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Effect of mild COVID-19 on health-related quality of life

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ABSTRACT

Background: Little is known about the effects of a mild SARS-CoV-2 infection on health-related quality of life.
Methods: This prospective observational study of symptomatic adults (18–87 years) who sought outpatient care for an acute respiratory illness, was conducted from 3/30/2020 to 4/30/2021. Participants completed the Short Form Health Survey (SF-12) at enrollment and 6–8 weeks later, to report their physical and mental health function levels as measured by the physical health and mental health composite scores (PHC and MHC, respectively). PHC and MHC scores for COVID-19 cases and non-COVID cases were compared using t-tests. Multivariable regression modeling was used to determine predictors of physical and mental health function at follow-up.
Results: Of 2301 enrollees, 426 COVID-19 cases and 547 non-COVID cases completed both surveys. PHC improved significantly from enrollment to follow-up for both COVID-19 cases (5.4 ± 0.41; $P < 0.001$) and non-COVID cases (3.3 ± 0.32; $P < 0.001$); whereas MHC improved significantly for COVID-19 cases (1.4 ± 0.51; $P < 0.001$) and decreased significantly for non-COVID cases (−0.8 ± 0.37; $P < 0.05$). Adjusting for enrollment PHC, the most important predictors of PHC at follow-up included male sex ($\beta = 1.17$; SE = 0.5; $P = 0.021$), having COVID-19 ($\beta = 1.99$; SE = 0.54; $P < 0.001$); and non-white race ($\beta = -2.01$; SE = 0.70; $P = 0.004$). Adjusting for enrollment MHC, the most important predictors of MHC at follow-up included male sex ($\beta = 1.92$; SE = 0.63; $P = 0.002$) and having COVID-19 ($\beta = 2.42$; SE = 0.67; $P < 0.001$).
Conclusion: Both COVID-19 cases and non-COVID cases reported improved physical health function at 6–8 weeks' convalescence; whereas mental health function improved among COVID-19 cases but declined among non-COVID cases. Both physical and mental health functioning were significantly better among males with COVID-19 than females.

1. Introduction

Infection with the SARS-CoV-2 virus resulting in symptomatic illness has been associated with a wide range of symptoms including respiratory, neurological, gastrointestinal symptoms; various combinations of presenting symptoms; and a range of severity from not requiring medical intervention to hospitalization, ICU admission and the need for extracorporeal membrane oxygenation (ECMO). Symptoms include cough, fever, loss of taste and/or smell, shortness of breath, fatigue, sleep disorders, among others. Many of these symptoms persist during the post-acute phase, involve the same systems (Willi et al., 2021) and can last 6 months or more (Nasserie et al., 2021) with significant physical, mental and cognitive impacts post COVID-19 hospital discharge (Evans et al., 2021). Declines in mental and cognitive functioning at 3 months post COVID-19 have been reported in 36% of patients with mild to critical cases (Van den Borst et al., 2021). While the primary predictors of persistent post-COVID-19 symptoms appear to be severity of disease and hospitalization (Kayaaslan et al., 2021), those with mild disease have also reported these symptoms. Among outpatients, including young adults and those with few high-risk conditions, high prevalence of symptoms persisting 14–21 days post COVID-19 testing have been reported (Tenforde et al., 2020). Other studies have reported significant "brain fog" and fatigue ≥6 weeks post COVID-19 that affect cognition and quality of life among non-hospitalized patients (Graham et al.,

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2021). In fact, a review of studies published through February 2021 reported the frequency of persistent post COVID-19 symptoms to be 10%–35% among patients with mild COVID-19 (van Kessel et al., 2022).

Persistence of symptoms alone does not describe their effect on day-to-day physical or mental functioning, typically assessed using health-related quality of life measures. The variability in severity and/or combination of symptoms, the organ systems affected, and a wide range of personal factors such as age, responsibilities, pre-existing conditions, etc., may influence the impact of persistent symptoms on perceived quality of life. Several studies have measured health-related quality of life using the Short Form Health Survey-36 item (SF-36) or -12 item (SF-12) at 1 month (Chen et al., 2020), ≤2months (Méndez et al., 2021), ≤3 months (Qu et al., 2021; González et al., 2021), and 12 months (Méndez et al., 2022) post COVID-19 hospitalization discharge. Two of these studies reported the frequency of low quality-of-life scores of 44% for physical functioning and 39% for mental functioning at ≤2 months' follow up and of 40% for physical functioning and 33% for mental functioning at twelve months' follow up. Few studies have measured the persistence of symptoms approximately two months after mild COVID-19 or its effect on quality of life.

