A national evaluation of outcomes in Long COVID services using digital PROM data from the ELAROS platform

NHS England commissioned the University of Leeds team and ELAROS digital company to evaluate outcomes in a sample of Long COVID (LC) services in England using the ELAROS Digital Patient Reported Outcome Measures (DPROM) platform for recording outcome measures. The aims of the evaluation were to understand a) the extent of symptom burden and functional disability in individuals accessing care in NHS-funded LC services; and b) condition trajectories and the extent of change in the severity of the condition in individuals receiving care in these services. This report provides details on data collection methods, participants, PROM data analysis, interpretation of results, and clinical implications. The report also describes the limitations in interpreting the results and makes recommendations for future work to be undertaken by NHS England, LC services, local commissioners, and individuals with LC.

NHS England will share outputs from any additional analyses of patient outcomes, healthcare utilisation and models of care in due course as these become available.

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Summary

Key findings of this service evaluation study

- **Patient characteristics:** A sample of 5318 patients from 14 participating NHS LC sites were analysed. The sample had a female: male ratio of 2.1:1. The average age was 48.4 yrs, with 87% (of those whose ethnicity was recorded) of white ethnicity and 9% of Black or Asian ethnicity.
- **Comorbidities:** This sample of patients had a low prevalence of co-morbidities (7%) with a clear onset of new LC symptoms after their COVID-19 infection supporting the onset of a new condition in this cohort of previously healthy individuals.
- **Duration of LC:** The average duration of LC in this sample was 384 days (>12 months) at first assessment in an LC site, with symptoms still ongoing at presentation, with more than 90% of the sample being non-hospitalised patients.
- **Digital platform:** A total of 17, 471 PROMs (C19-YRS and EQ5D-5L) were completed by this sample of patients with at least 1,532 participants completing multiple assessments on the same PROM on the DPROM platform. The completion of PROMs around the 3-month mark was low for both measures (11.7% for C19-YRS and 14.6% for EQ5D-5L). The ones who completed PROMs both around the 3-month mark and the 6-month mark were 4.3% for C19-YRS and 5% for EQ5D-5L. This limits the generalisability of the findings in this evaluation to all the LC population, but the findings remain valid for this cohort of individuals.
- **New-onset disability:** 3395 patients who completed at least one C19-YRS questionnaire at first assessment showed significant new-onset symptom burden, functional disability and deterioration of overall health since the COVID-19 infection.
- **Comparison between LC and other chronic conditions:** The cross-sectional EQ5D index value of 3438 patients suggests the burden and disability in LC are worse than that reported in the literature for Diabetes Mellitus, COPD, Heart Failure, and Multiple Sclerosis.
- **3-month follow-up:** Among those who completed an initial C19-YRS assessment and another at 3 months, there was a statistically significant improvement in symptom burden, functional disability and overall health. Patients at 3 months however still had significant LC symptom burden and disability compared to their pre-COVID-19 health status, i.e., their condition had improved, but they were far off from a complete recovery. Among those who completed EQ5D-5L, at first assessment and at 3 months, their EQ5D-5L index score did not show any statistically significant improvement, but the EQ5D-5L VAS showed a statistically significant improvement.
- **6-month follow-up:** Among those who completed measures at the first assessment, 3 months, and 6 months, C19-YRS and EQ5D-5L VAS showed statistically significant improvement whereas EQ5D Index Value showed statistically significant deterioration. Patients at 6 months still had significant LC symptom burden and disability compared to their pre-COVID-19 health status, i.e., their condition had improved but had not fully recovered. The follow-up changes in scores support the efficacy of interventions provided by LC services and suggest that continued specialist input is needed to manage these patients with persistent symptoms.
- **C19-YRS (condition-specific measure) vs EQ5D-5L (generic measure):** The 3-month month follow-up changes in scores and responsiveness of PROMs highlight that C19-YRS is a more sensitive measure than EQ5D-5L in this cohort of individuals with LC. This is in keeping with the literature recommending the use of condition-specific measures in addition to EQ5D-5L.

- **Vocational problems:** 62% of this sample had their work role affected with them having to either be on sick leave, reduce hours, change roles, or quit roles. Only 21% were able to maintain their previous roles held prior to their COVID-19 infection. This is suggestive of considerable productivity loss and financial implications to the country.
- **Fluctuating condition:** In patients who completed multiple assessments, it was evident that LC is a fluctuant condition with no necessary linear trend of improvement or deterioration between the domains of symptom burden, functional disability and overall health. This highlights the need to understand the triggers for the condition and invest in self-management and ongoing support from community healthcare services.
- **Long-term condition:** In most patients in this sample, LC has evidently become a long-term condition (LTC) with fluctuations in their condition causing disability and significant deterioration of their overall health status seen even after 18 months of LC with no complete resolution or full recovery. There needs to be a national investment in managing this new LTC along with other LTCs.

Introduction

Long COVID (LC) or Post-COVID Syndrome (PCS) or Post-COVID Condition (PCC) is a clinical syndrome of persistent symptoms after a confirmed or probable COVID-19 infection. LC is a patient-derived term[1] used broadly for symptoms persisting beyond 4 weeks after the infection whereas PSC or PCC are scientific terms used by NICE and WHO respectively for symptoms persisting beyond 12 weeks.[2, 3] There are an estimated 1.9 million individuals with LC in the UK with more 1.5 million reporting problems with daily activities affected and more than 750,000 have been experiencing symptoms for more than 2 years since the COVID-19 infection.[4]

NHS England (NHSE) established more than 90 specialist LC services in England since 2021, with an investment of £90 million last year, to provide diagnosis, treatment, and rehabilitation for those with persistent LC symptoms.[5] Their recommendation for services is to provide an integrated care model involving a multidisciplinary team of professionals tailored to individual needs and capture change using validated outcome measures.

The National Institute for Health and Care Research (NIHR) and UK Research and Innovation (UKRI) have so far invested over £50 million in more than 20 LC studies.[6] The purposes of these studies include examining LC epidemiology, underlying mechanisms, testing possible treatments, and determining what people can do to optimise their own recovery. Two of the largest platform studies funded to investigate treatment pathways are LOng COvid Multidisciplinary consortium: Optimising Treatments and servIces acrOss the NHS (LOCOMOTION) and Symptoms, Trajectory, Inequalities and Management: Understanding Long covid to Address and Transform Existing Integrated Care Pathways (STIMULATE-ICP).

A Digital platform for capturing Patient Reported Outcome Measures (DPROM) for LC patients was developed by ELAROS 24/7 Digital Company and the University of Leeds, in 2021.[7] The DPROM platform hosts over 30 PROMs, including the EuroQol Five Dimensions (EQ5D-5L) health-related quality of life measure. The other key PROM of the platform is COVID-19 Yorkshire Rehabilitation Scale (C19-YRS), a LC-specific PROM, developed by the University of Leeds research team. The C19-YRS is recommended by NHSE for clinical and research use and is being further validated through the NIHR LOCOMOTION study (task 2.2).[8] The DPROM platform is currently being used to collect PROMs in 40 LC services across England. Each service decides which PROMs to use, however, EQ-5D-5L and C19-YRS are used uniformly by most of the services and the additional PROMs chosen to vary considerably between services.

There is currently a need to evaluate these NHSE-funded LC services to maximise benefits for people with LC, assist with service planning, and identify transferable learning for managing other long-term conditions. Analysis of DPROM data, particularly the EQ-5D-5L and C19-YRS used across LC services, can help meet the need to evaluate NHSE services.

Methods

In 2023, NHSE awarded funding to the University of Leeds for the 'Evaluation of long COVID services using DPROM data' service evaluation project, which started in January 2023 and ends in September 2023. The project aim was to analyse PROM data from LC services using the ELAROS platform to assess the extent of symptom burden and functional disability in individuals accessing care in NHS-funded LC services and assess changes in these measures over time to understand the extent of improvement in patients accessing LC services.

Of the 40 LC services using the ELAROS platform, 14 were included in this evaluation as their Research and Development team had approved the use of patient data through approval of the service evaluation project (and signing a Data Sharing Agreement with ELAROS and the University of

Leeds) and/or approval of the linked NIHR LOCOMOTION study. Services using the ELAROS platform aim to capture C19-YRS and EQ-5D-5L measures from patients every 3 months while they are in the service, which is facilitated through automated mobile phone notifications. However, to increase PROM data completeness for the purposes of this evaluation, some patients who had not recently completed specific PROMs were contacted directly by a researcher or the service with a specific request to complete PROMs that were due for completion.

Instruments

C19-YRSm

The COVID-19 Yorkshire Rehabilitation Scale (C19-YRS) was specifically developed to measure the symptoms, functioning and disability associated with COVID-19.[9] The C19-YRS (original) comprises 22 items each rated on an 11-point numerical rating scale from 0 (none of this symptom) to 10 (extremely severe level or impact). The instrument has four subscales (range): Symptom Severity score (0–100), Functional Disability score (0–50), Additional symptoms (0–60), and Overall Health (0–10). The scale was the first condition-specific PROM to be validated in LC and has been shown to be reliable and have appropriate psychometric properties to be used in this population.[10] C19-YRSm is a modified version of the original C19-YRS with a 4-point response category: 0, no problem to 3, severe problem.[11] As with the unmodified 'original C91-YRS' instrument there are four subscales (range): Symptom Severity (0-30), Functional Disability (0-15), Other Symptoms (0-25), and Overall Health (0-10). Although the C19-YRSm was derived from the original version of the instrument the subscales are not fully compatible and there is yet no algorithm to equate the two measures. C19-YRSm has also been validated in individuals with LC and has been shown to have good psychometric properties.[12]

EQ-5D-5L

The EuroQol EQ-5D-5L is a preference-based instrument with five domains: Mobility, Usual Activities, Selfcare, Pain / Discomfort, and Anxiety / Depression. It has five response categories ranging from 1 (no problems) to 5 (severe problems). Responses to each domain are collated into a profile score which is converted into a health utility or index score using a country-specific algorithm (tariff or value set). Utilities reflect societal preferences for health states and are measured on a metric from 0 (dead) to 1 (perfect health). Utility values less than 0, indicating states worse than dead, are also captured. The EQ-5D-5L were mapped onto the EQ-5D-3L (an alternative version of the instrument with 3 response categories advocated by the National Institute for Health and Care Excellence (NICE) using the van Hout et al. (2012) mapping (crosswalk or CW) algorithm to derive UK utility values.[13]

Data import, cleaning, and coding

The data were downloaded in three batches from the ELAROS platform (21 June 2023). The three batches corresponded to each of the PROMs: Original C19-YRS, C19-YRSm and the EQ-5D-5L. The downloaded files were stored as comma separated values (csv) files (in MS Excel). Each dataset was imported separately into R-studio (version 2022.07.2) for data cleaning and analysis.

Each patient had been allocated a unique 13-character patient identification (ID) number. The last 2 to 3 digits in this ID number represented a cumulative total of the number of completions of the PROM. This number was independent of the assessment time, e.g., successive totals may represent a PROM being completed on either successive or the same assessment day. These digits were extracted from the patient ID and stored as a variable recording the number of PROMs completed.

The assessment time was stored as a composite of date (day/month/year; dd/mm/yyyy). The date component was extracted and stored as a separate assessment date variable. A variable was derived

for cumulative time by calculating the time difference in days between successive completed assessments. This cumulative time variable ranged from 0 to N days.

