

# Point of care testing for sepsis

<b>Submission date</b> 22/06/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 18/08/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 22/06/2022	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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 microorganisms (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. Radox 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)

ronan.mcmullan@belfasttrust.hscni.net

2. Mr Paul Doherty (public)

paul.doherty@nictu.hscni.net

## Contact information

### Type(s)

Scientific

### Contact name

Dr Ronan McMullan

### Contact details

Kelvin Laboratory Building

The Royal Hospitals

Grosvenor Road

Belfast

United Kingdom

BT12 6BA

+44 2890 634140

ronan.mcmullan@belfasttrust.hscni.net

### Type(s)

Public

### Contact name

Mr Paul Doherty

### Contact details

Northern Ireland Clinical Trials Unit

1st Floor Elliott Dynes

The Royal Group of Hospitals

Grosvenor Road

Belfast

United Kingdom

BT12 6BA  
+44 2890 63 5794  
paul.doherty@nctu.hscni.net

## **Additional identifiers**

**Protocol serial number**  
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

**Study type(s)**  
Diagnostic

**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(s)**

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

## **Key secondary outcome(s)**

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 TNF $\alpha$ , IL-1 $\beta$ , 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

## **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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

16 years

**Sex**

All

**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**

United Kingdom

England

Northern Ireland

Scotland

**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  
Manchester  
United Kingdom  
M23 9LT

**Study participating centre**  
**University Hospitals Birmingham**  
Mindelsohn Way  
Birmingham  
United Kingdom  
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  
Derry  
United Kingdom  
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  
Poole  
United Kingdom  
BH15 2JB

**Study participating centre**  
**Northern Health and Social Care Trust**  
Northern Health and Social Care Trust Trust Headquarters  
Bretten Hall  
Bush Road  
Antrim  
United Kingdom  
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  
Whitechapel  
London  
United Kingdom  
E1 1BB

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

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

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



**Study participating centre**  
**South Eastern Health and Social Care Trust**  
Upper Newtownards Road  
Dundonald  
Belfast  
United Kingdom  
BT16 1RH

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

## **Sponsor information**

**Organisation**  
Belfast Health and Social Care Trust (BHSCT)

**ROR**  
<https://ror.org/02tdmfk69>

## **Funder(s)**

**Funder type**  
Industry

**Funder Name**  
Innovate UK

**Alternative Name(s)**  
UK Research and Innovation Innovate UK, innovateuk

**Funding Body Type**  
Government organisation

**Funding Body Subtype**  
National government

**Location**  
United Kingdom

# Results and Publications

## 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?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No