As part of a COVID-19 vaccine effectiveness study, we assessed physical and mental functioning using the SF-12 at enrollment and 6–8 weeks post clinical/research testing for COVID-19 using reverse transcription polymerase chain reaction (PCR) assays. We compared SF-12 scores and sub-scores at enrollment and follow-up between symptomatic COVID-19 cases and non-COVID cases who were seeking outpatient care. Our objective was to determine the factors related to changes in scores in a prospective, observational study. Little is currently known about the short-term effects of mild disease associated with the novel coronavirus SARS-CoV-2, as measured by functional status. These data may offer insights for public health planning.

2. Methods

This study was conducted with the approval of the University of Pittsburgh Human Research Protection Office on a sample of participants of the U.S. Influenza Vaccine Effectiveness Network (US Flu VE) – Pittsburgh site. Methods for the US Flu VE study have been previously published. Briefly, symptomatic (fever, cough other respiratory symptoms, loss of taste or smell, with duration ≤10 days) patients presenting for COVID-19 testing and/or treatment of symptoms during the period 3/30/2020 through 4/30/2021 were eligible. This time period encompassed both the delta variant and omicron variant dominant periods of the pandemic. Patients who were younger than 18 years old, or who in the previous 14 days, had received COVID-19 vaccine or had enrolled in the study, were not eligible.

SARS-CoV-2 infections were confirmed by PCR tests from nasopharyngeal or nasal swabs at a centralized testing lab using standardized protocols. These singleplex tests for SARS-CoV-2, precluded identification of other infective agents related to symptoms in non-COVID cases.

All participants enrolled in person at emergency departments and urgent care centers, regardless of COVID-19 status, were eligible for inclusion in the survey study. For participants recruited online from among those receiving COVID-19 testing at the testing labs, all patients with positive COVID-19 tests (COVID-19 cases) and a random sample of those with negative COVID-19 tests (non-COVID cases) were invited to participate by email or phone within 2–5 days of testing. Because the parent study was a test-negative design, when COVID-19 cases were high and testing results were known, it was not necessary to enroll a large cohort of non-COVID cases in proportion to COVID-19 cases. The resulting ratio of COVID-19 cases to non-COVID cases varied between 2:3 and 1:20 depending on the total number of tests and relative numbers of cases and non-cases, so as not to over-enroll non-COVID cases for the parent study. Patients who provided informed consent were administered (phone) or self-administered (online) an enrollment survey that included the SF-12 (Appendix 1). Data on demographics, symptoms and other measures of current health and well-being, general health status, and self-report of influenza vaccination, were also collected during patient enrollment interviews. The SF-12 survey specifically asks respondents to think about the past 4 weeks when considering their responses. Approximately 6–8 weeks after enrollment, participants were recontacted by their preferred method and readministered the SF-12.

2.1. Statistical analyses

SF-12 surveys were scored according to the developer's instructions, and individual scale scores, as well as physical and mental health composite scores were recorded. The SF-12 is scored such that a lower score for any component indicates less good health. For example, lower scores indicate that the respondent reported having less energy, reduced emotional role and increased bodily pain. Furthermore, a score <50 for the PHC or MHC is considered to represent low functioning in that domain (Maruish and Turner-Bowker, 2009). The percent of participants who scored in the low range for PHC and MHC at enrollment and follow-up were calculated and compared using risk differences with 95% confidence intervals. In addition, the change in PHC and MHC score group (low <50, high ≥50) from enrollment to follow-up was determined and participants were grouped as "no change," "improved," and "worsened." Significance was tested using Chi-square tests to compare grouping differences between COVID-19 cases and non-COVID cases.

Mean PHC and MHC scores and sub-scores at enrollment and follow-up for COVID-19 cases and non-COVID cases were compared within groups using paired t-tests. Mean enrollment and follow-up scores were compared between groups using two-sample t-tests. To identify the factors independently associated with the change in physical and mental health composite scores, separate multivariable linear regression models were fitted to identify their predictors. All continuous variables used in the regression were subjected to Komolgorov-Smirnov D statistic tests to determine normality. Results are shown in Appendix 2. A type I error or a P value < 0.05 was used as the threshold for statistical significance. Data analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

