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DIAMONDS-SEARCH study: Designing new tests that can diagnose the causes of fever, including COVID-19

Submission date
29/05/2020

Recruitment status
No longer recruiting

Registration date
22/06/2020

Overall study status
Ongoing

Last Edited
16/06/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

DIAMONDS – Diagnosis and Management of Febrile Illness using RNA Personalised Molecular Signature Diagnosis – is a five-year collaborative, multi-partnered research project that will develop a new molecular diagnostic test to provide rapid diagnosis of common infectious bacterial disease, as well as viral and inflammatory diseases. It involves an international, multi-disciplinary team of researchers and scientists from across 28 institutions and 13 countries with 11 of those countries from Europe.

The DIAMONDS research team is addressing the problem that clinicians have when patients who have common symptoms (such as fever) come to hospital. Common infectious and inflammatory diseases account for up to a third of all unplanned hospital and primary care attendances. Currently, if a patient is admitted to hospital with a fever and non-specific symptoms, they could go through a whole series of investigations, such as blood tests, spinal fluid samples, MRI and CT scans, to help clinicians try to identify the cause of their symptoms. These tests can be uncomfortable, expensive and a patient could be waiting days or even weeks before they receive an accurate diagnosis and appropriate treatment, for example patients are often treated with antibiotics as a precautionary measure against serious bacterial infections, which have no effect if the real diagnosis is a self-resolving viral infection. All this puts a huge strain on the patient and the healthcare system.

When trying to find a solution to this problem, researchers have previously found that common diseases are characterised by unique patterns of gene expression (the process of DNA information being converted into instructions for cells to make proteins and other molecules). When a disease is associated with the switching on and off of genes in a patient's blood, it forms its own 'gene signature'. The gene signature has previously been shown to identify bacterial infections with a 95-100% accuracy.

The DIAMONDS research team will use expertise from previous gene signature research to make diagnosis faster and more accurate. The aim is to shorten the diagnosis time to under two hours, using a patient's first blood sample. This diagnostic test may save a patient from unnecessary and potentially painful tests, as well as revolutionise the way healthcare can be delivered and have a positive impact on the health system and medical practitioners delivering healthcare.

The first part of the project is recruitment patients with conditions caused by infection and inflammation into DIAMONDS Search. Samples will be taken during the episodes of acute and

convalescent illness. Selected optimal gene signatures for a wide range of infections and inflammatory conditions will be used to build a data library of the identifiable gene signatures of common inflammatory and infectious diseases. By comparing the pattern of genes in a patient's blood sample to the hundreds of gene signatures in the library, diagnosis can be made rapidly. Gene signatures selected from the data library will be used on both existing devices and new prototypes, such as lab-on-chip technology to create test devices, to enable diagnosis of multiple conditions on the same device - a concept called Personalised Molecular Signature Diagnosis (PMSD). PMSD-based care could transform the management of suspected infectious or inflammatory diseases, by driving more efficient and equitable organisation of the way care is delivered to the large numbers of patients presenting with symptoms of infection or inflammation.
As part of the global response to the coronavirus pandemic, the DIAMONDS consortium has re-purposed DIAMONDS Search to tackle the urgent global need for improved diagnostics to guide clinical management of patients with confirmed or suspected SARS-CoV-2. The DIAMONDS consortia is undertaking rapid development of novel host RNA-based diagnostic devices that can diagnose SARS-CoV-2 infection and comparator illnesses simultaneously at the point of testing and also to discriminate pure SARS-CoV-2 infection from that caused by co-infections, for instance with bacteria or other infections. DIAMONDS will also elucidate host gene expression signatures associated with different manifestations of Covid-19, inflammatory disease and uncontrolled viral disease.

DIAMONDS is recruiting patients of all ages with suspected and proven Covid-19, across the full spectrum of disease from mild (not admitted to hospital), moderate (admitted to ward only) and severe (intensive care). Samples and data from these highly characterised patients will be used by DIAMONDS consortium biotechnology partners to develop devices to detect diagnostic RNA signature of SARS-CoV-2 infection and signatures predictive of severe disease.

We will not be analysing the clinical information or samples while the patient is in hospital, but will be storing them to be analysed later, so the results are not likely to help manage the patient's illness and will not affect the patient's clinical care. However, the information gained by the study may help improve the diagnosis and treatment patients in the future.If we find significant results that would influence the patient's future care, the clinical care team will contact the patient.There are no disadvantages to joining the study. The small additional amount of blood and other samples taken should not make a difference to the patient's well-being.

DIAMONDS has research funding, totalling €22.5 million over five years, which is provided by the European Commission under the Horizon 2020 research and innovation programme.

Unfortunately, this study is not recruiting public volunteers at this time. This is because researchers are directly identifying volunteers in certain hospitals. Please do not contact the research team as they will not be able to respond. For more information about COVID-19 research, visit the Be Part of Research homepage.

