Self-Reported Everyday Functioning After COVID-19 Infection

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Abstract

IMPORTANCE Changes in everyday functioning are crucial to assessing the long-term impact of COVID-19 infection.

OBJECTIVE To examine the impact of COVID-19 infection on everyday functioning 18 months after infection among veterans with and without histories of COVID-19 infection.

DESIGN, SETTING, AND PARTICIPANTS This cohort study used data from the US Veterans Affairs (VA) and included 186 veterans who had COVID-19 between October 2020 and April 2021 (ie, COVID-19 cohort) and 186 matched comparators who did not have documented COVID-19 infections (ie, control cohort). This match balanced the risk of COVID-19 based on 39 variables measured in the 24 months before infection or match, using principles of target trial emulation. Data were analyzed from December 2022 to December 2023.

EXPOSURE First documented COVID-19.

MAIN OUTCOME AND MEASURES The differences in self-reported everyday functioning 18 months after COVID-19 infection were estimated and compared with their matched comparators. Within–matched pair logistic and linear regressions assessed differences in outcomes and were weighted to account for sampling and nonresponse.

RESULTS Among the 186 matched pairs of participants, their weighted mean age was 60.4 (95% CI, 57.5 to 63.2) years among veterans in the COVID-19 cohort (weighted sample, 91 459 of 101 133 [90.4%] male; 30 611 [30.3%] Black or African American veterans; 65 196 [64.4%] White veterans) and 61.1 (95% CI, 57.8 to 64.4) years among their comparators in the control cohort (91 459 [90.4%] male; 24 576 [24.3%] Black or African American veterans; 70 157 [69.4%] White veterans). A high proportion of veterans in the COVID-19 cohort (weighted percentage, 44.9% [95% CI, 34.2% to 56.2%]) reported that they could do less than what they felt they could do at the beginning of 2020 compared with the control cohort (weighted percentage, 35.3%; [95% CI, 25.6% to 46.4%]; within–matched pair adjusted odds ratio [OR], 1.52 [95% CI, 0.79 to 2.91]). There was no association of documented COVID-19 infection with fatigue, substantial pain, limitations in either activities of daily living and instrumental activities of daily living, severely curtailed life-space mobility, employment, or mean health-related quality of life on a utility scale.

CONCLUSIONS AND RELEVANCE In this cohort study of veterans with and without documented COVID-19, many reported a substantial loss of everyday functioning during the pandemic regardless of whether or not they had a documented infection with COVID-19. Future work with larger samples is needed to validate the estimated associations.


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Introduction

The World Health Organization's clinical case definition of post–COVID-19 condition specifies that an impact on everyday functioning is essential to the diagnosis. However, many studies describing the high burden of symptoms and accumulation of new diagnoses following COVID-19 infection have failed to capture function. Data from general population surveys comparing respondents who had previously had COVID-19 with respondents who had not had COVID-19 may conflate the impacts of COVID-19 with factors that increased risk COVID-19 infection. Recent work extrapolating disability-adjusted life-years from new diagnoses has suggested potentially high burdens of ongoing disability attributable to COVID-19 infection, but did not directly measure disability.

We conceptualized everyday functioning at several levels, consistent with the international classification of functioning conceptual model: (1) fatigue and pain; (2) limitations in activities of daily living; (3) limitations in social functioning (eg, life-space mobility and employment); (4) self-rated overall functioning; and (5) health-related quality of life. We measured these outcomes using a survey administered to both individuals who had previously had COVID-19 and their matched comparators. We test for differences in both the mean population and among those with the most severe symptoms.

We used target trial emulation methods to maximize rigor and compared the everyday functioning of veterans with electronic health record evidence of COVID-19 with veterans who had an equivalent risk of infection in the same month but without evidence of infection up to that point and the time of the survey (Table 1). This distinguished the impacts of the COVID-19 pandemic that may impact everyday function from specific adverse effects of documented viral infection.

Methods

This cohort study was approved by the institutional review boards (IRBs) of Ann Arbor VA and Durham VA Medical Center and uses secondary data analyses reviewed and approved by the IRBs of Durham VA Medical Center, VA Palo Alto Health Care System, VA Portland Health Care System, and VA Puget Sound Health Care System. Verbal informed consent was collected.

