LOng COvid Multidisciplinary consortium Optimising Treatments and servIces acrOss the NHS (LOCOMOTION)

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LOng COvid Multidisciplinary consortium Optimising Treatments and servIces acrOss the NHS (LOCOMOTION): protocol for a mixed-methods study in the UK

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ABSTRACT

Introduction Long COVID, a new condition whose origins and natural history are not yet fully established, currently affects 1.5 million people in the UK. Most do not have access to specialist long COVID services. We seek to optimise long COVID care both within and outside specialist clinics, including improving access, reducing inequalities, helping self-management and providing guidance and decision support for primary care. We aim to establish a 'gold standard' of care by systematically analysing current practices, iteratively improving pathways and systems of care.

Methods and analysis This mixed-methods, multisite study is informed by the principles of applied health services research, quality improvement, co-design, outcome measurement and learning health systems. It was developed in close partnership with patients (whose stated priorities are prompt clinical assessment; evidence-based advice and treatment and help with returning to work and other roles) and with front-line clinicians. Workstreams and tasks to optimise assessment, treatment and monitoring are based in three contrasting settings: workstream 1 (qualitative research, up to 100 participants), specialist management in 10 long COVID clinics across the UK, via a quality improvement collaborative, experience-based co-design and targeted efforts to reduce inequalities of access, return to work and peer support; workstream 2 (quantitative research, up to 5000 participants), patient self-management at home, technology-supported monitoring and validation of condition-specific outcome measures and workstream 3 (quantitative research, up to 5000 participants), generalist management in primary care, harnessing electronic record data to study population phenotypes and develop evidence-based decision support, referral pathways and analysis of costs. Study governance includes an active patient advisory group.

Ethics and dissemination LOng COvid Multidisciplinary consortium Optimising Treatments and servIces acrOss the NHS study is sponsored by the University of Leeds and approved by Yorkshire & The Humber—Bradford Leeds Research Ethics Committee (ref: 21/YH/0276). Participants will provide informed consent. Dissemination plans include academic and lay publications, and partnerships with national and regional policymakers.

Trial registration number NCT05057260, ISRCTN15022307.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Mixed-methods, real-world study co-designed with patients and frontline staff.
⇒ Largest cohort of non-hospitalised patients with long COVID followed up longitudinally.
⇒ Aims to identify condition phenotypes and traits, individual-level and group-level symptom to activity relationships, stratify and evaluate treatments, understand barriers to health equality and return to work and validate condition-specific patient-reported outcome measures.
⇒ Not designed to test specific hypotheses about efficacy of interventions or quantify the comparative effects of treatments.

INTRODUCTION

What is long COVID?

We use the patient-made term 'long COVID'[1] to embrace the official categories of 'ongoing symptomatic COVID-19' (symptoms between 4 and 12 weeks) and 'post-COVID-19 syndrome' (symptoms beyond 12 weeks) in any patient, irrespective of whether they were hospitalised or had a positive or negative SARS-CoV-2 test.[2] Long COVID's varied symptoms include fatigue, breathlessness, palpitations, dizziness, pain, neurocognitive

dysfunction ('brain fog'), sleep problems, exercise intolerance, functional disability in daily activities and reduced quality of life.[3–9]

Long COVID may be more common in people who had more severe acute illness or those with pre-existing conditions.[10 11] Dysregulated immune response, immunothrombosis, endothelial dysfunction, multiple organ damage and dysautonomia all appear to play a role in its aetiology.[10 12 13] Structural inequalities are important in the development and course of COVID and may play a role in long COVID.[5 14–20]

People with lived experience of long COVID have a strong track record of contributing to the knowledge base on their condition. Long COVID was initially characterised by patients who came together in online communities after healthcare professionals (who thought of COVID as a short-lived acute illness) had disbelieved or dismissed their stories.[1 21] Many of those affected were health professionals themselves.[22] Published patient-led research on long COVID includes large-scale symptom surveys,[18 23] personal testimony and autoethnography,[24 25] co-design of services[22 26] and a manifesto for assessment and treatment.[27]

Long COVID management and services

Long COVID symptoms are characterised by symptoms and functional impairment that are multidimensional, episodic and unpredictable in nature.[28] The cornerstone of management is prompt multidisciplinary assessment and treatment with an emphasis on excluding serious complications, managing specific symptom clusters and supporting whole-person rehabilitation.[22 26 29 30] But it is unclear which patients need to be referred to specialist clinics and which tests and treatments are needed for whom.[11 31] Recording of long COVID in primary care systems appears to be low.[32]

As of March 2022, 1.5 million people in the UK reported symptoms of long COVID.[33] In 2021, NHS England invested £24 million to set up over 80 multidisciplinary long COVID clinics in England.[34] Waiting lists for these specialist clinics are long and there are no equivalent services in Scotland, Wales or Northern Ireland. Specialist long COVID clinics vary in medical staffing levels, referral pathways, investigations and treatments. Demand exceeds supply, and the current demographics of clinic populations raise questions about inequalities of access in minority ethnic and other disadvantaged groups.

While many patients with long COVID could probably benefit from self-management resources (eg, 'Your COVID recovery' website),[35] these are not currently well signposted or universally accessible, nor is there adequate guidance on how to support self-monitoring patients or when they may need escalation of care.

