UK Covid-19 Public Inquiry

Module 3 – the impact of the Covid-19 pandemic on the healthcare systems of the UK

An expert report on the treatment of Long Covid

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I confirm that this is my own work and that the facts stated in the report are within my own knowledge. I understand my duty to provide independent evidence and have complied with that duty. I confirm that I have made clear which facts and matters referred to in this report are within my own knowledge and which are not. Those that are within my own knowledge I confirm to be true. The opinions I have expressed represent my true and complete professional opinions on the matters to which they refer.

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Dr Rachael Evans

9th April 2024

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We have sought advice from the following people:

Regarding Paediatric Long Covid:

Research:

Professor Sir Terence Stephenson: Nuffield Professor of Child Health at University College London (UCL) and current Chair of the Health Research Authority. Chief Investigator of the NIHR funded Long COVID in Children and Young People CLoCk study.

Professor Roz Shafnan: Professor of Translational Psychology at University College London Great Ormond Street Institute of Child Health. Honorary Consultant Clinical Psychologist. Co-Investigator of the CLoCk study.

Clinical:

Dr Terry Segal: Consultant in general paediatrics and adolescent medicine at University College Hospital London UCLH. Co-lead of the Pan London Post COVID service.

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Professor Keir Lewis (Wales): Professor of Respiratory Medicine and Biomedical Sciences at Swansea University and Honorary Respiratory Consultant and Respiratory Lead at Hywel Dda University Health Board.

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Professor James Chalmers (Scotland): Professor of Respiratory Medicine at University of Dundee and Honorary Consultant Respiratory Physician at Ninewells Hospital.

Dr Melissa Heightman (England): NHS-England National Specialty Advisor for Long Covid, Consultant Respiratory Physician, University College London Hospitals NHS Foundation Trust.

Contents

Introduction

1. This section of our report follows our M2 section and covers content relevant to M3 only. Our M2 section covers: how the understanding of the long-term sequelae of SARS-CoV-2 infection developed throughout the Covid-19 pandemic, the diagnosis and pathophysiology of Long Covid, the scientific advice provided to government, the SAGE response relevant to Long Covid, how foreseeable Long Covid was, and a summary of the UK funded research studies regarding Long Covid epidemiology. It included a summary of the current and future interventions to treat Long Covid and recommendations for addressing long-term sequelae of infection in future pandemics. The two reports should be read alongside each other.

2. This report covers an overview of the UK and international funding response to researching treatments for Long Covid, the UK healthcare response to Long Covid for children, adolescents, and adults in the context of the evolving understanding about Long Covid, access to healthcare and inequalities in Long Covid, research findings to date regarding treatments for Long Covid, clinical and cost-effectiveness of healthcare services, and lessons learned with future recommendations.

3. Since the writing of the M2 section Long Covid remains a significant health priority. In June 2023, Dr Hans Henri P. Kluge, WHO Regional Director for Europe stated to the press on Covid-19, 'Long COVID remains a complex condition we still know very little about. According to estimates from our collaborating centre, the Institute for Health Metrics and Evaluation at the University of Washington in Seattle, nearly 36 million people across the WHO European Region may have experienced long COVID in the first 3 years of the pandemic. That's approximately 1 in 30 Europeans over the past 3 years.'

4. 'Long Covid remains a glaring blind spot in our knowledge, that urgently needs to be filled. Unless we develop comprehensive diagnostics and treatment for Long Covid, we will never truly recover from the pandemic.' [Kluge H 2023]

5. For this report it is important to understand the chronology between healthcare support in the UK, research funding for Long Covid, and research studies being conducted (Figure 1).

6. For context, it takes typically 8 to 10 years from concept to availability of a new drug at a cost of $1 billion [Wouters OJ 2020, PhRMA]. Repurposing of existing therapies is faster but still usually requires a similar cost for large late phase clinical trials. The Human Insufficiency Virus (HIV) is an example of a virus with severe long-term sequelae which frequently ended in death. The pandemic was declared in 1981 and the first treatment was available within six years (1987).

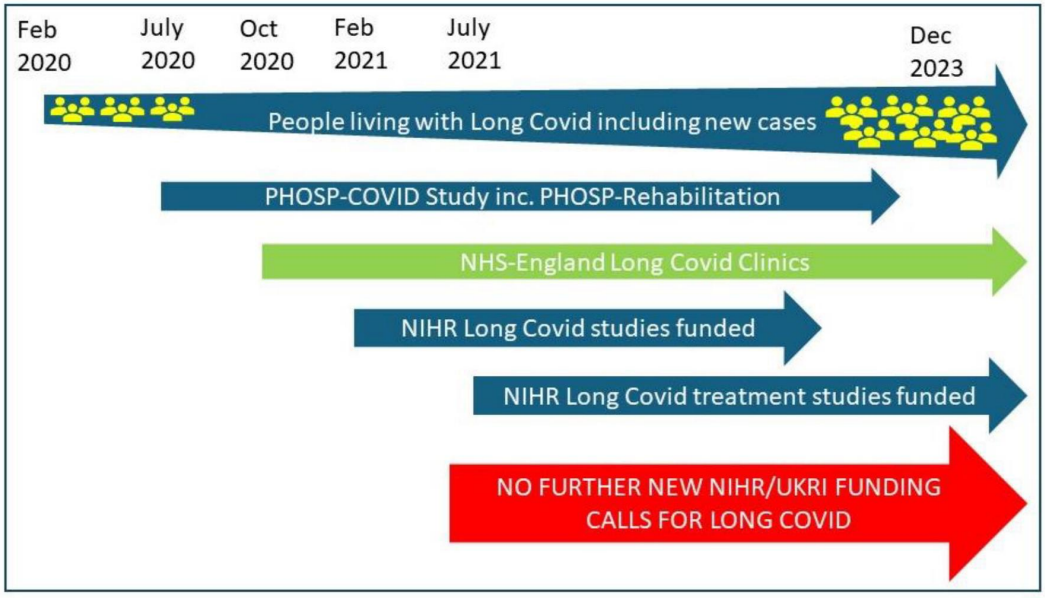


Figure 1. The chronology of funded Long Covid studies and healthcare for Long Covid in England

The figure highlights that Long Covid healthcare in England was provided prior to research being conducted and to date is being provided whilst research studies are being completed. This is important context for the evolution of healthcare described in the report.

Funded research for Long Covid including treatment in the UK and internationally

7. **UK** - The research landscape for Long Covid in the UK, funded predominately through the government via UKRI and NIHR in England and Chief Scientist Office in Scotland (£300K 23rd October 2021) [CSO 2021], was started earlier than other countries internationally. Even though funding in the UK was provided early in the pandemic the ongoing funding is limited with few Long Covid specific calls. There have been no specific Long Covid funding for treatments since 2021. In contrast other research-active nations internationally have largely responded later, but are now providing substantial research funding for Long Covid particularly in United States of America in recognition that this new condition is affecting a large number of people and its impact is persisting long after the initial SARS-CoV-2 infection.

8. PHOSP-COVID was the first study to be funded by UKRI/DHSC (July 2020) to study the consequences of Covid-19 in adults discharged from hospital following Covid-19. The PHOSP-COVID cohort is now complete and full cohort profile described, involving nearly 8,000 participants and over 2,700 participants who underwent in-person research visits for a wide range of biological samples, physical measurements, and validated questionnaires, enabling researchers to gain a better understanding of the disease [Elneima O 2023].

9. The timelines for NIHR/UKRI research support from October 2020 are shown below (Figure 2). The first call for Long Covid research for those non-hospitalised was November 2020. One of the studies funded from the November 2020 call was focused solely on children and adolescents. The studies focussing on the description and epidemiology of Long Covid and their timelines are shown in Figure 3.

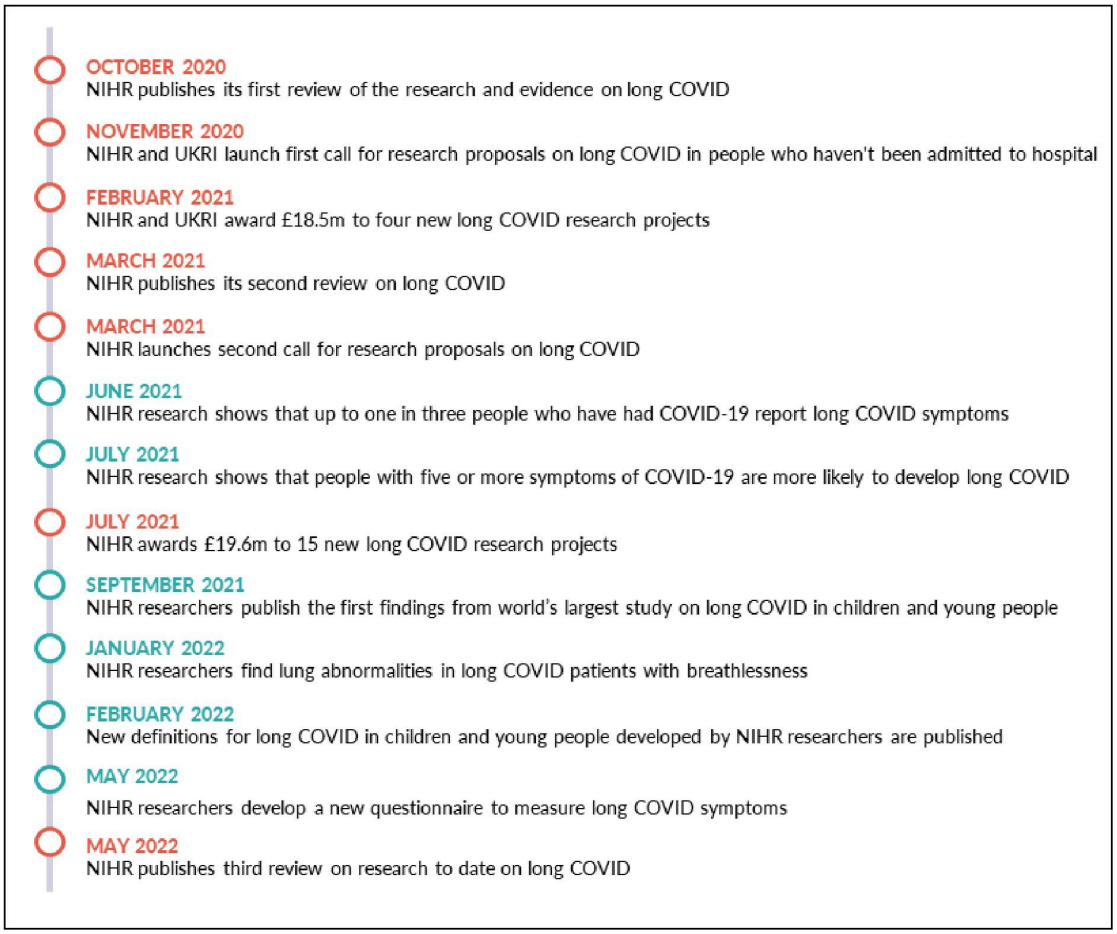


Figure 2. NIHR milestones in researching the long-term impact of Long Covid.

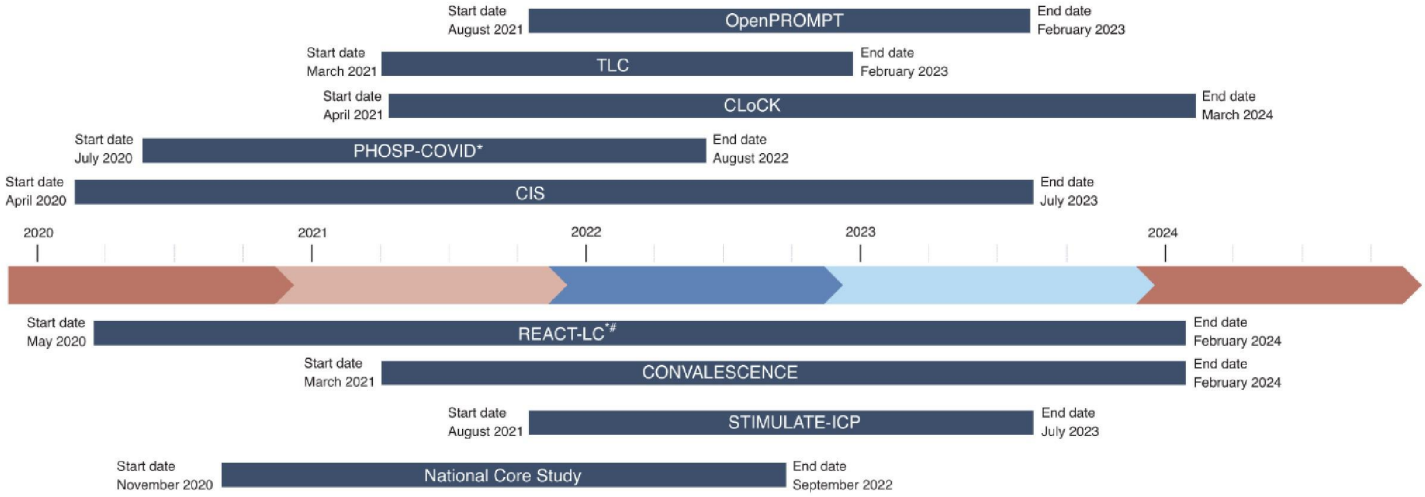


Figure 3. Timeline of major NIHR / UKRI funded epidemiological studies on Long Covid.

