

New research into treatment and diagnosis of long COVID

- 15 new studies across UK to expand research that will support thousands of vulnerable people
- Nearly £20 million for research projects will help improve understanding of long COVID and identify effective treatments
- Projects include the largest long COVID trial to date which will involve over 4,500 people

Thousands of people suffering with long COVID will benefit from new research programmes backed by £19.6 million to help better understand the condition, improve diagnosis and find new treatments.

An extensive programme of 15 new research studies, backed by government funding through the National Institute for Health Research (NIHR), will allow researchers across the UK to draw together their expertise from analysing long COVID among those suffering long-term effects and the health and care professionals supporting them.

The [latest research](#) shows that although many people make a full recovery following COVID-19, a significant proportion of people continue to experience chronic symptoms for months. These ground breaking studies aim to help those people affected return to their normal lives.

The projects will focus on:

- Better understanding the condition and identifying it
- Evaluating the effectiveness of different care services
- Better integrating specialist, hospital and community services for those suffering with long COVID
- Identifying effective treatments, such as drugs, rehabilitation and recovery to treat people suffering from chronic symptoms
- Improving home monitoring and self-management of symptoms, including looking at the impact of diet, and
- Identifying and understanding the effect of particular symptoms of long COVID, such as breathlessness, reduced ability to exercise and brain fog

Health and Social Care Secretary, Sajid Javid, said:

Long COVID can have serious and debilitating long term effects for thousands of people across the UK which can make daily life extremely challenging.

This new research is absolutely essential to improve diagnosis and treatments and will be life-changing for those who are battling long-term symptoms of the virus.

It will build on our existing support with over 80 long COVID

assessment services open across England as part of a £100 million expansion of care for those suffering from the condition and over £50 million invested in research to better understand the lasting effects of this condition.

Professor Nick Lemoine, Chair of NIHR's long COVID funding committee and Medical Director of the NIHR Clinical Research Network (CRN), said:

This package of research will provide much needed hope to people with long-term health problems after COVID-19, accelerating development of new ways to diagnose and treat long COVID, as well as how to configure healthcare services to provide the absolute best care. Together with our earlier round of funding, NIHR has invested millions into research covering the full gamut of causes, mechanisms, diagnosis, treatment and rehabilitation of long COVID.

The selection process for this broad range of innovative studies into long COVID involved people with lived experience at every stage and their input has been invaluable in shaping the outcome of this call and the research projects which will receive funding.

The projects include:

- STIMULATE-ICP at University College London which will be the largest long COVID trial to date, recruiting more than 4,500 people with the condition. With £6.8 million of funding, the project will test the effectiveness of existing drugs to treat long COVID by measuring the effects of 3 months' treatment, including on people's symptoms, mental health and outcomes such as returning to work. It will also assess the use of MRI scans to help diagnose potential organ damage, as well as enhanced rehabilitation through an app to track their symptoms.
- The immunologic and virologic determinants of long COVID at Cardiff University with nearly £800,000, which will look at the role of the immune system in long-term disease and whether overactive or impaired immune responses could drive long COVID by causing widespread inflammation.
- ReDIRECT at University of Glasgow backed by nearly £1 million, which will assess whether a weight management programme can reduce symptoms of long COVID in people who are overweight or obese.
- LOCOMOTION at University of Leeds with £3.4 million, which focuses on identifying and promoting the most effective care, from accurate assessments in long COVID clinics to the best advice and treatment in surgeries, as well as home monitoring methods that can show flare-ups of symptoms. The research aims to establish a gold standard of care that can be shared across England and the rest of the UK.
- EXPLAIN at University of Oxford backed by £1.8 million, which will seek to diagnose ongoing breathlessness in people with COVID-19 who were not admitted to hospital, using MRI scans to trace inhaled gas moving into and out of the lungs to assess their severity and whether they improve

over time.

UK Government Minister for Scotland Iain Stewart said:

Long Covid is a terrible illness affecting thousands of people across the UK, and as it's such a new disease, there's still a lot we don't know about it.

This UK Government funding, which is supporting studies led by the University of Glasgow and University of the West of Scotland, will help us make progress in understanding long Covid and hopefully improve treatment and support for patients right across the UK.

UK Government Minister for Wales Simon Hart said:

The development and distribution of the vaccine means we can now see an end to the pandemic and Wales has played a significant part via Wrexham's Wockhardt facility where the Oxford-AstraZeneca vaccine continues to be produced.

Following this investment I hope Cardiff University can play a similarly important role in understanding and countering the long-term effects of the virus as we emerge from the pandemic.