Among the 2301 enrollees, 2268 met the inclusion criteria (Fig. 1); 1295 (57%) completed only the enrollment survey and one individual had unmatched ID numbers; thus, they were not included in subsequent analyses. Of the remaining 973 (43%) participants, 426 (44%) tested positive for COVID-19 and 547 (56%) tested negative; infections with other viruses were not reported. Those who completed both enrollment and follow-up surveys compared with those who only completed the enrollment survey were significantly older (45.1 vs. 42.0 years; $P <$ 0.001, more often female (71.3% vs. 65.6%; $P = 0.004$), white (88.6% vs. 81.4%; $P < 0.001$), and vaccinated against influenza (70.1% vs. 60.9%; $P < 0.001$), had slightly fewer average number of symptoms at enrollment (4.7 vs. 4.9; $P = 0.028$) and less often reported nausea/vomiting (6.2% vs. 13.5%; $P < 0.001$; Appendix 3 Table 1).

When comparing demographic and health characteristics, several differences between COVID-19 cases and non-COVID cases were observed (Table 1). COVID-19 cases were less frequently female (62.7%) vs. 78.0% of non-COVID cases ($P < 0.001$), less frequently vaccinated against influenza (64.8% of COVID-19 cases vs. 74.2% of non-COVID cases; $P = 0.006$), experienced more symptoms (5.2 ± 1.6 COVID-19 cases vs. 4.4 ± 1.5 non-COVID cases; $P < 0.001$), and COVID-19 cases reported fever, chills, nasal congestion and diarrhea more frequently, and sore throat and shortness of breath less frequently (all $P < 0.043$) than non-COVID cases.

Table 2 shows the percent of COVID-19 cases and non-COVID cases who had low enrollment scores (<50) for the PHC and MHC, and the risk differences with 95% confidence intervals. COVID-19 cases and non-

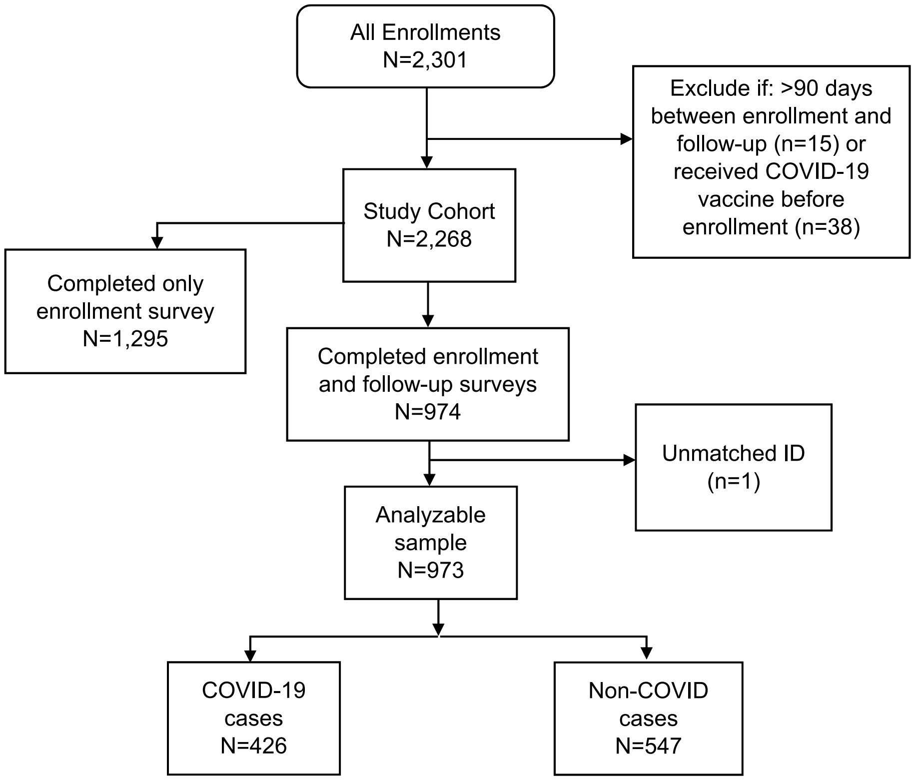

Fig. 1. Flow chart.

Table 1
Demographic and health characteristics of enrollees who completed enrollment and follow-up surveys (N = 973).