A new service specification expects primary care services to take on substantial elements of long COVID management.[36] General practitioners—who claim chronic underfunding, understaffing and task-shifting from secondary care—feel unable to cope with a new condition affecting large numbers of patients, especially in the absence of clear guidance and referral pathways.[19 37]

Given the numbers of people affected, the high levels of unmet need and burden of long-term disability, the disproportionate effect on disadvantaged people, the implications for the economy of long-term sickness absence and the limited capacity in primary care, long COVID is an impending 'system crisis'.[38] There is an urgent need for applied research to optimise services and care pathways in a way that takes account of resource constraints and recognises the potential of patients themselves and generalist services to contribute to care, given appropriate support and resources.

METHODS AND ANALYSIS

Research aim

To optimise all aspects of long COVID care in the UK, including access to services, care pathways and practices and equity.

Strategic objectives

Working in partnership with those who have lived experience of long COVID:

1. Establish a multisite learning network of long COVID clinics and services across the UK to capture and disseminate evidence-based practice.
2. Iteratively improve practices and protocols in long COVID clinics using a quality improvement collaborative and experience-based co-design to define best practice that ensures equitable access and care pathways.
3. Study self-management and symptom fluctuation in patients at home using a validated patient-reported outcome measure.
4. Use general practice electronic records to study population phenotypes and thereby develop evidence-based clinical templates, decision support, referral pathways and prioritisation criteria.
5. Evaluate the cost-effectiveness of different pathways.

Research questions

Our research questions are shown in box 1.

Study design

This mixed-method, multisite study is co-designed with patients with long COVID (whose stated priorities are prompt clinical assessment; evidence-based advice and treatment and help with returning to work and other roles[1 22]) and frontline clinicians.

The study has three workstreams, each designed to optimise assessment, treatment and monitoring in a different setting (figure 1). Workstream 1 addresses

Box 1 Research questions

1. For specialist long COVID clinics:
   - How can we use the quality improvement cycle to optimise the multidisciplinary assessment and care of people with long COVID?
   - How can we draw on patients' lived experience of services and the experience of frontline staff to inform this quality improvement?
   - How can we improve access and reduce inequalities for disadvantaged and underserved groups?
   - How can we best integrate clinical rehabilitation with vocational rehabilitation in the workplace?
   - How can we optimise peer support for patients with long COVID?
2. For patients at home:
   - How can we monitor fluctuations and triggers in long COVID and use these data to aid self-management?
   - How can we use patient-reported outcome measures to estimate condition severity, functional impact and quality of life in long COVID?
3. For integrated long COVID services across primary, secondary and community care:
   - What referral and triage criteria are appropriate for referring patients to specialist services?
   - What clinic investigations are appropriate for patients with specific symptoms or symptom clusters (eg, chest pain, resting or exertional hypoxaemia, dysautonomia, symptoms suggestive of mast cell disorder, cognitive difficulties)?
   - What is the effectiveness of specific interventions for patients with these and other relevant symptoms and symptom clusters?
   - What are the appropriate skill mix and staffing levels for long COVID services of different types?
   - What is the cost-effectiveness and healthcare utilisation of different care models?

specialist management in 10 long COVID clinics. Workstream 2 addresses patient monitoring at home using a validated outcome measure (box 1). Workstream 3 addresses generalist management in primary care and pathways (including cost-effectiveness) across the primary/secondary care interface. A cross-cutting theme of patient and public involvement informs and supports all workstreams.

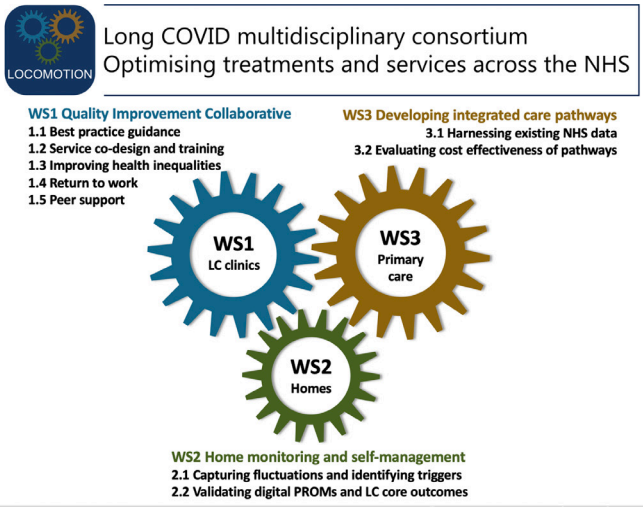

Figure 1 LOng COvid Multidisciplinary consortium Optimising Treatments and servIces acrOss the NHS (LOCOMOTION) project workstreams (WS) and tasks. LC, long COVID; NHS, National Health Service.

Workstream 1: long COVID specialist clinics

Multisite quality improvement collaborative

Quality improvement collaboratives are networks of healthcare organisations that engage collectively in a cycle of data gathering, goal setting, action and evaluation, meeting regularly to compare findings and share resources.[39] Although this model has had mixed success,[40] if core principles are followed (eg, good facilitation, clear goal setting, ensuring representatives from each organisation have clear channels for feeding their learning into a coordinated and strategic change effort),[39 41] results can be dramatic.[41 42]

We will establish a quality improvement collaborative across 10 geographically and organisationally diverse long COVID services, with participation from site principal investigators, embedded clinician-researchers and patient partners. The collaborative will be chaired by an experienced clinician-researcher (TG) and will meet approximately monthly in a 2-hour video conference. Participants will share experience-based knowledge and research evidence, deliberate on best practice and plan and evaluate practice change. The quality improvement cycle—prioritise a topic, set goals, identify data sources, implement change, collect data on performance and outcomes, then repeat—will be followed for both clinical (eg, investigations, treatments) and more operational (eg, referral criteria, service model, workforce) aspects of long COVID management.

