

## Summary of Long-COVID studies open to Welsh participants

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**Abstract:** Long-COVID is the term used to describe symptoms that continue or develop weeks or months after acute COVID-19 infection. Long-COVID can present as a variety of different symptoms including continuous breathlessness, muscle aches and cognitive impairment. As this is still very much a novel phenomenon, it is important that research is being conducted to further the understanding of this and work towards providing treatment and support to all those affected. A summary of active and prospective NIHR-funded Long-COVID studies was published in 2021 by the Wales COVID-19 Evidence Centre (WCEC) and this report provides an update on the studies highlighted. In addition, this report also includes a further search of an additional ten funding organisations to produce a summary of the new and ongoing studies of long-COVID open to Welsh participants. Whilst 57 studies were identified, only two additional studies were found to be relevant and open to Welsh participants, resulting in a total of five studies currently open to Welsh participants.

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# Summary of Long-COVID studies open to Welsh participants

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# Summary of Long-COVID studies open to Welsh participants Report Number – REM0011 (August 2023)

## EXECUTIVE SUMMARY

### Study Background / Aim

The term 'Long-COVID' refers to the symptoms that continue or develop as a result of COVID-19 infection, weeks or months following the acute infection. These symptoms can be varied across individuals and have been a prevalent topic of research across the world.

In 2021, the Wales COVID-19 Evidence Centre (WCEC) conducted a search of active and prospective NIHR Long-COVID research open to Welsh participants.

The aim of this report is to provide an update on the studies highlighted in that report as well as an updated search of new studies.

### Methodology

The updating of the studies identified in the 2021 report was done by searching for the study pages of each study. In the instance that there was no study page available, or insufficient detail, project leads were contacted by email to request an update.

The identification of new studies involved searching through relevant funding bodies, charities and study registries. A total of eleven resources were searched. Each resource was searched in July of 2023 and included all studies that opened from 2021 to 2023. Studies were screened based on titles, then abstract. Those deemed to be potentially relevant were further explored through study pages were available or through contacting project leads via email. Through this, studies that were relevant to those living with Long-COVID, still recruiting and open to those living in Wales were identified.

### Key Findings

Of the studies highlighted in 2021, only three were open to Welsh participants at the time of the search. Furthermore, one of these was due to close at the end of July 2023, and another is due to close at the end of August 2023.

The search for additional studies identified 57 potential studies, however after further investigation, it was found that only five were relevant and open to Welsh participants. Similarly to the studies highlighted in 2021, only one will remain open after August 2023.

### Conclusions and Potential for Future Research

With only five studies being identified at the time of this search, there is clearly a lack of new or current research into Long-COVID being conducted in Wales.

Many of the UK based studies identified in this search were recruiting participants from specific services local to the research centre carrying out the study. However, in 2021, the Welsh Government published a strategy for the 'Adferiad (Recovery) Long COVID programme', which will work to increase delivery of diagnosis, treatment, support and

care for those in Wales suffering with Long-COVID. This may provide opportunity for more Wales based studies into Long-COVID.

## Contents

|   |    |
|---|----|
| Background/context:.....  | 7  |
| Methods:.....   | 7  |
| Updating of 2021 summary: .....   | 7  |
| Search for new studies:.....  | 7  |
| Findings:.....  | 8  |
| Conclusion: .....   | 12 |
| Appendix A: List of studies identified through title and abstract screening ..... | 12 |
| References .....  | 14 |

## Background/context:

Long-COVID is the term used to describe symptoms that continue or develop weeks or months after acute COVID-19 infection and can vary greatly from person to person. The national Institute for Health and Care Excellence (NICE) defined Long-COVID as comprising of both ongoing symptomatic COVID-19, which is the presence of signs and symptoms of COVID-19 that persist for four to twelve weeks, and post COVID-19 syndrome which is when signs and symptoms develop or continue more than twelve weeks post initial infection [1]. An NIHR review into Long-COVID conducted in 2020 concluded that there is a significant need for research into this condition.

