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Point-of-care testing for respiratory pathogens in critical care

Submission date
19/06/2017

Recruitment status
No longer recruiting

Registration date
21/06/2017

Overall study status
Completed

Last Edited
28/02/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Current plain English summary as of 12/02/2020:
Background and study aims
Pneumonia (chest infection) is a serious illness which is usually caused by bacteria. When identified, it warrants swift treatment with antibiotics and sometimes requires high-dependency or intensive care unit admission.

The choice of which of the many antibiotics to use in patients with pneumonia is 'best-guess': it is guided by what bacteria are likely be present. As a result we use antibiotics which kill many different bacteria. We know that use of these antibiotics promotes antibiotic resistance. The World Health Organisation have identified antibiotic resistance as one of the biggest threats to global health today.

Current tests looking for bacteria in sputum take several days to generate results so do not allow doctors to be more targeted with their antibiotic use. Rapid 'point-of-care' tests for pneumonia have been developed which can provide accurate results in about 1 hour rather than several days. We wish to explore if using a rapid test improves the use of antibiotics and improves patient care.

Who can participate?
Adults aged 18 and older who are admitted to critical care and are on antibiotics for pneumonia.

What does the study involve?
After the patient is enrolled in the trial 3 samples are obtained: a sputum sample, a urine sample and a blood sample. They are allocated to either get the current standard clinical care or a new molecular test that looks for bacteria and viruses in the sputum. Those who get the new test also get a blood test which measures a marker of infection (called procalcitonin) and a urine test which looks for part of a bacteria which commonly causes chest infections.

Patients who get the new test have all tests done immediately by the research team which typically takes around 2 hours. The research team (who are infection speciality registrars or consultants) also interpret the results and feed them back to the responsible clinical team along with any antibiotic advice if the results facilitate a change in therapy.

What are the possible benefits and risks of participating?
Participants may benefit from identifying an organism which has caused their disease considerably quicker and this may better direct the antibiotic therapy they receive.

There are no notable risks with participating.

Where is the study run from?
Southampton General Hospital (UK)

When is the study starting and how long is it expected to run for?
August 2016 to July 2025

Who is funding the study?
The study is funded by Southampton Biomedical Research Centre (UK) and the National Institute for Health Research (UK)

Biofire Diagnostics are supplying the consumables free of charge but had no input into the design or running of the study.

Who is the main contact?
1. Dr Tristan Clark
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2. Dr Stephen Poole
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Previous plain English summary:
Background and study aims
Acute respiratory tract infections are responsible for over four million deaths each year and are the third most common cause of death worldwide. Respiratory viruses are the most common detectable pathogen (virus) in adults with acute respiratory infection. Influenza and other respiratory virus infections often remain undiagnosed in patients admitted to critical care due to lack of systematic testing. Even when testing occurs, treatment is often delayed because of slow turnaround times of laboratory methods. Treatment for influenza in hospitalised adults requires medications called neuraminidase (e.g. Tamiflu / oseltamivir). Prompt treatment with neuraminidase inhibitors reduces the risk of death and therefore the sooner patients receive them, the better their outcomes will be. Point-of-care tests (POCT) for respiratory viruses have been limited in clinical practice by unacceptably low sensitivities and by an inadequate range of detectable viruses. Newer molecular systems, such as the FilmArray Respiratory Panel, have comparable sensitivity to laboratory tests and are able to detect a wide range of viruses generating a result in about an hour. The aim of the study is to evaluate the impact of point-of-care testing for respiratory viruses in adults with severe acute respiratory illness in critical care units.

Who can participate?
Adults aged 18 and older who are admitted to the hospital with a respiratory issue

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive nose and throat swab taken (which is like a ‘cotton bud’) by research staff. This swab is taken immediately to and analysed for many different viruses that can cause respiratory on the POCT. The results are available in about one hour and participants are informed of the results, as will the doctors and nurses looking after them. Those in the second group receive the standard care.

