Article:
Gardiner, L.E., Lozano-Rojas, D., Smith, N. et al. (2026) Investigating prognostic classifications of preexisting multiple long-term conditions for health outcomes 1 year after COVID-19 hospitalization: A UK prospective observational study. International Journal of Infectious Diseases, 168. 108695. ISSN: 1201-9712

https://doi.org/10.1016/j.ijid.2026.108695

International Journal of Infectious Diseases 168 (2026) 108695

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Investigating prognostic classifications of preexisting multiple long-term conditions for health outcomes 1 year after COVID-19 hospitalization: A UK prospective observational study

Lucy E Gardiner[1], Daniel Lozano-Rojas[1], Nikki Smith[2], Jane Espley[2], Iain D Stewart[3], Kimon Ntotsis[1], Raminder Aul[4], Nawar Dair Bakerly[5], Paul Beirne[6], Charlotte E Bolton[7,8], Jeremy S Brown[9], Andrew Briggs[10], Trudie Chalder[11], James D Chalmers[12], Gourab Choudhury[13], Melanie J Davies[14,22], Anthony De Soyza[15], Annemarie B Docherty[16], Nicholas Easom[17], Carlos Echevarria[18], Claudia M Efstathiou[3], Omer Elneima[1], Jonathan Fuld[19], John R Geddes[20], Anne F Goemans[21,22], William Greenhalf[23], Neil J Greening[1], Beatriz Guillen-Guio[21,22,24], Victoria C Harris[1], Ewen M Harrison[16], Nicholas Hart[25], Liam G Heaney[26], Simon Heller[27], Ling-Pei Ho[28], Alex Horsley[29], Linzy Houchen-Wolloff[1], Luke Howard[30], John R Hurst[31], Muhammad Mamoon Iqbal[1], Joseph Jacob[9,32], Gisli Jenkins[3], Caroline Jolley[33], Mark Jones[34], Steven Kerr[35], Kamlesh Khunti[14,22], Olivia C Leavy[21,22], Keir Lewis[36], Nazir I Lone[16], Janet M Lord[37], Will D-C Man[38], Michael Marks[10], Hamish J C McAuley[1], Gerry P McCann[22,39], Stefan Neubauer[40], Peter JM Openshaw[3], Dhruv Parekh[41], Paul Pfeffer[42], Krishnah Poinasamy[43], Joanna C Porter[9], Jennifer K Quint[44], Najib M Rahman[45], Betty Raman[46], Matthew Richardson[1], Sarah DM Rowland-Jones[47], Matthew J Rowland[48], Ruth M Saunders[1], Janet T Scott[49], Malcolm G Semple[50], Marco Sereno[1], Ajay M Shah[33], Aziz Sheikh[16], Aarti Shikotra[1], Ananga Singapuri[1], Maxime Taquet[51], David Thomas[52], Roger Thompson[47], Mathew Thorpe[16], Mark Toshner[53], Lin Wang[1], Dan G Wootton[54], Bang Zheng[10], Louise V Wain[21,22], Christopher E Brightling[1], Sally J Singh[1], Rod S Taylor[55], Rachael A Evans[1,*], On behalf of the PHOSP-COVID study Collaborative Group

[1] *The Institute for Lung Health, NIHR Leicester Biomedical Research Centre Respiratory, University of Leicester, Leicester, UK*
[2] *Patient Advisory Group, Leicester, UK*
[3] *National Heart and Lung Institute, Imperial College London, London, UK*
[4] *St Georges University Hospitals NHS Foundation Trust, London, UK*
[5] *Manchester Metropolitan University, Manchester, UK*
[6] *The Leeds Teaching Hospitals NHS Trust, Leeds, UK*
[7] *NIHR Nottingham Biomedical Research Centre, Nottingham, UK*
[8] *Centre for Respiratory Research, Translational Medical Sciences, School of Medicine, University of Nottingham, Nottingham, UK*
[9] *UCL Respiratory, Division of Medicine, University College London Medical School, Rayne Institute, London, UK*
[10] *London School of Hygiene & Tropical Medicine, London, UK*
[11] *Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, Kings College London, London, UK*
[12] *University of Dundee, Ninewells Hospital and Medical School, Dundee, UK*
[13] *University of Edinburgh, Edinburgh, UK*
[14] *Diabetes Research Centre, University of Leicester, Leicester, UK*
[15] *Population Health Sciences Institute, Newcastle University, Newcastle Upon Tyne, UK*
[16] *The Usher Institute, University of Edinburgh, Edinburgh, UK*
[17] *Infection Research Group, Hull University Teaching Hospitals, Hull, UK*
[18] *The Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK*
[19] *Department of Respiratory Medicine, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK*
[20] *NIHR Oxford Health Biomedical Research Centre, University of Oxford, Oxford, UK*
[21] *Division of Public Health and Epidemiology, School of Medical Sciences, University of Leicester, Leicester, UK*

* **Corresponding author:** Tel.: 0116 2583663.
E-mail address: re66@leicester.ac.uk (R.A. Evans).

https://doi.org/10.1016/j.ijid.2026.108695

[22] NIHR Leicester Biomedical Research Centre, Leicester, UK
[23] University of Liverpool, Liverpool, UK
[24] Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain
[25] Lane Fox Clinical Respiratory Physiology Research Centre, Guy's and St Thomas' Hospital, London, UK
[26] Wellcome-Wolfson Institute for Experimental Medicine, Queens University Belfast, Belfast, UK
[27] Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK
[28] MRC Human Immunology Unit, University of Oxford, Oxford, UK
[29] NIHR Manchester Biomedical Research Centre, Division of Infection, Immunity & Respiratory Medicine, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK
[30] Imperial College Healthcare NHS Trust, London, UK
[31] University College London, London, UK
[32] UCL Hawkes Institute, University College London, London, UK; UCL Respiratory, University College London, London, UK
[33] Kings College London, London, UK
[34] Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, UK
[35] Roslin Institute, University of Edinburgh, Edinburgh, UK
[36] Hywel Dda University Health Board
[37] MRC-Versus Arthritis Centre for Musculoskeletal Ageing Research, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK
[38] Royal Brompton and Harefield Clinical Group, Guys and St Thomas NHS Foundation Trust, London, UK
[39] Department of Cardiovascular Sciences, University of Leicester, Leicester, UK; NIHR Leicester Biomedical Research Centre
[40] Division of Cardiovascular Medicine, Radcliffe Department of Medicine, University of Oxford, Oxford, UK
[41] University of Birmingham, Birmingham, UK
[42] Barts Health NHS Trust, London, UK
[43] Asthma and Lung UK, London, UK
[44] School of Public Health, Imperial College London, London, UK
[45] Oxford University Hospitals NHS Trust, Oxford, UK
[46] Radcliffe Department of Medicine, University of Oxford, Oxford, UK
[47] University of Sheffield, Sheffield, UK
[48] Kadoorie Centre for Critical Care Research, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK
[49] MRC-University of Glasgow Centre for Virus Research, Glasgow, UK
[50] NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, UK
[51] Department of Psychiatry, University of Oxford, Oxford, UK
[52] Imperial College London, London, UK
[53] VPD Heart and Lung Research Institute, Department of Medicine, University of Cambridge, Cambridge, UK
[54] Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, Liverpool, UK
[55] School of Health & Wellbeing, University of Glasgow, Glasgow, UK

ARTICLE INFO

Article history:
Received 16 December 2025
Revised 7 April 2026
Accepted 8 April 2026

Keywords:
COVID-19
Long COVID
Multiple long-term conditions
Multimorbidity

ABSTRACT

Background: Preexisting multiple (two or more) long-term conditions (MLTCs) may negatively affect recovery after COVID-19. We investigated how preexisting MLTCs, including different categorization and patterns of MLTCs, affect 1-year health outcomes after severe COVID-19.
Methods: Adults post-hospitalization after COVID-19 were recruited during 2020-2021. We compared recovery at 1 year after discharge using adjusted multivariable logistic regression in 1:1 propensity-matched adults (for age, sex, ethnicity, social deprivation, obesity, and smoking history) with and without preexisting MLTCs. In adults with MLTCs, different categorization such as number of conditions, number and types of body systems involved (e.g. respiratory, cardiovascular), and latent class analysis–derived patterns of condition co-occurrence were assessed for their association with recovery at 1 year.
Results: A total of 647 adults with MLTCs were matched with 647 adults without MLTCs (n = 1294; 61.9% male, 79.6% of White ethnicity, median age 59 [interquartile range 52-67] years). The presence of MLTCs was associated with lower odds of feeling fully recovered (odds ratio 0.66 [95% confidence interval 0.51-0.85], $P = 0.001$). In those with MLTCs, recovery was negatively affected by number and type of body systems involved (e.g. respiratory [odds ratio 0.49 (95% confidence interval 0.34-0.69), $P < 0.001$]) but not by the number of conditions ($P > 0.1$). Four latent classes of MLTC co-occurrence were estimated with different risks of recovery ($P < 0.01$).
Conclusion: Adults with preexisting MLTCs were 34% less likely to feel fully recovered at 1 year after COVID-19 hospitalization than adults without MLTCs. We describe prognostic classifications of MLTCs, with future work needed to understand whether they have prognostication in broader post-acute infection sequalae.

