ORIGINAL RESEARCH

Psychological and Cognitive Functioning Among Patients Receiving Outpatient Rehabilitation for Post-COVID Sequelae: An Observational Study

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Abstract

Objectives: To describe the characteristics of individuals receiving outpatient rehabilitation for post-acute sequelae of SARS-CoV-2 infection (PASC). Further, to examine factors associated with variation in their psychological and cognitive functioning and health-related quality of life.

Design: Observational study.

Setting: Outpatient COVID-19 recovery clinic at a large, tertiary, urban health system in the US.

Participants: COVID-19 survivors with persistent sequelae (N=324).

Interventions: : Not applicable.

Main Outcome Measures: Multivariable logistic and linear regression models were used to examine factors associated with COVID survivors' experience of severe anxiety, severe depression, post-traumatic stress disorder (PTSD), cognitive impairment, and self-reported health-related quality of life.

Results: About 38% of survivors seeking care for their persistent COVID symptoms suffered from severe anxiety, 31.8% from severe depression, 43% experiencing moderate to severe PTSD symptomology, and 17.5% had cognitive impairment. Their health-related quality of life was substantially lower than that of the general population (-26%) and of persons with other chronic conditions. Poor and African American/Black individuals experienced worse psychological and cognitive sequelae after COVID19 infection, even after controlling for age, sex, initial severity of the acute infection, and time since diagnosis.

Conclusions: Evidence of consistent disparities in outcomes by the patients' race and socioeconomic status, even among those with access to post-acute COVID rehabilitation care, are concerning and have significant implications for PASC policy and program development.

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Individuals with COVID-19 often continue to have persistent symptoms in the weeks to months after the resolution of their acute illness. Conservative estimates indicate that these persistent symptoms, referred to collectively as post-acute sequelae of SARS-CoV-2 infection (PASC), affect about 10%-30% of individuals with COVID-19 and can occur despite a relatively mild initial illness.[1-16] PASC, which afflicts individuals of all age groups,[14] sex,[9] and races, is long-lasting and can continue beyond 7 months after the resolution of their acute viral infection.[15,16]

Symptoms of PASC are diverse, ranging from pulmonary to cardiac, musculoskeletal, dermatologic, and gastrointestinal. Some of the most prevalent ongoing symptoms, however, are neurologic and psychological including cognitive dysfunction, anxiety, depression, and post-traumatic stress disorder (PTSD).[1-5,10-16] Given concerns about their potentially high burden for the large

and growing number of individuals with PASC,[17,18] the Society of Critical Care Medicine,[19] the International Multi-professional Steering Committee of Cochrane Rehabilitation for COVID-19,[20,21] and the US Multi-disciplinary Collaborative Task Force developing consensus statements for post-COVID rehabilitation[22] recommend evaluation and treatment of such neuropsychological outcomes for all persons presenting with persistent post-COVID symptoms.

Rehabilitation services provided in an outpatient setting are potentially well-suited to mitigate the debilitating sequelae of COVID-19 and related complications.[23-26] Notwithstanding their benefit and despite notable exceptions,[27-29] relatively limited data are available on the sociodemographic, psychological, and cognitive characteristics of patients with PASC who present for rehabilitation.

The purpose of this study was to describe the sociodemographic characteristics and psychological and cognitive presenting complaints of a population of COVID-19 survivors receiving outpatient rehabilitation at a racially diverse, urban COVID recovery clinic. We also examined the association between patient characteristics and the presence of severe, persistent psychological and cognitive sequelae and resulting health-related quality of life, with a special focus on the role of time since COVID diagnosis and severity of the acute illness. We hypothesize that both duration of symptoms and severity of the acute infection would be positively associated with the incidence of COVID-19 cognitive sequelae.

Methods

Setting

The study was performed at 1 of the first US post-COVID Assessment and Recovery Clinics within the University of Pennsylvania Department of Physical Medicine and Rehabilitation, an academic rehabilitation facility located in Philadelphia, PA. This work was done under the University of Pennsylvania IRB through an approved research protocol to analyze de-identified, archival data.