In 2021, the Wales COVID-19 Evidence Centre (WCEC) published a summary of active and prospective Long-COVID research in Wales[2]. This was produced with the aim of both describing the research climate at that time, and to highlight opportunities for participation for people with Long-COVID, and health care professionals involved in their care. In that summary, 19 ongoing and prospective NIHR-funded studies were identified.

Now, two years on, this report details the updated status of those 19 studies, as well as an updated search of new studies.

## Methods:

### Updating of 2021 summary:

The update of the status of the 19 studies highlighted in the 2021 summary was conducted in June 2023. This started with the identification of the study pages for each study. In the case that there was no update available, or there was insufficient detail, project leads were contacted by email to request an update.

### Search for new studies:

In order to identify any additional studies, an extensive search of relevant funding bodies, charities and study registries was undertaken. The list of searched resources can be seen in table 1. This list was finalised by the team including two public partnership group (PPG) members.

| Organisation Name   | Weblink   |
|---|---|
| <b>National Institute for Health and Care Research (NIHR)</b>         | <a href="https://bepartofresearch.nihr.ac.uk/results/search-results?query=long-covid&amp;location=">https://bepartofresearch.nihr.ac.uk/results/search-results?query=long-covid&amp;location=</a> |
| <b>Medical Research Council (MRC)</b>                                 | <a href="https://gtr.ukri.org/search/project?term=long+covid">https://gtr.ukri.org/search/project?term=long+covid</a>   |
| <b>Economic and Social Research Council (ESRC)</b>                    | <a href="https://gtr.ukri.org/search/project?term=long+covid">https://gtr.ukri.org/search/project?term=long+covid</a>   |
| <b>Biotechnology and Biological Sciences Research Council (BBSRC)</b> | <a href="https://gtr.ukri.org/search/project?term=long+covid">https://gtr.ukri.org/search/project?term=long+covid</a>   |

|  |   |
|--|---|
| <b>Science and Technology Facilities Council (STFC)</b>    | <a href="https://gtr.ukri.org/search/project?term=long+covid">https://gtr.ukri.org/search/project?term=long+covid</a>   |
| <b>Medical Research Foundation</b>                         | <a href="https://www.medicalresearchfoundation.org.uk/what-we-fund/what-weve-funded">https://www.medicalresearchfoundation.org.uk/what-we-fund/what-weve-funded</a>                             |
| <b>Diabetes Research &amp; Wellness Foundation</b>         | <a href="https://www.drwf.org.uk/news-and-events/news/how-you-can-take-part-in-diabetes-research/">https://www.drwf.org.uk/news-and-events/news/how-you-can-take-part-in-diabetes-research/</a> |
| <b>Crohn's in Childhood Research Association (CICRA)</b>   | <a href="https://www.cicra.org/our-research/current-research/">https://www.cicra.org/our-research/current-research/</a>   |
| <b>Alzheimer's Society</b>                                 | <a href="https://www.alzheimers.org.uk/research/our-research/research-projects/current-projects">https://www.alzheimers.org.uk/research/our-research/research-projects/current-projects</a>     |
| <b>Government Adferiad (recovery) Long COVID Programme</b> | <a href="https://www.gov.wales/adferiad-recovery-long-covid-programme-html#73085">https://www.gov.wales/adferiad-recovery-long-covid-programme-html#73085</a>                                   |
| <b>Cochrane Trials Registry</b>                            | <a href="https://www.cochranelibrary.com/advanced-search?q=*long%20covid&amp;t=6">https://www.cochranelibrary.com/advanced-search?q=*long%20covid&amp;t=6</a>                                   |

Table 1: Resources searched for new studies

Each resource was searched for studies dating from 2021 to 2023. Searches of all databases were run in July of 2023. Studies were first screened based on titles, then abstract. Studies still deemed to be potentially relevant were then further explored through locating study pages or contacting lead investigators via email. This exploration included determining whether or not the study was still recruiting, open to those living in Wales and relevant to those with long-COVID.

