

ABSTRACT

Background: No studies exist exploring psychiatric outcomes in patients with Long Covid (LC) as compared with those who had experienced Covid-19 and completely recovered, nor any that explore factors associated with psychiatric outcomes in those with persistent symptoms. Given the increased rates of psychiatric illness in disabling medical conditions, LC may be associated with comorbid psychopathology. In the setting of patient reports of providers attributing LC solely to psychiatric illness, we hypothesized that not all LC individuals experience psychiatric symptoms. In order to better characterize psychiatric symptoms in LC and understand the contributing factors, we administered an internet-based survey containing standardized psychiatric screeners to assess depression, anxiety, and suicidality in those who had recovered from Covid-19 and in those with LC.

Methods: Cross sectional design, with inclusion criteria of confirmed or suspected Covid-19 illness. LC was defined by at least two months of symptoms, and non-LC one week up to two months of symptoms. Total sample size was 6113, with 5638 LC and 475 non-LC.

Results: Depression, anxiety, or suicidality were identified in 42.8% of those with LC and 28.0% of those without LC ($p < 0.001$), while the majority of those with LC (57.2%) and those without LC (72%) did not experience these. Suicidal thoughts were reported by 17.3% of LC and 10.8% of non-LC ($p < 0.001$); 32.7% of LC and 21.8% of non-LC had Patient Health Questionnaire-2 (PHQ-2) scores ≥ 3 ($p < 0.001$), and 25.2% of LC and 16.7% of non-LC had General Anxiety Disorder-7 (GAD-7) scores ≥ 10 ($p < 0.001$). Individuals with LC displayed significantly higher rates of adaptive coping styles on the Brief-COPE scale. Factors that were associated with psychiatric outcomes in LC included younger age, greater reductions in overall health, income, psychiatric history, limitations to physical activity, financial pressure, sex, gender, impact of illness on employment, and negative experiences with support from medical professionals, family, friends, partners, and employers.

Conclusions: Long Covid is not in itself an entity defined by psychiatric challenges, but rather one that may include an element of psychiatric comorbidity in a subset of the LC population. Anxiety, depression, and suicidality in LC exist at similar rates to those in other debilitating medical conditions. Those with LC may be more at risk for these than those with Covid-19 who recover. Individuals with LC had higher rates of adaptive coping styles, and multiple illness-related and social factors were associated with psychiatric outcomes.

INTRODUCTION

Prolonged symptoms due to COVID-19 infection are prevalent¹ and can be debilitating.² These prolonged symptoms are referred to as Long Covid (LC)³, also known as post COVID-19 condition⁴ or Post-Acute Sequelae of Covid-19 (PASC)⁵. The World Health Organization's (WHO) consensus definition of post COVID-19 condition encompasses individuals with probable or confirmed SARS-CoV-2 infection with onset of prolonged symptoms usually within three months of infection, lasting for at least two months and generally impacting daily functioning.⁴ LC is a multi-systemic complex chronic disease that can involve the neurocognitive, respiratory, gastrointestinal, and cardiovascular systems, among others.⁶ Current theories about pathophysiology include viral persistence, endothelial dysfunction and persistent clotting, immune dysregulation and autoimmunity, and hyperinflammatory states.⁷

Given the increased rates of psychiatric illness in disabling medical conditions such as cancer and asthma,¹¹ Long Covid (LC) may be associated with comorbid psychopathology. The frequency with which mental health issues manifest after Covid-19 infection is poorly understood, with different reported results depending on study type, methodology, and research question asked. A systematic review assessing post-Covid psychiatric symptoms found that the most commonly reported psychiatric symptoms were depression and anxiety, with variability in incidence and follow up period. The majority of the studies in the review were of hospitalized

individuals and did not have a control group.⁹ Studies that include non-hospitalized cohorts and non-infected controls find elevated rates of anxiety and depression symptoms after Covid-19 compared to controls, but lower rates of anxiety and depression compared to severe cases.¹⁰ While suicidality has been postulated to occur in the LC population at higher frequencies compared to the general population¹¹, no studies have evaluated this.

Reported rates of psychiatric illness in those who have experienced prior Covid-19 illness are elevated compared to the general population¹². We have previously shown that individuals with LC experience a number of mood symptoms². LC patient reports highlight stigmatization¹³ and assumptions by others that all their symptoms are due to psychiatric disease^{14,15}, which can lead to misdiagnosis¹⁶. We hypothesized that not all LC individuals experience significant symptoms of depression, anxiety, or suicidality, and that the majority of those with LC did not utilize maladaptive coping techniques. The extent of psychiatric symptoms in LC compared to those who recovered from Covid-19, and how social, health, and demographic factors relate individually to depression, anxiety, and suicidality in LC, has not been evaluated. In order to better qualify these psychiatric symptoms, we utilized depression, anxiety, and suicidality screening measures, along with a coping scale, and compared responses between those with LC and those who were infected with SARS-CoV-2 but did not develop LC. We then evaluated associations of demographic, illness, and social factors with anxiety, depression, and suicidality in order to better describe the individuals who experience psychiatric comorbidity as part of their LC course.

METHODS

Study setting, sample & data collection: We created and distributed an internet-based cross-sectional survey.² Development of the survey began in June 2020, and the Qualtrics survey was

disseminated starting in September 2020 utilizing social media channels and internet-based support groups². Inclusion criteria for the survey were those 18 years and older with confirmed or suspected Covid-19 who were at least one week past their symptom onset date. The survey consisted of 128 sequential questions. We utilized adaptive questioning focused on severity and incidence of specific symptoms. Participants were given the option to take a break. There were no financial incentives. A reminder page at the end of the survey was included as a completeness check. Incomplete, expired, and duplicate entries were excluded from analysis.

The study was approved by the University College London Research Ethics Committee (16159.002, UCL, London, UK), and Oregon Health and Science University Institutional Review Board (IRB) (Portland, OR, USA), with UCL serving as the primary site. The Weill Cornell Medical College IRB granted an exemption. Participants gave written informed consent to participate in order to complete the survey.

To ensure data protection, an MD5 (message-digest algorithm) hash code was generated with participants' email addresses or phone numbers. This one-way cryptographic function ensures that participants cannot be de-anonymized within the Qualtrics database. Participant email addresses were stored in a General Data Protection Regulation (GDPR)-compliant server in a secure data center in the European Union. Cookies that expired between two weeks and one month were used to save progress. An IP check was used in conjunction with cookies to prevent multiple survey entries from a single device. Incomplete, expired, and duplicate entries based upon hash code were excluded from analysis.

To minimize biases related to testing accessibility and presence of anti-SARS-CoV-2 antibodies^{17,18}, we used the WHO consensus criteria of probable or confirmed Covid-19 infection with at least two months of illness⁴ to define Long Covid. Those who recovered in less than two months from a probable or confirmed Covid-19 course were included in a non-LC

control group. All participants had symptom onset dates between December 2019 and September 2021, which allowed for analyzing LC cases up to the start of the Omicron wave.