We report the results of a prospective telephone- and mail-based survey collection from veterans with a history of COVID-19 and matched comparators 18 months after COVID-19 infection during October 2020 to April 2021. We focused on these patients because their onset of COVID-19 infection was late enough in the epidemic that health systems had time to adapt after the initial shock, yet health care facility-based testing was ubiquitous and home-testing was less common than now, reducing measurement error in the classification of our primary exposure.

Study Population

As described previously, we assembled 14 separate monthly cohorts from March 2020 to April 2021 of individuals enrolled in the VA who were assigned to a VA primary care team or who had more than 1 visit to a VA primary care clinic in 2 years. Veterans included in the COVID-19 cohort were those who were first documented to be positive for COVID-19 in a given month identified via the VA COVID-19 Shared Data Resource and Medicare data. Uninfected potential comparators were those who did not have documentation of COVID-19 prior to or during the same month and met the same inclusion criteria. Comparators without a documented history of COVID-19 to date are henceforth referred to as the uninfected cohort, which is defined as no known infection. We excluded veterans with a history of COVID-19 who had COVID-19-related diagnostic codes in fee-for-service Medicare claims 15 or more days before their VA test. We convened multidisciplinary experts to select matching and control variables via a consensus-directed acyclic graph for the relationship between COVID-19 and several patient-centered outcomes. Patients with COVID-19 were exact matched with replacement to controls based on index month, sex, immunosuppressive medication use (binary), state of residence, and COVID-19 vaccination status (in January to April 2021 cohorts). Then, 39 covariates...
were included in month-specific propensity score models (eTable 1 in Supplement 1). Race and ethnicity were categorized as present in source VA data and included a mix of self-report and categorization by others. Race and ethnicity were included because of the racialization of COVID-19 exposures and access to care.

Within this broader cohort (eFigure 1 in Supplement 1), we took a stratified random sample of 100 veterans who had tested positive for COVID-19 for each month of October, November, and December 2020, and February, March, and April 2021 (eFigure 2 in Supplement 1), which was further stratified by 4 US Census regions and hospitalization. We identified up to 5 comparators for each sampled patient with COVID-19. Comparators were ranked based on how closely they were matched to a patient with COVID-19. We restricted eligible comparators to those who did not have evidence in VA or Medicare data of COVID-19 infection by April 2022, were not known to have died in VA data systems, and had an address in the US.

