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# The association between baseline physical and mental health and the risk of postacute sequelae of COVID-19 infection

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**Post-acute sequelae of COVID-19 infection (PASC) is a widely reported phenomenon wherein symptoms of COVID-19 infection persist for four weeks or more beyond acute infection. Risk factors at baseline (prior to infection) for the development of PASC are not well understood. This study aimed to identify baseline demographic, physical and mental health characteristics associated with the development of PASC. We identified 351 participants who reported contracting COVID-19 and 145 that experienced PASC symptoms. Baseline physical health, mental health, and demographic data were collected for all participants. Risk factors for the development of PASC were identified using multivariable logistic regression. PASC was associated with lower income, Hispanic ethnicity, younger age, and respiratory conditions (asthma or COPD). Worse self-reported mental health status, a diagnosis of depression, and a higher patient health questionnaire-2 (PHQ-2) score were also associated with PASC. We then used latent class analysis and identified two subtypes of PASC, one with fewer PASC symptoms ($n = 112$) and another with many PASC symptoms ($n = 33$). Risk factors for membership in each class were different, but a past diagnosis of depression predicted membership in both classes compared to those without PASC. A diagnosis of depression was more strongly associated with the "many symptoms" class compared to the "few symptoms" class. We find that several mental health and demographic risk factors are linked to PASC. More research is necessary to understand both the two subtypes of PASC identified in our analysis, and the underlying relationship between COVID-19 infection and PASC.**

**Keywords** Long COVID, PASC, Mental health

Severe acute respiratory coronavirus-2 (SARS-CoV-2) infection can lead to a range of symptoms that persist beyond the course of acute infection. The prevalence of this phenomenon, termed "long COVID", "post-COVID-19 conditions (PCC)", or "post-acute sequelae of COVID-19 infection (PASC)", is variable – estimates range from 4.7 to 80% in different studies[1]. The wide variance in observed prevalence may be due to the heterogeneity of populations across different studies, differences in methods used to measure self-reported symptoms, and the lack of definitive diagnostic criteria for PASC[1]. PASC can include both physical symptoms (e.g., persistent loss of smell and taste, headaches, body aches, fatigue) and mental symptoms (e.g., brain fog and anxiety)[1]. The specific risk factors that increase the risk of PASC are not well understood. There is also significant heterogeneity in the duration of PASC (how long symptoms persist after acute infection to be considered PASC) across existing literature[2]. The recent National Academies of Sciences Engineering and Medicine (NASEM) definition of Long COVID (LC), created in July 2024, defines PASC as persistent symptoms for 90 days after acute COVID-19 infection[3].

Studies have found a variety of risk factors at baseline for the development of PASC, including female sex, smoking, obesity, and severe acute illness or hospitalization. The effect of some of these characteristics, like age, is unclear: some studies[4–6] find that being older confers greater risk for PASC, while others[7,8] find the opposite. One study with hospitalized patients found that "life stressors" – including food insecurity, financial insecurity, and new disability – are associated with PASC[9].

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While many studies have been conducted on the relationship between physical health at baseline and PASC, the impact of baseline mental health on PASC prevalence and severity is not well studied. For instance, in a 2023 meta-analysis of 41 PASC risk factor studies, only four examined the effect of anxiety or depression on PASC risk[5]. One study of adolescents and children in England found that poorer baseline mental and physical health is correlated with more PASC symptoms[10]. Another study on adults hospitalized with COVID-19 found that depression and anxiety at baseline were associated with PASC[11]. A study surveying a cohort of primarily health-care workers found an association between baseline anxiety and depression with PASC[12]. However, many of these studies have limited cohorts – healthcare workers, for example, may experience more acute stressors related to COVID-19 than the general population – and rarely utilize multiple measures of baseline mental health, including diagnosed conditions (e.g. depression) and self-reported descriptors of mental health.

The most comprehensive study on this topic, conducted in the United Kingdom using electronic health record data and longitudinal study samples, found that older age, female sex, poor baseline physical and mental health, white race, obesity, and asthma were associated with a higher likelihood of PASC symptoms[6]. The lack of a clear consensus on specific physical health and mental health risk factors at baseline necessitates more research on the relationship between pre-infection baseline mental and physical health and the likelihood of developing PASC.