Participants have their hospital case notes and clinical data reviewed to see if a rapid testing can diagnose respiratory viruses sooner and improves health outcomes.

What are the possible benefits and risks of participating?
Participants may benefit from having diagnosed with a respiratory virus sooner than otherwise, leading to a more rapid use of antivirals and appropriate isolation facility use. There are no notable risks with participating.

Where is the study run from?
Southampton General Hospital (UK)

When is the study starting and how long is it expected to run for?
August 2016 to July 2025

Who is funding the study?
Biofire Diagnostics (UK)

Who is the main contact?
1. Dr Tristan Clark
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number
216585

ClinicalTrials.gov number

Secondary identifying numbers
34003, IRAS 216585

Study information

Scientific Title
Pragmatic randomized controlled trial of molecular point-of-care testing for respiratory pathogens versus routine clinical care in critically ill adults with Pneumonia: SARIPOC

Acronym
SARIPOC

Study objectives
Current study hypothesis as of 13/02/2020:
The aim of the study is to evaluate the clinical impact of molecular point-of-care testing for respiratory pathogens in adults with severe acute respiratory illness in critical care units.

Previous study hypothesis:
The aim of the study is to evaluate the clinical impact of molecular point-of-care testing for respiratory viruses in adults with severe acute respiratory illness in critical care units.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Regional Ethics Committee (REC) Southcentral – Berkshire, 25/05/2017, 17/SC/0110

Study design
Randomised; Interventional; Design type: Diagnosis, Management of Care

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

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

Health condition(s) or problem(s) studied
Infectious diseases

Interventions
Current interventions as of 12/02/2020:
Participants are randomly allocated to either the intervention or the control group using a 1:1 software randomization service.

Intervention group: Participants in this group receive testing for respiratory pathogens at the point-of-care using the FilmArray Pneumonia Panel with results communicated to the clinical team. Additionally, a procalcitonin blood test and pneumococcal urinary antigen testing are performed. The results are available in about two hours and patients will be informed of the results, as will the doctors and nurses looking after them. This is done in addition to standard care.

Control group: Participants in this group receive the standard clinical care alone. This may include sending a sputum sample to the laboratory for testing (the results for this usually take 1 to 2 days).

Retrospective hospital case notes and clinical data are evaluated.

Previous interventions:
Participants are randomly allocated to either the intervention or the control group using a 1:1 internet-based randomisation service.

Intervention group: Participants in this group receive nose and throat swabs, and have a lower respiratory sample taken if available, which is then tested for respiratory virus at the point-of-care using the FilmArray Respiratory Panel with results communicated to the clinical team. The results are available in about one hour and patients areinformed of the results, as will the doctors and nurses looking after them This is done in addition to the standard care.

Control group: Participants in this group receive the standard clinical care alone. This may include sending a nose and throat swab to the laboratory for testing (the results for this usually take 1 to 2 days).

Retrospective hospital case notes and clinical data are evaluated.

Intervention Type
Other

Primary outcome measure

Current primary outcome measure as of 19/03/2021:
The proportion of patients treated with results directed antimicrobials within 48 hours of a lower respiratory tract test result (this is defined as the use of antimicrobial agents that are started or continued on the basis of appropriateness (or the optimal choice) for a detected pathogen(s), where a putative pathogen(s) considered by the investigators to be plausibly causative, is identified; or the appropriate de-escalation or cessation of antimicrobials occurs where no pathogen is identified).

Previous primary outcome measure from 12/02/2020 to 19/03/2021:
All primary and secondary outcome measures are measured retrospectively using electronic hospital case notes at the end of hospital stay or 30 days, and 60 days.
The proportion of patients treated with results directed antimicrobials. This is defined as the use of antimicrobial agents that are started or continued on the basis of appropriateness (or the optimal choice) for a detected pathogen(s), where a putative pathogen(s) considered by the investigators to be plausibly causative, is identified; or the appropriate de-escalation or cessation of antimicrobials occurs where no pathogen is identified.