The cumulative time between successive assessments was used to categorise the data into a 90-day period after the first assessment allowing for 30 days on either side of the 90-day midpoint, in other words, a time period from 60 to 120 days after the first assessment. The same principle was used to derive a 180-day period after the first assessment (± 30 days, i.e., 150 to 210 days). These two timepoints were used in the longitudinal analysis described below (*Statistics*).

The time from the occurrence of the first COVID symptoms to a) first assessment and b) registration was calculated for each patient. As the infection date was occasionally recorded to a default fixed dy setting in the platform, this meant that some values for both the time to first assessment and registration were erroneous. These times were excluded in the analysis by recoding the times as missing data.

The domains for the original C19-YRS and C19-YRSm (Symptom Severity, Functional Disability, Overall Health and Other Symptoms) and the EQ-5D-5L (Mobility, Selfcare, Usual Activities, Pain/Discomfort and Anxiety/Depression) were recoded into a numeric format (from character format). The same was also applied to the variables for: age, height, weight, admission days and ICU days. Age was restricted to the adult population, i.e., age ≥ 18 years. Mis-recorded age values (negative values or age >120 years) were removed from the analysis.

Index scores were derived for the EQ-5D-5L using the van Hout et al. crosswalk algorithm[13] to map the profile scores onto the EQ-5D-3L (for compatibility with the other NHS England EQ-5D data sources and preferred by the National Institute for Health and Care Excellence, NICE), as well as the EuroQol Valuation Technology algorithm (EQ-VT).[14] The "eq5d" library (in R) was used to derive these indices.

Multiple site/centre names were unified into a single name for each site: BSW Healthy Futures & LCAC; Bradford; Cambridgeshire & Peterborough; Hertfordshire; Imperial; Leicester; Newcastle; RDASH; Oxford; Pennine Acute; and Salford. Records from the few Welsh and Scottish centres in the datasets (Cardiff and Vale University Health Board and NHS Highland) were removed.

The English Index of Multiple Deprivation (IMD) deciles were derived from postcode data (where available) using the Ministry of Housing, Communities & Local Government online tool: https://imd-by-postcode.opendatacommunities.org/imd/2019

Pre-COVID comorbidities had been recorded in a single cell for each patient. The cell was split to create a binary coded variable (yes/no; 1/0) for each of the following comorbidities: respiratory, mental health, cardiovascular, and other, as well as none.

Body Mass Index (BMI) was calculated using the standard formula namely, weight in kilograms divided by the square of height (measured in metres). Not all values for height and weight had been recorded in, respectively metres and kilograms. Therefore BMI values exceeding the extremes for published data in the UK population were excluded from the analysis, i.e., BMI <11 or >59 (https://therapies.heartofengland.nhs.uk/wp-content/uploads/bmi_chart.pdf.)

Statistics

Continuous data (e.g., age, BMI) were summarised using means, standard deviations; 95% confidence intervals were included for the PROMs (original C19-YRS, C19-YRSm and EQ-5D-5L scores). IMD deciles were summarised using medians and range (minimum to maximum). Categorical variables (e.g., ethnicity, smoking and occupational status) were described using totals and percentages.

Changes over time were assessed for the C19-YRSm scores and the EQ-5D-5L Index and Visual Analogue Scale (VAS) for those patients who had completed the first assessment and the 90-day assessment, and additionally for those who had additionally completed an assessment at 180 days (± 30 days). The standardised response mean (SRM) – an effect size measure - was derived to evaluate the relative responsiveness (i.e., the ability of the instruments to respond to or detect change over time) of the C19-YRSm and the EQ-5D-5L Index and VAS for those patients who had completed the two PROMs on the same day. The SRM was calculated as the difference in scores (on the C19-YRSm domains (Symptom Severity, Functional Disability, Overall Health and Other Symptoms) and EQ-5D-5L index and VAS between day 90 (± 30 days) and the first assessment divided by the standard deviation of the score difference.

Regression analyses were undertaken to evaluate the predictors for the changes in Symptom Severity over time. Given the potential differences between patients at first assessment (in terms of Symptom Severity scores) and differences in how individual symptom trajectories could evolve over time, linear mixed effects models were applied with random intercepts and slopes. The *lme4* library was used for this analysis. The following variables were included as covariates in the analysis: sex (male/female), age group (categorised as: 18-39, 40 to 49, 50 to 59, and 60 years and over); ethnicity (White, Black, Asian, Mixed and Other); duration of symptoms (<6 months; 6 to 12 months; 12+ months); hospital admission (yes/no), ICU admission (yes/no), co-morbidities (respiratory, mental health, diabetes, cardiovascular, none); and centre. Interactions between covariates and time were also derived. For ease of interpretation the regression slopes over time are presented as the change in symptom scores per 90 days.

Results

A total of 5318 patients were registered on the ELAROS system (Table 1a) across 14 participating centres. The number of registered patients varied across centres from 23 (Rotherham-Doncaster) to 1128 (Leeds). The mean age of the overall patient sample was 48.4 years, and the majority were female (68%). The main recorded ethnicity was White (71%) with the second largest recorded ethinicity being Asian (6.3%); ethnicity had not been recorded for 19% of the sample (Table 1b). The mean duration of LC was 398 days (standard deviation, SD: 276.9 days). This ranged from 343.4 days (Salford) to 583.4 days (Newcastle) between the centres (Table 1c).

The sample was predominantly non-hospitalised patients with around 10% of the patients reporting a hospital admission with a mean duration of 14.5 days (SD: 29.8 days). Only 2.4% of the sample had been admitted to an intensive care unit (ICU), with a mean duration of 18.8 days (SD: 21.4) (Table 1d). The mean time between the first COVID infection and clinic registration (Table 1e) was 384 days (SD: 274 days), which ranged between centres from 331 days (SD: 277 days, Salford) to 612 days (SD: 318.3 days, Imperial).

A small proportion of patients (7%) reported pre-COVID co-morbidities. The most frequently reported pre-COVID comorbidity was mental health issues (3.1%) (Table 1f). Just under 40% of the patient sample had never smoked (Table 1g); 21% were ex-smokers. Body mass index (BMI) was only available for 668 patients (Table 1h). This low number is largely due to a combination of missing and miscoded data for either the height or weight variables or both. The mean BMI of these patients was 27.9 kg/m2 (SD: 6.8 kg/m2) and 37% (244 patients) were obese (BMI ≥ 30 kg/m2).

Postcodes, required to derive IMD decline, were only available for 790 patients (15%) enabling the index of multiple deprivation (IMD) to be derived (Table 1i). The median IMD decile was 6 (range: 1 to 10). This ranged across centres from a median of 3 (Imperial, Newcastle, Salford) to 8 (Hertfordshire, Oxford).

Table 1a. Basic Demographics by Centre

Variable	Overall N = 5,318	BSW N = 804	B&S N = 63	Brad N = 631	C&P N = 718	Essex N = 479	Herts N = 78	Imp N = 61	Leeds N = 1,128	Leics N = 196	Newc N = 73	RDASH N = 23	Oxf N = 104	PA N = 501	Sal N = 459
Female	**3,614 (68%)**	562 (70%)	40 (63%)	431 (68%)	512 (71%)	310 (65%)	48 (62%)	41 (67%)	760 (67%)	126 (64%)	51 (70%)	16 (70%)	76 (73%)	321 (64%)	320 (70%)
Male	**1,704 (32%)**	242 (30%)	23 (37%)	200 (32%)	206 (29%)	169 (35%)	30 (38%)	20 (33%)	368 (33%)	70 (36%)	22 (30%)	7 (30%)	28 (27%)	180 (36%)	139 (30%)
Mean age (SD)	**48.4 (27.1)**	48.9 (15.1)	46.6 (11.7)	49.7 (13.5)	50.4 (63.8)	45.4 (18.6)	50.5 (12.1)	45.5 (12.4)	46.8 (13.7)	48.6 (16.0)	46.8 (12.6)	54.1 (16.7)	45.5 (13.5)	49.7 (14.5)	48.8 (13.6)
Missing values	**1**	0	0	0	0	0	0	0	0	0	0	0	0	1	0

Key (all tables): SD, standard deviation; BSW, BSW Healthy Futures & LCAC; Birm, Birmingham; Brad, Bradford; C&P, Cambridgeshire & Peterborough; Herts, Hertfordshire; Imp, Imperial; Leics, Leicester; Newc, Newcastle; RDASH; Oxf, Oxford; PA, Pennine Acute; Sal, Salford.

Table 1b. Ethnicity by Centre

Ethnicity (N,%)	Overall N = 5,318	BSW N = 804	B&S N = 63	Brad N = 631	C&P N = 718	Essex N = 479	Herts N = 78	Imp N = 61	Leeds N = 1,128	Leics N = 196	Newc N = 73	RDASH N = 23	Oxf N = 104	PA N = 501	Sal N = 459
Asian	**333 (6.3)**	16 (2.0)	10 (16)	130 (21)	18 (2.5)	12 (2.5)	1 (1.3)	10 (16)	69 (6.1)	18 (9.2)	1 (1.4)	0 (0)	1 (1.0)	33 (6.6)	14 (3.1)
Black	**70 (1.3)**	3 (0.4)	4 (6.3)	4 (0.6)	6 (0.8)	10 (2.1)	0 (0)	2 (3.3)	33 (2.9)	1 (0.5)	1 (1.4)	0 (0)	0 (0)	3 (0.6)	3 (0.7)
Mixed	**99 (1.9)**	10 (1.2)	3 (4.8)	16 (2.5)	12 (1.7)	7 (1.5)	3 (3.8)	3 (4.9)	24 (2.1)	2 (1.0)	2 (2.7)	1 (4.3)	5 (4.8)	2 (0.4)	9 (2.0)
White	**3,759 (71)**	573 (71)	46 (73)	352 (56)	535 (75)	367 (77)	71 (91)	35 (57)	802 (71)	151 (77)	67 (92)	22 (96)	80 (77)	346 (69)	312 (68)
Other	**36 (0.7)**	1 (0.1)	0 (0)	3 (0.5)	6 (0.8)	1 (0.2)	1 (1.3)	3 (4.9)	12 (1.1)	3 (1.5)	1 (1.4)	0 (0)	0 (0)	4 (0.8)	1 (0.2)
Not recorded	**1,021 (19)**	201 (25)	0 (0)	126 (20)	141 (20)	82 (17)	2 (2.6)	8 (13)	188 (17)	21 (11)	1 (1.4)	0 (0)	18 (17)	113 (23)	120 (26)

Table 1c. Long COVID Symptom Duration by Centre

Variable	Overall N = 3,307	BSW N = 428	B&S N = 38	Brad N = 385	C&P N = 497	Essex, N = 327	Herts N = 55	Imp N = 33	Leeds N = 699	Leics N = 137	Newc N = 46	RDASH N = 14	Oxf N = 55	PA N = 302	Sal N = 291
Mean LC duration in days (SD)	**398 (277)**	382 (272)	436 (246)	460 (274)	347 (282)	423 (274)	554 (325)	626 (320)	397 (247)	413 (264)	583 (245)	525 (378)	393 (309)	355 (281)	343 (280)

Table 1d. Hospital and ICU Admissions by Centre

Variable	Overall N = 5,318	BSW N = 804	B&S N = 63	Brad N = 631	C&P N = 718	Essex N = 479	Herts N = 78	Imp N = 61	Leeds N = 1,128	Leics N = 196	Newc N = 73	RDASH N = 23	Oxf N = 104	PA N = 501	Sal N = 459
Hospital Admission (%)	**517 (9.7%)**	51 (6.3%)	5 (7.9%)	91 (14%)	55 (7.7%)	55 (11%)	8 (10%)	7 (11%)	123 (11%)	18 (9.2%)	14 (19%)	1 (4.3%)	6 (5.8%)	45 (9.0%)	38 (8.3%)
Mean admission days (SD)	**14.5 (29.8)**	19.3 (53.4)	2.2 (1.7)	17.7 (32.9)	7.3 (10.4)	17.9 (31.8)	9.3 (16.7)	6.6 (12.6)	12.5 (19.9)	9.3 (9.8)	15.0 (13.3)	1.0 (NA)	1.7 (1.7)	13.4 (21.1)	22.7 (43.8)
ICU Admission (%)	**128 (2.4%)**	13 (1.6%)	1 (1.6%)	27 (4.3%)	14 (1.9%)	15 (3.1%)	2 (2.6%)	1 (1.6%)	24 (2.1%)	3 (1.5%)	6 (8.2%)	0 (0)	0 (0%)	9 (1.8%)	13 (2.8%)
Mean ICU days (SD)	**18.8 (21.4)**	18.0 (20.3)	1.0 (NA)	17.8 (25.0)	8.9 (7.9)	28.7 (29.6)	24.5 (27.6)	19.0 (NA)	18.5 (14.8)	8.0 (11.3)	8.7 (16.4)	NA (NA)	NA (NA)	20.0 (17.8)	28.2 (26.8)

* In tables where numbers do not sum to total N participants, this is due to incomplete or missing questionnaires/information.