Introduction

Although most people survive COVID-19, some individuals develop persistent symptoms beyond 12 weeks post-infection [1]. The overall global prevalence of "long COVID" [2] has been estimated to be 36% and 44% within hospitalized individuals [3]. Given the significant global health and economic impacts associated with long COVID [4], understanding factors that influence recovery is a priority. Risk factors associated with the development of long COVID in hospitalized and non-hospitalized cohorts include female sex, obesity, belonging to an ethnic minority [5], and having a preexisting long-term condition (LTC) [3,5,6]. Specifically, the presence of single preexisting LTCs including diabetes, airways disease, or cardiovascular disease are associated with worse health outcomes 1 year after COVID-19 hospitalization [7–9]. However, the impact of multiple (two or more [10]) LTCs (MLTCs) is not well understood. Given the prevalence of MLTCs, it is important to understand how

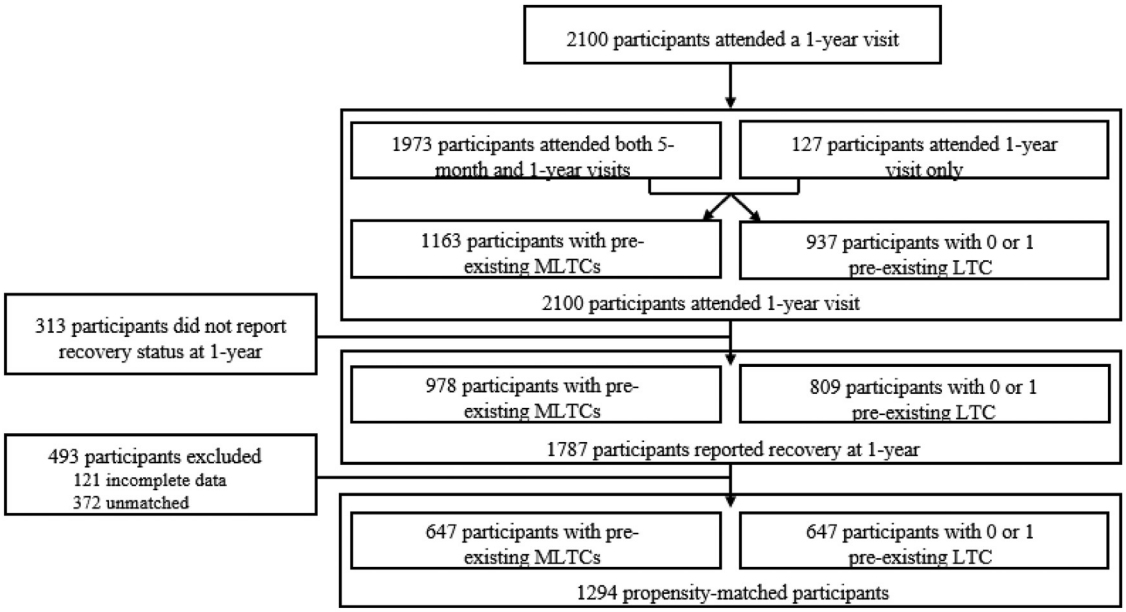


Figure 1. Consort filtering flowchart.

preexisting MLTCs may influence the development and severity of long COVID.

We know that over one in three adults overall and more than half over the age of 60 years are estimated to be living with MLTCs worldwide [11]. Living with MLTCs represents a significant burden to the individual, their support network, health care systems, and broader society, particularly, in disadvantaged communities and settings [10]. Beyond aging, intersectional risk factors associated with MLTCs include ethnicity, social deprivation, and lifestyle factors such as smoking, physical inactivity, and obesity [12–14]. Early in the COVID-19 pandemic, it was recognized that adults with MLTCs were more susceptible to severe COVID-19, hospitalization, and death [15]. Compared with those without MLTCs, adults with MLTCs are more likely to not feel fully recovered and have multiorgan abnormalities 6 months after COVID-19 hospitalization [16,17]. Furthering our understanding of underlying mechanisms that drive symptoms and/or organ impairment associated with long COVID was identified as a research priority by patients and clinicians [18] and it is recognized that specific underlying LTCs/MLTCs may exacerbate pathological mechanisms or reduce an individual's tolerance to organ injury associated with COVID-19 and post-acute sequalae [19].

Although the co-existence of two or more LTCs is a widely accepted definition of MLTCs [20], there is variability in what are considered qualifying LTCs [21,22]. The concept of "complex" MLTCs has been proposed in response to criticism of the "two or more LTCs" definition not differentiating the range of impact associated between different LTCs [10]. Various definitions have been proposed including increasing number of LTCs, involvement of multiple body systems, and the co-existence of mental and physical conditions [23]. However, consensus has not been established to date, in part, due to a paucity of evidence demonstrating the added value of nuanced classifications [20]. A growing body of work has explored groupings/clusters of LTCs, highlighting that certain condition combinations may confer distinct patterns of risk and impact [10,24–27]. Meaningful categorization of MLTCs may have the potential to facilitate targeted care to the those with the most need.

Furthering understanding of the development and severity of long COVID according to the presence and different phenotypes of MLTCs has the potential to provide insight into the underlying mechanisms causing long COVID (a patient priority question [18]) and be used to extend definitions of complex MLTCs. The post-hospitalization COVID-19 (PHOSP-COVID) study prospectively sought to investigate the relationship between patterns of preexisting LTCs and post–COVID-19 sequalae (ISRCTN10980107).

We, therefore, aimed to answer the following questions in adults 1 year after hospital discharge with COVID-19: (i) Are adults with preexisting MLTCs less likely to feel recovered with worse health and well-being outcomes than adults without preexisting MLTCs? (ii) Are there differences in recovery at 1 year according to how MLTCs are categorized (e.g. number or type of LTCs, body systems involved), including how certain LTCs group together?

Methods

The methods, analysis, and results are reported in line with Strengthening the Reporting of Observational Studies in Epidemiology guidelines [28].

Study design and participants

Recruitment to the PHOSP-COVID prospective longitudinal cohort study has been described previously [29]. In summary, adults (aged ≥18 years) discharged before March 31, 2021 from one of 39 National Health Service (NHS) hospitals across the four UK nations after admission to a medical assessment unit or ward with confirmed or clinician-diagnosed COVID-19 were included.

In accordance with the study objectives, the analyses included the subset of surviving PHOSP-COVID participants who attended a 1-year (between 10 and 14 months) study visit post-discharge (Figure 1). Participants were dichotomized into two groups based on the presence of preexisting MLTCs: (i) those with two or more LTCs (MLTCs group) and (ii) those with one or no LTCs (no MLTCs group). The study population was limited to participants with primary outcome (patient-perceived recovery at 1 year) data for the

primary analyses and the MLTCs group for the exploratory analyses of MLTCs. LTCs were collected from medical health care records reflecting the time of hospital admission. All 40 preexisting LTCs reported by PHOSP-COVID (full list available in Supplement S1) were considered qualifying LTCs informed by an international Delphi consensus study (on the definition and measurement of MLTCs in research) [20] and expert opinion. With recognition of equipoise regarding the status of obesity as a LTC vs a risk factor, obesity was not considered a qualifying LTC in accordance with the Delphi consensus and commonly used weighted MLTCs measures [20,22,30].

Ethics

Written informed consent was obtained from all study participants. The study was approved by the Leeds West Research Ethics Committee (20/YH/0225) and is registered on the ISRCTN Registry (ISRCTN10980107).

Outcome measures

The primary outcome was patient-perceived recovery (patient responses to the question "Do you feel fully recovered?" treated as a binary outcome "Yes" and "No" [grouping "No" and "Unsure" responses]) at 1 year after COVID-19 hospitalization in individuals with preexisting MLTC compared with those without, reported as an odds ratio (OR) with 95% confidence interval (CI).

Secondary outcome measures included symptoms (count and severity) and various measures of physical, mental, cognitive health, and social isolation at 1 year post-hospitalization (full list and details in Supplement S2). Physical health measures included exercise tolerance/functional capacity (e.g. incremental shuttle walk test, handgrip strength), disability measured by the Washington group short set on functioning, and frailty measured by the Rockwood clinical frailty score (RCF). Anxiety, depression, and post-traumatic stress disorder were measured by patient-reported questionnaires (e.g. patient health questionnaire). Cognitive impairment was measured by the Montreal cognitive assessment. Health-related quality of life (HRQoL) was measured by the five-level EuroQol five-dimensional questionnaire.

Statistical analysis

Continuous and categorical variables were descriptively summarized using means (SD) or medians (interquartile range [IQR]) and frequencies and percentages, respectively. Missing data were reported for each variable. A χ^2 test was used to identify differences in proportions within categorical variables. Differences in continuous variables were identified using an independent Student's *t*-test or Mann–Whitney U test. Normality was assessed using a Shapiro–Wilk test and visual inspection for each variable. Complete-case analysis was used for all analyses, based on the relevant variables included within the statistical models. Statistical significance was set at probability value (*P*-value) of less than 5%.

Sample size calculations were performed prospectively based on respective event rates for recovery in the PHOSP-COVID cohort. We subsequently checked and confirmed that the sample size of our propensity-matched population of 1294 participants was adequate to detect a recovery event (based on patient-perceived recovery after COVID-19 hospitalization), with 80% power at 5% significance level, using two independent data sets (Supplement S3) [31,32].

Participants were dichotomized into two groups based on the presence of preexisting MLTCs: (i) those with two or more LTCs (MLTCs group) and (ii) those with one or no LTCs (no MLTCs group).

Propensity score matching analyses

Propensity score matching of groups (MLTCs vs no MLTCs) was used to reduce the effects of selection bias and confounding. A directed acyclic graph (DAG) was constructed to identify confounders associated with the presence of MLTCs using existing evidence of relationships (including age, sex, ethnicity, index of multiple deprivation [IMD], obesity, and smoking history [12–14]) (Supplement S4a). A multivariable logistic regression model (adjusting for age, sex, ethnicity, IMD, obesity, and smoking history) was used to calculate a propensity score for each participant with complete data within the study population. Participants with preexisting MLTCs were then matched 1:1 to a participant without preexisting MLTCs, with a similar propensity score using a nearest neighbor matching algorithm and a pre-specified maximum difference in propensity score (caliper width) of 0.2 SDs. Balance in covariates between groups were assessed using standardized mean difference and variance ratio of covariates.

Patient-perceived recovery at 1 year post-hospitalization was modeled in the propensity-matched sample using multivariable logistic regression with adjustment by predefined covariates (age, sex, ethnicity, IMD, obesity, smoking history, severity of acute illness, and duration of admission [a DAG visual representation of potential confounders for the effect of MLTCs presence on recovery at 1 year is presented in Supplement S4b]) in the complete-case data set. Adjusted multivariable generalized linear (including logistic, multinomial, and linear) and beta regression models were also used to explore secondary outcome measures at 1 year post-hospitalization. Logistic and linear models were used for binary and continuous outcomes respectively (e.g. RCF $\geq$5 yes/no and handgrip strength [kilogram]). Linear, multinomial, and beta models were explored (as appropriate) for discrete/ordinal (generalized anxiety disorder-7 questionnaire [0-21]). Final model selection was informed by the Bayesian information criterion (BIC), with appropriate assumptions checked, including linearity (where applicable) and collinearity.

Exploratory analyses of MLTCs

Multivariable logistic regression was used to model the primary outcome according to MLTCs categorization (complex MLTCs definitions), such as the number and type of LTCs (description of the organ/body system involved), number of body systems involved, and the presence of physical and mental health LTCs (within those with MLTCs and complete primary outcome and covariate data).