Table 1. Target Trial Emulation Comparison Table

<table>
<thead>
<tr>
<th>Element</th>
<th>Unethical target trial</th>
<th>Emulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goal</td>
<td>To test the effect of individual infection with SARS-CoV-2 on everyday functioning 18 months after infection</td>
<td>Same as target trial</td>
</tr>
<tr>
<td>Setting</td>
<td>VA nationwide system</td>
<td>Same as target trial</td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>Veterans aged 18 years and older in care in the VHA with an assigned primary care team for at least 2 years on randomization date, or who had at least 1 VHA primary care clinic visit in that period</td>
<td>Same as target trial</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>Previous documented COVID-19 infection; address outside of Washington DC or 50 states</td>
<td>Previous documented SARS-CoV-2 infection in National Surveillance tool or Medicare-documented COVID-19 diagnosis or related diagnostic codes (ICD-10-CM: B97.29, U07.1, U09.9, J12.82, 179 286.16) listed in fee-for-service Medicare claims; address outside of DC or 50 States; missing or invalid key matching variables: age, height, weight, zip code; no suitable matches between infected patients and comparator</td>
</tr>
<tr>
<td>Enrollment period</td>
<td>October 2020 to April 2021</td>
<td>Same as target trial</td>
</tr>
<tr>
<td>Treatment strategies</td>
<td>Inoculum of SARS-CoV-2 sufficient to guarantee COVID-19 infection</td>
<td>SARS-CoV-2 infection with a confirmatory PCR test for SARS-CoV-2 in VA National Surveillance Tool</td>
</tr>
<tr>
<td>Comparator</td>
<td>Double-blinded inoculum of placebo</td>
<td>Best matched veteran with neither documented SARS-CoV-2 infection in National Surveillance tool nor Medicare-documented COVID-19 diagnosis through the month at which matched as a comparator</td>
</tr>
<tr>
<td>Approach to balancing confounders</td>
<td>1:1 Randomization, stratified by month and center</td>
<td>Up to 5:1 (comparator:infected) Matching on 5 exact criteria (including month and home state) and 39 propensity score criteria from VA data</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>Self-reported everyday functioning</td>
<td>Same as target trial</td>
</tr>
<tr>
<td>Follow-up period</td>
<td>18 Months from inoculation</td>
<td>18 Months from the earliest date of a documented positive test for those with COVID-19 infection; comparators began surveillance for outcomes from the same date (index date, the emulated equivalent of randomization and inoculation date) as that of their individually matched infected patient and were followed for 18 months</td>
</tr>
<tr>
<td>Causal contrast</td>
<td>Primary analysis: comparison of outcomes between individuals with a history of COVID-19 infection and those without contemporaneous infection</td>
<td>Primary analysis: same as target trial</td>
</tr>
<tr>
<td>Statistical analysis</td>
<td>Logistic regression for dichotomous outcomes and linear regression for continuous ones, coupled with applying inverse probability of censoring weights, compositing of death and functional outcomes, or survivor averaged effects to account for differential survival and loss to follow-up</td>
<td>Within-pair differences in outcomes, using logistic or linear regression as appropriate to adjust for any unbalanced matching variables. Surveying by matched pair and enrolling a survivor in both groups eliminates differential survivorship by group; survey and nonresponse weights reweight the estimates back to the overall population of interest</td>
</tr>
</tbody>
</table>

Abbreviations: ICD-10-CM, International Statistical Classification of Diseases, Tenth Revision, Clinical Modification; PCR, polymerase chain reaction; VA, US Department of Veterans Affairs; VHA, Veterans Health Administration.
Sample Size Rationale

This study was designed from 2020 to 2021 to evaluate for large mean associations. During that period, there were simultaneous discussions regarding COVID-19. For example, it was suggested that (1) COVID-19 was best understood exclusively through inpatient short-term outcomes (as in early drug trials); (2) COVID-19 might be a mass disabling event; and (3) the long-term disabling impacts of COVID-19 were independent of initial severity of illness. Thus, we designed our survey to evaluate effect sizes for activities of daily living, such as those seen in hospitalized patients with sepsis and pneumonia. For example, patients hospitalized with sepsis with no prior limitations in activities of daily living or instrumental activities of daily living reported a mean of 1.6 new limitations a year later. Similarly, hospitalizations for pneumonia were associated with 1.0 new health-related limitations in activities and instrumental activities of daily living among those with no or mild-to-moderate prehospitalization limitations.

In designing the present study, we prioritized a carefully matched comparator group and population-representativeness. This required building the national sampling frame and recruiting within a complex matching structure. National representativeness as a goal meant that a veteran with COVID-19 infection needed to be recruited quickly once sampled in order to also identify and recruit a comparator without infection to retain a matched pair, which required allocating substantial resources to recruit any sampled individual. Indeed, our internal validity hinged on a high response rate for matched comparators, which we achieved.

Furthermore, the time course of evolution of late impacts of COVID-19 was unknown. As such, we designed for repeat interviews every 6 months to follow respondents, which meant that our design favored depth over breadth. Therefore, we made a pragmatic decision based on a fixed budget and at-the-time plausible large effect sizes, to attempt to survey 100 COVID-19 survivors and their matched comparators per month for each of 6 months.