Table 1e. Time between first infection and registration by centre

Variable	Overall N = 3,297	BSW N = 428	B&S N = 38	Brad N = 378	C&P N = 497	Essex N = 327	Herts N = 55	Imp N = 33	Leeds N = 696	Leics N = 137	Newc N = 46	RDASH N = 14	Oxf N = 55	PA N = 302	Sal N = 291
Mean time between first infection and clinic registration in Days (SD)	**384 (274)**	372 (271)	409 (247)	408 (272)	342 (281)	417 (274)	537 (323)	612 (318)	391 (245)	405 (260)	556 (249)	504 (381)	387 (309)	343 (279)	331 (277)

Table 1f. Comorbidities by Centre

Variable N (%)	Overall N = 5,318	BSW N = 804	B&S N = 63	Brad N = 631	C&P N = 718	Essex N = 479	Herts N = 78	Imp N = 61	Leeds N = 1,128	Leics N = 196	Newc N = 73	RDASH N = 23	Oxf N = 104	PA N = 501	Sal N = 459
Respiratory	**95** **(1.8)**	0 (0)	0 (0)	0 (0)	1 (0.1)	5 (1.0)	12 (15)	2 (3.3)	44 (3.9)	8 (4.1)	9 (12)	0 (0)	4 (3.8)	0 (0)	10 (2.2)
Mental Health	**163** **(3.1)**	0 (0)	0 (0)	0 (0)	3 (0.4)	12 (2.5)	16 (21)	6 (9.8)	80 (7.1)	11 (5.6)	16 (22)	2 (8.7)	9 (8.7)	0 (0)	8 (1.7)
Cardiovascular	**34** **(0.6)**	0 (0)	0 (0)	0 (0)	1 (0.1)	3 (0.6)	4 (5.1)	3 (4.9)	16 (1.4)	1 (0.5)	4 (5.5)	0 (0)	1 (1.0)	0 (0)	1 (0.2)
Diabetes	**33** **(0.6)**	0 (0)	0 (0)	0 (0)	0 (0)	6 (1.3)	1 (1.3)	3 (4.9)	18 (1.6)	2 (1.0)	2 (2.7)	0 (0)	0 (0)	0 (0)	1 (0.2)
Other	**170** **(3.2)**	0 (0)	4 (6.3)	0 (0)	1 (0.1)	21 (4.4)	20 (26)	14 (23)	59 (5.2)	10 (5.1)	14 (19)	3 (13)	12 (12)	0 (0)	12 (2.6)
No comorbidities	**4,972** **(93)**	804 (100)	59 (94)	631 (100)	715 (100)	448 (94)	43 (55)	41 (67)	974 (86)	174 (89)	43 (59)	19 (83)	85 (82)	501 (100)	435 (95)

Table 1g. Smoking status by Centre

Smoking status N(%)	Overall N = 5318	BSW N = 804	B&S N = 63	Brad N = 631	C&P N = 718	Essex N = 479	Herts N = 78	Imp N = 61	Leeds N= 1,128	Leics N = 196	Newc N = 73	RDASH N = 23	Oxf N = 104	PA N = 501	Sal N = 459
Occasional smoker	**142** **(2.7)**	22 (2.7)	2 (3.2)	8 (1.3)	8 (1.1)	12 (2.5)	1 (1.3)	3 (4.9)	43 (3.8)	7 (3.6)	0 (0)	1 (4.3)	4 (3.8)	15 (3.0)	16 (3.5)
Regular smoker	**150** **(2.8)**	20 (2.5)	1 (1.6)	11 (1.7)	7 (1.0)	19 (4.0)	1 (1.3)	0 (0)	43 (3.8)	4 (2.0)	2 (2.7)	2 (8.7)	1 (1.0)	19 (3.8)	20 (4.4)
Ex-smoker	**1,114** **(21)**	180 (22)	11 (17)	85 (13)	78 (11)	135 (28)	43 (55)	15 (25)	238 (21)	48 (24)	17 (23)	5 (22)	21 (20)	141 (28)	97 (21)
Never smoked	**2,084** **(39)**	350 (44)	40 (63)	152 (24)	137 (19)	241 (50)	33 (42)	28 (46)	460 (41)	94 (48)	44 (60)	7 (30)	65 (63)	233 (47)	200 (44)
Not recorded	**1,828** **(34)**	232 (29)	9 (14)	375 (59)	488 (68)	72 (15)	0 (0)	15 (25)	344 (30)	43 (22)	10 (14)	8 (35)	13 (13)	93 (19)	126 (27)

Table 1h. Body Mass Index (BMI) by centre

Variable	Overall N = 668	BSW N = 127	B&S N = 11	Brad N = 31	C&P N = 57	Essex N = 65	Herts N = 17	Imp N = 22	Leeds N = 153	Leics N = 26	Newc N = 15	RDASH N = 1	Oxf N = 30	PA N = 60	Sal N = 53
Mean BMI (kg/m2) (SD)	**27.9 (6.8)**	26.7 (6.1)	27.1 (2.9)	31.0 (7.4)	28.5 (8.5)	27.6 (6.5)	31.0 (7.7)	24.4 (4.7)	27.4 (6.7)	26.8 (5.5)	28.2 (6.5)	38.5 (NA)	26.7 (5.0)	29.6 (7.1)	30.4 (7.7)
Number of obese individuals (BMI>29) (%)	**244 (37)**	35 (28)	3 (27)	17 (55)	22 (39)	26 (40)	7 (41)	4 (18)	53 (35)	10 (38)	6 (40)	1 (100)	9 (30)	25 (42)	26 (49)

Table 1i. Index of Multiple Deprivation (IMD) – Deciles by Centre

Variable	Overall, N = 5,318	BSW N = 804	B&S N = 63	Brad N = 631	C&P N = 718	Essex N = 479	Herts N = 78	Imp N = 61	Leeds N = 1,128	Leics N = 196	Newc N = 73	RDASH N = 23	Oxf N = 104	PA N = 501	Sal N = 459
IMD Median (min, max)	**6.0 (1, 10)**	7.5 (6, 9)	4 (1,9)	-	7 (6,10)	6 (1,10)	8 (1,10)	3 (1,8)	6 (1,10)	7 (1,10)	3 (1,10)	4 (1,9)	8 (3,10)	-	3 (1,10)
Missing data	**4,528**	802	43	631	713	398	10	26	847	109	24	0	40	501	384

Key: Min, Minimum; Max, Maximum

Patient Reported Outcome Measures (PROMs)

A total of 17,471 patient-reported outcome measure (PROM) measurements had been completed: 18% (N=3150) the original version of the C19-YRS; 39% (N=6770) the modified (m) version of the C19-YRS (C19-YRSm) and 43% the EQ-5D-5L (N=7551) (Table 2a). The number of completed PROMs per centre ranged from 45 (Rotherham-Doncaster, the most recent centre to register participation) to 4594 (Leeds).

The first assessment represented 51% (N=8985) of the total number of completed PROM assessments (Table 2b). A further 20% (N=3,469) and 9.8% (N=1,707) of PROMs completed were the second and third assessments, respectively (Assessments 2 and 3). Just under 90% of PROMs completed were a patient's 5th assessment or less. Less than 4% of patients PROMs completed were a 10th or more assessment.

A further 20% (N=3469) and 9.8% (N=1707) PROMs had been completed a second and third time respectively (Assessments 2 and 3). Just under 90% of PROMs had been completed up to and including the 5th assessment time. Less than 4% of patients had completed a PROM at 10 or more assessment times.

In terms of the individual PROMs, 68% (N=2152) completed the original 19-YRS (Table 2c) at the first assessment, and a further 17% (N=521) and 6.6% (N=209) at the subsequent two assessments. Similarly, 50% (N=3395) completed the C19-YRSm at the first assessment with 21% (N=1416) and 10% (N=691) at assessment 2 and 3, respectively (Table 2d). Finally, the figures for the EQ-5D-5L were 46% (N=3438), 20% (N=1532) and 11% (N=807) for assessments 1 to 3, respectively (Table 2e).

The scores for the PROMs are shown in Tables 3a to 4b. Both Symptom Severity and Functional Disability showed a substantial worsening, from the pre-COVID ratings, at first assessment: Symptom Severity had increased to a mean of 18.6 (SD: 5.8, 95% confidence intervals (CI): 18 to 19) at the first assessment from a retrospectively self-reported pre-COVID level of 4.1 (SD: 4.1, 95%CI: 3.9 to 4.2); Functional Disability had increased to 7.1 (SD: 3.8, 95%CI: 7.0 to 7.3) from 1.1 (SD: 2.2, 95%CI: 1.0 to 1.2) pre-COVID (Table 3a). Conversely, Overall Health had decreased down to 4.5 (SD: 1.9, 95%CI: 4.4 to 4.5) from 7.5 (SD: 2.5, 95%CI: 7.4 to 7.6) pre-COVID.

There were 396 patients who had completed the C19-YRSm at the first assessment and then subsequently at 90 days (± 30 days) following the initial assessment (Table 3b). For these patients, a trend was observable with a statistically significant reduction (between the first and 90-day assessment) in both Symptom Severity and Functional Disability and a concomitant statistically significant improvement in Overall Health. Other Symptoms were also observed to reduce over this time period.

A total of 146 patients had completed the C19-YRSm at the first assessment, and subsequently at 90 (± 30) days and 180 (± 30) days) (Table 3c). These patients demonstrated a further statistically significant improvement in Symptom Severity between the 90 and 180-day assessments. Also, a statistically significant improvement was observed over this time period for Functional Disability and Overall Health.