Latent class and co-occurrence analyses

To understand whether meaningful groups of patients (phenotypes) could be described by how LTCs group together, latent class analysis (LCA) was used in all participants with MLTCs with complete LTC data who attended a 1-year visit (Figure 1), following the guide provided in Weller *et al.* (2020) [33]. A succession of LCA models were explored with 1:30 classes based on the presence of preexisting LTCs. LCA model selection was guided by statistical criteria (Akaike information criterion [AIC], consistent AIC [CAIC], AIC with penalty factor of 3 [AIC3], BIC, sample-adjusted BIC [SABIC], log likelihood, and entropy) to narrow down the best fitted models and clinical interpretation of the model outcome for final selection. Participants were assigned to one class based on their respective posterior probabilities and naming of classes was based on a set of rules based on between- and within-class prevalence of LTCs (full details are provided in Supplement S5). Multivariable logistic regression (adjusted for age, sex, ethnicity, IMD, obesity, severity of acute illness, and duration of admission) was

used to model recovery at 1 year post-hospitalization according to LTC classes derived from LCA using complete-case data. Network analysis was implemented to determine relationships of pair co-occurrence among the LTCs and frequent itemset mining for evaluation of co-occurrence of more than two LTCs.

R (version 2023.12.1, R Foundation for Statistical Computing) was used (with packages *tidyverse, dplyr, ggplot2, matchit, betareg, nnet, performance, lmtest, sandwich, rms, finalfit, car,* and *poLCA*) for the statistical analyses.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Patient and public involvement

This study was informed by research priorities identified by patients and clinicians [18]. A patient advisory group comprising seven individuals living with preexisting MLTCs and long COVID were involved in the design, reporting, and dissemination of this research. Two members (N.S. and J.E.) were involved in interpretation of the analyses and reviewing the manuscript.

Results

Of 2100 participants, a total of 1787 had primary outcome data, 978 (54.7%) of whom had preexisting MLTCs (Figure 1; Supplement S6). Before matching, the MLTCs group were older, less diverse in ethnicity, more deprived, more likely to be obese, and had more participants with a smoking history than the non-MLTCs group (Table 1).

Of the 978 participants with MLTCs and primary outcome (patient-perceived recovery at 1 year) data (Figure 1), the majority had two to four preexisting LTCs (76.4%) involving one to three body systems (89.8%) (Supplement S11). Cardiovascular was the most prevalent LTC type (72.4%) and the median Charlson comorbidity index score [30] of this cohort was 3 (IQR 2-4) (associated with an estimated 10-year survival rate of 77%).

Are adults with preexisting MLTCs less likely to feel recovered with worse health and well-being outcomes than adults without preexisting MLTCs?

A total of 647 participants with preexisting MLTCs were matched 1:1 with 647 participants without MLTCs, with no significant difference in age group, ethnicity, deprivation, presence of obesity, and smoking history (details of the matching process are listed in Supplement S7 and S8). The propensity score–matched population (n = 1294) had a median age of 59 (IQR 52-67) years, 61.9% were male, 79.6% of White British ethnicity, median admission duration of 8 (IQR 4-16) days, and 19.3% were intubated and mechanically ventilated during their admission.

Compared with adults without MLTCs, adults with MLTCs were 34% (OR 0.66 [95% CI 0.51-0.85], $P = 0.0013$) less likely to feel fully recovered at 1 year post-discharge (Figure 2; Supplement S9). Physical, mental, and cognitive health outcomes at 1 year were also worse in adults with MLTCs than in those without (Table 2; Supplement S10). In addition to health outcomes, adults with MLTCs were more likely to frequently feel lonely (OR 0.46 [95% CI 0.30-0.68], $P = 0.0002$) and isolated at 1 year (OR 0.52 [95% CI 0.35-0.76], $P = 0.0010$).

Are there differences in recovery at 1 year according to how MLTCs are categorized (e.g. number or type of LTCs, body systems involved) including how certain LTCs group together?

Of the 978 participants with MLTCs, 922 had complete data relevant to the regression analyses of the primary outcome (i.e. complete data for age, sex, ethnicity, IMD, severity of acute illness, duration of admission, obesity, and smoking history). Patient-perceived recovery at 1 year was associated with type of LTCs and number of body systems involved but not with increasing number of LTCs beyond two (Table 3; Supplement S10). Within participants with MLTCs, recovery was negatively associated with multiple body systems involved (two or more) and the co-existence of mental and physical health LTCs (Table 3). Worse outcomes in adults with multiple body system involvement or co-existent mental and physical health LTCs were also reflected across a range of physical and mental health outcomes at 1 year post-hospitalization (Supplement S13), including HRQoL and feeling isolated.

A total of 1139 of 1163 (97.9%) participants with MLTCs and complete LTC data were included in the LCA to identify MLTCs classes based on the presence of frequently co-occurring preexisting LTCs. According to information criterion measures, AIC indicated 11 classes, CAIC 3 classes, AIC3 5 classes, BIC 3 classes, and SABIC 4 classes selection (a comparison of criteria and models are provided in Supplement S14a). For each of these, entropy, class sizes, posterior probabilities of class members, and clinical meaning were evaluated (Supplement S14b-d). Four MLTCs classes were identified: coronary heart disease (n = 90), depression/anxiety and asthma (n = 345), cardiovascular risk factors (n = 662), and no dominant, numerous conditions (n = 42) (Supplement S15). Overall, combinations among hypertension, hypercholesterolemia, and diabetes were the most frequently co-occurring LTCs (Supplement S16a-b).

The coronary heart disease class was primarily characterized by high prevalence of preexisting myocardial infarction and ischemic heart disease (Figure 3a). Compared with the other classes, members of this class were older (median 66.5 [IQR 60.0-74.8] years), predominantly male (86.7%), and of White ethnicity (85.6%) (Supplement S17a). Despite the relatively small size (<10% of the LCA cohort), this class had a high prevalence of myocardial infarction and a high proportion of the total of participants (85%) with this condition (Figure 3a, b). Members of the depression/anxiety and asthma class were younger (median 57.0 [IQR 49.0-64.0] years), predominantly females (57.4%), and of White ethnicity (87.8%). The cardiovascular risk factors class was primarily characterized by high prevalence of preexisting hypertension, hypercholesterolemia, and diabetes. Although male sex (67.1%) and White ethnicity were predominant (73.2%), this class had the highest proportion of adults of Black (10.4%) and South Asian ethnicity (10.3%). The no dominant, numerous conditions class had no dominant LTCs or demographic characteristics; however, notably, members have the highest number of LTCs (median 9 [IQR 7-10]) and body systems involved (median 4 [IQR 4-5]). Further details regarding class characterization are provided in Supplement S17.

There was a difference in patient-perceived recovery at 1 year across classes ($P = 0.0016$). Compared with the cardiovascular risk factors class, members of the depression/anxiety and asthma class were less likely to report full recovery at 1 year post-discharge (OR 0.64 [95% CI 0.42-0.96], $P = 0.035$) (Figure 4). A limited range of physical and mental health outcomes were worse in the depression/anxiety class than in the cardiovascular risk factors class, including HRQoL and feeling isolated. The no dominant, numerous conditions class was associated with a broader range of worse secondary outcomes, including additional physical measures and symptom severity (Supplement S18).

Table 1
Baseline characteristics of propensity score–matched population (n = 1294).

		Matched population *n = 1294*		No MLTCs group *n = 647*		MLTCs group *n = 647*		Standardized mean difference post-propensity score matching	*P*-value (χ^2 or Mann–Whitney U test)
		N	%	n	%	N	%		
Median age (years)		59 (52-67)		58 (50-66)		59 (53-67)			0.015
Age group[a] (years)	<30	16	1.2	10	1.5	6	0.9	0.044	0.38
	30-39	57	4.4	32	4.9	25	3.9	0.039	
	40-49	191	14.8	106	16.4	85	13.1	0.087	
	50-59	411	31.8	201	31.1	210	32.5	−0.030	
	60-69	397	30.7	190	29.4	207	32.0	−0.060	
	70-79	202	15.6	96	14.8	106	16.4	−0.046	
	80+	20	1.5	12	1.9	8	1.2	0.049	
Sex[a]	Female	493	38.1	260	40.2	233	36.0	0.086	0.14
	Male	801	61.9	387	59.8	414	64.0	−0.086	
Gender	Female	485	37.5	256	39.6	229	35.4		0.25
	Male	772	59.7	373	57.7	339	52.4		
	Intersex, non-binary or prefer not to say	11	0.9	..	..	..	..		
	Missing values	26	2.0	13	2.0	73	11.3		
Ethnicity[a]	Black	69	5.3	39	6.0	30	4.6	0.058	0.52
	Mixed	27	2.1	15	2.3	12	1.9	0.029	
	Other	53	4.1	30	4.6	23	3.6	0.051	
	South Asian	115	8.9	60	9.3	55	8.5	0.026	
	White	1030	79.6	503	77.7	527	81.5	−0.087	
Disability	Yes	254	19.6	80	12.4	174	26.9		<0.0001
	No	929	71.8	512	79.1	417	64.5		
	Prefer not to say	48	3.7	19	2.9	6	0.9		
	Missing values	63	4.9	36	5.6	50	7.7		
Index of multiple deprivation quintile[a]	1 - most deprived	284	21.9	144	22.3	140	21.6	0.015	0.90
	2	260	20.1	136	21.0	124	19.2	0.046	
	3	243	18.8	119	18.4	124	19.2	−0.020	
	4	245	18.9	118	18.2	127	19.6	−0.036	
	5 - least deprived	262	20.2	130	20.1	132	20.4	−0.008	
Pre-COVID employment status	Full-time employment	456	35.2	258	39.9	198	30.6		<0.0001
	Part-time employment	100	7.7	51	7.9	49	7.6		
	Caring for an adult or children, or in education	19	1.5	8	1.2	11	1.7		
	Unemployed	38	2.9	11	1.7	27	4.2		
	Off sick	38	2.9	14	2.2	24	3.7		
	Retired	219	16.9	89	13.8	130	20.1		
	Missing values	424	32.8	216	33.4	208	32.1		
Caring responsibilities	None	905	69.9	448	69.2	457	70.6		0.48
	Primary carer of a child/children (<18)	154	11.9	86	13.3	68	10.5		
	Primary carer of a disabled child/children	11	0.9	..	..	..	..		
	Primary carer or assistant for an older person/people (>65)	46	3.6	24	3.7	22	3.4		
	Primary carer or assistant of a disabled adult (>18)	36	2.8	13	2.0	23	3.6		
	Secondary carer (another person carries out main caring role)	48	3.7	22	3.4	26	4.0		
	Prefer not to say	37	2.9	19	2.9	18	2.8		
	Missing values	57	4.4	29	4.5	28	4.3		
Living arrangements	Spouse/partner	833	64.4	416	64.3	417	64.5		0.94
	Children 0-16 years	51	3.9	30	4.6	21	3.2		
	Own/partner's children >16 years	62	4.8	31	4.8	31	4.8		
	Own/partner's parents	13	1.0	7	1.1	6	0.9		
	Other adult relatives	50	3.9	23	3.6	27	4.2		
	Other non-related adults	15	1.2	8	1.2	7	1.1		
	Prefer not to say	70	5.4	37	5.7	33	5.1		
	Missing values	200	15.5	95	14.7	105	16.2		
Median body mass index		31.2 (27.8-36.1)		30.9 (27.8-35.1)		31.5 (27.9-37.1)			
Obesity[a]	<30 kg/m^2	526	40.6	266	41.1	260	40.2	0.019	0.024
	>30 kg/m^2	768	59.4	381	58.9	387	59.8	−0.019	0.78
Smoking[a]	Current	19	1.5	11	1.7	8	1.2	0.037	
	Ex	543	42.0	268	41.4	275	42.5	−0.022	0.75
	Never	732	56.6	368	56.9	364	56.3	0.013	
Severity of acute illness (WHO clinical progression scale)	WHO Class 3-4	195	15.1	100	15.5	95	14.7		
	WHO Class 5	552	42.7	273	42.2	279	43.1		0.58
	WHO Class 6	297	23.0	141	21.8	156	24.1		
	WHO Class 7-9	250	19.3	133	20.6	117	18.1		
Admission duration (days)		8 (4-16)		8 (4-17)		8 (4-15)			0.44

Data are presented as n (%) or median (interquartile range). Values are omitted where >0 and ≤5 for data protection purposes, denoted by "‥"
[a] Propensity matching factors.MLTCs, multiple long-term conditions; WHO, World Health Organization.