There were 231,160 veterans who had a positive SARS-CoV-2 test between March 2020 and April 2021 known to VA, and 9,291,822 who did not. As previously described, 208,536 matched groups were created, and standardized mean differences (SMDs) for 39 variables between the matched groups of individuals who had previously had COVID-19 and their comparators were all less than 0.1. From the matched groups in October through December 2020 and February through April 2021, 600 potential patients with previous COVID-19 infection were identified in a stratified random sample, along with up to 5 best matched comparators (eFigure 2 in Supplement 1). Of these, 548 veterans with a history of COVID-19 infection were known to be alive and living in the US at the time of survey, and 235 (43%) consented to participate and completed surveys. Of those, 194 (83%) well-matched comparators consented and completed a survey, and 8 (4.1%) of these comparators were noted to have COVID-19 after sampling and before survey completion, resulting in 186 matched pairs.

Survey Operations and Instruments

Approximately 18 months after the initial documented infection for COVID-19 (in monthly cohorts, April to December 2022, or to matched comparators), we sent a letter describing the survey and giving the option to opt out. Those who did not opt out were called and offered the opportunity to provide verbal informed consent for participation. Those who consented were surveyed via telephone, with an option to complete by mail or by a proxy of their choosing. Surveys could be divided throughout multiple sessions for respondents. Given the high English fluency rates among veterans of the US military, surveys were only conducted in English. A $10 token of appreciation was provided regardless of whether they completed all or part of the survey. Telephone surveys were administered by trained interviewers entering data directly into a VA Research Electronic Data Capture database with built-in validity, consistency, and completeness checks.

Once a veteran with a history of COVID-19 provided informed consent for a survey, the team attempted to recruit one of his or her 5 best matched comparators of those who were still alive and not documented to have COVID-19 per propensity score. While interviewers were aware of which
cohort respondents were drawn from, they were carefully trained to administer the surveys identically and to make no reference to whether the respondent themselves had COVID-19. When asked to compare with a previous period, the respondents were to compare with the beginning of 2020, which was a time anchor relevant to all individuals.

We assembled the survey from well-validated instruments. Fatigue was assessed using the PROMIS Short Form version 1.0 Fatigue 7a and its standardized scoring,\(^2\) with a general population mean (SD) of 50 (10) points, with higher scores indicating more fatigue. Pain was assessed using the pain single item from the EuroQol 5-Dimension 5-Level (EQ-5D-5L). Activities of daily living and instrumental activities of daily living, were assessed using items from the Health and Retirement Study and other studies of individuals with a history of COVID-19, and tabulated as a count.\(^1\) Life-space mobility was assessed as in the UAB Study of Aging, with a composite score that runs from 0 to 120 with higher numbers indicating a larger, more independent life-space. EQ-5D-5L health-related quality of life scores were derived using US norms.\(^2\)

**Statistical Analyses**

Covariate balance was assessed using standardized mean differences (SMDs), where differences of less than 0.1 indicate excellent covariate balance.\(^1\) Associations between COVID-19 infection and survey outcomes were examined using within-pair conditional logistic regression for dichotomous outcomes and linear regression on the within-pair differences (\(y_{COVID-19} - y_{comparator}\)) for continuous outcomes. All regression analyses adjusted for race and ethnicity because they were not well balanced in surveyed populations. Analyses were conducted in Stata version 17 (StataCorp) and unless otherwise noted include for both sampling weights and nonresponse weights using Stata's probability weight adjustment procedure; R version 4.2.2 (R Project for Statistical Computing) was used to obtain the weighted SMDs for categorical variables with more than 2 categories. Stata code and log files can be found in Supplement 1 and Github.\(^4\)

Weights incorporating both complex sampling and survey-level nonresponse were created, and the weighted results are reported here. Logistic regression was used to estimate the probability of nonresponse among eligible COVID-19 participants invited to participate. Age, sex, race, and Gagne comorbidity score were forced into the equation and other variables selected using a lasso procedure from among the variables in the matching for the month of infection. Final probability weights were the product of sampling weights and nonresponse weights.

We present analyses among individuals with a history of COVID-19 infection who were alive 18 months after onset and did not adjust for death in these estimates, as mortality analyses have been published separately.\(^4\) To assess robustness, we also reanalyzed the outcomes without applying weights and, separately analyzed the outcomes without removing any individuals with a history of COVID-19 prior to survey. We also conducted hypothesis-generating post hoc analyses\(^6,7\) separately by whether or not the COVID-19 cohort was hospitalized within 7 days of their first positive test. Statistical significance was defined as \(P < .05\). Data were analyzed from December 2022 to December 2023.

