ISRCTN97997760 https://doi.org/10.1186/ISRCTN97997760

Point of care testing for sepsis

Submission date
22/06/2016

Recruitment status
No longer recruiting

Registration date
18/08/2016

Overall study status
Completed

Last Edited
22/06/2022

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
Sepsis is the term used to describe serious infections. Up to half of all hospitalised patients with sepsis may die. It is caused by microrganisms (microbes), such as bacteria, and one of the most important parts of treating patients with sepsis is to give them the right antibiotics as soon as possible to treat the underlying infection. Many different microbes can cause sepsis. Currently the only way to find out for sure which one to target in any particular patient is to wait for it to grow in a laboratory from a sample of their blood, or other samples (culture). As it takes at least 24-48 hours to grow in the laboratory, doctors choose 'best guess' antibiotics that can treat a lot of different microbes before they know which one would be the best fit. These are not always the right antibiotics for that particular individual, and sometimes patients only get the right treatment once there is a result from the laboratory. Randox Ltd has recently developed a new bedside device based on technology that is able to identify bacteria in patients' blood within just one hour. Looking only for characteristic fragments of over 40 different microbes means that doctors’ decisions about which treatment to give patients will not need to wait for over a day for the microbe to grow in a laboratory. This will allow treatments to be better targeted from a much earlier stage. The aim of this study is to investigate how well the new test is able to identify microbes in comparison to blood culture, which is currently the best method of measurement (gold standard).

Who can participate?
Patients aged 16 years who are admitted to ICU and are suspected of having sepsis.

What does the study involve?
Patients are screened daily by members of the clinical team and where a patient suspected of having sepsis requires a blood sample taken as part of routine clinical care; additional blood will be taken at this time and stored. At the time that the standard care blood culture is taken from a potential participant, a 5ml research sample of blood is also be collected for analysis with the new test.
An additional 10ml sample of blood is also collected on the first sampling occasion for a given patient when research staff are available at that time to process and store the sample. Each patient can contribute more than one sample to this study but there must be five days between each sample being taken.

What are the possible benefits and risks of participating?
There are no direct benefits or risks involved to the patients taking part in this study.

Where is the study run from?
At least 18 intensive care units in NHS hospitals in Northern Ireland and England (UK)

When is the study starting and how long is it expected to run for?
May 2015 to November 2022

Who is funding the study?
Innovate UK (UK)

Who is the main contact?
1. Dr Ronan McMullan (scientific)
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2. Mr Paul Doherty (public)
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
15176RMcM-SS

Study information

Scientific Title
PoinT of carE teSTing for sepsIs: a diagnosTic accuracy study

Acronym
TEST-IT

Study objectives
The Randox POC Multiplex PCR test has high diagnostic accuracy, in comparison with conventional culture, for detecting pathogens in critically ill adults with suspected sepsis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. South Central - Oxford C Research Ethics Committee, 06/07/2016, ref: 16/SC/0277
2. Scotland A REC, 07/07/2016, ref: 16/SS/0108

Study design
Prospective observational multi-centre cross sectional diagnostic accuracy study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet

Health condition(s) or problem(s) studied
Sepsis

Interventions
Adult patients admitted to ICU who undergo blood culture testing for suspected sepsis are eligible for this study and will be screened daily, on the basis of the inclusion/exclusion criteria as specified in the protocol. Blood cultures will be taken in the usual manner in the course of routine care. At the time that each blood culture is taken from an eligible patient, a 5ml sample of blood will also be collected for multiplex PCR testing. An additional 10ml sample of blood will also be collected where it is the first sample or research staff are available to process and store the sample. Each patient can contribute more than one sample to this study; however an interval of at least 5-days must lapse between consecutive samples obtained.

Reference standard: Automated blood culture technology, in place as standard NHS care in microbiology laboratories at participating sites, and performed prospectively as part of usual clinical care.

Index test: Microarray-based multiplex PCR for detection of DNA from a range of at least 40 sepsis pathogens. It will be carried out using an instrument which has been developed by Randox Ltd specifically for this test. The index test will be performed retrospectively in a centralised laboratory for the first part of the study and prospectively at study sites in the latter part of the study.

Intervention Type
Other

Primary outcome measure
Diagnostic accuracy of the multiplex PCR test, expressed as sensitivity, specificity, and positive and negative predictive values, with uncertainty expressed using 95% confidence limits.

Secondary outcome measures
1. Resource use associated with the multiplex PCR testing and conventional blood culture is measured by study-specific data collection forms at randomly generated time points over the course of the trial
2. The time required to complete testing will be measured for both Multiplex PCR and the paired blood culture. In the case of the blood culture two measures will be recorded at:
2.1. The time between sampling and the test first being reported to clinical teams as positive
2.2. The time between sampling and a final pathogen identification first being reported to clinical teams. It is acknowledged that, for both of these, the result will usually be ‘first’ reported verbally
Blood cultures that do not flag positive after 5-days of incubation will be categorised as negative with a time to result of 5-days.