Both the mean EQ-5D-5L Index and visual analogue scale (VAS) scores were low at the first assessment (Table 4a) at 0.50 (SD: 0.30, 95%CI: 0.53 to 0.55) and 51 (SD: 21, 95%CI: 51 to 52) respectively. A total of 503 patients had completed the EQ-5D-5L at the first assessment and subsequently at 90 (± 30) days (Table 4b). No statistically significant improvement was observed on

the EQ-5D-5L Index for these patients (0.50 at both time periods); the improvement in the EQ-5D-5L VAS was however statistically significant, increasing to 50.9 (SD: 21.6) from 48.7 (SD: 21.1).

A group of patients (N=171) had also completed the EQ-5D-5L at 90 and 180 days as well as at the first assessment (Table 4c). There was a statistically significant improvement in the VAS scores from 48 (SD: 20) at first assessment to 51 (SD: 22) at the 90-day assessment. There was, on the other hand, a statistically significant worsening of the EQ-5D-5L index score.

A total of 168 patients had completed both the C19-YRSm and EQ-5D-5L (and VAS) on the same day both the first and day 90 assessment (± 90 days) (Table 4d). The SRM for the C19-YRSm domains was as follows: Symptom Severity 0.38; Functional Disability 0.21, Overall Health 0.17 and Other Symptoms 0.22. In contrast, the SRM for the EQ-5D-5L was 0.06 and 0.04 for the VAS. These results demonstrate that the C19-YRSm - a condition-specific PROM – is significantly more responsive to change in patient symptoms than a generic PROM, i.e., the EQ-5D-5L and supports the (statistically significant) improvements observed on the C19-YRSm Symptom Severity and Functional Disability domains and the absence of any noticeable change on the EQ-5D-5L Index values.

Table 5 and Figure 1 show the correlation between the various domains of C19-YRS and EQ-5D-5L.

Table 2a. Overall number of completed Patient-Reported Outcome Measures (PROMS) by centre

Number of each PROM completed (%)	Overall N = 17,471	BSW N = 2,970	B&S N = 503	Brad N = 1,315	C&P N = 1,311	Essex N = 1,583	Herts N = 584	Imp N = 242	Leeds N = 4,594	Leics N = 1,231	Newc N = 414	RDASH N = 45	Oxf N = 784	PA N = 716	Sal N = 1,179
C19-YRS Original	**3,150 (18)**	7 (0.2)	142 (28)	147 (11)	596 (45)	664 (42)	35 (6.0)	5 (2.1)	146 (3.2)	263 (21)	41 (9.9)	0 (0)	117 (15)	480 (67)	507 (43)
C19-YRS Modified	**6,770 (39)**	1,558 (52)	123 (24)	793 (60)	202 (15)	128 (8.1)	260 (45)	137 (57)	2,208 (48)	390 (32)	185 (45)	24 (53)	270 (34)	236 (33)	256 (22)
EQ-5D-5L	**7,551 (43)**	1,405 (47)	238 (47)	375 (29)	513 (39)	791 (50)	289 (49)	100 (41)	2,240 (49)	578 (47)	188 (45)	21 (47)	397 (51)	0 (0)	416 (35)

Table 2b. Total number of completed assessments by centre

Number of assessments completed (N,%)	Overall N = 17,471	BSW N = 2,970	B&S N = 503	Brad N = 1,315	C&P N = 1,311	Essex N = 1,583	Herts N = 584	Imp N = 242	Leeds N = 4,594	Leics N = 1,231	Newc N = 414	RDASH N = 45	Oxf N = 784	PA N = 716	Sal N = 1,179
1	**8,985 (51)**	1,575 (53)	127 (25)	856 (65)	1,091 (83)	822 (52)	158 (27)	103 (43)	2,236 (49)	404 (33)	137 (33)	42 (93)	227 (29)	538 (75)	669 (57)
2	**3,469 (20)**	730 (25)	80 (16)	211 (16)	158 (12)	260 (16)	109 (19)	49 (20)	1,122 (24)	250 (20)	69 (17)	3 (6.7)	146 (19)	99 (14)	183 (16)
3	**1,707 (9.8)**	318 (11)	64 (13)	80 (6.1)	37 (2.8)	126 (8.0)	83 (14)	31 (13)	534 (12)	152 (12)	46 (11)	0 (0)	111 (14)	29 (4.1)	96 (8.1)
4	**977 (5.6)**	161 (5.4)	46 (9.1)	42 (3.2)	9 (0.7)	74 (4.7)	60 (10)	18 (7.4)	278 (6.1)	97 (7.9)	39 (9.4)	0 (0)	80 (10)	11 (1.5)	62 (5.3)
5	**624 (3.6)**	78 (2.6)	35 (7.0)	28 (2.1)	6 (0.5)	46 (2.9)	50 (8.6)	14 (5.8)	149 (3.2)	69 (5.6)	35 (8.5)	0 (0)	63 (8.0)	8 (1.1)	43 (3.6)
6	**446 (2.6)**	43 (1.4)	33 (6.6)	20 (1.5)	5 (0.4)	38 (2.4)	37 (6.3)	13 (5.4)	94 (2.0)	55 (4.5)	28 (6.8)	0 (0)	42 (5.4)	6 (0.8)	32 (2.7)
7	**310 (1.8)**	24 (0.8)	26 (5.2)	14 (1.1)	3 (0.2)	28 (1.8)	27 (4.6)	8 (3.3)	53 (1.2)	44 (3.6)	18 (4.3)	0 (0)	35 (4.5)	6 (0.8)	24 (2.0)
8	**223 (1.3)**	13 (0.4)	17 (3.4)	8 (0.6)	2 (0.2)	25 (1.6)	22 (3.8)	5 (2.1)	31 (0.7)	31 (2.5)	11 (2.7)	0 (0)	30 (3.8)	6 (0.8)	22 (1.9)
9	**165 (0.9)**	10 (0.3)	15 (3.0)	6 (0.5)	0 (0)	25 (1.6)	17 (2.9)	1 (0.4)	22 (0.5)	27 (2.2)	7 (1.7)	0 (0)	16 (2.0)	4 (0.6)	15 (1.3)
10*	**116 (0.7)**	5 (0.2)	12 (2.4)	6 (0.5)	0 (0)	21 (1.3)	8 (1.4)	0 (0)	12 (0.3)	23 (1.9)	5 (1.2)	0 (0)	10 (1.3)	3 (0.4)	11 (0.9)

***The full table including assessments 11 to 34 are shown in Appendix 2b.**

Table 2c. Total number of original C19-YRS assessments completed by centre

Number of original C19-YRS assessments completed (%)	Overall N = 3,150	BSW N = 7	B&S N = 142	Brad N = 147	C&P N = 596	Essex N = 664	Herts N = 35	Imp N = 5	Leeds N = 146	Leics N = 263	Newc N = 41	Oxf N = 117	PA N = 480	Sal N = 507
1	**2,152 (68)**	1 (14)	54 (38)	91 (62)	516 (87)	414 (62)	20 (57)	5 (100)	91 (62)	135 (51)	25 (61)	65 (56)	356 (74)	379 (75)
2	**521 (17)**	1 (14)	30 (21)	29 (20)	59 (9.9)	112 (17)	11 (31)	0 (0)	36 (25)	72 (27)	9 (22)	30 (26)	62 (13)	70 (14)
3	**209 (6.6)**	1 (14)	18 (13)	14 (9.5)	11 (1.8)	50 (7.5)	4 (11)	0 (0)	13 (8.9)	32 (12)	3 (7.3)	14 (12)	22 (4.6)	27 (5.3)
4	**103 (3.3)**	1 (14)	12 (8.5)	7 (4.8)	3 (0.5)	30 (4.5)	0 (0)	0 (0)	4 (2.7)	15 (5.7)	2 (4.9)	7 (6.0)	7 (1.5)	15 (3.0)
5	**50 (1.6)**	1 (14)	7 (4.9)	4 (2.7)	3 (0.5)	14 (2.1)	0 (0)	0 (0)	1 (0.7)	5 (1.9)	1 (2.4)	1 (0.9)	6 (1.3)	7 (1.4)
6	**35 (1.1)**	1 (14)	6 (4.2)	1 (0.7)	3 (0.5)	11 (1.7)	0 (0)	0 (0)	1 (0.7)	4 (1.5)	1 (2.4)	0 (0)	5 (1.0)	2 (0.4)
7	**17 (0.5)**	1 (14)	3 (2.1)	1 (0.7)	1 (0.2)	5 (0.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (1.0)	1 (0.2)
8	**13 (0.4)**	0 (0)	3 (2.1)	0 (0)	0 (0)	4 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (1.0)	1 (0.2)
9	**11 (0.3)**	0 (0)	3 (2.1)	0 (0)	0 (0)	4 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.6)	1 (0.2)
10*	**10 (0.3)**	0 (0)	2 (1.4)	0 (0)	0 (0)	4 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.6)	1 (0.2)

***The full table including assessments 11 to 34 are shown in Appendix 2c.**

Table 2d. Total number of C19-YRSm (modified) assessments completed by centre

Number of C19-YRSm assessments completed (%)	**Overall** N = 6,770	**BSW** N = 1,558	**B&S** N = 123	**Brad** N = 793	**C&P** N = 202	**Essex** N = 128	**Herts** N = 260	**Imp** N = 137	**Leeds** N = 2,208	**Leics** N = 390	**Newc** N = 185	**RDASH**N = 24	**Oxf** N = 270	**P&A** N = 236	**Sal** N = 256
1	**3,395 (50)**	802 (51)	26 (21)	549 (69)	184 (91)	108 (84)	64 (25)	57 (42)	1,055 (48)	112 (29)	52 (28)	21 (88)	67 (25)	182 (77)	116 (45)
2	**1,416 (21)**	398 (26)	17 (14)	124 (16)	13 (6.4)	15 (12)	47 (18)	28 (20)	529 (24)	81 (21)	30 (16)	3 (13)	49 (18)	37 (16)	45 (18)
3	**691 (10)**	168 (11)	17 (14)	39 (4.9)	4 (2.0)	4 (3.1)	38 (15)	17 (12)	256 (12)	51 (13)	21 (11)	0 (0)	41 (15)	7 (3.0)	28 (11)
4	**404 (6.0)**	83 (5.3)	14 (11)	22 (2.8)	1 (0.5)	1 (0.8)	29 (11)	11 (8.0)	135 (6.1)	35 (9.0)	19 (10)	0 (0)	30 (11)	4 (1.7)	20 (7.8)
5	**251 (3.7)**	36 (2.3)	10 (8.1)	14 (1.8)	0 (0)	0 (0)	25 (9.6)	8 (5.8)	75 (3.4)	24 (6.2)	17 (9.2)	0 (0)	26 (9.6)	2 (0.8)	14 (5.5)
6	**187 (2.8)**	24 (1.5)	9 (7.3)	9 (1.1)	0 (0)	0 (0)	19 (7.3)	7 (5.1)	53 (2.4)	20 (5.1)	15 (8.1)	0 (0)	19 (7.0)	1 (0.4)	11 (4.3)
7	**131 (1.9)**	14 (0.9)	8 (6.5)	6 (0.8)	0 (0)	0 (0)	13 (5.0)	5 (3.6)	30 (1.4)	19 (4.9)	12 (6.5)	0 (0)	15 (5.6)	1 (0.4)	8 (3.1)
8	**90 (1.3)**	8 (0.5)	6 (4.9)	5 (0.6)	0 (0)	0 (0)	11 (4.2)	3 (2.2)	17 (0.8)	13 (3.3)	7 (3.8)	0 (0)	13 (4.8)	1 (0.4)	6 (2.3)
9	**57 (0.8)**	7 (0.4)	4 (3.3)	3 (0.4)	0 (0)	0 (0)	8 (3.1)	1 (0.7)	12 (0.5)	10 (2.6)	3 (1.6)	0 (0)	6 (2.2)	1 (0.4)	2 (0.8)
10*	**38 (0.6)**	5 (0.3)	3 (2.4)	3 (0.4)	0 (0)	0 (0)	2 (0.8)	0 (0)	8 (0.4)	9 (2.3)	3 (1.6)	0 (0)	3 (1.1)	0 (0)	2 (0.8)