Identifying PASC cases also presents challenges. One study on a population of individuals aged 12–25 found no significant difference in PASC symptoms between those with and without a prior COVID-19 infection, suggesting that measurement of PASC may have limited accuracy, as symptoms are nonspecific and can result from other health conditions[13]. There is also evidence that there may be different "subtypes" of PASC, with groups of patients reporting clusters of different symptoms[7,10].

Our study, on a large, diverse population of adults in Los Angeles County (LAC), California, utilizes survey data on a group of adults who experienced COVID-19 symptoms that persisted more than four weeks after acute infection[14]. We utilize a variety of physical and mental health metrics – including a history of diagnosed conditions like depression, self-assessment of physical and mental health, and standardized mental health subscales – to identify risk factors for a wide array of mental and physical PASC symptoms. Based on previous studies, we hypothesized that female gender, non-white ethnicity, specific self-reported conditions like obesity, respiratory conditions (asthma, COPD), diagnosed depression, and poor mental health at baseline would be associated with an increased likelihood of PASC. Finally, we examine PASC symptoms in our dataset to identify possible subtypes of PASC and their risk factors, to better understand the varying manifestations of PASC.

## Methods

### Study design and population

The LA County (LAC) COVID-19 Pandemic Surveillance Cohort Study is a longitudinal, ongoing survey of a representative sample of residents of LAC recruited during the pandemic. Study recruitment was conducted by LRW Group, a market research firm that maintains a database of roughly 2.5 million LAC residents. Surveys were administered between March and April 2021, and enrollment quotas based on age, income, gender, and ethnic distribution were set for recruitment representative of the LAC population. Additional details on recruitment and survey procedures are described in detail elsewhere[15,16].

1,222 participants completed the initial survey for this study in May 2021, which collected demographic and baseline health information. Of this group, 724 participants completed two follow-up surveys in May 2022 and January 2023. On follow-up surveys, 412 adults self-reported testing positive for COVID-19, and 195 experienced PASC. Some members of this group reported a COVID-19 test positivity date before baseline data were collected and therefore were excluded from analysis. The remaining 351 participants were our analytic sample, of which 145 experienced PASC.

## Measures

We defined the outcome measure of PASC as any self-reported symptoms persisting for four or more weeks (approximately 30 or more days) after COVID-19 infection[14]. To assess PASC, we asked the following question in the administered surveys:

> Some people experience a broad range of mental or physical symptoms that last for many weeks to months after their original COVID-19 infection. This is commonly referred to as "long COVID," "long-haul COVID," "post-COVID conditions," or "post-acute sequelae of SARS-CoV-2 infection" (also known as "PASC").
>
> Did you experience any of the following symptoms that lasted for more than 4 weeks after your original COVID-19 infection?

Included symptoms are outlined in Table 1. Participants who did not meet this criterion were classified as non-PASC. The baseline survey assessed self-reported physical and mental health information including the Patient Health Questionnaire-2 (PHQ-2)[17] and the emotional well-being subscale of the 36-item short form survey (SF-36)[18], history of diagnosed physical and mental illness (history of chronic health conditions, heart attack or disease, stroke, asthma, diabetes, high blood pressure, cancer, obesity, COPD, depression, kidney disease, arthritis, immunocompromised state, pregnancy, hepatitis, history of diagnosed depression, and feelings of anxiety and depression), and demographic information (gender identity, annual household income, race/ethnicity, and age).