## Findings:

Of the 19 studies detailed in the 2021 summary, six were still open for recruitment as of the beginning of July 2023. However, two of these studies are due to close recruitment on the 31<sup>st</sup> of July 2023. Furthermore, of the six still open, only three are recruiting Welsh participants. Table 2 details the recruitment status of all 19 studies.

| <b>Study Name</b>  | <b>Recruitment Status</b>                |
|--|--|
| <b>Post-hospitalisation COVID-19 study: a national consortium to understand and improve long-term health outcomes (PHOSP-COVID)</b>    | Closed                                   |
| <b>HElping Alleviate the Longer-term consequences of COVID-19 (HEAL-COVID): a national platform trial</b>                              | Closed                                   |
| <b>Rehabilitation Exercise and psycholoGical support After covid-19 InfectioN (REGAIN): a multi-centre randomised controlled trial</b> | Closed                                   |
| <b>Understanding Experiences of Long COVID in Families</b>   | Closed                                   |
| <b>Long Covid Multidisciplinary Consortium: Optimising Treatments and services acROss the NHS (LOCOMOTION)</b>                         | Closed                                   |
| <b>Long Covid Personalised Self-management support- co-design and Evaluation (LISTEN)</b>  | Open until 31/08/23 (Welsh participants) |



|   |  |
|---|--|
| <b>The immunologic and virologic determinants of Long-COVID</b>   | Open until 31/07/23 (Welsh participants)     |
| <b>HypErpolarised Xenon magnetic resonance PuLmonary imAging in patieNts with Long COVID (EXPLAIN)</b>  | Closed                                       |
| <b>Cognitive Impairment in long COVID: PhEnotyping and RehabilitatiOn (CICERO)</b>  | Open until January 2024 (Welsh participants) |
| <b>Symptoms, Trajectory, Inequalities and Management: Understanding Long-COVID to Address and Transform Existing Integrated Care Pathways (STIMULATE-ICP)</b>     | Closed                                       |
| <b>ReDIRECT: Remote Diet Intervention to Reduce long Covid symptoms Trial</b>   | Closed                                       |
| <b>Quality-of-life in patients with long COVID: harnessing the scale of big data to quantify the health and economic costs</b>                                    | Open until 31/07/23                          |
| <b>Percutaneous Auricular Nerve Stimulation for Treating Post-COVID Fatigue (PAuSing-Post-COVID Fatigue)</b>  | Open (end date not specified)                |
| <b>Immune analysis of long COVID to inform rational choices in diagnostic testing and therapeutics</b>  | Closed                                       |
| <b>Understanding and using family experiences of managing long COVID to support self care and timely access to services</b>                                       | Closed                                       |
| <b>Development of a robust T cell assay to retrospectively diagnose SARS-CoV-2 infection and assays as diagnostic and monitoring tools in long COVID patients</b> | Open until end of September 2023             |
| <b>Using Activity Tracking and Just-In-Time Messaging to Improve Adaptive Pacing: A Pragmatic Randomised Control Trial</b>  | Closed                                       |
| <b>Impact of COVID-19 vaccination on preventing long COVID: a population-based cohort study using linked NHS data</b>   | Closed                                       |
| <b>Long COVID Core Outcome Set (LC-COS) project</b>   | Closed                                       |

*Table 2: Recruitment status of studies highlighted in the 2021 NIHR search*

By searching the resources listed in table 1, 57 studies were identified as being potentially relevant through title and abstract screening. Of these 57 studies, only two met the criteria of being relevant for those with Long-COVID and having recruitment open for Welsh participants. A list of the 57 studies identified can be found in appendix a. Overall there are currently five studies into Long-COVID that are open to Welsh participants, but only one will remain open after the end of August 2023. This updated summary is detailed in table 3.