Experience-based co-design

Experience-based (co-)design is an established improvement approach intended to ensure that health services are designed, redesigned and improved around the needs and experiences of patients and frontline staff.[43] Key features include a grounding in the perceptions and reactions of individual patients and staff, a focus on 'emotional touch-points' (points in the patient pathway that generate strong emotions such as frustration, anger, fear or hopelessness). Experience-based co-design has a solid theoretical grounding in phenomenology (which, in this context, approximates to lived experience).[44] This approach has been extensively applied in health service research and quality improvement.[45 46]

As a first step in the experience-based co-design method, a maximum-variety sample of approximately 15 adult patients and staff from each site will be interviewed about their experience of services using semi-structured or narrative interviews. Patient interviews will focus on emotional touch-points as these are likely to identify aspects of the service that need improvement.[47] Staff interviews will capture ideas for service improvement.

Interviews will be analysed thematically and fed back into local quality improvement.

Addressing inequalities

A qualitative substudy will seek to understand and address the multiple intersecting inequalities in long COVID service utilisation.[12] Working with and through participating NHS organisations, as well as community and advocacy organisations and selected social media outlets, we will recruit a maximum-variety sample of 30 people with long COVID representing key characteristics of underserved groups who have not (yet) been seen in a long COVID clinic. Sampling criteria include: poverty, homelessness, non-white ethnic groups (including traveller communities) and those with disabilities; within all these groups, we will seek to include a gender balance and recruit diverse age groups. In addition, we will interview a diverse sample of 15 key informants (individuals with relevant expertise on long COVID and health inequalities) via clinical, academic, policy and advocacy organisations. Interviews will explore symptom recognition (both self-reported and by clinicians), health-seeking behaviour, care pathways, motivations and disincentives to accessing healthcare support and attitudes towards long COVID and stigma (eg, relating to psychological symptoms). We will also explore emotional touch-points, patient support networks and trajectories of care for those not receiving specialist long COVID healthcare.

All interviews will be transcribed, entered into a qualitative software package and thematically analysed before being synthesised and fed into the work of the quality improvement collaborative (see section 'Multisite quality improvement collaborative'), co-design (see section 'Experience-based co-design'), rehabilitation (see section 'Vocational rehabilitation'), home management (workstream 2) and trajectories of care and pathway redesign (workstream 3).

Vocational rehabilitation

People living with long COVID can find it difficult to return to work, and those who have been able to return to work are experiencing work instability (defined as a mismatch between an individual's abilities and the demands of their job).[48] We will explore the needs of 20 working-age people recruited from long COVID clinics and selected for diversity in age, gender, ethnicity, occupation and career stage to inform the development of appropriate return-to-work programmes (vocational rehabilitation pathway). To understand return-to-work policies and procedures, we will interview a purposive sample of occupational health, human resource and managerial professionals from a representative range of organisations, recruited via social media and researchers' local contacts. Based on these interviews and our experience of designing vocational rehabilitation programmes for other acute-onset, long-term conditions, we will develop an individually tailorable, co-ordinated programme of support, education and advice. This advice will be relevant for people with long COVID, their family and others involved in the person's vocational role such as employers and disability employment advisors. We will test the proposed programme for acceptability and feasibility with a further sample of 20 diverse participants, as well as clinicians and therapists.

Peer support

Long COVID was first characterised in online peer support groups and several participating sites have local peer support groups, but it is not known how best to structure and support such groups. We will undertake a hermeneutic literature review of peer support models in comparable conditions (eg, chronic pain) and conduct interviews with stakeholders involved in delivering or supporting peer support for long COVID. We will share findings with workstream 'Multisite quality improvement collaborative'. Through discussion, we will identify which features of successful peer support are relevant to long COVID and consider how to improve existing models (if present) or establish new peer support services. Using the quality improvement cycle, we will collect data to evaluate and improve as the peer support groups evolve.

Workstream 2: home monitoring and self-management by patients with long COVID

Monitoring fluctuations, symptoms and associated triggers

Long COVID is characterised by fluctuating and difficult to manage symptoms with high variability between individuals. Its relapsing and remitting presentation may be exacerbated by triggers, although patients report difficulty with pacing strategies, and little is known about what causes fluctuations or the nature of triggers. We propose disordered relationships in symptoms and activities are underpinned by possible pathologies across multiple body systems including the central nervous system and interoceptive pathways.

This substudy uses an intensive longitudinal design. Some of the key COVID-19 Yorkshire Rehabilitation Scale questions (box 2) have been embedded into a bespoke digital platform which monitors general health, symptom fluctuations and potential triggers, and is linked to wearable sensors. We hypothesise that physical, cognitive and emotional triggers will predict symptoms experienced at subsequent timepoints the same day or day after. The relationship between triggers and symptoms will vary within and between individuals and bespoke understanding is required for effective self-management.

We will recruit a diverse sample of 400 patients who are awaiting their initial long COVID appointment. We will conduct a time-series study (referral, 6 weeks, 12 weeks) comprising brief symptom surveys six times daily for a 7-day period, along with sensor and accelerometer data plus self-reported activities and emotional triggers. This daily ecological momentary assessment includes continuous data collection of the following using activity sensors (Axivity): physical activity levels (step count, intensity of physical activity, timings and duration of physical activity), sleep (timing and duration). Participants will also answer

Box 2 The COVID-19 Yorkshire Rehabilitation Scale: a validated patient-reported outcome measure for long COVID

We have previously developed the COVID-19 Yorkshire Rehabilitation Scale, the first patient-reported outcome measure for long COVID. This instrument is recommended in the National Institute for Health and Care Excellence (NICE) rapid guideline for long COVID and NHS England service guidance and adapted in the WHO self-management booklet.[2 66–68]

The scale has been digitised by a private digital health company (ELAROS). The patient completes the questionnaire on a smartphone application and the clinicians access the results on a web portal and both use the system to monitor progress, fluctuations and response to ongoing treatments for long COVID.