Original primary outcome measure:
Proportion of influenza-positive patients treated with neuraminidase inhibitors (NAI) within 7 days of admission to hospital, measured retrospectively on discharge or at 30 days, using electronic hospital prescribing systems

Secondary outcome measures

Current secondary outcome measures as of 19/03/2021:
1. Median time to results directed antimicrobial therapy within 48 hours of a lower respiratory tract test result, days
2. Proportion with results-directed escalation or de-escalation in antimicrobial therapy within 48 hours of a lower respiratory tract test result. Escalation/de-escalation defined as addition/ cessation of a second agent or increase/decrease in antibiotic stewardship 'ranking'
3. Median time to results directed escalation/ de-escalation within 48 hours of lower respiratory tract result, hours
4. Proportion treated with ineffective empirical antimicrobial therapy (defined by the absence of an antimicrobial agent active against the specific class of microorganisms responsible for the infection or the administration of an antimicrobial agent to which the microorganism responsible for infection is resistant) at recruitment
5. Median duration of ineffective antimicrobial therapy (hours), up to 14 days
6. Median duration of all antimicrobial therapy for this episode of pneumonia (hours), up to 14 days
7. Median number of different antimicrobial agents used for this episode of pneumonia (hours) up to 14 days
8. Number of antibiotic-free hours in the 14 days following recruitment
9. Median number of hours piperacillin/tazobactam in the 14 days following recruitment
10. Median number of hours of meropenem in the 14 days following recruitment
11. Median turn-around time for results, hours and days
12. Proportion of patients with a credible pathogen identified for this episode of pneumonia. Credible pathogen as determined by two independent infection specialists, with a third adjudicating in event of disagreement.
13. Concordance between pathogen identification between molecular methods (FilmArray) and culture
14. Concordance between genotypic and phenotypic isolate sensitivities

15. Proportionate in-hospital, 30- and 60-day mortality
16. Median duration of hospitalisation (days), measured for the duration of hospitalisation or up to 30 days (whichever is shortest)
17. Median time on non-invasive ventilation (days), measured for the duration of hospitalisation or up to 30 days (whichever is shortest)
18. Median time on invasive ventilation (days), measured for the duration of hospitalisation or up to 30 days (whichever is shortest)
19. Median time on ionotropic support (days), measured for the duration of hospitalisation or up to 30 days (whichever is shortest)
20. Median time in critical care (days), measured for the duration of hospitalisation or up to 30 days (whichever is shortest)
21. Proportion with antimicrobial associated adverse events, measured for the duration of hospitalisation or up to 30 days (whichever is shortest)
22. Relationship between sputum pathogen quantification within 48 hours of recruitment (colony-forming units/CFUs and/or genome copies/ml) and clinical outcome measures (30-day mortality, length of stay and time on organ support)
23. Utility of serum biomarkers (Procalcitonin) at recruitment in differentiating between bacterial and viral infection (as detected by microbiological sampling) and predict outcome (clinical outcome measures as described above)
24. Proportion and nature of pathogen detection in pneumonia occurring following macro-aspiration
25. Proportion and nature of pathogen detection in patients with SARS-CoV-2 infection
26. Proportion and nature of pathogen detection in relation to the preceding duration of antibiotic therapy (hours)

