Engineering and Physical Sciences Research Council

Understanding Long COVID

a challenge led sandpit

13 – 14 September 2022

Integrating data-driven **BIO**physical models into **RE**spiratory **ME**dicine, BIOREME Network

Contents

Welcome to The BIOREME Sandpit

Welcome to Nottingham and to the first BIOREME Sandpit.

BIOREME is a collaborative Healthcare Technologies NetworkPlus, funded by UKRI:EPSRC. We welcome members from a diverse range of disciplines working in academia, medicine, industry and charity with an interest in the applications of mathematical modelling to lung health and respiratory medicine.

Our aim is to catalyse research in these areas that will result in new technologies and treatments, as well as better understanding of lung disease.

BIOREME activities are focussed on three research themes with potential for collaborative and translational research to transform patient health in respiratory medicine

- Theme 1: Improving treatment delivery and clinical trial design.
- Theme 2: Developing the next generation of clinical lung function measurement.
- Theme 3: Modelling the acute and long-term physiological effects of COVID-19.

BIOREME hosts events and offers funding opportunities to bring our network members together and drive future collaborations and grant applications within the remit of our three themes.

Sandpit format

This event falls within **theme 3** "modelling the acute and long-term physiological effects of COVID-19". We are delighted to be joined by a diverse group of researchers who can add real value to this subject area.

Our diverse group of speakers will present **data from national and international studies** looking at a range of quantitative and qualitative indicators. We are also pleased to have the patient voice represented through clinical experts, patient advocates and charity groups.

During the subsequent breakout sessions on day one, there will be facilitated group discussions centred around the three **starter challenge areas** to identify specific research questions. On day two, focussed working groups will be formed around the research questions identified, each of which may generate a research project outline and a proposal for seed funding of up to £10,000. These will be "pitched" at the final session.

Starter Challenge Areas

1. Can we demonstrate, through combination of quantitative and qualitative data the scale and significance of Long COVID? Can this raise awareness and provide evidence to funders and policy makers?

2. How can data from the different trials and studies be combined to draw correlations; can this generate new hypotheses?

3. Can data from the different trials and studies be combined to inform new mechanistic models to provide insight into causes and test hypotheses that arise from data analysis?

Sandpit Impact

Our key goals for this sandpit are

- To **identify key research challenges** for Long COVID that can be addressed using the data presented and the expertise of the participants.
- To spark **new interdisciplinary collaborations** that will propose solutions to these challenges
- To **fund follow-up activities** (e.g. workshops or meetings) that will enable these collaborations to develop competitive grant proposals
- To **publish a statement piece** in an academic journal to outline the challenges and proposed solutions developed in the sandpit.

Publication of Outcomes

A medical writer is attending the event to summarise the presentations and discussion sessions into a meeting report. Subsequently, this will be developed into a peer-reviewed academic publication taking into consideration the wider literature in this area. This piece will highlight opportunities for data-driven approaches, including biophysical modelling, to add real value to Long COVID research and discuss what further experimental evidence is needed. This piece will provide expert and patient-informed justification to strengthen future funding applications in this area.

Seed funding details

The £10,000 seed funding will support further activities for successful projects to mature into competitive grant applications. This may include e.g. a grant-development workshop focussed on the particular problem identified, or the collection of pilot data to support a grant proposal. Note that funding will be awarded at 80% FEC and so the award is conditional on agreement between the awarded

institution(s) and BIOREME, which will need to be reached after the event. Note that the final funding awarded to successful proposals will be expected to fall within 10% of the original cost proposed at the sandpit and need not use all of the funding available. Depending on the costings proposed at the sandpit, it may be that more than one proposal can be funded. The BIOREME team will facilitate onward activities that develop from this funding.

Potential funding calls

Regardless of which proposal(s) is(are) awarded funding on the day, we encourage all new collaborations formed to consider ways they can develop their proposals into competitive grant applications. The BIOREME Team will be happy to provide a Letter of Support for proposals arising from the sandpit and to facilitate with reviewing the application prior to submission, given sufficient notice. In particular, we highlight the following funding calls that participants may be interested in:

- UKRI:MRC - *Build on existing COVID-19 infrastructure, partnerships and resources* Closing dates Round 2: 11 Jan 2023, Round 3: 10 May 2023
- NIH: NIH Long COVID Computational Challenge (L3C): AI/ML models to predict susceptibility and likelihood of developing PASC/Long COVID. Closing date: 15 Dec 2022
- UKRI – clinical academic research partnerships Closing date: 17 Nov 2022
- UKRI – EPSRC mathematical sciences small grants scheme Quarterly review
- BIOREME – Small Starter Grant – Quarterly review, next deadline 1st October 2022