The original COVID-19 Yorkshire Rehabilitation Scale is a 23-item patient-reported outcome measure which grades the severity of key symptoms, functional limitations, overall health and additional symptoms on an 11-point Likert scale and also captures pre-COVID-19 scores for comparison.[50] Questions 1–10 form the symptom severity subscale (score 0–100), 11–15 the functional disability subscale (0–50), 16 is the overall health score (0–10) and 17–23 the additional symptoms subscale (0–60). The psychometric analysis in a sample of 187 patients with long COVID showed good data quality, satisfactory scaling and targeting and good reliability both overall (Cronbach's alpha 0.891) and for individual subscales.[69]

Initial testing of a previous version of the COVID-19 Yorkshire Rehabilitation Scale in 370 community patients from a single long COVID clinic (Leeds) appears to reveal three clinical severity phenotypes (mild, moderate and severe) for both individual symptom clusters and functional disability (figure 2).[12] Such condition severity phenotypes with remitting relapsing nature of the condition suggest common mechanisms driving the array of symptoms but this is yet to be fully established.

Preliminary Rasch analysis of the original version of COVID-19 Yorkshire Rehabilitation Scale revealed dysfunctional scale response categories. The instrument was modified by replacing the 11-point Likert scale with a simpler 4-point scale. This version will be made available on the digital platform for the LOng COvid Multidisciplinary consortium Optimising Treatments and servIces acrOss the NHS study so it can be used to gather individual data for clinical assessment and also present these data in pseudonymised form for aggregated analysis (eg, to derive psychometric properties of the scale).

A full version of the modified COVID-19 Yorkshire Rehabilitation Scale is available in online supplemental appendix file 1.

a series of questions throughout the day about their sleep, daily activities, symptoms and symptom impact, postexertional malaise, stress and anxiety.

We will also recruit 50 participants from one site (Oxford) who will additionally be monitored to explore the potential for using heart rate and heart rate variability in biofeedback therapy. Physiological phenotyping will include the COVID-19 Yorkshire Rehabilitation Scale plus additional measures of heart rate and heart rate variability (using a wrist or chest-worn sensor—Fitbit Sense and Polar H10).

Part-way through the main workstream 2 study, a small qualitative evaluation will be undertaken using semi-structured interviews with 20 patient and 10 clinician participants. For patients this will include reflections

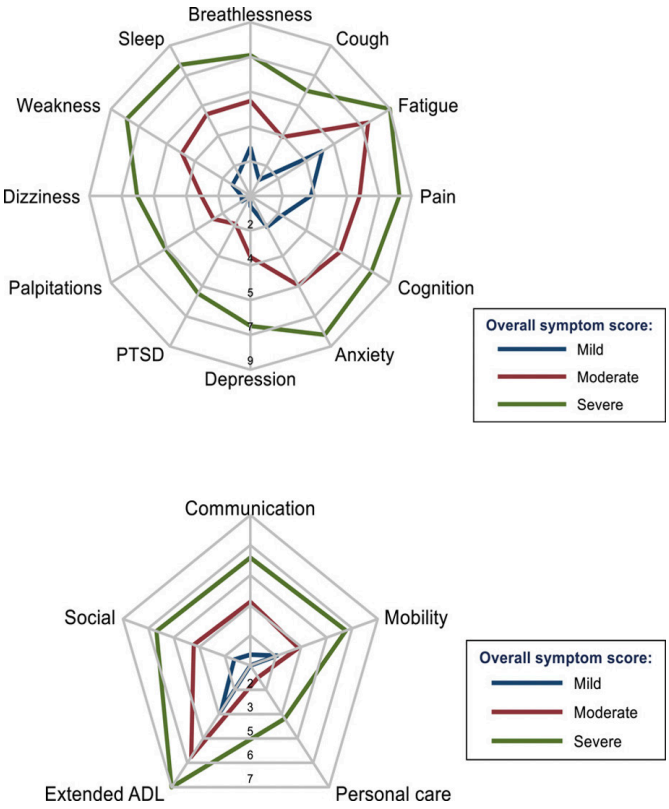

Figure 2 Aggregate scores from a clinic population on the COVID-19 Yorkshire Rehabilitation Scale patient-reported outcome measure. (A) Mean symptom severity score of 370 patients, plotted as three subgroups (severe >6, moderate 3–5.9 and mild <3). Since radar plots do not intersect, these preliminary data suggest a single syndrome rather than several different syndromes of long COVID. (B) Mean functional ability scores on same sample. Figure reproduced with permission from Sivan *et al*.[12] ADL, Activities of Daily Living; PTSD, post-traumatic stress disorder.

on their COVID-19 experience, a think-aloud exercise informed by theories of technology usability (dimensions of efficiency, effectiveness and satisfaction) and suggestions for improving the app or the study. Data will be analysed thematically using insights from sociotechnical theories.

Findings from 'Monitoring fluctuations, symptoms and associated triggers' section will feed into the quality improvement collaborative (workstream 'Multisite quality improvement collaborative') and the pathway redesign (workstream 'Pathway development').