Supportive quotes

Professor Amitava Banerjee, Associate Professor in Clinical Data Science and Honorary Consultant Cardiologist, University College London, Chief investigator of the STIMULATE-ICP (Symptoms, trajectory, inequalities and management: understanding long COVID to address and transform existing integrated care pathways) trial, said:

Individuals with long COVID have long been asking for recognition, research and rehabilitation. In our two-year study across six clinical sites around England, we will be working with patients, health professionals, scientists across different disciplines, as well as industry partners, to test and evaluate a new 'integrated care' pathway from diagnosis to rehabilitation, and potential drug treatments in the largest trial to-date. We will also be trying to improve inequalities in access to care and investigating how long COVID compares with other long-term conditions in terms of use of healthcare and burden of disease, which will help to plan services.

Dr Dennis Chan, Principal Research Fellow, Institute of Cognitive Neuroscience, University College London, Chief investigator of the CICERO (Cognitive Impairment in long COVID: PhEnotyping and RehabilitatiOn) project, said:

Cognitive impairment, referred to informally as 'brain fog', is a major component of long COVID that compromises people's daily activities and ability to return to work. The aim of this study is twofold; first, to understand better the nature of this 'cognitive COVID' in terms of the cognitive functions affected and the associated brain imaging changes, and second, to test whether neuropsychological rehabilitation can improve people's outcomes. If this study is successful we will not only understand much better the way in which COVID affects the brain but also provide NHS services with new tools to help people recover from their cognitive difficulties.

Professor Fergus Gleeson, Professor of Radiology and Consultant Radiologist, Oxford University, Chief Investigator of EXPLAIN (Hyperpolarised Xenon Magnetic Resonance Pulmonary Imaging in PATIENTS with Long-COVID) project, said:

Following on from our earlier work using hyperpolarised xenon MRI in patients following hospitalisation with COVID-19 pneumonia, where we showed that their lungs may be damaged even when all other tests were normal, it is critical to determine how many patients with long COVID and breathlessness have damaged lungs, and if and how long it takes for their lungs to recover.

Hyperpolarised xenon MRI is a safe scanning test that requires the patient to lie in the MRI scanner and breathe in one litre of the inert gas xenon that has been hyperpolarised so that we can see it using MRI. The scan takes a few minutes and does not require radiation exposure, so it may be repeated over time to see lung changes. Using this technique, we can see the xenon – which behaves in a very similar way to oxygen – move from the lungs into the blood stream. In this way, we can see if there has been damage to the airways in the lungs, or to the areas where oxygen crosses into the blood stream, which appears to be the area damaged by COVID-19.

Background information

- The projects were funded following a UK-wide research call for ambitious and comprehensive research into understanding and addressing the longer term physical and mental health effects of COVID-19 in non-hospitalised people and will build on the existing research already commissioned to look at long COVID.
- In February 2021, 4 projects funded by NIHR and UK Research and Innovation (UKRI) were announced, following the first research call.
- The UK began the commissioning of long COVID research in 2020 and some projects are already producing results that are informing the understanding of long COVID. This research call adds to the existing investment of over £30 million of research funding taking the total investment to £50 million.

- The National Institute for Clinical Excellence (NICE) has issued official guidance on best practice for recognising, investigating and rehabilitating patients with long COVID. According to NICE guidance, 'long COVID describes signs and symptoms that continue or develop after acute COVID-19. It includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more).'
- In October 2020, NHS England and Improvement launched a 5 point plan for long COVID. There are now 89 specialist post COVID-19 clinics operating in England.
- On 15 June 2021, NHSEI published a new 10 point plan and announced an additional £100 million expansion of care for patients with long COVID.

Annex A: Study summaries

Developing and testing the best ways to diagnose, treat and provide rehabilitation for people with long COVID

Dr Amitava Bannerjee, University College of London – £6.8m The wide-ranging symptoms of long COVID are debilitating and need coordinated care from specialists, hospitals and community services. The STIMULATE-ICP (Symptoms, trajectory, inequalities and management: understanding long COVID to address and transform existing integrated care pathways) trial, developed with the help of patient organisations, will be the largest long COVID trial to date, recruiting more than 4,500 people with the condition. This project will test the efficacy of existing drugs to treat long COVID, and measure the different effects of three months' treatment on patients with regards to their symptoms, mental health and outcomes such as returning to work. It will also assess the use of MRI scans to help diagnose potential organ damage in those recovering from the coronavirus, as well as enhanced rehabilitation – the provision of joined-up specialist care centred around an app for patients allowing them to track their symptoms.