Table 2
Outcomes at 1 year in propensity score–matched population (n = 1294).

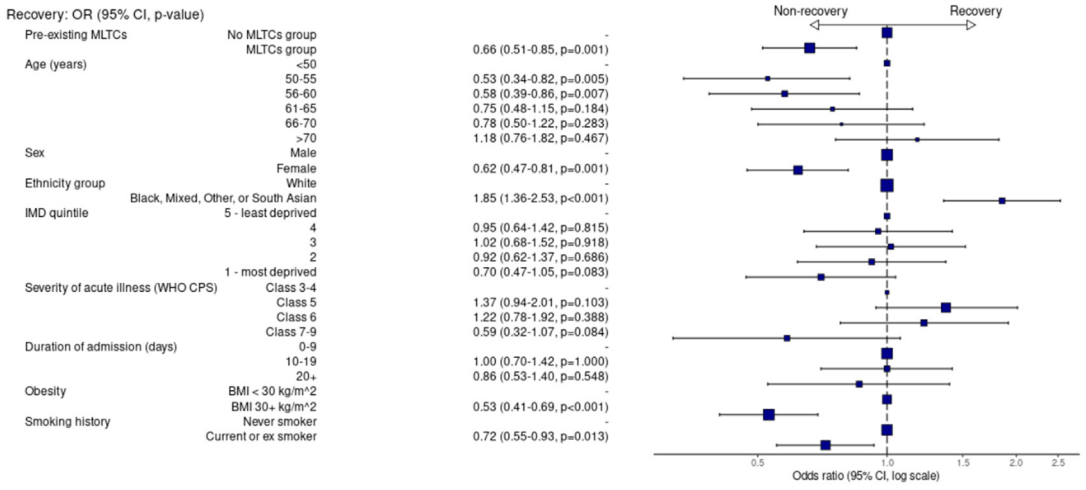
			Matched population *n = 1294*		No MLTCs group *n = 647*		**MLTCs group** *n = 647*		***P*-value**[a]
			n	%	n	%	**n**	**%**	
Recovery	Patient-perceived recovery	Recovered	392	30.3	221	34.2	171	26.4	0.0030
		Not recovered	902	69.7	426	65.8	476	73.6	
Frailty	RCF score	1 – Very fit	157	12.1	95	14.7	62	9.6	<0.0001
		2 – Well	387	29.9	256	39.6	131	20.2	
		3 – Managing well	421	32.5	169	26.1	252	38.9	
		4 – Vulnerable	166	12.8	51	7.9	115	17.8	
		5 – Mildly frail	29	2.2	7	1.1	22	3.4	
		6/7 – Moderately or severely frail	20	1.5	..	..	..	..	
		8/9 – Very severely frail or terminally ill	0	0.0	0	0.0	0	0.0	
	RCF summary	≥5 Yes (frail)	49	3.8	11	1.7	38	5.9	0.00022
		≥5 No (not frail)	1131	87.4	571	88.3	560	86.6	
		Missing values	114	8.8	65	10.0	49	7.6	
HRQoL	EQ-5D-5L – UI	Median post-hospitalization	0.77 (0.62-0.88)		0.8 (0.68-1.00)		0.72 (0.54-0.84)		<0.0001
		Missing values	133	10.3	68	10.5	65	10.0	
	EQ-5D-5L – VAS	Median post-hospitalization	75 (60-88)		80 (65-90)		70 (50-80)		<0.0001
		Missing values	144	11.1	72	11.1	72	11.1	
Symptoms	Symptom count	Median	9 (4-16)		7 (3-15)		11 (5-19)		<0.0001
		Missing values	0	0	0	0	0	0	
Breathlessness	Severity (0-10)	Median	2 (0-5)		2 (0-4)		2 (1-5)		<0.0001
		Missing values	28	2.2	13	2.0	15	2.3	
	Dyspnea-12	Median score	2 (0-7)		1 (0-5)		3 (0-10)		<0.0001
		Missing values	94	7.3	50	7.7	44	6.8	
Cough	Severity (0-10)	Median	0 (0-2)		0 (0-2)		0 (0-2.25)		0.00038
		Missing values	32	2.5	17	2.6	15.0	2.3	
Fatigue	Severity (0-10)	Median	3 (1-6)		2 (0-5)		4 (1-7)		<0.0001
		Missing values	30	2.3	15	2.3	15	2.3	
	Functional assessment of chronic illness therapy – Fatigue scale	Median summary score	39 (27-46)		42 (32-48)		36 (22.75-44)		<0.0001
		Missing values	92	7.1	49	7.6	43	6.6	
Poor sleep	Severity (0-10)	Median	3 (0-6)		2 (0-5)		4 (1-6)		<0.0001
		Missing values	30	2.3	15	2.3	15	2.3	
Pain	Severity (0-10)	Median	1 (0-5)		1 (0-4)		2 (0-6)		<0.0001
		Missing values	34	2.6	16	2.5	40	6.2	
	Questionnaires – brief pain inventory	Median - Severity	12 (4-20)		10 (2-18)		14 (5-22)		<0.0001
		Missing values	309	23.9	171	26.4	138	21.3	
		Median - Interference	14 (1-33)		10 (0-26)		17 (3-39)		<0.0001
		Missing values	345	26.7	192	29.7	153	23.6	
Functional capacity	Walk test	Median ISWT distance (m) (n = 771)	420 (280-590)		450 (330-650)		360 (240-550)		<0.0001
		Missing values	131/771		54/771		77/771		
		Median ISWT level	7 (6-9)		8 (6-9)		7 (5-9)		<0.0001
		Missing values	136/771		56/771		80/771		
	Short physical performance battery	Median total score	11 (9-12)		11 (9-12)		10 (9-12)		<0.0001
		≥10 Yes	537	41.5	234	36.2	303	46.8	<0.0001
		≥10 No	607	46.9	340	52.6	267	41.3	
		Missing values	150	11.6	73	11.3	77	11.9	
	Muscle strength	Median handgrip strength (kg)	32 (23.7-41.6)		32.6 (24.5-42.2)		31 (22.4-40.5)		0.014
		Missing values	133	10.3	64	9.9	69	10.7	
		Median quadriceps strength (kg)	22.7 (17.3-31)		23.4 (17-30.3)		22.4 (17.4-31.3)		0.80
		Missing values	1133	87.6	561	86.7	572	88.4	
	Nottingham extended activities of daily living scale	Median total score	20 (18-22)		21 (19-22)		20 (16-22)		<0.0001
		Missing values	106	8.2	52	8.0	54	8.3	
	General practice physical activity questionnaire	Median physical activity index	2 (1-3)		2 (1-3)		1 (1-3)		<0.0001
		Missing values	117	9.0	65	10.0	52	8.0	
		Median exercise score	0 (0-2)		0 (0-2)		0 (0-1)		0.87
		Missing values	111	8.6	61	9.4	50	7.7	
		Median occupation score	1 (1-2)		1 (1-2)		1 (1-1)		<0.0001
		Missing values	102	7.9	55	8.5	47	7.3	
Disability	WG-SS - Disability	Yes	254	19.6	92	14.2	162	25.0	<0.0001
		No	1034	79.9	552	85.3	482	74.5	
		Missing values	6	0.5	..	..	..	..	
	WG-SS – New disability	Yes	69	5.3	25	3.9	44	6.8	0.071
		No	274	21.2	135	20.9	139	21.5	
		Missing values	951	73.5	487	75.3	464	71.7	

(*continued on next page*)

Table 2 (*continued*)

			Matched population *n = 1294*		No MLTCs group *n = 647*		**MLTCs group** *n = 647*		***P*-value**[a]
			n	%	n	%	**n**	**%**	
Mental Health	Anxiety – Generalized anxiety disorder questionnaire-7	Median summary score	3 (0-8)		2 (0-7)		4 (0-10)		<0.0001
		>8 Yes	284	21.9	114	17.6	170	26.3	0.00030
		>8 No	925	71.5	487	75.3	438	67.7	
		Missing values	85	6.6	46	7.1	39	6.0	
	Depression – Patient health questionnaire-9	Median summary score	4 (1-10)		3 (1-8)		5 (2-12)		<0.0001
		≥10 Yes	311	24.0	118	18.2	193	29.8	<0.0001
		≥10 No	895	69.2	481	74.3	414	64.0	
		Missing values	88	6.8	48	7.4	40	6.2	
	Post-traumatic stress disorder checklist for DSM -5	Median total score	7 (2-21)		6 (1-15.75)		9 (3-26)		<0.0001
		≥37 Yes	134	10.4	39	6.0	95	14.7	<0.0001
		≥37 No	1070	82.7	559	86.4	511	79.0	
		Missing values	90	7.0	49	7.6	41	6.3	
Cognitive	Cognitive impairment – Montreal cognitive assessment	Median total score	27 (25-29)		27 (26-29)		27 (25-28)		<0.0001
		Median total corrected score	28 (26-29)		28 (26-29)		27 (25-29)		0.00046
		<23 Yes	99	7.7	37	5.7	62	9.6	0.012
		<23 No	944	73.0	484	74.8	460	71.1	
		Corrected – Yes	88	6.8	34	5.3	54	8.3	0.035
		Corrected – No	955	73.8	487	75.3	468	72.3	
		Missing values	251	19.4	126	19.5	125	19.3	
Other	Occupation status	Full-time employment	461	35.6	271	41.9	190	29.4	<0.0001
		Part-time employment	170	13.1	94	14.5	76	11.7	
		Caring for an adult or children, or in education	23	1.8	11	1.7	12	1.9	
		Unemployed	40	3.1	16	2.5	24	3.7	
		Off sick	99	7.7	29	4.5	70	10.8	
		Retired	305	23.6	132	20.4	173	26.7	
		Prefer not to say	8	0.6	..	..	..	..	
		Missing values	188	14.5	92	14.2	96	14.8	
	Loneliness	Often	117	9.0	40	6.2	77	11.9	<0.0001
		Some of the time	326	25.2	135	20.9	191	29.5	
		Hardly ever	817	63.1	454	70.2	363	56.1	
		Missing values	34	2.6	18	2.8	16	2.5	
	Isolation	Often	125	9.7	46	7.1	79	12.2	<0.0001
		Some of the time	302	23.3	118	18.2	184	28.4	
		Hardly ever	841	65.0	466	72.0	375	58.0	
		Missing values	26	2.0	17	2.6	9	1.4	