Previous secondary outcome measures from 12/02/2020 to 19/03/2021:
1. Median number of days to treatment with results directed antimicrobials
2. Proportion of participants with an escalation in antimicrobial therapy following test results (defined as addition of second agent or increase in antibiotic stewardship 'ranking')
3. Proportion of participants with a de-escalation (defined as either removal of a second agent or de-escalation according to ranking above) in antibiotics following results
4. Median number of days to escalation or de-escalation in antimicrobial therapy
5. Proportion of participants treated with inappropriate empirical antimicrobial therapy (defined by the absence of an antimicrobial agent active against the specific class of microorganisms responsible for the infection or the administration of an antimicrobial agent to which the microorganism responsible for infection is resistant).
6. Median number of days of inappropriate antimicrobial therapy
7. Median number of days of all antimicrobial therapy
8. Median number of days of intravenous antimicrobial therapy
9. Median number of different antimicrobial agents used
10. Proportion of participants correctly treated with influenza antivirals
11. Median number of days to treatment with appropriate influenza antivirals
12. Median number of days of treatment with inappropriate influenza antivirals
13. Proportion of participants correctly isolated in single room accommodation
14. Median number of days to appropriate isolation facility use
15. Median number of days of inappropriate isolation facility use
16. Median turn-around time for results (h)
17. Proportion of participants with a pathogen identified
18. Concordance between pathogen identification between molecular methods (FilmArray) and culture
19. Concordance between genotypic and phenotypic isolate sensitivities
20. Proportionate in-hospital mortality at 30 and 60 days

21. Median number of days of hospitalisation
22. Median number of days on organ support
23. Median number of days in critical care
24. Proportion of participants re-presenting to hospital within 30 days post discharge
25. Proportion of participants readmitted to hospital within 30 days post discharge
26. Proportion of participants with Clostridium difficile infection
27. Proportion of participants with antimicrobial associated adverse events
28. Proportion of participants with detection of multi-resistant pathogens whilst in hospital
29. Proportion of participants with recurrent infection

Previous secondary outcome measures:
1. Proportion of cases of influenza identified are measured using electronic hospital case notes at end of hospital stay or 30 days
2. Proportion of cases of non-influenza respiratory viruses detected are measured using electronic hospital prescribing systems at end of hospital stay or 30 days
3. Proportion of all NAI use occurring in influenza positive patients are measured using electronic hospital prescribing systems at end of hospital stay or 30 days
4. Time from admission to NAI commencement in hours are measured using electronic hospital prescribing systems
5. Duration of NAI use in influenza positive and negative patients in days are measured using electronic hospital prescribing systems
6. Proportion of patients treated with antibiotics are measured using electronic hospital prescribing systems at end of hospital stay or 30 days
7. Duration of antibiotic use (in days) are measured using electronic hospital prescribing systems
8. Number of antibiotic agents received and spectrum are measured using electronic hospital prescribing systems at end of hospital stay or 30 days
9. Proportion of patients isolated are measured using hospital case notes at end of hospital stay or 30 days
10. Duration of isolation facility use are measured using hospital case notes at end of hospital stay or 30 days
11. Proportion of influenza cases correctly isolated are measured using hospital case notes at end of hospital stay or 30 days
12. Time from admission to isolation of influenza cases are measured using hospital case notes at end of hospital stay or 30 days
13. Time from admission to de-isolation of influenza negative cases are measured using hospital case notes at end of hospital stay or 30 days
14. Time on organ support (in days) is measured using hospital case notes
15. Time on supplementary oxygen (in days) is measured using hospital case notes
16. Time in critical care unit (level 2 /3 duration) (in days) is measured using hospital case notes
17. Duration of hospitalisation (in days) is measured using hospital case notes
18. Proportion of patients with complications and serious adverse events are measured using hospital case notes at end of hospital stay or 30 days
19. In hospital, 30 and 60 day mortality is measured

Overall study start date
01/08/2016

Completion date
01/07/2025

Eligibility

Key inclusion criteria

Current participant inclusion criteria as of 12/02/2020:
1. Admitted to the Respiratory High Dependency Unit (RHDU), or an Intensive Care Unit (ICU), or about to be transferred to RHDU, GICU, NICU or under the care of the RHDU or ICU team in another hospital area, within University Hospital Southampton NHS Foundation Trust (UHS)
2. Aged ≥18 years
3. Has a working diagnosis of CAP, HAP or VAP* and physician decides to start new antibiotic treatment or modify existing antibiotic treatment.