Optimising standards of care for long COVID in hospitals, doctors' surgeries and at home

Dr Manoj Sivan, University of Leeds – £3.4m Although there are 83 long COVID clinics in England, most people have not had access to them, and face long waiting times to be seen. The LOCOMOTION (long COVID multidisciplinary consortium: optimising treatments and services across the NHS) project focuses on identifying and promoting the most effective care, ranging from accurate assessments in these clinics to the best advice and treatment in surgeries, as well as home monitoring methods that can show flare-ups of symptoms. Drawing from the experiences of current long COVID patients and NHS professionals, the research aims to establish a 'gold standard' of care that can be shared across England and the rest of the UK. Analysis will be conducted in 10 long COVID clinics, at home and in doctors' surgeries, and the study will track referrals and evaluate different services through patient interviews to make sure they are efficient, accessible and cost-effective. Specialists in healthcare inequality will also ensure that views are sought and recorded from people who are not visiting clinics.

Explaining why long COVID patients experience breathlessness and a reduced ability to exercise

Professor Fergus Gleeson, University of Oxford – £1.8m One of the most prevalent and persistent symptoms among long COVID patients has been discomfort in breathing following physical activity. The EXPLAIN (Hyperpolarised xenon magnetic resonance pulmonary imaging in patients with Long-COVID) project will seek to diagnose ongoing breathlessness in coronavirus patients who were not admitted to hospital, using MRI scans to trace inhaled gas moving into and out of the lungs. A 15-minute scan using low levels of xenon gas will display lung function and – if abnormalities are found – comparisons of data across different groups of participants recruited from Oxford and Sheffield can help assess their severity and whether they improve over time. Some EXPLAIN patients will also have a separate scan to see if heart damage can be identified. If the MRI scans separate patients with and without lung disease, further CT scans can be analysed, using artificial intelligence and blood samples to identify associated conditions and inform the development of treatments.

Understanding and treating ‘brain fog’

Dr Dennis Chan, University College London – £1.2m Up to three quarters of people who experience long-term symptoms after COVID-19 report problems with memory, attention or other cognitive functions – symptoms known collectively as ‘brain fog’. The CICERO (Cognitive Impairment in long COVID: PhEnotyping and Rehabilitati0n) project will first determine which elements of brain function are most affected in people with long COVID. The relationship between brain function and other symptoms of long COVID, such as fatigue and anxiety, will be explored, and MRI scanning will be used to identify the affected brain networks. The researchers will then develop and test a new rehabilitation strategy to help people recover from the cognitive aspects of long COVID and return to normal life and working ability. This will support production of a freely available COVID-19 Cognitive Recovery Guide on how best to offer the new rehabilitation approach depending on the patient’s symptoms.

Co-designing personalised self-management for patients at home

Professor Fiona Jones, Kingston University – £1.1m Long COVID describes more than 200 different symptoms that can interact and fluctuate. Although fatigue and problems with brain function are the most common symptoms, each patient can experience a different set of symptoms. The LISTEN (Long COVID Personalised Self-management support – co-design and Evaluation) project will work in partnership with people who have long COVID to design and evaluate a package of self-management support that can be personalised to individual needs. The researchers will first work with people living with or recovered from long COVID, plus a social enterprise with expertise in reaching seldom heard populations, to design the package and associated patient and training resources. The team will then test the self-management package alongside up to six one-to-one virtual coaching sessions from trained rehabilitation practitioners, to test whether the treatment improves how people with long COVID feel and how they cope with everyday activities. The researchers will

also evaluate how the package could be implemented more widely, with the aim that self-management for people with long COVID can be delivered at scale.

ReDIRECT: Remote Diet Intervention to Reduce long Covid symptoms Trial

Dr David Blane, University of Glasgow – £999,679

The immunologic and virologic determinants of long COVID

Professor David Price, Cardiff University – £774,457

Quality-of-life in patients with long COVID: harnessing the scale of big data to quantify the health and economic costs

Dr Rosalind Eggo, London School of Hygiene and Tropical Medicine – £674,679

Percutaneous Auricular Nerve Stimulation for Treating Post-COVID Fatigue (PAuSing-Post-COVID Fatigue)

Dr Mark Baker, Newcastle University – £640,180

Immune analysis of long COVID to inform rational choices in diagnostic testing and therapeutics

Professor Daniel Altmann, Imperial College – £573,769

Understanding and using family experiences of managing long COVID to support self care and timely access to services

Professor Sue Ziebland, University of Oxford – £557,674

Development of a robust T cell assay to retrospectively diagnose SARS-CoV-2 infection and IFN- γ release assay as diagnostic and monitoring assay in Long COVID patients

Dr Mark Wills, University of Cambridge – £372,864

Using Activity Tracking and Just-In-Time Messaging to Improve Adaptive Pacing: A Pragmatic Randomised Control Trial

Professor Nicholas Sculthorpe, University of the West of Scotland – £317,416

Impact of COVID-19 vaccination on preventing long COVID: a population-based cohort study using linked NHS data

Professor Daniel Prieto-Alhambra, University of Oxford – £224,344

Long COVID Core Outcome Set (LC-COS) project

Dr Tim Nicholson, King's College London – £139,619