Variable	COVID-19 cases n = 426	Non-COVID-19 cases n = 547	*P* value
Age, mean (SD)	46.1 (15.8)	44.4 (13.5)	0.059
Female sex, ref. = male, n (%)	266 (62.7)	423 (78.0)	**<0.001**
Non-white race, ref. = White, n (%)	54 (12.7)	57 (10.4)	0.272
Self-reported influenza vaccination, ref. = not vaccinated, unknown, refused, n (%)	276 (64.8)	406 (74.2)	**0.006**
Symptoms at enrollment			
Fever, n (%)	291 (68.8)	330 (62.5)	**0.043**
Chills, n (%)	284 (66.7)	319 (58.8)	**0.012**
Cough n (%)	368 (86.6)	466 (85.4)	0.582
Sore throat, n (%)	206 (48.7)	365 (67.1)	**<0.001**
Shortness of breath, n (%)	190 (44.8)	305 (56.2)	**<0.001**
Nasal congestion, n (%)	332 (80.8)	313 (59.5)	**<0.001**
Vomiting/Nausea, n (%)	30 (7.0)	30 (5.5)	0.327
Diarrhea, n (%)	193 (45.5)	211 (38.9)	**0.037**
Number of symptoms,[a] mean (SD)	5.2 (1.6)	4.4 (1.5)	**<0.001**

Note: Missing values < 4% for all variables.
[a] Sum of baseline symptoms fever, chills, cough, sore throat, shortness of breath, nasal congestion, vomiting/nausea, diarrhea, loss of smell or taste, and other symptoms (increased fatigue n = 1).

COVID cases did not differ at enrollment for PHC, however at follow-up, COVID-19 cases were 6.4% (95% CI = 12.3, 0.6%) less likely to have a low score (<50) than non-COVID cases ($P = 0.032$). At both enrollment and follow-up, low MHC scores were significantly less frequent (−11%; 95% CI = −17.3%, −4.9%; $P < 0.001$) among COVID-19 cases than non-COVID cases (−18.3%; 95% CI = −24.5, −12.2; $P < 0.001$).

Fig. 2 shows the percentages of those whose scores did not change from <50 or ≥50 at enrollment to follow-up, improved or worsened over that time. Although not statistically significant ($P = 0.081$), COVID-19 cases slightly more frequently improved their PHC score (29%) than

Table 2
Frequency of low function physical and mental health composite scores.

SF-12 Physical Health Composite score	Percent with score <50 = low function			
	COVID-19 cases, %	Non-COVID cases, %	Risk difference (95% CI)	*P* value
Enrollment	52.8	51.7	0.011 (−0.053, 0.074)	0.738
Follow-up	27.9	34.4	−0.064 (−0.123, −0.006)	**0.032**
SF-12 Mental Health Composite score				
Enrollment	53.8	64.9	−0.111 (−0.173, −0.049)	**<0.001**
Follow-up	47.7	66.0	−0.183 (−0.245, −0.122)	**<0.001**

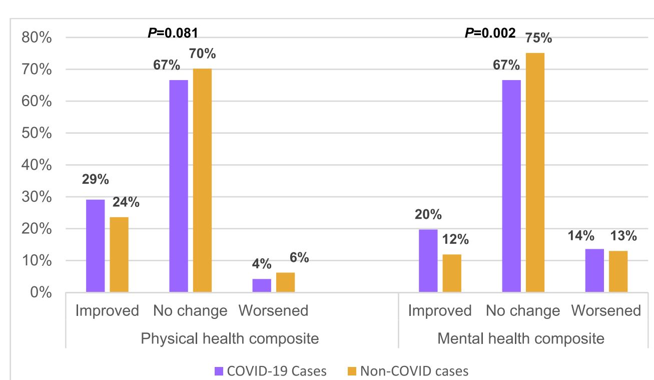

Fig. 2. Change in functional status group (<50 low vs. ≥50 high) from enrollment to follow-up for COVID-19 cases and non-COVID cases.

non-COVID cases (24%), while the latter more frequently had no change in their score group (70% for non-COVID cases vs. 67% for non-COVID cases). For MHC scores, significant improvements were observed for COVID-19 cases compared with non-COVID cases. For example, 20% of COVID-19 cases improved compared with 12% of non-COVID cases and 45% of COVID-19 cases and 55% of non-COVID cases worsened ($P = 0.002$) Scatter plots of the individual scores at both time points are shown in Appendix 3, Fig. 1a and b.

