LONGER-TERM MENTAL HEALTH CONSEQUENCES OF COVID-19 INFECTION: MODERATION BY RACE AND SOCIOECONOMIC STATUS

by

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To my family

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ABSTRACT

While evidence suggests that the mental health consequences of coronavirus disease 2019 (COVID-19) can persist for several months following infection, little is known about the longer-term mental health consequences and whether certain sociodemographic groups may be particularly impacted. The study objectives were to characterize the longer-term mental health consequences of COVID-19 infection and examine whether such consequences are more pronounced in Black people and people with lower socioeconomic status. 277 Black and White adults (age ≥ 30 years) with a history of COVID-19 (cases; tested positive ≥ 6 months prior to participation) or no history of COVID-19 infection (controls) completed a 45-minute online questionnaire battery. Unadjusted *t*-tests revealed that cases had greater depressive ($d = 0.24$), anxiety ($d = 0.34$), PTSD ($d = 0.32$), and insomnia ($d = 0.31$) symptoms than controls. These differences remained significant for symptoms of anxiety, PTSD, and insomnia after adjusting for age, sex, race, education, income, and smoking status. No case-control differences were detected for perceived stress and general psychopathology. Cases had more than double the odds of clinically significant symptoms of anxiety ($OR = 2.22$) and PTSD ($OR = 2.40$). Case-control status was more strongly and positively associated with depressive, anxiety, PTSD, perceived stress, and general psychopathology symptoms at lower education levels. Race and income were not moderators of the relationships. The mental health consequences of COVID-19 may be significant, widespread, and persist for at least 6 months after infection, and people with lower education levels may face a greater burden of these consequences.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has dealt a devastating blow to the physical and mental health of many millions of people on an international scale. The U.S. carries the highest case load and death toll internationally, with more than 80 million cases and 984,000 deaths (1). Given these troubling numbers, it is important to investigate what the recovery process entails for the considerable and growing number of people who have been infected with COVID-19. While many people who are symptomatic recover within two weeks from the acute phase, marked by symptoms such as fever, cough, and difficulty breathing (2), 54% of those who survive COVID-19 infection have persistent symptoms for at least six months (3). The persistence of COVID-19-related symptoms beyond three weeks post-infection is often referred to as long COVID (4), and the various symptoms suggest that multiple organ systems are affected (5). In particular, the longer-term mental health consequences of COVID-19 infection are a major area of concern, as accumulating literature suggests that these consequences are highly prevalent (6).

Evidence of the mental health consequences of COVID-19 months after infection is alarming. People with COVID-19 have a higher incidence of any psychiatric diagnosis 14-90 days after onset compared to people who have had other health events, such as having influenza (HR = 1.79) or other respiratory illnesses (HR = 1.33) (7). Notably, people who have survived the acute phase have elevated rates of depression (20%), anxiety (30%), post-traumatic stress disorder (PTSD) (13%), and sleep disorders (27%) months after COVID-19 infection (3). Furthermore, studies have found that in the months after hospital discharge, 23-56% of COVID-19 patients have clinical elevations in at least one psychological dimension – i.e., depression, anxiety, insomnia, PTSD, or obsessive-compulsive symptoms (8-10). While there is a growing body of evidence that illustrates the high rates of mental health consequences several months following COVID-19 infection, it remains unclear whether these symptoms begin to take a chronic trajectory.

Candidate mechanisms that could explain the mental health consequences of COVID-19 infection fall into two broad categories, which could have synergistic effects: (1) biological pathways related to SARS-CoV-2 and the body's response to the virus or treatments and (2) psychosocial pathways related to the COVID-19 illness experience (11). One possible biological pathway is the immune response to COVID-19. The immune response to COVID-19 infection can become dysregulated and lead to a persistent inflammation process that may contribute to long-term mental health consequences (12). The ability of COVID-19 to cause chronic, low inflammation directly in the central nervous system may also explain the longer-term mental health symptoms (13). Vascular and hematological changes following COVID-19 infection is a second possible biological pathway. The psychiatric symptoms reported by people with a history of COVID-19 may be related to blood clots in the brain that can occur after COVID-19 infection (14, 15). Multiple psychosocial pathways related to the COVID-19 illness experience (e.g., the treatment experience, quarantine, stigma, and stress) could also explain the mental health consequences. For example, receiving treatment such as intubation and enduring stays in the ICU could trigger acute and long-term mental health consequences of trauma in COVID-19 patients (16). Additionally, the self-isolation that people with COVID-19 endure while in quarantine may impact their mental health (17). Furthermore, stress has been identified as one of the main factors that trigger symptom relapse in people still experiencing physical and psychological COVID-19 symptoms six months later (18).

As there is reason to suspect that the consequences of COVID-19 may be greater in certain marginalized groups, it would be remiss to investigate these consequences without exploring whether or not they are more profound in these populations. Much is still unknown about which populations may be most impacted by the longer-term mental health consequences of COVID-19 infection. Given that Black people and people with lower socioeconomic status (SES) have been disproportionately burdened by the physical health consequences of COVID-19 infection (19-21), it is plausible that its mental health consequences are also more pronounced in these groups. Several of the candidate mechanisms that could underlie the mental health consequences of COVID-19 infection may be greater in these two overlapping groups. These mechanisms relate to factors that produce greater inflammation (22-24), stigma (25-27), and stressors (28-30).

At present, there are crucial aspects of the mental health consequences of COVID-19 infection that remain unexplored. While a growing literature is examining the mental health consequences of COVID-19 several months following infection, the longer-term consequences (≥ 6 months post-infection) are largely unknown. Furthermore, many studies to date suffer from limited generalizability, as most consist of majority White samples and many focus on COVID-

19 patients meeting highly specific criteria (e.g., healthcare professionals or hospitalized patients) within a single site or network (31). Consequently, it remains unclear whether the mental health consequences are greater in Black people and people with lower SES. To anticipate the needs of and develop interventions for the considerable and growing number of people with long COVID, it is critical that the longer-term mental health consequences are well characterized and that the potential roles of race and SES in these outcomes are examined. Thus, the present study assessed the longer-term mental health consequences of COVID-19 infection and examined race and SES as moderators in a sample of middle-aged adults with good representation of Black people.