Measures: The survey included assessments of individuals' symptom trajectories over time as previously reported², in addition to social and psychological factors. Question formats included Likert scales and check-all-that-apply, with an option to add comments in open-ended form. Participants were asked to identify whether they were completely recovered, and if so to approximate their last day of symptoms. Participants who were transgender may have chosen to identify as either a specific gender or as non-binary depending on their preference. Sex was included as a separate variable, assessed by asking participants whether their gender matched their sex at birth. Standardized measures included the Patient Health Questionnaire-2 (PHQ-2)¹⁹ to assess depressive symptoms, General Anxiety Disorder-7 (GAD-7)²⁰ to assess anxiety, and Brief-COPE²¹ to assess coping. We elected to use the PHQ-2 over the PHQ-9, as the PHQ-9 contains several questions assessing somatic symptoms that are common in LC in the absence of psychiatric comorbidity², and thus was expected to create measurement error. The PHQ-2 and GAD-7 have established reliability and validity in the medical population,^{20,22} while reliability and validity of the Brief-COPE is established in individuals experiencing traumatic events.²¹ Depression was defined²² as PHQ-2 greater than or equal to 3, and anxiety was defined²⁰ as GAD-7 greater than or equal to 10, thereby minimizing flooring effects. These cut points are supported by sensitivity and specificity of 0.72 and 0.85 for PHQ-2 scores of 3 or greater²³, and 0.74 and 0.83 for GAD-7 scores of 10 or greater²⁴. Cut points of 5, 10, and 15²⁰ corresponding to mild, moderate, and severe anxiety were used for graphical depiction in Figure 1. Those who scored any points on the PHQ suicidality question were grouped together to create a binary suicidality variable. The suicidality question of the PHQ-9 was retained as a separate question to assess suicidality in the prior two weeks. An additional question allowed individuals to check types of suicidality or self-harm throughout their LC course. We favored

standardized measures as outcomes in the analysis, as they minimize recall bias. Participants were asked to rate, on a scale of 1-10, their overall health pre- and post-Covid-19 illness. Differences between these scores were calculated to obtain an overall change in health score. Participants were also asked to assess their overall health on the day of survey completion as a function of their pre-Covid-19 health. Participants were able to check off whether they found their providers, friends, partners, and family members “harmful,” “dismissive,” “skeptical,” or “apathetic,” which we defined broadly as a “negative experience,” and “supportive” or “actively engaged in support,” which we defined as a “positive experience.” Financial pressure was defined as “lost job or can’t work if self employed,” “can’t afford basic necessities,” or “under pressure but able to make ends meet.” Participants were asked whether their persistent symptoms impacted their employment, with this defined as “I needed to reduce my hours working remotely or in person,” or “I had to quit my job or was fired.”

The survey also assessed demographics, presence or absence of specific LC symptoms from a provided list, whether participants found a support group helpful to their overall wellbeing, and whether they had access to PCR testing. Participants were also given the option to check off from a list what new diagnoses they were given by a provider.

Statistical Analyses

Univariate & Bivariate Analysis

We compared rates of depression, anxiety, and suicidality between those with LC and those without. We then examined relationships between demographic factors, illness factors, social factors, and psychiatric outcomes, in the LC group. Finally, 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 the low rates of missing data. Analyses on coping strategies and non-psychiatric symptoms were performed by applying a Bonferroni correction to α of 0.05 to assess significance. Chi-squared tests were performed to evaluate relationships between categorical variables and binary psychiatric outcomes, with the chi-squared test statistic (χ^2) and p-values reported. For those variables that had more than two categories, pairwise Z-tests with Bonferroni-corrected p value of 0.05 were used to determine significantly different proportions within a group. T-tests were performed to evaluate relationships between continuous variables and binary psychiatric outcomes, with the t-test statistic (t) and p-values reported. 95% confidence intervals were calculated for all proportions. Effect size for chi-square tests was estimated using the ϕ coefficient or Cramer's V, considered small at 0.1, medium at 0.3, and large at 0.5. To estimate effect size for t-tests, we calculated Cohen's d, considered small at 0.2, medium at 0.5, and large at 0.8.

Predictive models

We developed formative models to identify how the biological and social variables assessed were associated with participants' psychiatric health. Estimates and confidence intervals were estimated using generalized linear models (GLM) for the three psychiatric outcomes: depression symptoms, anxiety symptoms, and suicidal ideation. Since this model was developed with a non-probability sample, GLM estimates were then compared to more conservative estimates identified using least absolute shrinkage and selection operator (LASSO) regression to improve generalizability.^{25,26}

Missing data was imputed using single imputation with the MICE package, as multiple imputation is not compatible with LASSO. Odds of screening positive for depression and odds of reporting any suicidal ideation were both modeled using logistic regression, and anxiety

symptom severity was estimated using linear regression. For each outcome and using the full LC sample, we first regressed the mental health outcome of interest on all covariates with the exception of variables capturing participants' negative and positive post-illness experience with employers due to higher rates of missingness. We then conducted a secondary analysis on a subsample of participants who were employed at organizations prior to the start of the COVID-19 Pandemic (i.e. excluded unemployed and self-employed participants) in order to include employer-related variables in the models [see supplementary]. Some variables, such as income, provider disbelief, and perception of appropriate medical care were not included in the models due to theoretical considerations of collinearity and collider bias.^{27,28} Variance inflation factors were calculated for all variables in the model, ranging from 1.00-1.38.²⁶

Models for both the full and employed samples were then replicated using LASSO regression for each of the three psychiatric outcomes. LASSO regression was selected to account for issues related to model overfitting using regularization²⁵. Using the glmnet model, we used k-fold cross-validation to identify the optimal regularization parameter (λ) for each model.²⁹ We then regressed each psychiatric outcome on the covariates to identify how our original GLM models compared to more conservative point estimates generated with LASSO. Of note, regularization techniques for regression do not calculate confidence intervals or standard errors.

A post-hoc statistical power analysis identified that the final models were fully powered.

RESULTS

Demographics for the cohort are depicted in Table 1. 82% of those who completed the consent form started the survey, and 58.5% of those who started the survey completed it. The total sample consisted of 5638 participants with LC and 475 without LC. Over 50 countries were represented, with the majority (54.8%) from the United States and Canada, and 26.3% from the U.K. 19.8% of the participants were healthcare workers. The median duration of illness in the non-LC group was 16 days, while the median duration of illness in the LC group was 190 days and ongoing at time of survey completion.

LC vs. non-LC

As shown in Table 1, there were significant differences in sex, age, and area of residence between those with LC and those without, with non-LC individuals more likely to be male ($\chi^2 = 7.38, p = 0.007$), younger ($\chi^2 = 53.04, p < 0.001$), and more likely to report living in a rural or suburban area ($\chi^2 = 42.32, p < 0.001$). The proportion of healthcare workers was higher in the LC group ($\chi^2 = 4.93, p = 0.026$). There were no significant differences in hospitalization between LC and non-LC groups, with 9.2% of individuals with LC hospitalized compared with 6.5% of non-LC. There were no significant differences in prior psychiatric history between those with LC (44.4%) and those without (40.3%).

The majority of participants did not meet cutoffs for any of the three psychiatric outcomes, with 42.8% (95% CI 41.5,44.1) of those with LC and 28.0% (95% CI 24.0,32.3) of those without LC meeting a cutoff for either depression, anxiety, or suicidality ($\chi^2 = 39.57, p < 0.001$). Of those who experienced significant depression, anxiety, or suicidality, 44.4% (95% CI 42.2, 46.2) in LC, and 44.2% (95% CI 35.8, 53.2) in the non-LC group had no psychiatric history.

There was no significant difference in reported new psychiatric diagnoses between LC (3.0%, 95% CI 2.5, 3.4) and non-LC (0.1%, 95% CI 0.0, 2.4) respondents ($\chi^2 = 0.94$, $p=0.33$).