Study design and variable definitions

This observational cohort study includes all consecutive, unique patients receiving treatment at the study health system post-COVID clinic from June 2020 to April 2021 to address their PASC symptoms.

Data are drawn from a combination of medical records and structured surveys conducted at the time of the initial visit. Demographic characteristics include age, sex, race/ethnicity (coded as Black/African American, Hispanic, White, and a residual category of other race/ethnicity, which included persons self-identified as Asian, Pacific Islander, Alaska Native, and a small number of observations with unreported race/ethnicity), and health insurance coverage status (coded as Medicare, Medicaid, private/commercial, or other insurance). As proxies for the severity of the acute

List of abbreviations:

CI	confidence interval
OR	odds ratio
PASC	post-acute sequelae of SARS-Cov-2 infection
PTSD	post-traumatic stress disorder

SARS-CoV-2 infection, we collected information on whether the patient was hospitalized or admitted to an intensive unit for COVID-19. Finally, we calculated the weeks since the diagnosis based on the date of the first positive COVID test and the date of the initial post-COVID clinic visit. Patients with symptoms persisting longer than 12 weeks were classified as experiencing post-COVID syndrome, according to the conventional criterion.[28]

Outcome measures

All patients underwent the same standardized assessment, which included a structured survey of COVID-related symptoms and associated impairments. Measures were selected based on the US Society of Critical Care Medicine as well as recommendations from the Multi-disciplinary Collaborative Consensus task force for assessment of symptoms in patients with PASC.[19,22] The hospital anxiety scale and Hospital depression scale,[30,31] each a validated 14-item assessment, were used to identify anxiety and depression, respectively, while the impact of event scale, a widely-used epidemiologic screening tool for PTSD, was used to assess the extent of COVID-related traumatic experience.[32,33] Cognitive functioning was assessed by trained clinical staff using the Montreal Cognitive Assessment,[34] a 12-item assessment of global cognitive performance designed to detect mild cognitive dysfunction. Finally, health-related quality of life was assessed using the visual analog scale (0-100) of the preference-based European Quality of Life Scale instrument.[35,36] Consistent with the established thresholds that identify clinically meaningful dysfunction, patients were coded as having severe anxiety if they scored >8 in the hospital anxiety scale score >8 scale; severe depression if they scored >8 in the hospital depression scale, and PTSD if they scored >1.75 in the impact of event scale. Patients were coded as experiencing cognitive impairment if they scored <18 in the education-adjusted Montreal Cognitive Assessment scale.

Data analysis

The sample was characterized by means (and SD) and median (and interquartile range) for normally and non-normally distributed data, respectively. For binary variables, including the prevalence of severe depression, severe anxiety, PTSD, and cognitive impairment, we report the number and percentage of patients experiencing those symptoms. With exception of the continuous measure of health-related quality of life for which we applied ordinary linear regression analysis, a multivariable logistic specification was used to examine factors associated with the presence of each outcome.

Results

Sample characteristics

Of the 324 patients assessed at the study health system's post-COVID clinic between June 2020 and April 2021, most (58.6%) were younger than 50 years old and were women (68.8%; table 1). Approximately 16% were African American, 5.2% were of Latino or Hispanic descent, and 10.5% were of other races. Nearly 1 in 8 had less than a high school education and about 9.1% were living under the poverty threshold as proxied by Medicaid enrollment.