| Few symptoms ($n=112$) | Margin | SE[2] | [95% CI] | |
|---|---|---|---|---|
| Likelihood of membership | 0.760 | 0.047 | 0.653 | 0.837 |
| Body Aches | 0.160 | 0.040 | 0.096 | 0.253 |
| Depression | 0.161 | 0.038 | 0.100 | 0.248 |
| Sleep Problems | 0.130 | 0.040 | 0.070 | 0.230 |
| Fatigue | 0.397 | 0.049 | 0.305 | 0.498 |
| Headaches | 0.127 | 0.036 | 0.072 | 0.216 |
| Joint Pain | 0.108 | 0.031 | 0.060 | 0.187 |
| Loss of Taste | 0.176 | 0.039 | 0.112 | 0.264 |
| Cough | 0.387 | 0.050 | 0.298 | 0.485 |
| Memory Issues | 0.384 | 0.042 | 0.305 | 0.469 |
| Shortness of Breath | 0.137 | 0.034 | 0.083 | 0.220 |
| **Many symptoms ($n=33$)** | **Margin** | **SE** | **[95% CI]** | |
| Likelihood of membership | 0.242 | 0.040 | 0.096 | 0.253 |
| Body Aches | 0.723 | 0.093 | 0.512 | 0.867 |
| Depression | 0.550 | 0.093 | 0.370 | 0.720 |
| Sleep Problems | 0.730 | 0.087 | 0.532 | 0.870 |
| Fatigue | 0.920 | 0.063 | 0.684 | 0.983 |
| Headaches | 0.710 | 0.093 | 0.504 | 0.856 |
| Joint Pain | 0.572 | 0.100 | 0.374 | 0.749 |
| Loss of Taste | 0.332 | 0.087 | 0.186 | 0.517 |
| Cough | 0.751 | 0.088 | 0.546 | 0.884 |
| Memory Issues | 0.805 | 0.083 | 0.594 | 0.920 |
| Shortness of Breath | 0.510 | 0.096 | 0.330 | 0.690 |

**Table 1**. Distribution of PASC symptoms in latent class analysis[1]. [1]Model goodness of fit: AIC: 1580.21, BIC: 1648.71. [2]Standard Error.

## Statistical analysis

We first used chi-squared tests to compare baseline demographic, physical, and mental health data for participants exhibiting PASC versus those without PASC. We then used a multivariable logistic regression model to examine risk factors at baseline for reporting of PASC. For this analysis, we focused on self-reported diagnosis of depression as the primary measure of mental health risk factor to avoid collinearity, as all measures of mental health were highly correlated and a prior diagnosis of depression seemed to be the most objective metric available. Finally, we used latent class analysis (LCA) to create clusters of PASC symptomatology within our sample. LCA uses selected variables for each participant to define disparate classes within the sample and assigns participants to classes based on probability of membership in each class. We assigned participants to the class for which they had the had the highest probability of membership. We attempted the LCA with two classes based on results from a prior analysis of PASC subtypes[10]. Once classes were identified, we conducted a PASC subtype analysis using a multinomial logistic regression with non-PASC participants and the two PASC classes to assess risk factors for the two PASC classes.

All statistical analysis was conducted using STATA version 17.0 and alpha levels were set at 0.05. Goodness of fit measures for LCA are provided in the footnotes of Table 1.

This study was reviewed and approved by the Institutional Review Board of the Los Angeles County Department of Public Health. Written informed consent was obtained from all study participants. Our study follows the STROBE reporting guidelines for cohort studies and all relevant guidelines and regulations for research with human participants.

## Results

Our analytic sample of 351 adults who self-reported testing positive for COVID-19 after the baseline survey consisted of 131 males (37.4%) and 217 females (61.9%). The largest race/ethnicity groups in our sample were white (44.4%) and Hispanic (30.5%) (Table 2).

145 participants (41.3%) experienced PASC. In univariate analysis, PASC was associated with female gender, Hispanic ethnicity, and younger age. (Table 2) PASC was also associated with pre-existing respiratory conditions (asthma or COPD). Obesity and poorer reported physical health were not associated with PASC. Similarly, the total number of physical conditions experienced at baseline was not associated with PASC.