The end dates provided on Figure 3 are the planned end dates, but some studies have needed extensions.

10. To date, more than £50 million of UK government funding has been invested in Long Covid research projects. The bulk of this (£39.2 million) has been awarded to 19 projects commissioned through two dedicated calls for Long Covid research (summarised in Figure 4).

11. These 19 studies examine the underlying mechanisms of Long Covid, investigate symptoms, and test possible treatments. They explore whether NHS services, such as Long Covid clinics, meet people's needs, and look at what people can do to optimise their own recovery. The majority of NIHR funded studies included patient and public involvement [Routen A 2023] with variation in patient involvement particularly with the development of the studies.

12. Three projects were considering who gets Long Covid and why, and two were investigating the biological causes of the condition. Three studies were investigating diagnosis including an immunology study. Four studies were evaluating treatments, and three others were considering recovery and rehabilitation. One study was investigating the impact of Covid-19 vaccination on preventing Long Covid, and the final two studies were researching how health services can treat the condition, and the health and economic costs of the disease.

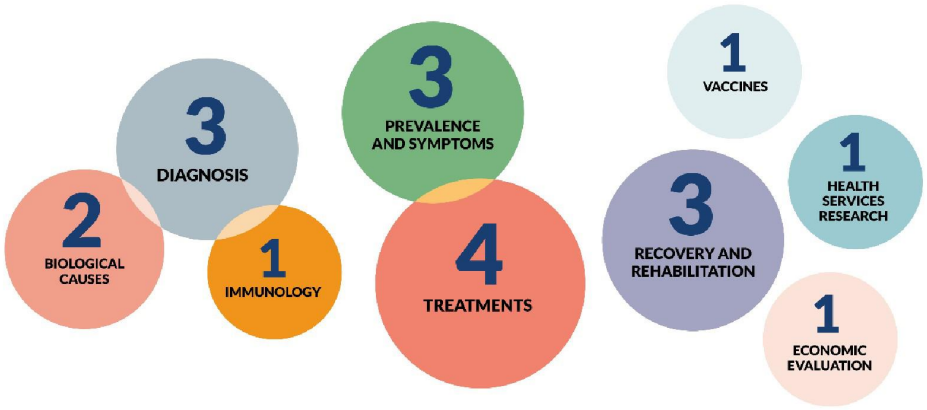


Figure 4. Topics in NIHR-funded studies researching the long-term impact of Long Covid [NIHR 1].

13. The Stimulate-ICP study (Symptoms, Trajectory, Inequalities, and Management: Understanding Long-COVID to Address and Transform Existing Integrated Care Pathways), funded by NIHR in July 2021 with a £6.9m grant [NIHR 2)], is one of few NIHR funded trials to investigate pharmacological management [Forshaw D 2023]. Eligibility criteria are adults who were not hospitalised for the acute illness and were referred to a Long Covid clinic involved in the study. The primary outcome is self-reported fatigue 12 weeks after starting treatment, measured using a validated questionnaire. Two elements of the study design are being used to measure the effectiveness of the interventions at reducing fatigue (though many other outcomes such as breathlessness, quality of life, and

healthcare utilisation are also being measured). One part of the study is a more typical individually randomised trial to test the effectiveness of three different drugs (famotidine/loratadine, an antihistamine; rivaroxaban, a "blood-thinner" which prevents blood clots; and colchicine, an anti-inflammatory drug usually used for gout). Each individual participant entering the study can consent to be randomly allocated to receive one of these drugs or no medication. This is an open-labelled study with no placebo. It is a platform trial, so further drugs can be added for testing if required.

14. In January 2021 NIHR funded the HEAL-Covid (HElping Alleviate the Longer-term consequences of COVID-19) study which was an Urgent Public Health badged trial (ISRCTN15851697) and Clincialtrials.gov (NCT04801940)). Eligibility criteria were patients who had survived a hospital admission with Covid-19 and were recruited prior to being discharged, so the trial was designed to prevent long-term consequences rather than treat established Long Covid. It was a platform trial so different medications could be added. Patients were randomised to either usual care for 12 months or Apixaban (a blood thinner) (2021 -2022) or Atorvastatin(2022-2023). The main outcome was hospital free survival for 12 months after research. Patients also completed patient reported outcome measures as questionnaires for their symptoms and health-related quality of life. From the symptom questionnaires it would be possible to estimate any difference in the development of Long Covid between the two groups. Participating sites were across the four nations [Toshner MA 2022]

15. **European Union** - The EU-Commission is funding research to understand and tackle Long Covid. Approximately €66 million has supported large cohort studies on Covid-19 to determine long-term consequences and symptoms of Covid-19 infections (ec.europa.eu). These include the Horizon 2020 project ORCHESTRA (€26 million) and four Horizon Europe projects funded from the HERA Incubator call in 2021 (around €10 million per project). The Commission set-up a Cohorts Coordination Board to facilitate coordination between consortia on topics such as data standards and data harmonisation. The DRAGON project (The RapiD and SecuRe AI enhAnced DiaGnosis, Precision Medicine and Patient EmpOwerment Centered Decision Support System for Coronavirus PaNdemics) was funded (€11.5 million) by IMI2 in October 2020. DRAGON started on 1 October 2020 to identify patients who have got Covid-19 or novel coronaviruses that may arise in the future with a major focus on the acute infection but has used its approaches to explore the longer-term consequences of Covid-19. In response to the 2021 Horizon Europe call, "Personalised medicine and infectious diseases: understanding the individual host response to viruses" the Commission funded six projects that started between June-September 2022 and receive a total budget of €42.3 million.

16. **The European Respiratory Society** (ERS) formed the clinical research collaboration END-COVID. The END-COVID CRC in September 2021 surveyed 130 centres across 26 European countries about Long Covid services [Valenzuela 2022]. There was considerable variability across the centres in terms of access to services with a mix of virtual versus face-to-face clinics, inconsistent access to tests, rehabilitation, and mental health provision.

17. **Australia** - Improving health outcomes for people living with Long Covid. A new research plan to improve health outcomes for people living with Long Covid will shape $50 million

in funding from the Medical Research Future Fund. An independent Expert Advisory Panel formed the plan. Members tell us how it meets an urgent need. https://www.health.gov.au/news/improving-health-outcomes-for-people-living-with-post-acute-sequelae-of-covid-19-long-covid

18. **Canada** - In Canada there is a Long Covid taskforce but we are not aware of specific research funding for this condition. The taskforce objective is to develop a scientific roadmap that provides a framework to manage Long Covid. The roadmap will identify the evidence required and data gaps to be filled and will provide recommendations for action on the health and socioeconomic impacts of Long Covid in the Canadian context. https://science.gc.ca/site/science/en/office-chief-science-advisor/initiatives-covid-19

19. **USA** - In December 2020, the NIH held a workshop to summarise what is known about Long Covid [NIH 2020]. This led to the announcement on 23 February 2021 by the director of the NIH of Congress providing $1.15 billion in funding over four years for NIH to support research into the prolonged health consequences of SARS-CoV-2 infection. The funding is being released in tranches to address a series of research questions via core funding and calls. Some of the initial underlying questions this initiative called the NIH-RECOVER program aimed to answer were:

    a. What does the spectrum of recovery from SARS-CoV-2 infection look like across the population?

    b. How many people continue to have symptoms of Covid-19, or even develop new symptoms, after acute SARS-CoV-2 infection?

    c. What is the underlying biological cause of these prolonged symptoms?

    d. What makes some people vulnerable to this but not others?

    e. Does SARS-CoV-2 infection trigger changes in the body that increase the risk of other conditions, such as chronic heart or brain disorders?

https://www.nih.gov/about-nih/who-we-are/nih-director/statements/nih-launches-new-

20. NIH-RECOVER (https://recovercovid.org) has a series of embedded studies including: i) autopsy and tissue pathology studies to determine effects on organs and tissues, ii) longitudinal observational and cohort studies, iii) electronic health care records to study real-world data from large groups of people and iv) clinical trials of interventions to target 5 key areas: autonomic dysfunction, cognitive dysfunction, fatigue, sleep disturbance and viral persistence.

Healthcare and treatment for Long Covid across the UK

21. Healthcare had to evolve before any specific treatments (medication or rehabilitation) for Long Covid were known to be effective through clinical trials. Individuals with Long Covid needed healthcare support to establish a diagnosis, exclude other diagnoses, understand their diagnosis, for self-management support, and for recovery support with therapies including rehabilitation programmes and mental health support.

22. Access to healthcare for Long Covid has been and remains variable within and across the four nations of the UK. A high-level summary is provided in Table 1.

	England	Wales	Scotland	Northern Ireland
Dedicated Long Covid Clinics	Y community and secondary care	N	N	Y
Dedicated funding for primary care	Y	Y	N	N
Long Covid service central funding and amount announced	Oct 2020 – March 2025 £124M announced 2020-21	July 2021 – present £18.4 M to date	Sept 2021-2026 £10M announced 2021	November 2021 – present ? amount
Nationally provided public/patient information on Long Covid	Y Website	Y App	Y Booklet	Y Website with links to Apps
Long Covid Rehabilitation	Y 2021	Y	Y September 2021	Y November 2021
Nationally provided GP training	Y RCGP, E-learning for health	Y RCGP, E-learning for health, [GovWales 2021]	Y RCGP, E-learning for health.	Y RCGP, E-learning for health
Long Covid Taskforce or similar	Y Oct 2020	Y	Y March 2022	N

Table 1. A high-level summary of dedicated centrally funded Long Covid Services across the four UK nations 2020 to present.

23. Qualitative reports of patient experience of NHS (or equivalent for the four nations) care for Long Covid highlight inconsistency in access, approach, interventions or specific therapies and patient experience of Long Covid healthcare [Macpherson 2022]. A qualitative systematic review found five studies, with the number of participants ranging from 24 participants for interviews to 3,762 survey respondents. One identified theme was around healthcare experiences, which were mixed, exemplified by the following two quotes from interviews by patients with Long Covid: *"…I feel like there's a lack of knowledge. And I really wasn't able to get any answers, I know, you know this is obviously a novel illness. But just even for one doctor to look into it a bit and come back to me, didn't happen"* in contrast to *"I have to say it was a really powerful experience speaking to the GPs … the two more recent ones, actually just the experience of being heard and feeling like somebody got it and was being kind about it, but you know it was okay that they couldn't do anything, I just kind of needed to know that I wasn't losing it really and it was real what I was experiencing, I think so that was really helpful."* [Macpherson K 2022].

24. Overall, study participants included in the same systematic review found access care to be *"complex, difficult and exhausting"* [Macpherson K 2022]. Other qualitative data highlighted patients having to seek and create their own care pathways and often sought advice from medical professionals that were part of their Long Covid support networks [Ladds E 2020]. Patients perceived a lack of support with 'ping-ponging' between NHS 111 and GPs [Macpherson K 2022]. Patient experience appeared better where they had been offered follow-up appointments and where they felt their healthcare providers had listened to them. The study authors concluded: *"It appears that greater knowledge of long COVID is required by a number of stakeholders and that the design of emerging long COVID services or adaptation of existing services for patients with long COVID should take account of patients' experiences in their design"* [Macpherson K 2022]. Local patients should also be involved in the ongoing adaptations and delivery of Long Covid services.

25. The first point of contact to access healthcare across the UK is typically through primary care. The Royal College of General Practitioners provided education including eLearning on their website led by Dr Gail Allsopp to help GPs better support people with Long Covid [RCGP]. An important part of this work was promoting consistent coding for Post-COVID syndrome / Long Covid within electronic health records. The NIHR funded Locomotion study has a workstream involving quality improvement for Long Covid clinics and as part of this has published a series of BMJ Best Practice pointers on Long Covid [Greenhalgh T 2022], Orthostatic Tachycardia (a condition that causes an abnormal heart-rate increases with sitting or standing) [Espinosa-Gonzalez A 2023], Breathlessness [Evans RA 2023], and Cognitive Dysfunction after COVID-19 [Ladds E 2024] to date. These are intended as succinct summaries for GPs and primary care and have been widely read and shared by clinicians, evidenced by excellent metrics of the attention the articles received (Altmetrics) The Health Education England in partnership with Central London Community Healthcare NHS Trust, NHS England and NHS Improvement and Health Education England also developed a series of educational material for clinicians hosted on the "E-learning for health" [eLFH 2021] website which hosts distance learning material for healthcare professionals.