METHODS

Study Design

This online study utilized a cross-sectional, case-control design. The Indiana University-Purdue University Indianapolis (IUPUI) Institutional Review Board approved this study.

Participants and Procedure

Participants were recruited from June 2021 – September 2021 through Amazon Mechanical Turk (MTurk), an online data collection platform yielding reliable and valid data and more diverse samples than traditional college samples (32). The MTurk platform was managed through CloudResearch, a commonly used MTurk extension for social science research, to improve data quality and increase sample representativeness (33). On Mturk, participants were invited to complete a 45-minute, online questionnaire battery via Qualtrics (34). Participant eligibility was based on the following inclusion criteria: (1) country of residence: U.S., (2) spoken language: English, (3) age: ≥ 30 years, (4) race: identify as Black or White, (5) ethnicity: not Hispanic or Latinx/o/a, and (6) COVID-19 status: (a) self-report of a positive COVID-19 test ≥ 6 months before study participation and at least 1 COVID-19 symptom during the acute phase (cases) or (b) self-report of never testing positive for COVID-19 (controls). Age ≥ 30 years was selected as an inclusion criterion to prevent the sample from being skewed to a young demographic, as Mturk participants aged 18-24 years old are overrepresented on the platform compared to nationally representative surveys (35). This criterion may also help guard against overrepresentation of COVID-19 cases with mild symptoms, as younger age groups tend to have milder symptom severity (36). Identifying as non-Hispanic was selected as an inclusion criterion to avoid introducing factors related to Hispanic ethnicity when examining Black and White racial differences. Participants gained access to the questionnaire battery after providing informed consent and passing the screening questions.

For inclusion in data analysis, participants needed to pass three of the four quality checks in the questionnaire battery, such as: "I am reading all the questions on this survey (select very strongly agree)." Quality checks are considered a satisfactory way to attain high quality MTurk data (37). Upon completion of the questionnaire battery, participants received a verification code to earn $5.50 in compensation after confirmation that they passed the quality check benchmark. Of the 325 people who completed the questionnaire battery, 22 respondents were excluded for attempting the screening questions multiple times. An additional 21 respondents were excluded for failing to enter the verification code. To ensure high quality data, 5 more respondents were excluded for failing to pass the quality check benchmark, leaving a sample of 277 adults.

Measures

Mental Health Outcomes

The questionnaire battery included measures assessing symptoms of depression, anxiety, PTSD, insomnia, perceived stress, and general psychopathology.

Depression symptom severity was measured using the Patient Health Questionnaire (PHQ-9) (38), a 9-item questionnaire. Participants rated how often they have been bothered by each depressive symptom over the past two weeks on a scale of 0 (not at all) to 3 (nearly every day). Higher scores indicate greater depressive symptom severity. A score ≥ 10 reflects moderate to severe symptom severity.

Anxiety symptom severity was measured using the Generalized Anxiety Disorder-7 (GAD-7) (39), a 7-item questionnaire. Participants rated how often they have been bothered by each anxiety symptom over the past two weeks on a scale of 0 (not at all) to 3 (nearly every day). Higher scores indicate greater anxiety symptom severity. A score ≥ 10 reflects moderate to severe anxiety symptom severity.

PTSD symptom severity was assessed by the PTSD Checklist for DSM-5 (PCL-5) (40), a 20-item questionnaire. Participants rated how much they have been bothered by each PTSD symptom over the past month on a scale of 0 (not at all) to 4 (extremely). A score ≥ 31 reflects a provisional diagnosis of PTSD.

The Insomnia Severity Index (ISI) (41), a 7-item questionnaire, was used to assess insomnia symptom severity. Participants rated their symptoms and consequences of insomnia over the past two weeks on a scale of 0 to 4, with higher scores indicating greater insomnia symptom severity. A score of 8-14 reflects subthreshold insomnia, and a score ≥ 15 reflects moderate to severe insomnia.

The Perceived Stress Scale-10 (PSS) (42), a 10-item questionnaire, was used to measure the degree to which individuals perceive their lives to be stressful. Participants rated how often over the last month, on a scale of 0 (never) to 4 (very often), they have thought or felt a certain way. Higher scores are indicative of greater perceived stress.

The Hopkins Symptom Checklist-90 (SCL-90) (43), a 90-item questionnaire, was used to measure a broad range of mental health problems and symptoms to ensure that important mental health consequences of COVID-19 infection that currently have little preliminary support were not overlooked. The SCL-90 consists of the following nine subscales: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. Participants rated how much they were bothered by each symptom over the past week, from 0 (not at all) to 4 (extremely). Higher scores indicate greater general psychopathology.

Sociodemographic Factors, Clinical Characteristics, and COVID-19 Characteristics

The questionnaire battery included items and validated scales assessing sociodemographic factors (e.g., age, sex at birth, gender, race, ethnicity, education, annual household income, employment status, and health insurance status), medical and mental health history (including COVID-19 vaccination status), current height and weight for controls (for body mass index [BMI] calculation), height and weight for cases at the time of first positive COVID-19 test (for BMI calculation), tobacco use (Behavioral Risk Factor Surveillance System Tobacco Use Questionnaire) (44), alcohol use (Alcohol Use Disorders Identification Test [AUDIT]) (45), and sedentary time (one item from International Physical Activity Questionnaire [IPAQ]) (46). The questionnaire battery included an additional questionnaire, administered to cases only, assessing factors related to COVID-19 history (e.g., months since positive test, acute symptom severity, treatment setting, and recovery status). The questionnaire battery for cases and controls also assessed other factors that are not part of this report.