[a] χ^2 or Mann–Whitney U test.Data are presented as n (%) or median (interquartile range). Values are omitted where >0 and ≤5 for data protection purposes, denoted by "·.."EQ-5D-5L UI and VAS, EuroQol-5 dimensions-5 levels utility index and visual analog scale; ISWT, incremental shuttle walk test; MLTCs, multiple long-term conditions; RCF, Rockwood clinical frailty score; WG-SS, Washington group short set on functioning.



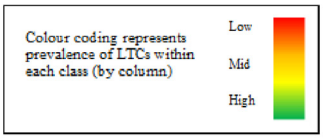
BMI = body mass index; CI = confidence interval; IMD = Index of Multiple Deprivation; LTC = long-term condition; MLTCs = multiple long-term conditions; OR = odds ratio; WHO CPS = World Health Organisation Clinical Progression Scale.

Figure 2. Patient-perceived recovery at 1 year post–hospital discharge.

Discussion

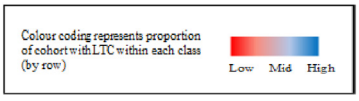
Adults with preexisting MLTCs were 34% less likely to report full recovery at 1 year after COVID-19 hospitalization than those without MLTCs (propensity-matched). Within those with MLTCs, having a preexisting respiratory, gastrointestinal, or neurologic/psychiatric LTC; two or more body system involvement; co-existing mental and physical health LTCs; or co-occurring depression/anxiety and asthma was associated with being less likely to report full recovery at 1 year. Conversely, those with an "endocrine/renal/metabolic" LTC were more likely to feel recovered. Prognostic classifications of preexisting MLTCs in the post–COVID-

(a) Prevalence of pre-existing long-term conditions within 1:4 classes heatmap



LTC	Class 1 (n=90)	Class 2 (n=345)	Class 3 (n=42)	Class 4 (n=662)
MI	0.844	0.014	0.119	0.005
IHD	0.667	0.014	0.190	0.065
AF	0.178	0.020	0.262	0.085
Hypertension	0.667	0.125	0.905	0.761
HCD	0.433	0.061	0.690	0.443
CVA or TIA	0.044	0.032	0.119	0.066
COPD	0.178	0.078	0.095	0.085
Asthma	0.022	0.388	0.310	0.177
OSA	0.022	0.096	0.524	0.063
GORD	0.211	0.272	0.357	0.092
RA	0.000	0.084	0.143	0.027
OA	0.022	0.243	0.619	0.127
Depression/anxiety	0.156	0.577	0.738	0.121
CFS/fibromyalgia/chronic pain	0.022	0.200	0.667	0.003
DM	0.256	0.087	0.524	0.512
Hypothyroidism	0.022	0.128	0.190	0.065
CKD	0.211	0.000	0.286	0.074
Cancer	0.033	0.035	0.048	0.077

(b) Proportion of cohort with long-term conditions within 1:4 classes heatmap



LTC	Class 1 (n=90)	Class 2 (n=345)	Class 3 (n=42)	Class 4 (n=662)
MI	0.854	0.056	0.056	0.034
IHD	0.517	0.043	0.069	0.371
AF	0.178	0.078	0.122	0.622
Hypertension	0.093	0.067	0.059	0.781
HCD	0.102	0.055	0.076	0.767
CVA or TIA	0.063	0.172	0.078	0.688
COPD	0.155	0.262	0.039	0.544
Asthma	0.008	0.504	0.049	0.440
OSA	0.020	0.333	0.222	0.424
GORD	0.101	0.497	0.079	0.323
RA	0.000	0.547	0.113	0.340
OA	0.010	0.429	0.133	0.429
Depression/anxiety	0.043	0.614	0.096	0.247
CFS/fibromyalgia/chronic pain	0.020	0.683	0.277	0.020
DM	0.056	0.072	0.053	0.819
Hypothyroidism	0.021	0.454	0.082	0.443
CKD	0.238	0.000	0.150	0.613
Cancer	0.044	0.176	0.029	0.750

AF = atrial fibrillation; CFS = chronic fatigue syndrome; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CVA or TIA = cerebrovascular accident or transient ischaemic attack; DM = diabetes mellitus; GORD = gastro-oesophageal reflux disease; HCD = hypercholesterolaemia; HTN = hypertension; IHD = ischaemic heart disease; LTC = long-term condition; MI = myocardial infarction; OA = osteoarthritis; OSA = obstructive sleep apnoea; RA = rheumatoid arthritis.

Figure 3. Latent class and co-occurrence analyses: (a) prevalence of preexisting long-term conditions within 1:4 classes heatmap, (b) proportion of cohort with long-term conditions within 1:4 classes heatmap, (c) frequent itemset mining.

(c) Frequent itemset mining: UpSet plots showing co-occurrence of long-term conditions in individual classes

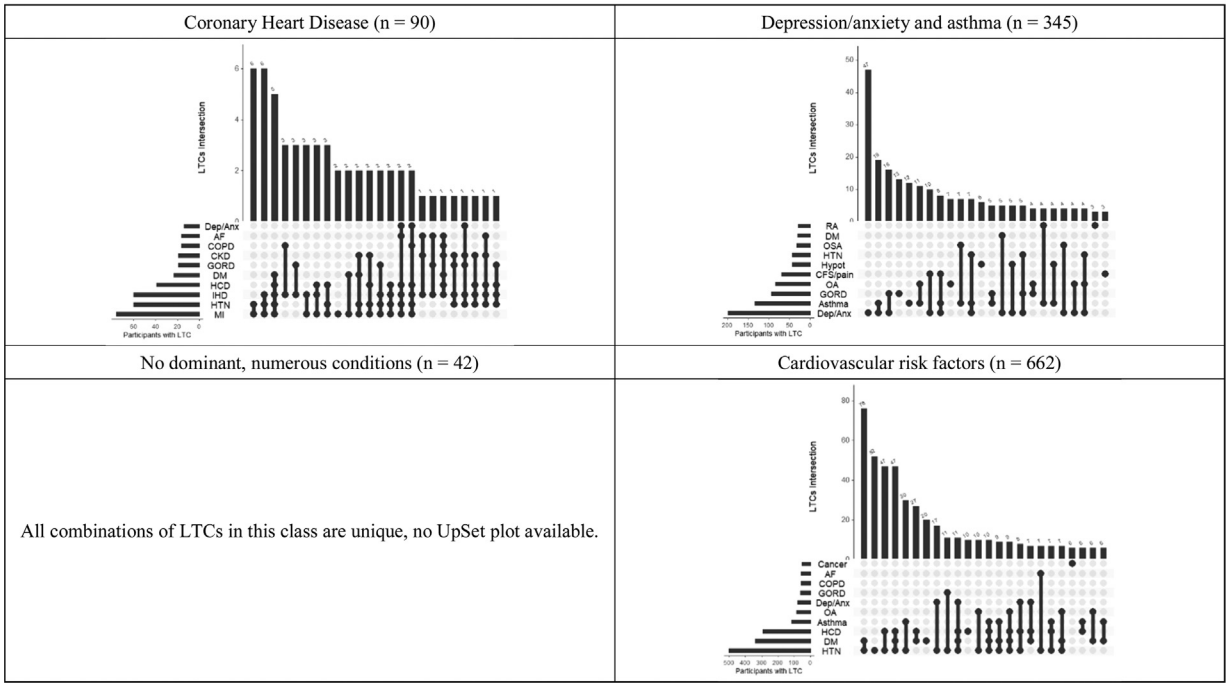
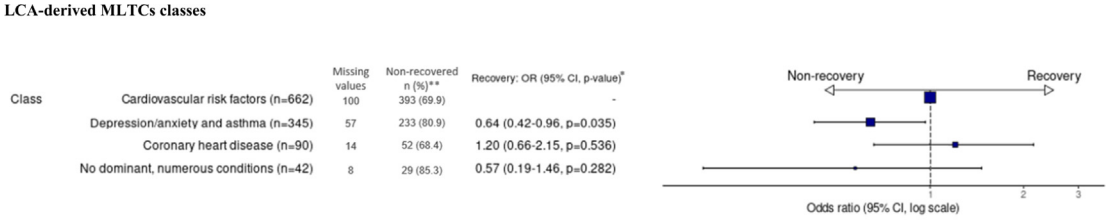


Figure 3. Continued



*Adjusted for age, sex, ethnicity, IMD, severity of acute illness, duration of admission, obesity and smoking history.
** Percentages excluding missing values.
CI, confidence interval; MLTCs, multiple long-term conditions.

Figure 4. Patient-perceived recovery 1 year post–hospital discharge (preexisting MLTCs). Latent class analysis–derived MLTCs classes. CI, confidence interval; MLTCs, multiple long-term conditions.

Table 3
Patient-perceived recovery at 1 year after COVID-19 hospitalization according to further categorization of preexisting MLTCs (n = 922): (a) "complex" MLTC definitions, (b) latent class analysis–derived MLTCs classes.