Programme – Day 1

10.30 – 11.00	Arrivals and Coffee	
11.00 – 11.15	Introduction	Professor Bindi Brook, BIOREME Chair
11.15 – 12.00	COVID-19 and Long COVID research: Trying to understand the challenge	Dr Mark Faghy, University of Derby and Patient groups
12.00 –12.30	UK Long Covid lung MRI studies EXPLAIN/PCILD/MURC/CMORE	Professor Jim Wild, University of Sheffield
12.30 – 12.45	Getting to know you 1	Presentations from attendees
12.45 -13.45	Lunch	
13.45 – 14.15	PHOSP-COVID study	Professor Chris Brightling, University of Leicester
14.15 – 14.45	WILCO Long COVID Study	Professor Danny Altmann, Imperial College London
14.45 – 15.00	Getting to know you 2	Presentations from attendees
15.00 – 15.30	What Causes Long COVID? Microclots	Professor Resia Pretorious, Stellenbosch University
15.30 – 16.00	Break	
16.00 – 16.30	Living with Long COVID	Dr Binita Kane Respiratory physician and Long COVID kids champion
16.30 – 16.45	Introduction to sessions	BIOREME Team
16.45 – 17.45	Explore Challenge	All attendees
17.45 – 18.15	Feedback session	All attendees
18.15 – 18.30	Close	
18.30 – 19.30	Drinks reception	
19.30	Optional evening meal	

Programme Day 2

8.30 – 9.00	Arrivals and Coffee	
9.00 – 9.15	Introduction to Day 2	BIOREME Team
9.15 – 9.45	How to make FAIR fair?	Hon. Professor Phil Quinlan, University of Nottingham
9.45 – 10.30	**Explore the themes** Discuss and identify key research questions within the themes	**All attendees**
10.30 – 11.00	Break	
11.00 – 12.00	**Formation of Groups** Discuss how to address key research questions	**All attendees**
12.00 – 13.00	**Work in progress and peer review** Present work in progress and feedback	**All attendees**
13.00 – 14.00	Lunch	
14.00 – 15.00	Implement feedback and develop plan	**All attendees**
15.00 – 16.00	Final presentations and Q and A	**All attendees**
16.00-16.30	Meeting close	BIOREME Team

Map of campus

Useful Information

COVID precautions

We have taken a number of measures to safely run this event including:

- A well-ventilated room (through opening windows and doors) with more than double the capacity of the expected number of attendees and a similarly sized second room for breakout sessions
- Ask all attendees to wear masks during indoor sessions, we will provide FFP2s.
- Ask attendees to take an LFT before the event, and if they feel unwell to not attend (we will have a remote option for those unable to attend in person)

Getting here

By car: If arriving by car it is best to enter campus via the West entrance. If staying at the De Vere Hotel, you can park at the Hotel carpark for free (grid ref C3). For others, you can park at the visitor parking at grid ref E2 for £10/day.

By public transport: If arriving by train into Nottingham station, you can get the tram towards Toton Lane to the stop "University Boulevard". The Monica Partridge building is a 10 min walk from the stop (Grid ref D3, building no.62)

Supporting Information – Long COVID Research

University of Derby Long COVID Research Summary
Led by Dr Mark Faghy and Dr Ruth Ashton

We have been running several projects in Long COVID since 2020. This summary is to provide an insight into the work that has been done, to stimulate discussion and encourage collaboration to improve patient outcomes:

Profiling recovery: PREPP-19: A 16-week cohort observation of patients discharged from hospital following a COVID-19 infection/referral to an established Long COVID clinic. Profiling of the symptom profile, biological physiological, and psychological markers alongside cognitive function, quality of life, functional status and lived experience. Patients engage in five face-to-face visits and four telephone consultations. The regular patient interaction has provided vast quantitative and qualitative data highlighting significant issues with quality of life and the episodic nature of Long COVID. The aim is to improve the understanding and changes in symptoms over time to identify where the most important and opportune moments in the recovery process are to develop bespoke support mechanisms.
We are close to 100 patients completing the trial in the UK and this work is also taking place in America (Chicago) and India (Ramiah).