Use the COVID-19 Yorkshire Rehabilitation Scale to monitor symptoms in clinic cohorts

Preliminary validation data from the COVID-19 Yorkshire Rehabilitation Scale, a condition-specific outcome measure for long COVID,[49] suggest that patients scoring low on one symptom tend to score low on other symptoms too (see figure 2)[12]—consistent with severity phenotypes seen in the posthospitalisation COVID-19 study,[10] and suggesting that long COVID may be driven by common mechanisms affecting multiple body systems. Workstream

'Use the COVID-19 Yorkshire Rehabilitation Scale to monitor symptoms in clinic cohorts' will test this hypothesis to determine the extent to which the COVID-19 Yorkshire Rehabilitation Scale can be used for triage, targeting interventions and capturing the response to treatments.

Longitudinal COVID-19 Yorkshire Rehabilitation Scale data on a large sample of clinic patients with long COVID will be collected quarterly from participants using the ELAROS digital app and web portal[50] or equivalent. The COVID-19 Yorkshire Rehabilitation Scale has been modified based on increasing knowledge of the condition and preliminary psychometric analysis.[51] Further psychometric evaluation of the modified COVID-19 Yorkshire Rehabilitation Scale in this new sample will use a Rasch measurement model to explore the scale item's model fit, local dependency, response category functioning and differential item functioning. If necessary, we will refine the scale through an iterative process of psychometric testing and modifications. Each Rasch scale assessment will use data from 500 to 600 patients who have completed the COVID-19 Yorkshire Rehabilitation Scale as part of their standard assessment procedures across our 10 clinics. We anticipate iterations to the scale during the project depending on findings of the Rasch scale assessment. When a stable item set is decided, the total available sample will be used to provide final scale calibrations.

The digital platform will also capture other aspects of long COVID using symptom-specific patient-reported outcome measures and quality of life measures. Data from patient-completed COVID Yorkshire Rehabilitation Scale and EuroQoL EQ-5D questionnaires will be collected from all sites uniformly and each site can capture other measures in the digital platform if they wish. The platform will also have the ability to include WHO's core set of outcome measures that is currently being developed.[52] This work will enable testing of a core set of measures that can capture this new condition comprehensively and compare with the WHO's International Classification of Functioning Disability and Health framework.[53]

Workstream 3: developing and evaluating long COVID integrated care pathways

Pathway development

We will use both retrospective and prospective cohorts to answer research questions 3a–3d in box 1. For patients newly referred to long COVID clinics, we will collect prospective data (to inform national standards for routine data collection moving forward) and link to clinical information captured in routine care. In a second cohort of patients suspected of having long COVID but not referred to long COVID clinics, routine data capture from healthcare provision will be used to understand pathways and demographic factors to increase appropriate referrals moving forward. An integrated dataset will be constructed from primary care, community care and specialist long COVID clinics to develop and evaluate effective and cost-effective service models which incorporate the quality principles and best practice guidance developed in workstream 'Multisite quality improvement collaborative'.

Box 3 Datasets that will contribute towards modelling long COVID phenotypes and cost-effectiveness of treatments

Data resource 1: iCARE/North West London Whole Systems Integrated Care is a Heath Data Research UK Alliance Trusted Research Environment and Salford—unique health management platforms covering a population of 2.6 million in NW London and the Salford Integrated Record (includes the Imperial College Healthcare NHS Trust (ICHT) and Salford long COVID clinics).

Data resource 2: The Oxford-Royal College of General Practitioners Research and Surveillance Centre[70] is one of Europe's oldest sentinel networks and recruited to be nationally representative. It now consists of a network of in excess of 1800 practices' data (n>18 million, 32% of the English national population). Data from this Research and Surveillance Centre, as well as other data from across LOCOMOTION are being made available via ORCHID (http://orchid.phc.ox.ac.uk), a Health Data Research UK listed trusted research environment and meets NHS Digital's Data Security and Protection requirements. Researchers across LOCOMOTION with an approved analysis requirement can apply to access data remotely within ORCHID. Data go through a privacy protecting statistical disclosure control process prior to leaving the ORCHID trusted research environment. ORCHID is supporting national COVID surveillance of the UK Health Security Agency and four national core studies.[54] ORCHID is a pseudonymised dataset using an NHS Digital-approved method allowing data to be linked to national test results, immunisation, emergency care, hospital and death datasets at an individual patient level.

Data resource 3: National General Practice Data for Research and Planning via the National Core Studies Portal.

LOCOMOTION, LOng COvid Multidisciplinary consortium Optimising Treatments and servIces acrOss the NHS.

We will use advanced analytical techniques (such as latent class analysis and clustering) pertinent to providing insight into long COVID phenotypes based on pseudonymised patient-level variables, including patient outcomes and comorbidities. These patient groupings will then be analysed in the context of healthcare settings, using network analysis to understand the effect of patient trajectories, enabling validation or modification of existing guidelines, leading to implementation of new clinical decision support tools in electronic record systems.

We will use approved mechanisms for data linkage via NHS Digital and work within established trusted research environments. Data linkage for practice data and patient clinic data for Imperial will take place in North West London Whole Systems Integrated Care, Salford's Integrated Record for Salford and via the Oxford-Royal College of General Practitioners Clinical Informatics Digital Hub for all other sites.[54] Brief details of these datasets are shown in box 3 and further detail given in online supplemental appendix file. All research analysis will be undertaken on de-identified data.

