nature mental health

Article

https://doi.org/10.1038/s44220-023-00064-6

Factors associated with psychiatric outcomes and coping in Long COVID

Received: 16 June 2022

Accepted: 6 April 2023

Published online: 10 May 2023

Check for updates

Yochai Re'em [1,2] ✉, Elisabeth A. Stelson [2,3], Hannah E. Davis [2], Lisa McCorkell [2], Hannah Wei [2], Gina Assaf [2] & Athena Akrami [2,4]

The relationship between Long COVID (LC) and psychiatric outcomes, as well as factors associated with presence and absence of these, has so far been insufficiently studied. Here we evaluated psychiatric symptoms and coping among patients with LC and patients recovered from COVID-19 who participated in a large international survey. Given increased rates of psychiatric illness with chronic medical conditions and known immune-inflammatory contributors to psychiatric disease, we hypothesized that a subset, but not the entirety, of LC respondents may have comorbid psychopathology. A substantial minority of both groups experienced suicidality, depression and anxiety symptoms, with these symptoms being more common in the LC group. LC respondents used more adaptive coping styles. Psychiatric outcomes in LC were associated with younger age, greater reductions in overall health, higher symptom severity, limitations to physical capability, lower income, financial hardship, psychiatric history, employment impact, male sex, men and non-binary gender, and negative experiences with medical professionals, family, friends, partners and employers.

Long COVID (LC) following coronavirus disease 2019 (COVID-19) infection is prevalent[1] and can be debilitating[2]. LC is a complex chronic disease that can involve multiple systems[3]. Current theories on pathophysiology include viral persistence, endothelial dysfunction and microclotting, immune dysregulation and autoimmunity, and hyperinflammatory states[4].

Given higher rates of psychiatric illness in disabling medical conditions such as cancer and asthma compared with the general population[5], LC may be associated with comorbid psychopathology. Studies that include non-hospitalized cohorts and non-infected controls find slightly elevated rates of anxiety and depression symptoms after COVID-19 compared with controls, with mild acute cases experiencing lower rates compared with severe acute cases[6]. A 6 month electronic health record study found higher rates of psychiatric diagnoses post-COVID when compared with other respiratory tract infections[7]. A 2 year electronic health record-based retrospective cohort study found that the increased risk of mood and anxiety disorders returned to baseline within 2 months of COVID infection, while other conditions such as cognitive dysfunction and psychoses, remained elevated[8]. Despite several large-scale studies examining rates of mental health conditions following COVID-19 infection, few studies have explored psychiatric sequelae explicitly in those with persistent symptom burden following COVID-19 illness, and fewer have identified factors associated with these psychiatric sequelae. Additionally, while suicidality has been postulated to occur in the LC population at higher frequencies compared with the general population[9], no studies have evaluated this.

We have previously shown that individuals with LC experience a number of mood symptoms[2]. In addition to these, patients with LC report stigmatization[10] and assumptions that all their symptoms are due to psychiatric disease[11,12], which can lead to misdiagnosis[13]. In this Article, we hypothesize that a subset, but not a majority, of individuals with LC experience substantial symptoms of depression, anxiety or suicidality, and that the majority of those with LC use adaptive coping.

To better qualify these psychiatric symptoms, we disseminated an internet-based survey to a large international cohort, utilizing depression, anxiety and suicidality screeners, along with a coping

[1]Weill Cornell Medical College, Department of Psychiatry, New York, NY, USA. [2]Patient-Led Research Collaborative, New York, NY, USA. [3]Department of Social & Behavioral Sciences, Harvard TH Chan School of Public Health, Boston, MA, USA. [4]Sainsbury Wellcome Centre, University College London, London, UK. ✉e-mail: yreemmd@gmail.com

https://doi.org/10.1038/s44220-023-00064-6

Table 1 | Demographics of survey respondents

Factor	Number of respondents (*N*=6,113)	Long Covid (*N*=5,638)	Non-Long Covid (*N*=475)
Gender[a]			
Woman	4,756 (77.80%)	4,413 (78.27%)	343 (72.21%)
Man	1,247 (20.40%)	1,126 (19.97%)	121 (25.47%)
Non-binary	92 (1.50%)	81 (1.44%)	11 (2.32%)
Prefer not to say	10 (0.17%)	10 (0.18%)	0 (0.0%)
Other	8 (0.13%)	8 (0.14%)	0 (0.0%)
Age group, years[a]			
18–29	580 (9.50%)	495 (8.78%)	85 (17.89%)
30–39	1,416 (23.20%)	1,299 (23.04%)	117 (24.63%)
40–49	1,746 (28.60%)	1,639 (29.07%)	107 (22.53%)
50–59	1,443 (23.60%)	1,354 (24.02%)	89 (18.74%)
60–69	707 (11.60%)	652 (11.56%)	55 (11.58%)
70–79	202 (3.30%)	183 (3.25%)	19 (4%)
80+	19 (0.30%)	16 (0.28%)	3 (0.63%)
Ancestry[a]			
Asian, South Asian, South East Asian	171 (2.80%)	150 (2.66%)	21 (4.42%)
Black	116 (1.90%)	98 (1.74%)	18 (3.80%)
Hispanic, Latino or Spanish origin	197 (3.22%)	174 (3.09%)	23 (4.84%)
White	5,061 (82.79%)	4,695 (83.27%)	366 (77.05%)
Other, including Pacific Islander, Indigenous Peoples, Middle Eastern/North African	118 (1.93%)	110 (1.95%)	8 (1.68%)
White and Hispanic, Latino or Spanish origin	89 (1.46%)	81 (1.44%)	8 (1.68%)
White and Black and either Asian or Other and/or Asian, and/or other, as above	268 (4.38%)	255 (4.52%)	13 (2.74%)
Black and either Asian or other and/or Asian, and/or other	65 (1.06%)	52 (0.92%)	13 (2.74%)
Prefer not to answer	28 (0.46%)	23 (0.41%)	5 (1.05%)
Hospitalization			
Non-hospitalized	5,566 (91.05%)	5,122 (90.85%)	444 (93.47%)
Hospitalized	547 (8.95%)	516 (9.15%)	31 (6.53%)
History of psychiatric diagnosis			
Yes	2,678 (43.81%)	2,488 (44.1%)	190 (40.0%)
No	3,392 (55.49%)	3,111 (55.2%)	281 (59.2%)
Not available	43 (0.70%)	39 (0.7%)	4 (0.8%)
Healthcare worker[a]			
No	4,924 (80.55%)	4,523 (90.22%)	401 (84.42%)
Yes	1,189 (19.45%)	1,115 (19.78%)	74 (15.58%)
Country of residence[a]			
United States	3,119 (51.02%)	2,901 (51.46%)	218 (45.89%)
United Kingdom and Northern Ireland	1,609 (26.32%)	1,502 (26.64%)	107 (22.53%)
Canada	232 (3.80%)	220 (3.90%)	12 (2.53%)
France	191 (3.12%)	184 (3.26%)	7 (1.47%)
Spain	113 (1.85%)	109 (1.93%)	4 (0.84%)
The Netherlands	81 (1.32%)	75 (1.33%)	6 (1.26%)
Germany	78 (1.28%)	74 (1.31%)	4 (0.84%)
Ireland	69 (1.13%)	64 (1.14%)	5 (1.05%)
Russian Federation	67 (1.10%)	39 (0.69%)	28 (5.89%)
Other	554 (9.06%)	470 (8.34%)	84 (17.68%)

[a]Significantly different between LC and non-LC at the α=0.05 level. Differences between groups were assessed utilizing chi-square test.

scale, and compared responses between those with LC and those who were infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) but did not develop LC. We then evaluated associations of demographic, illness and social factors with anxiety, depression and suicidality to better describe psychiatric comorbidity in LC.

Results

Of those who completed the consent form, 82% started the survey and 58.5% of those who started the survey completed it. Rates of missing responses for the three primary outcomes were: 1.6% suicidal thoughts, 2.7% Patient Health Questionnaire-2 (PHQ-2) and 3.8% Generalized Anxiety Disorder scale-7 (GAD-7). Over 50 countries were represented, with the majority (54.8%) from the United States and Canada and 26.3% from the UK (Table 1). Healthcare workers represented 19.8% of respondents. Participants found the survey through support groups (59%) and other online sources (41%). The median duration of illness in the non-LC group was 16 days (10–28 days), while the median duration of illness in the LC group was 190 days (164–229 days) at survey submission and ongoing.