GAD-7

GAD-7 scores, categorized by severity of anxiety, are depicted in Figure 1.1. 25.2% (24.0, 26.4) of LC and 16.7% (13.4, 20.5) of non-LC experienced moderate to severe anxiety, using a binary cutoff of $GAD \geq 10$, though medians and means of both groups were below the screening cutoff GAD-7 score of 10. This difference between groups was significant ($\chi^2 = 16.12$, $p < 0.001$, effect size $\phi = .052$).

PHQ2

PHQ-2 scores are depicted in Figure 1.2. Using a PHQ-2 cutoff value of 3, 32.7% (31.5, 34.0) of LC and 21.8% (18.1, 25.8) of non-LC were depressed; this difference was significant ($\chi^2 = 23.20$, $p < 0.001$, effect size $\phi = .062$).

Suicidality

Suicidality is detailed in Figure 1.3 and Figure 1.4. 17.2% (16.3, 18.3) of LC and 10.8% (8.1, 14.0) of non-LC reported suicidal thoughts in the prior two weeks. This difference was significant ($\chi^2 = 12.7$, $p < 0.001$, effect size $\phi = .046$).

Coping

Overall, the most utilized coping strategies in LC were acceptance, planning, active coping, and use of emotional support. The least utilized were denial, substance use, behavioral disengagement, and self-blame. As detailed in table 2, compared to non-LC, LC displayed significantly higher scores on adaptive coping, use of emotional support, venting, use of instrumental support, planning, behavioral disengagement, and self-blame. These differences remained significant when eliminating those with a PHQ-2 score of ≥ 3 from both groups.

Factors associated with psychiatric outcomes in LC

Demographic-related factors

Depression was significantly different by gender overall ($\chi^2 = 9.48$, $p = 0.009$), with 32.0% (30.6,33.4) of women significantly less likely than 46.3% (35.0,57.8) of non-binary/gender nonconforming respondents to be depressed. 34.6% (31.8,37.5) of men were depressed, which was not significantly different from women or non-binary/gender nonconforming groups. Anxiety was significantly different by gender overall ($\chi^2 = 8.58$, $p = 0.014$), with 39.2% (28.4,50.9) of non-binary/gender nonconforming respondents significantly more anxious than 24.5% (21.9,27.1) of men, and 25.1% (23.8,26.5) of women. 20.7% (18.3,23.2) of those with male sex experienced suicidal thoughts, significantly more ($\chi^2 = 14.21$, $p < 0.001$) than female sex at 15.9% (14.8,17.0). There were no significant differences in anxiety or depression by sex.

Overall, 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. 24.3% (23.1,25.6) of those who reported their ancestry as white were anxious, significantly less than those with mixed race other than white at 41.9% (30.5,53.9). Those who reported their ancestry as white also had lower rates of suicidality than all the other groups (16.4%), and lower rates of depression (32%), especially compared to those with mixed ancestry other than white (41.9%), though these were both not significant after Bonferroni correction.

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 significantly more likely to be younger, particularly in the 18-29 year old age range.

We analyzed income in currencies that represented at least 10% of the responses (USD and GBP) and created 5 income categories (USD: \$0-10k, \$10-40k, \$40-80k, \$85-150k, >\$150k; UK: £0-20k, £20-40k, £40-60k, £60-80k, >£80k). Participants were asked to report their income before the Covid-19 pandemic, and at the time of the survey. Lower income brackets before and during the pandemic were associated with higher levels of psychiatric outcomes [income before pandemic: anxiety ($t = 4.37$, $p < .001$), depression ($t = 7.54$, $p < .001$), and suicidal thoughts ($t = 6.94$, $p < .001$); [income during the pandemic: anxiety ($t = 6.05$, $p < .001$), depression ($t = 9.82$, $p < .001$), and suicidal thoughts ($t = 9.05$, $p < .001$)].

Those with a prior psychiatric diagnosis were significantly more likely to experience suicidality ($\chi^2 = 94.47$, $p < 0.001$), depression ($\chi^2 = 150.74$, $p < 0.001$), and anxiety ($\chi^2 = 163.67$, $p < 0.001$).

Symptom and Severity-related factors

Rates of psychiatric conditions and their relationships with illness factors are detailed in Table 3.

There were no significant relationships between the number of days of symptoms and suicidality, depression, or anxiety.

Individuals with depression and suicidality had greater overall reductions in health (drops of 2.15 and 2.17 on a 10-point scale, respectively), with no significant relationship observed between change in health and anxiety. Those with depression ($t = 19.18$, $p < 0.001$), anxiety ($t = 10.96$, $p < 0.001$) and suicidality ($t = 12.03$, $p < 0.001$) reported lower overall health on the day of the survey compared to baseline.

Those with limitations to their physical activity, compared to those without, were more likely to experience depression ($\chi^2 = 90.20$, $p < 0.001$), suicidality ($\chi^2 = 33.55$, $p < 0.001$), and anxiety ($\chi^2 = 20.72$, $p < 0.001$).

Participants who were hospitalized, compared to those who were not, had higher levels of depression ($\chi^2 = 9.63$, $p < 0.05$) and suicidal thoughts ($\chi^2 = 4.23$, $p < 0.05$), with no significant differences in anxiety.

We also explored the individual relationships between presence or absence of 144 non-psychiatric symptoms, and each of the three psychiatric outcomes in the LC group. After Bonferroni correction, 26 symptoms were significantly associated with at least one mental health outcome and a weak effect size (Cramer's V of 0.1 to 0.3). No symptom had a medium or large effect size (Cramer's V > 0.3). Significant symptoms included eye and vision symptoms, muscle and joint pain, more severe symptoms such as slurring words, hallucinations, and acute confusion, several headache and cognitive symptoms, and sexual dysfunction. For any subset with a given symptom, the proportion with depression ranged from 31.8%-49.2%, the proportion with anxiety ranged from 21.3%-41.9%, and the proportion with suicidal thoughts ranged from 16.6%-33.8%. A full list of symptoms and mental health outcomes is in Supplemental Table 1.

Participants were given the option of reporting new diagnoses made by a medical provider.

Using a minimum of 25 responses per diagnosis, we identified 14 new non-psychiatric diagnoses 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 ($\chi^2 = 1.7$, $p = 0.02$).

3% with LC reported being given a new psychiatric diagnosis. Of those given a new psychiatric diagnoses, 33.5% (26.4%, 40.7%) did not meet the threshold for depression, anxiety, or suicidal thoughts in the past two weeks.

Social factors

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

Those who experienced any financial pressure, compared to those who did not, experienced more suicidality ($\chi^2 = 137.91$, $p < 0.001$), depression ($\chi^2 = 173.62$, $p < 0.001$), and anxiety ($\chi^2 = 145.38$, $p < 0.001$). Those whose illness affected their employment experienced more suicidality ($\chi^2 = 17.80$, $p < 0.001$), depression ($\chi^2 = 25.58$, $p < 0.001$), and anxiety ($\chi^2 = 13.31$, $p < 0.001$).

Negative experiences with providers were the most frequently reported type of negative experience, with 52.9% of respondents reporting them within a median 190 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 reported that at least one of their doctors conveyed they did not believe them, compared to those who did not, were more likely to be depressed ($\chi^2 = 23.77$, $p < 0.001$), anxious ($\chi^2 = 33.55$, $p < 0.001$), and suicidal ($\chi^2 = 29.16$, $p < 0.001$). In order to account for the possibility that those with psychiatric symptoms might be more likely to report not being believed by a provider, we also compared rates of affirmative responses to this question in those with LC compared to those without, after removing all those with a psychiatric condition, finding that significantly more with LC reported a doctor did not believe them (71.0% vs. 32.6%, $\chi^2 = 145.8$, $p < 0.001$)

Those who experienced negative interactions with their provider, family, friends, partner, or employer were more likely to report suicidal thoughts , more likely to be depressed , and more likely to be anxious . (p<0.001, Table X).