Data Analysis

To characterize the longer-term mental health consequences of COVID-19 infection, cases and controls were compared on continuous measures of the mental health outcomes (i.e., PHQ-9, GAD-7, PCL-5, ISI, PSS-10, and SCL-90 total scores) through a series of independent-samples *t*-tests. In addition, a parallel series of supplemental ANCOVAs was conducted, adjusting for the following pre-selected covariates: age, sex, race, education, income, and smoking status. These covariates were selected because they could influence both COVID-19 infection risk and the mental health consequences of interest (47-52). In a second set of supplemental ANCOVAs, BMI was added as another covariate to further adjust for an observed difference between cases and controls. To illustrate clinical significance, percentages of participants scoring above the clinical cut points on relevant questionnaires were computed (i.e., ≥ 10 on the PHQ-9, ≥ 10 on the GAD-7, ≥ 31 on the PCL-5, and ≥ 8 on the ISI), and chi-square tests were performed comparing cases to controls on these dichotomous measures (e.g., % with clinically significant depressive symptoms). Additionally, supplemental logistic regression models were run, adjusting for age, sex, race, education, income, and smoking status.

To examine race (Black vs. White), education (years), and income (U.S. dollars) as moderators of the relationships between COVID-19 status (cases vs. controls) and the mental health outcomes, a regression-based path analysis approach employing PROCESS model 1 (53) was utilized. Separate analyses were conducted for each candidate moderator and included the following covariates: age, sex, race, education, income, and smoking status. The statistical significance of moderation effects was determined through a bias-corrected bootstrap 95% confidence interval with 10,000 bootstrap samples. Moderation was considered statistically significant if the confidence interval did not cross zero. Subsequently, if the moderation effect was statistically significant, the conditional effect of COVID-19 status on the mental health outcomes was examined at different values of the moderator (for race: each level of the factor; for education and income: one standard deviation below the mean, the mean, and one standard deviation above the mean). All analyses were conducted using SPSS version 27.

RESULTS

Participant Characteristics

Sociodemographic Factors

Participant characteristics are shown in Table 1. A total of 277 people (60.3% female) were included in this study. Participants reported a mean age of 43.2 years, a mean education level of 15.2 years, and a mean annual household income of $69,501. In our sample, 45.8% identified as Black, 54.2% identified as White, and 98.9% identified as not Hispanic or Latinx/o/a. Most participants reported that they were employed (82.3%) and had health insurance (88.4%). Independent-samples *t*-tests and chi square analyses were conducted to determine whether there were characteristic differences between cases and controls. For most sociodemographic factors, no differences were detected between cases and controls. A significant difference was found for age (t (271) = 3.9, p < .001), as cases were an average of 5.2 years younger than controls.

Clinical Characteristics

As is also displayed in Table 1, participants reported histories of mental health disorders, including depression (28.9%) and anxiety (36.1%). Some reported currently taking medication (19.9%) or receiving psychotherapy/counseling (11.6%) for a mental health disorder. Among the participants, 59.6% received at least one dose of a COVID-19 vaccine, 13.9% reported a medical condition classified as a COVID-19 comorbidity (54), 33.5% reported a medical condition classified as a potential COVID-19 comorbidity (54), and 18.1% were current smokers. Furthermore, participants had a mean BMI of 29.1 kg/m^2 (falling in the overweight category) and averaged 8.4 hours of daily sedentary behavior. For most clinical characteristics, no significant differences were detected between cases and controls. However, a higher percentage of cases had a history of sleep disorders (χ^2 (1, 277) = 5.4, p = .02) and COVID-19 comorbidities (χ^2 (1, 273) = 3.9, p = .049), and cases on average reported a higher BMI (t (270) = 2.5, p = .01) and sedentary hours per day (t (253) = 2.1, p = .04).

Table 1. Participant Characteristics

	All (N = 277)	Cases (n = 127)	Controls (n = 150)
Sociodemographic Factors			
Age, years, *M* (*SD*)	**43.2 (11.4)**	**40.4 (10.4)**	**45.6 (11.7)**
Sex, *n* (%) female	167 (60.3)	80 (63.0)	87 (58.0)
Gender, *n* (%)			
Female	164 (59.2)	78 (61.4)	86 (57.3)
Male	110 (39.7)	48 (37.8)	62 (41.3)
Transgender	1 (0.4)	0 (0.0)	1 (0.7)
Non-binary/Fluid Queer/Gender Queer	2 (0.7)	1 (0.8)	1 (0.7)
Race[1], *n* (%)			
Black	127 (45.8)	52 (40.9)	75 (50.0)
White	150 (54.2)	75 (59.1)	75 (50.0)
Ethnicity, *n* (%)			
Hispanic or Latinx/o/a	3 (1.1)	3 (2.4)	0 (0.0)
Not Hispanic or Latinx/o/a	272 (98.9)	124 (97.6)	148 (100.0)
Education, years, *M* (*SD*)	15.2 (2.1)	15.3 (2.1)	15.1 (2.1)
Income[2], U.S. dollars, *M* (*SD*)	69,501 (51,251)	76,036 (54,371)	63,976 (47,949)
Employed, *n* (%)	228 (82.3)	105 (82.7)	123 (82.0)
Have Health Insurance, *n* (%)	245 (88.4)	113 (89.0)	132 (88.0)
Clinical Characteristics			
Received ≥ 1 dose of COVID-19 vaccine, *n* (%)	165 (59.6)	82 (64.6)	83 (55.3)
History of Mental Health Disorder, *n* (%)			
Depression	80 (28.9)	37(29.1)	43 (28.7)
Anxiety	100 (36.1)	50 (39.4)	50 (33.3)
PTSD	18 (6.5)	8 (6.3)	10 (6.7)
Sleep Disorder	**25 (9.0)**	**17 (13.4)**	**8 (5.3)**
Bipolar	13 (4.7)	5 (3.9)	8 (5.3)
Schizophrenia/Psychotic Disorder	1 (0.4)	0 (0.0)	1 (0.7)
Alcohol Use Disorder	7 (2.5)	3 (2.4)	4 (2.7)
Current Treatment for Mental Health Disorder, *n* (%)			
Medication	55 (19.9)	28 (22.0)	27 (18.0)
Talk Therapy/Counseling	32 (11.6)	16 (12.6)	16 (10.7)
History of Medical Conditions, *n* (%)			
COVID-19 Comorbidities[3]	**38 (13.9)**	**23 (18.4)**	**15 (10.1)**
COVID-19 "At Risk" Comorbidities[4]	91 (33.5)	45 (36.3)	46 (31.1)
BMI, kg/m², *M* (*SD*)	**29.1 (7.9)**	**30.5 (7.6)**	**28.0 (8.0)**
Current Smoker, *n* (%)	50 (18.1)	24 (18.9)	26 (17.3)
AUDIT total score, *M* (*SD*)	3.1 (4.7)	3.1 (4.5)	3.0 (4.8)
Sedentary Hours per Day, *M* (*SD*)	**8.4 (3.8)**	**7.9 (3.9)**	**8.9 (3.7)**