***The full table including assessments 11 to 34 are shown in Appendix 2d.**

Table 2e. Total number of EQ-5D-5L assessments completed

Number of EQ-5D-5L assessments completed (%)	Overall N = 7,551	BSW N = 1,405	B&S N = 238	Brad N = 375	C&P N = 513	Essex N = 791	Herts N = 289	Imp N = 100	Leeds N = 2,240	Leics N = 578	Newc N = 188	RDASH N = 21	Oxf N = 397	Sal N = 416
1	**3,438 (46)**	772 (55)	47 (20)	216 (58)	391 (76)	300 (38)	74 (26)	41 (41)	1,090 (49)	157 (27)	60 (32)	21 (100)	95 (24)	174 (42)
2	**1,532 (20)**	331 (24)	33 (14)	58 (15)	86 (17)	133 (17)	51 (18)	21 (21)	557 (25)	97 (17)	30 (16)	0 (0)	67 (17)	68 (16)
3	**807 (11)**	149 (11)	29 (12)	27 (7.2)	22 (4.3)	72 (9.1)	41 (14)	14 (14)	265 (12)	69 (12)	22 (12)	0 (0)	56 (14)	41 (9.9)
4	**470 (6.2)**	77 (5.5)	20 (8.4)	13 (3.5)	5 (1.0)	43 (5.4)	31 (11)	7 (7.0)	139 (6.2)	47 (8.1)	18 (9.6)	0 (0)	43 (11)	27 (6.5)
5	**323 (4.3)**	41 (2.9)	18 (7.6)	10 (2.7)	3 (0.6)	32 (4.0)	25 (8.7)	6 (6.0)	73 (3.3)	40 (6.9)	17 (9.0)	0 (0)	36 (9.1)	22 (5.3)
6	**224 (3.0)**	18 (1.3)	18 (7.6)	10 (2.7)	2 (0.4)	27 (3.4)	18 (6.2)	6 (6.0)	40 (1.8)	31 (5.4)	12 (6.4)	0 (0)	23 (5.8)	19 (4.6)
7	**162 (2.1)**	9 (0.6)	15 (6.3)	7 (1.9)	2 (0.4)	23 (2.9)	14 (4.8)	3 (3.0)	23 (1.0)	25 (4.3)	6 (3.2)	0 (0)	20 (5.0)	15 (3.6)
8	**120 (1.6)**	5 (0.4)	8 (3.4)	3 (0.8)	2 (0.4)	21 (2.7)	11 (3.8)	2 (2.0)	14 (0.6)	18 (3.1)	4 (2.1)	0 (0)	17 (4.3)	15 (3.6)
9	**97 (1.3)**	3 (0.2)	8 (3.4)	3 (0.8)	0 (0)	21 (2.7)	9 (3.1)	0 (0)	10 (0.4)	17 (2.9)	4 (2.1)	0 (0)	10 (2.5)	12 (2.9)
10	**68 (0.9)**	0 (0)	7 (2.9)	3 (0.8)	0 (0)	17 (2.1)	6 (2.1)	0 (0)	4 (0.2)	14 (2.4)	2 (1.1)	0 (0)	7 (1.8)	8 (1.9)

***The full table including assessments 11 to 34 are shown in Appendix 2e**

Table 3a. Overall C19-YRSm scores at first assessment

Mean C19-YRSm score (SD) [95%CI] N = 3,395	Pre-Covid	First assessment
Symptom Severity (Score: 0-30)	4.1 (4.1) [3.9, 4.2]	18.6 (5.8) [18,19]
Functional Disability (Score: 0-15)	1.1 (2.2) [1.0,1.2]	7.1 (3.8) [7.0,7.3]
Overall Health (Score: 0-10)	7.5 (2.5) [7.4,7.6]	4.5 (1.9) [4.4,4.5]
Other Symptoms (Score: 0-25)	-	5.7 (4.4) [5.6,5.9]

Key: 95%CI, confidence interval

*At first assessment, the C19-YRSm records Symptom Severity, Functional Disability and Overall Health for both before pre- COVID and current status. However, pre-COVID scores are not recorded for 'Other Symptoms'

Table 3b. Changes in C19-YRSm scores at 90 (± 30) day follow-up assessment

C19-YRSm (Mean, SD) [95%CI] N=396	Pre-Covid	1st Assessment	2nd Assessment 90 days (± 30 days)
Symptom Severity (Pre-Covid)	3.9 (3.8) [3.5, 4.3]	18.4 (5.6) [18,19]	16.7 (5.9)** [16,17]
Functional Disability (1st Assessment)	1.1 (2.3) [0.85,1.3]	7.6 (3.6) [7.2,7.9]	6.9 (3.7)* [6.6,7.3]
Overall Health (1st Assessment)	7.8 (2.1) [7.6,8.0]	4.4 (2.0) [4.2,4.6]	4.7 (1.8)** [4.6,4.9]
Other Symptoms		5.9 (4.2) [5.5,6.3]	5.4 (4.3)† [5.0,5.8]

Key: CI, Confidence Interval

*p<0.05; **p<0.01 (repeated measures t-test, Assessment 1 vs 2)

†p=0.1

Table 3c. Changes in C19-YRSm scores at 180 (± 30) day follow-up assessment

C19-YRSm (Mean, SD) [95%CI] N=146	1st Assessment	Day 90 (± 30 days)	Day 180 (± 30 days)
Symptom Severity (0-30)	19.1 (5.2) [18,20]	17.5 (5.7) [17,18]	16.6 (6.2) [16,18]*
Functional Disability (0-15)	8.3 (3.5) [7.7,8.8]	7.7 (3.6) [7.1,8.3]	7.5 (3.7) [6.9,8.1]**
Overall Health (0-10)	4.2 (2.0) 3.8,4.5]	4.6 (1.9) [4.3,4.9]	4.8 (1.7) [4.5,5.1]*

*p<0.05; **p<0.01 (oneway analysis of variance, ANOVA)

Table 4a. Overall EQ-5D-5L Index and Visual Analogue Scale (VAS) scores at first assessment

Mean EQ-5D scores (SD) [95%CI] N = 3,438	First assessment
Index	0.50 (0.30) [0.53,0.55]
VAS	51 (21) [51,52]

Key: CI, confidence interval

Table 4b. Changes in EQ-5D-5L Index and VAS scores at the 90 (± 30) day follow-up assessment

EQ-5D (Mean, SD) [95%CI]	Assessment 1 N = 503	Assessment 2: 90 days (± 30 days) N = 503
Index	0.50 (0.30) [0.50,0.54]	0.50 (0.30) [0.51,0.56]†
VAS	48.7 (21.1) [47,51]	50.9 (21.6) [49,53]*

* p=0.048; †p=0.31 (repeated measures t-test)

Table 4c. Changes in EQ-5D-5L and VAS scores over time (180 days)

EQ-5D (Mean, SD) [95%CI] N=171	1st Assessment	Day 90 (± 30 days)	Day 180 (± 30 days)
EQ-5D-5L	0.511 (0.27) [0.47,0.55]	0.51 (0.28) [0.47,0.55]	0.50 (0.31)*** [0.45,0.55]
VAS	48 (20) [45,51]	49 (21) [46,52]	51 (22) [48,55]**

**p<0.01; ***p<0.001 (one way ANOVA)

Table 4d. Standardised Response Mean (SRM) for the C19-YRSm and EQ-5D-5L

Domain / Instrument	Mean change from baseline (SD)	Standardised Response Mean*
Symptom Severity (C19-YRSm)	-1.57 (4.12)	-0.38
Functional Disability (C19-YRSm)	-0.54 (2.6)	-0.21
Overall Health (C19-YRSm)	0.33 (1.88)	0.18
Other Symptoms (C19-YRSm)	-0.64 (2.9)	-0.22
EQ-5D-5L	0.011 (0.2)	0.06
EQ-5D VAS	0.79 (19.2)	0.04

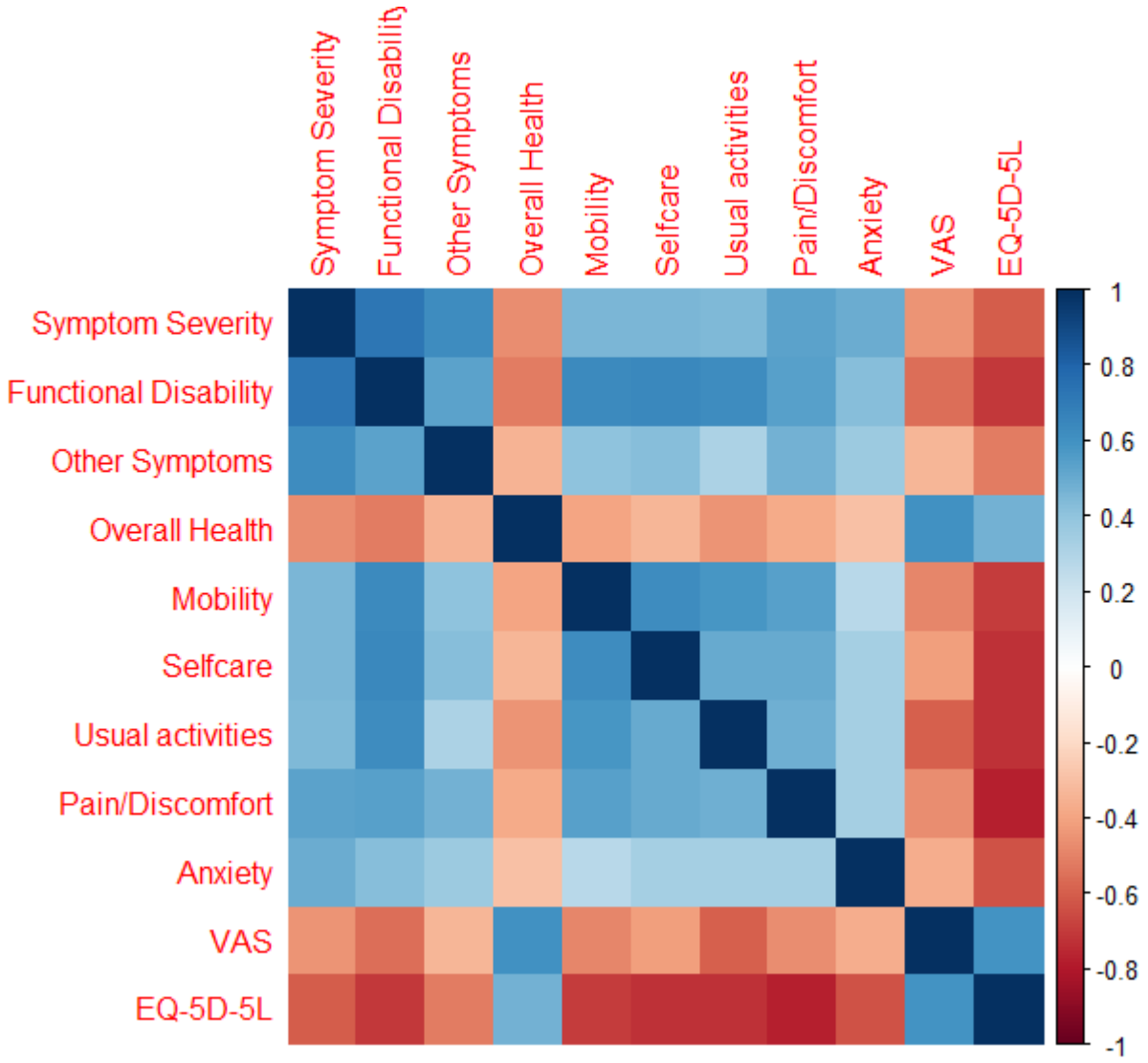
*****Presented as absolute values in the Results.