**Results**

Weighted characteristics of the 186 pairs included mean age of 60.4 (95% CI, 57.5-63.2) years among respondents with previous COVID-19-infection (91 459 of 101 133 in the weighted sample [90.4%] male; 30 611 [30.3%] Black or African American veterans; 65 196 [64.4%] White veterans; 40 721 [40.3%] had never smoked; 11 194 [11.1%] had been prescribed immunosuppressant medicines in the previous 24 months) and 61.1 (95% CI, 57.8-64.4) years among their comparators (91 459 [90.4%] male; 24 576 [24.3%] Black or African American veterans; 70 157 [69.4%] White veterans; 37 956 [37.5%] had never smoked; 11 194 [11.1%] had been prescribed immunosuppressant medicines by VA in previous 24 months) (Table 2).
Fatigue and Pain
Fatigue scores reported 18 months after COVID-19 infection had a mean of 54.6 (95% CI, 52.6-56.7), where higher is worse. Rates of fatigue were similar in the comparator group, with a mean fatigue score of 51.7 (95% CI, 49.5 to 53.9). The within–matched pair adjusted regression showed no statistically significant association between COVID-19 infection and fatigue score (Table 3). Of veterans in the COVID-19 cohort, 51.1% (95% CI, 40.1% to 62.0%) reported moderate, severe, or extreme pain at 18 months vs 65.7% (95% CI, 54.7% to 75.3%) of their comparators. The within–matched pair conditional logistic regression showed no statistically significant difference in odds of reporting substantial pain by group (odds ratio [OR], 0.50 [95% CI, 0.24 to 1.05]) (Table 4).

Activities of Daily Living
The distribution of health-related limitations in activities of daily living and instrumental activities of daily living at 18 months after COVID-19 infection is the Figure. Veterans in the COVID-19 cohort reported a mean of 3.4 (95% CI, 2.6 to 4.2) limitations, and 37.3% (95% CI, 27.5% to 48.3%) reported 4 or more activities of daily living or instrumental activities of daily living limitations. Matched
comparators reported a mean of 3.0 (95% CI, 2.4 to 3.6) limitations, and 30.2% (95% CI, 21.3% to 40.9%) reported 4 or more limitations. There was no difference in the within-pair analysis of the mean (SMD, −0.04 [95% CI, −1.24 to 1.15] fewer limitations in COVID-19 cohort), nor in the odds of reporting 4 or more ADL or IADL limitations (OR, 1.46 [95% CI, 0.75 to 2.84]).

Life-Space Mobility and Employment
Life-space mobility at 18 months after infection was similar for the COVID-19 cohort and their matched comparators (mean [SD], 70.4 [33.1] vs 66.6 [28.3], where higher is better; within–matched pair adjusted regression nonsignificant difference of 8.89 points better life-space mobility after COVID-19, 95% CI, −3.90 to 21.69). There was also a similar concentration of individuals with severely curtailed life-space mobility among both cohorts, with 37.0% (95% CI, 27.1% to 48.1%) of the COVID-19 cohort and 41.1% (95% CI, 30.6% to 52.4%) of the control cohort having scores less than 60 (within–matched pair adjusted conditional logistic regression OR, 0.90; 95% CI, 0.44 to 1.82).

Table 3. COVID-19 and Thresholds of Morbidity at 18 Months*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Weighted association with COVID-19, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain (moderate, severe, extreme limitation)</td>
<td>0.50 (0.24-1.05)</td>
</tr>
<tr>
<td>Severe (4 or more) I/ADL limitation</td>
<td>1.46 (0.75-2.84)</td>
</tr>
<tr>
<td>Curtained life space (&lt;60)</td>
<td>0.90 (0.44-1.82)</td>
</tr>
<tr>
<td>Not employed</td>
<td>0.89 (0.45-1.77)</td>
</tr>
<tr>
<td>Poor health-related quality of life, EQ-5D-5L&lt;0.5)</td>
<td>1.37 (0.64-2.91)</td>
</tr>
<tr>
<td>At least 75% of 2020 functioning</td>
<td>1.52 (0.79-2.91)</td>
</tr>
</tbody>
</table>