Note: All variables had complete data except (n): age (273), ethnicity (275), education (274), income (275), COVID-19 comorbidities (273), COVID-19 "at risk" comorbidities (272), BMI (272), and sedentary hours (255). Bolded elements indicate significant differences. COVID-19 = coronavirus disease 2019; PTSD = post-traumatic stress disorder; BMI = body mass index; AUDIT = Alcohol Use Disorders Identification Test.

[1]Categories were collapsed into a dichotomous variable (Black, White). Those who identified both as Black and any other racial group (*n* = 3) were coded as Black. Those who identified both as White and any racial group other than Black (*n* = 1) were coded as White.

[2]Income was winsorized (an extreme outlier was replaced by the next highest value) to limit the effect of one extreme outlier on the mean.

[3]COVID-19 Comorbidities were: active cancer or current cancer treatment, chronic kidney disease, chronic obstructive pulmonary disease [COPD], Down Syndrome, heart conditions, HIV/AIDS, immunocompromised state [from solid organ transplant], sickle cell disease, and type 2 diabetes.

[4]COVID-19 "At Risk" Comorbidities: asthma (moderate-to-severe), cerebrovascular disease, cystic fibrosis, hypertension, immunocompromised state [from blood or bone marrow transplant, immune deficiencies, HIV, use of corticosteroids, or use of other immune weakening medicines], liver disease, neurologic conditions, pulmonary fibrosis, thalassemia, and type 1 diabetes.

COVID-19 Characteristics

As can be seen in Table 2, cases reported that they first tested positive for COVID-19 an average of 9.5 months (*SD* = 3.2) before participation, and most rated their symptoms during the acute phase as mild or moderate. About 20% went to the emergency department for their symptoms; however, only 3.9% were hospitalized, and none had an ICU stay. Notably, 85.5% of cases endorsed that they still had one or more symptoms of COVID-19, and 29.9% reported that they still had not returned to their usual health.

Table 2. Cases Characteristics

COVID-19 Severity and Treatment	
Months since positive test, *M (SD)*	9.5 (3.2)
Acute symptom severity, *n* (%)	
None	0 (0.0)
Mild	52 (40.9)
Moderate	61 (48.0)
Severe	14 (11.0)
Went to emergency department, *n* (%)	25 (19.7)
Hospitalized, *n* (%)	5 (3.9)
ICU stay, *n* (%)	0 (0.0)
COVID-19 Recovery Status	
Feeling now compared to at your worst, *n* (%)	
Much Better	110 (86.6)
Slightly Better	15 (11.8)
No change	2 (1.6)
Slightly worse	0 (0.0)
Much worse	0 (0.0)
Feeling now compared to before having COVID-19, *n* (%)	
Much better	23 (18.4)
Slightly better	21 (16.8)
No change	41 (32.8)
Slightly worse	38 (30.4)
Much worse	2 (1.6)
Returned to usual health, *n* (%)	
Yes	89 (70.1)
No	38 (29.9)
Still have symptoms, *n* (%)	94 (85.5)

Note: All variables had complete data except (n): Months since positive test (125), feeling now compared to before having COVID-19 (125), and still have symptoms (110). COVID-19 = coronavirus disease 2019; ICU = intensive care unit.

COVID-19 Case-Control Differences in Mental Health Outcomes

Across multiple mental health outcomes, cases had greater symptom severity than controls (see Table 3). Unadjusted *t*-tests revealed that cases had significantly greater depressive (d = 0.24), anxiety (d = 0.34), PTSD (d = 0.32), and insomnia (d = 0.31) symptoms than controls. The detected differences were small in magnitude (44). The case-control difference for the PSS-10 fell just short of statistical significance (d = 0.23). In ANCOVA models adjusted for age, sex, race, education, income, and smoking status, significant differences remained for anxiety, PTSD, and insomnia symptoms but not for depressive symptoms. There were no significant case-control differences in perceived stress and general psychopathology.

Table 3. Mental Health Outcomes by COVID-19 Status

Mental Health Outcomes	***Cases*** (*n* = 127) *M (SD)*	***Controls*** (*n* = 150) *M (SD)*	***t-tests*** *t*	*df*	*p*	***ANCOVAs*** *F* (*df*1, *df*2)	*p*
PHQ-9	**6.07 (5.79)**	**4.71 (5.51)**	**1.99**	**273**	**.047**	2.72 (1,259)	.10
GAD-7	**5.25 (5.21)**	**3.60 (4.62)**	**2.78**	**270**	**.01**	**4.56 (1,256)**	**.03**
PCL-5	**15.73 (17.92)**	**10.63 (13.86)**	**2.64**	**269**	**.01**	**5.35 (1,255)**	**.02**
ISI	**8.61 (6.21)**	**6.78 (5.76)**	**2.53**	**273**	**.01**	**5.44 (1,259)**	**.02**
PSS-10	15.09 (8.76)	13.07 (8.65)	1.90	268	.06	2.00 (1,254)	.16
SCL-90	0.58 (0.67)	0.47 (0.57)	1.46	275	.14	1.65 (1,261)	.20

Note: ANCOVA models are adjusted for age, sex, race, education, income, and smoking status. Bolded elements indicate significant differences. Sample sizes were (*n*): PHQ-9 (275), GAD-7 (272), PCL-5 (271), ISI (275), PSS-10 (270), and SCL-90 (277). PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder-7; PCL-5 = PTSD Checklist for DSM-5; ISI = Insomnia Severity Index; PSS-10 = Perceived Stress Scale-10; SCL-90 = Hopkins Symptom Checklist-90.