Table 1 Summary of characteristics

	Total N=324	Severe Anxiety n=123	Severe Depression n=103	PTSD n=138	Cognitive Impairment n=52
Age (y)					
Mean ± SD	46.6 (14.0)	45.3 (14.3)	47.3 (15.0)	45.8 (14.7)	52.6 (15.2)
Median (IQR)	46.0 (21.0)	43.0 (20.0)	46.0 (18.0)	43.0 (23.0)	50.0 (20.5)
Age (y), n (%)					
<30	38 (11.7)	17 (13.8)	15 (14.6)	18 (13.0)	2 (3.8)
30-39	66 (20.4)	25 (20.3)	15 (14.6)	36 (26.1)	8 (15.4)
40-49	86 (26.5)	38 (30.9)	31 (30.1)	29 (21.0)	16 (30.8)
50-59	76 (23.5)	26 (21.1)	22 (21.4)	31 (22.5)	12 (23.1)
60-69	38 (11.7)	9 (7.3)	10 (9.7)	14 (10.1)	4 (7.7)
70+	28 (6.2)	8 (6.5)	10 (9.7)	10 (7.2)	10 (19.2)
Sex, n (%)					
Women	221 (68.8)	88 (72.7)	70 (69.3)	94 (69.6)	38 (74.5)
Men	100 (31.2)	33 (27.3)	31 (30.7)	41 (30.4)	13 (25.5)
Race/ethnicity, n (%)					
Black	52 (16.0)	24 (19.5)	21 (20.4)	31 (22.5)	17 (32.7)
Hispanic	17 (5.2)	8 (6.5)	7 (6.8)	5 (3.6)	0 (0.0)
White	221 (68.2)	80 (65.0)	67 (65.0)	87 (63.0)	31 (59.6)
Other/Unknown	34 (10.5)	11 (8.9)	8 (7.8)	15 (10.9)	4 (7.7)
Education, n (%)					
<12 years formal education	37 (11.9)	15 (12.5)	14 (14.0)	17 (12.5)	2 (3.8)
Insurance, n (%)					
Medicaid	29 (9.1)	19 (15.6)	14 (13.7)	21 (15.4)	3 (5.9)
Medicare	31 (9.7)	10 (8.2)	11 (10.8)	10 (7.4)	8 (15.7)
Commercial	258 (81.1)	93 (76.2)	77 (75.5)	105 (77.2)	40 (78.4)

Abbreviation: IQR, interquartile range.

More than one-third of the sample scored in the range endorsing dysfunction in each of the 4 psychological and cognitive metrics, with 123 (37.9%) suffering from severe anxiety, 103 (31.8%) having symptoms consistent with severe depression, 138 (43%) experiencing moderate to severe PTSD symptomology, and 52 (17.5%) having cognitive impairment. The right panel of table 1 shows the demographic and socioeconomic characteristics of these patients, by outcomes.

Although there were no marked differences in the demographic characteristics of COVID survivors experiencing severe depression, severe anxiety, or moderate-to-severe PTSD symptoms, a higher proportion of individuals experiencing cognitive dysfunction was older, female, and African American/Black than those without cognitive dysfunction. Of note, about 30% of those with severe depression and 38% of those scoring in the cognitive impairment range of the assessment tools had been hospitalized for COVID, compared with 17.9% and 21% among those with severe anxiety and PTSD.

In table 2, we present the patients' unadjusted health-related quality of life as well as their psychological and cognitive functioning at the assessment visit, overall and by (tertiles of) time since COVID diagnosis and severity of the acute viral infection, proxied by hospitalization.

Less than one-quarter (22.8%) of the full sample had been hospitalized for COVID-19 during their acute infection. The mean number of weeks since diagnosis among all patients was 21.9 (SD=12.7), range 13-51 weeks. Nearly 70% (n=225) met the criteria for PASC with symptoms persisting longer than 12 weeks since disease diagnosis. As seen in figure 1, about one-third of all patients experienced symptoms lasting more than 30 weeks.

The mean health-related quality of life for the overall sample was 59.5 (SD=21.1). Across all measures, outcomes were generally more prevalent among patients with symptoms lasting more than 12 weeks although there were no marked differences among patients in the top 2 tertiles of the COVID symptoms duration distribution (ie, 12-29 and 30+ weeks since onset). With increasing severity of the acute SARS-CoV-2 infection, more problems were reported on all dimensions except anxiety for which a substantially smaller proportion of the hospitalized sample scored in the range of severe symptoms (29.7%) as compared with non-hospitalized COVID survivors (40.7%).