Pathway cost-effectiveness analysis and model testing

This workstream aims to assess the cost-effectiveness of different care pathways and develop and test efficient service models. Service models vary substantially across England.[55] Comparing these using standardised health economic outcome measures will enable an understanding of the cost-effectiveness aspects of service delivery.

Following established frameworks for model conceptualisation, we will incorporate collaborative stakeholder and public involvement,[56 57] and address known methodological challenges for public health economic modelling.[58] We will evaluate the cost-effectiveness of alternative care pathways from a societal perspective, incorporating health and social care costs incurred by the public sector as well as productivity losses and out-of-pocket expenditures. The primary analysis will assess the cost-effectiveness of alternative strategies in terms of incremental cost per quality-adjusted life year gained. We will use cost-effectiveness thresholds of £20 000–30 000 and £60 000 per quality-adjusted life year gained.[59 60] Secondary analysis will evaluate cost-consequences of alternative care pathways and disaggregate these in terms of disparate outcomes such as the proportions of individuals who return to pre-COVID levels of productivity and those who continue to experience excessive out-of-pocket expenditures.[61]

We will validate models using real-world data from existing platforms (data resources 1–3, box 3).[62] Probabilistic sensitivity analysis will assess the impact of uncertainties of all incorporated parameters.[63] We will use cost-effectiveness acceptability curves to show the probability of cost-effectiveness of each evaluated strategy at alternative cost-effectiveness thresholds held by decision-makers. Scenario analyses will assess the impacts of different model structural assumptions.

Equality, diversity and inclusion

Meeting the needs of all patients with long COVID is at the heart of the LOCOMOTION study. Specifically, workstream 1.3 is dedicated to exploring the experiences of underserved population groups. This workstream will identify key facilitators and barriers to delivering good quality healthcare to these communities and findings will feed into co-design of long COVID clinics, understanding the features of long COVID and validating patient-reported outcome measures. In addition, workstreams exploring vocational rehabilitation, home management, peer support and care pathway redesign will specifically gather and analyse data relating to populations most at risk of long COVID.

To further understand the disproportionate impact of long COVID across the population, we created a seven-member overarching patient advisory group inclusive of diverse cultural, ethnic and socioeconomic groups. This group contributes to the governance of LOCOMOTION and provides overall management of patient and public involvement, which is embedded throughout the study. Members of the group link into each workstream to ensure relevant and meaningful involvement activity within each one. The advisory group has worked with all workstreams to maximise inclusivity and reduce exclusion by design. Revisions to plans include widening accessibility to the COVID-19 Yorkshire Rehabilitation Scale and EuroQol EQ-5D patient-reported outcome measures and supporting alternative formats for interviews where digital/remote attendance may be difficult.

To support recruitment across all workstreams, we will offer translation services on an individual basis required to facilitate qualitative interviews and the consent process. This will include translation of patient information sheets, consent forms and outcome measures and use of bilingual researchers or interpreters as necessary. For participants not currently receiving specialist support for long COVID, we will also try to offer incentive payments in recognition of the barriers to engaging with research experienced by underserved groups.[64]

Patient and public involvement

For the outputs of LOCOMOTION to meet patient need, the study must be responsive to the patient voice that lies at the centre of its design, development and delivery. Members of the patient advisory group attended proposal research planning meetings and met separately to analyse and develop the research aims, objectives and questions, ensuring these align with the key research priorities of those with long COVID. All advisory group members have lived experience of long COVID. Some also have experience of design and evaluation of research bids and policy task forces. They have contacts with wider patient community groups. The advisory group meets quarterly to review progress, ensure the research continues to answer relevant issues and that findings can inform long COVID care. In addition, two patients from each of the 10 long COVID NHS clinics will form the patient advisory network, which will liaise with the advisory group, providing local intelligence about long COVID experiences and clinic access. The advisory group and advisory network are supported by an experienced Patient and Public Involvement/Engagement Manager. The patient-level and service-level measures have been determined by patients, healthcare professionals and researchers using consensus methods (tables 1 and 2).

Statistical analysis

The rationale for sample size for the tasks involving quantitative data (task 2.1, task 2.2, tasks 3.1 and 3.2) is uploaded as a separate document (see online supplemental file 2).

ETHICS AND DISSEMINATION

Ethics approval was obtained from Bradford and Leeds Research Ethics Committee on behalf of Health Research Authority and Health and Care Research Wales on 6 January 2022 (reference: 21/YH/0276). Participants will provide informed consent for workstreams 1 and 2.

Table 1 Patient-level measures to be used in LOCOMOTION sites

Name of instrument	Description	Use case
C19-YRS	Every 1-3 months. Patient-completed measures for long COVID; 4-point Likert scale assessment of 12 symptoms, with direct mapping to functional impact across the five key domains (communication, mobility, personal care, social interaction and activities of daily living).	Validated rehabilitation score, developed specifically for long COVID.
EQ-5D	Every 1-3 months. Standardised patient-completed quality of life assessment; single page questionnaire to evaluate mobility, self-care, engagement with usual activities, pain/discomfort and mental health.	Widely used for health studies; allows cross-referencing of functional ability for comparison with other conditions.
EQ-5D-VAS	Every 1-3 months. Single value indicator of general health status on a scale from 0 to 100.	Widely used for health studies; allows cross-referencing for comparison with other conditions.
Ecological Momentary Assessments	Six times/day over 7 days ('Monitoring fluctuations, symptoms and associated triggers' patient cohort only). EMA includes continuous data collection of the following using activity sensors (Axivity) and, in the substudy, heart rate using the Fitbit Sense and polar H10 Heart rate monitor: physical activity levels (step count, intensity of physical activity, timings and duration of physical activity), sleep (timing and duration). Participants also answer a series of questions throughout the day about their sleep health, daily activities, symptoms and symptom impact, postexertional malaise, stress and anxiety.	Repeated measures enable data capture of symptom fluctuation and identification of potential triggers.
System Usability Scale	10-item scale designed to assess user satisfaction with digital systems.	Widely used scale allows comparison across systems. Overall scores >70 are considered to reflect above average levels of user satisfaction.[71]