PASC was associated with all markers of mental health at baseline, including worse self-reported mental health, diagnosed depression, and a higher PHQ-2 score. PASC was not associated with any baseline non-respiratory physical conditions, including history of heart disease, stroke, diabetes, high blood pressure, cancer, kidney disease, arthritis, hepatitis, pregnancy, and immunocompromised status (not shown). PASC was also not associated with alcohol use, cigarette or e-cigarette use, or marijuana use (not shown).

| | Total *n* (%) | No PASC *n* (%) | PASC *n* (%) | *P*-value |
|---|---|---|---|---|
| **Total** | 351 (100) | 206 (100) | 145 (100) | |
| **Demographic Information** | | | | |
| Gender | | | | **0.02**** |
| Male | 131 (37.3) | 89 (43.2) | 42 (29.0) | |
| Female | 217 (61.8) | 116 (56.31) | 101 (70.0) | |
| Non-binary | 3 (0.9) | 1 (0.5) | 2 (1.4) | |
| Income | | | | 0.065 |
| Under $50,000 | 93 (26.5) | 44 (21.4) | 49 (33.8) | |
| $50,000 - $99,999 | 103 (29.3) | 64 (31.1) | 39 (26.9) | |
| $100,000 or more | 141 (40.2) | 88 (42.7) | 53 (36.6) | |
| Prefer no answer | 14 (4.0) | 10 (4.9) | 4 (2.8) | |
| Ethnicity | | | | **0.047**** |
| Hispanic | 107 (30.5) | 52 (25.2) | 55 (37.9) | |
| White | 156 (44.4) | 105 (51.0 | 51 (35.2) | |
| Black | 26 (7.4) | 14 (6.8) | 12 (8.3) | |
| Asian | 46 (13.1) | 26 (12.6) | 20 (13.8) | |
| Other | 16 (4.6) | 9 (4.4) | 7 (4.8) | |
| Age | | | | **0.006**** |
| 18–29 | 40 (11.4) | 16 (7.8) | 24 (16.6) | |
| 30–49 | 193 (54.6) | 111 (53.9) | 82 (56.6) | |
| 50–64 | 94 (26.8) | 59 (28.6) | 35 (24.1) | |
| 65+ | 24 (6.8) | 20 (9.7) | 4 (2.8) | |
| **Markers of Physical Health** | | | | |
| Self-reported Physical Health | | | | 0.515 |
| Poor or Fair | 39 (11.1) | 21 (10.2) | 18 (12.4) | |
| Good, Very Good or Excellent | 312 (88.9) | 185 (89.8) | 127 (87.6) | |
| Respiratory Conditions (Asthma or COPD) | | | | **0.001**** |
| Yes | 57 (16.2) | 22 (10.7) | 35 (24.1) | |
| No | 294 (83.8) | 184 (89.3) | 110 (75.9) | |
| Number of chronic conditions | | | | 0.393 |
| 0 | 164 (46.7) | 102 (49.5) | 62 (46.7) | |
| 1–2 | 144 (41.0) | 78 (37.9) | 66 (45.5) | |
| 3–4 | 38 (10.8) | 22 (10.7) | 16 (11.0) | |
| 5–6 | 5 (1.4) | 4 (1.9) | 1 (0.7) | |
| Obesity | | | | 0.744 |
| Yes | 96 (27.4) | 55 (26.7) | 41 (28.3) | |
| No/Not sure | 255 (72.7) | 151 (83.3) | 104 (71.7) | |
| **Markers of Mental Health** | | | | |
| Self-reported Mental Health | | | | **0.004**** |
| Poor or Fair | 42 (12.0) | 16 (7.8) | 26 (17.9) | |
| Good, Very Good or Excellent | 309 (88.0) | 190 (92.2) | 119 (82.1) | |
| Diagnosed with depression | | | | **0.000**** |
| Yes | 84 (23.9) | 32 (15.5) | 52 (35.9) | |
| No or Not Sure | 267 (76.1) | 174 (84.5) | 93 (64.1) | |
| Patient Health Questionnaire 2 Score | | | | **0.000**** |
| At Risk for major depressive disorder (3–6) | 45 (12.8) | 14 (6.8) | 31 (31.4) | |
| Not at risk for major depressive disorder (0–2) | 306 (87.2) | 192 (93.2) | 114 (78.6) | |