Cases also had significantly higher rates of clinically significant symptoms than controls (see Table 4). To illustrate, more cases (19.0%) had moderate to severe anxiety symptoms than controls (9.6%). Similarly, 20.2% of cases, versus 9.5% of controls, met criteria for a provisional diagnosis of PTSD. Unadjusted chi-square tests revealed that cases had more than double the odds of clinically significant anxiety and PTSD symptoms (*ORs* = 2.22 and 2.40, respectively).

In logistic regression models adjusted for the covariates listed above, the elevation in the odds of clinically significant PTSD symptoms for cases remained statistically significant (*OR* = 2.39); however, the elevation in the odds of clinically significant anxiety symptoms did not. Of note, cases also had an elevated odds of clinically significant insomnia symptoms that fell just short of statistical significance (*ORs* = 1.59 and 1.48).

Table 4. Case-Control Differences in Percentage Scoring Above Clinical Cut Points for the Mental Health Outcomes

			Chi-Square Tests		***Logistic Regressions***	
Mental Health Outcomes	% Cases	% Controls	*OR*	*p*	*OR*	*p*
PHQ-9	22.2	16.8	1.42	.25	1.28	.47
GAD-7	**19.0**	**9.6**	**2.22**	**.03**	1.79	.15
PCL-5	**20.2**	**9.5**	**2.40**	**.01**	**2.39**	**.03**
ISI	52.8	41.2	1.59	.06	1.48	.13

Note: Clinical cut points were: PHQ-9 ≥ 10 (moderate to severe depressive symptoms); GAD-7 ≥ 10 (moderate to severe anxiety symptoms); PCL-5 ≥ 31 (provisional PTSD diagnosis); ISI ≥ 8 (subthreshold to severe insomnia). Logistic regression models were adjusted for age, sex, race, education, income, and smoking status. Bolded elements indicate significant differences. Sample sizes were (*n*): PHQ-9 (275), GAD-7 (272), PCL-5 (271), ISI (275), PSS-10 (270), and SCL-90 (277). *OR* = odds ratio; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder-7; PCL-5 = PTSD Checklist for DSM-5; ISI = Insomnia Severity Index.

Supplemental ANCOVA models further adjusting for BMI showed that significant differences remained for anxiety ($p = .03$), PTSD ($p = .03$), and insomnia ($p = .03$) symptoms. No additional adjustments were made for other participant characteristics for which there were case-control differences – i.e., history of sleep disorders, COVID-19 comorbidities, and sedentary hours per day (see Table 1) – due to the ambiguity in whether they represent differences that existed prior to COVID-19 infection or additional consequences of COVID-19 infection.

Race as a Moderator of COVID-19 Case-Control Differences in Mental Health Outcomes

Moderation analyses employing PROCESS revealed that race did not moderate the relationship between case-control status and any of the mental health outcomes (all *p*s for case-control status x race interaction > .30; see Table 5).

Table 5. Results of Analyses Examining Race as a Candidate Moderator of COVID-19 Case-Control Differences in Mental Health Outcomes

Mental Health Outcomes	Case-Control Status x Race Interaction		
	b	*SE*	*p*
PHQ-9	-0.57	1.35	.67
GAD-7	-0.06	1.16	.96
PCL-5	-3.91	3.82	.31
ISI	-0.79	1.48	.59
PSS-10	-1.46	2.07	.48
SCL-90	-0.09	0.15	.56

Note: Race was coded as Black = 0 and White = 1. Models were adjusted for age, sex, education, income, and smoking status. Sample sizes were (*n*): PHQ-9 (275), GAD-7 (272), PCL-5 (271), ISI (275), PSS-10 (270), and SCL-90 (277). PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder-7; PCL-5 = PTSD Checklist for DSM-5; ISI = Insomnia Severity Index; PSS-10 = Perceived Stress Scale-10; SCL-90 = Hopkins Symptom Checklist-90.

Socioeconomic Status as a Moderator of COVID-19 Case-Control Differences in Mental Health Outcomes

In the present sample, the correlation between the two indicators of SES – education and income – was $r = .32$ ($p < .001$). Moderation analyses demonstrated that education did moderate the relationship between case-control status and five of the six mental health outcomes, and post-hoc probing of the significant case-control status x education interactions revealed that they all had a similar form (see Table 6 and Figure 1). Specifically, case-control status was more strongly and positively associated with depressive, anxiety, PTSD, perceived stress, and general psychopathology symptoms at lower education levels. As education increased, the strength of associations between case-control status and the mental health outcomes decreased, becoming nonsignificant in most instances. Of note, a similar pattern was also observed for insomnia symptoms, although the case-control status x education interaction for this outcome fell just short of significance. In contrast, results of moderation analyses indicated that income did not moderate the relationship between case-control status and any of the mental health outcomes (all *p*s for case-control status x income interaction > .07; see Table 7).

Table 6. Results of Analyses Examining Education as a Candidate Moderator of COVID-19 Case-Control Differences in Mental Health Outcomes

Mental Health Outcomes	**Interaction with Education**			**Post-Hoc Probing Results**								
				1 SD Below			*Mean*			*1 SD* Above		
	b	*SE*	*p*	*b*	*SE*	*p*	*b*	*SE*	*p*	*b*	*SE*	*p*
PHQ-9	**-0.83**	**0.31**	**.01**	**2.94**	**0.97**	**.003**	1.18	0.69	.09	-0.58	0.95	.54
GAD-7	**-0.60**	**0.27**	**.03**	**2.55**	**0.83**	**.002**	**1.29**	**0.59**	**.03**	0.03	0.81	.97
PCL-5	**-2.39**	**0.89**	**.01**	**9.69**	**2.73**	**<.001**	**4.65**	**1.94**	**.02**	-0.39	2.68	.88
ISI	-0.67	0.35	.05	3.22	1.06	.003	1.80	0.76	.02	0.38	1.04	.71
PSS-10	**-1.07**	**0.50**	**.03**	**3.78**	**1.48**	**.01**	1.53	1.06	.15	-0.72	1.46	.62
SCL-90	**-0.07**	**0.03**	**.03**	**0.26**	**0.11**	**.02**	0.10	0.08	.18	-0.06	.10	.58

Note: Education was examined as a continuous variable. Models were adjusted for age, sex, race, income, and smoking status. Bolded elements indicate significant associations. Sample sizes were (*n*): PHQ-9 (275), GAD-7 (272), PCL-5 (271), ISI (275), PSS-10 (270), and SCL-90 (277). PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder-7; PCL-5 = PTSD Checklist for DSM-5; ISI = Insomnia Severity Index; PSS-10 = Perceived Stress Scale-10; SCL-90 = Hopkins Symptom Checklist-90.