26. The Scottish Government published an 'Implementation Support note on managing the long-term effects of COVID-19' which is supplementary to the SIGN/NICE/RCGP guidelines and has a particular focus on primary care [SIGN 2021].

Wales

27. Wales took a different approach to the other three nations and funded Long Covid services centrally through a specific funding stream. £5 million (non-recurrent) was provided for the 'Adferiad' (Recovery) programme, launched in June 2021 and delivered exclusively through primary care (https://gov.wales/adferiad-recovery-long-covid-programme-html) and a further £5 million (non-recurrent) in 2022/23. A new suite of patient pathways was introduced, combined with new or expanded primary and community rehabilitation services to support people with Long Covid. The services were delivered by GPs, occupational therapists, and physiotherapists. Each of the seven Health Boards could implement the central guidance/framework locally so some variation in local services and approach is likely. The majority of reviews are online with less face-to-face assessments. Some Health Boards offered a direct on-line referral scheme on-line i.e. individuals could refer themselves. A further £8.4 million was allocated for 2023/24 (recurring) to Adferiad (Recovery) services with the to widen access to these services on a symptom-based need for people with other long-term conditions who may have similar needs such as other post-viral syndromes.

Scotland

28. The provision of Long Covid services in Scotland was left to the discretion of health boards for the first 18 months of the pandemic and therefore there was variation in access and quality. Some health boards accommodated referrals for Long Covid care and rehabilitation within existing services, while some commenced limited dedicated Long Covid rehabilitation services. On 30 September 2021, funding of £10 million for Long Covid support was announced to provide Health Boards "with the resource in a flexible and tailored manner to the needs of people with Long Covid" [GovScot 2021]. Shortly after the Long Covid service funding was announced a website was launched with self-management advice for Long Covid (https://www.nhsinform.scot/long-term-effects-of-covid-19-long-covid/). The Scottish Intercollegiate Guidelines Network (SIGN) published 'Managing the long-term effects of COVID-19' on 5 May 2021 [SIGN 2 2021]. However, it is unclear how widely these guidelines were implemented.

29. A report funded by the Scottish Government Chief Scientist Office up to July 2022 indicated that once the public became aware of one of the Long Covid services they were unable to meet demand and the service closed after 18 months due to a lack of funding, with the waiting list distributed to local community rehabilitation teams. Existing services which were not specifically dedicated to Long Covid tended to receive considerably fewer referrals, and reluctance of health boards to promote services for fear of being overwhelmed has been reported [Duncan E 2023].

30. Over three years into the Covid pandemic in July 2023, NHS Education Scotland hosted an e-learning module about Long Covid designed for a range of healthcare professionals [NES 2023].

Northern Ireland

31. In Northern Ireland there was no central funding until November 2021 and Long Covid clinics were therefore either not provided or developed at the discretion of local clinicians

and health services,. On 01 November 2021 the Health Minister for Northern Ireland Robin Swann launched the first dedicated assessment and treatment services for patients with Long Covid (DoHNI 2021). According to the launch, services were to include a multi-disciplinary clinic, bespoke pulmonary rehabilitation / dysfunctional breathing services, additional support for patients discharged from critical care, strengthening psychology support to all Trusts and signposting to self-management resources. It is unclear how much funding was provided. An example of the implementation and timing at one trust included the MDT assessment clinic and rehabilitation from November 2021, but the post critical care support was yet to be provided, the psychology support was strengthened but only available from May 2023, a regional MDT for clinical physiology, speech and language therapy and dietetic support was available since 2022, and there was signposting to self-management support. The self-management support included a webpage https://online.hscni.net/about-us/commissioning-directorate/long-covid-recovery-support/, signposting to the Your COVID Recovery website and a directory of Digital support for Long Covid (Available at: https://view.pagetiger.com/longcoviddigitalsupport). The latter included COVID Recovery developed by NHS Wales, Wysa ("an emotionally intelligent chatbot that uses AI to react to the emotions" expressed), Stronger Together (a community App which included a Long Covid group to access community support), Coronavirus Support (general advice around Covid-19), COVID coach (designed to help build resilience, manage stress and increase well-being), and Ada (a symptom checker App). The date when the host website was first available is unknown.

England

32. As discussed in our M2 report section 1.9, in England Long Covid assessment clinics were funded from 7 Oct 2020 as part of the five-point plan for Long Covid. 40 clinics were launched and by Dec 2020 69 clinics were operating [NHS England 1 2020]. The initial launch of the clinics was primarily focused on patients discharged from hospital [NHS England 1 2020]. Since 05 July 2021 monthly published reports are in the public domain [NHS England 2023] which include the number of patients referred and rejected, time to first appointment, age, sex, ethnicity, and indices of multiple deprivation. An extensive Long Covid service specification was first published in 2021, which included patients who had not been admitted to hospital for their acute Covid illness, to help provide a consistent approach and reduce health inequity [NHS England 1 2021 and NHS England 2 2021]. Multiple adults with lived experience of Long Covid and representatives from the national Long Covid charities were part of the NHS England taskforce and contributed to the service specification alongside the other task force members which includes clinicians, researchers, voluntary sector and policy experts.

33. The 'Your COVID Recovery' website led by Professor Sally Singh (University of Leicester/ University Hospitals of Leicester NHS Trust) was funded by NHS England as part of the Long Covid five-point plan. The website included information about post-covid symptoms and advice to support self-management. It was developed at pace and was first launched on 05 July 2020. The website content was designed by healthcare professionals and people with lived experience of post-covid syndrome and a patient and public involvement group for the website was formed (this was completely separate to the Long Covid Taskforce which formed in Oct 2020 and the patient and public voices (PPV) that were part of the team). The initial team in 2020 before the website went live included at least

eight diverse patients. Although the primary original intended audience was for adults with ongoing difficulties after a hospital admission, it was intended for other people with ongoing problems after Covid-19 to use. A paediatric component was developed and launched in 2021. Since the launch, over 14 million users from 189 countries have access the information form Your Covid Recovery website. For the first two million website uses from 31st July 2020 to 31st July 2021, cough, fatigue and musculoskeletal pain were the most accessed information pages.

34. The Your Covid Recovery website has been amended in response to public, patient and clinician feedback including a major restructure of the site in July 2022 with further content added. There was a detailed governance flow chart (available from the University Hospital Leicester NHS Trust Your Covid Recovery team). The website was divided into four phases to further incorporate advice for people that were not hospitalised for their initial Covid illness, and for early support to be accessed where symptoms were ongoing beyond four weeks. Other feedback was supplemented by integrated feedback forms with the website itself where any user could provide feedback through ten questions. This information was also used to amend content. The site was intended to provide early information and support for people with ongoing symptoms after COVID-19 particularly those with mild or improving symptoms. Individuals with more complex needs need further support such as through the Long Covid clinics for individually, tailored advice.

35. There was initial consternation from clinicians and Long Covid Taskforce members that interventions such as rehabilitation had not been funded alongside the assessment clinics in October 2020 as it was clear to the clinical community that whilst assessments could provide information, diagnostic clarity, and support, interventions to improve symptoms, physical and mental health, and return to work were necessary. Early on, adults living with Long Covid who were not hospitalised provided clear accounts to the Taskforce that the severity of Long Covid could be as severe compared to people who had been hospitalised and therefore highlighted that the clinical services needed to be for anyone with persisting symptoms. Data from PHOSP-COVID, ONS and other studies supported the latter highlighted in our M2 expert report.

36. Akin to the NHS England Your Covid Recovery website, in Wales a specific App: the 'NHS Wales COVID Recovery App' was designed by the Respiratory Health Implementation Group (RHIG), hosted by Cardiff and Vale University Health Board and delivered by a private company, the Institute of Clinical Science and Technology. The app provides symptom tracking, education and sign-posting, but experience and reviews have been mixed, with problems mainly recognising or registering the GP practice (especially if patients were registered with England-based practices). The Elaros App [Sivan M 2023], which collects patient reported outcome measures including the Covid 19 Yorkshire Recovery Scale [Sivan M 2022] and can be used for symptom tracking, was used across the Scottish Long Covid services.

37. In June 2021, NHS England announced an additional £100 million in funding to expand and enhance Long Covid services, see Figure 5 [NHS England 2021 3]. Between July 2021 and July 2022 over 45 000 people experiencing severe or complex symptoms were seen by a specialist Long Covid service [NHS England 2022 3]. To date, 113 619 patients have been assessed by a specialist Long Covid service (accepted out of 125 951 referrals) with 359 375 follow-up appointments (data from NHS-England). 118 000

patients have been entered onto the NHS-England Long-Covid registry from 90/101 adult post-COVID providers and 8/13 Post-COVID children and young people (CYP) hub providers.

- £70 million to expand Long COVID services to add to the £24 million already spent on Post-COVID Assessment Clinics.
- £30 million for the rollout of an enhanced service for general practice to support patients to be managed in primary care, where appropriate, and enable more consistent referrals to clinics for specialist assessment and treatment.
- Care coordination.
- Establish 15 Post-COVID assessment children and young people's hubs across England in order to coordinate care across a range of services.
- Develop standard rehabilitation pathway packages to treat the commonest symptoms of Long COVID
- Extend the use of the Your COVID Recovery online rehabilitation platform
- Collect and publish data to support operational performance, and clinical and research activities.
- Focus on equity of access, outcomes and experience.
- Promote good clinical practice through the national learning network on Long COVID for healthcare professionals
- Support our NHS staff suffering from Long COVID

Figure 5. Ten key steps of the Long Covid NHS England plan 2021/22.

38. Phase II of Your Covid Recovery was part of this funding which involved a modular website with remote delivery by rehabilitation teams over one year. The evolution and efficacy of rehabilitation is further described in paragraphs 59-71. The majority of people with Long Covid are of working age. The ONS report in December 2022 on long Covid and the labour market found that among working-age people not in full-time education, the odds of inactivity (excluding retirement) for those reporting Long Covid nearly a year (40 to 51 weeks) after a first test-confirmed SARS-CoV-2 infection were 34% higher compared with before infection; this was after adjusting for background rates of inactivity in the labour market [ONS 1 2022]. The Institute for Fiscal Studies in their July 2022 report estimated that the loss of earnings in the UK due to long Covid is approximately £1.5 billion per annum [Reuschke D 2022]. This has highlighted a need and gap in NHS care for vocational rehabilitation. The true economic impact worldwide is unknown. One estimate from David Cutler of Harvard University suggests that the total economic cost of Long Covid in the USA is some $3.7 trillion, including reduced quality of life, reduced earnings and increased medical spending [JHEOR 2022].

39. The Improving Access to Psychological Therapies team led by Professor David Clark (a member of the NHS England Long Covid Task Force) held an upskilling webinar in autumn 2020 to improve their team's knowledge of Long Covid and subsequently a further set of webinars were available on E-learning for health website [eLFH 2 2022]

40. There are no specific pharmacological treatments for Long Covid, but clinicians are using medications to try and improve symptoms. These include anti-histamines due to mast cell activation syndrome (MCAS) being postulated as an underlying mechanism. MCAS is a condition of unknown cause which can cause flushing, skin hives and rashes, nausea, diarrhoea, abdominal pain and bloating, breathlessness and wheeze, headaches, brain fog, palpitations. Other treatments used are a mix of non-pharmacological and pharmacological therapy for symptoms of dysautonomia / postural orthostatic tachycardia syndrome in line with existing guidance. Dysautonomia is an abnormality with the body's self-regulating system – the autonomic nervous system which controls blood pressure and heart rate amongst other functions. Postural orthostatic tachycardia syndrome is a condition which causes an abnormal increase in heart rate with sitting or standing. However, there is no specific evidence base for the use of these approaches in Long Covid, so the balance of risk and benefit is currently unknown. Trials of treatment are therefore urgently needed. The Stimulate-ICP trial, described in paragraph 13, includes dual anti-histamines as one of the treatments under evaluation.

41. People with Long Covid can experience changes to their voice, swallowing, upper away and communication all of which can be helped by Speech and Language Therapists (SALT). Unfortunately, SALT are often not part of the Long Covid MDT due to a lack of available staff. Data from the PHOSP-COVID study, highlighted a high prevalence of swallow, communication, voice and cognitive problems particularly in people who received invasive mechanical ventilation [Dawson C 2023]. Data collated by the Royal College of Speech and Language Therapists (RCSLT) highlights a range of symptoms experienced including difficulty swallowing, voice change, brain fog affecting communication, difficulty with word finding. Over 80% of 153 patients reported improvement in at least one area on the Therapy Outcome Measure [data from the RCSLT].

42. Outside of NHS care, many patients have self-medicated with over-the-counter medications such as antihistamines, whilst others have sought private healthcare where non-evidenced based therapies have been accessed [Brown K 2022],. These therapies include nutritional supplements and hyperbaric oxygen, and some have travelled abroad to access plasmapheresis [Hadanny A 2024, Achleitner 2023]. Multiple private Long Covid clinics are available.