Psychiatric symptoms and coping in LC versus non-LC

Those who recovered from acute COVID-19 illness were more likely to be male ($\chi^2 = 7.38$, $P = 0.007$), younger ($\chi^2 = 53.04$, $P < 0.001$) and non-healthcare workers ($\chi^2 = 4.93$, $P = 0.026$) (Table 1). The rates of prior psychiatric history were similar between LC and non-LC (Table 1). There were no significant differences in hospitalization between LC and non-LC (Table 1).

The majority of participants did not meet cut-offs for any of the three psychiatric outcomes, with 42.8% (95% confidence interval (CI) 41.5% to 44.1%) of those with LC and 28.0% (95% CI 24.0% to 32.3%) of those without LC meeting a cut-off for depression, anxiety or suicidality ($\chi^2 = 39.57$, $P < 0.001$). Of those who met the cut-off for at least one psychiatric outcome, 44.4% (95% CI 42.2% to 46.2%) in LC and 44.2% (95% CI 35.8% to 53.2%) in the non-LC group had no prior psychiatric history.

GAD-7

A total of 25.2% (24.0–26.4) of LC and 16.7% (13.4–20.5) of non-LC experienced moderate to severe anxiety, though medians and means of both groups were below the screening cut-off GAD-7 score of 10. This difference between groups was significant ($\chi^2 = 16.12$, $P < 0.001$, effect size $\varphi = 0.052$) (Fig. 1a).

PHQ-2

A total of 32.7% (31.5–34.0%) of LC and 21.8% (18.1–25.8%) of non-LC screened above the depression threshold; this difference was significant ($\chi^2 = 23.20$, $P < 0.001$, effect size $\varphi = 0.062$) (Fig. 1b).

Suicidality

A total of 17.2% (16.3–18.3%) of LC and 10.8% (8.1–14.0%) of non-LC reported suicidal thoughts in the prior 2 weeks. This difference was significant ($\chi^2 = 12.7$, $P < 0.001$, effect size $\varphi = 0.046$) (Fig. 1c,d).

Coping

Overall, the most utilized coping strategies by LC respondents were acceptance, planning, active coping and use of emotional support. The least utilized were denial, substance use, behavioural disengagement and self-blame. Compared with their non-LC counterparts, LC respondents displayed significantly higher scores on adaptive coping, use of emotional support, venting, use of instrumental support, planning, behavioural disengagement and self-blame (Table 2). These differences remained significant when eliminating those with a PHQ-2 score of ≥3 (that is, those who screened positive for depression) from both groups.

Factors associated with psychiatric outcomes in LC

Demographic-related factors. LC respondents with a prior psychiatric diagnosis were significantly more likely to experience all psychiatric outcomes (Supplementary Table 1).

Depression, anxiety and suicidality were significantly different by gender. Women were less likely to be depressed, anxious and suicidal compared with non-binary/gender nonconforming (GNC) respondents. Men were significantly more likely to be suicidal than women. GNC respondents were significantly more likely to be suicidal and anxious than men and women (Supplementary Table 1). Those with male sex were more likely to experience suicidality than female sex, with no differences between sexes in depression or anxiety (Supplementary Table 1).

There were significant differences in anxiety ($\chi^2 = 18.64$, $P = 0.001$), depression ($\chi^2 = 13.66$, $P = 0.034$) and suicidality ($\chi^2 = 18.74$, $P = 0.005$) by ancestry (Supplementary Table 1). Those with depression ($t = -4.10$, $P < 0.001$), suicidality ($t = -6.74$, $P < 0.001$) and anxiety ($t = -12.34$, $P < 0.001$) were also significantly more likely to be younger, particularly in the 18–29 year age range. Additionally, lower income brackets, both before COVID-19 and current, were associated with higher levels of psychiatric outcomes (Supplementary Table 1).

Symptom and severity-related factors. Rates of psychiatric conditions and their relationships with LC factors are detailed in Table 3.

Change in overall health was determined by asking participants to rate their overall health retrospectively pre-COVID-19 illness and post-COVID-19 illness. Individuals with depression and/or suicidality reported greater overall reductions in health, with no significant relationship between reductions in health and presence of anxiety symptoms (Table 3). A separate question specifically asked participants to rate their overall health on the day of the survey as compared with their pre-COVID baseline. Those with depression, anxiety and/or suicidality reported lower overall health on the day of the survey compared with their pre-COVID baseline (Supplementary Table 1). There was no significant relationship between the number of days respondents had experienced symptoms and psychiatric outcomes (Table 3). Those hospitalized had higher levels of depression and suicidal thoughts, with no significant differences in anxiety (Table 3). Those with limitations to their physical activity, compared with those without, were more likely to experience depression, suicidality and/or anxiety (Table 3).

We explored the individual relationships between the presence or absence of 144 non-psychiatric symptoms and each of the psychiatric outcomes. After Bonferonni correction, 26 symptoms were significantly associated with at least one outcome, all with a weak effect size (Cramer's V of 0.1–0.3). Significantly associated symptoms included eye and vision symptoms, muscle and joint pain, several headache and cognitive symptoms, sexual dysfunction, slurring words, hallucinations and acute confusion. For any subset of individuals with a given symptom, the majority did not have depression, anxiety or suicidal thoughts. A full list of symptoms and mental health outcomes is presented in Supplementary Table 1.

We identified 14 new non-psychiatric diagnoses after COVID-19 infection with at least 25 responses and explored their relationship to mental health outcomes. Of these, polyneuropathy was associated with depression ($\chi^2 = 7.04$, $P = 0.008$) and motor, peripheral or cranial neuropathies were associated with suicidal thoughts ($\chi^2 = 1.7$, $P = 0.02$). No new diagnosis was associated with anxiety. New diagnoses of postural orthostatic tachycardia syndrome, myalgic encephalomyelitis/chronic fatigue syndrome, stroke, migraine, costochondritis, blood clots, traumatic brain injury, small fibre neuropathy, autonomic neuropathy, myocarditis, neuralgia and encephalopathy were not associated with psychiatric outcomes in this dataset (Supplementary Table 4).