Those who experienced positive interactions with their provider, family, friends, partner, or employer were less likely to report suicidal thoughts (, less likely to be depressed , and less likely to be anxious (. (p<0.001, Table X)

To assess the need for medical care, participants were able to indicate whether they did not need any medical care, and whether they received the appropriate amount of care or less care than they needed. 71.1% of respondents reported receiving below the appropriate amount of medical care. 21.8% received the appropriate amount of care, and 7.1% reported not needing medical care. Those with depression were significantly more likely to report receiving *significantly below* and *somewhat below* the appropriate amount of care ($\chi^2 = 38.99$, $p < 0.001$).

Those with suicidal thoughts were significantly more likely to report experiencing *significantly below* and *somewhat below* the appropriate amount of care and less likely to report receiving the appropriate amount of care ($\chi^2 = 66.00$, $p < 0.001$). Those with anxiety were significantly more likely to report receiving *significantly below* the appropriate amount of care, and less likely to report receiving the appropriate amount of care ($\chi^2 = 50.97$, $p < 0.001$).

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 well-being, with 21.5% reporting no effect, and 8.5% reporting psychological worsening.

There were no observed significant relationships between psychiatric symptoms and access to SARS-CoV-2 diagnostic PCR or antibody testing.

Overall, those with children were slightly less likely to be anxious ($\chi^2 = 4.63$, $p = 0.031$), depressed ($\chi^2 = 5.732$, $p = 0.017$), and suicidal ($\chi^2 = 30.43$, $p < 0.001$). In order to attempt to account for the age of children, participants were analyzed separately by age group. Only those in the age groups 40-49 ($\chi^2 = 9.23$, $p = .002$) and 50-59 ($\chi^2 = 5.661$, $p = .017$) who had children were less likely to experience suicidality. Those in the age group 30-39 with children had higher GAD-7 scores ($\chi^2 = 4.42$, $p = .036$). There were no age group specific relationships between having children and depression.

Predictive Models

GLM and LASSO estimates for these three psychiatric outcomes (depression, anxiety, and suicidal ideation) conducted with the full LC sample are presented in Table Xa. GLM and LASSO estimates for LC participants employed at organizations (which includes employer response variables) are included in Table Xb. Across models, the magnitude of effect for variables was modest. LASSO estimates resembled GLM estimates, and were consistently attenuated. Observations across models are provided below.

Full LC Sample

Demographics

All results controlled for other covariates. Age greater than 30 years was consistently protective against screening positive for depression, anxiety, and suicidal ideation. Men experienced increased odds of depression and suicidal ideation compared to women, and non-binary/genderqueer participants were at increased odds of suicidal ideation. Identifying with multiple ancestries was associated with all three mental health outcomes compared to white participants. Not having children was associated with increased risk of suicidality but not depression, and was associated with decreased risk of anxiety.

Medical and Social Support

Across all three psychiatric outcomes, positive and negative experience with partners was a significant factor, while experience with family was less often significant. A positive experience with a physician lowered the odds of depression and anxiety; a negative experience increased the odds of both.

Health

When controlling for other variables in the model, LC-related physical limitations were associated with depression and anxiety, and having been hospitalized was associated with depression and suicidal ideation. Severity of LC symptoms was associated with all psychiatric outcomes. Having “much worse” health emerged as a significant risk factor in the suicidal ideation GLM model, when controlling for the other variables. More number of days sick was inversely associated with anxiety and depression but positively associated with suicidal thoughts. Access to COVID testing was not significant in any of the models. Not having had a previous psychiatric diagnosis before becoming ill was consistently associated with better depression, anxiety, and suicidal ideation outcomes after developing LC, when controlling for other covariates.

Employment and Finances

Both financial hardship and job loss since becoming ill was positively associated with depression, anxiety, and suicidal ideation. While having reduced number of hours of work trended towards significance as a risk factor in suicidal ideation model, it was not significant in the other models and was shrunk to zero in the LASSO model estimating odds of depression.

An additional model, of LC patients who were employed at organizations before getting sick, is included in the supplementary materials. Negative responses from employers were positively associated with screening positive (trend) and severity of anxiety symptoms (significant), but not with suicidal ideation. Further information can be found in [TABLE X].

DISCUSSION

In this first study of psychiatric symptoms in Long Covid as compared with those experiencing Covid-19 illness and recovering, we found that LC was associated with greater psychiatric symptom burden, while the majority of those with LC do not experience psychiatric symptoms. We additionally found that psychiatric symptoms in LC are associated with younger age, greater reductions in overall health, symptom severity, loss of income, positive psychiatric history, limitations to physical activity, financial pressure, sex, gender, employment impacted by illness, and negative experiences with support systems (medical professionals, family, friends, partners, and employers).

Psychiatric symptoms are commonly experienced in chronic and debilitating illnesses such as cancer, diabetes, and asthma^{11,20-23}, and our findings show similar rates of depression, anxiety, and suicidality in LC. Our results also suggest that while both those with LC and those who experienced Covid-19 and recovered^{8,24,25} are at risk for psychiatric sequelae, those with LC may be at higher risk due to factors related to dealing with chronic illness. Importantly, 57.2% of those with LC did not meet any cutoff for anxiety, depression, and suicidality, reinforcing that LC is not in itself an illness defined by psychiatric symptoms. Considering the prevalence of physical symptoms in LC without psychiatric comorbidity, screening tools that rely on somatic markers of psychiatric illness such as fatigue or tachycardia are likely to overrepresent the burden of psychiatric illness in this population. Accounting for this and offering psychiatric intervention only to those experiencing psychological difficulties would allow for improved utilization of an already taxed mental healthcare system.

[Ancestry discussion]

Our result 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 historically marginalized populations in the wake of the global COVID-19 pandemic, which are related to disparities in access to healthcare, psychosocial stressors, and social determinants of health, all factors that disproportionately impact marginalized communities. Our findings suggest that future studies should explore these disparities in greater detail, and that comprehensive care for Long COVID patients should include assessing for social and community assets and barriers to care³⁰.

Comparing coping styles in those with LC to 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 had more adaptive approaches to coping, with the largest effect sizes seen in increased active coping, instrumental support, and planning, regardless of depressive symptoms.

Alarming, 52.9% of the participants reported a negative experience with medical providers within the first 6-7 months of illness, and 11.6%-26.3% experienced this with friends, partners, family, and employers. This may be partly addressed with improved messaging from health groups and governmental bodies emphasizing the symptoms and prevalence of Long Covid. Additionally, psychiatric referral in the absence of continued medical workup and treatment is one of many ways the stigma of psychologization³² affects patient care. This is partly evidenced by the Long Covid 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 to other supports, future studies may

shed further light on the interplay between healthcare experiences and mental health outcomes in this population. Finally, the high prevalence of these negative experiences suggests medical harm should be incorporated into mental health research in Long Covid and associated conditions moving forward.

70% of participants who joined an online Covid-19 support group found that the group had a positive impact on their psychological well-being, suggesting that support groups may have potential to be of benefit if led by peers and well moderated.³³

Our symptom analysis showed that association of non-psychiatric symptoms with psychiatric comorbidity is inconsistent among symptoms in the same organ system: only some cognitive, dermatologic, respiratory, headache, smell/taste symptoms were associated with psychiatric outcomes, where others in the same category were not. This suggests that symptom analysis may be more helpful when symptoms are assessed individually rather than as symptom categories. Importantly, of all respondents with cognitive dysfunction, the majority did not have a psychiatric condition, further solidifying that the cognitive dysfunction in LC occurs independent of psychiatric conditions.