Definition		Reference	Odds ratio [95% confidence interval] for recovery at 1-year[a]	*P*-value
Number of LTCs	≥3 LTCs	Two LTCs	0.91 [0.45-1.27]	0.57
	≥4 LTCs	≤3 LTCs	0.87 [0.62-1.21]	0.42
	≥5 LTCs	≤4 LTCs	0.78 [0.52-1.14]	0.21
Multiple bodily system involvement	≥2 systems	One system	0.67 [0.47-0.95]	0.026
	≥3 systems	≤2 systems	0.61 [0.42-0.88]	0.0093
Mental and physical health LTCs		Physical only	0.64 [0.42-0.96]	0.033

[a] Adjusted for age, sex, ethnicity, index of multiple deprivation, severity of acute illness, duration of admission, obesity, and smoking history.MLTCs, multiple long-term conditions.

19 hospitalization population have potential implications for providing clinical care and future research in long COVID. By extension, these prognostic classifications may have utility beyond infection (e.g. stratifying risk of functional decline after acute exacerbation of chronic disease). Relative to non-recovery rates reported within the reverse power calculation data sets (55% of 327 hospitalized adults at 3 months [31] and 49% of 1192 hospitalized adults in Wuhan at 1 year [32]) and the estimated global prevalence of long COVID (36% overall and 44% within hospitalized individuals [3]), a substantially higher proportion of our post-hospitalization matched cohort did not feel fully recovered at 1 year (70%). Although our cohort had a relatively low proportion of females (38.1%), they were notably more obese (59.4% vs 22.4%) and more deprived (21.9% vs 14.4% in IMD decile 1) than a cohort of 171,662 adults hospitalized with COVID-19 in England [5]. The risk profile of our cohort may have influenced our findings and may not be directly translated to the broader population.

Recent meta-analyses identifying the presence of single preexisting LTCs as risk factors for the development of long COVID have

evaluated limited lists of LTCs (seven [6] and 10 physical health LTCs only [3]) and the presence of MLTCs was not considered, perhaps limited by the extent and nature of reporting of preexisting LTCs. A population-based longitudinal cohort study of 1,554,040 adults in the United Kingdom with confirmed SARS-CoV-2 infection (hospitalized and non-hospitalized) used a more comprehensive list of 33 physical and nine mental health preexisting LTCs [5]. Anxiety, somatic symptom disorder, and type 2 diabetes were reported as the most significant risk factors for long COVID over a year later, but, again, the co-existence of two or more LTCs was not investigated.

There is equipoise as to whether obesity is considered a LTC vs a risk factor given its potential long-term impact but modifiable nature. Obesity has not been consistently included in weighted measures of MLTCs [21] and was not included as a listed LTC within a relevant Delphi consensus [20]. In keeping with previous analyses [5,6], our results indicate that obesity is an independent risk factor for non-recovery after matching and adjusting for all other variables.

Reflective of the patient-perceived recovery findings, secondary outcomes at 1 year spanning physical, mental, and cognitive health were all less favorable in those with MLTCs than in those without. Of particular note, with consideration of the prevalence of MLTCs in disadvantaged communities, the presence of MLTCs was associated with worse HRQoL and feeling lonely and isolated. A qualitative synthesis (of eight studies) reported an association with MLTCs and loneliness [34]; however, the directionality of the relationship was debated. The compounding psychosocial impacts of those living with preexisting MLTCs and long COVID warrants further attention.

Although the potential value of complex MLTCs definitions in categorizing individuals beyond the standard two or more LTCs definitions has been recognized [20,23], there are limited data comparing clinical outcomes by differing definitions. Inconsistency in reporting and defining MLTCs limits evidence synthesis [21]. We report significant differences in recovery at 1 year after COVID-19 hospitalization according to type and number of body systems involved. Although the challenges associated with complex MLTCs definition standardization across the heterogenous clinical landscape are recognized, consistent reporting is essential to progress this field of research.

Mental health conditions and cardiometabolic conditions (respectively) are the most consistent and replicable MLTCs clusters described in existing literature, with mental health clusters often being associated with worse outcomes [10,24–26]. Similarly, we report worse recovery at 1 year after COVID-19 hospitalization in our depression/anxiety and asthma class than others. Outside of an infectious insult, LCA was used in two British cohorts to identify associations between age-stratified MLTCs clusters and HRQoL [27]. Chronic pain and cardiometabolic clusters were consistently associated with worse HRQoL across age groups compared with other clusters.

Although PHOSP-COVID is a large, prospective multi-center study, the data are observational and reflective of the impact of circulating SARS-CoV-2 variants of the period in a mostly unvaccinated population, limiting the extent to which findings can be generalized to the onward phases of the pandemic. The absence of objective baseline data limits our ability to account for preexisting health status and may, therefore, had led to an overestimation of worse 1-year outcomes. The primary outcome of recovery at 1 year is based on subjective patient-reported assessment, which may be influenced by additional broader psychosocial influences that are not captured by our data. Attrition bias may have been introduced by exclusion of participants lost to follow-up and deaths. Further, not all participants with preexisting MLTCs could be matched (with participants without MLTCs), potentially introducing selection bias and limiting the generalizability of our findings. Although missingness is less than 10% for the majority of variables reported, missingness according to site was identified to affect several variables, limiting the use of multiple imputation, potentially introducing bias if the missingness was not random. The absence of an observed association between number of LTCs and recovery at 1 year among those with MLTCs may have been reflective of survivor bias, whereby those with a greater number of LTCs may have a higher mortality and are, therefore, missing in follow-up.

Our findings confirm the increased vulnerability of adults living with MLTCs to post-acute sequalae of SARS-CoV-2 infection. Categorizing adults with preexisting MLTCs by type and number of body systems affected and frequently co-occurring LTCs has potential utility for clinical care and for future research definitions. The ability to identify and target those adults post–COVID-19 hospitalization most in need has the potential to improve health and wellbeing outcomes and reduce inequalities, for example, stratification for the vaccination program and targeted interventions such as access to anti-viral therapies or specific monoclonal antibodies in the advent of re-infection.

In conclusion, adults with preexisting MLTCs hospitalized due to COVID-19 were less likely to feel fully recovered at 1 year. Certain types of LTCs, multiple body system involvement, and co-occurring LTC class phenotypes were associated with worse recovery at 1 year. We describe novel prognostic classifications of MLTCs relevant for targeted clinical care and furthering the field of complex MLTC definitions. These classifications of MLTCs need further investigation in other post-acute infection syndromes, including the underlying pathophysiology.

Declaration of competing interest

L.E. Gardiner declares that they were awarded funding from a Wellcome Trust doctoral fellowship (Leicestershire Health Inequalities Improvement Programme [grant number UNS144807]) to complete this work. R. Aul declares lecture fees and support for attending a meeting from Boehringer Ingelheim. N.D. Bakerly declares they have received nonrestrictive educational grants from Chiesi, AZ, and Teva for attending conferences; honoraria from Teva, AZ, and GSK; support for attending meetings and/or travel from Chiesi and AZ; participation on a Data Safety Monitoring Board or Advisory Board for Teva; and receipt of equipment from Global Access Diagnostics (previously Mologic Inc). C.E. Bolton declares that their institute received grant funding from NIHR/UKRI and NIHR to complete this work; and their institute received grant funding from Nottingham Hospitals Charity, NIHR, and University of Nottingham. G. Choudhury declares funding from GlaxoSmithKline and AstraZeneca; received honoraria for delivering talks from GSK, AZ, Chiesi, and BI; participation on a Data Safety Monitoring Board or Advisory Board as Chair on the Act on COPD Programme for AZ in Scotland; and a leadership or fiduciary role as Chair for the Lothian Respiratory Managed Clinical Network. C.E. Brightling declares that their institute received grant funding from MRC/NIHR and NIHR to complete this work; their institute received grant funding from Areteia, AstraZeneca, Chiesi, Genentech, GSK, Regeneron Pharmaceuticals, Roche, and Sanofi; and consulting fees from Areteia, AstraZeneca, Chiesi, Genentech, GSK, Regeneron Pharmaceuticals, Roche, and Sanofi. A. Briggs declares consulting fees from Roche, Merck, Sanofi and GSK. J.D. Chalmers declares funding from AstraZeneca, Boehringer Ingelheim, Chiesi, Grifols, Genentech, Gilead, Insmed, and Trudell; consulting fees from AstraZeneca, Chiesi, Glaxosmithkline, Insmed, Grifols, Novartis, Boehringer Ingelheim, Pfizer, Janssen, Antabio, and Zambon. G. Choudhury declares funding from GlaxoSmithKline and AstraZeneca; received honoraria for delivering talks from GSK, AZ, Chiesi, and BI; participation on a Data Safety Monitoring Board