**Table 2**. Demographic and baseline information by PASC.

## Multivariable logistic regression

Using a multivariable logistic regression model comparing participants with PASC and non-PASC participants (Table 3), we found that PASC was associated with many of the same risk factors. Hispanic ethnicity (aOR: 1.90 [1.04–3.47], $p = 0.036$) was a risk factor for developing PASC. Older age was a protective factor against PASC (aOR for 65 + age group: 0.11 [0.02–0.53], $p = 0.006$). Female gender had a trending association with PASC but was not a significant risk factor at the $p < 0.05$ level (female gender (aOR:1.62 [0.98–2.70], $p = 0.063$). PASC was

| | aOR[1] (95% CI) | *P*-value |
|---|---|---|
| **Gender** | | |
| Male | Ref | |
| Female | 1.62 (0.98–2.70) | 0.063 |
| Non-binary | 1.68 (0.11–24.70) | 0.703 |
| **Income** | | |
| Under $50,000 | Ref | |
| $50,000-$99,999 | 0.50 (0.27–0.95) | **0.034**** |
| $100,000 or more | 0.60 (0.33–1.10) | 0.103 |
| No answer | 0.28 (0.07–1.09) | 0.067 |
| **Race/Ethnicity** | | |
| White | Ref | |
| Hispanic | 1.90 (1.04–3.47) | **0.036**** |
| Black | 1.63 (0.65–4.11) | 0.297 |
| Asian | 1.45 (0.70–3.05) | 0.326 |
| Other | 1.63 (0.52–5.09) | 0.404 |
| **Age** | | |
| 18–29 | Ref | |
| 30–49 | 0.60 (0.27–1.33) | 0.208 |
| 50–64 | 0.49 (0.20–1.21) | 0.123 |
| 65+ | 0.11 (0.02–0.53) | **0.006**** |
| **Physical Conditions** | | |
| Self-Reported Physical Health | 0.98 (0.41–2.34) | 0.969 |
| Respiratory Conditions | 2.77 (1.33–5.79) | **0.006*** |
| No. of chronic conditions | 1.13 (0.68–1.89) | 0.644 |
| Obesity | 0.64 (0.31–1.31) | 0.219 |
| **Mental Conditions** | | |
| Depression Diagnosis | 3.02 (1.71–5.33) | **0.000**** |

**Table 3**. Adjusted odds ratio of demographic, physical and mental health covariates on PASC symptoms. [1]Adjusted odds ratio. ** $p < 0.05$.

also associated with respiratory conditions, defined as a diagnosis of asthma or COPD (aOR: 2.77 [1.33–5.79], $p = 0.006$). A diagnosis of depression at baseline was also associated with PASC (aOR: 3.02 [1.71–5.33], $p = 0.000$)

## Latent class analysis

Latent class analysis yielded optimal fit with two classes, one with "few" symptoms ($n = 112$) and the other with "many" symptoms ($n = 33$). Members of the few symptoms class experienced an average of 2.3 symptoms (minimum 1, maximum 5) while members of the many symptoms class experienced an average of 6.9 symptoms (minimum 5, maximum 10). (Table 1) Latent class proportions and probabilities of symptoms are presented in Table 1. The most common PASC symptoms for those in the class with few symptoms were fatigue, cough, and memory issues. Less than 25% of the participants with PASC were placed in the class with many PASC symptoms, who reported a higher proportion of body aches, depression, sleep problems, fatigue, headaches, joint pain, cough, memory issues, and shortness of breath.

## PASC subtype analysis

We then conducted a multinomial logistic regression to assess risk factors at baseline for developing either PASC subtype or risk factors between the two subtypes. Risk factors for the class with few symptoms vs. no PASC included Hispanic ethnicity (aOR: 2.02 [1.07–3.87], $p = 0.03$) and diagnosed depression (aOR: 2.44 [1.33–4.50], $p = 0.004$). (Table 4) Income between $50,000 and $99,999 was a protective factor for membership in the few symptoms class when compared to income under $50,000 (aOR income $50,000-$99,999: 0.49 [0.25–0.96], $p = 0.04$; reference group income under $50,000).