Mean SF-12 scores and subscores comparing COVID-19 cases and non-COVID cases were examined in two ways (Table 3). First, paired t-tests were used to compare enrollment and follow-up scores within groups. All COVID-19 cases' SF-12 scores, including the PHC and MHC, increased significantly from enrollment to follow-up (range of differences = 4.5–20.2; $P < 0.001$), with the exception of the general health subscore (difference = 1.3; NS). Among non-COVID cases, six of ten scores, including the PHC, increased significantly (difference range = 3.3–11.5; $P < 0.001$). Notable exceptions were the general health, emotional role, and mental health subscores that did not change (difference range = −0.9-0.2) and the MHC that decreased slightly (−0.8), but significantly ($P < 0.001$). The mean differences from enrollment to follow-up were generally larger among COVID-19 cases than non-COVID cases.

Secondly, mean enrollment scores and mean follow-up scores were compared between groups using two-sample t-tests (Table 3). At enrollment, COVID-19 cases scored significantly ($P \leq 0.007$) higher than non-COVID cases on four domains, including having less bodily pain, better general health, better mental health subscore and better MHC. Whereas, at enrollment non-COVID cases scored significantly ($P \leq 0.010$) higher than COVID-19 cases on two domains, better physical functioning, and better social functioning. Of note, there was a significantly larger improvement in the social functioning subscore among COVID-19 cases than among non-COVID cases that may be explained by the social distancing/quarantine recommendations for those with COVID-19 until recovery. There were no significant differences between COVID-19 cases and non-COVID cases at enrollment for four domains, physical role, energy level, emotional role, and PHC. At 6–8 weeks' follow-up, COVID-19 cases scored significantly better than non-COVID cases on all domains ($P \leq 0.042$).

Linear regression analyses were conducted in two ways – stratified by COVID status and unstratified but including COVID status as a predictor variable. It should be noted that the enrollment and follow-up PHC were significantly related, as were the enrollment and follow-up MHC, therefore, only one was selected to be included in the regression analyses, such that for each follow-up value (PHC or MHC) the corresponding enrollment value was used, but only the follow-up value for the other scale was included. The predictors of follow-up PHC and MHC varied when the regressions were stratified by COVID-case status, as shown in Appendix 3 Tables 2 and 3 Thus, the final regression models were conducted using COVID case status as a predictor variable. The predictors of higher overall physical functioning at follow-up as measured by the PHC (Table 4) include enrollment PHC (β = 0.57; SE = 0.03; $P < 0.001$), male sex (β = 1.17; SE = 0.5; $P = 0.021$), and having COVID-19 (β = 1.99; SE = 0.54; $P < 0.001$); whereas, the predictors of lower PHC were higher follow-up MHC (β = −0.09; SE = 0.02; $P < 0.001$), older age (β = −0.11; SE = 0.02; $P < 0.001$), and non-white race (β = −2.01; SE = 0.70; $P = 0.004$).

The predictors of higher mental health at follow-up as measured by

Table 4
Predictors of physical health and mental health composite scores at follow-up by linear regression modeling.

Predictor variable	*Follow-up Physical Health*		*Follow-up Mental Health*	
	Estimate (SE)	*P* value	Estimate (SE)	*P* value
Intercept	32.01 (2.18)	**0.001**	20.83 (2.94)	**<0.001**
Enrollment physical health composite score	0.57 (0.03)	**<0.001**	–	–
Follow-up mental health composite score	−0.09 (0.02)	**<0.001**	–	–
Enrollment mental health composite score	–	–	0.56 (0.03)	**<0.001**
Follow-up physical health composite score	–	–	−0.09 (0.03)	**0.007**
Days between enrollment and follow-up surveys	0.03 (0.02)	0.192	0.07 (0.03)	**0.008**
Age, years	−0.11 (0.02)	**<0.001**	0.07 (0.02)	**<0.001**
Male sex, ref. = Female	1.17 (0.50)	**0.021**	1.92 (0.63)	**0.002**
Non-white race, ref. = White	−2.01 (0.70)	**0.004**	−1.01 (0.88)	0.253
Self-reported influenza vaccination	0.75 (0.49)	0.123	−0.36 (0.61)	0.560
Number of symptoms at enrollment	−0.18 (0.15)	0.246	−0.67 (0.18)	**<0.001**
COVID-19 case, ref. = non-COVID case	1.99 (0.54)	**<0.001**	2.42 (0.67)	**<0.001**
	R-square	**Significance**	**R-square**	***P* value**
Overall model	**0.45**	**<0.001**	**0.39**	**<0.001**

Table 3
SF-12 subscores and composite scores at enrollment and follow-up by COVID-19 status.