Children and young people

43. Across the four nations there has been a different approach to Long Covid services. To our knowledge, there are no dedicated children or young person (CYP) Long Covid clinics in Wales, Scotland, or Northern Ireland. The Scottish Government had allocated funding for one Scottish Health Board to establish a CYP Long Covid service, but the Health Board was unable to develop this service due to low numbers of referrals and an inability to recruit clinicians to deliver the service. There is a CYP sub-group of the Scottish Long Covid Network established in March 2022. In Northern Ireland and Wales, the plan was for children and young people to be referred paediatric specialists. There were tensions between the need for Long Covid paediatric specialists and the demand, and it was felt that this approach would be more equitable.

44. In England, a Pan London CYP Post-Covid clinical reference group met November 2020, and a CYP Post COVID Pan London Task and Finish group met 2nd Dec 2020 which was led by Dr Terry Segal (adolescent paediatrician with experience in ME/CFS), Dr Elizabeth Whittaker (Infectious Disease Consultant) and Zara Brookes (Clinical Network Clinical Senior Manager, Registered Children's nurse, NHS England and NHS Improvement (NHS London)). The tasks were to create and set up a standardised referrals process into the Post COVID-19 assessment services. A clinical guidance summary was created [NHS London 2020]. The April 2021 National Guidance for Post Covid Syndrome assessment clinics incorporated advice around services for children and young people for the first time [NHS England 2021 4]. The advice included an early, holistic, medical assessment to identify need for specialist input, organ impairment, and support for the large range of symptoms that can significantly affect quality of life. The guidance included the patient pathway, referral routes to secondary care and post-covid assessment clinics, and recommended the availability of a virtual multi-disciplinary team meeting for the referring paediatrician to discuss cases.

45. In Spring 2021, NHS-England created a CYP Post COVID Clinical Network and a CYP workstream within the NHS-England Long Covid Taskforce. The workstream met twice a month to collate numbers and share good practice, experience, learn from each other and plan services as well as inform the National guidance. They also met regularly and were supported by Dr Melissa Heightman the NHS-England Long Covid National Specialty Advisor.

46. Fifteen Children and Young Person (CYP) Long Covid Hubs were announced as part of the NHS England strategy for Long Covid with a hub and spoke format in July 2021 [NHS-E 2021 2]. The principles were to assess CYP to identify complications, provide a holistic assessment and support to enable supported self-management and support local care to continue where possible. The CYP NHS England Long Covid Taskforce workstream developed resources to support CYP with Long Covid and these were incorporated into the Your COVID Recovery website. Representatives from the CYP workstream attended a Long Covid ministerial Round Table March 2022. By the end of July 2023, 1265 children and young people had been assessed by the CYP Post Covid clinics. 8/13 current CYP hubs contribute data to the NHS-England national registry.

47. The mainstay of treatment for the CYP hubs is to provide advice to local teams via the virtual MDT for mild cases with signposting to resources and bespoke advice. For children and young people who are assessed at the clinical hubs, a multidisciplinary holistic biopsychosocial assessment is conducted to exclude any secondary organ damage and assess for comorbidities such as autonomic dysfunction including postural orthostatic tachycardia syndrome (POTS) a condition which causes an abnormal increase in heart rate with sitting or standing, and low mood or depression, as well as the effects on the child or young person's life [Walds M 2023]. Self-management advice delivered by 'Your COVID Recovery' leaflets, webinars and groups to support sleep, pacing activity and wellbeing are delivered in some hubs. Ongoing follow up from physiotherapy, occupational therapy, psychological input and medical reviews as well as ongoing subspeciality referrals are made where needed. Medication is given to support symptoms such as melatonin for sleep, amitriptyline for pain and sleep, autonomic medications such as midodrine or ivabradine under cardiac supervision.

48. There has been an 'assurance report' from NHS-England regarding CYP hubs. Most services were accepting referrals from both primary and secondary care and provided a full holistic assessment. The most common staff involved were consultants, physiotherapists, occupational therapists and psychologists and the multi-disciplinary team model was working well in most areas. Where recorded (proportion unknown), most clinics reported positive outcomes. However, vacancies were high particularly for allied health professionals and psychologists. There were difficulties in some areas accessing rehabilitation in the community due to lack of local resource. A few needs were flagged including needs for ongoing support with ME/CFS as clinical services not resourced in some areas, a clinical forum was desired to discuss complex clinical cases and share best practice, regular meetings with commissioners. There was variation noted in accessing the assessment service and local treatment pathways.

49. Similar to adults, private medicine has been sought for some children and young adults and a variety of approaches undertaken.

Evolving research evidence for the treatment of Long Covid

This section includes an update of progress and any results from clinical trials of interventions for Long Covid (including trials with an endpoint of reducing the incidence of Long Covid). There are sections for both pharmacological and non-pharmacological management.

Research on drug treatments

There was one only one NIHR funded clinical trial for the treatment of established Long Covid which involved medication - the Stimulate-ICP trial introduced in paragraph 13.

Stimulate-ICP study – testing colchicine (an anti-inflammatory), rivaroxaban (a blood thinner) and anti-histamines.

50. The project started 01 August 2021 and took a year to set up and gain the necessary approvals. None of the medications were approved by the COVID-19 Therapeutics Advisory Panel (UK-CTAP) in a meeting on 9th September. A subsequent meeting with a new expert panel (which Professor Chris Brightling was part of) approved famotidine/loratadine, but not colchicine or rivaroxaban until provision of further information which was collated and discussed at another meeting on 29 Nov 2021, and all three medications were approved. The protocol and documents were submitted to the Research Ethics Committee and Health Research Authority (REC/HRA) 01 Feb 2022, and given favourable approval by 11th March 2022. Medicines and Healthcare products Regulatory Agency (MHRA) approval was granted by August 2022.

51. The target sample size for the cluster randomised trial comparing enhanced care versus usual care was 1,130 participants. There was an ambitious recruitment target of 4,520 participants across six to ten sites for the individual randomised controlled trial involving medications. Over 800 participants were recruited by August 2023. Further sites have been added and started September 2023; the first submission of an amendment to include sites to the medication trial only to MHRA took from 24 Jan 2023 until 26 May to be approved [Financial Times 2023].

52. The drug treatments were selected according to the potential underlying mechanisms causing Long Covid (at the time the study was initiated). These were an anti-inflammatory (colchicine) to target ongoing inflammation, an anti-coagulant (blood thinner – Rivaroxaban) to target ongoing clot formation (involving a particular component of the complex clotting cascade), and anti-histamines to target MCAS.

UKRI HEAL-COVID

53. The HEAL-COVID study (introduced in paragraph 14) has completed recruitment with 1,245 participants over 109 sites. Recruitment was slower than anticipated in part due to prescription of anticoagulation (blood thinners) after an admission becoming part of 'usual care' for some clinicians and therefore patients were not entered into the trial. The first results were published in preprint (not peer-reviewed) 07 12 2022 [Toshner MR 2022]. 801 participants were recruited, 402 to apixaban (a blood thinner) and 399 to usual care. The apixaban arm of the trial was stopped early after the interim analysis showed no indication of benefit reviewed by the oversight committee. There was no statistically significant difference between death or hospitalisation between those people receiving apixaban and those receiving usual care only [Toshner MR 2022].

USA - NIH Recover

54. The first three areas (paragraph 19) of NIH Recover started initially and the clinical trials were launched September 2023 [NIH 2023]. The first two trial platforms launched were RECOVER-VITAL and RECOVER-NEURO followed by RECOVER-SLEEP and RECOVER-Autonomic. Studies targeting fatigue and possible rehabilitation trials have not started. **RECOVER-VITAL** tests the possibility of SARS-CoV-2 persistence with a longer dose regimen of the antiviral PAXLOVID (nirmatrelvir and ritonavir) than is used for treating acute Covid. **RECOVER-NEURO** examines interventions for cognitive dysfunction related to Long Covid, including brain fog, memory problems and difficulty with attention, thinking clearly and problem solving such as the web-based brain training program called BrainHQ. **RECOVER-SLEEP** will test interventions for changes in sleep patterns or ability to sleep after having COVID-19. A trial for hypersomnia, or excessive daytime sleepiness, will test two wakefulness-promoting drugs compared to a placebo control. A second trial for sleep disturbances, such as problems falling or staying asleep, will test other interventions designed to improve sleep quality to learn if these interventions may help regulate sleep patterns in adults with Long Covid. **RECOVER-AUTONOMIC** will examine interventions to help treat symptoms associated with problems in the autonomic nervous system.

55. These trials are likely to take over a year to report, and if successful, will likely require further trials to confirm findings before treatments for Long Covid become available.

Other trials - non-government funded

56. USA – COVID-OUT: Early Outpatient Treatment for SARS-CoV-2 infection. ClinicalTrials.gov NCT04510194. In brief, the COVID-OUT trial included non-hospitalised participants at the time of their SARS-CoV-2 infection. There were three aims for the study, the first two were to reduce progression to severe Covid -19 and to reduce viral load of the pathogen. The third aim was to understand if any of the active treatment arms prevented Long Covid. Participants were randomised to six groups which included three drugs in current use for different conditions. The six groups were Metformin alone, Metformin and Fluvoxamine (a type of medication known as selective serotonin reuptake inhibitors (SSRIs), and used to treat obsessive compulsive disorders), Metformin and Ivermectin (a medication used for parasite infections), Placebo, Ivermectin and Fluvoxamine, Fluvoxamine alone, Ivermectin alone. The treatments were given for 14 days and the primary outcome measures were recorded at Day 14 of the trial. The outcome for the third aim 'patient reported receipt of a Long Covid diagnosis' was recorded after Day 180. 1126 participants consented for long-term follow-up between Dec 30, 2020 and Jan28 2022 [Bramante C 2023]. 1074 completed at least 9 months of follow-up (95%). 8.3% (n=93) of participants reported a Long Covid diagnosis by Day 300. The main result was a reduction in the development of Long Covid by 41% in participants that received Metformin compared with placebo. There was no effect with Ivermectin or Fluvoxamine. Whilst these results are important and encouraging, they require replication, mechanisms to be understood (particularly for only two weeks of treatment), and safety and cost-effectiveness to be evaluated in future studies.

57. Early results investigating a metabolic modulator which improves cellular energy metabolism (i.e. improves energy production of a cell) are promising [Finnigan LEM 2023].

A small early phase randomised controlled trial was conducted. The participants were adults with fatigue dominant Long Covid. They were randomly allocated to the medication or placebo twice a week by mouth for four weeks. The main outcome measure was a sophisticated measure of energy production during exercise. In this small, early phase trial there was no difference in the main outcome. However, there were promising reductions in secondary end points including an established patient reported fatigue measure. Larger trials are needed to draw any firm conclusions.

58. The potential role of Covid -19 vaccinations to reduce the likelihood of developing Long Covid after breakthrough infections and the potential effect on Long Covid symptoms was covered in the M2 section of our report.

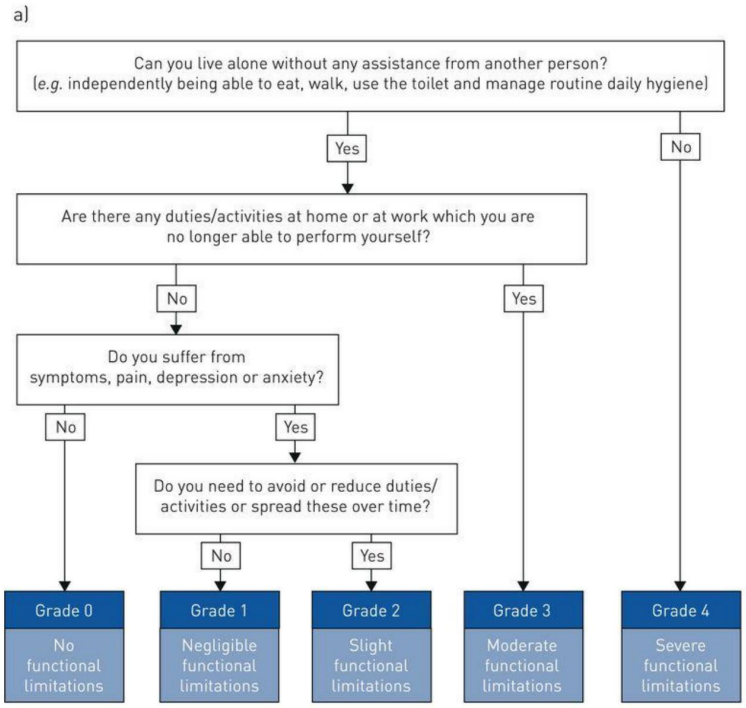
Research on non-drug treatments such as rehabilitation

59. At the start of the pandemic, many clinicians and researchers quickly identified the likely need for rehabilitation programmes for some people surviving a hospital admission, mainly inferred by pre-existing knowledge of post-intensive care syndrome. The rehabilitation needs and strategy for the complex nature of Long Covid particularly in adults who were non-hospitalised was less clear within the first six months of the Covid-19 pandemic. Rehabilitation guidance for adults post-hospital admission for Covid-19 was collated quickly based on expert opinion involving modification of existing pulmonary rehabilitation programmes [Spruit M 2020, Singh S 2020]. Pulmonary Rehabilitation is an evidence-based programme of individually prescribed aerobic and strength training, self-management support and multi-disciplinary education. A typical programme duration is six to eight weeks with a minimum of two supervised sessions per week. Different models of care have been evaluated to improve access such as virtual programmes, web-based programmes, and home programmes. At the start of the Covid pandemic, most pulmonary rehabilitation programmes stopped due to social distancing and lock-down policies. Virtual web-based models were implemented for people with chronic lung diseases although many patients did not have the levels of digital literacy needed [Polgar O 2022]. These programmes were modified for people with Long Covid by many sites as the need for Long Covid rehabilitation became apparent.