Factors associated with quality of life, psychological, and cognitive functioning

Table 3 presents the results from our multivariable regression models. After controlling for sociodemographic characteristics and other potential confounders, time since COVID-19 diagnosis was significantly associated with lower health-related quality of life: -5.49 [95% confidence interval [CI] -11.19 to -0.22, P=.03] and -5.12 [95% CI -11.0 to -0.95, P=.05] points for persons in the 12-29 weeks and >30 weeks since COVID diagnosis, respectively). With the exception of a marginally higher likelihood of PTSD symptoms (odds ratio [OR]=1.71; 95% CI 0.96 to 3.07, P=.07) among those in the 12-29 weeks since COVID diagnosis, time since acute viral infection was not associated with patients' experience of other severe mental health, psychological, or cognitive impairments.

The severity of the acute infection, proxied by whether the person was hospitalized for COVID was associated with an increased likelihood of severe depression (OR=1.60, 95% CI 0.89 to 2.88, P=.06) and cognitive impairment (OR=1.92, 95% CI 1.09 to 4.11, P=.05). In contrast, the severity of acute infection was not

Table 2   Quality of life, psychological, and cognitive functioning of patients seeking rehabilitation care for COVID-19 sequelae

	Total Sample	Health-related Quality of Life (EQ-VAS)	Severe Anxiety (HADS-A)	Severe Depression (HADS-D)	PTSD (IES-6)	Cognitive Impairment (Montreal Cognitive Assessment -Blind)
	n (%)	Mean ± SD Median (IQR)	n (%)	n (%)	n (%)	n (%)
Overall	324 (100)	59.5 (21.1) 65.0 (25.0)	123 (37.9)	103 (31.8)	138 (43.0)	52 (17.5)
Time since COVID DX						
<12 weeks	99 (30.6)	63.0 (19.2)	33 (33.7)	29 (29.9)	36 (37.1)	13 (14.9)
12-29 weeks	121 (37.4)	65.0 (26.0)	46 (39.0)	39 (33.1)	57 (48.7)	18 (17.1)
30+ weeks	104 (32.1)	57.1 (22.9)	43 (42.2)	33 (32.4)	43 (42.6)	19 (19.0)
		65.0 (35.0)				
		58.2 (20.6)				
		60.0 (30.0)				
Severity of acute disease			22 (29.7)	31 (41.3)	29 (44.0)	20 (30.3)
Hospitalized	74 (22.8)	58.3 (19.4)	101 (40.2)	72 (28.9)	109 (39.7)	32 (13.9)
Not hospitalized	250 (77.2)	60.0 (20.0)				
		59.8 (21.7)				
		65.0 (28.5)				

NOTES. Patients were coded as having severe anxiety if they scored >8 in the HADS-A score >8 scale; severe depression if they scored >8 in the HADS-D, and PTSD if they scored >1.75 in the IES-6. Patients were coded as having cognitive impairment if they scored <18 in the education-adjusted Montreal Cognitive Assessment-Blind scale. Because of a small number of missing/incomplete values, the sample size varies by functioning domains. The sample is n=313 for the EQ-VAS, n=310 for severe anxiety, n=309 for severe depression, n=307 for PTSD, and n=271 for cognitive impairment based on the Montreal Cognitive Assessment-Blind.