Certain symptoms may reflect a phenotype of LC that is more likely to experience psychiatric comorbidity. The presence of acute confusion, vision and hearing symptoms, and hallucinations among significant symptoms with higher effect sizes in relation to psychiatric outcomes suggests a relevance of encephalopathy/delirium, or clinical pictures similar to post-concussive syndrome, though further research is required to better elucidate this.

There have been various prevalence rates reported for suicidality related to the Covid-19 pandemic^{34,35}, 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 to those who experienced Covid-19 and recovered, which is consistent with higher rates of suicidality in chronic illnesses.³⁶ Further studies exploring the factors associated with suicidality in LC may add additional insight into areas for intervention and prevention. Having children is classically thought of as a protective factor for suicidality²⁹ and this was seen in the group overall. However, an analysis by age showed only those aged 40-59 with children had lower rates of suicidality, suggesting that there are unique considerations for those with children of particular ages.

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. These findings reinforce existing clinical and epidemiological understanding that LC is not in itself a psychiatric or somaticized illness. Increased age (i.e. greater than 30 years) also was also consistently inversely associated with any of the psychiatric outcomes, potentially indicating that change in health status may be more emotionally challenging for younger adults to navigate. As can be seen in these models, positive response from medical providers, family, friends, patients, and employers is not the same as the absence of negative responses and vice versa.

STRENGTHS & LIMITATIONS

This study has several strengths. To our knowledge, these findings represent the first assessment of psychiatric symptoms in a geographically diverse LC population with a large sample size as compared with those who experienced Covid-19 and recovered. It also

represents one of the few assessments of psychiatric functioning in those who experienced Covid-19 and were not hospitalized, and additionally looks at the absence of psychiatric symptoms and coping strategies in this population. Additionally, it does not use inappropriate depression and anxiety scales for patients with fatigue and autonomic dysfunction. This study also has a number of limitations. These results are obtained from a cross-sectional design, so causality cannot be inferred. The study also has a non-random cross-sectional sample, which comes with a potential for self-report, recall, and social desirability biases. The non-randomness in particular requires that the prevalence rates presented be interpreted with caution, as this cohort cannot be considered as a representation of all those with LC. 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 these also increase the likelihood of a presence of a confounder when evaluating psychiatric outcomes. We also urge additional caution with interpreting our formative predictive models, since unmeasured confounding is likely, which may affect point estimates and confidence intervals.³⁷ Instead we suggest these models be used as a guide to generate new hypotheses for future research.

CONCLUSION

In order 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 in and of itself not a psychiatric entity. Those with LC may be at increased risk for psychiatric disease compared with those who experienced Covid-19 illness without developing LC, which is consistent with the development of psychiatric comorbidity in other chronic debilitating medical conditions. Appropriate psychiatric interventions in LC should focus on those who experience psychiatric challenges while ensuring concomitant workup and treatment of ongoing medical issues.

TABLES & FIGURES

Table 1. Demographics of survey respondents

Factor	Number of Respondents (N=6113)	Long COVID (N=5638)	Non Long COVID (N=475)
Gender*			
Woman	4756	4413	343
Man	1247	1126	121
Non-Binary	92	81	11
Prefer not to say	10	10	0
Other	8	8	0
Age Group*			
18-29	580	495	85
30-39	1416	1299	117
40-49	1746	1639	107
50-59	1143	1354	89
60-69	707	652	55
70-79	202	183	19

80+	19	16	3
Ancestry			
Asian, South Asian, South East Asian	171	150	21
Black	116	98	18
Hispanic, Latino, or Spanish Origin	197	174	23
White	5061	4695	366
Other, including Pacific Islander, Indigenous Peoples, Middle Eastern/North African	118	110	8
White, and Hispanic, Latino, or Spanish Origin	89	81	8
White and Black and either Asian or Other and/or Asian, and/or other, as above	268	255	13
Black and either Asian or Other and/or Asian, and/or Other	65	52	13
Prefer not to answer	28	23	5
Hospitalization			
Non-hospitalized	5566	5122	444
Hospitalized	547	516	31
Healthcare Worker*			
No	4924	4523	401
Yes	1189	1115	74

Country of Residence			
United States of America	3119	2901	218
United Kingdom and Northern Ireland	1609	1502	107
Canada	232	220	12
France	191	184	7
Spain	113	109	4
Netherlands	81	75	6
Germany	78	74	4
Ireland	69	64	5
Russian Federation	67	39	28
Other	554	470	77

*significantly different between LC and non-LC at the $\alpha = .05$ level.

Table 2.

Coping in Long Covid vs. Non-Long Covid																																																																																																																																																	
Type of Coping	Long Covid (N=5135) Non-LC (N=399)	Mean	SD	t	df	p	Effect Size																																																																																																																																										
Self Distraction	Yes	2.603	0.797	1.368	5532	0.171	0.07																																																																																																																																										
	No	2.546	0.847					Active Coping	Yes	2.876	0.884	8.296	5532	<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	5532	<0.001	0.18	No	2.556	0.931	Behavior 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	5532	<0.001	0.24	No	1.947	0.764	Use of Instrumental Support	Yes	2.567	0.862	7.471	5532	<0.001	0.39	No	2.231	0.910	Positive Reframing	Yes	2.357	0.929	1.421	5532	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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532
Active Coping	Yes	2.876	0.884	8.296	5532	<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	5532	<0.001	0.18	No	2.556	0.931	Behavior 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	5532	<0.001	0.24	No	1.947	0.764	Use of Instrumental Support	Yes	2.567	0.862	7.471	5532	<0.001	0.39	No	2.231	0.910	Positive Reframing	Yes	2.357	0.929	1.421	5532	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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056						
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	5532	<0.001	0.18	No	2.556	0.931	Behavior 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	5532	<0.001	0.24	No	1.947	0.764	Use of Instrumental Support	Yes	2.567	0.862	7.471	5532	<0.001	0.39	No	2.231	0.910	Positive Reframing	Yes	2.357	0.929	1.421	5532	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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																	
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	5532	<0.001	0.18	No	2.556	0.931	Behavior 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	5532	<0.001	0.24	No	1.947	0.764	Use of Instrumental Support	Yes	2.567	0.862	7.471	5532	<0.001	0.39	No	2.231	0.910	Positive Reframing	Yes	2.357	0.929	1.421	5532	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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																												
Use of Emotional Support	Yes	2.721	0.906	3.496	5532	<0.001	0.18																																																																																																																																										
	No	2.556	0.931					Behavior 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	5532	<0.001	0.24	No	1.947	0.764	Use of Instrumental Support	Yes	2.567	0.862	7.471	5532	<0.001	0.39	No	2.231	0.910	Positive Reframing	Yes	2.357	0.929	1.421	5532	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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																																							
Behavior 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	5532	<0.001	0.24	No	1.947	0.764	Use of Instrumental Support	Yes	2.567	0.862	7.471	5532	<0.001	0.39	No	2.231	0.910	Positive Reframing	Yes	2.357	0.929	1.421	5532	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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																																																		
Venting	Yes	2.123	0.738	4.577	5532	<0.001	0.24																																																																																																																																										
	No	1.947	0.764					Use of Instrumental Support	Yes	2.567	0.862	7.471	5532	<0.001	0.39	No	2.231	0.910	Positive Reframing	Yes	2.357	0.929	1.421	5532	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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																																																													
Use of Instrumental Support	Yes	2.567	0.862	7.471	5532	<0.001	0.39																																																																																																																																										
	No	2.231	0.910					Positive Reframing	Yes	2.357	0.929	1.421	5532	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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																																																																								
Positive Reframing	Yes	2.357	0.929	1.421	5532	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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																																																																																			
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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																																																																																														
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	5532	0.094	-0.09	No	2.065	0.914	Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																																																																																																									
Humor	Yes	1.987	0.893	-1.676	5532	0.094	-0.09																																																																																																																																										
	No	2.065	0.914					Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15	No	2.982	0.803	Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																																																																																																																				
Acceptance	Yes	3.092	0.748	2.799	5532	0.005	0.15																																																																																																																																										
	No	2.982	0.803					Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10	No	1.860	1.056																																																																																																																															
Religion	Yes	1.961	1.027	1.886	5532	0.059	0.10																																																																																																																																										
	No	1.860	1.056																																																																																																																																														