60. The 'Your Covid Recovery' website highlighted in previous sections, funded by NHS England, aimed to support self-management in primary and community care. It was flagged by a pop-up within electronic health records so clinicians such as general practitioners could offer it as a resource to patients during consultations. It was designed as an information resource for a 'light touch' self-management approach to support people with ongoing symptoms particularly for those with milder symptoms and impact.

61. The COVID-19 functional status scale tool published July 2020 (Figure 6) is a potentially useful tool for healthcare professionals in primary care and other settings to stratify healthcare needs [Klok F 2020]. It's unclear if this was widely used in the UK. It is very similar to the widely used Medical Research Council Dyspnoea Scale Grade for adults with chronic respiratory disease for prognostication purposes, and as a broad tool to guide referrals to rehabilitation. The COVID-19 Functional Status Scale has subsequently been shown to have construct validity (i.e. the scale from slight to severe functional limitations

is appropriately associated with worse and more symptoms, reduced quality of life and impairment with work and usual activities [Machado FVC 2021].



b)

How much are you currently affected in your everyday life by COVID-19? (Please indicate which one of the following statements applies to you most)	Corresponding PCFS scale grade
I have no limitations in my everyday life and no symptoms, pain, depression or anxiety related to the infection.	0
I have negligible limitations in my everyday life as I can perform all usual duties/ activities, although I still have persistent symptoms, pain, depression or anxiety.	1
I suffer from limitations in my everyday life as I occasionally need to avoid or reduce usual duties/activities or need to spread these over time due to symptoms, pain, depression or anxiety. I am, however, able to perform all activities without any assistance.	2
I suffer from limitations in my everyday life as I am not able to perform all usual duties/ activities due to symptoms, pain, depression or anxiety. I am, however, able to take care of myself without any assistance.	3
I suffer from severe limitations in my everyday life: I am not able to take care of myself and therefore I am dependent on nursing care and/or assistance from another person due to symptoms, pain, depression or anxiety.	4

Figure 6. COVID Functional Scale

62. Phase II of 'Your Covid Recovery' was specifically designed as a modular website for remote delivery during the first year of the pandemic and was to be more widely implemented as part of the NHS England Long Covid 2021/2022 plan (Figure 5). The modules were further adapted for patients who were non-hospitalised and developed Long Covid, and were co-produced by patients and clinicians, with endorsement from a wide range of national professional societies. Phase II of Your COVID Recovery was delivered by rehabilitation teams and when it became possible patients attended assessments before and after the programme similar to other rehabilitation programmes for long term conditions. There was also telephone support by healthcare professionals.

63. Tensions exist around the use of physical activity and exercise in rehabilitation programmes for some patients with Long Covid particularly those suffering from severe flare-up of symptoms after exercise such as post-exertional malaise and post-exertional symptom exacerbation. For the first couple of years into the pandemic there was little research-based evidence to direct programmes. One aim for exercise-based support in the form of an individually tailored rehabilitation programme is to partially reverse the deconditioning (loss of fitness) caused by prolonged periods of reduced physical activity from either severe symptoms and/or a hospital admission. Rehabilitation can provide individual support in managing symptoms and improve the loss of physical function [Singh S 2023]. The timing of when to start a programme also needs to be individualised particularly for those with very severe fatigue. Rehabilitation may help despite deconditioning not being the primary origin of symptoms in Long Covid. As stated

previously, the primary underlying causes Long Covid remain major therapeutic targets which need urgent investigation.

64. Concerns have been raised by both patients and healthcare professionals about the role of exercise in people with fatigue and post-exertional symptom exacerbation. Post-exertional symptom exacerbation (PESE) is defined as worsening of symptoms following physical or mental exertion, typically 12 to 48 hours after activity and lasting days or (rarely) weeks. The 'world physiotherapy' group [operating name of the World Confederation for Physical Therapy, a registered UK charity describe post-exertional symptom exacerbation as "*disabling and often delayed exhaustion disproportionate to the effort made. It is sometimes described as a "crash". The activity that can trigger this worsening of symptoms can be something that was easily tolerated before.*" Post exertional symptom exacerbation or malaise is frequently described by people with myalgic encephalomyelitis/ chronic fatigue syndrome and forms part of the definitions. It is important to distinguish that although some people with Long Covid may develop ME/CFS the two conditions are not interchangeable. Despite PESE being a well-recognised symptom in ME/CFS, little is known about how to accurately measure it, the underlying mechanisms and how to treat it. This is a priority area that requires further research for all people living with this very debilitating symptom.

65. To ensure the NHS England Covid recovery and rehabilitation programmes were designed appropriately, people with lived experience were involved in development and adaptations of the material. Pragmatically, rehabilitation programmes have been adapted to provide a personalised approach to manage PESE including pacing advice [Parker M 2022]. A recent report highlighted a different post-exertion molecular response to exercise in people with Long Covid experiencing post-exertional malaise compared with well matched (age, sex, body mass index) healthy controls [Appelman B 2024]. The results highlight a biological abnormality in the muscle of this group which exercise highlights. A small study of highly physiologically characterised adults with Long Covid and PESE (described by the DePaul Symptom Questionnaire) compared different bouts of exercise between people with Long Covid and PESE and healthy controls [Tryfonos A 2024]. Exercise capacity was lower in patients by at least a fifth compared with controls and 62% had evidence of a myopathy (abnormal skeletal muscle). The exercise bouts were set at an individualised relative intensity (to a person's maximum performance). Patients managed the exercise bouts reporting similar fatigue scores at 48hrs after exercise to controls but higher muscle pain and more concentration difficulties. However, there were no differences seen in systemic inflammatory markers such as interleukin 6, or markers of muscle damage (creatinine kinase). The authors conclude that 'cautious exercise adoption could be recommended to prevent further muscle deconditioning and health impairment in patients with Post Covid Condition' (Long Covid). Further research is needed to understand whether the myopathy reported in these studies is specific to people who report post-exertional symptom exacerbation or Long Covid more broadly. The role of therapeutics needs urgently exploring.

66. There are concerns that if reduced physical activity is left unmanaged for years then long-term quality of life and health will be negatively affected with a potential increased risk of developing other long-term conditions. Research is urgently needed to inform these discussions around safety, efficacy, and effectiveness of personalised exercise-based rehabilitation programmes.

67. To date the evidence around rehabilitation is rapidly increasing. At the start of the pandemic, evidence was limited to uncontrolled pre-post studies but there have now been multiple small randomised controlled trials of various types of rehabilitation strategies compared with usual care and multiple systematic reviews. Populations, types of interventions, timing of interventions, and outcomes all vary and restrict definitive conclusions. One of the most recently conducted systematic reviews identified 14 studies involving respiratory training and exercise-based rehabilitation with a control comparator [Pouliopoupou D 2023]. Rehabilitation was associated with increased exercise / functional capacity compared with control comparators in a meta-analysis involving 1,244 participants with a moderate effect size. However, there was uncertainty around the probability of exercise induced adverse events due to a combination of a lack of reporting in some studies and a low number of events.

68. The largest rehabilitation randomised controlled trial to date is the 'Rehabilitation Exercise and psycholoGical support After covid-19 InfectioN (REGAIN) trial [McGregor G 2024] with 485 participants randomised to either a digital supervised intervention of physical health and mental health support or usual care. Participants discharged from hospital after Covid-19 with ongoing physical or mental health sequelae at least three months after discharge were eligible. The primary outcome was the patient reported outcomes measurement information system (PROMIS) preferences score at three months which is a measure of health-related quality of life. In a prespecified adjusted model, there was a significant improvement in the primary outcome measure at three months which was sustained at 12 months in the intervention group compared with usual care. There was no difference between groups at any timepoint in the unadjusted model. There were a similar proportion of adverse events and serious adverse events between the groups with one serious adverse event potentially related to an exercise session (syncope and vomiting 24 hours after the exercise session).

69. A randomised controlled trial (PHOSP-Rehabilitation [Daynes E 2023) of either Your Covid Recovery PHASE II or face to face Covid rehabilitation versus usual care has finished recruiting over 180 participants. The results will be available Spring 2024. The participants are post-hospital discharge so the results may not be directly applicable to the non-hospitalised group.

70. Other rehabilitation interventions such as breathing control exercises and respiratory muscle training are being evaluated. The English National Orchestra offered singing therapy early in the pandemic with some effect on breathlessness [Phillip KEJ 2022] and the Scottish Opera and Scottish Ballet have similarly supported symptom management. One of the earliest randomised controlled trials of a rehabilitative intervention to be completed evaluated inspiratory muscle training [McNarry M 2022]. Although there was no between group difference in the primary endpoint, the intervention group showed potential to improve breathlessness.

71. There are other ongoing NIHR funded studies investigating how to best support patients with Long Covid via enhanced self-management or rehabilitation. These include, but are not limited to, investigating the use of a self-management App (Living Well - https://www.ucl.ac.uk/healthcare-engineering/living-covid-recovery) [Murray E 2022] as part of the Stimulate-ICP trial [Stimulate-ICP 2021], and LISTEN (Long COVID Personalised Self-managemenT support - co-design and EvaluatioN) study.

Access to Long Covid services

Adults

72. It is now clear that Long Covid can result in a long-term condition and therefore patients need access to dedicated clinics with trained healthcare professionals, the process to referral and appointments should be timely and efficient, the services should provide good patient experience and improve health outcomes in line with the triple aims of the Health Care Act 2022. Robust data and service evaluation are needed to identify the true health inequality gap and this has been limited by the recognition of Long Covid, accuracy of coding for Long Covid across health sectors, and mapping SARS-CoV-2 incidence with expected Long Covid prevalence.

73. As highlighted in M2 section 1.9, at the start of the pandemic spring 2020 there were no dedicated centrally funded UK NHS services to follow-up people after SARS-CoV-2 either for people surviving a hospital admission or people with persisting symptoms after infection in the community (non-hospitalised). Access was therefore variable. At the start of the pandemic, hospital specialists often followed up patients relevant to their particular specialty rather than providing a multi-system approach that a dedicated Long Covid clinic can provide [Houchen-Wolloff L 2023]. Face to face appointments were limited due to the social restrictions which limited a full examination of patients with routine observations such as resting heart rate, blood pressure and peripheral oxygen saturation (oxygen level), and access to simple diagnostics was either limited or more complicated. Services were therefore provided according to clinician enthusiasm (an example of 'situated' resilience) with local managerial support (an example of 'structural' resilience) [Overton C 2023, Houchen-Wolloff 2023] until Autumn 2020 in England.

74. As previously described, dedicated Long Covid clinics were funded in England from October 2020. Clinicians running dedicated clinics became familiar with the clinical syndromes of Long Covid utilising new research as it appeared and were supported by national webinars through research studies such as PHOSP-COVID in summer/autumn 2020 supported by the British Thoracic Society [BTS 2020], Long Covid NHS England Taskforce weekly webinars from 2022, and resources on e-learning from health [eLFH 2021, eLFH 2022]. However, as Long Covid is a new condition there is no specific training for a Long Covid physician or other healthcare professionals so naturally there will be variation in approaches. There is also wide variation in the type of clinicians delivering these services including but not limited to nurses, physiotherapists, general practitioners, integrated care physicians (doctors who work across primary, community and secondary care), rehabilitation specialists, respiratory physicians, infectious diseases specialists, chronic fatigue experts. The NHS-England Long Covid Service specification was designed to provide a framework for clinics and commissioners to work towards to reduce unwanted variation (some variation is expected and wanted where services are different to fit the needs of the local population and to integrate with existing services in that area). The service specification provides suggested Long Covid clinical pathways, the post-covid service requirements including support for primary care, multi-disciplinary rehabilitation, children and young people, workforce support, data, key service outcomes, and governance.

75. There was a reasonable geographical spread of clinics across England within the first 70 set up except for the South West of England (Figure 7). Clinics were requested to provide monthly data as situational reports: 'sitreps' as discussed above and questionnaire data including individual EQ5D-5L was collected.