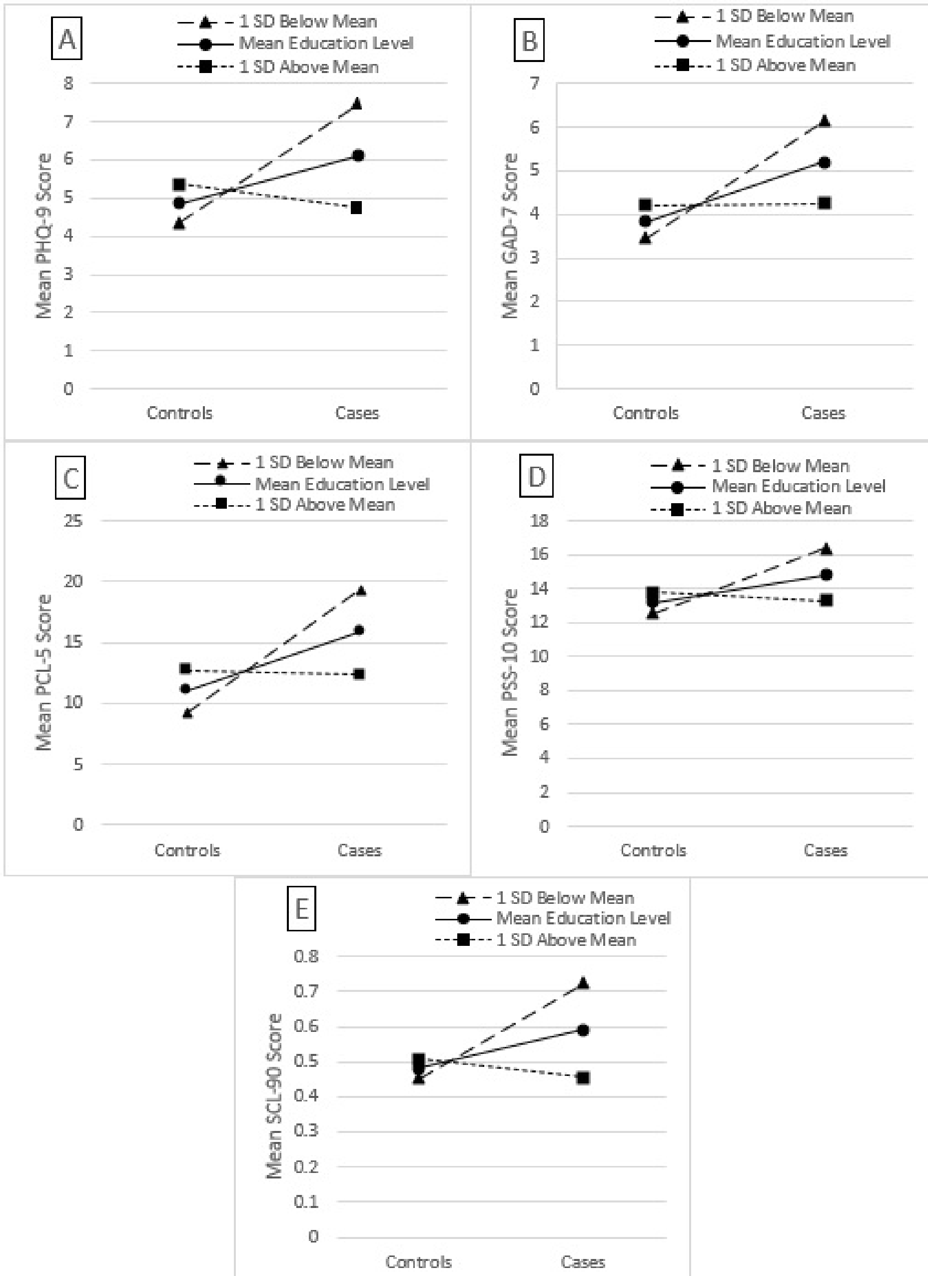

Figure 1. Association between case-control status and the mental health outcomes as a function of education level. Results shown for depressive symptoms (PHQ-9; Panel A), anxiety symptoms (GAD-7; Panel B), PTSD symptoms (PCL-5; Panel C), perceived stress (PSS-10; Panel D), and general psychopathology (SCL-90; Panel E). PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder-7; PCL-5 = PTSD Checklist for DSM-5; PSS-10 = Perceived Stress Scale-10; SCL-90 = Hopkins Symptom Checklist-90.

Table 7. Examining Income as a Candidate Moderator of COVID-19 Case-Control Differences in Mental Health Outcomes

Mental Health Outcomes	Interaction with Income		
	b	*SE*	*p*
PHQ-9	-.002	.001	.10
GAD-7	-.001	.001	.29
PCL-5	-.006	.004	.10
ISI	-.001	.001	.51
PSS-10	-.004	.002	.08
SCL-90	0.00	0.00	.18

Note: Income was examined as a continuous variable. Models were adjusted for age, sex, race, education, and smoking status. Sample sizes were (*n*): PHQ-9 (275), GAD-7 (272), PCL-5 (271), ISI (275), PSS-10 (270), and SCL-90 (277). PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder-7; PCL-5 = PTSD Checklist for DSM-5; ISI = Insomnia Severity Index; PSS-10 = Perceived Stress Scale-10; SCL-90 = Hopkins Symptom Checklist-90.