https://doi.org/10.1038/s44220-023-00064-6

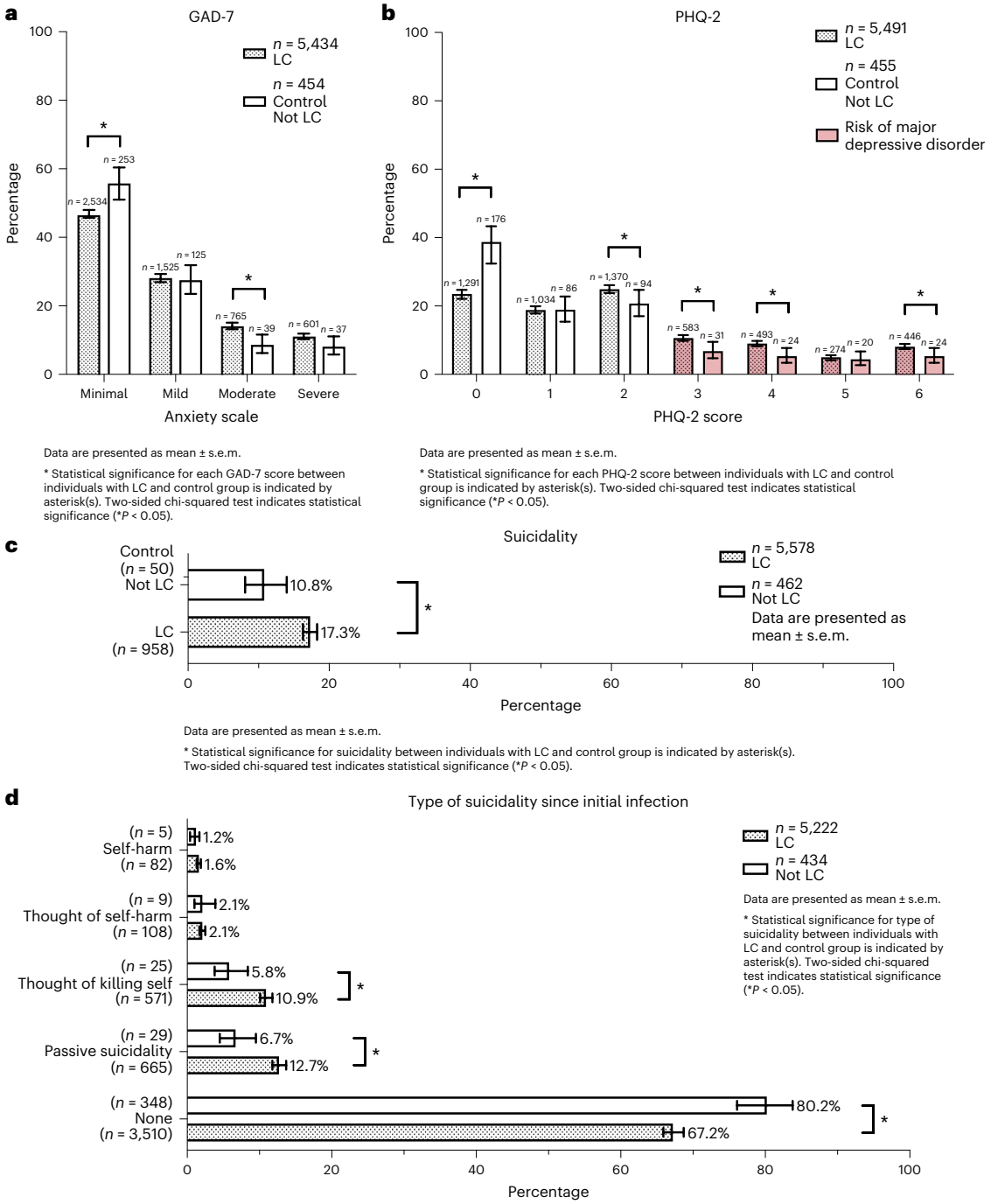

Fig. 1 | Mental health symptoms of long COVID (LC) patients compared to patients without long COVID. a, Comparison of anxiety symptom severity. **b**, Comparison of depressive symptom severity. **c**, Comparison of suicidal ideation. **d**, Comparison of suicidal ideation type. All variables are dichotomous with the exception of gender variables (categorical with female/woman as reference group); ancestry variables (categorical with white as reference group); change in health variables (with same or better pre-COVID health as reference group); change in job hours or employment (categorical with no change in job as reference group); severity of LC symptoms (continuous); and number of days with LC symptoms (continuous).

Social factors. Rates of psychiatric symptoms and their relationships with social factors are detailed in Table 3 and Supplementary Table 1.

Financial pressure and illness affecting employment were each associated with more suicidality, depression and anxiety symptoms (Table 3)

Negative experiences with providers were the most frequently reported type of negative experience, with 52.9% of respondents reporting having at least one within a median 190 days (164–229 days) of illness. This was followed by negative experiences with friends (26.3%), employers (22.9%), family (20%) and spouse or partner (11.6%). Those who experienced a negative interaction with a provider were significantly more likely to be depressed, anxious and suicidal (Table 3). Those who reported that at least one of their doctors conveyed they did not believe them were more likely to be depressed, anxious and suicidal (Supplementary Table 1).

We found that, of those who did not have any of the three primary psychiatric outcomes, those with LC were still significantly more likely than non-LC respondents to report that a provider did not believe them (71.0% versus 32.6%, $\chi^2 = 145.8$, $P < 0.001$), removing the possibility that those with psychiatric symptoms could be more likely to report not being believed by a provider.

https://doi.org/10.1038/s44220-023-00064-6

Table 2 | Coping in long covid patients (LC) versus non-long covid patients (non-LC)

Type of coping	LC (*N*=5,135), non-LC (*N*=399)	Mean	s.d.	*t*	df	*P*	Effect size (Cohen's *d*)
Self-distraction	Yes	2.603	0.797	1.368	5,532	0.171	0.07
	No	2.546	0.847				
Active coping	Yes	2.876	0.884	8.296	5,532	<0.001	0.43
	No	2.495	0.885				
Denial	Yes	1.260	0.523	2.667	483	0.008	0.12
	No	1.195	0.457				
Substance use	Yes	1.330	0.680	−1.555	454	0.121	−0.09
	No	1.380	0.723				
Use of emotional support	Yes	2.721	0.906	3.496	5,532	<0.001	0.18
	No	2.556	0.931				
Behavioural disengagement	Yes	1.454	0.628	5.381	481	<0.001	0.25
	No	1.297	0.556				
Venting	Yes	2.123	0.738	4.577	5,532	<0.001	0.24
	No	1.947	0.764				
Use of instrumental support	Yes	2.567	0.862	7.471	5,532	<0.001	0.39
	No	2.231	0.910				
Positive reframing	Yes	2.357	0.929	1.421	5,532	0.155	0.07
	No	2.288	0.925				
Self-blame	Yes	1.741	0.824	3.962	474	<0.001	0.19
	No	1.584	0.759				
Planning	Yes	2.926	0.878	11.587	451	<0.001	0.65
	No	2.351	0.961				
Humor	Yes	1.987	0.893	−1.676	5,532	0.094	−0.09
	No	2.065	0.914				
Acceptance	Yes	3.092	0.748	2.799	5,532	0.005	0.15
	No	2.982	0.803				
Religion	Yes	1.961	1.027	1.886	5,532	0.059	0.10
	No	1.860	1.056				

Coping assessed using brief-COPE scale. Differences between groups assessed utilizing two-sided *t*-test.

Those who experienced negative interactions, and those who did not experience positive interactions, with their family, friends, partner or employer were more likely to be depressed, be anxious and report suicidal thoughts (Supplementary Table 1).

Participants were able to indicate whether they did not need any medical care, as well as whether they received the appropriate amount of care or less care than they needed. A total of 71.1% of respondents reported receiving below the appropriate amount of medical care, 21.8% receiving the appropriate amount of care and 7.1% not needing medical care. Among those with LC, receiving "significantly below the appropriate amount of care" was associated with depression, suicidal thoughts and anxiety (Supplementary Table 1). There were no observed relationships between psychiatric outcomes and access to SARS-CoV-2 polymerase chain reaction testing.

There was no significant difference in rates of depression, anxiety and suicidal thoughts between those who joined and did not join a support group. Of those who did join a COVID-specific support group, 70% reported that the group "moderately to significantly improved their psychological wellbeing," with 21.5% reporting no effect and 8.5% reporting psychological worsening.

Overall, those with children were slightly less likely to be anxious, depressed and suicidal (Table 3). To attempt to account for the age of children, participants were analysed separately by age group. Only those in the age groups 40–49 and 50–59 with children were less likely to experience suicidality compared with those in the respective age groups without children. The age groups 30–39 and 70–79 with children had slightly higher anxiety compared with those in the age group without children. There were no statistically significant differences in prevalence of depression for those with and without children by age group (Supplementary Table 2).

Predictive models. Generalized linear model (GLM) and least absolute shrinkage and selection operator (LASSO) estimates for the three psychiatric outcomes (depression, anxiety and suicidal ideation) conducted with the full LC sample are presented in Table 4, while GLM and LASSO estimates for LC participants employed at organizations (which includes employer response variables) are included in Supplementary Table 3. Across models, the magnitude of effect for variables was modest. LASSO estimates resembled GLM estimates and were consistently attenuated.