76. Each clinic will have had different referral pathways depending on which sector the clinic was within. Most required a clinician referral and some patients described barriers to getting referred by their GP – either not knowing about the condition or being unfamiliar with local services [Ladds E 2020]. Patient advocates were keen on a self-referral pathway, but few clinics offer this (which is typical of NHS outpatient clinics). NHS England prioritised trying to understand the health inequalities and encouraging local teams to understand or reduce their particular issues. However, the ability to do this accurately was limited by availability of data particularly when routine Covid-19 testing stopped.

- **England**
  - **London n=10**
    - University College London Hospital Trust (UCLH)
    - Homerton University Hospital Foundation Trust, Homerton University Hospital
    - Barts Health NHS Trust, Royal London Hospital and St Bartholomew's Hospital
    - Barking, Havering and Redbridge University Hospitals NHS Trust, King George Hospital
    - London North West University Healthcare NHS Trust, Northwick Park Hospital
    - Imperial College Healthcare NHS Trust, St Mary's Hospital
    - Chelsea and Westminster Hospital NHS Trust, Chelsea and Westminster Hospital
    - Kings Health Partners (Guy's and St Thomas' NHS Foundation Trust), St Thomas' site
    - King's Health Partners (King's College Health Foundation Trust), King's College Hospital
    - St George's NHS Trust, St George's Hospital
  - **South East n=15**
    - Oxford University Hospitals NHS Foundation Trust
    - Oxford Health NHS Foundation Trust
    - Royal Berkshire NHS Foundation Trust – Berkshire Long Covid Integrated Service
    - Buckinghamshire Healthcare NHS Foundation Trust
    - Virgin Care Services Limited & Frimley Health NHS Foundation Trust
    - Berkshire Healthcare NHS Foundation Trust
    - Royal Surrey County Hospital
    - East Surrey and west Sussex – First Community Health & Care
    - Community Surrey Health Surrey and Ashford and St Peter's Hospital
    - Surrey Downs Health & Care Partnership
    - East Sussex Healthcare NHS Trust
    - Sussex Community NHS Foundation Trust
    - Essex Partnership University NHS Foundation Trust

        - East Suffolk and North Essex NHS Foundation Trust
        - Milton Keynes University Hospital NHS Foundation Trust
    - **South West n=4**
        - Bath, Swindon and Wiltshire – Wiltshire Health and Care
        - Bristol, North Somerset and South Gloucestershire – Sirona care and health
        - Gloucestershire Hospitals NHS Foundation Trust
        - Gloucestershire Health and Care NHS Foundation Trust
    - **East England n=3**
        - Cambridge University Hospitals NHS Foundation Trust
        - Mid and South Essex – Provide Community Interest Company
        - Hertfordshire Community Service Health Care Trust
    - **East Midlands n=5**
        - University Hospitals Leicester NHS Trust and Provider Company Ltd arm of the Leicester, Leicestershire and Rutland Alliance
        - Norfolk Community Health and Care Trust
        - North Lincolnshire and Goole NHS Foundation Trust
        - University Hospitals Coventry and Warwickshire NHS Trust (UHCW)
        - Northamptonshire Healthcare NHS Foundation Trust, Northampton General Hospital, Kettering General Hospital
    - **West Midlands n=6**
        - Worcestershire Acute Hospitals NHS Trust
        - Shropshire Community Health Trust
        - Birmingham Community Healthcare Trust
        - Dudley Group NHS Foundation Trust
        - Walsall Healthcare NHS Trust
        - The Royal Wolverhampton NHS Trust
    - **North West n=10**
        - Liverpool University Hospitals NHS Foundation Trust
        - Manchester University NHS Foundation Trust (Manchester Royal Infirmary, Wythenshawe Hospital)
        - North Care Alliance (Salford Royal NHS Foundation Trust, Royal Oldham Hospital)
        - North Manchester General Hospital
        - Tameside & Glossop Integrated Trust
        - Stockport NHS Foundation Trust
        - Wrightington Wigan and Leigh NHS Foundation Trust
        - Bolton NHS Foundation Trust
        - Lancashire and South Cumbria NHS Foundation Trust
        - North Cumbria Integrated Care NHS Foundation Trust
    - **North East n=16**
        - The Newcastle upon Tyne Hospitals NHS Foundation Trust
        - Northumbria Healthcare NHS Foundation Trust
        - County Durham and Darlington NHS Foundation Trust
        - North Tees and Hartlepool NHS Foundation Trust
        - South Tees Hospitals NHS Foundation Trust
        - York Teaching Hospital NHS Foundation Trust
        - Harrogate and District NHS Foundation Trust

- Hull University Teaching Hospitals NHS Trust
- Sheffield Teaching Hospitals NHS Foundation Trust
- The Rotherham NHS Foundation Trust
- Barnsley Healthcare Federation
- Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust
- Bradford Teaching Hospitals NHS Foundation Trust
- Leeds Teaching Hospitals NHS Trust
- The Mid Yorkshire Hospital NHS Trust
- Calderdale and Huddersfield NHS Foundation Trust

Figure 7. List of the first 69 Long Covid clinics by geographical region, December 2020.

77. From Wales, the relative numbers attending the services in each Health Board and different survey response rates from the Health Boards suggest inequity. The reasons for this are not known. The actual services also differ between the seven Health Boards in terms of staff composition, durations and types of intervention similarly described across the UK in the PHOSP-COVID healthcare pathway mapping [Houchen-Wolloff L 2023]. Comparing outcomes between the services provided by Health Boards has not been done, but would allow better implementation of the most effective interventions. A community of practice across the local Health Boards in Wales was established in 2023 to enable shared learning, networking opportunities, and dissemination of good and promising practice. A set of national standards, outcome indicators and performance improvement measures are being developed.

78. Integrated care is essential for people with Long Covid; it should be viewed as 'everybody's business' rather than siloed [van der Feltz-Cornelis C 2023]. The approach in Wales potentially upskills primary care whereas for example in some secondary care Long Covid clinics the learning and expertise has not been transferred to primary care and patients have found hurdles in being referred. However, the complex multi-system nature of Long Covid requires specialism and trust from patients that they are seeing someone knowledgeable who can appropriately answer their questions [van der Feltz-Cornelis C 2023]. Primary care is currently overwhelmed, and some incentives might be necessary with specific indicators for example to diagnose and code Long Covid. NHS England provided an uplift in funding for primary care for 'Long Covid Enhanced service' [NHS England 2 2022] and a self-assessment had to be completed for the payment to confirm that workforce education and training on Long Covid was in place, that there was a local clinical pathway to support self-management, that the practice were aware of how to signpost for support and refer to a specialist clinic where necessary, that comprehensive data coding was in place using the specified clinical codes (SNOMED and ICD codes [Pfaff ER 2023]) to appropriately record the diagnosis in the patient's medical records), and has an equity of access plan in place. What difference these steps made in patient care are largely unknown.

79. To improve 'access' to Long Covid clinical care, the first step is to improve awareness of the general public equitably about Long Covid, to enable people to recognise their ongoing symptoms and to encourage seeking healthcare when needed. Social deprivation is known to be a key driver of health inequalities and was associated with both

risk of severe Covid-19 and Long Covid [Vandentorren S 2022, Shabnam S 2023]. Therefore, a proactive approach of public awareness for certain groups of people to improve healthcare seeking behaviour may be necessary to reduce health inequalities. Specifically, public awareness needs to incorporate accessibility and appropriate material for example, but not limited to different ethnicities, cultural appropriateness, health literacy, languages and target carers. Little is known about how Long Covid is affecting people with learning difficulties for example what health inequalities exist around accessing Long Covid care.

80. In England, going forward it is essential that the transfer of funding of Long Covid care to Integrated Care Systems leads to continued Long Covid services for as long as they are needed and capacity increased if there are future waves of Covid-19.

81. In future, Long Covid care should be standardised across the UK to provide health equity. More is already known about what a clinically and cost-effective model looks like for hospitalised populations, and over the next few months more research will be coming out from the Locomotion and Stimulate-ICP studies to help inform future NICE guidelines and inform policy.

Children and young people

82. As far as we are aware, there are no dedicated funded services for Long Covid for children and young people in Northern Ireland, Wales and Scotland. Similar to adults, services in 2020 and early 2021 in England developed organically. It was more difficult for some regions in England to set up a clinic at speed especially if they did not already have existing ME/CFS services and hence longer waits. This is in contrast with adult services where respiratory was the dominant specialty before centrally funded services [Houchen-Wolloff L 2023] due to the acute lung injury sustained requiring hospital admission for many adults at the beginning of the pandemic (described in the M2 section of this report). NHS England announced funding to set up 15 Post-COVID hubs for children and young people in June 2021 [NHS-E 3 June 2021] as part of the £100M investment in Long Covid.

83. Figure 8 lists the proposed post-covid hub sites.

- London - London hub led by the Evelina, Imperial, University College London Hospital (UCLH) and Great Ormond Street Hospital for Children (GOSH)
- South East
  - Oxford University Hospitals NHS Foundation Trust
  - Queen Alexandra Hospital, Portsmouth
  - University Hospital Southampton NHS Foundation Trust
- South West
  - Bristol Royal Hospital for Children
- East England
  - Cambridge University Hospitals NHS Foundation Trust
- East Midlands
  - University Hospitals of Leicester NHS Trust
- West Midlands

    - Birmingham Women's and Children's NHS Foundation Trust
- North East
    - The Newcastle upon Tyne Hospitals NHS Foundation Trust
    - South Tees NHS Foundation Trust
    - Hull University Teaching Hospitals NHS Trust
- North West
    - Sheffield Children's NHS Foundation Trust
    - Leeds Children's Hospital
    - Alder Hey Children's NHS Foundation Trust
    - Royal Manchester Children's Hospital

Figure 8: Sites of NHS-England Post Covid Hubs for children and young people

84. Regions with lower rates of Covid-19 and fewer patients with Long Covid are likely to have inexperienced healthcare professionals, supporting the role of a 'hub and spoke' model and the virtual MDT delivered by the post-covid CYP hubs. Similar to adults, clinic models varied in their delivery, with some predominantly using telephone assessments; although the latter can prevent fatigued children and young adults having to travel long distances, observations and clinical examination are missed, so it is important to link in with primary care to ensure these have been done.

85. There remains inequality of access to Long Covid clinics for children and young people. In the pan London service, there are disproportionately more patients from higher socioeconomic groups, in contrast to the local demographics.

86. The Long Covid hubs could be improved by enabling specialists access to the busier hubs for learning, and outreach practitioners could help. Similar to adults being able to self-present, accepting referrals from schools might reduce health inequities and improve access. Clinicians, academics and policy makers need to be mindful that school attendance is not always a marker of wellness as some children will be strongly encouraged to attend even though they are not well enough. In adults, occupation can similarly be misleading as a sign of wellness, as often work is prioritised over all other aspects of life for a variety of reasons.

Long Covid treatment and health inequalities

87. As described in the M2 section of this report, Long Covid is more common in females, middle age, pre-existing health conditions including obesity and social deprivation. It is also known that female sex, obesity, and pre-existing health conditions make someone more likely to develop severe Long Covid rather than milder disease.

88. NHS England and Wales record demographics of adults attending Long Covid clinics monthly which are publicly available [NHS England 2023]. Not all protected characteristics are recorded. The data from July 2021 – July 2022 [NHS England 2022 1] shows the demographics of the >50,000 patients who had access the clinics:

    - 62% of people assessed were women
    - 69% of people were aged 35 to 64
    - 64% of people were white
    - 7% of people were Asian or Asian British
    - 3% of people were Black
    - 3% of people were mixed or other ethnic groups
    - [assumption for this report that 20% of people had missing data for ethnicity]
    - 19% were people classified as living in areas of greatest socio-economic deprivation; that is, among the 20% of people in groups 1 and 2 on the Index of Multiple Deprivation (IMD).

89. Published data from individual clinics suggest the demographics are reasonably representative of the local populations [Heightman M 2022]. However, unpublished data from the 'Pan London CYP Long Covid Service' suggested a disproportionate number of children from higher socioeconomic groups are seen compared to the local population (unpublished data from Dr Terry Segal).

90. Another strength of having dedicated Long Covid clinics is to be able to record data on the people who access support to identify any gaps. It will be difficult to track if care becomes absorbed in generic long term condition follow-up in primary and community care without access to specialists. More detailed analysis on the Long Covid clinic data is being performed by researchers including from the Stimulate-ICP consortium.

91. The limited data on health inequalities in Long Covid care is due to a combination of limited coding by healthcare professionals which limits the use of routinely collected data from electronic healthcare records, there is no national registry or national audit data, data that is collected from the clinics is reliant on research teams performing the analysis and then there are data governance hurdles regarding data protection. All of these factors limit our current understanding of health inequalities.