Abbreviations: HADS-A, hospital anxiety scale; HADS-D, hospital depression scale; IES-6, impact of event scale; IQR, interquartile range.
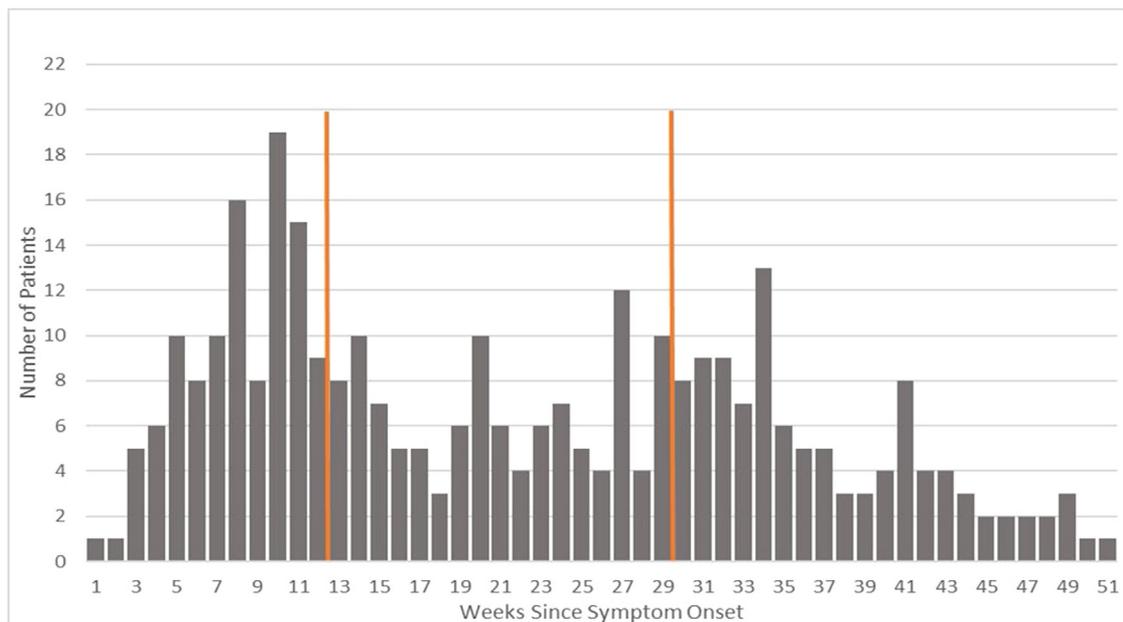
Fig 1   Distribution of patients by time since COVID-19 diagnosis. NOTE: Vertical orange line indicates tertile thresholds.

associated with health-related quality of life or experience of moderate to severe PTSD symptoms. Consistent with the unadjusted differences, hospitalization had a marginally protective effect on the patients' experience of severe anxiety (OR=0.57, 95% CI 0.31 to 1.06, P=.07).

The results also revealed a consistent negative association between poverty and, to a lesser extent, Black race and psychological and cognitive functioning among COVID survivors. Controlling for severity and duration of disease as well as other potential confounders, the health-related quality of life of Medicaid beneficiaries (ie, those patients with income and assets low enough to qualify for the indigent US public health insurance program, Medicaid) was 13.8 points lower than that of privately-insured COVID survivor counterparts. Medicaid beneficiaries were also 3 times (OR=3.33, 95% CI 1.42 to 7.80, P<.001) more likely to experience severe anxiety, almost twice (OR=1.94, 95%