SF-12 subscore	COVID-19 cases (n = 426)			Non-COVID cases (n = 547)			Comparison of mean scores between COVID-19 cases and non-COVID cases at	
	Enrollment Mean (SD) (a)	Follow-up Mean (SD) (b)	Difference Mean (SE) (b-a)	Enrollment Mean (SD) (c)	Follow-up Mean (SD) (d)	Difference Mean (SE) (d-c)	Enrollment *P* value[d] (a-c)	Follow-up *P* value[d] (b-d)
Physical functioning	65.2 (37.3)	84.5 (25.8)	19.2 (1.70)[c]	71.4 (32.6)	80.2 (28.0)	8.8 (1.29)[c]	**0.007**	**0.014**
Role, physical	61.4 (31.1)	81.6 (24.9)	20.2 (1.51)[c]	64.3 (28.0)	75.8 (27.5)	11.5 (1.12)[c]	0.128	**<0.001**
Bodily pain	75.7 (27.0)	83.2 (25.6)	7.6 (1.34)[c]	70.8 (28.1)	75.9 (28.4)	5.1 (1.07)[c]	**0.007**	**<0.001**
General health	73.4 (22.6)	74.8 (20.9)	1.3 (0.92)	68.2 (23.1)	68.4 (24.2)	0.2 (0.78)	**<0.001**	**<0.001**
Energy/fatigue	45.2 (26.1)	52.1 (25.5)	6.9 (1.42)[c]	43.1 (25.0)	45.6 (25.4)	2.5 (1.06)[a]	0.200	**<0.001**
Social functioning	59.2 (35.3)	78.5 (28.5)	19.2 (1.85)[c]	64.9 (31.2)	69.6 (30.3)	4.7 (1.41)[c]	**0.010**	**<0.001**
Role, emotional	77.2 (27.4)	81.7 (23.9)	4.5 (1.40)[c]	75.8 (24.8)	74.9 (24.6)	−0.9 (1.02)	0.417	**<0.001**
Mental health	66.8 (21.8)	69.4 (21.8)	2.6 (0.98)[b]	59.8 (21.2)	59.3 (22.4)	−0.5 (0.78)	**<0.001**	**<0.001**
Physical health composite	47.6 (9.5)	53.0 (8.4)	5.4 (0.41)[c]	48.5 (9.1)	51.8 (9.7)	3.3 (0.32)[c]	0.137	**0.042**
Mental health composite	47 (10.6)	48.4 (10.6)	1.4 (0.51)[b]	45.2 (9.8)	44.4 (10.7)	−0.8 (0.37)[a]	**0.006**	**<0.001**

SD: Standard Deviation; SE: Standard Error.
[a] $P < 0.05$; mean difference (Follow-up – Enrollment), using paired *t*-test for significance.
[b] $P < 0.01$; mean difference (Follow-up – Enrollment), using paired *t*-test for significance.
[c] $P < 0.001$; mean difference (Follow-up – Enrollment), using paired *t*-test for significance.
[d] Statistical significance using the two-sample *t*-test - comparison of means between cases and non-cases at enrollment and follow-up.

the MHC include enrollment MHC (β = 0.56; SE = 0.03; $P < 0.001$), days between surveys (β = 0.07; SE = 0.03; $P = 0.008$), older age (β = 0.07; SE = 0.02; $P < 0.001$), male sex (β = 1.92; SE = 0.63; $P = 0.002$) and having COVID-19 (β = 2.42; SE = 0.67; $P < 0.001$); whereas predictors of lower follow-up MHC were follow-up PHC (β = −0.09; SE = 0.03; $P = 0.007$), and the number of symptoms present at enrollment (β = −0.67; SE = 0.18; $P < 0.001$). Male sex, white race and having COVID-19, as opposed to another respiratory infection, had the largest positive impact on follow-up PHC, while male sex, and having COVID-19 had the largest positive impact on follow-up MHC.

4. Discussion

This study assessed health-related quality of life measured by physical health function and mental health function before and around the time of testing for COVID-19 among those with respiratory infection symptoms. The assessment was repeated after 6–8 weeks of convalescence. The rate of low physical health functioning among COVID-19 cases (28%) in this study was considerably lower than a previous report of 44% among hospitalized COVID-19 cases at 2 months post discharge (Méndez et al., 2021) but higher than another report of 16% among hospitalized COVID-19 cases at 3 months post discharge (Qu et al., 2021). Forty-eight percent of mild COVID-19 cases in our study reported low mental health functioning at 6–8 weeks post testing compared with other reports of 39% at 2 months post hospital discharge (Méndez et al., 2021) and 33% at 3 months post hospital discharge (Qu et al., 2021). These differences may be due to a shorter time between diagnosis and follow-up testing among outpatients, compared with inpatients whose time of follow-up testing did not account for the time spent in the hospital following disease onset/diagnosis.