Risk factors for the class with many symptoms vs. no PASC included a diagnosis of asthma or COPD (aOR: 5.90 [1.83–18.73] $p = 0.003$), and a diagnosis of depression (aOR: 6.64 [2.63–16.74], $p < 0.001$). (Table 4) Older age was a protective factor for this class (aOR 50–64: 0.10 [0.02–0.50], $p = 0.005$; aOR 65+: 0.02 [0.01–0.32], $p = 0.006$)

When examining the risk factors between the many symptoms and few symptoms class, a significant risk factor for membership in the many symptoms class was a diagnosis of depression (aOR = 2.72 [1.08–6.82], $p = 0.03$). Age 50–64 was protective in this analysis when compared to the 18–29 age group (aOR age 50–64 = 0.14 [0.03–0.73], $p = 0.02$; reference group age 18–29).

| | Few Symptoms ($n=112$) vs. No PASC ($n=206$) | | Many symptoms ($n=33$) vs. No PASC ($n=206$) | | Many Symptoms ($n=33$) vs. Few symptoms, ($n=112$) | |
|---|---|---|---|---|---|---|
| | aOR (95% CI) | *P*-value | aOR (95% CI) | *P*-value | aOR (95% CI) | *P*-value |
| **Demographic Information** | | | | | | |
| Gender | | | | | | |
| Male | Ref | | Ref | | Ref | |
| Female | 1.52 (0.90–2.60) | 0.12 | 2.40 (0.85–6.80) | 0.10 | 1.57 (0.55–4.52) | 0.84 |
| Non-binary | 1.38 (0.07–28.85) | 0.84 | 1.60 (0.05–52.90) | 0.80 | 1.16 (0.04–35.53) | 0.09 |
| Income | | | | | | |
| Under $50,000 | Ref | | Ref | | Ref | |
| $50,000 - $99,999 | 0.49 (0.25–0.96) | **0.04**** | 0.53 (0.17–1.70) | 0.28 | 1.08 (0.34–3.40) | 0.9 |
| $100,000 or more | 0.60 (0.32–1.13) | 0.11 | 0.55 (0.18–1.67) | 0.29 | 0.93 (0.31–2.77) | 0.89 |
| Race/Ethnicity | | | | | | |
| White | Ref | | Ref | | Ref | |
| Hispanic | 2.02 (1.07–3.87) | **0.03**** | 1.55 (0.55–4.37) | 0.41 | 0.89 (0.27–2.91) | 0.85 |
| Black | 1.56 (0.57–4.26) | 0.39 | 2.20 (0.45–10.67) | 0.33 | 1.95 (0.29–12.94) | 0.49 |
| Asian | 1.75 (0.82–3.75) | 0.15 | 0.28 (0.03–2.60) | 0.26 | 0.16 (0.02–1.60) | 0.12 |
| Other | 2.43 (0.77–7.72) | 0.13 | N/A (sample size) | | N/A (sample size) | |
| Age | | | | | | |
| 18–29 | Ref | | Ref | | Ref | |
| 30–49 | 0.70 (0.30–1.64) | 0.41 | 0.33 (0.10–1.12) | 0.08 | 0.47 (0.14–1.54) | 0.22 |
| 50–64 | 0.67 (0.26–1.74) | 0.41 | 0.10 (0.02–0.50) | **0.005**** | 0.14 (0.03–0.73) | **0.02**** |
| 65+ | 0.16 (0.03–0.86) | 0.33 | 0.02 (0.01–0.32) | **0.006**** | 0.11 (0.06–2.18) | 0.14 |
| **Measures of Physical Health** | | | | | | |
| Self-Reported Physical Health | | 0.87 | | 0.94 | | 0.86 |
| Poor or Fair | Ref | | Ref | | Ref | |
| Good, Very Good or Excellent | 0.93 (0.35–2.33) | | 1.06 (0.25–4.40) | | 1.14 (0.27–4.72) | |
| Obesity | 0.49 (0.22–1.09) | 0.08 | 1.37 (0.42–4.50) | 0.6 | 2.81 (0.84–9.35) | 0.84 |
| No. of Chronic Conditions | 1.08 (0.76–1.53) | 0.68 | 1.20 (0.65–2.23) | 0.56 | 1.12 (0.60–2.10) | 0.73 |
| Respiratory Conditions (Asthma/COPD) | 2.14 (0.96–4.76) | 0.06 | 5.90 (1.83–18.73) | **0.003**** | 2.74 (0.86–8.72) | 0.09 |
| **Measures of mental health** | | | | | | |
| Diagnosed depression | 2.44 (1.33–4.50) | **0.004**** | 6.64 (2.63–16.74) | <**0.001**** | 2.72 (1.08–6.82) | **0.03**** |