Lived Experience Survey: Developed in collaboration with our PPIE representatives, we collected detailed insight into the lived experience of Long COVID patients and the 185 responses provided over 500 pages of quantitative and qualitative data that has been thematically analysed and highlighted the key challenges facing Long COVID patients. To

date, we have focused the analysis on Long COVID but there is a broader insight into the acute phase, recovery, impact upon family life/employment and data about treatment and interventions that have been offered.

COVID-19 Symptom Survey: Launched in late 2020, we ran an online survey to capture information about the acute phase of COVID-19 which gave a real insight into the developing nature of persistent symptom profiles. Completed by almost 400 people, the data gives insight into symptoms; Quality of Life; sleep quality; breathlessness; physical activity and mental health.

Delphi Consensus Statement: Data collection has just been completed for this project and the aim was to establish consensus on what Long COVID support/rehabilitation approaches should contain. Seeking input from patients, healthcare workers, clinicians, physiotherapists, and academic researchers (which can be split into those with and without Long COVID).

SHEDding light on Long COVID: A unique collaboration between scientists, and artists from regional and national stakeholders that use Long COVID research data to create physical and virtual exhibitions that can raise awareness of Long COVID. This public engagement work will also give hope to patients that they are being listened to and that the scientists are working hard to understand and find resolutions to the long-term issues they are living with.

Service Development and Blueprinting: Using the data collected over two years and bringing together established Long COVID research groups we want to devise screening tools and bespoke services that can increase patient outcomes in Long COVID. We feel that engaging all important stakeholders (e.g., clinical, academic, public-sector

organisations, hospital trusts and patients with lived experience) in a system science model will lead to the development and implementation of safe and accepted support services that can achieve broad outcomes.

University of Sheffield – Long COVID MRI Studies

Longitudinal lung function assessment of patients hospitalised with COVID-19 using ^{1}H and ^{129}Xe lung MRI – PRE PRINT

Imperial College London – WILCO Long COVID study

Investigating the immunology of long-term effects of SARS-CoV-2

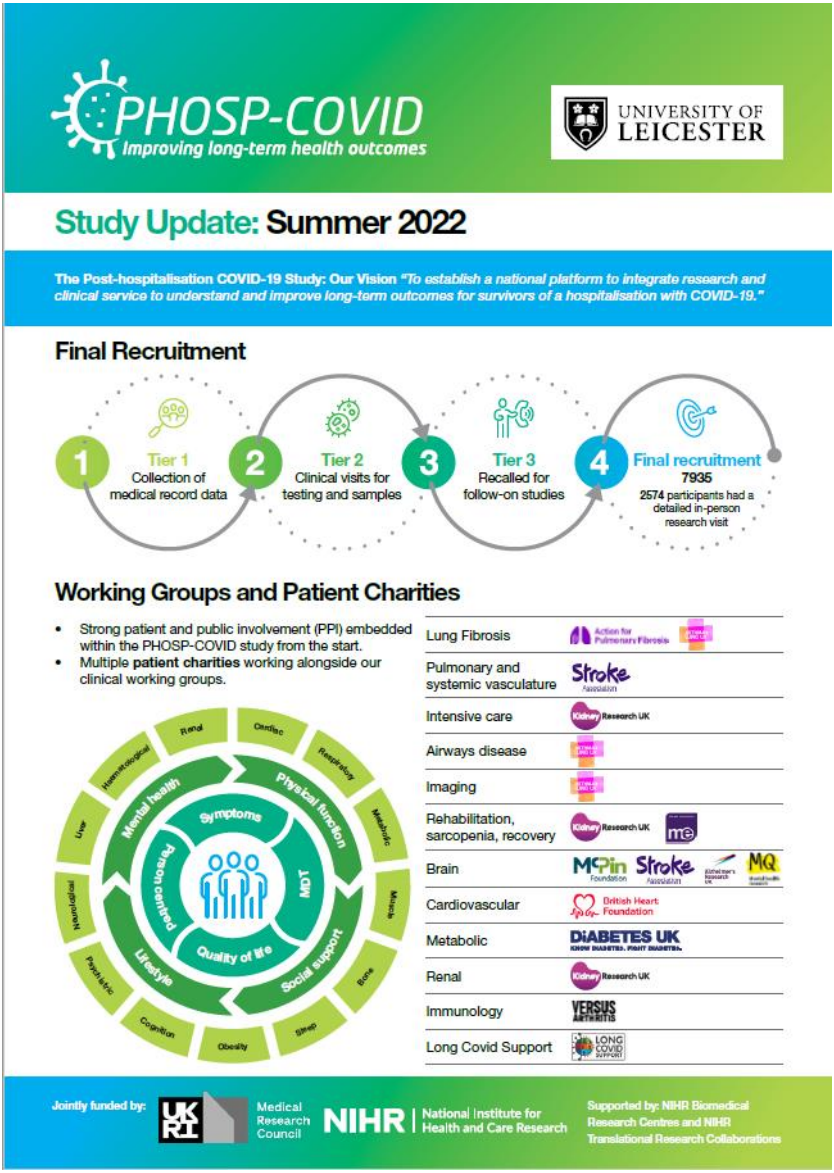
Professor Danny Altmann, Professor Rosemary Boyton, Fahimah Amini