| Study Name and Weblink  | Study Aim   | Eligibility   | Recruitment status  |
|---|---|---|---|
| <p><b>Long Covid Personalised Self-management support- co-design and Evaluation (LISTEN)</b></p> <p><a href="https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/listen">https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/listen</a></p>     | <p>This study is developing an intervention consisting of a package of self-management support, co-designed with individuals living with long COVID and other stakeholders. The aim is to compare this intervention with usual care in the NHS to explore whether it can help patients manage Long COVID symptoms in everyday life. In the first part of this study, participants living with Long COVID will work with researchers to design a package of self-management support personalised to their needs. In the second part of this study, individuals with Long COVID will be recruited to a clinical trial to evaluate the new intervention.</p>   | <p>Participants must be aged 18 or over and experience persistent illness following COVID-19 infection for over 12 weeks.</p>   | <p>Recruitment open until 31st August 2023</p>                    |
| <p><b>The immunologic and virologic determinants of Long-COVID</b></p> <p><a href="https://www.cardiff.ac.uk/news/view/2535247-cardiff-university-awarded-major-funding-to-research-long-covid">https://www.cardiff.ac.uk/news/view/2535247-cardiff-university-awarded-major-funding-to-research-long-covid</a></p> | <p>This research aims to provide new insights into the cause of Long COVID and to explore whether Long COVID results from the impact of the coronavirus on the body's immune system. The researchers will evaluate whether the virus causes reactive autoimmune diseases (through coronavirus stimulation of the body's natural defence systems); also, they will assess if the virus persists in the body longer term triggering ongoing immune activation. The project hopes to identify markers to indicate which patients with COVID-19 subsequently develop Long COVID. These biomarkers will, in turn, contribute to the development of new diagnostic tests and treatments for Long COVID.</p> | <p>Study participants should be aged 18 years or over and able to provide informed consent. All participants should have a clinical diagnosis of Long COVID made through specialist assessment in a designated Long COVID clinic/service. Those receiving immunosuppressive medication or suffering from underlying immunological disease are not eligible to participate. The Long COVID clinic at University Hospital of Wales, Cardiff will be participating in this study in Wales. Referrals can be made to this clinic via your GP.</p> | <p>Study end date is 31/07/23. Recruiting until the end date.</p> |
| <p><b>Cognitive Impairment in long COVID: PhEnotyping and RehabilitatiOn (CICERO)</b></p>   | <p>This study will look at why patients develop long term problems with memory, attention or other cognitive function (sometimes called 'brain fog') following</p>  | <p>There are no recruiting sites for this study in Wales. However, clinics in England recruiting for this study are able to receive referrals from your</p>   | <p>Recruitment open. Completion</p>                               |

|   |  |   |   |
|---|--|---|---|
| <p><a href="https://fundingawards.nihr.ac.uk/award/COV-LT2-0014">https://fundingawards.nihr.ac.uk/award/COV-LT2-0014</a></p>  | <p>COVID-19 infection. Magnetic Resonance Imaging (MRI) scanning will be used to identify affected brain networks. The findings will be used to 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</p>   | <p>GP in Wales. Participants should be aged between 30 and 60 years, have evidence of prior COVID-19 infection and have cognitive impairment persisting over 3 months from the acute infection</p>  | <p>date estimated for January 2024.</p>                               |
| <p><b>An investigation to explore the use of a type of MRI scan using an inhaled gas in identifying lung damage associated with long COVID sufferers</b></p> <p><a href="https://www.isrctn.com/ISRCTN14304264">https://www.isrctn.com/ISRCTN14304264</a></p> | <p>The aim of this study is to further the understanding of some of the factors that cause symptoms in long COVID and provide a much-needed explanation to individuals struggling with breathlessness. Learning more about the nature of damage within the lungs through xenon MRI may help with the future development of treatments, and provide a reliable way of measuring the treatment response over time.</p> | <p>Participant is willing and able to give informed consent for participation in the study. Aged 18 years or above. One of the following criteria: Microbiological evidence of COVID-19 infection OR Diagnosis of long COVID or 'post-COVID syndrome' (as defined by NICE 2020) made through specialised assessment at a designated long COVID clinic</p>                                     | <p>Recruitment open until 13th August 2023</p>                        |
| <p><b>Ayurveda for promoting recovery in long COVID</b></p> <p><a href="https://www.lshtm.ac.uk/research/centres-projects-groups/april">https://www.lshtm.ac.uk/research/centres-projects-groups/april</a></p>  | <p>APRIL is a randomised, placebo-controlled trial of a traditional Indian herbal medicine for treating Long COVID, led by researchers at the London School of Hygiene &amp; Tropical Medicine, UK, and the All-India Institute of Ayurveda, India.</p>  | <p>Adults (18 years or older) with the capacity to provide informed consent. Have been diagnosed with Long COVID as per the NICE Guidelines (NG188) that has reduced their ability to carry out day-to-day activities compared with the time before they had COVID-19. Not taking any other herbal medicines, or willing to stop taking any such medicines for the duration of the trial.</p> | <p>Recruitment open. Must apply through GP. No end date specified</p> |