Table 5. Correlation matrix for EQ-5D-5L (Index and domains), EQ-5D-VAS and the C19-YRSm (at Assessment 1, N=2667)

Variables	Symptom Severity	Functional Disability	Other Symptoms	Overall Health	Mobility	Selfcare	Usual activities	Pain/ Discomfort	Anxiety/ Depression	EQ-5D VAS	EQ-5D-5L
Symptom Severity	1.00	0.72	0.63	-0.47	0.46	0.46	0.45	0.53	0.49	-0.45	-0.61
Functional Disability	0.72	1.00	0.54	-0.52	0.63	0.64	0.62	0.54	0.42	-0.56	-0.70
Other Symptoms	0.63	0.54	1.00	-0.34	0.40	0.43	0.32	0.47	0.37	-0.33	-0.51
Overall Health	-0.47	-0.52	-0.34	1.00	-0.39	-0.34	-0.45	-0.38	-0.30	0.60	0.47
Mobility	0.46	0.63	0.40	-0.39	1.00	0.62	0.59	0.55	0.28	-0.48	-0.70
Selfcare	0.46	0.64	0.43	-0.34	0.62	1.00	0.51	0.50	0.34	-0.42	-0.72
Usual activities	0.45	0.62	0.32	-0.45	0.59	0.51	1.00	0.48	0.34	-0.59	-0.73
Pain/Discomfort	0.53	0.54	0.47	-0.38	0.55	0.50	0.48	1.00	0.34	-0.46	-0.77
Anxiety/ Depression	0.49	0.42	0.37	-0.30	0.28	0.34	0.34	0.34	1.00	-0.36	-0.63
EQ-5D VAS	-0.45	-0.56	-0.33	0.60	-0.48	-0.42	-0.59	-0.46	-0.36	1.00	0.59
EQ-5D-5L	-0.61	-0.70	-0.51	0.47	-0.70	-0.72	-0.73	-0.77	-0.63	0.59	1.00

*EQ-5D-5L domains: Mobility, Selfcare, Usual activities, Pain/Discomfort, Anxiety/Depression
#All correlations statistically significant at *p<0.01*.

Figure 1. Heatmap of correlation matrix for EQ-5D-5L, EQ-5D-VAS and the C19-YRSm (at Assessment 1, N=2667)



The impact of LC on occupational status is shown in Table 6. Although the occupational status of just over a fifth (21%, 25% after excluding 'not recorded/missing' data) of the patient sample had not changed, for a majority of patients (62%, 75% after excluding 'not recorded/missing' data) their work had been affected by LC (e.g., change in role or working arrangements, lost their job, reduced working hours).

Table 6. Occupational Status

Occupation status	N = 3,395
No change	696 (21%)
Changes made to role/ working arrangements (such as working from home or lighter duties)	708 (21%)
Reduced working hours	415 (12%)
Had to retire/ change job	240 (7.1%)
Lost job	150 (4.4%)
Sick leave	603 (18%)
Not recorded / Missing	583 (17%)

*Taken from the original C19-YRS and C19-YRSm

Modelling symptom trajectories based on Patient Reported Outcome Measures (PROMS)

Figure 2 shows the change in Symptom Severity score over time (the grey area indicates the standard errors). The average score at the first assessment is around 18 (out of 30); this gradually improves over time with an average score of approximately 14 for those patients completing assessments around day 500 after their first assessment.

Figure 2a. Symptom Severity over Time

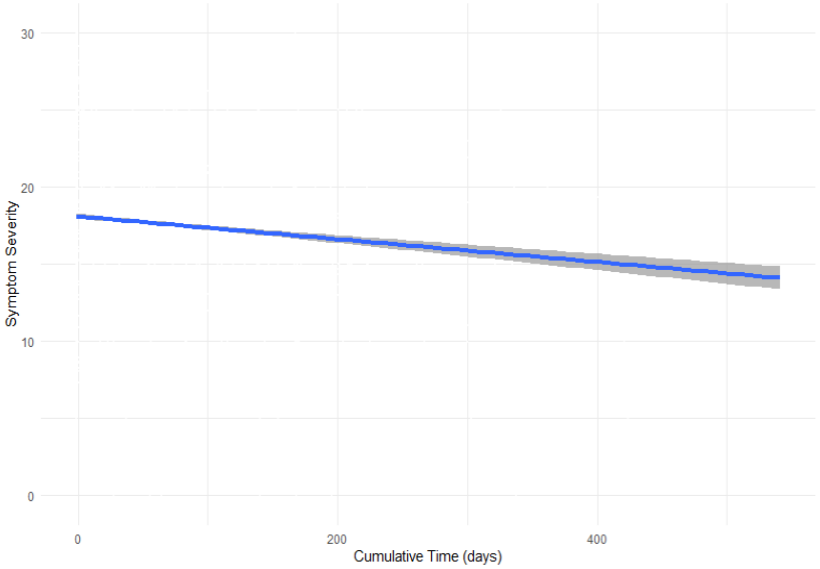


Figure 2b. Functional Disability over Time

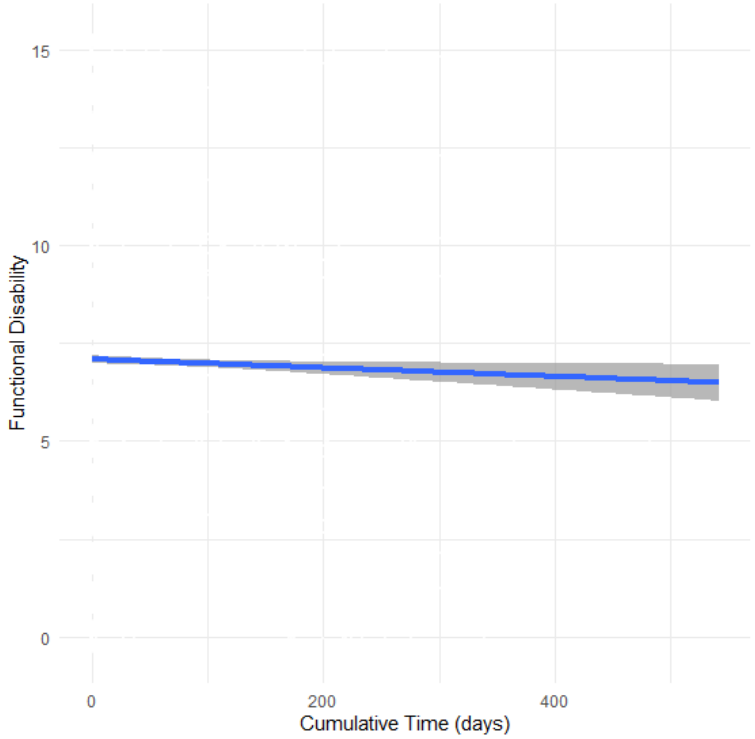


Figure 2c. Overall Health over Time

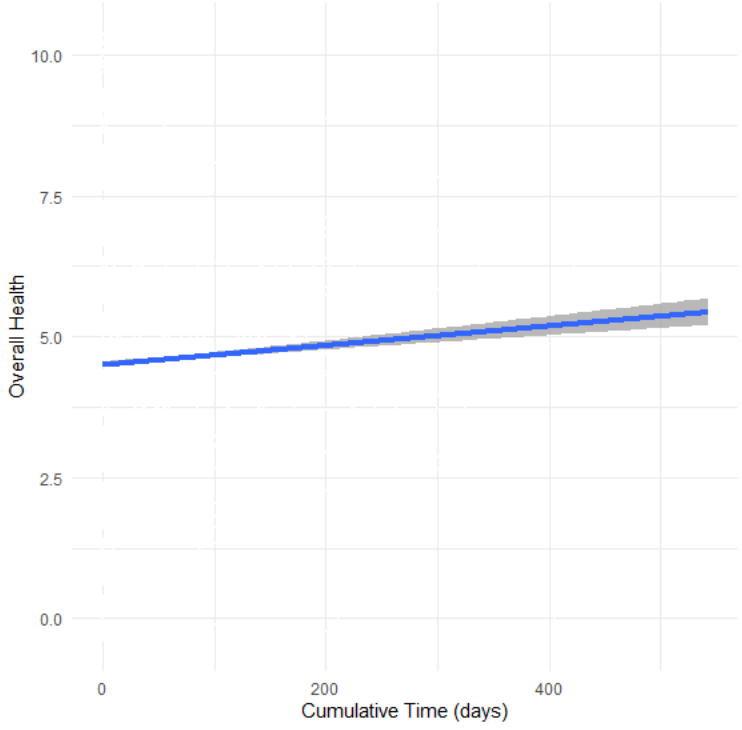


Table 7 shows the results of the first regression model (random intercepts only, no covariates) indicating an average Symptom Severity score of 18.3 at the first assessment ("intercept"). The cumulative time predictor indicates that over a 90-day period, the Symptom Severity score will improve, on average, by roughly 1 point (negative values indicate a lessening in severity). Similarly, over 180 days, Symptom Severity will improve on average by approximately 2 points (1.8).

Table 7. Random intercepts model / random slopes model for Symptom Severity

Symptom Severity		
Predictors	*Estimates*	*95%CI*
Change in Symptom Severity per 90 days unadjusted for covariates*	-0.87	-0.95 to -0.78
Change in Symptom Severity per 90 days adjusted for covariates*	-0.96	-1.07 to -0.82

*****Cumulative time from 1st assessment multiplied by 90 to provide an indication of change over 90 days
Covariates: Sex, Age category, Co-morbidity, Ethnicity and Centre

Symptom trajectory subgroup analyses

The Symptom Severity score trajectories over time, separated by sex, are shown in Figure 3. Whilst female patients had, on average, worse Symptom Severity scores at the first assessment compared to males, and both males and females improved, there was a suggestion that males may see slightly better improvement (lowering of Symptom Severity scores) compared to females over the course of time. However, when symptom trajectories for males and females were formally compared, the differences were not statistically significant (p=0.09, Table 8) and follow-up data on more men and women is needed to confirm this tentative finding.