Demographics. Holding all other covariates constant, individuals 30 years and older were consistently less likely to screen positive for depression, anxiety or suicidal ideation compared to younger participants (18–29 years). Men experienced increased odds of depression and suicidal ideation symptoms compared with women, and GNC participants were at increased odds of suicidal ideation. Identifying with multiple ancestries was associated with all three mental health

https://doi.org/10.1038/s44220-023-00064-6

Table 3 | Illness and social factors associated with suicidality, depression and anxiety in LC

		Suicidality			Depression			Anxiety		
		Mean±s.d. in suicidal	Mean±s.d. in non-suicidal	Test statistic and *P* value	Mean±s.d. in depressed	Mean±s.d. in non-depressed	Test statistic and *P* value	Mean±s.d. in anxious	Mean±s.d. in non-anxious	Test statistic and *P* value
Illness factors		*N*=958	*N*=4,593		*N*=1,796	*N*=3,695		*N*=1,366	*N*=4,059	
Days of illness		203.99±90.16	203.38±85.02	*t*=0.20, *P*=0.84	200.59±91.71	204.46±82.83	*t*=1.51, *P*=0.13	201.36±91.93	204.06±84.16	*t*=−0.96, *P*=0.34
Change in overall health		2.17±1.10	2.00±1.10	*t*=−4.34, *P*<0.001	2.15±1.09	1.96±1.10	*t*=−5.87, *P*<0.001	2.07±1.07	2.01±1.11	*t*=−1.78, *P*=0.075
		Prevalence suicidal	95% CI	Test statistic and *P* value	Prevalence depressed	95% CI	Test statistic and *P* value	Prevalence anxious	95% CI	Test statistic and *P* value
Physically limited by illness	Limited in physical activity	904/4,943=18.3%	17.2 to 19.4	χ^2=33.55, *P*<0.001	1,702/4,888=34.8%	33.5 to 36.2	χ^2=90.20, *P*<0.001	1,261/4,827=26.1%	24.9 to 27.4	χ^2=20.72, *P*<0.001
	Not limited in physical activity	54/608=8.9%	6.7 to 11.4		94/603=15.6%	12.8 to 18.7		105/598=17.6%	14.6 to 20.8	
Hospitalization	Hospitalized	104/506=20.6%	17.1 to 24.3	χ^2=4.23, *P*=0.04	196/504=38.9%	34.6 to 43.3	χ^2=9.63, *P*=0.002	134/493=27.2%	23.3 to 31.3	χ^2=1.15, *P*=0.28
	Not hospitalized	854/5,045=16.9%	15.9 to 18.0		1,600/4,987=32.1%	30.8 to 33.4		1,232/4,932=25.0%	23.8 to 26.2	
Social factors										
Financial challenges	Any financial hardship	606/2,548=23.8%	22.1 to 25.5	χ^2=140.44, *P*<0.001	1,055/2,530=41.7%	39.8 to 43.6	χ^2=172.34, *P*<0.001	817/2,482=32.9%	31.1 to 34.8	χ^2=145.38, *P*<0.001
	No financial hardship	352/3,003=11.7%	10.6 to 12.9		741/2,961=25.0%	23.5 to 26.6		549/2,943=18.7%	17.3 to 20.1	
Employment	Illness affected employment	425/2,314=18.4%	16.8 to 20.0	χ^2=17.20, *P*<0.001	769/2,292=33.6%	31.6 to 35.5	χ^2=25.58, *P*<0.001	614/2,258=27.2%	25.4 to 29.1	χ^2=13.32, *P*<0.001
	Illness did not affect employment	106/868=12.2%	10.1 to 14.6		207/856=24.2%	21.3 to 27.2		177/851=20.8%	18.1 to 23.7	
Medical care	Significantly below care needed	446/1,977=22.6%[a]	20.7 to 24.5	χ^2=66.00, *P*<0.001	742/1,955=38.0%[a]	35.8 to 40.1	χ^2=38.99, *P*<0.001	588/1,930=30.5%[a]	28.4 to 32.6	χ^2=50.97, *P*<0.001
	Somewhat below care needed	306/1,968=15.5%[b]	14.0 to 17.2		566/1,946=29.1%[b]	27.1 to 31.2		458/1,924=23.8%[b]	21.9 to 25.8	
	Recevied appropriate care	149/1,212=12.3%[b]	10.5 to 14.3		369/1,202=30.7%[b]	28.1 to 33.4		234/1,187=19.7%[c]	17.5 to 22.1	
	Did not need care	57/394=14.5%[b]	11.1 to 18.3		119/388=30.7%[b]	26.1 to 35.5		86/384=22.4%[b,c]	18.3 to 26.9	
Provider experience	Negative provider experience	596/2,938=20.3%	18.8 to 21.8	χ^2=34.91, *P*<0.001	1,042/2,907=35.8%	34.1 to 37.6	χ^2=23.54, *P*<0.001	847/2,872=29.5%	27.8 to 31.2	χ^2=57.62, *P*<0.001
	No negative experience	323/2,302=14.0%	12.6 to 15.5		671/2,278=29.5%	27.6 to 31.4		454/2,249=20.2%	18.5 to 21.9	
Support group	Joined online COVID-19 support group	582/3,297=17.7%	16.4 to 19.0	χ^2=1.13, *P*=0.29	1,046/3,263=32.1%	30.5 to 33.7	χ^2=1.30, *P*=0.25	797/3,223=24.7%	23.2 to 26.3	χ^2=0.92, *P*=0.34
	Did not join online COVID-19 support group	370/2,235=16.6%	15.0 to 18.2		741/2,210=32.7%	31.6 to 35.5		566/2,187=25.9%	24.1 to 27.8	
Access to testing	Had access to testing	665/3,845=17.3%	16.1 to 18.5	χ^2=0.70, *P*=0.40	1,279/3,809=33.6%	32.1 to 35.1	χ^2=2.56, *P*=0.11	968/3,767=25.7%	24.3 to 27.1	χ^2=0.36, *P*=0.55
	Did not have access to testing	192/1,043=18.4%	16.1 to 20.9		318/1,028=30.9%	28.1 to 33.9		271/1,018=26.6%	23.9 to 29.5	
Has children	Has children	440/2,998=14.7%	13.4 to 16.0	χ^2=30.43, *P*<0.001	927/2,961=31.3%	29.6 to 33.0	χ^2=5.73, P=0.02	705/2,936=24.0%	22.5 to 25.6	χ^2=4.63, *P*=0.03
	Does not have children	518/2,553=20.3%	18.7 to 21.9		869/2,530=34.3%	32.5 to 26.2		661/2,489=26.6%	24.8 to 28.3	

For multivariable analyses, prevalences with different superscripts are significantly different at the α=0.05 level. Differences between groups of illness factors assessed utilizing two-sided *t*-test. Differences between groups of social factors assessed using chi-square test.

outcomes compared with white participants. Not having children was associated with suicidality but not depression or anxiety symptoms.

Medical and social support. Across all three psychiatric outcomes, positive and negative experiences with partners were a significant factor, while experiences with family and friends were less often statistically significant. A positive experience with a provider significantly lowered the odds of depression symptoms. Anxiety scores were positively associated with positive provider experiences and negatively associated with negative provider experiences—both of which were significant when controlling for covariates.

Health. LC-related physical limitations were positively associated with depression and anxiety symptoms, and hospitalization was positively associated with depression and suicidal ideation, adjusting for other covariates. Severity of LC symptoms was significantly negatively associated with all psychiatric outcomes, although the effect was small. Not having had a previous psychiatric diagnosis before becoming ill was consistently negatively associated with depression, anxiety and suicidal ideation symptoms.

Employment and finances. Both experience of financial hardship and loss of job since becoming ill were significantly positively associated with depression, anxiety and suicidal ideation after controlling for other covariates.

Discussion

To our knowledge, this is the first study of psychiatric symptoms in LC as defined by the World Health Organization that utilizes a comparison with those recovered from COVID-19 and explores associations with a range of variables associated with psychiatric symptoms. We found that LC was associated with greater psychiatric outcome burden, but that the majority of those with LC do not experience psychiatric outcomes. We additionally found that psychiatric outcomes in LC are associated with younger age, greater reductions in overall health, higher symptom severity, limitations to physical capability, lower income brackets, loss of income, presence of a psychiatric history, financial pressure, employment impacted by illness, male sex, men and non-binary gender, and negative experiences with support systems (medical professionals, family, friends, partners and employers).

Psychiatric symptoms are common in chronic and debilitating illnesses such as cancer, diabetes and asthma[5,14–17], and our findings show similar rates of depression, anxiety and suicidality in LC. Our results suggest that, while both those with LC and those who recovered from COVID-19 are at risk for psychiatric sequelae[7,8,18], those with LC may be at higher risk due to factors related to dealing with chronic illness as well as direct and indirect biological effects of the SARS-CoV-2 virus. Considering the emerging developments in understanding of immune and inflammatory aspects of LC[19,20], there may be particular relevance to similar immune-inflammatory aspects known to confer greater psychiatric risk[21,22].