or Advisory Board as Chair on the Act on COPD Programme for AZ in Scotland; and a leadership or fiduciary role as Chair for the Lothian Respiratory Managed Clinical Network. M.J. Davies declares grant funding from AstraZeneca, Boehringer Ingelheim, and Novo Nordisk; consulting fees from Boehringer Ingelheim, Lilly, and Novo Nordisk; payment for speaking for AstraZeneca, Boehringer Ingelheim, Lilly, Novo Nordisk, and Sanofi; support for attending meetings and/or travel from Boehringer Infelheim, Lilly, Novo Nordisk, Amgen, AstraZeneca, Biomea Fusion, Regneron, and Zealand Pharma; and participation on a Data Safety Monitoring Board or Advisory Board for Amgen, AstraZeneca, Biomea Fusion, Sanofi, Zealand Pharma, Carmot/Roche, Regeneron, EktaH, AbbVie, GSK, and Daewoong Pharmaceutical. A. De Soyza declares grant funding from Bayer, Gilead, Pfizer, AstraZeneca, Insmed, and Novartis, unrelated to the submitted manuscript; consulting fees from Boehringer, Bayer, Gilead, Pfizer, GSK, Insmed, AstraZeneca, and Novartis in work unrelated to the submitted manuscript; speaker fees from Bayer, Gilead, Pfizer, GSK, Insmed, AstraZeneca, Innogen, and Fischer&Paykel; support for attending meetings and/or travel from AstraZeneca, Chiesi, GSK, and Insmed; and participation on a Data Safety Monitoring Board or Advisory Board for Bayer. A.B. Docherty declares that they were awarded funding from the Wellcome Trust (227856/Z/23/Z). A.F. Goemans declares that they were awarded funding from a Wellcome Trust fellowship. B. Guillen-Guio declares that they were awarded funding from a Sir Henry Wellcome Postdoctoral Fellowship (grant number 221680/Z/20/Z). L.G. Heaney declares that their institute received funding from GSK, AstraZeneca and Roche/Genentech; payment for lectures received from AstraZeneca, Novartis, Roche/Genentech, Sanofi, Circassia, GlaxoSmithKline, Chiesi, and Teva; support to travel to meetings from AstraZeneca and GSK; participation on a Data Safety Monitoring Board or Advisory Board for Novartis, Roche/Genentech, GSK, Teva, and Celltrion; and funding from the NIHR (RfPB grant PB-PG-0317-20032). S. Heller declares consulting fees from NovoNordisk; and participation on a Data Safety Monitoring Board or Advisory Board for Eli Lilly with payments made to their institution. A. Horsley declares that their institute was awarded funding from UK Research and Innovation (MR/V027859/1) and NIHR Manchester BRC; and is Chair for the NIHR Respiratory Translational Research Collaboration. J.R. Hurst declares funding from AstraZeneca; consulting fees from AstraZeneca and GSK; payment for lectures and presentations from AstraZeneca, Boehringer Ingelheim, Chiesi, Sanofi, and Takeda; support for attending meetings and/or travel from AstraZeneca; participation on a Data Safety Monitoring Board or Advisory Board for AstraZeneca; and receipt of equipment from Nonin. J. Jacob declares funding from the Wellcome Trust, Microsoft Research GlaxoSmithKline, Gilead Sciences, Cancer Research UK, Rosetrees Trust, Cystic Fibrosis Trust, and Chan Zuckerberg Initiative; consulting fees from Boehringer Ingelheim, Roche, GlaxoSmithKline, and NHSX; payment for lectures and presentations received from Boehringer Ingelheim, Roche, GlaxoSmithKline, and Takeda; support for attending meetings and/or travel from Boehringer Ingelheim and Takeda; patents planned, issued or pending (UK patent application number 2113765.8 and UK patent application number GB2211487.0); and participation on a Data Safety Monitoring Board or Advisory Board for Boehringer Ingelheim and Roche. R.G. Jenkins declares that their institute received funding from AstraZeneca, Biogen, Galecto, GlaxoSmithKline, Nordic Biosciences, RedX, and Pliant; consulting fees from AstraZeneca, Brainomix, Bristol Myers Squibb, Chiesi, Cohbar, Daewoong, GlaxoSmithKline, Veracyte, Resolution Therapeutics, and Pliant; payment for lectures and presentations received from Boehringer Ingelheim, Chiesi, Roche, PatientMPower, and AstraZeneca; payment for expert testimony from Pinsent Masons LLP; participation on a Data Safety Monitoring Board or Advisory Board for Boehringer Ingelheim, Galapagos and Vicore; and a leadership or fiduciary role for NuMedii and is president for Action for Pulmonary Fibrosis. M. Jones declares funding from the MRC to complete this work; funding from the MRC, British Lung Foundation, and Boehringer Ingelheim; consulting fees from Skyhawk Therapeutics; and a leadership or fiduciary role in the AAIR Charity Scientific Committee. K. Khunti declares funding from AstraZeneca, Boehringer Ingelheim, Lilly, MSD, Novo Nordisk, Sanofi, Servier, Oramed Pharmaceuticals, Roche, Daiichi-Sankyo, and Applied Therapeutics; consulting fees from Amgen, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Lilly, Novo Nordisk, Sanofi, Servier, Pfizer, Roche, Daiichi-Sankyo, Embecta, and Nestle Health Science; and payment for lectures and presentations from Amgen, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Lilly, Novo Nordisk, Sanofi, Servier, Pfizer, Roche, Daiichi-Sankyo, Embecta, and Nestle Health Science. O.C. Leavy declares that their institute received joint funding from UKRI and NIHR (MR/ V027859/1 and COV0319) to complete this work. N.I. Lone declares leadership or fiduciary roles as director of research for the Intensive Care Society UK, and Chair of the Scottish Intensive Care Society Audit Group, Public Health Scotland. W.D.-C. Man declares that their institute received funding from National Institute for Health Research and NHS Accelerated Access Collaborative; and is Honorary President of the Association for Respiratory Technology and Physiology, and an associate editor of ERJ Open Research. G.P. McCann declares funding from NIHR (RP-2017-ST2-007) to complete this work; funding from the British Heart Foundation, Wellcome Trust and NIHR; and research support from Resonance Health, Circle CVi and Perspectum. M. Marks declares being a recipient of the PHOSP grant. G.P. McCann declares funding from the British Heart Foundation and NIHR; and royalties or licenses from Circle and Perspectum. P.J.M. Openshaw declares funding from UKRI-MRC/DHSC NIHR and UKRI-BEIS. D. Parekh declares funding from NIHR and MRC; and a leadership or fiduciary role for the Faculty of Intensive Care Medicine Board. P. Pfeffer declares funding from NIHR. K. Poinasamy declares funding from UKRI and NIHR to complete this work. A. Briggs declares consulting fees from Roche, Merck, Sanofi and GSK. J.C. Porter declares funding from a Boehinger Ingelheim studentship; and a leadership or fiduciary role as medical director of Breathing Matters. J.K. Quint declares that their institute received funding from UKRI, NIHR, Health Data Research UK, BI, AZ, and Insmed; and consulting fees from GlaxoSmithKline and BI. S.D.M. Rowland-Jones declares that their institute received funding from UKRI to complete this work; and their institute received funding from NIHR Sheffield Biomedical Research Centre, Bill and Melinda Gates Foundation, UKRI (MRC), and EDCTP. M. J. Rowland declares support for attending meetings and/or travel from Novartis Pharmaceuticals; stock or stock options from Novartis Pharmaceuticals and Roche Pharmaceuticals; and is employed full time as a Senior Clinical Development Medical Director at Novartis Pharmaceuticals. M.G. Semple declares grant funding from National Institute of Health Research UK, Medical Research Council UK and Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool to complete this work; participation on a Data Safety Monitoring Board or Advisory Board for Pfizer and GSK; leadership or fiduciary roles as Chair of Infectious Disease Scientific Advisory Board for Integrum Scientific LLC and Director of MedEx Solutions Ltd; stock or stock options as minority owner of Integrum Scientific LLC and majority owner of MedEx Solutions Ltd; receipt of equipment, materials, drugs, medical writing, gifts, or other services from Chiesi Farmaceutici SpA; and is a nonremunerated independent member of HMG UK Scientific Advisory Group for Emergencies (SAGE), COVID-19 Response (March 2020 to March 2022), nonremunerated independent member of HMG UK New Emerging Respiratory Virus Threats Advisory

Group (NERVTAG) (2014 to July 2023), and has been seconded to the Scottish Government (from August 2025). M. Sereno declares that their institute received grant funding from NIHR/UKRI and NIHR to complete this work. A. Sheikh declares that their institute was awarded grant funding from NIHR and UKRI to complete this work; participation on a Data Safety Monitoring Board or Advisory Board for AstraZeneca's Thrombotic Thrombocytopenic Taskforce; and leadership or fiduciary roles for UK and Scottish Government COVID-19 advisory groups. A. Shikotra declares that their institute was awarded joint funding from UKRI and NIHR to complete this work. A.A.R. Thompson declares grant funding to their institution Heart Research UK and Janssen-Cilag Ltd and fellowship funding to their institution from British Heart Foundation; payment for lectures and presentations from Janssen-Cilag Ltd; and support for attending meetings from Janssen-Cilag Ltd. M. Toshner declares grant funding from the NIHR Cambridge BRC and NIHR HTA to complete this work; consulting fees from Janssen; support for attending meetings and/or travel from GSK and Janssen; and participation on a Data Safety Monitoring Board or Advisory Board for ComCov and FluCov. L.V. Wain declares funding from UK Research and Innovation (MR/V027859/1), GSK/Asthma+Lung UK (Professorship [C17-1]) and National Institute of Health Research (COV0319) to complete this work; funding from Orion Pharma, GSK, Genentech, and AstraZeneca; consulting fees to their institution from Galapagos, Boehringer Ingelheim, and GSK; support for attending meetings and/or travel from Genentech; participation on Advisory Board for Galapagos; and leadership or fiduciary role as an associate editor for the European Respiratory Journal. S. J. Singh declares grants or contracts from NIHR (programme grant [NIHR 202020], Wellcome Doctoral Training Programme, HTA Project Grant [NIHR 131015], NIHR DHSC/UKRI COVID-19 Rapid Response Initiative, NIHR Global Research Group [NIHR 17/63/20]), Actegy Limited, and NIHR Senior Investigator; payment for presentations for Ministry of Justice; participation on NICE Expert Adviser Panel (Long COVID), Wales Long COVID Advisory Board, and NHS-E Long COVID Your COVID Recovery working group; and leadership or fiduciary roles as ATS Pulmonary Rehabilitation Assembly Chair, Clinical Lead RCP Pulmonary Rehabilitation Accreditation Scheme, and Clinical Lead NACAP Audit for Pulmonary Rehabilitation. R.A. Evans declares funding from UKRI/MRC/NIHR to complete this work; funding from NIHR, UKRI, Wolfson Foundation, Genentech/Roche, and Synairgen; consulting fees from AstraZeneca/Evidera for long COVID; speaking fees from Boehringer and Moderna; support for attending meetings from Chiesi; and leadership or fiduciary roles as ERS Group 01.02 Pulmonary Rehabilitation and Chronic Care Secretary and ATS Pulmonary Rehabilitation Assembly Chair. The remaining authors declare no conflicts of interest.

Funding

UK Research and Innovation, National Institute for Health and Care Research, and Wellcome Trust. MR/V027859/1 and COV0319.

Ethical approval statement

Written informed consent was obtained from all study participants. The study was approved by the Leeds West Research Ethics Committee (20/YH/0225) and is registered on the ISRCTN Registry (ISRCTN10980107).

Acknowledgments

PHOSP-COVID is jointly funded by a grant from the MRC-UK Research and Innovation and the Department of Health and Social Care through the National Institute for Health Research (NIHR) rapid response panel to tackle COVID-19 (grant references: MR/V027859/1 and COV0319). The views expressed in the publication are those of the author(s) and not necessarily those of the National Health Service (NHS), the NIHR or the Department of Health and Social Care. Lucy Gardiner (first author) is funded through a Wellcome Trust doctoral fellowship as part of the Leicestershire Health Inequalities Improvement Programme [223512/Z/21/Z]. This study was supported by the National Institute for Health and Care Research (NIHR) Leicester Biomedical Research Centre (BRC). Professor Rachael Evans was funded by a NIHR clinician scientist fellowship (CS-2016-020) throughout the PHOSP-COVID award. The views expressed are those of the authors and not necessarily those of the Wellcome Trust, the NIHR or the Department of Health and Social Care. Professor Sally Singh is supported by the NIHR Leicester Biomedical Research Centre (BRC) and the NIHR Cross NIHR Collaboration for Multiple Long Term Conditions. Professor Kamlesh Khunti is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands (ARC EM), NIHR Global Research Centre for Multiple Long Term Conditions, and the British Heart Foundation (BHF) Centre of Excellence. The views expressed are those of the author(s) and not necessarily those of the NIHR, NHS or the Department of Health and Social Care. Professor Malcolm G Semple is now seconded to the Scottish Government. The views expressed in this paper are those of the authors and do not necessarily reflect the views or policies of the authors' employers, the Scottish Government or any other organizations with which the authors are affiliated. A Patient Advisory Group comprising seven individuals living with preexisting multiple long-term conditions and long COVID were involved in the design, reporting and dissemination of this research.