Table 3 Multivariable model estimates

	Health-related Quality of Life (EQ-VAS) N=313	Severe Anxiety (HADS-A) N=310	Severe Depression (HADS-D) N=309	PTSD (IES-6) N=307	Cognitive Impairment (Montreal Cognitive Assessment-Blind) N=271
	Coefficient (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (y)	−0.006 (−0.199, 0.188)	0.99 (0.97, 1.01)	1.00 (0.98, 1.02)	1.00 (0.98, 1.02)	1.03 (1.00, 1.06)*
Sex					
Women	REF	REF	REF	REF	REF
Men	−0.041 (−5.08, 5.00)	0.71 (0.42, 1.20)	0.93 (0.55, 1.57)	0.96 (0.57, 1.60)	0.78 (0.37, 1.63)
Race/ethnicity					
Black	−2.17 (−8.84, 4.49)	1.77 (0.94, 3.46)†	1.26 (0.64, 2.47)	2.43 (1.22, 4.84)*	2.02 (0.96, 4.55)†
Hispanic	8.33 (−2.59, 19.25)	1.11 (0.36, 3.37)	1.04 (0.35, 3.16)	0.40 (0.12, 1.40)	—
White	REF	REF	REF	REF	0.82 (0.25, 2.64)
Other/unknown	1.71 (−6.27, 9.69)	1.03 (0.46, 2.32)	0.80 (0.33, 1.92)	1.43 (0.65, 3.13)	REF
Insurance					
Medicaid	−13.81 (−22.04, −5.58)*	3.33 (1.42, 7.81)*	1.94 (0.96, 4.39)†	4.83 (1.84, 12.68)*	0.54 (0.11, 2.68)
Medicare	−5.08 (−14.21, 4.06)	1.25 (0.49, 3.20)	1.24 (0.49, 3.16)	0.80 (0.31, 2.04)	0.83 (0.27, 2.54)
Commercial	REF	REF	REF	REF	REF
Hospitalized	−0.67 (−6.49, 5.16)	0.57 (0.31, 1.06)†	1.60 (0.89, 2.88)†	0.70 (0.38, 1.28)	1.92 (0.90, 4.11)†
Weeks since diagnosis					
<12	REF	REF	REF	REF	REF
12 to <29	-5.49 (−11.19, 0.22)*	1.30 (0.72, 2.33)	1.15 (0.64, 2.09)	1.71 (0.96, 3.07)†	1.46 (0.63, 3.34)
30+	-5.12 (−11.00, 0.95)†	1.39 (0.76, 2.52)	1.11 (0.59, 2.06)	1.24 (0.68, 2.26)	1.54 (0.67, 3.54)

NOTES. The cognitive impairment regression also controls for educational level. Patients were coded as having severe anxiety if they scored >8 in the HADS-A score >8 scale; severe depression if they scored >8 in the HADS-D, and PTSD if they scored >1.75 in the IES-6. Patients were coded as having cognitive impairment if they scored <18 in the education-adjusted Montreal Cognitive Assessment-Blind scale. All regressions also include a constant term and an indicator for missing race/ethnicity.

Abbreviations: HADS-A, hospital anxiety scale; HADS-D, hospital depression scale; IES-6, impact of event scale; REF.

* $P \le .05$.
† $0.05 < P \le .1$.

CI 1.10 to 4.39, P=.04) as likely to experience severe depression and nearly 5 times (OR=4.83, 95% CI 1.84 to 12.68, P<.001) as likely to have moderate to severe PTSD symptoms than commercially-insured patients. African American/Black COVID survivors were 1.8 times more likely than white COVID patients to experience severe anxiety (OR=1.77, 95% CI 1.01 to 3.46, P=.05), nearly two and a half times more likely to have PTSD symptoms (OR=2.43, 95% CI 1.22 to 4.84, P<.01), and twice as likely to have cognitive impairment (OR=2.02, 95% CI 1.06 to 4.55, P=.05).

With the exception of a higher likelihood of cognitive impairment among older patients, age and sex were not associated with any of the outcomes considered here once other factors were accounted for. Finally, in variants of the main models in which we included interaction terms between certain sociodemographic characteristics, such as race and poverty, and time since diagnosis or severity of initial infection revealed no statistically significant modifying effects.

Discussion

Despite the growing number of studies describing the characteristics and functioning of patients undergoing inpatient rehabilitation after hospitalization with COVID-19 in the United States and elsewhere, little is known about patients seeking care at the emerging outpatient post-COVID clinics. Our study contributes to this incipient literature.

Our findings indicate that the health-related quality of life of survivors seeking care for their persistent COVID symptoms is rather low when compared with the general population. The mean health-related quality of life for the overall sample was 59.5, nearly 21 points, or 26%, below the normal threshold of 80.4 for the general US population.[37] This value is also markedly lower than that of persons with other chronic conditions, such as arthritis (-14.7 points), asthma (-16.6 points), and diabetes mellitus (-14.6).[37] Health-related quality of life was lower among patients suffering from more prolonged symptoms, although time since disease diagnosis and symptom onset were not significantly associated with specific psychological metrics, except for PTSD.