Importantly, 57.2% of those with LC did not meet any cut-off for anxiety, depression and suicidality, and overall the LC group used more adaptive coping, reinforcing that LC is not in itself an illness defined by presence of these psychiatric symptoms nor maladaptive coping. Considering the prevalence of physical symptoms in LC without psychiatric comorbidity[2], screening tools that rely heavily on somatic markers of psychiatric illness, such as fatigue or tachycardia, are likely to overrepresent the burden of psychiatric illness in this population. Improving the accuracy of screening for people with LC and offering psychiatric intervention specifically to those experiencing psychological difficulties would allow for improved utilization of an already taxed mental healthcare system.

Comparing coping styles in those with LC with those without allows for differentiating between coping with acute COVID-19 illness and the stress of the pandemic to coping with LC illness. Those with LC displayed more adaptive approaches to coping, with the largest effect sizes seen in increased active coping, instrumental support and planning, regardless of depressive symptoms. Seventy per cent of participants who joined an online COVID-19 support group found that the group had a positive impact on their psychological wellbeing, and participation was negatively associated with depression and suicidal ideation symptoms, suggesting that support groups may have potential to be of benefit if led by peers and well moderated[23].

Notably, 52.9% of the participants reported a negative experience with medical providers, and 11.6–26.3% reported negative experiences with friends, partners, family and employers. This may be partially addressed with improved education and messaging from health groups and governmental bodies on the symptoms and prevalence of LC. Additionally, psychiatric referral in the absence of continued medical workup and treatment is one of many ways the stigma of psychologization[24] affects patient care. This is partly evidenced by the LC respondents who reported not receiving the medical care they needed being significantly more likely to experience psychiatric symptoms. Considering the relatively higher rates of negative experiences with providers compared with other supports, future studies may shed further light on the interplay between healthcare experiences and mental health outcomes in this population.

Our results also showed higher rates of psychiatric symptoms in some racial/ethnic groups. This is in line with recent national data on mental health disparities in racially and ethnically marginalized populations, which are related to disparities in access to healthcare, psychosocial stressors and social determinants of health[25]. However, these groups in our sample were not sufficiently represented, which may partly explain the lack of significant differences between some subgroups. Future studies should explore these disparities in greater detail, and comprehensive care for patients with LC should include assessing for social and community assets and barriers to care[25].

Our preliminary symptom analysis showed that association of non-psychiatric symptoms with psychiatric comorbidity is inconsistent among symptoms in the same organ system. Further research is needed to better understand the relationship between psychiatric outcomes and specific LC symptoms. Importantly, of all respondents with cognitive dysfunction, the majority did not meet the threshold for psychiatric outcomes, further solidifying that cognitive dysfunction in LC can occur independently of psychiatric conditions.

There have been various prevalence rates reported for suicidality related to the COVID-19 pandemic[26,27], while no prior studies have evaluated rates of suicidality in those with LC. We found those with LC were significantly more likely to experience suicidality compared with those who experienced COVID-19 and recovered. These rates are consistent with higher rates of suicidality in chronic illnesses[14], making it critical to provide necessary support for those with chronic illnesses while also considering the biological factors that could be driving this symptom at different timepoints in recovery[21,22]. Multiple factors in our survey were associated with suicidality risk, and should be addressed where possible, particularly in male and non-binary patients, patients under age 30, patients who reported they did not receive adequate medical care, and patients who had more severe symptoms.

Across predictive models, not having a pre-existing psychiatric diagnosis before contracting COVID significantly reduced risk of post-infection psychiatric symptoms when controlling for other covariates. Young adults (under age 30) were consistently at greatest risk for all three psychiatric outcomes, which may be an indication that age-related factors may partially explain differentials in psychiatric symptom presentation.

Strengths and limitations

To our knowledge, these findings represent the first assessment of psychiatric symptoms in a geographically diverse LC population with a

https://doi.org/10.1038/s44220-023-00064-6

Table 4 | Multivariable analysis of protective and risk factors for developing depressive symptoms, anxiety symptoms or suicidal ideation among patients with Long COVID (*N*=5,208)

Variable group	Variable	PHQ-2			GAD-7			Suicidal Ideation		
		GLM OR and significance	95% CI	LASSO OR	GLM coefficient and significance	95% CI	LASSO coefficient	GLM OR and significance	95% CI	LASSO OR
Demographics	Age (>30 years)	0.64[a]	0.51 to 0.80	0.66	−2.09[a]	−2.61 to −1.57	−2.01	0.81	0.65 to 1.00	0.83
	Male/man identification (ref. female/woman)	1.25[b]	1.07 to 1.47	1.22	0.10	−0.25 to 0.45	0.02	1.21[c]	1.04 to 1.41	1.16
	Non-binary/ gender queer identification (ref. female/woman)	1.23	0.77 to 1.94	1.14	0.34	−0.74 to 1.42	0.16	2.59[a]	1.66 to 4.10	2.36
	No children	1.03	0.90 to 1.17	1.01	−0.04	−0.34 to 0.25	.	1.28[a]	1.12 to 1.45	1.26
	African American/ Black (ref. white)	1.61[c]	1.02 to 2.51	1.46	0.54	−0.51 to 1.59	0.34	1.50	0.96 to 2.32	1.35
	Asian (ref. white)	1.41	0.96 to 2.06	1.30	0.71	−0.16 to 1.58	0.54	1.24	0.85 to 1.79	1.15
	Non-white Latinx (ref. white)	1.02	0.70 to 1.45	.	0.41	−0.39 to 1.20	0.27	0.92	0.64 to 1.30	0.98
	White Latinx (ref. white)	1.12	0.66 to 1.87	1.01	0.18	−0.99 to 1.34	.	0.73	0.42 to 1.23	0.81
	Multiple ancestries (ref. white)	1.41[c]	1.07 to 1.86	1.34	1.01[b]	0.38 to 1.64	0.90	1.40[c]	1.07 to 1.82	1.33
	Other ancestries (ref. white)	0.58[c]	0.34 to 0.95	0.64	−0.66	−1.67 to 0.36	−0.48	1.42	0.92 to 2.18	1.30
Positive and supportive community response	Positive medical provider response	0.72[a]	0.62 to 0.83	0.76	−0.67[a]	−1.00 to −0.34	−0.65	0.90	0.78 to 1.04	0.93
	Positive friend response	0.74[c]	0.58 to 0.96	0.75	−0.56	−1.14 to 0.02	−0.54	1.12	0.88 to 1.43	1.01
	Positive partner response	0.88	0.65 to 1.19	0.89	−0.72[c]	−1.42 to −0.02	−0.69	0.73[c]	0.55 to 0.98	0.76
	Positive family response	0.70[c]	0.52 to 0.92	0.70	−0.18	−0.83 to 0.47	−0.15	0.98	0.75 to 1.29	.
	Support group participation	0.80[b]	0.70 to 0.92	0.83	−0.21	−0.52 to 0.10	−0.15	1.22[b]	1.06 to 1.40	1.20
Negative and stigmatizing community response	Negative medical provider response	0.89	0.76 to 1.05	0.96	0.42[c]	0.08 to 0.77	0.39	1.13	0.97 to 1.32	1.15
	Negative friend response	1.13	0.92 to 1.38	1.10	0.24	−0.22 to 0.69	0.22	1.20	0.99 to 1.45	1.13
	Negative partner response	1.58[a]	1.24 to 2.08	1.55	0.99[a]	0.42 to 1.57	0.99	1.37[b]	1.08 to 1.74	1.37
	Negative family response	1.12	0.89 to 1.41	1.10	0.39	−0.13 to 0.91	0.38	1.07	0.86 to 1.33	1.07
Health	No pre-existing psychiatric diagnosis	0.51[a]	0.45 to 0.58	0.53	−2.00[a]	−2.29 to −1.71	−1.96	0.58[a]	0.51 to 0.66	0.60
	Change in health—worse (ref. same or better health)	0.99	0.76 to 1.31	.	0.06	−0.51 to 0.63	0.06	1.17	0.90 to 1.53	.
	Change in health—much worse (ref. same or better health)	1.02	0.76 to 1.36	.	−0.29	−0.91 to 0.33	−0.22	1.30	0.98 to 1.73	1.11
	Severity of LC symptoms	0.98[a]	0.97 to 0.98	0.98	−0.03[a]	−0.04 to −0.02	−0.03	0.99[a]	0.99 to 1.00	0.99