**Table 4**. Adjusted odds ratios of demographic, physical and mental health covariates on PASC symptoms. **$p<0.05$.

## Discussion

The main findings of this analysis are threefold. First, the risk of PASC is associated with demographic characteristics including younger age and Hispanic ethnicity. Second, several baseline health risk factors were associated with PASC. Only one physical risk factor – a diagnosis of either asthma or COPD – was associated with a higher risk for PASC in both univariate and multivariate analyses, while many metrics of adverse mental health, including a poorer self-reported mental health, a diagnosis of depression, and a higher score on the PHQ-2 scale, were associated with PASC in the univariate analysis. A diagnosis of depression was also a significant risk factor in the multivariate model. Finally, PASC appears to present in two subtypes – a smaller group with many symptoms, and a larger group with few symptoms (primarily fatigue, cough, and memory issues). Both subgroups were associated with a prior diagnosis of depression, but we observed distinct physical and demographic risk factors for each subtype. A diagnosis of depression was also a unique risk factor for membership in the many symptoms class when compared to the few symptoms class.

The prevalence of PASC in our sample was high (145 of 351 or 41% participants experienced PASC) but consistent with other studies that have found estimates ranging from 4.7 to 80%[1]. The somewhat high prevalence of PASC in our study might reflect that we measured PASC as experiencing any symptoms 4 weeks post-infection while other studies' definition of PASC requires symptoms to last up to 3 months post-infection[3]. It is also notable that the group experiencing "many symptoms" was a smaller portion of our sample ($n=33$ or 9.4%) – further study on PASC prevalence among subtypes is necessary.

The relationship between female gender and PASC risk has been consistently identified in the literature, including a recent meta-analysis of 41 studies on PASC risk factors[4,5,8,11,19]. Possible factors underlying this association include a higher mortality rate for men with COVID-19 and a more active immune response in women[19]. We did not find a relationship between female gender and PASC at the $p=0.05$ level in the multivariate analysis (the relationship was significant at the $p<0.10$ level and in univariate analysis), which may be due to sample size or adjusting for chronic conditions, many of which are more prevalent in women and may have symptom overlap with PASC[20].

Younger age was a significant risk factor for PASC in both univariate and multivariate analysis. This is consistent with studies that find a positive correlation between younger age and likelihood of PASC[4–7] but is not in accord with other studies on this topic[8,9,11]. This difference may be due to some studies (including ours) having a relatively healthy cohort and undercounting hospitalized patients. Older patients who contract COVID-19 are more likely to be hospitalized than young people, meaning that a cohort made up of mostly non-hospitalized cases may be under-representing severe COVID-19 infections among the elderly. While our study could have included patients who were previously hospitalized, our methodology (administering surveys) may present a response bias towards healthier patients, as sicker or hospitalized patients may have less capacity to respond to surveys and may have less inclination to reflect on their illness course. It also may be true that young people are more attuned to deviations from perfect health (and therefore more likely to attribute them to PASC symptoms), while older people are used to PASC-like symptoms in daily life. Additionally, the duration post-infection that defines PASC has changed: while our survey asked participants if they had experienced symptoms four weeks or more after infection, newer studies may adopt the NASEM definition (symptom experienced three months or more after infection)[1,6]. Thus, we may overrepresent milder PASC cases in our cohort, as milder PASC cases may have a shorter symptom duration.

We did not find a clear association between baseline physical health upon future risk and severity of PASC. Chronic conditions: immunosuppression, diabetes, heart disease[5–7,21] were not associated with PASC in our study. Overall measures of physical health (self-reported physical health at baseline, number of physical conditions at baseline) were also not associated with PASC. Asthma, COPD and obesity, the only physical health risk factors associated with PASC in our analysis, have been linked to PASC risk in previous studies[6,22]. The overall picture of the relationship between physical health and PASC remains unclear, but asthma and COPD seem to have the clearest link to PASC among all physical health risk factors at baseline.