*CAP defined by the BTS as: 'symptoms and signs of acute lower respiratory tract infection associated with new radiographic shadowing for which there is no other explanation'. CAP patients who are intubated and ventilated remain classified as CAP.

HAP defined as by the IDSA as: 'new lung infiltrate, plus clinical evidence that the infiltrate is of an infectious origin, which includes the new onset of fever, purulent sputum, leucocytosis, and decline in oxygenation... arising >48 h after hospital admission'. HAP patients who are intubated and ventilated remain classified as HAP.

VAP defined as by the IDSA as: 'new lung infiltrate plus clinical evidence that the infiltrate is of an infectious origin, which include the new onset of fever, purulent sputum, leucocytosis, and decline in oxygenation... occurring >48 h after endotracheal intubation'

Previous participant inclusion criteria:
1. Admitted to the Respiratory High Dependency Unit (RHDU), or an Intensive Care Unit (ICU), or about to be transferred to either RHDU or ICU, or under the care of the RHDU or ICU team in another hospital area, within University Hospital Southampton NHS Foundation Trust (UHS)
2. Aged ≥18 years old
3. Duration of respiratory illness less than 10 days prior to hospitalisation
4. Presented to hospital less than 72 hours prior to enrolment
5. Has a severe acute respiratory illness*

*An episode of severe acute respiratory illness is defined as an acute pulmonary illness (including pneumonia, bronchitis and influenza-like illness) or an acute exacerbation of a chronic respiratory illness (including exacerbation of COPD, asthma or bronchiectasis), requiring high dependency or intensive care. For the study, a severe acute respiratory illness as a provisional, working, differential or confirmed diagnosis must be made by a treating clinician.

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 200; UK Sample Size: 200

Total final enrolment
200

Key exclusion criteria
Current participant exclusion criteria as of 12/02/2020:
1. A purely palliative approach being taken by the treating clinicians
2. Previously included in this study
3. Consent declined or consultee consent declined
4. Underlying Cystic Fibrosis or other condition characterized by persistent colonization with resistant organisms
5. Not expected to survive the next 24 h in the opinion of the responsible clinical team

Involvement in observational trials may not exclude a participant from this trial, and this is at the CI's discretion.

Previous participant exclusion criteria:
1. Not fulfilling all the inclusion criteria
2. A purely palliative approach being taken by the treating clinicians
3. Previously included in this study
4. Declines nasal / pharyngeal swabbing
5. Consent declined or consultee consent declined
6. Severe acute respiratory illness is related to solely to critical illness and/or is not the principal illness leading to ICU/HDU admission

Date of first enrolment
01/07/2017

Date of final enrolment
01/07/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Southampton General Hospital
University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
Southampton General Hospital

Sponsor details
Mailpoint 18
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/011cztj49

Funder(s)

Funder type
Industry

Funder Name
Biofire Diagnostics

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 12/02/2020:
We plan to publish the results of this trial in a high-impact peer-reviewed journal in September 2022.

Previous publication and dissemination plan:
We plan to publish the results of this trial in a high-impact peer reviewed journal in September 2021.

Intention to publish date
30/09/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Tristan Clark (t.w.clark@soton.ac.uk). Data will be made available in 3 months following publication for a period of 5 years. All of the individual participant data

collected during the trial, after de-identification will be made available. It will be available to researchers who provide methodologically sounds proposal to achieve the aims in the approved proposal including individual participant meta-analysis. Proposals should be directed to the above PI. All data will be de-identified. Informed consent will be obtained from all patients. There are no known ethical or legal restrictions currently.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version v4.1	08/02/2021	13/07/2021	No	No
Results article		09/09/2022	30/09/2022	Yes	No
HRA research summary			28/06/2023	No	No