Table 4 (continued) | Multivariable analysis of protective and risk factors for developing depressive symptoms, anxiety symptoms or suicidal ideation among patients with Long COVID (*N*=5,208)

Variable group	Variable	PHQ-2			GAD-7			Suicidal Ideation		
		GLM OR and significance	95% CI	LASSO OR	GLM coefficient and significance	95% CI	LASSO coefficient	GLM OR and significance	95% CI	LASSO OR
	Number of days with LC symptoms	1.0[b]	0.998 to 0.999	1.00	−0.003[b]	−0.004 to −0.001	−0.002	1.00[a]	1.000 to 1.002	1.00
	Post-illness physical limitations	1.61[a]	1.24 to 2.10	1.55	0.53[c]	0.04 to 1.03	0.44	1.13	0.90 to 1.43	1.13
	Hospitalized for COVID	1.28[c]	1.03 to 1.59	1.23	0.40	−0.09 to 0.89	0.31	1.32[b]	1.07 to 1.63	1.26
	COVID testing access	0.91	0.78 to 1.07	0.93	0.03	−0.32 to 0.38	.	1.08	0.93 to 1.25	1.05
Employment and finances	Post-illness work hours reduced (ref. no change in job)	1.06	0.88 to 1.28	.	−0.19	−0.59 to 0.21	−0.14	1.20	0.99 to 1.44	1.13
	Post-illness job loss (ref. no change in job)	1.40[c]	1.06 to 1.86	1.30	0.71[c]	0.07 to 1.35	0.70	1.34[c]	1.03 to 1.78	1.26
	Post-illness financial hardship	1.55[a]	1.35 to 1.77	1.53	1.26[a]	0.96 to 1.56	1.24	1.67[a]	1.46 to 1.90	1.65

[a]P=0.001. [b]P=0.01. [c]P=0.05. Lasso estimates of '.' are variables that are completely minimized in the model.

large sample size as compared with those who recovered from COVID-19. It also represents one of a few assessments that explore psychiatric functioning in a largely non-hospitalized population, examine potential contributors and correlates to these, and additionally investigate coping strategies and absence of psychiatric sequelae. That said, this study has several limitations. These results are obtained from a non-random cross-sectional design, with a potential for self-report, recall, social desirability and selection biases. As such, causality cannot be inferred. Despite checks such as manual review of data for outliers and inconsistencies, and limiting responses from the same Internet Protocol address, accuracy of responses was not verified via in-person evaluation. The non-randomness requires that the prevalence rates presented be interpreted with caution. Additionally, the majority of recruitment sources being from social media and support networks means that these results, especially prevalence, cannot be considered a representation of all those with LC. However, recruitment through these means allowed for an efficient, wide recruitment that crossed international boundaries, while trust in the research team being composed of patients with LC themselves may have improved participation. The time period of the study, from the beginning of the pandemic through 2021, as well as the international sample, means that differences in societal understanding and appreciation of LC during this time may have impacted factors such as social support received and work accommodations.

The lack of matching between LC and non-LC groups is both a strength and limitation, in that these groups may be different in key areas, though this also increases the likelihood of a presence of a confounder when evaluating psychiatric outcomes. That said, despite the statistical tests being adequately powered at $\beta = 0.1$, the non-LC group is considerably smaller, and this is a key limitation. One potential factor to consider is that those who recovered may have been less motivated to participate and contribute to studies. Another important limitation is lack of follow-up to ensure that those in the non-LC group remained fully recovered.

Additionally, we have previously shown that the clinical syndrome of this population is nearly identical in those testing positive and those untested, testing negative, or testing too late[2]. As a result, to minimize biases related to access to testing and production of antibodies, positive tests were not required to participate (breakdown of participant test status can be found in Supplementary Table 5). While the lack of a reliable, non-biased objective measure of infection is a limitation, these results are probably a closer approximation of the real-world clinical status of those with LC compared with studies that require documentation of positive testing.

While using standardized measures for psychiatric symptoms is a strength and recall bias is minimized by restricting recall to 2 weeks, the results may therefore not be representative of the entirety of an individual's LC symptom experience, especially given the fluctuation in symptoms throughout the illness course[2].

This study was primarily focused on psychosocial aspects of LC, while biological factors, especially immune-inflammatory, are known to influence both LC[19,20] and psychiatric symptomatology[21,22], and should be considered as important aspects of understanding pathophysiology. We also urge additional caution with interpreting our formative predictive models, since unmeasured confounding is likely, which may affect point estimates and confidence intervals[28].

Conclusion

To best address the psychiatric comorbidities in LC, it is important to recognize that the majority of those with LC do not experience psychiatric disease, and that LC is not itself a somaticized illness[3]. However, those with LC are at increased risk for psychiatric disease compared with those who experienced COVID-19 illness without developing LC. This is consistent with the high rates of psychiatric comorbidity in other chronic debilitating medical conditions. Appropriate psychiatric interventions in LC should focus on those who experience psychiatric challenges, emphasize modifiable factors and ensure concomitant workup and treatment of ongoing medical issues.

Methods

Study setting, sample and data collection

We created an internet-based cross-sectional 128-question Qualtrics survey, distributed in September 2020, utilizing social media channels, internet-based support groups and health networks[2]. All participants were infected between December 2019 and September 2021, allowing for analysis up to the start of the Omicron wave. Inclusion criteria for the survey were adults with confirmed or suspected COVID-19 at

least 1 week past symptom onset date. To minimize biases related to testing accessibility and presence of SARS-CoV-2 antibodies[29–32], we used the World Health Organization consensus criteria of probable or confirmed COVID-19 infection with at least 2 months of illness[33] to define LC. We have previously shown that the clinical syndrome in LC is nearly identical in those testing positive and those untested or testing negative[2], which further supports this approach.

Those who recovered in less than 2 months were included in a non-LC control group. We utilized adaptive questioning, with options to take a break and a completeness check.

The study was approved by the University College London Research Ethics Committee (16159.002, UCL, London, UK). Participants gave written informed consent with no financial incentives or compensation.

The following responses were removed from the dataset: did not start survey or un-submitted survey (n = 5,095), onset date before December 2019 (n = 57), 0 days of symptoms (n = 5), poorly formatted symptom date (n = 1), duplicate participants (n = 196) and participants who were sick for longer than 2 months then recovered (n = 212). Responses with ongoing symptoms who had not reached 2 months (n = 1,268) were then removed, resulting in complete data from 5,638 LC respondents and 475 non-LC (respondents who were sick for longer than 1 week and recovered before 2 months). This allowed for comparison of those with ongoing LC symptoms with those who had recovered from COVID-19, eliminating those who recovered from LC after 2 months of illness. Those with LC who recovered were removed from this study as this was thought to be a clinically different subpopulation with different psychiatric outcomes.

Data were collected using Qualtrics v Sept 2020, and exported using Microsoft Excel v16.71. Data were analysed in SPSS v27, R v 4.1.3 with MICE package v3.15.0 and Python v3.7.1 with: pandas 1.1.5, numpy: 1.19.4, pingouin: 0.5.0, scipy: 1.7.3, statsmodels: 0.13.1, datetime and math modules.

Measures

The survey assessed LC symptoms previously reported[2], in addition to social and psychological factors. Recovered participants were asked to approximate their last day of symptoms. The PHQ-2 (ref. 34), GAD-7 (ref. 35) and Brief-COPE[36] were used to assess depression, anxiety and coping, respectively. PHQ-2 with the addition of the suicidal ideation item from the PHQ-9 was used instead of the full PHQ-9, as the PHQ-9 contains some questions assessing somatic symptoms that are common in LC in the absence of psychiatric comorbidity[2], and is thus expected to create measurement error. An additional question allowed individuals to check types of suicidality or self-harm throughout their LC course. PHQ-2 and GAD-7 have established reliability and validity in those with medical illness[35,37], while reliability and validity of the Brief-COPE is established in individuals experiencing adverse events[36]. Depression was defined[34] as PHQ-2 greater than or equal to 3 (sensitivity and specificity of 0.72 and 0.85 (ref. 38)), and anxiety was defined[35] as GAD-7 greater than or equal to 10 (sensitivity and specificity of 0.74 and 0.83 (ref. 39)), minimizing flooring effects. Cut points of 5, 10 and 15 (ref. 35) corresponding to mild, moderate and severe anxiety were used for graphical depiction in Fig. 1. Change in overall health was determined by asking participants to rate their overall health retrospectively pre-COVID-19 illness and post-COVID-19 illness, subtracting the value post-illness from the value pre-illness. A separate question specifically asked participants to rate their overall health on the day of the survey as compared with their pre-COVID baseline. Additional variable details are described in Supplementary Details 1.