Table 3: Summary of studies of Long-COVID open to Welsh participants

## Conclusion:

Overall, the search conducted has highlighted five studies into Long-COVID that are open to Welsh participants. As three of these are studies from the original 2021 search, this indicates that there is a lack of new or current research being conducted in Wales in this area.

Many of the UK based studies found recruited participants from specific services local to the research centre carrying out the study. Through this search, it was found that there are notably smaller numbers of Wales based research centres conducting studies into Long-COVID. It is currently unknown whether this may be a reflection of services available to those in Wales suffering with Long-COVID.

In 2021, Welsh Government published a policy and strategy for the 'Adferiad (Recovery) Long COVID programme' [3]. In this they detail the use of a £5million package to expand the provision of diagnosis, treatment, rehabilitation and care for those suffering from the long term effects of COVID-19. Although no studies have yet been highlighted, this is a potential area of recruitment for future studies, either experimental or to evaluate these services.

## Acknowledgments

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## Appendix A: List of studies identified through title and abstract screening

| Study Title   | Database/Resource           |
|---|-----------------------------|
| Pausing post-COVID fatigue  | Cochrane Trials Registry    |
| Ayurveda for promoting recovery in long COVID   | Cochrane Trials Registry    |
| Is Signposting to Online Peer Support Helpful in Decreasing Loneliness in Parents of Children With Long-term Conditions and Disabilities? | Cochrane Trials Registry    |
| REGAIN: RCT of Oxaloacetate for Fatigue in Long COVID   | Cochrane Trials Registry    |
| Developing chamomile as a potential long COVID therapy: clinical evaluation of Roman chamomile extract in healthy volunteers              | Cochrane Trials Registry    |
| A Randomised Phase II Study to Investigate the Effectiveness of ACUpuncture for the Relief of Long COVID Related Fatigue                  | Cochrane Trials Registry    |
| Tools to help clinicians swiftly diagnose neurological problems in COVID-19 patients  | Medical Research Foundation |
| Improving Long COVID patient recovery through voice-based AI symptom tracking and personalised rehabilitation                             | Innovate UK                 |
| Genomics of bacterial coinfections from COVID-19 patients: insights into disease severity and antimicrobial resistance                    | MRC                         |