DISCUSSION

The present study sought to characterize the longer-term mental health consequences of COVID-19 infection and examine whether such consequences are more pronounced in certain sociodemographic groups. We found that COVID-19 status was indeed associated with mental health outcomes an average of 9.5 months after infection. Compared to those without a history of COVID-19 (controls), people with a history of COVID-19 (cases) had significantly greater depressive, anxiety, PTSD, and insomnia symptoms. Aside from depressive symptoms, these group differences remained after adjustment for sociodemographic factors and smoking status. In addition, some of these differences were potentially clinically meaningful, as cases had more than twice the odds of reporting clinically significant levels of anxiety and PTSD symptoms compared to controls. However, COVID-19 status was not significantly associated with perceived stress or general psychopathology. We also found that, contrary to our expectations, race and income (one indicator of SES) did not moderate relationships between COVID-19 status and the mental health outcomes. However, education (another indicator of SES) did moderate most of the relationships of interest, suggesting that people with lower education levels may be particularly susceptible to the longer-term mental health consequences of COVID-19 infection.

Our findings from adults at least six months post-infection suggest that the longer-term mental health consequences of COVID-19 infection is an area of concern. Our results are in line with emerging evidence that people with a history of COVID-19 continue to experience mental health symptoms (e.g., anxiety and depression) about one year after infection (45). In our study, participants with a history of COVID-19 had greater mental health symptom severity than those with no history of COVID-19. This is consistent with previous studies which found that people with a history of COVID-19 have greater anxiety, depression, insomnia, and PTSD symptom severity several months to a year after infection (46-49). While severe symptoms during the acute phase have been linked with a greater risk of mental health disorders at 6-month follow-up (50), our results indicate that COVID-19 infection may have long-lasting mental health effects even among those with an initial mild to moderate illness. Our results are supported by a study which found that, compared to those with no history of COVID-19, non-hospitalized patients with a history of COVID-19 had a greater burden of anxiety, stress, trauma, and sleep disorders at 6-month follow-up (51). In that study (as in the present study), people with a history of COVID-19 did not display markedly greater levels of perceived stress and general psychopathology, possibly indicating that the longer-term effects of COVID-19 infection preferentially impact certain overlapping psychological dimensions (e.g., depression, anxiety, PTSD, and sleep disturbance).

We found that people experience the longer-term mental health consequences of COVID-19 infection at alarming rates. Furthermore, some of the case-control differences in mental health outcomes appear to be clinically meaningful, as people with a history of COVID-19 had more than twice the odds of people without of a history of COVID-19 of reporting clinically significant symptoms of anxiety and PTSD. Specifically, in our sample, people with a history of COVID-19 reported high rates of clinically significant anxiety (19.0%) and PTSD (20.2%) symptoms. While there were no significant differences in the rates of clinically significant depressive and insomnia symptoms, people with a history of COVID-19 did have numerically and potentially meaningfully higher rates for these mental health outcomes as well. In our sample, one in five people with a history of COVID-19 had clinically significant depressive symptoms, and more than half had clinically significant insomnia symptoms. A Swedish study of hospitalized COVID-19 patients with persistent symptoms found even higher rates of clinically significant depressive symptoms (43%) and anxiety symptoms (29%) at 5-month follow-up (52). The higher rates observed in that study may have been due to participation being restricted to those who were hospitalized and had persistent symptoms and lower clinical cut points that captured mild symptoms in addition to moderate and severe symptoms. A meta-analysis of the long-term mental health consequences of other coronaviruses (SARS and MERS) also noted high point prevalence rates for depression (14.9%), anxiety (14.8%), and PTSD (32.2%) (53). Additionally, 50% of people with a history of SARS have reported difficulty sleeping six months after hospital discharge (54). Still, there is notable variability across studies in the reported prevalence rates of persistent symptoms of COVID-19. For example, an Iranian study of hospitalized COVID-19 patients six months after hospital discharge found a drastically lower rate of clinically significant PTSD symptoms (5.8%) (55).

Such a range across studies could be due to differences in study design and sample composition. In the Iranian study, patients who had taken psychiatric medication in the last year were excluded, and the majority of their sample were male, which is notable because women have greater odds of experiencing the longer-term mental health consequences of COVID-19 infection (47, 56). In addition, differing results across studies could reflect the inherent variability in the presentation of the disease itself (57). Psychological symptoms may vary between individuals depending on the region of the brain that may be affected by COVID-19 induced coagulation and neuronal damage (58). Differences in psychological symptom presentation may also emerge based on the level of chronic immune response to COVID-19 infection. In a preprint investigating the immune response in people with persistent neurological symptoms of COVID-19, higher depression scores were associated with a greater and more dysfunctional T-cell response to COVID-19 viral proteins (59).

We found that race did not moderate the relationship between COVID-19 status and the mental health outcomes. However, to properly contextualize this finding, several factors should be considered. First, the null race moderation results might be due, in part, to our sample characteristics. Although 19.7% of our participants with a history of COVID-19 went to the emergency department, only 11.0% reported severe acute symptoms, and only 3.9% were hospitalized (none were admitted to the ICU). While the literature is mixed on whether COVID-19 acute illness severity is a major risk factor for persistent symptoms (60), a more severe acute illness may be a risk factor for persistent mental health symptoms (10). This is pertinent because Black patients with COVID-19 are at greater risk of ICU admission than White patients with COVID-19 (61). It is plausible that, if COVID-19 severity and treatment setting strongly contribute to the longer-term mental health consequences in Black adults, those mechanisms were not fully captured in our sample. Second, considering the variability in COVID-19 disease expression, it is possible that certain symptoms may be more pronounced in Black adults, while other symptoms may be less affected. A study through the U.S. Department of Veteran Affairs found that, while Black adults with a history of COVID-19 had a greater burden of physical outcomes (e.g., diabetes and thromboembolism) at 6 month follow-up, they had similar incidence rates for anxiety, mood, and sleep disorders to White adults with a history of COVID-19 (62). At present, it is difficult to draw firm conclusions because there remains a dearth of literature examining the longer-term mental health consequences of COVID-19 infection in Black adults. However, there is now increased interest in research exploring the mechanisms of long COVID and racial disparities (63).