Table 4. COVID-19 With Continuous Measures of Morbidity at 18 Months*

<table>
<thead>
<tr>
<th>Measure</th>
<th>Interpretation of direction of coefficient</th>
<th>Weighted association with COVID-19 coefficient (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue score</td>
<td>Higher is more fatigued (score ranges 0-1)</td>
<td>0.33 (−3.19 to 3.85)</td>
</tr>
<tr>
<td>I/ADL limitations count</td>
<td>Higher is more limitations (score ranges 0-13)</td>
<td>−0.04 (−1.24 to 1.15)</td>
</tr>
<tr>
<td>Composite life space score</td>
<td>Lower is more curtained life space (score ranges 0-120)</td>
<td>8.89 (−3.90 to 21.69)</td>
</tr>
<tr>
<td>EQ-5D utility index</td>
<td>Lower is worse health-related quality of life (score ranges 0-1)</td>
<td>−0.02 (−0.14 to 0.10)</td>
</tr>
<tr>
<td>Extent to which respondent feels back to January 2020 functioning</td>
<td>Lower is worse functioning (score ranges 0-100)</td>
<td>−5.22 (−14.65 to 4.21)</td>
</tr>
</tbody>
</table>

Figures. Distributions of Self-Reported Limitations in Activities and Instrumental Activities of Daily Living and Answers Regarding Physical and Mental Ability Since 2020

Abbreviations: EQ-5D, EuroQol 5-Dimension 5-Level; I/ADL, activities and instrumental activities of daily living; OR, odds ratio.

* Weighted within-pair conditional logistic regression, adjusted for race and ethnicity. Confidence intervals including 1 indicate no statistically significant association; odds ratios greater than 1 indicate more common after COVID-19 than in matched comparators.
Overall, 62.6% (95% CI, 51.7% to 72.4%) of COVID-19 cohort was not employed at the 18-month follow-up compared with 64.7% (95% CI, 53.7% to 74.3%) of their comparators. The OR from within-pair adjusted regression was 0.89 (95% CI, 0.45 to 1.77).

Quality of Life
Respondents were asked “Think about what you could do physically and mentally at the beginning of the year 2020. On a scale of 1 to 100, with 100 being all the way back to what you could do at the start of 2020, how close to being back are you?” Of the veterans in the COVID-19 cohort, 44.9% (95% CI, 34.2% to 56.2%) reported they could do less than 75% of what they felt they could do at the beginning of 2020, in contrast with 35.3% (95% CI, 25.6% to 46.4%) of their comparators (Figure). The within–matched pair adjusted OR was 1.52 (95% CI, 0.79 to 2.91). Mean (SD) EQ-5D-5L health utility scales at 18 months were 0.57 (0.35) in the COVID-19 cohort and 0.61 (0.25) in the comparators, with a within–matched pair adjusted difference of −0.02 (95% CI, −0.14 to 0.10).

Sensitivity Analyses
eTables 3 to 6 in Supplement 1 shows similar results in unweighted analyses and in weighted analyses that did not exclude the 8 comparators ascertained from medical records to have COVID-19 after sampling but prior to survey completion. Hypothesis-generating post hoc analyses26,27 shown in eTables 7 and 8 suggest possible enduring impacts of COVID-19 among the hospitalized group on fatigue and function, 18 months later, but standard errors were large. eTable 9 in Supplement 1 examines health care use among survey respondents with documented COVID-19 compared with those sampled but who did not participate in the survey and shows somewhat greater rates of primary care interaction by survey respondents, but no statistically significant differences in inpatient admission rates, specialty care interactions, or mental health interactions.

Discussion
Our results suggested a high burden of ongoing fatigue, pain, and disability among veterans after the COVID-19 pandemic. When asked in 2022, they rated their own physical and mental functioning as substantially worse than it was in 2020. Our sample, as finally collected, was too small to provide precise evidence as to whether or not this morbidity was more common among those with documented COVID-19 infection than among those who without.