Study website
https://www.diamonds2020.eu

Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
278651

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

20SM5903, IRAS 278651, CPMS 45537

Study information

Scientific Title
Diagnosis and management of febrile illness using RNA personalised molecular signature diagnosis

Acronym
DIAMONDS

Study objectives
The aim of DIAMONDS is to design new diagnostic tests that can tell quickly and accurately what illness a patient has when they come to hospital with common symptoms such as fever. This would help the right treatment to be given to the right patient, at the right time ('personalised medicine').

There are two recruitment studies in DIAMONDS; DIAMONDS Search which will recruit patients and controls for the first 3 years of the study and DIAMONDS Pilot Demonstration study which will subsequently recruit patients and controls for one year.

Patients with suspected infectious disease or inflammatory disease will be recruited into DIAMONDS Search. Samples will be taken during the acute illness and convalescence, RNA will be extracted from blood samples and the optimum RNA signatures (gene transcripts) for each infectious and inflammatory condition will be selected.

The selected RNA signatures will be used to develop a European Diagnostic Transcriptomic Library (EDTL) whose molecular taxonomy of infectious and inflammatory disease will be used as the basis for personalised diagnosis ("Personalised Molecular Signature Diagnosis (PMSD)"). RNA signatures from EDTL will be used to develop a diagnostic test device which can be used to diagnose infectious and inflammatory conditions. The performance of PMSD will be evaluated by recruitment of patients with infectious disease or inflammatory disease and controls study into the DIAMONDS Pilot Demonstration study.

The COVID-19 pandemic has presented the opportunity to undertake rapid development of a host blood host RNA test to distinguish SARS-CoV-2 Infection from other viral and bacterial infection.

Hypothesis:
The underlying diagnosis in patients presenting with illness suggestive of infection or inflammation can be accurately discriminated using tests that interrogate the gene expression levels of a modest number of transcripts in whole blood.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/04/2020, London - Dulwich Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH, United Kingdom; +44 (0)207 104 8241; dulwich.rec@hra.nhs.uk), ref: 20/HRA/1714

Study design
Observational case-control laboratory study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital

Study type(s)
Other

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
Patients with suspected infection or suspected inflammatory conditions including patients with suspected COVID-19 (SARS-CoV-2 infection)

Interventions
The researchers will use case-controlled groups of patients presenting to hospital, recruited across Europe, The Gambia and Asia to discover biomarkers of infectious and inflammatory disease, using multi-omic analysis of blood samples from already-available, and prospectively recruited patient samples, from patients with clearly defined clinical conditions, comprising the discovery group. After establishing the gene expression profiles for different conditions, they will validate these on a second, validation group of patients, including prospectively recruited patients in DIAMONDS Search, and samples from other similar ethically approved studies. They will establish a molecular taxonomy of infectious and inflammatory disease and will develop and configure diagnostic devices to rapidly detect gene transcripts required for Personalised Molecular Signature Diagnosis (PMSD).

Intervention Type
Genetic

Primary outcome measure
Gene expression measured using RNA sequencing at presentation in children and adults with different infectious and inflammatory conditions

RNA biomarker signature with a sensitivity of 95% and specificity of 95% based on groups of at least 50 patients in each diagnostic category, which would allow capture of the effect sizes between the different comparator groups of as little as 1.5 fold change.

Secondary outcome measures
Healthcare resource use of patients presenting with infectious and inflammatory illness measured using qualitative questionnaire during admission and 3-6 months after admission

Overall study start date

01/01/2020

Completion date
31/03/2026

Eligibility

Key inclusion criteria
1. A patient of any age who attends or who is admitted at a participating hospital
2. AND who has one or more of the following;
2.1. Fever (≥38.0 °C) or history of fever in the preceding 24 hours
2.2. Symptoms (including non-specific signs) suggestive of infection
2.3. Symptoms suggestive of inflammation (including exacerbation of pre-existing inflammatory disease), and including non-specific signs/symptoms such as fever, joint pains, muscle pains, headaches, lymphadenopathy/fatigue, abdominal pain, rashes, mucosal inflammation, elevated inflammatory markers, unexplained cytopenias
3. AND EITHER who gives consent for samples to be taken for research
4. OR who retrospectively gives consent, according to a deferred consent model in which consent is obtained after initial sample collection

Participant type(s)
Patient

Age group
All

Sex
Both

Target number of participants
5000

Total final enrolment
14091

Key exclusion criteria
1. Patients who do not give consent
2. RNA sample is not taken

Date of first enrolment
27/04/2020

Date of final enrolment
31/05/2025

Locations

Countries of recruitment
Austria

England

France

Gambia

Germany

Greece

Italy

Latvia

Nepal

Netherlands

Slovenia

Spain

Switzerland

Taiwan

United Kingdom

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Sponsor type
University/education

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ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, Ευρωπαϊκής Επιτροπής, Европейската комисия, Evropské komise, Commission européenne, Choimisiúin Eorpaigh, Europskoj komisiji, Commissione europea, La Commissione europea, Eiropas Komisiju, Europos Komisijos, Európai Bizottságról, Europese Commissie, Komisja Europejska, Comissão Europeia, Comisia Europeană, Európskej komisii, Evropski komisiji, Euroopan komission, Europeiska kommissionen, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal around 1 year after the overall end of the study. No additional files are available.

Intention to publish date
30/09/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publically available repository.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

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