Improvements in overall physical health function during convalescence were most significantly related to male sex, white race, and having a COVID-19 positive PCR test. In a study among Chinese COVID-19 inpatients three months post discharge, higher PHC scores were related to male sex, younger age and not having physical symptoms at follow-up (Qu et al., 2021). Although males are more likely to have severe COVID-19 than females (Gomez et al., 2021), based on these two studies, females seem to recover more slowly, regardless of whether they experienced severe or mild disease. Racial disparities in COVID-19 incidence and mortality are widely acknowledged, but are not attributable to a higher prevalence of high-risk conditions (Mackey et al., 2021). However, it is possible that lower PHC during COVID-19 convalescence among non-whites is related to higher frequency of high-risk conditions, as a similar relationship between presence of high risk conditions and self-reported fair/poor general health has been previously reported (Gandhi et al., 2020).

Improvements in mental health function during convalescence were most significantly related to being male and having a COVID-19 positive test. In contrast, a study of hospitalized COVID-19 patients found only presence of symptoms at follow-up to be significantly related to low MHC at 3 months post discharge (Qu et al., 2021), while in another study of Chinese hospitalized COVID-19 patients, female sex was related to low MHC (Chen et al., 2020). Thus, post COVID MHC of men seems to rebound better than women's whether their disease was severe or mild. These findings are summarized in Fig. 3.

Only one other study was identified that compared health-related quality of life in COVID-19 cases and non-COVID cases. In that observational study, outpatients attending a "long COVID" neurological clinic >6 weeks post infection were sequentially enrolled, neurological symptoms and health-related quality of life were measured and compared with non-COVID cases (Graham et al., 2021). Quality-of-life scores did not differ significantly between the 22 COVID cases and 12 non-COVID cases who took the patient Reported Outcome Measurement Information System (PROMIS) assessment, but were significantly lower in both groups than demographically matched US normative population for cognition and fatigue (Graham et al., 2021).

In our study of symptomatic outpatients seeking testing for COVID-19, improvements in average physical and mental function were observed among both COVID-19 cases and non-COVID cases over 6–8 weeks of convalescence. While there was no difference in physical function at enrollment, physical function at follow-up improved more among COVID-19 cases than among non-COVID cases. Furthermore,

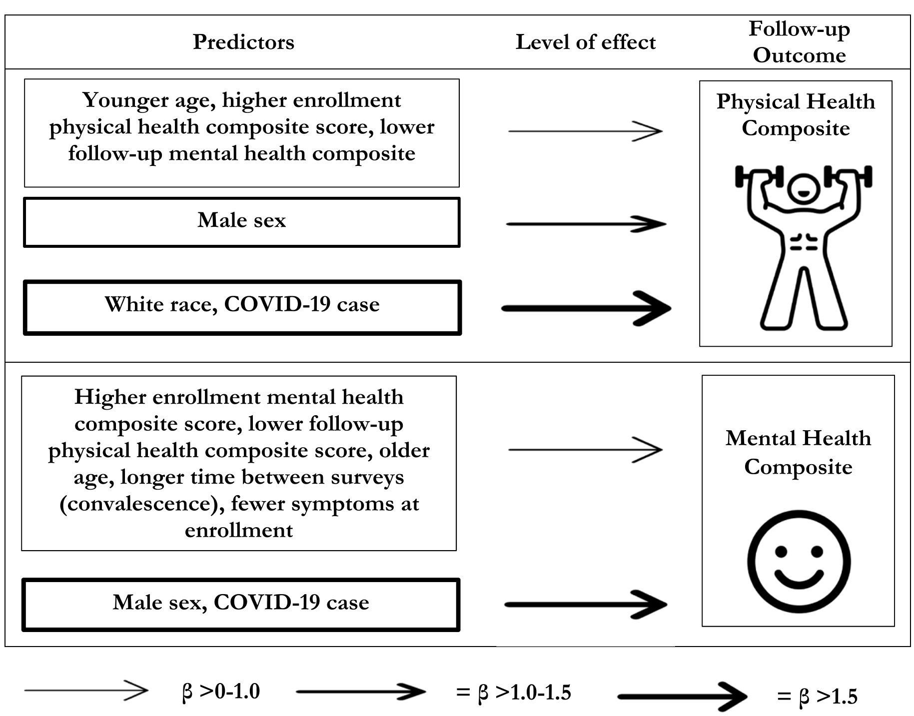

Fig. 3. Predictors of higher SF-12 composite score (better functional status) following acute respiratory illness.