Our findings add to the existing literature demonstrating the association between poorer mental health and increased risk of PASC[5,6,9–12]. A prior diagnosis of depression was strongly associated with PASC in our analysis. While other metrics of baseline mental health may be more transient or vary in severity between individuals, depression evaluated and diagnosed by a medical professional provides a standardized metric for poor mental health prior to COVID infection. It may be true that individuals with poorer pre-existing mental health are more attentive to interruptions to their mental health, and therefore more likely to identify and label their symptoms. However, a study in young adults finds that a past mental health diagnosis reduces the likelihood of PASC-associated mental health symptoms[23], which may imply the opposite (that pre-existing mental illness may mitigate some of the effect of PASC-associated mental health symptoms). The link between depression and PASC may also be a result of serotonin reduction due to COVID–19 infection – Wong et al. found that serotonin reduction is associated with development of PASC[24].

Finally, we observed two subtypes of PASC using latent class analysis. Different subgroups of PASC infection have been observed in the literature[7,10,25]. Stephenson et al.[10] found two subtypes of PASC, one with few symptoms and one with many, while Subramanian et al.[7] and Kisiel et al.[25] found three subgroups with an increasing number of symptoms differentiating each group. All these analyses found varying risk factors for membership in different subgroups. Our study also identified different risk factors for the two subtypes of PASC – Hispanic ethnicity was associated with the few symptoms class, while younger age and respiratory conditions were associated with the many symptoms class. Diagnosed depression was associated with membership in both groups and was more strongly associated with membership in the many symptoms class compared to membership in the few symptoms class.

These results indicate that the underlying causes of different PASC subtypes may vary. It is possible that some classes of PASC may be caused by factors entirely unrelated to acute COVID-19 infection, especially the class with few symptoms, and thereby may not be "true" PASC. It is also possible that each class of PASC has a different etiology, and the PASC subtype with many symptoms has causal factors more closely linked to prior depression (i.e., serotonin suppression). (25) Finally, as discussed previously, our definition of PASC (4 weeks post infection) is earlier than more recent studies. The makeup of each subgroup may change through the PASC disease course – PASC in the many symptoms class may persist longer than the few symptoms class, for instance. Importantly, however, the results of our study are not adequately powered to draw strong conclusions, as the sample size of the "many symptoms" class is very small (33 participants or 9.4%).

Our findings suggest that accurately measuring the extent of PASC symptoms in the population, especially those with pre-existing mental health issues, requires further study. It is important to note that this does not imply that PASC is psychosomatic, but rather it may suggest that some symptoms attributed to PASC are caused by external mental health stressors – including social isolation due to COVID-19 stay-at-home orders, worries and anxieties about the pandemic, or entirely unrelated stressors -- rather than COVID-19 infection. This is consistent with a study that finds no association between COVID-19 infection and symptoms attributed to PASC[13]. A major limitation of our study is the lack of a control group who never had COVID-19 – it is possible PASC would have been observed in patients who did not contract COVID-19. The accuracy of our results may also be limited by our sample size. Finally, it is possible that PASC at 4 weeks post-infection is significantly different than PASC 12- or 24-weeks post infection. Further research that compares PASC risk factors at multiple time points after acute infection, is needed.

In sum, we find that a variety of risk factors are associated with COVID-19 symptoms persisting past the course of acute infection. More research is needed to disentangle the specific effects of COVID-19 infection (both direct and indirect) on PASC and better understand the directionality of the relationship between adverse mental health at baseline and mental health symptoms of PASC. Our research also adds to the growing body of evidence that PASC manifests in different subtypes, and the causes and risk factors for each of these subtypes may differ. Further analysis to understand the biological underpinnings of the different manifestations of PASC is necessary.

## Data availability

Data are available from the corresponding author upon request.

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## Author contributions

NK and CL prepared tables, NK wrote the main manuscript. NS, CL, JU and RL oversaw data analysis and writing of the manuscript.

## Declarations

## Competing interests

The authors declare no competing interests.

## Additional information

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