Figure 3. Symptom Severity over Time by Sex

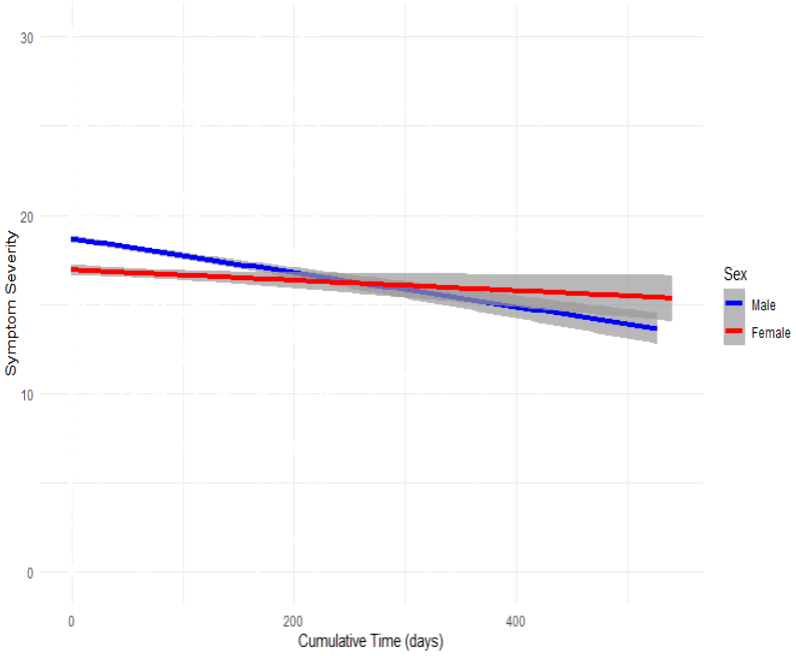


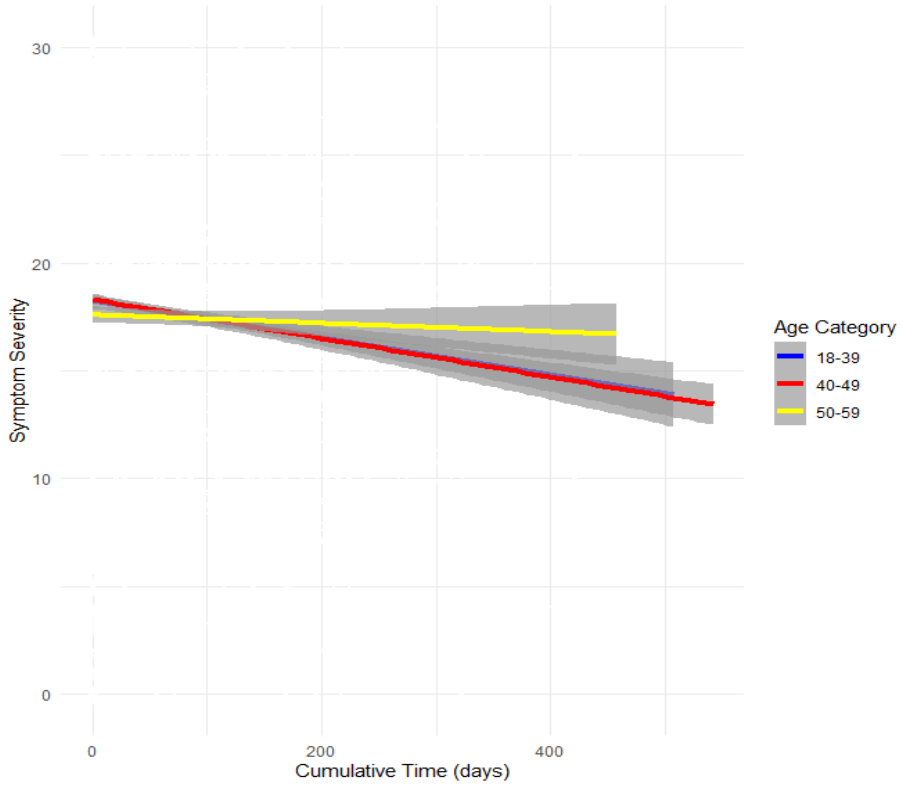
Table 8. Random intercepts and slopes model for Symptom Severity (with covariates and interaction terms)

Symptom Severity			
Interactions	*Estimates*	*CI*	*p-value for the interaction*
Time			
≤90 days from 1st assessment	-1.89	-2.29 – -1.49	<0.001
>90 days from 1st assessment	-0.44	-0.73 – -0.17	
Sex			
Male	-0.80	-1.10 – -0.50	0.16
Female	-1.01	-1.25 – -0.77	
Age			
18-39 years	-0.93	-1.26 – -0.61	0.83
40-49 years	-0.86	-1.19 – -0.58	
50-59 years	-1.04	-1.35 – -0.73	
60+ years	-0.90	-1.26 – -0.53	
Duration of symptoms			
<6 months	-0.81	-3.23 – 1.67	0.96
6 – 12 months	-0.92	-1.36 - -0.47	
12+ months	-0.98	-1.11 - -0.85	
Hospital admission			
No	-0.99	-1.13 - -0.86	0.31
Yes	-0.79	-1.16 - -0.41	
ICU admission			
No	-0.98	-1.11 - -0.86	0.36
Yes	-0.65	-1.35 – 0.06	
Pre-existing respiratory problem			
No	-0.94	-1.16 – -0.71	0.71
Yes	-1.04	-1.61 – -0.48	
Pre-existing mental health problem			
No	-0.94	-1.16 – -0.71	0.71
Yes	-1.02	-1.47 – -0.57	
Pre-existing cardiovascular problem			
No	-0.95	-1.18 – -0.73	0.16
Yes	-0.05	-1.29– 1.19	
Pre-existing diabetes			
No	-0.95	-1.18 – -0.73	0.19
Yes	-0.28	-1.31 – 0.75	
Other pre-existing health problems			
No	-0.95	-1.18 – -0.72	0.65
Yes	-0.84	-1.33 – -0.35	
Pre-existing health problems*			
No	-1.02	-1.38 – -0.66	0.58
Yes	-0.93	-1.16 – -0.70	
Ethnicity			
Asian	-0.86	-1.43 – -0.28	0.50
Black	-0.61	-1.55 – 0.33	
Mixed	-0.92	-1.82 – -0.02	
White	-0.98	-1.21 – -0.75	
Other	0.03	-1.17 – 1.23	

NB: Comorbidity data were not recorded for all patients.
*Pre-existing health problems refers to any of the comorbidities, i.e., respiratory, cardiovascular, mental health and diabetes.

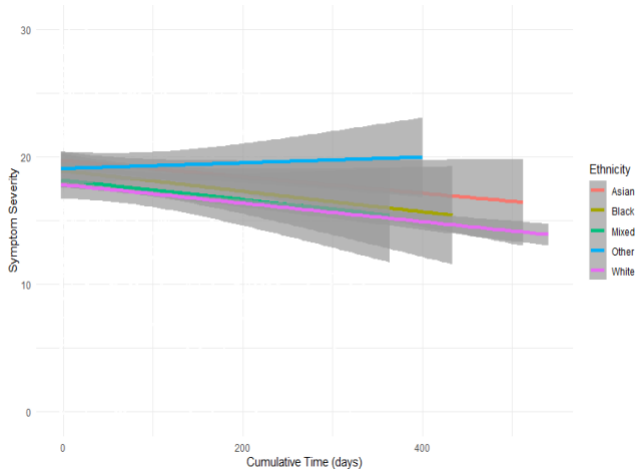
Figure 4 demonstrates that age groups between 18 to 59 years achieved similar levels of improvement in Symptom Severity over time. Overall, there was no evidence of a difference in symptom trajectories across all the age groups (p=0.69, Table 8). However, the oldest age category (60 and above) appeared to show little or no improvement in Symptom Severity over time, compared to observed improvements in all the younger age groups, so further investigation of symptom trajectories in older age groups is recommended.

Figure 4. Symptom Severity over Time by Age Category



Black and Asian patients had the highest Symptom Severity scores at the first assessment (on average 1 point higher compared to the other ethnicities), whereas White patients scored on average 0.6 points lower (better). This may indicate that some ethnic groups are more susceptible to worse symptoms, or a difference in referral patterns resulting in only Black and Asian people with worse symptoms being referred. However, there was no evidence of different symptom trajectories over time (Figure 5) between ethnic groups (p=0.56, Table 8). It is worth noting that the confidence intervals were very wide, and it is therefore recommended that more data be collected on minority ethnic groups to ensure their needs are met.

Figure 5. Symptom Severity over Time by Ethnicity



Time since the first assessment was dichotomised into ≤ 90 days and >90 days after the first assessment). This showed that patients experienced faster improvement (steeper decline symptom scores on average) during the first 90 days from first assessment, compared to over subsequent assessments. Symptoms improved approximately four times faster during the first 3 months in the care of a LC clinic than subsequently ($p<0.001$) although improvements were still seen beyond that point (Table 8). Note that 90 days was an arbitrary cut-off and that further work would be needed to quantify exactly when most improvement was seen. Furthermore, the slower improvement beyond 90 days may reflect a different population with more persistent problems, who take longer to discharge and therefore provide longer-term data, rather than indicating any lack of benefit of intervention beyond the first 90 days.

Figure 6 is an illustration of a random sample of 20 patients across the 3 time points showing the variation in Symptom Severity, Functional Disability and Overall Health scores suggesting non-linear trends of changes or in other words, fluctuations seen in LC. Even at the second time point (180 day assessment), the scores are higher when compared to pre-COVID scores suggesting a lack of complete resolution of the condition

Figure 6a. Individual Symptom Severity scores at 3 time points (N=20)

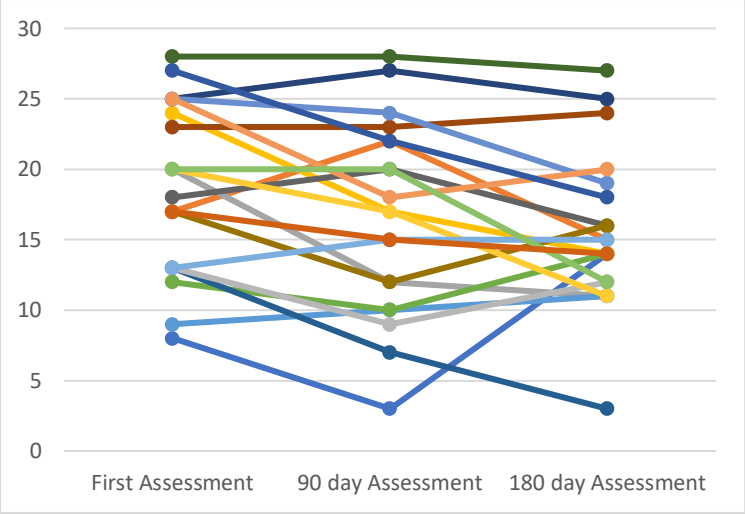


Figure 6b. Individual Functional Disbility scores at 3 timepoints (N=20)

