclusion and exclusion criteria, eligible participants will have demographic and clinical data gathered daily, along with blood samples which will be sent to the laboratory for processing as per protocol (see section 8.2). Patients will have an uncomplicated hospital stay and recovery and some will develop organ dysfunction and/or need step-up care. Up to four sequential daily samples will be collected, following admittance to the study, for example days 0, 1, 2 and 3. Sampling will stop when the patient has been either:
1. Discharged alive or deceased
2. End of Life care is initiated (based on a clinical decision patient will not survive acute illness)
3. Inotropic support is initiated
4. COVID PCR test indicates patient should be assigned to a cohort already fully recruited or not allowed to be recruited (relevant to later stages of the study). These instances will be minimized by taking account of the results of community COVID PCR tests in the past 14 days, and rapid lateral flow COVID-19 screening tests done in Emergency Departments.

Patients will be followed up as long as they remain in hospital up to day 6 (7 days since admission).

Outcome data will be collected, censored after 7 days since admission. Pertaining to point d), where patients have been consented and had the first set of research blood tests and it is subsequently found that the COVID-19 PCR places the patient in the fully recruited cohort, then those patients will be followed up to 3 days after the blood tests or until the outcomes outlined above has occurred, if earlier than 3 days.

To enable recruitment to occur all weekdays Monday to Friday, it will be accepted that patients recruited on Wednesdays, Thursdays and Fridays will only have their research blood tests taken when the research team is on duty.

Most participating sites lacking weekend cover, will only be able to take the blood samples on weekdays.

The implications for recruited patients will be:
Recruited Wednesday: samples for days 0, 1 and 2 taken
Recruited Thursday: samples for days 0 and 1 taken
Recruited Friday: samples for days 0, and 3 taken.
These patients will still be followed up for 7 days to determine if the outcomes of interest have occurred. Participating sites that have a 7-day research team presence, can recruit patients and take blood samples on weekend days as well.

Throughout the study, participants will continue to be managed according to their clinical needs.

Intervention Type
Other

Primary outcome(s)
1. The accuracy of the GADx multi-channel lateral flow device to detect bacterial infection and differentiate it from viral infection or no infection, measured using proteomic host-response biomarker signatures at a single time point within 24 hours of presentation to the hospital
2. The accuracy of Presymptom Health host response signature to predict sepsis, measured using 7-gene and 14-gene transcriptome signatures within 24 hours of presentation to the hospital, and daily up to 3 days thereafter
3. Biomarker signatures to predict organ dysfunction in all ALTRI patients, COVID-19+ve patients

and COVID-19-ve patients, measured using 7-gene and 14-gene transcriptome signatures within 24 hours of presentation to the hospital, and daily up to 3 days thereafter

Key secondary outcome(s))
1. Differences in biomarker signatures between COVID-19+ve and COVID-19-ve ALTRIs, measured using GADx proteomic and Presmyptom transcriptome signatures once within 24 hours of presentation to the hospital
2. Comparison of gene expression biomarkers with other known sepsis biomarker trajectories and illness severity scores to predict adverse outcomes in ALTRIs, measured using comparative proADM, IL-6, IL-8, IL-10, CRP and procalcitonin levels, measured within 24 hours of presentation to the hospital, and daily up to 3 days thereafter
3. The ability of GADx point of care multi-channel lateral flow technology to predict disease progression to sepsis, measured using proteomic host-response biomarker signatures at a single time point (initial presentation to the hospital)

Completion date
30/04/2024

Eligibility

Key inclusion criteria
1. Patients aged over 18 years
2. Patients admitted to hospital with symptoms associated with ALRTI
3. Have objective signs of acute lower respiratory tract infection as denoted by ONLY ONE of the following criteria:
3.1. New oxygen requirement
3.2. Clinical signs of acute lung infiltration or consolidation e.g. crackles, dullness to percussion, aegophony
3.3. Radiological signs of new lung infiltrates or consolidation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Patients <18 years of age
2. Pregnant patients
3. Patients with severe anaemia, defined as a haemoglobin less than 80 g/l at presentation
4. Patients with prior oxygen dependency due to chronic lung disease with chronic respiratory

failure.
5. Immunosuppressed patients (e.g. HIV disease, anti-rejection medication)
6. Patients admitted for palliation only, or not expected to survive longer than 24 hours from ED attendance
7. Patients who already meet the criteria for sepsis at the time of hospital presentation
8. Recruitment to another study already at the time of presentation that would result in duplication of blood sampling

Date of first enrolment
30/04/2021

Date of final enrolment
01/04/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queen Alexandra Hospital
Southwick Hill Road
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Study participating centre
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Study participating centre
University Hospital of North Tees
Hardwick Road
Stockton-on-tees
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Study participating centre
Rotherham General Hospital
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Study participating centre
St George's Hospital
Blackshaw Road
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SW17 0QT

Study participating centre
St Peter's Hospital
Guildford Road
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Study participating centre
Bristol Royal Infirmary
Marlborough Street
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Study participating centre
Royal Surrey County Hospital
Egerton Road
Guildford
United Kingdom
GU2 7XX

Study participating centre
Gloucester Royal Hospital
Great Western Road

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GL1 3NN

Sponsor information

Organisation
Portsmouth Hospitals NHS Trust

ROR
https://ror.org/009fk3b63

Funder(s)

Funder type
Industry

Funder Name
Presymptom Health & Global Access Diagnostics Ltd

Results and Publications

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