In contrast to race, one indicator of SES, education, was a moderator of the relationships between COVID-19 status and most of the mental health outcomes. A biological pathway could help explain the more pronounced mental health consequences of COVID-19 infection observed in people with lower education. As people with lower SES often have increased baseline inflammation, COVID-19 infection could further trigger an overactive inflammatory response (23) and greater mental health consequences may arise because of the prolonged inflammatory response to COVID-19 infection (12). Increased baseline inflammation in people with lower SES may be due to a higher prevalence of poor health behaviors (e.g., smoking and poor diet quality) and greater exposure to proinflammatory environments (e.g., infections in overcrowded areas and limited access to sanitation) (22). In addition, a psychosocial pathway (i.e., stigma) could help explain the more pronounced mental health consequences in people with lower education. People infected with COVID-19 may face stigma similar to that seen during other outbreaks of infectious diseases, which may exacerbate the mental health consequences (64). This is notable because stigma may be greater in people with lower education. For example, people with lower education are more likely to be unemployed (65), and being unemployed is a predictor of COVID-19-related stigma (e.g., minimized social communication and loss of friends) (26). Furthermore, stigma can disproportionately affect people with lower education through the public health response, as social distancing and quarantine can instill a sense of "othering" towards already stigmatized groups (27). Concurrently, higher education may have been a protective factor against the longer-term mental health consequences of COVID-19. At higher education levels, people with a history of COVID-19 may have experienced a buffering effect of education, as people with more education engage in more health promoting behaviors and have greater social support (66). Engaging in more health promoting behaviors, such as increased fruit and vegetable intake and physical activity, may improve mental health (67, 68). Additionally, greater social support could bolster mental health because it may help people cultivate effective coping strategies and resilience in stressful situations (69).

Surprisingly, another SES indicator, income, was not a moderator of these associations. One potential explanation is restriction of range in the income-related sample characteristics. Participants with a history of COVID-19 had a relatively high mean annual household income ($76,036), and most had health insurance (89%). Thus, people with extremely low incomes, who may be most affected by the longer-term mental health consequences of COVID-19, are not represented well in our sample. Another potential explanation is self-report error. Income is difficult to measure because household income often consists of multiple sources from several people in the home (70), which may result in self-report error from a misreported source of income (71). Greater error in the measure of income, versus that of education, would make it more difficult to detect moderation.

Although our study has key strengths (e.g., a sample with good representation of Black adults, a validated and broad assessment of mental health outcomes, and the testing of sociodemographic factors as moderators), there are also important limitations to consider. First, the present sample was restricted to Amazon Mturk users, which could have weakened case-control differences and may limit the generalizability of our results. Of note, the average employment rate in our sample was higher than in the general U.S. population (72). Furthermore, our sample had a restricted range in acute illness severity and subsequent treatment setting, which may have led to an underestimation of the true longer-term mental health consequences. However, in comparison to traditional college samples, Mturk provides more representative samples (32). Second, our eligibility criteria required that people with a history of COVID-19 participate in this study only if they had tested positive for COVID-19. Therefore, true cases who were unable to receive a COVID-19 test (e.g., due to poor healthcare access) were excluded from this study, which could also limit the generalizability of our results. Third, because we collected self-report data only, we are unable to verify factors such as COVID-19 status and dates of positive COVID-19 tests with health records. Thus, there could be some misclassification of cases and controls, which could weaken group differences (73). Fourth, given the cross-sectional nature of our data, reverse causality and confounding remain plausible alternative explanations for our findings. Concerning reverse causality, poor mental health present before COVID-19 infection could lead to an increased risk of COVID-19 infection. Regarding confounding, while we adjusted for several covariates in our models, other unmeasured or unexamined factors could still be operating as confounders of relationships between COVID-19 status and mental health outcomes.

There is an urgent and growing need to further characterize the longer-term mental health consequences of COVID-19 infection, to identify the sociodemographic groups at greatest risk, and to develop and test treatments designed to lessen these consequences. In a recent call to action from an international, multidisciplinary group of experts, the authors highlighted the lack of consistency in the assessment of longer-term COVID-19 outcomes across studies and recommend creating a minimum list of outcomes that should be assessed in all related studies (74). They also acknowledged the importance of additional considerations that are particularly relevant for marginalized groups, such as differentiating whether outcomes were due to COVID-19 or other risk factors and including alternative definitions and measurement methods to account for limited access to COVID-19 testing and resources. Like the present investigation, future studies should utilize a broad set of validated mental health assessments, which will allow for comparisons to existing results (e.g., norms when available) and aggregation of results across COVID-19 studies (e.g., in meta-analyses). Future studies should also consider including validated measures assessing racism and/or discrimination, as systemic racism has been identified as a key contributor to the disproportionate burden of mental health consequences from the COVID-19 pandemic in Black people (75). Notably, it appears that stress from experiencing discrimination, rather than general stress, is associated with more persistent physical and psychological COVID-19 symptoms (76). Another relevant topic for consideration in future studies is the intersection of race, education, and income. The protective effect of higher education and income on mental health may be dependent on race, as education and income may introduce protective benefits for White adults but introduce additional stressors, such as increased discrimination, for Black adults (77).

To summarize, this study provides new insights into the nature of the longer-term mental health consequences of COVID-19 infection and identifies a sociodemographic group that may be particularly susceptible to these poor outcomes. While prior studies have largely focused on hospitalized COVID-19 patients, our study examined people across the spectrum of COVID-19 severity in the acute phase. Our results highlight that the mental health consequences of COVID-19 remain highly prevalent for at least 6 months after initial infection. In addition to the many physical symptoms that persist following COVID-19 infection, many mental health symptoms across multiple domains persist as well. In particular, symptoms of anxiety and PTSD should be closely monitored and treated when detected in the months following COVID-19 infection. Furthermore, people with lower education levels may be particularly susceptible to these consequences and thus are in need of greater monitoring and treatment resources. Future efforts are needed to continue to identify the sociodemographic groups at greatest risk for the mental health consequences of COVID-19 infection and develop effective treatments for these symptoms in these populations.

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