Coping assessed using the Brief-COPE scale

Table 3:

		Illness & Social factors contributing to suicidality, depression, and anxiety in Long Covid								
		Suicidality			Depression			Anxiety		
		Mean +/- SD in suicidal	Mean +/- SD in non-suicidal	Test Statistic	Mean +/- CI in depressed	Mean +/- SD in non-depressed	Test Statistic	Mean +/- CI in anxious	Mean +/- CI in non-anxious	Test Statistic
Illness Factors		N = 958	N = 4593		N = 1796	N = 3695		N = 1366	N = 4059	
Days of Illness		203.99 +/- 90.16	203.38 +/- 85.02	t = .20	200.59 +/- 91.71	204.46 +/- 82.83	t = 1.51	201.36 +/- 91.93	204.06 +/- 84.16	t = -.96
Change in Overall Health		2.17 +/- 1.10	2.00 +/- 1.10	t = -4.34**	2.15 +/- 1.09	1.96 +/- 1.10	t = -5.87**	2.07 +/- 1.07	2.01 +/- 1.11	t = -1.78
		Prevalence Suicidal	95% CI	Test Statistic	Prevalence Depressed	95% CI	Test Statistic	Prevalence Anxious	95% CI	Test Statistic
Physically limited by illness	Limited in physical activity	904/4943 = 18.3%	17.2-19.4	$\chi^2 = 33.55^{**}$	1702/4888 = 34.8%	33.5-36.2	$\chi^2 = 90.20^{**}$	1261/4827 = 26.1%	24.9-27.4	$\chi^2 = 20.72^{**}$
	Not limited in physical activity	54/608 = 8.9%	6.7-11.4		94/603 = 15.6%	12.8-18.7		105/598 = 17.6%	14.6-20.8	
Hospitalization	Hospitalized	104/506 = 20.6%	17.1-24.3	$\chi^2 = 4.23^*$	196/504 = 38.9%	34.6-43.3	$\chi^2 = 9.63^*$	134/493 = 27.2%	23.3-31.3	$\chi^2 = 1.15$
	Not Hospitalized	854/5045 = 16.9%	15.9-18.0		1600/4987 = 32.1%	30.8-33.4		1232/4932 = 25.0%	23.8-26.2	
Social Factors										
Financial Challenges	Any financial hardship	606/2548 = 23.8%	22.1-25.5	$\chi^2 = 140.44^{**}$	1055/2530 = 41.7%	39.8-43.6	$\chi^2 = 172.34^{**}$	817/2482 = 32.9%	31.1-34.8	$\chi^2 = 145.38^{**}$
	No financial hardship	352/3003 = 11.7%	10.6-12.9		741/2961 = 25.0%	23.5-26.6		549/2943 = 18.7%	17.3-20.1	
Employment	Illness affected employment	425/2314 = 18.4%	16.8-20.0	$\chi^2 = 17.20^{**}$	769/2292 = 33.6%	31.6-35.5	$\chi^2 = 25.58^{**}$	614/2258 = 27.2%	25.4-29.1	$\chi^2 = 13.32^{**}$
	Illness did not affect employment	106/868 = 12.2%	10.1-14.6		207/856 = 24.2%	21.3-27.2		177/851 = 20.8%	18.1-23.7	
Medical Care	Significantly below care needed	446/1977 = 22.6% ^a	20.7-24.5	$\chi^2 = 66.00^{**}$	742/1955=38.0% ^a	35.8-40.1	$\chi^2 = 38.99^{**}$	588/1930 = 30.5% ^a	28.4-32.6	$\chi^2 = 50.97^{**}$
	Somewhat below care needed	306/1968=15.5% ^b	14.0-17.2		566/1946=29.1% ^b	27.1-31.2		458/1924=23.8% ^b	21.9-25.8	
	Received appropriate care	149/1212 = 12.3% ^b	10.5-14.3		369/1202=30.7% ^b	28.1-33.4		234/1187=19.7% ^c	17.5-22.1	
	Did not need care	57/394=14.5% ^a	11.1-18.3		119/388=30.7% ^a	26.1-35.5		86/384 = 22.4% ^a	18.3-26.9	
Provider Stigma	Negative provider experience	596/2938 = 20.3%	18.8-21.8	$\chi^2 = 34.91^{**}$	1042/2907 = 35.8%	34.1-37.6	$\chi^2 = 23.54^{**}$	847/2872 = 29.5%	27.8-31.2	$\chi^2 = 57.62^{**}$
	No negative experience	323/2302 = 14.0%	12.6-15.5		671/2278 = 29.5%	27.6-31.4		454/2249 = 20.2%	18.5-21.9	
Support Group	Joined online covid-19 support group	582/3297 = 17.7%	16.4-19.0	$\chi^2 = 1.13$	1046/3263 = 32.1%	30.5-33.7	$\chi^2 = 1.30$	797/3223 = 24.7%	23.2-26.3	$\chi^2 = .92$
	Did not join online covid-19 support group	370/2235 = 16.6%	15.0-18.2		741/2210 = 32.7%	31.6-35.5		566/2187 = 25.9%	24.1-27.8	
Access to Testing	Had access to testing	665/3845 = 17.3%	16.1-18.5	$\chi^2 = .70$	1279/3809 = 33.6%	32.1-35.1	$\chi^2 = 2.56$	968/3767 = 25.7%	24.3-27.1	$\chi^2 = .36$
	Did not have access to testing	192/1043=18.4%	16.1-20.9		318/1028 = 30.9%	28.1-33.9		271/1018 = 26.6%	23.9-29.5	
Has Children	Has children	440/2998 = 14.7%	13.4-16.0	$\chi^2 = 30.43^{**}$	927/2961 = 31.3%	29.6-33.0	$\chi^2 = 5.73^*$	705/2936 = 24.0%	22.5-25.6	$\chi^2 = 4.63^*$
	Does not have children	518/2553 = 20.3%	18.7-21.9		869/2530 = 34.3%	32.5-26.2		661/2489 = 26.6%	24.8-28.3	
*p<0.05	Note: For multivariable analyses, prevalences with different superscripts are significantly different at the $\alpha = 0.05$ level									
** p<0.001										

Table 4: Multivariable analysis of protective and risk factors for developing depressive symptoms, anxiety symptoms, or suicidal ideation among patients with long COVID