University of Leicester – The Post-hospitalisation COVID-19 study (PHOSP-COVID)

A consortium of leading researchers and clinicians from across the UK working together to understand and improve long-term health outcomes for patients who have been in hospital with confirmed or suspected COVID-19.

Chief Investigator – Professor Chris Brightling

University of Leicester – PHOSP-COVID Study update



Our Research Priorities

We have jointly set research priorities from the PHOSP-COVID study with patients and clinicians. Our Top 10 priorities are not ranked and have an emphasis on:

Underlying mechanisms

- What are the underlying mechanisms of Long Covid that drive symptoms and/ organ impairment?
- What imaging techniques or scans may be able to detect & predict the development of organ problems or wider systemic issues?
- What happens to the immune system throughout patients' recovery from COVID-19?
- What can data at 6 & 12 months tell us about the long-term trajectory of illness?

Interventions

- What is the impact of treatment(s) during the acute stage of COVID-19 on recovery?
- What are the problems within the muscles associated with symptoms limiting activity/ function/ exercise? What can be done to help?
- What medications, dietary changes, supplements, rehabilitation & therapies aid recovery?
- What can be done to support mental wellbeing during recovery?

Diagnostic/ prognostic tools

- What blood/ other laboratory tests may be able to detect and predict the development of organ problems or wider systemic issues?
- What is the risk of future adverse health events (e.g. stroke, heart attack)?

The full article by PHOSP-COVID Collaborative Group (2022) can be accessed here: https://thorax.bmj.com/content/77/7/717

Key Findings

3/10 felt recovered at 1 year after hospital discharge.

Reported **four clusters**: very severe, severe, moderate and mild, relating to the level of physical health, mental health and cognitive impairment.

Health-related quality of life was reduced at 1 year compared with before hospital admission.

Systematic inflammation and obesity are potential risk factors that can be treated. **Other risk factors include being female and receiving mechanical ventilation.**

- The full articles in the Lancet Respiratory Medicine by the PHOSP-COVID Collaborative Group (2022) can be accessed here: https://www.thelancet.com/action/showPdf?pii=S2213-2600%2821%2900383-0 & https://www.thelancet.com/action/showPdf?pii=S2213-2600%2822%2900127-8
- PHOSP-COVID has sparked ideas for other research projects. Further details of current/ planned projects can be found on our website: https://www.phosp.org/

Stellenbosch University - What Causes Long COVID? Microclots

Could tiny blood clots cause long COVID's puzzling symptoms? –News Feature, Nature

The potential role of ischaemia–reperfusion injury in chronic, relapsing diseases such as rheumatoid arthritis, Long COVID, and ME/CFS: evidence, mechanisms, and therapeutic implications – Review paper, Biochemical journal

Professor Resia Pretorious

Respiratory physician and Long COVID kids champion – Living with Long COVID

Dr Binita Kane will talk about supporting her daughter's journey with Long COVID, an international search for answers and how this has led her to become a patient advocate, researcher and Long COVID Kids champion

Dr Binita Kane

University of Nottingham – How to make FAIR fair

A link to co-connect project – a curated and open access research platform to help scientists across the UK to access the data they need more easily to help develop potential therapies and treatment for COVID-19

Hon. Professor Phil Quinlan

Future opportunities with BIOREME

Events

- British Science Festival – Leicester **17th September 2022**
- Annual network wide meeting – Warwick University, **13 January 2023**
- Coming soon: Study group Spring 2023 and sandpit summer 2023
- Quarterly Webinars

Funding

- Small starter grants **next deadline 1st October**
- UG summer internships for 2023 project proposal **deadline 27th September**
- 1 year Fellowship funding –next **call to open in Feb 2023**

Networking

- Sign up to our updates at bioreme.net/signup and follow us on Twitter @BIOREMEnet
- Join our slack channel – just email contact@bioreme.net to be sent an invite
- Coming soon – a directory of members on Bioreme.net to find collaborators