|   |      |
|---|------|
| Understanding the importance of inflammasomes and interleukin-1 to hyper-inflammatory syndromes, including COVID-19                                     | MRC  |
| Real-time modelling and inference of Covid-19 transmission and control  | MRC  |
| Understanding T cell immunity to SARS-CoV-2 natural infection and vaccination in healthy and immunocompromised individuals                              | MRC  |
| COVID-19 and lung disease: developing therapy through immune cell re-programming (Ref: 3949)  | MRC  |
| Pain Mechanisms in long-Covid   | MRC  |
| "Plugging the holes in COVID-19 therapy"  | MRC  |
| Development of an intradermal or inhaled DNA vaccine for COVID-19 and beyond<br>Childhood evolution of B cell responses to COVID-19 vaccination         | MRC  |
| Determinants of immune response following COVID-19 natural infection and vaccination in elderly residents of UK long term care home facilities          | MRC  |
| Explaining the differential severity of COVID-19 between Indians in India and the UK  | MRC  |
| Therapies for Long COVID in non-hospitalised individuals: From symptoms, patient-reported outcomes and immunology to targeted therapies (The TLC Study) | MRC  |
| AGILE: Seamless Phase I/IIa Platform for the Rapid Evaluation of Candidates for COVID-19 treatment  | MRC  |
| REACT Long COVID (REACT-LC)   | MRC  |
| Characterisation, determinants, mechanisms and consequences of the long-term effects of COVID-19: providing the evidence base for health care           | MRC  |
| Repurposing approved drugs as potent antiviral combinations to treat COVID-19 disease   | MRC  |
| COVID-19 therapeutics and beyond: An HTS to identify inhibitors of SARS-CoV-2 nsp12 and starting points for other Coronavirus inhibitors                | MRC  |
| Non-hospitalised Children & young people (CYP) with Long Covid (The CLoCk Study)  | MRC  |
| Genomics of bacterial coinfections from COVID-19 patients: insights into disease severity and antimicrobial resistance                                  | MRC  |
| Covid Social Mobility and Opportunities study (COSMO): Wave   | ESRC |
| Exploring directions for post-pandemic disaster education through interdisciplinary collaboration between the UK and South Korea                        | ESRC |
| DfT Covid Recovery User Focus ESRC Policy Fellowship  | ESRC |
| The impact of the Covid-19 pandemic on the mental health of workers in health services: building resilience in post-conflict territories                | ESRC |
| Inequalities in informal caregiving over the adult life course in Europe: social participation, health and the influence of Covid-19                    | ESRC |
| Understanding the challenges of living with Parkinson's in a post COVID health and social context: a mixed methods proposal                             | ESRC |
| Joint Pain in Long COVID  | NIHR |
| Long COVID and HRQoL v0.1   | NIHR |
| Musculoskeletal Pain in Long COVID  | NIHR |

|  |      |
|--|------|
| Ayurveda for promoting recovery in long COVID  | NIHR |
| COVID-19 hearing loss project v1.8   | NIHR |
| Cognitive Rehabilitation for People With Cognitive Covid19   | NIHR |
| An investigation to explore the use of a type of MRI scan using an inhaled gas in identifying lung damage associated with long COVID sufferers | NIHR |
| HEART Rate Variability Biofeedback in LOng COVID-19 (HEARTLOC)   | NIHR |
| Helping alleviate the longer-term consequences of COVID-19   | NIHR |
| The UK Interstitial Lung Disease Long-COVID19 Study (UKILD-Long COVID): Understanding the Burden of Interstitial Lung Disease in Long COVID.   | NIHR |
| Uninterrupted and Interrupted Sitting in Long COVID-19   | NIHR |
| Health-related Quality of Life and Long COVID  | NIHR |
| Long term effects of COVID-19 in people with diabetes  | NIHR |
| Aerosol clearance in patients with and without long COVID  | NIHR |
| Symptoms, trajectory, inequalities and management: understanding Long COVID to address and transform existing integrated care pathways         | NIHR |
| Connecting breath and mind for CYP with post-COVID syndrome  | NIHR |
| Randomised Study to Investigate the Effectiveness of Acupuncture for the Relief of Long COVID-19 Related Fatigue                               | NIHR |
| Feasibility of Personalised Health Behaviour Coaching to Support Symptoms and Activities of Daily Living in Those With Long COVID-19.          | NIHR |
| MUlti-nuclear MR Imaging Investigation of Respiratory Disease-associated CHanges in Lung Physiology  | NIHR |
| Acute kIDnEy Injury in covid-19  | NIHR |
| MODEL-COV  | NIHR |
| Evaluating video and hybrid group consultations in general practice: Mixed-methods, participatory study  | NIHR |
| BEAT-CORONA: Building evidence to advance treatments for COVID-19  | NIHR |
| The EPIC Project: the mental and physical health impact of the COVID-19 pandemic on healthcare professionals, patients and the general public  | NIHR |

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Our dedicated team works together with Welsh Government, the NHS, social care, research institutions and the public to deliver vital research to tackle health and social care challenges facing Wales.

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