	Models					
	PHQ-2		GAD-7		Suicidal Ideation	
	OR	95% CI & Significance	Coefficient	95% CI & Significance	OR	95% CI & Significance
Demographic						
Age (>30 years)	0.664	0.4780 - 0.927 ***	-1.634	-2.388 - -0.880 ***	0.740	0.560 - 0.979 *
Male/Man identification (ref female/woman)	-	-	-	-	1.234	1.024 - 1.484 *
Non-binary/ Gender queer identification (ref female/woman)	-	-	-	-	2.106	1.237 - 3.613 **
Not having children	-	-	-	-	1.216	1.038 - 1.424 *
Positive, supportive response						
Positive medical provider response	0.708	0.579 - 0.863 ***	-0.534	-0.997 -0.071 *	-	-
Positive friend response	0.566	0.430 - 0.746 ***	-1.034	-1.684 - -0.384 **	-	-
Positive partner response	-	-	-	-	1.524	1.245 - 1.863 ***
Negative, stigmatizing response						
Negative medical provider response	-	-	0.502	0.0306 - 0.974 *	-	-
Negative friend response	-	-	-	-	1.180	0.994 - 1.398
Negative family response	1.289	1.016 - 1.632 *	0.690	0.146 1.233 *	-	-
Negative partner response	1.658	1.279 - 2.1460 ***	1.400	0.796 - 2.003 ***	-	-
Negative employer response	1.261	1.033 - 1.534 *	0.730	0.281 - 1.179 **	-	-
Health outcomes						
Pre-existing psychiatric diagnosis	0.613	0.509 - 0.739 ***	-1.604	-2.017 - -1.191 ***	0.597	0.515 - 0.693 ***
Severity of LC symptoms	0.978	0.973 - 0.982 ***	-0.024	-0.034 - -0.013 ***	0.992	0.988 - 0.995 ***
Number of days with LC symptoms	-	-	-0.004	-0.006 - -0.001 **	1.001	1.001 - 1.002 ***

Post-illness physical limitations	1.600	1.099 - 2.384 *	0.755	0.037 - 1.474 *	-	-
Required a higher level of COVID care than received	0.745	0.597 - 0.931 **	-	-	1.428	1.2015 - 1.701 ***
Hospitalized for COVID	-	-	-	-	1.314	1.025 - 1.679 *

Employment outcomes

Post-illness job loss	-	-	1.162	0.156 - 2.168 *	1.442	1.023 - 2.033 *
Post-illness financial hardship	1.481	1.222 - 1.794 ***	1.123	0.685 - 1.562 ***	-	-

Significance codes: 0 '****' 0.001 '***' 0.01 '**' 0.05 '.' 0.1 '.' 1

Variables not selected by stepwise algorithm for any of the models: Any race/ethnicity/ ancestry identification; Positive family response; Positive employer response; Testing access; COVID-related support group; Reduced work hours; Change in overall health

All variables are dichotomous with the exception of gender variables (categorical with female/woman as reference group); Severity of LC symptoms (continuous); and Number of days with LC symptoms (continuous)

Ref reference category; OR odds ratio, CI confidence interval

Figure 1 Comparison of depression, anxiety and suicidality in the past 2 weeks between participants with and without Long-COVID

Fig. 1.1 GAD-7

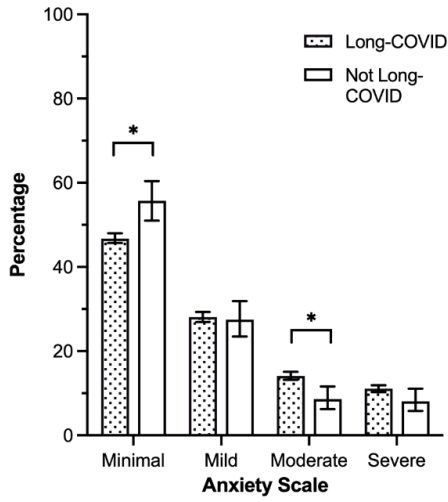


Fig. 1.2 PHQ-2

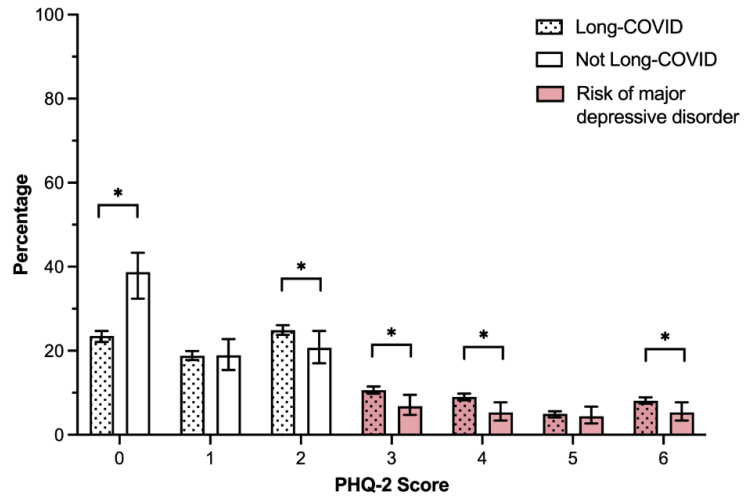


Fig. 1.3 Suicidality

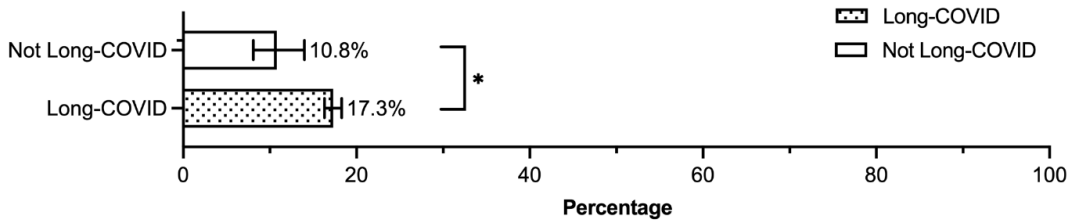
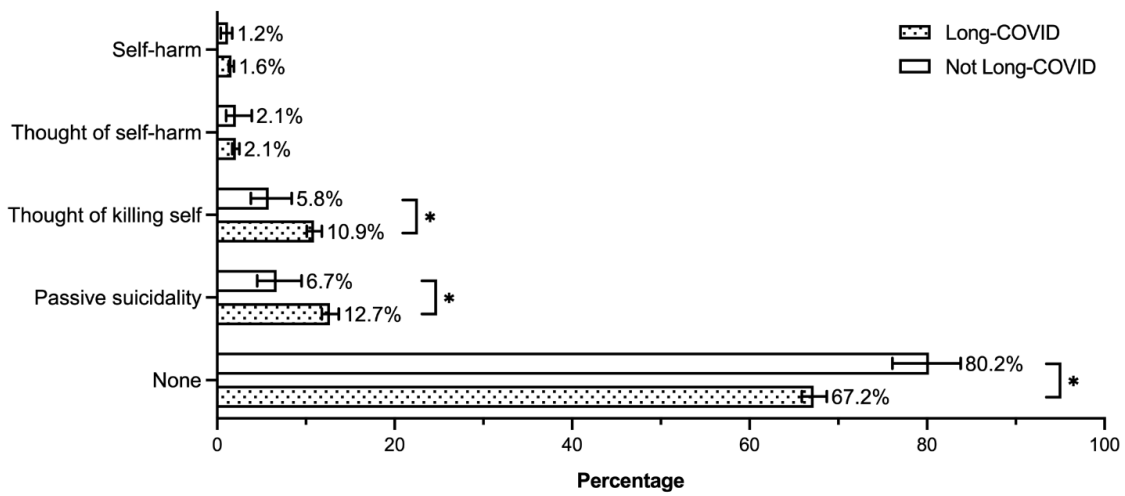