Consistent with the emerging literature on the subject, our findings highlight the extent of the pandemic's psychological, emotional, and mental health toll on individuals, either through its effect on the development of new or the worsening of pre-existing stressors.[38-41] Studies have shown that the disabling effects of conditions such as depression, anxiety, and PTSD often lead to significant occupational, financial, and social distress.[15,39] Somewhat surprisingly, the severity of the acute infection, although increasing the likelihood of patients experiencing severe depression and cognitive impairment, was not associated with PTSD and, in fact, was protective against severe anxiety. Patients who were hospitalized may have had more consistent follow-up care and greater certainty about the cause of their residual symptoms leading to less anxiety. This conjecture should be explored in future research.

The findings of worse functioning among poor, and to a lesser extent, African American/Black individuals with PASC are concerning. Low-income and African Americans/Black individuals are more likely to test positive and to experience more severe acute COVID-19-related outcomes, including hospitalization and death.[42,43] Our findings suggest that poor and African American/

Black individuals also endure worse psychological and cognitive sequelae after COVID-19 infection, and that such socioeconomic and racial disparities persist even after controlling for initial severity of the acute infection and time since diagnosis.

Our findings, combined with robust evidence about the extent of PASC among individuals with history of COVID-19 infections, raise concerns about how the US and other countries will meet the unprecedented demand for outpatient rehabilitation services for this population. It is unlikely that the release of COVID-19 vaccines will lead to the end of PASC given the high numbers of individuals with continued symptoms several months from their initial infection. High rates of hesitancy and refusal to become vaccinated, both in the US and worldwide, will also contribute to the persistence of PASC, as may the risk of breakthrough infections due to new virus variants.

Developing and promoting access to PASC treatments that ameliorate these symptoms is, therefore, an urgent public policy imperative. Minority individuals, in particular, may require more intensive and comprehensive services to fully address some of these problems. In addition, in view of the observed socioeconomic disparities in access, governmental income support, rent subsidies, and prevention of eviction may all play a role in helping low-income individuals suffering from PASC, and add another justification for a larger role of targeted government support for a duration that might promote resolution of sequelae.

Study limitations

There are important limitations of our study that warrant mentioning. Despite relatively large and diverse, patients in our sample, it represents a self-selected group of individuals who had information about and access to the study health system's post-COVID clinic. For this reason, our findings may not be representative of the larger population of individuals with PASC. In addition, the study is cross-sectional in nature: patients' health-related quality of care, psychological and cognitive functioning were evaluated only at the initial visit precluding us from examining the content and potential effectiveness of the PASC clinical program. Increasingly, there have been recommendations for a standardized set of comprehensive measures for the COVID patient population in order to more uniformly analyze treatment protocols and efficacy.[44] Finally, perhaps the most substantial limitation of the study is the absence of pre-COVID measures of the outcomes. Given the opportunistic nature of our sample, we are unable to ascertain whether the observed associations between patients' psychological and cognitive functioning with race and poverty predate the individuals' infection and subsequent PASC.

Despite these limitations, the use of numerous validated standardized measures applied consistently to a relatively large sample of patients referred to or seeking outpatient rehabilitation care for their persistent COVID-19 symptoms is a unique strength of this study, which highlight the importance of incorporating psychological assessment, referral, and treatment in the context of outpatient PASC recovery programs.

Conclusions

Information about the characteristics and functioning of persons suffering from PASC is critical to understanding their needs and preparing for their treatment. Given the large and growing number of patients suffering from post-acute sequelae of SARS-CoV-2 infection, the consistent and persistent disparities in disease incidence and new evidence, as documented here, of disparities in outcomes by the patients' race and socioeconomic status even among those with access to post-acute COVID rehabilitation care, the results of this study have significant implications for both policy and program development.

Keywords

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