Exploratory outcome measures:
1. Neutrophil activation biomarkers are measured by plasma MPO and MMP-8 in sample taken at time of reference standard
2. Plasma and serum inflammatory response biomarkers are measured by CRP, cytokines (including but not limited to TNFα, IL-1β, IL-6, IL-8), proteases and anti-proteases, activation molecule expression (including but not limited to sICAM-1), coagulation factors (including but not limited to thrombin-anti-thrombin complex, tissue factor, protein C, thrombomodulin and plasminogen activator inhibitor-1), RAGE ligands and vitamin D status

3. Pulmonary and systemic epithelial and endothelial function and injury are assessed through measuring plasma and serum biomarkers (including RAGE, Ang I/II, SP-D, vWF and PCP3) and urinary albumin/creatinine ratio in sample taken at time of reference standard
4. Surrogate markers of inflammation are measured through primary cultures fresh human neutrophils monocytes and macrophages as well as mesenchymal stromal cells in sample taken at time of reference standard

Overall study start date
01/05/2015

Completion date
30/11/2022

Eligibility

Key inclusion criteria
1. Aged 16 years and over
2. Patients with suspected sepsis
3. Undergoing blood sampling for culture in the course of routine care

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
4501 samples

Total final enrolment
3185

Key exclusion criteria
1. Patients aged <16 years old
2. Patients previously recruited to the study
3. Consent declined

Date of first enrolment
01/09/2016

Date of final enrolment
28/02/2018

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Study participating centre
Belfast Health and Social Care Trust
274 Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
South Wharf Road
St Mary's Hospital
London
United Kingdom
W2 1NY

Study participating centre
Heart of England NHS Foundation Trust
Bordesley House
Birmingham Heartlands Hospital
Bordesley Green East
Birmingham
United Kingdom
B9 5SS

Study participating centre
University Hospital South Manchester NHS Foundation Trust
Southmoor Road
Wythenshawe
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M23 9LT

Study participating centre
University Hosptials Birmingham
Mindelsohn Way
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B15 2TH

Study participating centre
Royal Liverpool and Broadgreen University Hospital
Thomas Drive
Liverpool
United Kingdom
L14 3LB

Study participating centre
University Hospitals Bristol NHS Trust
Bristol Royal Infirmary
Upper Maudlin Street
Bristol
United Kingdom
BS2 8HW

Study participating centre
Western Health and Social Care Trust
Altnagelvin Area Hospital site
Glenshane Road
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BT47 6SB

Study participating centre
Royal Berkshire NHS Foundation Trust
London Road
Reading
United Kingdom
RG1 5AN

Study participating centre
Poole Hospital NHS Foundation Trust
Longfleet Road

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BH15 2JB

Study participating centre
Northern Health and Social Care Trust
Northern Health and Social Care Trust Trust Headquarters
Bretten Hall
Bush Road
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BT41 2RL

Study participating centre
Chelsea & Westminster Hospital NHS Foundation Trust
369 Fulham Road
London
United Kingdom
SW10 9NH

Study participating centre
Barts Health NHS Trust
The Royal London Hospital
Whitechapel Road
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E1 1BB

Study participating centre
Kings College Hospital NHS Foundation Trust
Denmark Hill
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United Kingdom
SE5 9RS

Study participating centre
University Hospital Southampton NHS Trust
Tremona Road

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United Kingdom
SO16 6YD

Study participating centre
Lothian Universities Hospital Trust (NHS Lothian)
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1 Lauriston Place
Edinburgh
United Kingdom
EH3 9YW

Study participating centre
South Eastern Health and Social Care Trust
Upper Newtownards Road
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BT16 1RH

Study participating centre
Salford Royal NHS Foundation Trust
Stott Lane
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M6 8HD

Sponsor information

Organisation
Belfast Health and Social Care Trust (BHSCT)

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Research Governance
King Edward Building
The Royal Hospitals
Grosvenor Road
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BT12 6BN

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/02tdmfk69

Funder(s)

Funder type
Industry

Funder Name
Innovate UK

Alternative Name(s)
innovateuk

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
It is anticipated that the study findings will be published in national and international peer review journals which will be led by the Co-CI's. This will secure a searchable compendium of these publications and make the results readily accessible to the public and health care professionals. In addition study findings may be presented at both national and international meetings and also to appropriate patient groups.

Intention to publish date
30/05/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Paul Doherty at NICTUTEST-IT@nictu.hscni.net

IPD sharing plan summary
Available on request

Study outputs

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