This reduced sample size provides an important nuance to interpreting the lack of a statistically significant association. Consider our results for activities of daily living. We found an effect size of potential interest (OR, 1.46) in the association of COVID-19 and having 4 or more activities of daily living or instrumental activities of daily living limitations, but the confidence interval was wide (95% CI, 0.75 to 2.84). This means that our data cannot reject the null hypothesis that the rates of substantial activities of daily living limitation are the same in among surviving individuals in the COVID-19 cohort and their risk-matched comparators. However, our data are also consistent with individuals with a history of COVID-19 having double the odds of substantial disability—the sample we were able to obtain may have lacked the power to distinguish these quite different scenarios. Our results do establish bounds such that effect sizes as large as the mean increase in activities of daily living or instrumental activities of daily living limitations seen in inpatient sepsis17 are inconsistent with our data.

In the face of lack of power, there is sometimes a temptation to seek signal in point estimates, or in consistency of direction across multiple outcome measures. Our data suggest the limits of such a strategy for providing strong, reproducible evidence. The point estimates were inconsistent across different tests of association in the same measure. For example, the potentially large OR of 1.46 for more than 4 limitations coexists with a mean difference of −0.04 fewer activities of daily living or instrumental activities of daily living limitations in the COVID-19 cohort, with a broad 95% CI. We did
not possess strong a priori reasons for preferring one approach to testing for a difference associated with COVID-19.

These data have advantages and weaknesses. Unlike some assessments of COVID-19, we use self-reported data for the infection and control groups. Doing so in our sampling and within–matched pairs analysis controls for the unequal distribution of COVID-19 among the population, which evolved throughout the first years of the epidemic. Our use of self-report with the same questions allowed direct comparisons of the results between matched pairs. We reduced bias by using a national sampling frame and weighting to incorporate sampling and nonresponse. The baseline burden of morbidity among VA patients may limit the ability to detect disease impacts and generalizability to other populations. This combination of features are uncommon among the more than 196 studies summarized in recent major publications and systematic reviews. Our results contrast with studies extrapolating disability-adjusted life-years from new diagnoses attributed to COVID-19 infection, but that do not directly measure disability. Differential ascertainment may be a greater risk for claims-based studies, and our study attempted to minimize this.

These data are consistent with an interpretation that the COVID-19 pandemic has had adverse effects outside of solely infectious or postinfectious mechanisms. Other adverse effects may have been due to psychological, behavioral, social, policy, and economic mechanisms. These data cannot rule out the possibility that COVID-19–confirmed viral infection may be associated with disability among some individuals who had COVID-19. We value the assessments of respondents themselves, in which they self-reported decline in physical and mental capacity relative to 2020.

**Limitations**

This study has limitations. We prioritized self-report rather than physiological or objective functional testing, which could introduce recall bias in cases where veterans were asked to compare with their own recalled prior capacity. The age and sex distribution of the sample reflect the VA, which may not be generalizable across the whole population.

Because our data were collected via survey, we did not include individuals who had died, which may violate target trial emulation conditioned on postrandomization information. We have previously measured that the population-weighted differences in mortality, which could introduce censoring of the extreme phenotype bias. Our study was further limited by the small sample size, which was partially due to a lower-than-expected recruitment rate, which has been seen in other studies. Future work should include larger sample sizes to better estimate the association of COVID-19 with everyday functioning.

We sampled too few female or nonbinary respondents to explore sex and gender differences. Occupation information was also not available. Although an acyclic directed graph-informed target trial emulation was used to maximize rigor, unmeasured confounding could persist. The degree of undocumented infection among comparators is unknown.

**Conclusions**

In this cohort study, veterans reported high rates of ongoing fatigue, pain, and disability after the COVID-19 pandemic, regardless of history of COVID-19. There were no statistically significant results between these symptoms and COVID-19 illness. These results highlight the importance of acknowledging and addressing the broader impacts of the COVID-19 pandemic on health beyond those directly associated with documented infection.
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REFERENCES


**SUPPLEMENT 1.**

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SUPPLEMENT 3.
Data Sharing Statement