Fig. 1.4 Type of suicidality since initial infection



REFERENCES

1. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK - Office for National Statistics. Accessed April 7, 2022. <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/7april2022>
2. Davis HE, Assaf GS, McCorkell L, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *eClinicalMedicine*. 2021;38. doi:10.1016/j.eclinm.2021.101019
3. Why we need to keep using the patient made term “Long Covid.” The BMJ. Published October 1, 2020. Accessed April 21, 2022. <https://blogs.bmj.com/bmj/2020/10/01/why-we-need-to-keep-using-the-patient-made-term-long-covid/>
4. A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021. Accessed January 24, 2022. https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1
5. Xie Y, Bowe B, Al-Aly Z. Burdens of post-acute sequelae of COVID-19 by severity of acute infection, demographics and health status. *Nat Commun*. 2021;12(1):6571. doi:10.1038/s41467-021-26513-3
6. Mehandru S, Merad M. Pathological sequelae of long-haul COVID. *Nat Immunol*. 2022;23(2):194-202. doi:10.1038/s41590-021-01104-y
7. Proal AD, VanElzakker MB. Long COVID or Post-acute Sequelae of COVID-19 (PASC): An Overview of Biological Factors That May Contribute to Persistent Symptoms. *Front Microbiol*. 2021;12:1494. doi:10.3389/fmicb.2021.698169
8. Preventing Chronic Disease: January 2005: 04_0066. Accessed January 26, 2022. https://www.cdc.gov/pcd/issues/2005/jan/04_0066.htm
9. Schou TM, Joca S, Wegener G, Bay-Richter C. Psychiatric and neuropsychiatric sequelae of COVID-19 – A systematic review. *Brain Behav Immun*. 2021;97:328-348. doi:10.1016/j.bbi.2021.07.018
10. Caspersen IH, Magnus P, Trogstad L. Excess risk and clusters of symptoms after COVID-19 in a large Norwegian cohort. *Eur J Epidemiol*. Published online February 25, 2022. doi:10.1007/s10654-022-00847-8
11. Sher L. Post-COVID syndrome and suicide risk. *QJM Int J Med*. 2021;114(2):95-98. doi:10.1093/qjmed/hcab007
12. Taquet M, Geddes JR, Husain M, Luciano S, Harrison PJ. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. *Lancet Psychiatry*. 2021;8(5):416-427. doi:10.1016/S2215-0366(21)00084-5
13. Marija Pantelic and Nisreen Alwan: The stigma is real for people living with long covid. The BMJ. Published March 25, 2021. Accessed May 5, 2022. <https://blogs.bmj.com/bmj/2021/03/25/marija-pantelic-and-nisreen-alwan-the-stigma-is-real->

for-people-living-with-long-covid/

14. Alwan NA. Lessons from Long COVID: working with patients to design better research. *Nat Rev Immunol*. 2022;22(4):201-202. doi:10.1038/s41577-022-00692-6
15. Roth PH, Gadebusch-Bondio M. The contested meaning of “long COVID” – Patients, doctors, and the politics of subjective evidence. *Soc Sci Med*. 2022;292:114619. doi:10.1016/j.socscimed.2021.114619
16. Seidl E, Seidl O. Do my feelings fit the diagnosis? Avoiding misdiagnoses in psychosomatic consultation services. *J Healthc Risk Manag J Am Soc Healthc Risk Manag*. 2021;41(2):9-17. doi:10.1002/jhrm.21456
17. CDC. Cases, Data, and Surveillance. Centers for Disease Control and Prevention. Published February 11, 2020. Accessed March 30, 2022. <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/burden.html>
18. Cervia C, Zurbuchen Y, Taeschler P, et al. Immunoglobulin signature predicts risk of post-acute COVID-19 syndrome. *Nat Commun*. 2022;13(1):446. doi:10.1038/s41467-021-27797-1
19. Kroenke K, Spitzer RL, Williams JBW. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care*. 2003;41(11):1284-1292. doi:10.1097/01.MLR.0000093487.78664.3C
20. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097. doi:10.1001/archinte.166.10.1092
21. Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. *Int J Behav Med*. 1997;4(1):92-100. doi:10.1207/s15327558ijbm0401_6
22. Löwe B, Kroenke K, Gräfe K. Detecting and monitoring depression with a two-item questionnaire (PHQ-2). *J Psychosom Res*. 2005;58(2):163-171. doi:10.1016/j.jpsychores.2004.09.006
23. Levis B, Sun Y, He C, 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*. 2020;323(22):2290-2300. doi:10.1001/jama.2020.6504
24. 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*. 2016;39:24-31. doi:10.1016/j.genhosppsy.2015.11.005
25. McNeish DM. Using Lasso for Predictor Selection and to Assuage Overfitting: A Method Long Overlooked in Behavioral Sciences. *Multivar Behav Res*. 2015;50(5):471-484. doi:10.1080/00273171.2015.1036965
26. Vittinghoff E, Glidden D, Shiboski S, McCulloch C. Predictor Selection. In: *Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models*. Springer Publishing Company; 2005:253-288.
27. Elwert F, Winship C. Endogenous Selection Bias: The Problem of Conditioning on a Collider Variable. *Annu Rev Sociol*. 2014;40:31-53. doi:10.1146/annurev-soc-071913-043455
28. Arah OA. 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*. 2008;5(1):5. doi:10.1186/1742-7622-5-5
29. Friedman JH, Hastie T, Tibshirani R. Regularization Paths for Generalized Linear Models via Coordinate Descent. *J Stat Softw*. 2010;33:1-22. doi:10.18637/jss.v033.i01
30. McKnight-Eily LR. 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*. 2021;70. doi:10.15585/mmwr.mm7005a3
31. Nan H, Lee PH, McDowell I, Ni MY, Stewart SM, Lam TH. Depressive symptoms in people with chronic physical conditions: prevalence and risk factors in a Hong Kong community

- sample. *BMC Psychiatry*. 2012;12(1):198. doi:10.1186/1471-244X-12-198
32. Byrne EA. Understanding Long Covid: Nosology, social attitudes and stigma. *Brain Behav Immun*. 2022;99:17-24. doi:10.1016/j.bbi.2021.09.012
 33. Corrigan PW, Sokol KA. The Impact of Self-Stigma and Mutual Help Programs on the Quality of Life of People with Serious Mental Illnesses. *Community Ment Health J*. 2013;49(1):1-6. doi:10.1007/s10597-011-9445-2
 34. Shi L, Que JY, Lu ZA, et al. Prevalence and correlates of suicidal ideation among the general population in China during the COVID-19 pandemic. *Eur Psychiatry J Assoc Eur Psychiatr*. 2021;64(1):e18. doi:10.1192/j.eurpsy.2021.5
 35. Knudsen AKS, Stene-Larsen K, Gustavson K, 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*. 2021;4:100071. doi:10.1016/j.lanep.2021.100071
 36. Rogers ML, Joiner TE, Shahar G. Suicidality in Chronic Illness: An Overview of Cognitive-Affective and Interpersonal Factors. *J Clin Psychol Med Settings*. 2021;28(1):137-148. doi:10.1007/s10880-020-09749-x
 37. Westreich D, Greenland S. The Table 2 Fallacy: Presenting and Interpreting Confounder and Modifier Coefficients. *Am J Epidemiol*. 2013;177(4):292-298. doi:10.1093/aje/kws412