C19-YRS, COVID-19 Yorkshire Rehabilitation Scale; EMA, European Medicines Agency; LOCOMOTION, LOng COvid Multidisciplinary consortium Optimising Treatments and servIces acrOss the NHS; VAS, visual analogue scale.

Retrospective data required for workstream 3 general practice and hospital episode statistics linkage cannot be provided in anonymised form. These data will be collected under the Control of Patient Information notice initially and subsequently under authorisation from the Health Research Authority Confidentiality Advisory Group.

Dissemination will include both academic publications and lay summaries in various formats. Relevant long COVID phenotypes will be published in the Health Data Research UK National Phenotype Library, together with their computable definition, and assigned a Digital Object Identifier. Policy impact will be aided by our strong existing links to NHS England, and by the fact that several of the co-investigators are on the UK Long COVID National Task Force. MS, who co-leads LOCOMOTION, is advisor for WHO (Europe) on COVID-19 rehabilitation

Table 2 Service-level measures to be used in LOCOMOTION sites

Measure	How measured	Type of data
Evidence of patient-focused iterative change to clinic services	Ongoing data collection throughout the study from interactions with sites (principal investigators, research fellows, patients and local multidisciplinary teams) and simple summary statistics will provide evidence of changes to and evaluation of long COVID clinic services.	Qualitative and quantitative
Patient experiences of efforts to reduce inequalities	Interviews with patients and key informants will explore symptom recognition, health-seeking behaviour, care pathways, motivations/disincentives to accessing healthcare support, attitudes towards long COVID and stigma.	Qualitative
Patient experiences of tailored vocational rehabilitation as per guidelines	Qualitative data from interviews with patients, professionals involved in long COVID clinics and key informants will explore the impact of long COVID on return-to-work and job retention, including access to and from work and within work, adaptations required for work.	Qualitative
Cost per quality-adjusted life year (QALY)	Cost-effectiveness of alternative models of service delivery will be expressed in terms of incremental cost per QALY.	Quantitative
Cost-effectiveness acceptability curves	Cost-effective acceptability curves will be used to show the probability of cost-effectiveness of each of the evaluated strategies at alternative cost-effectiveness thresholds held by decision makers,	Quantitative

LOCOMOTION, LOng COvid Multidisciplinary consortium Optimising Treatments and servIces acrOss the NHS.

and is also involved in the WHO working party to develop a core set of outcome measures for long COVID.

We have links with other long COVID projects based in the UK and beyond to enable co-learning and maximise impact. In particular, our links with the Symptoms, Trajectory, Inequalities and Management: Understanding Long-COVID to Address and Transform Existing Integrate Care Pathways (STIMULATE ICP) study (https://www.stimulate-icp.org/) will enable sharing and evaluating clinic data for exploring mechanisms and developing treatment algorithms. Links with the therapies for long COVID platform[65] will facilitate development of condition-specific measures for long COVID and compare the psychometric properties of these new measures.

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Competing interests MS is advisor to WHO for long COVID policy in Europe. TG is member of the UK long COVID national task force and member of the National Institute for Health and Care Excellence (NICE) postacute COVID guideline oversight committee and Independent SAGE member. SdeL is the Director of the Oxford-RCGP RSC (primary care surveillance network); has received grants through his University from AstraZeneca, Eli Lilly, GSK, MSD, NovoNordisk, Sanofi, Seqirus and Takeda; and has sat on advisory boards for AstraZeneca, Sanofi and Seqirus. CR Member of Society of Occupational Medicine Taskforce on long COVID; member of WHO guideline development group on rehabilitation for post-COVID condition; community representative on the Access to COVID-19 Tools Accelerator (ACT-A) committee; member of long COVID support employment group (unpaid advocacy work for workers with long COVID); and has undertaken paid work for Nestle, advising on support for employees with long COVID.

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Modified COVID-19 Yorkshire Rehabilitation Screening (C19-YRS)

Self-report version

Participant Identification Number:

HEARTLOC C19YRS form number:

Date: Time:

The purpose of this questionnaire is to find out more about your current problems following COVID-19 illness. Your responses will be recorded in your clinical notes. We will use this information to monitor your symptoms, offer treatments and assess response to treatment.

This questionnaire will take around 15 minutes. If there are any topics you don't want to talk about you can choose not to respond.