Author contributions

R.A.E. conceptualised the study. L.E.G. and D.L.R. conducted the statistical analyses. The manuscript was initially drafted by L.E.G. and R.A.E., and further developed by D.L.R., N.S., J.E., S.J.S. and R.S.T. All authors reviewed the manuscript.

Data sharing statement

The protocol, consent form, definition and derivation of clinical characteristics and outcomes, training materials, regulatory documents, requests for data access and other relevant study materials are available online at https://www.phosp.org.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2026.108695.

References

[1] O'Mahoney LL, Routen A, Gillies C, Ekezie W, Welford A, Zhang A, et al. The prevalence and long-term health effects of Long Covid among hospitalised and non-hospitalised populations: a systematic review and meta-analysis. *EClinicalmedicine* 2023;**55**:101762. doi:10.1016/j.eclinm.2022.101762.

[2] Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV. WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis* 2021;**22**:e102–7. doi:10.1016/S1473-3099(21)00703-9.

[3] Hou Y, Gu T, Ni Z, Shi X, Ranney ML, Mukherjee B. Global prevalence of long COVID, its subtypes, and risk factors: an updated systematic review and meta-analysis. *Open Forum Infect Dis* 2025;**12**:ofaf533. doi:10.1093/ofid/ofaf533.

[4] Bansal A. Economic burden of long COVID: macroeconomic, cost-of-illness and microeconomic impacts. *npj Prim Care Respir Med* 2025;**35**:53. doi:10.1038/s41533-025-00460-8.

[5] Wang H-I, Doran T, Crooks MG, Khunti K, Heightman M, Gonzalez-Izquierdo A, et al. Prevalence, risk factors and characterisation of individuals with long COVID using Electronic Health Records in over 1.5 million COVID cases in England. *J Infect* 2024;**89**:106235. doi:10.1016/j.jinf.2024.106235.

[6] Tsampasian V, Elghazaly H, Chattopadhyay R, Debski M, Naing TKP, Garg P, et al. Risk factors associated with post-COVID-19 condition: a systematic review and meta-analysis. *JAMA Intern Med* 2023;**183**:566–80. doi:10.1001/jamainternmed.2023.0750.
[7] Gharibzadeh S, Routen A, Razieh C, Zaccardi F, Lawson C, Gillies C, et al. Long term health outcomes in people with diabetes 12 months after hospitalisation with COVID-19 in the UK: a prospective cohort study. *EClinicalmedicine* 2025;**79**:103005. doi:10.1016/j.eclinm.2024.103005.
[8] Elneima O, Hurst JR, Echevarria C, Quint JK, Walker S, Siddiqui S, et al. Long-term impact of COVID-19 hospitalisation among individuals with pre-existing airway diseases in the UK: a multicentre, longitudinal cohort study—PHOSP-COVID. *ERJ Open Res* 2024;**10**:00982–2023. doi:10.1183/23120541.00982-2023.
[9] Lawson CA, Moss AJ, Arnold JR, Bagot C, Banerjee A, Berry C, et al. Long COVID and cardiovascular disease: a prospective cohort study. *Open Heart* 2024;**11**:e002662. doi:10.1136/openhrt-2024-002662.
[10] Skou ST, Mair FS, Fortin M, Guthrie B, Nunes BP, Miranda JJ, et al. Multimorbidity. *Nat Rev Dis Primers* 2022;**8**:48. doi:10.1038/s41572-022-00376-4.
[11] Chowdhury SR, Chandra Das DC, Sunna TC, Beyene J, Hossain A. Global and regional prevalence of multimorbidity in the adult population in community settings: a systematic review and meta-analysis. *EClinicalmedicine* 2023;**57**:101860. doi:10.1016/j.eclinm.2023.101860.
[12] Valabhji J, Barron E, Pratt A, Hafezparast N, Dunbar-Rees R, Turner EB, et al. Prevalence of multiple long-term conditions (multimorbidity) in England: a whole population study of over 60 million people. *J R Soc Med* 2023;**117**:01410768. doi:10.1177/01410768231206033.
[13] Eto F, Samuel M, Henkin R, Mahesh M, Ahmad T, Angdembe A, et al. Ethnic differences in early onset multimorbidity and associations with health service use, long-term prescribing, years of life lost, and mortality: a cross-sectional study using clustering in the UK Clinical Practice Research Datalink. *PLoS Med* 2023;**20**:e1004300. doi:10.1371/journal.pmed.1004300.
[14] Freisling H, Viallon V, Lennon H, Bagnardi V, Ricci C, Butterworth AS, et al. Lifestyle factors and risk of multimorbidity of cancer and cardiometabolic diseases: a multinational cohort study. *BMC Med* 2020;**18**:5. doi:10.1186/s12916-019-1474-7.
[15] Chudasama YV, Zaccardi F, Gillies CL, Razieh C, Yates T, Kloecker DE, et al. Patterns of multimorbidity and risk of severe SARS-CoV-2 infection: an observational study in the U.K. *BMC Infect Dis* 2021;**21**:908. doi:10.1186/s12879-021-06600-y.
[16] Evans RA, McAuley H, Harrison EM, Shikotra A, Singapuri A, Sereno M, et al. Physical, cognitive, and mental health impacts of COVID-19 after hospitalisation (PHOSP-COVID): a UK multicentre, prospective cohort study. *Lancet Respir Med* 2021;**9**:1275–87. doi:10.1016/S2213-2600(21)00383-0.
[17] Group C-MORE/PHOSP-COVID Collaborative. Multiorgan MRI findings after hospitalisation with COVID-19 in the UK (C-MORE): a prospective, multicentre, observational cohort study. *Lancet Respir Med* 2023;**11**:1003–19. doi:10.1016/S2213-2600(23)00262-X.
[18] Houchen-Wolloff L, Poinasamy K, Holmes K, Tarpey M, Hastie C, Raihani K, et al. Joint patient and clinician priority setting to identify 10 key research questions regarding the long-term sequelae of COVID-19. *Thorax* 2022;**77**:717–20. doi:10.1136/thoraxjnl-2021-218582.
[19] Russell CD, Lone NI, Baillie JK. Comorbidities, multimorbidity and COVID-19. *Nat Med* 2023;**29**:334–43. doi:10.1038/s41591-022-02156-9.
[20] Ho ISS, Azcoaga-Lorenzo A, Akbari A, Davies J, Khunti K, Kadam UT, et al. Measuring multimorbidity in research: Delphi consensus study. *BMJ Med* 2022;**1**:e000247. doi:10.1136/bmjmed-2022-000247.
[21] Ho IS-S, Azcoaga-Lorenzo A, Akbari A, Black C, Davies J, Hodgins P, et al. Examining variation in the measurement of multimorbidity in research: a systematic review of 566 studies. *Lancet Public Health* 2021;**6**:e587–97. doi:10.1016/S2468-2667(21)00107-9.
[22] Payne RA, Mendonca SC, Elliott MN, Saunders CL, Edwards DA, Marshall M, et al. Development and validation of the Cambridge Multimorbidity Score. *CMAJ* 2020;**192**:E107–14. doi:10.1503/cmaj.190757.
[23] MacRae C, Mercer SW, Henderson D, McMinn M, Morales DR, Jefferson E, et al. Age, sex, and socioeconomic differences in multimorbidity measured in four ways: UK primary care cross-sectional analysis. *Br J Gen Pract* 2023;**73**:e249–56. doi:10.3399/BJGP.2022.0405.
[24] Busija L, Lim K, Szoeke C, Sanders KM, McCabe MP. Do replicable profiles of multimorbidity exist? Systematic review and synthesis. *Eur J Epidemiol* 2019;**34**:1025–53. doi:10.1007/s10654-019-00568-5.
[25] Fisher K, Griffith LE, Gruneir A, Kanters D, Markle-Reid M, Ploeg J. Functional limitations in people with multimorbidity and the association with mental health conditions: baseline data from the Canadian Longitudinal Study on Aging (CLSA). *PLoS One* 2021;**16**:e0255907. doi:10.1371/journal.pone.0255907.
[26] Tang LH, Thygesen LC, Willadsen TG, Jepsen R, la Cour K, Frølich A, et al. The association between clusters of chronic conditions and psychological well-being in younger and older people-A cross-sectional, population-based study from the Lolland-Falster health Study. *Denmark. J Comorbidity* 2020;**10** 2235042X20981185. doi:10.1177/2235042×20981185.
[27] Steell L, Krauth SJ, Ahmed S, Dibben GO, McIntosh E, Hanlon P, et al. Multimorbidity clusters and their associations with health-related quality of life in two UK cohorts. *BMC Med* 2025;**23**:1. doi:10.1186/s12916-024-03811-3.
[28] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007;**147**:573–7. doi:10.7326/0003-4819-147-8-200710160-00010.
[29] Elneima O, McAuley HJ, Leavy OC, Chalder T, Chalmers JD, Horsley A, et al. Cohort profile:: post-hospitalisation COVID-19 (PHOSP-COVID) study. *Int J Epidemiol* 2024;**53**:dyad165. doi:10.1093/ije/dyad165.
[30] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;**40**:373–83. doi:10.1016/0021-9681(87)90171-8.
[31] Sigfrid L, Drake TM, Pauley E, Jesudason EC, Olliaro P, Lim WS, et al. Long Covid in adults discharged from UK hospitals after Covid-19: a prospective, multicentre cohort study using the ISARIC WHO clinical characterisation Protocol. *Lancet Reg Health Eur* 2021;**8**:100186. doi:10.1016/j.lanepe.2021.100186.
[32] Huang L, Li X, Gu X, Zhang H, Ren L, Guo L, et al. Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study. *Lancet Respir Med* 2022;**10**:863–76. doi:10.1016/S2213-2600(22)00126-6.
[33] Weller BE, Bowen NK, Faubert SJ. Latent class analysis: a guide to best practice. *J Black Psychol* 2020;**46**:287–311. doi:10.1177/0095798420930932.
[34] Hajek A, Kretzler B, König H-H. Multimorbidity, loneliness, and social isolation. A systematic review. *Int J Environ Res Public Health* 2020;**17**:8688. doi:10.3390/ijerph17228688.