92. Health inequities can result from different health-seeking behaviour. Early findings from the PHOSP-COVID study highlighted that over two-thirds of people did not feel fully recovered many months after hospital [Evans R 2021 and Evans R 2022]. We therefore recommended proactive follow-up of patients discharged from hospital after Covid-19 stratified by need to include a holistic multi-system assessment in patients who were not recovered, integration of physical and mental health, and a multi-disciplinary (for example doctors, nurses, physiotherapists, occupational therapists) team approach with access to

multiple specialities (for example respiratory, cardiology, neurology, diabetes, psychology / psychiatry). Proactive care potentially improves health equity as it does not rely on an individual seeking healthcare usually through primary care if there are ongoing problems (reactive care). There were concerns that proactive care (meaning healthcare professional initiated) could be unmanageable and costly particularly when there were vast numbers of patients hospitalised.

93. However, there are systems using artificial intelligence that can be deployed to telephone large numbers of patients using natural voice clinical consultations. These systems are currently in use within other areas of the NHS particularly after surgery to see if a patient has recovered (ufonia.com). Such a system has been piloted post-hospital discharge at University Hospitals of Leicester NHS Trust Long Covid service reducing healthcare professional time and thereby efficiently stratifying care based on whether a patient feels recovered [Ufonia 2023].

94. Healthcare workers were at higher risk of exposure to SARS-CoV-2 infection throughout the Covid-19 pandemic and early studies highlighted the risk of severe disease associated with certain ethnic backgrounds [Sze S 2020]. In response, the UK Research study into Ethnicity and COVID-19 outcomes in Healthcare workers (UK-REACH) study was supported by a MRC-UK research and innovation grant (MR/V027549/1) and the Department of Health and Social Care through the NIHR in 2020. The study cohort includes 17 891 healthcare workers across the UK with online questionnaires completed at baseline, six- and twelve-months follow-up with consent for data linkage for 25 years from consent [Bryant L 2023]. Data from 10 772 healthcare workers who had worked during the first UK lockdown in March 2020 highlighted occupational risk factors associated with increased risk of infection included attending a high number of COVID-19 positive patients, a nursing or midwifery role, reporting a lack of access to personal protective equipment, working in an ambulance or an inpatient hospital setting. People working in intensive care units were less likely to have been infected [Martin CA 2022]. The authors are careful not to infer a causal link from their cross-sectional data.

95. Many healthcare workers have therefore subsequently developed Long Covid particularly after infections in 2020 with the earlier SARS-CoV-2 strains and before vaccinations were available. However, to date there is little to suggest that healthcare workers are at further increased risk of developing Long Covid after a single infection, but the impact of repeated infections is also poorly understood. There is a systematic and meta-analyses currently being conducted to understand the risk of Long Covid in healthcare workers in more detail [Al-Oraibi A 2023].

Efficacy and cost-effectiveness of treatment provided at Long Covid clinics

Adults

96. The need for treatment and rehabilitation in Long Covid is set out in the M2 section of this report.

97. As part of an affiliated grant to PHOSP-COVID funded through the NIHR policy research programme (NIHR reference: 202708)), Dr Evans and co-authors mapped healthcare pathways across the UK using the PHOSP-COVID sites [Houchen-Wolloff 2023]. The results highlighted a wide range of healthcare pathways after a hospital admission for Covid-19 including no proactive follow-up (8/45 (18%)). The services were mapped according to level of assessment, rehabilitation, and psychology support, and the level of patient access (i.e., whether all patients could potentially access the services or whether there were restrictions such as only patients who had required a high level of respiratory support during the admission). A complex assessment required availability of complex diagnostics, a face-to-face clinic, presence of a multi-disciplinary team (e.g. nurses, doctors, physiotherapists, and other allied healthcare professionals, and different specialities available for example respiratory, neurology and cardiology. A complex rehabilitation programme would involve a holistic multi-dimensional approach and a series of contacts.

98. In summary, the results highlighted considerable variation across services of the availability of any service, and the level of patient access, assessment and interventions available. There was a mismatch at sites between complexity of the assessment and interventions available, with only 7/45 sites (16%) offering the highest level of service that all patients could potentially access.

99. Analysis using data one year after hospital discharge from over 1,000 PHOSP-COVID participants and the hospital site healthcare service mapping (patient access, complexity of assessment, rehabilitation, and psychological support) has shown that the complex assessment and rehabilitation are more clinically effective compared to no service (presented Sept 2023 at the European Respiratory Society). Our data suggest the comprehensive services have the potential to be cost-effective (unpublished data, NIHR grant final report under review) although the confidence intervals (precision) are wide. An early version of this data was presented to NHS-England Dec 2022, and was included in our PHOSP public webinar (July 2023). Further cost-effectiveness analyses for non-hospitalised Long Covid are being conducted as part of the NIHR Locomotion, Stimulate-ICP, Open Prompt and TLC studies, and the lead health economists for each trial are collaborating to enable combined analyses in future (a further collaboration which originated through the national Long Covid research working group). Our results from PHOSP-COVID are promising but there are caveats – the analysis was performed based on the level of service available for the particular hospital site and assumes that all patients recruited from that site accessed the services on offer.

100. Researchers from the NIHR Stimulate-ICP consortium are accessing the NHS England data which includes a generic health-related quality of life questionnaire (Euroqol 5 dimension 5 level questionnaire – EQ5D-5L) to evaluate the clinical and cost-

effectiveness of Long Covid clinics, but this remains in the data analysis stage currently. The NIHR Locomotion collaborative have prospectively collected patient reported outcome measures in over 2,000 patients through 10 Long Covid clinics across the UK using an App (elaros.com). Data collection is ongoing and evaluation of clinical and cost-effectiveness of different types of services is planned. Data from the Locomotion study is requested to be completed monthly to further understand the described fluctuating nature of Long Covid, but currently, there is a lack of existing peer-reviewed evidence to provide certainty on the cost-effectiveness of Long Covid clinics

101. The Welsh Government previously reviewed their Long Covid programme every six months to monitor and assess the efficacy of the new services provided. The reviews now form part of the routine planning and assurance processes. The Centre for healthcare Evaluation Device Assessment and Research (CEDAR) and the Welsh Value in Health Centre (WViHC) have supported the Local Health Boards in facilitating data collection via a survey, and by providing data analysis, reporting and summary at a national level. The data collected includes patient-reported outcome and experience measures (PROMs and PREMs). Several Local Health Boards have also commissioned Cedar to carry out additional work in the form of patient case studies, and focused reports including a social return on investment analysis. Figure 9 lists the evaluation reports for Long Covid Services in Wales.

102. The results suggest a general improvement in various measures of quality of life from point-of-referral to point-of-discharge, but variable response rates preclude some comparisons. Some of the improvement may have been independent of service but is likely to be small, for example there was either no or minimal improvement across all health domains at one year compared to five months in data from the PHOSP-COVID study (PHOSP 2022).

- A preliminary national evaluation report was released by Cedar on the 14th of January 2022

'Adferiad' (Recovery) Long COVID Service National Evaluation (First update - Eng)

This report has been used by Welsh Government in their review of the Long COVID services and it has been mentioned in their web communication (https://gov.wales/community-and-primary-care-services-are-helping-treat-people-long-covid).

- A second national evaluation report was released on the 30th of April 2022

'Adferiad' (Recovery) Long COVID Service National Evaluation (Second update - Eng)

- A third release of the national evaluation report was released on the 23rd September 2022

'Adferiad' (Recovery) Long COVID Service National Evaluation (Third update - Eng)

- A fourth release of the national evaluation report was released on the 14th March 2023

'Adferiad' (Recovery) Long COVID Service National Evaluation (Fourth update - Eng)

Figure 9. Recovery Long Covid Service National Evaluation reports (Wales).

Children and young people

103. As mentioned previously, as far as we are aware there are no funded rehabilitation services for children and young people with Long Covid in Northern Ireland, Wales and Scotland, so this section only refers to specialist Long Covid clinics for children and young people in England.

104. Prior to the establishment of the NHS England 15 paediatric post-COVID hubs in July 2021, it was clear from the referrals to paediatricians in London, early in the pandemic from June 2020, that there was a need for supporting CYP with Long Covid symptoms. Children were reporting ongoing fatigue and other symptoms, and a similar picture was evolving around the country. Long COVID kids is a charity to highlight Long Covid in children. It was established in October 2020 and registered as a charity in 2021. The Long COVID CYP Pan London group and NHS-England Long Covid Taskforce have established links with Long Covid Kids to understand the patient experience better and improve services.

105. Clinicians became aware that thorough physical assessment was needed to check for secondary organ damage and holistic assessment was also very important. In London CYP were given treatment for comorbidities and provided with tailored multidisciplinary rehabilitation with the aim of supporting their development. Those who were out of education were supported in reintegration and return to social and other activities, where possible.

106. The budgets were decided by NHS England for the post-COVID hubs in line with the number of COVID cases per geographical area. Each service has looked at their results and some have presented at national meetings. There were meetings regarding outcome measures led by NHS England and these were specified in the NHS England service specification [NHS England 2 2022]. Assurances were reported regularly, patient and referrer feedback were obtained from most hubs and the results acted on. Fortnightly 'sit rep' reports with individual data were returned to the NHSE team for each of the hubs and this included waiting times, demographics and follow up.

Current situation and future prospects for healthcare systems to improve longer-term management of Long Covid

107. The estimated prevalence of Long Covid in the UK was over 2 million people in Feb 2023 [ONS] which is similar to the most common lung and heart conditions, Chronic Obstructive Pulmonary Disease and Chronic Heart Failure, combined [Hopkinson N 2019, NICOR], and over half the prevalence of Type II Diabetes which is one of the commonest long-term conditions [NICE 2018]. Healthcare for these long-term conditions is stratified according to need from annual reviews in primary care, to nursing specialists, to specific rehabilitation programmes with a multi-disciplinary care, and to medical specialists in secondary and tertiary care. Care for people with Long Covid similarly requires dedicated, trained specialists working across the health sector in an integrated approach. Currently, there is inequity of the level of care between Long Covid long term care and other long-term conditions. Disbanding existing services will make this worse whereas there needs to be continuation of existing services and creation of services where they currently do not exist.

108. The previous sections highlight the disparity in care provided across the four nations over the last three years. Whilst some of this hesitance may have been due to the lack of an evidence base around what services are clinically and cost-effective, care should have been provided for people with Long Covid with inbuilt research to develop and amend services according to the findings. Hospital acute care for COVID-19 developed rapidly in this way and healthcare for Long Covid should have followed a similar strategy. Unfortunately, this reflects the common disparity between acute and chronic care within the NHS.

109. Despite the investment into Long Covid services and providing healthcare support in some form across the four nations, most of these services are vulnerable. It is essential that the expertise developed is retained and expanded as required in future. The transfer of centrally funded Long Covid services to the Integrated Care Systems from 1st April, 2024 requires scrutiny to ensure eligible patients with Long Covid have access to

dedicated assessment clinics and rehabilitation especially as early data supports clinical and cost-effectiveness. There have been new ways of working between healthcare professionals making use of virtual technology rapidly implemented because of the social restrictions in the first year of the pandemic. These 'MDT' meetings need to be supported and funded, and care of other long-term conditions could be improved by the learning in Long Covid particularly where individuals are living with multiple long-term conditions and healthcare can become burdensome for both the individual and the healthcare system.

110. The first Long Covid conference held June 2023 in Birmingham had excellent attendance, highlighting the need for specialists to learn together and to share the challenges and stresses of looking after a new condition, often in addition to existing busy clinical schedules. The second Long Covid conference held March 2024 was similarly well attended with excellent networking opportunities. If Long Covid clinics are disintegrated it will be much more challenging to unify shared learning at this sort of scale. There have been challenges recruiting patients with Long Covid to clinical therapeutic trials, but it is going to be much harder and potentially further slow research if people with Long Covid are not seen in dedicated research clinics as they will be much harder to identify.

111. With an estimated two million people in the UK experiencing Long Covid and with a significant proportion likely experiencing significant negative impact on daily life including occupation, caring responsibilities, and family life, it may have been prudent in England to sustain the central funding for Long Covid care for a couple more years alongside local plans being drawn up and agreed prior to moving funding to the integrated care systems.

112. In Wales, despite a drive to upskill and fund primary and community care to fund Long Covid support over the last couple of years, this funding is not recurrent. It is unclear what healthcare pathways people with Long Covid will be able to access. In Scotland the health boards do not have a central, unified approach, and similarly it is unclear what healthcare people will be able to access in Scotland or Northern Ireland going forward.

113. For the most severe, complex cases there is a need for dedicated Long Covid clinics and rehabilitation services, and it is a concern that this expertise and healthcare may not be available in future in any of the UK four nations. Having a Long Covid clinic network maintained and expanded together with embedded research will help drive the discovery of mechanisms, tests and new treatments. These can then be implemented into the services and cascaded to primary care alongside training and capacity building.