Do you consent for this information to be used for audit and research as well ? **Yes** ☐ **No** ☐

SYMPTOM SEVERITY

Please answer the questions below to the best of your knowledge.
'Now' refers to how you feel now/this week (last 7 days).
"Pre-COVID" refers to how you were feeling prior to contracting the illness.
If you are unable to recall this, just state 'don't know'

Rate the severity of each problem on a scale of 0-3:
0 = None; no problem
1 = Mild problem; does not affect daily life
2 = Moderate problem; affects daily life to a certain extent
3 = Severe problem; affects all aspects of daily life; life-disturbing

		Now	**Pre-COVID**
1. Breathlessness	Breathlessness:		
	a) At rest	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	b) Changing position e.g. from lying to sitting or sitting to lying	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	c) On dressing yourself	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	d) On walking up a flight of stairs	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
2. Cough/ throat sensitivity/ voice change	Cough/ throat sensitivity	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Change of voice	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
3. Fatigue (tiredness	Fatigue levels in your usual activities	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐

not improved by rest)			
4. Smell/taste	Altered smell	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Altered taste	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
5. Pain/discomfort	Chest pain	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Joint pain	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Muscle pain	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Headache	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Abdominal pain	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
6. Cognition	Problems with concentration	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Problems with memory	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Problems with planning	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
7. Palpitations/ dizziness	Palpitations in certain positions, activity or at rest	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Dizziness in certain positions, activity or at rest	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
8. Post-exertional malaise (worsening of symptoms)	Crashing or relapse hours or days after physical, cognitive or emotional exertion	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
9. Anxiety/ mood	Feeling anxious	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Feeling depressed	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Having unwanted memories of your illness or time in hospital	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Having unpleasant dreams about your illness or time in hospital	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
	Trying to avoid thoughts or feelings about your illness or time in hospital	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
10. Sleep	Sleep problems, such as difficulty falling asleep, staying asleep or oversleeping	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐

FUNCTIONAL ABILITY

11. Communication	Difficulty with communication/word finding difficulty/understanding others	**Now**	**Pre-COVID**
		0 ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
12. Walking or moving around	Difficulties with walking or moving around	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
13. Personal care	Difficulties with personal tasks such as using the toilet or getting washed and dressed	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
14. Other activities of Daily Living	Difficulty doing wider activities, such as household work, leisure/sporting activities, paid/unpaid work, study or shopping	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐
15. Social role	Problems with socialising/interacting with friends* or caring for dependants *related to your illness and not due to social distancing/lockdown measures	**0** ☐ **1** ☐ **2** ☐ **3** ☐	**0** ☐ **1** ☐ **2** ☐ **3** ☐

OTHER SYMPTOMS

Please select any of the following symptoms you have experienced since your illness in the last 7 days.Please also select any previous problems that have worsened for you following your illness.

☐ Fever
☐ Skin rash/ discolouration of skin
☐ New allergy such as medication, food etc
☐ Hair loss
☐ Skin sensation (numbness/tingling/itching/nerve pain)
☐ Dry eyes/ redness of eyes
☐ Swelling of feet/ swelling of hands
☐ Easy bruising/ bleeding
☐ Visual changes
☐ Difficulty swallowing solids
☐ Difficulty swallowing liquids
☐ Balance problems or falls
☐ Weakness or movement problems or coordination problems in limbs
☐ Tinnitus
☐ Nausea
☐ Dry mouth/mouth ulcers
☐ Acid Reflux/heartburn
☐ Change in appetite
☐ Unintentional weight loss
☐ Unintentional weight gain
☐ Bladder frequency,urgency or incontinence
☐ Constipation, diarrhoea or bowel incontinence

☐ Change in menstrual cycles or flow
☐ Waking up at night gasping for air (also called sleep apnea)
☐ Thoughts about harming yourself

Other symptoms – free text

OVERALL HEALTH

How good or bad is your health overall in the last 7 days?

For this question, a score of 10 means the BEST health you can imagine. 0 means the WORST health you can imagine.

a) Now: WORST HEALTH 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐ BEST HEALTH
b) Pre-Covid: WORST HEALTH 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐ BEST HEALTH

EMPLOYMENT

Occupation: _____

Has your COVID-19 illness affected your work??

☐ No change
☐ On reduced working hours
☐ On sickness leave
☐ Changes made to role/ working arrangements (such as working from home or lighter duties)
☐ Had to retire/ change job
☐ Lost job

Any other comments/concerns:_____

PARTNER/FAMILY/CARER PERSPECTIVE

This is space for your partner, family or carer to add anything from their perspective:

Statistical appendix

Task 2.1:

For the main workstream we will recruit 400 participants with the anticipation of a 30% dropout, giving 300 patients (40 per site) using consecutive sampling. For the single site sub-study we will invite 50 participants, allowing for dropouts and leaving approximately 30 participants to ensure meeting central limit theorem criteria for reliability analysis and between 25-50 for meeting feasibility criteria.[1]

Task 2.2:

There are no fixed or established guidelines on the sample size required for the psychometric testing in this task. Each analysis will vary depending upon its specific purpose. A sample size of between five and six hundred is robust to obtain a confidence level of 99% for item calibrations to be stable within less than half a logit,[2] although additional parameters also need to be considered, such as targeting and item-bias testing group sizes.

Larger sample sizes (eg approximately 5000 across the ten clinics) will provide more stable calibrations, making them less susceptible to random variations within the data. Larger sample sizes also allow for a cross-validation methodology (splitting the sample and replicating the analysis), reducing the risk of incorporating random error into final conclusions.

Patients will be excluded from the analysis if they have missing data for more than 50% of the main-body YRS items to reduce large errors and fluctuations.

Tasks 3.1 and 3.2:

There is no basis for calculating a sample size at this point in time as analyses will be hypothesis-driven, iterative and exploratory, responding to WS1. With over 7 million patients across the datasets, we have sufficient data.

References

1. London NRDS. Justify sample size for a feasibility study. NIHR RDS: London 2022.

2. Linacre J. Sample size and item calibration stability. *Rasch Mes Trans* 1994;7:328.