COVID-19 cases had higher mental function at enrollment than non-COVID cases, yet mental function improved significantly among COVID-19 cases, while it decreased significantly among non-COVID cases. When adjusting for demographic factors and baseline quality of life scores, COVID-19 cases fared better at follow-up than non-COVID cases with acute respiratory illness on both physical and mental measures of quality of life. These results are consistent with declines in mental health status that have been reported among high functioning adults hospitalized for acute respiratory illness including influenza and RSV, approximately five weeks after enrollment (Nowalk et al., 2020). One might speculate that having experienced and recovered from a mild case of COVID-19 offered those participants a sense of freedom from pandemic-mandated social distancing without fear of contracting or spreading disease, thus leading to better mental health quality of life.

Considerable attention is being given to persistent symptoms of COVID-19, with a meta-analysis estimating that globally, 43% of all COVID-19 patients and 34% of non-hospitalized COVID-19 patients experience persistent symptoms (Chen et al., 2022). The most frequent persistent symptoms were identified as fatigue, memory problems and shortness of breath and were associated with female sex, older age and presence of high-risk conditions such as asthma. In our study, two risk factors for lower physical function were consistent with those of persistent symptoms – female sex and older age. However, among those who experienced mild respiratory illnesses not requiring hospitalization, non-COVID-19 cases reported worse physical and mental function after 6–8 weeks of convalescence than those with COVID-19. In addition to knowing that a significant number of COVID-19 patients are experiencing persistent COVID-19 symptoms, medical professionals who care for patients with ARI should be aware that some non-COVID cases may take an extended period of time to return to their baseline mental health functional status.

4.1. Strengths and limitations

The strengths of this study include its large sample size; direct comparisons between COVID and non-COVID respiratory illness patients; inclusion of only those seeking outpatient care, similar to the majority of all COVID cases; and a study period that spanned many waves of the pandemic and several virus variants. Most of the previous research included much smaller samples of mostly moderate to severe, hospitalized patients, many of whom had been in the ICU, some who were seeking care specifically for persistent symptoms, and most studies were conducted in the first six months of the pandemic. One limitation is that we did not measure symptoms at follow-up and cannot therefore evaluate their effect on physical or mental functioning, nor did we measure health related factors such as body weight. Secondly, we were not able to identify the infective agent related to symptoms in non-COVID cases because tests were primarily singleplex for SARS-CoV-2. Thirdly, this study was conducted relatively soon after diagnosis, and differences between COVID-19 cases and non-COVID cases may arise after a longer convalescent period, when persistent symptoms of COVID may become more apparent. These findings do not address potential changes in physical and mental status among patients with neurodegenerative disorders such as Parkinson's or Alzheimer's Disease (Rai et al., 2022). We did not evaluate physical activity levels before, during or after illness. Pandemic mitigation measures likely restricted physical activity and social interaction and may have diminished pre-illness PHC and MHC levels overall. Finally, there were some significant differences between those who completed the follow-up survey and those who did not including reporting fewer symptoms at enrollment. These demographic and illness differences may limit generalizability to all patients with mild acute respiratory illness.

5. Conclusions

This study is the first to compare physical and mental functional status of symptomatic COVID-19 outpatient cases with non-COVID cases. At six to eight weeks of convalescence, COVID-19 cases reported better health-related quality of life, as measured by physical and mental health functioning, than non-COVID cases. Both physical and mental health functioning were significantly better among males with COVID-19 than females. Further research is needed to determine physical and mental functional status following severe cases of COVID-19 and which infectious agents or patient characteristics may be associated with the lower mental function following non-COVID infections.

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Declaration of competing interest

Drs. Nowalk and Balasubramani have grant funding from Merck & Co., Inc. for an unrelated project. Drs. Zimmerman, Nowalk and Balasubramani have grant funding from Sanofi on an unrelated project. Mr. Clarke, Ms. Clarke, Mr. Susick, Ms. Dauer, Ms. Sax, Dr. Taylor, Dr. Moehling Geffel have no conflicts to report.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbih.2023.100596.

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