Statistical analyses

Univariate and bivariate analysis. We compared rates of depression, anxiety and suicidality between those with LC and those without, and examined relationships between demographic, illness and social factors with psychiatric outcomes in LC. Multivariate analyses were performed to further describe correlates of psychiatric outcomes in the LC group.

Statistical tests were performed in SPSS version 27, R and Python, and results were cross-checked to confirm accuracy. Complete case analysis on a variable-by-variable basis was utilized given low rates of missingness. Chi-squared tests were performed to evaluate relationships between categorical variables and binary psychiatric outcomes. For variables with more than two categories, pairwise Z-tests and Bonferroni-correcting an α of 0.05 were used to determine different proportions within a group. t-Tests were performed to evaluate relationships between continuous variables and binary psychiatric outcomes. The 95% CIs were calculated for all proportions.

Predictive models. Estimates and confidence intervals were calculated using GLMs for the three psychiatric outcomes. Missing data for the predictive model analysis were imputed with the MICE package[40]. Odds of depression and suicidal ideation were both modelled using logistic regression, and anxiety was estimated using linear regression. For each outcome, we first regressed the mental health outcome of interest on all covariates. Variables capturing participants' experience with employers were excluded due to higher rates of missingness since not all participants had an employer (see analysis of subsample of workers in Supplementary Table 3). Income, provider disbelief and perception of appropriate medical care were not included in the models due to theoretical considerations of collinearity and collider bias[41,42]. Variance inflation factors were calculated for all variables in the model, ranging from 1.00 to 1.38 (ref. 43).

Since this model was developed with a non-probability sample, GLM estimates were then compared with more conservative estimates identified using LASSO methods to improve generalizability and account for issues related to overfitting[44]. Using the glmnet model, we used k-fold cross-validation to identify the optimal regularization parameter (λ) for each model[45]. We then regressed each psychiatric outcome on the covariates to identify how our original GLM models compared with more conservative point estimates generated with LASSO.

A post-hoc statistical power analysis identified all final models as fully powered. De-identified data are available upon request.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The full survey is available at http://patientledresearch.com. At the time of survey completion, participants were informed that their responses may be made available to others in de-identified form. Due to the inclusion of text write-in responses, which may erroneously include identifiers, a completely de-identified dataset can be created only with robust manual removal of potential identifiers. As such, a de-identified dataset is not immediately available, but can be made available by request.

References

1. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK. *Office for National Statistics* https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/7april2022 (2022).
2. Davis, H. E. et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *eClinicalMedicine* https://doi.org/10.1016/j.eclinm.2021.101019 (2021).
3. Davis, H. E., McCorkell, L., Vogel, J. M. & Topol, E. J. Long COVID: major findings, mechanisms and recommendations. *Nat. Rev. Microbiol.* https://doi.org/10.1038/s41579-022-00846-2 (2023).

4. Proal, A. D. & VanElzakker, M. B. Long COVID or post-acute sequelae of COVID-19 (PASC): an overview of biological factors that may contribute to persistent symptoms. *Front. Microbiol.* **12**, 1494 (2021).
5. Chapman D. P., Perry, G. S. & Strine T. W. The vital link between chronic disease and depressive disorders. *Prev. Chronic Dis.* http://www.cdc.gov/pcd/issues/2005/jan/04_0066.htm (2005).
6. Caspersen, I. H., Magnus, P. & Trogstad, L. Excess risk and clusters of symptoms after COVID-19 in a large Norwegian cohort. *Eur. J. Epidemiol.* https://doi.org/10.1007/s10654-022-00847-8 (2022).
7. Taquet, M., Geddes, J. R., Husain, M., Luciano, S. & Harrison, P. J. 6-Month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. *Lancet Psychiatry* **8**, 416–427 (2021).
8. Taquet, M. et al. Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients. *Lancet Psychiatry* https://doi.org/10.1016/S2215-0366(22)00260-7 (2022).
9. Sher, L. Post-COVID syndrome and suicide risk. *QJM* **114**, 95–98 (2021).
10. Pantelic, M. & Alwan, N. The stigma is real for people living with long COVID. *Br. Med. J.* https://blogs.bmj.com/bmj/2021/03/25/marija-pantelic-and-nisreen-alwan-the-stigma-is-real-for-people-living-with-long-covid/ (2021).
11. Alwan, N. A. Lessons from Long COVID: working with patients to design better research. *Nat. Rev. Immunol.* **22**, 201–202 (2022).
12. Roth, P. H. & Gadebusch-Bondio, M. The contested meaning of 'long COVID'—patients, doctors, and the politics of subjective evidence. *Soc. Sci. Med.* **292**, 114619 (2022).
13. Seidl, E. & Seidl, O. Do my feelings fit the diagnosis? Avoiding misdiagnoses in psychosomatic consultation services. *J. Healthc. Risk Manag.* **41**, 9–17 (2021).
14. Rogers, M. L., Joiner, T. E. & Shahar, G. Suicidality in chronic illness: an overview of cognitive-affective and interpersonal factors. *J. Clin. Psychol. Med. Settings* **28**, 137–148 (2021).
15. Uhlenbusch, N., Swaydan, J., Höller, A., Löwe, B. & Depping, M. K. Affective and anxiety disorders in patients with different rare chronic diseases: a systematic review and meta-analysis. *Psychol. Med.* **51**, 2731–2741 (2021).
16. Ferro, M. A. et al. Suicidal behaviour among adolescents and young adults with self-reported chronic illness. *Can. J. Psychiatry* **62**, 845–853 (2017).
17. Khuwaja, A. K. et al. Anxiety and depression among outpatients with type 2 diabetes: a multi-centre study of prevalence and associated factors. *Diabetol. Metab. Syndr.* **2**, 72 (2010).
18. Xie, Y., Xu, E. & Al-Aly, Z. Risks of mental health outcomes in people with COVID-19: cohort study. *Br. Med. J.* **376**, e068993 (2022).
19. Klein J., et al. Distinguishing features of Long COVID identified through immune profiling. Preprint at *medRxiv* https://doi.org/10.1101/2022.08.09.22278592 (2022).
20. Choutka, J., Jansari, V., Hornig, M. & Iwasaki, A. Unexplained post-acute infection syndromes. *Nat. Med.* **28**, 911–923 (2022).
21. Gananca, L. et al. Relationships between inflammatory markers and suicide risk status in major depression. *J. Psychiatr. Res.* **134**, 192–199 (2021).
22. Vasupanrajit, A., Jirakran, K., Tunvirachaisakul, C. & Maes, M. Suicide attempts are associated with activated immune-inflammatory, nitro-oxidative, and neurotoxic pathways: a systematic review and meta-analysis. *J. Affect. Disord.* **295**, 80–92 (2021).
23. Corrigan, P. W. & Sokol, K. A. The impact of self-stigma and mutual help programs on the quality of life of people with serious mental illnesses. *Community Ment. Health J.* **49**, 1–6 (2013).
24. Byrne, E. A. Understanding Long COVID: nosology, social attitudes and stigma. *Brain Behav. Immun.* **99**, 17–24 (2022).
25. McKnight-Eily, L. R. Racial and ethnic disparities in the prevalence of stress and worry, mental health conditions, and increased substance use among adults during the COVID-19 pandemic—United States, April and May 2020. *MMWR Morb. Mortal Wkly Rep.* https://doi.org/10.15585/mmwr.mm7005a3 (2021).
26. Shi, L. et al. Prevalence and correlates of suicidal ideation among the general population in China during the COVID-19 pandemic. *Eur. Psychiatry* **64**, e18 (2021).
27. Knudsen, A. K. S. et al. Prevalence of mental disorders, suicidal ideation and suicides in the general population before and during the COVID-19 pandemic in Norway: a population-based repeated cross-sectional analysis. *Lancet Reg. Health Eur.* **4**, 100071 (2021).
28. Westreich, D. & Greenland, S. The Table 2 Fallacy: presenting and interpreting confounder and modifier coefficients. *Am. J. Epidemiol.* **177**, 292–298 (2013).
29. Vashisht, R. et al. Age- and sex-associated variations in the sensitivity of serological tests among individuals infected with SARS-CoV-2. *JAMA Netw. Open* **4**, e210337 (2021).
30. Cases, data, and surveillance. *Centers for Disease Control and Prevention* https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/burden.html (2020).
31. Cervia, C. et al. Immunoglobulin signature predicts risk of post-acute COVID-19 syndrome. *Nat. Commun.* **13**, 446 (2022).
32. Krishna, B. A. et al. Evidence of previous SARS-CoV-2 infection in seronegative patients with long COVID. *eBioMedicine* https://doi.org/10.1016/j.ebiom.2022.104129 (2022).
33. A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021. *World Health Organization* https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1 (2021).
34. Kroenke, K., Spitzer, R. L. & Williams, J. B. W. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med. Care* **41**, 1284–1292 (2003).
35. Spitzer, R. L., Kroenke, K., Williams, J. B. W. & Löwe, B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch. Intern. Med.* **166**, 1092–1097 (2006).
36. Carver, C. S. You want to measure coping but your protocol's too long: consider the brief COPE. *Int. J. Behav. Med.* **4**, 92–100 (1997).
37. Löwe, B., Kroenke, K. & Gräfe, K. Detecting and monitoring depression with a two-item questionnaire (PHQ-2). *J. Psychosom. Res.* **58**, 2163–171 (2005).
38. Levis, B. et al. Accuracy of the PHQ-2 alone and in combination with the PHQ-9 for screening to detect major depression: systematic review and meta-analysis. *JAMA* **323**, 2290–2300 (2020).
39. Plummer, F., Manea, L., Trepel, D. & McMillan, D. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. *Gen. Hosp. Psychiatry* **39**, 24–31 (2016).
40. van Buuren, S. & Groothuis-Oudshoorn, K. mice: multivariate imputation by chained equations in R. *J. Stat. Softw.* **45**, 1–67 (2011).
41. Elwert, F. & Winship, C. Endogenous selection bias: the problem of conditioning on a collider variable. *Annu. Rev. Sociol* **40**, 31–53 (2014).
42. Arah, O. A. The role of causal reasoning in understanding Simpson's paradox, Lord's paradox, and the suppression effect: covariate selection in the analysis of observational studies. *Emerg. Themes Epidemiol.* **5**, 5 (2008).
43. Vittinghoff, E., Glidden, D., Shiboski, S., & McCulloch, C. in *Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models* 253–288 (Springer Publishing Company, 2005).