Lessons for diagnosis and treatment of the long-term consequences of a future pandemic pathogen

114. There are multiple key lessons from the COVID pandemic that could be taken forward. The NIHR infrastructure including the Biomedical Research Centres, Translational Research Collaborations, Clinical Research Facilities and Clinical Research Networks were critical in forming collaborations, setting up, and delivering research at scale and pace during the COVID pandemic. The UK was often heralded as being at the forefront of COVID research internationally [GAVI 2022]. Despite this, dedicated research funding for Long Covid ceased after February 2021 which was only one year into the UK pandemic and, despite it being critically required.

115. More pre-pandemic preparedness is needed for the longer-term sequelae of any pathogen for both research studies and clinical care. Embedding research into clinical care improves efficiency and underpins scalability. The ISARIC study was a huge success for recording observational data during acute care; it was up and running by April 2020 due to the protocols all being written and approved. Similar hibernated studies are needed to investigate the post-infectious sequelae alongside hibernated clinical care sites to deliver care alongside embedded research to learn at pace – this approach can be scaled as needed. The RECOVERY study was an outstanding example of embedding an intervention study into clinical care and was set-up at pace early in the pandemic. A combination of a broad observational study and a framework for an interventional study is essential for future acute pandemics and alongside these there is a need for similar hibernated studies for the long-term consequences of a future pandemic infection that are ready for rapid deployment. Such an approach could be developed by a task force supported by government funders NIHR/UKRI with periodic review of the protocols, hosted by a nominated sponsor organisation and the network supported by the NIHR clinical research network or future similar organisations.

116. Although multi-centre research studies such as PHOSP-COVID, Stimulate-ICP, Locomotion have all worked across the UK and recruited thousands of patients between them, it has taken significant amounts of time to set up contracting for low-risk collaborations. Having research governance with ethical approvals and contracting in place for key studies ahead of a pandemic is critical as many of the same people were delivering acute care, setting up new studies and dealing with governance issues simultaneously in the early months of the pandemic.

117. Whilst it is challenging to predict the exact pathogen, acute illness, severity and incidence of post-infectious sequelae, there is a broad principle of holistic and a multi-system approach spanning physical and mental health that could be used. The numerous protocols for UK Long Covid studies could be used to provide a skeleton protocol to be adapted ahead of the next pandemic. A panel of experts in post-viral syndromes, post-infectious sequelae, post intensive care syndrome, and multiple long-term conditions, children and adult specialities, together with patients could ensure optimal use of prior expertise rather than trying to gain this during an acute pandemic. Core outcome sets need to be agreed to enable easy sharing and combining of data.

118. Similarly, core service specifications could be drafted to be modified for a specific condition or pathogen; these do not need to be started from scratch. Healthcare systems

need to be prepared, agile, flexible, expandable, and resilient. Where exactly technology and artificial intelligence can be used to support healthcare needs to be pre-planned and to learn from innovative solutions used for the Covid-19 pandemic.

119. Whilst certain governance rules were lifted to aid science during the Covid-19 pandemic, challenges with data linkage with either electronic health records and NHS digital or between studies have hampered collaboration and enhanced learning. Whilst data governance needs to protect individuals' data, staffing needs to be adequate to manage the needs of pandemic research. The same is true for the staffing of other research infrastructure such as the MHRA. For example, the "PHOSP-I" clinical trial governance application (https://doi.org/10.1186/ISRCTN46454974) was submitted Nov 2022, and received ethical and HRA approval Dec 2022, the first response from MHRA was received July 2023, and final approval provided Dec 2023, 13 months after first submission. This study is one of few internationally investigator led randomised controlled trial testing a therapeutic agent (Tocilizumab) in Long Covid and the delays are another setback for patients.

120. It might be that a future pandemic presents in a very similar way and that retaining the knowledge of the last pandemic and building on lessons learned are sufficient. The bigger problem is that the next pandemic might behave very differently and this will then require integrated research and data systems to be able to learn and adapt quickly from any new threat. Future pandemic pathogens could have a range of characteristics, and in some, the long-term consequences of infection could be the primary driver of mortality, morbidity, and broader societal impacts. High-quality longitudinal research, with experimental medicine clinical trials, will therefore be essential to inform policy-makers about the threat and guide timely and effective responses.

Recommendations regarding prevention and treatment of Long Covid

121. Long Covid was foreseeable as a consequence of the acute Covid pandemic and remains a major health problem. More focus on long-term consequences as part of pandemic preparedness is important and greater attention to the cause, diagnostics, and treatment of Long Covid is critical.

122. There remains to be an urgent need for dedicated national research funding for Long Covid particularly for further clinical trials testing both pharmacological and non-pharmacological therapies for children, young people and adults living with Long Covid. We now know there are different types of Long Covid with different underlying mechanisms (see M2 section of this report). Clinical trials need to be targeted to the relevant type of Long Covid – a personalised medicine approach know to work in other long-term conditions (see M2 section).

123. Keys issues to consider alongside those highlighted in our M2 report include:

Preventing Long Covid

124. The cessation of national COVID-19 testing, and minimal recommendations around individual testing, both deprioritise the importance of reducing spread of infection to reduce the serious long-term consequences of COVID-19. Other measures of minimising the spread of infection such as mandatory mask wearing have ceased even in healthcare settings and prioritising clean air in public spaces such as hospitals and schools has largely been left to local decisions. The UK public are not fully aware of the need to prevent Long Covid including the role for vaccination alongside its utility in preventing severe acute illness.

125. Long Covid needs to be re-considered as an indication for prioritising vaccination. Whilst definitive evidence is still lacking, it is a reasonable rationale that an individual who has developed Long Covid is at further risk of Long Covid with future SARS-CoV-2 infections. The evidence to date suggests that being vaccinated prior to developing SARS-CoV-2 infection reduces the rate of Long Covid and so far, there is no signal of harm in those with Long Covid who are subsequently vaccinated (see M2 section of this report). This is therefore a rationale to prioritising booster vaccinations for people at high risk of getting severe COVID-19 and/or Long Covid.

Assessing and treating Long Covid

126. Earlier development of a dedicated Long Covid clinical service with a clear ambition to embed research into the clinical care might have led to earlier recognition of Long Covid by healthcare professionals (rather than those with lived experience being the first to highlight it and have minimal healthcare support). The reality was clinical care followed the research. Similarly, treatment trials should have been funded at scale to embed into clinical care with early adoption of findings. The existing treatment trials needed to be fast-tracked through the regulatory processes akin to the acute trials such as the Recovery study. This has led to an unjustifiable delay in results and hence delays to improvements in patient care.

127. All four nations took a different approach to provide Long Covid care and externally appeared to be uncoordinated across the nations. At the start of the pandemic which approach was either clinically or cost-effective was unknown. If research had been embedded in clinical care across the nations a natural experiment of these conditions could have been set up from the start; delayed dedicated funding for Long Covid clinics and rehabilitation so reactive follow-up only (Scotland / Northern Ireland), primary care / community care led care (Wales), and dedicated specialist Long Covid services (England). For clarity, proactive follow-up can be achieved post-hospital by contacting all patients discharged to enquire if they have fully recovered or not. There was potential to learn more quickly what services for Long Covid are effective and therefore what should be provided at scale.

128. Dedicated Long Covid services involving assessment and rehabilitation enabled development of healthcare expertise in a new multi-system condition.

129. The disruption of Long Covid on ability to work highlighted the need for upskilling healthcare professionals around occupational advice, better communication with occupational health teams (public and private), and the need for vocational rehabilitation. Vocational rehabilitation incorporates a series of services that are designed to facilitate return to work by people with a variety of different disabilities including health issues. As discussed, healthcare professionals are at high risk of Long Covid due to their high exposure to infections particularly in 2020. The British Medical Association Long Covid report highlights the need for better support for people living with Long Covid to return to work safely including a flexible approach to the use of work place adjustments (BMA 2023). Phased returns in the NHS tend to be fixed whereas people with Long Covid require these to be individually tailored to increase the likelihood of success. Anecdotally, flexible, individualised, prolonged phased returns appear better managed in the private sector.

130. Emerging evidence suggests that Long Covid services are clinically and cost-effective where they are stratified by patient need, include a holistic assessment, a multi-system approach, involve the multi-disciplinary team and have access to a range of specialty advice. Providing care in a dedicated service has enabled learning within and across teams to improve the care provided to patients and has prevented multiple speciality referrals for the wide range of clinical problems experienced by people with Long Covid. The latter approach is less burdensome for patients with predominant fatigue and also efficient for the healthcare system. Long Covid also highlights the need for clinical expertise in people with multiple long term conditions (multi-morbidity) outside of medicine for the elderly specialists ("Geriatricians").

131. Whilst Long Covid services are the gold standard according to the writers of this report, there are potential health inequities where they do not exist and or patients are unable to access them. Further work is needed to understand the health inequalities in order to reduce them.

132. Dedicated funding in England is ceasing to be centrally administered from April 2024 and the Integrated Care Systems (ICS) will be tasked to deliver these. There needs to be careful monitoring to ensure Long Covid clinics are not stopped and all the learning of the last three and half years lost. The ICS provide the ability to commission services according

to local need and enable further integration across primary, community and secondary care, which in principle could improve the Long Covid pathway.

133. The approach across the four nations needs to be unified to ensure access to Long Covid care is not pre-determined by where someone lives.

Future pandemics

134. Currently there appears minimal focus on pandemic preparedness for long-term consequences. This needs to be optimised to reduce current and future individual burden of illness, improve health outcomes and healthcare experience, and improve both health economy and equity in line with the triple aims of the Health and Care Act 2022. As part of this, there needs to be prepared healthcare services for the next pandemic that are agile, flexible, expandable, and resilient.

135. Whilst the next pandemic may not be a respiratory virus similar to COVID-19, with unknown long-term consequences at an unknown incidence, having hibernated healthcare pathways that use a holistic and multi-system approach utilising multi-specialty team meetings would quickly be able to flex when the sequelae became apparent through integrated hibernated research and data systems. This could include pre-agreed lead sites with hub and spoke models across regions. How to embed the research studies into these clinical care models needs to be pre-established.

The authors' role in advising the healthcare systems across the UK on their response to the Covid-19 pandemic.

136. As members of the NHS England Taskforce for Long Covid since inception, Professor Christopher Brightling and Dr Rachael Evans have provided input to the NHS England service specifications (NHS England 2021, NHS England 2022) particularly highlighting research findings. The Long Covid Taskforce was originally subdivided into a research subgroup, clinical subgroup, and rehabilitation subgroup. The latter two were combined in 2022 and all the subgroups ceased in 2023. Professor Christopher Brightling and Dr Rachael Evans are also part of the National Long Covid research group chaired by Professor Kamlesh Kunti where minutes of the meetings have previously been available for NHS England.

137. Data from the first 1,000 participants of the Post-Hospital COVID-19 (PHOSP-COVID study described in the M2 section of this report) were published initially in preprint Dec 2020 [Evans R 2020] prior to peer-reviewed publication [Evans R 2021] and Dr Rachael Evans presented separately to the DHSC, NHS England Long Covid taskforce, and to the Lord Bethell Roundtable, and together with other information from national and international studies were referenced in the NICE guidance for Long Covid [NICE 2021]. The PHOSP-COVID study is the largest of its kind internationally and includes in-person research data at two time points after hospital admission for COVID-19, the first between five to six months and the second at one year [Elneima O 2023]. The report of the first 1,000 PHOSP-COVID participants were the first to highlight the extent of non-recovery, with less than 1 in 3 participants feeling fully recovered a few months after discharge from hospital [Evans R 2021]. Participants were experiencing a wide range (>50) of ongoing symptoms with an average of nine different symptoms in an individual, multi-organ effects, and a negative impact on physical function, mental health and cognitive impairment. Alongside the health impacts there were negative social impacts, reflected in occupation change after COVID-19, with 18% of those who were working before hospitalisation no longer working, and 19% had a change in work status due to COVID-19 [Evans R 2021].

138. Unpublished data described in paragraph 99 highlights that a more complex/comprehensive approach to healthcare for Long Covid appeared clinically effective and likely cost-effective. These results were presented to the Long Covid programme managers and team at NHS England by Dr Rachael Evans and the principle investigatory Professor Andrew Briggs (Professor of Health Economics, London School of Hygiene and Tropical Medicine) at a designated ad hoc meeting November 2022 to help service planning. The results were subsequently presented at an NHS England Long Covid webinar for Long Covid clinical teams 15th May 2023.

139. Alongside patients, clinicians and academics, Dr Rachael Evans presented at the Westminster Health Forum policy conference for 'Priorities for Long Covid services, care and research' 31st January 2023 in the research section 'Taking forward clinical research and understanding of Long Covid - priorities for improving patient outcomes, advancing clinical trials, prediction and prevention, investment, utilising data, and areas for focus such as cardiology'.

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