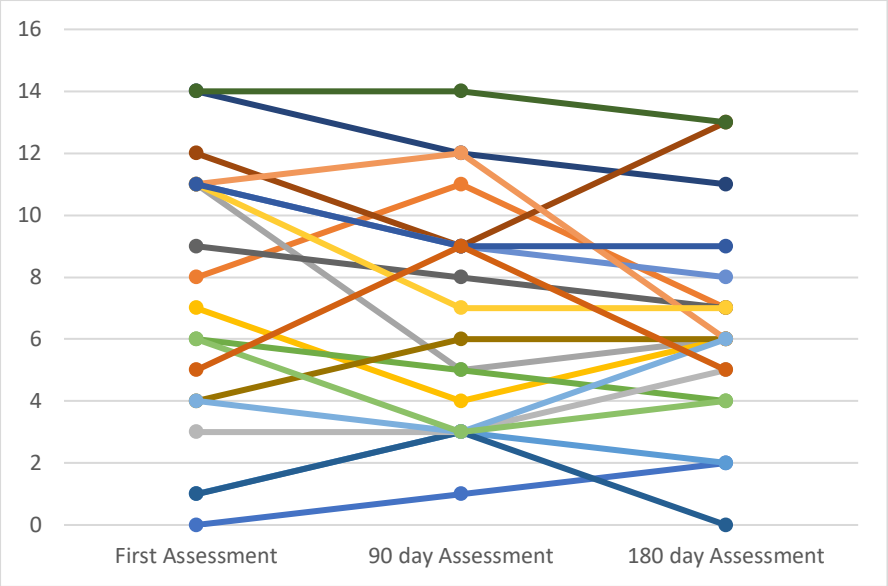
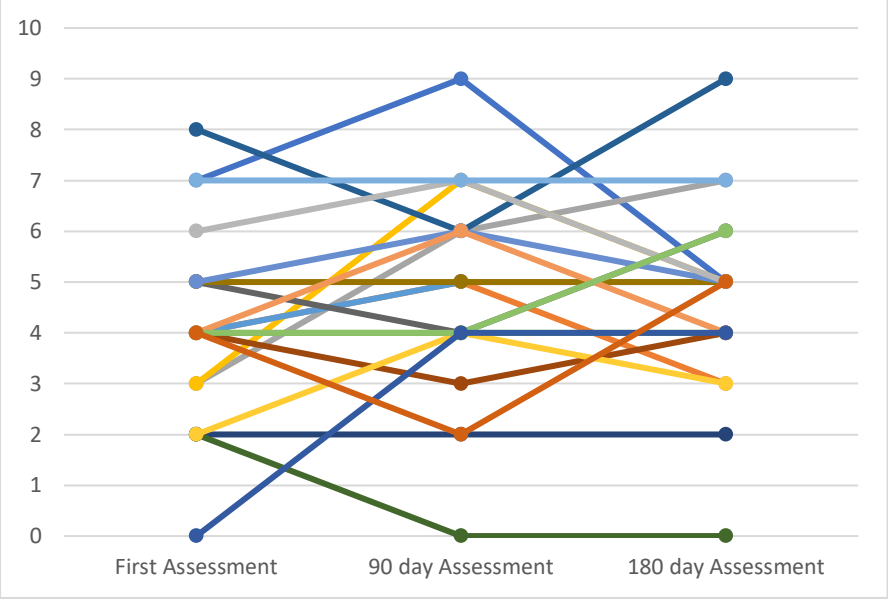


Figure 6c. Individual Overall Health scores at 3 timepoints (N=20)



Discussion

The key finding of this national evaluation is that LC is a new condition and patients have a new-onset of symptoms and functional disability following an acute COVID-19 infection that seems to persist in some even at 180 days (6 months) after referral to (and starting to be seen in) a specialist LC clinic. 3395 participants who completed at least one C19-YRS questionnaire at first assessment showed a significant new-onset symptom burden, functional disability and deterioration of overall health since the COVID-19 infection.

The LC services have a greater proportion of middle-aged females, in keeping with other LC studies reported in the literature. This sample predominantly had non-hospitalised patients (90%) with a low prevalence (7%) of co-morbidities supporting other studies that have reported previously fit and well individuals struggling with LC even after mild acute COVID-19 infection. Even though the sample in this evaluation is not fully representative of the LC population in the country, it is suggestive of the existence of a cohort of individuals with severe symptoms and persistence even after 1 year since the acute illness.

The DPROM platform in this service evaluation was used to complete a total of 17, 471 PROMs (C19-YRS and EQ5D) which is encouraging in terms of a novel concept of using an interactive digital system for patients to complete PROMs in their own time. This reduces administrative time in LC services to collect PROM in traditional paper-based form and analyse manually. It is also reassuring that several patients (1532 participants) completed multiple assessments on the same PROM on the DPROM platform.

The cross-sectional EQ5D-5L index value of 3438 patients suggests the burden and disability in this cohort of LC patients were worse than in Diabetes Mellitus, COPD, Heart Failure, and Multiple Sclerosis (Table 9).[15, 16] This highlights the need for prioritisation of services to provide comprehensive management programmes for LC and also develop research programmes to improve our understanding of the condition and test novel treatments.

Table 9. Comparison of EQ5D-5L Index Scores in LC and other chronic long-term conditions

Condition	EQ-5D Index (SD)
Healthy population	0.92 (0.17)
Diabetes mellitus (type 2)	0.79 (0.22)
COPD	0.68 (0.24)
Heart failure	0.60 (0.25)
Multiple sclerosis	0.59 (0.29)
Long Covid (this service evaluation study)	0.50 (0.30)

There are small albeit statistically significant improvements in symptom burden, functional disability and overall health at 3 month and 6 months, suggestive of the effect of interventions provided in the specialist clinics. Results of the evaluation show that 3 months following their initial PROM assessment, patients showed a statistically significant improvement in most of the analysed measures. However, they still had significant new-onset LC symptom burden and disability compared to their pre-COVID-19 health status. Similar results were also found in patients who completed a PROM assessment at 6 months following their initial assessment. These findings show that some patients require longer than 6 months under the care of LC service to achieve complete recovery, and longer-term follow-up data will provide an insight into how far this extends.

Changes in scores at both the 3 and 6-month follow-up assessments provide evidence that the C19-YRS, a LC-specific PROM, is a more sensitive measure in LC than EQ-5D-5L, a generic PROM. This demonstrates the requirement for including the use of a LC-specific PROM to provide a more accurate assessment of outcomes.[17] This is particularly applicable to LC as >200 symptoms have been reported and it is not feasible to capture this using symptom-specific scales or generic scales. EQ5D-5L should however remain the mandatory PROM to be measured to enable comparison with other long-term conditions.

Only 21% of our sample were able to maintain their work role prior to their COVID-19 infection without changes to their working arrangements, with 62% requiring sick leave, reduced hours, a change in role, retirement, or quitting their role. This highlights the clear need to create and implement effective vocational rehabilitation programmes within LC services to ensure patients can return to or maintain work, for the benefit of the patient and the UK economy, both in terms of preventing productivity loss and the reduced utilisation of state benefits.

Multiple assessments within the same patient have shown that LC is a fluctuating condition, as there is not necessarily a linear trend of improvement or deterioration in the symptom burden, functional disability, and overall health of patients. This means that the conclusions inferred from changes in PROM scores over time are subject to be influenced by these fluctuations and more regular assessments are required to assess changes with more certainty. The overall health score of C19-YRS or VAS scale of the EQ5D-5L might be a better reliable indicator of the condition and is likely to be less influenced by symptom and function fluctuations seen in the condition.

It is clear from the results that persistent LC in some patients is a Long-Term Condition (LTC) that can continue to cause functional decline and disability even 18 months after onset. This should be considered when determining how ongoing care of persistent LC is going to be planned in future. These patients are likely to re-present to services even after discharge when they have a relapse of symptoms. Healthcare authorities should recognise persistent LC as a new LTC and prioritise their management along with other LTCs such as mental health problems, Diabetes Mellitus, COPD and persistent pain syndromes.

Limitations

There are several limitations to this study. Firstly, this sample includes only those using a single digital platform (ELAROS); we don't have data from those completing paper forms or other digital platforms. This limitation however does not influence the conclusions that in a subset of patients, LC symptom burden, functional limitation burden, and vocational problems, evolve into a long-term condition.

The repeated PROMs completeness rates are not good (drops by > 50% between first and second assessments) but these rates comparable to reported rates in the literature. Multiple studies have explored the use of digital Patient Reported Outcomes (PROs) in other conditions [18]. Some studies have reported non-use rates to be as high as 72% [19, 20] However given the advantages and the emphasis on digitalisation of NHS services and move to bring care as close as possible to patients homes, the use of digital PROMs is an efficient way of collecting PROMs in future. Automatic integration of these digital tools into the electronic health records (HER) remains a challenge due to the various EHR systems in place and needs further development work.

Digital exclusion is a limitation of these approaches and we have not been able to analyse the trends in those individuals filling out PROMs in a traditional manner. This is more work needed on

minimising the digital exclusion of less privileged individuals and integration of clinician-entered EHR results with the digital platform results so that the analysed sample is as inclusive as possible.

Having two timepoints is useful, but LC is a fluctuating condition and difficult to make conclusions based on changes in outcome measures. We need to encourage patients to complete measures on a frequent basis (at least 3 monthly) using the digital platform and perform further analysis of the data collected in the long run. The overall health VAS scale of PROMs could be a more stable indicator of the condition than the fluctuating specific symptoms in the condition. This needs to be investigated in future research.

Recommendations

Recommendations for Healthcare Authorities

- Recognise LC is a new-onset condition with a significant burden of symptoms, functional disability and decline of overall health in affected individuals. Even though there is a lack of consensus on a single uniform biomarker for the condition, the findings of this study support a significant healthcare burden in previously healthy and fit individuals.
- Recognise that in some individuals, persistent LC (> 2 years of symptoms) is an LTC with fluctuations that require long-term care with a similar strategy as other LTCs. The funding and commissioning plan needs to have persistent LC included under the LTCs category and prioritise LC as much as other LTCs.
- Encourage all LC services to use regular PROMs (if possible digital PROMs platform) as they are an efficient and cost-effective way of capturing true trajectories of the condition.
- With digital PROMs platforms, there is a need to address the barriers of digital exclusion and ensure adequate training facilities are available for individuals to take up the use of such technology.
- Encourage more sites to contribute data to national evaluation studies. With more than 700,000 patients with LC > 2 years (persistent LC), there is a need to capture long-term outcomes on a bigger dataset of patients than this evaluation.
- We need to ensure we don't lose sight of the magnitude of LC and its burden on people's lives (finding of this study). The key is to operationalise existing LC clinics as clinical research centres and facilitate as much translational research as possible to understand the condition better and improve outcomes for patients. Studies such as LOCOMOTION and other NIHR-funded studies aim to achieve this. We need more investment in clinical interventional research.

Recommendations for LC services

- Continue to provide specialist care to individuals with LC. Many individuals improve substantially and are successfully discharged, but services also have a considerable number of patients struggling with long-term symptoms and disability which require close monitoring and targeted interventions. NHSE has plans to do more work on how these services will integrate/ work with other services for other long-term conditions so that the care provided is cost-effective.
- Services need to include the use of LC condition-specific measures such as C19-YRSm or others (for e.g., Symptom Burden Questionnaire (SBQ)) as LC is a novel condition and the using a combination of symptom-based measures is cumbersome and burdensome to the patients. Using C19-YRSm along with a healthcare utility measure such as EQ5D-5L provides the right balance of measuring symptom burden and disability for the patient accurately (C19-YRSm) and cost-effectiveness of services for the service providers and commissioners (EQ5D-5L).

Recommendations for individuals with LC

- A clinical diagnosis of LC is key to successful intervention and long-term management. Individuals with persistent symptoms need to present to their clinicians and seek specialist input.
- Complete PROMs on a regular basis to understand the fluctuations in the conditions and self-manage the condition in terms of adjusting to triggers and dealing with complications and functional limitations seen in the condition. This will also enable clinicians and researchers to understand the long-term trajectories of the condition.
- Continue to peer-support each other and work closely with healthcare professionals and healthcare providers to enhance our understanding of the condition and inform policy decisions on long-term care and clinical research in LC.

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