44. McNeish, D. M. Using LASSO for predictor selection and to assuage overfitting: a method long overlooked in behavioral sciences. *Multivar. Behav. Res.* **50**, 471–484 (2015).
45. Friedman, J. H., Hastie, T. & Tibshirani, R. Regularization paths for generalized linear models via coordinate descent. *J. Stat. Softw.* **33**, 1–22 (2010).

Acknowledgements

The authors acknowledge the contributions of A. Sbrana, J. Seltzer, A. Meriquez Vázquez and K. Phillips, who reviewed and offered feedback on the draft. We also thank G. Pasupathy for assistance creating and formatting supplementary materials. This work was non-funded; the authors all contributed to this project on a voluntary basis.

Author contributions

Y.R., H.E.D., L.M., H.W., G.A. and A.A. created the survey. All authors contributed to the study design and research questions. Y.R., H.E.D. and E.A.S. drafted the initial manuscript. Y.R. and H.E.D. performed the univariate and bivariate analyses. E.A.S. performed predictive modelling. All authors contributed to editing and creating the final manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s44220-023-00064-6.

Correspondence and requests for materials should be addressed to Yochai Re'em.

Peer review information *Nature Mental Health* thanks Jolanta Zawilska, Simon Faissner and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

nature portfolio

Corresponding author(s): Yochai Re'em

Last updated by author(s): Mar 18, 2023

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☐	☒	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data was collected using Qualtrics v Sept 2020, and exported using Microsoft Excel v16.71
Data analysis	Data was analyzed in SPSS v27, R v 4.1.3 with MICE package v3.15.0 and Python v3.7.1 with: pandas 1.1.5 numpy: 1.19.4 pingouin: 0.5.0 scipy: 1.7.3 statsmodels: 0.13.1 datetime and math modules

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

De-identified data is available upon request. The full survey is available at https://patientresearchcovid19.com/.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Sex and Gender are both reported. Sex was determined by asking whether gender matches gender assigned at birth.
Population characteristics	See below.
Recruitment	Participants were recruited from social media channels, online support groups, and health systems. These results are obtained from a non-random cross-sectional design, with a potential for self-report, recall, and social desirability biases, and causality cannot be inferred.
Ethics oversight	The study was approved by the University College London Research Ethics Committee (16159.002, UCL, London, UK).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	Quantitative cross sectional. A large international survey was disseminated via social media and health networks. Participants included those with confirmed or suspected covid-19 infection. Questions asked participants to reflect on their recovery experience retrospectively and also answer questions relating to their experience at the time of survey completion. The survey was distributed in September 2020 and remained open indefinitely, with data analysis restricted to end at infection date September 1 2021 to account for the beginning of the Omicron wave. Standardized survey instruments included brief-COPE, PHQ-9, GAD-7.
Research sample	The survey "Information Sheet" (accessible here: patientresearchcovid19.com/survey2) stated: "You are being invited to participate in this research study because you have had a COVID-19, or suspected COVID-19 infection (still suffering or suffered symptoms) for longer than 1 week and you are 18 years of age or older." This study sample was chosen in order to obtain a high N from international sources, with the survey easily accessible on the internet. The goal at the time was to obtain as much information as possible as quickly as possible given the novelty of the virus and the rapidly evolving landscape of Covid-19. This was distributed via online support groups, social media sites, and health networks, resulting in an international population with a majority of women, and age range peak 30-49. Given the lack of adequate existing demographic data describing Long Covid, the demographic features of the underlying population remain unknown. However, we suspect that our population is not sufficiently representative of the larger Long Covid population, to a degree, given the internet-based recruiting and emphasis on reliance on support groups, and this is discussed in our limitations.
Sampling strategy	Convenience sampling, The survey was open to all adults who chose to participate.
Data collection	Participants entered their answers to the survey on their personal devices via computer or mobile. Qualtrics was used to collect the data. For data protection, an MD5 (message-digest algorithm) hash code was generated with participants' email addresses or phone numbers. Participant email addresses were stored in a secure data center. Cookies that expired between two weeks and one month were used to save progress. Incomplete, expired, and duplicate entries based upon hash code were excluded from analysis. Researchers were not present at the time of data collection and were unblinded to the hypothesis.

Timing	Survey was distributed in September 2020 and kept open indefinitely. A data pull for the analysis was performed on June 1, 2022. Data analysis was restricted to participants who were infected between December 1 2019 and September 1 2021, allowing for analysis up to the start of the Omicron wave, with total N=6113.
Data exclusions	Exclusion criteria were pre-established. The following responses were removed from the dataset: did not start survey or un-submitted survey (n = 5095), onset date before December 2019 (n = 57), 0 days of symptoms (n = 5), poorly formatted symptom date (n=1), duplicate participants (n = 196), test response (n=1), and participants who were sick for longer than two months then recovered (n=212). Responses with ongoing symptoms who had not reached 2 months (n = 1268) were then removed, resulting in complete data from 5638 Long Covid respondents and 475 non-LC (respondents who were sick for longer than one week and recovered before two months).
Non-participation	Of those who completed the consent form, 82% started the survey, and 58.5% of those who started the survey completed it.
Randomization	Not random, covariates controlled in multivariate model using LASSO.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging